Ontario
Agency for Health Protection and Promotion
Agence de protection et de promotion de la santé

Labstract

December 2008

Diagnostic Interpretation of Viral Specific IgM and IgG Serology

To Health Care Providers

The following information provides a general guide to the interpretation of viral specific IgM and IgG serology. For information regarding a specific viral agent, please contact the appropriate section within the Public Health Laboratory to discuss the availability of testing and the interpretation of results.

General Principles

After a primary viral infection both specific IgM and IgG antibodies become detectable in serum approximately three days after the appearance of a rash or the onset of other symptoms. Levels of both antibodies then increase rapidly before reaching a plateau around the tenth day.

At approximately one month after onset of infection, the level of IgM begins to decline gradually and typically becomes undetectable within two to three months. Levels of IgG however, remain elevated for a longer period of time, gradually declining over a number of years and usually remaining detectable for life. A similar antibody response is also observed following immunization. Thus the presence of IgG provides an indicator of immunity and/or evidence of past infection. For some viruses that result in chronic or persistent infection (e.g. HIV, HCV), the presence of IgG generally indicates ongoing infection and not immunity.

Because the level of antibody development varies from patient to patient, there is no absolute level of antibody that is considered normal, i.e. there is no “normal range”. Diagnosis is assessed with regard to the presence or absence of both IgM and/or IgG, and results are usually reported qualitatively rather than quantitatively (e.g. IgM Non-Reactive; IgG Reactive). Occasionally, an antibody result will be reported as indeterminate. This indicates that the level of antibody is in the “grey zone” or “borderline” range of detection and is considered neither reactive nor non-reactive. This may occur for several reasons including the following. The sample may have been collected too early in the disease process (acute phase) and thus the individual may not have produced sufficient antibodies to yield a reactive result with the diagnostic test. For IgM antibodies, the sample may have been collected late in the course of the infection (convalescent phase) when the level is falling and will eventually become non-reactive. In addition, an indeterminate result may occur because of a non-specific antibody cross-reaction, particularly with other unrelated IgM antibodies (e.g. Rheumatoid factor).

IgM antibodies may or may not be detectable following viral re-infection or reactivation. In some cases where there has been a long period of latency following primary infection (e.g. shingles), IgM may become detectable following reactivation. In other cases such as those viruses that result in chronic infection (e.g. Hepatitis B), IgM antibodies may be detectable intermittently following flares of disease activity and do not indicate a recent or acute infection.

Timing of specimen collection is important in interpretation of antibody results. Whenever possible, the first sample should be collected as early as possible following the onset of symptoms followed by a second sample collected 10 to 14 days later.

Diagnostic Interpretation

Depending on the viral agent suspected, serologic tests may be available which detect IgM antibodies alone, IgG antibodies alone, or total antibodies (i.e. both IgG and IgM together). For some viral agents, no reliable antibody test may be available and thus laboratory diagnosis requires an alternative method (e.g. virus isolation, direct detection, etc.).

Since virus-specific IgM is usually only detectable for two to three months after primary infection its presence serves as a marker of acute or recent infection. However, in order to accurately assess the significance of IgM results, one must also consider the patient's IgG results. By looking at both antibody results, one can usually make a more reliable interpretation and also estimate the timing of possible infection.

It is important to note that in newborns, maternal transfer of IgG antibodies may remain detectable for up to 12 months of age making interpretation of serologic results difficult. However, the detection of virus-specific IgM antibodies in the newborn usually indicates an acute or recent infection.

The following tables serve as a guide to the interpretation of virus-specific serology. All results must be interpreted in conjunction with knowledge of the clinical history and the timing of specimen collection in relation to the onset of infection.

In early infection, one may expect to see any of the following four antibody profiles:

1)	IgM **-** IgG **-**	No evidence of current infection. May be too early to detect antibody, therefore, follow-up sample needed for result comparison. In patients with otherwise healthy immune systems, the continued absence of both IgM and IgG antibodies to a specific viral agent is consistent with ongoing susceptibility to that agent and no evidence of prior infection or immunization.
2)	IgM + IgG **-**	Possible primary infection or recent immunization. However, depending on the clinical history, a follow-up sample may be needed to rule out test non-specificity and/or a false positive IgM result. Failure to develop a subsequent detectable IgG antibody response is consistent with the latter two scenarios.
3)	IgM + IgG +	Antibody response is consistent with recent infection and/or immunization.
4)	IgM **-** IgG +	Presence of IgG antibodies in the absence of detectable IgM is consistent with past infection, prior vaccination, or ongoing infection (e.g. HIV)

Follow-up Testing

This is usually requested to aid in result interpretation by ruling out or confirming recent infection. e.g. The presence of virus-specific IgM antibodies without subsequent development of IgG antibodies suggests a false positive IgM result and therefore no recent infection. Persistence of IgM beyond the normal time frame of 2-3 months may also signify a false positive result or an abnormal antibody response consistent with past infection rather than recent (e.g. WNV).

In general, the following antibody profiles are consistent with recent infection to a specific viral agent:

	Specimen 1	Specimen 2
1)	IgM-	IgM+ (IgM development)
	IgG-	IgG+ (IgG development)
or		
2)	IgM+	IgM+ (IgM persistence) or IgM- (IgM resolution)
	IgG-	IgG+ (IgG development)

NOTE: Samples drawn late in the cycle of antibody production may not show typical profiles.

For Further Information:

- Contact the Public Health Laboratory at **416-235-5725** and ask to speak to the Head Technologist responsible for testing for the specific viral agent(s) of interest.