

# Measles

## CLINICAL CASE DEFINITION

An illness characterized by all of the following:

- ◆ a generalized rash lasting at least 3 days AND
- ◆ a temperature of 101° F (38.3°C) or higher AND
- ◆ at least one of:
  - cough,
  - coryza (runny nose), or
  - conjunctivitis (redness and inflammation of the conjunctiva which lines the eyelid and covers the eyeball)

## CASE CLASSIFICATION

- ◆ **Suspect:** Rash illness with fever
- ◆ **Probable:** A case that meets the clinical case definition, has non-contributory or no serologic or virologic testing, and is not epidemiologically linked to a confirmed case.
- ◆ **Confirmed:** A case that is laboratory confirmed (see [LABORATORY CONFIRMATION](#), below), or that meets the clinical case definition **AND** is epidemiologically linked to a confirmed case. A laboratory-confirmed case does not need to meet the clinical case definition.

## TRANSMISSION

- ◆ Person-to-person via airborne transmission or droplets from the respiratory secretions of infected persons.
- ◆ Droplets can become aerosolized and remain suspended in the air for an extended period of time (documented up to 2 hours). Measles is highly communicable.

## INCUBATION PERIOD

From exposure to prodrome (symptoms preceding rash) the average incubation is 10 – 12 days. From exposure to rash onset the average is 14 days (range 7 – 18). See [Measles Timeline](#), below.

## PERIOD OF COMMUNICABILITY

From 4 days before rash onset to 4 days after.

## REPORTING/INVESTIGATION

- ◆ Health care providers should **immediately** report any possible case of measles to local health department of the patient's residence.
- ◆ Local health department responsibilities:
  - Contact case/guardian and health care provider.
  - Determine if case meets clinical case definition. If definition met (probable or confirmed cases), investigate using report form/surveillance worksheet and control guidelines below.
  - Measles is an important public health concern; if clinical presentation suggests a likely measles case(s), notify MDHHS Immunization Division by phone 517/335-8159.
  - Report/ensure reporting of case to the Michigan Disease Surveillance System (MDSS).

[CDC Measles Surveillance Worksheet](#) may be helpful in field investigation to collect and capture data. Obtain immunization history information from provider record or MI Care Improvement Registry (MCIR - state immunization registry).

- Update the MDSS record in a timely manner with new or additional info as it becomes available. Finalize MDSS record when case investigation is complete.
- In the event of a measles-related death, obtain and send copies of hospital discharge summary, death certificate, and autopsy report to MDHHS Immunization Division.

## LABORATORY CONFIRMATION

Essential; should be attempted for all potential cases meeting the clinical case definition. Collect serum and viral specimen (throat swab, urine, etc). Laboratory confirmation for measles is defined as one of the following:

- ◆ Positive serologic test for measles-specific IgM antibody (**this is the preferred confirmation**)

**NOTE:** Measles IgM tests that are negative and were collected less than 72 hours after the rash onset should be repeated using sera collected 72 or more hours after rash onset.

- ◆ Significant rise in measles IgG antibody by any standard serologic assay
  - Collection of sera for these paired assays should be appropriately spaced: 10 or more days should separate the collection of the acute and convalescent sera.
  - Sera should be tested **in parallel** (i.e., run together in the same test/assay batch).
- ◆ Isolation of measles virus from a clinical specimen.
- ◆ Detection of measles-virus-specific nucleic acid by polymerase chain reaction (PCR).

Serum and viral (culture, PCR testing for virus RNA and sequencing) specimens should be collected from suspected cases. See additional information under [LABORATORY SPECIMENS: PROCEDURES AND CONSIDERATIONS](#), below.

Measles testing is available through the MDHHS laboratory but is subject to reagent availability. Pre-approval arrangements must be made through the MDHHS VPD Surveillance Coordinator at 517/335-8159. Measles testing (serologic and virologic) is also available through commercial clinical laboratories.

## IMMUNITY/SUSCEPTIBILITY

Individuals should be considered immune (protected against) measles **only** if they meet one or more of the following conditions:

- ◆ Born before 1957 (exceptions are women who might become pregnant and health care workers; these groups should have documentation of immunity by one of the methods immediately following below)
- ◆ Laboratory confirmation of a measles disease diagnosis;
- ◆ Serologic (lab) evidence of immunity to measles
- ◆ Documentation of receipt of 2 doses of measles-containing vaccine administered at least 28 days apart (1 dose is acceptable for preschool-age children and adults not considered at high risk, ie.

adults who do not work in healthcare, who do not travel internationally, and who are not students at post-high school educational institutions).

NOTE: All persons who work in a health care setting *in any capacity* should have evidence of immunity to measles, mumps, rubella, varicella, pertussis, hepatitis B, and seasonal influenza.

## CONTROL MEASURES

- ◆ Investigate reports of possible measles **immediately**.
- ◆ If Clinical Case Definition is met, regard as true measles case; implement control actions unless measles is ruled out by lab testing or other information.
- ◆ Cases should be excluded and isolated from group activity settings (e.g. schools, day-care centers, work place, camps, etc.) immediately and through the 4th day after the onset of rash to limit further exposures. In health care settings, use of Airborne Precautions is recommended.
- ◆ Identify exposed contacts.  
**Measles is highly communicable.** Measles cases are communicable (contagious) starting 3-5 days before rash onset through the 4th day after rash onset; exposure includes household contact and same-room contact.
- ◆ Assess susceptibility of contacts (see Immunity/Susceptibility, above). Measles vaccine is universally recommended as part of the routine childhood immunization schedule, thus persons  $\geq 4$  years of age and born after 1956 should have a history of 2 doses of MMR vaccine, and persons  $\geq 1$  year and  $<4$  years of age should have a history of at least 1 dose of MMR vaccine.
- ◆ Susceptible contacts should be recommended to receive post-exposure prophylaxis with either:
  - Measles (MMR) vaccine, if given within 72 hours of exposure
  - Immune globulin (IG), if given within 6 days of exposure

Comment: In most situations vaccine is preferable to use of immune globulin, provided vaccine can be given within 72 hours. However, IG, rather than vaccine, should be used for infants under 6 months of age, pregnant women, and severely immunocompromised persons:

- Infants aged  $<12$  months who have been exposed to measles should receive 0.5 mL/kg [0.11ml/lb] of body weight of IG given intramuscularly (IGIM) (maximum dose = 15 mL). Alternatively, MMR vaccine can be given instead of IGIM, to infants age 6–11 months, if it can be given within 72 hours of exposure.
  - Pregnant women without evidence of measles immunity who are exposed to measles should receive 400 mg/kg of IG given intravenously (IGIV).
  - Severely immunocompromised† persons who have been exposed to measles should receive 400 mg/kg of IG given intravenously (IGIV), even if they have past evidence of measles immunity
  - Other people who do not have evidence of measles immunity can receive an IG dose of 0.5 mL/kg of body weight. Give priority to people who were exposed to measles in settings where they have intense, prolonged close contact (e.g., household, child care, classroom, etc.). Give IG intramuscularly; the maximum dose is 15 mL.
- ◆ Exclusion of exposed, susceptible contacts: Exposed persons attending group-activity settings (e.g. schools, day-care centers, work place, camps) who cannot provide documentation of

measles immunity (including those with medical, religious and philosophical exemptions) should be vaccinated as soon as possible.

- Those who are receiving their 1<sup>st</sup> dose of measles vaccine (MMR or MMRV) and are receiving it within 72 hours of exposure to measles may in general be re-admitted to the activity setting (however the local health officer may opt not to grant readmission until 21 days after the last know case onset, depending on the situation). The 2<sup>nd</sup> dose of measles vaccine in should be scheduled for 28 days after the first dose.
  - Those who had received one dose of measles-containing vaccine prior to the exposure and who now receive a second dose following the exposure do not need to be excluded from public settings or group activities.
  - Those who refuse vaccination, and those who receive vaccine more than 72 hours after exposure, should be excluded from the setting for 21 days after the onset of the final case of measles in the group activity outbreak setting.
  - Although the 2<sup>nd</sup> dose of measles, mumps, rubella vaccines is not routinely given until 4 – 6 years of age, in outbreak situations involving day care, pre-school, and other settings with children under 4 years of age, consideration should be given to requiring the 2<sup>nd</sup> dose as a control measure, following appropriate minimum intervals between doses.
- ◆ Provide information about measles to persons at risk and/or the general public. An excellent Question-&-Answer [measles information sheet](#) in .PDF format is available from the Immunization Action Coalition (<http://www.immunize.org/catg.d/p4209.pdf> )

## LABORATORY SPECIMENS: PROCEDURES AND CONSIDERATIONS

- ◆ Collect a serum and specimen(s) for PCR/viral isolation/molecular epidemiology testing (a respiratory specimen, such as throat or nasopharyngeal swab; urine can also be considered). Collect specimens at the same time. See below for details.
- ◆ Laboratory support for measles case investigations fulfills 2 important and distinct objectives:
  - 1) confirmation of cases which improves overall surveillance
  - 2) characterization of circulating measles virus strains
- ◆ It is important to pursue **both** serologic and virologic testing; i.e., it is important to collect both serum and viral specimens from suspected cases.
- ◆ To obtain MDHHS serology and virology specimen collection and container kits, call MDHHS Laboratory Support Unit: 517-335-9040.

## MEASLES SEROLOGY

**Purpose:** to confirm a case of measles by detecting measles-specific antibodies.

**Specimen needed:** serum, 2 ml.

**MDHHS lab kit:** unit 8

**Specimen container description:** plastic serum tube with skirted cap

**MDHHS lab form:** [DCH-0583](#)

**Preferred test:** measles IgM antibody. This test is available at or through MDHHS laboratory, using highly sensitive and highly specific direct capture ELISA (EIA) methodology.

**Alternate tests:** other methods of measles IgM; paired IgG demonstrating significant rise in measles IgG antibody.

### **Specimen collection/submission procedure:**

- ◆ Collect at least 5 ml of whole blood in red-top or other tube without anticoagulant. Separate serum from blood by centrifugation and pour into PLASTIC serum tube, store at 2 - 8 C, or freeze serum if it cannot be shipped and received in MDHHS lab within 3 days. Do not freeze whole blood.
- ◆ Timing of specimen collection
  - **For IgM testing:** collect one serum between the 3rd and 30th day after onset of rash.
  - **NOTE:** Measles IgM tests that are negative and were collected less than 72 hours after the rash onset should be repeated using sera collected 72 or more hours after rash onset.
  - **For paired IgG testing;** note that IgG testing **requires 2 serum specimens**, acute phase and convalescent phase:
    - Acute-phase specimen - collect as soon after rash onset as possible;
    - Convalescent-phase specimen - collect 10-30 days (no earlier than 10 days) after acute-phase specimen.

Test will be done when both specimens are received (specimens can be sent individually or acute can be held at 2 - 8°C and sent to lab with convalescent specimen). If the specimens are sent to MDHHS lab separately, be sure to indicated on the Lab Request form that this is an acute serum and that the convalescent specimen will follow in approximately 10 -14 days.
- Label tube(s) with patient name, date of birth, and date of specimen collection.
- ◆ Complete MDHHS Virology Test Requisitions Form [DCH-0583](#); complete all information in the Patient Information and Specimen Information sections.
  - Request “measles IgM” and “rubella IgM” in the Test Requested area
  - NOTE: testing for rubella is encouraged for all suspected measles cases (likewise, testing for measles is encouraged for all suspected rubella cases).
- ◆ Be sure MDHHS Immunization Division has been notified of the case investigation.
- ◆ Ship specimens on a cold pack by overnight delivery if possible.
- ◆ Mail specimens to:
  - Michigan Department Health & Human Services
  - Bureau of Laboratories
  - 3350 N. Martin Luther King Blvd.
  - Building 44, Room 155
  - Lansing, MI 48909

## **MEASLES VIROLOGY/MOLECULAR EPIDEMIOLOGY TESTING**

**Collect a respiratory specimen for PCR/viral isolation in addition to the serum described above).**

**Use a synthetic swab (not cotton).**

**Purpose:**

Virus isolates and viral RNA detection/sequencing can confirm a measles case, and are also important for molecular epidemiologic surveillance, specifically to help determine

- ◆ the geographic origin of the virus,
- ◆ the viral strains circulating in the U.S., and
- ◆ whether these strains have become endemic in the U.S.

Note: Specimens for measles virology should be routinely collected along with serum when investigating potential measles cases. **Do not delay collection of viral specimens until serologic confirmation is obtained**, since the success of virus isolation is greatest for specimens collected within 7 days of rash onset. Do not collect viral specimens if more than 10 days have elapsed since rash onset.

**Specimens:**

- ◆ Respiratory specimen - throat swabs (oropharyngeal) or nasopharyngeal (NP) swabs are the preferred samples for virus isolation or detection of measles RNA by RT-PCR
- ◆ Urine - Urine samples may also contain virus and when feasible to do so, collection of both throat swab and urine can increase the likelihood of detecting the virus

**MDHHS lab kit:** 45

**Specimen container(s)**

- ◆ Throat swabs and other respiratory specimens: Viral Transport Media test tube
- ◆ Urine: 50 ml centrifuge tube or other sterile container

**Specimen collection/submission procedure:**

Label all specimen containers used with patient name, date of birth, and date of specimen collection.

**Respiratory specimens: throat swab (preferred), nasopharyngeal swab, nasal swab, or nasal wash**

- ◆ Collect as soon as possible after onset of rash (no later than 10 days after rash onset).
- ◆ **Throat swabs (and/or nasal or NP swab):** Use sterile Dacron (or other synthetic) swab to swab back of throat or the nasopharynx; if collecting more than one specimen use separate Dacron/synthetic swabs. Try to collect epithelial cells. Place swab(s) in a tube containing 2-3 ml of viral transport medium; submerge swab in transport medium and express the swab against the inside wall of the specimen container. Swab may be left in tube but make sure tube cap is securely screwed on; swab shaft may need to be cut down in order to fit if swab is to be left in tube.
- ◆ **Nasal wash:** use syringe with small plastic tube and 3-5 ml of Viral Transport Medium (VTM). Tilt head back, instill VTM in one nostril, holding other nostril closed; aspirate VTM fluid and specimen material quickly and gently. Rinse the tube with approximately 2ml of VTM to obtain any residual specimen.
- ◆ Keep specimens at 4°C (refrigerated).
- ◆ Ship specimens on cold pack by overnight delivery if possible.

**If immediate cold shipment (within 48 hours) cannot be arranged or is not convenient:**

- Nasal wash specimens** can be centrifuged at 500 × g (approximately 1500 rpm) for 5 minutes, preferably at 4°C, and the pellet re-suspended in 1 ml of cell culture medium. If

possible, the supernatant can be saved in a separate tube. The samples should be frozen and shipped at -70° C (dry ice). If centrifugation is not available, the whole specimen can be frozen (preferably at -70°C) and shipped on dry ice.

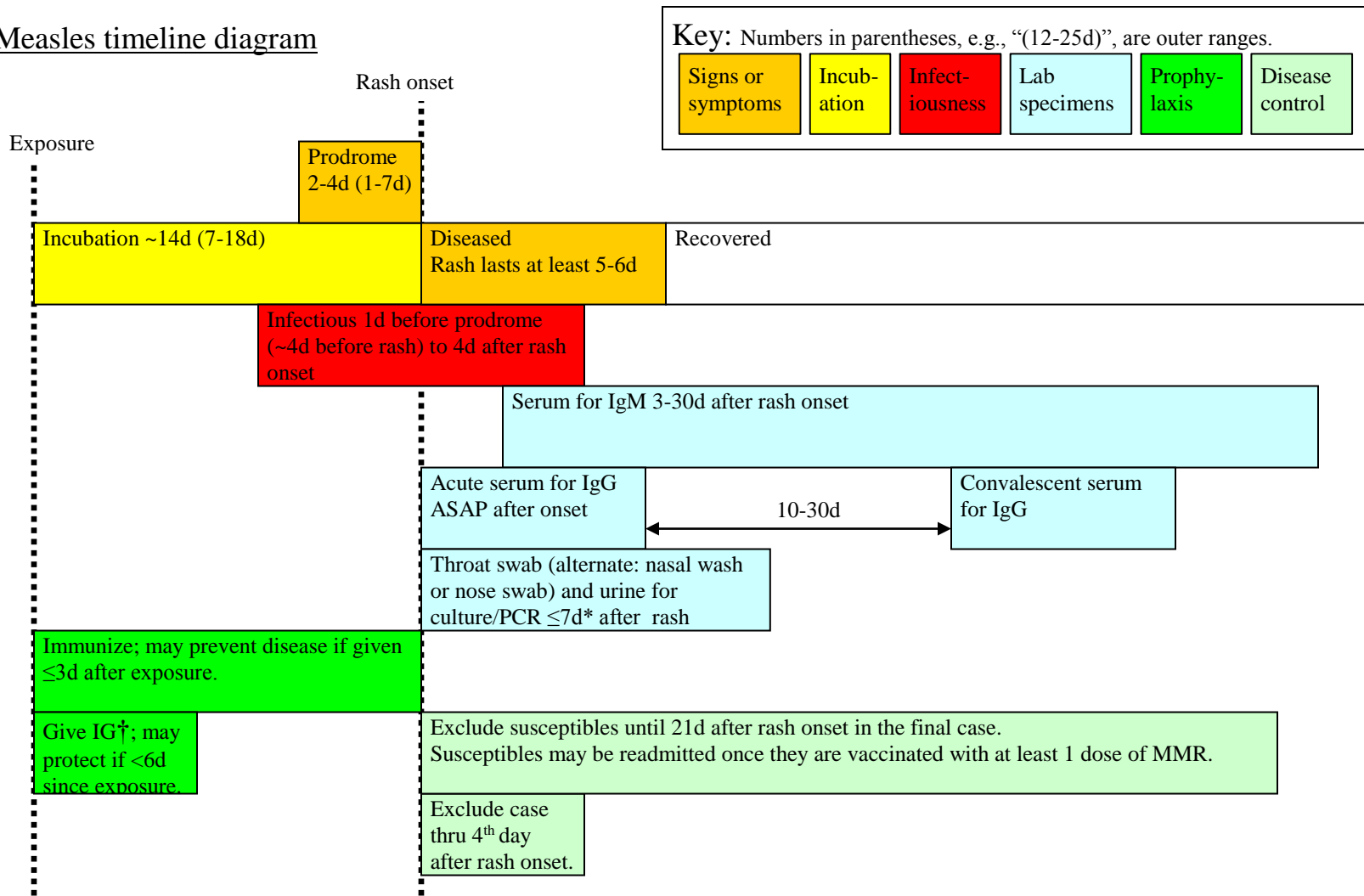
- **Nose and throat swabs** can be removed from the transport medium after allowing some time for elution of virus. The specimen can then be frozen at -70°C and shipped on dry ice.

**Urine specimens:**

- ◆ Collect within the first week after rash onset.
- ◆ Collect 50-100 ml of urine in a clean urine specimen container (50 ml centrifuge tubes work well); first morning void is preferable, collect urine “clean catch mid-stream.”
  - If centrifugation is available: Centrifuge at 500xg (approximately 1500 rpm) for 5 to 10 minutes to pellet the sediment. The supernatant should be discarded; re-suspend the sediment in 2-3 ml of viral transport medium or any cell culture medium. Ship frozen at -70°C on dry ice. If dry ice is not available, store at 4°C and ship on cold pack within 48 hours.
  - If centrifugation is not available, do not freeze the urine sample. The entire urine specimen should be stored at 4°C and shipped to the lab on cold pack.
- ◆ Complete a MDHHS Virology Test Requisition Form [DCH-0583](#) for each specimen. Indicate “measles virus by culture/PCR” in the “other” section of the Test Requested area.
- ◆ Mail specimens on a cold pack to:  
Michigan Department Health & Human Services  
Bureau of Laboratories  
3350 N. Martin Luther King Blvd.  
Building 44, Room 155  
Lansing, MI 48909



## Measles timeline diagram



\* For best results with viral culture, collect specimens  $\leq 3d$  after rash onset. Do not collect such specimens  $> 10d$  after rash onset.  
 $^\dagger$  Give IG only if the person is immunocompromised, or MMR is contraindicated, or  $> 72h$  to  $< 6d$  have passed since exposure.

Sources: APHA Control of Communicable Diseases Manual, AAP Red Book, CDC Pink Book, CDC VPD surveillance manual