THE DIFFERENCE OF

ONE INNOVATIVE PARTNER

IN ADVANCING THE WORLD OF HEALTH

COMBATING ANTIMICROBIAL RESISTANCE (AMR): ECCMID 2018

The 28th European Congress of Clinical Microbiology and Infectious Diseases (ECCMID) was hosted in the Feria de Madrid from 21-24 April, 2018. The packed programme featured world expert talks on current hot topics. Naturally, BD Life Sciences was in the middle of the action as a ECCMID gold-level sponsor and with our must-attend symposium,

'Fighting antimicrobial resistance: diagnostic solutions that lead to an appropriate use of antibiotics and help reduce the spread of AMR'.

On Sunday morning, hundreds of delegates were welcomed by David Hickey, President of BD Diagnostic Systems (USA). He opened the symposium by setting the scene of the clear and present danger arising from AMR.

BD

AMR: A WORLD-WIDE KILLER

'Right now in the USA, AMR costs $20 billion each year. AMR is attributed to 700,000 preventable deaths worldwide annually. It is predicted that by 2050, AMR will become the leading cause of death world-wide and cost more than $1 trillion per year. However, we do not have to accept that AMR will become the biggest problem facing human health: with effective processes, communication and tools, we have an opportunity to make a difference'.

THE INTERNATIONAL FIGHT AGAINST AMR

Mr. Hickey then outlined the areas which are key to fighting AMR, including antimicrobial surveillance, infection prevention and control. He draws particular attention to the issue of antimicrobial stewardship, which currently has rather a patchy approach internationally. However, there is hope: the United Nations recently formed the Interagency Coordination Group on Antimicrobial Resistance which has in progress a five-pronged attack on AMR, namely

- Awareness and education
- Surveillance and research
- Reduction of infection rates
- Optimisation of antimicrobials
- Increased innovation

BD'S GLOBAL PRESENCE IN THE BATTLE AGAINST AMR

BD is also taking the issue of AMR very seriously. We have products that are relevant across the continuum of patient care, including devices for infection prevention and control, and systems for rapid screening, detection and identification of infectious agents. New product development also aims to support these measures against AMR:

We aspire to provide timely, meaningful information to prescribing clinicians, in order to help them manage their antimicrobial use.

In terms of health and policy development, BD is also a global presence, collaborating with other vested parties to support the fight against AMR. Our company is uniquely positioned to engage 'top down' by aligning around national AMR action plans, as well as 'bottom up' by mobilising AMR initiatives at hospital level. We intend to use our unique position to do just that.

BLOOD CULTURE OPTIMISATION AND AMR

Next up to the podium was Dr. Michael Weinbren, Consultant Microbiologist and doctor in charge of Infection Control at the King's Mill Hospital, Sutton-in-Ashfield, England, United Kingdom. The title of his talk was, 'Antibiotic stewardship. Does optimisation of the blood culture pathway have a role to play?'

Dr. Weinbren opened with a shocking statement: 30 years ago, AMR was rare. Now, due to AMR it is possible that we are entering the end of the antibiotic era.

Recognising his responsibilities in the fight against AMR, Dr. Weinbren instigated changes to the way his NHS Trust handles blood cultures, which are the gold standard investigation in the diagnosis and treatment of sepsis. The rationale was this: rapid identification of infection leads to rapid instigation of correct antimicrobial therapy, cutting the necessary duration of treatment. This ultimately results in better outcomes for the patient and reduces the risk of developing AMR.

Prior to his pathway intervention, Dr. Weinbren carried out an initial survey of current practice. He noticed various problems which impacted on the delivery of blood culture results, including inadequate sample volumes and delays in getting samples to the laboratory. There were also delays in sample processing and in positive results being picked up by staff. To further impact these issues, throughout the Trust, there was a commonly held misconception that blood cultures took 48 hours to yield a result, while in reality, positive results can be obtained from 6 hours after collection, the majority signaling positive within 12 hours.

So, Dr. Weinbren went to work, making changes to optimise the blood culture pathway within the Trust:

- The blood culture bottles were changed from glass to plastic to ensure they could be placed in the air tube delivery system along with other blood samples, rather than languishing for hours in a separate box before being picked up.
- A campaign was instigated in order to educate staff on the new pathway and to emphasise the need for expediting samples
- The blood culture analyser was moved to the Blood Science Department, for unlike the Microbiology Laboratory, it was open 24 hours a day. This ensured blood cultures were loaded on to the analyser 24 hours / day.
- Outside of routine microbiology working hours blood science staff remove positive blood cultures subculturing samples on to media for growth / identification and also setting up direct routine sensitivity plates as well as rapis antibiotic sensitivity plates.
- Dr. Weinbren's new blood culture pathway reduced the time taken to provide meaningful results to the treating clinicians (85% of blood cultures completed (from collection to identity of organism with antibiotic sensitivities within 36 hours compared to a teaching hospital which had partially optimized the pathway which took more than 66 hours to achieve the same result)). The impact of the changes were immediate and positive: in a review of the pathway he identified 2 patients who were likely not to have survived without the rapid intervention afforded by the new protocols.

SEPSIS AND STEWARDSHIP

To round off his presentation, Dr. Weinbren talked about the future management of sepsis. He recognises that with new technologies come new possibilities, enabling the early prediction of antibiotic failure as well as the rapid identification of causative microorganisms and the management of sepsis within a period of 12 hours (for the majority of gram-positive organisms where the identity is key as antibiotic sensitivities are largely predictable) or 19 hours for gram-negative organisms where new technology will give antibiotic sensitivity results in 7 hours or less- the latter is key for gram-negative organisms because antibiotic sensitivities are unpredictable overall. Dr. Weinbren concluded that in the fight against AMR and sepsis, diagnostic and antibiotic stewardship is key.

QUESTION FROM THE FLOOR:

How did you manage positive results obtained outside of normal Microbiology working hours?

ANSWER:

It is vital to have cross disciplinary working and commitment from the staff to make the system work. At night simple algorithms are hopefully the way forward in order to place patients on the correct treatments. It is also important that when testing provides new information, these results are communicated to clinicians, who should then act accordingly.

MICROBIOLOGY LABORATORIES AND AMR

Dr. Rafael Cantón, ESCMID Fellow from the Hospital Universitario Ramón y Cajal and the Instituto Ramón y Cajal de Investigación Sanitaria (IRYCIS), followed Dr Weinbren with his talk entitled, 'Strategies and challenges of microbiology labs in the fight against AMR: diagnostic solutions that lead to an appropriate use of antibiotics and help reduce the spread of AMR'.

AMR DEFINITIONS

Dr. Cantón opened by explaining how the definition of AMR varies according to clinical perspective. For clinicians, it equates to the absence of an adequate clinical outcome, despite maximum antimicrobial dose. For clinical microbiologists, it means the presence of a gene within a microbe - a gene which expresses a particular resistance mechanism, which in turn inhibits a related antimicrobial effect. Accordingly, antimicrobial susceptibility testing (AST) and AMR testing are two key tools in the microbiology laboratory. Indeed, Dr. Cantón described AMR testing as complementary to AST testing and when used together, they are particularly useful in addressing challenging clinical cases where resistance mechanisms are pertinent to both public and individual health.

AMR AND THE ROLE OF CARBAPENEMASE

Dr. Cantón continued: The dissemination and evolution of AMR is complex. Take for example the case of carbapenemase-producing *Enterobacteriaceae* (CPE), which render ineffective many common antibiotics including penicillins and cephalosporins. These bacteria are a significant threat to public health and exemplify both the limitations of antimicrobial susceptibility testing and the need for resistance testing. There are various techniques for screening and identifying CPE in the microbiology laboratory, including colorimetric assay, mass spectrometry, immunochromatography and polymerase chain reaction (PCR) as well as commercial molecular tests. In order to confirm and precisely characterise active resistance mechanisms, Dr. Cantón recommends combining phenotypic ancillary tests with molecular testing.

TACKLING CARBAPENEM-RESISTANT ENTEROBACTERIACEAE (CRE) IN THE CARE SETTING

From a clinical perspective, identification of patients colonised with CPE is important as these people have a higher risk of becoming infected with multi-drug resistant organisms. To reduce transmission and infection from these resistant bacteria, effective management strategies include:

- Performing rectal swab cultures to identify carriers - molecular tests provide rapid results with high sensitivity and specificity
- Implementation of strict contact precautions in the nursing care of carriers
- Education, cleaning and hand washing programmes
- Antibiotic stewardship including carbapenem-sparing regimens

GLOBAL AND NATIONAL STRATEGIES

Finally, there are various national and international standards which guide clinical microbiologists in tackling AMR. The European Committee on Antimicrobial Susceptibility Testing (EUCAST) released new AMR guidelines in 2017 while in the same year, the World Health Organisation launched its paper entitled, 'Global priority list of antibiotic-resistant bacteria to guide research, discovery and development of new antibiotics'. In addition, local strategies such as carbapenemase screening and management have proved cost-effective as well as cost-saving.

QUESTION FROM THE FLOOR:

What type of patient should be surveilled for CRE?

ANSWER:

You should discuss this with your local infection control team, in order to find the most cost effective and appropriate surveillance pathways. However, a broad rule of thumb would be those patients transferred from another hospital and those coming from abroad.

THE VITAL ROLE OF AUTOMATION IN AMR

The final presentation was from Prof. Gilbert Greub, Director of the Microbiology Institute in Lausanne University, and Head of Diagnostic Microbiology at the University Hospital Center, Lausanne, Switzerland. His talk was entitled, 'Automation in the fight against AMR'.

AMR DUE TO INCREASED ANTIBIOTIC CONSUMPTION

Prof. Greub explained that AMR has developed from a global increase in the prescription of antibiotics and the subsequent increase in antibiotic consumption. What is more, every year the rate of AMR is increasing. However, from the automation of sample collection to the delivery of results, improved diagnostic tools and automated diagnostic technology have an important role to play in the fight against AMR.

RAPID IDENTIFICATION OF PATHOGENS AND EARLIER ANTIBIOTIC SUSCEPTIBILITY TESTING (AST)

Firstly, automation facilitates the rapid identification of etiological agents, which in turn helps streamline the application of appropriate therapies. For example, automated PCR enables the detection of bacteria, fungi, parasites and viruses on the same microplate while matrix-assisted laser desorption/ionization time-of-flight (MALDI-TOF) mass spectrometry reduces the time taken to identify any microbes present in a sample. By identifying pathogens quickly, techniques like PCR and MALDI-TOF facilitate early clinical intervention with appropriate treatments and reduce the time needed to successfully treat patients and make the development of AMR less likely.

Secondly, automation provides earlier AST results. For example, integrated MALDI-TOF and AST modules permit rapid carbapenemase detection: this information provided AST results much earlier than would be possible with PCR. Blood culture analysis based on blood pellets and atomic force microscopy is also likely to provide earlier AST results, primarily because the technology does not require the growth of bacteria.

EPIDEMIOLOGY OF AMR

Thirdly, automation may be exploited in the epidemiology of AMR. For example, telebacteriology may help a microbiologist located in a tertiary hospital read plates from another clinical base and provide appropriate advice on antibiotic use. Information technology will also play a significant role in the harvesting of useful data. Because automation relies on software, it is likely that statistics could be provided on a continual basis, rather than periodically. These statistics will inform sepsis management as well as provide automated epidemiological surveillance and antibiotic resistance statistics and ultimately facilitate a complete and automated antibiotic stewardship.

AUTOMATION REDUCES AMR

Ultimately, automation means improved diagnostic microbiology. It allows earlier identification of pathogens, earlier AST results and earlier detection of any outbreaks. This information affords timely and appropriate therapy as well as meaningful infection control measures, which will culminate in

a reduction in antibiotic consumption, and eventually a reduction in AMR.

QUESTION FROM THE FLOOR:

What about automation for *Klebsiella* and *E. coli* on chromogenic agars?

ANSWER:

Automation could help with identification and reporting. It will give you more time to read and identify more complex cases.

Learn more at amr.bd.com

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