PROCALCITONIN ALGORITHM FOR GUIDANCE IN ANTIBOTIC THERAPY DECISIONS IN RESPIRATORY TRACT INFECTIONS AND SEPSIS

OVERVIEW: Procalcitonin or PCT is an amino acid precursor of calcitonin which is produced under circumstances of inflammation including bacterial infections in various parts of the body. Levels are not elevated in PURE viral infections. It is detectable often within 3 hours of infection with maximum levels around 12-24 hours. PCT levels are proportionally elevated to the severity of infection and individuals with more severe disease often have higher levels.

PCT monitoring has been shown to decrease antibiotic exposure (duration of therapy) and antibiotic associated adverse effects in respiratory tract infections without increase in adverse outcomes and to reduce empiric antibiotic prescriptions in COPD exacerbations.

In septic patients, PCT serial monitoring protocols have been shown to reduce antibiotic treatment duration and exposure without apparent harm to patients.

GOALS:

1. Lower prescribing rates of empiric use of antibiotics in low-acuity primary care and ED patients
2. Shorter duration of therapy in moderate-and high-acuity ED and intensive care unit patients

ROLE IN THERAPY TO ASSIST IN DECISION MAKING:

- Differentiation of viral vs. bacterial respiratory tract infections
- Assist in Monitoring response to anti-infective therapy (source control) in sepsis and bacterial pneumonias
- Determining length of therapy of antibiotics.
- Monitoring by individual physicians or in conjunction with Antimicrobial Therapy Stewardship Program (ATMS).

LIMITATIONS:

PCT may be elevated in the following conditions

- **Renal insufficiency**: Baseline values, in the absence of infection, can rise to 1.5 ng/ml in ESRD (CrCl less than 30 ml/min) prior to initiation of dialysis; during regular hemodialysis, in the absence of infection, baseline values may be as high as 0.5 ng/ml.
- Procalcitonin levels may be elevated in conditions that allow “translocation” of intestinal bacteria: e.g., transiently (24 hrs) after general anesthesia, severe congestive heart failure, profound hypotension regardless of the etiology, end stage liver disease among others.
- Trauma, post-surgery, cardiac shock and burns – PCT levels should start to trend down after inciting event.
- Pancreatitis: Either due to sterile necrosis and/or secondary bacterial infection.
- Paraneoplastic production by medullary cancer of the thyroid gland or C cells of the lung.
- Immunotherapy- Anti-lymphocyte globulins, IL-2, Granulocyte transfusions, OKT3, Alemtuzumab: All stimulate an innate immune response.
- GVHD.
- May see mild elevations in some fungal infections.

**Note:** Procalcitonin levels usually do not increase in response to infection with organisms that lack a cell wall; e.g., Mycoplasma and Chlamydophila.
Adapted from Schuetz, P, et al, Role of procalcitonin in managing adult patients with respiratory tract infections, Chest 2012; 141:1063-1073. Values apply to patients with estimated CrCl of ≥ 30 ml/min. With Cr Cl < 30 ml/min, there is a gradual increase in baseline PCT levels to a maximum of 1.5 ng/ml in patients with ESRD; on HD, PCT levels can remain as high as 0.5 in absence of infection.

### A. An algorithm for Low-acuity nonpneumonic infections (ie, low risk) in primary care and emergency department (ED) settings.

<table>
<thead>
<tr>
<th>PCT result</th>
<th>Recommendation regarding use of Abx:</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;0.10 ng/ml</td>
<td>Strongly discouraged</td>
</tr>
<tr>
<td>&lt;0.25 ng/ml</td>
<td>Discouraged</td>
</tr>
<tr>
<td>≥0.25 ng/ml</td>
<td>Encouraged</td>
</tr>
<tr>
<td>&gt;0.50 ng/ml</td>
<td>Strongly encouraged</td>
</tr>
</tbody>
</table>

**Overruling the algorithm**
Consider use of antibiotics if patients are clinically unstable, have strong evidence or pneumonia, are at high risk (ie. COPD GOLD III-IV), or need hospitalization; can repeat in 4-6 hrs, neg. predictive value of two low values is 95%.

**Follow-up/other comments**
Follow-up only needed if no symptom resolution after 1 to 2 days; recheck PCT level every 1 to 2 days.

Recheck PCT level every 2-3 days; clinical re-evaluation as appropriate.

### B. Algorithm for Moderate-acuity pneumonic infections (ie, moderate risk) in hospital and ED settings.

<table>
<thead>
<tr>
<th>PCT result</th>
<th>&lt;0.10 mcg/ or drop&gt;90%</th>
<th>&lt;0.25 ng/ml or drop&gt;80%</th>
<th>≥0.25 ng/ml</th>
<th>&gt;0.50 ng/ml</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;0.25 ng/ml</td>
<td>Therapy strongly encouraged</td>
<td>Cessation of therapy strongly encouraged</td>
<td>Cessation of therapy encouraged</td>
<td>Cessation of therapy strongly discouraged</td>
</tr>
<tr>
<td>≥0.25 ng/ml</td>
<td>Cessation of therapy strongly encouraged</td>
<td>Cessation of therapy strongly discouraged</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Overruling the algorithm**
Consider alternative diagnosis, or Abx if patients are clinically unstable, are at high risk for adverse outcome (eg. PSI classes IV-V, immunosuppression), or have strong evidence of a bacterial pathogen.

**Follow-up/other comments**
Reassess patients’ condition and recheck PCT level after 6 to 12 hrs if no clinical improvement observed.

Recheck PCT level every 2 to 3 days to consider early cessation of Abx.

### C. Algorithm for High-acuity infections (ie, high risk, sepsis) in intensive care unit settings.

<table>
<thead>
<tr>
<th>PCT result</th>
<th>&lt;0.25 ng/ml</th>
<th>&lt;0.50 ng/ml</th>
<th>≥0.50 ng/ml</th>
<th>&gt;1.0 ng/ml</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;0.25 ng/ml</td>
<td>Therapy strongly discouraged</td>
<td>Cessation of Abx strongly encouraged</td>
<td>Encouraged</td>
<td></td>
</tr>
<tr>
<td>≥0.50 ng/ml</td>
<td>Therapy strongly discouraged</td>
<td>Cessation of Abx strongly discouraged</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Empirical antibiotic therapy recommended in all patients with clinical suspicion of infection**

**Overruling the algorithm**
Consider alternative diagnosis, reassess patients’ condition and recheck PCT level every 1-2 days.

Reassess patients’ condition and recheck PCT level every 1-2 days to consider cessation of Abx.

**Follow-up evaluation every 1 to 2 days**

**Follow-up/other comments**
Clinical reevaluation as appropriate; recheck PCT every 1-2d.

A failure of PCT to fall is consistent with inadequate "source control" and should stimulate a comprehensive clinical reassessment.

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**Figure 3.** Proposed algorithms for use of procalcitonin (PCT) values to determine antibiotic treatment of infections. A: An algorithm for low-acuity nonpneumonic infections (ie, low risk) in primary care and emergency department (ED) settings. B: Algorithm for moderate-acuity pneumonic infections (ie, moderate risk) in hospital and ED settings. C: Algorithm for high-acuity infections (ie, high risk, sepsis) in intensive care unit settings. Abx indicates antibiotics; COPD: chronic obstructive pulmonary disease; GOLD: Global Initiative for Chronic Obstructive Lung Disease; PSI: pneumonia severity index.