Viral Serology

The use of viral serology may be confusing. The following comments may assist you in ordering and interpreting these diagnostic tests. Should you have questions about what to request, contact the Client Services Department at Warde. We will be glad to assist you in determining whether viral culture, viral serology or antigen detection is appropriate in a given situation.

Using Viral Serology to Diagnose an Acute Infection

1. Documenting seroconversion

   Antibody production to an agent begins during the acute stage of an infection and continues during convalescence. Serum collected early in an infection will have fewer antibodies than serum collected later.

   Example:
   A patient has symptoms consistent with mumps infection (fever, swollen salivary glands, and headache). Blood is collected on the day the patient is first seen by a physician and a second specimen is collected two weeks later (when symptoms are no longer present). When the lab assays these two samples, specimen 1 has no antibody to mumps and specimen 2 is positive. The serology report supports the diagnosis of "mumps infection".

   Note: The convalescent serum should be obtained **no sooner than 2 weeks** after the acute serum. The two sera should be assayed together by the laboratory.

2. Detecting IgM

   In the setting of clinical signs and symptoms of infection by a particular virus, IgM antibody serology may be useful in the detection of acute infection; however, the use of lgM antibodies to detect acute viral infection should be approached with some caution, and with careful attention to pre-test probability. Such testing should be limited to patients with signs and symptoms that support infection with the virus being tested by IgM serology, in order to optimize positive predictive value. Applying IgM serology too broadly, for example in asymptomatic patients, increases the likelihood that a positive result will be a false positive. There are well known potential causes for IgM antibody cross-reactivity (rheumatoid factor, cross-reactivity with other viral antigens, etc). In 2018 the American Board of Internal Medicine Foundation's *Choosing Wisely* program published the following recommendation:

   "Don't order IgM antibody serologic studies to assess for acute infection with infectious agents no longer endemic in the US, and in general avoid using lgM antibody serologies to test for acute infection in the absence of sufficient pre-test probability."

   Finally, if lgM serologies return positive results for rare or vaccine-preventable diseases, it is important to notify local and state health departments as soon as results are known.

Warde Medical Laboratory

Using Viral Serology to Determine Previous Infection

1. The presence of IgG antibody to a virus in a single specimen collected from a patient who does not have symptoms indicates that the patient has, at some time in the past, been infected with or vaccinated against that virus.

   Example:
   The presence of mumps antibody in a patient indicates that this person has either had mumps infection or been vaccinated.

2. The presence of lgG antibody to a given virus in a single specimen collected from a patient who does have symptoms does not necessarily indicate that the patient currently has that viral infection-- even if the level of antibody is "high".

   Example:
   Most adults have antibody to cytomegalovirus (CMV). The presence of anti-CMV IgG in a patient with a mono-like illness does not prove that the illness is caused by CMV.

Using Viral Serology and Antigen Detection to "Stage" an Infection

1. Hepatitis B virus Infection

   A panel of tests is usually used to diagnose Hepatitis B infection and define the phase of the infection. The panel includes assays for the detection of Hepatitis B antigens, and antibodies to these antigens as shown in the following table (Key: HBsAg = Hepatitis B surface antigen; HBeAg = Hepatitis B "e" antigen (a marker of active viral replication); Anti HBc IgM = IgM Hepatitis B core antibody; Anti HBc IgG = IgG Hepatitis B core antibody; Anti HBe = antibody to Hepatitis B "e" antigen; Anti HBs = Hepatitis B surface antibody.)

Marker	Incubation	Acute Phase	Past Infection	Chronic Infection	Vaccination
HBsAg	+	+	-	+	-
HBeAg	+	+	-	+/-	-
Anti HBc IgM	-	+	-	-	-
Anti HBc IgG	-	+	+	+	-
Anti HBe	-	-	+/-	+/-	-
Anti HBs	-	-	+	-	+

2. Epstein-Barr Virus (EBV) infection

Primary infection with Epstein-Barr virus is usually asymptomatic and most adults have antibody to this virus. In some patients, particularly young adults, primary infection results in infectious mononucleosis (IM) which is characterized by swollen lymph glands, fever, sore throat and fatigue. Approximately 90% of patients with IM will produce heterophile antibodies that can be easily detected with the Monospot test. Some adults and a higher percentage of children do not develop heterophile antibodies. In these cases, tests that detect antibody to EBV related antigens provide evidence of an acute or recent infection.

Antibodies	No Past Infection	Acute Infection	Recent Infection	Past Infection
Anti-Viral Capsid Antigen (VCA) IgM	IgM-	IgM+	IgM+/-	IgM-
Anti-Viral Capsid Antigen (VCA) IgG	IgG-	IgG+	IgG+	IgG+
Anti-EB Nuclear Antigen (EBNA)	-	-	+	+
Anti-Early Antigen (EA)	-	+	+/-	-

Additional resources:

Editorial: Utilization and Interpretation of Epstein Barr Virus Serologies - Warde Medical Laboratory (wardelab.com)