Saint Luke's Regional Laboratories
Clinical Laboratory Letter

July 2014

Heartland Virus

Heartland virus is a newly identified phlebovirus that was first isolated from two northwestern Missouri farmers hospitalized with fever, leukopenia, and thrombocytopenia in 2009. Six cases were confirmed during 2012–2013. Five patients were Missouri residents and one was a Tennessee resident. Four of the patients were hospitalized and one died. Heartland virus is believed to be transmitted through infected ticks or other arthropods. (Pastula DM, etal. Notes from the Field: Heartland Virus Disease — United States, 2012–2013, MMWR Weekly, March 28, 2014 / 63(12);270-271).

In a recent study, 56,428 ticks were collected in northwest Missouri for analysis. Lone Star ticks (*Amblyomma americanum*) were the most common species identified and nymph stage Lone Star ticks were found to harbor the Heartland virus (Savage HM, Godsey MS Jr, Lambert A, et al. First detection of heartland virus (Bunyaviridae: *Phlebovirus*) from field collected arthropods. Am J Trop Med Hyg 2013;89:445–52).

Patients infected with Heartland virus typically present with fever, leukopenia and thrombocytopenia. Nonspecific findings include fatigue, anorexia, headache, nausea, myalgia, or arthralgia. These findings mimic the signs and symptoms of *Ehrlichia* and *Anaplasma* infection which need to be ruled out. Unlike these infections, patients with Heartland virus do not respond to doxycycline therapy. No vaccine or medication is available to prevent or treat Heartland virus disease.

Currently, testing for Heartland virus is only available through enrollment in a CDC clinical trial. Consultation with an infectious disease specialist is recommended, if Heartland virus infection is suspected.

C Reactive Protein versus Erythrocyte Sedimentation Rate

Erythrocyte sedimentation rate (ESR) is one of oldest laboratory tests in use. When anticoagulated whole blood is allowed to stand, red blood cells settle out. The rate at which they fall is known as the erythrocyte sedimentation rate and is a rough measure of abnormal concentrations of acute phase proteins and immunoglobulins. The acute phase proteins that affect ESR are fibrinogen, C-reactive protein, alpha-1 antitrypsin, and haptoglobin. Acute phase proteins increase with acute tissue damage and inflammation such as occurs in myocardial infarction, collagen vascular disease, malignancy and chronic infection. Elevated immunoglobulins, including monoclonal gammopathy, also increase ESR. This property makes ESR a sensitive, but nonspecific, indicator of tissue damage and inflammation. Historically, an elevated ESR has been recommended as an important diagnostic criterion for polymyalgia rheumatica and temporal arteritis, because these two diseases have few other laboratory markers.

C-reactive protein (CRP) is an acute phase protein synthesized in hepatocytes and alveolar macrophages in response to cytokines, particularly IL-6. It is a general marker of inflammation that begins to rise four to six hours after tissue injury. This is much earlier than other acute phase reactants, which do not begin to increase until 24 hours or more. CRP also increases to much higher levels than other acute phase proteins, making it the most sensitive indicator of small inflammatory stimuli.

Even though both ESR and CRP levels reflect similar pathologies, discordance between ESR and CRP has been documented and is thought to depend, in part, on serum albumin concentration, renal insufficiency, anemia and non-infectious inflammatory disorders.

ESR is a manual test, whereas CRP is performed on an automated chemistry analyzer. In this age of

laboratory automation and cost containment, some laboratories have replaced ESR with CRP. A recent study has clearly demonstrated that ESR still has important clinical utility and should be retained.

Dr. Gurmuhk Singh, The Shepeard Professor of Pathology and Chief of Clinical Pathology at Georgia Regents University, compared ESR and CRP values in 4527 instances when both tests were ordered (Adv Biol Chem: 2014; 4:5-9; DOI:10.4236/abc.2014.41002). He found 150 instances, involving 97 patients, where ESR was elevated more than twice the upper limit of normal (60 mm/h) but CRP was normal (≤1.0 mg/L). Average age of the patients was 55.5 years, and the sample included 71 women and 26 men. Medical records of these cases were reviewed to discern the cause of disparity between the ESR and CRP results. Of these patients, 39 had skin lesions, 33 joint lesions, 27 bone lesions and 11 colon disease.

Skin lesions were grossly visible and included cellulitis, vasculitis, gangrene, and lupus. The most common bone disease was osteomyelitis, often without any discharge or break in skin. Other bone and joint diseases included, gangrene, lytic bone lesions from myeloma, septic arthritis following joint replacement surgery, necrosis of bone implant and rheumatoid arthritis. Many patients had co-existing degenerative joint disease with or without synovitis and tendinitis. Colon lesions included inflammatory bowel disease due to ulcerative colitis, Crohns disease, and diverticulitis. A relevant negative finding was the lack of instances of pneumonia, acute appendicitis, and non-osseous pyogenic lesions in any of the patients with elevated ESR and normal CRP.

This study demonstrated that clinical laboratories should continue to offer ESR. ESR was particularly valuable in detecting inflammatory disorders that may not be obvious by clinical examination or CRP results. ESR is particularly useful in diagnosing bone disease in general and osteomyelitis in particular.

In many cases it is appropriate to order both CRP and ESR in the initial diagnostic workup. If both are elevated, the course of the disease should be followed with serial CRP levels since CRP responds more quickly to changing clinical conditions than ESR.

Serum Protein Electrophoresis Change

Serum proteins have different net charges and can be separated by electrophoresis into several distinct bands. The band that migrates fastest toward the anode is albumin followed by alpha 1-globulin, alpha 2-globulin, beta globulin, and gamma globulins. Protein concentrations may be altered as a result of different disease states. Interpretation of serum protein electrophoretic patterns is helpful in diagnosing some diseases The most commonly recognized electrophoretic patterns are acute inflammation, alpha-1 antitrypsin deficiency, chronic inflammation, cirrhosis, hypoalbuminemia, hypogammaglobulinemia, monoclonal gammopathy, polyclonal gammopathy and protein losing disorder.

In mid-August, Saint Luke's Regional Laboratories will be upgrading to a new automated protein electrophoresis method, the SPIFE 4000 Split Beta SPE system. This change necessitated a change in the reference ranges for each protein fraction. The new ranges will be:

Protein Fraction	Reference Range
Total Protein	6.0 – 8.0 g/dL
Albumin	3.4 – 5.0 g/dL
Alpha 1 globulin	0.2 – 0.4 g/dL
Alpha 2 globulin	0.5 – 1.1 g/dL
Beta globulin	0.9 – 1.5 g/dL
Gamma globulin	0.5 – 1.5 g/dL

Specimen requirement is a red top tube of blood.

Protime & INR Reference Range Change

The reference range for Protime and INR changed on July 16, 2014. The new ranges are 11.4 – 15.0 seconds and 0.8-1.2, respectively. Specimen requirement is a lavender top tube of blood.