Syndromic Testing for Infectious Diseases
Part 4: Multiplex Panels for Positive Blood Culture Bottles

Presenter:
Robin Patel, M.D.
Consultant, Divisions of Infectious Diseases and Clinical Microbiology, Chair, Division of Clinical Microbiology and the Elizabeth P. and Robert E. Allen Professorship in Individualized Medicine

Department of Laboratory Medicine and Pathology at Mayo Clinic, Rochester, Minnesota
Utilization Message

- As you view this presentation, consider the following important points regarding testing:
  - How is the test going to be used in your practice?
  - When should the test be used?
  - How will results impact patient management?

Disclosures

- Board Member: ASM
- Grant Recipient: CD Diagnostics, BioFire, Curetis, Merck, Hutchison Biofilm Medical Solutions, Accelerate Diagnostics, Allergan, The Medicines Company
- Consultant: Curetis, monies paid to Mayo Clinic
- Patent on Bordetella pertussis/parapertussis PCR issued, patent on a device/method for sonication with royalties paid to Mayo Clinic, patent on an anti-biofilm substance issued
- DSMB: Actelion, money paid to Mayo Clinic
- Editor's stipends: ASM, IDSA
- Honoraria: NBME, Up-to-Date, Infectious Diseases Board Review Course
Introduction

• Bacteremia – morbidity and mortality
• Septic shock
  • Delays in administration of effective antimicrobial therapy associated with increased mortality
• Treatment may be compromised by antibacterial resistance

Conventional Blood Culture Practices
FDA-Approved Multiplex Panels for Detection of Select Organisms and Resistance Genes in Positive Blood Cultures

<table>
<thead>
<tr>
<th></th>
<th>FILMARRAY®</th>
<th>VERIGENE</th>
<th>TOTAL NUMBER OF TARGETS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>GRAM-POSITIVE</strong></td>
<td></td>
<td></td>
<td>27</td>
</tr>
<tr>
<td>BACTERIA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>GRAM-NEGATIVE</strong></td>
<td></td>
<td></td>
<td>15</td>
</tr>
<tr>
<td>BACTERIA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>14</td>
</tr>
<tr>
<td>YEASTS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RESISTANCE GENES</td>
<td></td>
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<td></td>
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</tbody>
</table>

**TIME TO RESULT**

- 1 HOUR
- ~2.5 HOURS
- ~2 HOURS

FilmArray® Blood Culture Identification Panel (BioFire)
Randomized Controlled Clinical Trial
Mayo Clinic 2013-2014

Patients with positive blood cultures
Stratified randomization (age, ICU, transplant service)

- CONTROL
  - Gram stain called to service
  - Standard subculture and susceptibility (1-3 d)

- BCID ALONE
  - Gram stain called to service
  - Standard subculture and susceptibility (1-3 d)
  - Rapid test plus lab call with comments (1 h)

- BCID/STEWARDSHIP
  - Gram stain called to service
  - Standard subculture and susceptibility (1-3 d)
  - Rapid test plus lab call with comments (1 h)
  - ID MD/pharmacist call with specific treatment recommendations

Supported by the National Institute of Allergy and Infectious Diseases of the National Institutes of Health under Award Number UM1AI104681 (Antibacterial Resistance Leadership Group)
### Clinical Outcomes

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Control (n=207)</th>
<th>Rapid Test (n=198)</th>
<th>Rapid Test + Stewardship (n=212)</th>
<th>P –value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Length of stay (days)</td>
<td>8 (5,15)</td>
<td>8 (5,15)</td>
<td>8 (5,16)</td>
<td>0.60</td>
</tr>
<tr>
<td>30-day mortality</td>
<td>22 (10.6%)</td>
<td>20 (10.1%)</td>
<td>18 (8.5%)</td>
<td>0.74</td>
</tr>
<tr>
<td>30-day readmission w/same organism</td>
<td>6 (2.9%)</td>
<td>6 (3%)</td>
<td>8 (3.8%)</td>
<td>0.88</td>
</tr>
<tr>
<td>Toxicity/adverse drug reaction</td>
<td>3 (1.4%)</td>
<td>3 (1.5%)</td>
<td>2 (0.9%)</td>
<td>0.82</td>
</tr>
<tr>
<td>Blood culture clearance in 3d</td>
<td>147 (71%)</td>
<td>131 (66.2%)</td>
<td>146 (68.9%)</td>
<td>0.79</td>
</tr>
<tr>
<td>C. difficile/Drug-resistant organism within 30d</td>
<td>15 (7.2%)</td>
<td>16 (8.1%)</td>
<td>21 (9.9%)</td>
<td>0.62</td>
</tr>
</tbody>
</table>

*VRE, MRSA, extended-spectrum cephalosporin resistant Enterobacteriaceae, Pseudomonas aeruginosa and Acinetobacter species resistant to ≥3 antibiotic classes

### Comparison of Time To Identification, Susceptibility Results, and Antibiotic Modifications

<table>
<thead>
<tr>
<th>Timeline, hours (h)</th>
<th>0</th>
<th>12</th>
<th>24</th>
<th>36</th>
<th>48</th>
<th>60</th>
<th>72</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control (n=169)</td>
<td></td>
<td>△</td>
<td>△</td>
<td>△</td>
<td>△</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rapid test (n=147)</td>
<td>△</td>
<td>△</td>
<td>△</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rapid test + Stewardship (n=165)</td>
<td>△</td>
<td>△</td>
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</tbody>
</table>

- **Organism identification**
- **Phenotypic antimicrobial susceptibility report**
- **De-escalation**
- **Escalation**

*Significant vs. control; †Significant vs. control and rapid multiplex PCR alone
Limitations

- Cost (largely “add-on” tests)
- For maximal benefit, should be performed 24/7
- Does not cover all causes of bloodstream infection
- May not identify all pathogens in mixed infections
- False-positive results
- Narrow spectrum of genes associated with resistance in Gram-negative bacilli (especially BCID)

Advantages

- Minimal hands-on time, highly automated
- Rapid turnaround time
- To enable rapid escalation or de-escalation of antimicrobial therapy, results should be reported to providers as rapidly and directly as possible, and ideally communicated to an expert in antimicrobial stewardship who can work with providers to optimize therapy
References


Questions or requests…
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or call Mayo Laboratory Inquiry at 800-533-1710