



Saint Luke's Regional Laboratories Clinical Laboratory Letter



June 2006

Mumps Testing Guidelines And Outbreak Update

New cases of mumps continue to be reported in the Midwest outbreak that began in Iowa in December 2005. As of the first week of June, Kansas had 744 confirmed and probable mumps cases reported, while Missouri had 29 confirmed and 102 probable cases. The group most affected remains young adults, aged 18-24.

State specific outbreak guidelines for physicians & health care workers are available on the websites of the Kansas Department of Health & Environment (www.kdhe.state.ks.us) and Missouri Department of Health & Senior Services (www.dhss.mo.gov).

The clinical case definition of mumps infection includes acute onset of unilateral or bilateral tender swelling of parotid or other salivary glands, lasting \geq 2 days. KDHE suggests that these symptoms alone are sufficient for the diagnosis, if the patient resides in a county where mumps cases have been confirmed. Mumps is transmissible prior to symptom onset, having an incubation period of 14 days.

The laboratory diagnosis of mumps infection is accomplished through isolation of virus by culture or serologic testing. Virus cultures can be positive from 7 days before to 9 days after onset of salivary gland swelling. The preferred mumps culture specimen is parotid gland secretions, although throat, naso-pharyngeal swabs and urine are also acceptable. Swab specimens should be submitted in viral transport media and the suspected diagnosis should be noted on the requisition. Mumps virus cultures are performed by Saint Luke's Regional Laboratories (SLRL).

Serologic testing for suspected infection should include mumps IgM and IgG antibodies. According to the CDC, interpretation of IgM results is difficult, especially in previously vaccinated people. Neither the sensitivity nor specificity of mumps IgM is well-known, due to lack of experience with most of the IgM assays in a previous outbreak situation.

Although presence of mumps IgM antibody is diagnostic of acute infection, absence of IgM antibody with the appropriate clinical symptoms is also considered a reportable case. Mumps IgM and IgG antibody testing is forwarded to Mayo Medical Laboratories by SLRL.

Mumps IgG antibody is detectable in serum as soon as 7 days after the onset of symptoms and persists for many years after an infection, or may be indicative of previous effective vaccination. Mumps IgG only testing is performed twice weekly by SLRL Microbiology. The specimen type for serology testing is one red-top tube of blood.

Immature Platelet Fraction: An Index of Thrombopoietic Activity

In the evaluation of thrombocytopenia, it has been known for many years that quantification of immature platelets may be used as an index of bone marrow thrombopoietic activity, analogous to the red cell reticulocyte count in the evaluation of anemia. Newly released platelets, originally termed "reticulated platelets", contain residual RNA, and may be measured by flow cytometry, using a fluorescent dye that binds RNA. Measurement of reticulated platelets has been shown to be useful in differentiating whether thrombocytopenia is secondary to decreased production or peripheral destruction of platelets. A significant disadvantage of the flow cytometric method is that it is time-consuming and not widely available.

A fully automated rapid method for quantification of immature platelets, the "immature platelet fraction" (IPF), is now available on a standard hematology analyzer. The method used is fluorescent flow cytometry using an RNA-binding dye. The IPF value can be reported together with the routine complete blood count.

This automated IPF assay has been shown in two recent studies to be useful in differentiating aplastic from peripheral consumptive causes of thrombocytopenia. In one study (Br J Haematol.

2004;126:93-99) patients with immune thrombocytopenic purpura (ITP) demonstrated the highest IPF values of all the patients studied, indicating active platelet production in the setting of peripheral platelet destruction. Raised IPF values were seen in 73% of patients with ITP, and 100% of ITP patients with a platelet count below 50 th/uL. Patients with active thrombotic thrombocytopenic purpura (TTP) also had high IPF values. Patients with ITP and TTP in remission generally had low IPF values. Patients with thrombocytopenia secondary to chemotherapy had low IPF values, indicative of decreased platelet production.

In another study of thrombocytopenic patients (Am J Clin Pathol. 2006;125:282-287), patients with peripheral platelet destruction (ITP and DIC) had significantly higher IPF values than those with marrow suppression (aplastic anemia and cancer). In this study, elevated IPF values (greater than 9%) were 89% sensitive for diagnosis of ITP, 100% sensitive for diagnosis of DIC, and 100% specific for being found in patients with peripheral platelet destruction. In summary, IPF is a useful test in the initial evaluation of a patient with thrombocytopenia. An elevated level is indicative of peripheral platelet destruction, for example ITP, TTP, or DIC, whereas a normal level is suggestive of decreased platelet production, for example drug-induced marrow suppression or aplastic anemia. In selected cases (for example typical ITP), the availability of this simple test may make performance of a bone marrow examination unnecessary.

A study was recently completed by Saint Luke's Regional Laboratories to evaluate the ability of IPF to predict platelet recovery following peripheral blood hematopoietic progenitor cell (HPC) transplantation. Fifty patients undergoing peripheral blood HPC transplantation (38 autologous and 12 allogeneic) were followed daily after transplantation with measurement of IPF, immature reticulocyte fraction (IRF, previously shown to be an early predictor of hematopoietic recovery), platelet count, and absolute neutrophil count (ANC). IPF recovery (defined as a value greater than 7%) occurred significantly earlier than recovery of all the other parameters (3.1 days earlier than platelet count, 3.8 days earlier than ANC, 0.6 days earlier than IRF). IPF recovered at least one day prior to platelet count in 79% of patients, and was followed by platelet count recovery within an average of 4.1 days (range 1-12 days, 76% within 5 days). IPF is one of the earliest predictors of hematopoietic

recovery following peripheral blood HPC transplantation. In selected cases of marrow ablation, monitoring IPF may guide and possibly limit the use of prophylactic platelet transfusions, in view of anticipated imminent recovery of the platelet count.

IPF will be available in Saint Luke's Regional Laboratories in mid-June, 2006. The assay will be available 7 days a week, and sample requirement is one 5ml purple-top tube (IPF can be run on the same sample as the CBC). The reference range is 1.1-7.1%.

CCP Antibody Update

More aggressive forms of therapy are being used early in the course of rheumatoid arthritis in the hope of diminishing long term morbidity. Because this treatment is expensive and may be associated with major side effects, it is important to accurately diagnose rheumatoid arthritis before initiating therapy. Several studies in the past five years have demonstrated that the use of anti-CCP antibody in addition to rheumatoid factor (RF) has a better predictive value than RF alone in the detection of rheumatoid arthritis in high risk populations.

Saint Luke's Regional Laboratories (SLRL) introduced anti-CCP antibody testing in May 2003 to assist in the diagnosis of rheumatoid arthritis. On July 1, SLRL will upgrade to the third generation of the anti-CCP assay. It is about 5% more sensitive than the second generation assay, without loss of specificity. This upgrade will necessitate a change in the reference range from the current range of 0 – 20 to 0 – 30 units.

Mitochondrial Antibody Change

Anti-mitochondrial antibodies are found in almost all patients with primary biliary cirrhosis and are considered the serological hallmark of the disease. These antibodies are useful diagnostically in distinguishing primary biliary cirrhosis from other types of chronic liver disease. Recently, the enzyme immunoassay for detection of mitochondrial antibodies has been improved by incorporating a recombinant fusion protein that contains the immunodominant epitopes of the three major target antigens of mitochondrial antibodies; E2 subunits of pyruvate dehydrogenase, 2-oxo acid dehydrogenase, and 2-oxo glutarate dehydrogenase. The reference range has changed from <1.0 to 0 – 50 units.