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Letter to the Editor

Enhancing clinical impact by rapid bacterial identification from blood cultures: the York Teaching Hospital UK experience

***Madam*,**

Bloodstream infections (BSI) constitute a significant disease burden and are estimated to affect more than 30 million people worldwide every year resulting in over 6 million deaths [1]. Prompt identification of microorganisms grown in blood cultures facilitates earlier targeted clinical intervention for patients with sepsis. Therefore, reducing the turn-around time of species identification and antimicrobial susceptibility testing is a high priority. However, in many hospitals in the United Kingdom, the results of conventional bacterial culture techniques may only become available 24—48 hours after the patient has presented with an acute illness. Most blood cultures will flag positive within 12 hours of collection if loaded onto the blood culture analyser without delays. The national standard in the UK is that 100% of blood cultures should be loaded onto the analyser within four hours of collection. Load delays not only delay the time from collection to flagging positive but also have a negative impact on the rates of microbial detection - there is a 0.3% increase in false negative blood cultures for each hour's delay. In York Teaching Hospital majority of the blood culture bottles get loaded onto the analyser within 4—6 hours from collection.

The typical blood culture process involves Gram staining of blood smears made from positive blood culture bottles. This provides a presumptive microbial identification to aid clinical decision-making but it is difficult to make a clear distinction between contamination and a clinically significant BSI at this stage (particularly for Gram positive cocci in clusters) [2]. Broad-spectrum empiric treatment is often given pending the final identification and antibiotic susceptibilities; this approach could promote the development of nosocomial multi-drug-resistant infection [3]. Positive blood cultures are then inoculated onto solid agar plates which are incubated for 18—24 hours in order to yield pure bacterial colonies. Full identification of the organism(s) is then made using Matrix Assisted Laser Desorption Ionization-Time of Flight (MALDI ToF) mass spectrometry followed by antibiotic susceptibility profiling (that takes a further 18—24 hours to complete in the absence of a rapid susceptibility testing methodology).

In this project, we aimed to assess the effectiveness and impact of rapid MALDI-ToF identification of blood culture isolates after 6 hours of incubation on antimicrobial therapy choices in York Teaching Hospital. We used blood culture bottles inoculated with blood that were referred to the Microbiology laboratory of York Teaching Hospital from 1st October 2019 and 31st January 2020. A total of 154 blood culture samples were ultimately identified and included in the project.

Briefly, all new positive blood cultures from 20:00 of the previous day were retrieved from the BD Bactec FX blood culture analyser (Becton Dickinson, UK) and processed by 09:00 every weekday. Gram staining was performed and blood agar plates prepared. For the purpose of this project, only plates made from bottles with a pure Gram film result were processed by a short-term incubation method with formic acid and spun down deposit. Between 15:00 and 15:30, a biomedical scientist would check the plates for growth. Plates with mixed growth were excluded and only those with pure growth were sent for MALDI-ToF-based identification. Bacterial colonies were transferred to the Vitek MS MALDI ToF (BioMerieux) system using a 1-μL sterile plastic loop. The target plates were overlaid with 1 μL of a matrix solution, dried in room air and subsequently subjected to MALDI-ToF identification. Criteria for reliable identification included confidence scores of $\geq$1.7. The identification process was performed only once and results released to the clinical team to act upon. All culture plates were then re-incubated so that growth would be available for any follow-up work required the next day.

A total of 154 blood samples were prospectively collected from 149 patients of which 81 (54.4%) were males. The mean age was 67.9 (range 1—99). Initial Gram staining yielded Gram positive cocci in 96 (62.3%) samples; 52 (33.8%) were Gram negative bacilli; 5 (3.2%) were Gram positive bacilli and 1 (0.6%) was a Gram variable bacillus.

The MALDI ToF-based identification was successfully carried out after 6 hours of incubation in 114/154 (74%) of the samples. Earlier identification of an organism from MALDI ToF at 6-hours led to a switch of antibiotics in 50/149 (33.6%) of the patients. Overall, Escherichia coli (28/114, 28.6%), Staphylococcus aureus (17/114, 14.9%), Streptococcus pneumonia (9/114, 7.9%), Staphylococcus epidermidis (7/114, 6.1%) and Klebsiella pneumonia (5/114, 4.4%) were identified most commonly.

Of the 40 samples that could not be identified by MALDI ToF, 11 (27.5%) of these were clinically significant isolates; 30/40 (75%) were Gram positive cocci, 4/40 (10%) were Gram positive bacilli, 5/40 (12.5%) were Gram negative bacilli and 1/40 (2.5%) was a Gram variable bacillus which was later identified as Streptococcus salivarius (Table I). A total of 11 (27.5%) of the isolates were coagulase negative staphylococci which were not

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Table I
Final identification of organisms that could not be identified by MALDI-ToF testing at 6 hours

Gram stain	Organism
Gram Positive Cocci	*Staphylococcus haemolyticus*
Gram Positive Cocci	*Streptococcus group G*
Gram Positive Cocci	*Staphylococcus epidermidis*
Gram Positive Cocci	*Streptococcus dysgalactiae ssp. dysgalaciae, Staphylococcus hominis*
Gram Positive Cocci	*Streptococcus mitis/oralis*
Gram Positive Cocci	*Beta haemolytic Streptococcus group A*
Gram Positive Cocci	*Staphylococcus aureus*
Gram Positive Cocci	*Streptococcus pneumoniae*
Gram Positive Cocci	*Staphylococcus warneri*
Gram Positive Cocci	*Staphylococcus warneri, Staphylococcus homins*
Gram Positive Cocci	*Staphylococcus aureus*
Gram Positive Cocci	*Staphylococcus pettenkoferi*
Gram Positive Cocci	*Streptococcus pneumonia*
Gram Positive Cocci	*Streptococcus dysgalactiae*
Gram Positive Cocci	*Staphylococcus aureus*
Gram Positive Cocci	*Group A Streptococcus*
Gram Positive Cocci	*Streptococcus mitis/oralis*
Gram Positive Cocci	*Beta haemolytic Streptococcus group A*
Gram Positive Cocci	*Streptococcus dysgalactiae*
Gram Positive Cocci	*Staphylococcus capitis*
Gram Positive Cocci	*Staphylococcus pettenkoferi*
Gram Positive Cocci	*Staphylococcus capitis*
Gram Positive Cocci	*Staphylococcus epidermidis*
Gram Positive Cocci	*Staphylococcus epidermidis*
Gram Positive Cocci	*Alpha haemolytic Streptococci*
Gram Positive Cocci	*Globicatella sanguinis*
Gram Positive Cocci	*Mixed coagulase negative Staphylococcus*
Gram Positive Cocci	*Staphylococcus epidermidis*
Gram Positive Cocci	*Streptococcus mitis/oralis*
Gram Variable Bacilli	*Streptococcus salivarius*
Gram Positive Bacilli	*Actinomyces viscosus*
Gram Positive Bacilli	*Actinomyces naeslundii*
Gram Positive Bacilli	*Kocuria kristinae*
Gram Positive Bacilli	*Actinomyces naeslundii*
Gram Negative Bacilli	*Fusobacterium nucleatum*
Gram Negative Bacilli	*Escherichia coli*
Gram Negative Bacilli	*Escherichia coli*
Gram Negative Bacilli	*Klebsiella pneumonia*
Gram Negative Bacilli	*Staphylococcus capitis*
Gram Negative Bacilli	*Escherichia coli*

clinically significant. The Gram positive bacilli were, Actinomyces viscosus, Actinomyces naeslundii, Kocuria kristinae and Actinomyces naeslundii.

This project demonstrated the efficacy of MALDI ToF-based identification after 6 hours of incubation in 114/154 (74%) of the blood culture samples. The earlier species identification resulted in a switch of antibiotics in 50/149 (33.6%) of the patients. These results are promising as they represent a shortening of the traditional turn-around time of positive blood culture identification. Reduced costs, shorter lengths of hospital stay and improved clinical outcomes are some of the benefits of early administration of targeted antimicrobial therapy [4,5]. Although encouraging, this earlier identification should be complemented by robust antimicrobial stewardship programmes as an integrated approach is known to significantly improve the timeliness of targeted treatment administration [2].

In conclusion, rapid bacterial identification from blood cultures hold promise for the timely achievement of targeted antimicrobial therapy in the setting of BSI. Ways of maximizing the microbial identification, especially for the relatively slower growing gram positive bacteria, should be explored.

Conflict of interest statement

The authors have no competing interests to declare.

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