



Informing Antibiotic Decisions in Patients with LRTI

B·R·A·H·M·S PCT

A valuable tool for aiding antibiotic stewardship



Understanding Procalcitonin (PCT)

The utility of B-R-A-H-M-S PCT™ as a tool for informing antibiotic therapy decisions stems from its unique kinetics in response to systemic bacterial infection.

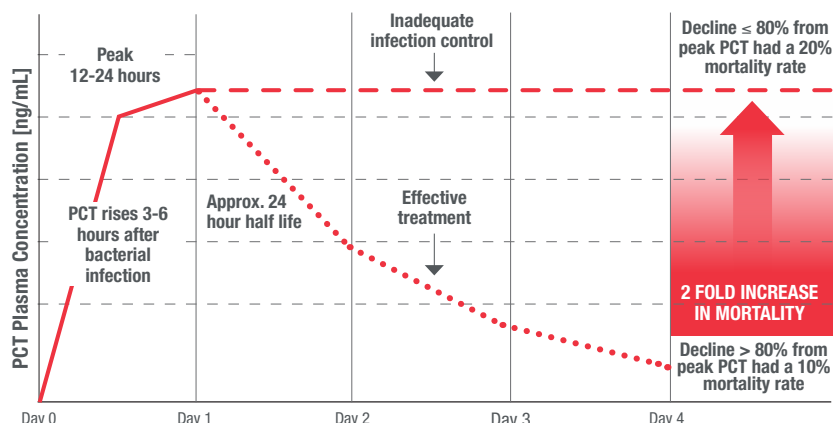
PCT is an immunoactive molecule involved in the body's immune response to bacterial infection. PCT can be produced by several cell types and organs in response to pro-inflammatory stimuli by bacteria.¹ In healthy individuals, PCT concentrations are less than 0.1 ng/mL.² PCT levels increase 2 to 3 hours after bacterial insult and peak within 12 to 24 hours.^{3,4,5} The magnitude of the increase in PCT concentration correlates with the severity of the bacterial infection.⁴

As the bacterial infection is controlled with appropriate antibiotic therapy, PCT levels decrease by up to 50% per day.^{6,7} If therapy is inadequate, bacteria will continue to stimulate PCT production and levels will remain high.

During viral infections, PCT production is attenuated by interferon- γ released during the host response to the virus, and thus will not rise as in bacterial infections.

PCT Kinetics Highlights

- **Levels increase 2-3 hours after bacterial insult and return to normal as the infection is resolved.**^{3,4,5}
- **Approximate half-life of 24 hours**
- **High specificity and sensitivity for bacterial infection**
- **Indicator for disease severity and treatment response**



Comparing PCT to Other Biomarkers

Lactate

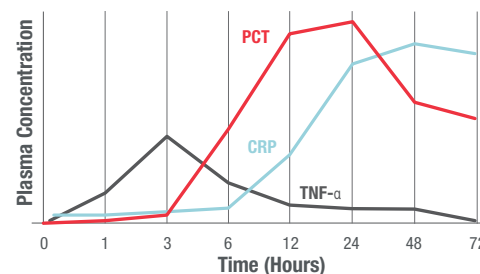
A marker of inadequate tissue perfusion, lactate (lactic acid) is not specific for bacterial infection; a wide range of clinical conditions can increase lactate levels.⁵ Lactate does not rise until late in the course of systemic bacterial infection.⁸ For patients evaluated in the ED for a suspected infection, the combination of lactate and PCT measurements, together with clinical data and vital signs, provide complementary information for risk stratification.⁹

C-Reactive Protein (CRP)

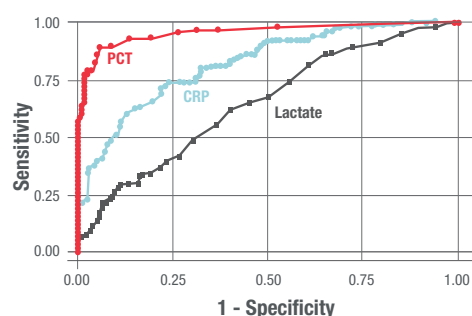
CRP is triggered in response to inflammation associated with bacterial, viral, or fungal infection, and conditions such as obesity and tissue injury. It has no correlation to Sepsis-related Organ Failure Assessment (SOFA) score and its kinetics are slow, peaking 36 to 50 hours after causal challenge.^{10,11,12} CRP has not been recommended because of its lack of specificity for systemic bacterial infection and its suppression when corticosteroids are used.¹³

Blood Cultures

Only 30% – 50% of patients with a clinical diagnosis of severe sepsis or septic shock have positive blood cultures.¹⁴ 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 systemic infection and sepsis.¹⁵



PCT has the best AUC as a marker of systemic bacterial infection, compared to CRP and Lactate.¹⁶

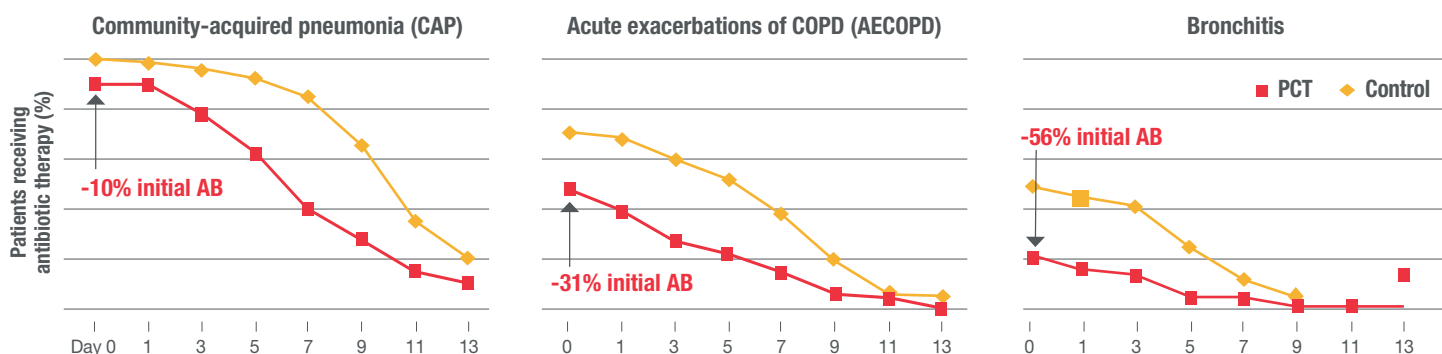
LRTI: Is it Bacterial or Viral?

As many as 75% of patients with acute respiratory-tract infections are treated with antibiotics, despite a mainly viral cause for these infections.¹⁷

B·R·A·H·M·S PCT has been shown to aid 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).^{18, 19-27}

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.¹⁸



Fewer antibiotics were initiated in the PCT-guided group.

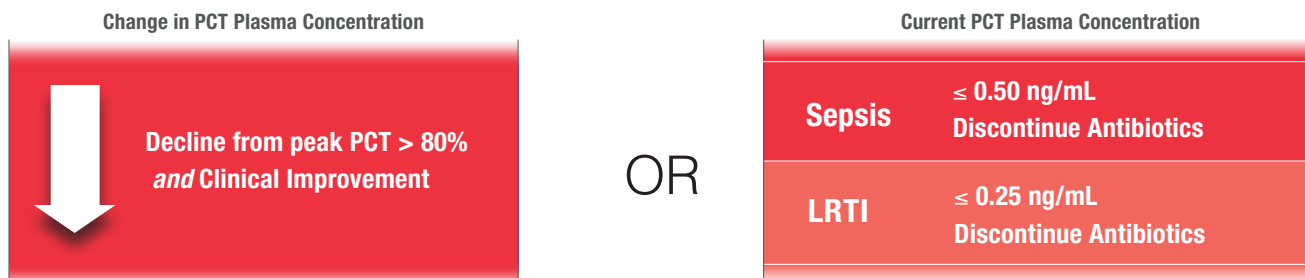
Guiding Antibiotic Therapy Decisions for LRTI

PCT Thresholds

PCT Plasma Concentration [ng/mL]	> 0.50 ng/mL	Antibiotics Strongly Encouraged
	> 0.25 – 0.50 ng/mL	Antibiotics Encouraged
	0.10 – 0.25 ng/mL	Antibiotics Discouraged
	< 0.10 ng/mL	Antibiotics Strongly Discouraged

Insight for Safely Discontinuing Antibiotic Therapy

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



PCT-guided therapy has been shown to aid antibiotic stewardship for LRTI:^{18,21,22,24-34}

19.2% reduction in relative antibiotic initiation

38% reduction in antibiotic exposure (3.6 days) for inpatients

51% reduction in antibiotic exposure for ED patients not admitted

No negative effects for mortality or length of stay

Clinical Challenge: Is it Heart Failure or LRTI?

In patients with a history of congestive heart failure (CHF) presenting with acute respiratory symptoms, differentiating acute heart failure (AHF) from LRTI is challenging due to overlapping clinical presentation and radiological findings.³⁵

- **18% of hospitalizations for acute heart failure are caused by infections.**³⁶
- **Infection (e.g. pneumonia, infective endocarditis, sepsis) is a known factor in triggering AHF.**³¹
- **Pneumonia is independently associated with higher in-hospital mortality for hospitalized heart failure patients (Odds Ratio 1.60).**³⁸
- **AHF precipitated by ACS or infection is independently associated with higher 90-day risk of death (Hazard Ratio 1.51).**³⁹

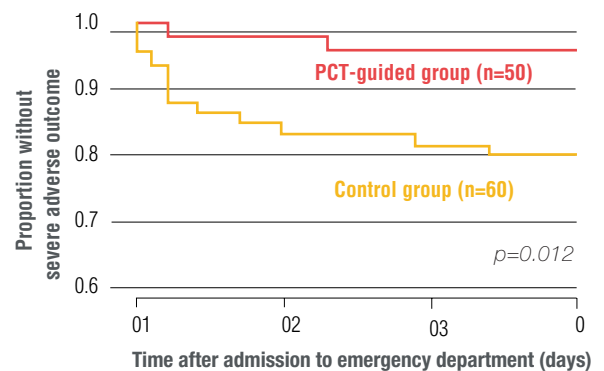
PCT-guided Antibiotic Therapy in HF Patients with Suspected Pneumonia

Secondary analysis of 233 patients with a history of CHF, formerly included in a multicenter, randomized-controlled trial, to compare antibiotic guidance with and without PCT algorithm.⁴⁰

In 110 patients with low initial PCT value (<0.25 ng/mL):

- **30-day adverse outcome was significantly decreased (-16%) in PCT-guided group.**
- **Antibiotic exposure was significantly reduced (-2.8 days) in PCT-guided group.**

For patients presenting with dyspnea, PCT >0.25ng/mL indicates bacterial infection that requires antibiotic treatment.⁴⁰



Time to the first adverse outcome by randomization group in patients with low initial PCT levels (<0.25 ng/mL); adverse outcome included all-cause mortality or ICU admission.⁴⁰

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. Decisions regarding antibiotic therapy should not be based solely on procalcitonin concentrations.



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:** 4000+ 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.
- **Standardization:** Standardized clinical cut-offs, independent of platform.
- **Precision:** Demonstrated high clinical equivalence to the B·R·A·H·M·S PCT reference.
- **Adoption:** PCT is included in antibiotic stewardship guidelines issued by IDSA (Infectious Disease Society of America) and the Surviving Sepsis Campaign.^{41,42}

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