

Local Health Department Guidelines for the Epidemiological Investigation and Control of Measles

Maryland Department of Health and Mental Hygiene
Prevention and Health Promotion Administration
Infectious Disease Bureau
Center for Immunization
January 2013

Introduction

Measles is an acute viral illness that can affect both children and adults. Although measles is no longer endemic in the United States, measles infection and outbreaks continue to occur sporadically, oftentimes in unvaccinated or under-vaccinated populations. Also, as measles is still endemic in many countries, cases in the United States often involve individuals who recently traveled to measles-endemic regions or who were exposed to imported cases of measles.

This document was written to provide guidance on the investigation of measles cases and outbreaks. The recommendations in this document are intended to provide general guidance. Measles incidents should be evaluated on an individual basis, with the consultation of local and state infection control staff if needed, to determine the appropriate steps for measles prevention and control.

Questions regarding this document can be directed to:

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Disease Description

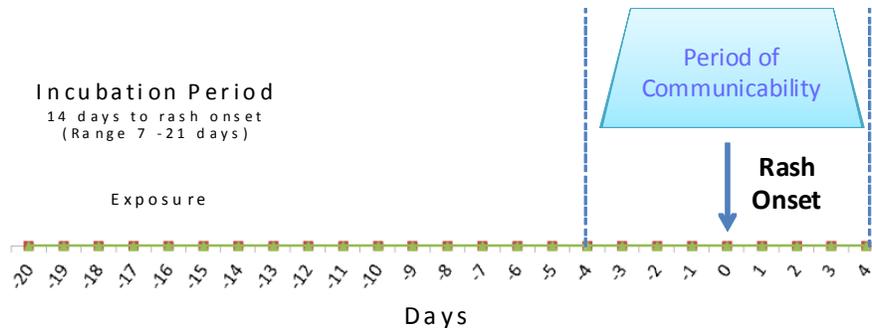
Mode of Transmission: Measles is highly contagious and can be transmitted from person to person via respiratory droplets. Although transmission occurs primarily through direct contact with infectious droplets, airborne transmission in closed areas has been documented for up to 2 hours after a person with measles was in the area.

Incubation Period: The incubation period of measles averages 14 days to rash onset (range: 7-21 days).

Clinical Manifestation: Measles infection is characterized by a *prodrome* of a rising fever (often peaking as high as 103⁰F – 105⁰F), cough, coryza (runny nose) and conjunctivitis lasting for approximately 2-4 days (range 1-7 days). This is followed by a maculopapular skin rash that spreads progressively from the hairline to the face, then torso and extremities, usually lasting for 5 to 6 days. Other symptoms include Koplik spots (a rash present on mucous membranes which appears as punctate blue-white spots on the bright red background of the buccal mucosa), lymphadenopathy (swelling of lymph nodes) and malaise.

Complications occur in approximately 30% of measles cases and are more commonly observed in children < 5 years of age and adults > 20 years of age. Common complications include: ear infections (7% of cases), diarrhea (8% of cases) and pneumonia (6% of cases). Less common complications are acute encephalitis (0.1% of cases) and seizures (0.6%-0.7% of cases). Measles can be fatal in 0.2% of cases.

Measles Disease Progression



Communicability Period: An infected individual is contagious from 4 days before to 4 days after onset of the rash. Measles is highly communicable, with greater than 90% secondary attack rates among susceptible persons.

CDC Surveillance Case Classification and Definitions

CDC Surveillance case classification of measles

1) Clinical Case Definition: An illness characterized by *all* of the following:

- A generalized rash lasting ≥ 3 days
- A fever $\geq 101^{\circ}\text{F}$ ($\geq 38.3^{\circ}\text{C}$)
- Cough, coryza, or conjunctivitis

2) Laboratory criteria for diagnosis: Laboratory confirmation of infection by *any* of the following: (see *Testing/Laboratory Diagnosis* Section for details)

- Significant (generally a fourfold) rise in measles antibody (IgG) level by any standard serologic assay
- Positive serologic test for measles IgM antibody
- Isolation of measles virus from a clinical specimen
- Detection of measles nucleic acid through polymerase chain reaction (PCR)

3) CDC Case Classification:

- **Suspect:** a case with fever illness and rash, which does not meet criteria for any other illness.
- **Probable:** a case meeting the clinical case definition without lab confirmation, and not epidemiologically linked to a confirmed case.
- **Confirmed:** a case that is laboratory confirmed -OR-meets the clinical case definition and is epidemiologically linked to a confirmed case.

Note: The most current CDC case definitions can be found at:

http://www.cdc.gov/osels/ph_surveillance/nndss/casedef/case_definitions.htm

4) Outbreak: An outbreak is defined as two or more epi-linked cases of measles where at least one is laboratory confirmed within 42 days of each other.

Definitions

Internationally Imported case: An internationally imported case results from measles exposure that occurs outside the United States, as evidenced by:

- at least some of the exposure period (7-21 days before rash onset) occurring outside the U.S. , and,
- rash onset occurring within 21 days after entry into the United States, and,
- no known exposure to measles in the U.S. during the exposure period.

U.S.-acquired case: A case is considered U.S.-acquired if travel outside of the U.S. did not occur in the 21 days before rash onset, or, if it can be linked to a domestic source. In addition, U.S.-acquired cases are sub-classified into 4 mutually exclusive categories:

- **Import-linked**, if the case is epidemiologically linked to an internationally imported case.
- **Imported-virus**, if the case is not epidemiologically linked to an internationally imported case but viral genetic evidence indicates infection with an imported measles genotype, defined as a genotype that is not occurring in the U.S. in a pattern of endemic transmission. Endemic transmission is defined as a chain of measles virus transmission that is continuous for ≥ 12 months within the U.S.
- **Endemic**, if evidence indicates that the case is epidemiologically or virologically linked to endemic transmission in the United States.
- **Unknown source**, if epidemiological and virological link to importation or endemic transmission in the U.S. cannot be established.

An import-associated case is defined as a case that is classified as internationally imported, import-linked or imported-virus.

Testing/Laboratory Diagnosis

Because measles is an extremely rare disease in the United States, clinical evidence is not sufficient to confirm a case. Laboratory diagnosis is crucial to confirm the few actual measles cases among the thousands of patients with suspected measles.

Serologic antibody testing is the recommended method for laboratory confirmation of measles. Serologic testing is widely available and results are generally available within 3 days. Laboratory confirmation of measles infection can also be obtained through virus isolation and PCR, preferably from a throat or nasopharyngeal swab. PCR results are generally available within a day; however, results of virus isolation procedures may take 1-3 weeks and therefore, have limited clinical usefulness. These tests are summarized in Table 1.

Patients with clinical signs and symptoms consistent with measles should receive laboratory testing to confirm measles diagnosis. People who are asymptomatic for measles, including asymptomatic close contacts of a confirmed measles case, should *not* be tested as this increases the likelihood of obtaining a falsely positive result.

Recommended steps for testing:

- 1) Obtain a serologic specimen for IgM and IgG testing at first contact with suspected case of measles.
- 2) If feasible, collect a throat swab and/or nasopharyngeal aspirate, for virus isolation at the same time a serologic specimen is collected. This will provide an alternate method of laboratory diagnosis in the case that serology results are inconclusive. Samples should be shipped on cold packs. Additionally, submission of specimens for virus isolation and analysis of viral strain is helpful for surveillance of measles in the United States.
- 3) If the IgM test result is inconclusive, obtain a convalescent serologic specimen 14-30 days after the first (acute-phase) specimen for a second IgG test to detect a rise in titer.
- 4) If an IgM negative result is obtained from a specimen collected before rash onset, or within 72 hours from rash onset, another specimen would need to be collected at least 72 hours after rash onset to confirm the result.

Interpretation of results:

Diagnosis of acute measles infection is most commonly 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. A positive IgM result indicates measles infection. A single measles IgG positive result may indicate past measles infection or measles vaccination. Neither clinical evidence alone nor a single IgG test is sufficient to confirm an acute case of measles.

IgM antibody detection using enzyme immunoassay (EIA) is highly accurate. However, falsely positive results may be obtained if:

- Testing is done for a patient with no rash or fever
- Patient has a rash due to parvovirus B19, rubella, roseola or dengue

- Patient received measles vaccination 6-45 days prior to specimen collection

Detection of measles virus by PCR or culture also confirms a measles diagnosis. However, a negative PCR or culture does not rule out measles because both methods are affected by the timing of specimen collection and the quality of the specimen.

Table 1: Summary of Laboratory Testing for Measles

	IgM Testing	IgG Testing	Virus Isolation (by PCR or Culture)
Window period for specimen collection	IgM can be detectable from day of rash onset to 2 months after rash onset. *If initially negative, a second sample can be collected at least 72 hours after rash onset	IgG is detectable 5-10 days after rash onset, and persists for a lifetime.	Ideally, specimen should be collected within 7 days of rash onset and <i>not</i> after 10 days from rash onset. Virus is most likely to be isolated within 3 days of rash onset.
Type of Specimen	Blood	Blood	Nasopharyngeal aspirate or swab or throat swab
Benefits	-Rapid results, high clinical usefulness -IgM testing widely available -An IgM positive result is sufficient for initiation of public health action -IgM can often be detected immediately after rash onset	-Rapid results, high clinical usefulness -IgG testing widely available	-A positive PCR or Culture result is sufficient for laboratory confirmation of measles
Limitations	-IgM result may be falsely negative if specimen is obtained in the first 72 hours after rash onset. -Recent measles vaccination and other rash illnesses (e.g. due to parvovirus, rubella, dengue) can cause a falsely positive IgM result.	-Requires an acute and convalescent specimen to confirm diagnosis (a single IgG positive result is not sufficient for laboratory confirmation of measles as it does not distinguish between acute and past infection)	- Sensitive to time of collection and quality of specimen. - Negative PCR or culture does not rule out measles -Slow processing time and therefore, limited clinical usefulness

Treatment

There is no specific antiviral treatment for measles.

Prevention/Vaccination

Vaccination remains the most effective way to prevent measles infection. Live attenuated measles virus vaccine is incorporated with mumps and rubella vaccine as a combined vaccine (MMR). The current ACIP recommendations for routine vaccination for children indicate a first dose of MMR at 12-15 months of age with a second dose at school entry (4-6 years). Two doses of MMR vaccine are also recommended for adults at high risk, such as international travelers, college students, or healthcare workers born during or after 1957. For healthcare workers born before 1957 without other evidence of immunity, one dose MMR should be considered.

Case/Outbreak Investigation

When a patient is suspected of having measles, a case investigation should be started immediately. Timely and thorough case investigation should: confirm the patient's diagnosis; ensure appropriate medical follow-up for affected persons; identify the source of infection; locate persons who may have been exposed; and isolate potentially infectious persons to prevent transmission of illness in the community.

Case investigation procedures should not be delayed pending confirmatory lab results. Interviewing the case-patient and case-patient's healthcare provider promptly after case notification is necessary so that infection control measures can be implemented immediately should laboratory results confirm measles infection.

Individuals who are suspected of having measles, and who plan to visit their medical provider, should be advised to inform their provider of the reason for their visit so that precautions can be taken to limit their exposure to other patients or susceptible staff. In addition, suspect measles cases should be advised to minimize interaction with others until measles can be ruled out.

Recommended case investigation procedures:

(Refer to *Special Settings* Section for additional guidance on case investigation procedures relevant to schools, hospitals, and settings where close contact may facilitate transmission of measles.)

1) Confirm measles diagnosis

- Obtain specimen for lab testing if patient is experiencing clinical symptoms of measles, particularly rash and fever (Refer to *Testing/Laboratory Diagnosis* Section for details)

2) Interview the case-patient and identify source of infection

- Interview patient about contact with other known measles cases or persons with symptoms of measles.

- Utilize the CDC Measles Surveillance Worksheet (attached) to guide the interview and collect other relevant information (i.e. demographics, clinical details, vaccine history, etc.).
- Assess whether patient traveled outside of the U.S. in the 21 days prior to rash onset to determine if measles infection was acquired in the U.S. or abroad.
- Assess whether patient was exposed to someone who traveled outside of the US in the 21 days prior to rash onset to determine if measles infection was acquired in the U.S. or abroad.
- Obtain an accurate and complete immunization history of the case (including manufacturer and lot number if possible).

3) Identify exposed and susceptible persons

Initiate a contact investigation to identify persons who may have been exposed to measles through contact with the case-patient during the infectious period (4 days before to 4 days after onset of rash), and may have been infected because they are not immune to measles.

A person can be considered **exposed to measles** if they shared the same airspace as a measles case during the case's infectious period (4 days before to 4 days after rash onset) or entered a closed area up to 2 hours after a person infectious with measles was in the area (e.g. a patient who is seen in the same exam room as a person infectious with measles, 2 hours after the infectious person left the exam room). Exposures can occur in various settings including: the home, workplace, school, prison, dormitory, airplane, waiting room at doctor's office, etc. Contact with case-patients may vary widely in type and duration. Therefore, measles exposures should be evaluated on a case-by-case basis following an interview with the case and/or contact person to determine the nature of the exposure.

A **susceptible individual** is defined as a person who has not received 2 doses of measles-containing vaccine on or after his/her 1st birthday or does not have documented history of disease. In general, a person can be considered immune to measles if they:

- 1) Have written documentation of receiving 2 measles-containing vaccines;
- 2) Have documentation of past measles infection, diagnosed by a physician;
- 3) Were born before 1957, or,
- 4) Have serologic evidence of immunity (IgG antibody detected in a lab test).

Note: Verbal confirmation of immunity is not acceptable. *Documentation of physician-diagnosed disease is no longer acceptable evidence of immunity for healthcare personnel.*

Additionally, although birth before 1957 is acceptable evidence of immunity, healthcare facilities should strongly consider vaccinating workers who were born before 1957 and have no documentation of receiving 2 measles-containing vaccines.

- Interview the case-patient regarding contact with others during his/her infectious period (4 days before to 4 days after rash onset).

- If the case-patient reports travel (e.g. via plane) during his/her infectious period, contact staff at Maryland Department of Health and Mental Hygiene Center for Immunization for assistance in identifying passengers and persons in other jurisdictions/locations who may need to be contacted.
- Obtain and document immunization histories for case-patient and all contacts.
- All symptomatic contacts should be tested for measles and managed as suspected measles cases.

4) Initiate measles control measures

Identification and vaccination of susceptible household contacts can occur immediately and should not be delayed because of pending laboratory results. Waiting for laboratory confirmation of measles infection prior to vaccination and prophylaxis of non-household contacts (e.g. schoolmates) may be reasonable in some situations; nevertheless, this should be evaluated on a case-by-case basis.

- Airborne precautions are appropriate until 4 days after onset of rash
- Measles vaccine should be provided to exposed susceptible persons who do not have a contraindication to MMR vaccine. Measles immunization may be effective as prophylaxis if given within 72 hours of exposure to measles. However, immunization should be administered to susceptible individuals regardless of time since exposure in order to provide protection against subsequent measles exposures.
- If vaccine cannot be given, immune globulin may be effective as a prophylaxis if administered to susceptible persons within 6 days from time of exposure.
- Susceptible persons who receive vaccination within 72 hours of exposure:
 - Can be immediately readmitted to childcare or school.
 - Must be excluded from direct patient contact and work in a medical facility from the 5th day after exposure through the 21st day after exposure, regardless of whether they received post –exposure vaccine or immune globulin.
 - Should be advised to monitor for signs and symptoms of measles.
- Persons who are exempt from measles vaccination, who decline to be vaccinated, or who receive vaccination greater than 72 hours after exposure should be excluded:
 - From schools and child care until at least the 22nd day after the onset of rash in the last case identified.
 - From medical settings from the 5th day after first exposure through the 21st day after last exposure.

During this time period, they should be monitored for the development of symptoms consistent with measles.

5) Conduct surveillance

Active surveillance should be maintained for at least 2 incubation periods (42 days) after the last reported confirmed case to ensure that all cases are identified.

Special Settings

In addition to following the recommended steps for case investigation described above, the following measles control measures should be conducted for cases and outbreaks occurring in settings where measles can be transmitted easily due to crowding and/or close contact of individuals.

1) Schools and Childcare Centers

- Assess immunization status of staff, students and siblings of students.
- Vaccinate staff and students who are exposed and susceptible to measles. In outbreak situations, vaccination of siblings of students may also be considered.
- Immune globulin may be administered instead of measles-containing vaccine. However, vaccination is the preferred method.
- Susceptible persons who receive measles vaccination (whether it is their 1st or 2nd dose) or immune globulin can return to the school or childcare immediately.
- Susceptible persons who refuse vaccination must be excluded from school or childcare until at least the 22nd day has passed from the onset of rash in the last case of measles identified in the school.
- Persons who develop symptoms of measles should be excluded from school or childcare for 4 days after rash onset.
- Request that the school notify parents/guardians that a measles case has been identified in the school. A letter and measles fact sheet should be sent to each parent/guardian.

2) Healthcare Settings

- Assess immunization status of all staff, including persons involved in direct patient care (e.g. nurses, physicians, phlebotomists) as well as persons who work in the patient care setting (e.g. clerical staff, front office staff, technicians).
- Vaccinate persons who are exposed and susceptible to measles.

Note: Persons born before 1957 are considered immune to measles. However, if they do not have documented evidence of immunity and have direct contact with patients, measles vaccination should be considered. Documentation of physician-diagnosed measles infection is **not** acceptable evidence of immunity for healthcare providers.

- Immune globulin may be administered instead of vaccination. However, vaccination is the preferred method.
- Susceptible persons who are exposed and have no immunity to measles should be excluded from direct patient contact and the affected medical facility from the 5th day after first exposure through the 21st day after last exposure, regardless of whether they receive vaccine or immune globulin after exposure. They can resume patient contact on the 22nd day after their exposure date provided they are not experiencing symptoms of measles infection.

- Healthcare personnel with documentation of 1 vaccine dose may remain at work and should receive the second dose of MMR.
- Susceptible persons who develop symptoms of measles should be excluded from the facility for 4 days after rash onset.

Reporting

All suspected measles cases must be reported to staff at the Maryland Department of Health and Mental Hygiene Center for Immunization within 24 hours after initial notification. All case investigations should be promptly entered into NEDSS (National Electronic Disease Surveillance System) and the information reviewed for completeness and accuracy. The following table summarizes information that should be collected during case/outbreak investigations and entered into NEDSS:

Table 2: Summary of information to collect during case/outbreak investigation

Type of Information	Information to be collected and reported
Demographic	Name Address Date of birth Sex Race/Ethnicity Reporting source Date reported Jurisdiction
Clinical	Date of rash onset Duration of rash Other symptoms Onset of other symptoms Hospitalizations Complications
Laboratory	Serologic test date(s) and result(s) Date of specimen collection for viral isolation
Epidemiologic	Source of exposure/infection (e.g. note epidemiologic link to confirmed cases or outbreaks) Import status (e.g. Imported, U.S.-acquired)
Vaccination History	Date(s) of measles vaccination(s) Reason for vaccination exemption, if applicable
Outcome	Case classification Date of death, if applicable

Vaccine Adverse Events

Adverse events that occur after administration of the measles vaccine should be reported to the Vaccine Adverse Event Reporting System (VAERS), a passive reporting system use to monitor vaccine safety. Any clinically significant events, unexpected events following vaccination and/or events listed on the vaccine manufacturer’s package insert, should be reported to VAERS. Adverse events may be reported by

submitting a VAERS form online, by fax or by mail. Visit <http://vaers.hhs.gov> for detailed instructions on reporting.

References

Centers for Disease Control and Prevention. Measles. In: *Manual for the surveillance of vaccine-preventable diseases*. 4th Ed. Centers for Disease Control, Atlanta, GA, 2008.

Centers for Disease Control and Prevention. Measles Virus Isolation (Updated 2009). In: *Manual for the surveillance of vaccine-preventable diseases*. 4th Ed. Centers for Disease Control, Atlanta, GA, 2008.

American Academy of Pediatrics. Measles. In: *Red Book: 2009 report of the committee on infectious diseases*. 28th Ed. Pickering LK, Baker CJ, Kimberlin DW, Long SS, eds. Elk Grove, IL; American Academy of Pediatrics; 2009:444-455.

Centers for Disease Control and Prevention. Measles. In: *Epidemiology and prevention of vaccine-preventable diseases*. 11th ed. Atkinson W, Wolfe S, Hamborsky J, McIntyre L, eds. Washington DC: Public Health Foundation, 2009.

Centers for Disease Control and Prevention. Immunization of Health-Care Personnel: Recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR* 2011 Nov25; 60(RR07); 1-45.

Centers for Disease Control and Prevention. *Immunization Works*. July 2009 issue. Centers for Disease Control, Atlanta, GA.

Measles (Rubeloa) Case Definition available at:

http://www.cdc.gov/osels/ph_surveillance/nndss/casedef/case_definitions.htm

Sample letter to parents:

Dear Parents,

We have just been notified of a suspect case of measles in your child's school. Measles is an extremely contagious disease that often begins with a high fever (103°F-105°F) and cold like symptoms such as cough, runny nose, and conjunctivitis. This is followed by a maculopapular rash which is red and covered with small bumps that can last for 5-6 days. The rash usually begins on the head and then spreads to the neck, torso, arms and legs. The rash usually appears 14 days after a person is exposed. The illness is usually mild or moderately severe but can result in complications such as pneumonia and death.

Measles is spread through the air and can even be spread in a closed area (e.g. classroom) up to 2 hours after a person with measles has left the area. A person with measles can be spread the disease from 4 days before a rash appears until 4 days after the rash appears.

Students suspected of having measles will be excluded from school and may return to school following the 4th day after the rash appears. Exposed unvaccinated students and staff should receive a dose of vaccine as soon as possible. Those unvaccinated students and staff that receive vaccine will be allowed back to school immediately. Unvaccinated students and staff that do not receive vaccine due to medical or religious reasons will be excluded from school until 21 days after the onset of rash in the last case of measles.

Measles can be prevented with appropriate vaccination. Measles vaccine is administered to children in combination with mumps and rubella vaccine (MMR) in a two dose series. Please check with your health care provider to make sure your child's shots are up-to-date.

Please watch your child for any symptoms of measles (cold-like symptoms, rash) over the next several weeks. If you notice any of these symptoms in your child, please notify your primary care physician and the (typically, school nurse and/or county health department) at (phone number) as soon as possible.

Sincerely,