Measles Outbreak Control Guidelines

Infectious agent
Virus: paramyxovirus, genus *Morbillivirus*. There is only one antigenic type of this RNA virus.

Clinical manifestations
Measles is an acute disease characterized by fever, cough, coryza, conjunctivitis, erythematous maculopapular rash and Koplik’s spots (pathognomonic enanthema).

Symptoms
Prodromal symptoms
- Begins 10-12 days after exposure.
- Duration 2-4 days with a range of 1-7 days.
- Fever increases gradually to 103° to 105° F.
- Symptoms include: cough, coryza, conjunctivitis, malaise, diarrhea, anorexia, and lymphadenopathy.
- Koplik’s spots:
  - White enanthem (rash) on mucous membranes, usually the buccal membrane.
  - Appears as scattered blue-white spots on a bright red background.
  - Occurs 1-2 days before rash to 1-2 days after rash.

Rash
- Maculopapular eruption that lasts 5-6 days.
- Occurs 2-4 days after prodrome (approximately 14 days after exposure).
- Rash usually begins on face/head and spreads downward and outward, reaching the hands and feet.
- The rash fades in the same order that it appears--from head to extremities.

ILLUSTRATION OF AVERAGE MEASLES ILLNESS TIMELINE (in days)
Beginning at time of exposure (-14).
Day 0 is day of rash onset.

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<th>Incubation Period</th>
<th>Prodrome</th>
<th>Rash</th>
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Period of Communicability
Complications
Occur in 30% of cases and are more common in those younger than 5 years and older than 20 years.

Diarrhea
- Diarrhea is reported in 8% of measles cases and is the most common complication of measles.

Otitis media
- Otitis media is reported in 7% of cases and occurs almost exclusively in children.

Pneumonia
- Pneumonia is reported in 6% of cases and may be identified as viral or superimposed bacterial.
- Most common cause of death.

Acute encephalitis
- Occurs in 0.1% of reported cases.
- Onset generally occurs 6 days after rash onset (range 1-15 days).
- It is characterized by fever, headache, vomiting, stiff neck, meningeal irritation, drowsiness, convulsions, and coma.
- Case fatality rate is approximately 15%.
- Some form of residual neurologic damage occurs in as many as 25% of cases.
- Seizures are reported in 0.6%-0.7% of cases.

Complications during pregnancy
- Measles infections during pregnancy have been associated with an increase in low-birth weight infants, premature labor, spontaneous abortion, and birth defects.

Death
- 0.2% of reported measles cases in the US are fatal.
- Pneumonia in children and acute encephalitis in adults are the most common causes of death.
- Measles mortality rates are much higher in developing countries due to nutritional deficiencies and the lack of medical case management.

Subacute sclerosing panencephalitis (SSPE)
- Symptoms include progressive deterioration of intellect and behavior followed by ataxia, seizures and death caused by persistent measles infection of the brain.
- Incidence can be as high as 1 in 8000 cases in children under 2 years.
- Average onset is 7 years after acute infection (range: 1 month-27 years).
- Persons with SSPE cannot transmit measles.
Treatment

- There is no specific antiviral therapy for measles
- Medical care is supportive
- Treat severe measles cases among children (e.g. hospitalized) with vitamin A
- Vitamin A
  - Give vitamin A immediately upon diagnosis and repeat the next day
    - Plays a role in preserving epithelial cell integrity and immune modulation
    - Has been associated with reductions in morbidity and mortality
  - Age-specific daily doses
    - 50,000 IU for infants age <6m
    - 100,000 IU for infants age 6-11m
    - 200,000 IU for children age >12m

Note: Even in developed countries such as the U.S. (where measles usually is not severe), vitamin A should be given to all children with severe measles (e.g. requiring hospitalization).

Incubation period

- From exposure to prodrome averages 10-12 days.
- From exposure to rash onset averages 14 days (range 7-18 days).
- Individuals prophylaxed with immunoglobulin (IG) may have extended incubation periods up to 28 days and mild disease presentation.

Period of communicability

- Highly communicable disease with greater than 90% secondary attack rate among susceptible individuals.
- Communicable from 4 days before to 4 days after rash onset.

Transmission

- Transmitted by respiratory droplets and airborne spread.
- Airborne transmission in a closed area has been reported for up to 2 hours after a person with measles occupied the area.

Basic epidemiology

- Humans are the only reservoir.
- Measles is the leading cause of vaccine-preventable disease mortality in children worldwide.
- The remaining burden is primarily attributable to vaccine underutilization.
- Measles is no longer endemic in the U.S.
  - Cases in the U.S. are attributable to importation.
  - Most measles cases occur in U.S. citizens returning from travel who do not have measles vaccine protection.
  - Consider international importation if rash onset is within 21 days of return from foreign travel.
Case definition

Case definition and classification published by CSTE January 2013

Clinical description

- Generalized maculopapular rash lasting ≥3 days, AND
- Fever of ≥101°F, AND
- Cough, coryza or conjunctivitis.

Case classification

Probable case
In absence of a more likely diagnosis, an illness that meets the clinical description with
- No epidemiologic linkage to a laboratory-confirmed measles case AND
- Non-contributory 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 PCR; OR
- IgG seroconversion from negative to positive (as documented in this illness) or a significant 4 fold rise in measles serologic IgG antibody OR
- A positive measles serologic IgM antibody that is not explained by MMR vaccination in the last 6-45 days; and performed at the public health laboratory OR
- Direct epidemiologic linkage to a case confirmed by one of the methods above.

Note: Temperature does not need to reach ≥101°F and rash does not need to last ≥3 days if laboratory criteria are met.

Outbreak
- For national reporting, an outbreak is defined as a chain of transmission including 3 or more cases linked in time and space.

Case classification for Import Status

Internationally Imported case
- A case that has its source outside of the U.S. as evidenced by at least some of the exposure period (7-21 days before rash onset) occurring outside the U.S. with a rash onset within 21 days of entering the U.S. and there is no known exposure to measles in the U.S. during that time.

U.S. – acquired case
- A case in which the patient had not been outside the U.S. during the 21 days before the rash onset or was known to have been exposed to measles within the U.S.
U.S. – acquired cases sub-classifications

- 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.
- Endemic case: a case for which epidemiological or virological evidence indicates an endemic chain of transmission. Endemic transmission is defined as a chain of measles virus transmission that is continuous for ≥12 months within the U.S.
- Unknown source case: a case for which an epidemiological or virological link to importation or to endemic transmission within the U.S. cannot be established after a thorough investigation.

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

Note: States may also choose to classify cases as “out-of-state-imported” when imported from another state in the U.S. However, for national reporting, cases will be classified as either internationally imported or U.S. acquired.

Laboratory criteria for diagnosis

Any of the following make the case confirmed:

- Isolation of measles virus from clinical specimen
- Detection of measles-virus-specific nucleic acid by PCR*
  - *Viral PCR testing is available only at Wadsworth
- Positive measles IgM antibody test
  - All positive IgM results from commercial laboratories must be forwarded to Wadsworth for confirmation
- Four-fold rise in measles IgG antibody level by standard serologic assay
- IgG seroconversion not due to MMR vaccination during the previous 6-45 days

PCR and Culture

- Detection and isolation of measles virus RNA from clinical specimens (e.g., nasopharynx, pharynx, or urine) confirms the diagnosis and is extremely important for molecular epidemiologic surveillance
- Specimens for PCR/culture should ideally be obtained at the same time as the acute serology specimen because virus is more likely to be isolated within 3 days of rash onset
  - Obtain viral specimen ASAP – within 72 hours of rash onset for best results
  - Do not collect viral specimens more than 10 days after rash onset

IgM antibody

- Antibodies are detected in samples for at least 28 days after rash onset and frequently longer
A proportion of specimens (up to 23% in a CDC study) collected within 72 hours of rash onset may give false negative results. If a negative result is obtained from serum collected within 72 hours after rash onset, a second serum should be collected ≥ 72 hours after rash onset.

Note: Recently vaccinated cases may have an elevated measles IgM titer for up to 6 weeks following vaccination. Confirmed case status in these individuals will need to be assessed on a case by case basis.

IgG antibody

- The IgG response begins at about 7 days after rash onset and typically persists for a lifetime.
- A rise in measles IgG antibody between acute and convalescent specimens by standard serological assay, defined as a “4 fold rise,” confirms measles.

Testing and diagnosis

All cases under investigation should have both viral and serologic testing.
- The viral tests and acute serum specimens should be collected at the first contact with the suspected measles case.
  - Up to 23% of IgM tests performed in the first 72 hours after rash onset may be falsely negative.
  - Any negative IgM drawn within 72 hours of rash onset should be repeated and obtained 72 hours after rash onset.
  - Testing for IgG along with IgM is recommended for suspected measles cases.
- Previously vaccinated persons may have a blunted and/or transient production of IgM. PCR testing may be the best method to confirm such cases. Additional serologic testing may also be needed. The Bureau of Immunization should be consulted for complete recommendations.
- Viral specimens and acute measles serology can be sent directly to Wadsworth to improve receipt of confirming results in a timely manner.
- For after hour or weekend specimen submission, recommendations will be made based on clinical compatibility, risk of community or facility exposure and the availability of laboratory staff, especially on weekends. Due to financial constraints and limited staffing, only the highest risk cases will be tested on the weekend.
  - Please consult with NYSDOH Bureau of Immunization prior to specimen shipment.
- The convalescent serum specimen should be drawn 14-30 days later, if necessary for confirmation.
  - For comparison of acute and convalescent samples (“paired sera”), assays must be run together in one laboratory at the same time and with the same test (“run in parallel”).

Specimen collection

Collection for viral testing and serology

- Contact commercial laboratory regarding instructions and notification for specimen shipment.
- Use a separate kit for each specimen.
New York State Department of Health
Bureau of Immunization

- Carefully complete the history form, including the clinical information, test results, provider name and phone number; patient name, DOB and county of residence.
- Viral test kits should be obtained through commercial laboratories. Contact the Bureau of Immunization for information on ordering viral test kits from Wadsworth Laboratory.
- Serology specimen kits are not routinely available from Wadsworth Laboratory. For questions or special requests, please contact the NYSDOH Bureau of Immunization (518) 473-4437 or Diagnostic Immunology at (518) 474-4177

Specimen source
- For measles PCR and culture: clinical specimen from nasopharynx or pharynx and urine.
- For measles IgM and IgG: serum.

Procedure
- Measles virus PCR and culture
  - Measles virus is most frequently recovered within the first 3 days following rash. Collect specimen no later than 10 days after rash onset.
  - Use separate specimen containers for each sample.
  - Carefully complete the history form as described above.
  - Label specimen containers with patient’s name and collection date; collect 2 specimens: NP or throat specimen AND urine specimen.
    - Nasopharyngeal (NP) swab or throat swab – use viral medium
      - Rub the 2 dry sterile swabs on the appropriate area.
      - Immerse swab tips in 5ml of stabilizing buffer in the screw cap specimen tube.
      - Break the swabs to fit and seal tightly.
    - Urine
      - Add specimen to a sterile centrifuge tube or screw-cap cup.
      - Insert specimen cup into plastic zip-lock bag or package specimen tube as for other samples.
- Measles IgG and IgM serology
  - Acute specimen: collect serum within 3-28 days of onset of symptoms.
  - Convalescent specimen: collect serum 14-30 days after the first (acute) specimen.
  - Separate acute and convalescent serum specimens need to be collected using serum separator tube.
  - Carefully complete the history form as described above.
  - Label specimen tube with patient’s name and collection date.
  - When possible, centrifuge serum separator tube 20–30 minutes after collection.
  - When testing for a four-fold rise in titer, acute and convalescent specimens are run simultaneously, so results will not be available until the convalescent specimen is collected, sent and tested.

Transport
- Viral PCR and culture sample
  - If unable to ship within 24 hours, preserve at -70°C.
  - Avoid freeze-thaw cycles.
  - Can ship with dry or wet ice or cold packs.
Serum
- Do NOT freeze.
- Refrigerate at 4°C until shipping.
- Ship with cold packs.
- Samples must have an outer packaging to prevent freezing.

Mailing instructions for Wadsworth Laboratories

Please consult with the NYSDOH Bureau of Immunization prior to specimen shipment at (518) 473-4437.

- Ship measles viral specimen submission by overnight mail
  - Put specimen kit into Styrofoam mailing box
  - Include 1-2 cold packs to keep specimen refrigerated
  - Before shipping specimen for delivery on a weekend or holiday, call the Virus Isolation Laboratory at (518) 474-4177.

Overnight delivery should be mailed to:
Virus Isolation Laboratory
David Axelrod Institute
Wadsworth Center, NYSDOH
120 New Scotland Ave
Albany, NY  12208

Questions?  Call Wadsworth Center at (518) 474-4177.

- Ship measles IgG and IgM serology submission by overnight mail
  - Put specimen kit into Styrofoam mailing box.
  - Include 1-2 cold packs to keep specimen refrigerated.
  - Before shipping specimen for delivery on a weekend or holiday, call Diagnostic Immunology in advance at (518) 474-4177.

Overnight delivery should be mailed to:
Diagnostic Immunology
David Axelrod Institute
Wadsworth Center, NYSDOH
120 New Scotland Ave
Albany, NY  12208

Questions?  Call Wadsworth Center at (518) 474-4177.

Case investigation

Demographics
- Name
New York State Department of Health
Bureau of Immunization

- Address
- DOB/age
- Occupation/Setting
- Race
- Ethnicity
- Gender
- Date reported

Reporting source
- Date Reported
- Source
- Provider
- County

Clinical Information
- Rash (describe)
- Rash duration
- Fever
- Cough
- Coryza
- Conjunctivitis
- Dates of onset of all symptoms

Complications
- Diarrhea
- Otitis media
- Pneumonia
- Acute encephalitis
- Seizures

Laboratory results
- Lab name
- Date of specimen
- Type of tests
- Results/Confirmation

Vaccine history
- Type
- Manufacturer
- Number of doses
- Vaccination dates
- Lot number
- Reason if not vaccinated

Outcome
- Case survived or died
New York State Department of Health
Bureau of Immunization

Control measures

♦ Review immunization and clinical status of all contacts. Measles immunity is defined as any of the following:
  o Born prior to 1957; or
  o Written documentation of 2 doses of measles-containing vaccine for children ≥ 4 years and adults at high risk for exposure transmission (i.e. health care personnel, international travelers and students at post high school educations institutions) with a minimum interval of 28 days from the first dose to the second dose; or
  o Written documentation of one or more doses of a measles-containing vaccine administered on or after the first birthday for children aged 1 through four years and adults not at high-risk; or
  o Laboratory evidence of immunity; or
  o Laboratory confirmation of disease.

♦ Post-exposure prophylaxis of susceptible contacts
  o Vaccination within 72 hours of exposure, or IG if administered within six days of exposure, may provide some protection or modify the clinical course of disease.
  o Contacts who are not vaccinated within 72 hours, and who are not candidates for IG, should still be immunized in order to offer protection against infection from future exposure.

♦ Post-exposure vaccination:
  o People born after 1/1/1957 (who are 1 year of age or older) with no recorded measles vaccination should:
    • Receive one dose of MMR vaccine.
    • Be allowed to return to school/work once vaccinated.
    • Receive a second dose of vaccine not less than 28 days later.
  o People born after 1/1/1957 with only one recorded dose of measles vaccine should:
    • Receive a second dose.
    • Be allowed to return to school/work once vaccinated.
  o Healthy children 6 through 11 months of age:
    • May receive MMR vaccine in place of IG (see below) if administered within 72 hours of exposure.
    • This vaccination does NOT count as part of the routine 2-dose MMR series. These children will receive a total of 3 doses of MMR.
  o The following groups should not receive MMR vaccine, but can receive IG:
    • Pregnant women, or women planning to become pregnant within the next month,
    • Severely immunocompromised persons,
    • Infants under 6 months of age, or
- Persons with a history of severe allergic reaction (e.g., anaphylaxis, after a previous dose or to a vaccine component).
  - Immunoglobulin (IG)
    - Indications:
      - Susceptible pregnant women.
      - Infants under 12 months of age.
      - Susceptible household contacts or persons in settings with intense, prolonged close contact not vaccinated within 72 hours of exposure.
      - Severely immunocompromised persons, regardless of immunization status.
    - Timing:
      - IG should be given within 6 days of exposure to prevent or modify disease.
    - Dosage:
      - Immunoglobulin Intramuscular (IGIM) is 0.5 ml/kg of body weight (maximum dose is 15 ml).
      - Immunoglobulin Intravenous (IGIV) is 400 mg/kg.
    - CDC recommends that individuals who receive IG within 6 days of exposure cannot return to health care settings for 28 days since IG can prolong the incubation period.
    - In other settings such as childcare, school or work, factors such as immune status, intense or prolonged contact and presence of populations at risk should be taken into consideration before allowing these individuals to return to normal activity.
      - Enhanced surveillance and a plan for follow-up should symptoms develop can also be provided by the LHD.
      - Regional and Central office staff are available for consultation on any special situations.

Note: Persons receiving intravenous immunoglobulin (IVIG) at regular intervals for other reasons do not need additional IG if their last dose of IVIG was within three weeks of exposure and the dose was greater than 400 mg/kg.

- Immunization after IG administration
  - Children should be at least 12 months old.
  - The interval between IG administration and MMR should be at least 6 months.

Note: Any susceptible contact who develops fever, cough, runny nose, conjunctivitis, or other cold-like symptoms should be:
  - Immediately excluded from school/work for at least 5 days.
  - Offered appropriate diagnostic testing if a rash develops.
  - Excluded for at least another 4 days after the onset of rash.

Control measures for school and daycare settings
  - Review immunization records of all contacts born on or after 1/1/1957.
  - Persons who cannot readily provide documentation of measles immunity as described above must be vaccinated or excluded from the school or institution.
  - Persons vaccinated with measles-containing vaccine may be immediately readmitted to the school or institution.
  - Persons who continue to be exempted from, or who refuse measles vaccination must be excluded from the school, childcare or other institution until 21 days after the onset of rash in the last case of measles.
  - School activities restrictions during an outbreak:
For extracurricular activities, all participating individuals must be in compliance with the standards of measles immunity, be properly vaccinated or excluded as defined above.

The LHD should be notified of the planned event in order to review the activity plans and the measles immunity status of the participating persons. The LHD, in consultation with the NYSDOH, may advise cancellation of travel events based on the nature of the outbreak.

- To reduce potential spread of measles disease, no spectators should be present at any indoor sporting or extracurricular activity involving students from the affected school. Outdoor activities may be permitted to have spectators only if the ability exists to restrict the spectators to those from the affected school.

LHDs where the school resides, as well as the LHD receiving the participants, will insure that all participants are properly protected and provide enhanced surveillance for measles during the outbreak period or 21 days after the last exposure to the last reported case of measles.

For school and post-secondary institutions, this guidance is in compliance with PHL 2164, PHL 2165 and NYCRR 66-1 and 66-2.

Control of outbreaks in summer camps:

- Review immunization records of all contacts born on or after 1/1/1957.
- List those who have not had 2 appropriately timed doses of measles vaccine or proof of immunity to measles.
- Persons who cannot readily provide documentation of measles immunity must be vaccinated, excluded or appropriately isolated in the camp setting. The LHD or NYSDOH can provide guidance for isolation recommendations.
- Persons vaccinated with measles containing vaccine may be immediately readmitted to the camp setting.
- For off-site or inter-camp activities, all participating individuals must be in compliance with the standards of measles immunity, be properly vaccinated or excluded.

The LHD should be notified of the planned event to review the activity plans and the measles immunity status of the participating persons. The LHD, in consultation with the NYSDOH, may advise cancellation of travel events based on the nature of the outbreak.

Also, based on the nature of the measles outbreak, camp activities may be confined to the camp grounds with no other groups attending until 21 days after the date of onset of the last case.

Control measures for healthcare settings

- **NOTE**: Regardless of presumptive immunity status, all healthcare staff entering a room with a patient who is potentially ill with measles should use respiratory protection consistent with airborne infection control precautions (use of an N95 respirator or a respirator with similar effectiveness in preventing airborne transmission). Because of the possibility, albeit low, of MMR vaccine failure in healthcare providers exposed to infected patients, they should all observe airborne precautions in caring for patients with measles.
Title 10 of NYS PHL requires all personnel working in health care facilities and home care agencies to have immunity to measles, or to be properly vaccinated with two measles containing vaccines (unless a licensed physician, physician’s assistant, specialist’s assistant, licensed midwife or nurse practitioner certifies that immunization with measles vaccine may be detrimental to the person’s health).

If an outbreak occurs within (or in the area served by) a medical office, hospital, clinic, or other medical or nursing facility, all personnel should receive a dose of MMR vaccine (and a second MMR dose 28 days after the first) unless they have written documentation of measles immunity. **This includes HCP born before 1957 that lack evidence of measles immunity or laboratory confirmation of disease.**

Serologic screening of health care personnel during an outbreak to determine measles immunity is not recommended. Results from serological testing, if performed, should not delay the administration of MMR vaccine while waiting for the results of testing; however, the results can inform the need for the second MMR vaccine dose.

Susceptible personnel who have been exposed to measles should be relieved from patient contact and excluded from the facility from the 5th to the 21st day after exposure, regardless of whether they received post-exposure prophylaxis.

Exposed personnel who become ill should be relieved from all patient contact and excluded from the facility for 4 days after they develop rash.

Hospital contacts of a case patient who do not have presumptive evidence of measles immunity should be vaccinated or offered IG (as discussed above) or quarantined for 21 days after their exposure to the case patient.

Contacts of people with measles compatible symptoms should be isolated with appropriate infection control measures to prevent additional spread.

If IG is administered to an exposed person, observation should continue for 28 days after exposure and they should be excluded from work.

### Reporting

- A Confidential Case Report Form (DOH-389) must be submitted.
- The LHD must be notified immediately by telephone as soon as a diagnosis of measles is suspected.
- The LHD must notify the NYSDOH Bureau of Immunization within 24 hours of their notification, preferably by telephone (518-473-4437), as soon as the case is reported to them. The Duty Officer system is available to LHDs and providers for consultation 24/7.

### Additional clinical information

- **Atypical Measles**
  - Occurs only in persons who received inactivated (killed) measles vaccine (KMV) and are subsequently exposed to wild-type measles virus.
  - Approximately 600,000-900,000 persons received KMV in the U.S. from 1963-67.
Illness is characterized by fever, pneumonia, pleural effusions and edema.

- Rash is usually maculopapular, petechial, but may have urticarial, purpuric, or vesicular components. It appears first on wrist and ankles.
- Atypical measles may be prevented by revaccinating with live measles vaccine.
  - Moderate to severe local reactions with or without fever may follow vaccination. However, these reactions are less severe than with wild type measles infection.

- Measles in vaccinated persons
  - May have a modified disease presentation and is usually detected during an outbreak or after known exposure to a confirmed case of measles
  - See testing and diagnosis section for recommended laboratory testing guidance.
  - Also has been described as secondary immune response (SIR).

- Measles vaccine reaction
  - Reactions following measles vaccine represent replication of measles vaccine virus with subsequent mild illness.
  - These events occur 5-12 days post-vaccination only in persons who are susceptible to infection.
  - Reactions include fever, transient rash and lymphadenopathy.