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LETTER TO THE EDITOR

Evaluation of a Rapid System for Antimicrobial Identification and Antimicrobial Susceptibility Testing in Pediatric Bloodstream Infections

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Rapid identification (ID) and antimicrobial susceptibility testing (AST) techniques promise to improve the management of patients with bloodstream infections (BSI). We used the Pheno system (version 1.0.0.59) by Accelerate Diagnostics (AXDX) to evaluate 65 pediatric patient samples and compared results to those from our standard of care (SOC). Bactec Peds Plus/F (Becton, Dickinson, Baltimore, MD)-positive samples were used on the Pheno system as instructed by the package insert. In our SOC, the Bruker Biotyper matrix-assisted laser desorption ionization–time of flight mass spectrometer (MALDI-TOF MS) (Bruker Daltonics, Billerica, MA) was used for ID and the Vitek 2 system (bioMérieux, Durham, NC) was used for AST, supplemented by results of the Verigene Gram-positive blood culture (BC-GP) test (Luminex Corp., Austin, TX) for Gram-positive bacteria.

Of 65 samples, 5 were excluded due to a time lapse of >8 h after blood culture positivity (4 samples) or instrument failure (1 sample). The Pheno system achieved identification results for 47 of the remaining 60 samples (78.3%). For 3 of the missed 13 samples, the instrument returned an "indeterminate" result, which is assigned when the signal from the sample exceeds a negative result but does not meet criteria for a positive result (1). "Indeterminate" results included those for multiple organisms, often *Staphylococcus* and *Candida* species. Nine of the remaining 10 samples, which included *Salmonella enterica* serovar Typhi, *Salmonella enterica* serovar non-Typhi, *Raoultella planticola* (2 samples), *Bacillus* spp. (not *anthracis*) (2 samples), *Pseudomonas putida*, *Acinetobacter* species, and *Ochrobactrum*, were appropriately labeled "off panel." In the remaining off-panel result, our SOC returned *E. coli*, an organism identifiable by the Pheno system. Overall, the Pheno system's reportable panel covered 81% of the organisms causing BSI at our institution.

Of the 47 identified samples, 40 were monomicrobial. Fourteen of 14 Gram-positive monomicrobial samples and 21 of 26 Gram-negative samples were consistent with the IDs provided by our SOC. Gram-negative performance was of interest, because our standard of care does not include a rapid system for identification of Gram-negative organisms. At our institution, the Pheno system adds little actionable information for Gram-positive organisms beyond that supplied by the Verigene BC-GP test, which provides clinically actionable resistance determinants in Gram-positive samples within 3 h (2). The Pheno test kits also come at significantly higher cost. Among the five incorrect Gram-negative results, the Pheno system identified two separate *Salmonella*-positive samples (*Salmonella paratyphi* A, *Salmonella* non-Typhi) as coagulase-negative *Staphylococcus* (CoNS) and ran CoNS AST panels. A trained technologist would have

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TABLE 1 Sensitivity and specificity of the Pheno system[a]

Organism(s)	TP/(TP+FN)	% sensitivity	TN/(TN+FP)	% specificity
Coagulase-negative *Staphylococcus*	4/4	100	41/43	95.3
Enterococcus faecalis	4/5	80	43/43	100
Staphylococcus aureus	4/4	100	43/43	100
Streptococcus spp.	4/4	100	43/43	100
Acinetobacter baumannii	2/2	100	45/45	100
Citrobacter spp.	2/2	100	45/45	100
Enterobacter spp.	4/5	80	41/42	97.6
Escherichia coli	7/8	87.5	40/41	97.6
Klebsiella spp.	11/11	100	35/36	97.2
Proteus spp.	0/2	0	47/47	100
Serratia marcescens	2/3	66.7	45/46	97.8

[a]TP, true positive; TN, true negative; FN, false negative; FP, false positive.

recognized the incompatibility with the Gram stain, but the results were concerning. As indicated in the previous paragraph, in two other instances, the Pheno system appropriately labeled *Salmonella* species as off panel, so these results cannot be generalized to all *Salmonella*-positive samples in our study. The Pheno system had an 88.0% sensitivity, which is lower than its performance in other pediatric populations (3) (Table 1).

Approximately 10% of bloodstream infections seen at our institution are polymicrobial. The Pheno system correctly identified all organisms in only two of seven polymicrobial samples. Of 17 total isolates recovered from these seven polymicrobial samples, only 11 were correctly identified. Additionally, the Pheno system possesses a feature that labels samples as "monomicrobial," which mischaracterized four of these samples (Table 2).

Of the AST results returned, 215 were concordant and 15 were discrepant, including 0 very major errors, 2 major errors, and 13 minor errors (91.6% essential agreement, 93.4% categorical agreement) (Table 3). For antimicrobials of low agreement (ampicillin-sulbactam, ceftazidime, and cefazolin), errors were found across species for ceftazidime, in *E. coli* and *Klebsiella oxytoca* for ampicillin-sulbactam, and only in *Klebsiella pneumoniae* for cefazolin. Mean times to ID and AST results (1.37 and 6.58 h, respectively) were a considerable reduction from times achieved by our SOC (25.26 and 48.53 h, respectively), consistent with other evaluations (4, 5, 6).

TABLE 2 Polymicrobial results

Organism(s)	Sample	Pheno system result	Monomicrobial call
K. pneumoniae	14	Detected	
Proteus mirabilis	14	Missed	Yes
E. faecalis	14	Missed	
E. coli	25	Detected	
E. faecalis	25	Detected	No
K. pneumoniae	35	Detected	
E. cloacae complex	35	Missed	Yes
E. cloacae complex	52	Detected	
S. marcescens	52	Missed	Yes
S. marcescens	55	Detected	
Pseudomonas putida	55	Off panel	Yes
K. pneumoniae	58	Detected	
E. coli	58	Detected	No
Proteus vulgaris	58	Missed	
K. pneumoniae	59	Detected	
E. faecalis	59	Detected	No
Staphylococcus haemolyticus	59	Detected	

TABLE 3 AST essential and categorical agreements[a]

Test and antibiotic(s)	No. of samples	Essential agreement	Categorical agreement
Gram-positive organism AST			
Ampicillin	2	100	100
Erythromycin	2	100	100
Linezolid	3	100	100
Vancomycin	6	100	100
Gram-negative organism AST			
Amikacin	24	100	100
Ampicillin-sulbactam	14	78.5	71.4
Cefepime	24	95.8	95.8
Ceftazidime	22	50.0	81.8
Ceftriaxone	22	100	86.4
Ciprofloxacin	22	100	100
Ertapenem	22	100	100
Gentamicin	22	95.4	100
Piperacillin-tazobactam	16	93.7	100
Tobramycin	22	90.9	90.9
Cefazolin	6	100.0	83.3
Daptomycin	1	100	100

[a]There were no results for ceftaroline, aztreonam, or meropenem.

We expect that the Pheno system will offer valuable information, particularly in the management of Gram-negative monomicrobial bloodstream infections. Our contribution highlights the limitation of the Pheno system to adequately detect polymicrobial infections, as well as the importance of an experienced microbiologist to review results. An effective stewardship program is also necessary to maximize the value of this type of technology. Since this evaluation, AXDX has made hardware and software upgrades, but it is unclear whether they have addressed the limitations mentioned here.

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