Saint Luke's Regional Laboratories
Clinical Laboratory Letter

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PCR Replaces Virus Culture for Skin Lesions

Primary infection with varicella zoster virus (VZV) causes chickenpox, while reactivation of the virus is responsible for varicella zoster, or shingles. The most common clinical manifestation of infection is dermal vesicles. Although viral culture of vesicular fluid has been the standard diagnostic test, the sensitivity of culture is low at less than 50%.

Saint Luke's Regional Laboratories replaced conventional herpes virus culture of genital lesions with herpes testing by PCR in June 2003. Effective March 3, 2005 all skin lesion specimens submitted for viral culture are tested by PCR for herpes simplex virus 1 & 2, and VZV. In addition to enhanced sensitivity, PCR results are available within 1-2 days instead of 3 -10 days required for cultures. The charge for PCR is comparable and specimen collection is the same as for viral cultures. Vesicular fluid can be collected with a tuberculin syringe and transferred to viral transport media, or vesicles can be unroofed and the base of the lesion swabbed to obtain infected epithelial cells. The test can be ordered as Virus Lesion PCR, and the CPT code is 87798.

Predictive Value of D-Dimer for Recurrence of Venous Thromboembolism

The aim of oral anticoagulation after an episode of venous thromboembolism (VTE) is to reduce the risk of recurrent VTE and post-thrombotic syndrome. It is generally accepted that the risk of recurrence is low if a first episode of VTE is associated with a reversible risk factor (such as surgery or immobilization), requiring short-term (3 months) oral anticoagulant therapy (OAT), whereas a longer period of anticoagulation is required if the episode is idiopathic (unprovoked), or if persistent risk factors are present (such as cancer or various thrombophilic defects). The optimal duration of OAT for a first episode of VTE is, however, controversial. The duration of OAT in each patient should be tailored to maximize its preventive benefit and minimize the risk of hemorrhage. A major problem is the absence of reliable markers to predict recurrent thrombosis, which would facilitate selection of patients for longer-term anticoagulation.

Several recent studies suggest that D-dimer levels measured after OAT is discontinued may be useful for predicting the likelihood of recurrent VTE. In one study (Thromb Haemost 2002; 87:7-12) 396 patients with a first episode of VTE had D-dimer assayed on the day OAT was discontinued, and after a further 3-4 weeks, and 3 months. Increased D-dimer was present in 15.5%, 40.3%, and 46.2% of the patients at the three respective time points. D-dimer was persistently elevated in 80 patients, 16.2% of whom developed recurrent VTE, and persistently normal in 127 patients, only 3.9% of whom had a recurrence. The negative predictive value of D-dimer for VTE recurrence was highest for the 3 month value (95.6%). In other words a normal D-dimer value at 3 months after OAT withdrawal was associated with a 95.6% likelihood of no recurrent VTE. In a subsequent study (Circulation 2003; 108:313-318) 599 patients with a first episode of VTE were tested for D-dimer at one month following OAT withdrawal, and were also screened for inherited thrombophilic defects. Once again, the D-dimer value had a high negative predictive value (94.2%) for VTE recurrence. An elevated D-dimer level one month after OAT discontinuation was associated with an increased risk of recurrent VTE, especially in those with idiopathic VTE (relative risk 2.75), and those with thrombophilic defects such as factor V Leiden (relative risk 5.88).

In summary, patients with a first episode of VTE who have a normal D-dimer level 1-3 months after withdrawal of OAT have a low risk of VTE recurrence. This may help clinicians determine the optimal duration of OAT in individual patients, avoiding unnecessarily prolonged anticoagulation in some. A clinical study is currently underway to evaluate this approach.

Transporting Arterial Blood Gas Specimens

Traditionally, arterial specimens were collected in glass syringes and placed in an ice slurry for transportation to the laboratory. Glass syringes provided an impermeable barrier to atmospheric gas pressures, but there was still a progressive decrease in pO_2 and increase in pCO_2 caused by metabolism of the leukocytes and erythrocytes over time. Storage in an ice slurry decreased the metabolic rate to approximately 10 % of the value at 37 degrees centigrade.

During the past few years, plastic syringes have largely replaced glass syringes because of concerns about safety, waste disposal, and cost. Plastic syringes are significantly more permeable than glass to both oxygen and carbon dioxide. Therefore, this change in practice necessitated a re-evaluation of the storage time and conditions on oxygen and carbon dioxide results.

Specimens collected in plastic syringes and stored on ice actually increase the rate of rise in pO_2 compared to plastic syringes stored at ambient temperature. The mean change is 8.4 mmHg at 30 minutes, 9.6 at 60 minutes and 10.3 at 90 minutes when the initial pO_2 is approximately 100 mm Hg. The pO_2 of blood collected in glass syringes and stored on ice also increases, but to a much lesser extent. This increase occurs due to the combination of a decreased metabolic utilization of oxygen and a rise in the rate of diffusive transfer of oxygen into blood secondary to the decreased temperature. In contrast, pO_2 does not change significantly when whole-blood samples collected in a plastic syringe are stored at ambient temperature for 30 minutes. The changes in pO_2 in plastic syringes stored at room temperature are the same order of magnitude as glass syringes stored in ice.

Because of these findings, the Clinical and Laboratory Standards Institute now recommends that arterial specimens be collected in a plastic syringe, left at room temperature and analyzed within 30 minutes. Accordingly, blood gas syringes should now be transported to the laboratory at room temperature.

ABG specimens collected from patients with severe anemia or leukocytosis should be analyzed as quickly as possible. When the hemoglobin concentration is decreased, the capacity for buffering oxygen may be reduced. The metabolic decrease in pO_2 and increase in pCO_2 in the presence of an elevated WBC count will be even more pronounced in blood gas specimens transported at room temperature.

Urine Myoglobin for Rhabdomyolysis

Myoglobin is an oxygen carrying heme protein present in high concentrations in the cytoplasm of cardiac and skeletal muscle. Small amounts of myoglobin are cleared from the plasma in one to six hours and metabolized to bilirubin. When plasma myoglobin levels exceed 1.5 mg/dL, it is excreted by the kidney.

Rhabdomyolysis is defined as an acute increase in plasma concentrations of creatine kinase to more than 5 times the upper limit of normal in the absence of a myocardial infarction. High concentrations of myoglobin are released into the plasma during muscle injury. Visible myoglobinuria (tea or cola colored urine) occurs when urinary myoglobin exceeds 250 ug/mL, corresponding to the destruction of >100 grams of skeletal muscle.

The major causes of myoglobinuria include skeletal muscle trauma, excessive muscle use, primary skeletal muscle diseases, hyperpyrexia, seizures, and gangrene. Insect and snakebites can also cause myoglobinuria. The most common drugs causing myoglobinuria are alcohol, cocaine, amphetamines, opiates, phencyclidine, neuroleptics, and statins.

Patients with skeletal muscle injury also have elevated serum CK, AST, LD, uric acid, potassium and creatinine levels. Creatine kinase levels may exceed 100,000 IU/L. Serum calcium is often decreased due to calcium binding by damaged muscle proteins and phosphate. Acute renal failure results from renal vasoconstriction, intraluminal myoglobin cast formation, and heme protein nephrotoxicity.

Myoglobinuria can be inferred by a positive urine dipstick test for heme in the absence of red blood cells on microscopic examination of urine sediment. If these criteria are met, requests for quantitation of urine myoglobin are forwarded to Mayo Medical Laboratories.

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