#6605

Comparison of the Accelerate Pheno®, Vitek®2, Verigene®, and MALDI Biotyper® Systems for Microbial Identification and AST

INDIANA UNIVERSITY SCHOOL OF MEDICINE

Jack G. Schneider, MD[1]; Christopher L. Emery, MD[2]; Thomas E. Davis, MD[2]; James B. Wood, MD[1]
John J. Manaloor, MD[1]; Ryan Relich, PhD.[2]; Brittany Bocian, MLS[2]; Bryan H. Schmitt, DO[2]

[1]Ryan White Center for Pediatric Infectious Disease and Global Health, Indiana University School of Medicine [2]Department of Pathology and Laboratory Medicine, Indiana University School of Medicine

INDIANA UNIVERSITY SCHOOL OF MEDICINE

INTRODUCTION

- Early recognition of sepsis and initiation of targeted antibiotic therapy is crucial in the treatment of gram-negative rod (GNR) bacteremia, as mortality increases for each hour of delay in effective antibiotic therapy.
- Historically, microbial identification and antimicrobial susceptibility testing methods have been limited by the need to test pure cultures of bacterial isolates.
- Because of the rapidly increasing prevalence of multi-drug resistant pathogens, quick and reliable methods that obviate the need for isolate procurement are essential for the timely implementation of appropriate antimicrobial therapy, especially for bloodstream infections.
- The Accelerate Pheno™ system (AXDX) is a new technology that can quickly identify the most common organisms in bloodstream infections and utilize morphokinetic cellular analysis to provide rapid susceptibility results for commonly used antibiotics.
- The aim of this study was to compare bloodstream pathogen identification (ID), antimicrobial susceptibility testing (AST), and turnaround times (TATs) of AXDX vs. standard-of-care (SOC) methods, including the VERIGENE®, Bruker MALDI Biotyper®, and VITEK®2 systems.

METHODS

- One hundred forty-two samples, including 17 contrived, 32 fresh pediatric (Age ≤ 21), and 93 fresh adult (Age > 21) samples all with monomicrobial GNR bacteremia were prospectively enrolled over a 3-month timespan.

Pathogen ID, AST and TAT

- SOC 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 (Figure 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.

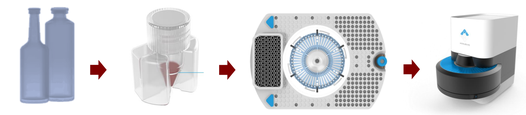


Figure 1: The Accelerate Pheno™ system workflow
A 0.5-mL blood aliquot was placed in the sample vial and run on the AXDX instrument. Sample was prepared using gel electrofiltration (GEF) by the instrument. FISH was used for ID of bacteria. Eligible bacteria were exposed to a panel of antimicrobials,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

RESULTS

Table 1. Mean time to assay result by method

Assay	Method	Instrument Run Time[a]	Time from Positivity[a]
ID	VERIGENE®	2.0 ± 0.38	4.3 ± 1.8
	MALDI-TOF MS	N/A	21.4 ± 6.9
	AXDX	1.3 ± 0.01	3.7 ± 1.9
AST	VITEK® 2	9.2 ± 1.50	35.7 ± 8.3
	AXDX	6.6 ± 0.05	9.0 ± 1.8

p<0.001 (ID: VERIGENE® vs MALDI-TOF MS; ID: MALDI-TOF MS vs AXDX; ID: VERIGENE® vs AXDX; AST: VITEK® 2 vs AXDX)

[a]Times presented are mean ± standard deviation in hours. N=142 for all methods except MALDI-TOF MS which has N=125 (seeded isolate samples not timed on MALDI-TOF MS) and N=136 for AXDX AST (6 samples produced AST non-reportable events on AXDX). Significance values computed using Mann-Whitney U-Test.

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

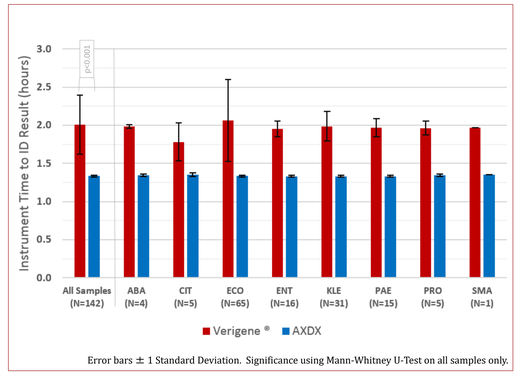
Microbe	PPA[a]	NPA[b]
E. coli	64/64 (100%)	76/76 (100%)
Klebsiella spp.	31/31 (100%)	109/110 (99.1%)
Enterobacter spp.	14/16 (87.5%)	126/126 (100%)
Proteus spp.	4/5 (80%)	137/137 (100%)
Citrobacter spp.	4/5 (80%)	137/137 (100%)
S. marcescens	1/1 (100%)	141/141 (100%)
P. aeruginosa	14/15 (93.3%)	125/125 (100%)
A. baumannii	4/4 (100%)	138/138 (100%)
Total	**136/141 (96.5%)**	**990/991 (99.9%)**

[a]1 indeterminate result was excluded from PPA calculation
[b]3 indeterminate results were excluded from NPA calculation

Table 3. Antimicrobial susceptibility testing performance of AXDX compared to the VITEK® 2 system

Antibiotic	EA	CA	VME	ME	S	I	R
Ampicillin-Sulbactam	84/94 (89.4%)	74/94 (78.7%)	0	2	48	14	32
Piperacillin-Tazobactam	93/101 (92.1%)	96/101 (95%)	1	0	85	2	14
Cefepime	117/129 (90.7%)	112/129 (86.8%)	0	1	101	8	20
Ceftazidime	112/127 (88.2%)	110/127 (86.6%)	0	1	92	3	32
Ceftriaxone	113/113 (100%)	111/113 (98.2%)	0	0	79	1	33
Meropenem	119/122 (97.5%)	119/122 (97.5%)	0	0	108	0	14
Amikacin	123/125 (98.4%)	124/125 (99.2%)	0	0	119	1	5
Gentamicin	120/126 (95.2%)	125/126 (99.2%)	0	0	107	1	18
Tobramycin	121/126 (96%)	120/126 (95.2%)	0	0	103	7	16
Ciprofloxacin	126/127 (99.2%)	125/127 (98.4%)	0	0	87	1	39
Aztreonam	0/1 (0%)	0/1 (0%)	0	1	1	0	0
Total	**1128/1191 (94.7%)**	**1116/1191 (93.7%)**	**1**	**5**	**930**	**38**	**223**

Abbreviations: EA=essential agreement; CA=categorical agreement; VME=very major error; ME=major error; S=susceptible; I=intermediate; R=resistant.
[a]VME/ME samples were adjudicated by a discrepancy laboratory using broth microdilution. Prior to discrepancy testing, there were 3 VME and 12 ME. 2 VME (1 ampicillin-sulbactam, 1 cefepime) and 7 ME (1 ampicillin-sulbactam, 3 cefepime, 3 ceftazidime) were adjudicated in favor of AXDX by broth microdilution.



Error bars ± 1 Standard Deviation. Significance using Mann-Whitney U-Test on all samples only.

Figure 2. Instrumentation mean time to ID result by organism for VERIGENE® vs. AXDX, all samples.

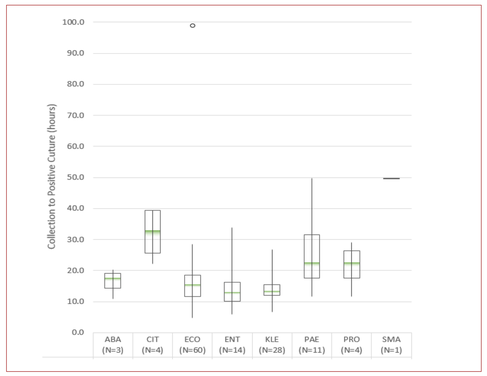


Figure 3. Time ranges by organism from collection to positive blood culture, all fresh patient samples.

Abbreviations: ABA=*A. baumannii*,; CIT=*Citrobacter* spp.; ECO=*E. coli*; ENT=*Enterobacter* spp.; KLE=*Klebsiella* spp.; PAE=*P. aeruginosa*; PRO=*Proteus* spp.; SMA=*S. marcescens*

SUMMARY OF RESULTS

Performance Results

- AXDX had a **PPA of 96.5% and NPA of 99.9%** for identification compared to both the VERIGENE® system and MALDI-TOF MS (Table 2).
  - There were 5 false-negatives (2 *Enterobacter* spp., 1 *Proteus* spp., 1 *Citrobacter* spp. and 1 *P. aeruginosa*)
  - The VERIGENE® system did not detect *Enterobacter gergoviae or Klebsiella variicola* in two different samples, which were detected by AXDX (identified as *Enterobacter* spp. and *Klebsiella* spp., respectively).
- AXDX had an overall **EA** and **CA** of **94.7%** and **93.7%**, respectively, for AST compared to the VITEK® 2 system (Table 3). Eleven percent (16/141) of isolates were found to be ESBL producers. AXDX had an overall **EA** and **CA** of **91.8%** for AST compared to the VITEK® 2 system with these specific isolates.
- Following discrepancy adjudication testing via broth microdilution:
  - Three initial AXDX VMEs were adjudicated to 1 VME against AXDX for piperacillin-tazobactam and 2 MEs against VITEK® 2
  - Twelve initial AXDX MEs were adjudicated to 5 ME's against AXDX (including 1 for cefepime with an ESBL *E. coli*) and 7 VMEs against VITEK® 2

Timing/Workflow Results

- Despite highly variable growth times for organisms from collection to positive culture (Figure 3), AXDX had a mean time of 1.3 hours for ID from time of set-up which was highly consistent (σ=0.01) compared to 2.0 hours for the VERIGENE® system, which was also consistent (σ=0.38) (Table 1 & Figure 2). Mean time for MALDI-TOF MS confirmatory testing was 21.4 hours from time of positivity, and was quite variable (σ=6.9).
- AXDX required a mean time of 6.6 hours from time of set-up and 9.0 hours from time of positivity for AST, compared to 9.2 and 35.7 hours, respectively, for the VITEK® 2 system.
- AXDX decreased the time required to prepare positive blood cultures with GNR's from nearly 30 minutes to approximately 3 minutes.

CONCLUSIONS

- AXDX provides reliable results that are comparable to other methods, including molecular and proteomics-based methods for organism ID and phenotypic and molecular methods for AST in positive blood cultures with GNR's.
- AXDX has the potential to significantly reduce turnaround time for positive blood culture ID and AST results, and thus can likely further aid in effective antimicrobial stewardship.
- Utilizing AXDX can substantially reduce overall hands-on time for lab technologists, allowing for more optimal work-flow.
- 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.

REFERENCES

*Banerjee, R, et al. 2015. *Clinical Infectious Diseases* 61: 10711080.
*Charnot-Katsikas, Angella, et al. 2018. *Journal of Clinical Microbiology*. 56e01166-17.
*Lutgring, JD, et al. 2018. *Journal of Clinical Microbiology* 56: e01672-17.
*Kumar, A, et al. 2006. *Critical Care Medicine* 34: 1589-1596.
*Marschal, M, *et al.* 2017. *Journal of Clinical Microbiology* 55: 2116-2126.
*Pancholi, P, et al. 2018. *Journal of Clinical Microbiology*: JCM-01329.

Jack Schneider, MD (jgschnei@iu.edu)
Indiana University School of Medicine, 705 Riley Hospital Drive, RI 3032, Indianapolis, IN 46202