SYMPTOMS

PRODROME STAGE

- Stepwise increase in fever to 103°F-105°F
- Cough, coryza, and conjunctivitis (itchy eyes)
- Koplik spots (on mucous membranes)

RASH

- Maculopapular eruption that persists 5 to 6 days
- Begins at hairline, then involves face and upper neck
- Proceeds downward and outward to hands and feet
- Severe areas peel off in scales
- Fades in order of appearance

COMMON COMPLICATIONS

- Diarrhea
- Ear infections

SEVERE COMPLICATIONS

- Pneumonia
- · Encephalitis (swelling of the brain)
- Death

LONGTERM COMPLICATIONS

 Subacute sclerosing panencephalitis (SSPE) is a very rare, but fatal disease of the central nervous system that results from a measles virus infection acquired earlier in life

DIFFERENTIAL

- Scarlet fever
- Staphylococcal toxin diseases
- Rubella
- Drug rash
- · Viral exanthem
- Infectious mononucleosis
- Dengue

Kentucky Public Health Prevent. Promote. Protect.

ETIOLOGIC AGENT

Measles/Rubeola virus

TRANSMISSION

 via large respiratory droplets and airborne transmission

COMMUNICABILITY

 4 days before through 4 days after rash onset

INCUBATION PERIOD

• 11 to 12 days (range, 7 to 21 days)

MEASLES VACCINES

- MMR (MMR-II)
- MMRV (ProQuad)

KENTUCKY MEASLES OCCURRENCE

MMWR Year	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
Confirmed Case Count	0	0	0	0	0	0	0	0	2	0	0	0

CASE DEFINITIONS

PROBABLE CASE

In the absence of a more likely diagnosis, an illness that meets the clinical description with:

- No epidemiologic linkage to a laboratoryconfirmed measles case: AND
- Noncontributory or no measles laboratory testing.

CONFIRMED CASE

An acute febrile rash illness† with:

- Isolation of measles virus‡ from a clinical specimen; OR
- Detection of measles-virus specific nucleic acid‡ from a clinical specimen using polymerase chain reaction; OR
- IgG seroconversion‡ or a significant rise in measles immunoglobulin G antibody‡ using any evaluated and validated method; OR
- A positive serologic test for measles immunoglobulin M antibody‡§; OR
- Direct epidemiologic linkage to a case confirmed by one of the methods above.
- † Temperature does not need to reach ≥101°F/38.3°C and rash does not need to last ≥3 days.
- ‡ Not explained by MMR vaccination during the previous 6-45 days.
- § Not otherwise ruled out by other confirmatory testing or more specific measles testing in a public health laboratory.

Preferred: LABORATORY CRITERIA

 Detection of viral RNA by reverse transcription polymerase chain reaction (RT- PCR). Preferred specimens are nasopharyngeal (NP) or oropharyngeal (OP) samples shipped in viral transport medium (VTM). Urine samples may also be collected in a sterile container. PCR testing for measles virus is available at <u>KDPH DLS</u>. Contact KDPH if testing is requested.

CDC recommend that both PCR and IgM testing is done

 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 KDPH DLS for testing. PCR testing done during the recommended timeframe can "rule out" measles in the setting of a false positive IgM.

*Recently vaccinated individuals can have false positive PCR and elevated IgM.

OUTBREAK

 Every case of Measles is to be investigated as a potential outbreak. *Enter the outbreak in the REDCap project: 2024 DEHP Outbreak Management

SPECIMEN COLLECTION FOR LABORATORY TESTING

Test Name	Specimens to take	Timing for specimen collection	Transport requirements		
Measles (Rubeola) isolation RT-PCR *Preferred specimen	Nasopharyngeal aspirates/swab or throat swabs	ASAP after rash onset	Transport specimens at 4°C if tests are to be performed within 72 hours; otherwise, freeze at -70°C until tests can be performed.		
IgM antibody	Serum	Collect at same time as other samples (less sensitive after 3 days of rash onset)	Ship on cold pack *IgM is detectable for at least 30 days after rash onset		

CDC | Measles- Specimen Collection, Storage, and Shipment



EPIDEMIOLOGIC CLASSIFICATION

INTERNATIONALLY IMPORTED CASE

An internationally imported case is defined as a case in which measles results from exposure to measles virus outside the United States as evidenced by at least some of the exposure period (7–21 days before rash onset) occurring outside the United States and rash onset occurring within 21 days of entering the United States 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

A U.S.-acquired case is defined as a case in which the patient had not been outside the United States during the 21 days before rash onset or was known to have been exposed to measles within the United States.

- *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 United States 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 United States
- *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 U.S

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.



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 <u>CDC</u> Measles Surveillance Worksheet
- 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 a 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
 - 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 <u>clinical presentation</u> is highly suggestive of measles, but no epidemiologic risk factor can be elicited, still consider measles and immediately mask the patient with or without risk factors and follow <u>guidelines</u> <u>for infection control</u>
- If measles is being considered, the <u>local health</u> department should be contacted immediately. If after hours call KDPH at (888)-9REPORT
- 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 positive 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

- · 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



High-risk contacts include healthcare personnel, pregnant or immunocompromised people, household contacts of a case, or persons in settings with known unvaccinated persons. Additional evidence of immunity should be required for exposed high-risk persons and during an outbreak. Immunity can be presumed if the exposed person:

[‡]Unless known to be unvaccinated for measles.

POSTEXPOSURE CHEMOPROPHYLAXIS (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 KDPH at (888) 9-REPORT.

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.

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. Persons who receive IG >6 days after the first exposure should be placed on quarantine until 21 days after their last exposure.

Important Points to Consider Regarding IG PEP:

- 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 <30kg (<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 people without evidence of measles immunity should receive 400 mg/kg of body weight of intravenous IG1 (IVIG is licensed in the U.S. as 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. In consultation with the Kentucky Department of Public Health, IGIV may be administered.
- Nonimmune persons who receive IG should not receive MMR vaccine earlier than 6 months after IGIM or 8 months after IGIV administration.
- 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.

§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/mm3 (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 0 (CDC recommends day 5 for healthcare workers) after the first exposure through day 21 after the last exposure (day of exposure is day 0).
- Quarantined persons should be instructed to notify their LHD if symptoms occur.
- Extending quarantine or exclusion beyond 21 days after exposure in persons who received IG PEP is not routinely recommended, 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 LHD.
- Susceptible adults should be instructed to stay home from work and other activities.

SCHOOL

Children in school and childcare settings shall be excluded through the fourth day after rash onset with rash onset as day zero or in the case of an outbreak, exclude unimmunized child for at least 21 days after the last date the unimmunized child was exposed.

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 (<u>Virazole®</u>) 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.



RECOMMENDED FOLLOW UP

Low-risk contacts (immunocompetent person, person >12 months of age, not pregnant, not a healthcare worker, or not a household contact)

	IgG testing	MMR PEP ¹	IG PEP ²	Quarantine if ³ no PEP	Exclusion ⁴	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 ⁵	If desired	If desired	No	No	Yes	Passive
Unknown or no documentation of vaccination or immunestatus, without presumption of immunity ^{5,6}	Yes ¹	Yes	Footnote ⁷	Yes	Yes	Active
Prior measles IgG negative test result ⁶	Yes	Yes	Footnote ⁷	Yes	Yes	Active
Known to be unvaccinated ⁶	No	Yes	Footnote ⁷	Yes	Yes	Active

High-risk contacts (immunocompromised person, infant <12 months of age, pregnant woman, healthcare worker, or household contact)

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	IgG testing	MMR PEP ¹	IG PEP ²	Quarantine if ³ no PEP	Exclusion ⁴	Symptom watch		
Unvaccinated infants <6 months of age	No	No	Yes ²	Yes	Yes	Active		
Unvaccinated infants 6-11 months of age ¹	No	IG Preferred ¹	Yes ²	Yes	Yes	Active		
Pregnant women without two documented MMR vaccine doses or serologic evidence of immunity	Yes	No	Yes ⁸	Yes	Yes	Active		
Severely immunocompromised people	No	No	Yes	Footnote ⁷	Yes	Active		
Household, healthcare worker or contact with prolonged exposure without two documented MMR vaccine doses or serologic evidence of immunity	Yes	Yes	Yes ⁷	Yes	Yes	Active		
Immunocompetent contact with two documented MMR vaccine doses or serologic evidence of immunity	No	No	No	No	No	Passive		

^{1.} MMR vaccine can be given as PEP <72hours 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 <12months 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.

Kentucky Public Health

^{2.} 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.

^{3.} Implement quarantine from 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.

^{4.} Exclude from high-risk settings (e.g., childcare facilities with infants and healthcare facilities) from day 0 (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.

^{5.} See presumption of immunity criteria. A self-reported history of measles disease without documentation is not acceptable as a presumption of immunity.

^{6.} 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.

^{7.} 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.

^{8.} KDPH should be consulted about severely immunocompromised measles contacts to assess the need for quarantine.