The Point-of-Care Ecosystem: Building a Friendly Diagnostic Environment

Disclosures: Advisory Board member for Roche Diagnostics (Non-cardiac immunoassays) and for Radiometer. StatStrip Lactate meters donated by Nova Biomedical

Nam K. Tran, PhD, FACB, Associate Clinical Professor
Director of Chemistry, Toxicology, POCT, and SARC
Co-Director of the Pathology Biorepository
Learning Objectives

• Identify elements of a point-of-care ecosystem and its role in healthcare.

• Describe case examples of good versus bad POC ecosystems and how they impact patient care.

• Discuss the future of POC ecosystem, as well as anticipated challenges and directions.
ec·o·sys·tem
/ˈɛkəˌsɪstəm/

noun ECOLOGY

a biological community of interacting organisms and their physical environment.

• (in general use) a complex network or interconnected system.

"Silicon Valley's entrepreneurial ecosystem"
Smart Phones and Smart Watches
Smart Phones, Smart Watches, Tablets and Laptops, and more!
Point-of-Care Testing

Examples:
- Disposable
- Handheld
- Portable
- Transportable
- Benchtop
- Monitoring
Point-of-Care Testing

Examples:
- Disposable
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- Smart devices
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Point-of-Care Testing

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• Handheld
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• Transportable
• Benchtop
• Monitoring
• Smart devices

Too many platforms and too many manufacturers!
Barriers to the Diagnostic Ecosystem
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Pre-existing User Bias

• “POCT is faster therefore it must be better”

• “Everyone uses this device, therefore it must be better”

• “Its just [analyte], what’s the big deal?”
Barriers to the Diagnostic Ecosystem

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• “We got a good deal since it was lumped into another reagent contract.”
• “How inaccurate or imprecise could it be?”
Barriers to the Diagnostic Ecosystem

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**Analytical Performance**
- “Its FDA approved, so therefore its acceptable.”
- “A bias of [insert number] is not clinically significant”
- ”Its POCT, accuracy is a trade off for portability”.
Barriers to the Diagnostic Ecosystem
Barriers to the Diagnostic Ecosystem

Not all Solutions are Wise Solutions
- Finding the cheapest platforms
- No POCT!
- Just let people do what they want
- Bring in rogue devices!
- Bigger challenges may lie ahead!
Barriers to the Diagnostic Ecosystem

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Information Technology
- Too expensive to connect devices
- IT says no
- Lets get connectivity later
Barriers to the Diagnostic Ecosystem

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Connectivity Counts!
Overview of POCT Connectivity

• Recognition that “modern pathology” requires dissemination of laboratory services to be part “networked services”.

• POCT is being used increasingly in hospitals, clinics, primary care, and home settings.

• “Knowing now matters”, but results need to appear at the right time right place, for the right person(s).

• Connectivity solutions are now critical for transmitting/receiving results, maintaining compliance, and enable monitoring of patient data trends.
Connecting Devices are Not New

“Network Centric Warfare”, United States military doctrine since the early 1990’s and proven in Desert Storm.
What we think it looks like…
Current one-way diagnostics results output.

What POCT connectivity probably looks like…
POCT CONNECTIVITY AT UC DAVIS (2015)
POCT CONNECTIVITY AT UC DAVIS (2015)
POCT CONNECTIVITY AT UC DAVIS (2015)

EMR

POCT Middleware

CLINIC#3

CLINIC#2

CLINIC#1

HOSPITAL
POCT CONNECTIVITY AT UC DAVIS (2015)
POCT Connectivity Challenges

• Significant number of POCT devices are developed each year with varying degrees of connectivity features.

• Most devices conform to POCT01-A2 CLSI standard for connectivity, however, there are still potential sources of incompatibility.

• Hospital infrastructure may not support connectivity due to variable WiFi network power, interfering instruments, and other environmental factors.

• WiFi vs. wired vs. both: Convenience vs. cost, reliability vs. mobility.

• Middleware software (IT1000, RALS, etc) may also be variable and adds to the complexity of integrating POCT into a hospital setting.

• Electronic Health Record systems may not be easily adapted to report POCT results. Not all POCT devices have bidirectional communications.

• No standard for field POCT connectivity other than CLSI standards. Unproven in recent disaster/field settings.
Consequences of Non-Connected POCT

• Results (patients and quality control) not quickly reported to other providers (if at all)—impairing follow-up and/or trending.

• Cannot control users who have received or maintained appropriate training.

• POCT may not be billed appropriately (loss of $$$$$$!).

• Increased risk for result reporting error (reliance on verbal or written results).

• How can you have an ecosystem without any form of connectivity?

• Unable to integrate timely POCT data with other medical test results to optimize clinical decision making.
Consequences of Non-Connected POCT

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• How can you have an ecosystem without any form of connectivity?

• Inability to integrate timely POCT data with other medical test results impacts the effectiveness of lab testing.
Consequences of Inadequate Connectivity

Case Example:
- Procalcitonin is a sepsis biomarker
- Timely action necessary for clinical impact.
- Study relied on paper-based reporting of results!
- Did not find any benefit of procalcitonin.
- Untimely accurate results (POCT or not) is not actionable, or at least less actionable!
POCT CONNECTIVITY AT UC DAVIS (TODAY)
POCT CONNECTIVITY AT UC DAVIS (TODAY)
Future of POCT Connectivity

More bidirectional connectivity, harmonization of systems, and increased diversity for user settings (e.g., home, ambulances, general wellness tracking).
Sensor fusion is a process by which data from several different sensors are "fused" to compute something more than could be determined by any one sensor alone.
Medical sensor future may be the future of patient care. Integration of multiple sources of medical information (POCT, lab, smart devices, genetic testing, EHR data) into meaningful and actionable results.
Point-of-Care Cardiac Biomarker Testing
Case Study: POC Cardiac Biomarkers

"Minutes Lost Means Muscle Lost!"
Point-of-Care cTn Testing Improves TAT?

• POCT does speed things up. Faster turnaround times approaching 18-20 minutes!!
• Enhances Emergency Department workflow
• Empowers providers for rapid rule out.
• However…
Criteria for acute myocardial infarction

The term acute myocardial infarction (MI) should be used when there is evidence of myocardial necrosis in a clinical setting consistent with acute myocardial ischaemia. Under these conditions any one of the following criteria meets the diagnosis for MI:

- Detection of a rise and/or fall of cardiac biomarker values [preferably cardiac troponin (cTn)] with at least one value above the 99th percentile upper reference limit (URL) and with at least one of the following:
  ✷ Symptoms of ischaemia.
  ✷ New or presumed new significant ST-segment–T wave (ST–T) changes or new left bundle branch block.
  ✷ Development of pathological Q waves in the ECG.
  ✷ Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality.
  ✷ Identification of an intracoronary thrombus by angiography or autopsy.

- Cardiac death with symptoms suggestive of myocardial ischaemia and presumed new ischaemic ECG changes if biomarkers were obtained, or before cardiac biomarker values would be increased.

- Percutaneous coronary intervention (PCI) related MI is arbitrarily defined by elevation of cTn values from baseline values (≤99th percentile URL) or a rise of cTn values >20% if the baseline values are elevated, suggestive of myocardial ischaemia or (ii) new ischaemic ECG changes or (iii) angiographic findings demonstrating new loss of viable myocardium or new regional wall motion abnormality are recorded.

- Stent thrombosis associated with MI when detected by coronary angiography or autopsy in the setting of cardiac biomarker values with at least one value above the 99th percentile URL.

- Coronary artery bypass grafting (CABG) related MI is arbitrarily defined by elevation of cardiac biomarker with normal baseline cTn values (≤99th percentile URL). In addition, either (i) new pathological Q wave or new native coronary artery occlusion, or (iii) imaging evidence of new loss of viable myocardium is recorded.

Criteria for prior myocardial infarction

Any one of the following criteria meets the diagnosis for prior MI:

- Pathological Q wave on electrocardiogram in the absence of acute chest pain.
3rd Universal Definitions of Myocardial Infarction

- Third universal definitions state that an MI is based on a rise and/or fall of a cardiac biomarker, preferably troponin, with at least one value above the 99th percentile of the upper reference limit (URL), plus signs of ischemia.
- Assays should also exhibit analytical imprecision of <10% CV at the 99th percentile of the URL.
Point-of-Care Cardiac Biomarker Testing

*Not FDA Approved

*Not FDA Approved
Point-of-Care Cardiac Biomarker Testing

CV = 16.5%

*Not FDA Approved

CV = 17%

*Not FDA Approved


No FDA approved POC assay meets 3rd Universal Definition Recommendations! Faster is not always better…if you can’t determine true changes, you’re not guideline compliant!
The Problem of Not Planning Your Ecosystem Ahead of Time!

- **Scenario:** Your hospital invested heavily in POC troponin testing over the last decade. The Emergency Department uses it for rapid “rule-out”, while patients being “ruled in” get follow-up serial contemporary troponin testing via the laboratory. However, you caught wind of ”high sensitivity troponin” becoming FDA approved in the United States…
“Current Practices” for Cardiac Troponins in AMI

- >8 million annual ED visits for chest pain in the US.
- ~300 adult patients undergo cTn testing each week in the UCD Health ED

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Can we do better?

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Can we do better?
New Era of Cardiac Troponin Testing in the United States

UC Davis among first to use highly sensitive test to quickly identify heart attacks

(SACRAMENTO) — Emergency medicine physicians at UC Davis Health are using the latest-generation cardiac troponin (cTn) test to more quickly identify heart attack patients who come to the medical center with chest pain.

The test, known as hs-cTnT (which stands for high-sensitivity cardiac troponin T) measures troponin T levels in the blood, which rise in response to heart muscle damage. Hs-cTnT was approved by the U.S. Food and Drug Administration last year.

The deployment of the test at UC Davis is the result of nearly two years of planning and the
Do we need POCT in the age of High Sensitivity Cardiac Troponin?

What defines a high sensitivity troponin assay?

- High sensitivity assays more precise than contemporary assays.

- High sensitivity assays can detect troponin in >50% of healthy individuals.

Take home message: Lower CV’s equals better ability to identify changes in troponin over time. Creates opportunity for 0/1 hour rule out protocols!
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Impact of high-sensitivity cardiac troponin on use of coronary angiography, cardiac stress testing, and time to discharge in suspected acute myocardial infarction

Raphael Twerenbold¹,², Cedric Jaeger¹,², Maria Rubini Gimenez¹,², Karin Wildi¹,², Tobias Reichlin¹,², Thomas Nestelberger¹,², Jasper Boeddinghaus¹,², Karin Grimm¹,², Christian Puelacher¹,², Berit Moehring¹,², Gil Pretre¹,², Nicolas Schaeerli¹,², Isabel Campodarve³, Katharina Rentsch⁴, Stephan Steuer⁵, Stefan Osswald¹,², and Christian Mueller¹,²*

¹Department of Cardiology, University Hospital Basel, Petersgraben 4, CH-4031 Basel, Switzerland; ²Cardiovascular Research Institute Basel (CRIB), University Hospital Basel, Basel, Switzerland; ³Servicio de Urgencias y Medicina Interna - Hospital del Mar, Barcelona, Spain; ⁴Laboratory Medicine, University Hospital Basel, Basel, Switzerland; and ⁵Emergency Department, Kantonsspital Luzern, Luzern, Switzerland

Received 21 October 2015; revised 25 March 2016; accepted 29 April 2016; online publish-ahead-of-print 29 June 2016

See page 3333 for the editorial comment on this article (doi:10.1093/eurheartj/ehw355)
Impact of high-sensitivity cardiac troponin on use of coronary angiography, cardiac stress testing, and time to discharge in suspected acute myocardial infarction


1Department of Cardiology, University Hospital Basel, Petersgraben 4, CH-4031 Basel, Switzerland; 2Cardiovascular Re. Switzerland; 3Servicio de Urgencias y Medicina Interna - Hospital del Mar, Barcelona, Spain; 4Laboratory Medicine, Univ. Department, Kantonsspital Luzern, Luzern, Switzerland

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Evaluation of High-Sensitivity Cardiac Troponin I Levels in Patients With Suspected Acute Coronary Syndrome

Introduction

High concentrations of high-sensitivity cardiac troponin I (hs-cTnI) have been shown to have excellent sensitivity and have been identified as markers of acute myocardial injury. The cardiac troponin I (cTnI) test has been shown to perform as an indicator of acute myocardial injury. The cTnI test is also used as a reference standard for the diagnosis of acute coronary syndromes (ACS).

Objectives

The primary objective of this study was to evaluate the diagnostic performance of hs-cTnI levels in patients with suspected ACS. The study aimed to determine if hs-cTnI levels could be used as a marker of acute myocardial injury in patients with suspected ACS.

Methods

The study was a prospective cohort study of patients with suspected ACS. Patients were enrolled at the time of presentation to the emergency department. The hs-cTnI test was performed in all patients at presentation and at 6 hours following presentation. The primary outcome was the presence of acute myocardial injury as determined by the hs-cTnI test.

Results

A total of 234 patients were enrolled in the study. The median age of the patients was 65 years (range: 23-93 years). The majority of patients were male (71.7%). The median hs-cTnI level at presentation was 5.6 ng/L (range: 0.0-111 ng/L). The median hs-cTnI level at 6 hours was 2.0 ng/L (range: 0.0-87.0 ng/L).

Conclusion

In conclusion, the study found that hs-cTnI levels were elevated in patients with suspected ACS. The results of this study support the use of hs-cTnI levels as a marker of acute myocardial injury in patients with suspected ACS.

Acknowledgements

This study was supported by the European Society of Cardiology. The authors would like to thank all the participating physicians and nurses for their support.

References


See page 3333 for the editorial comment on this article (doi:10.1093/eurheartj/ehw355)
**Clinical Research**

**Original Investigation**

**Evaluation of High-Sensitivity Cardiac Troponin I in Patients With Suspected Acute Coronary Syndrome**

Edward Greten, MD, Joel Gortmaker, MD, Louise Fellen, PhD, J. Andrew Bard, PhD, Meir P. Shahar, MD, PhD, and Martin W. Schenke, MD, PhD, Berlin, Germany; and Boston Children's Hospital, Boston, MA, USA

**Objective**: To determine the diagnostic performance of the hsTnI assay in patients with suspected ACS.

**Results**: The hsTnI assay showed a better diagnostic performance than the cTnI assay in patients with suspected ACS. The hsTnI assay showed a better diagnostic performance than the cTnI assay in patients with suspected ACS.

**Conclusion**: The hsTnI assay is a useful tool for the diagnosis of ACS.

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**Original Investigation**

**Diagnosis of Myocardial Infarction Using a High-Sensitivity Troponin I 1-Hour Algorithm**

Johannes Tobias Neumann, MD, Nilkker Sorensen, MD, Tjark Schütte, MD, Francisco Díaz, PhD, Johannes Tobias Neumann, MD, Nilkker Sorensen, MD, Tjark Schütte, MD, Francisco Díaz, PhD

**Objective**: To test a 1-hour diagnostic algorithm to diagnose AMI using a high-sensitivity troponin I assay with a myocardial infarction (AMI) currently constituting an urgent need.

**Design, Setting, and Participants**: The Berlin Heart: Acute Cardiac Care Study is a prospective study that explored the application of the troponin I assay for the diagnosis of AMI in 1040 patients presenting to the emergency department with acute chest pain. The study was conducted in 1000 patients presenting to the emergency department with acute chest pain.

**Exposure**: Acute chest pain suggestive of AMI.

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Received 21 October 2015; revised 25 March 2016; accepted 29 April 2016; published ahead of print 29 June 2016

See page 3333 for the editorial comment on this article (doi:10.1093/eurheartj/ehw3355)
International evidence is profound – nearly a decade of experience!!!

CLINICAL RESEARCH

...
Do we need POCT in the age of High Sensitivity Cardiac Troponin?

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Take home message: Lower CV’s equals better ability to identify changes in troponin over time. Creates opportunity for 0/1 hour rule out protocols!
Do we need POCT in the age of High Sensitivity Cardiac Troponin?

Rapid 0/1 hour algorithms have been shown to be safe in Europe and now deployed at UC Davis Health.
Point-of-Care cTn Complicates the Ecosystem

**Scenario:** Your hospital invested heavily in POC troponin testing over the last decade. The Emergency Department uses it for rapid “rule-out”, while patients being “ruled in” get follow-up serial contemporary troponin testing via the laboratory. However, you caught wind of “high sensitivity troponin” becoming FDA approved in the United States...

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- Can’t mix and match troponins (I vs. T, or contemporary vs. high sensitivity).
- Best case scenario, POC troponin goes away. Worst case scenario, your hospital gets to wait by the wayside as the rest of the world benefits form high sensitivity troponins.
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Take Home Message: When you don’t design a good ecosystem, your barriers to change become all that much harder to deal with and you could end up being behind the curve!
Rational Development of a POC Ecosystem: Molecular Infectious Disease Example
Sepsis Value Proposition

• Every hour delay in achieving appropriate antimicrobial therapy increases odds of death by 7.6% in severe sepsis.

• Sepsis bundles are designed to speed up recognition and treatment to improve outcomes.

• Novel technologies are now available to facilitate early recognition of sepsis and provide pathogen identification.
Procalcitonin (PCT) Basics

- Pro-hormone to calcitonin
- Normally produced in C-cells (normal serum levels <0.05 ng/mL)
- Bacterial infections: PCT released into bloodstream uncleaved
- Viral infections: PCT suppressed by IFNγ
- Low in non-specific inflammation, neutropenia, viral/fungal infections
Procalcitonin Studies

Figure 1 Available evidence concerning PCT in different infections derived from observational and randomized-controlled intervention studies. While for some infections, intervention studies have investigated benefit and harm of using PCT for antibiotic decisions (right side), for other infections only results from diagnostic (observation) studies are available with mixed results (left side). Abbreviations: PCT, procalcitonin, + moderate evidence in favor of PCT; ++ good evidence in favor of PCT; +++ strong evidence in favor of PCT; ? evidence in favor or against the use of PCT still undefined.
Procalcitonin Kinetics and Sepsis

- PCT appears within 2-4 hours in pts with infections
- PCT usually peaks 8-24 hrs
- Short T1/2: 24 hrs; decreases by 50% if effective therapy given
- PCT returns to normal with recovery
PCT Levels Correlate with Severity of Illness / Mortality

- ICU admission PCT >2.0 ng/mL \(\rightarrow\) Increased risk for severe sepsis / septic shock vs patients with levels <0.5 ng/mL
- PCT decline of ≤80% from the day that severe sepsis / septic shock clinically diagnosed to four days after diagnosis \(\rightarrow\) Higher 28-day risk of all-cause mortality vs patients with decline >80%

References:
PCT Impact: Antibiotic Stewardship

BRAHMS PCT has been shown to reduce antibiotic prescription rate and exposure duration in LRTI

PCT-supported decision making reduces unnecessary ABx exposure

- **Bronchitis**: 65% ABx reduction
- **Acute exacerbations of COPD (aeCOPD)**: 50.4% ABx reduction
- **Community-acquired pneumonia (CAP)**: 32.4% ABx reduction

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Procalcitinon and Value

Effect of Procalcitonin Testing on Health-care Utilization and Costs in Critically Ill Patients in the United States

Robert A. Balk, MD; Sameer S. Kadri, MD; Zhun Cao, PhD; Scott B. Robinson, MA, MPH; Craig Lipkin, MS; and Samuel A. Bozzette, MD, PhD

TABLE 3 Matched, Regression Adjusted Outcomes (N = 132,112)

<table>
<thead>
<tr>
<th>Variable</th>
<th>PCT Mean of Adjusted Value</th>
<th>95% CI</th>
<th>No PCT Mean of Adjusted Value</th>
<th>95% CI</th>
<th>Mean of Difference</th>
<th>95% CI</th>
<th>P Value</th>
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<tbody>
<tr>
<td>Total LOS</td>
<td>11.6</td>
<td>11.4 to 11.7</td>
<td>12.7</td>
<td>12.6 to 12.8</td>
<td>-1.2</td>
<td>-1.3 to -1.0</td>
<td>&lt;.001</td>
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<td>ICU LOS</td>
<td>5.1</td>
<td>5.1 to 5.2</td>
<td>5.3</td>
<td>5.3 to 5.4</td>
<td>-0.2</td>
<td>-0.3 to -0.1</td>
<td>.031</td>
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<tr>
<td>Total cost, $</td>
<td>30,454</td>
<td>29,968 to 31,033</td>
<td>33,213</td>
<td>32,964 to 33,556</td>
<td>-2,759</td>
<td>-3,321 to -2,156</td>
<td>&lt;.001</td>
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<tr>
<td>ICU cost, $</td>
<td>20,155</td>
<td>20,625 to 19,798</td>
<td>21,465</td>
<td>21,270 to 21,710</td>
<td>-1,310</td>
<td>-1,702 to -847</td>
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<td>Pharmacy cost, $</td>
<td>4,238</td>
<td>4,119 to 4,453</td>
<td>4,568</td>
<td>4,480 to 4,678</td>
<td>-331</td>
<td>-488 to -99</td>
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<td>Antibiotic cost, $</td>
<td>882</td>
<td>854 to 948</td>
<td>952</td>
<td>931 to 980</td>
<td>-70</td>
<td>-105 to 4</td>
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<td>Laboratory cost, $</td>
<td>1,807</td>
<td>1,778 to 1,839</td>
<td>1,726</td>
<td>1,710 to 1,744</td>
<td>81</td>
<td>51 to 114</td>
<td>.002</td>
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<tr>
<td>Total antibiotic exposure</td>
<td>16.2</td>
<td>16.1 to 16.5</td>
<td>16.9</td>
<td>16.8 to 17.1</td>
<td>-0.7</td>
<td>-0.9 to -0.4</td>
<td>.006</td>
</tr>
</tbody>
</table>

• Retrospective, propensity score-matched multivariable analysis
• Premier Healthcare Database
• >33K patients admitted to ICU w/ 1-2 PCT on ICU day 1 vs >98K patients w/o PCT

CHEST 2017; 151(1):23-33
PCT Impact: Mortality, Hospital-Acquired Infections and ABx Stewardship

*PCT can help reduce antibiotic use by providing diagnostic clarity on bacterial infection management*¹

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<tr>
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<th>% Reduction</th>
<th>Description</th>
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<tr>
<td>Days of therapy per patient</td>
<td>47.1%</td>
<td>Reduciton in Antimicrobial Days of Therapy</td>
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<tr>
<td></td>
<td>62.0%</td>
<td>Reduction in Mortality Due to Infectious Diseases</td>
</tr>
<tr>
<td></td>
<td>50.0%</td>
<td>Reduction in 30-day Readmissions</td>
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<tr>
<td></td>
<td>64.0%</td>
<td>Reduction in <em>Clostridium difficile</em> Infections</td>
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<tr>
<td></td>
<td>50.0%</td>
<td>Reduction in Adverse Drug Events</td>
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<table>
<thead>
<tr>
<th></th>
<th>Pre: 17.0 DOT</th>
<th>Post: 9.0 DOT</th>
<th>P &lt; 0.001</th>
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<tbody>
<tr>
<td>Days of therapy per patient</td>
<td>7.6%</td>
<td>2.9%</td>
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<tr>
<td>Mortality due to infectious diseases</td>
<td>Pre: 7.6%</td>
<td>Post: 2.9%</td>
<td>P &lt; 0.001</td>
</tr>
<tr>
<td>30-day readmission for infection</td>
<td>Pre: 22.4%</td>
<td>Post: 11.1%</td>
<td>P &lt; 0.001</td>
</tr>
<tr>
<td><em>Clostridium difficile</em> Rate</td>
<td>Pre: 2.5%</td>
<td>Post: 0.9%</td>
<td>P &lt; 0.002</td>
</tr>
<tr>
<td>Adverse drug events</td>
<td>Pre: 16.2%</td>
<td>Post: 8.1%</td>
<td>P &lt; 0.001</td>
</tr>
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</table>

¹Broyles; MR. Impact of Procalcitonin-Guided Antibiotic Management on Antibiotic Exposure and Outcomes: Real-world Evidence, Open Forum Infectious Diseases, Volume 4, Issue 4, 1 October 2017, ofx213,
Implementation of PCT – Optimizing Microbiology and Antimicrobial Resources
Implementation of PCT – Optimizing Microbiology and Antimicrobial Resources

Traditional Sepsis Workflow

qSOFA
SIRS
Other Variables

NEGATIVE
Implementation of PCT – Optimizing Microbiology and Antimicrobial Resources

Traditional Sepsis Workflow

3-5 DAYS

No value added for the laboratory:
• Cost of processing cultures and space taken up by a potentially negative sample.
• Other labs such as serial lactates, perhaps antibiotic levels.
• Laboratory staff time!

NEGATIVE
Implementation of PCT – Optimizing Microbiology and Antimicrobial Resources

Procalcitonin-Enhanced Sepsis Workflow

qSOFA SIRS
Procalcitonin Algorithm - Adults

In patients with Lower Respiratory Tract Infection

- **<0.1 ng/mL**
  - Bacterial etiology: Very unlikely
  - NO antibiotics!
  - ▪ Repeat PCT in 6-12 hrs if antibiotics not begun and no clinical improvement
  - ▪ Overrule if clinically unstable or immunosuppressed
  - ▪ Remember caveats

- **0.1-0.25 ng/mL**
  - Bacterial etiology: Unlikely
  - No antibiotics

- **>0.25-0.5 ng/mL**
  - Bacterial etiology: Likely
  - Antibiotics yes

- **>0.5 ng/mL**
  - Bacterial etiology: Very likely
  - Antibiotics YES!

- Consider repeat PCT every 2-3 days to consider antibiotic cessation
- Stop when 80-90% decrease of peak PCT

Implementation of PCT – Optimizing Microbiology and Antimicrobial Resources

VALUE ADDED for the laboratory:
- Appropriate labs performed = optimized staff / reagent, and instrument usage
- Increased revenue

Procalcitonin-Enhanced Sepsis Workflow

qSOFA SIRS

Abnormal PCT, Lactate, etc.
Implementation of PCT – Optimizing Microbiology and Antimicrobial Resources

Procalcitonin-Enhanced Sepsis Workflow

VALUE ADDED for the laboratory:
- Appropriate labs performed = optimized staff / reagent, and instrument usage
- No additional cultures or other tests required (e.g., $50/culture set x 1,000 cultures/year = $50,000/year in savings!!)

qSOFA SIRS

WORK UP FOR OTHER CAUSES OF SIRS

Normal PCT, lactate, etc
At UC Davis, from 2015-2016, the number of unnecessary blood cultures were reduced by 15% (equating about 1,000 cultures) after deploying PCT.

**VALUE ADDED for the laboratory:**
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Can we speed other aspects up by deploying POC lactate testing?
At UC Davis, from 2015-2016, the number of unnecessary blood cultures were reduced by 15% (equating about 1,000 cultures) after deploying PCT.

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**qSOFA**
**SIRS**

**Procalcitonin-Enhanced Sepsis Workflow**

**Normal PCT, lactate, etc**

**WORK UP FOR OTHER CAUSES OF SIRS**
*At UC Davis, from 2015-2016, the number of unnecessary blood cultures were reduced by 15% (equating about 1,000 cultures) after deploying PCT.*

POC lactate can be done in <30 seconds vs. 10 mins for a STAT lab vs. 30-45 mins for the Core Lab..however…
Are all Lactate Testing Method the Same?

**FACT:** Lactate measurements **ARE NOT** standardized and as many are aware, any delay in testing leads to falsely elevated results (despite placing on ice).
Are all Lactate Testing Method the Same?

Beckman DxC 800
Pavilion Core Lab

Siemens RapidLab
Davis 5 Blood Gas Lab

Radiometer ABL800
OR Lab (Retired)
ABG Lab vs. Mean Lactate Values

Mean (SD) Bias = -0.17 (0.29)
OR Lab vs. Mean Lactate Values

Mean (SD) Bias = -0.01 (0.22)
Core Lab vs. Mean Lactate Values

Mean (SD) Bias = 0.18 (0.18)
Comparison Study vs. Mass Spec

Population: n = 100 patients (65 sepsis, 27 severe sepsis, 8 septic shock)
Compared by mass spec

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<tr>
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<th>POC 2</th>
<th>POC 3*</th>
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4 MMOL/L CUTOFF
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4 MMOL/L CUTOFF
**Comparison Study vs. Mass Spec**

Population: n = 100 patients (65 sepsis, 27 severe sepsis, 8 septic shock)  
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**Pro Tip:** POCT may be a better option through at least reducing pre-analytical delays and improving lactate accuracy. However, whatever you use, stick to that same method!

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4 MMOL/L CUTOFF
Optimizing Microbiology and Antimicrobial Resources

Procalcitonin-Enhanced Sepsis Workflow

Can we do anything else to improve workflow?
mPOCT and Decision Making in ED

Results (n=61)
- 64% management changed
- 13-18% fewer CXR, blood draws, UAs
- 5% fewer admissions
- 15% less antibiotic use
- 8% more appropriate oseltamivir use

- Real-time interviews of MDs
- Stanford ED; Jan-March 2016
- NP swab/respiratory virus PCR in children <18 years triggered interview

- How would a hypothetical viral mPOCT (RSV, Flu A/B) that would have results within 20 min affect care?
Results

- Influenza diagnosis changed treatment plan vs empiric care plan in 61% of cases
- cobas Liat® Influenza A + B assay
- 30 minute turnaround

Results

- Influenza diagnosis changed treatment plan vs empiric care plan in 61% of cases
- cobas Liat equivalent to centralized lab-based testing (sens: 98.8%, spec: 98.5%)

Clinical decision making in the emergency department setting using rapid PCR: Results of the CLADE study group.

Enhancing Care Paths by Adding Molecular Testing

Diagnosis of Respiratory Tract Infections (RTI) in the ED

qSOFA
SIRS
Suspicion of RTI

+PCT

VALUE ADDED for the laboratory:
- Appropriate labs performed = optimized staff / reagent, and instrument usage
- No additional cultures or other tests required (e.g., $50/culture set x 1,000 cultures/year = $50,000/year in savings!!)
Enhancing Care Paths by Adding Molecular Testing

Multiplex Molecular Respiratory Panel ($109/test) + PCT

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Multiplex Molecular Respiratory Panel ($109/test)
Enhancing Care Paths by Adding Molecular Testing

Diagnosis of Respiratory Tract Infections (RTI) in the ED

Multiplex Molecular Respiratory Panel ($109/test)

qSOFA
SIRS
Suspicion of RTI

PCT

VALUE ADDED by Enhancing Quality of Care:
PCT aids in determining the risk for bacterial infection.
- PCT negative and PCR viral panel positive can avoid the need for antimicrobial therapy.
- PCT positive and PCR bacterial panel positive helps target appropriate antimicrobial therapy.
- Optimizes molecular revenue generation
Enhancing Care Paths by Adding Molecular Testing

Diagnosis of Respiratory Tract Infections (RTI) in the ED

qSOFA
SIRS
Suspicion of RTI

Multiplex Molecular Respiratory Panel ($109/test)

Optimizing Molecular Testing:
- Addition of bedside targeted molecular testing for common pathogens such as Flu/RSV and Strep A improves the cost-effectiveness.
Does the patient have signs and symptoms suggestive of influenza, including atypical clinical presentation, or findings suggestive of complications associated with influenza? Do the patient have signs and symptoms suggestive of influenza, including atypical clinical presentation, or findings suggestive of complications associated with influenza?

- Yes
- No

Is the patient being admitted to the hospital?

- Yes
- No

Influenza testing probably not indicated; consider other etiologies

- Yes
- No

Influenza clinically diagnosed; start empiric antiviral treatment if the patient is in a high-risk group for influenza complications, or has progressive disease, advise close follow-up if worsening.

Flu season= yes

CDC: Will flu test results influence clinical management= yes

Perform multiplex PCR

- Inpatients
- ED patients being admitted
- Immunocompromised outpatients

Low-risk outpatients
- ED patients not being admitted

Perform LIAT

https://www.cdc.gov/flu/professionals/diagnosis/consider-influenza-testing.htm
Integrating LIAT at UC Davis

Coexisting with Multiplex Assays

- Reduced ED demand on multiplex PCR testing by 40%
- Savings of $37,603 from January to April 2018 in unneeded multiplex testing alone.
- Among ED patients tested by LIAT, therapeutic turnaround time reduced by an average of 4.8 (3.3) hours.
- LIAT testing for inpatients reduced "droplet" isolation by at least a day.
- Interestingly, the 20 min turnaround time for LIATs at clinics forced providers to adhere more to CDC recommendations for molecular testing (e.g., test only when needed!).
A point-of-care ecosystem should consist of devices that synergistically adds value to patient care and works with other diagnostic systems such as central lab services.

Point-of-care testing is not necessary for ALL situations. Faster is not always better and in some cases, POCT could result in unintended problems.

Barriers to developing a productive POC ecosystem includes pre-existing biases, inadequate performance and cost, inappropriate application of the technology, and information technology.

Appropriate integration of POC technologies in an “ecosystem” of tests optimizes patient outcomes as in the case of POC molecular diagnostics and lactic acid testing, combined with core lab procalcitonin assays.
Questions