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Procalcitonin Testing and Antibiotic Stewardship

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Antibiotic Resistance

- >2 million people in the United States are infected with antibiotic-resistant bacteria each year (CDC)[1]
- One cause of antibiotic resistance is the over-prescribing of antibiotics
  - Viral infections
  - Inflammatory conditions without infectious origin
  - Continuing antibiotics after original infection has cleared
- At least 30% of all antibiotics prescribed are unnecessary[2]
- Unnecessary antibiotic use puts patients at a greater risk for antibiotic-related adverse drug events (ADEs): [1]
  - Emergence of antimicrobial resistance, selection of pathogens, drug side effects and allergic reactions.

Antibiotic stewardship

Monitor and improve the way antibiotics are prescribed and used

Early and accurate detection of pathogens

Initiation of optimal therapy

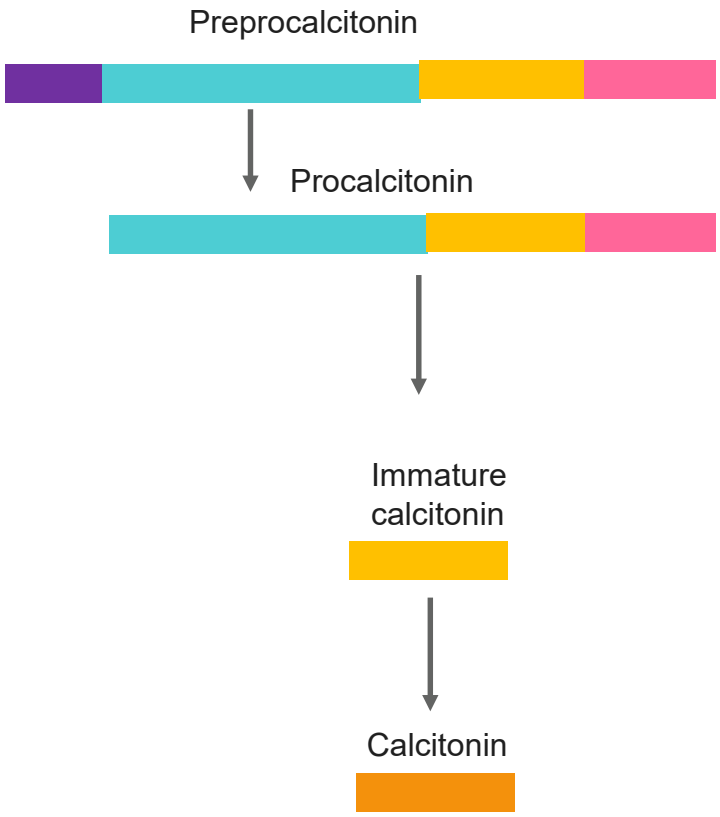
Tailor therapy for effectiveness and safety

Discontinue antibiotics when appropriate

Procalcitonin

116 amino acid protein

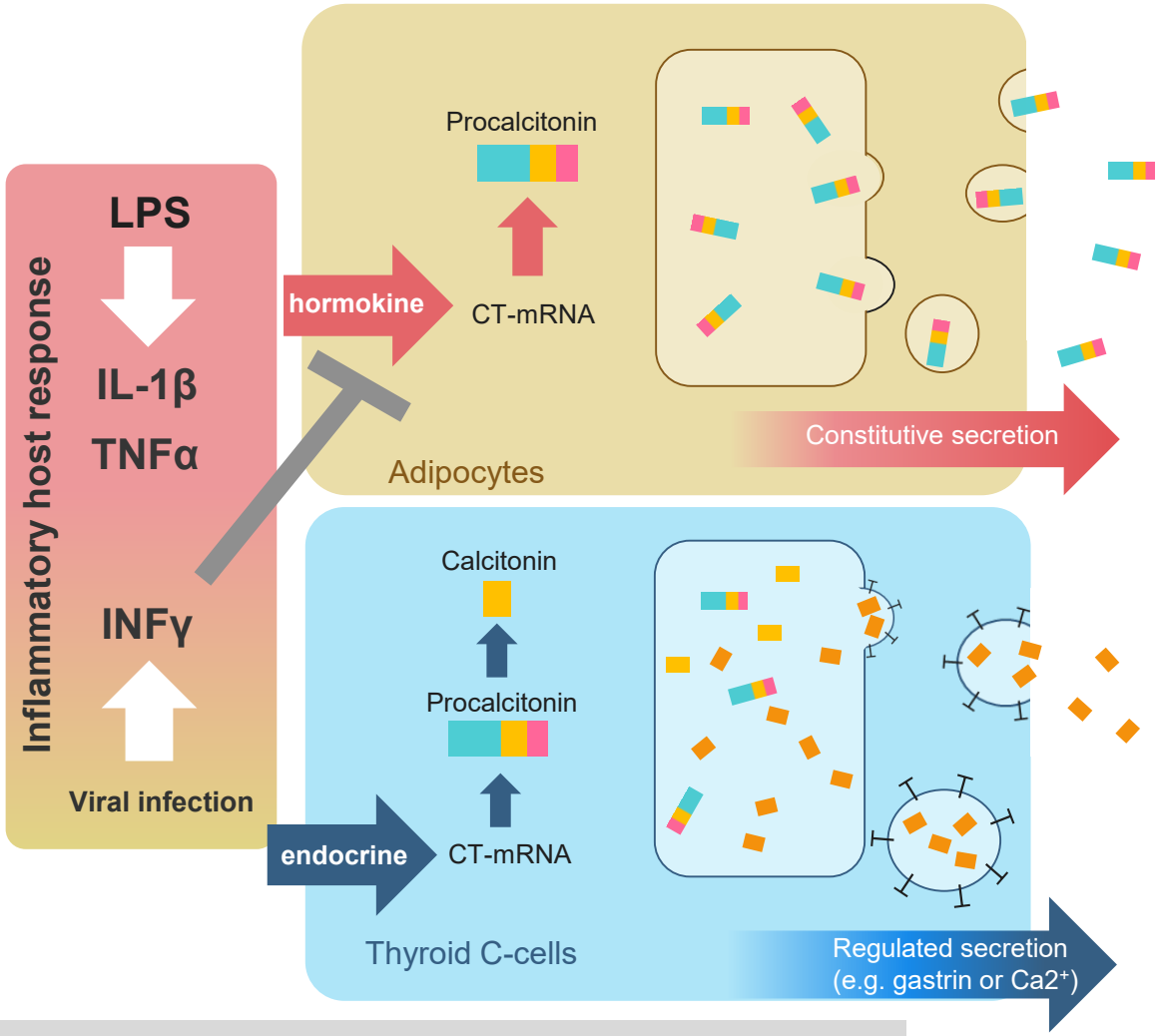
- Serum biomarker
- Produced in most cells and tissues
- Preprocalcitonin is cleaved into procalcitonin[3]
- Precursor of calcitonin in thyroid cells



Procalcitonin

Increased in response to cytokines released during a bacterial infection

Inhibited by interferon-gamma (INFγ) produced in a viral infection



Adapted with permission from: Lincheid P, Seboek D, Nylen E, Langer I, Schlatter M, Becker K, Keller U. In vitro and in vivo Calcitonin I gene expression in parenchymal cells: a novel product of human adipose tissue. Endocrinology 2003; 144(12): 5578-84.[4]

Procalcitonin kinetics

- Rises 4-6 hours after onset of infection and peaks within 15-24 hours[3].
- Procalcitonin decreases by half each day after the control of an infection[3]
  - In the setting of ongoing inflammation, procalcitonin reaches a plateau
- Greater sensitivity and specificity than other markers of inflammation in sepsis, such as CRP, lactate and IL-6[5]

Procalcitonin in antibiotic stewardship

- Blood biomarker used to measure a patient's response to infection
- Aid in risk assessment for critically ill patients upon intensive care unit (ICU) admission for progression to severe sepsis or septic shock
- Prognostic for mortality risk in severe sepsis or septic shock
- Assist in antibiotic therapy decision making for patients with suspected lower respiratory tract infection
- Aid in decision to discontinue antibiotics
- Not to be used as a sole marker to guide antibiotic therapy

Measurement of procalcitonin

- As of September 2019, 30 FDA-cleared procalcitonin assays/platforms
- Quantitative immunoassay
  - Electrochemiluminescence immunoassay (ECLIA)
  - Chemiluminescent microparticle immunoassay (CMIA)
  - Chemiluminescent enzyme immunoassay (CLEIA)
  - Latex particle enhanced immunoturbidimetry
  - Immunofluorescent assay with Time-Resolved Amplified Cryptate Emission (TRACE ® on KRYPTOR ® analyzers) technology
  - Enzyme-linked fluorescent assay (ELFA)
- Sample types; heparin or EDTA plasma, or serum
- Check the indications that are cleared to be used with your particular assay

Procalcitonin-guided treatment algorithms

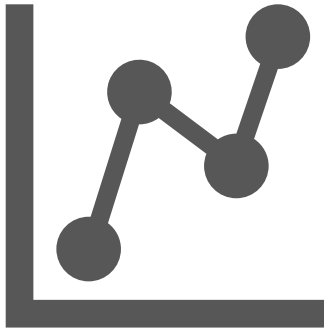
- Reference intervals vary across methods
- Many various procalcitonin-guided treatment algorithms proposed
- Algorithms may be specific to be used with certain patient populations and clinical condition[6].
  - For example, 0.25 µg/L as a cutoff level proposed to indicate bacterial infection in patients with mild or moderate illness who are not in the ICU and for whom bacterial infection is uncertain. For patients with severe illness and in the ICU, a cutoff of 0.5 µg/L is proposed.
  - A decline of >80% from peak values, or a return to a level below the cutoff, would support stopping antibiotics.
- Most procalcitonin algorithms incorporate guidelines for when to perform follow-up procalcitonin testing

Conditions that may elevate procalcitonin besides bacterial infection[7]

- Certain cancers
- Severe burns
- Trauma
- After prolonged resuscitation
- Myocardial infarction
- Rhabdomyolysis
- Newborns
- Some autoimmune disorders
- Organ transplantation
- Liver dysfunction or severe renal disease (especially with dialysis)
- Cardiogenic shock
- Malaria
- Invasive fungal infections
- Multiple organ dysfunction syndrome
- Systemic inflammatory response syndrome (SIRS), cytokine storm and/or antibody therapy

Considerations

- Does not identify pathogen
- Procalcitonin concentrations may be low early in infection, in localized infections, in some immunocompromised patients, and other conditions[7, 8]
- A single measurement has limited value
- Useful to evaluate the kinetics of a patient's procalcitonin results[9]



Considerations

- Caution should be taken in interpreting procalcitonin results in patients with conditions of non-infectious origin known to alter procalcitonin levels, as well as in patients with chronic infections[6].
- Retrospective studies of real-world application of procalcitonin-guided antibiotic therapy report mixed success[9].
- More studies are needed that evaluate the value of testing procalcitonin in infections other than respiratory infections and systemic infections
- Evidence for procalcitonin use with children and neonates, patients with acute conditions, pregnant women, and patients with compromised immune systems not discussed in this presentation
- Lack of harmonization across platforms

Implementing procalcitonin-guided antimicrobial stewardship

Choosing Wisely — An initiative of the ABIM Foundation

American Society for Clinical Pathology
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Thirty Things Physicians and Patients Should Question

25 Don't perform Procalcitonin testing without an established, evidence-based protocol.

- Evidence-based utilization plan[10]
- Identify major users of procalcitonin assay and establish guidelines that are appropriate for the institution, setting, and patient population.
- Consider the patient population (ED, ICU, outpatient vs. inpatient) and other co-morbidities patients may have
- Use appropriate reference intervals for the patient population and suspected type of infections detected (sepsis, lower respiratory tract infection, etc.)
- Quick turnaround times and test offered around the clock
- Education and training are crucial

Summary

- Procalcitonin testing can be incorporated into an institution's antibiotic stewardship program
- Facilities are encouraged to implement an evidence-based algorithm that is appropriate for the use of procalcitonin testing in their population
- Providing information and education to providers is essential when introducing procalcitonin testing
- Evaluation of procalcitonin results along with the entire clinical picture is important

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Disclosures/Potential Conflicts of Interest

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