Chapter 6: Measles

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I. Disease description

Measles is an acute viral illness caused by a virus in the family paramyxovirus, genus *Morbillivirus*. Measles is characterized by a prodrome of fever and malaise, cough, coryza, and conjunctivitis, followed by a maculopapular rash. Measles is usually a mild or moderately severe illness. However, measles can result in residual neurological impairment from encephalitis in approximately 5–10 cases per 10,000 reported cases and in death in approximately 1–3 cases per 1,000 reported cases. Pneumonia complicates 6% of measles in the United States, and 19% of cases are hospitalized.

II. Background

Before the introduction of measles vaccine in 1963, roughly one-half million cases of measles were reported each year in the United States. Since then, measles incidence has decreased to a record low of 86 reported cases in 2000.[1]

In recent years, outbreaks of measles have been small, with < 20 cases reported. Recent outbreaks do not have a predominant setting but typically involve people who are exposed to imported measles cases and who are unvaccinated or have received only one dose of measles vaccine.

Specific global goals for reduction in measles morbidity and mortality were set by the World Health Assembly in 1989[2] and the World Summit for Children in 1990.[3] Subsequently, target dates of 2000, 2007, and 2010 for its elimination were established for the Region of the Americas, the European Region, and the Eastern Mediterranean Region of the World Health Organization (WHO), respectively. Since adoption of the regional measles elimination goal at the Pan American Sanitary Conference in 1994 until present, most countries of the Region of the Americas implemented the Pan American Health Organization's recommended vaccination strategies for the interruption of measles virus transmission. The current surveillance data indicate that measles virus transmission in the Region of the Americas has been reduced in 2002 to historically low levels and possibly interrupted.[4]

However, measles continues to cause substantial morbidity and mortality globally. The Global Burden of Disease 2000 Study estimated that measles resulted in 777,000 deaths worldwide in 2000, of which 452,000 (58%) deaths were in the African Region of the WHO.[5] Thus, measles remains the leading cause of vaccine-preventable child mortality, with the remaining global disease burden being primarily attributable to the underutilization of measles vaccine. To address this issue, the WHO and the United Nation's Children's Fund developed

the Strategic Plan for Measles Mortality Reduction and Regional Elimination 2001–2005; the Plan seeks to (1) reduce the number of measles deaths by half by 2005 compared with 1999 levels, (2) achieve and maintain interruption of indigenous measles transmission in large geographical areas with established elimination goals, and (3) review the progress and assess the feasibility of global measles eradication at a global consultation in 2005.[6] The recommended strategies for reducing measles mortality include:

- providing the first dose of measles vaccine to successive cohorts of infants
- ensuring that all children have a second opportunity for measles vaccination through supplemental immunization activities, routine immunization services, or a combination of these
- enhancing measles surveillance with integration of epidemiological and laboratory information
- improving the management of every measles case[7]

To advocate for reduction of measles mortality in Africa, a new international partnership was formed in February 2001 at a meeting hosted by the American Red Cross. In the first year of the measles partnership, supplementary measles vaccination campaigns were conducted in eight countries (Benin, Burkina Faso, Cameroon, Ghana, Mali, Tanzania, Togo, and Uganda), vaccinating 21 million children. These campaigns are predicted to prevent an estimated 47,000 measles deaths over the next three years.[8]

III. Importance of rapid case 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 under-vaccinated 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 strains.[9] Current surveillance data indicate this goal has been achieved. 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. Current elimination strategies emphasize 90% measles vaccination coverage among children by 2 years of age and assuring vaccination with a second dose of measles vaccine for all school and college students.

VI. Case definitions

The following case definition for measles has been approved by the Council of State and Territorial Epidemiologists (CSTE) and was published in 1997.[10]

Clinical case definition

Measles is an illness characterized by all of the following:

- A generalized maculopapular 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
- Significant rise in measles antibody level by any standard serologic assay
- Isolation of measles virus from a clinical specimen

Case classification

Suspected: Febrile illness accompanied by generalized maculopapular 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 the National Notifiable Diseases Surveillance System (NNDSS). All confirmed cases should be classified as one of the following:

International importation: An imported case has its source outside the country, its rash onset occurs within 21 days after entering the country, and the illness cannot be linked to local transmission.

Indigenous case: Any case that cannot be proved to be imported should be classified as indigenous. Indigenous cases are sub-classified as follows:

- **Epidemiologically linked to importation:** Cases that are linked in a chain of transmission to imported cases should be classified as indigenous cases with an epidemiologic link to importation.

- **Virologic evidence of importation:** Cases in a chain of transmission from which a virus is cultured that is not endemic in the United States are classified as indigenous cases with virologic evidence of importation. It is essential to obtain specimens for virology from every sporadic case (or at least 5 specimens from large chains of transmission) to assure adequate virologic information. Often the virologic information is not available at the time of reporting and the sub-classification is determined later. Cases which are epidemiologically linked to importation and have virologic evidence of importation are sub-classified as epidemiologically linked.

- **Unknown source:** Indigenous cases which are not epidemiologically linked to importation and have no virologic evidence of importation are sub-classified as unknown source cases.

Out-of-state importation: Although the basic classification divides cases into international importations and indigenous cases, states may also choose to classify cases as out-of-state importations when a case is imported from another state in the United States. The possibility that a patient was exposed within his or her state of residence should be excluded; therefore, the patient either must have been out of state continuously for the entire period of possible exposure (at least 7–21 days before onset of rash) or have had one of the following types of exposure while out of state: a) face-to-face contact with a person who had either a probable or confirmed case, or b) attendance in the same institution as a person who had a case of measles (e.g., in a school, classroom, or childcare center). Out-of-state importations are uncommon.

To minimize the problem of false positive laboratory results, restrict case investigation and laboratory testing to patients most likely to have measles? those with fever and generalized maculopapular rash.

VII. Laboratory testing

Because measles is an extremely rare disease in the United States, 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 today do not have measles. Because measles is such a highly contagious disease, 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, it is crucial to use laboratory diagnosis to confirm the few actual measles cases among the thousands of patients with suspected measles.

Because measles is so rare, even with the excellent laboratory tests available, there will be some false positive results. (The positive predictive value of a test [PPV] is the proportion of people with positive results who actually have the disease. The PPV decreases when the disease becomes rare.) Some false

positive results are expected, and it is preferable to misclassify as measles a few cases that are not actually measles than to miss cases that are measles.

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 results.

Serologic testing

Serologic testing for antibodies to measles is widely available. Generally, in a previously susceptible person exposed to either vaccine-related or wild-type measles virus, the IgM response starts first around the time of rash onset and is transient, persisting 1–2 months. The IgG response starts more slowly, at about 7 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 drawn roughly two weeks apart. Uninfected persons are IgM negative and will either be IgG negative or IgG positive depending upon their previous infection or vaccination histories.

Recommendations for serologic testing for measles

- An enzyme immunoassay (EIA) test for IgM antibody to measles in a single serum specimen, drawn at the first contact with the suspected measles case, 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) may be tested for a rise 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 testing) neither IgM nor IgG antibody responses can distinguish measles disease from the response to vaccination.

Tests for IgM antibody

Although there are multiple possible methods for testing for IgM antibody, EIAs are the most consistently accurate tests and are therefore the recommended method. 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. Problems with removal of IgG antibodies can lead to false positive tests[11] 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. This is the preferred reference test for measles. One direct capture IgM EIA is commercially available.

EIA tests for measles are often positive on the day of rash onset. However, in the first 72 hours after rash onset, up to 30% of tests for IgM may give false negative results. Tests that are negative in the first 72 hours after rash onset should be repeated (**Table 1**); serum should be obtained for repeat testing 72 hours after rash onset. IgM is detectable for at least 28 days after rash onset and frequently longer.[12]

Tests that are negative in the first 72 hours after rash onset should be repeated; serum should be obtained for repeat testing 72 hours after rash onset. IgM is detectable for at least 30 days after rash onset and frequently longer.

When a laboratory IgM test is suspected of being false positive (**Table 1**), additional tests may be performed. False positive IgM results for measles may be due to the presence of rheumatoid factor in serum specimens. Serum specimens from patients with other rash illness, such as parvovirus B19, rubella, and roseola have been observed to result in false positive reactions in some IgM tests for measles. False positive tests may be suspected when thorough surveillance reveals no source or spread cases, when the case does not meet the clinical case definition, or when the IgG result is positive within 7 days of rash onset. In these situations, confirmatory tests may be done at the state public health laboratory or at CDC. IgM results by tests other than EIA can be validated with EIA tests. Indirect EIA tests may be validated with capture EIA tests.

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 the IgM tests remain inconclusive, a second (convalescent) serum specimen, collected 14–30 days after the first (acute) specimen, can be used to test for an increase in the 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 and include 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 plaque reduction neutralization test of IgG in acute and convalescent paired sera.

IgG testing for laboratory confirmation of measles requires the demonstration of a rise in the titer of antibody against measles. The tests for IgG antibody should be conducted on both acute and convalescent specimens at the same time. The same type of test should be used on both specimens. The specific criteria for documenting an increase in titer depend on the test. EIA values are not titers and increases in EIA values 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. However, a negative culture or RT-PCR does not rule out measles because the tests are not very sensitive and are much affected by the timing of specimen collection and the quality and handling of the clinical specimens. Since culture and RT-PCR take weeks to perform, they are rarely useful in confirming the diagnosis of measles. If positive, these tests can be useful adjuncts to diagnosing acute measles when serology results are inconclusive. Also, if measles virus is cultured or detected by RT-PCR, the viral genotype can be used to distinguish between measles disease, caused by a wild-type measles virus, and a response to measles vaccination, caused by a vaccine strain.

Although rarely useful to diagnose measles, viral culture and RT-PCR are extremely important for molecular epidemiologic surveillance to help determine 1) the origin of the virus, 2) which viral strains are circulating in the United States, and 3) whether these viral strains have become endemic in the United States. Isolation of measles virus is technically difficult and is generally performed in research laboratories.

Specimens (urine, nasopharyngeal aspirates, heparinized blood, or throat swabs) for virus culture should be obtained from clinically suspected cases of measles.

Specimens (urine, nasopharyngeal aspirates, heparinized blood, or throat swabs) for virus culture obtained from clinically suspected cases of measles should be shipped to the state public health laboratory or to the 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 6**). 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 if the opportunity to collect a specimen occurs more than 10 days after rash onset.

For additional information on laboratory support for surveillance of vaccine-preventable diseases, see Chapter 19, “Laboratory Support for Surveillance of Vaccine-Preventable Diseases.”

VIII. Reporting

Each state and territory has regulations or laws governing the reporting of diseases and conditions of public health importance.[13] These regulations and laws list the diseases to be reported and describe those persons or groups responsible for reporting, such as health-care providers, hospitals, laboratories, schools, daycare and childcare facilities, and other institutions. Contact your local or state health department for reporting requirements in your state.

Reporting to CDC

Provisional reports of suspected measles should be promptly reported to the CDC by the state health department or directly to the CDC by telephone at 404-639-8230 or by e-mail (sbr1@cdc.gov). Case information should then also be

reported by the state health department to the National Notifiable Diseases Surveillance System (NNDSS) through the National Electronic Telecommunications System for Surveillance (NETSS) or the National Electronic Disease Surveillance System (NEDSS), once available, 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: CDC, National Immunization Program (NIP), Epidemiology and Surveillance Division, publishes a monthly 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 (sbr1@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
  - Serological test results
  - Date of collection of specimen for virus isolation

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Information to collect (con't.)

- Vaccination status
  - Number of doses of measles vaccine received
  - Dates of measles vaccinations
  - Manufacturer name
  - Vaccine lot number
  - If not vaccinated, reason

- Epidemiological
  - Transmission setting
  - Source of transmission (e.g., age, vaccination status, relationship to decedent)
  - 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)
  - Travel history

IX. Vaccination

Measles vaccine is incorporated with mumps and rubella vaccine as a combined vaccine (MMR). The current Advisory Committee on Immunization Practices (ACIP) recommendations for routine vaccination indicate a first dose at 12–15 months of age with a second dose at school entry (4–6 years).[14]

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, the 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 16, "Enhancing Surveillance."

Reviewing death certificates

Mortality data are available through the vital records systems in all states. They may be available soon after deaths occur in states using electronic death certificates. Although no acute deaths from measles in the United States have been documented since 1992, each measles-associated death is important and warrants a full investigation. Mortality data should be reviewed each year to

identify deaths that may be due to measles. Any previously unreported cases identified through this review should be thoroughly investigated and reported.

Investigating contacts

Determining the source or chain of disease transmission, identifying all contacts (household, childcare, 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 during outbreaks. Local or state health departments should contact health-care 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.[15]

Monitoring 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 number of cases that meet the clinical case definition, but are not confirmed
- The number of cases that meet the clinical case definition in which measles is ruled out by appropriate laboratory testing
- The number of chains of transmission that have an imported source
- The number of chains of transmission for which at least one clinical specimen for virus isolation was collected and submitted to CDC

Another important indicator of the adequacy of the measles surveillance system is the level of investigative effort. This is measured as the number of suspected measles cases investigated and discarded for a particular area and may be expressed as a population rate. Even in the absence of measles, measles-like illnesses occur and should be investigated.[16] A program which reports no investigation of suspected cases cannot be assumed to have adequate measles surveillance. For more information on surveillance indicators, see Chapter 15, "Role of Surveillance in Disease Elimination Programs."

XI. Case investigation

All reports of suspected measles cases should be investigated immediately. The measles surveillance worksheet (see **Appendix 7**) 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 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 or not a reported case meets the clinical case definition (see "Case definitions"). If the case was reported within 3 days of onset of rash, there must be appropriate follow-up to establish rash of at least 3 days' duration.

Case investigation and vaccination of susceptible household contacts should not be delayed pending the return of laboratory results.

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.[16] 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 in the absence of laboratory confirmation. This is particularly important as the outbreak is ending; at that point, laboratory confirmation should be sought for all suspected cases.

The occurrence of measles-like illness in recently vaccinated persons can pose particular difficulties in the outbreak setting. Ten percent of recipients of measles-containing vaccine may develop fever and rash approximately one week after vaccination, and vaccination of susceptible persons results in the 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. Persons with measles-like illness who received measles vaccine 6–45 days before onset of rash should be classified as confirmed cases of measles **only if** (1) they meet the clinical case definition, and (2) 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.

Currently, very few of the suspected and probable cases investigated are confirmed as measles. 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, measles-rubella, or measles vaccine), two doses, three doses, or no doses of vaccine. The age of vaccination for each dose and the interval between doses should be noted. Written records with dates of vaccine administration are the only acceptable evidence of vaccination.

Some case-patients or their caregivers may have personal copies of immunization records available that include dates of administration; these are acceptable for reporting purposes. Usually immunization records must be sought from review of childcare or school records (generally available for children attending licensed childcare 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 searched 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 identify contacts. Transmission is particularly likely in households, schools, and other institutions (colleges, prisons, etc.), and in health-care settings. As part of the case investigation, the potential for further transmission should be assessed, and contacts of the case-patient during the infectious period (4 days before to 4 days after onset of rash) should be identified. In general, contacts who have not received two doses of measles-containing vaccine on or after the first birthday separated by at least 1 month are considered susceptible. These susceptible contacts are at risk for infection and further transmission to others and should be vaccinated as quickly as possible.

Obtain specimens (urine or nasopharyngeal mucus) for virus isolation from all cases (or from at least some cases in each outbreak) at the time of the initial investigation; do not wait to receive serologic test results.

Obtaining 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; do not wait until serologic test results are received (see **Appendix 6**). These isolates are essential for tracking the epidemiology of measles in the United States now that measles is not endemic in this country.[1] By comparing isolates from new case-patients to 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.

Currently, very few of the suspected and probable cases investigated are confirmed as measles. 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).

Organizing for outbreak investigation

Because investigating an outbreak requires many person-days of work, personnel are frequently transferred to the activity from other responsibilities in the health department or 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.

- Use a logbook (or large chalkboard) 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 ("draw blood," "call pediatrician for vaccination history," "notify contacts").

- 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.

- Keep the logbook in one well-defined location, preferably with folders with the case 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 lab results, and a separate stack of discarded cases.

- Establish protocols for control measures necessary for all likely situations (exposure in a childcare center, school, doctor's office, workplace, etc.) 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 a whole school).

General guidelines for outbreak control

Tracking what information is collected and what still needs to be collected. Tracking is easily accomplished by constructing a line listing of cases, allowing ready identification of known and unknown data and ensuring complete case investigation. A line listing can be maintained on a computer using database management or spreadsheet software but 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.

In general, the most effective outbreak control efforts are those that are targeted based upon epidemiologic data, rather that those that are directed at the entire community.

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, but fortunately no very large outbreaks (> 200 cases) have occurred in the United States since 1992.

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 17, “Analysis of Surveillance Data.”) These essential data elements allow public health officials to identify the population at risk of infection (unvaccinated preschool-age children, high school students who have only received one dose of measles vaccine, persons who visited the emergency room of Hospital A on a certain day,

etc.), determine where transmission is occurring (childcare centers, high schools, health-care settings), and identify persons who are at potential risk of infection (other unvaccinated preschool-age children, students attending other schools, etc.) In general**, the most effective outbreak control efforts are those that are targeted based upon 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 "Enhanced surveillance" are applicable in the outbreak setting. 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 1 month 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 in the population in which the outbreak is occurring. In practice, the population affected is usually rather narrowly defined (such as one or more schools); high immunity in the population is obtained by achieving high coverage with 2 doses of measles vaccine in the affected population. Persons who cannot readily document measles immunity should be vaccinated or excluded from the setting (school, hospital, 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. The 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 < 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.

Control of outbreaks in schools and other institutions

During outbreaks in elementary, junior, and senior high schools, and 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 revaccination with MMR vaccine is recommended in the affected schools or institutions. Recent 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 general, voluntary efforts have been much less successful than mandatory two-dose requirements for control of outbreaks. Therefore, public health officials should strongly consider implementing mandatory two-dose requirements for children in affected schools and other institutions. The scope of vaccination effort needed will depend on 1) age-appropriate first- and second-dose coverage with MMR in the community, 2) population density, 3) resources available, and 4) patterns of social contacts within the community. During an outbreak, strong consideration should be given to expanding two-dose requirements to all schools in the community.

In a school with a measles outbreak, all students and their siblings and all school personnel born in 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) should be vaccinated. Persons who cannot readily provide documentation of measles immunity should be vaccinated or excluded from the school or other institution. Persons revaccinated, 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, childcare, 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 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 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 in or after 1957 (including volunteers, trainees, nurses, physicians, technicians, receptionists, and other clerical and support staff) should receive a dose of MMR vaccine, unless they have documentation of measles immunity. Serologic screening of health-care workers during an outbreak to determine measles immunity is not generally recommended, because arresting measles transmission requires the rapid vaccination of susceptible health-care workers, which can be impeded by the need to screen, wait for results, and then contact and vaccinate the susceptible persons.

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 vaccine or immune globulin after the exposure. Personnel who become ill should be relieved from all patient contact and excluded from the facility for 7 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 epidemiological evidence that they are feasible or useful in controlling measles outbreaks.

Limited usefulness of quarantine in control of measles outbreaks

Imposing quarantine measures for outbreak control is usually 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. However, such actions are not recommended as a routine measure for control of most outbreaks.

Post-exposure 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, post-exposure vaccination is preferable to use of immune globulin. However, immune globulin should be given to pregnant women and immunosuppressed person who are exposed to measles. Immune globulin may be preferred for infants < 1 year of age who are household contacts of measles patients because it is likely that they will have been exposed more than 72 hours prior to measles diagnosis in the household member, and they are at highest risk of complications from the disease.

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

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

IgM result	Optimal time for specimen collection?[a]	Recent vaccination?[b]	Meets clinical case definition?[c]	Epidemiological linkage?[d]	Wild-type measles virus identified?	Case classification
+	Yes or No*	No	Yes or No	Yes or No	Yes or No	Confirmed[e]
+	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 or No	Yes or No	No	Discard[f]

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

[b] Recent vaccination means receipt of measles-containing vaccine 6–45 days before rash onset.

[c] Clinical case definition includes generalized maculopapular rash lasting = 3 days and fever (> 101º F or 38.3º C) and cough, coryza, or conjunctivitis.

[d] Epidemiological linkage means contact with a laboratory-confirmed case (source or spread case) during the appropriate period for transmission.

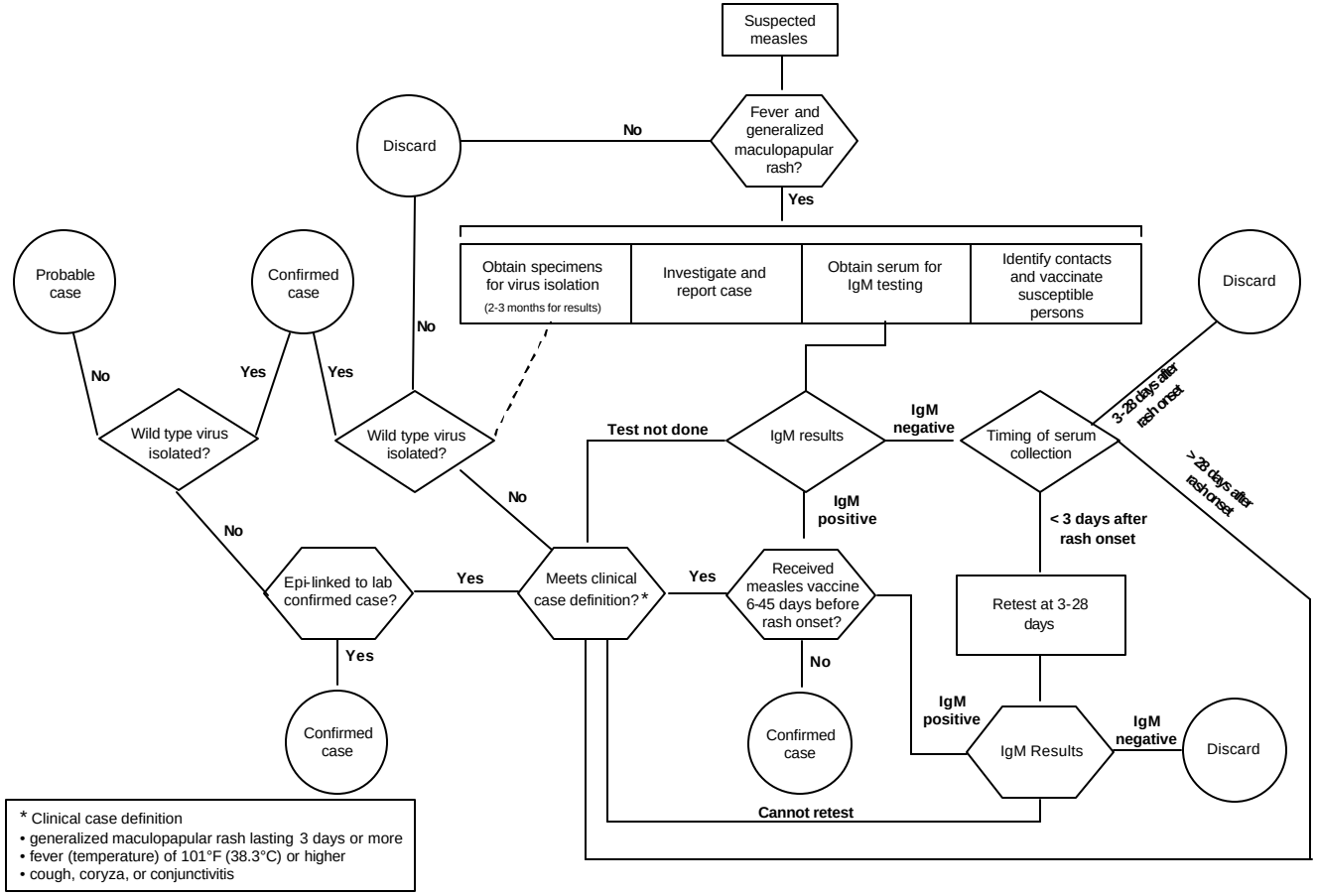
[e] The possibility of a false positive IgM test is increased when: 1) the IgM test was not an EIA test, 2) the case did not meet clinical case definition, 3) the case is an isolated indigenous cases (no epidemiological link to another confirmed case and no international travel), or 4) measles IgG is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

[f] Whenever possible, collect another serum specimen during optimum time for collection (3–28 days after rash onset), conduct an IgM test, and interpret the result according to this table. If a second specimen cannot be obtained, discard the case.

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

Case ID	Name (Last, First)	Age	Date of birth	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		?	—	—

Figure 1. Measles Case Investigation



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4	Smith, Joe	26 yr		12/30/1999	id#2	1/3/2000		?	--	--

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