

C. Ward¹, K. Stocker², J. Begum², P. Wade¹, U. Ebrahimsa¹, S. Goldenberg¹¹Department of Infectious Diseases, Guy's & St Thomas' NHS Foundation Trust, London, United Kingdom ; ²Department of Infection, GSTS Pathology, London, United Kingdom

Objectives

Delayed antimicrobial therapy in septic patients is associated with excess mortality. Blood cultures can take 48 hours or more to identify the causative pathogen and its resistance profile, during which patients are prescribed empirical broad-spectrum antimicrobials. Commercially developed assays are now available that can detect the presence of common pathogens associated with blood stream infection from positive blood culture bottles. Some of these panels also have antimicrobial resistance markers. We aimed to assess two such assays, their potential to reduce the time taken to identify organisms and to improve antimicrobial stewardship practice.

Methods

Positive blood cultures (BioMerieux BacTAlert) were tested using conventional methods (culture and species level identification using MALDI-TOF (Bruker) with antimicrobial sensitivity testing using Vitek2. Results and turnaround time were compared retrospectively with two rapid molecular methods; Nanosphere Verigene Blood culture Gram positive and/or Gram negative cartridges (according to preliminary Gram stain results), and the BioFire FilmArray Blood culture Identification Panel. All assays were performed according to manufacturers instructions. Antimicrobial prescribing data under conventional testing were collected and used to estimate theoretical benefit in antimicrobial stewardship had the rapid methods been used prospectively.

Results

A total of 173 patient samples were tested (first positive bottle per patient only, Gram stains with yeasts excluded). The mean time from blood culture positivity alert to species level identification was 25.68 hours for MALDI-TOF, 2.3 hours for Verigene and 1.07 hours for FilmArray. The mean time from sample collection to positivity alert was 31.65 hours, with a mean of 3.74 hours of sample transportation time.

The most common pathogens identified were Coagulase Negative *Staphylococci* (39%), *E. coli* (17%) and *Staphylococcus aureus* (8%).

When culture and phenotypic/MALDI-TOF identification were used as the gold standard the overall sensitivity, specificity, positive and negative predictive values were 97.4%, 99.8%, 94.4% and 99.8% respectively for Verigene and 98.1%, 98.6%, 85.3% and 99.8% respectively for FilmArray. The FilmArray produced 26 positives for *Pseudomonas aeruginosa* which could not be confirmed using culture or the Verigene; these were considered to be false positives and resulted in a specificity of 84.8% for this organism. There was significant theoretical opportunity for earlier intervention had either of the assays been used prospectively. This included opportunities for more directed therapy (including broader and narrower spectrum of activity) and for discontinuation of antimicrobials at an earlier time.

Conclusion

The diagnostic accuracy of both assays was very similar, resulting in excellent performance characteristics with the exception of several false positives for *Pseudomonas aeruginosa* with the FilmArray. Use of these assays could reduce the turnaround time to identification by a minimum of 23 hours and has the potential to improve antimicrobial stewardship and give important clues as to the source of the blood stream infection.

	Results for Nanosphere Verigene					Results for BioFire FilmArray				
	Sensitivity % (95%CI)	Specificity % (95%CI)	Positive Predictive Value % (95%CI)	Negative Predictive Value % (95%CI)	Kappa (95%CI)	Sensitivity % (95%CI)	Specificity % (95%CI)	Positive Predictive Value % (95%CI)	Negative Predictive Value % (95%CI)	Kappa (95%CI)
<i>Staphylococcus aureus</i>	100 (80.6-100)	100 (97.6-100)	100	100	1.0	100 (80.6-100)	100 (97.6-100)	100	100	1.0
<i>Staphylococcus spp</i>	95.5 (78.2-99.2)	99.3 (96.3-99.9)	95.5 (74.8-99.3)	99.3 (95.7-99.9)	0.95 (0.88-1.0)	98.5 (92.1-99.7)	100 (96.5-100)	100	99.1 (93.8-99.9)	0.99 (0.96-1.0)
<i>Staphylococcus epidermidis</i>	100 (92.3-100)	99.2 (95.7-99.9)	97.9 (86.7-99.7)	100	0.99 (0.96-1.0)					
<i>Micrococcus spp</i>	83.3 (43.6-97.0)	100 (97.8-100)	100	99.4 (86.5-99.9)	0.91 (0.72-1.0)					
<i>Streptococcus pneumoniae</i>	100 (20.7-100)	98.8 (95.9-99.7)	33.3 (11.2-66.5)	100	0.5 (-0.1-1.0)	100 (20.7-100)	100 (97.8-100)	100	100	1.0
<i>Enterococcus spp</i>						100 (87.8-100)	100 (97.7-100)	100	100	1.0
<i>Enterococcus faecalis</i>	50 (9.5-90.5)	100 (97.8-100)	100	99.4 (97.7-99.9)	0.66 (0.05-1.0)					
<i>Enterococcus faecium</i>	100 (56.6-100)	99.4 (96.7-99.9)	83.3 (41.5-97.2)	100	0.91 (0.72-1.0)					
<i>Streptococcus agalactiae</i>	100 (51-100)	100 (97.8-100)	100	100	1.0	100 (51-100)	100 (97.8-100)	100	100	1.0
<i>Streptococcus spp</i>	85.7 (48.7-97.4)	100 (97.7-100)	100	99.4 (96.4-99.9)	0.92 (0.96-1.0)	100 (64.5-100)	99.4 (96.7-99.9)	87.5 (49.8-98)	100	0.93 (0.79-1.0)
<i>E. coli</i>	100 (88.3-100)	100 (97.4-100)	100	100	1.0	100 (88.3-100)	100 (97.4-100)	100	100	1.0
<i>Pseudomonas aeruginosa</i>	100 (4.2-100)	100 (97.8-100)	100	100	1.0	100 (4.2-100)	84.8 (78.7-89.4)	100	7.1 (5.1-9.9)	0.11 (-0.03-0.26)
<i>Klebsiella pneumoniae</i>	100 (51-100)	100 (97.8-100)	100	100	1.0	100 (51-100)	100 (97.8-100)	100	100	1.0
<i>Klebsiella oxytoca</i>	100 (4.2-100)	100 (97.8-100)	100	100	1.0	50 (9.5-90.5)	100 (97.8-100)	100	99.4 (97.7-99.9)	0.66 (0.05-1.0)
<i>Citrobacter spp</i>	100 (43.9-100)	100 (97.8-100)	100	100	1.0					
<i>Enterobacter spp</i>	100 (51-100)	100 (97.8-100)	100	100	1.0	100 (51-100)	100 (97.8-100)	100	100	1.0
<i>Enterobacteriaceae</i>						66.7 (20.8-93.9)	100 (97.8-100)	100	99.4 (97.2-99.9)	0.80 (0.42-1.0)
<i>Acinetobacter spp</i>	50 (9.5-90.5)	100 (97.8-100)	100	99.4 (97.7-99.9)	0.66 (0.05-1.0)					