The Role of POCT in Management of Infectious Disease in the Critical Care Setting

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Learning Objectives

• Discuss the use of POC lactate in the management of sepsis
• Discuss the clinical impact of POCT Molecular Influenza assays and the reduction in duration in use of oseltamivir
• Discuss the use of near POCT molecular meningitis assays
Financial Disclosures

- Consultant
  - Nanosphere
  - ThermoFisher Scientific
  - LabCorp
  - iCubate
  - Copan Diagnostics
  - BD Diagnostics
  - GeneWeave
  - Affinity Biosciences
- Board Member
  - Evogen
- Research Grants
  - Meridian, Quidel, IMDx, Cepheid, BD, bioMérieux, Bruker Daltonics, Nanosphere, Seegene, Life Technologies, Prodesse, Great Basin Corp, iCubate, Biohelix, BioRad, Alere, Hardy Diagnostics, GenMark, Accelerate, BioFire, Copan Diagnostics

- Will discuss indications/products that are not FDA approved
Outline

• ID Tests most Important to Critical Care
• Needs of POCT in the Critical Care Setting
• The Case for Influenza
• POC in the Management of Sepsis
• The Future of POCT in the ICU
Infectious Diseases Tests Critical to Critical Care

- Sepsis Management
  - Blood culture
  - Gram Stain
  - Procalcitonin
  - Lactate
  - Molecular Pathogen Detection

- Meningitis
  - CSF Gram Stain
  - Molecular Pathogen Detection

- HIV Screening

- Hospital-Acquired Infections
  - *C. difficile*
  - MRSA/MSSA?
  - CRE

- Pneumonia/Respiratory
  - Gram Stain
  - Molecular Pathogen Detection
  - Molecular Resistance Detection

- Infections of the Immunocompromised
Goals of Point-of-Care

• Improve patient outcomes
• Improve patient satisfaction
  – Give the patient a diagnosis not the “best-guess”
• Reduce cost of providing care
  – Increased attention to institutional/system healthcare value scores
• Decrease turnaround
Antibiotic use in patients by detected aetiology from a study of hospitalised adults with acute respiratory illness.
Needs from Point-of-Care Testing in the ICU

• Results need to be available in 15-20 minutes or less to maintain patient flow
• Test performance should be independent of operator
  – Both traditional and non-traditional operators should be able to perform
  – Can clinic staffing meet the needs with large seasonal shifts in volume?
• Need strong evidence of effectiveness
The Case for Influenza
Needs from Point-of-Care Testing

• Need to optimize sensitivity and specificity
  – “The overuse of antibiotics for the treatment of outpatients is primarily due to the fact that in adults respiratory virus testing is either not performed or generally limited to rapid antigen direct tests (RADTs) for influenza. (Ginocchio, CID, 2011)”
  – Rapid Influenza tests have highly variable sensitivities (10%–75%) and specificities (50%–100%) depending on the viral target, age of the patient, sample collection, and duration of symptoms prior to testing (Ginocchio, JCV, 2009)
Molecular and non-Molecular Influenza tests in the ICU

- Significant differences in sensitivity
  - 17-80% reported sensitivity of RIDTs
  - 25-100% reported sensitivity in molecular POCT assays
    - Highly assay dependent
    - Requires balance of TAT and sensitivity
      - More amplification = greater TAT
- TAT generally similar
- Cost of molecular greater than RIDT
  - Molecular systems may also require capital purchase of equipment
- Guidelines generally allow molecular POCT replacement of lab-based testing
  - Confirmation recommended for RIDT – Treat high risk (including all critical care) patients while awaiting confirmation
Performance of molecular POCT, lab-based NAT, and antigen-based POCT

The Impact of Rapid PCR

Season 1: Standard Flu PCR

Season 2: Rapid Flu PCR

Number of days of oseltamivir

Respiratory Tract Infections: Diagnostic Challenge

• The Problem
  • Respiratory tract most common site of infection
  • Symptoms alone are not sufficient for clinicians to determine optimal patient management
    o True infection? Bacterial? Viral?
  • Wide array of known respiratory pathogens
  • Flu/RSV remain most common pathogens ordered/detected
  • Other pathogens requested:
    o Human Metapnuemovirus, Parainfluenza, Adenovirus, Rhinovirus, B. pertussis
Respiratory Tract Infections: Diagnostic Challenge

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We Practice What We Teach
Respiratory Tract Infections: Diagnostic Challenge

• The Problem
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    o True infection? Bacterial? Viral?
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### The Future of Respiratory Testing

<table>
<thead>
<tr>
<th>Virus</th>
<th>No. of true-positive specimens (<em>n</em> = 300 specimens tested)</th>
<th>% Sensitivity (95% CI) of:</th>
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<tbody>
<tr>
<td></td>
<td>FilmArray RP</td>
<td>eSensor RVP</td>
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<tr>
<td>AdV</td>
<td>35</td>
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<tr>
<td></td>
<td>57.1 (40.8, 72.0)</td>
<td>100 (88.2, 100)</td>
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<tr>
<td>Influenza virus</td>
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<tr>
<td>A</td>
<td>30</td>
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<td>86.2 (68.8, 95.1)</td>
<td>100 (86.5, 100)</td>
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<td>A H1/09</td>
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<td>73.3 (47.6, 89.5)</td>
<td>100 (77.3, 100)</td>
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<td>A H3</td>
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<td>100 (74.9, 100)</td>
<td>100 (74.9, 100)</td>
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<td>B</td>
<td>22</td>
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<td>77.3 (56.2, 90.3)</td>
<td>100 (82.5, 100)</td>
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<tr>
<td>MPV</td>
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<td>96.2 (79.6, 99.9)</td>
<td>100 (84.8, 100)</td>
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<td>100 (74.9, 100)</td>
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<td>92.3 (64.6, 99.9)</td>
<td>100 (73.4, 100)</td>
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<td>86.4 (65.8, 96.1)</td>
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<td>RhV/EV</td>
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<td>83.7 (69.7, 92.2)</td>
<td>90.7 (77.8, 96.9)</td>
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</table>

Popowitch, et al. JCM 2013

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We Practice What We Teach
POC in the Management of Sepsis
Early Antibiotics Improves Survival in Septic Shock
Need for Rapid Results: Patient Outcomes

- Up to 40% of bacteremia patients receive inadequate initial antibiotic treatment.\(^1\)

- Each hour that appropriate antimicrobial treatment is delayed increases a patient’s mortality rate 7.6%.\(^2\)

- Delaying appropriate treatment up to 45 hours is an independent predictor of infection-related mortality in patients with \textit{S. aureus} bacteremia.\(^3\)
  - Typical organism identification and susceptibility methods require 24-72 hours.

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Current Blood Culture Workflow

- Bottle culture
- Gram stain
- Culture positive
- Pathogen group
- Samples plated for sub-culturing
- Pathogen ID
- Pathogen resistance

Workflow with Rapid Tests

- Bottle culture
- Gram stain
- Culture positive
- Pathogen group
- Rapid - Test
- Pathogen ID and resistance

Blood drawn in ER, ICU, hospital floors

We Practice What We Teach

We Practice What We Teach
Lactate for Sepsis

• Guidelines recommend early measurement of lactate levels in order to identify patients with tissue hypoperfusion who are at the greatest risk of morbidity and mortality, especially in patients with cryptic shock in which hypotension is not yet apparent.

• A major limitation with reliance on early lactate measurements is the delays associated with central laboratory testing.
  – Further, limited by individual patients physiology for monitoring and using as a measure for response to resuscitation.
Specimen Matters

Fig. 3. Scatter diagram and regression line between arterial blood lactate (ABL POC) vs venous blood lactate (VBL POC) concentrations. All measurements are made with a POC method on microsamples of whole blood.

## POC Lactate Outcomes

### Table 2.

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Before</th>
<th>After</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality</td>
<td>15 (19%)</td>
<td>5 (6%)</td>
<td>0.02</td>
</tr>
<tr>
<td>Time from arrival to SOC result, min.</td>
<td>122 (82-149)</td>
<td>71 (53-101)*</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Time from arrival to POC result (after group only), min.</td>
<td>-</td>
<td>34 (26-55)</td>
<td>-</td>
</tr>
<tr>
<td>Time from order to test SOC results, min.</td>
<td>71 (53-91)</td>
<td>38 (26-53)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Time from order to POC test results (after group only), min.</td>
<td>3 (2-3)</td>
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</tr>
<tr>
<td>Time to IV fluids, min.</td>
<td>71 (42-110)</td>
<td>55 (34-83)</td>
<td>0.03</td>
</tr>
<tr>
<td>Time to antibiotic order, min.</td>
<td>62 (26-114)</td>
<td>69 (34-133)</td>
<td>0.27</td>
</tr>
<tr>
<td>Time to antibiotics, min.</td>
<td>97 (55-160)</td>
<td>89 (63-182)</td>
<td>0.59</td>
</tr>
<tr>
<td>Total ED LOS, min</td>
<td>326 (249-436)</td>
<td>352 (246-457)</td>
<td>0.50</td>
</tr>
<tr>
<td>ICU admits, No. (%)</td>
<td>41 (51%)</td>
<td>26 (33%)</td>
<td>0.02</td>
</tr>
<tr>
<td>ICU length of stay, days</td>
<td>4 (2-6)</td>
<td>3 (2-6)</td>
<td>0.90</td>
</tr>
<tr>
<td>Hospital length of stay**, days</td>
<td>8 (4-13)</td>
<td>7 (3-13)</td>
<td>0.27</td>
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</table>

After group: Time to POC vs. time to SOC (values above): P < 0.001.

Time to SOC, retrospective vs. prospective (see values above): P < 0.001.

* All patients in the prospective arm receiving a POC lactate test result also had their serum lactate levels measured in the central laboratory. The purpose of the central laboratory testing was to assess the performance of the POC lactate assay compared with the standard of care (SOC). It is important to note that treatment was initiated based on the POC result; it was not delayed or contingent on the value or the availability of the central lab serum lactate result.

** excludes deaths.
The Future of POC for Infectious Diseases
Future Trends

- Syndromic panels will likely be POC-usable
  - Meningitis Panel
  - Respiratory Virus Panel
  - Bacterial Pneumonia Panel
  - STI Panel

- Need to balance the needs of POC without turning the ICU into a laboratory
  - Providers need to provide care to patients, not be laboratorians
    - The lab needs to meet the needs of the clinician
    - May mean diversity of testing locations
Future Trends

• Continued expansion of molecular POC tests
  – *C. difficile* and Norovirus
    • Specimen will present significant challenges to POC testing
  – Respiratory Pathogens
    • Outcomes research will drive utilization
    • Expect up to 35% of lab volumes to move to POC

• HIV
  – Next generation assays will demonstrate improved specificity compared to 4\textsuperscript{th}/5\textsuperscript{th} generation lab assays
Conclusions

• Outcomes data demonstrate increase in appropriate antibiotic regimen when rapid testing is provided.

• POC Molecular assays have the potential to eliminate the need for confirmatory testing and address the poor sensitivity of rapid tests of the past.