Measles

CLINICAL CASE DEFINITION

An acute illness characterized by all 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, or
  coryza (runny nose), or
  conjunctivitis (redness and inflammation of the conjunctiva which lines the eyelid and covers the eyeball)

CASE CLASSIFICATION

♦ **Probable:** In the absence of a more likely diagnosis, 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:** An acute febrile rash illness† with:

- Isolation of measles virus‡ from a clinical specimen; or
- Detection of measles-virus specific nucleic acid‡ from a clinical specimen using polymerase chain reaction; or
- IgG seroconversion‡ or a significant rise in measles immunoglobulin G antibody‡ using any evaluated and validated method; or
- A positive serologic test for measles immunoglobulin M antibody‡§; or
- Direct epidemiologic linkage to a case confirmed by one of the methods above.

† Temperature does not need to reach ≥101°F/38.3°C and rash does not need to last ≥3 days.
‡ Not explained by MMR vaccination during the previous 6-45 days.
§ Not otherwise ruled out by other confirmatory testing or more specific measles testing in a P.H. Lab.

See LABORATORY CONFIRMATION below.

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 (documented up to 2 hours). Measles is highly communicable.

INCUBATION PERIOD

The average time from exposure to rash onset is 14 days (range 7 – 21). Prodrome symptoms generally precedes rash by 1-3 days. 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, investigate using report form/surveillance worksheet and control guidelines below.
    - Measles is an important public health concern; if clinical presentation suggests a measles diagnosis is likely, 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 attach copies of hospital discharge summary, death certificate, and autopsy report to the MDSS case. Notify the MDHHS Immunization Division (517-335-8159).

LABORATORY CONFIRMATION

Laboratory confirmation is essential for all outbreaks and all sporadic measles cases and should be attempted for all potential cases meeting the clinical case definition when a measles diagnosis is suspected, and no other more likely explanation exists for the illness. Collect serum and viral specimen (generally a throat (oropharyngeal) swab is preferred; a nasopharyngeal swab is an alternate, and urine may be advisable in some situations).

Laboratory confirmation for measles is defined as one of the following:

- Detection of measles-virus-specific nucleic acid by polymerase chain reaction (PCR).
- Isolation of measles virus from a clinical specimen.
- Positive serologic test for measles-specific IgM antibody

  NOTE: Measles IgM tests that are negative on serum collected less than 72 hours after the onset of rash should be repeated using sera collected 72 or more hours after rash onset.
- Significant rise in measles IgG antibody by any standard serologic assay – this is no longer commonly done but may be useful in certain situations.
    - Collection of sera for these paired IgG antibody 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).

Serum and a viral specimen 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) may also be available through commercial clinical

laboratories.

IMMUNITY/SUSCEPTIBILITY

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

- Birth before 1957 (note: this is not a valid criterion of measles immunity for women who might become pregnant and is also not valid for health care workers. These groups should have documentation of immunity by one of the methods mentioned below)
- Laboratory confirmation of a past measles disease diagnosis;
- Serologic (lab) evidence of immunity to measles (positive IgG);
- 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, i.e. 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.

Self-reported doses and a history of vaccination provided by a parent or other caregiver, or a clinical diagnosis of measles, should not be accepted.

CONTROL MEASURES

- Investigate reports of possible measles **immediately**.
- If Clinical Case definition (see above) is met, begin implementing control actions discussed below 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, workplace, camps, etc.) immediately and through the 4th day after the onset of rash to limit further exposures. In health care settings, the patient should be placed in a negative pressure room and use of Airborne Precautions is recommended.
- Identify exposed contacts:
  Measles is highly communicable. Measles cases are contagious starting 4 days before rash onset through the 4th day after rash onset. Exposures of greatest concern include 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 ≥ 4 years of age and born after 1956 should have a history of 2 doses of MMR vaccine, and persons ≥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 first exposure
  - Immune globulin (IG), if given within 6 days of first exposure

  Comment: In most situations, vaccination 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 first 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, workplace, 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 1st dose of measles vaccine (MMR or MMRV) **and** who do so within 72 hours of first 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 known exposure depending on the situation). These persons should be monitored closely for measles signs and symptoms for 21 days after their last exposure. The 2nd dose of measles vaccine should be scheduled for 28 days after the first dose.
        - Susceptible persons who receive their 1st dose of measles of vaccine more than 72 hours after first exposure are less likely to receive post-exposure prophylactic benefit from that dose of vaccine and thus should be considered for exclusion from the setting until 21 days after the onset of the final case of measles in the group activity outbreak setting.
    - Susceptible contacts that had received one dose of MMR prior to the exposure and receive a second dose within 72 hours of exposure do not need to be excluded from group-activity settings. If the second dose is received more than 72 hours after exposure, the LHD may choose to exclude the contact based on the contact's exposure setting (e.g., community or household) and the risk of transmission to others (e.g., daycare attendee). In both scenarios, the LHD should monitor for 21 days following their last exposure (28 days if IG was received).
    - Those who refuse vaccination, and those who receive vaccine more than 72 hours after exposure, should be excluded from school, day-care, camp, and other public/congregate settings for 21 days after the rash onset of the final case of measles in the group activity outbreak setting. Other social distancing measures, such as home quarantine of these susceptible exposed persons should be considered. These persons should be monitored for development of measles signs and symptoms for 21 days (28 days if received IG).
    - Although the 2nd 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 2nd 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. For testing at the state public health laboratory, throat or nasopharyngeal swabs are the preferred specimen for measles virus molecular detection. Urine specimens if collected will be submitted to a Vaccine Preventable Disease Reference Center for testing. Collect serum and viral specimen(s) 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 (IgM) and viral specimens from suspected cases. IgG serum results may assist in the evaluation of a suspect case, and in some instances may be useful for further testing.

- To obtain MDHHS serology and virology specimen collection/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-6084
(This form will automatically download)

Detection of measles IgM antibody can be diagnostic for measles because measles IgM antibody is produced in non-immune person when they are infected with measles virus. IgM antibody may not be detectable earlier than 72 hours after onset of rash. IgM serology is preferred over paired IgG antibody serology (acute-phase and convalescent-phase IgG antibody testing to demonstrate measles IgG antibody seroconversion) since only 1 serum specimen is needed and result turn-around time is shorter.

Also note that persons recently vaccinated against measles will have IgM (and IgG) response which is indistinguishable from the immune response as a result of measles virus infection; thus use of serology for diagnostic confirmation is not recommended in recently vaccinated persons (6-45 days since vaccination).

Serology 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 received by 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.

  NOTE: Two unique patient identifiers (generally first/last name and date of birth) are required by federal regulation, so please ensure the name and date of birth match on the tube and laboratory requisition form to prevent untestable samples or delays in diagnosis.

- Complete the MDHHS Virology/Serology Test Requisition Form DCH-6084; 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 suspected measles cases in situations where rubella may be as likely a diagnosis as measles (likewise, testing for measles is encouraged for suspected rubella cases).

- Be sure MDHHS Division of Immunization has been notified of the case investigation.

- Ship specimens on a cold pack by overnight delivery.

Ship 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 - throat swabs are generally preferred, nasopharyngeal (NP) swabs are an acceptable alternate. For PCR/viral isolation this should be collected in addition to the serum described above. Use a synthetic swab such as Dacron, nylon, or polyester; do not use cotton swab. Please refer to Instructions for Collection and Submission of Specimens for Viral Isolation and Viral PCR for additional information: DCH-0772

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.

Timing of specimen collection:

- **For PCR testing**: ideally, collect swab days 1-3 after rash onset (see note below).

  Note: Specimens for measles virology should be routinely collected along with serum when investigating potential measles cases. **Do <u>not</u> delay collection of viral specimens until serologic confirmation is obtained**, since the success of virus isolation is more likely to be successful when specimens are collected early (ideally within 3 days of rash onset, but up to 10 days post rash may be successful). Do not collect viral specimens if more than 10 days have elapsed since rash onset. Negative PCR tests do not necessarily rule out measles, especially if the swab was collected more than 3 days after rash onset. Evaluate other factors to determine case classification and public health follow-up, such as clinical presentation and the presence or absence of epidemiological risk factors (e.g., a known exposure).

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 a throat swab (or NP swab) and urine can assist in diagnosis, particularly if it has been more than 5 days since rash onset Consider day 0 as rash onset date:
  Day 0-5 of rash: throat/NP swab
  Day 6-9 of rash: throat/NP swab **and** urine

MDHHS lab kit: 45

Specimen containers

- Throat swabs and/or nasopharyngeal swabs: Viral Transport Media test tube
- Urine: if urine is collected, obtain in a 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.

NOTE: Two unique patient identifiers (generally first/last name and date of birth) are required by federal regulation, so please ensure the name and date of birth match on the tube and laboratory requisition form to prevent untestable samples or delays in diagnosis.

- **Respiratory specimens: throat swab (preferred) or nasopharyngeal swab:** Collect as soon as possible after onset of rash (no later than 10 days after rash onset).

Throat (oropharyngeal) swabs (and/or nasopharyngeal 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.

- Keep specimens at 4°C (refrigerated).

- Ship specimens on cold pack by overnight delivery.

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

- ❑ **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 9 days 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-6084 for each specimen. If using the previous form, please indicate "measles virus by culture/PCR" in the "other" section of the Test Requested area.

- Mail specimens on a cold pack to:

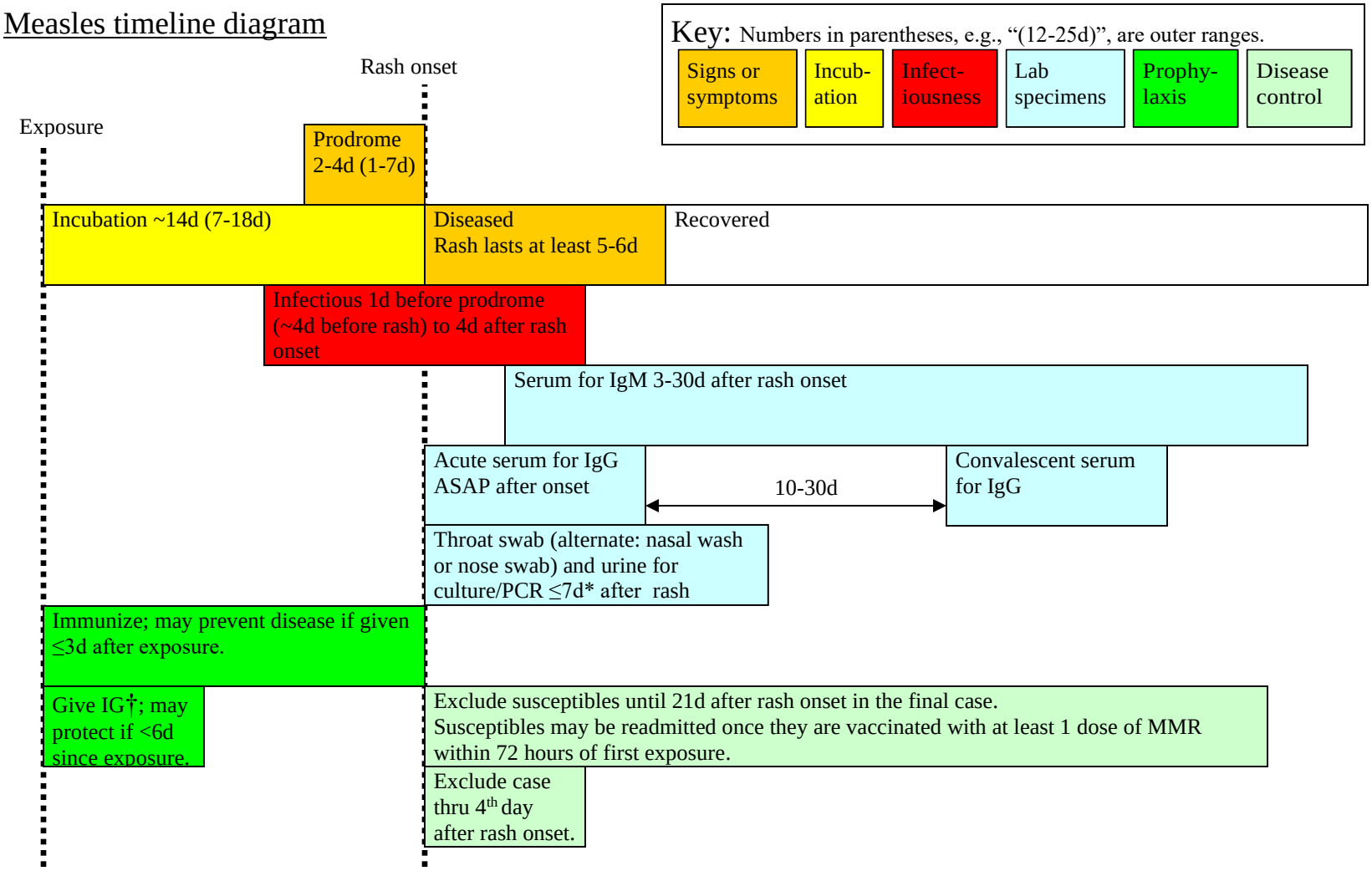
Michigan Department Health & Human Services
Bureau of Laboratories
3350 N. Martin Luther King Blvd.
Building 44, Room 155
Lansing, MI 48909

Discordant Laboratory Results

- If there are discordant laboratory results (e.g., negative PCR and positive IgM), evaluate additional factors to determine case classification and public health follow-up. These factors would include the clinical presentation, the presence or absence of epidemiologic risk factors (e.g., a known exposure), and specimen collection timing with regards to rash onset, and specimen shipment conditions.

❖

Measles timeline diagram



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

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