Effective Wednesday, December 19, 2012

ACL Laboratories Offers Improved Tests for Detection of Heparin Dependent Platelet Antibodies

Effective Wednesday, December 19, 2012, the PF4 Hep AB IgG will be performed on all samples submitted for heparin associated platelet antibody-PF4 testing. The Serotonin Release Assay will replace HAAG as the reflex test for pos/equiv PF4 ELISA. Test Order Code HDAC will be deactivated.

ACL Laboratories will offer a new Platelet Factor 4 Heparin Associated Antibody IgG test (Test Order Codes PF4IGG and PF4IGR) to improve detection of heparin associated platelet antibodies. The new method detects only IgG antibodies. This new specific IgG ELISA shows very close correlation with the serotonin release assay (Test Order Code SRAUH) and can be used as a screen for heparin induced thrombocytopenia (HIT) with greater specificity (fewer false positives) than our current non-specific method. A strong positive result in the improved test correlates well with the clinical likelihood of heparin induced thrombocytopenia “Type II” (HIT).

The new PF4 Heparin Associated Platelet Antibody IgG is a sensitive and specific assay for HIT antibodies in patients with a reasonable likelihood of having HIT based on clinical findings. The test will detect clinically significant IgG HIT antibodies, while avoiding detection of more non-clinically significant antibodies compared to the PF4 Hep AB IgGAM.

PF4 Hep AB IgG includes a heparin inhibition step to improve assay specificity. In addition, a positive or equivocal IgG will reflex to the confirmatory platelet functional assay, Serotonin Release Assay (Test Order Code SRAUH), when ordered as the reflex Test Order Code PF4IGR. Note: The Heparin Dep AB IGAM with Reflex (Test Order Code HDAC) will be deactivated 12/19/12.

The Serotonin Release Assay (performed at Blood Center of Wis) will replace the Heparin Platelet Aggregation (Test Order Code HAAG). The Platelet Aggregation assay using Platelet Rich Plasma is confounded by numerous variables that result in false-positive and false-negative test results. The Serotonin Release Assay is still considered the “gold standard” assay for the detection of heparin-dependent antibodies in HIT. Various studies have reported the sensitivity and specificity of the SRA to be as high as 90% and 100%, respectively.2,3 Because of its high specificity, the SRA is often useful for confirmation of weak or “inconclusive” results obtained with the highly sensitive PF4/ELISA.4,5

Although IgG heparin dependent platelet reactive antibodies are responsible for most HIT cases, patients may develop IgA or IgM antibodies in the absence of IgG that may or may not be associated with HIT. The screening test PF4 Hep AB IgGAM (Test Order Code HDA) will continue to be offered (without reflex) to detect and identify these unusual antibodies. It is recommended that if the HDA is ordered for diagnostic purposes, to also order the PF4 IgG with Reflex. In the rare situation where clinical necessity dictates confirmatory testing despite a negative anti-PF4 result, the SRAUH is the recommended confirmatory assay.

REFERENCES:
5) Visentin TP, Ford SE, Scott JP, Aster RH. Antibodies from patients with heparin induced thrombocytopenia/ thrombosis are specific for platelet factor 4 complexed with heparin or bound to endothelial cells. JCI 1994, 93:81-88.

Please refer to the ACL Laboratories Directory of Services (acllaboratories.com/tests-directory/search-tests.asp) for specimen collection requirements.

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ACL Laboratories Announces New Test Codes for Azole Monitoring, Diagnostic Marker for Fungus (including *Pneumocystis*)

**Test Order Codes:**
- Posaconazole, Quantitation by LC-MS/MS (POSQTR)
- Voriconazole, Quantitation by LC-MS/MS (VORQTR)
- (1,3)-Beta-D-Glucan (Fungitell®) (13BDGR)

ACL Laboratories now offers new test codes for azole therapeutic drug monitoring to facilitate ordering and reporting of posaconazole, voriconazole and itraconazole serum concentrations. Due to variability in absorption and drug interactions, monitoring levels of these agents is advised for treatment of invasive fungal infections. Data on target values continues to evolve and although prospective, controlled trials are needed to establish definitive recommendations, serum drug levels in conjunction with clinical assessment may assist in evaluation of therapeutic failure or drug toxicity. Suggested values using liquid chromatography – mass spectrometry (LC-MS/MS) are summarized below (Table 1). Samples for quantitative assay are sent twice weekly, every Monday and Thursday, to ARUP reference laboratory.

ACL Laboratories also now offers a new test code for diagnosing fungal infections (including *Pneumocystis jirovecii*): (1,3)-Beta-Glucan (Fungitell®) (Test Order Code 13BDGR). This assay is indicated for the presumptive diagnosis of invasive fungal disease. The Fungitell® Beta-D Glucan Assay detects (1,3)-Beta-D-Glucan from the following pathogens: *Candida* spp., *Acremonium*, *Aspergillus* spp., *Coccidioides immitis*, *Fusarium* spp., *Histoplasma capsulatum*, *Trichosporon* spp., *Sporothrix schenckii*, *Saccharomyces cerevisiae*, and *Pneumocystis jirovecii*.

### Table 1. Serum Azole Concentrations: Timing & Suggested Targets

<table>
<thead>
<tr>
<th>Agent (Test Order Code)</th>
<th>Duration of Therapy Prior to First Level*</th>
<th>Suggested Serum Concentrations for Treatment of Invasive Fungal Infections**</th>
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</table>
| Itraconazole (ITFUNR)   | Initial level after 2 weeks (t_{1/2} ~ 60hrs) | Trough Levels: >1mcg/mL  
Potentially Toxic Levels: >10mcg/mL  
Timing: Because of its long half-life, serum concentrations of itraconazole are expected to vary little during a 24-h dosing interval, and the blood specimen can be collected, if needed, at any time relative to drug administration. *Hydroxyitraconazole*: When measured by HPLC, both itraconazole and its bioactive hydroxy-itraconazole metabolite are reported, the sum of which should be considered in assessing drug levels. |
| Posaconazole (POSQTR)   | Initial level after 7-10 days (t_{1/2} ~ 20-66hrs) | Trough Levels: >0.7mcg/mL |
| Voriconazole (VORQTR)   | Initial level after 5-7 days               | Trough Levels: >1mcg/mL  
(drawn 15min prior to next dose)  
Potentially Toxic Trough Levels: >5.5mcg/mL  
Serum concentrations <1 mcg/mL have been associated with poor response, and levels >5.5 mcg/mL have been associated with neurologic toxicity |

*Earlier levels may be checked to verify absorption –but may not represent steady state values.  
**Suggested target concentrations for treatment of IFI listed. Data on serum triazole levels continues to evolve and may be organism specific. Consult disease specific guidelines as needed.

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