Saint Luke's Regional Laboratories
Clinical Laboratory Letter

May 2011

Interpreting Herpes simplex Testing

Genital herpes simplex virus (HSV) infection is among the most common sexually transmitted diseases and is frequently under-recognized due to subclinical infections. The seroprevalence of HSV-2 has increased steadily over the last decade, and genital infections due to HSV-1 are becoming more frequent. Differentiation of HSV-1 from HSV-2 is important prognostically, since genital HSV-2 infection is twice as likely to reactivate and recurs 8-10 times more frequently than genital HSV-1 infection. Recurrence of genital HSV-1 is less common after the first year of infection. Acquisition of new HSV-1 infection in an individual with HSV-2 antibodies is unusual, however women with genital HSV-1 infection are still at risk for HSV-2 acquisition. Extragenital complications of primary HSV infection include meningitis, urinary retention syndromes, and proctitis. The Centers for Disease Control (CDC) recently updated Sexually Transmitted Disease Guidelines (MMWR 2010;59, RR#12), including recommendations for herpes infection diagnostic testing.

In patients with new or recurrent genital ulcers, PCR testing is 1.5 to 4 times more sensitive than viral culture for diagnosis. HSV PCR differentiates between types 1 and 2, and is useful for lesions at any stage of healing. In the absence of lesions, or when PCR is negative despite high clinical suspicion, HSV IgG type-specific antibody testing is recommended. IgG antibody to HSV is detectable 2-12 weeks after infection and persists indefinitely. Importantly, seroconversion can take longer than 12 weeks in patients who are treated with anti-viral chemotherapy. False negative serologic results are most common in early stages of infection. Only tests based on detection of antibody to HSV glycoprotein G-2 are type-specific, due to cross-reactivity between viruses. Compared to Western blot, the sensitivity of type-specific HSV antibodies is 96-100%, with a specificity of 97-98%. Type-specific antibody testing of asymptomatic partners of persons with genital herpes is recommended to determine risk for acquiring new HSV infection. HSV IgM testing is not particularly useful in suspected primary genital infection due to low sensitivity (50%), ambiguity for primary vs. recurrent infection, and lack of type specificity.

Saint Luke's Regional Laboratories has performed HSV PCR for genital specimens since June 2003. Specimens for PCR testing should be submitted on a swab in M4-RT viral transport media. Type-specific HSV antibody testing is also available through Mayo Medical Laboratories. The test should be requested as 'HSV Type 1 & 2 Specific Antibodies' and the specimen requirement is one red top tube of blood.

Fetal Lung Maturity Testing Changes Again

Due to improvements in gestational age dating, maternal administration of corticosteroids that accelerate fetal lung maturity in at-risk pregnancies, and exogenous surfactant replacement therapies, the number of newborn deaths due to respiratory distress syndrome has declined considerably over the last 15 years. Most clinical laboratories in the United States have noted a steady decline in the number of fetal lung maturity tests that they perform each year. Saint Luke's Regional Laboratories (SLRL) experienced a similar trend from 2006 through 2009 with a slight uptick in 2010.

Year	FLM Tests per Year
2006	304
2007	275
2008	250
2009	233
2010	269

Many obstetricians in the United States have indicated that laboratory tests for fetal lung maturity are no longer needed for patient care (Grenache DG et al. Clinica Chimica Acta 2010;411:1746-9). Furthermore, European physicians rarely, if ever, order these tests and yet the rates of infant death due to respiratory distress are no worse than they are in the US.

Currently, more than 80% of laboratories in the United States use the FLM II assay from Abbott

Laboratories to assess fetal lung maturity. Unfortunately, Abbott recently announced that it will cease production of FLM II on Dec 31, 2011. SLRL has used FLM II as its initial test for fetal lung maturity for the past 10 years. In spite of decreasing clinical demand, SLRL has validated Lamellar Body Counts (LBC) as a replacement for FLM II. In order to give physicians time to acquaint themselves with this test, SLRL will begin reporting LBC together with FLM II results in June.

Type II pneumocytes package surfactant into intracellular storage granules called lamellar bodies, which are excreted into the alveolar space. Lamellar bodies appear in the amniotic fluid at 28 to 32 weeks and increase exponentially as gestation continues. Thus, LBC is a direct measurement of surfactant production. Due to the similar size of lamellar bodies and platelets, automated hematology analyzers can accurately count amniotic fluid lamellar bodies using the platelet channel.

Outcome-based studies have demonstrated that LBC performs at least as well as the TDx FLM II test (Ghidini A, et al. Arch Gynecol Obstet 2005;271:325-8, Haymond S et al. Am J Clin Path 2006;126:894-9 and Karcher R, et al. Am J Obstet Gynecol 2005; 193:1680). A meta-analysis calculated receiver-operating characteristic curves based upon data from six studies and showed the lamellar body count performed slightly better than the lecithin/sphingomyelin ratio in predicting respiratory distress (Wijnberger LD et al. BJOG 2001; 108:583).

SLRL has adopted the interpretive guidelines published by a consensus panel (Neerhof, MG. Obstet Gynecol 2001;97:318-20).

LBC (counts/uL)	Interpretation
0 – 15,000	Immature
15,000 – 50, 000	Indeterminate
>50, 000	Mature

Amniotic fluid is a heterogeneous mixture of fluid, sloughed cells, hair and other fetal debris that can have varying effects on LBC measurement. Blood contamination can lead to false elevation of the lamellar body count because platelets are counted as lamellar bodies. Meconium has been shown to lower LBC. Mucus artificially increases LBC. Vaginal pool samples can be counted if they are free of mucus. Amniotic fluid specimens contaminated with meconium or mucus cannot be run through the hematology analyzer. If amniotic fluid appears bloody, a red cell count is performed. LBC can be reported if the RBC count is <30,000/uL. Specimens with higher RBC counts are rejected. Physicians can request that a fetal lung profile be sent to a reference laboratory if either LBC or FLM II is indeterminate or the specimen is unacceptable for testing.

Specimens should be delivered to the laboratory at ambient temperature. LBC are stable at room temperature for up to 10 days. Frozen samples are not acceptable because freezing decreases LBC. Testing for LBC is available on a 24 x 7 basis.

Your Patience Please

The clinical laboratory on B level of Saint Luke's Hospital is nearing completion of the first phase of renovation. Before phase 2 can begin, Laboratory Support, Chemistry and Hematology must relocate. This is a huge undertaking involving most of the large automated instrumentation in the laboratory. A comprehensive contingency plan has been devised to minimize disruption of service. However, we ask for your understanding if turnaround times are slower during relocation on June 7-9.

Stimulating Bath Salts

The latest designer drugs are being marketed as bath salts in head shops and on the internet. Some popular names include Zoom, White Rush, Cloud Nine, Sextasy, White Dove and Ocean Snow. They have no legitimate use for bathing and are intended for substance abuse. These products contain stimulant compounds such as 3,4-methylene-dioxypyrovalerone (MDPV) or 4-methylmeth-cathinone (mephedrone). Users have snorted, injected and ingested these products. No relationship has been found between exposure route and severity of illness. Clinical findings are consistent with exposure to stimulants and include hypertension, tachycardia, tremors, mydriasis, agitation, delusions, hallucinations, paranoia and rhabdomyolysis. Fatalities have occurred.

Testing for these stimulants is available in the toxicology laboratory at Children's Mercy Hospital. Most patients abusing bath salts have tested positive for other drugs. Therefore, physicians should also order a urine TOX drug screen.