Laboratory Support for the Surveillance of VPD

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http://www.cdc.gov/nip/publications/surv-manual/chpt19_lab_support.pdf

MEASLES (also see Chapter 6)

Serologic testing

Serologic testing for antibodies to measles is widely available. Generally, in a previously susceptible person exposed to either vaccine- or wild-type measles virus, the IgM response starts first around the time of rash onset and is transient, persisting 1–2 months. The IgG response starts more slowly, at about 7 days after rash onset, but typically persists for a lifetime. The diagnosis of acute measles infection can be made by detecting IgM antibody to measles in a single serum specimen or by detecting a rise in the titer of IgG antibody in two serum specimens drawn roughly two weeks apart. Uninfected persons are IgM negative and will either be IgG negative or IgG positive depending upon their previous infection or vaccination histories.

Recommendations for serologic test for measles

An enzyme immunoassay (EIA) test for IgM antibody to measles in a single serum specimen, drawn at the first contact with the suspected measles case, is the recommended method for diagnosing acute measles.

A single specimen test for IgG is the most commonly used test for immunity to measles because IgG antibody is long lasting.

Testing for IgG along with IgM is recommended for suspected measles cases.

Paired sera (acute and convalescent) may be tested for a rise in IgG antibody to measles to confirm acute measles infection.

When a patient with suspected measles has been recently vaccinated (6-45 days prior to testing) neither IgM nor IgG antibody responses can distinguish measles disease from the response to vaccination.

Tests for IgM antibody

Although there are multiple possible methods for testing for IgM antibody, enzyme immunoassays (EIAs) are the most consistently accurate tests and are therefore the recommended method. There are two formats for IgM tests. The first and most widely available is the indirect format; IgM tests based on the indirect format require a specific step to remove IgG antibodies. Problems with removal of IgG antibodies can lead to false-positive tests[12] or, less commonly, false-negative results.

The second format, IgM capture, does not require the removal of IgG antibodies. CDC has developed a capture IgM test for measles, and trained personnel from every state public health laboratory. This is the preferred reference test for measles. One direct capture IgM EIA is commercially available.

EIA tests for measles are often positive on the day of rash onset. However, in the first 72 hours after rash onset, up to 30% of tests for IgM may give false-negative results. Tests that are negative in the first 72 hours after rash onset should be repeated (Table 1); serum should be obtained for repeat testing 72 hours after rash onset. IgM is detectable for at least 28 days after rash onset and frequently longer.[13]

When a laboratory IgM test is suspected of being false positive (Table 1), additional tests may be performed. False positive IgM results for measles may be due to the presence of rheumatoid factor in serum specimens. Serum specimens from patients with other rash illness, such as Parvovirus B19, rubella, and roseola have been observed to result in false positive reactions in some IgM tests for measles. False positive tests may be suspected when thorough surveillance reveals no source or spread cases, when the case does not meet the clinical case definition, or when the IgG result is positive within 7 days of rash onset. In these situations, confirmatory tests may be done at the state public health laboratory or at CDC. IgM results by tests other than

EIA can be validated with EIA tests. Indirect EIA tests may be validated with capture EIA tests.

Tests for IgG antibody

Because tests for IgG require two serum specimens and a confirmed diagnosis cannot be made until the second specimen is obtained, IgM tests are generally preferred. However, if the IgM tests remain inconclusive, a second (convalescent) serum specimen, collected 14-30 days after the first (acute) specimen, can be used to test for an increase in the IgG titer. These tests can be performed in the state laboratory or at CDC. A variety of tests for IgG antibodies to measles are available and include EIA, hemagglutination inhibition, indirect fluorescent antibody tests, and plaque reduction neutralization. Specimens (urine, nasopharyngeal aspirates, heparinized blood, or throat swabs) for virus culture should be obtained from clinically suspected cases of measles.

Complement fixation, although widely used in the past, is no longer recommended. The “gold standard” test for serologic evidence of recent measles virus infection is plaque reduction neutralization test of IgG in acute and convalescent paired sera.

IgG testing for laboratory confirmation of measles requires the demonstration of a rise in the titer of antibody against measles. The tests for IgG antibody should be conducted on both acute and convalescent specimens at the same time. The same type of test should be used on both specimens. The specific criteria for documenting an increase in titer depend on the test. EIA values are not titers and increases in EIA values do not directly correspond to titer rises.

Virus isolation

Isolation of measles virus in culture or detection of measles virus by reverse transcription polymerase chain reaction (RT-PCR) in clinical specimens confirms the diagnosis of measles. However, a negative culture or RT-PCR does not rule out measles because the tests are not very sensitive and are much affected by the timing of specimen collection and the quality and handling of the clinical specimens. Since culture and RT-PCR and take weeks to perform, they are rarely useful in confirming the diagnosis of measles. If positive, these tests can be useful adjuncts to diagnosing acute measles when serology results are inconclusive. Also, if measles virus is cultured or detected by RT-PCR, the viral genotype can be used to distinguish between measles disease, caused by a wild-type measles virus, and a response to measles vaccination, caused by a vaccine strain.

Although rarely useful to diagnose measles, viral culture and RT-PCR are extremely important for molecular epidemiologic surveillance to help determine 1) the origin of the virus, 2) which viral strains are circulating in the United States, and 3) whether these viral strains have become endemic in the United States. Isolation of measles virus is technically difficult and is generally performed in research laboratories.

Specimens (urine, nasopharyngeal aspirates, heparinized blood, or throat swabs) for virus culture obtained from clinically suspected cases of measles should be shipped to the state public health laboratory or to the CDC at the direction of the state health department as soon as measles is confirmed. Specimens should be properly stored while awaiting case confirmation (see Appendix 6). Clinical specimens for virus isolation should be collected at the same time as samples taken for serologic testing. Because virus is more likely to be isolated when the specimens are collected within 3 days of rash onset, collection of specimens for virus isolation should not be delayed until laboratory confirmation is obtained. Clinical specimens should ideally be obtained within 7 days of rash onset and should not be collected if the opportunity to collect a specimen is more than 10 days after rash onset.