Chapter 7: Measles

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I. Disease Description

Measles is an acute viral illness caused by a virus in the family Paramyxoviridae, genus *Morbillivirus*. Measles is characterized by a prodrome of fever and malaise, cough, coryza, and conjunctivitis, followed by a maculopapular rash. The illness is usually mild or moderately severe; however, measles can result in complications such as pneumonia, encephalitis and death. During 1987–2000, in the United States, nearly one-third (29%) of measles cases had some complication, with 6% complicated by pneumonia and 19% requiring hospitalization. During that period, measles resulted in encephalitis in 1 of 1,000 reported cases, and death was reported in 0.3% of cases.[1] The most severe sequela of measles virus infection is subacute sclerosing panencephalitis (SSPE), a fatal disease of the central nervous system that generally develops 7–10 years after infection. Among persons who contracted measles during the resurgence in the United States in 1989–1991, the risk of SSPE was estimated to be 6.5–11 cases/100,000 cases of measles. The risk of developing SSPE may be higher when measles occurs before the second year of life.[2]

The average incubation period for measles is 14 days, with a range of 7–21 days.3 Persons with measles are usually considered infectious from 4 days before until 4 days after onset of rash.[4]

II. Background

Before the introduction of measles vaccine in 1963, roughly one-half million cases were reported each year in the United States. In 1989, a second-dose vaccination schedule was recommended,[5] and in 1998, the Advisory Committee on Immunization Practices (ACIP) and the American Academy of Pediatrics (AAP) jointly recommended that states ensure second-dose coverage of children in all grades by 2001.[6] The current elimination strategy has led to a dramatic decline in measles cases. Fewer than 150 cases were reported each year during 1997–2004,[7–9] and measles incidence decreased to a record low of 37 reported cases in 2004.[9] In recent years, outbreaks of measles have been small, with fewer than 35 cases reported.[8–10] Recent outbreaks do not have one predominant transmission setting but mostly involve persons who are exposed to imported measles cases and who are unvaccinated or have received only one dose of measles vaccine. Moreover, recent outbreaks have been typically related to lack of adherence to existing recommendations for measles prevention among high-risk groups such as travelers and healthcare workers, groups who routinely refuse vaccination.[11, 12]

Globally, more than 30 million people are affected each year by measles.

While measles is now rare in many industrialized countries, it remains a common illness in many developing countries. Globally, more than 30 million people are affected each year by measles. In 2004, an estimated 454,000 measles deaths occurred globally; this translates to more than 1,200 deaths every day or 50 people dying every hour from measles. The overwhelming majority (more than 95%) of measles deaths occur in countries with per capita gross national income of less than US $1,000. In countries where measles has been largely eliminated, cases imported from other countries remain an important source of infection.[13]

In May 2003, the 56th World Health Assembly unanimously adopted a resolution[14] to reduce measles deaths by 50% by the end of 2005, compared with 1999 levels. This goal was established a year earlier by the United Nations General Assembly Special Session on Children, "World Fit for Children." In May 2005, the 58th World Health Assembly adopted the WHO/UNICEF Global Immunization Vision and Strategy (GIVS). GIVS calls on countries to reduce global measles deaths by 90% (compared with 2000 estimates) by 2010. In the Americas, under the leadership of the Pan American Health Organization (PAHO), Ministries of Health implemented an aggressive measles elimination program. Based on the success in the Americas using PAHO's strategies, measles elimination targets have been established in the European and Eastern Mediterranean regions for the year 2010, and in the Western Pacific region for 2012. The African and Southeast Asian regions have set goals for sustainable reductions in measles mortality. These initiatives will have direct benefits in the United States.

The WHO/UNICEF Comprehensive Strategy for Sustainable Measles Mortality Reduction includes the following:[13]

- Strong routine immunization, assuring that at least 90% of children are reached by routine immunization services every year, in every district.
- A second opportunity for measles immunization provided to all children, either through routine immunization services (if high coverage can be achieved and maintained over time) or through periodic supplementary immunization activities (SIAs). SIAs target large populations (entire nations or large regions) and aim to achieve immunization coverage of over 90%.
- Enhancing surveillance, ensuring prompt recognition and investigation of measles outbreaks, and assuring the implementation of appropriate outbreak response activities.
- Improving clinical management of measles cases, including vitamin A supplementation and adequate treatment of complications, if needed, with antibiotics.

The highly contagious measles virus is frequently imported into the United States by persons from other countries.

To advocate for reduction of measles mortality, the Measles Initiative was launched in February 2001. The Measles Initiative is a long-term commitment to control measles deaths, starting in Africa by vaccinating at-risk children 15 years of age and younger. Leading this effort are the American Red Cross, United Nations Foundation, the Centers for Disease Control and Prevention (CDC), United Nation's Children's Fund (UNICEF), and the World Health Organization (WHO). Other key players in the fight against measles include the International Federation of Red Cross and Red Crescent Societies and countries and governments affected by measles. As of the end of 2005, the Measles Initiative helped to decrease related mortality by 60% by vaccinating 213 million children in more than 40 African countries, saving more than 1.2 million lives. Because of the Measles Initiative's success in Africa, the program has expanded into Asia, where the measles burden remains high.[15]

III. Importance of Rapid Identification

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.

IV. Importance of Surveillance

The highly contagious measles virus is frequently imported into the United States by persons from other countries. Each imported measles case could start an outbreak, especially if undervaccinated groups are exposed. Surveillance and prompt investigation of cases and contacts help to halt the spread of disease.

Information obtained through surveillance is also used to assess progress towards disease elimination goals. Surveillance data are used to characterize persons, groups, or areas in which additional efforts are required to reduce disease incidence.

V. Disease Reduction Goals

The United States has established the goal of eliminating the transmission of endemic measles.[16] Current surveillance data indicate this goal has been achieved, and endemic measles was declared eliminated in the United States in 2000.[17] To prevent imported strains of measles virus from establishing endemic chains of transmission, rapid detection of cases is necessary so that appropriate control measures can be quickly implemented. The major challenges to sustaining the elimination of measles from the United States are a) continuing to vaccinate all children aged 12–15 months with a first dose of MMR, b) ensuring that all school-aged children receive a second dose of MMR vaccine, and c) working with other countries to set and achieve national measles elimination goals.[6]

VI. Case Definition

The following case definition for measles has been approved by the Council of State and Territorial Epidemiologists (CSTE) and was published in 2007.[18] The following case classifications for importation status were approved by the CSTE in 2006.[19]

Clinical case definition

An illness characterized by all of the following:

- A generalized rash lasting ≥3 days
- A temperature ≥101°F (≥38.3°C)
- Cough, coryza, or conjunctivitis

Laboratory criteria for diagnosis

- Positive serologic test for measles immunoglobulin M (IgM) antibody, or
- Significant (generally a fourfold) rise in measles antibody (lgG) level by any standard serologic assay, or
- Isolation of measles virus from a clinical specimen*

** Identification of measles genotype by RT-PCR and sequencing by WHO reference laboratory (CDC) from clinical samples confirms infection.*

Case classification

Case classification requires a consideration of the clinical presentation.

Suspected: Any febrile illness accompanied by rash.

Probable: A case that meets the clinical case definition, has noncontributory or no serologic or virologic testing, and is not epidemiologically linked to a confirmed case.

Confirmed: A case that is laboratory confirmed or that meets the clinical case definition and is epidemiologically linked to a confirmed case. A laboratory-confirmed case does not need to meet the clinical case definition.

Comment: Confirmed cases should be reported to CDC via the National Notifiable Diseases Surveillance System (NNDSS). All confirmed cases should be classified as one of the following:

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 United States 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.

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 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.

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

States may also choose to classify cases as "out-of-state-imported" when imported from another state within the United States. For national reporting, cases will be classified as either internationally imported or U.S.-acquired

Many clinicians have never seen a case of measles, and most patients who present with measles-like illness today do not have measles.

VII. Laboratory Testing

Because measles is an extremely rare disease in the United States, clinical evidence is not sufficient to confirm a case. Many clinicians have never seen a case of measles, and most patients who present with measles-like illness today do not have measles. Because measles is highly contagious with the potential for explosive spread following importation of the virus, it is critical to rapidly identify the few measles cases that do occur. For these reasons, laboratory diagnosis is crucial to confirm the few actual measles cases among the thousands of patients with suspected measles.

Even with the excellent laboratory tests available, some false-positive results will occur. (The positive predictive value [PPV] of a test is the proportion of persons with positive results who actually have the disease. The PPV decreases when the disease becomes rare.) Some false-positive results are expected, so it is preferable to misclassify a few false-positive cases than to miss cases that are measles.

To minimize the problem of false-positive laboratory results, case investigation and laboratory tests should be restricted to patients most likely to have measles, i.e., 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 results.

For additional information on laboratory support for surveillance of vaccine-preventable diseases, see Chapter 22, "Laboratory Support for Surveillance of Vaccine-Preventable Diseases", and visit the CDC measles laboratory website at http://www.cdc.gov/ncidod/dvrd/revb/measles

Serologic testing

Serologic testing for antibodies to measles is widely available. Generally, in a previously susceptible person exposed to wild-type measles virus, the IgM response starts around the time of rash onset and may be detected for 1–2 months. The IgG response starts more slowly, at about 5–10 days after rash onset, but typically persists for a lifetime. The diagnosis of acute measles infection can be made by detecting IgM antibody to measles in a single serum specimen or by detecting a rise in the titer of IgG antibody in two serum specimens obtained approximately 2 weeks apart.

The serologic response following vaccination is slower; IgM and IgG may not be detectable until 8–21 days postvaccination.

Recommendations for serologic testing for measles

- An enzyme immunoassay (EIA) test for IgM antibody to measles in a single serum specimen, obtained at the first contact with the suspected measles patient, is the recommended method for diagnosing acute measles.
- A single-specimen test for IgG is the most commonly used test for immunity to measles because IgG antibody is long-lasting.
- Testing for IgG along with IgM is recommended for suspected measles cases.
- Paired sera (acute- and convalescent-phase) may be tested for increase in IgG antibody to measles to confirm acute measles infection.
- When a patient with suspected measles has been recently vaccinated (6–45 days prior to blood collection) neither IgM nor IgG antibody responses can distinguish measles disease from the response to vaccination.

Tests for IgM antibody

Although multiple methods are available for testing for IgM antibody, EIA is the most consistently accurate test and is therefore recommended. There are two formats for IgM tests. The first and most widely available is the indirect format; IgM tests based on the indirect format require a specific step to remove IgG antibodies. Failure to remove IgG antibodies can sometimes lead to false-positive[20] or, less commonly, false-negative results.

The second format, IgM capture, does not require the removal of IgG antibodies. CDC has developed a capture IgM test for measles and has trained personnel from every state public health laboratory in its use. Although the IgM capture format is the preferred reference test for measles, several commercially available indirect measles IgM tests perform equally well. In contrast, only one capture IgM EIA is commercially available. This is the preferred reference test for measles.

EIA tests for measles are often positive on the day of rash onset. However, 30% of serum samples obtained in the first 72 hours after rash onset may give false-negative results. Negative results from serum collected in the first 72 hours after rash onset should be confirmed with a second serum obtained 72 hours or longer after rash onset (Table 1). IgM is detectable for at least 30 days after rash onset and frequently longer.[21]

When a laboratory IgM result is suspected of being false-positive (Table 1), additional testing may be performed. False-positive IgM results for measles may be due to the presence of rheumatoid factor in serum specimens and have also been documented when a patient has a rash illness caused by parvovirus B19, rubella, roseola or dengue. False-positive tests may be suspected when thorough surveillance reveals no source or spread of cases or when the case does not meet the clinical case definition. In these situations, confirmatory tests may be done at the state public health laboratory or at CDC.

Tests for IgG antibody

Because tests for IgG require two serum specimens and because a confirmed diagnosis cannot be made until the second specimen is obtained, IgM tests are generally preferred. However, if IgM tests remain inconclusive, a second (convalescent-phase) serum specimen, collected 14–30 days after the first (acute-phase) specimen, can be used to test for an increase in IgG titer. These tests can be performed in the state laboratory or at CDC. A variety of tests for IgG antibodies to measles are available, including EIA, hemagglutination inhibition, indirect fluorescent antibody tests, and plaque reduction neutralization. Complement fixation, although widely used in the past, is no longer recommended. The gold standard test for serologic evidence of recent measles virus infection is the plaque reduction neutralization test (PRNT). This is a quantitative assay for anti-measles IgG, and a fourfold rise in titer between acute- and convalescent-phase paired sera is indicative of recent measles infection. EIA values are not titers and increases in EIA values between paired sera do not directly correspond to titer rises.

Virus isolation

Isolation of measles virus in culture or detection of measles virus by reverse transcription polymerase chain reaction (RT–PCR) in clinical specimens confirms the diagnosis of measles. Among persons with a recent MMR vaccination, determination of the measles genotype is necessary to distunguish between wild-type virus infection and a rash caused from measles vaccination.[22] A negative culture or negative RT–PCR does not rule out measles because both methods are much affected by the timing of specimen collection and the quality and handling of the clinical specimens.

Collection of viral samples is extremely important for molecular epidemiologic surveillance to identify the genotypes associated with imported cases of measles. This information is used to document the absence of endemic circulation of measles in the United States. Isolation of measles virus is technically difficult and is generally performed in research laboratories. Nevertheless, the introduction of recombinant cell lines bearing the receptor(s) for measles virus has vastly improved the measles isolation in cell culture.

Aggressive case investigations of persons with acute disease provide the best opportunity to administer postexposure prophylaxis to contacts

Specimens (urine, nasopharyngeal aspirates, heparinized blood, or throat swabs) for virus culture obtained from persons with clinically suspected cases of measles should be shipped to the state public health laboratory or to CDC at the direction of the state health department as soon as measles is confirmed. Specimens should be properly stored while awaiting case confirmation (see Appendix 7). Clinical specimens for virus isolation should be collected at the same time as samples taken for serologic testing. Because virus is more likely to be isolated when the specimens are collected within 3 days of rash onset, collection of specimens for virus isolation should not be delayed until laboratory confirmation is obtained. Clinical specimens should ideally be obtained within 7 days of rash onset and should not be collected more than 10 days after rash onset.

VIII. Reporting

Each state and territory has regulations or laws governing the reporting of diseases and conditions of public health importance.[23] These regulations and laws list the diseases to be reported and describe those persons or groups responsible for reporting, such as healthcare providers, hospitals, laboratories, schools, daycare and childcare facilities, and other institutions. Persons reporting these conditions should contact their state health department for state-specific reporting requirements

Reporting to CDC

Provisional reports of suspected measles should be promptly reported to CDC by the state health department or directly to CDC by telephone at 404-639-8230 or by e-mail (sbrl@cdc.gov). Information on confirmed cases should then also be electronically reported by the state health department to the National Notifiable Diseases Surveillance System (NNDSS) within 14 days of the initial report to the state or local health department. Although only data from confirmed cases are published in the Morbidity and Mortality Weekly Report (*MMWR*), states are encouraged to notify CDC of all suspected cases by phone as soon as possible.

Note: *The Division of Viral Diseases, National Center for Immunization and Respiratory Diseases (NCIRD), CDC, publishes periodically a measles update that is distributed by mail, fax, or e-mail to all states. The update describes details of recent measles activity (sporadic cases and epidemics) by state. To receive the update, call your state health department or send an e-mail request to CDC (sbrl@cdc.gov).*

Information to collect

The following data are epidemiologically important and should be collected in the course of case investigation. Additional information also may be collected at the direction of the state health department.

- **Demographic information**
  - Name
  - Address
  - Date of birth
  - Age
  - Sex
  - Ethnicity
  - Race
  - Reporting source
  - County
  - Earliest date reported
- **Clinical**
  - Date of rash onset
  - Duration of rash
  - Rash presentation
  - Symptoms
  - Date of onset of symptoms
  - Hospitalizations
  - Complications
- **Outcome (case survived or died)**
  - Date of death
- **Laboratory**
  - Serologic test results
  - Date of collection of specimen for virus isolation
- **Vaccination status**
  - Number of doses of measles vaccine received
  - Dates of measles vaccinations
  - Manufacturer name
  - Vaccine lot number
  - If not vaccinated, reason
- **Epidemiologic**
  - Transmission setting
  - Source of infection (e.g., age, vaccination status, relationship to case-patient)
  - Source of exposure (contact with probable or confirmed case, or contact with immigrants or travelers)
  - Import status (indigenous, international import, or out-of-state import, linked or traceable to an international importation)
  - Residency (Did the patient reside in the United States?)
  - Travel history

IX. Vaccination

Measles vaccine is incorporated with mumps and rubella vaccine as a combined vaccine (MMR). The Advisory Committee on Immunization Practices (ACIP) recommends a first dose at 12–15 months of age with a second dose at school entry (4–6 years) for routine vaccination.[6]

Measles vaccine is also now available incorporated with mumps, rubella and varicella vaccines as a combined vaccine (MMRV). ACIP recommends a first dose of MMRV for children aged 12 months to 12 years who need a first dose of measles, mumps, rubella (MMR), AND varicella vaccine, or children aged 12 months to 12 years who need a second dose of MMR and either a first or second dose (as indicated) of varicella vaccine.[3]

X. Enhancing Surveillance

As measles incidence declines, additional effort may be required to ensure that appropriate and timely diagnosis of rash illnesses and reporting of suspected cases continues. In addition, rapid investigation and reporting of all suspected cases and recording of vaccination history and import status for all cases will become increasingly important.

The activities listed below can improve the detection and reporting of measles cases and improve the comprehensiveness and quality of reporting. Additional guidelines for enhancing surveillance are given in Chapter 19, "Enhancing Surveillance."

Obtaining accurate and complete immunization histories

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 immunization records provided by the case-patient. Verbal history of receipt of measles vaccine is not considered adequate proof of vaccination.

Laboratory testing

If measles is suspected, laboratory testing should be performed to confirm or rule out the case. If a case is confirmed, a case investigation should be conducted. Measles specimens should also be sent to CDC for testing if this resource is needed.

Investigating contacts

Determining the source or chain of disease transmission, identifying all contacts (household, child care, and other close contacts), and following up with susceptible persons may reveal previously undiagnosed and unreported cases.

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 healthcare providers in outbreak areas to inform them of the outbreak and request reporting of any suspected cases. These activities are especially important in large cities and in cities with large numbers of international visitors.

Special projects

Special projects, such as reviewing hospital and managed care administrative databases and emergency department logs to identify rash illnesses that may have been unreported cases of measles, can be used to evaluate surveillance sensitivity and completeness of reporting.[24]

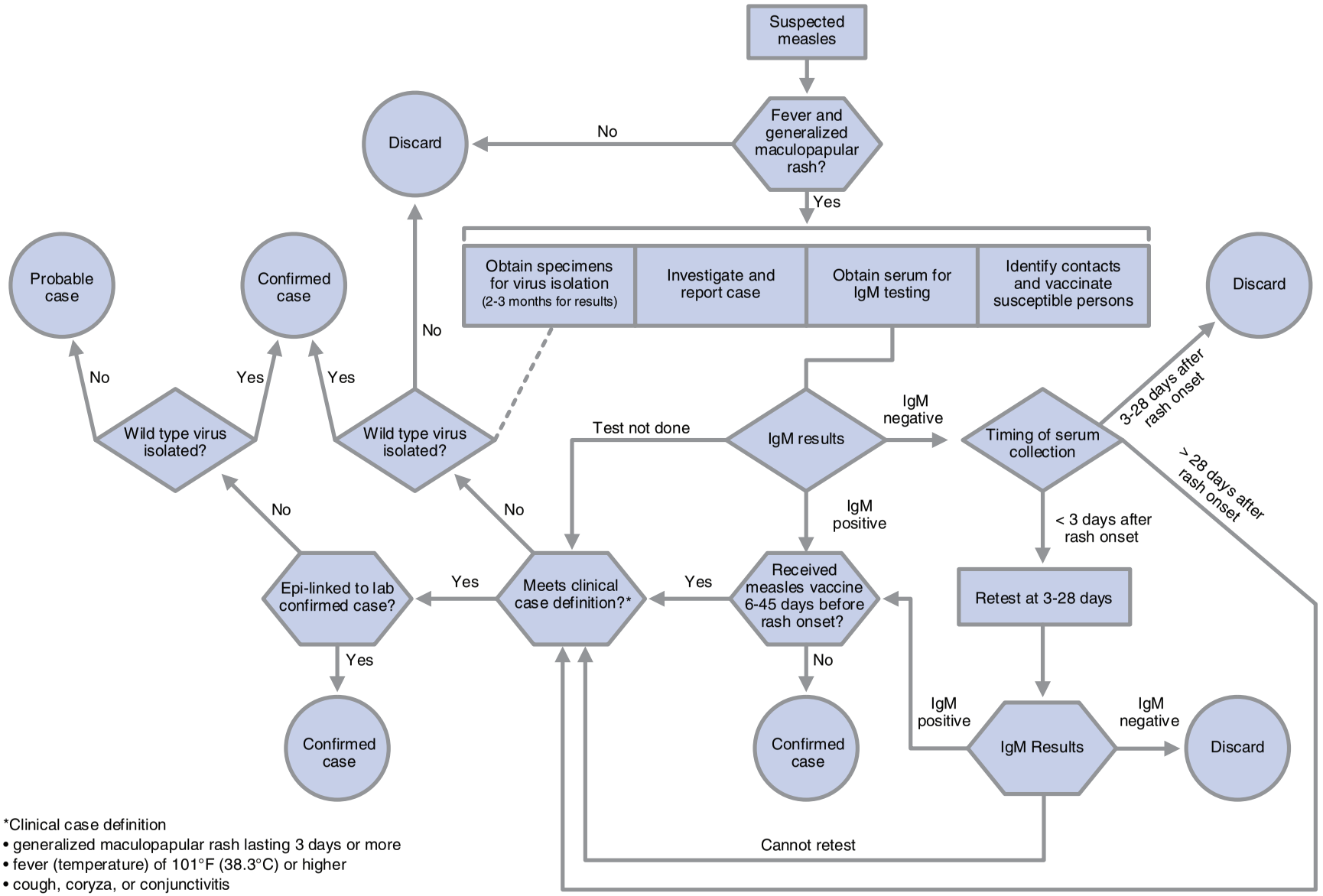
Monitering surveillance indicators

Regular monitoring of surveillance indicators, including time intervals between diagnosis and reporting and completeness of reporting, may identify specific areas of the surveillance and reporting system that need improvement. These indicators should be monitored:

- The proportion of confirmed cases reported to the NNDSS with complete information
- The median interval between rash onset and notification of a public health authority, for confirmed cases
- The proportion of confirmed cases that are laboratory confirmed
- The proportion of cases that have an imported source
- The proportion of cases for which least one clinical specimen for virus isolation was collected.

Another important indicator of the adequacy of the measles surveillance system is the detection of importations. In the absence of measles endemic transmission, imported cases or cases linked to importations should be detected. A program that reports no imported cases in settings where endemic measles has been eliminated cannot be assumed to have adequate measles surveillance. For more information on surveillance indicators, see Chapter 18, "Surveillance Indicators."

Figure 1. Measles Case Investigation



Virus isolation or positive RT–PCR. *Among persons with a recent MMR vaccination, determination of the measles genotype is necessary to distinguish between wild-type virus infection and a rash caused from measles vaccination.*[22]

XI. Case Investigation

All reports of suspected measles cases should be investigated immediately. The Measles Surveillance Worksheet (see Appendix 8) may be used as a guideline for collecting demographic and epidemiologic data during case investigation. Essential components of case investigation include establishing a diagnosis of measles, obtaining immunization histories for persons with confirmed cases, identifying sources of infection, assessing potential for transmission, and obtaining specimens for viral isolation.

Establishing a diagnosis of measles (Figure 1)

Necessary clinical information must be obtained to establish whether a reported case meets the clinical case definition (see "Case definitions"). If the case was reported within 3 days of onset of rash, appropriate follow-up is necessary to establish a rash duration of at least 3 days.

Laboratory confirmation is essential for all outbreaks and all isolated (sporadic) cases (those cases that are not part of a known outbreak). In an area of low measles incidence, most cases that meet the clinical case definition are not measles.[25] Even in outbreaks, laboratory confirmation should be obtained for as many cases as possible. Once community awareness is increased, many cases of febrile rash illness may be reported as suspected measles, and the magnitude of the outbreak may be exaggerated if these cases are included without laboratory confirmation. This is particularly important as the outbreak is ending; at that point, laboratory confirmation should be sought for all suspected cases.

Table 1. Classifying Suspected Measles Cases Based on Results of Case Investigation

IgM result	Optimal time for specimen collection?*	Recent vaccination?†	Meets clinical case definition?§	Epidemiologic linkage?¶	Wild-type measles virus identified?	Case classification
+	Yes or No	No	Yes or No	Yes or No	Yes or No	Confirmed**
+	Yes or No	Yes	Yes	Yes	Yes or No	Confirmed
+ or -	Yes or No	Yes or No	Yes or No	Yes or No	Yes	Confirmed
+	Yes or No	Yes	Yes	No	No	Probable
+	Yes or No	Yes	No	Yes or No	No	Discard
-	Yes	Yes or No	Yes or No	Yes or No	No	Discard
-	No[†]	Yes or No	Yes	Yes	No	Confirmed
-	No[†]	Yes or No	Yes	No	No	Probable
-	No[†]	Yes or No	No	Yes or No	No	Discard

Note: *Cells with "Yes or No" values do not affect the case classification.*

* *Optimal time for collection of IgM serum specimen is 3–28 days after rash onset.*

† *Receipt of measles-containing vaccine 6–45 days before rash onset.*

§ *Generalized maculopapular rash lasting ≥3 days and fever (>101° F or 38.3° C) and cough, coryza, or conjunctivitis.*

¶ *Contact with a laboratory-confirmed case (source or spread case) during the appropriate period for transmission.*

** *The possibility of a false-positive IgM test is increased when 1) the IgM test was not an EIA, 2) the case did not meet clinical case definition, 3) the case is an isolated indigenous case (no epidemiologic link to another confirmed case and no international travel), or 4) measles IgG was detected within 7 days of rash onset. Consider confirmatory testing for these cases.*

†† *Whenever possible, collect another serum specimen 3–28 days after rash onset, conduct an IgM test, and interpret the result according to this table*

The occurrence of measles-like illness in recently vaccinated persons can pose particular difficulties in an outbreak setting. Ten percent of recipients of measles-containing vaccine may develop fever and rash approximately 1 week after vaccination, and vaccination of susceptible persons results in production of IgM antibody that cannot be distinguished from the antibody resulting from natural infection. A positive measles IgM test cannot be used to confirm the diagnosis of measles in persons with measles-like illness who received measles vaccine 6–45 days before onset of rash. A negative test would exclude the diagnosis. Cases in persons with

measles-like illness who received measles vaccine 6–45 days before onset of rash should be classified as confirmed cases only if a) they meet the clinical case definition, and b) they are epidemiologically linked to a laboratory-confirmed case. For persons receiving vaccine 6–14 days prior to rash onset, specimens for viral isolation should be obtained in addition to serologic testing (see "Laboratory testing"); isolation of wild-type measles virus would allow confirmation of the case (Table 1).

Currently, very few of the suspected and probable cases investigated 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).

Obtaining accurate and complete immunization histories on all confirmed cases

Measles case investigations should include complete immunization histories that document all doses of measles-containing vaccine. All confirmed case-patients should then be classified as recipients of one dose of measles-containing vaccine (as MMR, MMRV, MR or M), two doses, three doses, or no doses of vaccine. The age at vaccination for each dose and the interval between doses should be noted. Written or electronic records with dates of vaccine administration are the only acceptable evidence of vaccination.

Efforts should be made to identify the source of infection for every confirmed case of measles.

Case-patients or their caregivers may have personal copies of immunization records that include dates of administration; these are acceptable for reporting purposes. Usually immunization records must be sought from review of child care or school records (generally available for children attending licensed child care centers or kindergarten through high school), or from providers. Immunization registries, if available, can readily provide vaccination histories. In the absence of a registry, immunization records should be reviewed at providers' clinics or offices. As part of the initial case investigation, case-patients or their parents should be asked where all vaccines were received, including the names of private physicians and out-of-town or out-of-state providers. Records at public health departments and health centers should be reviewed, and private physicians should be contacted and asked to review patient records for this information. With careful planning in an outbreak setting, it is possible to contact providers with a list of all case-patients reported to date for whom data are needed, and to call back at a prearranged time, rather than repeatedly contacting providers for records on individual children.

Identifying 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. In outbreak settings, such histories can often be obtained. 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. Unless a history of exposure to a known case within 7–21 days prior to onset of rash in the case is confirmed, case-patients or their caregivers should be closely queried about all these possibilities.

Assessing potential for transmission and identifying contacts

Transmission is particularly likely in households, schools, healthcare settings and other institutions (e.g., colleges, prisons). As part of the case investigation, the potential for further transmission should be assessed, and exposed contacts of the case-patient during the infectious period (4 days before to 4 days after onset of rash) should be identified. If the case-patient was traveling by plane or ship during the infectious period, the CDC Quarantine Station (operated by the Division of Global Migration and Quarantine) with jurisdiction for the reporting state should be contacted for assistance in the investigation and contact tracing of potentially exposed passengers and crew. This information is available at http://www.cdc.gov/ncidod/dq/quarantine_stations.htm. If unable to contact the Quarantine Station, call the DGMQ 24-hour number at 866-694-4867 for assistance.

Because susceptible contacts are at risk for infection and further transmission to others, they should be vaccinated as quickly as possible. In general, contacts who have not received two doses of measles-containing vaccine on or after the first birthday (doses should be given at least 1 month apart) are considered susceptible. One dose of measles-containing vaccine can be used as evidence of immunity for preschool-aged children and adults not at high risk.[6]

Obtaining specimens for viral isolation.

Efforts should be made to obtain specimens (urine or nasopharyngeal mucus) for virus isolation from all case-patients at the time of the initial investigation; do not wait until serologic test results are received (see Appendix 7). These isolates are essential for tracking the epidemiology of measles in the United States now that measles is not endemic in this country.[1, 7] By comparing isolates from new case-patients with other virus samples, the origin of particular virus types in this country can be tracked. For more information on obtaining and shipping these specimens, see "Laboratory testing."

XII. Outbreak Investigation

Although a complete description of activities to be undertaken in an investigation of a measles outbreak is beyond the scope of this manual, the following guidance may be useful to local health department personnel responsible for outbreak investigations.

Organizing for outbreak investigation

Because investigating an outbreak requires many person-days of work, personnel are frequently transferred to the activity from other duties, or even from other health departments, and may only be involved in outbreak investigation for a few days before they are replaced by others. This turnover in personnel can cause problems unless activities are organized so that the status of the investigation is documented at all times. Some practical suggestions for organizing this activity are listed here.

- Identify a team leader for case investigators so that at least one person knows about all the new cases called in that day and what still needs to be done. Daily briefings are a good way of keeping the whole staff informed of the status of the investigation.
- Use a logbook (or large chalkboard) or an electronic database to record all suspected cases as they are received. The person who receives the initial telephone call should attempt to obtain the information needed to fill in the line listing (see Table 2).
- Create a column in the logbook for actions needed for each suspected case (e.g., "draw blood," "call pediatrician for vaccination history," "notify contacts").
- Keep the logbook in one well-defined location, preferably with folders from investigations of all the cases that have been reported. It is useful to have one stack of all confirmed cases, one stack of suspected or probable cases awaiting further investigation or laboratory results, and a separate stack of discarded cases.
- Establish protocols for control measures necessary for all likely situations (e.g., exposure in a child care center, school, doctor's office, workplace) and clearly define who (local health officer, immunization program manager) will make the decision to proceed when a case investigator identifies a situation that might require major investments of health department resources (such as vaccinating an entire school).

Table 2. Example of line listing for recording data in a measles outbreak investigation

Case ID	Name (Last, First)	Age	Rash onset date	Source of exposure	Blood draw date	IgM result	MMR-1 date	MMR-2 date	Case status
1	Doe, Jane	15 yr	12/31/1999	id #2	1/3/2000		9/16/1985	—	—
2	Smith, Stacey	13 mo	12/16/1999		12/27/1999	+	—	—	lab confirmed
3	Doe, Henry	11 yr	12/26/1999	id #2	1/3/2000		—	—	—
4	Smith, Joe	26 yr	12/30/1999	id #2	1/3/2000		?	—	—

General guidelines for outbreak investigation

Tracking what information is collected and what still needs to be collected. Tracking is easily accomplished by constructing a line listing of cases, which allows ready identification of known and unknown data and ensures complete case investigation. A line listing can be maintained on a computer by using database management or spreadsheet software, but it often is most useful when filled in by hand on a form such as shown in Table 2. Such a line listing provides a current summary of the outbreak and of ongoing case investigations. The line listing is an essential component of every outbreak investigation.

Identifying the population affected by the outbreak. In the course of the outbreak investigation, every suspected case (whether reported through active or passive surveillance or identified through contact investigation) should be investigated thoroughly, as described above. In very large outbreaks, it may not be possible to investigate each reported case thoroughly.

Based on the findings of individual case investigations, the population affected by the outbreak should be characterized in terms of *person* (who is getting measles and how many case-patients have had zero, one, and two doses of measles vaccine?), *place* (where are the cases?), and *time* (when did it start and is it still going on?). For more information on data analysis, see Chapter 20, "Analysis of Surveillance Data." These essential data elements allow public health officials to identify the population at risk of infection (e.g., unvaccinated preschool-age children, high school students who have only received one dose of measles vaccine, persons who visited the emergency department of Hospital A on a certain day), determine where transmission is occurring (child care centers, high schools, healthcare settings), and identify persons who are at potential risk of infection (other unvaccinated preschool-age children, students attending other schools) In general, the most effective outbreak control efforts are those that are targeted on the basis of epidemiologic data rather than those that are directed at the entire community. Neither susceptibility nor risk of exposure is uniformly distributed throughout the community, and resources available for outbreak control are always limited. Therefore, it is essential that data be used to determine the scope of the current outbreak and the potential for spread and that interventions be based on those determinations.

Enhancing surveillance for measles. Many of the activities outlined in the section "Enhancing surveillance" are applicable in the outbreak setting. Previously unreported cases may be identified by reviewing emergency department logs or laboratory records. As part of outbreak response, active surveillance for measles should be established to ensure timely reporting of suspected cases in the population known to be affected by the outbreak, as well as in 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 departments and physicians serving affected communities are usually recruited to participate in active surveillance. Active surveillance should be maintained for at least two incubation periods after the last confirmed case is reported.

XIII. Outbreak Control

The primary strategy for control of measles outbreaks is achieving a high level of immunity (i.e., two doses of measles vaccine) in the population affected by the outbreak. In practice, the population affected is usually more 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, daycare). 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. Recent experience in measles outbreaks shows that almost all persons who are excluded from an outbreak area because they lack documentation of immunity quickly comply with vaccination requirements.

If many cases are occurring among infants younger than 12 months of age, measles vaccination of infants as young as 6 months of age may be undertaken as an outbreak control measure. Monovalent measles vaccine is preferred, but MMR may be administered to children before

the first birthday if monovalent measles vaccine is not readily available. In practice, this recommendation may take several months to implement, and several months to halt once the outbreak has ended. Note that children 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.

Postexposure vaccination and use of immunoglobulin to prevent measles in exposed persons

If given within 72 hours of exposure to measles, measles vaccine may provide some protection. In most settings, postexposure vaccination is preferable to use of immune globulin. Immune globulin can be administered within 6 days of exposure.[3] Immune globulin is indicated for susceptible household or other close contacts of patients with measles, particularly contacts younger than 1 year of age, pregnant women and immunocompromised persons, for whom risk of complications is highest.

Use of quarantine in control of measles outbreaks

Imposing quarantine measures for outbreak control is both difficult and disruptive to schools and other institutions. Under special circumstances, such as during outbreaks in schools attended by large numbers of persons who refuse vaccination, restriction of an event or other quarantine measures might be warranted.

Control of outbreaks in schools and other institutions

During outbreaks in schools, colleges and other institutions of higher education, and other institutions where young adults may have close contact (such as prisons), a program of vaccination with two 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 persons who are not immune to measles should be vaccinated; this includes all students and their siblings and all school personnel born during or after 1957 who cannot provide documentation that they have received two doses of measles-containing vaccine on or after their first birthday or cannot provide other evidence of measles immunity (such as serologic testing). Persons who cannot readily provide documentation of measles immunity should be vaccinated or excluded from the school or other institution. Persons receiving second doses, as well as previously unvaccinated persons receiving their first dose as part of the outbreak control program may be immediately readmitted to school. Persons who continue to be exempted from or who refuse measles vaccination should be excluded from the school, child care, or other institution until 21 days after the onset of rash in the last case of measles.

Control of outbreaks in medical settings

Persons who work in healthcare 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 be immune to measles to prevent any potential outbreak. If an outbreak occurs within or in the areas served by a hospital, clinic, or other medical or nursing facility, all personnel born during or after 1957 should receive two doses of MMR vaccine, unless they have documentation of measles immunity. Personnel born before 1957 without documentation of measles immunity should receive one dose of MMR. Serologic screening of healthcare workers during an outbreak to determine measles immunity is not generally recommended, because stopping measles transmission requires the rapid vaccination of susceptible healthcare workers, which can be impeded by the need to screen, wait for results, and then contact and vaccinate susceptible persons.

Susceptible personnel who have been exposed to measles should be relieved from patient contact and excluded from the facility from the fifth to the 21st day after exposure, regardless of whether they received vaccine or immune globulin after the exposure. Personnel who become ill should be relieved from all patient contact and excluded from the facility for 4 days after they develop rash.

Role of community-wide vaccination efforts in outbreak control

Mass revaccination of entire communities is not of demonstrated benefit in control of measles outbreaks. Such activities may sometimes have to be undertaken because of political or other community demands for "action" and concerns about the acceptability of targeted interventions directed toward selected high-risk populations, but there is no epidemiologic evidence that they are feasible or useful in controlling measles outbreaks.

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