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Reducing Antibiotic Exposure

B·R·A·H·M·S PCT (Procalcitonin) sensitive KRYPTOR

An Effective Tool to Aid in Antibiotic Stewardship and Assessing the Risk of Bacterial Infection

ThermoFisher SCIENTIFIC

B·R·A·H·M·S PCT (Procalcitonin)

Expanded Insight for Reducing Antibiotic Use

The Centers for Disease Control and Prevention (CDC) estimates that at least 30% of antibiotics prescribed in the United States are unnecessary.[1] The use of antibiotics is believed to be a primary cause of the spread of antibiotic-resistant bacteria.[2]

Thermo Scientific™ B·R·A·H·M·S PCT™ sensitive KRYPTOR™ provides clinicians in the emergency department, intensive care unit and hospital wards with a sensitive, specific STAT biomarker that provides newly expanded insight to aid clinicians in making decisions regarding antibiotic therapy, as well as differential diagnosis of bacterial infection and sepsis.

1/3 of Antibiotic Prescriptions are Unnecessary[1]

The Surviving Sepsis Campaign International Guidelines for Management of Severe Sepsis and Septic Shock (2016) suggests that PCT measurements can be used to support shortening the duration of antimicrobial therapy in sepsis patients.[3]

B·R·A·H·M·S PCT: The Quality Standard

When using PCT assays to support clinical decisions, quality and experience count. Clinicians worldwide rely on B·R·A·H·M·S PCT quality to make confident patient care decisions due to:

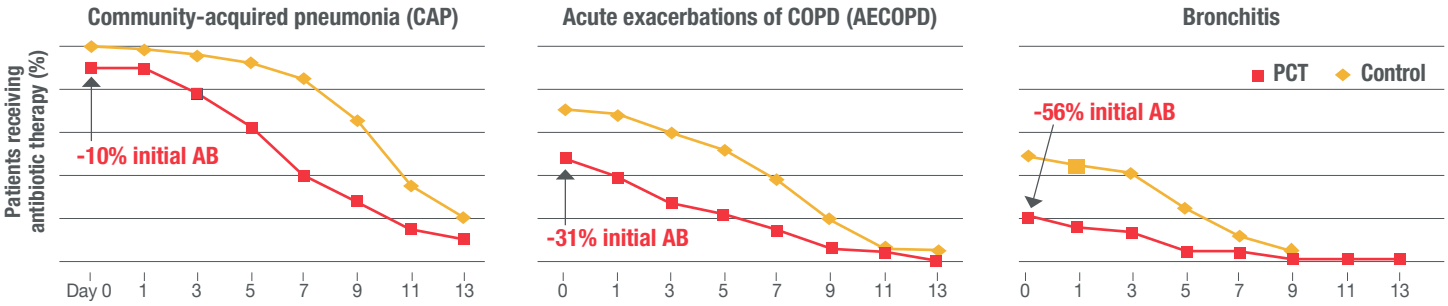
- **Evidence:** 4,500+ publications in both the U.S. and Europe demonstrate the clinical utility of PCT.
- **Experience:** B·R·A·H·M·S PCT has been in clinical use since 1996.
- **Precision:** Demonstrated high concordance at clinically relevant cut-offs.
- **Standardization:** Standardized, comparable clinical cut-offs, independent of platform.
- **Adoption:** PCT is included in antibiotic stewardship guidelines issued by IDSA (Infectious Disease Society of America) and the Surviving Sepsis Campaign.[3,4]

Insight for Initiating Antibiotics

As many as 75% of patients with acute respiratory-tract infections are treated with antibiotics, despite a mainly viral cause for these infections.[5] B·R·A·H·M·S PCT aids clinicians in the emergency room or inpatient hospital settings in determining whether antibiotics are appropriate for patients with suspected or confirmed lower respiratory tract infections (LRTI), defined as community-acquired pneumonia (CAP), acute bronchitis, and acute exacerbation of chronic obstructive pulmonary disease (AECOPD).

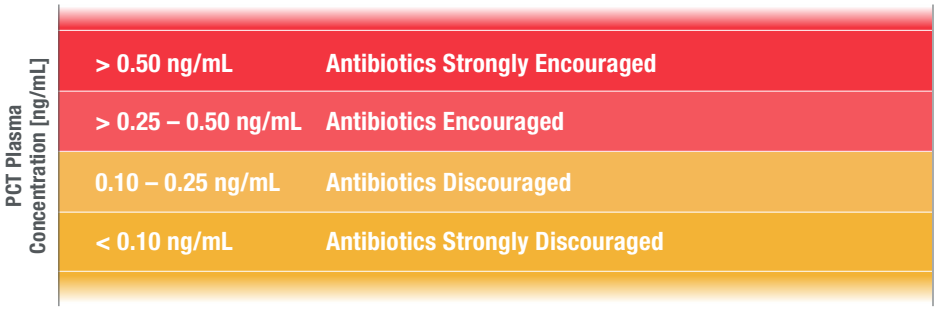
B·R·A·H·M·S PCT has been shown to reduce antibiotic prescription rate and exposure duration in LRTI.

Duration of antibiotic exposure and antibiotic prescription rates were significantly reduced in the PCT group in comparison to the standard of care group for community-acquired pneumonia (CAP) (n=925), acute exacerbations of COPD (n=228) and bronchitis (n=151) in the ProHosp trial.[5]



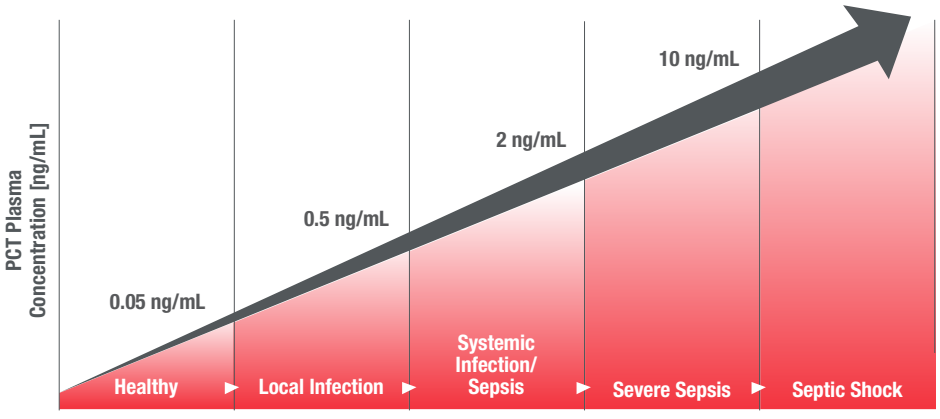
Guiding Antibiotic Therapy Decisions for LRTI

PCT Cut-offs



Aiding Differential Diagnosis

As a sensitive and specific biomarker of the inflammatory response to bacterial infection[6] B·R·A·H·M·S PCT aids clinicians in determining a critically ill patient's risk of progression to severe sepsis and septic shock.



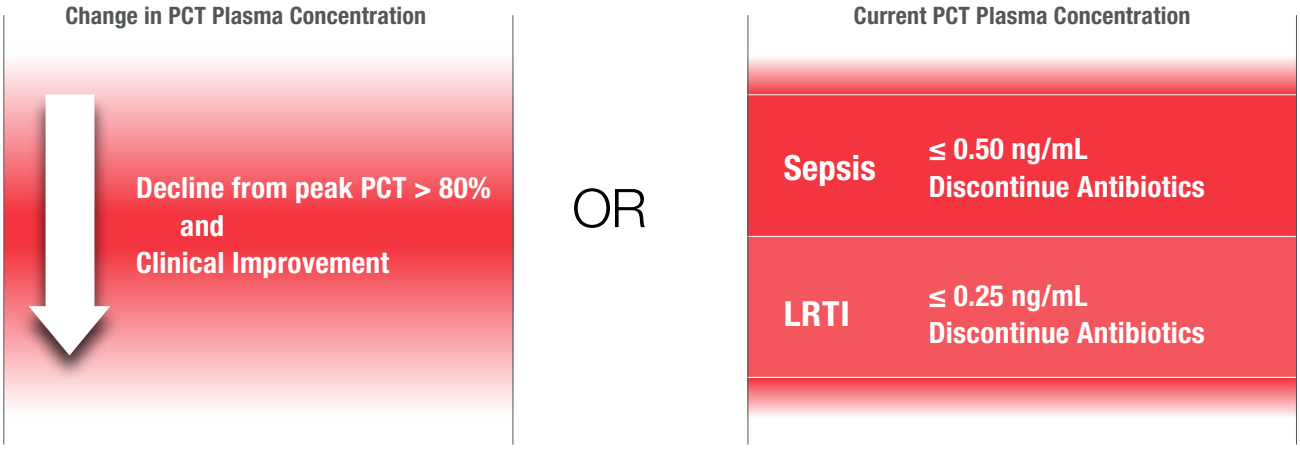
7,8,9,10

The short turn around time of B·R·A·H·M·S PCT sensitive KRYPTOR assay supports clinicians' decisions.

Decisions regarding antibiotic therapy should NOT be based solely on B·R·A·H·M·S PCT concentrations, but only in conjunction with clinical signs and symptoms and other diagnostic evidence.

Insight for Safely Discontinuing Antibiotics

Paired with clinical assessment, B·R·A·H·M·S PCT also aids decisions about whether to discontinue antibiotic therapy for patients with LRTI, or with suspected or confirmed sepsis.

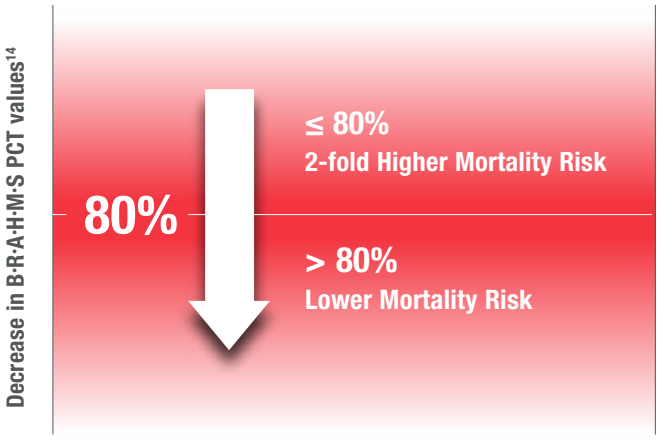


PCT-supported therapy has been shown to reduce inpatient antibiotic exposure by ↓ 35% for LRTI patients[5] ↓ 23% for critically ill ICU patients[11] without negative effects for mortality or length of stay.[5,11-21]

Aiding Assessment of Mortality Risk

Following ICU admission, evaluating serial B·R·A·H·M·S PCT measurements over consecutive days aids in assessing the host response to antibiotic therapy and the risk of all-cause mortality. When the infection is controlled, PCT will decline daily.[22] If the PCT level has not declined, the patient and therapy should be reassessed.

A baseline PCT measurement greater than 2.0 ng/mL on Day 0 is an additional factor to consider when evaluating PCT measurements on subsequent days.[23]



Decisions regarding antibiotic therapy should NOT be based solely on B·R·A·H·M·S PCT concentrations, but only in conjunction with clinical signs and symptoms and other diagnostic evidence.

Understanding PCT Kinetics

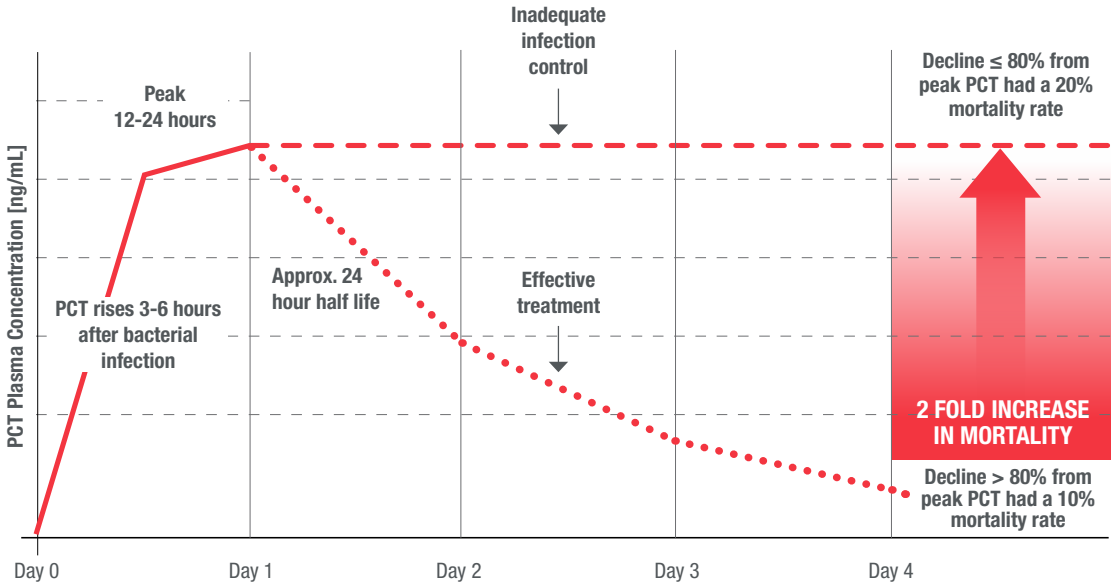
The utility of B·R·A·H·M·S PCT as a tool for assessing the risk of bacterial infection stems from its unique kinetics in response to severe bacterial infection.

PCT levels increase 3-6 hours after bacterial insult and return to normal as the infection is resolved.[7,8,9]

- **Approximate half-life of 24 hours**
- **High specificity and sensitivity for bacterial infection**
- **Indicator for disease severity and treatment response**

PCT Kinetics

PCT values rise in relation to sepsis severity, providing clinicians with a valuable tool for assessing patients suspected of sepsis.



The U.S. Multicenter MOSES Study[23]

The ability of B·R·A·H·M·S PCT to support mortality risk assessment over multiple days was demonstrated in a major multi-site U.S. study. The Procalcitonin Monitoring Sepsis Study (MOSES) included 858 adult patients with sepsis recruited across 13 investigational sites in the U.S. Key findings of the study included:

- The change of PCT over time aids in assessing the cumulative 28-day risk of all-cause mortality for patients diagnosed with severe sepsis or septic shock.
- A 2-fold increased risk of death is seen for patients showing a decrease in PCT less than or equal to 80 percent during the first four days following diagnosis of severe sepsis or septic shock compared to those who experienced a decrease in PCT greater than 80 percent. Mortality was the same for men and women.
- The initial PCT level (≤ 2.0 ng/mL or > 2.0 ng/mL) provided important additional information about the mortality risk when evaluating the patient's clinical course with PCT measurements on subsequent days.

Comparing PCT to Other Biomarkers

The sensitivity and specificity of B·R·A·H·M·S PCT to the host response to severe bacterial infection, together with its rapid rise after an infectious insult, offer clinical advantages that complement existing biomarkers.

Lactate

Lactate (lactic acid) is produced due to inadequate tissue perfusion, a defining parameter of late sepsis. However, lactate is not specific for bacterial infection. Clinical conditions including microcirculatory dysfunction, shunting, regional blood flow maldistribution, exaggerated aerobic or anaerobic glycolysis, hypovolemia or arterial hypotension can increase lactate levels.[24] In addition, lactate does not rise until late in the course of sepsis.[25]

For patients evaluated in the ED for a suspected infection, the combination of lactate and B·R·A·H·M·S PCT measurements, together with clinical data and vital signs, provide complementary information for risk stratification.[26]

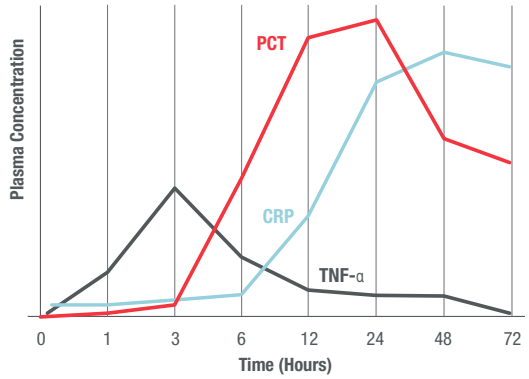
C-Reactive Protein (CRP)

CRP secretion is triggered by cytokines (IL-6, IL-1, TNF-α) in response to acute or chronic inflammation associated with bacterial, viral, or fungal infection, and conditions such as obesity and tissue injury. It has no correlation to Sepsis-related Organ Failure Assessment (SOFA) score and its kinetics are slow, peaking 36 to 50 hours after causal challenge.[27,28,29] In recent years, CRP has not been recommended because of its lack of specificity for systemic bacterial infection and its suppression when corticosteroids are used.[10]

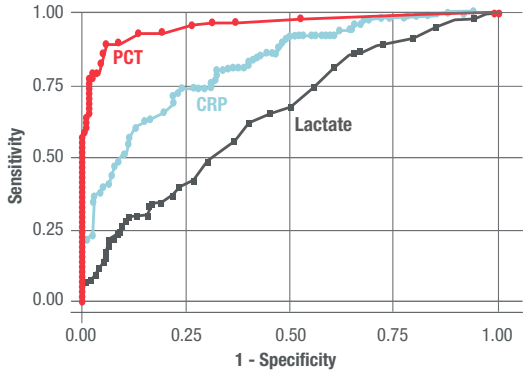
Blood Cultures

Only 30–50% of patients with a clinical diagnosis of severe sepsis or septic shock have positive blood cultures.[30] One U.S. study found that more than 50% of patients diagnosed with sepsis had normal white blood cell count (WBC).[31] Challenges with relying on blood cultures for assessing systemic infection include the delay for response, decreased sensitivity in patients already on antibiotics, and potential for false-positive results due to sample contamination.

The unique kinetics of PCT make it a valuable complement to other biomarkers of sepsis.[32]



PCT's sensitivity and specificity as a marker of systemic bacterial infection make it a valuable complement to traditional biomarkers used in sepsis risk assessment.[8]



Important Considerations When Interpreting PCT Results

Increased B·R·A·H·M·S PCT levels may not always be related to systemic bacterial infection.[9,33,34,35] They may also be associated with:

- Injuries including major trauma, burns and heat stroke
- Acute medical conditions such as biliary pancreatitis, chemical pneumonitis, viral hepatitis and/or decompensated severe cirrhosis (Child-Pugh Class 3), prolonged or severe cardiogenic shock, prolonged severe organ perfusion anomalies, and post-cardiac arrest
- Unusual infectious diseases including invasive fungal infections and acute plasmodium falciparum malaria
- Active medullary C-cell carcinoma, small cell lung carcinoma, and bronchial carcinoid
- Following interventions such as surgery with extracorporeal circulation, treatment with drugs stimulating release of pro-inflammatory cytokines or resulting in anaphylaxis, peritoneal or hemodialysis
- Neonates during the first three days of life. B·R·A·H·M·S PCT values should be interpreted using a specific nomogram during the first 72 hours following birth

B·R·A·H·M·S PCT results should be evaluated in context of all laboratory findings and the total clinical status of the patient. In cases where the laboratory results do not agree with the clinical picture or history, additional tests should be performed.

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