Procalcitonin (PCT) is the prohormone of calcitonin. In healthy hosts, calcitonin is produced in the thyroid gland. PCT is ubiquitously and uniformly expressed in multiple tissues throughout the body in response to bacterial stimuli. Elevated circulating levels of PCT are important markers in response to microbial infection. In clinical practice, it can be used to help determine the likelihood of the presence of bacterial infection and guide cessation of antibiotic therapy. PCT has excellent correlation with severity of infection (higher levels indicate more severe infection and higher mortality risk). Although, PCT is a helpful tool to differentiate between bacterial vs. viral infection, decisions regarding antimicrobial therapy should not be based solely on PCT serum concentrations alone. PCT should be placed into the clinical context of 1) site of infection, 2) likelihood of bacterial infection, 3) severity of illness and any other pertinent clinical data.

Clinical situations where PCT may be useful:

- Determination of antibiotic de-escalation and treatment duration in sepsis
- Differentiation of bacterial vs. viral lower respiratory tract infections (LRTI)
- Determination of antibiotic treatment duration in LRTI

Advantages of PCT:

- Not affected by corticosteroids
- Not affected by most autoimmune diseases
- Not affected by decreasing immune function/oncology therapy (i.e. neutropenia)
- Can use with disease modifying drugs
- Can use with other medications affecting inflammatory mediators

PCT kinetics:

- Rises rapidly 3-6 hours after bacterial infection
- Peak occurs 12-24 hours
- Half-life 24 hours (rapid decline with immune control on infection)
- Can take 24 hours of appropriate antibiotic therapy to see reduction in serum PCT
- PCT production and serum concentrations will decrease by up to 50% per day with appropriate antibiotic treatment
- If antibiotic therapy is inadequate, PCT levels will remain high

Situations where PCT elevations may be due to a non-bacterial cause:

- Acute graft vs. host disease
- Cytokine stimulating agent (OKT3, anti-lymphocyte globulins, alemtuzumab, IL-2, granulocyte transfusion)
- End stage renal disease (ESRD), hemodialysis (HD), peritoneal dialysis (PD)-see page 7 for details
- Malaria
- Massive stress: severe trauma, surgery, burns, prolonged severe cardiac shock or organ perfusion abnormalities (in absence of infection, PCT levels trend down after inciting event)
- Newborns (<48-72 hours after birth)
- Pancreatitis
- Paraneoplastic syndromes due to medullary thyroid and small cell lung cancer

**Situations where PCT can be falsely decreased:**
- Localized infections (osteomyelitis, abscess, subacute endocarditis)
- PCT is checked too early in the course of bacterial infection (i.e. acute bacterial sepsis)

**Procalcitonin levels and interpretation** *(Please see MMC Empiric Regimens guide for syndrome-based antibiotic recommendations)*

### Procalcitonin for Sepsis
(Strongly consider antibiotic initiation if high suspicion of serious bacterial infection regardless of PCT value)

<table>
<thead>
<tr>
<th>PCT value</th>
<th>Antibiotic Use Recommendation</th>
<th>Antibiotic Use Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;0.25 ng/ml</td>
<td>Strongly discouraged</td>
<td>Repeat PCT level in 24 hours if strong suspicion of early bacterial sepsis</td>
</tr>
<tr>
<td>0.25-0.49 ng/ml</td>
<td>Discouraged</td>
<td>Refer to flow chart (page 3-4) for specific guidance and PCT follow up monitoring</td>
</tr>
<tr>
<td>&gt;0.5-1.0 ng/ml</td>
<td>Encouraged</td>
<td></td>
</tr>
<tr>
<td>&gt;1.0 ng/ml</td>
<td>Strongly encouraged</td>
<td></td>
</tr>
</tbody>
</table>

### Procalcitonin for LRTI
(Pneumonia, COPD exacerbation, bronchitis)

<table>
<thead>
<tr>
<th>PCT value</th>
<th>Antibiotic Use Recommendation</th>
<th>Antibiotic Use Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;0.1 ng/ml</td>
<td>Strongly discouraged</td>
<td>Repeat PCT level in 24 hours if strong suspicion of early bacterial infection</td>
</tr>
<tr>
<td>0.1-0.24 ng/ml</td>
<td>Discouraged</td>
<td>Refer to flow chart (page 5-6) for specific guidance and PCT follow up monitoring</td>
</tr>
<tr>
<td>0.25-0.5 ng/ml</td>
<td>Encouraged</td>
<td></td>
</tr>
<tr>
<td>&gt;0.5 ng/ml</td>
<td>Strongly encouraged</td>
<td></td>
</tr>
</tbody>
</table>
Sepsis Procalcitonin (PCT) Algorithm

Patient in ER/floor with suspected sepsis (Time 0)

Activate “Sepsis Order Set”, within the order set:
- Order and start appropriate empiric antibiotic therapy ASAP
- Send serum PCT level (PCT 0) along with labs (i.e. CBC, lactate, ABG, etc.)

Is PCT level > 0.5 ng/ml?

- Yes: Continue appropriate antibiotic therapy
  - Go to “Sepsis Follow up PCT Algorithm”

- No: Strong clinical suspicion of bacterial sepsis?
  - Yes: Stop empiric antibiotics and consider alternative diagnosis
  - No: Continue appropriate antibiotic therapy and repeat PCT level after 24 hours from PCT 0 or time with morning lab if patient is on the floor (PCT 24)

Is PCT level > 0.5 ng/ml?

- Yes: Stop empiric antibiotics and consider alternative diagnosis
- No: Continue appropriate antibiotic therapy and repeat PCT level after 24 hours from PCT 0 or time with morning lab if patient is on the floor (PCT 24)

Yes

No
Sepsis Follow Up Procalcitonin (PCT) Algorithm

Patient with PCT > 0.5 mg/ml and on empiric antibiotic therapy

Repeat PCT levels daily for 3 days:
PCT 24, PCT 48, PCT 72

PCT 72 level < 0.5 ng/ml or drop by > 80% from peak or level not rising?

Yes

“3Ds” - Deescalate, Define a course, and Document in Epic:
- Complete the shortest most appropriate course of antibiotic therapy based on culture results.
- See MMC Empiric Regimens guide for syndrome-based antibiotic recommendations

No

Broaden empiric antibiotic coverage, and strongly consider ID consult. Repeat PCT level as per ID consult recommendation.

Is patient improving clinically and hemodynamically? (i.e. end organ dysfunction, lactate, etc.)

Yes

No

Use clinical judgment and consider other etiologies of shock. Contact Antimicrobial Stewardship Team as needed.
Lower Respiratory Tract Infections (LRTI) Procalcitonin (PCT) Algorithm

** If patient has severe sepsis or septic shock, please see “Sepsis Procalcitonin Protocol” **

Patient in ER/floor with suspected bacterial LRTI

Start appropriate empiric antibiotic therapy

Send serum PCT level (PCT 0) along with:
- CAP: CBC, CXR, urine Ag for Legionella/S. pneumoniae, sputum culture, influenza/RSV PCR if in season
- HAP/VAP: sputum culture, CXR or CT thorax

Is PCT level > 0.25 ng/ml?

- Yes: Continue appropriate antibiotic therapy
- No:
  - No: Go to “LRTI Follow up PCT Algorithm”
  - Yes: Strong clinical suspicion of bacterial LRTI?

Strong clinical suspicion of bacterial LRTI?

- Yes: Stop empiric antibiotics and consider nonbacterial cause of LRTI (i.e. viruses)
- No: Continue appropriate empiric antibiotic therapy and repeat PCT level after 24 hours from PCT 0 or time with morning labs (PCT 24)

IS PCT level > 0.25 ng/ml?

- Yes: Stop empiric antibiotics and consider nonbacterial cause of LRTI (i.e. viruses)
- No: Go to “LRTI Follow up PCT Algorithm”
Lower Respiratory Tract Infections (LRTI) Follow Up

Procalcitonin (PCT) Algorithm

** If patient has severe sepsis or septic shock, please see “Sepsis Follow up Procalcitonin Protocol” **

Patient with PCT > 0.25 mg/ml and on empiric antibiotic therapy

Repeat PCT level after 72 hours from PCT 0 (PCT 72)

Is PCT 72 level < 0.25 ng/ml or drop by > 80% from peak or level not rising?

Yes
- Is patient improving clinically?

No
- Broaden empiric antibiotic coverage and strongly consider ID consult. Repeat PCT level as per ID consult recommendation

Is patient improving clinically?

Yes
- “3Ds” - Deescalate, Define a course, and Document in Epic:
  - Complete the shortest most appropriate course of antibiotic therapy based on culture results.

No
- Consider nonbacterial etiologies. Contact Antimicrobial Stewardship Team as needed.
General PCT interpretation:

Sepsis:
PCT levels of >2 ng/ml predicts sepsis and levels of >10 ng/ml indicates likely septic shock. Higher PCT levels have shown to be associated with a worse prognosis, but have not generally added to well validated clinical scoring systems such as APACHE.

Bacterial Meningitis:
Levels <0.5 ng/ml make bacterial meningitis very unlikely. Most patients with bacterial meningitis have much higher PCT levels (>5 ng/ml).

Febrile children:
PCT levels >2 ng/ml make a serious infection much more likely while levels of <0.5 ng/ml make a serious infection much less likely. Values between 0.5 and 2 ng/ml are equivocal. Decisions on antibiotic administration in newborn patients should be based on clinical judgment.

PCT in ESRD patients:
PCT is known to be higher in ESRD due to decreased clearance. See table below for PCT threshold

<table>
<thead>
<tr>
<th>Renal Impairment</th>
<th>PCT value</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 5 CKD (GFR&lt;15ml/min)</td>
<td>&gt;0.5 ng/ml</td>
<td>Suspect bacterial infection</td>
</tr>
<tr>
<td>HD</td>
<td>Predialysis level &gt;0.5</td>
<td>Suspect bacterial infection</td>
</tr>
<tr>
<td>PD</td>
<td>Predialysis level &gt;0.5</td>
<td>Use clinical judgment and other infection markers</td>
</tr>
<tr>
<td>Renal transplant</td>
<td>&gt;0.14-0.22?</td>
<td>Use clinical judgment and other infection markers</td>
</tr>
</tbody>
</table>

References:

8. https://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/MedicalDevices/MedicalDevicesAdvisoryCommittee/MicrobiologyDevicesPanel/ucm515517.htm