#19163

Evaluation of the Accelerate Pheno™ System and its Potential Clinical Impact in a Pediatric Academic Center

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INTRODUCTION

- Early recognition of sepsis and initiation of targeted antibiotic therapy is crucial in the treatment of children with Gram-negative rod (GNR) bacteremia, as mortality increases for each hour of delay in effective antibiotic therapy.
- Currently, pathogen identification (ID) and antimicrobial susceptibility testing (AST) rely primarily on culture-based methods, taking >48 hours for results.
- Given the crisis of rising antimicrobial resistance, reliable and rapid diagnostic tests are needed to select effective antimicrobial therapy while also impacting antibiotic stewardship.
- The Accelerate Pheno™ system (AXDX) is a new technology that can quickly identify the most common organisms in bloodstream infections by utilizing morphokinetic cellular analysis to provide rapid susceptibility results for commonly used antibiotics.
- The aim of this study was to compare pathogen identification, AST results, and turnaround time (TATs) of AXDX vs. standard of care methods and assess potential clinical impact of AXDX in children with GNR bacteremia.

METHODS

- Pediatric patients ≤21 years of age admitted to Riley Hospital for Children with monomicrobial GNR bacteremia were prospectively enrolled.
- Testing used the Accelerate Pheno™ system (AXDX; Software Version 1.3.1.15) and the Accelerate PhenoTest™ BC kit (*Fig. 1*).
- Current laboratory methods for ID (Verigene® system and Bruker Biotyper MALDI-TOF MS system) and AST (VITEK® 2 system) were run in tandem with AXDX after blood cultures were flagged as positive by the BACTEC® FX instrument.
  - Sensitivity (SN) and specificity (SP) were calculated for routine identification.
  - Essential (EA) and categorical agreement (CA), major errors (ME) and very major errors (VME) were calculated for AST.
  - AXDX turnaround times were compared to TATs of conventional methods.

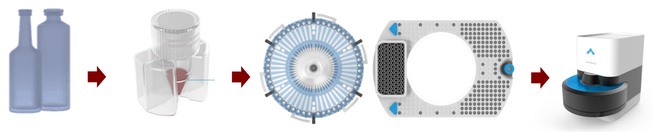

Figure 1: The Accelerate Pheno™ system workflow
A 0.5mL blood aliquot was placed in the sample vial and run on the AXDX instrument. Sample was prepared using gel electrofiltration (GEF) by the instrument. FISH was used for identification of bacteria. Eligible bacteria were exposed to a panel of antimicrobials, and the system analyzed bacterial growth to determine susceptibility (based on morphokinetic cellular analysis).

RESULTS

Table 1. Characteristics of Patient Population

Characteristics	N=32
Age Range	No. Patients
1 month-1 year	8
>1 year ≤18 years	20
>18 year ≤21 years	4
Location	
Pediatric ICU	2
General Wards	16
Bone Marrow Transplant	5
Heme/Onc	9

Table 2. Mean time to assay result by method

Assay	Method	Instrument Run Time (hours)	Time from Positivity (hours)
ID	Verigene® system	2.2	4.5
	MALDI-TOF MS	N/A	36.3
	AXDX	1.3	3.6
AST	VITEK® 2 system	9.1	35.9
	AXDX	6.6	8.9

Table 3. Identification performance of AXDX vs. both the Verigene® system and MALDI-TOF MS.

Microbe	Sensitivity
Enterobacter spp.	8/9 (88.9%)
Escherichia coli	8/8 (100%)
Klebsiella spp.	9/9 (100%)
Pseudomonas aeruginosa	4/4 (100%)
Serratia marcescens	1/1 (100%)
Total	**30/31* (96.8%)**

*One sample excluded due to technical failure

Table 4. Antimicrobial susceptibility testing performance of AXDX compared to the VITEK® 2 system

Antibiotic	EA	CA	VME	ME	S	I	R
Amikacin	29/29 (100%)	29/29 (100%)	0	0	29	0	0
Ampicillin-Sulbactam	13/16 (81.3%)	10/16 (62.5%)	0	1	9	4	3
Cefepime	26/30 (86.7%)	26/30 (86.7%)	0	0	27	2	1
Ceftazidime	22/30 (73.3%)	22/30 (73.3%)	0	0	25	2	3
Ceftriaxone	26/26 (100%)	25/26 (96.2%)	0	0	20	0	6
Ciprofloxacin	29/30 (96.7%)	28/30 (93.3%)	0	0	28	1	1
Gentamicin	27/30 (90%)	30/30 (100%)	0	0	28	0	2
Meropenem	27/29 (93.1%)	27/29 (93.1%)	0	0	29	0	0
Piperacillin-Tazobactam	13/15 (86.7%)	14/15 (93.3%)	0	0	13	1	1
Tobramycin	27/29 (93.1%)	27/29 (93.1%)	0	0	26	2	1
Total	**239/264 (90.5%)**	**238/264 (90.2%)**	**0**	**1**	**234**	**12**	**18**

Abbreviations: EA=essential agreement; CA=categorical agreement; VME=very major error; ME=major error; S=susceptible; I=intermediate; R=resistant.

SUMMARY OF RESULTS

- The Accelerate Pheno™ system had a **sensitivity of 96.8%** for pathogen identification compared to both the Verigene® system and the Bruker Biotyper MALDI-TOF MS system.
  - There was one false-negative *Enterobacter* spp.
  - The Verigene® system did not detect *E. cloacae* in one sample that was detected by AXDX, MALDI-TOF MS, and routine culture.
- AXDX had an overall **essential** and **categorical agreement** of **90.5%** and **90.2%**, respectively, for AST compared to the VITEK®2 system.
- Following discrepancy testing:
  - 1 ME for ampicillin-sulbactam in a *K. oxytoca* isolate remained.
  - Two other major errors (one *E. cloacae* with cefepime and one *K. oxytoca* with ampicillin-sulbactam) were converted to minor errors following broth microdilution discrepancy testing.
  - One ESBL *E. coli* with 2 ME's for cefepime and ceftazidime were converted to minor errors following broth microdilution discrepancy testing.
- AXDX required a mean time of 1.3 hours for identification from time of set-up compared to 2.2 hours for Verigene®. Mean time for MALDI-TOF MS confirmatory testing was 36.3 hours from time of positivity (Range: 21.8-81.1 hours).
- AXDX required a mean time of 6.6 hours from time of set-up and 8.9 hours from time of positivity for AST, compared to 9.1 and 35.9 hours, respectively, for the VITEK® 2 system.

CONCLUSIONS

- AXDX provides fast and reliable results compared to conventional laboratory methods.
- AXDX has the potential to significantly reduce turnaround time for positive blood culture results, potentially decreasing the time to optimal antibiotic therapy and thus, improving patient outcomes.
- Prospective studies evaluating the clinical impact of AXDX on patient outcomes are needed and planned.

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