Procalcitonin for Bacterial Infection

Procalcitonin (PCT) is the precursor peptide of calcitonin which under normal circumstances is secreted by thyroid C-cells in response to hypercalcemia. PCT is normally undetectable in serum, but is produced in large quantities by many organs and cells in response to severe inflammation, especially in the setting of bacterial infection.

The association between elevated PCT and bacterial infection was first described in 1993, and the assay has been used clinically in Europe for many years. PCT rises within 2-4 hours of onset of systemic bacterial infection and peaks within 6-24 hours. Sensitivity and specificity range from 60-90% for predicting sepsis. PCT testing is being used to differentiate bacterial versus viral infections and reduce antimicrobial therapy, especially in patients with lower respiratory tract infections and sepsis.

Unlike other markers of inflammation (*e.g.* CRP & ESR), PCT is thought to be more specific for bacterial infection. Its predictable half-life of 24 hours makes it useful for serial monitoring of therapeutic response. PCT level of a patient who is responding to antibiotic therapy should decrease by half every 24 hours. Also, unlike other inflammatory markers, PCT is usually low in viral infections, chronic inflammation and autoimmune disease. PCT level reportedly correlates with severity of inflammation. For example, in the appropriate clinical setting, PCT >2 ng/mL predicts sepsis or severe localized bacterial infection, and a level of >10 ng/mL is indicative of septic shock. Mortality is increased when PCT levels are >20 ng/mL.

A meta-analysis of 8 studies with 3431 patients indicated that PCT monitoring of patients with lower respiratory tract infections resulted in a 31% decrease in antibiotic prescriptions and a decrease in antibiotic therapy duration of 1.3 days (Li H et al. Antimicrob Agents Chemother 2011;53:379-87). Likewise, an international multicenter study including 1759 patients documented a 20% reduction in duration of antibiotic administration,

when an algorithm for PCT-guided therapy was followed (Albrich, et al. Arch Intern Med 2012;172:715-723).

PCT has limitations and may be elevated in clinical situations other than systemic bacterial infections. Therefore it is imperative that PCT testing is used & interpreted in conjunction with other clinical & laboratory data. PCT can also be elevated by:

- Major trauma, major surgery, and severe burns.
- Cardiogenic shock and multiorgan failure with hypoperfusion.
- Medullary thyroid cancer & small cell lung cancer.
- Untreated end-stage renal failure. Stable hemodialysis or peritoneal dialysis patients have PCT levels comparable to healthy adults with normal renal function.

PCT is run daily. Specimen requirement is one red top tube of blood. Results are reported quantitatively with reference range <0.1 ng/mL.

Universal Lipid Screening in Children

The increasing prevalence of obesity has led to a much larger population of children with dyslipidemia. Today, the predominant dyslipidemic pattern in childhood is a combination of moderate to severe elevation in triglycerides, normal to mild elevation in LDL cholesterol, and reduced HDL cholesterol level. This pattern has been associated with initiation and progression of atherosclerosis in children and adolescents.

Previous studies have repeatedly demonstrated that solely relying on family history of premature cardiovascular disease or cholesterol disorders misses 30 to 60% of children with dysplipidemia. Recently, an expert panel sponsored by the National Heart, Lung, and Blood Institute (NHLBI) and endorsed by the American Academy of Pediatrics issued comprehensive guidelines on cardiovascular health and risk reduction in children and adolescents that included universal screening of children at ages 9–11 and again at ages 17–19 (Pediatrics 2011;128: S213-256).

The expert panel published the following cut-points for low, acceptable, borderline, and high lipid levels in children and adolescents up to age 19.

	Acceptable	Borderline High	High
Total Cholesterol	<170	170–199	≥200
LDL Cholesterol	<110	110–129	≥130
Non-HDL Cholesterol	<120	120–144	≥145
HDL Cholesterol	>45		
Triglycerides (0–9 years)	<75	75–99	≥100
Triglycerides (10–19 years)	<90	90–129	≥130

It is important to note that non-HDL cholesterol was included in the lipid screening panel. Non-HDL cholesterol has been shown to be a more significant predictor of persistent dyslipidemia and atherosclerosis in children and adolescents than total cholesterol, LDL cholesterol or HDL cholesterol alone. A major advantage of non-HDL cholesterol is that it can be accurately calculated in nonfasting specimens with elevated triglycerides.

The expert panel recommended repeating abnormal results with a fasting lipid panel within 2 weeks to 3 months. Decisions regarding the need for medication therapy should be based on the average of results from at least 2 fasting lipid panels.

P2Y12 Platelet Reactivity Testing Change

Saint Luke's Regional Laboratories(SLRL) began offering P2Y12 Reactivity testing in June 2010 to measure the antiplatelet effect of clopidogrel. At that time, three values were reported including: P2Y12 Reaction Units (PRU), baseline PRU, and

percent inhibition. Accumetrics, the manufacturer of the VerifyNow® P2Y12 test has recently notified the laboratory that the instrument's software will be updated in August. This update will eliminate the baseline and percent inhibition results. Following the update, PRU will be the only value reported. SLRL supports this modification because our own studies have shown poor correlation between PRU and percent inhibition. For example, a PRU value of 230 is associated with percent inhibition values ranging from 5 to 50%.

PRU is the amount of residual P2Y12 receptor mediated aggregation. Therefore, a lower PRU indicates good response to anti-platelet medication, while a higher number indicates less than optimal response. Responders usually have PRU <200. PRU values >230 have been associated with an increased risk of ischemic events.

Previously, percent inhibition was primarily used preoperatively to determine if a patient who was taking Plavix, or another P2Y12 receptor inhibitor, was at increased risk of bleeding. After the update, a PRU value of >230 can be used as an indicator that the patient has sufficient residual platelet reactivity to minimize the risk of bleeding.

Accuracy of Creatinine Clearance

The accuracy of the creatinine clearance calculation depends on the accuracy of the urine collection. Twenty four-hour urine collections are considered optimal because they account for diurnal variation in creatinine clearance. The creatinine clearance report includes "grams of creatinine per 24 hours". This calculation is valuable in determining if a 24-hour urine collection is complete. Creatinine values <1g/24 hours for men or <0.9g/24 hours for women nearly always mean that the urine collection was incomplete. Normal urine volume is 0.6 to 2.0 liters per day, but most people produce between 1.0 and 1.5 liters per day.

Changes in Critical Values

The June issue of the Clinical Laboratory Letter announced several changes in critical values. These changes will become effective on August 1.