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SmartNotes

The future of AST: Towards faster results and quicker clinical decisions

Microbial identification and antibiotic susceptibility testing (AST) are vital to patient care, public health, and antimicrobial stewardship, but traditional methods have one major limitation – the time it takes to yield a result.

Traditional methods of AST, which can define pathogens and guide right first-time treatment plans, can take up to 72 hours due to the requirement for overnight cultures. But new ways of doing things are emerging, and microbiologists are leading the charge.

Patient care and public health

Laboratories play a vital role in patient management, with 70% of all clinical decisions being taken dependent on the result of *in vitro* testing.[1] What's more, these laboratories do so at just 2-4% of a hospital's overall budget, making them an extremely efficient use of resources.[2]

Data demonstrates that in bacterial infections, including relevant septic shock cases and bacterial meningitis, earlier antimicrobial treatment is a significant indicator of better outcomes.[3] This relationship is also documented in relation to sepsis, where every hour of delay in administering antibiotics after emergency department triage, or the onset of organ dysfunction or shock, can increase the likelihood of a poor outcome by between 3-7%.[4]

With all this in mind, clinicians are regularly required to prescribe broad-spectrum antibiotics while they wait for AST data. An unfortunate side-effect of this practice, however, is that it may contributing to antimicrobial resistance (AMR). There is a risk of the bacteria becoming resistant while the patient is on empiric therapy.[5]

Traditional AST methods

The route from suspected infection and sampling to a definitive laboratory report, via culturing, pathogen identification, and susceptibility testing, takes up to 72 hours using traditional means. This is mainly because more conventional susceptibility testing methods tend to require three overnight culture steps: culture, subculture, and AST.

Decision-making may ultimately involve multiple touchpoints, following interpretation of a combination of phenotypic tests to determine minimum inhibitory concentration (MIC), genotype and proteomic tests, to detect antimicrobial resistant genes or their products, as well as scientific and medical deduction.

While there are many advantages to this well-established approach, the result can be a slow march to optimized therapy. In turn, this can impact on patient care, contribute to AMR, and extend expensive hospital stays.

"The perception a clinician may have of a clinical microbiology laboratory is that we are using tools from the last century," said Dr Rafael Canton, Head of the Clinical Microbiology Department at the University Hospital Ramón y Cajal. "We need to make a change."

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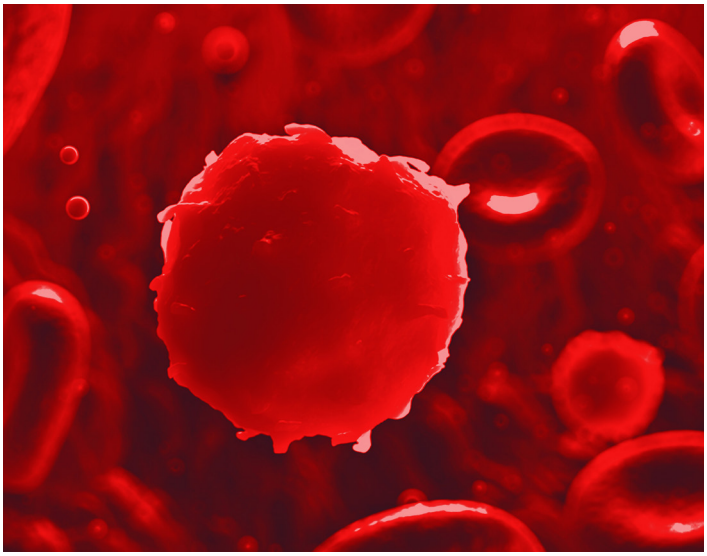
Further, the 72-hour turnaround time only relates to the optimal time-to-result in the microbiology laboratory. It does not take into account delays associated initial detection of the illness, a lack of weekend or overnight cover, or the processes of getting relevant data to the bedside ready for review, and implementing any required changes to patient care.



Advancing methods

Over the last decade, mass spectrometry (MS) has reduced the time it takes to identify microorganisms from 24 hours to just minutes.

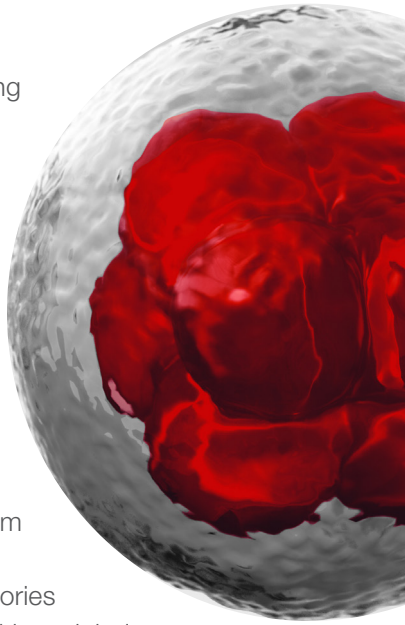
Rapid AST, however, has been harder to achieve. But new methods are now promising a step change that will benefit patients, infection control specialists, epidemiologists, and healthcare systems alike.

Microscopic techniques have been shown to be able to determine the antimicrobial susceptibility of bacteria from a positive blood culture bottle in just six hours.[6] Initial attempts involved incubating the sample with antimicrobial, and embedding it into agarose. Microbiologists then used a microscope to detect colony formation.

Recent advances in flow cytometry, namely the application of bacterial viability dyes, improved resolution, and increased sophistication of multi-parameter analysis, have contributed to the method's use in AST. A 2017 study found the approach combined rapid susceptible/non-susceptible classification and quantitative MIC measurements into a single process that took less than four hours.[7] However, advanced flow cytometry techniques are currently still limited to laboratories with a high degree of scientific expertise.

Isothermal calorimetric methods are also being investigated for use in AST and MIC. By measuring the heat generated by biological processes in the living cells, laboratories can track heat flow curves that can be affected by the presence of resistant microorganisms or their products. A study co-authored by Dr. Canton and published earlier this year found the method could accurately determine the MICs among drug-resistant clinical isolates of *Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa* and *Acinetobacter baumannii.*[8]

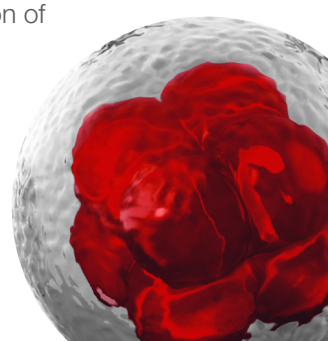
Bright future for AST

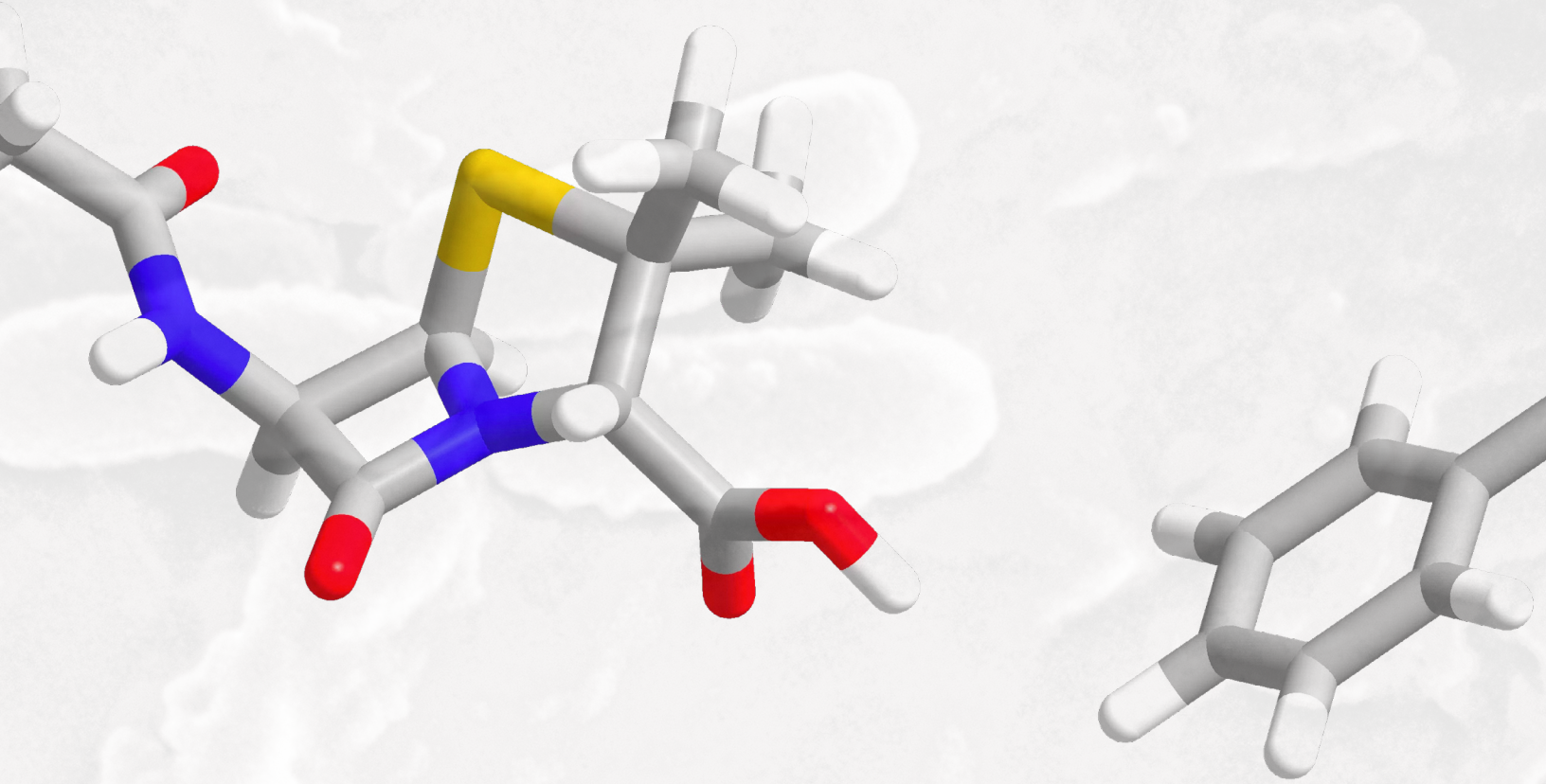


The potential impact of modernizing AST processes is huge. Studies have shown that returning an AST result 24 hours earlier than standard time frames could deliver per patient cost savings of between $2,500 and $20,000 through reducing disease severity and hospital stay duration,[9] and cut mortality rates by around 40%.[10]

Combining the rapid microorganism identification afforded by MS with rapid AST presents clinical laboratories with an exciting opportunity to tackle a global threat, said Dr. Canton.

"If we use these methods to treat patients more appropriately, the impact on the selection of antimicrobial resistance will be lower. If we introduce this rapid AST, we expect AMR will decrease in the future."





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