

# Accelerating Time to Pathogen-adapted Antibiotic Treatment by Subculture-independent Antimicrobial Susceptibility Testing in Patients suffering from Sepsis

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## Introduction:

- accurate & fast pathogen identification with subsequent antimicrobial susceptibility testing (AST) and minimum inhibitory concentration (MIC) detection is important for antibiotic treatment adaptation in patients suffering from sepsis.

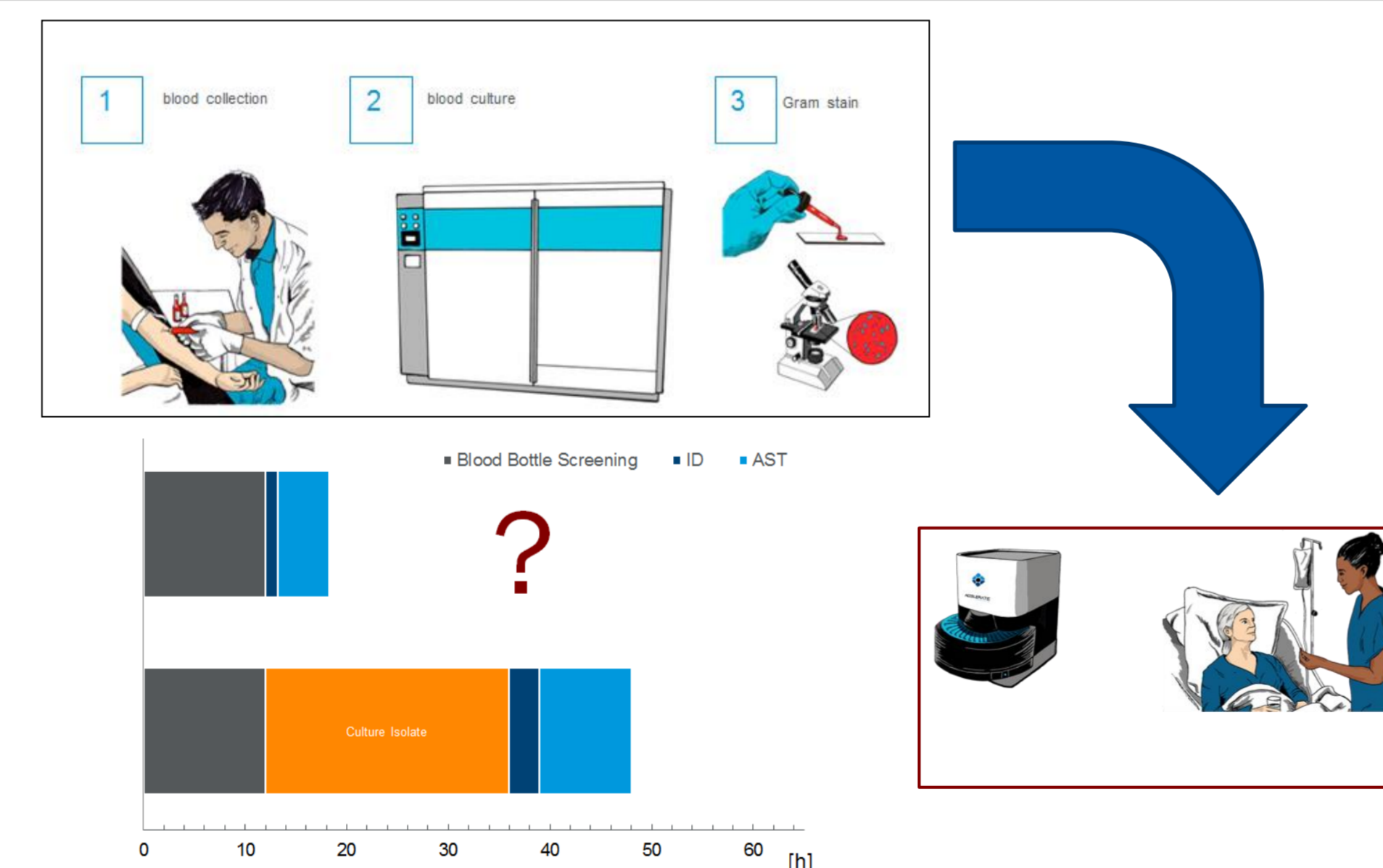
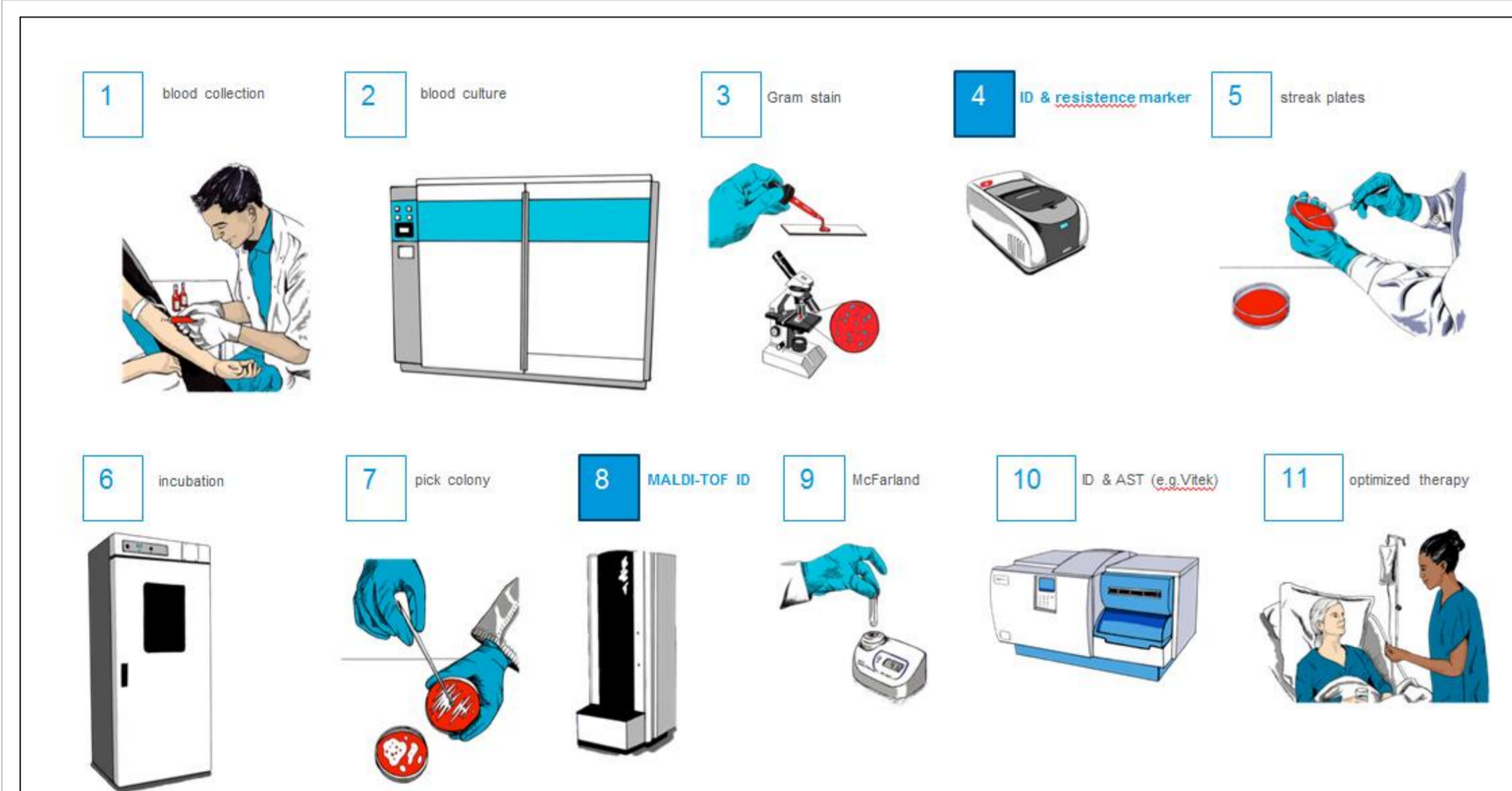
## Methods:

- Accelerate Pheno™ system is a new, fully automated, subculture-independent diagnostic method for both pathogen identification (ID) and antimicrobial susceptibility testing (AST) from positive blood cultures.
- ID/AST results were not reported to treating physicians as part of our internal evaluation process.

Gram-Negative	Antibiotic Susceptibility														
	Ampicillin-Sulbactam	Piperacillin-Tazobactam	Cefazolin	Cefepime	Ceftazidime	Ceftriaxone	Ertapenem	Meropenem	Amikacin	Gentamicin	Tobramycin	Ciprofloxacin	Minoxycycline	Acetaminophen	Colistin
<i>E. coli</i>	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•
<i>Klebsiella spp.</i>	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•
<i>Enterobacter spp.</i>	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•
<i>Proteus spp.</i>	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•
<i>Citrobacter spp.</i>	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•
<i>S. marcescens</i>	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•
<i>P. aeruginosa</i>	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•
<i>A. baumannii</i>	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•
<i>Candida albicans</i>	ID only														
<i>Candida glabrata</i>	ID only														

Gram-Positive	Antibiotic Susceptibility									
	Ampicillin	Ceftazidime	Doxycycline	Erythromycin	Trimethoprim-Sulfamethoxazole	Daptomycin	Linezolid	Vancomycin	MRSA (Cefoxitin)	MLSB (Erythromycin/Clotrimazole)
<i>S. aureus</i>	•	•	•	•	•	•	•	•	•	•
<i>S. lugdunensis</i>	•	•	•	•	•	•	•	•	•	•
<i>CoNS spp.</i>	•	•	•	•	•	•	•	•	•	•
<i>E. faecalis</i>	•	•	•	•	•	•	•	•	•	•
<i>E. faecium</i>	•	•	•	•	•	•	•	•	•	•
<i>S. pneumoniae</i>	ID only									
<i>S. agalactiae</i>	ID only									
<i>Streptococcus spp.</i>	ID only									



- positive blood cultures from critically ill patients with new onset of sepsis were tested using both conventional standard methods (FilmArray®, MALDI-TOF, VITEK® 2 system) (left panel) and the Accelerate Pheno™ system (right panel)
- Time-to-result was measured.

## Conclusion:

- Accelerate Pheno™ system significantly improved time-to-ID/AST when compared to standard methods.
- Due to short hands-on-time, subculture-independence & fast generation of results, this system represents a promising new diagnostic method for pathogen-adapted antibiotic treatment in selected patients
- ID/AST results would have led to a reduced time-to-treatment, if reported. System could thus serve as an innovative antibiotic stewardship (ABS) diagnostic tool.
- Accelerate Pheno™ system is not yet applicable for a high throughput of patient samples, preselection of critical patient specimens within a routine microbiology laboratory setting is needed.
- Microbiology laboratories should independently evaluate how this system fits into their workflow and their patient population, based on a risk stratification.

## Results:

Gram-positive pathogens	n	TP	FP	FN	TN (= 89-T)	Sensitivity (=TP/(TP+FN))	Specificity (=TN/(TN+FP))
<i>E. faecalis</i>	4	4	0	0	85	100%	100%
<i>E. faecium</i>	4	3	0	1	85	75%	100%
CNS	11	11	0	0	78	100%	100%
<i>S. aureus</i>	4	3	1	0	85	100%	98,8%
<i>Streptococcus spp.</i>	1	1	0	0	88	100%	100%
Total GP	24	22	1	1	421	95,7%	99,8%

## ID Performance for 89 evaluable organisms:

sensitivity: 92,2%, specificity: 99,8%

Antibiotic Agents Against Gram-positive pathogens	Count (EA/CA)	EA	CA
Ampicillin	7	100% (7/7)	100% (7/7)
Linezolid	14/15	100% (14/14)	100% (15/15)
Vancomycin	13/17	100% (13/13)	100% (17/17)
Doxycycline	0/6	N/A*	100% (6/6)
Daptomycin	6	83,3% (5/6)	100% (6/6)
Trimethoprim/Sulfamethoxazole	2	0% (0/2)	100% (2/2)
Methicillin-Resistance screen	7	N/A	100% (7/7)
MLSB screen	2	N/A	100% (2/2)

## AST Performance for 74 evaluable organisms:

- EA: 91,7%
- CA: 95,5%

## Overall AST Error Rate:

- minor error: 5,7% (27/471)
- major error: 1,5% (7/471)
- very major error: 0,6% (3/471)

Organism	Ø ID-Time AXDX	Ø AST-Time AXDX	Ø ID-Time SOC	Ø AST-Time SOC	Δ ID-Time	Δ AST-Time
<i>E. coli</i>	1,3	6,6	19,6	30,9	18,2	24,3
<i>P. aeruginosa</i>	1,4	6,6	7,0	31,0	5,6	24,4
<i>Klebsiella spp.</i>	1,4	6,6	23,2	31,5	21,9	24,9
<i>Proteus spp.</i>	1,3	6,6	23,3	32,1	22,0	25,5
<i>Enterobacter spp.</i>	1,4	6,6	17,2	33,3	15,8	26,7
<i>A. baumannii</i>	1,4	6,5	24,8	33,5	23,4	27,0
	1,37	6,58	19,18	32,05	17,82	25,47

Organism	Ø ID-Time AXDX	Ø AST-Time AXDX	Ø ID-Time SOC	Ø AST-Time SOC	Δ ID-Time	Δ AST-Time
<i>Ent. faecalis</i>	1,3	6,5	12,9	33,0	11,5	26,5
<i>Ent. faecium</i>	1,4	6,5	7,3	30,4	6,0	24,0
CNS	1,3	6,5	13,2	32,3	11,8	25,9
<i>S. aureus</i>	1,4	6,5	9,3	33,3	8,0	26,7
	1,35	6,50	10,68	32,25	9,33	25,78

Gram-negative pathogens	n	TP	FP	FN	TN (= 89-T)	Sensitivity (=TP/(TP+FN))	Specificity (=TN/(TN+FP))
<i>E. coli</i>	43	41	1	1	46	97,6%	97,9%
<i>P. aeruginosa</i>	3	3	0	0	86	100%	100%
<i>Klebsiella spp.</i>	6	6	0	0	83	100%	100%
<i>Proteus spp.</i>	4	3	0	1	85	75%	100%
<i>Enterobacter spp.</i>	3	3	0	0	86	100%	100%
<i>A. baumannii</i>	2	2	0	0	87	100%	100%
<i>Citrobacter spp.</i>	0	0	0	0	89	NA	100%
Total GN	61	58	1	2	473	96,7%	99,8%

Antibiotic Agents Against Gram-negative pathogens	Count (EA/CA)	EA	CA
Ampicillin/Sulbactam	43	81,4% (35/43)	93% (40/43)
Piperacillin/Tazobactam	49/50	91,8% (45/49)	86% (43/50)
Ceftazidime	51/52	92,2% (47/51)	90,4% (47/52)
Ceftriaxone	48	N/A*	97,9% (47/48)
Ertapenem	49	93,9% (46/49)	100% (49/49)
Meropenem	53/54	94,4% (50/53)	96,3% (52/54)
Gentamicin	51	96,1% (49/51)	96,1% (49/51)
Ciprofloxacin	53/54	94,3% (50/53)	94,4% (51/54)
Amikacin	2	50% (1/2)	100% (2/2)
Tobramycin	2	100% (2/2)	100% (2/2)
Aztreonam	2	50% (1/2)	100% (2/2)
Colistin	2	100% (2/2)	100% (2/2)

## average time to result reduction for GN:

- ID: 17,82 hours
- AST: 25,47 hours

## average time to result reduction for GP:

- ID: 9,33 hours
- AST: 25,78 hours

## average time to result reduction (GP+GN):

- ID: 14,42 hours
- AST: 25,59 hours

**definitions & abbreviations:** GN: Gram negative; GP: Gram positive; n: total number; TP: true positive; FP: false positive; FN: false negative; TN: true negative; AXDX: Accelerate Pheno™ system; EA: essential agreement: MIC result obtained with the AST device that is within plus or minus one doubling dilution step from the MIC value established with the reference method (ISO 20776-1); CA: categorical agreement: agreement of SIR results between a breakpoint test or an MIC test and the reference method (ISO 20776-1); error definitions: EA error: MIC discrepancy >1 dilution level; minor error: categorical discrepancy between S/I or R/I; major error: AXDX: R and SOC: S; very major error: AXDX: S and SOC: R

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