D-Dimer Do’s and Don’ts

D-Dimer is a type of fibrin degradation product that is only formed when a stable fibrin clot is formed and is being dissolved somewhere within the body. D-Dimer results are most commonly used in the evaluation and exclusion of deep vein thrombosis (DVT) and pulmonary embolism (PE). Many studies have indicated that the combination of pretest clinical probability assessment and D-Dimer testing is a safe and effective model for excluding DVT and reducing the number of more expensive imaging studies. In patients that have a low pretest probability score and a negative D-Dimer, a diagnosis of DVT may be excluded without imaging studies. In addition, the use of D-Dimer testing has also been shown to reduce the need for repeated ultrasound testing in patients whose score indicates that DVT is likely. This approach leads to reduced costs per patient and shorter time to diagnostic decision. D-Dimer testing alone should not be used to exclude DVT in patients with high pretest probability scores. In these cases, imaging studies should be performed.

In hemodynamically stable patients, the diagnosis of PE should follow a sequential diagnostic workup consisting of clinical pretest probability assessment, D-Dimer testing and, if necessary, computed tomography (CT) or ventilation-perfusion scanning. D-Dimer is most helpful in assessing patients with a low or intermediate clinical probability of PE, where a normal result avoids unnecessary further investigation. The use of D-Dimer is of limited value in patients with a high clinical probability of PE because they need to undergo imaging regardless of the D-Dimer result.

D-Dimer is useful in excluding the diagnosis of DVT and PE because a highly sensitive quantitative assay has a negative predictive value (NPV) of nearly 100%. The trade-off for this high sensitivity is relatively low specificity. A positive result is not useful in confirming the diagnosis of DVT or PE. Physicians need to remember that D-Dimer is often elevated in many disorders associated with activation of the coagulation cascade. Common examples include: myocardial infarction, congestive heart failure, stroke, atrial fibrillation, thrombolytic therapy, venous malformations, disseminated intravascular coagulation (DIC), preeclampsia and eclampsia, acute and chronic renal failure, nephrotic syndrome, sickle cell disease, advanced liver disease, surgery, trauma and malignancy. Because of this lack of specificity, D-Dimer testing should not be ordered on most hospitalized inpatients when DVT or PE is suspected.

It should also be remembered that D-Dimer levels are always elevated in the second and third trimesters of normal pregnancies. Elevated levels are also frequently seen in elderly patients due to their higher fibrinogen concentration and decreased urinary excretion of D-Dimer.

Revolutionary Gene Array for Rapid Detection of Respiratory Pathogens

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. Bacterial atypical pneumonia pathogens include Mycoplasma pneumoniae and Chlamyphila pneumoniae. M. pneumoniae typically infects younger age groups, while C. pneumoniae has a higher incidence in the elderly. Long-lasting immunity does not occur following infection with either organism.

Traditional methods for detection of respiratory pathogens include rapid antigen detection tests, direct fluorescent antibody (DFA) staining, culture, and serology. 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. Additionally, sensitivity of culture for respiratory viruses can be as low as 60%, and varies considerably depending on specimen collection and handling. Serologic testing for respiratory pathogens usually requires acute and convalescent samples and is usually not effective for early diagnosis.

Testing for respiratory pathogens 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 pathogens, PCR detects several orders of magnitude less organism 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.

A new FDA-cleared test for detection of multiple respiratory pathogens has recently become available. This assay combines PCR and gene array technology to detect 17 viral and 3 bacterial pathogens, including M. pneumoniae, C. pneumoniae, and B. pertussis. This test is available through Saint Luke’s Microbiology and should be ordered as ‘Respiratory Panel by PCR’. Testing will be performed daily and is available on nasopharyngeal swabs, nasal washes, and bronchoscopy specimens.

**Sample rejection for AFB cultures**

Sample quality is crucial in obtaining accurate results from culture specimens. Swabs are a suboptimal collection device for many specimens including body fluids, abscesses, and tissue. False negative results are probable when swab specimens from these sources are submitted for AFB culture. Mycobacterial cell walls are particularly hydrophobic, making it difficult to extract the organisms from swab material.

Regulatory agencies, such as Clinical Laboratory Standards Institute (CLSI) and College of American Pathologists (CAP) consider rejection of swabs for mycobacterial culture to be the best practice.

Effective immediately, Saint Luke’s Microbiology will reject specimens submitted on swabs for AFB culture, with the exception of pediatric specimens. Tissue, body fluids or abscess drainage for AFB culture should be submitted in a sterile container.

**Postvaccination Serologic Testing of Infants Exposed to Hepatitis B Virus at Birth**

An estimated 25,000 infants are born to hepatitis B surface antigen (HBsAg)-positive women annually in the United States. With no intervention, 40%–90% of these infants will acquire hepatitis B virus (HBV) infection. Approximately 90% of infected infants develop chronic HBV infection and 15%–25% are at increased risk for premature death from cirrhosis or cancer of the liver. To prevent perinatal HBV transmission, the Advisory Committee on Immunization Practices (ACIP) recommends that infants born to HBsAg-positive women receive postexposure prophylaxis with hepatitis B vaccine (HepB) and hepatitis B immune globulin (HBIG) within 12 hours of birth, and complete the 3-dose HepB vaccine series. If this regimen is followed, more than 90% of infants are protected (MMWR September 28, 2012 / 61(38):768-771).

To determine infant outcomes after postexposure prophylaxis, ACIP recommends postvaccination serologic testing between 9 and 18 months of age. Postvaccination serologic testing is critical for guiding medical management of infants born to HBsAg-positive women, identifying infants with HBV infection and in need of further care, and monitoring progress toward the elimination of perinatal HBV transmission.

**Alkaline Phosphatase Reference Range Change**

The reference range for serum alkaline phosphatase has changed to 42–140 from 42-128 IU/L.