



Saint Luke's Regional Laboratories Clinical Laboratory Letter

March 2014

New CDC Guidelines for Hepatitis B Exposure

CDC has recently updated the guidelines for post-exposure management of hepatitis B in health-care personnel (HCP) in MMWR 2013;62:RR-10, available at the CDC's website (cdc.gov). Hepatitis B vaccine has been recommended for HCP since 1982, resulting in markedly decreased infections in this population. However, post-vaccination serologic testing for hepatitis B antibody (anti-HBs) to determine immune status was not performed routinely until after 1991. Vaccine-induced anti-HBs decreases over time in most individuals, therefore post-exposure testing several years after vaccination may not distinguish between nonresponders and responders whose antibody has waned. The updated guidelines address revaccination and use of HBIG in HCP with unknown vaccine response, undetectable anti-HBs, and nonresponders.

Hepatitis B (HBV) is highly infectious. In addition to blood, other body fluids including cerebrospinal, synovial, pleural, peritoneal, pericardial and amniotic fluid are considered potentially infectious. Notably, HBV is transmissible in the absence of visible blood and remains infectious on environmental surfaces for at least 7 days. Acute HBV infection progresses to chronic infection in 90% of infants, but <10% of adults. However, 25% of childhood-acquired chronic infections and 15% of adult chronic infections result in premature death from cirrhosis or hepatocellular carcinoma.

Anti-HBs levels of ≥ 10 mIU/mL measured 1-2 months after completion of the vaccine series are considered seroprotective. By 18 years post-vaccination, 74% of individuals vaccinated at age ≥ 1 year have seroprotective anti-HBs detected. Among immunocompetent known responders, protection is believed to persist for ≥ 22 years post-vaccination. Per Table 2 of the above-referenced CDC guideline, exposed HCP with unknown vaccine response should have anti-HBs testing

performed post-exposure, regardless of source patient results. Saint Luke's Regional Laboratory performs anti-HBs testing Monday through Friday. Qualitative results are reported as positive or negative. A positive result corresponds to an antibody level greater than 10 mIU/mL, and is indicative of immunity.

Seroprevalence of Herpes Simplex Virus Types 1 & 2

Herpes simplex virus (HSV-1 and HSV-2) infections are found worldwide, even in remote populations. Herpes simplex virus (HSV) infections have no seasonal prevalence. The incubation period ranges from 1 to 26 days (median 6-8 days). Contact with active ulcerated lesions or asymptotically excreting persons can result in transmission. HSV has been isolated from nearly all body sites and is associated with a variety of clinical syndromes including mucocutaneous infections, central nervous system, and visceral infections. HSV infections vary widely in severity, from common cold sores to life-threatening infections in infants and immunocompromised hosts. Both viral subtypes can cause genital and oral-facial infections. HSV-2 infections increase risk of acquiring and transmitting HIV infection.

The epidemiology of HSV in the U.S. has been followed through NHANES data since 1976. A recent update (JID 2014;209:325-33) compares seroprevalence from years 1999-2004 and 2005-2010. HSV-2 seroprevalence (15.7%) has not changed significantly. Comparatively, HSV-1 seroprevalence has declined among all age groups, most substantially among 14- to 19-year olds. Current seroprevalence of HSV-1 among 14- to 49-year olds is 53.9%. Although HSV-1 incidence has decreased, the proportion of genital HSV infections attributable to HSV-1 has significantly increased. Data collected during a recent vaccine trial revealed that nearly 60% of genital herpetic infections were due to HSV-1.

Saint Luke's Regional Laboratory offers testing for herpes simplex by type-specific serology or HSV PCR. Differentiation of HSV-1 from HSV-2 is important prognostically, since genital HSV-2 infection may recur 8-10 times more frequently than genital HSV-1 infection. Likewise, oral-facial HSV-1 infection recurs more frequently than oral-facial HSV-2 infection. Occasionally, HSV is detected by PCR, but results are indeterminate for the subtype. This phenomenon has been described by Mayo Medical Laboratories (JCM 2005;43:1843-1845) and is attributable to polymorphisms within the HSV virus.

Predicting Type 1 Diabetes

Type 1 diabetes mellitus (T1DM) is an autoimmune disease that results from the cell-mediated destruction of islet beta cells. Onset of T1DM is preceded by the synthesis of autoantibodies to insulin and islet cell antigens. Detection of one or more islet cell autoantibodies is a strong predictor for progression to type I diabetes. The five year cumulative risk for developing diabetes has been estimated to be 17% if seropositive for 1 antibody, 39% if seropositive for 2 antibodies, and 70% if seropositive for 3 antibodies. Autoantibodies can often be detected by age 3.

A recent meta-analysis of three prospective studies involving 13,377 children genetically at risk of T1DM demonstrated that 8% (1059) of subjects seroconverted, and of these, 55% had multiple autoantibodies. Almost half of the antibody positive children developed T1DM; 44% within 5 years, 70% within 10 years and 84% within 15 years after seroconversion. The hazard ratio for developing diabetes in children with multiple antibodies was 395 (JAMA 2013;309:2473-9).

Some adults have slowly-progressive T1DM that has been classified as latent autoimmune diabetes of adulthood. They may be initially diagnosed as having type 2 diabetes because of their adult onset of disease and their initial insulin independence. Testing for islet cell autoantibodies is helpful in distinguishing type 1 from type 2 diabetes in these patients.

Presently, four autoantibodies to islet cell antigens have been discovered: insulin, insulinoma

associated antigen 2 (IA-2), glutamic acid decarboxylase 65 (GAD65) and zinc transporter 8 (ZnT8). Individual sensitivities of these autoantibodies for diagnosis of type 1 diabetes are 91% for GAD65 antibody, 74% for IA-2 antibody, 70% for ZnT8 and 49% for insulin antibody. Together, the combined sensitivity increases to 96%, with a specificity of 98%.

Detection of insulin antibodies in a patient who has never been treated with insulin is consistent with predisposition to T1DM. Detection of insulin antibodies is not as informative in patients who have already received insulin therapy because antibody can arise secondary to treatment. They are the least specific autoantibody for diabetes because they also are detectable in autoimmune thyroid disease and chronic hepatitis.

IA-2 is a transmembrane protein tyrosine phosphatase in neuroendocrine tissues. Autoantibodies to IA-2 usually appear later than autoantibodies to insulin and GAD, and are highly associated with expression of multiple anti-islet autoantibodies and progression to diabetes.

GAD is an enzyme involved in the synthesis of gamma-aminobutyric acid. Detection of GAD65 antibody in non-diabetic individuals predicts later development of T1DM. It is also helpful in distinguishing between type 1 and type 2 diabetes in adults. GAD65 autoantibody also serves as a marker of predisposition to other autoimmune disease that occur with type 1 diabetes such as Graves' disease, Hashimoto's thyroiditis, hypothyroidism, pernicious anemia, premature ovarian failure, Addison's disease and vitiligo. Unfortunately, GAD65 antibodies are not specific for T1DM and may be present in patients with a variety of autoimmune neurologic disorders. Approximately 3% of the general population has detectable GAD65 antibodies.

ZnT8 is the most recently discovered autoantigen associated with T1DM. ZnT8 antibodies are detected in 14% of subjects with new onset T1DM who test negative for the other autoantibodies. ZnT8 autoantibodies appear later than insulin autoantibodies. ZnT8 autoantibody is typically lost very early after the onset of diabetes. This test is not yet widely available.