Saint Luke's Regional Laboratories
Clinical Laboratory Letter

February 2005

Blood Culture Round-up

Saint Luke's Regional Laboratories processed 16,412 blood cultures in 2004, a 10% increase over 2003. The positive rate was comparable to last year at 11.3%, or 1846 positive cultures. The overwhelming majority of positive blood cultures yielded gram positive bacteria (76%), followed by gram negative bacteria (18%), anaerobic bacteria (4%) and fungus (2%). A breakdown of the most common isolates is as follows:

Organism	# Isolates (%)
Coagulase-negative staphylococci	671 (36)
S. aureus, methicillin-resistant	221 (12)
S. aureus, methicillin-sensitive	135 (7)
E. coli	156 (9)
Viridans streptococci	81
Enterococcus species, non-VRE	82
Enteroccus, vancomycin-resistant (VRE)	35
Streptococcus pneumoniae	46
Pseudomonas aeruginosa	32
Candida species	30

Generally, the following isolates nearly always represent true bacteremia or fungemia when isolated from blood cultures, even if only one culture is positive: *Staphylococcus aureus*, *Streptococcus pneumoniae, Pseudomonas aeruginosa, Candida* species, and enteric gram-negative bacteria such as E. coli. Other less commonly isolated organisms that are almost always pathogens include *Streptococcus pyogenes, Streptococcus agalactiae*, *Haemophilus influenzae, Bacteroides fragilis*, and *Neisseria meningitidis.* Enterococci are found to be significant 80% of the time.

The primary organisms responsible for blood culture contamination are skin flora. Coagulase-negative staphylococci are found to be contaminants 60-80% of the time. Other common potential contaminants include viridans streptococci, *Corynebacterium* species, *Propionibacterium*, *Bacillus* species, and *Micrococcus*. The overall blood culture contamination rate for Saint Luke's Hospital in 2004 was 1.47%, which is well below the national standard of 3%.

BNP Fluctuates Too Much to be used for Monitoring Treatment

BNP was originally approved as a diagnostic test for ruling out acute heart failure in patients presenting with dyspnea in emergency departments. Very high or very low BNP levels are helpful diagnostically for these patients. A dyspneic person with a BNP <100 has less than a 5% likelihood of having CHF. On the other hand, a person with known heart disease, who has a BNP level >1200 most likely does have CHF. Unfortunately, cardiac diseases other than CHF can produce BNP levels between 100 and 1200. This is the reason why the specificity of BNP for CHF is only 70 - 75%.

Since its introduction, many physicians have begun ordering daily BNP levels to monitor therapy. However, the value of this BNP application has never been proven. A recent article investigating the biological variability of BNP within an individual patient strongly suggests that serial monitoring is not good practice (Clinical Chemistry 2004; 50: 2052-58). The within day, day-to-day and week-to-week variability of BNP in 43 patients with stable chronic heart failure and a left ventricular ejection fraction <40% was studied. BNP levels ranged from 100 to 1630, with a median of 134. Within day variation was calculated from six samples that were collected every 2 hours starting at 08:00. Day to day variation was calculated from five samples collected between 08:00 and 10:00 on consecutive days within 1 week. Week to week variation was calculated on samples drawn between 08:00 and 10:00 once weekly for 6 consecutive weeks. The analytical imprecision of BNP measurement was 8.4%.

BNP values within individual patients fluctuated as much as 12% during a single day, 27% from day to

day, and 41% from week to week. BNP increased 25% during the day, with the lowest values occurring in the morning and the highest values in the evening. Using biological variation and analytical imprecision, it is possible to calculate how much BNP must change to be medically significant.

BNP Variability	Medically Significant Change
Within Day	31%
Day to Day	73%
Week to Week	113%

As seen in the table, BNP must change almost twofold from one day to the next, or one week to the next to be medically significant. This magnitude of change is greater than the 45 - 55% reduction in BNP that is expected with standard CHF therapy. Also, the majority of patients required more than 5 days of treatment to decrease their BNP levels more than the fluctuation due to biological variation. This study clearly demonstrates that daily orders for BNP are not warranted or helpful. In most cases, BNP should only be ordered twice during an admission: once for diagnosis and then again prior to discharge.

Also, it is important to remember that specimens for BNP levels should be drawn at the same time of the day to eliminate diurnal variation. BNP should not be measured while a patient is receiving nesiritide (Natrecor) because results will be falsely elevated. Maximum decrease in endogenous BNP will be detected at 6 hours post-infusion.

New Anti-beta-2-Glycoprotein I Assay

The antiphospholipid antibody syndrome (APS) is defined as the occurrence of arterial or venous thrombosis or fetal loss, in association with persistently positive immunoassays for IgG or IgM anticardiolipin antibody (ACA), or coagulation tests for lupus anticoagulant. The APS may be associated with autoimmune disorders, especially SLE (secondary APS) or may occur independently (primary APS). Positivity for anti-beta-2-glycoprotein I (anti-B2GPI) has been shown to be more closely associated with clinical manifestations of APS, including thrombosis, than the ACA assays. An immunoassay for anti-B2GPI has been available at Saint Luke's Regional Laboratories since 1998, and is a component of our "Antiphospholipid III" panel, which includes coagulation tests for lupus anticoagulant and immunoassays for ACA (IgG and IgM).

The anti-B2GPI assay currently being performed will detect only the IgG isotype of the antibody. Recently an immunoassay for the IgM isotype of anti-B2GPI has become available. A recent study evaluated a number of different antiphospholipid antibodies (including both IgG and IgM anti-B2GPI) as predictors of thrombosis, in 100 patients with primary APS, and 90 patients with SLE, 40 of whom had secondary APS. In the patients with SLE, both IgG and IgM anti-B2GPI were strongly associated with the clinical manifestations of APS, with specificity greater than 95%, and positive predictive values (PPV) greater than 90%. In the patients with primary APS, both IgG and IgM anti-B2GPI were strong predictors of thrombosis, especially arterial thrombosis (PPV greater than 90% for both antibodies).

The presence of anti-B2GPI antibody has not yet been included in the formal definition of APS, but may be in the future. In any event, detection of IgG or IgM anti-B2GPI would add credence to a diagnosis of APS, especially in borderline cases. Assay for IgM anti-B2GPI will be available in Saint Luke's Regional Laboratories starting in March 2005. Both IgG and IgM anti-B2GPI will be performed when anti-B2GPI is ordered. IgM anti-B2GPI will also be added to all panels in which IgG anti-B2GPI is already a component (this includes the Antiphospholipid III panel and venous thrombosis panel). Sample requirement for anti-B2GPI is one red-top tube (minimum 1.0 ml serum). The reference range for both IgG and IgM anti-B2GPI is 0-20 units. The test will be run twice per week.

Lithium Critical Value

The critical value for lithium has been changed from 3.5 to 2.0 mEq/L.