Potential for Faster Diagnosis of Bacteraemia Using Accelerate Pheno™

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INTRODUCTION

There is a direct relationship between appropriate antibiotic administration and survival in patients with bacteremia and sepsis. Additionally, the use of narrower spectrum antibiotics reduces adverse events and the development of resistance. Results from rapid diagnostic testing support timely and accurate treatment, thus improving clinical outcomes in patients with positive blood cultures. The Accelerate Pheno™ system (AXDX) is a platform for rapid identification (ID: ~ 90 minutes) and antimicrobial susceptibility testing (AST: ~ 7 hours) from positive blood culture bottles. We assessed the potential for more timely ID and AST for 158 positive blood cultures from unique patients, based on Gram stain morphology results that are consistent with on-panel organisms. We followed all patients until AST results were available and assessed the impact that culture results had on had on treatment by medical and surgical teams as well as the recommendations made by medical microbiologists.

The AXDX Pheno is not authorized for sale or marketing in Canada. For Research Use Only – Not for Clinical Diagnostic Use.

All activities in this study were based on Standard of Care.

AIMS

1. To assess Accelerate Pheno™ system (AXDX) in comparison to standard of care (SOC) in a convenience sample of selected positive blood cultures.

2. To assess the potential impact of AXDX testing on timely appropriate prescribing of antimicrobial agents for patients with bacteraemia.

METHODS

Sample selection

- Positive blood cultures from a convenience sample of 158 patients
- Samples were monomicrobial Gram-negative Rods, Gram-positive Cocci or yeast by initial gram stain
- Medical microbiologist and treating team interventions were collected prospectively at each intervention point (Gram stain, ID and AST) during routine patient care based on SOC results per existing practice
- Time to intervention by the microbiologist or team using the SOC were compared to the potential time provided by AXDX data availability

SOC

- BACTEC™ Lytic/10 Anaerobic/F and Plus Aerobic/F medium for growth
- Subculture to solid media and Gram stain, reported verbally to ward
- ID by rapid MALDI-TOF (Bruker, MALDI Biotyper® LT/SH) at 4-8, then 24 hours
- Failure to ID tested with API strips and 16S PCR at reference lab
- AST performed with **BD Phoenix™** PMIC-84 and -404 cards

AXDX

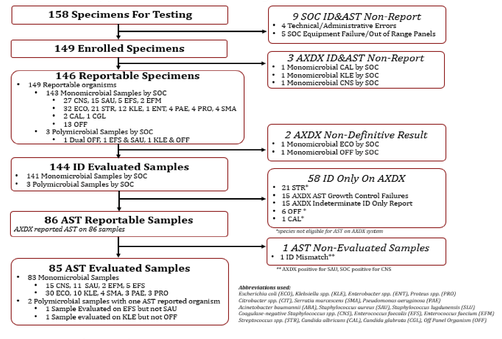
- Samples loaded in parallel with Gram stain and subculture plates
- AXDX used software version 1.2.1.22 and 1.3.0.22

Discrepancy resolution

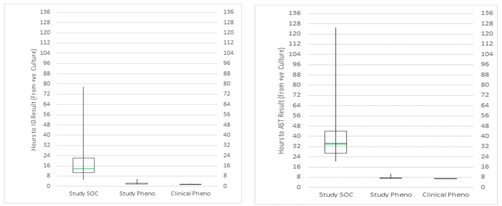
- Specimen tested by Vitek® 2 and MALDI-TOF (Vitek® MS) for ID
- Specimen tested in triplicate using broth microdilution and modal MIC as "correct" value

RESULTS

Organism Types and Results – Figure 1



Timing of Results – Figure 2



Box-plot shows 25th -75th percentile and range (lines) of time to results of ID and AST using SOC, AXDX Pheno including hands-on laboratorian time (study) vs. theoretical hands-on time with AXDX from positive culture bottle signal.

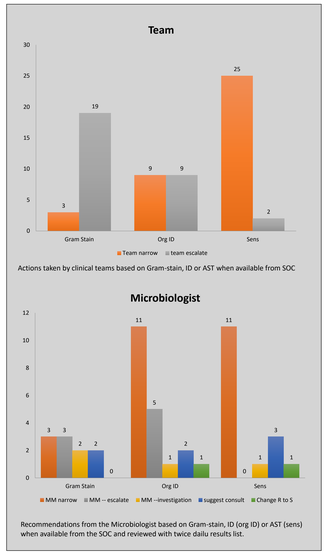


Figure 3 – Interventions by the treating team and medical microbiologist at the different intervention points.

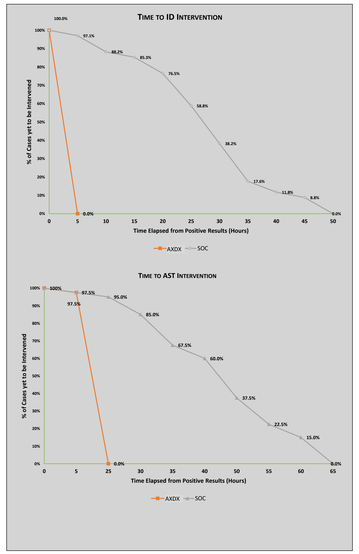


Figure 4 – Comparison of the intervention using SOC to the theoretical intervention time based on data availability from AXDX

Identification (see figure 1)

- Of 158 specimens selected for testing, 146 were reportable
- AXDX correctly identified 12 "off panel" streptococci and staphylococci
- 141 cultures were mono-microbial including correct "off panel" organisms
- When ID was provided, AXDX was 98.5% accurate

AST (see figure 1)

- AST was provided for 86 specimens (60%), One ID result was incorrect
- Overall **99.9% essential (EA) and 97.5% categorical (CA) agreement**
- For erroneous ID, reported AST had CA except for 1 minor error (MiE)
- No very major (VME) errors, and 3 major (ME) and 19 minor errors (MiE)

Timing (see figure 2)

- **Time to ID was 2.1 ± 1.2 h** (AXDX) compared to 16.3 ± 9.8 h (SOC)
- **Time to AST was 7.3 ± 1.6 h** (AXDX) compared to 36.3 ± 12.2 h (SOC)
- Difference to ID was 14 h and to AST was 29 h

ID	Median	3rd Quart.	Max	Min	1st Quart.	StdDev	Std Error
Study SOC	14	22	78	5.3	11	13	1.0
Study Pheno	2.1	2.4	5.4	1.6	1.9	0.65	0.055
Clinical Pheno	1.8	1.9	1.9	1.6	1.8	0.048	0.0040
AST	**Median**	**3rd Quart.**	**Max**	**Min**	**1st Quart.**	**StdDev**	**Std Error**
Study SOC	35	44	125	21	27	12	0.36
Study Pheno	7.3	7.7	11	6.8	7.1	0.66	0.022
Clinical Pheno	7.1	7.1	7.2	6.8	7.0	0.079	0.0026

Potential Clinical Impact (see figures 3 & 4)

- 100 of 146 positive cultures had actions attributable to culture results
- Most interventions (55%) involved narrowing antibiotics
- Narrowing was done most frequently when AST was available
- Using AXDX results, interventions could have been accomplished
  - **24.2 h earlier** for ID
  - **38.4 h earlier** for AST

CONCLUSIONS

- AXDX provides timely and accurate results for common pathogens in blood cultures
- Efficiency is optimized by using Gram stain to choose organisms likely to be on-panel
- This technology correctly identifies some off-panel members of on-panel groups
- Accuracy and reliability are improved by using Gram-stain and other easy lab tests
- Gram stain results are likely to result in broadening of therapy
- ID and AST results offer an opportunity to optimize antibiotic therapy
- The primary activity resulting from ID and AST is to narrow broad empiric therapy
- Microbiologists are more likely than clinical teams to narrow therapy with ID alone
- Clinical teams are most likely to narrow with ID and AST results data available
- These findings would need to be validated by real-time interventions
- Possible limitations to full impact of implementation include off-hours coverage and time for other diagnostics and clinical improvements

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FUTURE

These data will be used to support ongoing efforts to combine rapid diagnostic testing and antimicrobial stewardship to improve patient care and reduce antimicrobial resistance.

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