PROCALCITONIN
A Specific Marker for Diagnosis of Bacterial Infection and Sepsis
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## Contents

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Despite advances in critical care medicine, sepsis and septic shock are leading causes of death in intensive care units (ICUs). Sepsis is the systemic inflammatory response to infections. Worldwide, there are 18 million cases of diagnosed sepsis per year – and the incidences are rising at 8 to 10 percent annually.\(^1\)

In the United States, there are approximately 2 million new annual incidence of severe sepsis with a mortality rate of approximately 22.67%. Sepsis ranks as the 10th leading cause of death, and costs over $17 billion annually.\(^2,3\)

In the developing world, an estimated 1,400 people die from sepsis each day (~511,000 each year).\(^3,4\) Patients at risk of sepsis include infants, mothers after childbirth, the elderly, those with weakened immune systems, or those who have experienced significant trauma/injury, invasive surgery, or burns.

Early diagnosis and antibacterial therapy are therefore very important for patients with infections and/or sepsis.\(^5\) Delayed diagnosis leads to progression of the disease and the need for more invasive and costly treatment.\(^6\) The conventional method to diagnose sepsis is to perform blood cultures before the initiation of antibiotic therapy. Unfortunately, blood culture tests not only takes days to complete but also have low test result sensitivity (25-42%).\(^7,8\) In some cases, clinical signs of sepsis may develop without bacteriological evidence of infection. Furthermore, negative results do not exclude the presence of infection or sepsis.\(^9,10\) Therefore, a rapid, early and reliable test for detection of bacteremia and sepsis is highly desired.

Procalcitonin (PCT), a propeptide synthesized in the C-cells of the thyroid, has been identified to be more clinically useful and superior than currently used common clinical variables and laboratory tests in the diagnosis of sepsis.\(^11\) Moreover, it has been shown to correlate with the extent and severity of microbial invasion.\(^12-16\)

Since the mid 1990s, there has been a rapid increase in the use of PCT measurements in identifying systemic bacterial infections.\(^17\) Rising PCT concentrations can be detected in plasma within 2-6 hours after infectious challenges and peak within 6-24 hours. Once an infection is under control, PCT levels decrease. This rapid response is highly specific to bacterial infections and has made PCT one of the most pertinent biomarker’s used in detecting bacterial infection or sepsis.

More recently, PCT has been used to guide the initiation and duration of antibiotic therapy, not only for septic patients but also for patients of suspected lower respiratory tract infections.
PCT is used to differentiate between viral and bacterial infections, and helps physicians decide whether or not prescribing antibiotic therapy is necessary. Antibiotic prescriptions not only impose a burden on healthcare resources but, more importantly, contribute to the worldwide problem of antimicrobial resistance. Up to 50% of antimicrobial use in the inpatient setting is unneeded or inappropriate.\textsuperscript{19}

Viruses are typically the cause of acute bronchitis, but despite this, as much as 80% of patients will be prescribed antibiotics.\textsuperscript{20} Clinical studies demonstrated that PCT-guided antibiotics stewardship can reduce the rate of antibiotics prescription by more than 40%, and can reduce the duration of hospital stay by 60%.\textsuperscript{21,22}

With proven clinical advantages over other biomarkers, PCT testing is widely used in clinical laboratories for diagnosis of bacterial infection and sepsis, as well as for making therapeutic decisions about initiation and duration of antibiotic therapy.

**PCT Testing and Guidelines: Major Western Nations**

- American guidelines for evaluation of newly diagnosed critically ill adult patients with fever recommend serum PCT levels as an adjunctive diagnostic tool for discriminating infection as the cause for fever or sepsis presentations.\textsuperscript{23}

- PCT is recommended for early sepsis diagnosis and discontinuation of antibiotic therapy by German Sepsis Guidelines\textsuperscript{24} and Surviving Sepsis Guidelines.\textsuperscript{25}

- German guidelines for the management of adult lower respiratory tract infections (LRTI) recommend PCT for antibiotic stewardship in patients with ADCOPD and community-acquired pneumonia.\textsuperscript{26}

- Recently, PCT was also included into the European Guidelines for management of adult LRTI.\textsuperscript{27}

- Agency of Healthcare Research and Quality (AHRQ) of US Department of Health and Human Services issued a comparative effectiveness review on “Procalcitonin-Guided Antibiotic Therapy” in Oct. 2012 with a conclusion stating: Procalcitonin guidance reduces antibiotic use when used to discontinue antibiotics in adult ICU patients and to initiate or discontinue antibiotics in patients with respiratory tract infections.\textsuperscript{28}
Procalcitonin (PCT) Molecule & its Kinetics

Procalcitonin (PCT) is a 116 amino acid protein with a molecular weight of approximately 13 kDa as depicted in Figure 1. The molecule is encoded by a gene called CALC-1 that is located on chromosome 11. The PCT molecule is produced in the C-cells of the thyroid, and is a precursor of calcitonin. Under normal conditions, hormonally active calcitonin is produced and secreted in the C-cells of the thyroid gland after specific intracellular proteolytic processes of the prohormone PCT (see cleave sites indicated in Figure 1), whereas, the production of PCT outside the neuroendocrine cells of the thyroid gland is suppressed in healthy individuals. Therefore, the PCT plasma level in healthy individuals is low (< 0.1 ng/ml).

However, in the presence of bacterial infection, a ubiquitous increase of CALC-1 gene expression occurs, and PCT is produced nearly in all cell systems including liver, kidney, adipose tissue and muscle, and is directly released into the blood circulation. This leads to a rapid increase of the PCT (up to 1000 ng/ml) concentration in the blood of patients with severe bacterial infection and sepsis or sepsis shock.

PCT concentrations can be detected in plasma within 2-6 hours after infectious challenges and peak within 6-24 hours. Once an infection is under control, PCT levels decrease. The kinetics of PCT in the blood after endotoxin challenge is shown in Figure 2 and compared with the kinetics of C-Reactive Protein (CRP).

Figure 1
Molecular Structure of Procalcitonin

Figure 2
Kinetics of PCT Compared to Other Inflammatory Markers Upon Infection
Advantages of PCT Over Other Inflammatory Biomarkers

The short half-life (25–30 hours in plasma) of PCT, coupled with its specificity for bacterial infections, gives it a clear advantage over the other inflammatory biomarkers, including C-reactive protein (CRP), white blood cell counting (WBC), and interleukin-6 (IL-6)¹²:

1. PCT concentration will not rise because of minor infections unless they are accompanied by systemic inflammation.

2. Viral infection only causes minimal elevation of PCT levels. Blood levels of PCT are usually below 0.25 ng/mL, whereas bacterial infection results in a rapid and sharp increase of PCT levels (PCT from 0.5 ng/mL to > 10 ng/mL). This makes the PCT test the most useful diagnostic tool in differentiating viral infection from bacterial infection.

3. PCT concentration increases at an earlier stage in infection, and PCT levels become detectable within 2-4 hours and peaks within 6-24 hours. In comparison, CRP is an acute-phase protein which reacts to relatively minor infections, and CRP levels take 12 to 24 hours to rise. It also takes a longer time to fall. In contrast, PCT levels decrease rapidly when the infection is controlled by the immune system and supported by antibiotic therapy.

4. PCT levels correlate with the extent and severity of infection and has prognostic implications, namely predicting the course of disease and the risk for mortality in critically ill patients.¹³⁻¹⁶

In a clinical study¹², Muller et al. from the Division of Medical Intensive Care, University Hospitals, Basel, Switzerland compared the effectiveness of PCT as a marker for diagnosis of sepsis of patients in a medical ICU with other known inflammatory biomarkers including C-reactive protein (CRP), interleukin-6 (IL-6), and lactate. In a receiver operating characteristic curve (ROC) analysis, as shown in Figure 3, serum concentrations of PCT were found to be the most reliable laboratory variable for the diagnosis of sepsis as compared with CRP, IL-6, and lactate (p < .01, for each comparison). PCT concentrations of >1 ng/mL had a sensitivity of 89% and a specificity of 94% for the diagnosis of sepsis.

Figure 3
PCT is a Better Biomarker Than Other Conventional Inflammatory Markers
Where PCT May Be Useful

- Diagnosis, risk stratification, and monitoring of sepsis and septic shock
- Differentiation of bacterial verses viral respiratory tract infection
- Determination of antibiotic treatment length in respiratory infections
- Monitoring response to antibacterial therapy
- Diagnosis of systemic secondary infection: post-surgery, post-organ transplant, and in severe burns, multi-organ failure, and severe trauma
- Diagnosis of bacteremia and sepsis in adults and children (including neonates)
- Differentiating bacterial verses viral meningitis
- Diagnosis of renal involvement in pediatric urinary tract infections
- Diagnosis of bacterial infection in neutropenic patients
- Diagnosis of septic arthritis
A number of randomized trials have been performed evaluating the utility of PCT levels in guiding antibiotic therapy. Three separate systematic reviews/meta-analyses summaries showed a decrease in antimicrobial exposure of 19-38% without increases in mortality, length of hospital stay, or relapsed/persistent infection.\textsuperscript{41-43} Most studies in sepsis have evaluated using PCT to discontinue antibiotics although one large trial did use PCT levels to assist in the decision to initiate treatment.\textsuperscript{44}

At the present time, PCT has been demonstrated to be more clinically useful than commonly used clinical variables and laboratory tests in the diagnosis of sepsis. A clinical study conducted by The University of Geneva Hospitals, Geneva, Switzerland assessed the diagnostic value of procalcitonin (PCT), IL-6, and IL-8 as standard measurements in identifying critically ill patients with sepsis.\textsuperscript{36} Figure 4 shows that by adding PCT results to the routine value-based model, the AUC value increased from 0.77 to 0.94. At a cutoff of 1.1 ng/ml, PCT yielded a sensitivity of 97% and a specificity of 78% to differentiate patients with SIRS from those with sepsis.\textsuperscript{36}

Moreover, it has been shown that PCT values are correlated with the extent and severity of microbial invasion.\textsuperscript{12-16} In a clinical study led by Dr. Stephan Harbarth at The University of Geneva Hospitals, Geneva, Switzerland where 78 adult ICU patients were enrolled including; 18 SIRS, 14 sepsis, 21 severe sepsis, and 25 septic shock\textsuperscript{36} patients. It was found that the serum PCT levels are linearly correlated with the extent and severity of microbial infection. Figure 5 shows the dose response between serum PCT levels and the severity of sepsis.\textsuperscript{36}
It was concluded that PCT appeared to be most helpful in differentiating patients with sepsis from those with SIRS. Median PCT levels on admission (ng/ml, range) were 0.6 (0 to 5.3) for SIRS; 3.5 (0.4 to 6.7) for sepsis, 6.2 (2.2 to 85) for severe sepsis; and 21.3 (1.2 to 654) for septic shock (p<0.001).

Based upon the above information it is recommended that patients admitted to the ICU with presumed sepsis/septic shock/etc. have PCT levels analyzed on admission and that PCT measurement be repeated during the next 2 days. Decisions regarding antibiotic therapy can then be made based upon PCT dynamics, culture data, and patient specific clinical data. According to published studies, Algorithm 1 is recommended for initial diagnosis of sepsis and use of antibiotics, and Algorithm 2 is recommend for follow up and determination of the duration of antibiotic use.45-47

Interpretation should be based upon the clinical context and algorithms available on the Antimicrobial Stewardship Website. The specific comment included on the laboratory report should include the following information:

**Normal:** < 0.1 ng/mL (infants >72 hours – adults)

**Suspected Sepsis:** Strongly consider initiating antibiotics in all unstable patients.

- 0.1 – 0.5 ng/mL – Low likelihood for sepsis; Antibiotics discouraged.
- > 0.5 ng/mL – Increased likelihood sepsis; Antibiotics encouraged.
- > 2.0 ng/mL – High risk of sepsis/septic shock; Antibiotics strongly encouraged.
Algorithm 1

### Sepsis Algorithm: Initial PCT Value and Antibiotic Use

<table>
<thead>
<tr>
<th>PCT Value</th>
<th>Antibiotic Use Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;0.25 µg/L</td>
<td>Strongly Discouraged</td>
</tr>
<tr>
<td>0.25 - 0.49 µg/L</td>
<td>Discouraged</td>
</tr>
<tr>
<td>≥0.5 - 1.0 µg/L</td>
<td>Encouraged</td>
</tr>
<tr>
<td>&gt;1.0 µg/L</td>
<td>Strongly Encouraged</td>
</tr>
</tbody>
</table>

- Strongly consider antibiotic initiation in all patients with suspicion of infection
- Consider alternative diagnosis
- Repeat PCT in 6-12 hours if antibiotics not begun
- If clinically unstable, immunosuppressed or high risk consider overruling

Repeat daily for 3 days to consider early antibiotic discontinuation
See Algorithm 4

Algorithm 2

### Sepsis Algorithm: Follow Up PCT Value and Antibiotic Use

<table>
<thead>
<tr>
<th>PCT Value</th>
<th>Antibiotic Use Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;0.25 µg/L</td>
<td>Cessation Strongly Encouraged</td>
</tr>
<tr>
<td>0.25 - 0.49 µg/L</td>
<td>Cessation Encouraged</td>
</tr>
<tr>
<td>≥0.5 µg/L and decreased by &lt;80%</td>
<td>Cessation Discouraged</td>
</tr>
<tr>
<td>≥0.5 µg/L and rising or not decreasing</td>
<td>Cessation Strongly Discouraged</td>
</tr>
</tbody>
</table>

- Consider continuation if clinically unstable
- A PCT value which is rising or not declining at least 10% per day is a poor prognostic indicator and suggests infection is not controlled
- Consider expanding antibiotic coverage or further diagnostic evaluation
The evidence supporting the use of PCT assisting clinicians in antibiotic management of LRTI including; pneumonia, exacerbations of chronic bronchitis, and other assorted lower respiratory tract infections is very strong. A meta-analysis of 8 studies with 3,431 patients found that the use of PCT in LRTI resulted in a 31% decrease in antibiotic prescriptions and a decrease in antibiotic duration of 1.3 days. In one of these studies Dr. Philipp Schuetz and his colleagues from The University Hospital Basel Switzerland at the Department of Internal Medicine conducted a clinical study to assess the diagnostic and prognostic value of PCT in the management of patients with lower respiratory tract infections (LRTI). The study utilized antibiotic stewardship based on PCT cut-off ranges, which has been successfully implemented in patients with LRTI in different clinical settings. Specific PCT cut-off ranges reflecting the setting-specific likelihood of relevant bacterial infections have been proposed using multi-level likelihood ratios and have been translated into an easy-to-use and pragmatic clinical algorithm.

Based on the specific cut-off ranges, initiation or continuation of antibiotics was discouraged at levels <0.1 µg/L or <0.25 µg/L and encouraged at levels >0.5 µg/L or >0.25 µg/L respectively. In cases in which antibiotics were withheld, clinical re-evaluation and a repeated measurement of PCT were recommended after 6–24 hours. If PCT values were increased and antibiotic therapy was initiated, repeated PCT measurements were recommended and antibiotics were discontinued using the same cut-off ranges. In patients with very high PCT values on admission (e.g. >10 µg/L), discontinuation of antibiotic therapy was encouraged if levels decreased to below 80–90% of the initial value.

Based upon this evidence, it is suggested that patients considered at risk for LRTI have their PCT value measured on admission and subsequently every 2-3 days. Interpretation of values is listed below in Algorithms 3 and 4.

The specific comment included on the laboratory report should include the following information:

- PCT levels: 0.1 – 0.25 ng/mL - Low likelihood for bacterial infection; antibiotics discouraged.
- PCT levels: > 0.25 ng/mL - Increased likelihood for bacterial infection; antibiotics encouraged.

Decisions on antibiotic use should not be based solely on PCT levels. If antibiotics are administered, then repeat PCT testing should be obtained every 2-3 days to consider early antibiotic cessation. PCT is a dynamic biomarker and most useful when trends are analyzed over time in accompaniment with other clinical data. Interpretation should be based upon clinical context and algorithms available on the Antimicrobial Stewardship Website.
Algorithm 3

**LRTI Algorithm: Initial PCT Value and Use of Antibiotics**

<table>
<thead>
<tr>
<th>PCT Value</th>
<th>Bacterial Infection Probability</th>
<th>Antibiotic Use Recommendation</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;0.1 µg/L</td>
<td>Very Unlikely</td>
<td>Strongly Discouraged</td>
<td>• Consider alternative diagnosis</td>
</tr>
<tr>
<td>≥0.1 - &lt;0.25 µg/L</td>
<td>Unlikely</td>
<td>Discouraged</td>
<td>• Repeat PCT in 6-12 hours if antibiotic treatment has not been initiated and there is no clinical improvement</td>
</tr>
<tr>
<td>≥0.25 - &lt;0.5 µg/L</td>
<td>Likely</td>
<td>Encouraged</td>
<td>• If clinically unstable, immunosuppressed or high risk consider overruling (PSI Class IV-V, CURB&gt;2, GOLD III or IV)</td>
</tr>
<tr>
<td>≥0.5 µg/L</td>
<td>Very Likely</td>
<td>Strongly Encouraged</td>
<td>Repeat every 2-3 days to consider early antibiotic cessation, See Algorithm 2</td>
</tr>
</tbody>
</table>

**Algorithm 4**

**LRTI PCT Follow Up Algorithm**

<table>
<thead>
<tr>
<th>PCT Value</th>
<th>Antibiotic Use Recommendation</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;0.1 µg/L or drop by &gt;90%</td>
<td>Cessation Strongly Encouraged</td>
<td>Consider continuing if clinically unstable</td>
</tr>
<tr>
<td>0.1 - 0.24 µg/L or drop by &gt;80%</td>
<td>Cessation Encouraged</td>
<td></td>
</tr>
<tr>
<td>≥0.25 - 0.5 µg/L</td>
<td>Cessation Discouraged</td>
<td></td>
</tr>
<tr>
<td>&gt;0.5 µg/L</td>
<td>Cessation Strongly Discouraged</td>
<td></td>
</tr>
</tbody>
</table>

If PCT rising or not adequately decreasing consider possible treatment failure and evaluate for need for expanding antibiotic coverage or further diagnostic evaluation.
As the septic infection prognosis improves, PCT reliably returns to values below 0.5 ng/mL, with a half-life of 24 hours. With this in consideration, in-vitro determinations of PCT can be used to monitor the course and prognosis of life-threatening systemic bacterial infections and to tailor therapeutic interventions more efficiently as shown in Figure 6. This has been demonstrated for the monitoring of patients with ventilator-associated pneumonia (VAP).
A simple PCT test can help primary care physicians decide which patients suffering from a respiratory tract infection will benefit from a course of antibiotics.

Until now, deciding whether antibiotics are needed for treating a respiratory tract infection seemed less systematic and more reactionary. Doctors are taught to prescribe antibiotics on the basis of clinical features such as pus in the sputum or high fever, which point to the presence of a bacterial pathogen. However, basing this decision on clinical judgment alone is not always easy. As PCT testing has become more available to clinical laboratories, clinical practices for primary care physicians have improved significantly. A simple PCT test can help primary care physicians to distinguish between a viral and a bacterial infection, and to make decisive decisions with greater accuracy in consideration of initiating antibiotic therapy.

Antibiotic prescriptions not only impose a burden on healthcare resources but also contribute to the worldwide problem of rapidly growing antimicrobial resistance. A study published in the European Respiratory Journal in 2010 found that including a new diagnostic marker PCT in a therapeutic strategy reduces antibiotic prescription rates by more than 40%.22

In a clinical study, Dr. Nobre Vandack et al. from School of Medicine, University of Geneva, Switzerland tested the hypothesis that an algorithm based on serial measurements of PCT allows reduction in the duration of antibiotic therapy compared with empirical rules, and does not result in more adverse outcomes in patients with severe sepsis and septic shock.21

The study found that PCT guided patients had 3.5-day shorter median duration of antibiotic therapy for the first episode of infection than non-PCT guided control subjects. It was also found that there was a 2-day shorter intensive care unit stay for patients guided with PCT testing than that for non-PCT guided control subjects.

The study results suggested that a protocol based on serial PCT measurement allows reducing antibiotic treatment duration and exposure in patients with severe sepsis and septic shock without apparent harm. Figure 7 shows the comparison of antibiotic therapy duration between a PCT guided group and non-PCT guided control group.21, 56 Figure 8 shows the reduction of duration of antibiotic therapy for patients in ICU.21, 56 (All figures are provided for illustration purposes only.)
Figure 7
Effectiveness of PCT-Guided Management in Reducing the Duration of Antibiotic Therapy for Patients of Sepsis

Figure 8
Effect of PCT-Guided Management in Patients With Sepsis on ICU Length of Stay
In healthy people, plasma PCT concentrations are found to be below 0.05 µg/L, (others reported to be below 0.1 µg/L) but PCT concentrations can increase up to 1,000 µg/L in patients with sepsis, severe sepsis or septic shock. PCT levels are usually low in viral infections. A person’s immune response may vary in concentration regarding the production of PCT in the presence of nosocomial infection. Therefore, clinicians should use the PCT results in conjunction with the patient’s clinical situation. The reference ranges (Figure 9) and the PCT result interpretations are listed in Table 1. Table 2 highlights the differential diagnosis of lower respiratory tract infection. (All figures are provided for illustration purposes only.)
<table>
<thead>
<tr>
<th>PCT (ng/mL)</th>
<th>Possible Clinical Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 0.1</td>
<td>Normal Values</td>
</tr>
<tr>
<td></td>
<td>Infection very unlikely; systemic inflammatory response unlikely</td>
</tr>
<tr>
<td>&lt; 0.5</td>
<td>On first day of ICU admission this indicates a low risk for progression to severe sepsis and/or septic shock, sepsis unlikely</td>
</tr>
<tr>
<td></td>
<td>Local inflammation or infection is possible: systemic inflammatory response unlikely</td>
</tr>
<tr>
<td>≥ 0.5 and &lt; 2.0</td>
<td>Severe trauma, major surgery or cardiogenic shock, If the patient has a proven infection it is likely sepsis</td>
</tr>
<tr>
<td></td>
<td>Moderate risk for progression to severe systemic infection (severe sepsis)</td>
</tr>
<tr>
<td></td>
<td>The patient should be closely monitored both clinically and by re-assessing PCT within 6-24 hours</td>
</tr>
<tr>
<td>≥ 2.0 and &lt; 10</td>
<td>Very likely to be sepsis</td>
</tr>
<tr>
<td></td>
<td>On first day of ICU admission this indicates a high risk for progression to severe sepsis and/or septic shock</td>
</tr>
<tr>
<td>≥ 10</td>
<td>Severe sepsis or septic shock</td>
</tr>
<tr>
<td></td>
<td>Organ dysfunction</td>
</tr>
<tr>
<td></td>
<td>High risk of death</td>
</tr>
</tbody>
</table>

Table 2  Differential diagnosis of Lower Respiratory Tract Infections (LRTI)^49

<table>
<thead>
<tr>
<th>Plasma PCT Concentration</th>
<th>Possible Clinical Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCT &lt;0.1 µg/L</td>
<td>Use of antibiotics strongly discouraged, also in the presence of impaired pulmonary reserve in AECOPD</td>
</tr>
<tr>
<td>PCT ≥0.1 - &lt;0.25 µg/L</td>
<td>The use of antibiotics is discouraged</td>
</tr>
<tr>
<td>Bacterial infection unlikely</td>
<td></td>
</tr>
<tr>
<td>PCT ≥0.25 - &lt;0.5 µg/L</td>
<td>Advice to initiate antimicrobial therapy</td>
</tr>
<tr>
<td>Bacterial infection is possible</td>
<td></td>
</tr>
<tr>
<td>PCT ≥0.5 µg/L</td>
<td>Advice to initiate antimicrobial therapy</td>
</tr>
<tr>
<td>Suggests the presence of bacterial infection</td>
<td></td>
</tr>
</tbody>
</table>
False positive and false negative results can occur with any test. Clinical context should guide interpretation of PCT results. The following is a list of situations where the PCT elevations may be due to a non-bacterial cause:

- Newborns (<48-72 hours; after 72 interpret levels as usual)
- Massive stress (severe trauma, surgery, cardiac shock, burns)
- Treatment of agents which stimulate cytokines (OKT3, anti-lymphocyte globulins, alemtuzumab, IL-2, granulocyte transfusion)
- Malaria and some fungal infections
- Prolonged, severe cardiogenic shock or organ perfusion abnormalities
- Some forms of vasculitis and acute graft vs. host disease
- Paraneoplastic syndromes due to medullary thyroid and small cell lung cancer
- Significantly compromised renal function, especially ESRD/hemodialysis

In absence of infection PCT levels trend down after inciting event.

The following conditions need to be considered when PCT results are interpreted:

1. Interpret in the clinical context of the patient. For example: patients with septic shock should not have antibiotics withheld based on normal PCT. Patients with mild elevations in PCT who exhibit no signs or symptoms of infection may be closely monitored.

2. Serial measurements are preferred and provide more useful information. For example: patients very early in the onset of infection may have a normal PCT value. Patients who have persistently normal PCT levels are unlikely to have bacterial infection.

3. Consider the dynamics of the disease. For example: patients with severe trauma without infection should have PCT levels which steadily decline. Also, a patient with rising PCT suggests there is a lack of control of the infection. Patients with severe infections (bacteremic pneumonia) will generally take longer for PCT levels to normalize.

4. Be aware of conditions which may affect PCT levels. For example: a patient with peritonitis who returns to the OR for a washout is expected to have a transitory increase in PCT value post-operatively but should continue to trend down if the infection is adequately controlled.
3. Sarah M Pernan, Munish Goyal and David F Galeski., Initial Emergency Department Diagnosis and Management of Adult Patients with Severe Sepsis and Septic Shock. Scandinavian Journal of Trauma, Resuscitation and Emergency Medicine, 2012; 20:41
6. Kumar, A et al., Duration of hypotension prior to initiation of effective antimicrobial therapy is the critical determinant of survival in human septic shock. Crit Care Med., 2006; 34(6):1593
18. Philipp Schnetz, Mirjam Christ-Crain, Beat Müller Procalcitonin and Other Biomarkers for the Assessment of Disease Severity and Guidance of Treatment in Bacterial Infections. ADVANCES IN SEPSIS., 2008; Vol 6 No 3 page 82-89
24. Reinhardt K et al., Prevention, diagnosis, therapy and follow-up care of sepsis: 1st revision of S-2k guidelines of the German Sepsis Society (Deutsche Sepsis Gesellschaft e.V. (DSG)) and the German Interdisciplinary Association of Intensive Care and Emergency Medicine (Deutsche Interdisziplinäre Vereinigung für Intensiv- und Notfallmedizin (DIVI)). Ger Med Sci., 2010; 8: Doc14
25. Dellinger R., 41st Critical Care Congress (SCCM), Houston, Tx; 2012
27. Woodhead M et al., Guidelines for the management of adult lower respiratory tract infections. Clin Microbiol Infect., 2011; 17 (Suppl. 6): E1-E59

*Diazyme PCT assay is not used for differentiating non-infection caused inflammation from infection induced inflammation.

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