



# Saint Luke's Regional Laboratories Clinical Laboratory Letter



February 2009

## All Laboratories are not Created Equal

The two large publicly traded lab companies, Quest Diagnostics and Laboratory Corporation of America (LabCorp), have continually cut costs over the past ten years in order to satisfy Wall Street investors, win national managed care contracts and gain market share. Their efforts have caused many payers and regulators to regard clinical laboratories as nonessential commodities.

However, recent evidence suggests that this competitive strategy has backfired. Sustained cost cutting by the national laboratories appears to have finally reached the tipping point. Robert Michel, a leading laboratory expert, has recently suggested that staffing and resources have been cut so drastically that the quality and integrity of Quest's lab test results can no longer be guaranteed (Dark Daily Jan 26, 2009). The best example was the recent announcement in the Dark Daily (Jan 5, 2009) and the New York Times (Jan 8, 2009) that Quest has reported tens of thousands of inaccurate Vitamin D results during the past 18 months, even though their laboratory scientists recognized that a problem existed in early 2007.

Another recent study determined that one of these laboratories misclassified the HER-2 status of approximately 10% of breast cancers (Clinical Cancer Research 2008;14:7861-70). The errors were detected by parallel testing in an academic laboratory. Both laboratories used the same technology, but the national laboratory allowed technicians to assign a score, while the academic laboratory had licensed clinical laboratory scientists enumerate the fluorescent signals and board certified pathologists score each tumor. Different levels of laboratory staffing and oversight clearly impact medical outcomes.

To offset their cost cutting strategy for high volume routine testing, the national laboratories have actively promoted expensive esoteric tests often before their clinical efficacy has been established. In October, 2008, LabCorp halted sales of Ovasure, which they promoted as a screening test for ovarian

cancer, after receiving a warning letter from the FDA. More recently, the Evaluation of Genomic Applications in Practice and Prevention Working Group, which was supported by the Centers for Disease Control and Prevention (CDC), found no evidence of clinical utility for Quest's Breast Cancer Gene Expression Ratio assay (Genetics in Medicine 2009;11:66-73). These practices enhanced the laboratory's bottom line, but inappropriately increased health care spending without providing demonstrable clinical benefit.

Saint Luke's Regional Laboratories (SLRL) performs 98% of ordered laboratory tests in house. This testing is performed by highly competent clinical laboratory scientists and is overseen by four board certified clinical pathologists. SLRL takes great pride in the quality of their work. Data submitted to the College of American Pathologists External Comparison Report demonstrated that Saint Luke's Hospital laboratory's error rate was very low and the lab was ranked in the top 10<sup>th</sup> percentile of our customer defined peer group. When an error does occur, a clinical pathologist is readily available to address the issue. Clinical pathologists also continuously review the test menu to make certain that the tests being offered are medically appropriate.

The 2% of tests that are not performed in a Saint Luke's Hospital laboratory are sent to a reference laboratory. Whenever possible these tests are sent to one of the laboratories participating in the Regional Laboratory Alliance, which is an integrated network of hospital and independent laboratories that are committed to providing excellent patient care within the local health care system. If a test cannot be performed in one of these laboratories, it is referred to Mayo Medical Laboratories. For more than 25 years, Mayo Medical Laboratories has served as our primary reference laboratory because of their solid reputation for service, quality and integrity. We believe that all of these efforts define Saint Luke's Regional Laboratories as the laboratory of choice.

## Newborn Screening Update

Biotinidase deficiency is an autosomal recessive disorder that results in multiple carboxylase deficiencies. Individuals with profound biotinidase deficiency have less than 10% of mean normal serum biotinidase enzyme activity, while individuals with partial biotinidase deficiency have 10%-30%. Both profound and partial biotinidase deficiencies are usually identified by newborn screening. Missouri State Newborn Laboratory began reporting biotinidase on all infants on December 31, 2008. The estimated incidence of profound and partial deficiencies is 1 in 60,000 births.

Infants with profound biotinidase deficiency appear normal at birth but develop one or more of the following symptoms after the first few weeks of life: seizures, hypotonia, ataxia, developmental delay, vision problems, hearing loss, and cutaneous abnormalities such as alopecia, skin rash and candidiasis. Once vision problems, hearing loss, and developmental delay occur, they are usually irreversible, even with biotin therapy. Individuals with partial biotinidase deficiency may have hypotonia, skin rash, and hair loss, particularly during times of stress. Children with biotinidase deficiency identified by newborn screening should remain asymptomatic if biotin therapy is instituted early and continuously maintained.

All abnormal results are faxed to the physician of record and to Children's Mercy Hospital, which is the designated follow up center. The follow-up center will order confirmatory testing of biotinidase enzyme activity in serum or plasma. Biotinidase test results should be abnormal in all infants with profound or partial deficiency even if the specimen is obtained before formula or milk feeding or collected before 24 hours of age. A newborn screen should be collected prior to transfusion since transfusion may mask the deficiency.

## Procalcitonin for Bacterial Infection

Procalcitonin (PCT) is the precursor peptide of calcitonin, which is secreted by thyroid C-cells in response to hypercalcemia. PCT is normally undetectable in serum, but is produced by many organs & 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 3-6 hours of onset of systemic bacterial infection and peaks at 6-12 hours. Sensitivity and specificity range from 60-90% for predicting sepsis. The PCT literature continues to evolve & investigations are underway regarding utility of serial PCT testing in reducing antimicrobial use, differentiation of viral vs. bacterial pneumonia and need for antimicrobial therapy in COPD exacerbation.

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 & autoimmune disease. PCT level reportedly correlates with severity of inflammation. For example, in the appropriate clinical setting, PCT >2 ng/mL predicts sepsis, and a level of >10 ng/mL is indicative of septic shock. Mortality is increased when PCT levels are >20 ng/mL.

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

PCT is run daily. Specimen requirement is one red top tube of blood. Results are reported quantitatively with interpretive guidelines for sepsis diagnosis.

PCT level	Interpretive comment
≤ 0.5 ng/mL	Low risk for progression to severe systemic infection
>0.5 and ≤ 2 ng/mL	Moderate risk for progression to severe systemic infection
>2 ng/mL	High risk for progression to severe systemic infection