Saint Luke's REGIONAL LABORATORIES

Clinical Laboratory News

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RBC Antibody Titers in Pregnancy

Alloimmunization is production of antibodies against RBC antigens triggered by RBC transfusions or pregnancies. Alloantibodies in pregnant females "maternal antibodies" can cross into the fetal circulation via the placenta and lead to hemolytic disease in fetus and neonate (HDFN). Severity of the fetal anemia depends on the degree of antigenicity, amount and type of antibodies involved.

Rh antibody (anti-D) was the most common cause of HDFN and lead to significant morbidity and mortality before routine use of prophylactic Rh immunoglobulin in clinical practice. Other Rh antibodies (C, c, E, e) and non-Rh antibodies (K, Jka, Fya, etc) have also been implicated in HDFN.

All pregnant women should have an ABO-Rh type and antibody screen at the time of first prenatal visit for each pregnancy. If a pregnant female is found to be alloimmunized, antibody titers should be performed. Titers are performed upon detection, repeated at 18-20 weeks gestation and subsequently every 2-4 weeks if below critical titer. A critical titer is that titer associated with a significant risk for severe HDFN and is usually 1:16 or 1:32 in most centers.

To clarify, the purpose of titrating potentially significant antibodies detected in pregnancy is not to predict the severity of HDFN. Coupled with obstetric history, antibody titers are only 62% accurate in predicting severe HDFN. Rather, titration is a screening test. It is done to determine when to monitor for HDFN by non-serologic means, such as spectrophotometric analysis of amniotic fluid or middle cerebral artery (MCA) Doppler testing.

The following requests for titration of maternal antibodies are considered inappropriate:

- To differentiate between active and passive immunity (anti-D vs Rh immunoglobulin)
- Titrating non-IgG antibodies, as these don't cross placenta to cause HDFN
- Once the critical titer has been attained or the decision made to monitor the pregnancy by an alternative procedure such as amniocentesis or MCA Doppler testing
- Mother has history of previously affected fetus or neonate, current pregnancy is at higher risk of HDFN and titers are not found to be helpful
- Postnatal or antenatal titers to predict risk of HDFN in the subsequent pregnancy. Fetus is at higher risk of HDFN
- Antibodies detected at delivery, titration studies at this time serve no useful purpose
- Monitoring Kell-sensitized (anti-K) patients because Kell titers do not correlate with fetal status

At Saint Luke's Health System, Transfusion Medicine physicians are always available to help with prei-natal immunohematologic testing.

Quantiferon Updated Assay and Reporting Change

According to World Health Organization data, 25% of the world's population is infected with tuberculosis (TB). In 2016, there were 1.7 million tuberculosis-related deaths worldwide. In recent years, *Mycobacterium tuberculosis* (MTB) has become more deadly due to emergence of strains that are resistant to most or all TB drugs.

Interferon-gamma release assays, also known as IGRA's, have been available for several years as an alternative to tuberculin skin testing for detection of MTB infection. IGRA tests, including Quantiferon, detect the production of interferon produced by memory T-cells which are activated in vitro by re-exposure to TB antigen in the test collection tubes. Saint Luke's Laboratory has performed the Quantiferon-TB Gold (QFT) test in-house since

March 2013. This assay has been recently updated by the manufacturer and is now designated Quantiferon-TB Gold Plus (QFT-Plus).

The original QFT assay has 3 collection tubes which include a TB antigen tube, nil tube, and mitogen tube. The TB antigen tube measures the CD4 T-cell response to the MTB proteins ESAT-6 and CFP-10. This measurement is the primary basis for interpretation. However, results are also dependent upon measurement of background interference in the nil tube and ability of the patient's T-cells to produce interferon in the control mitogen tube. The major difference between QFT and QFT-Plus is the addition of a fourth collection tube. This tube also contains ESAT-6 and CFP-10 and measures interferon produced by CD8 T-cells. CD8 natural killer T-cells have recently been shown to kill TB infected cells and lyse intracellular organisms, as well as produce interferon.

The QFT-Plus assay is designed for higher sensitivity in active TB cases and after recent TB exposures as well as detecting infections in patients who lack CD4 T-cells. As with the previous test versions, QFT-Plus cannot distinguish active from latent tuberculosis. Likewise, positive results may occur due to previous or current infection with other mycobacterial organisms, including *M. kansasii, M. szulgai*, and *M*. *marinum*. ESAT-6 and CFP-10 are absent from TB vaccine (BCG) strains.

Saint Luke's Regional Laboratory will transition to QFT-Plus in August 2018. Results are reported as negative, indeterminate or positive. Reporting of positive tests will now include a numerical value for both TB1 & TB2 antigens, reflecting results obtained from the two antigen-containing collection tubes. Values over the cut-off on either or both TB1 or TB2 antigens (≥0.35 IU/mL) are interpreted as positive. Physicians should refer to the most recent CDC guidance for detailed recommendations on diagnosing MTB infection & selecting patients for testing. (https://www.cdc.gov/tb/publications/guidelines/default.htm)

A special collection kit with specific handling requirements is needed for these specimens, due to the presence of antigens and controls within the collection tubes. Specimens must be received by the laboratory as soon as possible after collection to decrease the likelihood of indeterminate results. Specimens received greater than 16 hours after collection cannot be processed.

Biotin Interference Update

Biotin is a form of vitamin B, many people take biotin supplements in hopes of treating hair loss, cradle cap in infants, and brittle nails. Increase in the use of biotin supplements by the public is producing an increase in the number of reports of analytic interference in biotin-based immunoassays (BBAs) used to evaluate endocrine function.

Recently, the manufacturer of BBAs released a list of assays affected by biotin interference. The effect of interference is dependent on assay method and can be positive or negative. If biotin interference is suspected, a repeat test 24-48 hours after stopping oral biotin may be requested. The following table lists the assays affected (Laboratory Test Directory available via EPIC and Saint Luke's web site provide interference details with each affected test).

NEGATIVE INTERFERENCE	POSITIVE INTERFERENCE
AFP	Vitamin B12
CA 125	Cortisol
CEA	Estradiol
CK-MB	Folate
Ferritin	Progesterone
FSH	Testosterone
PTH	
LH	
NTproBNP	
Prolactin	
PSA	
Beta HCG	
Troponin I	
TSH	