

## Chapter 7: 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 (as high as 105°F) and malaise, cough, coryza, and conjunctivitis, followed by a maculopapular rash.<sup>1</sup> The rash usually appears 14 days after exposure and spreads from head to trunk to lower extremities. Measles is usually a mild or moderately severe illness. However, measles can result in complications such as pneumonia, encephalitis, and death. Postinfectious encephalitis may occur approximately one per 1,000 reported measles cases.<sup>2,3</sup> Approximately two to three deaths may occur for every 1,000 reported measles cases.<sup>4</sup>

One rare long-term sequelae 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 (U.S.) in 1989–1991, the risk of SSPE was estimated to be 4–11 cases/100,000 cases of measles.<sup>5,6</sup> The risk of developing SSPE may be higher when measles occurs prior to the second year of life.<sup>5</sup>

The average incubation period for measles is 14 days, with a range of 7–21 days.<sup>7</sup> Persons with measles are usually considered infectious from four days before until four days after onset of rash with the rash onset being considered as day zero.

### II. Background

#### *Epidemiology of measles in the United States*

##### **Pre-elimination era**

In the decade prior to the licensure of live measles vaccine in 1963, an average of 549,000 measles cases and 495 measles deaths were reported annually.<sup>8</sup> However, almost every American was affected by measles during their lifetime; it is estimated that 3–4 million measles cases occurred each year.<sup>9–13</sup> Following implementation of the one dose measles vaccine program, there was significant reduction in the reported incidence in the United States by 1988 resulting in decline in measles-related hospitalizations and death.<sup>13–15</sup>

During 1989–1991, a resurgence of measles occurred when over 55,000 cases and 123 deaths were reported. The epidemiology during the resurgence was characterized mainly by cases in unvaccinated preschool-age children who had not been vaccinated on time with one dose of measles vaccine.<sup>16</sup> In addition, outbreaks were reported among highly vaccinated school-age children who received one dose of measles-containing vaccine. In 1989, a second-dose vaccination schedule was recommended by the Advisory Committee on Immunization Practices (ACIP), the American Academy of Pediatrics (AAP), and the American Academy of Family Physicians (AAFP).<sup>15, 17–19</sup> In 1998, the ACIP recommended that states ensure second dose coverage of children in all grades by 2001.<sup>20</sup> Following the resurgence, improved implementation of the timely administration of the first dose of MMR vaccine and increased implementation of two doses among school-age children led to a dramatic decline in measles cases.

In 2000, endemic measles was declared “eliminated<sup>17</sup>” from the United States.<sup>21</sup>

<sup>1</sup> Elimination is defined as the absence of endemic measles cases for a period of twelve months or more, in the presence of adequate surveillance (World Health Organization)

### Post-elimination era

During 2001–2011, 911 measles cases were reported.<sup>22</sup> The median number of measles cases reported per year was 62 (range: 37–220 cases/year). Measles incidence has continuously remained below one case per million since 1997. The majority of measles cases were unvaccinated (65%) or had unknown vaccination status (20%). Of the 911 reported measles cases, 372 (40%) were importations (on average 34 importations/year), 239 (26%) were epidemiologically linked to these importations, 190 (21%) either had virologic evidence of importation or had been linked to those cases with virologic evidence of importation, and 110 (12%) had unknown source. Unknown source cases represent cases where epidemiologic- or virologic-link to an imported case was not detected.

The highest incidence of measles cases in recent years occurred in 2008 (0.48 cases/million) and 2011 (0.72 cases/million). The epidemiology of measles in 2008 was characterized by (1) a high proportion (95%) of cases among U.S. residents who were unvaccinated or who had unknown vaccination status, most of whom were U.S. school-age children whose parents had religious or philosophical objections to vaccination, and (2) more spread from imported cases than other years.<sup>23</sup> In 2011, 220 measles cases were reported, the highest number of reported measles cases since 1996; 80 (36%) were importations, 144 (65%) were unvaccinated, and 47 (21%) had unknown vaccination status. Most of the importations were the result of unvaccinated U.S. travelers who had traveled to measles endemic countries, mainly Western Europe and India.<sup>24</sup>

Although measles elimination has been achieved in the United States, importation of measles will continue to occur as measles remains endemic in many other parts of the world.<sup>23, 25–28</sup> Thus, current measles epidemiology in the United States is determined by characteristics of the imported case and their susceptible contacts.

### Measles outbreaks in the United States in the post-elimination era

From 2001 through 2011, 63 outbreaks<sup>2</sup> of measles were reported; they were small with a median of six cases (range: 3–34). The outbreaks mostly involved individuals who were exposed to imported measles cases or were infected during a resulting chain of transmission and who were either unvaccinated or had unknown vaccine status. Lack of adherence to existing recommendations for measles prevention among groups at high risk (for example, individuals who travel internationally), can spread measles to susceptible populations, including infants too young to be vaccinated and groups who routinely oppose vaccination.<sup>28–32</sup> However, the size of the outbreaks was limited due to immediate control measures, high population immunity, and high measles vaccine effectiveness.

The settings, when known, included households, educational facilities (e.g., schools, day care), churches, health care, homeless shelters, and congregate settings. Traveling to measles endemic regions was also commonly reported. The most commonly reported setting in 2011 was associated with household.

Responding to measles cases and outbreaks is time consuming and costly for state health departments.<sup>25, 27, 33, 34</sup> An outbreak in San Diego in 2008 cost the public health department \$124,517 to contain, with additional medical costs and costs incurred by families for quarantining unvaccinated contacts at home. Total outbreak costs were \$176,980.<sup>25</sup> Another outbreak in 2008 affecting several hospitals cost about \$800,000 to contain, more than \$100,000 per case.<sup>27</sup>

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<sup>2</sup> National reporting: An outbreak is defined as a chain of transmission including 3 or more cases linked in time and space.

### *Global measles*

Despite tremendous achievements towards global measles mortality reduction and measles elimination goals, globally, in 2010, there were 327,305 measles cases reported and an estimated 139,300 measles deaths (i.e., approximately 380 deaths/day).<sup>35,36</sup> During 2009–2010, measles outbreaks were reported in Europe, Africa and Asia.<sup>37–43</sup> In 2010–2011, Western Europe saw a rise in measles cases with at least 33 countries reporting more than 68,743 measles cases, resulting in importations into the Americas.<sup>44–49</sup> In countries where measles has been eliminated, cases imported from other countries remain an important source of infection.

In the Americas, under the leadership of the Pan American Health Organization (PAHO), Ministries of Health have implemented an aggressive measles elimination program. In 2004, scientific evidence suggested that endemic transmission of measles virus in the Americas was interrupted for  $\geq 12$  months in 2002.<sup>50</sup> The Region of the Americas is in the process of verifying elimination of measles or maintenance of elimination in every country in the Region.<sup>51</sup>

Important measures are underway to achieve measles elimination in Europe, the Eastern Mediterranean, and the Western Pacific regions by 2015, and the African region by 2020. Achieving these elimination goals will have direct benefits in the United States.

Outbreak preparedness and response is one of the five core strategies in the 2012–2020 WHO strategic plan for global measles and rubella.<sup>52</sup>

## **III. Maintenance of Elimination**

Endemic measles was declared “eliminated” in the United States in 2000.<sup>11,21</sup> To maintain elimination, rapid detection of cases is necessary so that appropriate control measures can be quickly implemented. This is to prevent imported strains of measles virus from establishing endemic chains of transmission. The key challenges to maintaining the elimination of measles from the United States are

- vaccinating children at age 12–15 months with a first dose of MMR vaccine,
- ensuring that school-age children receive a second dose of MMR vaccine,
- vaccinating high-risk groups, such as health care personnel and international travelers including infants aged 6 to 11 months,
- maintaining measles awareness among health care personnel and the public, and
- working with US Government agencies and international agencies, including World Health Organization (WHO), on global measles mortality reduction and elimination goals.

In addition, pockets of unvaccinated populations can pose a risk to maintaining elimination.<sup>23,53</sup>

## **IV. Vaccination**

Live attenuated measles virus vaccine is incorporated into combination MMR vaccine and combination measles, mumps, rubella, and varicella (MMRV) vaccines. Monovalent measles vaccine is not available in the United States.

For prevention of measles, two doses of MMR vaccine are recommended routinely for children, with the first dose at age 12 through 15 months and the second dose at ages four through six years (school entry).<sup>13</sup>

For prevention of measles among adults, two doses of MMR vaccine are also recommended for adults at high risk, including international travelers, college and other post-high school students, and health care personnel born during or after 1957.<sup>13</sup> All other adults, born during or after 1957, without other presumptive evidence of measles immunity should be vaccinated with one dose of MMR vaccine. Vaccination recommendations for an outbreak setting are discussed in the “Control Measures” section later in this chapter.

MMRV vaccine is currently available in limited supply.<sup>54</sup> For supply status, see [http://www.cdc.gov/vaccinesafety/Vaccines/MMRV/MMRV\\_qa.html](http://www.cdc.gov/vaccinesafety/Vaccines/MMRV/MMRV_qa.html)

For more details on health care personnel please see the section ‘Health care settings’ in this chapter.

### *Travel recommendations*

Children aged 6–11 months who travel internationally should receive one dose of MMR vaccine optimally at least two weeks prior to travel. Because serologic response to the measles component of the vaccine varies among infants aged 6–11 months, children vaccinated before age 12 months should receive two additional doses of MMR or MMRV vaccine on or after the first birthday according to the routine recommended schedule.<sup>13, 55</sup>

Children aged  $\geq 12$  months and adults who plan to travel outside the United States should receive two doses of MMR vaccine, separated by at least 28 days. Other presumptive evidence of immunity includes laboratory evidence, or birth before 1957, or laboratory confirmation of disease. (See below under *Presumptive evidence of immunity*).

## **V. Presumptive Evidence of Immunity**

Acceptable presumptive evidence of measles immunity includes at least one of the following<sup>13</sup>:

- written documentation of adequate vaccination: receipt of one or more doses of a measles-containing vaccine administered on or after the first birthday for preschool-age children and adults not at high risk, and two doses of measles-containing vaccine for school-age children and adults at high risk for exposure transmission (i.e., health care personnel, international travelers, and students at post-high school educational institutions); or
- laboratory evidence of immunity; or
- birth before 1957; or
- laboratory confirmation of disease.

Persons who do not meet the above criteria are considered susceptible and should be vaccinated unless contraindicated.

*For health care settings please see the section ‘Health care settings’ below as the criteria are slightly different.*

## **VI. Case Definition**

The following case definition for case classification of measles cases, including case classifications for importation status, has been approved by the Council of State and Territorial Epidemiologists (CSTE) and was published in 2012.<sup>56</sup>

### *Disease-specific data elements:*

#### **Clinical information**

Date of onset, fever

Date of onset, rash

#### **Epidemiological risk factors**

Contact with measles case

Recent travel destination(s), if any

Travel return date

Measles-containing vaccine (total) doses

Last measles vaccination date

#### **Case definition for case classification**

**Clinical description:**

- An acute illness characterized by:
  - Generalized, maculopapular rash lasting  $\geq 3$  days; and
  - temperature  $\geq 101^\circ\text{F}$  or  $38.3^\circ\text{C}$ ; and
  - cough, coryza, or conjunctivitis

**Probable:**

- In the absence of a more likely diagnosis, an illness that meets the clinical description with:
  - no epidemiologic linkage to a laboratory-confirmed measles case; and
  - noncontributory or no measles laboratory testing.

**Confirmed:**

- An acute febrile rash illness<sup>†</sup> with:
  - isolation of measles virus<sup>‡</sup> from a clinical specimen; or
  - detection of measles virus-specific nucleic acid<sup>‡</sup> from a clinical specimen using polymerase chain reaction; or
  - IgG seroconversion<sup>‡</sup> or a significant rise in measles immunoglobulin G antibody<sup>‡</sup> using any evaluated and validated method; or
  - a positive serologic test for measles immunoglobulin M antibody<sup>§</sup>; or
  - direct epidemiologic linkage to a case confirmed by one of the methods above.

<sup>†</sup> Temperature does not need to reach  $\geq 101^\circ\text{F}/38.3^\circ\text{C}$  and rash does not need to last  $\geq 3$  days.

<sup>‡</sup> Not explained by MMR vaccination during the previous 6–45 days.

<sup>§</sup> Not otherwise ruled out by other confirmatory testing or more specific measles testing in a public health laboratory.

*Note: Genotype identification by a WHO reference laboratory (CDC or a public health laboratory that has validated their measles virus sequence analysis) is required to distinguish wild type from vaccine strain if vaccinated within 18 days of rash onset.*

**Epidemiologic classification of internationally-imported and U.S.-acquired**

**International importation:** An internationally imported case is defined as a case in which measles results from exposure to measles virus outside the United States as evidenced by at least some of the exposure period (7–21 days before rash onset) occurring outside the United States and rash onset occurring within 21 days of entering the United States and there is no known exposure to measles in the U.S. during that time.

All other cases are considered U.S.-acquired.

**U.S.-acquired case:** An 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.

Genotype identification by a WHO reference laboratory (CDC or a public health laboratory that has validated their measles virus sequence analysis) is required to distinguish wild type from vaccine strain if vaccinated within 18 days of rash onset.

**U.S.-acquired cases are sub-classified 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  $\geq 12$  months). Any genotype that is found repeatedly in U.S.-acquired cases should be thoroughly investigated as a potential endemic genotype, especially if the cases are closely related in time or location.

**Endemic case:** A case for which epidemiological or virological evidence indicates an endemic chain of transmission. Endemic transmission is defined as a chain of measles virus transmission that is continuous for  $\geq 12$  months within the United States.

**Unknown source case:** A case for which an epidemiological or virological link to importation or to endemic transmission within the United States 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 United States.

*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, however, cases will be classified as either internationally imported or U.S.-acquired. 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 probable or confirmed measles, or b) attendance in the same institution as a person with measles (e.g., in a school, classroom, or childcare center).

## VII. Laboratory Testing

*Collection of virologic and serologic specimens is recommended for every case.*

Laboratory confirmation is essential for all outbreaks and all sporadic measles cases. Detection of measles-specific IgM antibody and measles RNA by real-time RT-PCR are the most common methods for confirmation of measles infection. Efforts should be made to obtain a serum sample and throat swab (or nasopharyngeal swab) from suspected cases at first contact. Urine samples may also contain virus and when feasible to do so, collection of both respiratory and urine samples can increase the likelihood of detecting virus. Staff at the CDC measles laboratory is available for consultation and can assist with confirmatory testing as needed for measles. For details on all types of specimens (serum, respiratory, urine) collection and transport, see the CDC measles lab website: <http://www.cdc.gov/measles/lab-tools/index.html>.

Because measles is a rare disease in the United States, even with the excellent laboratory tests available, false positive results for measles IgM will occur. 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 (i.e., those who meet the clinical case definition, especially if they have risk factors for measles, such as being unvaccinated, recent history of travel abroad, without an alternate explanation for symptoms, for example epi-linked to known parvovirus case) or those with fever and generalized maculopapular rash with strong suspicion of measles.

During a measles investigation when community awareness is increased, many cases of febrile rash illness may be reported as suspected measles, and the magnitude of the situation may be exaggerated if these cases are included in the absence of laboratory confirmation. This is particularly important as the investigation is ending; at that point, laboratory confirmation should be sought for all suspected cases. Rarely, suspected cases may include vaccinated individuals. For these cases, laboratory confirmation may be challenging. An overview of diagnostic tools is described below.

### *Virus isolation in cell culture and measles RNA detection (RT-PCR)*

Clinical specimens for real-time polymerase chain reaction (RT-PCR) and virus isolation should be collected at the same time as samples taken for serologic testing. The preferred specimens for virus isolation or RT-PCR are throat or nasopharyngeal swabs, but urine may also contain virus. Virus isolation and RNA detection are more likely to be successful when the specimens are collected early (ideally within three days of rash onset, but up to ten days post rash may be successful). Isolation of measles virus in culture or detection of measles RNA by RT-PCR in

clinical specimens confirms the diagnosis of measles. *However, a negative culture or negative RT-PCR results do 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.*

Successful isolation of measles virus in culture or direct detection of measles RNA by RT-PCR in the clinical sample is particularly helpful for case confirmation when serology results are inconclusive. The Vero/hSLAM cell line, a recombinant cell line with a receptor for measles virus, has greatly improved the ability to isolate measles virus in cell culture.

### **Molecular analysis to determine genotype of measles**

Determination of the measles genotype provides the only means to distinguish between wild type virus infection and a rash caused from a recent measles vaccination. In addition, the collection of appropriate specimens from which virus or viral RNA can be obtained or amplified is extremely important for molecular epidemiologic surveillance to identify the genotypes associated with imported cases of measles. This information is used to track transmission pathways, link cases to countries overseas, and to document the absence of endemic circulation of measles in the United States.<sup>57</sup> Sequence analysis and genotyping for measles virus is conducted at the CDC measles laboratory. Refer to the CDC measles laboratory website for additional information on sample collection, processing and the genetic analysis of measles.

### *Serologic testing*

The state health department can provide guidance regarding available laboratory services. At the direction of the state health department, health care providers and state and local health departments may send serum specimens from suspected measles cases to the CDC measles laboratory. For detailed information on blood collection and shipping, refer to the CDC measles laboratory website: <http://www.cdc.gov/measles/lab-tools/index.html>.

There is no single laboratory test capable of confirming with 100% confidence every true case of measles. Public health laboratories that use commercial measles assay kits are encouraged to fully characterize and validate the kits in their laboratories using known test panels of positive and negative specimens. Information regarding the performance characteristics of many of the commercially available enzyme immunoassays (EIA) kits is available by contacting the CDC measles laboratory.

### **Use of IgM for confirmation of measles:**

#### **a. Unvaccinated persons**

Following measles virus infection in an unvaccinated individual, measles IgM antibodies appear within the first few days (1–4 days) of rash onset, peak within the first week post rash onset and are rarely detected after 6–8 weeks. Measles IgG antibodies are generally produced and detectable a few days after the IgM response. The timing of the IgM and the IgG response varies among individuals but IgG should be detectable by 7–10 days postrash onset. IgG levels peak approximately two weeks post rash onset and persist for life.

Upon exposure to wild type measles virus, an unvaccinated person may have detectable IgM as soon as the first day of rash onset. However, depending on the sensitivity of the assay used, a proportion of serum samples (23% in a study using CDC capture IgM assay<sup>58</sup>) collected within 72 hours after rash onset may give false negative results. If a negative result is obtained from serum collected within 72 hours after rash onset, a second serum should be collected  $\geq 72$  hours after rash onset. Measles IgM is detectable for at least 30 days after rash onset and frequently longer.

The serologic response following vaccination is slower; measles IgM may not be detectable until 8–14 days after vaccination and measles IgG may not be detectable for up to three weeks post vaccination.<sup>59</sup>

*Note: 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. Determination of the measles genotype is necessary when measles symptoms occur following an exposure to wild type virus and MMR vaccine had been provided as postexposure prophylaxis.*

#### **b. Vaccinated persons**

Individuals who have been previously exposed to measles antigen may have a modified disease presentation. These cases are usually detected during an outbreak or after a known exposure to a confirmed measles case. In rare instances, such cases can occur without a known exposure or other risk factor.

Often there is a blunted and/or transient production of IgM and therefore a negative IgM test in vaccinated persons suspected of having measles should not be used to rule out the case; RT-PCR testing may be the best method to confirm such cases. If viral testing results are noncontributory, additional testing can be performed for highly suspicious cases. See the sections below.

#### *Additional tests for measles infection*

Testing for measles-specific IgM from persons with rash and fever can produce false positive IgM results. As discussed above, false negative results can also occur in a previously vaccinated person.

#### **Ruling out a false positive IgM by testing a second serum:**

- If the acute sample was IgG negative, a second serum can be collected at  $\geq 10$  days after the acute sample. If this serum is IgG negative, measles can be ruled out.
- If the acute serum was IgG positive, a second serum can be tested for a significant rise in IgG between paired serum samples.

Tests for IgG rise or seroconversion such as plaque reduction neutralization (PRN) and avidity testing may be helpful in certain situations. A brief description for the utility of these assays is given below. More information is available on the CDC Measles webpage. Requests for testing should be directed to the Measles laboratory at CDC. (See Chapter 22, *Laboratory Support for the Surveillance of Vaccine-Preventable Diseases*)

#### **IgG antibody seroconversion or demonstration of a rise in titer using IgG EIA:**

##### **a. Unvaccinated persons**

If classification of a case cannot be made after testing a serum sample collected  $\geq 72$  hours after rash or detection of measles virus from a viral specimen was not successful, a convalescent serum sample can be collected. A convalescent serum sample should be collected 10–30 days after the acute serum. In immunologically naïve persons, the measles IgG response starts slowly and, depending on the assay, can be detected by day 3–7 after rash onset (range: 1–10 days), but typically persists for a lifetime.

*Note: IgG testing of paired serum samples requires the demonstration of a significant (usually four-fold) rise in the titer of antibody against measles using an assay that has been validated for this use. The test for IgG antibody should be conducted with acute and convalescent serum samples at the same time using the same test. IgG avidity assessments would also be informative on such specimens, since low avidity results would rule in a case of measles in this instance (See Avidity of IgG below).*

##### **b. Vaccinated persons**

When measles is suspected in previously vaccinated persons, the acute serum may be IgM negative and IgG positive. Measles infection in such cases is characterized by a rapid and robust IgG response.<sup>60, 61</sup> If a second serum sample collected 5–10 days later remains IgM negative, then the paired serum samples can be tested in a PRN assay or a quantitative or semi-quantitative IgG EIA validated for such use. Refer to the CDC measles laboratory website for more information: <http://www.cdc.gov/measles/lab-tools/index.html>.

The occurrence of measles-like illness in recently vaccinated persons can pose particular difficulties. Fever and rash are known to occur 6–12 days post-vaccination in a small percent of vaccinated persons.<sup>1</sup> 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 due to the measles IgM antibody response to the vaccine. Specimens for viral isolation should be obtained in addition to serologic testing (see “Laboratory testing” section above); isolation of wild type measles virus would allow confirmation of the case. In the absence of strain typing to confirm wild type infection, 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.

#### **Plaque reduction neutralization assay (PRN)**

The gold standard test for serologic evidence of recent measles infection is a four-fold rise in titer as measured in a measles virus plaque reduction neutralization test (PRN or PRNT) between acute and convalescent serum samples. Unlike the IgG EIA, this test measures measles functional (neutralizing) antibodies, requires specialized reagents, and is labor and time intensive. Only in rare situations would such testing be deemed necessary. Prior approval should be obtained from the CDC measles laboratory.

#### **Avidity of IgG**

A single acute-phase serum sample can be tested for IgG avidity; however samples must have detectable IgG. Low avidity IgG confirms a recent measles infection (or recent vaccination). Avidity testing can distinguish between primary and secondary vaccine failures. Avidity testing requires specialized reagents and their use is limited to unusual cases (prior approval required) usually in an outbreak setting when cases with modified or nonclassic presentation of measles are detected.

### **VIII. Reporting**

Each state and territory has regulations or laws governing the reporting of diseases and conditions of public health importance.<sup>62</sup> 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. You may contact your local or state health department for reporting requirements in your state.

#### *Reporting to CDC*

Since continuous endemic measles transmission has been eliminated, measles is an immediately notifiable disease. Measles cases should be reported promptly (within 24 hours<sup>3</sup>) by the state health department to the CDC or directly to Susan Redd at NCIRD, CDC by telephone: 404-639-8763 or by e-mail (SBR1@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) with the next regularly scheduled electronic transmission.

<sup>3</sup> *CSTE List of Nationally Notifiable Diseases:*  
<http://www.cste.org/resource/resmgr/PDFs/CSTENotifiableConditionListA.pdf>

### *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
  - Country of birth
  - If not born in the United States, length of time in the United States
- Reporting source
  - County
  - Date first reported
- Clinical
  - Symptoms onset date; including date of rash onset
  - Prodromal symptoms (i.e., cough, coryza, conjunctivitis, fever [note highest temperature])
  - Rash duration
  - Rash presentation
  - Symptoms
  - Hospitalizations
  - Complications
- Outcome (case survived or died)
  - Date of death
  - Results of postmortem examination
  - Death certificate diagnoses
- Laboratory
  - Serological tests: date collected, results
  - Virus isolation tests: type of specimen, date of collection of specimen for PCR and culture
- Vaccination status (including postexposure prophylaxis)
  - Number of doses of measles vaccine received
  - Dates of measles vaccinations
  - Name of manufacturer
  - Lot numbers of vaccines
  - If not vaccinated, reason
- Epidemiological
  - Transmission setting (e.g., household, school, health care setting, event)
  - Source of infection (e.g., age, vaccination status, relationship to case, contact with probable or confirmed case, or contact with immigrants or travelers, or international travel)
  - Import status (indigenous, international import, or out-of-state import, linked or traceable to an international importations)
  - Residency (e.g., Did the case reside in the U.S.?)
  - Travel history in the three weeks prior to symptom onset
  - Number of contacts
  - Postexposure prophylaxis (including whether measles immunoglobulin was administered, with dates of administration)

## IX. Importance of Rapid Identification and Surveillance

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.

### *Confirmed and suspect case identification*

Active surveillance for measles disease should be conducted for every confirmed measles case to assure timely reporting of suspected cases in the population known to be affected 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. Efforts should be made to obtain clinical specimens for viral detection (see “Laboratory testing” section above). Active surveillance should be maintained until at least two incubation periods after the last confirmed case is reported.

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: <http://www.cdc.gov/quarantine/QuarantineStationContactListFull.html>. If unable to contact the QS, call the DGMQ 24-hour number at 866-694-4867 for assistance.

### *Enhancing surveillance*

Because measles importations occur every year in the United States, additional surveillance 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 has become increasingly important.

Additional guidelines for enhancing surveillance are given in Chapter 19, “Enhancing Surveillance.”

### *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 proportion of cases that have an imported source
- The proportion of cases for which at 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 which 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.”

## X. Case and Contact Investigation

All reports of suspected measles cases should be investigated immediately.

In the measles post-elimination era, a single case of measles is considered a public health priority that requires rapid evaluation for likelihood of measles and appropriate public health response; additional effort is required to ensure that appropriate and timely diagnosis of rash illnesses and reporting of suspected cases continues in order to prevent outbreaks and re-establishment of endemic disease transmission.

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 confirmed cases, identifying sources of infection, assessing potential for transmission and identifying contacts without presumptive evidence of immunity, classifying importation status, and obtaining specimens for viral isolation.

Prompt recognition, reporting, and investigation of measles is important because the spread of the disease can be limited with early case identification and public health response including vaccination and quarantine of susceptible contacts without presumptive evidence of immunity.

As measles continues to be endemic in many regions of the world, importations of measles occur every year in the United States. Each imported measles case could result in transmission of measles to susceptible individuals if exposed. Surveillance and prompt investigation of cases and their susceptible contacts help to halt the spread of disease. However, because some imported measles cases are not detected in our surveillance system, maintaining a high alertness for measles is needed since not every “sporadic” case occurring in the community can be linked to an importation.

Information obtained through surveillance is also used to describe current measles epidemiology and to evaluate prevention policies and achievement of goals including maintenance of disease elimination. Surveillance data are used to characterize persons, groups, or areas in which additional efforts are required to reduce risk of measles disease and outbreaks.

### *Identify cases and establish a diagnosis*

An essential first step in a measles case investigation is to obtain necessary clinical information to determine whether or not a reported case is clinically compatible with measles and to obtain key epidemiological information. If the case was reported within three days of onset of rash, the case may not meet the clinical case definition (see “Case definitions”) and there should be appropriate follow-up to establish a rash duration of at least three days. However public health action, if needed, should not be delayed. Suspected cases of measles should have laboratory confirmation. Efforts should be made to obtain clinical specimens for viral testing (see the section “Laboratory testing”).

In the measles post-elimination era, most cases of febrile rash illness seen in physician’s offices that meet the clinical case definition will not be measles. However, health care providers should maintain a high index of suspicion for measles in clinically compatible cases especially among unvaccinated persons and among persons who recently traveled abroad or who have had contact with persons such as travelers or international visitors. In addition, not every sporadic measles case is linked to a known importation, so cases that raise high suspicion of measles, irrespective of associated risk factors, should be investigated for measles unless an alternative diagnosis is likely (e.g., known epidemiological link to a parvovirus case).

When evaluating patients with suspected measles who have negative serologic tests for acute measles infection (i.e., negative serum measles IgM), additional testing for rubella can be considered.

### *Obtain accurate and complete immunization histories*

Measles case investigations should include complete immunization histories that document all doses of measles-containing vaccine. Acceptable proof of vaccination is documented administration of live measles virus-containing vaccine. Written or electronic records with dates of vaccine administration are the only acceptable evidence of vaccination. 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/college records or from providers; if the case is a health care personnel, immunization records may be available at the health care facility. Immunization registries are now very useful sources of vaccination histories for children and adolescents.

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 of vaccination for each dose and the interval between doses should be noted.

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.

### *Identify the source of infection*

Efforts should be made to identify the source of infection for every confirmed case of measles. Case-patients or their caregivers should be asked about contact with other known cases. 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), in healthcare settings, or in churches. 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.

### *Assess potential for transmission and identify contacts without presumptive evidence of immunity*

In the event of a confirmed measles case, local or state health departments should contact health care providers in their areas to inform them of the confirmed case and request immediate reporting of any suspected cases through the media or Epi-X. Previously unreported cases may be identified by reviewing emergency room logs, electronic medical records, or laboratory records. Hospital emergency rooms and physicians serving affected communities are usually recruited to participate in active surveillance.

### **General guidelines**

- i. **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. The line listing is an essential component of every outbreak investigation.(Table 1).
- ii. **Identifying risk of transmission in the population affected by the outbreak.** As part of the case investigation, the potential for further transmission should be evaluated, and an assessment should be made of exposed contacts of the case-patient (and their presumptive evidence of immunity during the infectious period (four days before to four days after onset of rash, day of rash onset being day zero). In a closed setting the measles virus has been reported to have been transmitted by airborne or droplet exposure up to two hours after the measles case occupied the area.<sup>63</sup>

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 (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),
- determine where transmission is occurring or likely to occur. Transmission is particularly likely in households, daycare, schools, health care settings, and in congregate settings such as churches and other institutions (colleges, prisons, etc.), and
- identify persons who are at highest risk of infection or transmission (other unvaccinated children, students attending other schools, immunocompromised persons, pregnant women, health care personnel, infants aged <12 months etc.).

**Table 1. 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	Viral specimen (type, date and result)	MMR-1 date	MMR-2 date	Reason for Not Vaccinating	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			?	—		—

## XI. Control Measures

In general, the most effective 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 control may be limited. Therefore, it is essential that data be used to determine the scope of the investigation and the potential for spread and that intervention be based on those determinations using public health judgment to guide investigation and control efforts. The primary strategy is achieving a high level of immunity in the population affected.<sup>13</sup>

### *Initiation of investigation and prioritization of contacts*

State and local health departments should use their judgment to prioritize such investigations according to epidemiology and identified transmission settings. Settings at highest risk of transmission based on the epidemiology of the outbreak may be prioritized for public health response.

If suspected and probable cases are investigated, postexposure prophylaxis of household contacts without presumptive evidence of immunity should not be delayed pending the return of laboratory results. Other high priority groups for contact investigation are 1) close contacts other than household (e.g., persons who shared the same room or airspace in various settings), 2) health care settings because of the risk of transmission to persons at high risk of serious complications, and 3) schools/child care centers, colleges or other close settings where a defined number of persons have congregated (e.g., churches) because of high contact rates and transmission potential. In all these settings, exposures usually result in an identified number of susceptible contacts to follow up on individually. However, efforts to identify the likelihood of exposure in larger settings such as hospitals (e.g., patients and health care personnel in ER) may be helpful. In particular, one should identify individuals at high risk for severe disease including infants who are not vaccinated, immunocompromised individuals, and pregnant women.

Initial preparation for major control activities may need to be started before the laboratory results are known. However, it is reasonable to delay major control activities, such as checking presumptive evidence of immunity and enforcing student exclusion, pending the return of laboratory results, which should be obtained as quickly as possible (within 24 hours).

If resources are constrained, other exposure settings will more commonly be lower priority to investigate, though public health decisions should be guided by the epidemiologic investigation. For exposures at such venues as restaurants, stadiums, and malls, radio, TV, Epi-X, or other media to reach the general public may be used to reach potentially exposed persons rather than individual contact tracing. Persons can be guided to their physicians or the health department for assessment of immunity status and the need for vaccination. Additional guidelines for enhancing surveillance are given in Chapter 19, “Enhancing Surveillance.”

#### *Isolation of cases and exclusion of contacts without presumptive evidence of immunity*

Case-patients should be isolated for four days post rash onset. Respiratory etiquette and airborne precautions should be instituted in health care settings.

Persons who cannot readily document presumptive evidence of measles immunity should be offered postexposure prophylaxis (PEP) or excluded from the setting (school, hospital, day care). For assessment of presumptive evidence of immunity of contacts, 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 and who do not receive appropriate postexposure prophylaxis within the appropriate time should be excluded from affected institutions in the outbreak area until 21 days after the onset of rash in the last case of measles.

#### **Quarantine and its use**

Quarantine (most commonly voluntary quarantine) has been implemented especially where unvaccinated or populations at high risk were affected. In such situations, quarantine has helped to contain the spread of the disease to the surrounding community.<sup>25, 33, 34</sup> Compliance with quarantine can be ensured at the discretion of the health department. When deciding about quarantine, factors to consider include

- immune status of the individual,
- presumptive evidence of immunity,
- whether the person is at high risk or not, and
- transmission settings.

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.

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

Presumptive evidence of measles immunity should be assessed for all identified contacts.

There is limited data regarding the effectiveness of MMR vaccine and immunoglobulin (IG) PEP against disease prevention. Individuals who receive MMR vaccine or IG as PEP should be monitored for signs and symptoms consistent with measles for at least one incubation period.<sup>13</sup>

The MMR vaccine, if administered within 72 hours of initial measles exposure, and IG, if administered within six days of exposure, may provide some protection or modify the clinical course of disease. Except in health care settings, unvaccinated persons who receive their first dose of MMR vaccine within 72 hours postexposure may return to child care, school, or work.

However, vaccination should be offered at any interval following exposure in order to offer protection from future exposures.

Individuals who are at risk for severe disease and complications from measles (e.g., infants aged <12 months, pregnant women without evidence of measles immunity, and severely immunocompromised persons) should receive IG. Intramuscular IG (IGIM) can be given to other persons who do not have evidence of measles immunity, but priority should be given to persons exposed in settings with intense, prolonged, close contact (e.g., household, daycare, classroom). For exposed persons without evidence of measles immunity, a rapid IgG antibody test can be used to inform immune status, provided that administration of IG is not delayed. After receipt of IG, individuals cannot return to health care settings. In other settings such as childcare, school, or work, factors such as immune status, intense or prolonged contact, and presence of populations at risk, should be taken into consideration before allowing these individuals to return. These factors may decrease the effectiveness of IG or increase the risk of disease and complications depending on the setting to which they are returning.

The recommended dose of IG given intramuscularly (IGIM) is 0.5 mL/kg of body weight (maximum dose = 15 mL) and the recommended dose of IG given intravenously (IGIV) is 400 mg/kg. IGIM should be given to all infants aged <12 months who have been exposed to measles. For infants aged 6 through 11 months, MMR vaccine can be given in place of IG, if administered within 72 hours of exposure.<sup>13</sup>

If many cases are occurring among infants <12 months of age, measles vaccination of infants as young as six months of age may be undertaken as an outbreak control measure.<sup>13</sup> Note that children vaccinated before their first birthday should be revaccinated when they are 12–15 months old and again when they are 4–6 years of age.

#### *Role of communitywide vaccination efforts in outbreak control*

Physicians in affected communities should use the opportunity of a confirmed measles case for reminder/recall to ensure that all their patients are up to date with MMR vaccine requirements.

Community-wide vaccination clinics are rarely indicated but targeted clinics may be held to reach affected populations (e.g., vaccination for health care workers or clinic at a work setting with affected adults).

#### *Day care centers, schools and other educational institutions*

Measles cases in schools, colleges, and other institutions, such as day care centers where close contact may exist, require rapid public health investigation for response and for evaluation of risk of further transmission. In educational institutions where there are high rates of vaccine exemptors, the potential risk of spread of the disease is high. Control measures include:

- Exclusion and isolation of cases (they can return on the fifth day after rash onset if not immunocompromised);
- Offering vaccine for those who are not up-to-date with age-appropriate vaccination (first dose to unvaccinated, second dose to those with one documented dose can be given at least 28 days after the first dose);
- IG if immunocompromised (please refer the following section: Vaccination and use of immunoglobulin in exposed persons)
- Persons who continue to be exempted from or who refuse measles vaccination should be excluded from the school, child care, or other institutions until 21 days after rash onset in the last case of measles.<sup>20, 25</sup>

All students and all school personnel born in or after 1957 who cannot provide adequate presumptive evidence of immunity should be vaccinated. Persons receiving their second dose and previously unvaccinated persons receiving their first dose as part of the outbreak control program may be immediately readmitted to school. However these individuals should be monitored for signs and symptoms of measles.

### Health care 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 at increased risk of transmission to persons at high risk of severe measles. All persons who work in such facilities in any capacity should have presumptive evidence of immunity to measles to prevent any potential outbreak.<sup>64</sup>

### Presumptive evidence of immunity and routine vaccine recommendations for health care personnel

Health care personnel (HCP) have slightly different criteria for acceptable presumptive evidence of immunity. All persons who work in health care facilities should have presumptive evidence of immunity to measles.<sup>64</sup> This information should be documented and readily available (ideally through electronic medical records) at the work location.

Presumptive evidence of immunity to measles for health care personnel includes any of the following:

- Written documentation of vaccination with 2 doses of live measles or MMR vaccine administered at least 28 days apart,<sup>†</sup>
- Laboratory evidence of immunity,<sup>§</sup>
- Laboratory confirmation of disease, or
- Birth before 1957.<sup>¶</sup>

Although birth before 1957 is considered as presumptive evidence of immunity, for unvaccinated HCP born before 1957 that lack laboratory evidence of measles immunity or laboratory confirmation of disease, health care facilities should consider vaccinating personnel with two doses of MMR vaccine at the appropriate interval.

### Prevention and control strategies in medical settings

In a medical setting, both the employee health and infection control practitioners have a role. When a measles case occurs in a health care facility, including outpatient and long-term care facilities, the following measure should be undertaken:

- Immediate review of evidence of measles immunity in all exposed staff (see “Presumptive evidence of immunity for health care personnel”).
- Vaccination of personnel without presumptive evidence of immunity
- Exclusion of HCP with active measles illness
- HCP without presumptive evidence of immunity should be offered the first dose of MMR vaccine and excluded from work from day 5 to day 21 following exposure
- Isolation of patient in whom measles is suspected in a negative air pressure isolation room, also known as airborne infection isolation (AII) or airborne infection isolation room (AIIR).
- Implementation of airborne precautions in addition to respiratory etiquette

An effective vaccination program is the best approach to prevent health care associated measles transmission. Health Care Infection Control Practices Advisory Committee (HICPAC) and CDC have recommended that secure, preferably computerized, systems should be used to manage vaccination records for HCP so records can be retrieved easily as needed.<sup>64</sup> Failure to have such records can be costly and can increase resources needed to respond to the outbreak.<sup>27</sup>

<sup>†</sup> The first dose of measles-containing vaccine should be administered on or after the first birthday; the second dose should be administered no earlier than 28 days after the first dose

<sup>§</sup> Measles immunoglobulin (IgG) in the serum; equivocal results should be considered negative

<sup>¶</sup> The majority of persons born before 1957 is likely to have been infected naturally and may be presumed immune, depending on current state or local requirements. For unvaccinated personnel born before 1957 who lack laboratory evidence of measles immunity or laboratory confirmation of disease, health-care facilities should consider vaccinating personnel with 2 doses of MMR vaccine at the appropriate interval. For unvaccinated personnel born before 1957 who lack laboratory evidence of measles immunity or laboratory confirmation of disease, health-care facilities should recommend 2 doses of MMR vaccine during an outbreak of measles.

If a measles case or an outbreak occurs within or in the areas served by a hospital, clinic, or other medical or nursing facility, all personnel regardless of birth year, should receive two doses of MMR vaccine, unless they have other documentation of measles immunity.<sup>64</sup> Birth year before 1957 is not acceptable presumptive evidence of immunity during an outbreak. Health care facilities should provide MMR vaccine to all personnel without presumptive evidence of measles immunity at no charge. Recently vaccinated HCP do not require any restriction in their work activities.

Serologic screening of HCP during an outbreak to determine measles immunity prior to vaccination is not recommended, because preventing measles transmission requires the rapid vaccination of HCP without presumptive evidence of immunity, which can be impeded by the need to screen, wait for results, and then contact and vaccinate susceptible persons. Results from serological testing, if performed, can inform on need for the second MMR vaccine dose.

HCP without presumptive evidence of immunity who have been exposed to measles should be relieved from patient contact and excluded from the facility from the 5th day after the first exposure through the 21st day after the last exposure, regardless of whether they received vaccine or intramuscular immune globulin after the exposure. Personnel who develop measles should be relieved from all patient contact and excluded from the facility for four days after they develop rash.<sup>64</sup>

Hospital contacts of a case-patient, who do not have presumptive evidence of measles immunity, should be vaccinated and offered immune globulin. The recommended dose of IG given intramuscularly (IGIM) is 0.5 mL/kg of body weight (maximum dose = 15 mL) and the recommended dose of IG given intravenously (IGIV) is 400 mg/kg, which is the standard dosage for nonimmunocompromised persons,<sup>13</sup> or quarantined until 21 days after their exposure to the case-patient. Contacts of people with measles compatible symptoms should be isolated, and appropriate infection control measures should be implemented to prevent further spread.<sup>65</sup> If immune globulin is administered to an exposed person, observations should continue for signs and symptoms of measles for 28 days after exposure since immune globulin may prolong the incubation period.<sup>64</sup>

### *Additional information*

Because investigating an outbreak requires many person-days of work, personnel are frequently transferred to the activity from other areas 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.

- 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 (electronic spreadsheet preferred) 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 1).
- Create a column in the logbook for actions needed for each suspected case (“draw blood,” “call pediatrician for vaccination history,” “notify contacts”).
- Keep the logbook in one well defined location, preferably with folders containing 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) 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).

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