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*Recommendations
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Reports*

MORBIDITY AND MORTALITY WEEKLY REPORT

Case Definitions for Infectious Conditions Under Public Health Surveillance

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

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Centers for Disease Control and Prevention David Satcher, M.D., Ph.D.
Director

The material in this report was prepared for publication by:

Epidemiology Program Office..... Stephen B. Thacker, M.D., M.Sc.
Director

Division of Public Health Surveillance
and Informatics (proposed)Scott F. Wetterhall, M.D., M.P.H.
Director

The production of this report as an *MMWR* serial publication was coordinated in:

Epidemiology Program Office..... Stephen B. Thacker, M.D., M.Sc.
Director

Richard A. Goodman, M.D., M.P.H.
Editor, MMWR Series

Office of Scientific and Health Communications (proposed)
Recommendations and Reports..... Suzanne M. Hewitt, M.P.A.
Managing Editor

Nadine W. Martin
Project Editor

Peter M. Jenkins
Visual Information Specialist

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The following CDC staff members prepared this report:

Denise Koo, M.D., M.P.H.
Epidemiology Program Office

Melinda Wharton, M.D., M.P.H.
National Immunization Program

in collaboration with

Guthrie Birkhead, M.D., M.P.H.
Council of State and Territorial Epidemiologists

Case Definitions for Infectious Conditions Under Public Health Surveillance

Summary

State and local public health officials rely on health-care providers, laboratories, and other public health personnel to report the occurrence of notifiable diseases to state and local health departments. Without such data, trends cannot be accurately monitored, unusual occurrences of diseases might not be detected, and the effectiveness of intervention activities cannot be easily evaluated.

In the United States, requirements for reporting diseases are mandated by state laws or regulations, and the list of reportable diseases in each state differs. In October 1990, in collaboration with the Council of State and Territorial Epidemiologists, CDC published Case Definitions for Public Health Surveillance (MMWR 1990;39[No. RR-13]), which, for the first time, provided uniform criteria for reporting cases.

This report provides updated uniform criteria for state health department personnel to use when reporting the nationally notifiable infectious diseases listed in Part 1 of this report. A revision date is listed for each case definition that has been revised. Newly generated case definitions that have not been published previously are designated as "adopted" on the specified date. Case definitions for some infectious conditions not designated as nationally notifiable are included in Part 2 of this report. Some of these conditions may have been nationally notifiable or may become so; definitions are included here to facilitate interpretation of data for these diseases. These conditions may be reportable in some states.*

INTRODUCTION

State and local public health officials rely on health-care providers, laboratories, and other public health personnel to report the occurrence of notifiable diseases to state and local health departments. Without such data, trends cannot be accurately monitored, unusual occurrences of diseases might not be detected, and the effectiveness of intervention activities cannot be easily evaluated.

In the United States, requirements for reporting diseases are mandated by state laws or regulations, and the list of reportable diseases in each state differs. CDC and the Council of State and Territorial Epidemiologists (CSTE) have established a policy that requires state health departments to report cases of selected diseases (Table 1) to CDC's National Notifiable Diseases Surveillance System (NNDSS) (1,2). However, before 1990, the usefulness of such data was limited by the lack of uniform case definitions for public health surveillance. Without explicit criteria for identifying cases

*These case definitions were developed in collaboration with epidemiologists at CDC and the Council of State and Territorial Epidemiologists (CSTE). They were approved by a full vote of the CSTE membership and also endorsed for use by the Association of State and Territorial Public Health Laboratory Directors (ASTPHLD).

TABLE 1. Infectious diseases designated as notifiable at the national level — United States, 1997

Acquired immunodeficiency syndrome (AIDS)	Lyme disease
Anthrax	Malaria
Botulism	Measles
Brucellosis	Meningococcal disease
Chancroid	Mumps
<i>Chlamydia trachomatis</i> , genital infections	Pertussis
Cholera	Plague
Coccidioidomycosis	Poliomyelitis, paralytic
Cryptosporidiosis	Psittacosis
Diphtheria	Rabies, animal
Encephalitis, California serogroup	Rabies, human
Encephalitis, eastern equine	Rocky Mountain spotted fever
Encephalitis, St. Louis	Rubella
Encephalitis, western equine	Rubella, congenital syndrome
<i>Escherichia coli</i> O157:H7	Salmonellosis
Gonorrhea	Shigellosis
<i>Haemophilus influenzae</i> , invasive disease	Streptococcal disease, invasive Group A <i>Streptococcus pneumoniae</i> , drug-resistant invasive disease
Hansen disease (leprosy)	Streptococcal toxic-shock syndrome
Hantavirus pulmonary syndrome	Syphilis
Hemolytic uremic syndrome, post-diarrheal	Syphilis, congenital
Hepatitis A	Tetanus
Hepatitis B	Toxic-shock syndrome
Hepatitis, C/non-A, non-B	Trichinosis
HIV infection, pediatric	Tuberculosis
Legionellosis	Typhoid fever
	Yellow fever

for public health surveillance purposes, state health departments and individual practitioners often applied different criteria for reporting similar cases (3).

In October 1990, in collaboration with CSTE, CDC published *Case Definitions for Public Health Surveillance* (4), which, for the first time, provided uniform criteria for reporting cases to increase the specificity of reporting and improve the comparability of diseases reported from different geographic areas. This report supersedes the 1990 report, which included infectious diseases and one noninfectious condition (i.e., spinal cord injury). The CDC Surveillance Coordination Group has established a steering committee that is charged with the development of a broad range of case definitions for noninfectious conditions (e.g., environmental or occupational conditions, chronic diseases, adverse reproductive health events, and injuries). This report provides updated uniform criteria for public health professionals to use when reporting the nationally notifiable infectious diseases listed in Part 1. A revision date is included for

each case definition that has been revised. Newly generated case definitions that have not been previously published are designated as “adopted” on the specified date.

Data for nationally notifiable diseases reported by the 50 states, New York City, the District of Columbia, and the U.S. territories are collated and published weekly in the *Morbidity and Mortality Weekly Report (MMWR)*. Cases reported by state health departments to the NNDSS for weekly publication are provisional because of ongoing revision of information and delayed reporting; thus, these numbers may change. Updated final reports are published annually in CDC’s *Summary of Notifiable Diseases, United States (1)*.

The CDC/CSTE surveillance case definitions included in this report differ in their use of clinical, laboratory, and epidemiologic criteria to define cases. Some clinical syndromes do not have confirmatory laboratory tests; however, laboratory evidence may be one component of a clinical definition (e.g., toxic-shock syndrome). Most case definitions include a brief clinical description; however, unless this description is explicitly cited in the case classification section, it is included only as background information.

Some diseases require laboratory confirmation for diagnosis regardless of clinical symptoms, whereas others are diagnosed based on epidemiologic data. Many case definitions for the childhood vaccine-preventable diseases and foodborne diseases include epidemiologic criteria (e.g., exposure to probable or confirmed cases of disease or to a point source of infection [i.e., a single source of infection, such as an event resulting in a foodborne-disease outbreak, to which all confirmed case-patients were exposed]). In some instances, the anatomic site of infection may be important; for example, respiratory diphtheria is notifiable, whereas cutaneous diphtheria is not.

Substantial amounts of information, including results of laboratory tests, must be collected for many diseases before a final case classification is possible. State health departments should continue prompt reporting of provisional cases to CDC, and records should be updated with the appropriate classification status when additional surveillance information becomes available. Cases should be categorized as *laboratory-confirmed* (a subset of all confirmed cases) only if they meet the laboratory criteria specified. For additional information about procedures for reporting diseases to CDC, see the *Manual of Procedures for the Reporting of Nationally Notifiable Diseases to CDC (5)*.

Case definitions for some infectious conditions not considered nationally notifiable also are included in this report. Some of these conditions may have been nationally reportable or may become so; definitions are included here to facilitate interpretation of data for these diseases (Table 2). State health departments also provide CDC with information regarding certain conditions of public health interest, whether nationally reportable, through supplementary surveillance systems that collect more detailed, condition-specific information (5).

The usefulness of public health surveillance data depends on its uniformity, simplicity, and timeliness. The case definitions contained in this report establish uniform criteria for disease reporting and should not be used as the sole criteria for establishing clinical diagnoses, determining the standard of care necessary for a particular patient, setting guidelines for quality assurance, or providing standards for reimbursement. Use of additional clinical, epidemiologic, and laboratory data may enable a physician to diagnose a disease even though the formal surveillance case definition may not be met.

TABLE 2. Infectious diseases and conditions that are not nationally notifiable but for which case definitions may be useful for surveillance*

Amebiasis	Granuloma inguinale
Aseptic meningitis	Leptospirosis
Bacterial meningitis, other	Listeriosis
<i>Campylobacter</i> infection	Lymphogranuloma venereum
<i>Cyclospora</i> infection	Mucopurulent cervicitis
Dengue fever	Nongonococcal urethritis
Ehrlichiosis	Pelvic inflammatory disease
Genital herpes (herpes simplex virus)	Rheumatic fever
Genital warts	Tularemia
Giardiasis	Varicella (chickenpox)

*This list includes only the diseases and conditions that are not nationally notifiable for which case definitions are provided in this report; it is not a complete list of such diseases for which CDC and state and territorial health departments maintain surveillance systems.

The list of nationally reportable infectious diseases changes periodically. Diseases may be added to the list as new pathogens emerge or deleted as their incidence declines. Public health officials at state health departments and CDC collaborate in determining which diseases should be nationally notifiable; CSTE, in conjunction with CDC, makes recommendations annually for additions and deletions to the list of nationally notifiable diseases (1,2). As knowledge increases and diagnostic technology improves, some definitions will change to reflect those trends. Thus, future revisions can be expected. This report also is available in Adobe™ Acrobat™ portable document format (.pdf) through the World-Wide Web at http://www.cdc.gov/epo/mmwr/other/case_def/about.html. Future changes to the case definitions for nationally notifiable infectious diseases will be announced in the *MMWR* and made available in the electronic version.

How to Use Information in This Report

Terms that are used in case classifications for both Parts 1 and 2 are defined (see Definition of Terms Used in Case Classification). Because each case definition in Parts 1 and 2 is intended to stand alone, abbreviations are defined the first time they appear in each case definition section and abbreviated throughout the rest of that section. A publications list is included only for the section on acquired immunodeficiency syndrome (AIDS); this list provides further sources regarding AIDS.

These case definitions are to be used for identifying and classifying cases, both of which are often done retrospectively, for national reporting purposes. They should not be used as criteria for public health action. For many conditions of public health importance, action to contain disease should be initiated as soon as a problem is identified; in many circumstances, appropriate public health action should be undertaken even though insufficient information is available to determine whether cases meet the case definition.

Definition of Terms Used in Case Classification

Clinically compatible case: a clinical syndrome generally compatible with the disease, as described in the clinical description.

Confirmed case: a case that is classified as confirmed for reporting purposes.

Epidemiologically linked case: a case in which a) the patient has had contact with one or more persons who either have/had the disease or have been exposed to a point source of infection (i.e., a single source of infection, such as an event leading to a foodborne-disease outbreak, to which all confirmed case-patients were exposed) and b) transmission of the agent by the usual modes of transmission is plausible. A case may be considered epidemiologically linked to a laboratory-confirmed case if at least one case in the chain of transmission is laboratory confirmed.

Laboratory-confirmed case: a case that is confirmed by one or more of the laboratory methods listed in the case definition under Laboratory Criteria for Diagnosis. Although other laboratory methods can be used in clinical diagnosis, only those listed are accepted as laboratory confirmation for national reporting purposes.

Probable case: a case that is classified as probable for reporting purposes.

Supportive or presumptive laboratory results: specified laboratory results that are consistent with the diagnosis, yet do not meet the criteria for laboratory confirmation.

Suspected case: a case that is classified as suspected for reporting purposes.

PART 1. CASE DEFINITIONS FOR NATIONALLY NOTIFIABLE INFECTIOUS DISEASES

Acquired Immunodeficiency Syndrome (AIDS) (Effective 1/1/93)

Case definition

CDC has expanded the acquired immunodeficiency syndrome (AIDS) surveillance case definition to include all human immunodeficiency virus (HIV)-infected adolescents and adults aged ≥ 13 years who have either a) < 200 CD4+ T-lymphocytes/ μL ; b) a CD4+ T-lymphocyte percentage of total lymphocytes of $< 14\%$; or c) any of the following three clinical conditions: pulmonary tuberculosis, recurrent pneumonia, or invasive cervical cancer. The expanded definition retains the 23 clinical conditions in

the AIDS surveillance case definition published in 1987. (See publication [1] in Publications List in this section for complete information referring to this case definition.)

The AIDS surveillance case definition for children aged <13 years has not changed and retains the clinical conditions listed in the AIDS surveillance case definition published in 1987. However, definitions for HIV encephalopathy, HIV wasting syndrome, and HIV infection in children have been revised and the 1987 definition has been updated. (See Publication [2] in Publications List for complete information pertaining to this case definition.)

Laboratory criteria for diagnosis

See Publication (1) in Publications List.

Case classification

CDC has revised the classification system for HIV infection to emphasize the clinical importance of the CD4+ T-lymphocyte count in the categorization of HIV-related clinical conditions. This classification system replaces the system published by CDC in 1986. (See Publication [1] in Publications List for complete information pertaining to this case definition.)

Publications list

- (1) CDC. 1993 Revised classification system for HIV infection and expanded surveillance case definition for AIDS among adolescents and adults. MMWR 1992;41(No. RR-17).
- (2) CDC. 1994 Revised classification system for human immunodeficiency virus infection in children less than 13 years of age. MMWR 1994;43(No. RR-12).
- (3) CDC. Interpretation and use of the Western blot assay for serodiagnosis of human immunodeficiency virus type-1 infection. MMWR 1989;38(No. S-7).
- (4) Revision of the CDC surveillance case definition for acquired immunodeficiency syndrome. MMWR 1987;36(suppl:)1–15s.

Anthrax (Revised 9/96)

Clinical Description

An illness with acute onset characterized by several distinct clinical forms, including the following:

- Cutaneous: a skin lesion evolving during a period of 2–6 days from a papule, through a vesicular stage, to a depressed black eschar
- Inhalation: a brief prodrome resembling a viral respiratory illness, followed by development of hypoxia and dyspnea, with radiographic evidence of mediastinal widening
- Intestinal: severe abdominal distress followed by fever and signs of septicemia
- Oropharyngeal: mucosal lesion in the oral cavity or oropharynx, cervical adenopathy and edema, and fever

Laboratory criteria for diagnosis

- Isolation of *Bacillus anthracis* from a clinical specimen, or
- Anthrax electrophoretic immunotransblot (EITB) reaction to the protective antigen and/or lethal factor bands in one or more serum samples obtained after onset of symptoms, or
- Demonstration of *B. anthracis* in a clinical specimen by immunofluorescence

Case classification

Confirmed: a clinically compatible case that is laboratory confirmed

Botulism, Foodborne (Revised 9/96)**Clinical description**

Ingestion of botulinum toxin results in an illness of variable severity. Common symptoms are diplopia, blurred vision, and bulbar weakness. Symmetric paralysis may progress rapidly.

Laboratory criteria for diagnosis

- Detection of botulinum toxin in serum, stool, or patient's food or
- Isolation of *Clostridium botulinum* from stool

Case classification

Probable: a clinically compatible case with an epidemiologic link (e.g., ingestion of a home-canned food within the previous 48 hours)

Confirmed: a clinically compatible case that is laboratory confirmed or that occurs among persons who ate the same food as persons who have laboratory-confirmed botulism

Botulism, Infant (Revised 9/96)**Clinical description**

An illness of infants, characterized by constipation, poor feeding, and "failure to thrive" that may be followed by progressive weakness, impaired respiration, and death

Laboratory criteria for diagnosis

- Detection of botulinum toxin in stool or serum or
- Isolation of *Clostridium botulinum* from stool

Case classification

Confirmed: a clinically compatible case that is laboratory-confirmed, occurring in a child aged <1 year

Botulism, Wound**Clinical description**

An illness resulting from toxin produced by *Clostridium botulinum* that has infected a wound. Common symptoms are diplopia, blurred vision, and bulbar weakness. Symmetric paralysis may progress rapidly.

Laboratory criteria for diagnosis

- Detection of botulinum toxin in serum or
- Isolation of *C. botulinum* from wound

Case classification

Confirmed: a clinically compatible case that is laboratory confirmed in a patient who has no suspected exposure to contaminated food and who has a history of a fresh, contaminated wound during the 2 weeks before onset of symptoms

Botulism, Other**Clinical description**

See Botulism, Foodborne.

Laboratory criteria for diagnosis

- Detection of botulinum toxin in clinical specimen or
- Isolation of *Clostridium botulinum* from clinical specimen

Case classification

Confirmed: a clinically compatible case that is laboratory confirmed in a patient aged ≥ 1 year who has no history of ingestion of suspect food and has no wounds

Brucellosis**Clinical description**

An illness characterized by acute or insidious onset of fever, night sweats, undue fatigue, anorexia, weight loss, headache, and arthralgia

Laboratory criteria for diagnosis

- Isolation of *Brucella* sp. from a clinical specimen, or

- Fourfold or greater rise in *Brucella* agglutination titer between acute- and convalescent-phase serum specimens obtained ≥ 2 weeks apart and studied at the same laboratory, or
- Demonstration by immunofluorescence of *Brucella* sp. in a clinical specimen

Case classification

Probable: a clinically compatible case that is epidemiologically linked to a confirmed case or that has supportive serology (i.e., *Brucella* agglutination titer of ≥ 160 in one or more serum specimens obtained after onset of symptoms)

Confirmed: a clinically compatible case that is laboratory confirmed

Chancroid (Revised 9/96)

Clinical description

A sexually transmitted disease characterized by painful genital ulceration and inflammatory inguinal adenopathy. The disease is caused by infection with *Haemophilus ducreyi*.

Laboratory criteria for diagnosis

- Isolation of *H. ducreyi* from a clinical specimen

Case classification

Probable: a clinically compatible case with both a) no evidence of *Treponema pallidum* infection by darkfield microscopic examination of ulcer exudate or by a serologic test for syphilis performed ≥ 7 days after onset of ulcers and b) either a clinical presentation of the ulcer(s) not typical of disease caused by herpes simplex virus (HSV) or a culture negative for HSV.

Confirmed: a clinically compatible case that is laboratory confirmed

Chlamydia trachomatis, Genital Infections (Revised 9/96)

Clinical description

Infection with *Chlamydia trachomatis* may result in urethritis, epididymitis, cervicitis, acute salpingitis, or other syndromes when sexually transmitted; however, the infection is often asymptomatic in women. Perinatal infections may result in inclusion conjunctivitis and pneumonia in newborns. Other syndromes caused by *C. trachomatis* include lymphogranuloma venereum (see Lymphogranuloma Venereum) and trachoma.

Laboratory criteria for diagnosis

- Isolation of *C. trachomatis* by culture or
- Demonstration of *C. trachomatis* in a clinical specimen by detection of antigen or nucleic acid

Case classification

Confirmed: a case that is laboratory confirmed

Cholera (Revised 9/96)**Clinical description**

An illness characterized by diarrhea and/or vomiting; severity is variable.

Laboratory criteria for diagnosis

- Isolation of toxigenic (i.e., cholera toxin-producing) *Vibrio cholerae* O1 or O139 from stool or vomitus, or
- Serologic evidence of recent infection

Case classification

Confirmed: a clinically compatible case that is laboratory confirmed

Comment

Illnesses caused by strains of *V. cholerae* other than toxigenic *V. cholerae* O1 or O139 should not be reported as cases of cholera. The etiologic agent of a case of cholera should be reported as either *V. cholerae* O1 or *V. cholerae* O139. Only confirmed cases should be reported to NNDSS by state health departments.

Coccidioidomycosis (Revised 9/96)**Clinical description**

Infection may be asymptomatic or may produce an acute or chronic disease. Although the disease initially resembles an influenza-like febrile illness primarily involving the bronchopulmonary system, dissemination can occur to multiple organ systems.

Clinical case definition

An illness characterized by one or more of the following:

- Influenza-like signs and symptoms (e.g., fever, chest pain, cough, myalgia, arthralgia, and headache)
- Pneumonia or other pulmonary lesion, diagnosed by chest radiograph

- Erythema nodosum or erythema multiforme rash
- Involvement of bones, joints, or skin by dissemination
- Meningitis
- Involvement of viscera and lymph nodes

Laboratory criteria for diagnosis

- Cultural, histopathologic, or molecular evidence of presence of *Coccidioides immitis*, or
- Positive serologic test for coccidioidal antibodies in serum or cerebrospinal fluid by:
 1. Detection of coccidioidal immunoglobulin M (IgM) by immunodiffusion, enzyme immunoassay (EIA), latex agglutination, or tube precipitin, or
 2. Detection of rising titer of coccidioidal immunoglobulin G (IgG) by immunodiffusion, EIA, or complement fixation, or
- Coccidioidal skin-test conversion from negative to positive after onset of clinical signs and symptoms

Case classification

Confirmed: a case that meets the clinical case definition and is laboratory confirmed

Cryptosporidiosis (Adopted 3/95)**Clinical description**

An illness caused by the protozoan *Cryptosporidium parvum* and characterized by diarrhea, abdominal cramps, loss of appetite, low-grade fever, nausea, and vomiting. Infected persons may be asymptomatic. The disease can be prolonged and life-threatening in severely immunocompromised persons.

Laboratory criteria for diagnosis

- Demonstration of *Cryptosporidium* oocysts in stool, or
- Demonstration of *Cryptosporidium* in intestinal fluid or small-bowel biopsy specimens, or
- Demonstration of *Cryptosporidium* antigen in stool by a specific immunodiagnostic test (e.g., enzyme-linked immunosorbent assay)

Case classification

Probable: a clinically compatible case that is epidemiologically linked to a confirmed case

Confirmed: a case that is laboratory confirmed

Diphtheria (Revised 3/95)

Clinical description

An upper-respiratory tract illness characterized by sore throat, low-grade fever, and an adherent membrane of the tonsil(s), pharynx, and/or nose

Laboratory criteria for diagnosis

- Isolation of *Corynebacterium diphtheriae* from a clinical specimen or
- Histopathologic diagnosis of diphtheria

Case classification

Probable: a clinically compatible case that is not laboratory confirmed and is not epidemiologically linked to a laboratory-confirmed case

Confirmed: a clinically compatible case that is either laboratory confirmed or epidemiologically linked to a laboratory-confirmed case

Comment

Cutaneous diphtheria should not be reported. Respiratory disease caused by non-toxicogenic *C. diphtheriae* should be reported as diphtheria. All diphtheria isolates, regardless of association with disease, should be sent to the Diphtheria Laboratory, National Center for Infectious Diseases, CDC.

Encephalitis, Arboviral (Revised 9/96)

Clinical description

Arboviral infection may result in a febrile illness of variable severity associated with neurologic symptoms ranging from headache to aseptic meningitis or encephalitis. Arboviral encephalitis cannot be distinguished clinically from other central nervous system (CNS) infections. Symptoms can include headache, confusion or other alteration in sensorium, nausea, and vomiting. Signs may include fever, meningismus, cranial nerve palsies, paresis or paralysis, sensory deficits, altered reflexes, convulsions, abnormal movements, and coma of varying degree.

Laboratory criteria for diagnosis

- Fourfold or greater change in serum antibody titer, or
- Isolation of virus from or demonstration of viral antigen or genomic sequences in tissue, blood, cerebrospinal fluid (CSF), or other body fluid, or
- Specific immunoglobulin M (IgM) antibody by enzyme immunoassay (EIA) antibody captured in CSF or serum. Serum IgM antibodies alone should be

confirmed by demonstration of immunoglobulin G antibodies by another serologic assay (e.g., neutralization or hemagglutination inhibition).

Case classification

Probable: a clinically compatible case occurring during a period when arboviral transmission is likely, and with the following supportive serology: a stable (\leq twofold change) elevated antibody titer to an arbovirus (e.g., ≥ 320 by hemagglutination inhibition, ≥ 128 by complement fixation, ≥ 256 by immunofluorescence, and ≥ 160 by neutralization, or ≥ 400 by enzyme immunoassay IgM).

Confirmed: a clinically compatible case that is laboratory confirmed

Comment

The seasonality of arboviral transmission is variable and depends on the geographic location of exposure, the specific cycles of viral transmission, and local climatic conditions. Reporting should be etiology-specific (see below; the four encephalitides printed in bold are nationally reportable to CDC):

- **St. Louis encephalitis**
- **Western equine encephalitis**
- **Eastern equine encephalitis**
- **California encephalitis serogroup** (includes infections from the following viruses: LaCrosse, Jamestown Canyon, Snowshoe Hare, Trivittatus, Keystone, and California encephalitis viruses)
- Powassan encephalitis
- Other CNS infections transmitted by mosquitos, ticks, or midges (e.g., Venezuelan equine encephalitis and Cache Valley encephalitis)

***Escherichia coli* O157:H7 (Revised 9/96)**

Clinical description

An infection of variable severity characterized by diarrhea (often bloody) and abdominal cramps. Illness may be complicated by hemolytic uremic syndrome (HUS) or thrombotic thrombocytopenic purpura (TTP); asymptomatic infections also may occur.

Laboratory criteria for diagnosis

- Isolation of *Escherichia coli* O157:H7 from a specimen or
- Isolation of Shiga toxin-producing *E. coli* O157:NM from a clinical specimen*

*Strains of *E. coli* O157:H7 that have lost the flagellar "H" antigen become nonmotile and are designated "NM."

Case classification

Suspected: a case of postdiarrheal HUS or TTP (see HUS case definition)

Probable:

- A case with isolation of *E. coli* O157 from a clinical specimen, pending confirmation of H7 or Shiga toxin or
- A clinically compatible case that is epidemiologically linked to a confirmed or probable case

Confirmed: a case that is laboratory confirmed

Comment

Laboratory-confirmed isolates are reported via the Public Health Laboratory Information System (PHLIS), which is managed by the Foodborne and Diarrheal Diseases Branch, Division of Bacterial and Mycotic Diseases, National Center for Infectious Diseases, CDC. Both probable and confirmed cases are reported to the National Notifiable Diseases Surveillance System (NNDSS), but only confirmed cases are reported to PHLIS. Confirmation is based on laboratory findings, and clinical illness is not required.

Gonorrhea (Revised 9/96)**Clinical description**

A sexually transmitted infection commonly manifested by urethritis, cervicitis, or salpingitis. Infection may be asymptomatic.

Laboratory criteria for diagnosis

- Isolation of typical gram-negative, oxidase-positive diplococci (presumptive *Neisseria gonorrhoeae*) from a clinical specimen, or
- Demonstration of *N. gonorrhoeae* in a clinical specimen by detection of antigen or nucleic acid, or
- Observation of gram-negative intracellular diplococci in a urethral smear obtained from a male

Case classification

Probable: a) demonstration of gram-negative intracellular diplococci in an endocervical smear obtained from a female or b) a written morbidity report of gonorrhea submitted by a physician

Confirmed: a case that is laboratory confirmed

***Haemophilus influenzae* (Invasive Disease)**

Clinical description

Invasive disease caused by *Haemophilus influenzae* may produce any of several clinical syndromes, including meningitis, bacteremia, epiglottitis, or pneumonia.

Laboratory criteria for diagnosis

- Isolation of *H. influenzae* from a normally sterile site (e.g., blood or cerebrospinal fluid [CSF] or, less commonly, joint, pleural, or pericardial fluid)

Case classification

Probable: a clinically compatible case with detection of *H. influenzae* type b antigen in CSF

Confirmed: a clinically compatible case that is laboratory confirmed

Comment

Positive antigen test results from urine or serum samples are unreliable for diagnosis of *H. influenzae* disease.

Hansen Disease (Leprosy)

Clinical description

A chronic bacterial disease characterized by the involvement primarily of skin as well as peripheral nerves and the mucosa of the upper airway. Clinical forms of Hansen disease represent a spectrum reflecting the cellular immune response to *Mycobacterium leprae*. The following characteristics are typical of the major forms of the disease:

- *Tuberculoid*: one or a few well-demarcated, hypopigmented, and anesthetic skin lesions, frequently with active, spreading edges and a clearing center; peripheral nerve swelling or thickening also may occur
- *Lepromatous*: a number of erythematous papules and nodules or an infiltration of the face, hands, and feet with lesions in a bilateral and symmetrical distribution that progress to thickening of the skin
- *Borderline (dimorphous)*: skin lesions characteristic of both the tuberculoid and lepromatous forms
- *Indeterminate*: early lesions, usually hypopigmented macules, without developed tuberculoid or lepromatous features

Laboratory criteria for diagnosis

- Demonstration of acid-fast bacilli in skin or dermal nerve, obtained from the full-thickness skin biopsy of a lepromatous lesion

Case classification

Confirmed: a clinically compatible case that is laboratory confirmed

Hantavirus Pulmonary Syndrome (Revised 9/96)**Clinical description**

Hantavirus pulmonary syndrome (HPS), commonly referred to as hantavirus disease, is a febrile illness characterized by bilateral interstitial pulmonary infiltrates and respiratory compromise usually requiring supplemental oxygen and clinically resembling acute respiratory disease syndrome (ARDS). The typical prodrome consists of fever, chills, myalgia, headache, and gastrointestinal symptoms. Typical clinical laboratory findings include hemoconcentration, left shift in the white blood cell count, neutrophilic leukocytosis, thrombocytopenia, and circulating immunoblasts.

Clinical case definition

An illness characterized by one or more of the following clinical features:

- A febrile illness (i.e., temperature >101.0 F [>38.3 C]) characterized by bilateral diffuse interstitial edema that may radiographically resemble ARDS, with respiratory compromise requiring supplemental oxygen, developing within 72 hours of hospitalization, and occurring in a previously healthy person
- An unexplained respiratory illness resulting in death, with an autopsy examination demonstrating noncardiogenic pulmonary edema without an identifiable cause

Laboratory criteria for diagnosis

- Detection of hantavirus-specific immunoglobulin M or rising titers of hantavirus-specific immunoglobulin G, or
- Detection of hantavirus-specific ribonucleic acid sequence by polymerase chain reaction in clinical specimens, or
- Detection of hantavirus antigen by immunohistochemistry

Case classification

Confirmed: a clinically compatible case that is laboratory confirmed

Comment

Laboratory testing should be performed or confirmed at a reference laboratory. Because the clinical illness is nonspecific and ARDS is common, a screening case definition can be used to determine which patients to test. In general, a predisposing medical condition (e.g., chronic pulmonary disease, malignancy, trauma, burn, and surgery) is a more likely cause of ARDS than HPS, and patients who have these underlying conditions and ARDS need not be tested for hantavirus.

Hemolytic Uremic Syndrome, Postdiarrheal (Revised 9/96)

Clinical description

Hemolytic uremic syndrome (HUS) is characterized by the acute onset of microangiopathic hemolytic anemia, renal injury, and low platelet count. Thrombotic thrombocytopenic purpura (TTP) also is characterized by these features but can include central nervous system (CNS) involvement and fever and may have a more gradual onset. Most cases of HUS (but few cases of TTP) occur after an acute gastrointestinal illness (usually diarrheal).

Laboratory criteria for diagnosis

The following are both present at some time during the illness:

- Anemia (acute onset) with microangiopathic changes (i.e., schistocytes, burr cells, or helmet cells) on peripheral blood smear and
- Renal injury (acute onset) evidenced by either hematuria, proteinuria, or elevated creatinine level (i.e., ≥ 1.0 mg/dL in a child aged < 13 years or ≥ 1.5 mg/dL in a person aged ≥ 13 years, or $\geq 50\%$ increase over baseline)

Note: A low platelet count can usually, but not always, be detected early in the illness, but it may then become normal or even high. If a platelet count obtained within 7 days after onset of the acute gastrointestinal illness is not $< 150,000/\text{mm}^3$, other diagnoses should be considered.

Case classification

Probable:

- An acute illness diagnosed as HUS or TTP that meets the laboratory criteria in a patient who does not have a clear history of acute or bloody diarrhea in preceding 3 weeks or
- An acute illness diagnosed as HUS or TTP, that a) has onset within 3 weeks after onset of an acute or bloody diarrhea and b) meets the laboratory criteria except that microangiopathic changes are not confirmed

Confirmed: an acute illness diagnosed as HUS or TTP that both meets the laboratory criteria and began within 3 weeks after onset of an episode of acute or bloody diarrhea

Comment

Some investigators consider HUS and TTP to be part of a continuum of disease. Therefore, criteria for diagnosing TTP on the basis of CNS involvement and fever are not provided because cases diagnosed clinically as postdiarrheal TTP also should meet the criteria for HUS. These cases are reported as postdiarrheal HUS.

Hepatitis, Viral, Acute (Revised 9/96)

Clinical case definition

An acute illness with a) discrete onset of symptoms and b) jaundice or elevated serum aminotransferase levels

Laboratory criteria for diagnosis

- *Hepatitis A*: immunoglobulin M (IgM) antibody to hepatitis A virus (anti-HAV) positive
- *Hepatitis B*:
 1. IgM antibody to hepatitis B core antigen (anti-HBc) positive (if done) or hepatitis B surface antigen (HBsAg) positive
 2. IgM anti-HAV negative (if done)
- *Hepatitis C*:
 1. Serum aminotransferase levels >2.5 times the upper limit of normal, and
 2. IgM anti-HAV negative, and
 3. IgM anti-HBc negative (if done) or HBsAg negative, and
 4. Antibody to hepatitis C virus (anti-HCV) positive, verified by a supplemental test
- *Non-A, Non-B hepatitis*:
 1. Serum aminotransferase levels >2.5 times the upper limit of normal, and
 2. IgM anti-HAV negative, and
 3. IgM anti-HBc negative (if done) or HBsAg negative, and
 4. Anti-HCV negative (if done)
- *Delta hepatitis**: HBsAg or IgM anti-HBc positive and antibody to hepatitis delta virus positive

Case classification

Confirmed: a case that meets the clinical case definition and is laboratory confirmed or, for hepatitis A, a case that meets the clinical case definition and occurs in a person who has an epidemiologic link with a person who has laboratory-confirmed hepatitis A (i.e., household or sexual contact with an infected person during the 15–50 days before the onset of symptoms)

Comment

- 1) Persons who have chronic hepatitis or persons identified as HBsAg positive or anti-HCV positive should not be reported as having acute viral hepatitis unless they have evidence of an acute illness compatible with viral hepatitis (with the

*Delta hepatitis is not a nationally notifiable disease.

exception of perinatal hepatitis B infection). (See Hepatitis, Viral, Perinatal Hepatitis B Virus Infection Acquired in the United States or U.S. Territories.)

- 2) Up to 20% of acute hepatitis C cases will be anti-HCV negative when reported and will be classified as non-A, non-B hepatitis because some (5%–10%) have not yet seroconverted and others (5%–10%) remain negative even with prolonged follow-up (6).
- 3) Available serologic tests for anti-HCV do not distinguish between acute and chronic or past infection. Thus, other causes of acute hepatitis should be excluded for anti-HCV positive patients who have an acute illness compatible with viral hepatitis.

Hepatitis, Viral, Perinatal Hepatitis B Virus Infection Acquired in the United States or U.S. Territories (Adopted 3/95)

Clinical description

Perinatal hepatitis B in the newborn may range from asymptomatic to fulminant hepatitis.

Laboratory criteria for diagnosis

- Hepatitis B surface antigen (HBsAg) positive

Case classification

HBsAg positivity in any infant aged >1–24 months who was born in the United States or in U.S. territories to an HBsAg-positive mother

Comment

Infants born to HBsAg-positive mothers should receive hepatitis B immune globulin (HBIG) and the first dose of hepatitis B vaccine within 24 hours of birth, followed by the second and third doses of vaccine at 1 and 6 months of age, respectively. Postvaccination testing for antibody to HBsAg and HBsAg is recommended from 3 to 6 months following completion of the vaccine series. If HBIG and the initial dose of vaccine are delayed for >1 month after birth, testing for HBsAg may determine if the infant is already infected.

HIV Infection, Pediatric

Case definition

Refer to *1994 Revised Classification System for Human Immunodeficiency Virus Infection in Children <13 Years of Age* (MMWR 1994;43[No. RR-12]:1–10).

Legionellosis (Revised 9/96)

Clinical description

Legionellosis is associated with two clinically and epidemiologically distinct illnesses: Legionnaires disease, which is characterized by fever, myalgia, cough, pneumonia, and Pontiac fever, a milder illness without pneumonia.

Laboratory criteria for diagnosis

- Isolation of *Legionella* from respiratory secretions, lung tissue, pleural fluid, or other normally sterile fluids, or
- Demonstration of a fourfold or greater rise in the reciprocal immunofluorescence antibody (IFA) titer to ≥ 128 against *Legionella pneumophila* serogroup 1 between paired acute- and convalescent-phase serum specimens, or
- Detection of *L. pneumophila* serogroup 1 in respiratory secretions, lung tissue, or pleural fluid by direct fluorescent antibody testing, or
- Demonstration of *L. pneumophila* serogroup 1 antigens in urine by radioimmunoassay or enzyme-linked immunosorbent assay

Case classification

Confirmed: a clinically compatible case that is laboratory confirmed

Comment

The previously used category of "probable case," which was based on a single IFA titer, lacks specificity for surveillance and is no longer used.

Lyme Disease (Revised 9/96)

Clinical description

A systemic, tickborne disease with protean manifestations, including dermatologic, rheumatologic, neurologic, and cardiac abnormalities. The best clinical marker for the disease is the initial skin lesion (i.e., erythema migrans [EM]) that occurs in 60%–80% of patients.

Laboratory criteria for diagnosis

- Isolation of *Borrelia burgdorferi* from a clinical specimen or
- Demonstration of diagnostic immunoglobulin M or immunoglobulin G antibodies to *B. burgdorferi* in serum or cerebrospinal fluid (CSF). A two-test approach using a sensitive enzyme immunoassay or immunofluorescence antibody followed by Western blot is recommended (7).

Case classification

Confirmed: a) a case with EM or b) a case with at least one late manifestation (as defined below) that is laboratory confirmed.

Comment

This surveillance case definition was developed for national reporting of Lyme disease; it is not intended to be used in clinical diagnosis.

Definition of terms used in the clinical description and case definition:

- *Erythema migrans.* For purposes of surveillance, EM is defined as a skin lesion that typically begins as a red macule or papule and expands over a period of days to weeks to form a large round lesion, often with partial central clearing. A single primary lesion must reach ≥ 5 cm in size. Secondary lesions also may occur. Annular erythematous lesions occurring within several hours of a tick bite represent hypersensitivity reactions and do not qualify as EM. For most patients, the expanding EM lesion is accompanied by other acute symptoms, particularly fatigue, fever, headache, mildly stiff neck, arthralgia, or myalgia. These symptoms are typically intermittent. The diagnosis of EM must be made by a physician. Laboratory confirmation is recommended for persons with no known exposure.
- *Late manifestations.* Late manifestations include any of the following when an alternate explanation is not found:
 1. *Musculoskeletal system.* Recurrent, brief attacks (weeks or months) of objective joint swelling in one or a few joints, sometimes followed by chronic arthritis in one or a few joints. Manifestations not considered as criteria for diagnosis include chronic progressive arthritis not preceded by brief attacks and chronic symmetrical polyarthritis. Additionally, arthralgia, myalgia, or fibromyalgia syndromes alone are not criteria for musculoskeletal involvement.
 2. *Nervous system.* Any of the following, alone or in combination: lymphocytic meningitis; cranial neuritis, particularly facial palsy (may be bilateral); radiculoneuropathy; or, rarely, encephalomyelitis. Encephalomyelitis must be confirmed by demonstration of antibody production against *B. burgdorferi* in the CSF, evidenced by a higher titer of antibody in CSF than in serum. Headache, fatigue, paresthesia, or mildly stiff neck alone are not criteria for neurologic involvement.
 3. *Cardiovascular system.* Acute onset of high-grade (2° or 3°) atrioventricular conduction defects that resolve in days to weeks and are sometimes associated with myocarditis. Palpitations, bradycardia, bundle branch block, or myocarditis alone are not criteria for cardiovascular involvement.
- *Exposure.* Exposure is defined as having been (≤ 30 days before onset of EM) in wooded, brushy, or grassy areas (i.e., potential tick habitats) in a county in which Lyme disease is endemic. A history of tick bite is not required.
- *Disease endemic to county.* A county in which Lyme disease is endemic is one in which at least two confirmed cases have been previously acquired or in which established populations of a known tick vector are infected with *B. burgdorferi*.

Malaria (Revised 3/95)

Clinical description

Signs and symptoms are variable; however, most patients experience fever. In addition to fever, common associated symptoms include headache, back pain, chills, sweats, myalgia, nausea, vomiting, diarrhea, and cough. Untreated *Plasmodium falciparum* infection can lead to coma, renal failure, pulmonary edema, and death. The diagnosis of malaria should be considered for any person who has these symptoms and who has traveled to an area in which malaria is endemic. Asymptomatic parasitemia can occur among persons who have been long-term residents of areas in which malaria is endemic.

Laboratory criteria for diagnosis

- Demonstration of malaria parasites in blood films

Case classification

Confirmed: an episode of microscopically confirmed malaria parasitemia in any person (symptomatic or asymptomatic) diagnosed in the United States, regardless of whether the person experienced previous episodes of malaria while outside the country

Comment

A subsequent attack experienced by the same person but caused by a different *Plasmodium* species is counted as an additional case. A subsequent attack experienced by the same person and caused by the same species in the United States may indicate a relapsing infection or treatment failure caused by drug resistance.

Blood smears from questionable cases should be referred to the National Malaria Repository, CDC, for confirmation of the diagnosis.

Cases also are classified according to the following World Health Organization categories:

- *Autochthonous:*
 - Indigenous:* malaria acquired by mosquito transmission in an area where malaria is a regular occurrence
 - Introduced:* malaria acquired by mosquito transmission from an imported case in an area where malaria is not a regular occurrence
- *Imported:* malaria acquired outside a specific area (e.g., the United States and its territories)
- *Induced:* malaria acquired through artificial means (e.g., blood transfusion, common syringes, or malariotherapy)
- *Relapsing:* renewed manifestation (i.e., of clinical symptoms and/or parasitemia) of malarial infection that is separated from previous manifestations of the same infection by an interval greater than any interval resulting from the normal periodicity of the paroxysms

- *Cryptic*: an isolated case of malaria that cannot be epidemiologically linked to additional cases

Measles (Revised 9/96)

Clinical case definition

An illness characterized by all the following:

- a generalized rash lasting ≥ 3 days
- a temperature ≥ 101.0 F (≥ 38.3 C)
- cough, coryza, or conjunctivitis

Laboratory criteria for diagnosis

- Positive serologic test for measles immunoglobulin M antibody, or
- Significant rise in measles antibody level by any standard serologic assay, or
- Isolation of measles virus from a clinical specimen

Case classification

Suspected: any febrile illness accompanied by rash

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

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

Comment

Confirmed cases should be reported to NNDSS. An *imported* case has its source outside the country or state. Rash onset occurs within 18 days after entering the jurisdiction, and illness cannot be linked to local transmission. Imported cases should be classified as:

- *International*. A case that is imported from another country
- *Out-of-State*. A case that 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 7–18 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 day care center).

An *indigenous* case is defined as a case of measles that is not imported. Cases that are linked to imported cases should be classified as indigenous if the exposure to the imported case occurred in the reporting state. Any case that cannot be proved to be imported should be classified as indigenous.

Meningococcal Disease

Clinical description

Meningococcal disease manifests most commonly as meningitis and/or meningococemia that may progress rapidly to purpura fulminans, shock, and death. However, other manifestations might be observed.

Laboratory criteria for diagnosis

- Isolation of *Neisseria meningitidis* from a normally sterile site (e.g., blood or cerebrospinal fluid [CSF] or, less commonly, joint, pleural, or pericardial fluid)

Case classification

Probable: a case with a positive antigen test in CSF or clinical purpura fulminans in the absence of a positive blood culture

Confirmed: a clinically compatible case that is laboratory confirmed

Comment

Positive antigen test results from urine or serum samples are unreliable for diagnosing meningococcal disease.

Mumps (Revised 9/96)

Clinical case definition

An illness with acute onset of unilateral or bilateral tender, self-limited swelling of the parotid or other salivary gland, lasting ≥ 2 days, and without other apparent cause

Laboratory criteria for diagnosis

- Isolation of mumps virus from clinical specimen, or
- Significant rise between acute- and convalescent-phase titers in serum mumps immunoglobulin G antibody level by any standard serologic assay, or
- Positive serologic test for mumps immunoglobulin M (IgM) antibody

Case classification

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 or probable case

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

Comment

Two probable cases that are epidemiologically linked would be considered confirmed, even in the absence of laboratory confirmation. False-positive IgM results by immunofluorescent antibody assays have been reported (8).

Pertussis (Revised 9/96)

Clinical case definition

A cough illness lasting ≥ 2 weeks with one of the following: paroxysms of coughing, inspiratory "whoop," or post-tussive vomiting, without other apparent cause

Laboratory criteria for diagnosis

- Isolation of *Bordetella pertussis* from clinical specimen or
- Positive polymerase chain reaction for *B. pertussis*

Case classification

Probable: a case that meets the clinical case definition, is not laboratory confirmed, and is not epidemiologically linked to a laboratory-confirmed case

Confirmed: a case that is laboratory confirmed or one that meets the clinical case definition and is either laboratory confirmed or epidemiologically linked to a laboratory-confirmed case

Comment

The clinical case definition is appropriate for endemic or sporadic cases. In outbreak settings, a case may be defined as a cough illness lasting ≥ 2 weeks. Because some studies have documented that direct fluorescent antibody testing of nasopharyngeal secretions has low sensitivity and variable specificity, it should not be relied on as a criterion for laboratory confirmation (9,10). Serologic testing for pertussis is available in some areas but is not standardized and, therefore, should not be relied on as a criterion for laboratory confirmation for national reporting purposes. Both probable and confirmed cases should be reported to NNDSS.

Plague (Revised 9/96)

Clinical description

Plague is transmitted to humans by fleas or by direct exposure to infected tissues or respiratory droplets; the disease is characterized by fever, chills, headache, malaise, prostration, and leukocytosis that manifests in one or more of the following principal clinical forms:

- Regional lymphadenitis (bubonic plague)
- Septicemia without an evident bubo (septicemic plague)
- Plague pneumonia, resulting from hematogenous spread in bubonic or septicemic cases (secondary pneumonic plague) or inhalation of infectious droplets (primary pneumonic plague)
- Pharyngitis and cervical lymphadenitis resulting from exposure to larger infectious droplets or ingestion of infected tissues (pharyngeal plague)

Laboratory criteria for diagnosis

Presumptive

- Elevated serum antibody titer(s) to *Yersinia pestis* fraction 1 (F1) antigen (without documented fourfold or greater change) in a patient with no history of plague vaccination or
- Detection of F1 antigen in a clinical specimen by fluorescent assay

Confirmatory

- Isolation of *Y. pestis* from a clinical specimen or
- Fourfold or greater change in serum antibody titer to *Y. pestis* F1 antigen

Case classification

Suspected: a clinically compatible case without presumptive or confirmatory laboratory results

Probable: a clinically compatible case with presumptive laboratory results

Confirmed: a clinically compatible case with confirmatory laboratory results

Poliomyelitis, Paralytic

Clinical case definition

Acute onset of a flaccid paralysis of one or more limbs with decreased or absent tendon reflexes in the affected limbs, without other apparent cause, and without sensory or cognitive loss

Case classification

Probable: a case that meets the clinical case definition

Confirmed: a case that meets the clinical case definition and in which the patient has a neurologic deficit 60 days after onset of initial symptoms, has died, or has unknown follow-up status

Comment

All suspected cases of paralytic poliomyelitis are reviewed by a panel of expert consultants before final classification occurs. Confirmed cases are then further classified based on epidemiologic and laboratory criteria (11). Only confirmed cases are included in Table I in the *MMWR*. Suspected cases are enumerated in a footnote to the *MMWR* table.

Psittacosis (Revised 9/96)**Clinical description**

An illness characterized by fever, chills, headache, photophobia, cough, and myalgia

Laboratory criteria for diagnosis

- Isolation of *Chlamydia psittaci* from respiratory secretions, or
- Fourfold or greater increase in antibody against *C. psittaci* by complement fixation or microimmunofluorescence (MIF) to a reciprocal titer of ≥ 32 between paired acute- and convalescent-phase serum specimens, or
- Presence of immunoglobulin M antibody against *C. psittaci* by MIF to a reciprocal titer of ≥ 16

Case classification

Probable: a clinically compatible case that is epidemiologically linked to a confirmed case or that has supportive serology (e.g., *C. psittaci* titer of ≥ 32 in one or more serum specimens obtained after onset of symptoms)

Confirmed: a clinically compatible case that is laboratory confirmed

Comment

The serologic findings by CF also may occur as a result of infection with *Chlamydia pneumoniae* or *Chlamydia trachomatis*. The MIF might be more specific for infection with *C. psittaci*, but experience with and availability of this newer test are more limited.

Rabies, Animal**Laboratory criteria for diagnosis**

- A positive direct fluorescent antibody test (preferably performed on central nervous system tissue)
- Isolation of rabies virus (in cell culture or in a laboratory animal)

Case classification

Confirmed: a case that is laboratory confirmed

Rabies, Human**Clinical description**

Rabies is an acute encephalomyelitis that almost always progresses to coma or death within 10 days after the first symptom.

Laboratory criteria for diagnosis

- Detection by direct fluorescent antibody of viral antigens in a clinical specimen (preferably the brain or the nerves surrounding hair follicles in the nape of the neck), or
- Isolation (in cell culture or in a laboratory animal) of rabies virus from saliva, cerebrospinal fluid (CSF), or central nervous system tissue, or
- Identification of a rabies-neutralizing antibody titer ≥ 5 (complete neutralization) in the serum or CSF of an unvaccinated person.

Case classification

Confirmed: a clinically compatible case that is laboratory confirmed

Comment

Laboratory confirmation by all of the above methods is strongly recommended.

Rocky Mountain Spotted Fever (Revised 9/96)**Clinical description**

A tickborne febrile illness most commonly characterized by acute onset and usually accompanied by myalgia, headache, and petechial rash (on the palms and soles in two thirds of the cases)

Laboratory criteria for diagnosis

- Fourfold or greater rise in antibody titer to *Rickettsia rickettsii* antigen by immunofluorescence antibody (IFA), complement fixation (CF), latex agglutination (LA), microagglutination (MA), or indirect hemagglutination antibody (IHA) test in acute- and convalescent-phase specimens ideally taken ≥ 3 weeks apart, or
- Positive polymerase chain reaction assay to *R. rickettsii*, or
- Demonstration of positive immunofluorescence of skin lesion (biopsy) or organ tissue (autopsy), or
- Isolation of *R. rickettsii* from clinical specimen

Case classification

Probable: a clinically compatible case with a single IFA serologic titer of ≥ 64 or a single CF titer of ≥ 16 or other supportive serology (fourfold rise in titer or a single titer ≥ 320 by Proteus OX-19 or OX-2, or a single titer ≥ 128 by an LA, IHA, or MA test)

Confirmed: a clinically compatible case that is laboratory confirmed

Rubella (Revised 9/96)***Clinical case definition***

An illness that has all the following characteristics:

- Acute onset of generalized maculopapular rash
- Temperature >99.0 F (>37.2 C), if measured
- Arthralgia/arthritis, lymphadenopathy, or conjunctivitis

Laboratory criteria for diagnosis

- Isolation of rubella virus, or
- Significant rise between acute- and convalescent-phase titers in serum rubella immunoglobulin G antibody level by any standard serologic assay, or
- Positive serologic test for rubella immunoglobulin M (IgM) antibody

Case classification

Suspected: any generalized rash illness of acute onset

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

Confirmed: a case that is laboratory confirmed or that meets the clinical case definition and is epidemiologically linked to a laboratory-confirmed case

Comments

Serum rubella IgM test results that are false positives have been reported in persons with other viral infections (e.g., acute infection with Epstein-Barr virus [infectious mononucleosis], recent cytomegalovirus infection, and parvovirus infection) or in the presence of rheumatoid factor. Patients who have laboratory evidence of recent measles infection are excluded.

Rubella, Congenital Syndrome (Revised 9/96)

Clinical description

An illness usually manifesting in infancy resulting from rubella infection in utero and characterized by signs or symptoms from the following categories:

- Cataracts/congenital glaucoma, congenital heart disease (most commonly patent ductus arteriosus, or peripheral pulmonary artery stenosis), loss of hearing, pigmentary retinopathy
- Purpura, splenomegaly, jaundice, microcephaly, mental retardation, meningoencephalitis, radiolucent bone disease.

Clinical case definition

Presence of any defects or laboratory data consistent with congenital rubella infection

Laboratory criteria for diagnosis

- Isolation of rubella virus, or
- Demonstration of rubella-specific immunoglobulin M antibody, or
- Infant rubella antibody level that persists at a higher level and for a longer period than expected from passive transfer of maternal antibody (i.e., rubella titer that does not drop at the expected rate of a twofold dilution per month)

Case classification

Suspected: a case with some compatible clinical findings but not meeting the criteria for a probable case

Probable: a case that is not laboratory confirmed and that has any two complications listed in paragraph a) of the clinical description or one complication from paragraph a) and one from paragraph b), and lacks evidence of any other etiology

Confirmed: a clinically compatible case that is laboratory confirmed

Infection only: a case that demonstrates laboratory evidence of infection, but without any clinical symptoms or signs

Comment

In probable cases, either or both of the eye-related findings (i.e., cataracts and congenital glaucoma) are interpreted as a single complication. In cases classified as infection only, if any compatible signs or symptoms (e.g., hearing loss) are identified later, the case is reclassified as confirmed.

Salmonellosis

Clinical description

An illness of variable severity commonly manifested by diarrhea, abdominal pain, nausea, and sometimes vomiting. Asymptomatic infections may occur and the organism may cause extraintestinal infections.

Laboratory criteria for diagnosis

- Isolation of *Salmonella* from a clinical specimen

Case classification

Probable: a clinically compatible case that is epidemiologically linked to a confirmed case

Confirmed: a case that is laboratory confirmed

Comment

Laboratory-confirmed isolates are reported to CDC via the Public Health Laboratory Information System (PHLIS), which is managed by the Foodborne and Diarrheal Diseases Branch, Division of Bacterial and Mycotic Diseases, National Center for Infectious Diseases, CDC. Both probable and confirmed cases are reported to the National Notifiable Diseases Surveillance System, but only confirmed cases are reported to PHLIS. Both asymptomatic infections and infections at sites other than the gastrointestinal tract, if laboratory confirmed, are considered confirmed cases that should be reported to PHLIS.

Shigellosis

Clinical description

An illness of variable severity characterized by diarrhea, fever, nausea, cramps, and tenesmus. Asymptomatic infections may occur.

Laboratory criteria for diagnosis

- Isolation of *Shigella* from a clinical specimen

Case classification

Probable: a clinically compatible case that is epidemiologically linked to a confirmed case

Confirmed: a case that is laboratory confirmed

Comment

Laboratory-confirmed isolates are reported to CDC via the Public Health Laboratory Information System (PHLIS), which is managed by the Foodborne and Diarrheal

Diseases Branch, Division of Bacterial and Mycotic Diseases, National Center for Infectious Diseases, CDC. Both probable and confirmed cases are reported to the National Notifiable Diseases Surveillance System, but only confirmed cases are reported to PHLIS. Confirmation is based on laboratory findings, and clinical illness is not required.

Streptococcal Disease, Invasive, Group A (Adopted 3/95)

Clinical description

Invasive group A streptococcal infections may manifest as any of several clinical syndromes, including pneumonia, bacteremia in association with cutaneous infection (e.g., cellulitis, erysipelas, or infection of a surgical or nonsurgical wound), deep soft-tissue infection (e.g., myositis or necrotizing fasciitis), meningitis, peritonitis, osteomyelitis, septic arthritis, postpartum sepsis (i.e., puerperal fever), neonatal sepsis, and nonfocal bacteremia.

Laboratory criteria for diagnosis

- Isolation of group A *Streptococcus* (*Streptococcus pyogenes*) by culture from a normally sterile site (e.g., blood or cerebrospinal fluid, or, less commonly, joint, pleural, or pericardial fluid)

Case classification

Confirmed: a case that is laboratory confirmed

Comment

See also Streptococcal Toxic-Shock Syndrome.

***Streptococcus pneumoniae*, Drug-Resistant Invasive Disease (Revised 9/96)**

Clinical description

Streptococcus pneumoniae causes many clinical syndromes, depending on the site of infection (e.g., acute otitis media, pneumonia, bacteremia, or meningitis).

Laboratory criteria for diagnosis

- Isolation of *S. pneumoniae* from a normally sterile site (e.g., blood, cerebrospinal fluid, or, less commonly, joint, pleural, or pericardial fluid) and

- “Nonsusceptible” isolate (i.e., intermediate- or high-level resistance of the *S. pneumoniae* isolate to at least one antimicrobial agent currently approved for use in treating pneumococcal infection (12,13)*)

Case classification

Probable: a clinically compatible case caused by laboratory-confirmed culture of *S. pneumoniae* identified as “nonsusceptible” (i.e., an oxacillin zone size of <20 mm) when oxacillin screening is the only method of antimicrobial susceptibility testing performed

Confirmed: a clinically compatible case that is laboratory confirmed

Streptococcal Toxic-Shock Syndrome (Revised 9/96)

Clinical description

Streptococcal toxic-shock syndrome (STSS) is a severe illness associated with invasive or noninvasive group A streptococcal (*Streptococcus pyogenes*) infection. STSS may occur with infection at any site but most often occurs in association with infection of a cutaneous lesion. Signs of toxicity and a rapidly progressive clinical course are characteristic, and the case-fatality rate may exceed 50%.

Clinical case definition

An illness with the following clinical manifestations occurring within the first 48 hours of hospitalization or, for a nosocomial case, within the first 48 hours of illness:

- Hypotension defined by a systolic blood pressure ≤ 90 mm Hg for adults or less than the fifth percentile by age for children aged <16 years
- Multi-organ involvement characterized by two or more of the following:
 1. **Renal impairment:** Creatinine ≥ 2 mg/dL (≥ 177 $\mu\text{mol/L}$) for adults or greater than or equal to twice the upper limit of normal for age. In patients with preexisting renal disease, a greater than twofold elevation over the baseline level.
 2. **Coagulopathy:** Platelets $\leq 100,000/\text{mm}^3$ ($\leq 100 \times 10^6/\text{L}$) or disseminated intravascular coagulation, defined by prolonged clotting times, low fibrinogen level, and the presence of fibrin degradation products
 3. **Liver involvement:** Alanine aminotransferase, aspartate aminotransferase, or total bilirubin levels greater than or equal to twice the upper limit of normal for the patient’s age. In patients with preexisting liver disease, a greater than two-fold increase over the baseline level

*Resistance defined by National Committee for Clinical Laboratory Standards (NCCLS)-approved methods and NCCLS-approved interpretive minimum inhibitory concentration (MIC) standards ($\mu\text{g/mL}$) for *S. pneumoniae*. NCCLS recommends that all invasive *S. pneumoniae* isolates found to be “possibly resistant” to beta-lactams (i.e., an oxacillin zone size of <20 mm) by oxacillin screening should undergo further susceptibility testing by using a quantitative MIC method acceptable for penicillin, extended-spectrum cephalosporins, and other drugs as clinically indicated (11,12).

4. *Acute respiratory distress syndrome*: defined by acute onset of diffuse pulmonary infiltrates and hypoxemia in the absence of cardiac failure or by evidence of diffuse capillary leak manifested by acute onset of generalized edema, or pleural or peritoneal effusions with hypoalbuminemia
5. A generalized erythematous macular rash that may desquamate
6. Soft-tissue necrosis, including necrotizing fasciitis or myositis, or gangrene

Laboratory criteria for diagnosis

- Isolation of group A *Streptococcus*

Case classification

Probable: a case that meets the clinical case definition in the absence of another identified etiology for the illness and with isolation of group A *Streptococcus* from a nonsterile site

Confirmed: a case that meets the clinical case definition and with isolation of group A *Streptococcus* from a normally sterile site (e.g., blood or cerebrospinal fluid or, less commonly, joint, pleural, or pericardial fluid)

Comment

See also Streptococcal Disease, Invasive, Group A and Toxic-Shock Syndrome.

Syphilis (All Definitions Revised 9/96)

Syphilis is a complex sexually transmitted disease that has a highly variable clinical course. Classification by a clinician with expertise in syphilis may take precedence over the following case definitions developed for surveillance purposes.

Syphilis, primary

Clinical description

A stage of infection with *Treponema pallidum* characterized by one or more chancres (ulcers); chancres might differ considerably in clinical appearance.

Laboratory criteria for diagnosis

- Demonstration of *T. pallidum* in clinical specimens by darkfield microscopy, direct fluorescent antibody (DFA-TP), or equivalent methods

Case classification

Probable: a clinically compatible case with one or more ulcers (chancres) consistent with primary syphilis and a reactive serologic test (nontreponemal: Venereal Disease Research Laboratory [VDRL] or rapid plasma reagin [RPR]; treponemal: fluorescent treponemal antibody absorbed [FTA-ABS] or microhemagglutination assay for antibody to *T. pallidum* [MHA-TP])

Confirmed: a clinically compatible case that is laboratory confirmed

Syphilis, secondary

Clinical description

A stage of infection caused by *T. pallidum* and characterized by localized or diffuse mucocutaneous lesions, often with generalized lymphadenopathy. The primary chancre may still be present.

Laboratory criteria for diagnosis

- Demonstration of *T. pallidum* in clinical specimens by darkfield microscopy, DFA-TP, or equivalent methods

Case classification

Probable: a clinically compatible case with a nontreponemal (VDRL or RPR) titer ≥ 4

Confirmed: a clinically compatible case that is laboratory confirmed

Syphilis, latent

Clinical description

A stage of infection caused by *T. pallidum* in which organisms persist in the body of the infected person without causing symptoms or signs. Latent syphilis is subdivided into early, late, and unknown categories based on the duration of infection.

Case classification

Probable: no clinical signs or symptoms of syphilis and the presence of one of the following:

- No past diagnosis of syphilis, a reactive nontreponemal test (i.e., VDRL or RPR), and a reactive treponemal test (i.e., FTA-ABS or MHA-TP)
- A past history of syphilis therapy and a current nontreponemal test titer demonstrating fourfold or greater increase from the last nontreponemal test titer

Syphilis, early latent

Clinical description

A subcategory of latent syphilis. When initial infection has occurred within the previous 12 months, latent syphilis is classified as early latent.

Case classification

Probable: latent syphilis (see Syphilis, latent) in a person who has evidence of having acquired the infection within the previous 12 months based on one or more of the following criteria:

- Documented seroconversion or fourfold or greater increase in titer of a nontreponemal test during the previous 12 months
- A history of symptoms consistent with primary or secondary syphilis during the previous 12 months

- A history of sexual exposure to a partner who had confirmed or probable primary or secondary syphilis or probable early latent syphilis (documented independently as duration <1 year)
- Reactive nontreponemal and treponemal tests from a person whose only possible exposure occurred within the preceding 12 months

Syphilis, late latent

Clinical description

A subcategory of latent syphilis. When initial infection has occurred >1 year previously, latent syphilis is classified as late latent.

Case classification

Probable: latent syphilis (see Syphilis, latent) in a patient who has no evidence of having acquired the disease within the preceding 12 months (see Syphilis, early latent) and whose age and titer do not meet the criteria specified for latent syphilis of unknown duration.

Syphilis, latent, of unknown duration

Clinical description

A subcategory of latent syphilis. When the date of initial infection cannot be established as having occurred within the previous year and the patient's age and titer meet criteria described below, latent syphilis is classified as latent syphilis of unknown duration.

Case classification

Probable: latent syphilis (see Syphilis, latent) that does not meet the criteria for early latent syphilis, and the patient is aged 13–35 years and has a nontreponemal titer ≥ 32

Neurosyphilis

Clinical description

Evidence of central nervous system infection with *T. pallidum*

Laboratory criteria for diagnosis

- A reactive serologic test for syphilis and reactive VDRL in cerebrospinal fluid (CSF)

Case classification

Probable: syphilis of any stage, a negative VDRL in CSF, and both the following:

- Elevated CSF protein or leukocyte count in the absence of other known causes of these abnormalities

- Clinical symptoms or signs consistent with neurosyphilis without other known causes for these clinical abnormalities

Confirmed: syphilis of any stage that meets the laboratory criteria for neurosyphilis

Syphilis, late, with clinical manifestations other than neurosyphilis (late benign syphilis and cardiovascular syphilis)

Clinical description

Clinical manifestations of late syphilis other than neurosyphilis may include inflammatory lesions of the cardiovascular system, skin, and bone. Rarely, other structures (e.g., the upper and lower respiratory tracts, mouth, eye, abdominal organs, reproductive organs, lymph nodes, and skeletal muscle) may be involved. Late syphilis usually becomes clinically manifest only after a period of 15–30 years of untreated infection.

Laboratory criteria for diagnosis

Demonstration of *T. pallidum* in late lesions by fluorescent antibody or special stains (although organisms are rarely visualized in late lesions)

Case classification

Probable: characteristic abnormalities or lesions of the cardiovascular system, skin, bone, or other structures with a reactive treponemal test, in the absence of other known causes of these abnormalities, and without CSF abnormalities and clinical symptoms or signs consistent with neurosyphilis

Confirmed: a clinically compatible case that is laboratory confirmed

Comment

Analysis of CSF for evidence of neurosyphilis is necessary in the evaluation of late syphilis with clinical manifestations.

Syphilitic Stillbirth

Clinical description

A fetal death that occurs after a 20-week gestation or in which the fetus weighs >500 g and the mother had untreated or inadequately treated* syphilis at delivery

Comment

For reporting purposes, syphilitic stillbirths should be reported as cases of congenital syphilis.

Syphilis, Congenital (Revised 9/96)

Clinical description

A condition caused by infection in utero with *Treponema pallidum*. A wide spectrum of severity exists, and only severe cases are clinically apparent at birth. An infant

*Inadequate treatment consists of any nonpenicillin therapy or penicillin administered <30 days before delivery.

or child (aged <2 years) may have signs such as hepatosplenomegaly, rash, condyloma lata, snuffles, jaundice (nonviral hepatitis), pseudoparalysis, anemia, or edema (nephrotic syndrome and/or malnutrition). An older child may have stigmata (e.g., interstitial keratitis, nerve deafness, anterior bowing of shins, frontal bossing, mulberry molars, Hutchinson teeth, saddle nose, rhagades, or Clutton joints).

Laboratory criteria for diagnosis

- Demonstration of *T. pallidum* by darkfield microscopy, fluorescent antibody, or other specific stains in specimens from lesions, placenta, umbilical cord, or autopsy material

Case classification

Probable: a condition affecting an infant whose mother had untreated or inadequately treated* syphilis at delivery, regardless of signs in the infant, or an infant or child who has a reactive treponemal test for syphilis and any one of the following:

- Any evidence of congenital syphilis on physical examination
- Any evidence of congenital syphilis on radiographs of long bones
- A reactive cerebrospinal fluid (CSF) venereal disease research laboratory (VDRL)
- An elevated CSF cell count or protein (without other cause)
- A reactive fluorescent treponemal antibody absorbed—19S-IgM antibody test or IgM enzyme-linked immunosorbent assay

Confirmed: a case that is laboratory confirmed

Comment

Congenital and acquired syphilis may be difficult to distinguish when a child is seropositive after infancy. Signs of congenital syphilis may not be obvious, and stigmata may not yet have developed. Abnormal values for CSF VDRL, cell count, and protein, as well as IgM antibodies, may be found in either congenital or acquired syphilis. Findings on radiographs of long bones may help because radiographic changes in the metaphysis and epiphysis are considered classic signs of congenitally acquired syphilis. The decision may ultimately be based on maternal history and clinical judgment. In a young child, the possibility of sexual abuse should be considered as a cause of acquired rather than congenital syphilis, depending on the clinical picture. For reporting purposes, congenital syphilis includes cases of congenitally acquired syphilis among infants and children as well as syphilitic stillbirths.

*Inadequate treatment consists of any nonpenicillin therapy or penicillin administered <30 days before delivery.

Tetanus (Revised 9/96)

Clinical case definition

Acute onset of hypertonia and/or painful muscular contractions (usually of the muscles of the jaw and neck) and generalized muscle spasms without other apparent medical cause

Case classification

Confirmed: a clinically compatible case, as reported by a health-care professional

Toxic-Shock Syndrome

Clinical case definition

An illness with the following clinical manifestations:

- **Fever:** temperature ≥ 102.0 F (≥ 38.9 C)
- **Rash:** diffuse macular erythroderma
- **Desquamation:** 1–2 weeks after onset of illness, particularly on the palms and soles
- **Hypotension:** systolic blood pressure ≤ 90 mm Hg for adults or less than fifth percentile by age for children aged < 16 years; orthostatic drop in diastolic blood pressure ≥ 15 mm Hg from lying to sitting, orthostatic syncope, or orthostatic dizziness
- **Multisystem involvement (three or more of the following):**
 - Gastrointestinal:* vomiting or diarrhea at onset of illness
 - Muscular:* severe myalgia or creatine phosphokinase level at least twice the upper limit of normal
 - Mucous membrane:* vaginal, oropharyngeal, or conjunctival hyperemia
 - Renal:* blood urea nitrogen or creatinine at least twice the upper limit of normal for laboratory or urinary sediment with pyuria (≥ 5 leukocytes per high-power field) in the absence of urinary tract infection
 - Hepatic:* total bilirubin, alanine aminotransferase enzyme, or aspartate aminotransferase enzyme levels at least twice the upper limit of normal for laboratory
 - Hematologic:* platelets $< 100,000/\text{mm}^3$
 - Central nervous system:* disorientation or alterations in consciousness without focal neurologic signs when fever and hypotension are absent

Laboratory criteria

Negative results on the following tests, if obtained:

- Blood, throat, or cerebrospinal fluid cultures (blood culture may be positive for *Staphylococcus aureus*)

- Rise in titer to Rocky Mountain spotted fever, leptospirosis, or measles

Case classification

Probable: a case in which five of the six clinical findings described above are present

Confirmed: a case in which all six of the clinical findings described above are present, including desquamation, unless the patient dies before desquamation occurs

Comment

See also Streptococcal Toxic-Shock Syndrome.

Trichinosis (Revised 9/96)**Clinical description**

A disease caused by ingestion of *Trichinella* larvae. The disease has variable clinical manifestations. Common signs and symptoms among symptomatic persons include eosinophilia, fever, myalgia, and periorbital edema.

Laboratory criteria for diagnosis

- Demonstration of *Trichinella* larvae in tissue obtained by muscle biopsy, or
- Positive serologic test for *Trichinella*

Case classification

Confirmed: a clinically compatible case that is laboratory confirmed

Comment

In an outbreak setting, at least one case must be laboratory confirmed. Associated cases should be reported as confirmed if the patient shared an epidemiologically implicated meal or ate an epidemiologically implicated meat product and has either a positive serologic test for trichinosis or a clinically compatible illness.

Tuberculosis (Revised 9/96)**Clinical description**

A chronic bacterial infection caused by *Mycobacterium tuberculosis*, characterized pathologically by the formation of granulomas. The most common site of infection is the lung, but other organs may be involved.

Clinical case definition

A case that meets the following criteria:

- A positive tuberculin skin test

- Other signs and symptoms compatible with tuberculosis (e.g., an abnormal, unstable [i.e., worsening or improving] chest radiographs, or clinical evidence of current disease)
- Treatment with two or more antituberculosis medications
- Completed diagnostic evaluation

Laboratory criteria for diagnosis

- Isolation of *M. tuberculosis* from a clinical specimen* or
- Demonstration of *M. tuberculosis* from a clinical specimen by nucleic acid amplification test,[†] or
- Demonstration of acid-fast bacilli in a clinical specimen when a culture has not been or cannot be obtained

Case classification

Confirmed: a case that meets the clinical case definition or is laboratory confirmed

Comment

A case should not be counted twice within any consecutive 12-month period. However, cases in which the patients had previously had verified disease should be reported again if the patients were discharged from treatment. Cases also should be reported again if patients were lost to supervision for >12 months and disease can be verified again. Mycobacterial diseases other than those caused by *M. tuberculosis* complex should not be counted in tuberculosis morbidity statistics unless there is concurrent tuberculosis.

Typhoid Fever

Clinical description

An illness caused by *Salmonella typhi* that is often characterized by insidious onset of sustained fever, headache, malaise, anorexia, relative bradycardia, constipation or diarrhea, and nonproductive cough. However, many mild and atypical infections occur. Carriage of *S. typhi* may be prolonged.

Laboratory criteria for diagnosis

- Isolation of *S. typhi* from blood, stool, or other clinical specimen

*Use of rapid identification techniques for *M. tuberculosis* (e.g., DNA probes and mycolic acids high-pressure liquid chromatography performed on a culture from a clinical specimen) are acceptable under this criterion.

†Nucleic acid amplification (NAA) tests must be accompanied by culture for mycobacteria species. However, for surveillance purposes, CDC will accept results obtained from NAA tests approved by the Food and Drug Administration (FDA) and used according to the approved product labeling on the package insert. Current FDA-approved NAA tests are only approved for smear-positive respiratory specimens.

Case classification

Probable: a clinically compatible case that is epidemiologically linked to a confirmed case in an outbreak

Confirmed: a clinically compatible case that is laboratory confirmed

Comment

Isolation of the organism is required for confirmation. Serologic evidence alone is not sufficient for diagnosis. Asymptomatic carriage should *not* be reported as typhoid fever. Isolates of *S. typhi* are reported to the Foodborne and Diarrheal Diseases Branch, Division of Bacterial and Mycotic Diseases, National Center for Infectious Diseases, CDC, through the Public Health Laboratory Information System. (See *Salmonella*.)

Yellow Fever**Clinical description**

A mosquito-borne viral illness characterized by acute onset and constitutional symptoms followed by a brief remission and a recurrence of fever, hepatitis, albuminuria, and symptoms and, in some instances, renal failure, shock, and generalized hemorrhages

Laboratory criteria for diagnosis

- Fourfold or greater rise in yellow fever antibody titer in a patient who has no history of recent yellow fever vaccination and cross-reactions to other flaviviruses have been excluded or
- Demonstration of yellow fever virus, antigen, or genome in tissue, blood, or other body fluid

Case classification

Probable: a clinically compatible case with supportive serology (stable elevated antibody titer to yellow fever virus [e.g., ≥ 32 by complement fixation, ≥ 256 by immunofluorescence assay, ≥ 320 by hemagglutination inhibition, ≥ 160 by neutralization, or a positive serologic result by immunoglobulin M-capture enzyme immunoassay]. Cross-reactive serologic reactions to other flaviviruses must be excluded, and the patient must not have a history of yellow fever vaccination.)

Confirmed: a clinically compatible case that is laboratory confirmed

PART 2. CASE DEFINITIONS FOR NON-NOTIFIABLE INFECTIOUS DISEASES

Amebiasis

Clinical description

Infection of the large intestine by *Entamoeba histolytica* may result in an illness of variable severity ranging from mild, chronic diarrhea to fulminant dysentery. Infection also may be asymptomatic. Extraintestinal infection also can occur (e.g., hepatic abscess).

Laboratory criteria for diagnosis

Intestinal amebiasis

- Demonstration of cysts or trophozoites of *E. histolytica* in stool or
- Demonstration of trophozoites in tissue biopsy or ulcer scrapings by culture or histopathology

Extraintestinal amebiasis

- Demonstration of *E. histolytica* trophozoites in extraintestinal tissue

Case classification

Confirmed, intestinal amebiasis: a clinically compatible illness that is laboratory confirmed

Confirmed, extraintestinal amebiasis: a parasitologically confirmed infection of extraintestinal tissue, or among symptomatic persons (with clinical or radiographic findings consistent with extraintestinal infection), demonstration of specific antibody against *E. histolytica* as measured by indirect hemagglutination or other reliable immunodiagnostic test (e.g., enzyme-linked immunosorbent assay)

Comment

Asymptomatic intestinal carriage of *E. histolytica* should not be reported. Among asymptomatic persons, a positive serologic test does not necessarily indicate extraintestinal amebiasis.

Aseptic Meningitis

Clinical description

A syndrome characterized by acute onset of meningeal symptoms, fever, and cerebrospinal fluid pleocytosis, with bacteriologically sterile cultures

Laboratory criteria for diagnosis

- No evidence of bacterial or fungal meningitis

Case classification

Confirmed: a clinically compatible case diagnosed by a physician as aseptic meningitis, with no laboratory evidence of bacterial or fungal meningitis.

Comment

Aseptic meningitis is a syndrome of multiple etiologies, but many cases are caused by a viral agent.

Bacterial Meningitis, Other (Adopted 9/96)**Clinical description**

Bacterial meningitis manifests most commonly with fever, headache, and a stiff neck; the disease may progress rapidly to shock and death. However, other manifestations may be observed.

Laboratory criteria for diagnosis

- Isolation of a bacterial species from the cerebrospinal fluid

Case classification

Confirmed: a clinically compatible case that is either laboratory confirmed or is accompanied by a positive blood culture

Comment

Cases of bacterial meningitis caused by *Haemophilus influenzae*, *Neisseria meningitidis*, group A *Streptococcus*, and *Listeria monocytogenes* should be reported to CDC's National Notifiable Diseases Surveillance System under the disease codes specific for these organisms. Only cases of bacterial meningitis caused by organisms other than those specified should be reported as cases of "bacterial meningitis, other."

Campylobacter Infection**Clinical description**

An infection that may result in diarrheal illness of variable severity

Laboratory criteria for diagnosis

- Isolation of *Campylobacter* from any clinical specimen

Case classification

Probable: a clinically compatible case that is epidemiologically linked to a confirmed case

Confirmed: a case that is laboratory confirmed

Comment

Only confirmed cases are reported to the laboratory-based surveillance system managed by the Foodborne and Diarrheal Diseases Branch, Division of Bacterial and Mycotic Diseases, National Center for Infectious Diseases, CDC.

Cyclospora Infection (Adopted 9/96)**Clinical description**

An illness of variable severity caused by the protozoan *Cyclospora cayetanensis* and commonly characterized by watery diarrhea, loss of appetite, weight loss, abdominal bloating and cramping, increased flatus, nausea, fatigue, and low-grade fever. Vomiting also may be noted. Relapses and asymptomatic infections can occur.

Laboratory criteria for diagnosis

- Demonstration of *Cyclospora* oocysts (by morphologic criteria or by demonstration of sporulation) or *Cyclospora* DNA (by polymerase chain reaction) in stool, duodenal/jejunal aspirates or small-bowel biopsy specimens

Case classification

Probable: a clinically compatible case that is epidemiologically linked to a confirmed case

Confirmed: a case that is laboratory confirmed

Comment

Direct person-to-person transmission is unlikely because *Cyclospora* oocysts are not infectious at the time of excretion.

Dengue Fever (Revised 9/96)**Clinical description**

An acute febrile illness characterized by frontal headache, retro-ocular pain, muscle and joint pain, and rash. The principal vector is the *Aedes aegypti* mosquito and transmission usually occurs in tropical or subtropical areas. Severe manifestations (e.g., dengue hemorrhagic fever and dengue shock syndrome) are rare but may be fatal.

Laboratory criteria for diagnosis

- Isolation of dengue virus from serum and/or autopsy tissue samples, or
- Demonstration of a fourfold or greater rise or fall in reciprocal immunoglobulin G (IgG) or immunoglobulin M (IgM) antibody titers to one or more dengue virus antigens in paired serum samples, or
- Demonstration of dengue virus antigen in autopsy tissue or serum samples by immunohistochemistry or by viral nucleic acid detection

Case classification

Probable: a clinically compatible case with supportive serologic findings (a reciprocal IgG antibody titer of ≥ 1280 or a positive IgM antibody test on a single acute (late)- or convalescent-phase serum specimen to one or more dengue virus antigens)

Confirmed: a clinically compatible case that is laboratory confirmed

Comment

Dengue hemorrhagic fever is defined as an acute febrile illness with minor or major bleeding phenomena, thrombocytopenia ($\leq 100,000/\text{mm}^3$), and evidence of plasma leakage documented by hemoconcentration (hematocrit increased by $\geq 20\%$) or other objective evidence of increased capillary permeability. The definition of dengue shock syndrome follows all of the above criteria for dengue hemorrhagic fever and also includes hypotension or narrow pulse pressure (≤ 20 mm Hg).

Ehrlichiosis (Adopted 9/96)**Clinical description**

A tickborne febrile illness most commonly characterized by acute onset, accompanied by headache, myalgia, rigors and/or malaise. Clinical laboratory findings may include intracytoplasmic microcolonies (morulae) in leukocytes of peripheral smear, cerebrospinal fluid (CSF), or bone marrow aspirate or biopsy, cytopenias (especially thrombocytopenia and leukopenia), and elevated liver enzymes (especially alanine aminotransferase or aspartate aminotransferase).

There are two clinically similar yet serologically distinct forms of ehrlichiosis: a) human granulocytic ehrlichiosis (HGE), caused by infection with an *Ehrlichia equi*-like agent and found primarily in the upper midwest and northeast, and b) human monocytic ehrlichiosis (HME) caused by *Ehrlichia chaffeensis* infection and found primarily in the southeastern quadrant of the United States.

Laboratory criteria for diagnosis

- Fourfold or greater change in antibody titer to *Ehrlichia* spp. antigen by immunofluorescence antibody (IFA) test in acute- and convalescent-phase specimens ideally taken ≥ 4 weeks apart. HME diagnosis requires *E. chaffeensis* and HGE currently requires *E. equi* or HGE-agent antigen, or

- Positive polymerase chain reaction assay. Distinct primers are used for the diagnosis of HGE and HME, or
- Intracytoplasmic morulae identified in blood, bone marrow, or CSF leukocytes, **and** an IFA antibody titer ≥ 64

Case classification

Probable: a clinically compatible case with either a single IFA serologic titer ≥ 64 or intracytoplasmic morulae identified in blood, bone marrow, or CSF leukocytes

Confirmed: a clinically compatible case that is laboratory confirmed

Comment

All laboratory testing should be conducted by experienced personnel with appropriate training and should include appropriate controls and reagents necessary for accurate etiologic diagnosis. States in which cases of HGE and/or HME have occurred may submit reports to CDC.

Genital Herpes (Herpes Simplex Virus) (Revised 9/96)

Clinical description

A condition characterized by visible, painful genital or anal lesions

Laboratory criteria for diagnosis

- Isolation of herpes simplex virus from cervix, urethra, or anogenital lesion, or
- Demonstration of virus by antigen detection technique in clinical specimens from cervix, urethra, or anogenital lesion, or
- Demonstration of multinucleated giant cells on a Tzanck smear of scrapings from an anogenital lesion

Case classification

Probable: a clinically compatible case (in which primary and secondary syphilis have been excluded by appropriate serologic tests and darkfield microscopy, when available) with either a diagnosis of genital herpes based on clinical presentation (without laboratory confirmation) or a history of one or more previous episodes of similar genital lesions

Confirmed: a clinically compatible case that is laboratory confirmed

Comment

Genital herpes should be reported only once per patient. The first diagnosis for a patient with no previous diagnosis should be reported.

Genital Warts (Revised 9/96)

Clinical description

An infection characterized by the presence of visible, exophytic (raised) growths on the internal or external genitalia, perineum, or perianal region

Laboratory criteria for diagnosis

- Histopathologic changes characteristic of human papillomavirus infection in specimens obtained by biopsy or exfoliative cytology or
- Demonstration of virus by antigen or nucleic acid detection in a lesion biopsy

Case classification

Probable: a clinically compatible case without histopathologic diagnosis and without microscopic or serologic evidence that the growth is the result of secondary syphilis

Confirmed: a clinically compatible case that is laboratory confirmed

Comment

Genital warts should be reported only once per patient. The first diagnosis for a patient with no previous diagnosis should be reported.

Giardiasis

Clinical description

An illness caused by the protozoan *Giardia lamblia* and characterized by diarrhea, abdominal cramps, bloating, weight loss, or malabsorption. Infected persons may be asymptomatic.

Laboratory criteria for diagnosis

- Demonstration of *G. lamblia* cysts in stool, or
- Demonstration of *G. lamblia* trophozoites in stool, duodenal fluid, or small-bowel biopsy, or
- Demonstration of *G. lamblia* antigen in stool by a specific immunodiagnostic test (e.g., enzyme-linked immunosorbent assay)

Case classification

Probable: a clinically compatible case that is epidemiologically linked to a confirmed case

Confirmed: a case that is laboratory confirmed

Granuloma Inguinale

Clinical description

A slowly progressive ulcerative disease of the skin and lymphatics of the genital and perianal area caused by infection with *Calymmatobacterium granulomatis*. A clinically compatible case would have one or more painless or minimally painful granulomatous lesions in the anogenital area.

Laboratory criteria for diagnosis

- Demonstration of intracytoplasmic Donovan bodies in Wright or Giemsa-stained smears or biopsies of granulation tissue

Case classification

Confirmed: a clinically compatible case that is laboratory confirmed

Leptospirosis

Clinical description

An illness characterized by fever, headache, chills, myalgia, conjunctival suffusion, and less frequently by meningitis, rash, jaundice, or renal insufficiency. Symptoms may be biphasic.

Laboratory criteria for diagnosis

- Isolation of *Leptospira* from a clinical specimen, or
- Fourfold or greater increase in *Leptospira* agglutination titer between acute- and convalescent-phase serum specimens obtained ≥ 2 weeks apart and studied at the same laboratory, or
- Demonstration of *Leptospira* in a clinical specimen by immunofluorescence

Case classification

Probable: a clinically compatible case with supportive serologic findings (i.e., a *Leptospira* agglutination titer of ≥ 200 in one or more serum specimens)

Confirmed: a clinically compatible case that is laboratory confirmed

Listeriosis

Clinical description

Infection caused by *Listeria monocytogenes*, which may produce any of several clinical syndromes, including stillbirth, listeriosis of the newborn, meningitis, bacteremia, or localized infections

Laboratory criteria for diagnosis

- Isolation of *L. monocytogenes* from a normally sterile site (e.g., blood or cerebrospinal fluid or, less commonly, joint, pleural, or pericardial fluid)

Case classification

Confirmed: a clinically compatible case that is laboratory confirmed

Lymphogranuloma Venereum**Clinical description**

Infection with L₁, L₂, or L₃ serovars of *Chlamydia trachomatis* may result in a disease characterized by genital lesions, suppurative regional lymphadenopathy, or hemorrhagic proctitis. The infection is usually sexually transmitted.

Laboratory criteria for diagnosis

- Isolation of *C. trachomatis*, serotype L₁, L₂, or L₃ from clinical specimen, or
- Demonstration by immunofluorescence of inclusion bodies in leukocytes of an inguinal lymph node (bubo) aspirate, or
- Positive microimmunofluorescent serologic test for a lymphogranuloma venereum strain of *C. trachomatis*

Case classification

Probable: a clinically compatible case with one or more tender fluctuant inguinal lymph nodes or characteristic proctogenital lesions with supportive laboratory findings of a single *C. trachomatis* complement fixation titer of >64

Confirmed: a clinically compatible case that is laboratory confirmed

Mucopurulent Cervicitis (Revised 9/96)**Clinical description**

Cervical inflammation that is not the result of infection with *Neisseria gonorrhoeae* or *Trichomonas vaginalis*. Cervical inflammation is defined by the presence of one of the following criteria:

- Mucopurulent secretion (from the endocervix) that is yellow or green when viewed on a white, cotton-tipped swab (positive swab test)
- Induced endocervical bleeding (bleeding when the first swab is placed in the endocervix)

Laboratory criteria for diagnosis

- No evidence of *N. gonorrhoeae* by culture, Gram stain, or antigen or nucleic acid detection, and no evidence of *T. vaginalis* on wet mount

Case classification

Confirmed: a clinically compatible case in a female who does not have either gonorrhea or trichomoniasis

Comment

Mucopurulent cervicitis (MPC) is a clinical diagnosis of exclusion. The syndrome may result from infection with any of several agents (see *Chlamydia trachomatis*, Genital Infections). If gonorrhea, trichomoniasis, and chlamydia are excluded, a clinically compatible illness should be classified as MPC. An illness in a female that meets the case definition of MPC and *C. trachomatis* infection should be classified as chlamydia.

Nongonococcal Urethritis (Revised 9/96)**Clinical description**

Urethral inflammation that is not the result of infection with *Neisseria gonorrhoeae*. Urethral inflammation may be diagnosed by the presence of one of the following criteria:

- A visible abnormal urethral discharge, or
- A positive leukocyte esterase test from a male aged <60 years who does not have a history of kidney disease or bladder infection, prostate enlargement, urogenital anatomic anomaly, or recent urinary tract instrumentation, or
- Microscopic evidence of urethritis (≥ 5 white blood cells per high-power field) on a Gram stain of a urethral smear

Laboratory criteria for diagnosis

- No evidence of *N. gonorrhoeae* infection by culture, Gram stain, or antigen or nucleic acid detection

Case classification

Confirmed: a clinically compatible case in a male in whom gonorrhea is not found, either by culture, Gram stain, or antigen or nucleic acid detection

Comment

Nongonococcal urethritis (NGU) is a clinical diagnosis of exclusion. The syndrome may result from infection with any of several agents (see *Chlamydia trachomatis*, Genital Infection). If gonorrhea and chlamydia are excluded, a clinically compatible

illness should be classified as NGU. An illness in a male that meets the case definition of NGU and *C. trachomatis* infection should be classified as chlamydia.

Pelvic Inflammatory Disease (Revised 9/96)

Clinical case definition

A clinical syndrome resulting from the ascending spread of microorganisms from the vagina and endocervix to the endometrium, fallopian tubes, and/or contiguous structures. In a female who has lower abdominal pain and who has not been diagnosed as having an established cause other than pelvic inflammatory disease (PID) (e.g., ectopic pregnancy, acute appendicitis, and functional pain), all the following clinical criteria must be present:

- Lower abdominal tenderness, and
- Tenderness with motion of the cervix, and
- Adnexal tenderness

In addition to the preceding criteria, at least one of the following findings must also be present:

- Meets the surveillance case definition of *C. trachomatis* infection or gonorrhea
- Temperature >100.4 F (>38.0 C)
- Leukocytosis >10,000 white blood cells/mm³
- Purulent material in the peritoneal cavity obtained by culdocentesis or laparoscopy
- Pelvic abscess or inflammatory complex detected by bimanual examination or by sonography
- Patient is a sexual contact of a person known to have gonorrhea, chlamydia, or nongonococcal urethritis

Case classification

Confirmed: a case that meets the clinical case definition

Comment

For reporting purposes, a clinician's report of PID should be counted as a case.

Rheumatic Fever

Clinical description

An inflammatory illness that occurs as a delayed sequela of group A streptococcal infection

Major criteria: carditis, polyarthritis, chorea, subcutaneous nodules, and erythema marginatum

Minor criteria: a) previous rheumatic fever or rheumatic heart disease; b) arthralgia; c) fever; d) elevated erythrocyte sedimentation rate, positive C-reactive protein, or leukocytosis; and e) prolonged PR interval on an electrocardiogram

Laboratory criteria for diagnosis

- No specific laboratory test exists for the diagnosis of rheumatic fever

Case classification

Confirmed: an illness characterized by a) two major criteria or one major and two minor criteria (as described in Clinical Description) and b) supporting evidence of preceding group A streptococcal infection (14).

Comment

Supporting evidence to confirm streptococcal infection includes increased anti-streptolysin-O or other streptococcal antibodies, throat culture positive for group A streptococcus, or recent scarlet fever. The absence of supporting evidence of preceding streptococcal infection should make the diagnosis doubtful, except in Sydenham chorea or low-grade carditis when rheumatic fever is first discovered after a long latent period from the antecedent infection.

Tularemia (Revised 9/96)

Clinical description

An illness characterized by several distinct forms, including the following:

- Ulceroglandular (cutaneous ulcer with regional lymphadenopathy)
- Glandular (regional lymphadenopathy with no ulcer)
- Oculoglandular (conjunctivitis with preauricular lymphadenopathy)
- Oropharyngeal (stomatitis or pharyngitis or tonsillitis and cervical lymphadenopathy)
- Intestinal (intestinal pain, vomiting, and diarrhea)
- Pneumonic (primary pleuropulmonary disease)
- Typhoidal (febrile illness without early localizing signs and symptoms)

Clinical diagnosis is supported by evidence or history of a tick or deerfly bite, exposure to tissues of a mammalian host of *Francisella tularensis*, or exposure to potentially contaminated water.

Laboratory criteria for diagnosis*Presumptive*

- Elevated serum antibody titer(s) to *F. tularensis* antigen (without documented fourfold or greater change) in a patient with no history of tularemia vaccination or
- Detection of *F. tularensis* in a clinical specimen by fluorescent assay

Confirmatory

- Isolation of *F. tularensis* in a clinical specimen or
- Fourfold or greater change in serum antibody titer to *F. tularensis* antigen

Case classification

Probable: a clinically compatible case with laboratory results indicative of presumptive infection

Confirmed: a clinically compatible case with confirmatory laboratory results

Varicella (Chickenpox) (Revised 9/96)**Clinical case definition**

An illness with acute onset of diffuse (generalized) papulovesicular rash without other apparent cause

Laboratory criteria for diagnosis

- Isolation of varicella virus from a clinical specimen or
- Significant rise in serum varicella immunoglobulin G antibody level by any standard serologic assay

Case classification

Probable: a case that meets the clinical case definition, is not laboratory confirmed, and is not epidemiologically linked to another probable or confirmed case

Confirmed: a case that is laboratory confirmed or that meets the clinical case definition and is epidemiologically linked to a confirmed or probable case

Comment

Two probable cases that are epidemiologically linked would be considered confirmed, even in the absence of laboratory confirmation.

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State and Territorial Epidemiologists and Laboratory Directors

The case definitions contained in this report were developed in collaboration with the Council of State and Territorial Epidemiologists. They were also endorsed for use by the Association of State and Territorial Public Health Laboratory Directors. Both the epidemiologists and the laboratory directors listed below were in the position shown as of December 1996.

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