# Utilization of the Accelerate Pheno™ System for Gram-Negative Bloodstream Infections in a Pediatric Academic Center


INDIANA UNIVERSITY SCHOOL OF MEDICINE

Riley Hospital for Children, Indiana University Health

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## INTRODUCTION

- Currently, pathogen identification (ID) and antimicrobial susceptibility testing (AST) rely primarily on culture-based methods, often taking >48 hours for results.
- There is a critical need for rapid and reliable diagnostics for the timely selection of antimicrobial therapy and enhanced antibiotic stewardship.
- The Accelerate Pheno™ system (AXDX) is a new technology that quickly identifies the most common organisms in bloodstream infections by utilizing morphokinetic cellular analysis to provide rapid AST results.
- The aim of this study was to compare pathogen ID, AST, and turnaround times (TATs) of AXDX against current standard of care (SOC) methods.
- Secondarily, we assessed the potential time to active and optimal antibiotic therapy if the AXDX was utilized for children with gram-negative rod (GNR) bacteremia.

## METHODS

- Patients ≤21 years of age admitted to Riley Hospital for Children with monomicrobial GNR bacteremia were prospectively enrolled over a 3-month timespan.

***Pathogen ID, AST and TAT***

- Standard of care laboratory methods for pathogen ID (VERIGENE® and Bruker MALDI Biotyper® systems) and AST (VITEK® 2 system) were run in tandem with the Accelerate PhenoTest™ BC kit (Fig 1) on positive blood culture samples (BACTEC® FX). Testing used the Accelerate Pheno™ system software version 1.3.1.15.
  - Exclusion criteria included samples with off-panel organisms or recurrent bacteremia within 30 days.
  - ID positive percent agreement (PPA) and negative percent agreement (NPA) were calculated for on-panel target organisms.
  - AST essential agreement (EA), categorical agreement (CA), major errors (ME), and very major errors (VME) were calculated.
  - Turnaround times of patient results were compared between AXDX and conventional methods.

***Theoretical Clinical Data***

- Demographic and clinical data, including selection and timing of antibiotics, were collected on all eligible patients.
- Exclusion criteria included samples with an off-panel organism, contaminated/impure growth, or a concurrent infection site that grew at least 1 organism that was not isolated from blood.
- Active therapy was defined as the first antimicrobial dose to which blood culture organism was susceptible by conventional antimicrobial testing.
- Optimal therapy was defined as the earliest optimal dose of antimicrobial therapy from time of blood culture positivity.
  - Cases that did not fall within evidence-based guidelines were adjudicated by an infectious diseases physician.
- Time to active and optimal therapy were compared to time when AXDX ID and AST results were available.

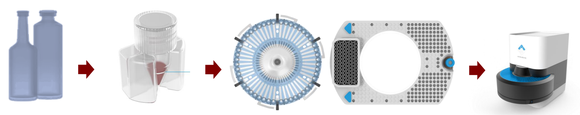



**Figure 1: The Accelerate Pheno™ system workflow**
A 0.5 mL blood aliquot was placed in the sample vial and run on the AXDX instrument. Eligible bacteria were exposed to a panel of antimicrobials, and the system analyzed bacterial growth to determine susceptibility based on morphokinetic cellular analysis.

## RESULTS

**Figure 2. Flow diagram of patient enrollment**

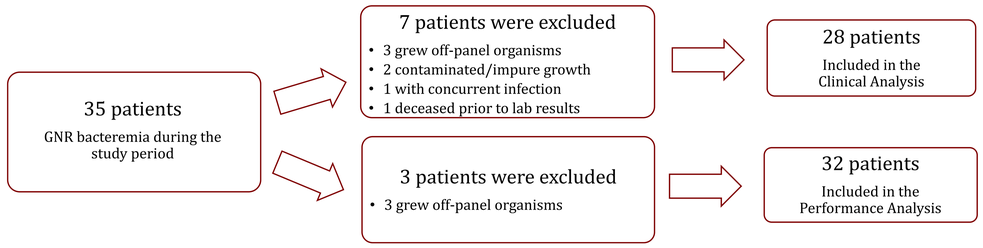
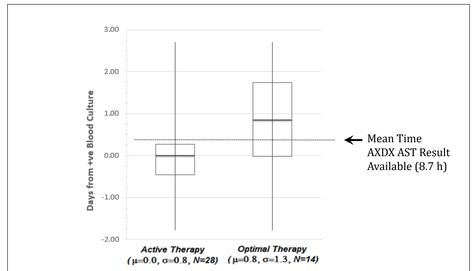



**Table 1. Characteristics of Patient Population (n=28)**

| Characteristic | No. Patients |
|---|---|
| **Age** | |
| 1 month-<1 year | 5 |
| ≥1 year ≤18 years | 20 |
| >18 year ≤21 years | 3 |
| **Sex** | |
| Male | 14 |
| Female | 14 |
| **Inpatient Location** | |
| Pediatric ICU | 2 |
| Bone Marrow/Stem Cell Transplant | 5 |
| Hematology/Oncology | 8 |
| General Wards | 13 |

**Figure 3. Time to active and optimal therapy**



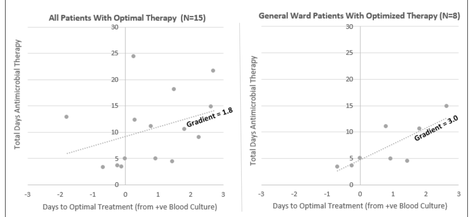

Days to active and optimal therapy from positive blood culture (t= 0.0 days) based on reviewed patient charts from current laboratory methods.

**Table 2. Identification performance of AXDX vs. both the VERIGENE® system and MALDI-TOF MS**

| Organism | PPA | NPA |
|---|---|---|
| *E. coli* | 8/8 (100%) | 27/27 (100%) |
| *Klebsiella* spp. | 10/10 (100%) | 25/25 (100%) |
| *Enterobacter* spp. | 8/9 (87.5%) | 25/26 (96.2%) |
| *S. marcescens* | 1/1 (100%) | 34/34 (100%) |
| *P. aeruginosa* | 4/4 (100%) | 31/31 (100%) |
| *Other** | No positive samples | 105/105 (100%) |
| **Total** | **31/32 (96.9%)** | **247/248 (99.6%)** |

*Other on panel gram-negative targets: *A. baumannii*, *Citrobacter* spp. and *Proteus* spp.

**Figure 4. Effect of optimizing patient therapy**




Patients receiving optimal therapy during treatment by institution guidelines based on chart review. All reviewed pediatric patients (left), and patients from general wards only (right). Gradient (slope) of simple linear regression added.

**Table 3. Antimicrobial susceptibility testing performance of AXDX vs. the VITEK® 2 system**

| Antibiotic | EA | CA | VME | ME | S | I | R |
|---|---|---|---|---|---|---|---|
| Ampicillin-Sulbactam | 13/17 (76.5%) | 10/17 (58.8%) | 0 | 2 | 10 | 4 | 3 |
| Piperacillin-Tazobactam | 13/15 (86.7%) | 14/15 (93.3%) | 0 | 0 | 13 | 1 | 1 |
| Cefepime | 27/31 (87.1%) | 27/31 (87.1%) | 0 | 0 | 28 | 2 | 1 |
| Ceftazidime | 22/31 (71.0%) | 22/31 (71.0%) | 0 | 0 | 26 | 2 | 3 |
| Ceftriaxone | 27/27 (100%) | 26/27 (96.3%) | 0 | 0 | 21 | 0 | 6 |
| Meropenem | 27/29 (93.1%) | 27/29 (93.1%) | 0 | 0 | 29 | 0 | 0 |
| Amikacin | 30/30 (100%) | 30/30 (100%) | 0 | 0 | 30 | 0 | 0 |
| Gentamicin | 28/31 (90.3%) | 31/31 (100%) | 0 | 0 | 29 | 0 | 2 |
| Tobramycin | 28/30 (93.1%) | 28/30 (93.3%) | 0 | 0 | 27 | 2 | 1 |
| Ciprofloxacin | 30/31 (96.8%) | 29/31 (93.5%) | 0 | 0 | 29 | 1 | 1 |
| **Total** | **245/272 (90.1%)** | **244/272 (89.7%)** | **0** | **2** | **242** | **12** | **18** |

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

**Table 4. Mean time to assay result by method**

| Assay | Method | Instrument Run Time* | Time* from Positivity |
|---|---|---|---|
| ID | VERIGENE® | 2.0 ± 0.23 | 4.1 ± 1.8 |
| | MALDI-TOF MS | N/A | 23.9 ± 8.0 |
| | AXDX | 1.3 ± 0.01 | 3.4 ± 1.7 |
| AST | VITEK® 2 | 9.5 ± 1.50 | 37.1 ± 9.7 |
| | AXDX | 6.6 ± 0.03 | 8.7 ± 1.8 |

p<0.001 (Instrument Run Time*: MALDI-TOF MS vs AXDX; VITEK® 2 vs AXDX)
p<0.001 (Time* from Positivity: VERIGENE® vs AXDX; MALDI-TOF MS vs AXDX; VITEK® 2 vs AXDX)
p=0.08 (Time* from Positivity: VERIGENE® vs MALDI-TOF MS)

*Times presented are mean ± standard deviation in hours. Significance values computed using Mann-Whitney U-Test

## SUMMARY OF RESULTS

- The Accelerate Pheno™ system had a **PPA of 96.9%** and a **NPA of 99.6%** for pathogen identification compared to both the VERIGENE® system and the Bruker MALDI Biotyper® system (Table 2).
- AXDX had an **EA** and **CA** of **90.1%** and **89.7%**, respectively, for adjudicated AST compared to the VITEK® 2 system (Table 3).
  - All CA errors were minor, with the exception of 2 major errors for ampicillin-sulbactam.
- Mean time from **set-up to ID** was **1.3 h** for AXDX compared to **2.0 h** for the Verigene® system. Mean time from **set-up to AST result** was **6.6 h** for AXDX compared to **9.5 h** for VITEK® 2 system (Table 4).
- Mean time from **positivity to ID** was **3.4 h** for AXDX compared to **4.1 h** for Verigene® and **23.9 h** for MALDI-TOF MS confirmatory testing. Mean time from **positivity to AST result** was **8.7 h** for AXDX compared to **37.1 h** for the VITEK® 2 system
  - AXDX instrument timing is more consistent than the VITEK® 2 based on standard deviations (Table 4).
- 38% (11/28) of patients were not on active therapy at time of blood culture positivity. Of these, 5 were put on active therapy within a mean of 1.3 days (range: 16 h to 2.7 days) (Figure 3).
  - 17% could have potentially started on active therapy sooner had AXDX results been available clinically.
- 8 patients were put on optimal therapy within a mean of 1.8 days (range 19 h to 8 days) (Figure 3).
  - Thus, 28% of patients could have had therapy optimized earlier had AXDX AST results been available.
- Each day to optimize patient therapy could correlate to a 1.8-day reduction in overall treatment time across all patients, and potentially a 3.0-day reduction for general ward patients based on IU clinical data (Figure 4).

## CONCLUSIONS

- Diagnostic modalities with rapid ID and AST results have the potential to decrease time to active and optimal therapy, thus impacting clinical care and aiding in effective antimicrobial stewardship.
- The Accelerate Pheno™ system provides fast and reliable results compared to conventional laboratory methods.
- Prospective studies evaluating the clinical impact of AXDX on patient outcomes are needed and planned.

## ACKNOWLEDGEMENTS


- Accelerate Diagnostics, Inc. provided half the kits used in the study, however was not involved in study design, data collection or data interpretation.
- Special thanks to Nathan Smith, Christina Chantell, and John Prichard from Accelerate Diagnostics, Inc. for assistance with data management and figure design.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