Measles Investigation Quicksheet

August 2023

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. Atypical rashes have been reported. 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 is considered to be a measles exposure. Exposure criteria apply even if the infectious person was masked. Although CDC recommends using a 2-hour window, there is little evidence for measles transmission >60 minutes after an infectious person has left the setting. Exposures occur during the case's infectious period, which starts four days before rash onset through four days after rash onset (day of rash onset is day 0).

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. Local health jurisdictions may choose to notify the public of exposures in large public venues for situational awareness. CDPH does not consider such scenarios as exposures for the purposes of public health follow-up such as PEP and quarantine unless a person is a known close contact.

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. Suspected or confirmed measles cases should be isolated during their infectious period.

Measles incubation period

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[*] meeting at least one of the following criteria:

- Detection of measles virus-specific nucleic acid[†] from a clinical specimen using polymerase chain reaction (PCR) (preferred)
- Isolation of measles virus[†] from a clinical specimen
- IgG seroconversion[†] or a significant rise in measles immunoglobulin G antibody[†] using any evaluated and validated method
- A positive serologic test for measles immunoglobulin M antibody[†‡]
- 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. CDPH 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 testing

See detailed information on the measles laboratory testing guidance.

Preferred: Detection of viral RNA by reverse transcription polymerase chain reaction (RT-PCR). Urine and throat or nasopharyngeal (NP) swab are the preferred specimen types.

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 measles is suspected, specimens should be sent to a **public health laboratory** for PCR testing. Negative PCR testing done during the recommended timeframe can "rule out" measles in the setting of a false positive IgM. Some commercial labs offer measles PCR testing. PCR testing in a public health lab is generally preferred; advantages of public health testing include timeliness and an ability to easily track specimens and results for public health follow up.

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.
    - 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.

Isolation

- Isolation refers to the separation of those with suspected or confirmed illness from those without illness. Those with suspected or confirmed illness should self-isolate at home, away from non-household and unimmunized contacts.
- Confirmed measles cases should be isolated during their infectious period, from four days before rash onset through four days after rash onset (day of rash onset is day 0)
- Suspect measles cases should be isolated until measles has been ruled out, or until their presumed infectious period is over.

Low-Risk Contacts and Settings

Low-risk contact

A low-risk contact is a person who is not at high risk of experiencing severe measles illness, or to/from whom the transmission potential is not high. Examples of low-risk contacts include those who are: immunocompetent, ≥12 months of age, not pregnant, not a healthcare worker, and not a household contact.

Low-risk setting

A low-risk setting is one in which transmission risk is low and multiple high-risk contacts are not present.

"Presumption of Immunity" Criteria for Low-Risk Contacts:
Low-risk contacts can be presumed to be immune to measles for the purposes of measles case investigations if they meet one of the following criteria:

- were born in the U.S. prior to 1957
- were born outside the U.S. prior to 1970 **AND** moved to the U.S. in 1970 or later[§]
- were born in any country in 1970 or later **AND** attended a U.S. primary or secondary school[§]
- 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
- have a documented IgG positive test for measles
- have laboratory confirmation of previous measles disease
- served in the U.S. armed forces
- entered the U.S. as a permanent U.S. resident or became one in 1996 or later (i.e., have a "green card")[§]

[§] 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 Contacts and Settings

High-risk contact

A high-risk contact is a person who may experience severe illness if they become infected with measles or to whom the transmission potential is high. Examples of high-risk contacts include infants up to 11 months of age, immunocompromised persons, pregnant persons, household contacts, contacts with prolonged exposure, healthcare workers or persons in settings with known unvaccinated persons (e.g., infant care settings).

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, or an infant care setting), or where there are multiple high-risk contacts, particularly persons who could experience severe disease if infected with measles. Healthcare settings are considered high-risk settings.

Additional evidence of immunity is required for high-risk contacts and settings and may also be required during an outbreak. Acceptable evidence of immunity includes:

- 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
- If no documentation of two doses of measles vaccine, a documented IgG positive test for measles
- Laboratory confirmation of previous disease.

Exclusion for High-Risk Contacts/Settings

- Exclusion refers specifically to high-risk settings and can apply to contacts who are not otherwise quarantined.
- If exclusion of those other than healthcare workers is implemented, it should begin on day 7 after the date of first exposure through day 21 after the date of last exposure (day of exposure is day 0)
- For healthcare workers, CDC recommends starting exclusion on day 5.
- If symptoms consistent with measles develop, contact should be immediately isolated until day 4 after rash onset (day of rash onset is day 0)

- CDPH does not recommend extending 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; if symptoms occur ≤28 days of exposure, they should self-isolate and contact their local health department.

Quarantine

- Quarantine refers to the period of home isolation recommended for non-immune contacts who have not received appropriate post-exposure prophylaxis within the specified time period (see Tables 1-3)
- If quarantine is implemented, it should begin on day 7 after the date of first exposure through day 21 after the date of last exposure. Dates of potential exposure are during the case's infectious period, which starts four days before the case's rash onset through four days after the case's rash onset (day of rash onset is day 0)
- If symptoms consistent with measles develop, contact should be immediately isolated and tested for measles. Quarantined persons should be instructed to notify their local health department if symptoms occur.
- CDPH does not recommend extending quarantine 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.

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 (e.g., pregnant or immunocompromised). If you have questions about which type of PEP is appropriate, please contact CDPH at 510-620-3737 and/or vpdreport@cdph.ca.gov.

MMR vaccine for PEP

Susceptible persons ≥6 months of age with 1 or no documented doses of MMR may receive MMR vaccine to decrease their risk of developing disease 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** to the case while the case is infectious is considered adequate PEP for public health contact management. Except in high-risk settings, unvaccinated persons who receive their first dose of MMR vaccine within 72 hours postexposure may discontinue quarantine and may return to childcare, school, or work.

Immune globulin (IG) for PEP

IG may be given to exposed susceptible persons (and severely immunocompromised persons regardless of immune status) ≤6 days from date of **last exposure** to prevent infection. However, only IG administered ≤6 days after **first exposure** to the case while the case is infectious is considered adequate PEP for public health contact management. Persons who receive IG >6 days after the **first exposure** to the case while the case is infectious should be placed in quarantine.

Because the effectiveness of IG PEP at preventing measles varies, it is recommended that persons who receive IG PEP be excluded from high-risk settings during their potential incubation period (see Table 2).

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 rather than IG PEP. 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 persons 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.

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).

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 1. Recommended Follow-Up of High-risk Measles Contacts

High-risk contacts (persons with potential for severe illness if infected **or** to whom the transmission potential is high)	**IgG testing***	**PEP†**	**Quarantine if no PEP‡**	**Exclusion§**	**Monitoring****
Unvaccinated infants <6 months of age	No	IG only	Yes	Yes	Active
Unvaccinated infants 6-11 months of age††	No	IG preferred††	Yes	Yes	Active
Pregnant persons without 2 documented MMR vaccine doses or serologic evidence of immunity‡‡	Yes*	IG only	Yes	Yes	Active
Severely immunocompromised§§	No	IG only	Maybe***	Yes	Active
Household contact or contact with prolonged exposure **without** 2 documented MMR vaccine doses or serologic evidence of immunity	Yes*	MMR or IG†††	Yes	Yes	Active
Immunocompetent contact **with** 2 documented MMR vaccine doses or serologic evidence of immunity	No	No	No	No	Passive

Table 2. Recommended Follow-Up of Measles Contacts Who Work in a Healthcare Setting or Other High-Risk Setting

Contacts who work in a healthcare setting or other high-risk setting	**IgG testing***	**PEP**	**Quarantine if no PEP‡**	**Exclusion§**	**Monitoring**
High-risk for severe disease due to personal medical history and without 2 documented MMR vaccine doses or serologic evidence of immunity	See Table 1				
Low risk for severe disease and with 1 documented MMR vaccine dose and no serologic evidence of immunity	Yes	MMR	No	Yes	Active
Low risk for severe disease and with no documented MMR vaccine doses and no serologic evidence of immunity	Yes	MMR	Yes	Yes	Active
With 2 documented MMR vaccine doses or serologic evidence of immunity	No	No	No	No	Passive

Table 3. Recommended Follow-Up of Low-Risk Measles Contacts

Low-risk contacts (immunocompetent persons, persons ≥12 months of age, not pregnant, not a healthcare worker, not a household contact)	**IgG testing***	**PEP**	**Quarantine if no PEP‡**	**Exclusion§**	**Monitoring****
Two documented doses of MMR vaccine (3% will be susceptible)	No	No	No	No	Passive
Known to be measles IgG positive (<1% will be susceptible)					
Meets presumption of immunity criteria	If desired	MMR if desired	No	Yes	Passive
Unknown or no documentation of vaccination or immune status, **without** presumption of immunity‡‡‡	Yes*	MMR or IG†††	Yes	Yes	Active
Prior measles IgG negative test result*,‡‡‡					
Known to be unvaccinated‡‡‡	No	MMR or IG†††	Yes	Yes	Active

* For measles contacts who have tested measles IgG negative or equivocal in a commercial lab, CDPH should be consulted regarding potential retesting at CDPH VRDL. If a contact tests positive for IgG at VRDL or a commercial lab, consider them to be immune.

† Contacts at high risk of severe infection (severely immunocompromised people, unvaccinated infants, and susceptible pregnant persons) should receive IG PEP within 6 days or less from the date of last exposure to measles.

‡ Implement quarantine from day 7 after first exposure through day 21 after last exposure. If symptoms consistent with measles develop, the exposed person should be isolated and tested.

§ Exclude from high-risk settings (e.g., childcare facilities with infants and healthcare facilities; see definition above) from day 7 (day 5 for healthcare workers in healthcare settings) after first exposure through day 21 after last exposure. Those who have received IG should exclude through day 28 after last exposure.

** Persons who receive IG should be actively monitored for 21 days. They should then passively monitor (symptom watch) during days 22-28.

†† MMR vaccine can be given as PEP within 72 hours or less from the time 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 from 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.

‡‡ If it can be done rapidly, it is recommended that pregnant persons 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 person is IgG negative or IgG equivocal or has unknown status and IgG test results (or retest at VRDL) will not be known by day 6 after exposure, administer IGIV.

[§§] See page 5 for high-level immunosuppression criteria.

[***] CDPH should be consulted about severely immunocompromised measles contacts to assess the need for quarantine.

[†††] 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).

[‡‡‡] See page 2 for low risk "presumption of immunity" criteria. A self-reported history of measles disease without documentation is **not** acceptable as a presumption of immunity. If a low-risk contact has a measles IgG negative or IgG 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.

Algorithm. Measles Contact Management

This algorithm is intended to assist with prioritization and workflow during measles contact investigations. Please consult the detailed guidance in the above sections of the Quicksheet when applying the algorithm.

