ECCMID 2018 Meeting Highlights

The 28th European Congress of Clinical Microbiology and Infectious Diseases (ECCMID) meeting, organized by the European Society of Clinical Microbiology and Infectious Diseases, convened in Madrid, Spain, from Apr 21 through Apr 24, 2018. This event attracted the world’s leading experts along with more than 12,000 multidisciplinary international scientists, clinicians, and public health experts eager to engage about issues in infectious diseases, clinical microbiology, and infection control.

Attendees of this year’s conference had access to hundreds of presentations and symposia and more than several thousand poster presentations, some of which that focus on antimicrobial stewardship and resistance are outlined below. Highlights of this year’s conference were keynote addresses with topics on preparedness for epidemic influenza; SARS, MERS, and coronaviruses to come; virology and immunology; global action against antibiotic resistance; tolerance of microbes to antibiotics; treatment of extensively drug-resistant gram-negative infections; making sense of the microbiome; and the possibility of the elimination of tuberculosis. Additionally, the clinical results of several new antibiotics, immunotherapies, and microbiome strategies in development were presented. There was a noticeable increase in the number of symposiums and posters devoted to the increasing role of rapid diagnostics in antibiotic resistance surveillance, antimicrobial stewardship, and appropriate antibiotic prescribing.

A highly attended presentation was a keynote address given by Otto Cars, MD, PhD, titled “Global coordinated action against antibiotic resistance — are we achieving enough?” Cars is a senior professor of infectious diseases at Uppsala University, founder of the international network ReAct, and member of a UN group to coordinate international work on antibiotic resistance. Watch this important presentation here.

During his presentation, Cars described the importance of the development of collective global policies to manage the antibiotic resistance crisis. He highlighted that rapid point prevalence surveillance is important to understand the problem and make informed decisions on appropriate prescribing of antibiotics. In addition, understanding the fecal microbiome from individuals located throughout the world is key as multidrug resistance organisms are being isolated and are increasing. He called on the global community to better support developing countries, because many have action plans but lack appropriate support. In addition, the infrastructure for antibiotic discovery in academic and industry is broken and needs to be rebuilt, he said.

Cars highlighted the need for collaboration among drug developers and incentives from global organizations to support antibiotic development, noting that innovative partnerships to provide global access to antibiotics (old and new) should be the goal. He underscored the need to change fundamental behavioral approaches to the appropriate use of antibiotics, highlighting the role of antimicrobial stewardship and the need for targeted prescribing benchmarks specific to each country. Finally, he described the UN Sustainable Development Goals as an opportunity to incorporate the policies, sustainable funding, and global action plan for combating antimicrobial resistance within a coordinated international legal framework to address the problem and to hold governments accountable.

Next year’s conference, the 29th ECCMID, will be held in Amsterdam on Apr 13 through Apr 16, 2019.

-Marnie L. Peterson, PharmD, PhD
Randomized trial supports shorter antibiotic course for bacteremia

Israeli and Italian researchers reported that a 7-day course of antibiotics for treatment of gram-negative bacteremia (GNB) offered similar outcomes to a 14-day course.

In the multicenter, non-inferiority randomized trial, the researchers assessed the outcomes for 604 GNB patients admitted to three hospitals in Israel and Italy from January 2013 through August 2014. The source of the infection was urinary in 68% of the patients (411/604), and the causative pathogens were Enterobacteriaceae in 90% (543/604). The 7-day group included 306 patients, and the 14-day group 298 patients. Patients with ongoing sepsis were not included.

The primary outcome was a composite of all-cause mortality, clinical failure, and re-admission or extended (>14 days) hospital stay, evaluated at 90 days. The non-inferiority margin was set at 10%. Secondary outcomes included 30- and 90-day mortality, development of secondary infections, Clostridium difficile infection, total antibiotic and hospital days, functional capacity, time to return to baseline activity, development of resistance, and adverse events.

At 90 days, the composite primary outcome occurred in 141 of 306 patients in the 7-day group (46.1%) versus 149 of 298 in the 14-day group (50.0%). Total antibiotic days from randomization until post-randomization were significantly shorter in the 7-day group (median, 5 days) than in the 14-day group (median, 12 days), and the time to return to baseline activity was shorter in the 7-day group (median 2 weeks vs median 3 weeks). No significant differences in fatality rates at 90 days (11.8% vs 10.7%) or other secondary outcomes were demonstrated.

"In patients hospitalized with GNB and sepsis resolution before day seven, a course of seven antibiotic days was not inferior to 14 days, reduced antibiotic days, and resulted in a more rapid return to baseline activity," lead author Dafna Yahav, MD, said in a press release from the European Society of Clinical Microbiology and Infectious Diseases (ESCMID). "This could lead to a change in accepted management algorithms and shortened antibiotic therapy."

ECCMID abstract #O1120
Apr 21 ESCMID press release

Colistin-resistant bacteria found in Indian food samples

Researchers in India reported the presence of colistin-resistant bacteria in the Indian food chain.

The analysis, conducted as part of an extended infection control surveillance measure to identify the entry of drug-resistant bacteria into the food chain, looked at samples of chicken, fish, meat, and vegetables collected from multiple sources, including markets, fish and meat outlets, households, and hospital kitchens. Out of the 100 samples tested, 44 (12 chicken, 3 mutton, 9 fish, 19 vegetables, 1 fruit) grew colistin-resistant bacteria (8 Escherichia coli, 20 Enterobacter spp., 27 Klebsiella spp., 2 Citrobacter spp.).

The authors of the study say the presence of colistin-resistant bacteria in such a large number of community food samples is extremely worrying, and they call for an urgent ban on the use of colistin as a growth promoter in animal husbandry.

ECCMID abstract #O0056
Point prevalence survey shows declines in prescribing in US hospitals
A uniform and standardized method for surveillance of antimicrobial use in hospitals showed declines in overall antimicrobial prescribing in four US hospitals, according to researchers from Texas A&M and Antwerp University.

For the study, a point prevalence survey (PPS) was conducted at the four hospitals from March to September 2017. The survey included all patients receiving an antimicrobial on the day of the PPS, and the data collected included details on the antimicrobial agents, reasons and indications for treatment, and a set of quality indicators. All data were entered into the Global Point Prevalence Survey of Antimicrobial Consumption and Resistance (GLOBAL-PPS), a web-based application to collect global data on rates of antimicrobial prescribing in hospitalized patients. The data were compared to a similar survey from 2015.

The results showed that the overall antimicrobial prevalence rate in adults was 37%, down from 44.8% in 2015. The highest use was in transplant units and intensive care units. Overall antimicrobial use in children or neonatal units was 28.9% in 2017, compared with 27.6% in 2015. Fluoroquinolone use decreased from 17.0% to 11.7%, and carbapenem use dropped from 20.8% to 9.1%, but the researchers noted that vancomycin use remained considerable, despite low rates of methicillin-resistant Staphylococcus aureus (MRSA).

In terms of quality indicators, reasons for antibiotic use and compliance with guidelines were over 80%, and documentation of antibiotic review improved to over 60%.

"Although there are a few areas that have improved since 2015, these results highlight areas for continued improvement and enable hospitals to benchmark improvement over time," the authors wrote.

ECCMID abstract #E0040

Global data show prescribing rates vary by country, continent
In another GLOBAL-PPS study, European researchers surveyed antimicrobial use in 395 hospitals in 52 countries worldwide.

In total, 90,640 patients admitted to 5,573 wards were surveyed from January 2017 through December 2017. Overall antimicrobial prevalence was 36.9%, which varied between continents (range, 25.1% in Oceania to 56.6% in Africa), hospital type (29.1% in primary care to 40.4% in tertiary care) and countries (22.1% in Armenia to 77.9% in Egypt). Among all the 49,369 antimicrobials prescribed antibiotics, antifungals, and drugs to treat tuberculosis represented 89.3%, 3.5%, and 2.6%, respectively. Out of 44,090 antibiotics, 63.7% (28,064) were prescribed for treatment, including 22.4% for a hospital-acquired infection, and 31.3% (13,798) were prescribed for medical or surgical prophylaxis.

The top three antibiotics used were ceftriaxone (13.7%), amoxicillin/clavulanic acid (7.4%), and piperacillin/tazobactam (6.7%). Meropenem represented 4.9% of prescriptions, and polymyxins 1.0%. Among 31,426 treated patients, 25.5% got a targeted treatment, with 8.4% in east and south Asia and 15.8% in Latin America receiving an antibiotic targeting a multidrug-resistant (MDR) organism (MDRO). Extended-spectrum beta-lactamase (ESBL)-producing Enterobacteriaceae was the most often reported cause for multidrug resistance, with the highest rates in Latin America (5.8%). The reason for treatment was recorded in 71.8%, and a stop/review date was recorded in 34.7% of antibiotic prescriptions. Local guidelines were notably missing in Africa (44.7% of prescriptions).
"These data serve to identify targets for quality improvement of antibiotic prescribing, the development of local prescribing guidelines, education and practice changes, and for measuring the impact of interventions through repeated PPS," the authors concluded.  

**ECCMID abstract #P0145A**

**Improper prescribing found common for carbapenem-resistant infections**

One out of three patients with laboratory-confirmed carbapenem-resistant infections at US hospitals received inappropriate carbapenem therapy, according to scientists with the medical technology company Becton, Dickinson and Co of Franklin Lakes, N.J.

The researchers analyzed 1,504 monomicrobial carbapenem-resistant cases from 62 US hospitals. *Pseudomonas aeruginosa, Acinetobacter baumannii, or Enterobacteriaceae* isolates were classified as carbapenem resistant if they tested resistant to meropenem, imipenem, ertapenem, or doripenem as per Centers for Disease Control and Prevention definitions, and inappropriate treatment was defined as receiving a carbapenem during the hospital stay. Mortality risk associated with inappropriate treatment was also estimated.

Overall, 34% of the patients (513/1,504) received inappropriate carbapenem treatment (72% meropenem, 13% imipenem, 8% multi-carbapenem, 5% ertapenem, and 1% doripenem). In 90% of these cases (464/513), the inappropriate treatment was empiric, and 75% of the empiric treatment patients (348/464) received carbapenems for 48 hours or longer. The pathogen distribution was 67% *P aeruginosa*, 22% Enterobacteriaceae, and 11% *A baumannii*.

Patients receiving inappropriate treatment had significantly higher in-hospital mortality (20%, 102/513) compared with those who didn't receive inappropriate carbapenem treatment (11%, 110/991), with an adjusted odds ratio of 1.59.

"These results highlight the importance of reducing inappropriate antibiotic treatment through rapid susceptibility test and antibiotic stewardship," the authors wrote.  

**ECCMID abstract #O0051**

**Rapid diagnostic test could identify CRE patients, improve outcomes**

Researchers at a Spanish hospital reported positive results for a rapid diagnostic test for gram-negative carbapenemase-producing bacteria.

The prospective study was conducted by researchers with the microbiology service of the Consorcio Hospital General Universitario from December 2016 through August 2017. The purpose was to evaluate the performance of the Eazyplex SuperBug system, a qualitative genotypic test for the identification of resistance genes in gram-negative bacteria. The test uses isothermal amplification reaction to detect VIM, OXA-48, OXA-181, KPC carbapenemase, and CTX-M-1 and CTX-M-9 ESBLs and can produce results in 15 minutes. Gram-negative rods from 171 patients were included in the study after showing resistance to carbapenems, and phenotypic tests were performed for comparison.

The test detected resistance genes in 150 (87.7%) of the isolates. The most frequently characterized beta-lactamase was CTX-M-1, which was detected in 119 isolates. The most frequently characterized carbapenemase was OXA-48, found in 112 isolates, followed by New Delhi metallo-beta (NDM)-lactamase (14). Co-production of OXA-48 and NDM was detected in 16 cases, all of them in *Klebsiella* spp. Comparison with phenotypic detection of carbapenemase and ESBL production showed 100% agreement with the Eazyplex SuperBug system.
The authors concluded that the reliable and easy-to-use test could help improve outcomes in patients infected with gram-negative bacteria.

**ECCMID abstract #O0192**

**First hospital ASP in Sri Lanka shows promising results**

Sri Lankan researchers reported that the country's first-ever antimicrobial stewardship program (ASP) resulted in the reduction of carbapenem consumption and costs, along with the incidence of carbapenem resistance.

The retrospective observational study was conducted for 1 year in 2016 to 2017 at Sri Jayewardenapura General Hospital, where an ASP was introduced shortly after the creation of Sri Lanka's National Action Plan for Combating AMR. The plan specified that ASPs should be implemented in the country's hospitals within 2 years. Aggregated data for 6 months before and 6 months after introduction of the ASP were compared.

During the study period, mean carbapenem consumption was reduced by 27.3%, from 30.7 to 22.3 defined daily doses (DDD) per 1,000 inhabitants per day, despite an increase of 587 patients in the latter 6-month period. The cost saving was 1,516,800 rupees ($22,700) for the same period. Carbapenem non-susceptibility of all gram-negative organisms, including Enterobacteriaceae, was reduced by 21% and 27.9%, respectively, from the pre- to post-intervention period.

**ECCMID abstract #P0898**

**ESBLs, travel, and antibiotic use**

In a study to evaluate risk factors for colonization with ESBL-producing Enterobacteriaceae (ESBL-E), researchers from the United Kingdom found that individual risk factors like international travel and antibiotic use are more important than community-based risk factors.

*In the study, the researchers screened rectal swabs from* 1,633 inpatients for ESBL-E carriage as part of a universal admission screening project using chromogenic agar culture and semi-automated antimicrobial susceptibility testing (Vitek). Patients were linked by residential postcode to community-based risk factors including population density, population ethnicity, housing, length of residence in the country, and various social and material deprivation indices. Individual risk factor data, including international travel and antibiotic use, was collected at the time of specimen collection. Risk factors for ESBL-E carriage were determined by univariable and multivariable binary logistic regression.

A total of 9.6% of the patients were colonized with ESBL-E. In the univariable analysis, the following variables were associated with ESBL-E carriage: Asian or black ethnicity, travel to Asia or Africa in the past 12 months, the length of time spent overseas, two or more courses of antibiotics in the past 6 months, the proportion of residents with Arabic ethnicity, and living in a home with two or fewer rooms. In the multivariable analysis, the only variables associated with ESBL-E carriage were travel to Asia (odds ratio [OR], 5.0) or Africa (OR, 2.9) in the past 12 months, and two or more courses of antibiotics in the past 6 months (OR, 2.2).

"This information is useful when identifying risk groups for targeted screening," the authors wrote.

**ECCMID abstract #O0333**
MDR burden higher in low- and middle-income countries

An analysis of national and international AMR surveillance systems found that the burden of MDR gram-negative bacteria is higher in low- and middle-income countries (LMICs) than in high-income countries (HICs).

In the study, researchers from Tuebingen University in Germany and the University of Verona in Italy extracted surveillance data collected from 112 countries from 2005 through 2016, covering a total of nearly 2 million isolates. Prevalence values were pooled across the four World Bank classification groups using random-effect meta-analysis.

Analysis of the data showed that fluoroquinoline-resistant *Neisseria gonorrhea* was the most prevalent resistant bacteria in all regions but was higher in LMICs, with a rate of 73% in LMICs compared with 53% in HICs. Third-generation cephalosporin-resistant (3GCR) Enterobacteriaceae was also more prevalent in LMICs compared with HICs (3GCR *K pneumoniae* 40% vs 27%; 3GCR *E coli* 32% vs 16%), as was MRSA (37% vs 20%).

Carbapenem-resistant *A baumannii* was homogenously present in all regions, with rates higher than 30%, while no difference among regions was observed in the prevalence of resistant typhoidal and non-typhoidal *Salmonella* and *Shigella* spp.

Conversely, vancomycin-resistant *Enterococcus faecium* and ampicillin-resistant *Haemophilus influenzae* showed lower resistance rates in LMICs compared with HICs.

"Current data suggest that the burden of resistance of MDR-gram negatives is higher in LMICs/LICs economies compared to HICs," the authors wrote. "Active policy targeting surveillance network and antibiotic and diagnostic stewardship in low resource settings should be urgently promoted and financed to contain the global spread of resistance."

ECCMID abstract #O0036

Study: Whole-genome sequencing can help hospitals identify outbreaks

In a prospective multicenter study, Australian investigators showed that whole-genome sequencing (WGS) has the potential to provide a new level of resolution to identify MDRO transmission networks within hospitals.

From Apr 24 to Jun 17, 2017, investigators from eight university hospitals performed WGS on isolates from all patients with positive clinical or screening cultures for MDROs, including MRSA, *vanA* VRE, ceftriaxone-resistant *E coli* or *K pneumoniae*, and carbapenem-non-susceptible *P aeruginosa* or *A baumannii*. The isolates were identified prospectively, clinical data were collected contemporaneously, and core genome single-nucleotide polymorphisms from reference-based read alignment were used to infer phylogenetic relationships.

Overall, 428 MDRO isolates from 370 patients were included in the analysis (*E coli*, 52%; MRSA, 22%; *vanA* VRE, 15%; *K pneumoniae*, 8%; *P aeruginosa*, 2%; *A baumannii*, 1%). The dominant sequence type (ST) among *E coli* was ST131 (33%), while *K pneumoniae* isolates were polyclonal. MRSA isolates predominantly belonged to STs 22, 45, and 93. Fifty-seven percent of *vanA* VRE isolates belonged to a *pstS*-negative ST (dominant local clone), and 28% were ST207. Carbapenem-resistant *P aeruginosa* (9) and *A baumannii* (2) were uncommon, and four of five carbapenemase-producing isolates were imported.
WGS phylogenetic analysis highlighted potential transmission of ESBL *E. coli*, MRSA, and *vanA* VRE. This included possible unsuspected transmission of ESBL *E. coli* in an intensive care unit, and inter-hospital MRSA transmission networks. These genomic relationships were corroborated by hospital-admission and patient-movement data. Practical communication strategies regarding WGS data were developed that facilitated improved WGS-guided hospital infection prevention and control.

The authors said the study indicates that linking traditional epidemiology with improved near real-time WGS and translational data communication can have important practical benefits for infection prevention and control efforts.

**ECCMID abstract #O0571**

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**Data show increase in *Staph aureus* bacteremia in Denmark**

Danish researchers reported a major increase in *Staphylococcus aureus* bacteremia (SAB) incidence in Denmark, driven primarily by elderly patients.

In the study, the researchers used data from the ongoing national *Staphylococcal* registration surveillance study to assess temporal changes in SAB incidence and the associated short-term mortality in the Danish population from 2008 to 2015. A total of 11,342 cases of SAB were identified, for an overall incidence rate (IR) of 24.93 per 100,000 person-years. From 2008 to 2015, the IR increased 48%, from 20.8 to 30.7.

The risk of SAB increased rapidly with advanced age. Additionally, male gender was associated with an increased incidence of SAB (increased risk ratio, 2.0). After adjusting for age and gender, the researchers found an annual increase of 4% in the SAB rate for all age-groups, with the exception of age-groups 80 to 89 years and 90 years and older, in which they found an annual increase of 8.4% and 13%, respectively. During the study period, the relative proportion of patients over 80 increased from 19.7% to 26.2%, corresponding to a nearly doubling in the age-adjusted IR (105.5 vs 200.7). The 30-day case-fatality rate of SAB was 24% and remained stable throughout the study.

The authors of the study said the increasing burden of SAB warrants continued surveillance and improved preventive measures.

**ECCMID abstract #O0086**

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**Late-career physicians more likely to prescribe prolonged antibiotics**

A Canadian study found that late-career family physicians were more likely to prescribe prolonged courses of antibiotics.

The retrospective cohort analysis of all family physicians in Ontario prescribing more than 75 antibiotics was conducted from March 2016 through February 2017. Prolonged duration was defined as more than 8 days of therapy, and antibiotics were classified as "all," "respiratory," and "urinary," based on the most common indications for these agents. Covariates included in the model were: physician gender and career-stage (less than 11 years, 11-24, and more than 24 years in practice), geographic area of practice, community physician density, practice size, antibiotic volume, new patient volume, practice complexity score, and patient age and sex.

There were 10,616 family physicians included in the study, prescribing 6.65 million antibiotic courses, which represent 95% of all outpatient antibiotics prescribed by physicians in Ontario. Thirty-five percent of prescriptions were for a prolonged duration. Physician career stage, rural location, and a larger pediatric practice were significantly associated with greater use of prolonged durations.
In the multivariable regression model, prolonged courses were more likely to be prescribed by late-career physicians (adjusted OR [aOR], 1.48) and mid-career physicians (aOR, 1.25) when compared with early-career physicians. The association with career stage was significant for all, respiratory, and urinary antibiotic prescriptions.

"These findings highlight opportunities for community antimicrobial stewardship interventions to improve antibiotic use through addressing practice differences in later career stage physicians," the authors concluded.

ECCMID abstract #O0479