Procalcitonin as a Marker of Infection, Sepsis, and Response to Antibiotic Therapy

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### Program Objectives

- List clinical settings in which procalcitonin testing has been shown to be useful.

- Describe limitations to the use of procalcitonin as a marker to predict risk of developing severe sepsis.

- Discuss potential new applications for the use of procalcitonin in managing patients with known infection.
Calcitonin

Adapted from Thompson LDR, Endocrine Pathology, Elsevier, 2006

From zebrafish.org (U.S. EPA)
Procalcitonin (PCT)

Adapted from Christ-Crain M, Muller B, Swiss Med Wkly 2005; 135:451-460
Early PCT Reports


Elevated calcitonin in toxic shock syndrome - in “polymeric molecular species”

Elevated calcitonin in fulminant meningococcaemia in children
Mallet E et al, Lancet 1983; 321:294

Elevated PCT in sepsis
- continuum of elevation
- non-infectious stimuli
- extra thyroidal production
Assicot M et al, Lancet 1993; 341:515-518
Inflammatory Marker Expression

Modified from Faix JD, Biomarkers Med 2011; 5:117-130
Systemic Markers of Local Inflammation

Definition of Sepsis - 1992

• **SIRS**
  – Body temperature >38°C or <36°C
  – Tachycardia
  – Hyperventilation
  – WBC > 12,000/mm³ or <4000/mm³ (or >10% immature forms)

• **Infection**

Markers for Sepsis Diagnosis

From Muller B et al, Crit Care Med 2000; 28:977-983
Markers for Sepsis Stages

From Muller B et al, Crit Care Med 2000; 28:977-983
Markers for Sepsis Survival

From Meisner M et al, Crit Care 1999; 3:45-50

From Brunkhorst FM et al, Clin Microbiol Infect 2002; 8:93-100
Definition of Sepsis - 2002

• **SIRS**

• **Infection** (Documentation of infection may not be required for the diagnosis of sepsis if strong suspicion exists.)
  – Additional criteria, such as altered mental status; edema; hyperglycemia in the absence of diabetes; elevated C-reactive protein or elevated procalcitonin are also included.

PCT in the News!

Procalcitonin: seeking a niche

Dear Sirs, What is your PCT?

Procalcitonin: Clinical tool or laboratory curiosity?

Procalcitonin in bacterial infections – hype, hope, more or less?

Biomarkers of sepsis: is procalcitonin ready for prime time?
PCT & Sepsis: Meta-analyses


From Tang BMP et al, Lancet Infection 2007; 7:210-217
PCT Following Traumatic Injury

From Wanner GA et al, Crit Care Med 2000; 28:950-957
PCT Production by Adipose Cells

From Linscheid P et al, Endocrinology 2003; 144:5578-5584
PCT Assay Evolution

From Christ-Crain M, Muller B, Swiss Med Wkly 2005; 135:451-460
PCT Cut-offs?

From Clec’h C et al, Crit Care Med 2006; 34:102-107

From Chiesa C et al, Clin Inf Dis 1998; 26:664-672

Medical pts: 1.0 ng/ml
Surgical pts: 9.7 ng/ml

neonates: 10 ng/ml
PCT Time Course after Trauma

From Castelli GP et al, Crit Care Med 2009; 37:1845-1849
PCT & Survival in ICU

From Jensen JU et al, Crit Care Med 2006; 34:2596-2602
PCT: PASS Study Survival

From Jensen JU et al, Crit Care Med 2011; 39:2048-2058
The “perfect” sepsis marker?

From Osuchowski MF et al, Crit Care Med 2009; 37:1567-1573
Antibiotic Stewardship

Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America Guidelines for Developing an Institutional Program to Enhance Antimicrobial Stewardship

From Dellit TH et al, Clin Inf Dis 2007; 44:159-177
PCT Guided Rx: First Reports

Lower Respiratory Tract Infection

From Christ-Crain M et al, Lancet 2004; 363:600-607

Community Acquired Pneumonia

From Christ-Crain M et al, Am J Respir Crit Care Med 2006; 174:84-93
PCT Guided Rx: Sepsis

From Nobre V et al, Am J Respir Crit Care Med 2008; 177:498-505
PCT Guided Rx: Recent Summary

Adapted from Schuetz P et al, Arch Intern Med 2011; 171:1322-1331
# PCT & Blood Culture Results

![Graph showing PCT & Blood Culture Results](image)

### Table: Bacterial Infection Prevalence

<table>
<thead>
<tr>
<th></th>
<th>PCT &gt;0.5</th>
<th>PCT &gt; 1.35</th>
<th>PCT &gt; 2</th>
<th>PCT &gt; 5</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bacterial infection prevalence = 48.7%</strong></td>
<td></td>
<td></td>
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<tr>
<td>Sensitivity</td>
<td>1.00± 0.00</td>
<td>0.81± 0.11</td>
<td>0.67± 0.12</td>
<td>0.50± 0.13</td>
</tr>
<tr>
<td>Specificity</td>
<td>0.63± 0.12</td>
<td>0.77± 0.11</td>
<td>0.82± 0.08</td>
<td>0.90± 0.08</td>
</tr>
<tr>
<td>Positive predictive value</td>
<td>0.72± 0.06</td>
<td>0.77± 0.10</td>
<td>0.78± 0.08</td>
<td>0.83± 0.15</td>
</tr>
<tr>
<td>Negative predictive value</td>
<td>1.00± 0.00</td>
<td>0.81± 0.11</td>
<td>0.72± 0.08</td>
<td>0.65± 0.08</td>
</tr>
</tbody>
</table>

*From Bele N et al, BMC Infectious Diseases 2011; 11:224*
PCT Assay Performance

PCT: More than a Marker?

From Tavares E & Minano FJ, Clin Science 2011; 119:519-534
Calcitonin Peptide Receptors

From Christ-Crain M & Muller B, Eur Respir J 2007; 30:556-573
High-sensitivity PCT?

From Sinning CR et al, Circulation J 2011; 75:1184-1191
Multi-Marker Approach to Sepsis

From Kofoed K et al, Crit Care 2007; 11:R38
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Questions?