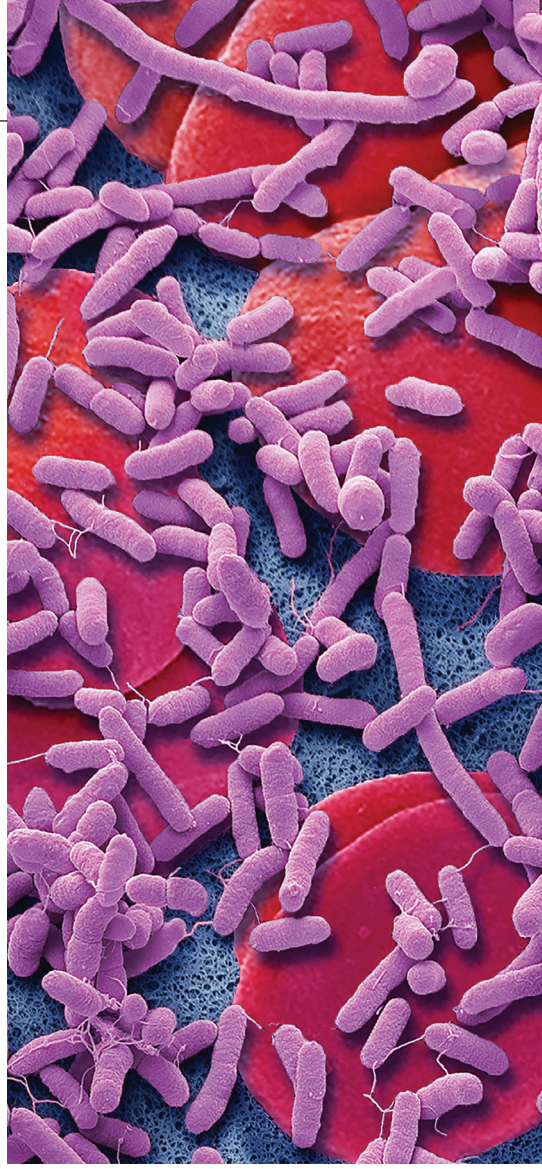
DETECTING THE SILENT KILLER

Rushana Hussain, Clinical Scientist at Royal Bolton Hospital, writes about rapid sepsis detection with MALDI mass spectrometry.



Sepsis – the overreaction of the body's immune system to infection – is a prevalent global health threat. It costs the NHS England approximately £2bn per year to treat, and claims the lives of around 31,000 people. Globally, there are an estimated 31 million cases of sepsis per year, with six million resulting in death.

There has long been a need for rapid detection and identification of the infecting organism in blood cultures to ensure a timely response for the management of sepsis. Without this, patients can suffer from septic shock and organ failure, often resulting in death. While broad spectrum antibiotics are generally the first step in treating sepsis patients, in a high proportion of cases, an early identification of the infecting organisms would enable a change in therapy where appropriate, therefore lowering mortality rates, decreasing treatment costs and improving patient outcomes.

A change in technology

Most clinical laboratories use biochemical methods as standard laboratory practice (SLP) to identify detected organisms from the sample, which can only provide information about the infecting organism once it is cultured, approximately after 24 hours. This uncertainty and delay in information limits the specificity of antibiotics that can be used for treatment.

Mass spectrometry (MS) has emerged as the gold standard for microorganism identification in clinical laboratories across the world. The Microbiology Department at the Royal Bolton Hospital (RBH), UK, has introduced matrix-assisted laser desorption/ionization (MALDI) time-of-flight (TOF) MS, alongside an innovative positive blood culture preparation kit, to accurately identify organisms in sepsis cases. Combining these methods is emerging as a powerful technique for rapid organism identification from a blood culture.

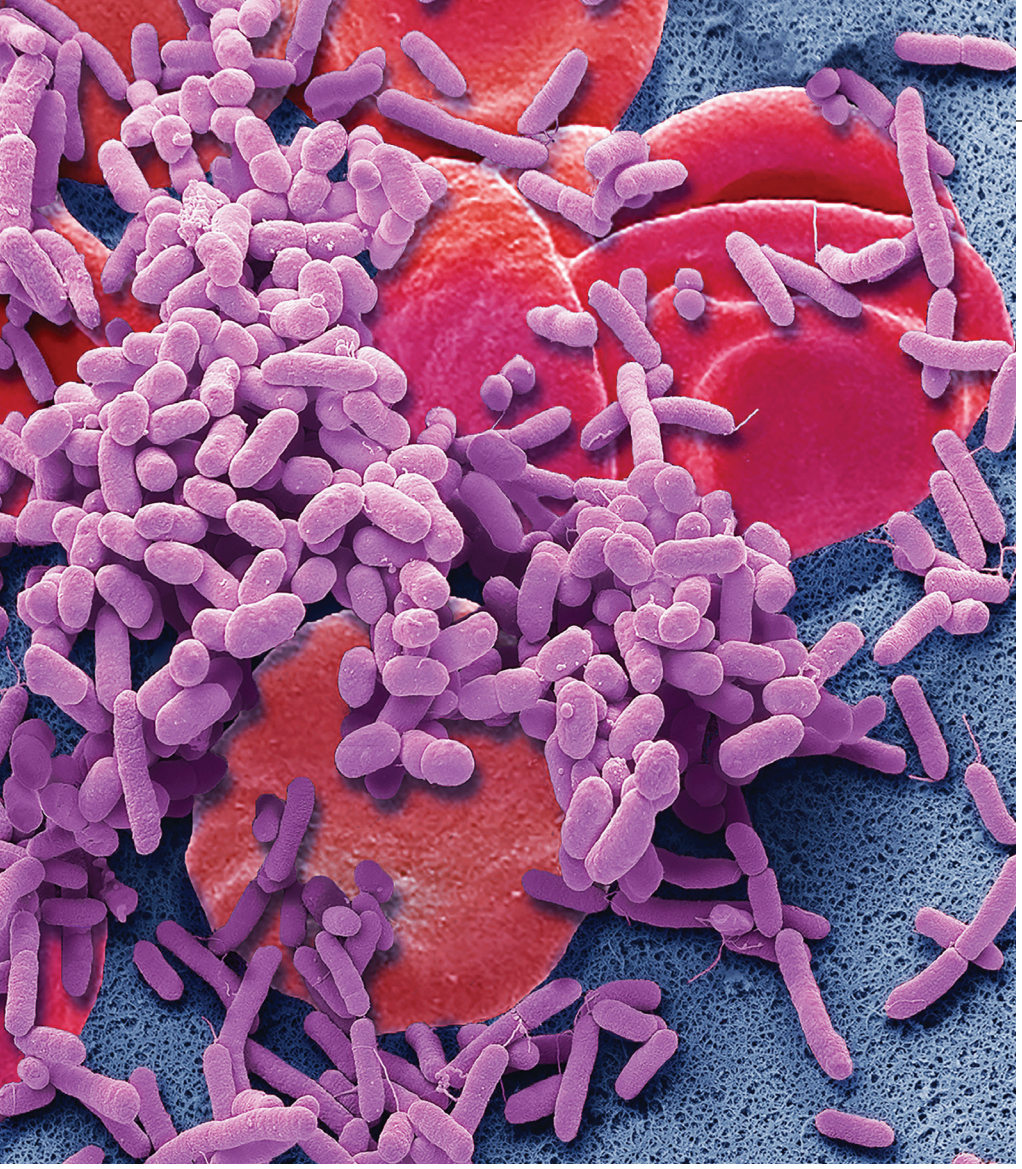
Evaluating MALDI-TOF MS

The RBH conducted a retrospective analysis of the processing of positive blood culture broths collected from patients admitted to the A&E department with suspected sepsis, to establish whether faster and more accurate diagnosis could be achieved using MALDI-TOF MS diagnostic tools, compared to the current SLP.

During April and May 2015, the microbiology laboratory implemented the MALDI-TOF MS protocol for processing positive blood culture broths, which was compared to the SLP (audit performed April to May 2014) to determine potential improvements in time to clinical results and patient pathways. Blood samples of patients who were suspected as having sepsis were sent to the microbiology laboratory for processing to determine the identity of the infecting organism, and all samples that were flagged positive for growth were subjected to Gram staining.

Cost savings and patient outcomes

The study found that although the use of MALDI-TOF MS takes additional time to perform, there was no delay to the availability of the Gram stain result and there was a significant improvement over the SLP of up to 23 hours in TAT for a presumptive identification. There was also a reduction of hospital stay duration for patients with bacteraemia during the MALDI-TOF MS period compared to the SLP. On average, for Gram positive bacilli, time spent in hospital was reduced by



Left. Sepsis. Composite coloured scanning electron micrograph. Bacteria amongst the red blood cells from the circulatory system

"This reduction is a reflection on the earlier and more accurate identification"

1.6 days, and 1.8 days for Gram positive cocci. This reduction corresponds to a significant cost reduction for the hospital.

In addition to length of stay in hospital, the cost implications of implementing the MALDI-TOF MS protocol considered the use of intravenous (IV) and oral antibiotics. Analysis of this data at RBH has shown a 33% reduction in doses of IV antibiotics and a 35% reduction in oral antibiotics using the MALDI-TOF MS protocol compared to SLP over a similar time period. This reduction is a reflection on the earlier and more accurate identification of the organism, enabling the clinical team to make informed decisions and alter antibiotic regimes 18 hours sooner. Knowing the actual identification of the organism enables clinicians to tailor antibiotic treatment and reduce overall antimicrobial use across the hospital.

An associated positive effect of a reduction in IV antibiotic usage is the expected reduction in nursing time to administer the therapy. In addition, reducing antibiotic use falls in line with National Institute for Health and Clinical Excellence (NICE) Guidelines on Antimicrobial Stewardship, by reducing the risk of multi-drug resistance through hospital acquired infections.

Hospital- and economy-wide advantages

For the clinical management of sepsis patients, it is important to identify the organism quickly in order to change empiric antibiotic regimens to a more targeted therapy. The MALDI-TOF MS protocol has shown 90% sensitivity and 100% specificity in laboratory investigations. This level of information enables clinicians to make confident, informed decisions in personalising antibiotic regimes, or altering patient pathways, which typically lead to better patient outcomes.

The benefits of treating sepsis in a targeted manner have significant impacts on quality of life for many patients who have sepsis. Faster diagnosis and treatment of the condition reduce the risk of long term patient morbidity (sometimes referred to as post sepsis syndrome or PSS) or life-changing physical and mental conditions.

Fighting sepsis in the future

MALDI-TOF MS can provide identification of an infecting organism in the blood approximately 18-23 hours earlier than traditional biochemical methods. This faster TAT provides the clinician with timely and accurate information, enabling an informed clinical assessment of the patient, to prescribe the correct antibiotics promptly, and instruct the removal of lines and indwelling catheters where possible, as well as request additional investigations.

Cost is often a barrier to organisations considering new technology. Although it is difficult to calculate all the financial implications across the patient pathway, data from RBH shows additional cost savings arise from a reduced length of hospitalisation and reduced use of antibiotics following the implementation of MALDI-TOF MS protocol into the hospital microbiology laboratory workflow. The laboratory is currently assessing how taking additional sets of blood cultures and improving transport time to the laboratory could improve the workflow and TATs further. BMS

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