Overview of the ID PRN

The Infectious Diseases Practice and Research Network (ID PRN) is composed of students, residents, fellows, pharmacists, and other clinical research specialists throughout the world who practice in the exciting realm of infectious diseases. Serving 2248 total members, which include 534 students, 141 residents, and 26 fellows, the ID PRN is the second largest research network within ACCP. Members are actively engaged in advancing pharmacy practice throughout an incredible variety of practice settings and believe strongly in education, research, credentialing, and professional stewardship. This has consistently been demonstrated through the PRN's substantial contributions to the Frontiers Fund, sponsorship of FIT and MERIT scholarships and of travel grants for students and trainees, and development of expert educational programming at state and national meetings. In addition, PRN members are active and dedicated leaders on committees and executive boards within ACCP and other organizations, including the PRN's close partnership with the Society of Infectious Diseases Pharmacists. PRN members are dynamic, collaborative, supportive, and innovative. Last year, the PRN revolutionized member involvement by broadcasting the Global Conference on Clinical Pharmacy business meeting through Periscope for all to watch live. In addition, the @accpinfdprn Twitter account was launched to share the latest practice advances in antimicrobial, antifungal, and antiviral pharmacotherapy with the PRN's membership. With such a diverse and passionate membership base, the PRN recognizes how essential it is to engage its members in consistently working together to extend the frontiers of clinical pharmacy practice. The PRN's mission in its work is to disseminate knowledge and promote career opportunities for infectious diseases specialists to optimize patient outcomes and demonstrate the pharmacist's value across the health care continuum.

Opportunities and Resources for Resident and Fellow Members of the ID PRN

The ACCP ID PRN was the first PRN to offer the opportunity for resident and fellow members to serve on the Executive Board of Officers. This year, two residents—a PGY1 and an infectious diseases PGY2—were appointed. In addition, students, residents, fellows, and pharmacists are encouraged to serve on the PRN's committees, including the Programming, Publications, Awards, Nominations, and Networking committees. To promote research and professional development, the PRN sponsors two $1000 awards to residents or fellows and two $1000 awards to students whose poster is accepted to the ACCP Annual Meeting. Award recipients must present their original research at the PRN business meeting. The PRN has also contributed $5000 to the Frontiers Fund in the past few years and has supported members who apply for FIT or MERIT scholarships within ACCP. The e-mail list associated with PRN membership is active daily, encouraging compelling clinical discussions and bringing attention to critical issues in practice. Networking is constantly promoted through e-mail list involvement, social media outlets, Annual Meeting attendance, research collaborations, and more. The PRN welcomes all who are interested in infectious diseases, even if it is not their current practice area. The PRN website has great tools and resources for resident and student members. It also contains the contact information for all Executive Board members. Please do not hesitate to reach out to PRN members!

Role of PCT in the Management of Patients with Infection

Procalcitonin (PCT) is a prohormone for calcitonin and is involved with calcium homeostasis. Unlike calcitonin, however, PCT is induced in severe stress in states such as bacterial infection. This is

advantageous when differentiating between bacterial infection and other etiologies is challenging. Alternative diagnoses may include viral or inflammatory causes. Availability of an assay that is sensitive and specific for bacterial etiologies would help determine the need for antibiotic therapy.

Procalcitonin is elevated in bacterial infections because of ubiquitous calcitonin gene expression. This increased gene expression results in increased PCT released from adipocytes.[1,2] Many studies have evaluated the sensitivity and specificity of PCT when used to predict bacterial infection. For example, when looking at patients with sepsis, PCT has been shown to be a more accurate diagnostic biomarker than other commonly used biomarkers for infection such as CRP and lactate.[3]

Normal PCT concentrations depend on the assay used. The first-generation assay used in most clinical trials is an immunometric assay that measures PCT plus the combination of calcitonin and calcitonin-carboxyl-peptide-I.[4] The defined upper limit of normal for this PCT assay is 0.5 ng/mL. The FDA-approved a second-generation assay that looks more specifically at PCT and also measures CCP-I concentrations. The upper limit of normal for the second-generation assay is 0.05 ng/mL.[5] For the remainder of this article, the first-generation assay will be referred to because this is the one most facilities use.

PCT-Guided Prescribing

Currently, numerous guidelines address the use of PCT to guide antibiotic therapy, and their recommendations should be considered when using PCT to make treatment decisions. However, many guidelines have reserved recommendations regarding PCT use because of limited evidence in specific patient populations or because new evidence has emerged since the guideline's publication. Most evidence for PCT use exists in patients with respiratory infections.

The Infectious Diseases Society of America (IDSA) hospital-acquired pneumonia and ventilator-associated pneumonia guidelines do not recommend using PCT when deciding to initiate antibiotic therapy. However, the guidelines recommend using PCT, in conjunction with clinical criteria, to guide discontinuation of antibiotic therapy.[6] Conversely, the IDSA guidelines for community-acquired pneumonia are currently being updated and provide no recommendation regarding PCT at this time.

In patients with sepsis, using PCT as a supplemental biomarker has been evaluated to guide antibiotic therapy. The most recent Surviving Sepsis Campaign guidelines advocate that PCT be used when deciding to discontinue antibiotic therapy either because of resolution of infection or when patients do not appear to have sepsis on subsequent evaluation.[7] There is no preferred method on how PCT should be used to make treatment decisions, only that therapy de-escalation using these various algorithms reduces antibiotic consumption.

Evidence supporting PCT use in other patient populations remains limited. Procalcitonin is identified as a potential adjunctive therapy in critically ill patients with new-onset fever. However, the IDSA guidelines do not recommend PCT for patients with febrile neutropenia either for initiating or discontinuing therapy.[8,9] Many of these guidelines have not been updated in several years, and recommendations may change as more studies evaluate PCT use in these specific populations and newer guidelines are released.

What Does and Does Not Affect PCT Concentrations

Clinicians must know what may or may not increase PCT concentrations. Research in this aspect is constantly being explored and updated, and it is evident that bacteria, rather than viral clinical syndromes, increase PCT. However, not all bacteria are capable of such induction. Exceptions include *Chlamydia* spp. and *Mycoplasma pneumoniae*. Thus, PCT cannot distinguish between viral and atypical pneumonia. Some fungi such as *Candida* spp. can increase PCT concentrations, whereas aspergillosis, coccidioidomycosis, and mucormycosis cannot.[10,11]

On the one hand, common bacterial diseases such as aspiration pneumonia, bacterial meningitis, pneumonia, peritonitis, septic arthritis, shock, trauma, and burn injuries may increase PCT concentrations. On the other hand, rheumatic diseases, inflammatory bowel diseases, and gout do not.[10-12] Procalcitonin may be a sensitive and specific marker for septic and non-septic arthritis.[13]

Regarding neoplasms, medullary thyroid cancer (MTC) is most strongly associated with PCT concentrations because PCT is the prohormone of calcitonin, the initial peptide isolated from MTC.[12] Elevated PCT concentrations with neuroendocrine tumors such as small cell lung cancer and carcinoid tumors are common. Other neoplasms such as lymphomas, sarcomas, and pancreas have not been linked to PCT.[10]

Most medications do not affect PCT concentrations unless they induce an innate inflammatory response. Thus, several immune-modulating medications increase PCT, such as alemtuzumab, interleukin-2, and rituximab. Of interest, glucocorticoids, even at therapeutic doses, did not affect PCT concentrations, which may be a useful marker in evaluating a patient's inflammatory response.[14] Other inflammatory mediators such as ibuprofen may modulate PCT.[15]

Future Direction in Using PCT

The evidence for microorganisms, clinical syndromes, and drugs affecting PCT concentrations is driven from observational studies with few patients and should thus be cautiously evaluated. Better prospective, controlled trials are warranted for definitive conclusions.[10] In addition, it is unclear whether some bacterial species are more potent than others. Moreover, in dual viral-bacterial infections, could a specific virus blunt the expected PCT response?[16] Finally, the exact biological role of the *PCT* gene in the innate immune response is not fully understood.

In conclusion, measuring PCT concentrations can streamline antimicrobial prescribing for patients, particularly in sepsis and respiratory tract infections; however, until more data are available, such evaluations should be done in conjunction with careful clinical assessments.[17]

References:

1. Carr JA. Procalcitonin-guided antibiotic therapy for septic patients in the surgical intensive care unit. J Intensive Care Med 2015;3:36.

2. Linscheid P, Seboek D, Schaer JD, et al. Expression and secretion of procalcitonin and calcitonin gene-related peptide by adherent monocytes and macrophage-activated adipocytes. Crit Care Med 2004;32:1715-21.

3. Tian G, Pan SY, Ma G, et al. Serum levels of procalcitonin as a biomarker for differentiating between sepsis and systemic inflammatory response syndrome in the neurological intensive care unit. J Clin Neurosci 2014;21:1153-8.

4. Becker KL, Snider R, Nylen ES. Procalcitonin assay in systemic inflammation, infection, and sepsis: clinical utility and limitations. Crit Care Med 2008;36:941-52.

5. Morgenthaler NG, Struck J, Fischer-Schulz C, et al. Sensitive immunoluminometric assay for the detection of procalcitonin. Clin Chem 2002;48:788-90.

6. Kalil AC, Metersky ML, Klompas M, et al. Management of adults with hospital-acquired and ventilator-associated pneumonia: 2016 clinical practice guidelines by the Infectious Diseases Society of America and the American Thoracic Society. Clin Infect Dis 2016;63:e61-111.

7. Rhodes A, Evans LE, Alhazzani W, et al. Surviving Sepsis Campaign: international guidelines for management of sepsis and septic shock 2016. Crit Care Med 2016;45:e486-552.

8. O'Grady NP, Barie PS, Bartlett JG, et al. Guidelines for evaluation of new fever in critically ill adult patients: 2008 update from the American College of Critical Care Medicine and the Infectious Diseases Society of America. Crit Care Med 2008;36:1330-49.

9. Freifeld AG, Bow EJ, Sepkowitz KA, et al. Clinical practice guidelines for the use of antimicrobial agents in neutropenic patients with cancer: 2010 update by the Infectious Diseases Society of America. Clin Infect Dis 2011;52:e56-e93.

10. Gilbert DN. Role of procalcitonin in the management of infected patients in the intensive care unit. Infect Dis Clin North Am 2017;31:435-53.

11. Dou YH, Du JK, Liu HL, et al. The role of procalcitonin in the identification of invasive fungal infection—a systemic review and meta-analysis. Diagn Microbiol Infect Dis 2013;76:464-9.

12. Becker KL, Nylén ES, White JC, et al. Clinical review 167: procalcitonin and the calcitonin gene family of peptides in inflammation, infection, and sepsis: a journey from calcitonin back to its precursors. J Clin Endocrinol Metab 2004;89:1512-25.

13 Hügle T, Schuetz P, Mueller B, et al. Serum procalcitonin for discrimination between septic and non-septic arthritis. Clin Exp Rheumatol 2008;26:453-6.

14 Tamaki K, Kogata Y, Sugiyama D, et al. Diagnostic accuracy of serum procalcitonin concentrations for detecting systemic bacterial infection in patients with systemic autoimmune diseases. J Rheumatol 2008;35:114-9.

15 Preas HL, Nylen ES, Snider RH, et al. Effects of anti-inflammatory agents on serum levels of calcitonin precursors during human experimental endotoxemia. J Infect Dis 2001;184:373-6.

16. Gilbert DN. Use of plasma procalcitonin levels as an adjunct to clinical microbiology. J Clin Microbiol 2010;48:2325-9.

17. Upadhyay S, Niederman MS. Biomarkers: what is their benefit in the identification of infection, severity assessment, and management of community-acquired pneumonia? Infect Dis Clin North Am 2013;27:19-31.