Laboratory Testing of Measles Virus

FAQ For Clinical Laboratories: Developed Jointly by ASM and APHL

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Please note that this document was written in August 2025 and the information included encompasses the available information at the time of writing. This is an evolving situation and test availability, requirements, and algorithms are subject to change. Contact your local public health authorities and consult the U.S. Centers for Disease Control and Prevention (CDC) website for the most up-to-date information or with questions.

1. What is measles?

Measles, also known as rubeola, is a highly contagious infectious illness caused by *Morbillivirus hominis*, a virus in the Paramyxoviridae family. The virus was renamed by the International Committee on Taxonomy of Viruses in 2022 from *Measles morbillivirus* to *Morbillivirus hominis* (1). Measles virus is a single-stranded, negative-sense, enveloped, non-segmented RNA virus. Humans are the only known reservoir (2).

The virus is transmitted exclusively between humans, typically via respiratory droplets. Infectious viral particles remain in the air and on surfaces for up to 2 hours. Immune naive persons exposed to a space in which an infected case has been are more than 90% likely to become infected (2). The typical incubation period for measles is 10-12 days after exposure to the development of prodromal symptoms. These symptoms include fever and the three C's: cough, coryza, and conjunctivitis. Koplik spots, which are pathognomonic for measles, appear on the buccal mucosa usually 2-3 days before the rash develops. The spots may persist for 1-2 days after the rash appears. The characteristic morbilliform rash

typically appears 14 days after exposure. This erythematous and maculopapular rash starts on the face then progresses down the chest and to the extremities over ~24-48 hours (3).

Measles vaccination (e.g., measles, mumps, and rubella, also known as MMR) is highly effective at preventing measles disease in children. The estimated vaccine effectiveness is 93-95% after one dose and 97-99% after two doses. Following introduction of the measles vaccine in 1963, the incidence decreased from 3,000 to 1.3 cases per 1,000,000 persons. After introducing the second dose in the late 1980s, the incidence fell to <1 per 1,000,000 persons. Measles was previously considered eliminated in the United States by the Centers for Disease Control and Prevention (CDC) in 2000 (4, 5).

In about 5% of children, a mild, self-limited, erythematous maculopapular rash can develop after receiving the first dose of MMR (3). This occurs typically within 7-14 days after administration of the vaccine dose. The appearance of this rash may be accompanied by a low-grade fever, but other symptoms, including the three C's, are notably absent. The appearance of this rash is a benign immune response to the vaccine itself. It does not indicate that the patient has developed an infection and the patient is not considered to be contagious (3).

2. How often does measles occur in the U.S.?

CDC tracks both recent and historic U.S. measles cases on their website.

Measles was officially considered "eliminated" from U.S. since 2000, meaning there had not been ongoing, domestic transmission for more than 12 months. Although the significant increase in cases in 2025 has threatened U.S. elimination status, measles is still uncommon. When testing for measles in an elimination setting and in the absence of known exposure, other causes of rash illness should be considered in addition to measles (6).

3. When should public health be contacted by providers regarding a suspected measles case?

In the U.S., measles is a mandatory, immediately notifiable disease for confirmed cases. Many jurisdictions also recommend that providers contact their local health department as soon as a provider suspects measles and before the patient leaves the facility (7, 8).

4. What tests are recommended for diagnosing active measles infection?

Measles nucleic acid amplification tests (NAATs) and IgM serology are the recommended tests for diagnosing active measles infection, and it is recommended that both be performed in cases of suspected active measles infection.

NAAT is most diagnostically sensitive if the appropriate specimen (see Table below) is collected promptly after rash onset. Although the yield decreases with time, NAAT may still be able to detect measles RNA up to 14 days after rash onset (9). Breakthrough cases of natural measles infection in vaccinated individuals are expected to test positive by NAAT, despite lower viral loads compared to vaccine-naïve cases (10).

Serum for measles IgM should be collected as soon as a measles case is suspected. However, specimens collected within 3 days of symptom onset may yield false negative IgM serology results in up to 23% of cases (11). Therefore, a second specimen should be collected 3-10 days after symptom onset if the initial IgM test was performed within 3 days of rash onset and was negative (9). Measles IgM may remain detectable 4-5 weeks after appearance of rash, though in previously vaccinated individuals this period may be shorter (11). It is expected that most previously vaccinated individuals will have detectable measles IgM when tested within the first 10 days of symptom onset in a natural measles virus infection (12).

Measles IgM testing in elimination settings, such as the U.S., may also yield false positive results due to cross reactivity with other antigens. Performing NAAT in parallel and considering other potential causes of rash illness are recommended to resolve potential false positive results (13).

Testing for measles by both IgM serology and NAAT is recommended in immunocompromised patients, though IgM may be falsely negative (14).

In the rare instances in which subacute sclerosing panencephalitis is suspected, serum and cerebrospinal fluid (CSF) should be tested for measles IgG antibody (15).

5. What is the role of IgG measles serology?

A single positive measles-specific IgG result is considered definitive laboratory evidence of immunity and is routinely accepted for employee clearance, school entry, and outbreak contact management. Because IgG antibody appears after the initial phase of illness or vaccination and persists for life, the absence or equivocal presence of measles-specific IgG signifies susceptibility and may prompt further discussions with public health personnel regarding post exposure prophylaxis (PEP) and/or treatment recommendations (16).

Measles IgG is not preferred in the diagnosis of active measles infection. However, either measles IgG seroconversion or a fourfold or greater increase in IgG titer between acute and convalescent specimens is considered supportive evidence of a recent infection. If performed, the acute serum sample should be collected within 7 days after onset of the rash and the convalescent sample should be collected 14 to 30 days later (17).

Previously, in special situations, IgG avidity testing has been used to help distinguish recent infection or recent vaccination (low avidity) from secondary vaccine failure (i.e. infection breakthrough despite producing high avidity IgG) (16). IgG avidity testing may not be available for clinical testing and is not recommended for routine use. As of August 2025, the CDC does not offer an IgG avidity test for clinical use.

6. What is/are the recommended specimen type(s) when testing for measles?

The recommended specimen type(s) and the preferred test method depends on the clinical indication and application for testing. See table 1.

Table 1: Recommended specimen types and measles testing methods

Application	Method	Specimen Type(s)	Notes
Diagnosing active infection	NAAT (nucleic acid amplification test)	Throat or NP (nasopharyngeal) swabs and urine; see notes.	Most sensitive when collected after rash onset; respiratory specimen is preferred 0-5 days after rash onset; respiratory plus urine 5-9 days aftert onset.
	Serology (IgM)	Serum	Serum collected for serology testing cannot be used for NAAT.
	Serology (IgG) *Not routinely recommended	Acute and convalescent serum	Measles IgG is not the preferred method for diagnosing infection. Acute (within 7 days after rash onset) and convalescent (14-30 days after acute) serum testing can offer supportive evidence of infection when NAAT and IgM are inconclusive.
Diagnosing subacute sclerosing panencephalitis	Serology (IgG)	Serum and cerebrospinal fluid	
Determining immunity	Serology (IgG)	Serum	
Differentiating between vaccine-derived rash and active measles infection	NAAT (nucleic acid amplification test)	Throat or NP (nasopharyngeal) swabs and urine; see notes.	Not all NAAT differentiate between wild-type and vaccine strain viruses. Contact the local health department if test selection guidance is needed. Consider ordering this test in patients who were exposed to wild-type measles after recent vaccination (18).

7. What are associated clinical laboratory findings?

According to the CDC, some documented abnormal laboratory findings have included lymphopenia and leukopenia, elevated C-reactive protein, and mildly elevated liver enzymes. Thrombocytopenia has been reported in a few cases (4, 8).

8. Where can measles be tested?

Public health, commercial, and some clinical laboratories offer serologic testing for measles. Public health and commercial laboratories offer molecular testing for measles, with limited performance at individual clinical laboratories. Molecular testing is also available through the APHL/CDC Vaccine-Preventable Disease (VPD) Reference Centers in California, New York, Minnesota, and Wisconsin. These centers were established by the CDC and APHL to provide diagnostic and characterization testing for measles. Laboratories should send residual positive specimens to their public health laboratory for additional nucleic acid sequencing-based characterization to assist in outbreak response and ongoing global surveillance.

9. What tests are used to differentiate between MMR vaccine-derived rash versus true measles infection?

Differentiating between vaccine-related rash and natural infection is not routinely required. If recently vaccinated (within the prior 21 days), the rash may be assumed to be related to the MMR vaccine. However, in recently vaccinated patients who were exposed to a known measles case or during outbreak situations, testing for wild-type virus may be indicated. Traditionally, vaccine reactions have been confirmed by broad measles NAAT followed by sequencing to determine the genotype. A more rapid method is a NAAT for specific detection of measles vaccine strains (MeVA) that can discriminate between vaccine and wild-type strains (18).

The MeVA test, which specifically detects measles vaccine strains, should be performed only on specimens collected from patients with a suspected vaccine reaction (i.e., a febrile rash illness occurring within 21 days after vaccination with a measles-containing vaccine) in a person also potentially exposed to wild-type measles virus, e.g., in an outbreak setting. The need for this testing should be discussed with local or state public health authorities. When indicated, the MeVA test should be performed in parallel with a standard measles NAAT, as a reflex test following a standard measles NAAT, or simultaneously if a single test that both detects and differentiates MeVA and wild-type measles virus is available. The MeVA test is currently being offered by the CDC, the VPD Reference Centers described above, and by some state public health laboratories. MeVA and MeV PCR testing may also be available at commercial reference laboratories.

10. Should asymptomatic people who have been exposed to measles virus be tested for measles infection?

No, *asymptomatic* people should not be tested, including close contacts of a confirmed case (19, 20). Post-exposure prophylaxis may be appropriate; providers should coordinate this with local public health authorities (21).

11. What laboratory precautions are recommended for handling specimens that potentially contain measles virus?

Clinical laboratory workers face increased exposure risks during outbreaks, particularly when handling throat and nasopharyngeal swabs and blood samples from infectious patients. These risks are significantly heightened during tasks involving respiratory specimens that generate aerosols, especially if such procedures are performed outside of biosafety cabinets. All respiratory specimens should be treated as potentially containing respiratory viruses, including measles virus, and laboratories should follow Biosafety Level 2 (BSL-2) precautions when handling specimens (22). Whenever aerosol-generating procedures (e.g., vortexing) are conducted, specimens must be processed in a Class II

biosafety cabinet equipped with HEPA-filtered exhaust air. Documented immunity to measles, through vaccination or prior infection, in laboratory team members is another important level of protection (23).

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