The field is moving on: new diagnostic and therapeutic tools presented at the 28th ECCMID 2018

Johannes R. Bogner¹

Published online: 7 May 2018
© Springer-Verlag GmbH Germany, part of Springer Nature 2018

This year's ECCMID in Madrid convened roughly 13,000 professionals to hear and discuss about 3500 contributions in more than 200 sessions, most of them in parallel. The field was covered extensively in all aspects from infections control over clinical microbiology, clinical infection management through vaccination and other preventive measures.

One contribution of the European Centre for Disease and Prevention Control (ECDC) by Dr. Robesyn summarized clinical characteristics of all 37,365 cases of measles reported to the ECDC from 2013 to 2017, 81% occurring in persons without vaccination. Countries which are represented with at least 5% of the reported cases are Italy, Romania, Germany, the Netherlands and the United Kingdom. The fact that 33% were hospitalized and 11% had pneumonia as well as the fact one in thousand patients died results once more in a call for higher vaccination rates. Odds ratio for mortality was seven times higher in children < 12 months of age as compared to older children and adults (O 0060). It has been discussed that this might especially be important in refugees to Europe [1].

Duration of antibiotic treatment in patients with cellulitis is mainly based on expert opinion and many say 10–14 days [2]. A Dutch study addressed the question whether 6 days of flucloxacillin treatment would be noninferior to treatment duration of 12 days. On a short term, 6 days of treatment appeared to be equivalent in efficacy to 12 days. However, those with a short treatment course did have significantly more and quicker relapses by day 90. Noteworthy in this trial: only 151 of 248 included participants (61%) had sufficiently improved by day 6. This was the inclusion criterion for randomisation. We could also take home this message: For 39% of patients in the Netherlands (probably equalling

patients in developed countries) flucloxacillin is not sufficient to result in sufficient clinical improvement by day 6. Moreover, in both groups only roughly 50% reached clinical cure opening the question, whether flucloxacillin can remain the suggested first line option for cellulitis (O 1122 [3]).

A putative “DEAD box RNA helicase” gene “helP” of *Pseudomonas* to be a killer: By sequencing and establishing a phylogenetic analysis of the core and accessory genome of *Pseudomonas* strains from blood stream infections a microbiology group from Tübingen in Germany (Oral presentation 0322 Willmann) found a novel and obviously clinically relevant virulence marker which they called “helP” (abbreviation for helicase of *Pseudomonas*). This is of importance because it seems to be suitable for clinical use and for its presumed high ability to predict negative outcome in *Pseudomonas* blood stream infection. The hazard ratio for poor clinical outcome was 1.96.

In the same session, there were two very promising talks on rapid diagnosis of organisms in sepsis using next generation sequencing (NGS [4]) and magnetic resonance technology (MRT): Silke Grumaz (O 0324) reported on the high performance of NGS diagnostics compared to culture-based microbiological diagnostics in patients suffering from septic shock. The talk made very clear that this is now a feasible tool that may come to clinical use. The same holds for MRT diagnostics, a test with very rapid and easy detection of the seven most likely organisms in sepsis [5], while in 112 samples in 95 patients only 15 were positive in blood culture the MR test had high sensitivity and detected organisms in 45 samples (O 0326 presented by Peter-Michael Rath).

It was not known whether Piperacillin–Tazobactam is an adequate carbapenem-sparing therapy for infections by *Escherichia coli* or *Klebsiella pneumoniae* which express extended-spectrum β -lactamases [ESBLs] mediating resistance to third-generation cephalosporins (3GCs). Using the concept of a multinational, randomised multi-continental trial in 32 trial sites in nine countries Harris and colleagues report that the use of

✉ Johannes R. Bogner
Johannes.Bogner@med.uni-muenchen.de

¹ Sektion Klinische Infektiologie, Klinik und Poliklinik IV, Klinikum der Universität München, Pettenkoferstr. 8a, 80336 Munich, Germany

Piperacillin–Tazobactam as definitive therapy for BSI caused by *E. coli* or *K. pneumonia* with non-susceptibility to 3GCs was inferior to Meropenem and should be avoided in this context. The trial had enrolled a total of 391 patients between 2014 and 2017. 60.9% of infections were urinary tract infections caused by *E. coli*. The majority of patients were enrolled in Singapore and Australia. In the intention to treat analysis, mortality was 12.3% with Piperacillin–Tazobactam as compared to 3.7% with Meropenem (O 1121).

New concepts against multidrug resistant (MDR) organisms are always welcome. One Saturday session was dedicated to new way in antibiotic targets. As outline for example by Anatol Luther (O 0246) outer membrane protein targeting antibiotics (OMPTAs) may constitute a novel antibiotic class with potent activity against Gram-negative organisms including XDR and colistin-resistant isolates. The MIC₉₀ values for the OMPTAs were reported to be between 0.03 and 0.25 mg/l for the organisms tested, whereas the MIC₉₀ for the comparators were generally > 8 mg/L. The OMPTA's showed no cross-resistance with comparator antibiotics, including colistin-resistant *A. baumannii* and *E. coli*; *K. pneumoniae* and *Enterobacter* spp. However, we must be aware that clinical trials showing efficacy in human infection and tolerability have to follow.

Possibly even more fascinating is the concept of using an artificial pharmacological activation of bacterial toxin–antitoxin (TA) genes as a tool to initiate something like bacterial suicide. This hypothesis and corresponding experiments were presented by Marcin Rownicki from Warsaw (O 0250). He studied the activation of *E. coli* TA “mazEF” and to achieve this he used antisense peptide nucleic acid (PNA) oligomers. The results showed promising antibacterial effect. Here also remains the question whether this can be translated in human application.

The Sunday morning session was intended to provide tips for publishing in infectious disease journals. How can a researcher find out whether a journal is really a reputable journal that has scientific influence? Sharon Bloom, one associate Editor of Emerging Infectious Diseases, pointed out that the mere fact that an abstract can be found in PubMed does mean that the journal is one that adheres to acceptable scientific conduct and is referenced in citation reports with an impact factor.

While in previous years the advent of new betalactam combinations against ESBL-producing Gram-negative organisms was celebrated, this year's conference even had one session in which resistance mechanisms against Cef-tazidime–Avibactam and Ceftolozane–Tazobactam were summarized, and cases and case series with treatment failure due to corresponding mutants were reported by Antonio Oliver and Romney M. Humphries. One conclusion of course is that wise use of the new compounds in correct

dosages must be promoted not to promote selection of new resistant strains.

One of the late breakers in a Monday session in infection control was presented by Friedericke Maechler (O 1130). The question was, whether intensified contact precautions (isolation, wearing gowns and gloves) would result in lower transmission rates of ESBL organisms as compared to standard precautions. Using a cluster randomized trial with cross-over design in 20 non-ICU wards in four countries with screening for ESBL bacteria and subsequent contact precautions they found no difference in subsequent transmissions. The rate of transmissions 4.6 per 1000 patients days in both groups. The question is, whether this will have influence on recommendations for isolation of ESBL harbouring individuals.

In the context of fungal diseases, new attention has been drawn to the Candida “super-bug” *Candida auris*. One group in the United Kingdom analysed a cluster of 70 colonised or infected patients of this profoundly difficult-to-treat fungus and found out that its distribution was linked to the use of multi-use thermometers (O 0172 Davie Eyre et al.). Again, high resistance rates against azole antifungals and even an 18% resistance rate against amphotericin B was detected, while no resistance was found against micafungin.

One of the virus catchlines deals with West Nile Virus in Greece. Prof. Tsakris reported 26 new neuro-invasive cases: “The re-emergence of WNV after a 2 years hiatus of reported human cases and its subsequent geographic expansion in newly affected areas demonstrates that Greece provides the appropriate ecological and climatic conditions for WNV circulation. The virus has been established in Greece and disease transmission may continue in the future”. INFECTION had already reported on cases even north of Greece [6].

Again, this conference showed not only that it earns a reputation of one the world's most interesting infectious disease assemblies but also that the quality of its program and contents as well as the expertise of all speakers is immense. Let us look forward to ECCMID 2019 in Amsterdam!

Compliance with ethical standards

Conflict of interest The author declares that he has no competing interests.

References

1. Jablonka A, Happle C, Grote U, et al. Measles, mumps, rubella, and varicella seroprevalence in refugees in Germany in 2015. *Infection*. 2016;44:781–7.
2. Ferreira A, Bolland MJ, Thomas MG. Meta-analysis of randomised trials comparing a penicillin or cephalosporin with a

- macrolide or lincosamide in the treatment of cellulitis or erysipelas. *Infection* 2016;44:607–15.
3. Cranendonk DR, Opmeer BC, van Agtmael M, et al. Antibiotic treatment for 6 days versus 12 days in patients with severe cellulitis: a multicentre randomised, double-blind, placebo-controlled, noninferiority. *ECCMID 2018*, 21–24. April 2018, Madrid Oral Presentation O 1122.
 4. Grumaz S, Stevens P, Grumaz C, et al. Next-generation sequencing diagnostics of bacteremia in septic patients. *Genome Med.* 2016;8:73.
 5. De Angelis G, Posteraro B, De Carolis E, et al. T2Bacteria magnetic resonance assay for the rapid detection of ESKAPEc pathogens directly in whole blood. *J Antimicrob Chemother.* 2018;73:iv20–iv6.
 6. Vilibic-Cavlek T, Kaic B, Barbic L, et al. First evidence of simultaneous occurrence of West Nile virus and Usutu virus neuroinvasive disease in humans in Croatia during the 2013 outbreak. *Infection.* 2014;42:689–95.