Saint Luke's Regional Laboratories
Clinical Laboratory Letter

December 2011

Respiratory Virus Detection by PCR

Respiratory viruses cause significant morbidity and mortality, particularly among the elderly, children, and immunocompromised individuals. There are an estimated 200,000 hospitalizations due to influenza and 125,000 RSV-related hospitalizations in the U.S. annually. Parainfluenzas, human metapneumovirus and adenoviruses can cause respiratory disease that is clinically indistinguishable from illness caused by influenza and RSV.

Traditional methods for detection of respiratory viruses include rapid antigen detection tests, direct fluorescent antibody (DFA) staining, and virus culture. None of these methods is ideal for diagnostic purposes. Rapid antigen testing is widely available but limited to detection of influenza and RSV, with sensitivity ranging from 50-90%. DFA testing has excellent sensitivity for most viruses, but is technically cumbersome to perform. Virus isolation by culture requires 2-10 days, so results are generally not available within a timeframe that is helpful for patient management. Importantly, the sensitivity of culture for respiratory viruses can be as low as 60%, and varies considerably depending on specimen collection and handling.

Testing for respiratory viruses by nucleic acid amplification tests, including PCR, greatly improves detection. The rate of viral identification increases by as much as 50% compared to traditional methods. For most respiratory viruses, PCR detects several orders of magnitude less pathogen than culture. The sensitivity of PCR for the eight most common respiratory viruses ranges from 95-100%, with specificity of 99-100%. Of note, mixed viral infections are detected in up to 30% of respiratory specimens tested by PCR.

In January 2012, SLRL's Molecular Diagnostics will begin PCR testing of respiratory specimens. Testing will be available for both nasopharyngeal swabs and bronchioalveolar lavage specimens. The assay detects and differentiates the following viruses:

- Influenza A including subtypes H1, H3, and H1N1
- Influenza B
- RSV types A & B
- Parainfluenza 1-4
- Human metapneumovirus types A & B
- Rhinovirus
- Coronavirus OC43, NL63, 229E, and HKU1
- Adenovirus types B, C, and E

Testing will be performed daily Monday through Saturday. For optimal results, specimens should be collected within 3 to 5 days of symptom onset. This test can only be ordered for inpatients within the Saint Luke's Health System.

Screening for Gestational Diabetes

The ongoing epidemic of obesity has increased the incidence of type 2 diabetes in women of childbearing age. For this reason, the American Diabetes Association (ADA) has recommended that pregnant women with risk factors for diabetes should be screened for type 2 diabetes at the first prenatal visit using standard diagnostic criteria (HbA1c $\geq$6.5, fasting glucose >126 mg/dL, or casual glucose >200 mg/dL). Women with diabetes found at this visit should be diagnosed with overt, not gestational, diabetes.

Gestational diabetes is defined as carbohydrate intolerance of varying degrees of severity with onset during pregnancy. The main purpose of identifying gestational diabetes is to detect women at risk of adverse perinatal outcomes. Gestational diabetes affects ~14% of pregnant women. After a pregnancy with GDM, a woman has an increased risk of developing type 2 diabetes mellitus within 10 years postpartum.

Fetal macrosomia affects 40% of the offspring of women with GDM. Macrosomia is associated with increased risk of birth injuries as a result of the large size of the fetus. Infants of women with GDM are at higher risk of developing obesity, impaired glucose tolerance or diabetes mellitus at an early age.

Keeping 1-hour postprandial blood glucose levels between 120 and 140 mg/dL minimizes the risk of macrosomia.

The International Association of Diabetes and Pregnancy Study Groups, which included representatives from the ADA, developed revised guidelines in 2009 for diagnosing GDM (Diabetes Care 2011; 34:s11). The group recommended that all women not known to have diabetes undergo a 75 g oral glucose tolerance test (OGTT) at 24 to 28 weeks of gestation. The test should be performed in the morning after an overnight fast of at least 8 hours. The diagnosis of GDM is made when any of the following plasma glucose values are exceeded:

Specimen	Diagnostic Threshold
Fasting	≥92 mg/dL (5.1 mmol/L)
One hour	≥180 mg/dL (10.0 mmol/L)
Two hour	≥153 mg/dL (8.5 mmol/L)

The new diagnostic criteria replace all of the previously published criteria. They will significantly increase the prevalence of GDM, primarily because only one abnormal value, not two, is sufficient to make the diagnosis. One abnormal glucose value on an OGTT is a common occurrence, and these women demonstrate fasting insulin concentrations and insulin resistance comparable to that of women with GDM. They are also more likely to deliver a macrosomic infant than women without GDM or women being treated for GDM. They are also more likely to develop impaired glucose tolerance later in life than women whose GTT values are all normal.

Capillary blood should not be used for screening unless the precision of the glucose meter is known, it has been correlated with simultaneously drawn venous plasma samples, and has met federal standards for laboratory testing. Specimen requirement is a gray top (potassium oxalate-sodium fluoride) tube of blood at each time interval.

Post-Prostatectomy PSA

PSA levels are most useful for monitoring patients with established cancer for residual disease after radical prostatectomy. When the entire prostate is removed for cancer, serum PSA should become undetectable. Previously, the chemistry analyzers used in the Saint Luke's Health System laboratories had a lower limit of detection of 0.01 ng/mL. The new analyzers introduced in November have a lower limit of detection of 0.06 ng/mL. Undetectable PSA levels that were previously reported as <0.01 ng/mL are now reported as <0.06 ng/mL. These results should be considered equivalent. A change to <0.06 from <0.01 should not be considered evidence of recurrence. The American Urological Association defines biochemical recurrence after prostatectomy as a PSA value of 0.2 ng/mL. This value should be confirmed by at least 2 PSA measurements.

Serum Acetone Reagent Shortage

Saint Luke's Health System has been notified by the manufacturer of a nationwide shortage of Acetest reagent. Because of this shortage, serum acetone testing is temporarily unavailable at most hospital laboratories. The laboratory is evaluating a rapid test for serum beta-hydroxybutyrate as a replacement for acetone.

Reference Range Changes

Saint Luke's Regional Laboratories has recently adjusted the reference ranges for three chemistry analytes. The new ranges are summarized below.

Analyte	Reference Range
Sodium	133-147 mEq/L
Chloride	96-112 mEq/L
Magnesium	1.4-2.7 mg/dL

HbA1c Interpretation Changes

In 2009, an International Expert Committee recommended the use of the HbA1c test to diagnose diabetes, with a threshold of 6.5% or greater (Diabetes Care 2009, 32 (7):1327-1334). The American Diabetes Association adopted this criterion in 2010. Patients who have an HbA1c of 5.7 to 6.4% are classified as having prediabetes.

Accordingly, Saint Luke's Regional Laboratories has changed the interpretive comments that accompany HbA1c results.

HbA1c Level	Interpretation
4.0-5.6%	Nondiabetes
5.7-6.4%	Prediabetes
6.5% or greater	Diabetes