Saint Luke's REGIONAL LABORATORIES

Clinical Laboratory News

July 2019

BPA for Urine Antigens

Legionella pneumophila and related species are uncommon causes of pneumonia in both immunocompromised and normal individuals. Legionella is ubiquitous in natural water habitats, and may colonize man-made water features which can then serve as a source of human infections. The gold standard for diagnosis of legionellosis is culture. However, *Legionella* requires charcoal-containing media for growth, cultures must be held for 14 days, and the reported sensitivity of culture is low at 25-80%. Serologic and urine antigen tests are also available, when respiratory specimens are difficult to collect. The urine antigen test detects a specific soluble antigen present in the urine of patients with *Legionella* infections and is the test of choice for diagnosis of early infection. It detects only *Legionella pneumophila* serogroup 1, which causes the majority of cases of legionellosis. The sensitivity is 70% with specificity near 100%. Antigen excretion may begin as early as 3 days after onset of symptoms and persist for up to 1 year afterward. The test remains positive for several weeks following antibiotic therapy.

Urine antigen testing is also a useful adjunct in the diagnosis of pneumococcal pneumonia, with sensitivity and specificity approximately 86% and 94%, respectively. The performance characteristics of this assay are unknown in patients who have been treated with antibiotics for more than 24 hours prior to specimen collection.

A review of 7758 SLHS urine antigen orders for 2018 revealed a duplicate testing rate of approximately 4.5%. Due to limited clinical utility of repeated urine antigen testing, an EPIC BPA has been initiated through Saint Luke's Care Infectious Disease EPT that will alert ordering physicians when urine antigen testing has been previously performed during a hospital admission.

Platelet Function Testing (PFT)

Platelet function testing is part of initial work-up in patients with bleeding disorders and in patients on anti-platelet therapy to evaluate efficacy. Platelets have become a critical target for pharmacotherapy due to rising incidence of atherothrombotic disease. In particular, percutaneous coronary intervention (PCI) with coronary artery stunts, a widely used intervention for ischemic heart disease management, requires treatment with dual anti-platelet therapy such as aspirin and platelet P2Y12 inhibitors, to prevent stunt thrombosis. In such patients, platelet function testing helps determine drug efficacy and/or sensitivity, compliance with medication, and optimal timing of urgent surgery after oral anti platelet therapy ends. PFT can also play a role in drug dosage optimization, especially P2Y12 inhibitors.

Methods for Assessing Platelet Function Available through Saint Luke's Laboratory include -

<u>VerifyNow (P2Y12 Response Assay)</u>
The P2Y12 assay is the simple reliable method to evaluate response to P2Y12 inhibitors in addition to sensitivity to aspirin. The assay is available for aspirin, P2Y12 inhibitors, and GIIb/IIIa inhibitors. Several studies have been performed to establish numeric thresholds for adequate and

inadequate platelet inhibition. A HPR value defined as P2Y12 units of (PRU) >235 was found to be predictive of stent thrombosis. Additional studies performed found that HPR is an independent predictor of stent thrombosis and/or MI in the first 12 months but not a predictor of death. In contrast, patients with low platelet reactivity (LPR) are found to have significant bleeding risk, especially in the setting of PCI. To delineate these risks and prevent bleeding and thrombotic risks, clinicians use PFT to target a therapeutic window of platelet reactivity, referred to as optimal level platelet reactivity (OPR) which is flanked by LPR and HPR cutoffs, respectively. However, there is lack of evidence that demonstrates this assay supports improved clinical outcomes.

VerifyNow or P2Y12 response assay uses anti-coagulated whole blood - two 2 mL light blue top Greiner tubes and one 2 mL white top tube. The test should be ordered STAT and specimen should reach Saint Luke's Laboratory within 2 hours of collection time.

Platelet Function Analyzer-100 (PFA-100)

The PFA-100 test is a sensitive screening tool for qualitative platelet defects but is not recommended for monitoring anti platelet therapy mainly due to lack of sensitivity and specificity for the effects of aspirin and P2Y12 inhibitors. It is a rapid, reproducible and standardized test. The endpoint of the test is a closure time (CT), measured as the duration from the start of the test to occlusion of the capillary aperture. The test is cartridge-based system, containing collagen and epinephrine or collagen and ADP. The PFA-100 CT varies with nature and severity of platelet defects. Various pre-analytical factors that can falsely prolong CT include platelet count less than 100,000 and hematocrit less than 30. In general, prolonged CT has limited specificity due to inability to distinguish severe platelet disorders from von Willebrand disorder (VWD).

Per recommendations by International Society on Thrombosis and Haemostasis, PFA-100 CT is an optional test for evaluation of platelet disorders and platelet function. Normal PFA-100 CT can help exclude a few severe platelet defects such as Glanzmann thrombasthenia and Bernard-Soulier syndrome, and moderate to severe VWD. However, if clinical suspicion for platelet function disorder is high, further work-up should be performed.

PFA-100 test requires two 4.0 ml whole blood sodium citrate (light blue top) tubes, should be ordered STAT and reach Saint Luke's Laboratory within 2 hours of collection. The specimen should be unprocessed and not send through pneumatic tube system. Laboratory hematology department should be informed at (816) 932-2415 prior to sending the specimen. The test is performed Monday through Sunday.

Light Transmittance Aggregometry (LTA) (Platelet Aggregation Studies)

LTA has been gold standard in function testing. However, fewer laboratories perform this test due to lack of standardization, problems with spurious platelet activation secondary to specimen centrifugation, and high complexity. The test uses turbidometric optical density to assess pharmacodynamic response to various agonists. The specimen translucency and light transmission increases as platelets aggregate. The final interpretation is based on platelet aggregation tracing produced in response to the agonist added. Common agonists used for testing include ADP, epinephrine, collagen, thrombin receptor

activating peptide, arachidonic acid, and antibiotic ristocetin. The recorded response depends on the normal functioning of the platelet, the presence of inhibitors of platelet function, and concentration of agonist used. Impaired platelet aggregation with one or more agonists may suggest inherited platelet function disorder.

Simultaneous measurement of ATP/ADP secretion, a marker for granule release, can be helpful in identification of platelet secretion defect. Both platelet aggregation (LTA) and lumi-aggregation tests are offered at Saint Luke's Hospital. The test requires five 4 ml whole blood sodium citrate tubes within 2 hours of collection time, which should arrive the laboratory between 8 am to 2 pm. For lumi-aggregation test, seven 4 ml sodium citrate tubes are required.

Other platelet functions tests including vasodilator-stimulated phosphoprotein phosphorylation assay (VASP) which uses flow cytometric analysis based testing to indirectly measure P2Y12 receptor inhibition are not available at Saint Luke's hospital.

Thromboelastography/Thromboelastometry (TEG)

Thromboelastography (TEG) technology uses whole blood to measure dynamic hemostatic changes in clot formation. The specimen, whole blood, is placed in a cup which oscillates during clot formation. This movement of the cup detects increased resistance and can assess bleeding, if due to anti-platelet therapy. Additional technology available in TEG is known as PlateletMapping, which can measure platelet function in the presence of anti-platelet therapy.

TEG is available at Saint Luke's Hospital and can be requested by calling blood bank at (816)932-2427 or (816)932-2412. PlateletMapping is currently unavailable at Saint Luke's Hospital.