Rapid identification and antimicrobial susceptibility testing of bacteria in bloodstream infections in paediatric patients using *the time-lapse microscopy* technology

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INTRODUCTION AND PURPOSE

Sepsis is one of the leading cause of morbidity and mortality worldwide and recent efforts have led to the development of new generation diagnostic methods. Accelerate Pheno ™ system (AXDX) is an automated microscopy platform that provides identification and antimicrobial susceptibility results in few hours, instead of days, from positive blood cultures. At the Bambino Gesù Children's Hospital, a tertiary care hospital in Rome, the AXDX system was evaluated and results were compared to those obtained using routine diagnostic methods.

METHODS

The bottles (BD BACTEC ™ PLUS) of the blood cultures are incubated in the BD BACTEC ™ FX automatic system. From positive blood culture, the identification (ID) of species is performed with mass spectrometry (Maldi-TOF, Bruker®) while the antimicrobial susceptibility testing (AST) is performed with VITEK®2 instrument (BioMérieux). A total of 26 positive blood cultures were also tested with the AXDX system, within 8 hours of blood culture positivity.

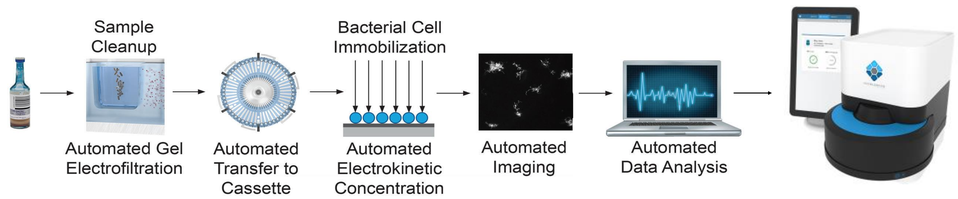


Figure. Workflow to get ID/AST from positive blood cultures with AXDX technology.

The evaluation of AXDX performance is based on sensitivity and specificity for ID and very major error (VME), major error (ME), minor error (MiE), categorical agreement (CA) and essential agreement (EA) for antimicrobial susceptibility testing (AST).

RESULTS

ID	CONCORDANT RESULTS	DISCORDANT RESULTS
Gram +	15	1
Gram -	5	1
Yeasts	1	0

4 Gram + were not identified. An infection was polymicrobial but the AXDX system identified only 2 bacteria. The third, a Gram -, was not identified because it was off-panel.

GRAM-POSITIVE	SENSITIVITY		SPECIFICITY		PPV	
Coagulase-negative Staphylococcus spp.	4/6	66,7%	15/15	100%	4/4	100%
Enterococcus faecalis	2/3	66,7%	18/18	100%	2/2	100%
Enterococcus faecium	1/1	100%	20/20	100%	1/1	100%
Staphylococcus aureus	6/8	75%	13/13	100%	6/6	100%
Staphylococcus lugdunensis	0/0	NA%	21/21	100%	0/0	NA%
Streptococcus spp.	0/0	NA%	20/21	95,2%	0/1	0%

GRAM-NEGATIVE	SENSITIVITY		SPECIFICITY		PPV	
Acinetobacter baumannii	0/0	NA%	21/21	100%	0/0	NA%
Citrobacter spp.	0/0	NA%	21/21	100%	0/0	NA%
Enterobacter spp.	0/0	NA%	21/21	100%	0/0	NA%
Escherichia coli	0/0	NA%	21/21	100%	0/0	NA%
Klebsiella spp.	2/3	66,7%	18/19	95%	2/3	66,7%
Proteus spp.	0/0	NA%	21/21	100%	0/0	NA%
Pseudomonas aeruginosa	2/2	100%	19/19	100%	2/2	100%
Serratia marcescens	0/0	NA%	21/21	100%	0/0	NA%

YEASTS	SENSITIVITY		SPECIFICITY		PPV	
Candida albicans	1/1	100%	19/19	100%	1/1	100%
Candida glabrata	0/0	NA%	20/20	100%	0/0	NA%

AXDX showed an overall sensitivity of 78% and specificity of 99.4% for pathogen ID, compared to our standard methods.

For AST, only 1 VME and no ME and MiE were detected.
The results show overall EA of 91.5% and CA of 100%.

ANTIBIOTICS	EA		CA		VME		ME		MiE	
Ampicillin	3	100%	3	100%	0	0%	0	0%	0	0%
Erythromycin	10	100%	10	100%	0	0%	0	0%	0	0%
Daptomycin	10	100%	10	100%	0	0%	0	0%	0	0%
Linezolid	13	100%	13	100%	0	0%	0	0%	0	0%
Vancomycin	13	100%	13	100%	0	0%	0	0%	0	0%

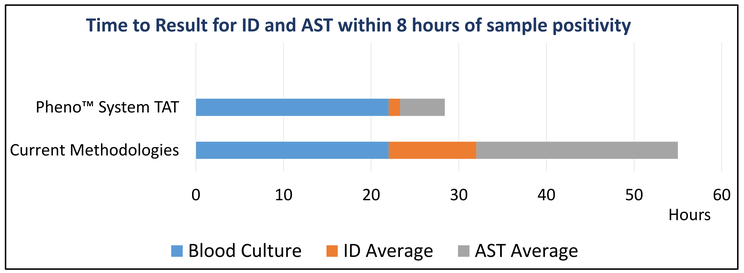
Antibiotics for Gram-positive tested with AXDX

ANTIBIOTICS	EA		CA		VME		ME		MiE	
Amikacin	2	66,67%	3	100%	0	0%	0	0%	0	0%
Cefepime	3	100%	3	100%	0	0%	0	0%	0	0%
Ceftazidime	2	66,67%	3	100%	0	0%	0	0%	0	0%
Ceftriaxone	1	100%	1	100%	0	0%	0	0%	0	0%
Ciprofloxacin	1	33,33%	3	100%	0	0%	0	0%	0	0%
Colistin	1	100%	1	100%	0	0%	0	0%	0	0%
Ertapenem	1	100%	1	100%	0	0%	0	0%	0	0%
Gentamycin	2	66,67%	3	100%	0	0%	0	0%	0	0%
Meropenem	2	66,67%	3	100%	0	0%	0	0%	0	0%
Piperacillin-Tazobactam	1	0%	0	0%	1	100%	0	NA%	0	0%

Antibiotics for Gram-negative tested with AXDX

CONCLUSIONS

For blood cultures tested within 8 hours of revealed positivity, the AXDX system shows an ID improvement of 8 hours and 30 minutes and an AST improvement of 18 hours and 22 minutes, compared to current methodologies.



The Accelerate Pheno™ system provides a final result (consisting of ID and AST), directly from positive blood cultures, faster than traditional methods with the potential to open a new era in rapid microbiological diagnostics.

This would enable better patient management with the benefit of decreasing the overall costs of care and the time of diagnosis. AXDX results will address clinicians to a most appropriate and timely therapeutic choice, reducing antimicrobial resistance.

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