Improving Sepsis Diagnosis and Treatment at BayCare Health System
Understanding the Lab's Potential to Deliver More Value in Collaboration with Physicians and Pharmacy

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Objectives

- Outline Sepsis and its outcomes
- Assess the clinical utility of sepsis biomarkers: Procalcitonin and Lactic Acid
- Initiatives to implement Sepsis Diagnosis and Management at BayCare Health System
- Physician Education and Information System initiatives
- Role of Clinical Laboratory in the diagnosis and monitoring of sepsis
- Quality Improvement measures to ensure appropriate utilization of laboratory testing
- Lessons Learned

Conflict of Interest Statement: NO affiliations with or involvement in any organization or entity with any financial or non-financial interest in the subject matter or materials discussed in this presentation
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200 Ave. F N.E.
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Winter Haven Women's Hospital
101 Ave. O S.E.
Winter Haven, FL 33880
(863) 294-7010
SIRS Disease Progression

**Insult**
- Bacterial
- Viral
- Fungal
- Parasitic
- Infection

**Sepsis**
SIRS + Infection
Clinical response to insult with ≥2 of the following:
- Temp > 38°C or ≤ 36°C
- Heart Rate ≥ 90 beats/min
- Respiration > 20 breaths/min or PaCO2 < 32mm Hg
- WBC > 12,000/mm3, < 4,000/mm3 or >10% immature bands

**Severe Sepsis**
Sepsis with at least one acute organ dysfunction

**Septic Shock**
Sepsis-induced refractory hypotension

Bone et al. *Chest* 1992
American College of Chest Physicians/Society of Critical Care Medicine consensus panel definitions - 2002
Sepsis is Costly

$17 billion  estimated cost per year (USA)

$50,000  average cost of treating sepsis

40%  of total ICU expenditures

>50%  Severe sepsis prolongs patient stay in the ICU and the hospital by more than 50%

Sepsis is Deadly

10th  Tenth leading cause of death (USA)

215,000  deaths per year

- Mortality rates associated with sepsis
  - 30-50% for severe sepsis
  - 50-80% for septic shock

- Early diagnosis/detection is critical to properly manage sepsis
- Initiation of early goal directed therapy is key to reducing mortality from severe sepsis and Septic Shock.

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Biomarkers and Early Diagnosis of Sepsis

**Procalcitonin: Marker of Sepsis**
- Severe bacterial infection
- Early course of reaction to infection
- Risk assessment: higher PCT = higher risk
- Kinetics help with assessing the course of infection
  - How is the patient responding to therapy
  - Results long before microbiological confirmation
- Helps differentiate patients with Sepsis from those with non-infectious SIRS

**Lactate: Marker of Septic Shock**
- Metabolite reaction to hypoperfusion and hypoxia of organs
- Severity marker/Surrogate marker in Septic Shock patients
- Strong predictor of organ dysfunction and mortality
- Lactate shift/Lactate Clearance is predictor of low mortality in critical ill patients
- Responds quickly to fluid resuscitation

Müller, B. Calcitonin Precursors are Reliable Markers of Sepsis in a Medical Intensive Care Unit. *Crit Care Med.* 28(4):977-983, April 2000


BayCare Sepsis Management Model

- Multidisciplinary approach
  - Engage Physicians, Nurses, Abstractors, Pharmacy, Lab and IS
- Emergency 3hr/6hr bundle compliance
  - Sepsis plan was created as per CMS guidelines
  - Evidence based guidelines
- Sepsis Detection Improvement Efforts in ER
  - Lactic Acid and Blood Culture orders included
- Sepsis Education Initiatives
  - Screening tools were created
  - Lab test alerts were created
  - Training and Education to team members
- Hospital-specific Sepsis committees
  - Monitor sepsis compliance rates
- Hospital-specific Post-sepsis huddle initiatives
  - Fall-out cases analysis
  - Gap analysis
Lab Initiative in Sepsis Management

• **Sepsis 3 hour bundle criteria**
  • Initial Lactic Acid Level
  • Draw blood cultures BEFORE antibiotics

• **Sepsis 6 hour bundle criteria**
  • Repeat Lactic Acid Level

**LACTATE RULE** for repeat Lactic Acid order

✓ If first STAT or ASAP Lactate is abnormal, system will automatically order another Lactate 4 hours from the initial lactate order time
Quality Improvements in Lactate testing

**Issue:** Providers ordering both “POC lab-Lactate” and “main lab- Lactate” at same time

➤ **Solution:** Lab with IS team designed a rule that “Cancel “main lab-lactate” if “POC lab- lactate” ordered in the same conversation”.

**Issue:** Duplicate orders. Timed study and Stat lactate orders received in lab at the same time, so lab was cancelling the timed orders, resulted in lactate fall-out
OR
Lactate rule did not fired on abnormal Timed lactate orders, so missing repeat lactate measurement on abnormal timed-study lactates

➤ **Solution:**
- The rule was modified to include Timed- study priority.
- This rule fires only 4 times per encounter
Quality Improvements in Lactate testing

**Issue:** Duplicate orders for lactic acid

**Solution:** Three scenarios where a lactic acid alert displays when a lactic acid order is entered within 4 hours of previous lactate order:

1. The results of previous Lactic acid order displayed:

2. The previous lactic acid result was abnormal and the lactate rule fired a repeat lactate:

3. The previous lactic acid result was abnormal and the lactate rule did NOT fired repeat lactic acid as this was 5th order on same encounter:
Lactic Acidosis in Sepsis

- Serial measurements of blood lactate levels may guide therapy

Serial lactate levels predictor of mortality

- Normal <2.0 mmol/L
- Mild acidosis 2.5-4.9 mmol/L (mortality 25-35%)
- Moderate acidosis 5.0-9.9 mmol/L (mortality 60-75%)
- Severe acidosis >10 mmol/L (mortality >95%)

Lactate is significantly elevated in Septic shock compared to Severe Sepsis patients

BayCare Health System- Oct 2015 to March 2016
Elevated Lactate predicts Mortality in Severe Sepsis and Septic Shock Patients (grouped)

Lactate (mmol/L) and Mortality

Individual standard deviations are used to calculate the intervals

*p<0.001 by 2-sample T test

BayCare Health System- Oct 2015 to March 2016
Lactate predicts Mortality in both Severe Sepsis and Septic Shock Patients

Severe Sepsis

Lactate and Mortality in Severe Sepsis Patients

- Lactate (mmol/L) vs. Mortality
- Non-survivors vs. Survivors
- n=207
- p<0.001 by 2-sample T test

Septic Shock

Lactate and Mortality in Septic Shock Patients

- Lactate (mmol/L) vs. Mortality
- Non-survivors vs. Survivors
- n=98
- ***p<0.001 by 2-sample T test
- n=271
Lactate Shift or Lactate Clearance

- Higher Lactate Shift/Clearance- associated with lower risk of death
- Rapid Lactate Clearance is a strong predictor of survival, and sustained elevation in lactate is a harbinger of adverse clinical outcome
- Lactate Clearance can be used to stratify mortality-risk among patients with severe sepsis or septic shock

Rapid Lactate Clearance is a strong predictor of survival in Severe Sepsis and Septic Shock Patients (grouped)

**Lactate Clearance and Mortality in Severe Sepsis & Septic Shock Patients**

- **n=186**
- **n=750**

***p<0.001 by 2-sample T test

*Individual standard deviations are used to calculate the intervals*
Rapid Lactate Clearance is a strong predictor of survival in Severe Sepsis, but not in Septic Shock

### Severe Sepsis

![Graph showing lactate clearance in severe sepsis patients with statistical significance.]

**Lactate Clearance in Severe Sepsis Patients**

- **n=750**
- **n=186**

***p<0.001 by 2-sample T test

### Septic Shock

![Graph showing lactate clearance in septic shock patients with no statistical significance.]

**Lactate Clearance in Septic Shock Patients**

- **n=247**
- **n=90**

NS- statistically not significant

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**BayCare Health System- Oct 2015 to March 2016**
Procalcitonin- Journey at BayCare Health System

- Discussed with Physicians and Pharmacists
- Procalcitonin- an expensive test
- SOC was used to make decision
  - Service
  - Outcome
  - Cost
PCT aids in Risk Assessment

BayCare Health System
PCT Results Guidelines

REFERENCE INTERVAL: 0.00 - 0.24 NG/ML

Lower Respiratory Tract Infection (Mild to Moderate Acuity)

- PCT < 0.1  Bacterial Infection VERY UNLIKELY
- PCT 0.1-0.24  Bacterial Infection UNLIKELY

Antibiotics NOT recommended for initial therapy. However, consider starting antibiotics if clinically unstable or high risk (PSI Class IV-V, CURB65 ≥2, GOLD III or IV). Repeat in 6-24 hours based on clinical status.

- PCT 0.25-0.5  Bacterial Infection LIKELY
- Antibiotics ARE recommended for initial therapy.
- PCT 0.5-1.0  Bacterial Infection VERY LIKELY

Antibiotics ARE recommended for initial therapy. Repeat PCT every 2-3 days for duration of antibiotics. CONSIDER STOPPING ABX when PCT decreases 80% from baseline or to ≤ 0.25 ng/mL, and patient is clinically stable. CONSIDER TX FAILURE if PCT remains elevated. (PCT will decrease 50% every 1 to 2 days in appropriately treated patients.) If PCT does not decrease appropriately, the patient may need expanded antibiotic coverage, or further diagnostic evaluation.

High Acuity Lower Respiratory Infections in ICU (including VAP), Severe Sepsis or Septic Shock

Antibiotics ALWAYS recommended for initial therapy.
- PCT < 0.25  Bacterial Infection VERY UNLIKELY
- PCT 0.25-0.5  Bacterial Infection UNLIKELY

ALWAYS order repeat level in 6 to 24 hours after initial PCT result. CONSIDER STOPPING ABX when 2 PCT results are <0.25 ng/mL.

- PCT 0.5-1.0  Bacterial Infection LIKELY
- PCT >1.0  Bacterial Infection VERY LIKELY

Antibiotics ALWAYS recommended for initial therapy. Repeat PCT every 1-2 days for duration of antibiotics. CONSIDER STOPPING ABX when PCT decreases 80% from baseline or to ≤ 0.5 ng/mL, and patient is clinically stable. CONSIDER TX FAILURE if PCT remains elevated. (PCT will decrease 50% every 1 to 2 days in appropriately treated patients.) If PCT does not decrease appropriately, the patient may need expanded antibiotic coverage, or further diagnostic evaluation.
Procalcitonin- Journey at BayCare Health System

A Proactive Approach

February 2008-
• Started pilot at Morton Plant Hospital (reference lab for other BayCare hospitals)
• Introduced VIDAS BRAHMS PCT assay (bioMérieux)
• Results available within 20 minutes
• Added PCT in “Sepsis Alert” Protocol and physician order sets

Antibiotic Stewardship

• The primary use of PCT assay was to risk assess the patients for Severe Sepsis and Septic Shock
• Feedback from Physicians and Medical Staff was Positive
• PCT was adapted as a tool to guide if antibiotic therapy is needed and helping the physicians to identify patients who do not need antibiotic therapy
Procalcitonin- Journey at BayCare Health System

Physician Education

- Physician Education was rolled out with guidelines to use the PCT test.

- A Committee was formed with Lab members, pharmacy and ICU/ED physicians to review PCT data with the goal of developing utilization protocol.

Procalcitonin- Journey at BayCare Health System

Quality Improvement for Appropriate Utilization

- A brief physician survey on ordering practices and diagnostics decisions related to PCT utilization was conducted

1. Have you ever ordered a PCT test from the Morton Plant clinical laboratory?
   - Yes: 88%
   - No: 12%

2. If yes, please indicate why you wanted to know the patient's PCT level:
   - A) To determine if the patient has a severe bacterial infection
   - B) To help select the proper antibiotic and duration of antibiotic
   - C) To provide further clarity when trying to diagnose a patient who presents with overlapping cardiac and pulmonary symptoms, signs and X-ray changes which could represent heart failure or pneumonia
   - D) Other, please specify:

3. How do you order procalcitonin?

- A) Per order set protocol: 40%
- B) As a single order: 36%
- C) Other: 24%

4. How often are the procalcitonin results helpful in guiding antibiotic therapy?

- A) Always: 13%
- B) Sometimes: 73%
- C) Seldom: 11%
- D) Never: 3%

5. Based on the available data (reference article in email) Would you follow an antibiotic treatment guideline as shown below?

- Yes: 84%
- No: 16%

Proposed Procalcitonin (PCT) guidelines for suspected LRTI or Sepsis (Bronchitis, AECOPD, CAP not HCAP)

- Initiation or continuation of antibiotics strongly discouraged if PCT is: < 0.1 µg/L
- Antibiotic use discouraged if PCT levels are: 0.1 - 0.25 µg/L
- Initiation or continuation of antibiotics is encouraged if PCT is: 0.25 - 0.5 µg/L
- Initiation or continuation of antibiotics is strongly encouraged if PCT is: > 0.5 µg/L

Antibiotics can be stopped if PCT level is < 0.25 on two or three draws in 24hrs and not rising; Consider stopping antibiotics once PCT level has dropped by 90% from peak level in first 24 hrs.
Quality/Utilization Improvement for PCT testing

- Reference Interval for PCT was low: 0 to 0.05 ng/ml
- PCT Guidelines needed to be revised for Low Acuity and High Acuity Indications
- Overutilization of PCT test in conditions not indicated for this test
  - Recommended for Sepsis, Meningitis, Respiratory tract infections
- Underutilization of PCT testing
  - Serial testing was not ordered to guide antibiotic treatment
The clinical decision reference range for PCT was changed to 0-0.24 ng/ml

- With the implementation of this clinical decision range, the results of PCT flag as abnormal for results ≥0.25 ng/ml
**REFERENCE INTERVAL: 0.00 - 0.24 NG/ML**

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**Lower Respiratory Tract Infection (Mild to Moderate Acuity)**

- **PCT < 0.1**  Bacterial Infection VERY UNLIKELY
- **PCT 0.1-0.24**  Bacterial Infection UNLIKELY

**Antibiotics NOT recommended for initial therapy.**
However, consider starting antibiotics if clinically unstable or high risk (PSI Class IV-V, CURB65 >2, GOLD III or IV). Repeat in 6-24 hours based on clinical status.

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- **PCT 0.25-0.5**  Bacterial Infection LIKELY
- **Antibiotics ARE recommended for initial therapy.**

**PCT > 0.5**  Bacterial Infection VERY LIKELY.
Antibiotics ARE recommended for initial therapy.

Repeat PCT every 2-3 days for duration of antibiotics. CONSIDER STOPPING ABX when PCT decreases 80% from baseline or to <= 0.25 ng/mL, and patient is clinically stable. CONSIDER TX FAILURE if PCT remains elevated. (PCT will decrease 50% every 1 to 2 days in appropriately treated patients.) If PCT does not decreases appropriately, the patient may need expanded antibiotic coverage, or further diagnostic evaluation.

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**High Acuity Lower Respiratory Infections in ICU (including VAP), Severe Sepsis or Septic Shock**

**Antibiotics ALWAYS recommended for initial therapy.**

- **PCT < 0.25**  Bacterial Infection VERY UNLIKELY
- **PCT 0.25-0.5**  Bacterial Infection UNLIKELY

ALWAYS order repeat level in 6 to 24 hours after initial PCT result. CONSIDER STOPPING ABX when 2 PCT results are <0.25 ng/mL.

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- **PCT 0.5-1.0**  Bacterial Infection LIKELY
- **PCT > 1.0**  Bacterial Infection VERY LIKELY

Antibiotics ALWAYS recommended for initial therapy.

Repeat PCT every 1-2 days for duration of antibiotics. CONSIDER STOPPING ABX when PCT decreases 80% from baseline or to <= 0.5 ng/mL, and patient is clinically stable. CONSIDER TX FAILURE if PCT remains elevated. (PCT will decrease 50% every 1 to 2 days in appropriately treated patients.) If PCT does not decreases appropriately, the patient may need expanded antibiotic coverage, or further diagnostic evaluation.
Appropriate utilization for PCT testing

- More single PCTs ordered
  - More single orders from emergency room and patient discharged
  - 56% single orders for admitted patients

- Serial testing not ordered to guide antibiotic treatment
  - In patients with PCT values >0.25 ng/ml
Scenarios: Inappropriate PCT testing

- Overutilization of PCT test in conditions not indicated for this test

<table>
<thead>
<tr>
<th>Reason of visit</th>
<th>ICD10: Diagnosis Desc</th>
</tr>
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<tbody>
<tr>
<td>CHEST PAIN</td>
<td>Other chest pain</td>
</tr>
<tr>
<td></td>
<td>Chest pain, unspecified</td>
</tr>
<tr>
<td>CELLULITIS</td>
<td>Cellulitis of left lower limb</td>
</tr>
<tr>
<td></td>
<td>Cellulitis of right lower limb</td>
</tr>
<tr>
<td></td>
<td>Cellulitis of left upper limb</td>
</tr>
<tr>
<td></td>
<td>Cellulitis of right upper limb</td>
</tr>
<tr>
<td></td>
<td>Cellulitis of abdominal wall</td>
</tr>
<tr>
<td></td>
<td>Cellulitis of left toe</td>
</tr>
<tr>
<td></td>
<td>Cutaneous abscess of left upper limb</td>
</tr>
<tr>
<td></td>
<td>Infection following a procedure, initial encounter</td>
</tr>
<tr>
<td>UTI</td>
<td>Urinary tract infection, site not specified</td>
</tr>
<tr>
<td>CP</td>
<td>Other chest pain</td>
</tr>
<tr>
<td>HEADACHE</td>
<td>Headache</td>
</tr>
<tr>
<td>ABNORMAL LABS</td>
<td>Acute kidney failure, unspecified</td>
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<tr>
<td></td>
<td>Acute kidney failure with tubular necrosis</td>
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<tr>
<td>BACK PAIN</td>
<td>Low back pain</td>
</tr>
<tr>
<td>GI BLEED</td>
<td>Melena</td>
</tr>
<tr>
<td></td>
<td>Acute duodenal ulcer with hemorrhage</td>
</tr>
<tr>
<td></td>
<td>Acute gastric ulcer with hemorrhage</td>
</tr>
<tr>
<td>LEG PAIN</td>
<td>Cellulitis of left lower limb</td>
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<tr>
<td></td>
<td>Acute embolism and thrombosis of left popliteal vein</td>
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<tr>
<td>ACUTE CHEST PAIN</td>
<td>Other chest pain</td>
</tr>
<tr>
<td>ASCITES</td>
<td>Alcoholic cirrhosis of liver with ascites</td>
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<tr>
<td>HIP FRACTURE</td>
<td>Displaced intertrochanteric fracture of left femur, initial encounter for closed fracture</td>
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<tr>
<td>Rectal Bleed</td>
<td>Gastrointestinal hemorrhage, unspecified</td>
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<tr>
<td>UNSTABLE ANGINA</td>
<td>Atherosclerotic heart disease of native coronary artery with unstable angina pectoris</td>
</tr>
<tr>
<td>CHOLECYSTITIS</td>
<td>Acute cholecystitis</td>
</tr>
<tr>
<td>KNEE PAIN</td>
<td>Acute embolism and thrombosis of left popliteal vein</td>
</tr>
</tbody>
</table>
Four PCT orderables created

Four Procalcitonin orders were created to guide appropriate use of Procalcitonin.

i. Procalcitonin- Sepsis
ii. Procalcitonin- Meningitis
iii. Procalcitonin- Respiratory
iv. Procalcitonin- Unspecified

Use of the “Procalcitonin Unspecified” order will result in an alert and the need to complete a PowerForm to provide additional information.
Procalcitonin is significantly elevated in Septic Shock compared to Severe Sepsis patients

BayCare Health System- Oct 2015 to March 2016

***p<0.001 by 2-sample T test

Individual standard deviations are used to calculate the intervals
Elevated PCT concentrations and PCT non-clearance are strongly associated with all-cause mortality in septic patients.

Procalcitonin Clearance for Early Prediction of Survival in Critically Ill Patients with Severe Sepsis

Mohd Basri Mat Nor and Azrina Md Railib

PCTc-48 is associated with prediction of survival in critically ill patients with sepsis.
Elevated Procalcitonin predicts Mortality in Severe Sepsis and Septic Shock Patients (grouped)

* *p<0.05 by 2-sample T test

n=181

n=789

*Individual standard deviations are used to calculate the intervals*

*p<0.05 by 2-sample T test*
Elevated Procalcitonin predicts Mortality in Severe Sepsis, but not in Septic Shock Patients

*"p<0.05 by 2-sample T test
NS: not significant
Weak Positive Correlation b/w Lactic Acid and PCT in Severe Sepsis, not in Septic Shock patients

P-value: NS
R-Squared: 0.012

P-value: < 0.001
R-Squared: 0.035
Both Lactic Acid and PCT weakly correlate and predicts Mortality in Severe Sepsis Patients

BayCare Health System - Oct 2015 to March 2016

P-value: < 0.001
R-Squared: 0.024 - 0.042
Lessons Learned

- The recognition of sepsis should be viewed as the first step in management
  - At ED presentation
- Multidisciplinary approach including various players (Labs, physicians, nurses, pharmacy, quality)
- Laboratories play a major role in diagnosis and management of Sepsis patients
  - Lactate rules and alerts
  - Data analysis to support:
    - Appropriate Utilization of lab testing
    - Evidence based practices
- PCT and Lactate concentrations are elevated in both Severe Sepsis and Septic Shock patients
  - Septic Shock- significantly higher Lactate and PCT than severe sepsis
- Elevated Lactate concentration predicts poor survival in both Severe Sepsis and Septic Shock patients
- Lactate Clearance- is a useful biomarker in predicting mortality in Severe Sepsis patients- rapid clearance in survival patients.
- Elevated PCT concentration predicts poor survival in Severe Sepsis patients
- In Severe Sepsis patients there is weak positive correlation between Lactate and PCT (first in ED) and both biomarkers predicts mortality.
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Pharmacy
Infection Control
Physicians
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Information System
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Quality and Clinical Outcomes
Enterprise Data Warehouse
Premier Quality Advisor
Visiun Performance Insight
Questions

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