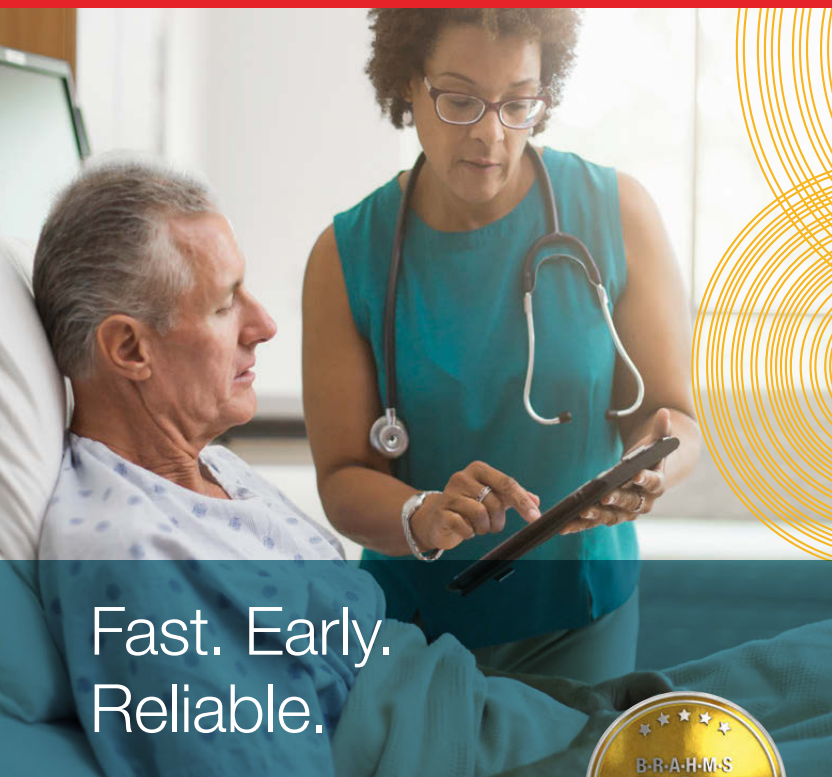


thermo scientific



Fast. Early.
Reliable.

B·R·A·H·M·S PCT: Sepsis
diagnosis and monitoring



Procalcitonin (PCT) – Clinical Guide

ThermoFisher
S C I E N T I F I C

This guide was created with the help of

Jérôme Pugin

Hôpitaux Universitaires de Genève, Switzerland

Michael Meisner

Städtisches Krankenhaus Dresden-Neustadt, Germany

Alain Léon

Hôpital Universitaire de Reims, France

Dominique Gendrel

Hôpital Necker, Paris, France

Anna Fernández López

Hospital Arnau de Vilanova, Lleida, Spain

We are grateful for their valuable contribution and critical discussion for practical use of PCT in the clinical setting.

14th edition: February 2017

Disclaimer

This guide is intended to give clinicians an additional orientation for practical utilisation of PCT measurement and interpretation of results. However, this does not relieve the clinician of the obligation to verify the interpretation of the laboratory result based on his or her clinical knowledge to assess the clinical status of each individual patient and to decide on appropriate treatment.

Neither B·R·A·H·M·S GmbH nor the contributing clinicians assume any liability for any injury and/or damage to persons or property arising from the information published. Liability claims regarding damage caused by the use of any information provided, including any information which is incomplete or incorrect, will therefore be rejected.

Table of contents

Introduction	4
What is Procalcitonin (PCT)?	5
Sepsis and SIRS definition	7
Clinical use of PCT for sepsis diagnosis in adults and children	8
Clinical use of PCT for diagnosis of neonatal sepsis	15
Recommended literature	19
Current options for measurement of PCT	20
Flow-charts: Diagnosis and monitoring with PCT	22

Introduction

Early diagnosis and appropriate therapy of sepsis is a daily challenge in the emergency room and in intensive-care units. Today, various therapeutic strategies are known to improve survival in patients with sepsis, therefore, rapid and accurate diagnosis is essential.

Sepsis suffers from a lack of specific clinical symptoms and signs. Microbiological cultures require time, do not reflect the host response of systemic inflammation nor the onset of organ dysfunction, and may not be positive in sepsis patients for a number of reasons.

Among the available biomarkers for sepsis, Procalcitonin (PCT) has the highest diagnostic accuracy. PCT levels rise rapidly (within 6 – 12 hours) after an infectious insult with systemic consequences. Since the outcome in patients with sepsis can significantly be improved if adequate therapy is started early, the measurement of PCT for an early and effective diagnosis is recommended in all patients in whom sepsis and a systemic inflammatory response is suspected.

Beyond its value for the diagnosis of sepsis, PCT has also proved to be useful in monitoring the course and severity of the systemic inflammatory response. Daily changes of plasma PCT levels give an indication on the course of the disease and the prognosis of the septic patient. Persistently elevated levels of PCT are associated with poor outcome and are now viewed as a failure of therapy or the lack of appropriate clearance of source of the infection.

A large database of 20 years of medical literature and clinical experience is available for PCT. This biomarker is now widely used in many countries across the world for the diagnosis of sepsis, the evaluation of the systemic inflammatory response and patient management.

This brochure intends to provide guidance for the utilisation of PCT and to introduce PCT as a routine tool for improved diagnosis and treatment of sepsis.

What is Procalcitonin (PCT)?

PCT is the prohormone of the hormone calcitonin, but PCT and calcitonin are distinct proteins. Calcitonin is exclusively produced by C-cells of the thyroid gland in response to hormonal stimuli, whereas PCT can be produced by several cell types and many organs in response to pro-inflammatory stimuli, in particular by bacterial products.

In healthy people, plasma PCT concentrations are found to be below 0.05 µg/L*, but PCT concentrations can increase up to 1000 µg/L in patients with sepsis, severe sepsis or septic shock. Usually, PCT concentrations exceeding 0.5 µg/L are interpreted as abnormal values suggestive of a sepsis syndrome. PCT values in the range of 0.5 and 2 µg/L represent a “grey” zone with uncertainty as far as the diagnosis of sepsis is concerned. In these cases, it is recommended to repeat the measurement after 6 – 24 hours, until a specific diagnosis is identified. PCT levels above 2 µg/L are highly suggestive of an infectious process with systemic consequences. Concentrations above 10 µg/L are almost exclusively found in patients with severe sepsis or septic shock.

The induction of PCT can be caused by different stimuli both *in vitro* and *in vivo*. Bacterial endotoxins and pro-inflammatory cytokines are powerful stimuli for the production of PCT. The exact biological role of PCT remains largely unknown, however, recent experimental studies suggest that PCT may play a pathogenic role in sepsis. The PCT protein carries leukocyte chemoattractant properties and modulates the production of NO by endothelial cells.

PCT is a stable protein in plasma and blood samples. At room temperature, more than 80% of the initial concentrations can be recovered after 24 hours of storage, and >90% is recovered when the sample is kept at 4 °C. Plasma PCT has a normal half life of 25 – 30 hours, and 30 – 45 hours in patients with severe renal dysfunction.

* Please note: PCT values are given in µg/L (≙ ng/mL).

A significant elevation of plasma PCT is found during sepsis, but particularly during the early days of severe sepsis and septic shock. In patients with non-bacterial "SIRS", PCT levels are usually found to be in the lower range ($<1 \mu\text{g/L}$). However, early after multiple trauma or major surgery, in severe burns or in neonates, PCT levels can be elevated independently of an infectious process. The return to baseline is usually rapid and in these cases a second increase of PCT can be interpreted as the development of a sepsis episode. Viral infections, bacterial colonisation, localised infections, allergic disorders, autoimmune diseases, and transplant rejection do not usually induce a significant PCT response (values $<0.5 \mu\text{g/L}$).

Sepsis and SIRS definition

Definitions for the terms of “SIRS”, “sepsis”, “severe sepsis” or “septic shock” have been proposed by the ACCP/SCCM consensus conference in 1992, and are now widely used (see Table 1).

Table 1 SIRS and sepsis definition (ACCP/SCCM-criteria)

SIRS (Systemic Inflammatory Response Syndrome)	2 or more of the following criteria: <ul style="list-style-type: none">• Temperature $>38^{\circ}\text{C}$ or $<36^{\circ}\text{C}$• Heart rate >90 beats/min• Respiratory rate > 20 breaths/min or $\text{PaCO}_2 <32$ torr (<4.3 kPa)• WBC >12000 cells/mm^3, <4000 cells/mm^3, or $>10\%$ immature (band) forms
Sepsis	Documented infection together with 2 or more SIRS criteria
Severe Sepsis	Sepsis associated with organ dysfunction, including, but not limited to, lactic acidosis, oliguria, hypoxemia, coagulation disorders, or an acute alteration in mental status
Septic Shock	Sepsis with hypotension, despite adequate fluid resuscitation, along with the presence of perfusion abnormalities. Patients who are on inotropic or vasopressor agents may not be hypotensive at the time when perfusion abnormalities are detected.

Sepsis Definition – New recommendations (Year 2016)

The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3):

- **Sepsis:** Life-threatening organ dysfunction due to a dysregulated host response to infection (The term ‘severe sepsis’ has been deemed redundant and removed, as sepsis has a mortality rate of 10 percent or higher, making the condition already severe. The SIRS criteria have been removed as they are overly non-specific and of poor clinical utility. There is a strong focus on non-homeostatic host response to infection and infection without organ dysfunction is not a part of new sepsis definition.)
- **Septic Shock:** Subset of sepsis in which particularly profound circulatory, cellular, and metabolic abnormalities substantially increase mortality

Clinical use of PCT in sepsis diagnosis in adults and children

► In which patients should PCT be measured?

In patients in whom sepsis is suspected.
These are patients presenting with

- SIRS criteria,
- perfusion abnormalities or
- unexplained shock or
- organ dysfunction,

or those who are at risk of developing such complications.

► When should PCT be determined?

At the time of admission or at any time during the hospital stay, when sepsis is suspected.

► How to interpret the PCT values?

Plasma PCT is a marker of the inflammatory response of the human body to a non-viral infection. Elevated values are highly suggestive of a bacterial infection with systemic consequences. When plasma PCT values are **below 0.5 µg/L**, bacterial sepsis is not likely.

PCT levels **above 2 µg/L** are associated with an increased likelihood of the presence of bacterial sepsis, unless other conditions for induction are known (see “When increased PCT levels may not be related to infection”, page 11).

When plasma PCT levels are measured **between 0.5 and 2 µg/L**, a systemic infection cannot be excluded. PCT levels should be remeasured within 6 – 24 hours.

A guideline for the interpretation of PCT serum and plasma concentrations is provided in table 2 (see page 14).

► When should PCT measurements be repeated?

- **Within 6 – 24 hours**
for differential diagnosis of sepsis, if concentrations are only slightly elevated (<2 µg/L) and/or if the patient presents with clinical signs symptomatic of sepsis.
- **Every 24 hours**
 - in patients who are at risk of developing sepsis and organ dysfunction.
 - in patients with sepsis to evaluate the response to therapy.

► How to use the information for clinical decision making?

- PCT <0.5 µg/L

In patients presenting with SIRS criteria, signs of organ failure or unexplained hypotension, PCT values below 0.5 µg/L usually rule out a bacterial systemic infection. This should lead the clinician to look for causes other than sepsis responsible for the patient's condition.

Important: PCT levels below 0.5 µg/L do not per se exclude an infection, because localised infections (without systemic signs) may be associated with such low levels (in this case lower cut-offs for exclusion of infection would be appropriate). Also if the PCT measurement is done very early after the bacterial infection process has started (usually <6 hours), these levels may still be low. In this case, PCT should be reassessed 6 – 24 hours later.

- PCT 0.5 – 2 µg/L

In patients with suspected sepsis, and when PCT levels are only slightly elevated (between 0.5 and 2 µg/L), the patient should be closely monitored both clinically and by re-assessing PCT levels for as long as systemic infection cannot be excluded, or can be confirmed by microbiological techniques.

- Persistently elevated PCT >2 µg/L

Persistently elevated daily plasma PCT concentrations >2 µg/L are an indication that the infectious process is not under control. Such a condition is associated with a poor prognosis and could trigger modifications in patient care, additional investigations, or even justify changes in treatment.

Flow-charts illustrating the use of PCT are provided on pages 22 – 23.

► Why increased PCT levels may not always be related to systemic bacterial infection?

There are a few situations described where PCT can be elevated by non-bacterial causes. These include, but are not limited to

- neonates <48 hours of life (physiological elevation)
- the first days after a major trauma, major surgical intervention, severe burns, treatment with OKT3 antibodies and other drugs stimulating the release of pro-inflammatory cytokines
- patients with invasive fungal infections or acute attacks of plasmodium falciparum malaria
- patients with prolonged or severe cardiogenic shock or prolonged severe organ perfusion anomalies
- patients with severe liver cirrhosis and acute or chronic viral hepatitis
- patients with small cell lung cancer or medullary C-cell carcinoma of the thyroid.

► Why low PCT levels do not automatically exclude the presence of bacterial infection?

Such low levels may be obtained, e.g., during the early course of infections, in localized infections and in subacute endocarditis.

Therefore, follow-up and re-evaluation of PCT in clinical suspicion of infection is pivotal.

The PCT measuring technique should be chosen dependent on intended clinical use.

Clinical examples

► Case 1

A 57-year-old male patient, undergoing cardiac surgery (CABG) with an uncomplicated course.

On day 7 after surgery, the patient presents with mild hypotension, a pale skin, sweating, mild hypothermia and loss of appetite. Because of hypotension, the patient is transferred to the ICU. Chest X-ray and echocardiography reveal normal findings: no pericardial effusion, no impaired ejection function, no pneumonia or pleural effusion.

The next day, the PCT value is 2.5 µg/L. Volume resuscitation improves hypotension and the patient is scheduled to return to the normal ward.

Due to the increased PCT value, which is inappropriately high for this patient, a CT-scan is performed, and shows a sternum osteomyelitis. The diagnosis is confirmed during a surgical procedure. A local drainage is performed and the patient recovered within 10 days.

The PCT was used as an aid for guidance in relation to diagnosis.

► Case 2

A 76-year-old woman admitted to the intensive care unit after peritoneal surgery for perforated sigmoiditis that had been developing for more than 24 hours. The operation consisted of a sigmoidectomy with a double-barrel colostomy and peritoneal lavage.

On admission, haemodynamic stability was dependent on volemic expansion and the administration of catecholamines. The PCT was 60 µg/L.

On day 6, while the patient was on antibiotics, the hemodynamic situation was unstable with regard to catecholamines and artificial ventilation; the patient was febrile, the PCT was 80 µg/L. The abdominal computer tomography confirmed the persistence of intra-peritoneal effusion.

On day 7, another laparotomy and peritoneal lavage were carried out within the context of a “second look”.

On day 9, the patient was weaned off the catecholamines, while it was also planned to take her off the ventilation. The PCT was 30 µg/L.

On day 12, the value was less than 10 µg/L.

The PCT was used as a re-evaluation aid within the context of the diagnostic and therapeutic strategy.

▶ **Case 3**

A 73-year-old man admitted to the intensive care unit via the emergency department due to unstable angina.

The temperature was 38.5 °C, the leucocytes were 11500/mm³ and the thoracic X-ray revealed bilateral pulmonary condensation. The echocardiography indicated a decrease in the ejection fraction from the left ventricle at 35%.

On admission, the PCT was <0.5 µg/L.

The treatment involved a mixture of antibiotics, inotropes and diuretics.

After 24 hours, the clinical condition had improved considerably, the thoracic X-ray was considered normal, the PCT of <0.5 µg/L allowed to exclude diagnosis of progressive bacterial bronchopneumopathy.

The PCT was used as a diagnostic aid.

Table 2 PCT reference ranges and interpretation of PCT serum or plasma levels

Normal values: <0.05 µg/L

Healthy individuals (age ≥3 days of life; normal value for neonates 0 – 48 hours of age see table 3, page 18)

Normal range for PCT (95% CI).
No systemic inflammatory response.

PCT <0.5 µg/L

Measurable, but clinically insignificant PCT response.

Minor or no significant systemic inflammatory response.
Local inflammation and local infection are possible.

PCT ≥0.5 – <2.0 µg/L

Significant, but moderate systemic inflammatory response. Infection is possible, but various conditions are known to induce PCT as well (severe trauma, major surgery, cardiogenic shock).

In case of proven infection:
Diagnosis of sepsis positive.
Follow up of PCT levels recommended (6 – 24 hours).

PCT ≥2 – <10 µg/L

Severe systemic inflammatory response, most likely due to infection (sepsis), unless other causes are known (see above).

High risk for developing organ dysfunction. In case of persistently elevated values >4 days: reconsider sepsis therapy. Poor outcome. Daily measurement of PCT levels recommended.

PCT ≥10 µg/L

Important systemic inflammatory response almost exclusively due to severe bacterial sepsis or septic shock.

Frequently associated with organ dysfunction. High risk of lethal outcome. Daily measurement of PCT levels recommended.

Clinical use of PCT for diagnosis of neonatal sepsis

► In which patients should PCT be measured?

In every case where sepsis is suspected due to clinical signs indicating a risk of feto-maternal infection or of nosocomial systemic infection.

Clinical signs of the neonate: tachypnea, bradycardia, tachycardia, arterial hypotension, hepatosplenomegaly, delayed recapillarisation, decreased muscular tension, seizures, irritability, moaning, increased oxygen demand, deteriorated blood gases, apnea, etc.

Feto-maternal risk factors: premature rupture of the amniotic sac, diabetes mellitus, HIV-infection, immunosuppression.

► When should PCT be determined?

At any time after delivery when sepsis is suspected according to clinical picture and/or risk factors.

► How to interpret the clinical values?

During the first 2 days of life, PCT levels are physiologically elevated, so that for this period specific reference ranges apply for each time point. PCT levels above these ranges indicate an early neonatal sepsis. (For reference ranges see page 18.)

Beginning with the 3rd day of life, the reference values for newborns are the same as for adults; thus, as in older patients in cases where PCT values are **below 0.5 µg/L**, a systemic infection is not very likely to be present.

At PCT values **above 2 µg/L** a systemic infection is very likely if other causes for PCT-induction have been excluded (see “When increased PCT levels may not be related to infection”, page 11).

At PCT levels **between 0.5 and 2 µg/L** systemic infection cannot be excluded and where clinical signs of sepsis are present, close patient monitoring is required. This should include clinical assessment and repetitive measurement of PCT levels which may increase within a couple of hours after the infection becomes systemic.

The presence of a systemic infection may be indicated already if PCT concentration persists on a level between 1 and 2 µg/L over several days.

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

► When should the PCT measurement be repeated?

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

PCT measurement 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, whereas a significant continuous decrease of PCT level by 30–50% per day is a sign of an improving condition of the patient.

► How to use the information for clinical decision making?

- During the first 2 days of life

Elevated PCT levels above the reference range strongly predict the presence of a systemic bacterial infection and represent an indication for early antibiotic treatment. Low PCT values (below reference values) indicate that systemic bacterial infection is not likely.

- From the 3rd day of life

PCT may be indicated as a useful surveillance marker in newborns at risk for severe nosocomial infections, and in those presenting with clinical signs of sepsis. As long as systemic infection cannot be excluded, newborns at risk for becoming septic should be closely monitored, both clinically and for the course of PCT development, in order to adapt the therapeutic approach.

PCT cut-offs for neonates

In healthy neonates, plasma PCT concentrations increase gradually after birth, reaching peak values at about 24 hours of age and then decrease to normal values below 0.5 µg/L by 48 – 72 hours of age.

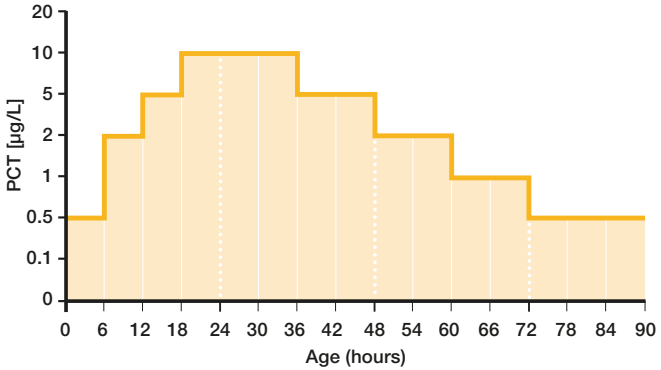





Figure 1 Age adjusted PCT cut-off values in newborns

Recommended literature

- Bouadma L et al.**, Use of procalcitonin to reduce patients' exposure to antibiotics in intensive care units (PRORATA trial): a multicentre randomised controlled trial, *Lancet* 2010, 375(9713):463-74
- Brunckhorst FM et al.**, Procalcitonin for early diagnosis and differentiation of SIRS, sepsis, severe sepsis, and septic shock, *Intensive Care Med* 2000, 26(Suppl 2): S148-152
- Charles PE et al.**, Procalcitonin kinetics within the first days of sepsis: relationship with the appropriateness of antibiotic therapy and the outcome, *Critical Care* 2009, 13:R38
- Chiesa C et al.**, Reliability of procalcitonin concentrations for the diagnosis of sepsis in critically ill neonates, *Clin Infect Dis* (1998), 26: 664-672
- Chiesa C et al.**, Procalcitonin as a marker of nosocomial infections in the neonatal intensive care unit, *Intensive Care Med* 2000, 26(Suppl. 2): 1175-7
- Chiesa C et al.**, C-reactive protein, interleukin-6, and procalcitonin in the immediate postnatal period: Influence of illness severity, risk status, antenatal and perinatal complications, and infection, *Clin Chem* 2003, 49(1): 60-68
- Falcoz PE et al.**, Usefulness of procalcitonin in the early detection of infection after thoracic surgery, *Eur J Cardiothorac Surg* 2005, 27(6): 1074-8
- Fernández López A et al.**, Procalcitonin in pediatric emergency departments for the early diagnosis of invasive bacterial infections in febrile infants: results of a multicenter study and utility of a rapid qualitative test for this marker, *Pediatr Infect Dis J* 2003, 22(10)
- Galetto Lacour A et al.**, Procalcitonin, IL-6, IL-8, IL-1 receptor antagonist and C-reactive protein as identifiers of serious bacterial infections with fever without localising signs, *Eur J Pediatr* 2001, 160: 95-100
- Gendrel D et al.**, Comparison of procalcitonin with C-reactive protein, interleukin 6 and interferon alpha for differentiation of bacterial vs viral infections, *Pediatr Infect Dis* 1999, 18: 875-881
- Gervais A et al.**, Usefulness of procalcitonin and C-reactive protein rapid tests for the management of children with urinary tract infection, *Pediatr Infect Dis J* 2001, 20: 507-512
- de Jong et al.**, Efficacy and safety of procalcitonin guidance in reducing the duration of antibiotic treatment in critically ill patients: a randomised, controlled, open-label trial, *Lancet Infect Dis* 2016; 3099: 1-9
- Han YY et al.**, Procalcitonin is persistently increased among children with poor outcome from bacterial sepsis, *Pediatr Crit Care Med* 2003, 4(1): 21-25
- Harbarth S et al.**, Diagnostic value of procalcitonin, interleukin-6 and interleukin-8 in critically ill patients admitted with suspected sepsis, *Am J Respir Crit Care Med* 2001, 164: 396-402
- Joram N et al.**, Umbilical cord blood procalcitonin and C reactive protein concentrations as markers for early diagnosis of very early onset neonatal infection, *Arch Dis Child Fetal Neonatal Ed* 2006, 91: F65-F66
- Kopterides P et al.**, Procalcitonin-guided algorithms of antibiotic therapy in the intensive care unit: a systematic review and meta-analysis of randomized controlled trials, *Crit Care Med* 2010, 38: 1-13
- Luyt CE et al.**, Procalcitonin Kinetics as a Prognostic Marker of Ventilator-associated Pneumonia, *Am J Respir Crit Care Med* 2005 Jan 1, 171(1): 48-53
- Meisner M et al.**, Postoperative plasma concentrations of procalcitonin after different types of surgery, *Intensive Care Med* 1998, 24: 680-684
- Meisner M.** Procalcitonin – Biochemistry and Clinical Diagnosis, ISBN 978-3-8374-1241-3 (UK, USA), ISBN 978-1-84815-163-5 (Germany), UNI-MED, Bremen 2010
- Müller B et al.**, Calcitonin precursors are reliable markers of sepsis in a medical intensive care unit, *Crit Care Med* 2000, 28(4): 977-983
- Müller B et al.**, Ubiquitous expression of the calcitonin-1 Gene in multiple tissues in response to sepsis, *J Clin Endocrinol Metab* 2001, 96(1): 396-404
- Schütz P**, Christ-Crain M and Müller B, Procalcitonin and Other Biomarkers for the Assessment of Disease Severity and Guidance of Treatment in Bacterial Infections, *Advances in Sepsis* 2008, 6(3): 82-89
- Simon L et al.**, Serum procalcitonin and C-reactive protein levels as markers of bacterial infection: a systematic review and meta-analysis, *Clin Infect Dis* 2004 Jul 15, 39(2): 206-17
- Singer M et al.**, The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3), *JAMA* 2016; 315(8): 801-810. doi:10.1001/jama.2016.0287
- Stocker M et al.**, Use of procalcitonin-guided decision-making to shorten antibiotic therapy in suspected neonatal early-onset sepsis: prospective randomized intervention trial, *Neonatology* 2010; 97: 165-174
- Uzzan B et al.**, Procalcitonin as a diagnostic test for sepsis in critically ill adults and after surgery or trauma: A systematic review and meta-analysis, *Crit Care Med* 2006 May, 17: 1-8
- van Rossum AM et al.**, Procalcitonin as an early marker of infection in neonates and children, *Lancet Infect Dis* 2004 Oct; 4(10): 620-30

Available PCT assays

Thermo Scientific™ B·R·A·H·M·S PCT™ assays

	Assay name/Characteristics	Measurement range
	B·R·A·H·M·S PCT™ sensitive KRYPTOR™	
	<ul style="list-style-type: none">• High-sensitive, quantitative automated assay• B·R·A·H·M·S KRYPTOR™ system required• Incubation time: 19 min	0.02 – 50 µg/L (direct measurement range) up to 1000 µg/L (extended measurement range)
	B·R·A·H·M·S PCT™ LIA*	
	<ul style="list-style-type: none">• Quantitative manual assay• Luminometer required• Incubation time: 1 h	0.1 – 500 µg/L
	B·R·A·H·M·S PCT™-Q	
	<ul style="list-style-type: none">• Semi-quantitative, rapid assay• No instrument required• Incubation time: 30 min	0.5 – 10 µg/L








* In the literature referred as LUMitest® PCT (former product name).

 Automated sensitive assay

 Manual assay

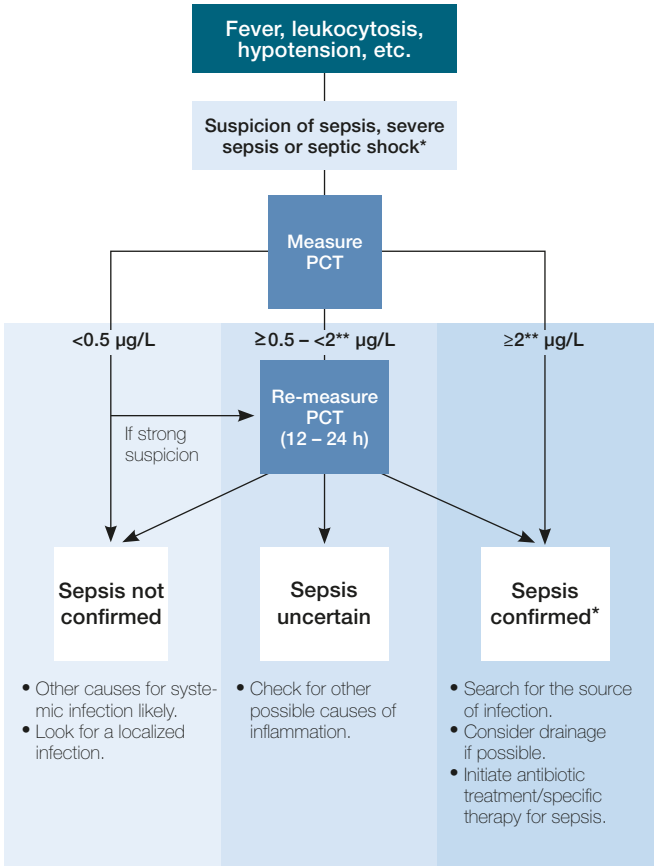
 Point of care test

B·R·A·H·M·S PCT™ assays on other IVD platforms

Assay name/Characteristics	Measurement range
 ADVIA Centaur® B·R·A·H·M·S PCT™ <ul style="list-style-type: none"> • Quantitative automated assay • ADVIA Centaur® system required • Time to result: <ul style="list-style-type: none"> - 26 min (Centaur® CP) - 29 min (Centaur® XP) 	0.02 – 75 µg/L
 ARCHITECT® B·R·A·H·M·S PCT™ <ul style="list-style-type: none"> • Quantitative automated assay • Architect® system required • Incubation time: 22 min 	0.02 – 100 µg/L
 ELECSYS® B·R·A·H·M·S PCT™ <ul style="list-style-type: none"> • Quantitative automated assay • Elecsys® or Cobas® system required • Incubation time: 18 min 	0.02 – 100 µg/L
 LIAISON® B·R·A·H·M·S PCT™ II GEN <ul style="list-style-type: none"> • Quantitative automated assay • LIAISON® system required • Incubation time: 16 min 	0.02 – 100 µg/L
 Lumipulse® G B·R·A·H·M·S PCT™ <ul style="list-style-type: none"> • Quantitative automated assay • Lumipulse® G system required • Incubation time: 30 min 	0.02 – 100 µg/L
 Samsung IB B·R·A·H·M·S PCT™ <ul style="list-style-type: none"> • Quantitative automated POC* assay • Samsung LABGEOIB10 system required • Incubation time: 20 min 	0.08 – 10 µg/L
 VIDAS® B·R·A·H·M·S PCT™ <ul style="list-style-type: none"> • Quantitative automated assay • VIDAS® system required • Incubation time: 20 min 	0.05 – 200 µg/L

* POC = Point of Care

Sepsis diagnosis with PCT

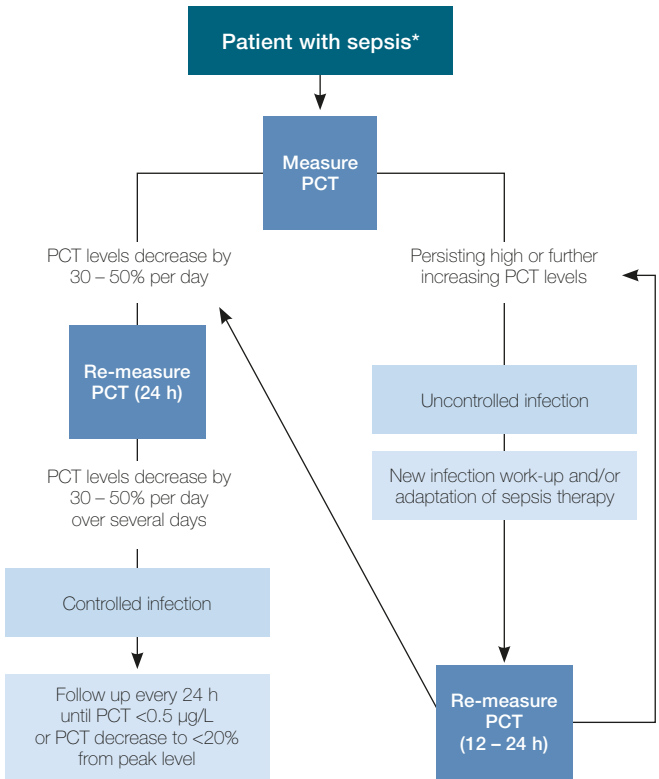


* In the absence of non-infectious causes for induction of PCT

(see page 11 "When increased PCT levels may not be related to infection")

** The cut-off of 2 $\mu\text{g/L}$ given in the scheme is for orientational purpose only. Each clinical department should adapt it according to its patient population. (Cut-off may be at PCT level higher or lower than 2 $\mu\text{g/L}$, depending on patient's background, e.g. major surgery (higher) or patient in medical ICU (lower).)

Monitoring patients with PCT



* Here: sepsis = sepsis, severe sepsis or septic shock

Clinical Diagnostics	Thermo Fisher Scientific B·R·A·H·M·S GmbH Neuendorfstr. 25 16761 Hennigsdorf Germany	+49 (0)3302 883 0 +49 (0)3302 883 100 fax info.pct@thermofisher.com www.thermoscientific.com/brahms
-----------------------------	--	--

Find out more at thermoscientific.com/procalcitonin

Thermo Fisher Scientific products are distributed worldwide; not all intended uses and applications mentioned in this printing are registered in every country. This indication for use is not cleared in the USA. The booklet is not valid for distribution in the USA.

© 2017 Thermo Fisher Scientific Inc. All rights reserved. B·R·A·H·M·S PCT and all other trademarks are the property of Thermo Fisher Scientific and its subsidiaries unless otherwise specified. ADVIA Centaur is a registered and protected trademark belonging to Siemens Healthcare Diagnostics. ADVIA Centaur B·R·A·H·M·S PCT is a product of Siemens Healthcare Diagnostics licensed from Thermo Fisher Scientific. ARCHITECT is a registered and protected trademark belonging to Abbott or one of its subsidiaries. ARCHITECT B·R·A·H·M·S PCT is a product of Abbott licensed from Thermo Fisher Scientific. Elecsys is a registered and protected trademark belonging to Roche or one of its subsidiaries. Elecsys B·R·A·H·M·S PCT is a product of Roche licensed from Thermo Fisher Scientific. LIAISON is a registered and protected trademark belonging to DiaSorin S.p.A. LIAISON B·R·A·H·M·S PCT II GEN is a product of DiaSorin S.p.A. licensed from Thermo Fisher Scientific. Lumipulse is a registered trademark of Fujirebio Inc. in Japan and in other countries. Lumipulse G B·R·A·H·M·S PCT is a product of Fujirebio Inc. licensed from Thermo Fisher Scientific. Samsung IB B·R·A·H·M·S PCT is a product of Samsung C&T Corporation licensed from Thermo Fisher Scientific. VIDAS is a registered trademark of bioMérieux S.A. or one of its subsidiaries. VIDAS B·R·A·H·M·S PCT is a product of bioMérieux licensed from Thermo Fisher Scientific. KRYPTOR is a registered trademark of CIS bio international, licensed for use by B·R·A·H·M·S GmbH, a part of Thermo Fisher Scientific.

The manufacture and/or use of this product is covered by one or more of the following patents: EP2028493, DE19903336, EP1026506, US7723492, JP5215250, JP5219939, EP2174143, JP5059943, JP5185460, EP2293076, EP2084545, CN101553733, HK1137807, JP5663531, JP5058263, US8465941, EP2548031, CN102939542, HK1180392, JP5681219, US8748195, EP2320237, CN102081101, HK1156690, JP5722587, US8383332, EP2545379, CN102822675, JP5798133, RU2580278.