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## Measles (Rubeola)

## Overview ${ }^{1,2,3,6,7}$

Measles (also called rubeola, red measles, or hard measles) is a highly contagious virus and is a serious illness. Persons who remain unvaccinated put themselves and others in their community, particularly those who cannot be vaccinated, at risk for this disease and its complications. Currently, measles most often occurs in susceptible persons (those who have never had measles or measles vaccine) who are traveling into and out of the United States (U.S.). Measles is transmitted person-to-person among close contacts by direct contact with infectious droplets (when a person with measles coughs, sneezes, or breathes out tiny droplets with measles virus into the air and another person breathes them in), or less commonly, by airborne spread (sometimes the virus can float in the air and infect others for approximately two hours after a person with measles leaves a room). Transmission may also occur by handling or touching contaminated objects and then touching your eyes, nose, and/or mouth. Measles may be transmitted from 4 days before to 4 days after rash onset. Maximum communicability occurs from onset of prodrome (or first symptoms) through the first 3-4 days of rash. ${ }^{3}$

The average incubation period for measles from exposure to prodrome is $10-12$ days, ${ }^{3}$ or from exposure to onset of rash averages 14 days with a range of 7-21 days. ${ }^{2}$ Measles is characterized by a prodrome that last 2-4 days (range 1-7 days) ${ }^{3}$ which appears like the beginning of a cold with a high fever, feeling run down, achy, watery eyes, and runny nose. Two or three days after symptoms begin; tiny white spots with bluish-white centers (Koplik’s spots) ${ }^{6}$ may appear inside the mouth and are considered pathognomonic for measles. A red blotchy rash appears 3 to 5 days after the prodrome, ${ }^{6}$ usually beginning on the face (hairline), spreading down the trunk and down the arms and legs. When the rash appears, a person's fever may spike to more than 104 degrees Fahrenheit. The rash usually lasts 4 to 7 days. ${ }^{7}$

Measles is highly contagious. If an individual has it, $90 \%$ of their susceptible close contacts who are not immune will also become infected with the measles virus. The illness is usually mild or moderately severe. However, approximately $30 \%$ of reported measles cases have one or more complications. The risk of severe complications and death is higher among children younger than five and adults 20 years of age and older. ${ }^{3}$ The most severe complications include diarrhea (8\%), middle ear infection (7\%), and pneumonia (6\%) which may be viral or superimposed bacterial, and is the most common cause of death ( $60 \%$ ). ${ }^{3}$

For a complete description of Measles, refer to the following texts:

- Control of Communicable Diseases Manual (CCDM), American Public Health Association, $19^{\text {th }}$ ed. 2008.
- American Academy of Pediatrics. Red Book: 2012 Report of the Committee on Infectious Diseases. 29th ed. 2012.
- Department of Health and Human Services, Centers for Disease Control and Prevention, Epidemiology and Prevention of Vaccine-Preventable Diseases, $12^{\text {th }}$ ed. Revised 2012.

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## 2013 Case Definition - Measles ${ }^{4}$

## Clinical description

An acute illness characterized by:

- Generalized maculopapular rash lasting $\geq 3$ days; and
- temperature $\geq 101^{\circ} \mathrm{F}$ or $38.3^{\circ} \mathrm{C}$; and
- cough, coryza, or conjunctivitis


## Case classification

Confirmed: An acute febrile rash illness $\dagger$

- With isolation of measles virus $\ddagger$ from a clinical specimen; or
- Detection of measles-virus specific nucleic acid $\ddagger$ from a clinical specimen using polymerase chain reaction; or
- IgG seroconversion $\ddagger$ or a significant rise in measles immunoglobulin $G$ antibody $\ddagger$ using any evaluated and validated method; or
- A positive serologic test for measles immunoglobulin M antibody $\ddagger \S$; or
- Direct epidemiologic linkage to a case confirmed by one of the methods above.
$\dagger$ Temperature does not need to reach $\geq 101^{\circ} \mathrm{F} / 38.3^{\circ} \mathrm{C}$ and rash does not need to last $\geq 3$ days. $\ddagger$ 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.


## 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.


## 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 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: An U.S.-acquired case is 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.
(Continued on next page)

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U.S.-acquired cases are subclassified 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 $\geq 12$ 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 $\geq 12$ 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 U.S.
NOTE: Internationally imported, import-linked, and imported-virus cases are considered collectively to be import-associated cases.

Case Classification COMMENT: The Centers for Disease Control and Prevention (CDC) does not request or accept reports of suspect cases so this category is no longer needed for national reporting purposes.

## Information Needed for Investigation ${ }^{3,10,11}$

Establish a diagnosis of measles: See "Figure 1 Measles Case Investigation" on the next page. Prompt recognition, reporting, and investigation of measles are important because the spread of the disease can be limited with early case identification and vaccination of susceptible contacts. Obtain demographic, clinical and laboratory information on the case from the attending physician, hospital, and/or laboratory. Obtain the other epidemiological information necessary to complete the Disease Case Report (CD-1) and Rash Investigation (IMMP-4) from the patient or a knowledgeable family member. NOTE: Do not wait for results of confirmatory testing to begin the case investigation. The need to initiate prophylaxis will be evaluated based on initial findings and defining any at-risk populations.
Measles is an extremely rare disease in the U.S., clinical evidence is not sufficient to confirm a case of measles. Many clinicians have never seen a case of measles, and most patients who present with measles-like illness in the U.S. today do not have measles. Because measles is such a highly contagious disease, with the potential for explosive spread, it is crucial to use laboratory diagnosis to rapidly confirm measles. COMMENT: An enzyme immunoassay (EIA) test for IgM antibody to measles in a single serum specimen is the recommended method for diagnosing acute measles.

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Figure 1. Measles Case Investigation

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Figure 1: Measles Case Investigation
Source: VPD Surveillance Manual, 4th Edition, 2008; Measles: Chapter 7 ${ }^{10}$

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## Information Needed for Investigation (continued) ${ }^{3,10,11}$

To minimize the problem of false positive laboratory results, it is important to restrict case investigation and laboratory tests to patients most likely to have measles; those with fever and generalized maculopapular rash. Testing for measles in patients with no rash, no fever, a vesicular rash, or a rash limited to the diaper area leads to false positive laboratory results.
Obtaining accurate and complete immunization histories on all confirmed cases: Measles case investigations should include complete immunization histories that document any doses of measles-containing vaccine. Acceptable proof of vaccination is documented administration of live measles vaccine virus. Vaccination histories may be obtained from schools, medical providers, or on immunization records provided by the case-patient. NOTE: Verbal history of receipt of measles vaccine is not considered adequate proof of vaccination.

Identify the source of infection: Efforts should be made to identify the source of infection for every confirmed case of measles. Case-patients or their caregivers should be asked about contact with other known cases within 7-21 days prior to onset of rash. When no history of contact with a known case can be found, opportunities for exposure to unknown cases should be sought. Such exposures may occur in schools (especially high schools with foreign exchange students), during air travel, through other contact with foreign visitors, while visiting tourist locations (casinos, resorts, theme parks), or in health-care settings.
Assess potential for transmission and identifying contacts: Goal: To rapidly identify primary contacts, evaluate immunity status, and vaccinate susceptible persons within 24 hours of the initial report. If exposure does not cause infection, postexposure vaccination should induce protection against subsequent exposures. ${ }^{11}$ Currently, very few of the suspected and probable cases investigated in the U.S. are confirmed as measles. However, case investigation and vaccination of susceptible household contacts should not be delayed pending the return of laboratory results. Initial preparation for major control activities also may need to be started before the laboratory results are known. However, it is reasonable to delay major control activities such as vaccinating an entire school, pending the return of laboratory results which should be obtained as quickly as possible (within 24 hours).
Obtain specimens for viral isolation: Efforts should be made to obtain specimens (urine or nasopharyngeal mucus) for virus isolation from all cases at the time of the initial investigation (virus is more likely to be isolated when specimens are collected within 3 days of rash onset); do not wait until serologic confirmation is obtained. Clinical specimens should be obtained within 7 days, and not more than 10 days after rash onset. ${ }^{3}$ These isolates are sent to CDC and are essential for tracking the epidemiology of measles in the U.S. now that measles is not endemic in this country.

Conduct active surveillance: Active surveillance for measles disease should be conducted for every confirmed measles case. In the case of an outbreak, local or state health departments should contact health-care providers in outbreak areas to inform them of the outbreak and request

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reporting of any suspected cases. These activities are especially important in large cities and in cities with large numbers of international visitors.

## Notification

- If measles is suspected, the local public health agency (LPHA) should immediately contact the District Communicable Disease Coordinator, or the Senior Epidemiology Specialist for the District, or the Missouri Department of Health and Senior Services (MDHSS) - BCDCP, phone \# (573) 751-6113, Fax \# (573) 526-0235, or for afterhours notification contact the MDHSS/ERC at (800) 392-0272 (24/7).
- If a case(s) is associated with a childcare center, BCDCP or the LPHA will contact the Bureau of Environmental Health Services, phone \# (573) 751-6095, Fax \# (573) 526-7377 and the Section for Child Care Regulation, phone \# (573) 751-2450, Fax \# (573) 526-5345.
- If a case(s) is associated with a long-term care facility, BCDCP or the LPHA will contact the Section for Long Term Care Regulation, phone \# (573) 526-8524, Fax \# (573) 751-8493.
- If a case is associated with a hospital, hospital-based long-term care facility, or ambulatory surgical center BCDCP or the LPHA will contact the Bureau of Health Services Regulation phone \# (573) 751-6303, Fax \# (573) 526-3621.


## Control Measures ${ }^{10,11}$

Investigate reports of possible measles immediately. If the "Clinical description" for measles is met, implement control measures unless measles is ruled out by lab testing or other information. NOTE: The case should be immediately isolated to minimize any possible ongoing transmission. If case attends school or child care/preschool, immunization records should be audited to determine the immunization status of the other attendees that may have been exposed. If the measles case is hospitalized, caregivers' immunization status should be evaluated and precautions taken.
Assess susceptibility of contacts. If administered within 72 hours of initial measles exposure, MMR vaccine might provide some protection against infection or modify the clinical course of disease. DO NOT wait to administer prophylaxis until serology is available. Persons 1 year and $<4$ years of age should have a history of at least 1 dose of MMR vaccine. Persons 4 years of age and born after 1956 should have a history of 2 doses of MMR vaccine. NOTE: Postexposure immunization and immunoglobulin administration are not 100\% effective; susceptible contacts may still be infectious from day 5 to 21 postexposure. COMMENT: To establish evidence of measles immunity requires laboratory diagnosis; measles immunity does not include documentation of physician diagnosed measles. ${ }^{11}$
Exclusion of exposed, susceptible contacts from group-activity settings, should occur if not properly vaccinated, or refusal to vaccinate, or contact was not vaccinated within 72 hours of exposure. Exposed persons attending group-activity settings (e.g. schools, day-care centers, work place, camps) who cannot readily provide documentation of measles immunity (including those with medical, religious philosophical exemptions) should be vaccinated or excluded from the setting. Exclusion should continue until 21 days after the onset of rash of the last case of measles in the group activity setting. In general, persons who are vaccinated (for the 1st time or

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receiving a required 2nd dose) may be re-admitted immediately to the group-activity setting; however, such a re-admittance policy may be modified depending upon the circumstances involved.
Measles is highly communicable. A measles case should not attend any group-activity settings until after the 4th day the rash appears. Measles cases are communicable (contagious) starting 4 days before rash onset through the 4th day after rash onset.
Provide information about measles to persons at risk and/or the general public. All measles contacts should be educated on symptoms of measles, instructed to watch for symptoms from 7 to 21 days after the last exposure, and told to isolate themselves and contact the health department if symptoms develop. An excellent Question-\&-Answer measles information sheet in .PDF format is available from the Immunization Action Coalition. For measles cases the World Health Organization currently recommends vitamin A for all children with acute measles. ${ }^{2}$ See the American Academy of Pediatrics, Red Book: 2012 Report of the Committee on Infectious Diseases for dosing information.
Enhancing surveillance for measles. Previously unreported cases may be identified by reviewing emergency room logs or laboratory records. As part of outbreak response, active surveillance for measles should be established to assure timely reporting of suspected cases in the population known to be affected by the outbreak, as well as other segments of the community that may be at high risk of exposure or in whom vaccination coverage is known to be low. Hospital emergency rooms and physicians serving affected communities are usually recruited to participate in active surveillance. Active surveillance should be maintained until at least 2 incubation periods after the last confirmed case is reported.

## Outbreak Control ${ }^{10}$

The primary strategy for control of measles outbreaks is achieving a high level of immunity (2 doses) in the population affected by the outbreak. In practice, the population affected is usually rather narrowly defined such as one or more schools. Persons who cannot readily document measles immunity should be vaccinated or excluded from the setting (school, hospital, day-care etc.). Only doses of vaccine with written documentation of the date of receipt should be accepted as valid. Verbal reports of vaccination without written documentation should not be accepted. Persons who have been exempted from measles vaccination for medical, religious, or other reasons should be excluded from affected institutions in the outbreak area until 21 days after the onset of rash in the last case of measles.

While routinely the 2nd dose of measles, mumps, rubella vaccines is not given until 4-6 years of age, in outbreak situations involving day care, pre-school, and other settings with children under 4 years of age, consideration should be given to requiring the 2nd dose as a control measure, following appropriately minimum intervals between doses.

If cases are occurring among infants < 12 months of age with ongoing risk for exposure, infants aged $\geq 6$ months can be vaccinated as an outbreak control measure. ${ }^{11}$ NOTE: Children

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vaccinated before the first birthday should be revaccinated when they are 12-15 months old and again when they are 4-6 years of age. Extra doses of measles vaccine are not harmful. ${ }^{2}$

## Control of Outbreaks in Schools and Other Institutions ${ }^{10}$

During outbreaks in elementary, junior, senior high schools, colleges and other institutions of higher education, as well as other institutions where young adults may have close contact (such as prisons), a program of vaccination with 2 doses of MMR vaccine is recommended in the affected schools or institutions. Past experience has indicated that measles outbreaks do not occur in schools in which all students are subject to a school requirement for two doses of measles vaccine.

In a school with a measles outbreak, all students and their siblings and all school personnel born after 1956 who cannot provide documentation that they have received two doses of measlescontaining vaccine on or after their first birthday or cannot provide other evidence of measles immunity (such as serologic testing) should be vaccinated. Persons who cannot readily provide documentation of measles immunity should be vaccinated or excluded from the school or other institution. Persons receiving 2nd doses, as well as previously unvaccinated persons receiving their 1st dose as part of the outbreak control program, may be immediately readmitted to school provided all persons without documentation of immunity have been excluded. All persons, including those vaccinated as part of the outbreak control program, should immediately report the onset of symptoms consistent with measles or its prodrome. Persons who continue to be exempted from or who refuse measles vaccination should be excluded from the school, childcare, or other institution until 21 days after the onset of rash in the last case of measles.

## Control of Outbreaks in Medical Settings ${ }^{6,10}$

An effective vaccination program is the best approach to prevent healthcare-associated measles transmission. Healthcare Infection Control Practices Advisory Committee (HICPAC) and CDC have recommended that secure, preferably computerized, systems should be used to manage vaccination records for healthcare personnel so records can be easily retrieved as needed. Facilities are also encouraged to review employee evidence of immunity status for measles and other vaccine preventable infections. COMMENT: To prevent disease and transmission in health-care settings, health-care institutions should ensure that all persons who work in healthcare facilities have documentation of adequate vaccination against measles or other acceptable evidence of immunity to measles. ${ }^{6}$ Healthcare facilities should provide MMR vaccine to all personnel without evidence of measles immunity.

Persons who work in health-care facilities (including volunteers, trainees, nurses, physicians, technicians, receptionists, and other clerical and support staff) are at increased risk of exposure to measles, and all persons who work in such facilities in any capacity should have evidence of immunity to measles to prevent any potential outbreak. If a measles case or an outbreak occurs within or in the areas served by a hospital, clinic, or other medical or nursing facility, all personnel irrespective of birth year should receive two doses of MMR vaccine, unless they have

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other documentation of measles immunity. Serologic screening of health-care workers during an outbreak to determine measles immunity is not recommended because stopping measles transmission requires the rapid vaccination of susceptible health-care workers without evidence of immunity, which can be impeded by the need to screen, wait for results, and then contact and vaccinate susceptible persons.

Healthcare personnel without evidence of immunity who have been exposed to measles should be relieved from patient contact and excluded from the facility from the 5th day after the first exposure to the 21st day after the last exposure, regardless of whether they received vaccine or immune globulin (IG) after the exposure. Personnel who develop measles should be relieved from all patient contact and excluded from the facility for 4 days after they develop rash. In health care settings use of Airborne Precautions is recommended.

## Postexposure Vaccination and use of Immunoglobulin (IG) to Prevent

 Measles in Exposed Persons ${ }^{1,2,10,11}$Postexposure Vaccination: If given within 72 hours of exposure to measles, measles vaccine may provide some protection. In most settings, post-exposure vaccination is preferable to use of immunoglobulin. If exposure results in infection, no evidence indicates that administration of MMR vaccine during the presymptomatic or prodromal stage of illness increases the risk for vaccine-associated adverse events. ${ }^{11}$ MMR vaccine is supplied in lyophilized form and must be stored at $-50^{\circ} \mathrm{C}$ to $8^{\circ} \mathrm{C}\left(-58^{\circ} \mathrm{F}\right.$ to $\left.46^{\circ} \mathrm{F}\right)$ and protected from light at all times. The vaccine in the lyophilized form can be stored in the freezer.
Reconstituted MMR vaccine should be used immediately or stored in a dark place at $2^{\circ} \mathrm{C}$ to $8^{\circ} \mathrm{C}\left(36^{\circ} \mathrm{F}\right.$ to $\left.46^{\circ} \mathrm{F}\right)$ for up to 8 hours and should not be frozen or exposed to freezing temperatures. ${ }^{11}$ Reconstituted MMRV vaccine must be discarded if not used within 30 minutes and should not be frozen. Improperly handled or stored vaccine may fail to protect against measles. ${ }^{1}$

Contraindications for MMR and MMRV vaccines include history of anaphylactic reactions to neomycin, history of severe allergic reaction to any component of the vaccine, pregnancy, and immunosuppression. Women who are given MMR vaccine should not become pregnant for at least 28 days. ${ }^{2}$ NOTE: MMR vaccine might interfere with the response to a tuberculin skin test, resulting in a temporary depression of tuberculin skin sensitivity. Therefore, if a tuberculin skin test is to be performed, it should be administered either any time before, simultaneously with, or at least 4-6 weeks after MMR or MMRV vaccine. For additional information on the contraindications and precautions associated with MMR and MMRV vaccines see: Morbidity and Mortality Weekly Report (MMWR), Prevention of Measles, Rubella, Congenital Rubella Syndrome, and Mumps, 2013: Summary Recommendations of the Advisory Committee on Immunization Practices (ACIP), Recommendations and Reports, June 14, 2013 / 62(RR04);1-34 http://www.cdc.gov/mmwr/preview/mmwrhtml/rr6204a1.htm.

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Postexposure Immunoglobulin: If administered within 6 days of exposure, IG can prevent or modify measles in persons who are nonimmune. IG is not indicated for persons who have received $\mathbf{1}$ dose of measles-containing vaccine at age $\geq \mathbf{1 2}$ months, unless they are severely immunocompromised. ${ }^{11}$ NOTE: IG should not be used to control measles outbreaks, but rather to reduce the risk for infection and complications in the person receiving it. Any nonimmune person exposed to measles who received IG should subsequently receive MMR vaccine, which should be administered no earlier than 6 months after IGIM administration or 8 months after IGIV administration, provided the person is then aged $\geq 12$ months and the vaccine is not otherwise contraindicated. ${ }^{11}$

The recommended dose of IG administered intramuscularly (IGIM) is $0.5 \mathrm{~mL} / \mathrm{kg}$ of body weight (maximum dose $=15 \mathrm{~mL}$ ) and the recommended dose of IG given intravenously (IGIV) is 400 $\mathrm{mg} / \mathrm{kg} .{ }^{11}$

Immunoglobulin is indicated for susceptible household or other close contacts of patients with measles, particularly infants younger than 1 year of age, pregnant women without evidence of measles immunity, and severely immunocompromised people for whom risk of complications is highest. IGIM can be administered to other persons who do not have evidence of measles immunity, but priority should be given to persons exposed in settings with intense, prolonged, close contact (e.g., household, daycare, and classroom). For exposed persons without evidence of measles immunity, a rapid IgG antibody test can be used to inform immune status, provided that administration of IG is not delayed. ${ }^{11}$

Because infants are at higher risk for severe measles and complications, and infants are susceptible to measles if mothers are nonimmune or their maternal antibodies to measles have waned, IGIM should be administered to all infants aged $<12$ months who have been exposed to measles. For infants aged 6 through 11 months, MMR vaccine can be administered in place of IG if administered within 72 hours of exposure.

Because pregnant women might be at higher risk for severe measles and complications, IGIV should be administered to pregnant women without evidence of measles immunity who have been exposed to measles. IGIV is recommended to administer doses high enough to achieve estimated protective levels of measles antibody titers.

Severely immunocompromised patients who are exposed to measles should receive IGIV prophylaxis regardless of immunologic or vaccination status because they might not be protected by the vaccine. Severely immunocompromised patients include patients with severe primary immunodeficiency; patients 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; patients on treatment for ALL within and until at least 6 months after completion of immunosuppressive chemotherapy; and patients with a diagnosis of AIDS or HIVinfected persons with severe immunosuppression defined as CD4 percent <15\% (all ages) or CD4 count $<200$ lymphocytes/mm3 (aged $>5$ years) and those who have not received MMR

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vaccine since receiving effective ART. Some experts include HIV-infected persons who lack recent confirmation of immunologic status or measles immunity.

## New Boxed Warning Highlights Thrombosis Risk from Human Immune Globulin ${ }^{8}$

 The U.S. Food and Drug Administration (FDA) is requiring manufacturers to add information on thrombosis to the current boxed warning in the labels of all intravenous human immune globulin products and to add a boxed warning to the labels of all subcutaneous and intramuscular human immune globulin products to highlight the risk of thrombosis and to add information on its mitigation.Although all human immune globulin products already contain some information related to the risk of thrombosis in the current WARNINGS and PRECAUTIONS sections of their labels, FDA recognizes that the communication of this risk and its mitigation are not standardized. FDA proposes that for thrombosis a more prominent placement of risk information and a uniform approach for communicating the risk and its possible mitigation will help to reduce the occurrence of these serious adverse events. For additional information, including Recommendations to Patients and Recommendations for Healthcare Professionals you can visit the FDA website at: http://www.fda.gov/BiologicsBloodVaccines/SafetyAvailability/ucm355986.htm.

## Laboratory Procedures ${ }^{3,10}$

Measles testing (serologic and virologic) is available through commercial clinical laboratories and the Missouri State Public Health Laboratory (MSPHL) who will also assist with shipment of samples to the CDC. Laboratory testing should be attempted for all potential cases meeting the clinical case definition. If measles is suspected, a blood test for measles-specific IgM antibody (this is the preferred confirmation) should be done 3 to 5 days after rash begins. If the clinic has contracts requiring the use of a commercial clinical laboratory, collect a second specimen or split the specimen, sending one to the MSPHL and one to the commercial clinical lab. NOTE: Measles IgM tests that are negative and were collected less than 72 hours after the rash onset should be repeated using sera collected 72 or more hours after rash onset. COMMENT: Persons who have been exposed to measles should contact their healthcare provider if they develop cold-like symptoms with a fever and/or rash. They should NOT go to any healthcare facility without calling first. The suspect case should be kept separate from others to prevent further spread.

Measles testing to be performed by the MSPHL should go through the Virology Unit, phone \# (573) 751-3334 before submission. Information on the collection or shipment of specimens for measles testing by the MSPHL may be viewed at: http://health.mo.gov/lab/measles.php for measles culture or http://health.mo.gov/lab/measlesrubella.php for IgM serology for measles. NOTE: Clinical specimens or isolates positive for measles performed by commercial clinical laboratories are to be submitted to the MSPHL for epidemiological or confirmation purposes.

Serum and viral (culture, PCR testing for virus RNA and sequencing) specimens should be collected at the same visit when the serum is taken; however, urine, nasopharyngeal or throat-

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swab specimens should not be substituted for serum specimens for measles diagnosis. Specimens should be properly stored while awaiting case confirmation. ${ }^{3,10}$ For detailed protocols for cell culture, virus isolation, collection, and handling of specimens for the isolation and identification of measles virus and information on biosafety and international shipping regulations, see: Measles Lab Manual from the World Health Organization; Manual for the Laboratory Diagnosis of Measles and Rubella Virus Infection, 2nd edition, August 2007 from the World Health Organization (WHO): http://www.cdc.gov/measles/lab-tools/WHO-labmanual.html. NOTE: Limit testing to those patients most likely to have measles. Testing for measles in patients with no rash, no fever, a vesicular rash, or a rash limited to the diaper area leads to false-positive results.

## Reporting Requirements

Measles is a Category 2 (A) State Reportable Disease reportable within one (1) calendar day of first knowledge or suspicion to the local health authority or to the Missouri Department of Health and Senior Services (MDHSS). All suspect cases of measles should be reported immediately to the local health authority, do not wait for lab confirmation.

As a Nationally Notifiable Condition, confirmed measles cases are an IMMEDIATE, URGENT report to the Centers for Disease Control and Prevention (CDC). IMMEDIATE, URGENT reporting requires MDHSS to call the CDC EOC at 770-488-7100 within 24 hours of a case meeting the notification criteria; followed by submission of an electronic case notification via (WebSurv) in the next regularly scheduled electronic transmission.

1. Health care providers should immediately report any possible case of measles to the local health agency of the patient's residence or MDHSS.
2. For suspect, probable, and confirmed cases local public health agencies should complete a Disease Case Report (CD-1) and "Rash Investigation" (IMMP-4).
3. MDHSS will notify the CDC within twenty-four hours by phone for all confirmed measles cases.
4. MDHSS will submit weekly electronic reports to CDC.
5. Entry of the CD-1 by the local public health agencies into WebSurv negates the need for the paper CD-1 to be forwarded to the District Health Office.
6. Send the completed "Rash Investigation" forms to the District Health Office.
7. All outbreaks or "suspected" outbreaks must be reported as soon as possible (by phone, fax, or e-mail) to the District Communicable Disease Coordinator. This can be accomplished by completing the Missouri Outbreak Surveillance Report (CD-51).
8. Within 90 days of the conclusion of an outbreak, submit the final outbreak report to the District Communicable Disease Coordinator.

## References

1. American Public Health Association. Measles (Rubeola, Hard Measles, Red Measles, Morbilli). In: Heymann D Ed. Control of Communicable Diseases Manual. $19^{\text {th }}$ ed. Washington, D.C. American Public Health Association, 2008: pp 402-408.

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2. American Academy of Pediatrics, Measles. In: Pickering LK, Baker CJ, Kimberlin DW, Long SS, eds. Red Book: 2012 Report of the Committee on Infectious Disease, 29 ${ }^{\text {th }}$ ed. Elk Grove Village, IL: American Academy of Pediatrics; 2012: pp 489-499.
3. Centers for Disease Control and Prevention. Epidemiology and Prevention of VaccinePreventable Diseases, Measles. Atkinson W, Hamborsky J, Wolfe S, eds. $12^{\text {th }}$ ed., second printing. Washington DC: Public Health Foundation, 2012. pp 173-192.
4. CDC’s National Notifiable Diseases Surveillance System (NNDSS) and Case Definitions. http://wwwn.cdc.gov/nndss/ (8/13)
5. Centers for Disease Control and Prevention, Vaccines \& Immunization: http://www.cdc.gov/vaccines/vpd-vac/measles/default.htm (8/13)
6. Centers for Disease Control and Prevention, Overview of Measles: http://www.cdc.gov/measles/about/overview.html (8/13)
7. Centers for Disease Control and Prevention, Travelers' Health - Yellow Book: http://wwwnc.cdc.gov/travel/yellowbook/2010/chapter-2/measles.aspx (8/13)
8. US Food and Drug Administration, FDA Safety Communication: New boxed warning for thrombosis related to human immune globulin products, June 10, 2013: http://www.fda.gov/BiologicsBloodVaccines/SafetyAvailability/ucm355986.htm (8/13)
9. Centers for Disease Control and Prevention, Measles (Rubeola), Lab Tools: http://www.cdc.gov/measles/lab-tools/index.html (8/13)
10. Centers for Disease Control and Prevention, Chapter 7: Measles, Manual for the Surveillance of Vaccine-Preventable Diseases (5th Edition, 2012) http://www.cdc.gov/vaccines/pubs/surv-manual/chpt07-measles.html (8/13)
11. Morbidity and Mortality Weekly Report (MMWR), Prevention of Measles, Rubella, Congenital Rubella Syndrome, and Mumps, 2013: Summary Recommendations of the Advisory Committee on Immunization Practices (ACIP), Recommendations and Reports, June 14, 2013 / 62(RR04);1-34
http://www.cdc.gov/mmwr/preview/mmwrhtml/rr6204a1.htm (8/13)

## Other Sources of Information

Gershon, Anne A. Measles Virus (Rubeola). In: Gerald L. Mandell, John E. Bennett, \& Raphael Dolin, Eds. Principles and Practice of Infectious Diseases, $7^{\text {th }}$ ed., Pennsylvania: Churchill Livingstone Elsevier, 2010: pp 2229-2236.

## Web Sites

1. Immunization Action Coalition: http://www.immunize.org. (8/13)
2. Morbidity and Mortality Weekly Report (MMWR), General Recommendations on Immunization, Recommendations of the Advisory Committee on Immunization Practices (ACIP), Recommendations and Reports January 28, 2011 / 60(RR02);1-60 http://www.cdc.gov/mmwr/preview/mmwrhtml/rr6002a1.htm (8/13)
