

**July 2016**

**Procalcitonin: Understanding its Utility and Limitations**

The novel biomarker procalcitonin (PCT) is an amino acid precursor of calcitonin, which under normal circumstances is produced by the C-cells of the thyroid gland. In healthy patients, circulating PCT concentrations are usually undetectable (<0.05 ng/mL). In the setting of acute bacterial infections, PCT concentrations are increased due to bacterial endotoxins and cytokines (IL-1, IL-6, and TNF $\alpha$ ). In contrast, interferon  $\gamma$  is released in the setting of viral infections which attenuates the upregulation of PCT. Thus, PCT may help to distinguish bacterial from viral infections due to its high specificity (Scheutz P., *et. al.* BMC Medicine 2011; 9(107):1-9). In addition, procalcitonin levels have been shown to be significantly lower in fungal in comparison to bacterial bloodstream infections (Cortegiani A., *et. al.* BMC Anesthesiology. 2014; 14(9):1-9). Procalcitonin becomes detectable within 2-4 hours of infection, peaks by 12-24 hours and is eliminated with a half-life of 24-36 hours.

Procalcitonin can be used as an adjunct to fever, leukocytosis, clinical presentation, and other factors to predict the likelihood of acute bacterial infections. The strongest evidence supports the use of PCT for assisting clinicians in antibiotic management in lower respiratory tract infections (LRTIs) (pneumonia, COPD exacerbations, bronchitis) and sepsis (Li H., *et. al.* Antimicrob Agents Chemother. 2011; 55: 5900-6).

In the setting of LRTIs, the use of PCT has resulted in an approximately 30% decrease in antibiotic use and a decrease in antibiotic duration of 1.3 days (Li H., *et. al.* Antimicrob Agents Chemother. 2011; 55: 5900-6). A PCT value of <0.25 ng/mL indicates a low risk of bacterial infection while a value > 0.25 ng/mL suggests an increased risk of LRTIs and the use of antibiotic therapy is more strongly considered. In the setting of elevated PCTs, testing should be repeated within 48 hours to guide antibiotic cessation. In SLHS, PCT is incorporated as a pre-checked lab on days 1, 3, and 5 in the

pneumonia and COPD order sets to assist clinicians in antibiotic use. An internal pilot study analyzing the effects of PCT incorporation into order sets led to decreased antibiotic use by 1.5 days (p=0.009), shorter length of stay by 1.4 days (p=0.035), decreased antibiotic costs by \$117, and no difference in mortality. It was also noted that PCT tends to peak on day 3 with consecutive lab draws as seen in figure 1 (Kelley P., *et. al.* Saint Luke's North Hospital. 2013).

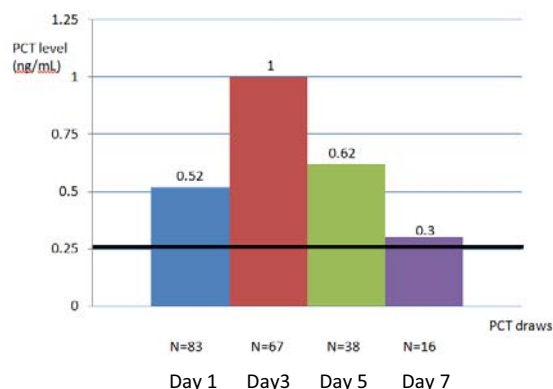


Figure 1: Average PCT levels on Days 1, 3, 5, and 7

In the setting of sepsis, the use of PCT has shown to decrease antibiotic exposure by 19-38% without increasing mortality, length of stay, or affecting persistence of infection. A PCT value of > 0.50 ng/mL is indicative of an increased risk of sepsis and a value > 2.00 ng/mL is indicative of high risk sepsis. When PCT is elevated in sepsis, studies suggest PCT should be repeated in 24 hours to guide antibiotic cessation (Bouadma L., *et. al.* Lancet. 2010; 375: 463-74). However, the Surviving Sepsis Guidelines suggest an alternative strategy with using low PCT levels or similar biomarkers to assist clinicians in the discontinuation of empiric antibiotics in patients who initially appear septic, but have no subsequent evidence of infection (Dellinger R., *et. al.* Critical Care Medicine. 2013; 41(2): 580-637).

Similar to other laboratory tests, PCT has its limitations. Severe trauma, major surgery, cardiogenic shock or burns can cause elevations in

PCT in the absence of sepsis. PCT can also be falsely elevated in patients with acute kidney injury, end stage renal disease, in patients with paraneoplastic syndromes due to medullary thyroid and small cell lung cancer and patients with other neuroendocrine tumors such as pheochromocytoma. In addition, PCT may not rise with localized infections such as cystitis, osteomyelitis or localized abscesses. Clinicians should be mindful of limitations of PCT use outside of the LRTI/sepsis arena as well in scenarios when PCT may be elevated at baseline due to underlying factors previously listed. Also various studies have suggested different cutoffs of PCT as a marker of acute infection.

In summary, the use of PCT is a valuable tool for guiding antibiotic decisions in LRTIs and sepsis. Its use in these settings has shown to decrease antibiotic use (without impacting mortality), which in turn may help prevent antibiotic resistance. PCT should not be used exclusively for antibiotic de-escalation or cessation; rather it should be used in combination with bedside exam and other clinical markers to guide antibiotic use.

### **Switching From CA 27.29 to CA 15.3**

Saint Luke's Laboratories will replace CA 27.29 assay with CA 15-3 assay in August, 2016. Both CA 27.29 and CA 15-3 are *MUC1* gene-derived circulating glycoproteins used primarily for follow-up of patients with history of breast cancer. The assay will be performed Monday - Friday. The specimen requirement is serum (plain red top or serum gel tube). Published data and an in-house comparative study performed revealed good correlation between CA 27-29 and CD15.3 assays.

### **Bias in Estradiol Assay**

Saint Luke's Laboratories recently received communication regarding possible interference in the serum estradiol immunoassay resulting in a positive bias. This effect may occur due to interference from drugs that are derivatives of estrogen, such as Fulvestrant (brand name Faslodex). Estrogen receptor antagonist medications including Fulvestrant are used in the treatment of patients with metastatic, postmenopausal, hormone receptor-positive breast cancer. A comment will accompany the assay

results noting potential interference, if the serum estradiol levels obtained are above 300 pg/mL.

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### **Annual Notice to Physicians/Reflex Testing**

Saint Luke's Regional Laboratories (SLRL) works to ensure compliance with all guidelines governing the submission of Medicare claims for laboratory services. This is to inform you that you need to be aware of the policies regarding medical necessity and Advance Beneficiary Notice (ABN) use, Medicare billing, CPT/HCPCS codes, Reflex Testing, Medicare National Limitation Amounts, and laboratory profiles that include a multichannel chemistry test or other automated multiple test results.

Medicare will only pay for tests that meet the Medicare definition of medical necessity. The Office of the Inspector General (OIG) wants to ensure that physicians order only medically necessary tests and that physicians know that the OIG may impose civil penalties on those who order otherwise. The OIG does recognize that a physician must be able to order any tests, including screening tests they believe appropriate for the treatment of their patients. Medicare may deny payment for a test that the physician believes appropriate but which does not meet the Medicare definition of medical necessity. In this case, the orders should be accompanied by a properly executed ABN.

SLRL does offer laboratory profiles that contain multichannel chemistry tests or other automated multiple test results. The individual components of these profiles and the corresponding CPT/HCPCS codes can be found in the on-line Lab Test Directory (see link information below) and on the back of the Saint Luke's Regional Laboratories requisition. Customized panels and profiles should not be used. The Medicare Limitation Amount for each CPT/HCPCS code can be found in the Medicare National Limitation Amount reference supplied to physician's offices by Medicare. Additional detailed information can be found with the on-line Lab Test Directory at <http://www.saintlukeshealthsystem.org/lab-test-directory>.