

Diagnosis of Sepsis- is Procalcitonin (PCT) the ideal marker? (...continued)

Table 1: PCT reference range and interpretation of serum PCT levels in adults and children

<0.05 ng/ml	Normal range, no systemic inflammatory response
<0.5 ng/ml	Measurable but clinically insignificant PCT response. This may indicate minor or no significant systemic inflammatory response, local inflammation, chronic inflammatory processes, autoimmune diseases, viral infections, and mild to moderate localized bacterial infections.
0.5- 2 ng/ml	Significant but moderate systemic inflammatory response. Possible bacterial infection, but non bacterial causes (severe trauma, major surgery, burns, cardiogenic shock, small cell lung cancer, medullary C-cell carcinoma invasive fungal infections, Plasmodium falciparum malaria, etc) have to be excluded. In the case of proven infection, diagnosis of sepsis is positive. Moderate risk for progression to severe systemic sepsis. Patient should be closely monitored both clinically and by re-assessing PCT within 6-24 hours. Serial monitoring recommended for response to therapy
≥ 2 - < 10 ng/ml	Severe systemic inflammatory response, most likely to bacterial infection (sepsis) unless other non-infective causes are known. High risk for progression to severe systemic sepsis. In case of persisting elevated values > 4 days, need to reconsider therapy and is associated with poor outcome. Continue serial PCT monitoring.
PCT ≥ 10 ng/ml	Systemic inflammatory response almost exclusively due to severe bacterial sepsis or septic shock. Frequently associated with organ dysfunction, and high risk of lethal outcome.

Note: It is important however to note that PCT levels below 0.5 ng/ml do not always indicate absence of bacterial infection, and falsely low PCT levels in the presence of bacterial infection may occur in the early course of localised infections and sub-acute infectious endo-carditis.

Also, if the PCT measurement is done very early following bacterial challenge (usually <6 hours), these values may still be low. In these cases, PCT should be re-assessed 6-24 hours later.

When to use PCT?

- PCT should be measured in patients in whom sepsis is suspected, in patients presenting with SIRS criteria, perfusion abnormalities, unexplained shock or organ dysfunction, those who are at risk of developing such complications post surgery or if a patient is intubated or ventilated.
- PCT increases 3h after bacterial infection, reaching maximum values after 6-12 hours.
- Serum or plasma only may be used. For monitoring of patients the same sample matrix should always be used.
- PCT values measured in patient samples of arterial blood are 4% higher than in samples from venous blood.
- PCT for monitoring patients should be done at a minimum of once per day. A 50% reduction of PCT concentration per day over several days is an indication of success of therapeutic intervention (surgery, antibiotic treatment). Persisting high or further increasing PCT levels are indicative of an uncontrolled infectious process justifying a re-assessment of therapeutic strategy.
- With no infectious complication, post-surgery PCT levels will be low or there will be a reduction of increased PCT levels during the succeeding days by 50% per day to reach normal values after a couple of days. With infectious complications post-surgery, persisting increased PCT levels or newly increasing PCT levels indicate infectious complications.

Pregnancy and neonates

PCT should be measured where sepsis is suspected due to clinical signs indicating a risk of fetomaternal infection and in neonates with tachypnoea, bradycardia, tachycardia, arterial hypotension, hepatosplenomegaly, delayed recapillarisation, decreased muscular tension, seizures, irritability, moaning, increased oxygen demand, deteriorated blood gases and apnoea.

It should also be done if fetomaternal risk factors are present i.e. premature rupture of the amniotic sac, diabetes mellitus, HIV-infection or immune-suppression; and at any time after delivery when sepsis is suspected according to clinical picture and/or risk factors.

PCT is physiologically elevated during the first 2 days of life, therefore period specific reference ranges should be used (Table 2). PCT levels above these ranges indicate early neonatal sepsis and may indicate the need for early antibiotic treatment. Low PCT levels indicate that systemic bacterial infection is not likely.

Table 2: PCT reference ranges for neonates of 0-48 hours of age

Age in hours	PCT (ng/ml)
0-6	2
6-12	8
12-18	15
18-30	21
30-36	15
36-42	8
42-48	2

In neonates onset and course of sepsis can be very rapid. In such cases induction of PCT may not have been taken place yet. For confirmation of diagnosis of clinically diagnosed sepsis at a later time point, re-measurement is then recommended.

In all cases where PCT levels are low or only slightly elevated (< 2 ng/ml) and clinical status of the patient is not definitely assessed, repeat measurements of PCT should be performed every 6-12 hours during the first two days of life, and within 12-24 hours in newborns older than 2 days.

PCT measurements should also be repeated to monitor the response of a septic newborn to therapy. Persistently elevated or further increasing levels of PCT above reference ranges indicate an ongoing infectious process and poor prognosis. This should alert the clinician to initiate further infection work-up and/or adaptation of the sepsis therapy.

A significant continuous decrease of PCT level by 30-50% per day is a sign of therapeutic response.

Current status regarding the 'ideal' marker of sepsis

Novel markers of infection include Interleukin 6 (IL-6) and other interleukins that form part of the inflammation cascade, Gamma interferon (IFN γ), tumor necrosis factor α (TNF α) and PCT discussed above. Because of the enormous number of factors influencing the inflammatory process, none can adequately be regarded as a "stand-alone" marker of infection. The more we try to find a "golden bullet" to diagnose infection as a cause of sepsis, the more evidence we find that we have to rely on our clinical skills in conjunction with serial measurements of all these markers.

Recommended References:

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