Section 8: Measles

BASIC EPIDEMIOLOGY

Infectious Agent
The measles virus—a single-stranded, RNA-encoded paramyxovirus.

Transmission
Virus is spread directly from person to person by inhalation of suspended droplet nuclei or by contact with infective nasopharyngeal secretions. It can also be transmitted indirectly by objects (fomites) contaminated with nasopharyngeal secretions. Measles is one of the most contagious of all infectious diseases, with >90% attack rates among susceptible close contacts.

Incubation Period
The incubation period ranges from 7–18 days (average 10–12 days) from exposure to the onset of prodromal symptoms.

Communicability
Measles is most communicable during the 3–4 days preceding rash onset. Persons with measles have been shown to shed virus between 4–5 days prior to rash onset (1–2 days prior to onset of prodromal symptoms) and for 4 days after the rash has appeared.

Clinical Illness
Measles is characterized by a generalized maculopapular rash (a flat, red area on the skin that is covered with small confluent bumps), fever, and one or more of the following: cough, coryza (runny nose), conjunctivitis (eye inflammation or pink eye), or Koplik's spots. There are three stages of illness:

- **Prodrome**
  - Measles has a distinct prodromal stage that begins with a mild to moderate fever and malaise. Usually within 24 hours there is an onset of conjunctivitis, photophobia (sensitivity to light), coryza (sneezing, nasal congestion, and nasal discharge), an increasingly severe cough, swollen lymph nodes (occipital, postauricular and cervical at the angle of the jaw), and Koplik's spots (seen only for a day or two before and after onset of rash). These spots are seen as bluish-white specks on a rose-red background appearing on the buccal and labial mucosa usually opposite the molars.
- **Rash**
  - The rash begins with flat, faint eruptions of upper lateral parts of the neck, behind the ears, along the hairline and on the posterior parts of the cheeks. The rash may appear from 1–7 days after the onset of the prodromal symptoms, but usually appears within 3–4 days. Individual lesions become more raised as the rash rapidly spreads over the entire face, neck, upper arms and chest. In severe cases, the lesions may merge together to form large rash masses. In mild cases, the rash may be macular and more nearly pinpoint, resembling that of scarlet fever.
- **Fever**
  - Fever is mild to moderate early in the prodrome, and goes up when the rash appears. Temperatures may exceed 40°C (104°F), and usually falls 2–3 days after

rash onset. High fever persisting beyond the third day of the rash suggests that a complication (e.g., ear infection) may have occurred.

DEFINITIONS

Clinical Case Definition
An illness characterized by all of the following criteria:

- A generalized rash lasting at least 3 days, and
- A temperature ≥ 101.0°F (≥ 38.3°C), and
- Cough, coryza, or conjunctivitis.

Laboratory Confirmation

- Positive serologic test for measles-specific IgM antibody performed at a public health laboratory, or
- Significant rise in measles antibody level by any standard serologic assay (i.e. four-fold rise in IgG antibody from acute to convalescent samples), or
- Isolation of measles virus from a clinical specimen, or
- Detection of measles-virus-specific nucleic acid by PCR.

Case Classification

- **Confirmed:**
  - A case that meets the clinical case definition and is laboratory confirmed by either: 1) a positive serologic test for measles immunoglobulin M antibody performed by a public health laboratory; 2) epidemiologic linkage to a confirmed measles case; or 3) travel to a measles endemic/outbreak area. OR
  - A compatible illness (may or may not meet the clinical description) with isolation of measles virus from a clinical specimen, detection of measles-virus specific nucleic acid by polymerase chain reaction from a clinical specimen, or a significant rise in measles immunoglobulin G antibody by any valid methodology.
- **Probable**: No probable case definition

CASE INVESTIGATION & INFECTION CONTROL

In the current setting of measles elimination in the United States, rapid investigation and reporting of all suspected measles cases is extremely important to ensure that measles remains controlled. The investigation steps below describe public health activities that should be completed when a suspect measles case is reported.

Establish diagnosis

- All suspect measles reports should be investigated immediately.
- Anyone with suspect measles should be isolated immediately - either at home or in the hospital under airborne precautions (respiratory isolation in negative air pressure room, if possible).
- Obtain the necessary clinical information to establish whether or not a suspect case meets the clinical case definition for measles.

- At a minimum, a suspect case should have an acute illness with fever >101°F and a generalized, maculopapular rash for which there is not a more compelling diagnosis.
- If the suspect case was reported within 3 days of rash onset, there should be appropriate follow-up to establish a rash duration of at least 3 days.
- **Alert appropriate local and regional health departments as well as DSHS IDCU in Austin immediately.**
- Assess vaccination history.
- Determine if suspect case has an epidemiological link or an epidemiological risk factor for measles in the three weeks prior to symptom onset, such as:
    - exposure to a confirmed or probable measles case;
    - travel to a measles endemic/outbreak area or contact with a traveler from a measles endemic/outbreak area;
    - transit through an international airport;
    - exposure to international visitors (includes visiting or working in U.S. tourist venues); or
    - use of public transit in a major U.S. city.
- Collect serological and virological specimens as soon as possible.

Laboratory confirmation is essential because in a setting of measles elimination, most cases that meet the clinical case definition are not measles. Additionally, because measles IgM assays may be falsely positive, collection of respiratory and/or urine specimens for PCR and viral isolation are encouraged. Testing at a public health laboratory is preferred. **If a private provider/hospital cannot or will not collect specimens, public health staff should make every arrangement to collect specimens instead.**

Determine whether to initiate a contact investigation

- If a case is highly suspicious for measles (e.g., clinically compatible illness in an unvaccinated person with history of travel to a measles endemic area), a contact investigation should be initiated even if laboratory confirmation of the case is not yet available.
- If a suspect measles case is not strongly suspicious for measles (e.g., clinically compatible illness in a person who has received one or two doses of MMR vaccine and does not have an epidemiologic risk factor for measles), the results of laboratory testing should be obtained before initiating a contact investigation.
- If an IgM positive test result has already been obtained on a suspect case who is not strongly suspicious for measles, repeat IgM testing or additional measles testing should be performed at a public health laboratory before a contact investigation is initiated.

Identify contacts

- A contact of a measles case is anyone who has shared the same airspace with a person who is infectious with measles (the infectious period is four days before rash onset through four days after rash onset [day of rash onset is day 0]), e.g., same classroom, home, clinic waiting room, airplane etc., or were in these areas up to 2 hours after the infectious person was present.
- No minimum time period has been established for exposure, but it is presumed that longer exposures are more likely to result in measles transmission than brief, transient exposures.
- When exposures have occurred in venues in which it is not possible to identify individuals, it is helpful to notify local health care providers so that they can be on the alert for possible cases. In addition, some health jurisdictions have issued press releases to notify the public.

- If the case was traveling by plane or ship during the infectious period, obtain all travel information (obtain boarding pass or e-reservation, if possible) and call IDCU, who will contact the CDC.

Prioritize contacts for investigation

If it is not feasible to investigate all possible contacts in an exposure setting, possible contacts may need to be prioritized for investigation. The following contacts, if susceptible to measles, are at the greatest risk of infection or severe disease, or are more likely to transmit measles to others and should be prioritized for investigation:

- household contacts;
- healthcare personnel of any age or others with occupations that require interaction with high risk populations;
- pregnant women;
- immunocompromised people;
- persons under five years of age in settings with known unvaccinated persons (e.g., childcare settings); and
- infants.

Other factors to consider

There are scant data on factors that make transmission of measles more likely, however if it is necessary to prioritize the investigation further, possible information to consider includes the following:

- length of time of exposure to case;
- proximity to case;
- ventilation in the exposure setting; and
- the time of exposure related to when the case left the setting.

In addition, the infectiousness of the case at the time of exposure may increase or decrease the possibility of transmission. Persons with measles are most infectious at the late prodromal phase of illness immediately prior to rash onset when cough and coryza are at their peak. The presence and frequency of cough in the case may affect the possibility of transmission. Cases who have received measles-containing vaccine in the past may be less symptomatic and also less infectious.

Provide post exposure prophylaxis for susceptible contacts

- The MMR vaccine may be given within 72 hours of exposure to persons $\geq$12 months of age with 1 or no documented doses of MMR, if not contraindicated.
- Immune globulin (IG) may be given to exposed susceptible people of any age through day six day after exposure.
  - The recommended dose of IG is 0.25 mL/kg (maximum dose=15 mL) intramuscularly (IM).
  - Immunocompromised persons should receive 0.5 mL/kg (maximum dose=15 mL) IM.
  - For persons receiving IVIG therapy, $\geq$400 mg/kg <3 weeks before measles exposure should be sufficient to prevent measles infection.

- It is unknown if administration of IG prolongs the incubation period. If symptoms consistent with measles occur ≤28 days of exposure, persons who have received IG should be instructed to isolate themselves immediately and notify their health department.

Monitor measles contacts

Measles contacts should monitor themselves for measles symptoms from day 5 after first exposure through day 21 after last exposure (day of exposure is day 0). Contacts should be instructed to isolate themselves immediately if measles symptoms develop and notify their health department (see Table 2 below). If they plan to seek medical care, they should contact the MD or ER ahead of time to notify them that they might have the measles and are coming in.

Control Measures

- Susceptible contacts to suspected cases should be vaccinated with measles vaccine within 72 hours of exposure OR should have immune globulin (IG) administered within six (6) days of exposure. Contact DSHS IDCU if IG/vaccine is needed.
- Children ≥1 year and <4 years should have history of at least one (1) dose of MMR vaccine.
- Persons ≥4 years and born after 1956 should have history of two (2) doses of MMR vaccine.
- If vaccination of exposed contact is contraindicated, exclude exposed contact from school or child-care facility for at least 14 days after last rash onset.
- Persons who cannot readily provide documentation of measles immunity should be vaccinated or excluded from the setting (e.g., school, child-care facility, work place).
- Anyone in the same airspace (same room, no minimum amount of time) with the suspected case up to 2 hours after the case has left should be considered exposed.

Exclusion

According to the Texas Administrative Code, children in school and childcare should be excluded for four (4) days from rash onset. In an outbreak, unvaccinated children should be excluded for at least 14 days after last rash onset. Adults should be instructed to stay home from work and any other activities.

Children as young as 6 months of age can receive measles vaccine if they have been exposed or are likely to be exposed.

Recommendations for prophylaxis, quarantine and monitoring of measles contacts

Category	IgG testing	MMR vaccine	Home quarantine‖	Symptom watch‖
People born before 1957¶ (5% will be susceptible)	No	No	No	Yes
People born during or after 1957 or high-risk people who were born before 1957, who:				
Have 2 documented doses of MMR (~1% will be susceptible)	No	No	No	Yes
Have 1 documented dose of MMR (5% will be susceptible) or no documented doses of MMR but are presumed to be immune to measles** and **are not** a high-risk person¶	If desired	If desired	No (unless tested and found to be susceptible)	Yes
Have no or 1 documented dose of MMR, but are presumed to be immune to measles** and **are** a high-risk person¶	If desired	Yes††	Work exclusion until immunity confirmed	Yes
First MMR dose given <72 hours of exposure	No	N/A	No	Yes
Immune globulin (IG) given ≤6 days of exposure‡‡	No	No	No	Yes
Unknown immune status, no presumption of immunity	If desired	Yes††	Yes	Yes
IgG negative/not vaccinated <72 hours of exposure/not given IG/known to be unvaccinated for measles	N/A	Yes††	Yes	Yes

‖If symptoms consistent with measles develop, person should be isolated. If there is concern about whether measles symptoms will be reported or compliance with quarantine, periodic calls to the exposed person to monitor for development of measles symptoms are recommended (see above for symptom watch time period and additional guidance).

¶ Ensure documentation of immunity (documented IgG+ or 2 documented doses MMR) in all high-risk persons, e.g., exposed healthcare personnel (including those born <1957), pregnant women, immunocompromised persons, and persons ≥4 years of age in settings with known unvaccinated persons, e.g., childcare settings (children aged 1-3 years should have 1 dose MMR).

**Immunity may be presumed in persons who have served in the U.S. armed forces, or were born in the U.S. in 1970 or later and attended a U.S. elementary school; or entered the U.S. in 1996 or later on an immigrant visa or have a green card (unless known to be unvaccinated).

††Vaccinate persons ≥1 year of age at the same time blood is drawn for serology unless IG is given.

‡‡IG may be administered ≤6 days of exposure to susceptible contacts of any age who did not receive MMR <72 hours of exposure. MMR should not be given until 5 months after IG in healthy people and until 6 months after IG in immunocompromised people. Persons who have received IG should monitor themselves for symptoms for 28 days.

Active surveillance for measles

In the case of an outbreak, local or state health departments should contact healthcare providers in the outbreak area to inform them of the outbreak and request reporting of any suspected cases. These activities are especially important in large cities and cities with large numbers of international visitors.

Testing of suspect cases who have recently received measles-containing vaccine

Ten percent of recipients of measles-containing vaccine may develop fever and rash approximately 1 week after vaccination, and vaccination of susceptible persons results in production of IgM antibody that cannot be distinguished from the antibody resulting from natural infection.

A positive measles IgM test cannot be used to confirm the diagnosis of measles in persons with measles-like illness who received measles vaccine 6–45 days before onset of rash. A negative test would exclude the diagnosis. For persons receiving vaccine 6–14 days prior to rash onset, a viral specimen should be obtained to distinguish between vaccine virus and wild-type virus.

REPORTING AND DATA ENTRY REQUIREMENTS

Provider, School & Child-Care Facilities, and General Public Reporting Requirements
Suspected measles cases are required to be reported immediately to the local or regional health department or the Texas Department of State Health Services (DSHS), Infectious Disease Control Unit (IDCU) at **(800) 252-8239 or (512) 776-7676**.

Local and Regional Reporting and Follow-up Responsibilities
DSHS Central Office must be notified immediately of any suspect cases of measles. Investigate any reported cases of measles. Identify and evaluate close contacts. Implement control measures and provide education to prevent further spread of disease. Measles investigation forms for must be sent to DSHS IDCU. In the event of a death, copies of the hospital discharge summary, death certificate, and autopsy report should also be sent to DSHS IDCU. Records must be faxed within 30 days of initial report to **(512) 776-7616** or mailed to the following address:

Infectious Disease Control Unit,
Texas Department of State Health Services
Mail Code: 1960
PO Box 149347
Austin, TX 78714-9347

Data Entry
The principle investigator (Local or Regional health department) is required to enter all measles investigations with a confirmed case status and submit notification in the NEDSS Base System (NBS) within 30 days of initial report. Please refer to the *NBS Data Entry Guidelines* for disease specific entry rules.

LABORATORY PROCEDURES

To obtain testing kits, contact the DSHS Laboratory at **(512) 776-7661**. Before shipping specimens, be sure to notify DSHS IDCU VPD staff at **(512) 776-7676.**

IgM Serology: A single specimen should be collected as soon as possible. A negative IgM result from a specimen collected before the fifth day of rash onset may not, however, rule out the diagnosis of measles. While we encourage early testing of patients with a rash-fever illness, testing may need to be repeated if specimen was collected before the fifth day of rash onset.

IgG Serology: Acute AND convalescent samples. Collect acute sample early in the course of illness and convalescent sample 10-14 days later. DSHS Laboratory can only conduct acute/convalescent testing if the first sample is negative (usually an unvaccinated individual). Otherwise, the acute/convalescent testing will need to be conducted through a private laboratory or hospital laboratory.

Measles serology results and interpretation

IgM result	IgG result	Previous infection history	Current infection/vaccination status	Comments
+	+ 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§

† 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.

Specimen Collection
Option 1:

- Collect at least 5 mL blood in red top tube.
- Label blood tubes with patient's first and last name, and we recommend a second identifier such as date of birth or medical record number or social security number. If the first and last name is not provided, the specimen will be rejected.
    - Centrifuge the **red top blood** collection tube within 2 hours from the time of collection to separate the serum from the red blood cells (clot).
    - Transfer the serum from the red top tube into a serum transport tube properly labeled with the patient's name and date of birth or social security number and ship cold with cool packs and must be received within 48 hours.
    - If the serum samples will not be delivered to the laboratory within 48 hours of collection, then the samples must be frozen at –20°C (frozen) or lower and shipped frozen with dry ice.
    - Do not freeze whole blood in red top tube for shipping.

Option 2:

- Collect at least 5 mL blood in **gold top** or **tiger top** blood collection tube containing a gel serum separator (Gold top or tiger top tubes are types of Serum Separator Tubes with the gel that keeps the serum separated from the clot after the centrifugation).
- Label blood tubes with patient's first and last name, and we recommend a second identifier such as date of birth or medical record number or social security number. If the first and last name is not provided, the specimen will be rejected.
    - Centrifuge the gold top blood collection tube within 2 hours from the time of collection to separate the serum from the red blood cells (clot) and ship cold with cool packs and must be received within 48 hours.
    - If more than 48 hours, transfer the serum into a serum transport tube properly labeled with the patient's name and date of birth or social security number and ship frozen with dry ice.
    - Do not freeze serum in SST for shipping. Freezing will cause hemolysis and hemolyzed specimens will be unsatisfactory for testing.

Submission Form

- Use the DSHS Laboratory current version of G-2A form (Dec 2011, Rev 4) for specimen submission.
- Make sure the patient's first and last name and date of birth / social security number match exactly what is written on the tube.
- Mark the laboratory test requested, date of onset, and date of collection. Be certain that the names on acute and convalescent sera match exactly.
- Call DSHS Laboratory at 512-776-7138 if needing information for specimen submission. Submitters must have a submitter number assigned by the DSHS Laboratory. If you do not have a submitter number, one can be obtained by calling 512-776-2377.

Specimen Shipping

- To avoid specimen rejection, ship separated serum or centrifuged SST Mon-Thurs to the DSHS laboratory via overnight delivery following the above guidelines.
- DO NOT mail on a Friday unless special arrangements have been pre-arranged with DSHS Laboratory.
    - If the serum samples will not be delivered to the DSHS laboratory within 48 hours of collection, transfer into a serum transport tube and freeze on Fridays. Ship frozen specimens with dry ice on Monday. Lone Star service will not deliver specimen to the DSHS lab on Saturday.
- Ship specimens to:

Laboratory Services Section, MC-1947
Texas Department of State Health Services
Attn. Walter Douglass (512) 776-7569
1100 West 49th Street
Austin, TX 78756-3199

Causes for Rejection:

- Discrepancy between name on tube and name on form.
- Insufficient quantity of serum for testing.
- Specimens received with extended transit time or received at incorrect temperature or no date of collection.

Viral Isolation

Viral isolation can confirm the diagnosis in measles, especially in vaccinated persons. Molecular epidemiologic techniques are used to genetically type measles viruses and identify the source of wild viruses and establish chains of transmission. The CDC can perform PCR testing on specimens forwarded to them.

Specimen Collection

- **Pharyngeal swab (preferred method):** The oropharynx should be rubbed vigorously with the swab to scrape off mucosal cells. The swab should then be placed in 2-3 mL of viral transport media. A viral culturette may also be used if 2-3mL of transport media is used.
- **Nasal Aspirates:** Obtain nasal specimen with a sterile rubber bulb aspirator. The aspirate should be discharged into a small sterile container.
- **Urine:** Urine specimens should be collected aseptically in a sterile container; up to 45 mL placed in a sterile 50 mL centrifuge tube.
- Specimen should be collected within four (4) days of rash onset.
- Keep specimen at 2-8ºC. Specimens received in the lab greater than 48 hours after collection should be stored frozen at -70 ºC and shipped on dry ice.

Submission Form

- Use Specimen Submission Form G-2A.
- Make sure the patient's name and date of birth / social security number match exactly what is written on the specimen container.
- Mark the laboratory test requested (virus isolation), disease suspected (measles), date of onset, and date of collection.

Specimen Shipping

- Ship specimen immediately via overnight delivery on wet ice.
- If specimen cannot be shipped immediately and received in the lab within 48 hours of collection, it may be stored at -70ºC and shipped on dry ice.
- DO NOT mail on a Friday unless special arrangements have been pre-arranged with DSHS Laboratory.
- Ship specimens to:

Laboratory Services Section, MC-1947
Texas Department of State Health Services
Attn. Walter Douglass (512) 776-7569
1100 West 49th Street
Austin, TX 78756-3199

Causes for Rejection:

- Specimens submitted on a preservative, such as formalin.
- Insufficient quantity of urine for testing.