FAST MICROBIOLOGY

Applicazioni cliniche

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Ferrara, 16 giugno 2016
The rapid molecular diagnostics strategy

Especially considering multidrug-resistant (MDR) Gram-negative bacteria, the rapid and accurate detection of antibiotic resistance determinants offers the potential to transform clinical practice by:

1) informing early appropriate and targeted antibiotic therapy;
2) shortening the duration and narrowing the spectrum of activity of empirical antibiotic regimens, thus limiting the selection of antibiotic-resistant bacteria;
3) improving clinical outcomes;
4) streamlining development of new antimicrobials by quickly identifying patients infected with antibiotic-resistant bacteria and enriching participant enrollment in clinical trials
5) Improving surveillance and epidemiological studies of transmissible diseases
Rapid Molecular Detection of Tuberculosis and Rifampin Resistance

Catharina C. Boehme, M.D., Pamela Nabeta, M.D., Doris Hillemann, Ph.D., Mark P. Nicol, Ph.D., Shubhada Shenai, Ph.D., Fiorella Krapp, M.D., Jenny Allen, B.Tech., Rasim Tahirli, M.D., Robert Blakemore, B.S., Roxana Rustomjee, M.D., Ph.D., Ana Milovic, M.S., Martin Jones, Ph.D., Sean M. O’Brien, Ph.D., David H. Persing, M.D., Ph.D., Sabine Ruesch-Gerdes, M.D., Eduardo Gotuzzo, M.D., Camilla Rodrigues, M.D., David Alland, M.D., and Mark D. Perkins, M.D.
With a single test, Xpert MTB/RIF identified 98% of patients with smear-positive and culture-positive tuberculosis (including more than 70% of patients with smear-negative and culture positive disease) and correctly identified 98% of bacteria that were resistant to rifampin.

- Prompt access to appropriate treatment
- Shortening the duration of hospitalization
- Reducing the overall drug exposure
- Decentralization of molecular diagnosis, since it potentially can be used at the point of treatment
- Improved epidemiological studies
Fast and low-cost decentralized surveillance of transmission of tuberculosis based on strain-specific PCRs tailored from whole genome sequencing data: a pilot study

Making possible to reconcile the high resolution offered by Whole Genomic Sequencing assay with the speed and ease of implementation of simple PCR-based strategies, could realize the «perfect tool» to provide an accurate picture of the transmission dynamics of M tuberculosis.

An allele-specific PCR targeting strain-specific single nucleotide polymorphisms, (TRAP) identified from WGS gives a substantial change to track actively transmitted Mycobacterium tuberculosis strains.
Galactomannan and Computed Tomography-Based Preemptive Antifungal Therapy in Neutropenic Patients at High Risk for Invasive Fungal Infection: A Prospective Feasibility Study

Maertens J et al, Clin Infect Dis, 2005
Galactomannan and Computed Tomography-Based Preemptive Antifungal Therapy in Neutropenic Patients at High Risk for Invasive Fungal Infection: A Prospective Feasibility Study

Maertens J et al, Clin Infect Dis, 2005;41:1242-50

136 High-risk episodes

19 Nonfebrile episodes

1 Probable IA (alive)

117 febrile neutropenic episodes

82 Defervesence

30 Persistent fever

5 Nonevaluable

28 Relapse neutropenic fever

7 Probable IA (1 death/6 alive)

1 Proven IA (death)

1 Probable IA (alive)

11 Unexplained fever

17 Breakthrough infection

4 Proven IA (3 death/1 alive)

1 Probable IA (alive)

9 treatments/41 FUO

10 treatments/109 episodes not clinically suspected of IFI
Direct comparison of galactomannan performance in concurrent serum and bronchoalveolar lavage samples in immunocompromised patients at risk for invasive pulmonary aspergillosis

Boch T et al, Mycoses, 2016, 59, 80-85

**Table 3** Diagnostic performance of BAL GM and serum GM for proven/probable ($n = 26$) and no IPA ($n = 8$).

<table>
<thead>
<tr>
<th>Test method</th>
<th>Sensitivity, % ($n = 26$)</th>
<th>Specificity, % ($n = 8$)</th>
<th>PPV, %</th>
<th>NPV, %</th>
<th>DOR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BAL GM</td>
<td>85</td>
<td>88</td>
<td>96</td>
<td>64</td>
<td>38.5 (3.7–404.2)</td>
</tr>
<tr>
<td>Serum GM</td>
<td>23</td>
<td>88</td>
<td>88</td>
<td>26</td>
<td>2.1 (0.2–20.7)</td>
</tr>
</tbody>
</table>
β-D-glucan (BDG) is a cell wall constituent of Candida species and other fungi.

The sensitivity and specificity of serum BDG testing for diagnosing invasive candidiasis have ranged from 57% to 97% and 56% to 93%, respectively.

**IN THE PRESENT META-ANALYSIS, REGARDING 28 STUDIES, AVERAGE SENSITIVITY AND SPECIFICITY RESULT 78% AND 81%**

The cutoff value of BDG at 80 pg/mL had the best diagnostic accuracy.

Optimal results are achieved if 2 consecutive tests are positive.

The major uncertainties for BDG detection are specificity and false-positivity, particularly among high-risk populations.

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He S et al, J Microbiol Immunol Infection 2014
b-Glucan Antigenemia Anticipates Diagnosis of Blood Culture-Negative Intra-abdominal Candidiasis  

Tissot F et al, Am J Respir Crit Care Med 2013;188: 1100-1109

434 Patients:
- Abdominal Surgery / Acute Pancreatitis
- AND
- Surgical ICU Stay ≥ 72h

101 Eligible Patients (23%):
- Recurrent GI Tract Perforation / Anastomotic Leakage
- OR
- Acute Necrotizing Pancreatitis

12 Patients not Included (3%):
- Informed consent not obtained:
  - 7
- Transferred before inclusion:
  - 2
- Died before inclusion:
  - 3

89 Patients Included (20%):
- Not colonized by Candida (subgroup Ia):
  - 2
- Colonized by Candida and not receiving antifungals (subgroup II):
  - 40
- Colonized by Candida and receiving pre-emptive antifungals for suspected intra-abdominal candidiasis, IAC (subgroup III):
  - 18
- Documented intra-abdominal candidiasis, IAC (subgroup IV):
  - 29
b-Glucan Antigenemia Anticipates Diagnosis of Blood Culture-Negative Intra-abdominal Candidiasis

Tissot F et al, Am J Respir Crit Care Med 2013;188: 1100-1109

Patients with BG ≥80 pg/ml / Patients in Subgrou

Median BDG

COLONIZED 99 pg/ml (8-440)

IAC 254 pg/ml (46-8557)
β-D-glucan (BDG) : open questions.

THE BEST CUT OFF?
(need for different cut offs?)

SINGLE OF SERIAL DETERMINATIONS?

TO MAKE OR TO EXCLUDE DIAGNOSIS OF IC?

ALONE or INCLUDED IN A NEW SCORE?

THE PROBLEM OF THE TURNROUND
Antifungal stewardship – a proposal

Selection of surgical ICU patients at highest risk for IC

Start antifungal treatment

Early de-escalation or early discontinuation according with b-D-G results and clinical outcome
Discontinuation of empirical antifungal therapy in ICU patients using 1,3-b-D-glucan


Screened patients
N=2148

Entry criteria

Yes
N=85

Start anidulafungin

Median BDG value
33 pg/mL

BDG+BC

All negative
N=21

Median BDG value
255 pg/mL

Recurrent candidaemia
N=0

BDG positive
N=57

Candidaemia
N=7 (8.2%)

Relative risk: 16.9

median BDG value
515 pg/mL

No
N=2063

Stop anidulafungin
T2 Magnetic Resonance Assay for the Rapid Diagnosis of Candidemia in Whole Blood: A Clinical Trial

Mylonakis E et al, Clin Infect Dis 2015;60:892-9

T2Dx lyse the red blood cells, concentrates the pathogen cells and cellular debris, lyse the Candida cells by mechanical bead beating, amplifies Candida DNA using a thermostable polymerase and pan-Candida primers for the intervening transcribed spacer 2 region within the Candida ribosomal DNA operon, and finally, detects amplified product by amplicon-induced agglomeration of supermagnetic particles and T2MR measurement.

Blood specimens were collected from 1801 hospitalized patients who had a blood culture ordered for routine standard of care; 250 of them were manually supplemented with concentrations from <1 to 100 colony forming units/mL for 5 different Candida species overall specificity 99.4% (95% CI 99.1%-99.6%)
overall sensitivity 91.1% (95% CI, 86.9%-94.2%)

The mean time to species identification was ...

4.4 \pm 1.0\text{ hours} for T2MR and

129.9 \pm 26.3\text{ hours} for the blood cultures (P < .001)
T2Candida Provides Rapid and Accurate Species Identification in Pediatric Cases of Candidemia.  

Hamula CL et al, Am J Clin Pathol March 2016;0:1-4

<table>
<thead>
<tr>
<th>Blood Culture Result</th>
<th>Candida albicans/ Candida tropicalis</th>
<th>Candida parapsilosis</th>
<th>Candida krusei/ Candida glabrata</th>
<th>Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>C parapsilosis</td>
<td>0</td>
<td>7</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>C albicans</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>C glabrata</td>
<td>0</td>
<td>0</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>C tropicalis</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Negative</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>9</td>
</tr>
</tbody>
</table>

The T2Candida panel provided the appropriate result for each specimen compared with blood culture-based species identification and correctly identified 15 positive and nine negative results in 3 to 5 hours.

Huang AM et al Clin Infect Dis 2013; 57: 1237-45

A pre-post quasi-experimental study was conducted to analyze the impact of MALDI-TOF with AST intervention in patients with bloodstream infections. The AST provided evidence based antibiotic recommendations after receiving real-time notification following blood culture Gram stain, organism identification, and antimicrobial susceptibilities. Outcomes were compared to a historic control group.

A total of 501 patients with bacteremia or candidemia were included in the final analysis: 245 patients in the intervention group and 256 patients in the pre-intervention group.
<table>
<thead>
<tr>
<th>Intervention</th>
<th>Gram Stain</th>
<th>Organism Identification</th>
<th>Antimicrobial Susceptibility</th>
<th>Total (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Narrowed coverage to target the isolated organism</td>
<td>2</td>
<td>22</td>
<td>48</td>
<td>72 (34.3)</td>
</tr>
<tr>
<td>Discontinued therapy targeting organisms not isolated</td>
<td>5</td>
<td>44</td>
<td>19</td>
<td>68 (32.4)</td>
</tr>
<tr>
<td>Initiated or broadened coverage</td>
<td>39</td>
<td>5</td>
<td>9</td>
<td>53 (25.2)</td>
</tr>
<tr>
<td>Other</td>
<td>8</td>
<td>4</td>
<td>5</td>
<td>17 (8.1)</td>
</tr>
<tr>
<td>Total (%)</td>
<td>54 (25.7)</td>
<td>75 (35.7)</td>
<td>81 (38.6)</td>
<td>210 (100)</td>
</tr>
<tr>
<td>Interventions accepted (%)</td>
<td>49 (90.7)</td>
<td>62 (82.7)</td>
<td>78 (96.3)</td>
<td>189 (90.0)</td>
</tr>
</tbody>
</table>

*Huang AM et al Clin Infect Dis 2013; 57: 1237-45*

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Preintervention (n = 256)</th>
<th>Intervention (n = 245)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinical outcomes</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>30-day all-cause mortality</td>
<td>52 (20.3)</td>
<td>31 (12.7)</td>
<td>.021</td>
</tr>
<tr>
<td>Time to microbiological clearance, d</td>
<td>3.3 ± 4.8</td>
<td>3.3 ± 5.7</td>
<td>.928</td>
</tr>
<tr>
<td>Length of hospitalization, d&lt;sup&gt;a&lt;/sup&gt;</td>
<td>14.2 ± 20.6</td>
<td>11.4 ± 12.9</td>
<td>.066</td>
</tr>
<tr>
<td>Length of ICU stay, d&lt;sup&gt;a&lt;/sup&gt;</td>
<td>14.9 ± 24.2</td>
<td>8.3 ± 9.0</td>
<td>.014</td>
</tr>
<tr>
<td>Recurrence of same BSI</td>
<td>15 (5.9)</td>
<td>5 (2.0)</td>
<td>.038</td>
</tr>
<tr>
<td>30-day readmission with same BSI</td>
<td>9 (3.5)</td>
<td>4 (1.6)</td>
<td>.262</td>
</tr>
<tr>
<td><strong>Treatment-related outcomes</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time to effective therapy, h</td>
<td>30.1 ± 67.7</td>
<td>20.4 ± 20.7</td>
<td>.021</td>
</tr>
<tr>
<td>Time to optimal therapy, h</td>
<td>90.3 ± 75.4</td>
<td>47.3 ± 121.5</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

<sup>a</sup> ICU: intensive care unit; BSI: bloodstream infection

**Outcomes**
<table>
<thead>
<tr>
<th>Study</th>
<th>Organisms</th>
<th>Population</th>
<th>Antibiotic use</th>
<th>Patient outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Perez et al APLM 2013</td>
<td>Gram-neg</td>
<td>201 pts with BSI (100 pre-intervention, 101 intervention)</td>
<td>Time to antibiotic optimization 46-h reduction (P = .004); Reduced time to active treatment</td>
<td>LOS (11.9 d vs 9.3 d; P = .01)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Hospital costs per pt (P = .009)</td>
<td></td>
</tr>
<tr>
<td>Huang et al CID 2013</td>
<td>Aerobic</td>
<td>501 pts with BSI (256 pre-intervention, 245 intervention)</td>
<td>Time to effective therapy of 30.1 vs 20.4 h (P = .021)</td>
<td>2.8-day decrease in mean LOS (P = .07)</td>
</tr>
<tr>
<td></td>
<td>Gram-pos,</td>
<td></td>
<td>Optimal antibiotic therapy (90.3 vs 47.3 h; P &lt; .001)</td>
<td><strong>Reduced mortality (20.3% vs 14.5%; P = .02)</strong></td>
</tr>
<tr>
<td></td>
<td>Gram-neg and yeast</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clerc et al CID 2013</td>
<td>Gram-neg</td>
<td>202 pts with BSI</td>
<td>Greater percentage of patients with ID consultation compared with Gram stain results alone (35.1% vs 20.8%; P = NR)</td>
<td>NR</td>
</tr>
<tr>
<td>Wenzler et al ECCMID 2014</td>
<td>A. baumannii</td>
<td>109 pts with BSI and/or pneumonia (66 pre-intervention, 53 intervention)</td>
<td>Time to effective therapy (77.7 h vs 36.6 h; P &lt; .0001)</td>
<td>Increase in clinical cure (15% vs 34%; P = .016)</td>
</tr>
<tr>
<td>Perez et al J Infect 2014</td>
<td>XDR Gram-neg</td>
<td>265 pts with BSI (112 pre-intervention, 153 intervention)</td>
<td>Time to optimal antibiotic therapy (80.9 h vs 23 h; P &lt; .001)</td>
<td><strong>Reduced mortality (21% vs 8.9%; P = .01)</strong></td>
</tr>
<tr>
<td>Carreno et al ICAAC 2014</td>
<td>Gram-neg</td>
<td>104 pts with BSI (78 pre and 26 post test)</td>
<td>NR</td>
<td>Time to sepsis resolution 4 vs. 3 days (P = 0.08)</td>
</tr>
</tbody>
</table>


single-center, quasi-experimental study. Adult patients with a CoNS blood culture identified via MALDI-TOF over a 3-month period were compared to a historical control group with CoNS identified by conventional methods. Patients were divided into 4 categories:
Pts with CoNS BSI before/after implementation of MADLI-TOF plus AST intervention
Pts with CoNS contamination before/after MADLI-TOF plus AST intervention

During the preintervention study period, prescribers were immediately notified of positive Gram stain results from blood cultures. The AST did not intervene for positive bacterial cultures in real time but AST reviewed daily reports from Monday through Friday for all patients receiving restricted antimicrobials and recommended therapy changes on the basis of institutional guidelines and clinical judgment.

All stewardship activities, except for the addition of real-time alerts for positive blood cultures during the intervention period, remained unchanged during the study time frame.


- **Gram positive cocci in clusters:**
  - Initiate broad spectrum gram-positive antimicrobial therapy (vancomycin, alternative: daptomycin). Draw repeat blood cultures prior to initiating antimicrobials if contamination suspected.

**If repeat cultures positive:**
- Continue gram-positive antimicrobial.
- Discontinue unnecessary gram-negative coverage.
- *consider antimicrobial de-escalation if isolate is susceptible and patient not critically ill*

**If repeat cultures negative + hemodynamically stable or no source identified:**
- Discontinue gram-positive antimicrobial.
- Discontinue unnecessary gram-negative coverage.

**If repeat cultures negative + [hemodynamically unstable or source identified]:**
- Continue gram-positive antimicrobial, consider obtaining ID consult. Discontinue unnecessary gram-negative coverage.

**OUTCOMES - CoNS bacteremia**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Preintervention group (n = 46)</th>
<th>AST intervention group (n = 32)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time to organism identification&lt;sup&gt;a&lt;/sup&gt; (h)</td>
<td>83.4 ± 29.5</td>
<td>57.0 ± 32.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Time to effective therapy&lt;sup&gt;a&lt;/sup&gt; (h)</td>
<td>37.7 ± 40.1</td>
<td>23.0 ± 10.7</td>
<td>0.064</td>
</tr>
<tr>
<td>Time to optimal therapy&lt;sup&gt;a&lt;/sup&gt; (h)</td>
<td>58.7 ± 56.4</td>
<td>34.4 ± 29.9</td>
<td>0.030</td>
</tr>
<tr>
<td>No. (%) of patients with 30-day all-cause mortality</td>
<td>10 (21.7)</td>
<td>1 (3.1)</td>
<td>0.023</td>
</tr>
<tr>
<td>Length of hospitalization&lt;sup&gt;a,b&lt;/sup&gt; (days)</td>
<td>14 ± 22</td>
<td>15 ± 14</td>
<td>0.954</td>
</tr>
<tr>
<td>Length of ICU stay&lt;sup&gt;a,b&lt;/sup&gt; (days)</td>
<td>28 ± 33</td>
<td>11 ± 11</td>
<td>0.188</td>
</tr>
<tr>
<td>No. (%) of patients with recurrent bacteremia</td>
<td>6 (13.0)</td>
<td>0 (0.0)</td>
<td>0.076</td>
</tr>
</tbody>
</table>


### OUTCOMES - CoNS contamination

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Preintervention group (n = 83)</th>
<th>AST intervention group (n = 85)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of CoNS antibiotic therapy&lt;sup&gt;a&lt;/sup&gt; (days)</td>
<td>4.4 ± 4.2</td>
<td>3.0 ± 1.6</td>
<td>0.015</td>
</tr>
<tr>
<td>Vancomycin utilization&lt;sup&gt;a&lt;/sup&gt; (g)</td>
<td>4.8 ± 6.3</td>
<td>3.0 ± 3.9</td>
<td>0.038</td>
</tr>
<tr>
<td>Daptomycin utilization&lt;sup&gt;a&lt;/sup&gt; (g)</td>
<td>2.88</td>
<td>0</td>
<td>0.243</td>
</tr>
<tr>
<td>No. of vancomycin serum assays obtained&lt;sup&gt;a&lt;/sup&gt;</td>
<td>2.0 ± 2.2</td>
<td>0.9 ± 1.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>No. (%) of patients with 30-day all-cause mortality</td>
<td>9 (10.8)</td>
<td>10 (11.8)</td>
<td>&gt;0.99</td>
</tr>
<tr>
<td>Length of hospitalization&lt;sup&gt;a&lt;/sup&gt; (days)</td>
<td>14.6 ± 22.9</td>
<td>15.8 ± 18.6</td>
<td>0.7</td>
</tr>
<tr>
<td>No. (%) of patients with recurrent bacteremia</td>
<td>3 (3.6)</td>
<td>2 (2.4)</td>
<td>0.68</td>
</tr>
</tbody>
</table>
Rapid Testing Using the Verigene Gram-Negative Blood Culture Nucleic Acid Test in Combination with Antimicrobial Stewardship Intervention against Gram-Negative Bacteremia.

Bork JT et al Antimicrob Agents Chemother. 2015;59:1588-95

Multiplex, automated molecular diagnostic test for identification of eight Gram-neg organisms and resistance markers from blood culture with a turnaround time of approximately 2 h.

A theoretical evaluation of time to effective and optimal antibiotic was performed, comparing actual antibiotic administration times from chart review ("control") to theoretical administration times based on BC-GN reporting and antimicrobial stewardship team review ("intervention").

132 first episodes of Gram- BSI were included
59% ICU pts

39% primary
26% urine
10% lung
9% CVC related
8% intra-abdominal

Correct identification by VERIGENE 95.6%
Sensitivity 97.1%
Specificity 99.5%

TIME to EFFECTIVE ATB 3.7 h earlier  p < .001
Allowing 12 h for ATB changes to be made based on Verigene

TIME to OPTIMAL ATB 18.3 h earlier  p < .001
The FilmArray PCR-based device integrates sample preparation, amplification, detection and analysis into one simple system that requires 2 min of hands-on time and has a total run time of about 1 hour.
FilmArray: Complete and Certified Offer

4 CE-IVD / FDA cleared panels
83 pathogens identification

Respiratory Panel
- 20 targets
- 3 bacteria
- 17 viruses

Blood Culture Identification Panel
- 27 targets
- 19 bacteria
- 5 yeast
- 3 resistance genes

Gastrointestinal Panel
- 22 targets
- 13 bacteria
- 5 viruses
- 4 parasites

Meningitis Encephalitis Panel
- 14 targets
- 6 bacteria
- 7 viruses
- 1 fungus
# FilmArray: Blood Culture Identification Panel

**27 pathogens**

<table>
<thead>
<tr>
<th>Gram + Bacteria:</th>
<th>Gram - Bacteria:</th>
<th>Fungi:</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Enterococcus spp.</em></td>
<td><em>A. baumannii</em></td>
<td><em>C. albicans</em></td>
</tr>
<tr>
<td><em>L. monocytogenes</em></td>
<td><em>Enterobacteriaceae</em></td>
<td><em>C. glabrata</em></td>
</tr>
<tr>
<td><em>Staphylococcus</em></td>
<td><em>Enterobacter cloacae</em></td>
<td><em>C. krusei</em></td>
</tr>
<tr>
<td><em>S. aureus</em></td>
<td><em>Complex</em></td>
<td><em>C. parapsilosis</em></td>
</tr>
<tr>
<td><em>Streptococcus spp.</em></td>
<td><em>E. coli</em></td>
<td><em>C. tropicalis</em></td>
</tr>
<tr>
<td><em>S. agalactiae (Group B)</em></td>
<td><em>H. influenzae</em></td>
<td></td>
</tr>
<tr>
<td><em>S. pyogenes (Group A)</em></td>
<td><em>K. oxytoca</em></td>
<td></td>
</tr>
<tr>
<td><em>S. pneumoniae</em></td>
<td><em>K. pneumoniae</em></td>
<td></td>
</tr>
</tbody>
</table>

**Antibiotic Resistance:**
- mecA
- Van A/B
- KPC

**Sample:** Positive Blood culture
Randomized Trial of Rapid Multiplex Polymerase Chain Reaction-Based Blood Culture Identification and Susceptibility Testing.

- Median time from Gram stain result to organism identification was shorter in both intervention groups (both 1.3 hours) versus the control group (22 hours) (P < .0001)

- Time from GS result to appropriate antimicrobial de-escalation and escalation was significantly shorter in INT 2 and INT versus control group respectively