Evaluation of a Rapid Identification and Antimicrobial Susceptibility Test System from Positive Blood Cultures

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ABSTRACT
Background: Sepsis is a significant cause of mortality, and the importance of rapid identification of antibiotics and subsequent tailoring of antibiotics in patient survival and preventing the emergence of resistant bacteria is well documented. Culture techniques can take up to 72 hours for definitive identification (ID) and determination of antimicrobial susceptibilities (AST). While PCR-based methodologies can provide rapid ID, they are limited in their ability to provide susceptibility data. Fast ID and AST systems like the Accelerate Pheno™ system (AXDX) dramatically reduce the time required to provide ID and susceptibility data for the organisms most commonly associated with sepsis.

Methods: AXDX was validated by Madigan Army Medical Center. 21 isolates (25 Gram-positive, 31 Gram-negative, 2 yeast and 3 off-panel) were run using AXDX and compared to the current laboratory method (ID: Vitek Blood Culture Identification panel, AST: VITEK 2 system). Validation included both seeded (n=36) and patient specimens (n=15), following AXDX validation, an additional 30 patient specimens (25 Gram-positive, 31 Gram-negative, 1 yeast, and 3 off-panel) were prospectively compared to the current methods (CM) as described. Results: In the validation study, the positive percent agreement (PPA) and negative percent agreement (NPA) were 91.8% and 99.7%, respectively, for identification. During AST testing, two major errors (both Gram-negative) and 12 minor errors were identified (1 Gram-positive and 11 Gram-negative). There was 100% concordance for the detection of methicillin resistance in Staphylococcus aureus (n=11) and coagulase-negative staphylococci (n=1) between AXDX and CM. From the time the blood culture was positive, the average time to ID was 2.0 hours and AST was 7.2 hours for AXDX, a potential reduction of 4.5 hours for ID and 7.4 hours for CM. During the prospective study, the PPA and NPA were 96.0% and 98.0%, respectively. Two major errors were detected, both XbaI/SpI/Phototak results that were amplification-subtactant resistant by AXDX, but susceptable by the VITEK 2 system. There were 5 minor errors. There was 100% concordance between methods for the enterococci (n=6) and indol-negativeProvidentiae strains (n=2).

CONCLUSIONS
- AXDX has dramatically reduced blood culture turnaround times. There were some discordant identifications. As a result, we continue to verify the AXDX results with a second method. While the technology is promising, there are some technical issues that need to be resolved. 

INTRODUCTION
- Sepsis remains a leading cause of death in the United States accounting for over 400,000 deaths in 2016
- The impact of timely, appropriate antibiotic therapy on patient survival has been well established
- Survival decreases by about 7.6% with each hour of delay
- Studies suggest median time to effective therapy is about 6 hrs
- Empiric therapy can guide initial treatment, however therapy should be narrowed, or may be incorrect
- De-escalation from broad spectrum agents
- Elimination of unneeded antimicrobials
- Traditional culture methods for identification and antimicrobial susceptibility testing can take in excess of 72 hrs
- Rapid ID and AST systems like the Accelerate Pheno have reduced the time required for ID and AST to approximately 8 hrs

MATERIALS AND METHODS
Part One
- Validation study performed following the procedures as described in the manufacturers’ package insert
- Three types of specimens used, total of 52 specimens
- Remnant positive patient specimens (n=18)
- Challenge isolates provided by Accelerate (n=13)
- Seeded specimens from MAAM Blood cultures (n=21)
- Subculture (Challenge or Seeded Sticks)
- Check purity, prepare 0.5 McFarland in sterile saline
- Time step 1: 100K dilution
- Incubate 1 ml of final dilution (10-100 cfu/ml) into a blood culture bottle
- Positive blood culture notification (Bar/Tec P)
- Perform Gram stain
- Load on the Accelerate following manufacturer’s guidance

Part Two
- Post validation
- Patient specimens tested using the Accelerate Pheno QC over an approximate three-month period (n=30)
- Compared to the current laboratory method
- Gram stain
- Blood Culture ID Panel multiplex PCR (BioFire)
- MALDI-ToF (Vitek-MS)
- Susceptibility Testing (Vitek 2)

RESULTS

WORKFLOW

Figure 1. Results for part one of the study which was a prospective data collection with the Accelerate Pheno being run in conjunction with the MAAM laboratories. Panel A: medical records (n=9) were reviewed and 52 positive blood cultures were identified. Of the total positive cultures, 18 were remnant positive patient specimens, 13 were challenge isolates from Accelerate, and 21 were seeded from MAAM blood cultures. Panel B: results from the Accelerate Pheno were compared to the current laboratory method. Panel C: positive blood culture results from the Accelerate were associated with an antimicrobial challenge. Panel D: results from the Accelerate Pheno were associated with a computed tomography scan of the patient. Panel E: results from the Accelerate Pheno were associated with a patient’s laboratory results.

Figure 2. Summary of the antimicrobial susceptibility testing results (AST) for the Challenge isolates. Panel A: antimicrobial susceptibilities were concluded using the VITEK-2 system. Panel B: antimicrobial susceptibilities were concluded using the Accelerate Pheno. Panel C: antimicrobial susceptibilities were concluded using the Vitek-MS system. Panel D: antimicrobial susceptibilities were concluded using the BioFire. Panel E: antimicrobial susceptibilities were concluded using the Vitek-2 system. Panel F: antimicrobial susceptibilities were concluded using the Accelerate Pheno. Panel G: antimicrobial susceptibilities were concluded using the Vitek-MS system. Panel H: antimicrobial susceptibilities were concluded using the BioFire. Panel I: antimicrobial susceptibilities were concluded using the Vitek-2 system. Panel J: antimicrobial susceptibilities were concluded using the Accelerate Pheno. Panel K: antimicrobial susceptibilities were concluded using the Vitek-MS system. Panel L: antimicrobial susceptibilities were concluded using the BioFire.

Figure 3. Results for part two of the study which was a retrospective data collection with the Accelerate Pheno being run in conjunction with the MAAM laboratories. Panel A: medical records (n=9) were reviewed and 52 positive blood cultures were identified. Of the total positive cultures, 18 were remnant positive patient specimens, 13 were challenge isolates from Accelerate, and 21 were seeded from MAAM blood cultures. Panel B: results from the Accelerate Pheno were compared to the current laboratory method. Panel C: positive blood culture results from the Accelerate were associated with an antimicrobial challenge. Panel D: results from the Accelerate Pheno were associated with a computed tomography scan of the patient. Panel E: results from the Accelerate Pheno were associated with a patient’s laboratory results.

Figure 4. Summary of the antimicrobial susceptibility testing results (AST) for the Challenge isolates. Panel A: antimicrobial susceptibilities were concluded using the VITEK-2 system. Panel B: antimicrobial susceptibilities were concluded using the Accelerate Pheno. Panel C: antimicrobial susceptibilities were concluded using the Vitek-MS system. Panel D: antimicrobial susceptibilities were concluded using the BioFire. Panel E: antimicrobial susceptibilities were concluded using the Vitek-2 system. Panel F: antimicrobial susceptibilities were concluded using the Accelerate Pheno. Panel G: antimicrobial susceptibilities were concluded using the Vitek-MS system. Panel H: antimicrobial susceptibilities were concluded using the BioFire. Panel I: antimicrobial susceptibilities were concluded using the Vitek-2 system. Panel J: antimicrobial susceptibilities were concluded using the Accelerate Pheno. Panel K: antimicrobial susceptibilities were concluded using the Vitek-MS system. Panel L: antimicrobial susceptibilities were concluded using the BioFire.

Figure 5. Results for part three of the study which was a retrospective data collection with the Accelerate Pheno being run in conjunction with the MAAM laboratories. Panel A: medical records (n=9) were reviewed and 52 positive blood cultures were identified. Of the total positive cultures, 18 were remnant positive patient specimens, 13 were challenge isolates from Accelerate, and 21 were seeded from MAAM blood cultures. Panel B: results from the Accelerate Pheno were compared to the current laboratory method. Panel C: positive blood culture results from the Accelerate were associated with an antimicrobial challenge. Panel D: results from the Accelerate Pheno were associated with a computed tomography scan of the patient. Panel E: results from the Accelerate Pheno were associated with a patient’s laboratory results.

Figure 6. Summary of the antimicrobial susceptibility testing results (AST) for the Challenge isolates. Panel A: antimicrobial susceptibilities were concluded using the VITEK-2 system. Panel B: antimicrobial susceptibilities were concluded using the Accelerate Pheno. Panel C: antimicrobial susceptibilities were concluded using the Vitek-MS system. Panel D: antimicrobial susceptibilities were concluded using the BioFire. Panel E: antimicrobial susceptibilities were concluded using the Vitek-2 system. Panel F: antimicrobial susceptibilities were concluded using the Accelerate Pheno. Panel G: antimicrobial susceptibilities were concluded using the Vitek-MS system. Panel H: antimicrobial susceptibilities were concluded using the BioFire. Panel I: antimicrobial susceptibilities were concluded using the Vitek-2 system. Panel J: antimicrobial susceptibilities were concluded using the Accelerate Pheno. Panel K: antimicrobial susceptibilities were concluded using the Vitek-MS system. Panel L: antimicrobial susceptibilities were concluded using the BioFire.

Conclusions
- The Accelerate Pheno system has been implemented in the MAAM Microbiology laboratory
- There has been a dramatic decrease in the turn-around-time for antimicrobial susceptibility testing
- Some identification issues
- Low cell numbers
- Debris
- System not fully integrated
- Continuing to use the system and monitor performance