



Laboratory Testing for Measles

For Public Health Staff

The California Department of Public Health (CDPH) Viral and Rickettsial Disease Laboratory (VRDL) encourages submission of specimens from suspected measles cases who meet the CDC clinical case definition.

CDC measles clinical case definition

An illness characterized by all the following:

- a generalized rash lasting ≥ 3 days;
- a temperature $\geq 101.0^{\circ}\text{F}$ ($\geq 38.3^{\circ}\text{C}$); and
- cough, coryza, or conjunctivitis.

Measles laboratory confirmation

Acute measles infection can be confirmed by:

- positive serologic test for serum measles IgM antibody; OR
- four-fold rise in measles IgG antibody between acute and convalescent titers; OR
- isolation of measles virus; OR
- detection of viral RNA by reverse transcription polymerase chain reaction (RT-PCR)

Specimen collection

Collection of a serum specimen for serologic detection of measles antibody in conjunction with a respiratory sample (nasopharyngeal swab or aspirate), and a urine specimen for molecular determination or virus isolation is helpful in the laboratory confirmation of a measles case.

IgM/IgG testing:

- Collect 7-10 ml of blood in a red top or serum separator tube (SST).
- The optimal time for collection of acute blood is as soon as measles is suspected and up to 7 days after symptom onset.
- If initial testing is negative and measles is strongly suspected, a convalescent serum sample should be collected 2-4 weeks after symptom onset.

IgM interpretation

- Detection of IgM in acute serum is the recommended test for rapid determination of acute measles infection.
- In unvaccinated persons, IgM antibody is generally detectable around the time of rash onset and can be detected for 1–2 months.
- If blood is drawn earlier than 72 hours after rash onset and the measles IgM antibody result is negative, draw another blood specimen and run for repeat testing.
- Other diseases, such as parvovirus infection, infectious mononucleosis, or rheumatologic disease can cause false positive measles IgM antibody results.
- If IgM results are positive and the patient does not have epi-links suggesting measles, the test should be confirmed at VRDL using the original serum sample, if possible.

IgG interpretation

- Obtain acute and convalescent serum specimens for measles-specific IgG antibody to confirm a measles diagnosis. This is especially important if the measles IgM antibody titer is drawn at the wrong time or if other infections are present.
- In unvaccinated persons, the IgG response starts at about 5–10 days after rash onset, but typically persists for a lifetime.
- In vaccinated persons, existing IgG antibody will begin to rise soon after exposure/infection and IgG may be quite elevated in the acute-phase blood sample, which may obviate the fourfold rise in IgG titer in the convalescent serum specimen.
- Paired acute and convalescent serum specimens that demonstrate a fourfold increase in IgG titer or a seroconversion from IgG negative to positive are considered positive diagnostic test results for measles.

Interpretations of a single positive measles IgG antibody result

- Current infection to which the individual is developing immunity; OR
- Immunity due to either a past infection or vaccination; OR
- Presence of maternal antibody (in infants < 15 months).

In recently vaccinated persons (6–45 days prior to rash onset) with suspected measles, neither IgM nor IgG antibody responses can distinguish measles disease from response to vaccination. A viral specimen should be obtained to distinguish between vaccine virus and wild-type virus.

PCR and viral culture

- The preferred specimen is a nasopharyngeal swab or aspirate.
- Urine is also an acceptable specimen for measles isolation or detection by RT-PCR.
- Attempt to obtain specimens as soon as possible after rash onset up to 10 days after onset. Virus is more likely to be isolated in culture when the specimens are collected within 4 days of rash onset.

Specimen collection for PCR and isolation

Respiratory specimens:

- Nasopharyngeal aspirate: use a syringe attached to a small, plastic tube and 2-3 ml of viral transport media (VTM). After placing VTM in the nose, aspirate as much of the material as possible and rinse the tube with 2 ml of VTM.
- Nasopharyngeal swab: firmly rub the nasopharyngeal passage with sterile daycron swab to dislodge epithelial cells. Place swabs in sterile VTM. Do not use special (e.g., anaerobic) media.

Urine:

- It is best if urine is collected from a first morning voided specimen during the first week after rash onset, although any urine specimen collected up to 10 days after rash onset will be accepted. Collect 50-100 ml urine in a sterile centrifuge or sediment tube.
- Urine specimens should be shipped within 24 hours of collection. Otherwise, urine should be centrifuged at 2,500 X g for 15 minutes at 4°C to pellet the sediment. The sediment should then be resuspended in 2-3 ml of VTM and frozen, preferably at -70°C.
- If centrifugation is not available, do not freeze the urine specimen. The entire specimen should be stored at 4°C and shipped on wet ice.

RT-PCR/viral culture interpretation

- While detection of viral RNA by RT-PCR confirms measles infection, failure to detect measles virus RNA by RT-PCR in samples from a person who meets the clinical case definition for measles does not rule out measles as a diagnosis. Successful detection of measles virus depends primarily on the timing of collection and the quality of the viral sample.
- Virus may be isolated from a nasopharyngeal or nasal wash/swab or urine collected at rash onset until up to 10 days, but optimally within 4 days after onset.
- Persons vaccinated within 3 weeks of symptom onset may yield a positive RT-PCR result due to detection of vaccine virus. Genetic characterization of viral isolates or RT-PCR products is the only laboratory test that can differentiate between vaccine-associated cases and wild-type infection.

Specimen storage and shipping (all specimen types):

Measles virus is sensitive to heat and desiccation and viability decreases when samples are not kept cold. Transport samples with cold packs as soon as possible following collection. If samples cannot be transported immediately, they can be held at 4°C for 72 hours before shipping. Otherwise, specimens should be frozen, preferably at -70°C and shipped on dry ice (except unprocessed urine – see above). Avoid repeat freeze-thaw cycles.

Measles Serology Results and Interpretation

IgM Result	IgG Result	Previous Infection History	Current Infection	Comments
+	+ or -	Not vaccinated, no history of measles	Recent 1st MMR	Seroconversion*
+	+ or -	Not vaccinated, no history of measles	Wild-type measles	Seroconversion*, classic measles
+	+ or -	Previously vaccinated, primary vaccine failure	Recent 2nd MMR	seroconversion*
-	+	Previously vaccinated, IgG+	Recent 2nd MMR	IgG level may stay same or boost
+	+	Previously vaccinated, IgG+	Wild-type measles	May have few or no symptoms**
+	+	Recently vaccinated	Exposed to wild-type measles	Cannot distinguish if vaccine or wild-type, evaluate on epidemiologic grounds***
+ or -	+	Distant history of measles	Wild-type measles	May have few or no symptoms**, if clinically compatible may have been misdiagnosed initially

* IgG response depends on timing of specimen collection

** If so, do not consider contagious unless clinical presentation is consistent with measles

*** If IgM negative, helpful to rule out wild-type measles infection

For more information on laboratory testing for measles, please see:

<http://www.cdc.gov/measles/lab-tools/index.html>