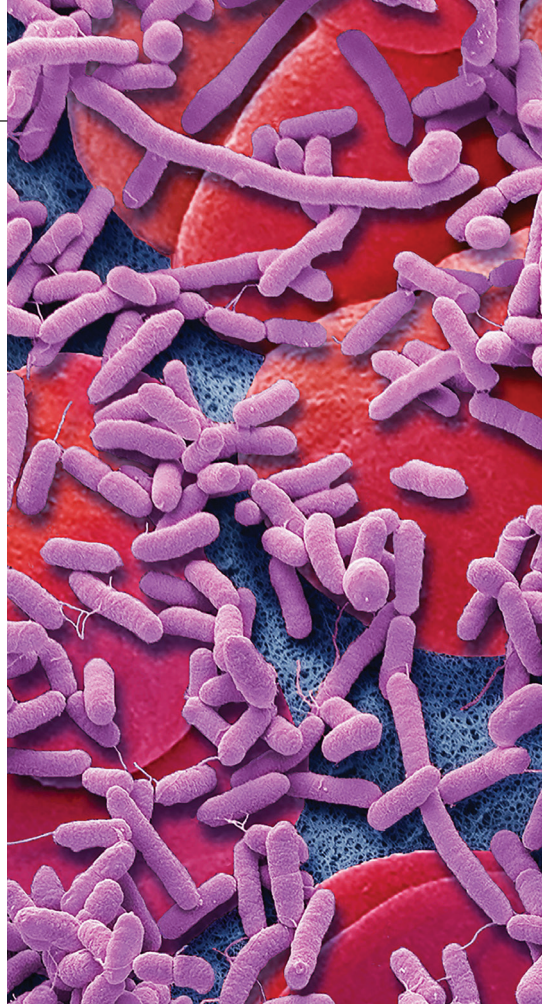
SEPSIS AND ANTIBIOTICS



The ADAPT-Sepsis Trial Coordinating team explains how NHS biochemistry teams are leading in the fight against antibiotic resistance.

Antibiotic resistance is a global concern and as a result the NHS and health organisations across the world are trying to reduce their use. Antibiotic use is a rich area for research and one trial looking into this area is ADAPT-Sepsis – a biomarker-guided trial in hospitalised patients with suspected sepsis seeking to reduce antibiotic duration. Laboratory biochemistry teams across the NHS, led by biochemical scientists, are integral to the delivery of this innovative trial.

The ADAPT-Sepsis trial aims to protect the effectiveness of currently available antibiotics for the whole UK population and develop treatment strategies that will prolong the effectiveness of new antimicrobial pharmaceuticals as they emerge. The trial is exploring whether treatment protocols based on serial monitoring of C-reactive protein (CRP) or procalcitonin (PCT) safely allow reduction in duration of antibiotic therapy in hospitalised patients with sepsis.

This is the first large-scale comparative study of CRP and PCT in this field and the first ever to include a blinding strategy to provide the highest quality evidence for these biomarkers during routine NHS care. This would not be possible without the input of NHS laboratory biochemistry teams across the UK.

A prolific killer

Sepsis results from overwhelming reactions to microbial infections where the immune system initiates dysregulated responses that can lead to remote organ dysfunction, shock and ultimately death. Sepsis is a prolific killer with a death occurring every 3.5 seconds globally. While immediate, appropriate antibiotic treatment for sepsis will help save lives, the current recommended duration of antibiotic therapy for sepsis is very uncertain and is based on low-quality evidence that may lead to antibiotic overuse, contributing to the development of antimicrobial resistance, a national and global priority.

CRP and PCT are circulating plasma proteins that are often raised in sepsis and usually fall in response to effective antibiotic treatment. They are readily measurable in NHS laboratories using standard equipment, providing a potential opportunity to personalise antibiotic duration, which could lead to reductions in population antibiotic usage, adverse effects for patients, improved healthcare resource utilisation and downstream effects relating to antimicrobial resistance.

The ADAPT-Sepsis trial will provide valuable insight into the treatment of sepsis and is also unique in its design, with the role of NHS laboratory biochemistry essential to ensuring high-quality assay performance and that

ADAPT-SEPSIS TRIAL TEAM

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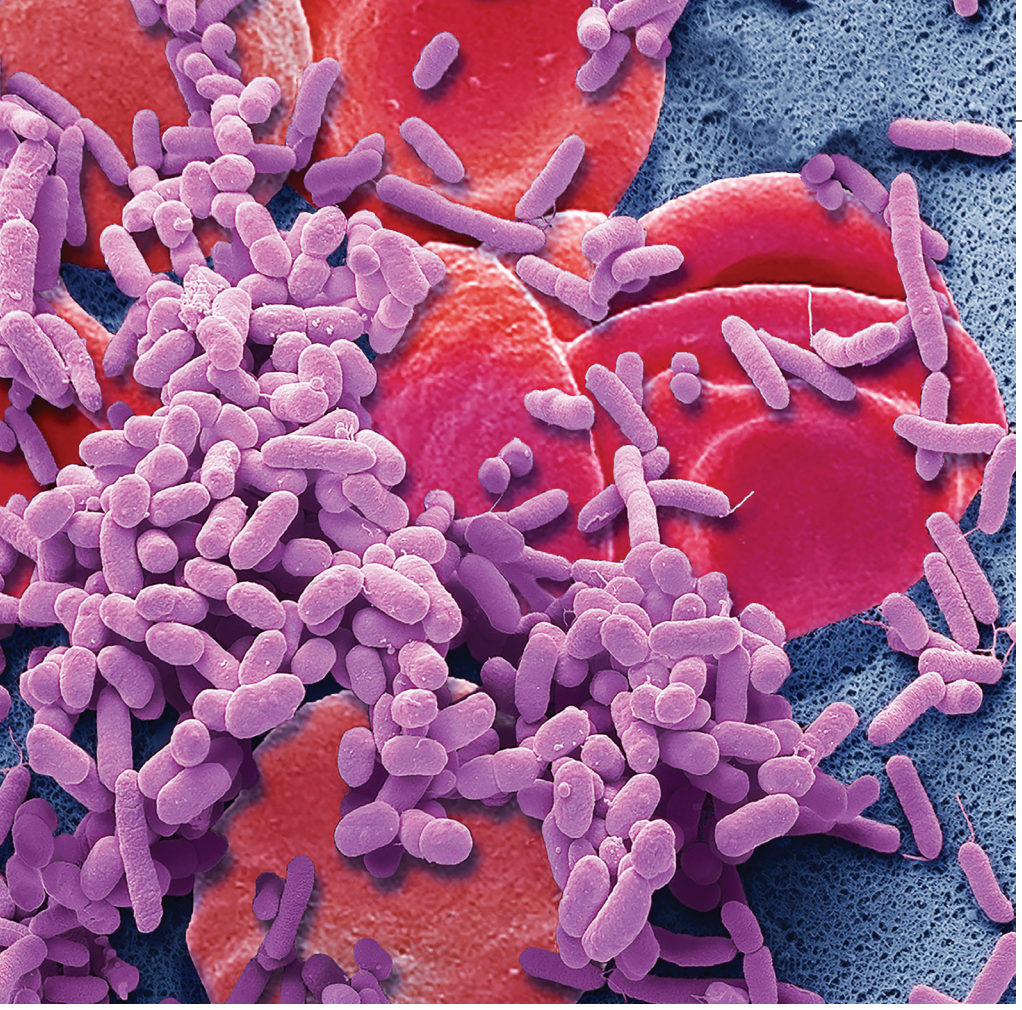

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the trial interventions can be followed successfully. After recruitment to the study, patients are randomised to one of either two treatment protocols in addition to standard care:
(a) Standard care
(b) Standard care + daily CRP monitoring
(c) Standard care + daily PCT monitoring.
ADAPT-Sepsis is a double-blinded trial, so the patient, site research team, treating clinical team and the trial coordinating team will not know which treatment allocation a patient receives. Only the biochemistry teams who perform the required biomarker test will know the treatment allocation.

Essential cog

Daily blood samples, from trial participants receiving antibiotics, are sent to laboratory biochemistry teams who perform the required assay and feedback results to the trial database. Antibiotic treatment advice for that patient for that day is automatically generated and sent to the treatment team (either supporting usual care or issuing two levels of antibiotic stoppage advice). This treatment advice is considered by the treating clinical team alongside other routine assessments to assist the clinical decision making process. Biochemistry teams are at the forefront of facilitating this essential trial process, which directly impacts upon patient care.

This study is a collaborative effort, with NHS clinical laboratory biochemistry teams as an essential cog in the wheel to deliver trial success for patients. Recognising that biochemistry departments are already under pressure to deliver routine practice, the trial has been designed to ensure it is implementable within an NHS laboratory setting. Jonathan Clayton, trial co-investigator and Senior Clinical Scientist at Salford Royal Hospital, has helped shape the study from its inception and has allowed the development of study processes, which are workable and achievable within real NHS labs. Trial education requirements are pragmatic and streamlined to enable training of large biomedical scientist bodies and the study online database has been designed to take just a few seconds to navigate.

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Delivering important research

The study is currently recruiting at 20 centres and continues to open additional sites. NHS laboratory biochemistry teams are involved in early site set-up discussions alongside the research and clinical care delivery teams to ensure each individual centre is able to deliver the study protocol. The trial team has developed bespoke solutions to overcome local barriers and existing lab leads, recognising the importance of this trial, has championed ADAPT-Sepsis and encouraged set up in neighbouring sites.

Whilst CRP is routinely used within the NHS, PCT remains a niche assay. The ADAPT-Sepsis team has helped the majority of participating centres to implement the PCT assay. These sites are now gaining experience of using the assay and the trial aims to contribute to a growing evidence base on PCT use in guiding antibiotic discontinuation.

The trial team would like to thank existing centres for their much-appreciated efforts to deliver this important research and to recognise the enthusiasm from the NHS laboratory biochemistry community as a whole. BMS

Any centres interested in taking part in ADAPT-Sepsis (ISRCTN47473244) are encouraged to get in touch.
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