Measles

Cases of measles occur worldwide[1–3]. In temperate zones, peak incidence occurs in late winter and early spring[1,4,5]. A single dose of MMR vaccine induces measles immunity in approximately 95% of those vaccinated[1,5]; however, due to measles extreme infectiousness, 2 doses are recommended[1,2,4,5]. In developing countries, case fatality rates average 3–5%[4] but can be as high as 10–30%[1,4]. Since 1995, the incidence of measles in the United States has been low with only a few hundred cases reported each year[6]. Endemic transmission of measles was declared eliminated in the U.S. in 2000[2,5]; however sporadic cases and outbreaks still occur nationally due to the virus being imported into the country through unvaccinated or incompletely vaccinated travelers (both native and non-native)[1–2,5]. There has been an increase of measles cases seen in the U.S. beginning in 2013[2,6]. In 2014, there were 667 cases of measles in the U.S., this is the highest number of cases since measles was eliminated in 2000[2].

A. Agent:

Measles virus is a member of the genus *Morbillivirus* of the family Paramyxoviridae[1–2,4,5]. It is an enveloped RNA virus[1,2,5] and has only one serotype[2,4].

B. Clinical Description:

Measles is a ***highly contagious disease*** characterized by fever, cough, coryza (runny nose), weight loss, generalized lymphadenopathy, conjunctivitis, and a generalized maculopapular rash[1,2,3–5]. Complications may include diarrhea, otitis media, pneumonia, seizures, meningitis, encephalitis, and subacute sclerosing panencephalitis (SSPE)[1–5]. SSPE is only from wild-type measles, no cases have been found in individuals vaccinated with the measles vaccine[3,5]. SSPE causes a degeneration of the central nervous system (CNS) and can occur 1 month to 27 years after infection[1]. The case fatality rate of measles ranges between 1 and 3 per 1,000 cases in the U.S.[5] Immunocompromised individuals are at increased risk for pneumonia, encephalitis, and death[3,4,5]. The characteristic rash sometimes does not develop in these patients[1,3,4,5]. An asymptomatic carrier state has not been observed[1]. Koplik spots can develop on the mucosa of the mouth and are considered to be pathognomonic for measles[1,5]. Occurring 1–2 days before to 1–2 days after the rash, they appear as punctate blue-white spots inside the mouth[1,4]. The maculopapular rash seen in measles begins at the hairline and then involves the face and upper neck[1,2,3,5]. During the 3 days after onset, the rash gradually proceeds downward and outward, reaching the hands and feet[1]. At the start of the rash the papules are discrete but may become confluent, particularly on the upper body[1,3]. Initially the lesions blanch with fingertip pressure, but not after 3–4 days[1]. Fine desquamation occurs over more severely involved areas[1,3]. Usually lasting 5–6 days, the rash fades in the same order that it appears, from head to extremities[1,3].

- Differential Diagnosis:
  Rubella, Kawasaki Syndrome, roseola infantum, enteroviruses, and drug rash[4].

C. Reservoirs:

The virus is only spread by humans[1,2,4,5].

D. Mode of Transmission:

Transmission occurs person-to-person by airborne droplets or direct contact with nasopharyngeal secretions of an infected person[1,2,4,5]. Measles virus is rapidly inactivated by heat, light, acidic pH, ether, and trypsin[1]. The virus can survive for up to 2 hours on a surface or in the air[1]. Measles virus is not spread by any other animal species[1,2].

E. Incubation Period:
The incubation period from exposure to prodrome ranges from 7–18 days (average 10–12 days[1]). The incubation period from exposure to rash ranges from 7–21 days (average 14 days)[1,2,4,5].

F. Period of Communicability:
Individuals with measles are usually considered infectious from 4 days before to 4 days after rash onset (count the day of rash onset as day zero)[1,2,4,5]. Immunocompromised patients may have prolonged excretion of virus in their secretions and can be infectious for the duration of their illness[5].

G. Susceptibility and Resistance:
Individuals born after 1957 that have not had the disease or have not been properly immunized are susceptible[1,2,5]. Proper immunization includes 2 MMR vaccinations (or 2 MMRV vaccinations)[1,2,4,5] with at least 28 days between the first and second dose[1,5]. Immunity is life-long after infection[1]. Two doses of MMR are recommended at 12–15 months and 4–6 years[1,2,5].

MMR efficacy:

- ≥99% immune after 2 doses[1,4,5]

Atypical measles - Occurs only in persons who received inactivated ("killed") measles vaccine (KMV) and are subsequently exposed to wild-type measles virus. An estimated 600,000 to 900,000 persons received KMV in the United States from 1963 to 1967. KMV sensitizes the recipient to measles virus antigens without providing protection. Subsequent infection with measles virus leads to signs of hypersensitivity polyserositis. The illness is characterized by fever, pneumonia, pleural effusions, and edema. The rash is usually maculopapular or petechial, but may have urticarial, purpuric, or vesicular components. It appears first on the wrists or ankles. Atypical measles may be prevented by revaccinating with live measles vaccine. Moderate to severe local reactions with or without fever may follow vaccination; these reactions are less severe than with infection with wild measles virus[1].

Modified measles - Occurs primarily in patients who received immune globulin (IG) as post-exposure prophylaxis and in young infants who have some residual maternal antibody. It is usually characterized by a prolonged incubation period, mild prodrome, and sparse, discrete rash of short duration. Similar mild illness has been reported among previously vaccinated persons[1].

H. Treatment:
Supportive care[2,4]; no specific antiviral therapy is available[2,5].

I. Clinical Case Definition[7]:

An acute illness characterized by:

- A generalized, maculopapular rash lasting ≥3 days; AND
- A temperature of ≥ 101.0°F (≥38.3°C); AND
- Cough, or coryza, or conjunctivitis.

J. Laboratory Criteria for Diagnosis[7]:

- 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.

*Not explained by MMR or MMRV vaccination during the previous 6–45 days

§ Not otherwise rules out by other confirmatory testing or more specific measles testing in a public health laboratory

Case Classification[7]	
Confirmed	An acute febrile rash illness× with: • Any of the laboratory criteria for diagnosis listed above; OR • Direct epidemiologic linkage to a case confirmed by one of the laboratory criteria for diagnosis listed above.
Probable	In the absence of a more likely diagnosis, an illness that meets the clinical description with: • No epidemiologic linkage to a laboratory-confirmed measles case; AND • Noncontributory or no measles laboratory testing.

× Temperature does not need to reach ≥ 101°F (≥38.3°C) and rash does not need to last ≥3 days.

K. Classification of Import Status[7]:

Internationally imported case: Defined as a case in which measles results from exposure to measles virus outside the U.S. 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 of entering the U.S. and there is no known exposure to measles in the U.S. during that time. All other cases are considered U.S.-acquired.

U.S.-acquired Case: Defined as a case in which the patient had not been outside the U.S. during the 21 days before rash onset or was known to have been exposed to measles within the U.S. U.S. acquired cases are sub-classified into four mutually exclusive groups:

Import-linked case: Any case in a chain of transmission that is epidemiologically linked to an internationally imported case.

Imported-virus case: A case for which an epidemiologic link to an internationally imported case was not identified, but for which viral genetic evidence indicates an imported measles genotype, i.e., a genotype that is not occurring within the U.S. in a pattern indicative of endemic transmission. An endemic genotype is the genotype of any measles virus that occurs in an endemic chain of

transmission (i.e., lasting ≥12 months). Any genotype that is found repeatedly in U.S.-acquired cases should be thoroughly investigated as a potential endemic genotype, especially if the cases are closely related in time or location.

Endemic case: A case for which epidemiological or virological evidence indicates an endemic chain of transmission. Endemic transmission is defined as a chain of measles virus transmission that is continuous for ≥12 months within the U.S.

Unknown source case: A case for which an epidemiological or virological link to importation or to endemic transmission within the U.S. cannot be established after a thorough investigation. These cases must be carefully assessed epidemiologically to assure that they do not represent a sustained U.S.-acquired chain of transmission or an endemic chain of transmission within the United States.

Internationally imported, import-linked, and imported-virus cases are considered collectively to be import-associated cases.

L. Laboratory Testing:

Collect both a serology and culture to be sent to the Arizona State Public Health Lab for testing.

TEST[8]	SPECIMEN TYPE	COLLECTION TIME
IgM*	Serum	Preferably 3 or more days after rash onset; will usually show up to one month out. Collection within first 3 days yields ~20% false negative results (draw may need to be repeated).
Culture **	Urine	At initial presentation (preferable); ≤10 days after rash onset
	NP or throat	At initial presentation (preferable); ≤5 days after rash onset
PCR***	Urine	≤14 days after rash onset
	NP or throat swab	≤3 days after rash onset

* The serologic response following vaccination is slower; IgM and IgG may not be detectable until 8–21 days post vaccination.

** Culture is necessary if case was vaccinated 6–45 days before testing.

*** Molecular typing of isolates is necessary to distinguish wild-type from vaccine-type Measles virus. It is done by RT-PCR through the CDC.

M. Assessing Laboratory Results:

Laboratory results should be interpreted in lieu of the epidemiologic evidence available. False positive IgM results can occur when measles IgM tests are ordered in the absence of clinical symptoms or soon after vaccination[2]. The IgM test has also been shown to cross react with antibodies to other organisms[2,8]. Ideally, specimens should be collected as soon as possible on all suspected measles cases to confirm the presence of the virus[1,2,8]. Travel to a measles endemic country or potential for exposure to somebody traveling to/from a measles endemic country is important to consider when triaging potential cases[1,2]. Positive measles IgM results at a commercial laboratory should be sent to the state laboratory for confirmatory testing and potential forwarding to CDC[1]. For highly suspect cases, additional blood draws may be necessary if the original specimen is no longer available.

N. Outbreak Definition:

An outbreak is one or more case(s) of confirmed measles in any setting. Confirmation must be done by Arizona State Public Health Laboratory (ASPHL), CDC, or another state laboratory. Cases identified within 21 days of the infectious period of the last known epi-linked case should be considered part of the same outbreak[7].

O. Time Frame[9]:

Providers	Submit a report to the Local Health Department by telephone or electronic reporting system authorized by ADHS within 24 hours after a case or suspect case is diagnosed, treated, or detected or an occurrence is detected.
Schools, Childcare establishments, Shelters	Submit a report to the Local Health Department within 24 hours after detecting a case or a suspect case.
Laboratories	- Submit a report to ADHS within 24 hours after obtaining a positive test result. - Submit an isolate or specimen, for each positive culture or test result, to ASPHL within 1 working day. - Report results of all other tests performed for the subject as part of the disease panel or as a reflex test to ADHS, when reporting a positive result for any of the specified tests.
Local Health Agencies	- Notify ADHS within 24 hours after receiving a report. - Submit an epidemiologic investigation report to ADHS within 30 calendar days after receiving a report. - Ensure isolate or specimen, for each positive culture or test result, are submitted to ASPHL within 1 working day.

P. Forms:

- CDC Measles Surveillance Worksheet

Q. Investigation Steps:

For a local health agency[9]:

A.A.C. R9-6-355. Measles (Rubeola)

A. Case control measures:

1. A local health agency shall:
   a. Upon receiving a report under R9-6-202 or R9-6-203 of a measles case or suspect case, notify the Department within 24 hours after receiving the report and provide to the Department the information contained in the report;
   b. Conduct an epidemiologic investigation of each reported measles case or suspect case;
   c. For each measles case, submit to the Department, as specified in Table 2.4, the information required under R9-6-206(D); and
   d. Ensure that one or more specimens from each measles case or suspect case, as required by the Department, are submitted to the Arizona State Laboratory.

B. Contact control measures:

1. A local health agency shall:
   a. Determine which measles contacts will be quarantined or excluded, according to R9-6-303, to prevent transmission; and
   b. Provide or arrange for immunization of each non-immune measles contact within 72 hours after last exposure, if possible.

Confirm Diagnosis

- Before contacting the patient or family, determine what information is available from medical records, physician, etc.

- For hospitalization, obtain medical records, including admission notes, times spent in each department if not isolated, progress notes, lab report(s), and discharge summary.
- Obtain information that supports clinical findings in the case definition and information on the onset date and order of the symptoms, including:
    - Rash (date of onset, duration & presentation), date of onset of each symptom, complications, hospitalizations, outcome status (survived or date of death).
- Obtain information on any laboratory tests performed and results or date results are expected.
- If laboratory tests have not been run to test for measles, coordinate testing with ADHS. Make a note of the laboratory (location and contact information) performing any tests and the expected turn-around time for testing.
- Obtain accurate and complete immunization histories on cases. Collect measles vaccine information, including:
    - Dates of vaccination, type, vaccine lot number, manufacturer, number of doses, and why case was not vaccinated (if applicable).

Conduct Case Investigation

Case investigation and vaccination of susceptible contacts should NOT be delayed pending laboratory results.

- Epidemiological investigation report should be submitted in MEDSIS by filling out the full DSO.
- Collect information as specified on the Measles Surveillance Worksheet, including:
    - Dates of exposure, demographic data (birth date, county, sex, race/ethnicity), vaccination status, travel history
- Dates of exit from and reentry to Arizona during infectious period, locations (include dates), mode of transportation including flight numbers. If travel by plane or ship, ADHS will contact CDC's regional Quarantine Station
- Identify potential source of infection; focus on incubation period of 7–21 days prior to rash onset.
- Collect information on the following:
    - Travel history should be captured in the travel table in MEDSIS and should include dates of travel.
    - Any potential exposure sites and exact dates and times, including provider visits, group settings, public venues, etc.
    - Any visitors from outside the U.S.
    - Case finding and defining transmission setting

Conduct Contact Investigation

- Consider those in contact with case 4 days before through 4 days after rash onset[4,5] (count the day of rash onset as day zero).

NOTE: Immunocompromised patients may have prolonged excretion of virus in their secretions and can be infectious for the duration of their illness[5]. Consider those in contact with an immunocompromised person 4 days before rash onset to the end of their illness.

    - Identify rash illnesses among close contacts, including household members or guests, neighbors, schoolmates, and other possible transmission setting(s).
    - Record immune status and collect immunization history; number and date of doses given.
    - Determine if case is involved in a high-risk occupation or if another special situation is involved (e.g., college, residential facility, health care).

- Presumptive evidence of immunity includes at least one of the following[2,5]:
  - Written documentation of adequate vaccination:
    - Receipt of one or more doses of a measles-containing vaccine administered on or after the first birthday for preschool-age children and adults not at high risk; **OR**
    - Receipt of two doses of measles-containing vaccine for school-age children and adults at high risk for exposure transmission (i.e., health care personnel, international travelers, and students at post-high school educational institutions); **OR**
  - Birth before 1957*; **OR**
  - Laboratory evidence of immunity; **OR**
  - Laboratory confirmation of disease.

***Although birth before 1957 is considered as presumptive evidence of immunity, for unvaccinated HCP born before 1957 that lack laboratory evidence of measles immunity or laboratory confirmation of disease, health care facilities should consider vaccinating personnel with two doses of MMR vaccine at the appropriate interval.**

NOTE: Verbal history of receipt of measles vaccine is NOT considered adequate proof of vaccination.

- Follow-up with symptomatic contacts as suspect cases.

Initiate Control and Prevention Measures

Due to the highly contagious nature of measles there are a variety of restrictions that may need to be placed upon cases, contacts and others within the community, these restrictions include:

- Hospitalized patients with measles must be under airborne precautions from the onset of illness through 4 days after the appearance of the rash. (i.e., 4 days before through 4 days after rash onset, with rash onset day counted as day 0)[4,5].
- Cases should be excluded from work, school, and other congregate settings during the period of communicability (i.e., 4 days before through 4 days after rash onset, with rash onset day counted as day 0)[4,5].
- Identify susceptible children and staff when measles has been identified in a school, daycare or health care facility. See Section 5: *Isolation, Work and Child Care Restrictions*
- Follow up with case(s) and contacts to assure compliance with recommendations. Initiate control measures immediately.
- Assure prophylactic measures are received by contact(s).

Isolation, Work and Child Care Restrictions

For a school or child care establishment[9]:

A.A.C. R9-6-355. Measles (Rubeola)

A. Case control measures:

1. An administrator of a school or child care establishment, either personally or through a representative, shall:
   a. Exclude a measles case from the school or child care establishment and from school- or child-care-establishment-sponsored events from the onset of illness through the fourth calendar day after the rash appears; and
   b. Exclude a measles suspect case from the school or child care establishment and from school- or childcare-establishment-sponsored events until the local health agency has determined that the suspect case is unlikely to infect other individuals.

B. Contact control measures:

1. When a measles case has been at a school or child care establishment, the administrator of the school or child care establishment, either personally or through a representative, shall:
   a. Consult with the local health agency to determine who shall be excluded and how long each individual shall be excluded from the school or child care establishment, and
   b. Comply with the local health agency's recommendations for exclusion.

For a health care provider or an administrator of a health care institution[9]:

A.A.C. R9-6-355. Measles (Rubeola)

A. Case control measures:

1. A diagnosing health care provider or an administrator of a health care institution, either personally or through a representative, shall isolate and institute airborne precautions for a measles case from onset of illness through the fourth calendar day after the rash appears.
2. An administrator of a health care institution, either personally or through a representative, shall exclude a measles:
    a. Case from working at the health care institution from the onset of illness through the fourth calendar day after the rash appears; and
    b. Suspect case from working at the health care institution until the local health agency has determined that the suspect case may return to work.

B. Contact control measures:

1. An administrator of a health care institution shall ensure that a paid or volunteer full-time or part-time worker at a health care institution does not participate in the direct care of a measles case or suspect case unless the worker is able to provide evidence of immunity to measles through one of the following:
    a. A record of immunization against measles with two doses of live virus vaccine given on or after the first birthday and at least one month apart;
    b. A statement signed by a physician, physician assistant, registered nurse practitioner, state health officer, or local health officer affirming serologic evidence of immunity to measles; or
    c. Documentary evidence of birth before January 1, 1957.

Case Management

Cases should be followed to determine compliance of control measures.

Contact Management, including Susceptible Contacts

The following are general guidelines for the effective use of immunization and/or IG:

- All susceptible contacts should be immunized or provided IG to prevent or modify disease development after exposure to measles[2,4,5,10].
- The use of post-exposure vaccine in susceptible individuals:
    - Immunization is preferred to the use of IG for post-exposure as it may protect the individual from disease and achieves the high level of population immunity needed to control a measles outbreak[1–2,4,5,10].
    - To protect those with contraindications to measles containing vaccine, who cannot receive the vaccine, ensure that household and close contacts are fully immunized to measles and exclude the individual from settings in which additional measles exposure may occur.
- Timing of immunization, for those without contraindications:
    - Give within 72 hours of exposure to attempt to provide protection. If >72 hours, vaccine is still recommended to prevent infection in future exposures[1–2,4,5,10].
    - Measles vaccine should not be given until at least 6 months have passed since the administration of IGIM or 8 months of IGIV[10].
- Use of post-exposure IG:
    - IG can be administered intramuscularly (IGIM), intravenously (IGIV), and subcutaneously (IGSC)[10].
    - IG should not be used to control measles outbreaks but may prevent or modify disease in susceptible contacts at risk for serious complications[2,10].
    - IG is only to provide temporary protection from an exposure to measles[1].
    - Without vaccination, individuals are still considered susceptible to future exposures and should be excluded from institutions affected by measles until 21 days after the onset of rash in the last case of measles[2,5].

- IG is especially indicated for susceptible household contacts of measles patients when contacts are younger than 6 months of age, pregnant, or immunocompromised[2,4,5,10]. (See Special Situations for more information on the use of IG in HIV-infected individuals.)

- Dosing of IG[10]:
  - IGIM: 0.5 mL/kg of body weight (maximum dose = 15 mL)
  - IGIV: 400 mg/kg of body weight
- Timing of IG[10]:
  - Temporary protection provided if given within 6 days of exposure.
  - If an individual has received IGIV (400 mg/kg) <3 weeks before exposure, no additional IG is required.
- Post-exposure immunization and IG administration are not 100% effective and may prolong the incubation period[2,5].
  - All contacts should be followed for signs and symptoms of measles for 3 weeks after exposure.
  - Any contact that develops signs or symptoms compatible with measles should be reported to the county health department and investigated as a case.
- Document compliance with post-exposure prophylaxis recommendations and the findings of contact follow-up.
  - Note any missing information when a contact is lost to follow-up.

Notifications

- ADHS and the local health department will jointly decide whether to send a health alert notice to providers, create a press release, or provide other public notifications.
- As appropriate, use the notification letter(s) and the disease fact sheet to notify the case, contacts and other individuals or groups.
- ADHS is responsible for notifying CDC upon identification of a confirmed/probable case.
- ADHS is responsible for submitting information from the investigation form to CDC.

R. Outbreak Guidelines:

Refer to the general outbreak guidelines section for general information on conducting an outbreak investigation.

Health Care Settings:
Refer to the Measles Surveillance Toolkit for Healthcare Settings**.**

HIV Infection in Contacts Susceptible to Measles[10]:

- The immune status and vaccination history of an HIV-infected individual exposed to measles is required to determine the need for prophylaxis.
- HIV-infected individuals are considered immune and do not require prophylaxis if they have:
  - No or moderate immune suppression, AND
  - Serologic evidence of immunity, OR
  - Receipt of 2 doses of measles vaccine after initiation of antiretroviral therapy.
- HIV-infected individuals who have not received measles vaccine after initiation of antiretroviral therapy or are severely immunosuppressed* should receive IGIV.

  ***Immunosuppression:**
  - **≤5 years of age: CD4 percentages <15% for 6 months or longer**
  - **>5 years of age: CD4 percentages <15% and CD4 count <200 cells/mm^2 for 6 months or longer**

- HIV-infected individuals with severe immunosuppression should not receive measles vaccine.
- HIV-infected individuals should not receive MMRV.
- Asymptomatic individuals do not need to be evaluated and tested for HIV infection before MMR or other measles vaccines are administered.

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