Measles Investigation Quicksheet

July 2022

Measles Basics

Signs and symptoms of measles infection

Measles typically begins with a mild to moderate fever accompanied by cough, coryza, and conjunctivitis. Some cases also report diarrhea, nausea, and vomiting. Two to three days later, Koplik's spots, a characteristic sign of measles, may appear. At this time the fever spikes, often to >104°F and a red blotchy maculopapular rash appears, usually first on the face, along the hairline, and behind the ears. This rash spreads downward to the trunk and then to the arms and legs. In approximately one week, the rash fades in the same sequence that it appeared. Complications of measles, including otitis media, bronchopneumonia, and laryngotracheobronchitis (croup) occur commonly in young children and immunocompromised hosts.

Measles exposure

Sharing the same airspace with a person infectious with measles e.g., same classroom, home, clinic waiting room, airplane etc., or being in these areas up to 1 hour after the infectious person has left the area. Although CDC recommends using a 2-hour window, there is only one report in the literature of measles transmission >60 minutes after an infectious person has left the setting.

No minimum duration has been established for an exposure, but it is presumed that exposures that are longer in duration and/or face to face 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 exposed individuals, it is helpful to notify local health care providers so that they can be on the alert for possible cases. In addition, some local health jurisdictions issue press releases to notify the public.

Measles infectious period

From four days before rash onset through four days after rash onset (day of rash onset is day 0). Immunocompromised patients who may have prolonged excretion of the virus in respiratory tract secretions can be contagious for the duration of the illness.

Measles incubation period for exposed contacts

From exposure to onset of prodromal symptoms is generally 8–12 days. The average interval between the appearance of rash in the index case and rash in secondary cases is 14 days (range 7-21 days).

Measles case definition

Clinical description: An acute illness characterized by:

- generalized, maculopapular rash lasting ≥3 days; and
- temperature ≥101°F or 38.3°C; and
- cough, coryza, or conjunctivitis

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.

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. VRDL can perform testing to distinguish between vaccine strain and wild type measles.
§ Not otherwise ruled out by other confirmatory testing or more specific measles testing in a public health laboratory.

Measles laboratory criteria for diagnosis

Preferred: Detection of viral RNA by reverse transcription polymerase chain reaction (RT- PCR)

Acceptable: Serum measles IgM antibody positive*; Isolation of measles virus; or significant rise in serum measles IgG antibody between acute and convalescent titers. Note that false positive measles IgM results are common.

If a patient is highly suspicious for measles, send specimens to a public health laboratory for testing; commercial labs cannot perform measles PCR testing. PCR testing done during the recommended timeframe can "rule out" measles in the setting of a false positive IgM. Detailed information on measles testing webpage.

*Measles IgM testing may be falsely positive.

Assessing Suspect Measles Cases

- Consider measles in patients of any age who have a fever ≥101 F, plus at least one of the 3 "Cs" (cough, coryza or conjunctivitis) and a descending rash that starts on the face. The rash typically follows the onset of illness within 4 days.
- If the patient has fever + ≥1 "C" + consistent rash (if ≥4 days since onset of fever) + an epidemiological risk factor, measles should be considered regardless of measles vaccination history.
- Epidemiological risk factors in the past 21 days:
  - Known contact with a measles case or an ill person with fever and a rash
  - Contact with an international visitor who arrived in the U.S. within the past 21 days
  - Travel outside the U.S., Canada or Mexico
  - Domestic travel through an international airport
  - Visited a U.S. venue popular with international visitors such as a large theme park
  - Lives in or visited a U.S. community where there are measles cases
- If the clinical presentation is highly suggestive of measles, but no epidemiologic risk factor can be elicited, still consider measles and immediately mask patient with or without risk factors and follow guidelines for infection control.
- If measles is being considered, the local health department should be contacted immediately.
- See detailed measles clinical guidance.
- If a suspect measles case reports air travel during their infectious period, please collect the following:
  - Departure and arrival cities
  - Flight number, date, and time
  - Terminal and/or gate number
  - Seat number
  - Information on any traveling companions

Assessing Measles Immunity in Contacts

Contacts who are not classified as high-risk† can be presumed to be immune to measles for the purposes of measles case investigations if they:

- were born
  - in the U.S. prior to 1957; or
  - outside the U.S. prior to 1970 **AND** moved to the U.S. in 1970 or later;‡ or
  - in any country in 1970 or later and attended a U.S. primary or secondary school;‡ or
- have written documentation with date of receipt of at least one dose of measles-containing vaccine given on or after their first birthday in 1968 or later; or
- have a documented IgG+ test for measles; or

- laboratory confirmation of previous disease; or
- served in the U.S. armed forces; or
- entered the U.S. in 1996 or later with an immigrant visa or have a green card‡

† A high-risk contact includes healthcare personnel of any age, pregnant women, immunocompromised people, household contacts of a case, or persons in settings with known unvaccinated persons (e.g., infant care settings). Additional evidence of immunity is required for exposed high-risk persons. Additional evidence of immunity may also be required during an outbreak. Immunity can be presumed if the exposed person:

- has documentation of a positive measles IgG test; or
- has documentation of two doses of measles vaccine given in 1968 or later, separated by at least 28 days, with the first dose on or after the first birthday.

‡Unless known to be unvaccinated for measles, e.g., having a medical contraindication to vaccination or being philosophically or religiously opposed to vaccinations.

High-risk contact

A high-risk contact is a person who may experience severe illness if they become infected with measles or from whom the transmission potential is high (large number of susceptible contacts or high intensity/duration of exposure). Examples of high-risk contacts include infants 6 to 11 months, immunocompromised persons, pregnant women, household contacts, and healthcare workers.

High-risk setting

A high-risk setting is one in which transmission risk is high (e.g., setting with a large number of measles-susceptible persons), particularly persons who could experience severe disease if infected with measles.

Postexposure Prophylaxis (PEP)

The administration of MMR vs. immune globulin (IG) as PEP to exposed contacts depends primarily upon time since exposure, age of the contact, and risk status of the contact (pregnant or immunocompromised). If you have questions about which type of PEP is appropriate, please contact CDPH at 510-620-3737.

MMR vaccine for PEP

Susceptible persons ≥6 months of age with 1 or no documented doses of MMR may receive MMR vaccine <72 hours after last exposure to measles, if not contraindicated (although administration of IG is preferred in infants 6-11 months of age). However, only MMR administered <72 hours after first exposure is considered PEP.

In some studies, the effectiveness of MMR PEP is low (though protection against future exposures is high) and likely depends upon the nature of the exposure, among other things. For this reason, exposed persons who have received MMR PEP should be excluded from high-risk settings (see Table).

Immune globulin (IG) for PEP

IG may be given to exposed susceptible persons (and severely immunocompromised persons regardless of immune status) ≤6 days of last exposure to prevent infection. However, persons who receive IG >6 days after the first exposure should still be placed on quarantine.

Because the effectiveness of IG PEP at preventing measles varies based upon a number of factors including the nature of the measles exposure, dosage and type of IG administered, etc., it is recommended that persons who receive IG PEP ≤6 days after last exposure be excluded from high-risk settings (see Table).

Important Points to Consider Regarding IG PEP:

- Detailed Information on IG administration
- If a person has no contraindications to MMR and it is <72 hours after the first exposure, give MMR and not IG PEP. Except in high-risk settings, unvaccinated persons who receive their first dose of MMR vaccine within 72 hours postexposure may return to childcare, school, or work.
- Infants <12 months of age should receive 0.5 mL/kg of body weight of intramuscular IG (IGIM); (max dose=15 mL).

- Unvaccinated children <30 kg (<66 lbs) who are not eligible for MMR PEP should receive 0.5 mL/kg of body weight of IGIM (max dose=15 mL).
- Pregnant women without evidence of measles immunity should receive 400 mg/kg of body weight of intravenous IG (IGIV).
- Severely immunocompromised persons[§], irrespective of evidence of measles immunity, should receive 400 mg/kg of body weight of IGIV.
- For persons already receiving IGIV therapy, administration of >400 mg IGIV/kg of body weight at least one time in the 3 weeks before first measles exposure should be sufficient to prevent measles infection.
- For patients receiving subcutaneous IG (IGSC) therapy, administration of ≥200 mg IGSC/kg of body weight once weekly for two consecutive weeks before first measles exposure should be sufficient.
- Persons weighing ≥30 kg (≥66 pounds) will not receive an adequate dose of measles antibodies from IGIM. Therefore, there is no recommendation to administer IGIM to such persons. If appropriate, IGIV should be administered.
- Nonimmune persons who receive IG should not receive MMR vaccine earlier than 6 months after IGIM or 8 months after IGIV administration.
- One source of IG is FFF Enterprises in Temecula CA, which can be reached 24/7 at 1-800-843-7477.
- After hematopoietic stem cell transplantation, duration of high-level immunosuppression is highly variable and depends on type of transplant, type of donor and stem cell source, and post-transplant complications such as graft vs. host disease and their treatments. Please contact CDPH at 510-620-3737 for consultation.

[§]Per CDC and IDSA guidance: Patients with high-level immunosuppression include those:

- with combined primary immunodeficiency disorder (e.g., severe combined immunodeficiency);
- who are receiving cancer chemotherapy;
- on treatment for ALL within and until at least 6 months after completion of immunosuppressive chemotherapy;
- within 2 months after solid organ transplantation;
- who have received a bone marrow transplant, until at least 12 months after finishing all immunosuppressive treatment, or longer in patients who have developed graft-versus-host disease;
- with HIV infection with a CD4 T-lymphocyte count <200 cells/mm^3 (age >5 years) and percentage <15 (all ages) (some experts include HIV-infected persons who lack recent confirmation of immunologic status or measles immunity);
- receiving daily corticosteroid therapy with a dose ≥20 mg (or >2 mg/kg/day for patients who weigh <10 kg) of prednisone or equivalent for ≥14 days; and
- receiving certain biologic immune modulators, such as a tumor necrosis factor-alpha (TNF-α) blocker or rituximab.

Quarantine/Exclusion of Contacts

- If quarantine/exclusion is implemented, it should begin on day 7 (CDC recommends day 5 for healthcare workers) after the first exposure through day 21 after the last exposure (day of exposure is day 0).
- If symptoms consistent with measles develop, contact should be immediately isolated until day 4 after rash onset (day of rash onset is day 0).
- Quarantined persons should be instructed to notify their local health department if symptoms occur.
- CDPH does not recommend extending quarantine or exclusion beyond 21 days after exposure in persons who received IG PEP, as it is unknown if IG prolongs the incubation period. However, such persons should monitor symptoms for an additional 7 days and if symptoms occur ≤28 days of exposure, they should self-isolate and contact their local health department.

Measles Treatment

No specific antiviral therapy is available for measles. Measles virus is susceptible in vitro to ribavirin, which has been given by the intravenous and aerosol routes to treat severely affected and immunocompromised children with measles. However, no controlled trials have been conducted,

and ribavirin is not approved by the U.S. Food and Drug Administration for treatment of measles. IV ribavirin (Virazole®) is available in the U.S. from Bausch Health. Contact Bausch Health at 877-361-2719 (24/7) if this product is requested.

Vitamin A. Vitamin A treatment of children with measles in developing countries has been associated with decreased morbidity and mortality rates. Low vitamin A levels have also been found in U.S. children, and children with more severe measles illness have lower vitamin A concentrations. The World Health Organization currently recommends vitamin A for all children with acute measles, regardless of their country of residence. Even in countries like the United States where measles usually is not severe, vitamin A should be given to all children with severe measles (e.g., those requiring hospitalization). Aquasol A™ appears to be the only parenteral vitamin A product available in the U.S.

Vitamin A for treatment of measles is administered once daily for 2 days, at the following doses:

- 200,000 IU for children 12 months or older;
- 100,000 IU for infants 6-11 months of age; and
- 50,000 IU for infants younger than 6 months.

An additional (i.e., a third) age-specific dose should be given 2 through 4 weeks later to children with clinical signs and symptoms of vitamin A deficiency.

Table. Recommended Follow-Up of Measles Contacts

***Low-risk* contacts** *(immunocompetent person, person ≥12 months of age, not pregnant, not a healthcare worker, or not a household contact)*	**IgG testing[1]**	**MMR PEP[2]**	**IG PEP[3]**	**Quarantine if no PEP[4]**	**Exclusion[5]**	**Symptom watch**
Two documented doses of MMR vaccine (3% will be susceptible)	No	No	No	No	No	Passive
Known to be measles IgG positive (<1% will be susceptible)	No	No	No	No	No	Passive
Born before 1957 (1% will be susceptible)	If desired	If desired	No	No	Yes	Passive
Have 1 documented dose of MMR vaccine (7% will be susceptible)	If desired	If desired	No	No	Yes	Passive
Unknown or no documentation of vaccination or immune status, **with** presumption of immunity[6]	If desired	If desired	No	No	Yes	Passive
Unknown or no documentation of vaccination or immune status, **without** presumption of immunity[6,7]	Yes[1]	Yes	Footnote[8]	Yes	Yes	Active
Prior measles IgG negative test result[1,7]	Yes[1]	Yes	Footnote[8]	Yes	Yes	Active
Known to be unvaccinated[7]	No	Yes	Footnote[8]	Yes	Yes	Active
***High-risk* contacts** *(immunocompromised person, infant <12 months of age, pregnant woman, healthcare worker, or household contact)*	**IgG testing[1]**	**MMR PEP[2]**	**IG PEP[3]**	**Quarantine if no PEP[4]**	**Exclusion[5]**	**Symptom watch**
Unvaccinated infants <6 months of age	No	No	Yes[3]	Yes	Yes	Active
Unvaccinated infants 6-11 months of age[2]	No	IG preferred[2]	Yes[3]	Yes	Yes	Active
Pregnant women without 2 documented MMR vaccine doses or serologic evidence of immunity	Yes[1]	No	Yes[9]	Yes	Yes	Active
Severely immunocompromised people (page 3)	No	No	Yes	Footnote[10]	Yes	Active
Household, healthcare worker or contact with prolonged exposure **without** 2 documented MMR vaccine doses or serologic evidence of immunity	Yes[1]	Yes	Yes[8]	Yes	Yes	Active
Immunocompetent contact **with** 2 documented MMR vaccine doses or serologic evidence of immunity	No	No	No	No	No	Passive
Local health jurisdictions may choose to do public notifications of exposures in large public venues such as movie theaters, lecture halls, supermarkets, big box stores, sports arenas, public transit, etc. for situational awareness. However, CDPH does not consider such exposures to constitute exposures for the purposes of public health follow-up such as PEP and quarantine, unless the person has had known close contact with the confirmed measles case.						

1. Measles contacts who are/have been measles IgG negative/equivocal in a commercial lab, should be retested at CDPH VRDL.
2. MMR vaccine can be given as PEP <72 hours of exposure to persons ≥6 months of age who do not have contraindications for MMR vaccine. However, IMIG is preferred as PEP for exposed infants <12 months of age ≤6 days of exposure. Persons ≥12 months of age who may have been vaccinated or had disease and receive MMR vaccine as PEP should have blood drawn and tested for measles IgG if measles IgG status is unknown at the time of MMR administration.
3. Contacts at high risk of severe infection (severely immunocompromised people, unvaccinated infants, and susceptible pregnant women) should receive IG PEP ≤6 days of last exposure to measles.
4. Implement quarantine from day 7 after first exposure (exposure day is day 0) through day 21 after last exposure. If symptoms consistent with measles develop, the exposed person should be isolated and tested.
5. Exclude from high-risk settings (e.g., childcare facilities with infants and healthcare facilities) from day 7 (day 5 for healthcare workers in healthcare settings) after first exposure through day 21 after last exposure. Some jurisdictions may choose to exclude from other settings with large numbers of unvaccinated persons.
6. See page 2 for presumption of immunity criteria. A self-reported history of measles disease without documentation is **not** acceptable as a presumption of immunity.
7. If a low-risk contact has a measles IgG negative/equivocal result, and subsequently provides documentation of two doses of MMR vaccine, base public health decisions on the two documented doses of MMR vaccine, i.e., presume immunity. Use “unknown or no documentation of vaccination or immune status, **with** presumption of immunity” row in the Table.
8. IGIM can be considered for susceptible persons in this category weighing <30 kg (<66 pounds). There is no recommendation for IGIM in susceptible persons ≥30 kg (≥66 pounds). If contact is ≥12 months of age, MMR PEP is preferred if <72 hours of exposure. IGIV is not recommended for low-risk contacts weighing ≥30 kg (≥66 pounds).
9. If it can be done rapidly, it is recommended that pregnant women be tested for measles IgG prior to administering IGIV if it is likely that they have received vaccine or had disease. If an exposed pregnant woman is IgG negative/equivocal or has unknown status and IgG test results (or retest at VRDL) will not be known by day 6 after exposure, administer IGIV.
10. CDPH should be consulted about severely immunocompromised measles contacts to assess the need for quarantine.