STI Case Definitions in Effect During 2023

A surveillance case definition is a set of uniform criteria used to define a disease for public health surveillance.¹ Surveillance case definitions enable public health officials to classify and count cases consistently across reporting jurisdictions. Surveillance case definitions are not intended to be used by healthcare providers for making a clinical diagnosis or determining how to meet an individual patient's health needs.

The Council of State and Territorial Epidemiologists (CSTE) recommends that health departments report cases of selected diseases to CDC's National Notifiable Diseases Surveillance System (NNDSS). The list of notifiable conditions and corresponding surveillance case definitions are reviewed annually by CSTE, and, if needed, are updated using CSTE's Position Statements.² This process provides uniform criteria for surveillance of nationally notifiable conditions, including the four nationally notifiable sexually transmitted infections (STIs).

To serve as a reference for *Sexually Transmitted Infection Surveillance*, 2023, the surveillance case definitions for nationally notifiable STIs in effect during 2023 are listed below.

Please see the NNDSS website (https://ndc.services.cdc.gov/) for historical case definitions and for the case definitions in use for the current calendar year.

References

- 1. National Notifiable Diseases Surveillance System. Case definitions. Available at: https://ndc.services.cdc.gov/
- 2. Council of State and Territorial Epidemiologist Position Statements. Available at: <u>https://www.cste.org/page/PSLanding</u>

Nationally Notifiable STIs Syphilis (Effective as of 1/2018)

Syphilis is a complex sexually transmitted disease that has a highly variable clinical course. Adherence to the surveillance case definitions will facilitate understanding the epidemiology of syphilis across the US.

Syphilis, primary

Clinical description

A stage of infection with *Treponema pallidum* characterized by one or more ulcerative lesions (e.g., chancre), which might differ considerably in clinical appearance.

Laboratory criteria for diagnosis

Confirmatory:

- Demonstration of *T. pallidum* by darkfield microscopy in a clinical specimen that was not obtained from the oropharynx and is not potentially contaminated by stool, OR
- Demonstration of *T. pallidum* by polymerase chain reaction (PCR) or equivalent direct molecular methods in any clinical specimen.

Supportive:

- A reactive nontreponemal serologic test (Venereal Disease Research Laboratory [VDRL], rapid plasma reagin [RPR], or equivalent serologic methods), OR
- A reactive treponemal serologic test (*T. pallidum* particle agglutination [TP-PA], enzyme immunoassay [EIA], chemiluminescence immunoassay [CIA], or equivalent serologic methods).*

* These treponemal tests supersede older testing technologies, including microhemagglutination assay for antibody to T. pallidum [MHA-TP].

Case classification

Probable: a case that meets the clinical description of primary syphilis and the supportive laboratory criteria.

Confirmed: a case that meets the clinical description of primary syphilis and the supportive confirmatory criteria.

Syphilis, secondary

Clinical description

A stage of infection caused by *T. pallidum* characterized by localized or diffuse mucocutaneous lesions (e.g., rash – such as non-pruritic macular, maculopapular, papular, or pustular lesions), often with generalized lymphadenopathy. Other symptoms can include mucous patches, condyloma lata, and alopecia. The primary ulcerative lesion may still be present. Because of the wide array of symptoms and signs possibly indicating secondary syphilis, serologic tests for syphilis and a physical examination are crucial to determining if a case should be classified as secondary syphilis.

Laboratory criteria for diagnosis

Confirmatory:

- Demonstration of *T. pallidum* by darkfield microscopy in a clinical specimen that was not obtained from the oropharynx and is not potentially contaminated by stool, OR
- Demonstration of *T. pallidum* by polymerase chain reaction (PCR) or equivalent direct molecular methods in any clinical specimen.

Supportive:

- A reactive nontreponemal serologic test (VDRL, RPR, or equivalent serologic methods), AND
- A reactive treponemal serologic test (TP-PA, EIA, CIA, or equivalent serologic methods).

Case classification

Probable: a case that meets the clinical description of secondary syphilis and the supportive laboratory criteria.

Confirmed: a case that meets the clinical description of secondary syphilis and the confirmatory laboratory criteria.

Syphilis, early non-primary non-secondary

Clinical description

A stage of infection caused by *T. pallidum* in which initial infection has occurred within the previous 12 months, but there are no signs or symptoms of primary or secondary syphilis.

Laboratory criteria for diagnosis

Supportive:

• A current nontreponemal test titer demonstrating fourfold or greater increase from the last nontreponemal test titer, unless there is evidence that this increase was not sustained for >2 weeks.

Case classification

Probable: a person with no clinical signs or symptoms of primary or secondary syphilis who has one of the following:

- No prior history of syphilis, AND a current reactive nontreponemal test (e.g., VDRL, RPR, or equivalent serologic methods), AND a current reactive treponemal test (e.g., TP-PA, EIA, CIA, or equivalent serologic methods), OR
- A prior history of syphilis and meets the supportive laboratory criteria.

AND 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, unless there is evidence that this increase was not sustained for >2 weeks
- Documented seroconversion of a treponemal test during the previous 12 months
- A history of symptoms consistent with primary or secondary syphilis during the previous 12 months
- Meets epidemiologic criteria.

Epidemiological criteria:

- A history of sexual exposure to a partner within the previous 12 months who had primary, secondary, or early non-primary non-secondary syphilis (documented independently as duration <12 months).
- Only sexual contact (sexual debut) was within the previous 12 months.

Syphilis, unknown duration or late

Clinical description

A stage of infection caused by *T. pallidum* in which initial infection has occurred >12 months previously or in which there is insufficient evidence to conclude that infection was acquired during the previous 12 months.

Case classification

Probable: a person with no clinical signs or symptoms of primary or secondary syphilis who meets one of the following sets of criteria:

- No prior history of syphilis, and a current reactive nontreponemal test (e.g., VDRL, RPR, or equivalent serologic methods), and a current reactive treponemal test (e.g., TP-PA, EIA, CIA, or equivalent serologic methods), OR
- A prior history of syphilis, and a current nontreponemal test titer demonstrating fourfold or greater increase from the last nontreponemal test titer, unless there is evidence that this increase was not sustained for >2 weeks, OR
- Clinical signs or symptoms and laboratory results that meet the likely or verified criteria for neurologic, ocular, otic, or late clinical manifestations syphilis (see below)

AND who has no evidence of having acquired the disease within the preceding 12 months (see Syphilis, early non-primary non-secondary).

Comments: Although cases of syphilis of unknown duration are grouped together with late syphilis for the purposes of surveillance, the conservative clinical and public health responses to these cases will differ when there is uncertainty about the duration of infection. When faced with uncertainty, clinicians should act conservatively and treat unknown duration syphilis as if it were late infection, with three doses of benzathine penicillin. In contrast, the most conservative approach for STD control programs would be to manage cases of syphilis of unknown duration as early non-primary non-secondary infections and search for partners who may have been recently infected. Because this would not be feasible for most STD control programs, programs should consider prioritizing cases of syphilis of unknown duration with higher nontreponemal titers (e.g., 1:32 or higher) for investigation and partner services. Although nontreponemal titers cannot reliably distinguish between early infection (<12 months duration) and late infection (>12 months duration), nontreponemal titers usually are higher early in the course of syphilis infection.

Syphilis, Congenital

Clinical description

A condition caused by infection in utero with *T. pallidum*. A wide spectrum of severity exists, from inapparent infection to severe cases that are clinically apparent at birth. An infant or child (aged less than 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 of lesions, body fluids, or neonatal nasal discharge, OR
- PCR or other equivalent direct molecular methods of lesions, neonatal nasal discharge, placenta, umbilical cord, or autopsy material, OR
- Immunohistochemistry (IHC), or special stains (e.g., silver staining) of 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 non-treponemal test for syphilis (VDRL, RPR, or equivalent serologic methods) AND any one of the following:

- Any evidence of congenital syphilis on physical examination (see Clinical description).
- Any evidence of congenital syphilis on radiographs of long bones.
- A reactive CSF VDRL test.
- In a non-traumatic lumbar puncture, an elevated CSF leukocyte (white blood cell [WBC]) count or protein (without other cause):
 - Suggested parameters for abnormal CSF WBC and protein values:
 - 1. During the first 30 days of life, a CSF WBC count of >15 WBC/mm3 or a CSF protein >120 mg/dL is abnormal.
 - 2. After the first 30 days of life, a CSF WBC count of >5 WBC mm3 or a CSF protein >40 mg/dL, regardless of CSF serology.

The treating clinician should be consulted to interpret the CSF values for the specific patient.

Confirmed: a case that is laboratory confirmed.

Comments: 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, WBC count, and protein 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. While maternal antibodies can complicate interpretation of serologic tests in an infant, reactive tests past 18 months of age are considered to reflect the status of the child. 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.

Syphilitic Stillbirth

Clinical case definition

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

* Adequate treatment is defined as completion of a penicillin-based regimen, in accordance with CDC treatment guidelines, appropriate for stage of infection, initiated 30 or more days before delivery.

Comments: For reporting purposes, congenital syphilis includes cases of congenitally acquired syphilis among infants and children as well as syphilitic stillbirths.

<u>Comments: Additional information to be collected on clinical manifestations of reported</u> <u>syphilis cases</u>

Syphilis is a systemic infection that, if untreated, can cause a variety of clinical manifestations, including:

• Signs and symptoms of primary and secondary syphilis (see above case definitions).

^{*} Adequate treatment is defined as completion of a penicillin-based regimen, in accordance with CDC treatment guidelines, appropriate for stage of infection, initiated 30 or more days before delivery.

- Latent infections (i.e., those lacking any signs or symptoms).
- Neurologic, ocular, or otic manifestations (neurosyphilis, ocular syphilis, or otosyphilis), which can occur at any stage of syphilis.
- Late clinical manifestations (tertiary syphilis), which generally occur after 15–30 years of untreated infection.

The following provides guidance for reporting neurologic, ocular, otic, and late clinical manifestations of syphilis. Cases should be reported according to stage of infection, as defined above (e.g., primary syphilis; secondary syphilis; early non-primary, non-secondary syphilis; or unknown duration or late syphilis) and the clinical manifestations should be reported in the case report data, as defined below.

Neurologic manifestations:

Neurologic manifestations (neurosyphilis) can occur at any stage of syphilis. If the patient has neurologic manifestations of syphilis, the case should be reported with the appropriate stage of infection (as if neurologic manifestations were not present) and neurologic manifestations should be noted in the case report data.

Clinical description

Infection of the central nervous system with *T. pallidum*, as evidenced by manifestations including syphilitic meningitis, meningovascular syphilis, general paresis, including dementia, and tabes dorsalis.

Classification of neurologic manifestations (neurosyphilis)

Possible: a person with a reactive nontreponemal test (e.g., VDRL, RPR, or equivalent serologic methods) and a reactive treponemal test (e.g., TP-PA, EIA, CIA or equivalent serologic methods) and clinical symptoms or signs that are consistent with neurosyphilis without other known causes for these clinical abnormalities.

Likely: a person with a reactive nontreponemal test (e.g., VDRL, RPR, or equivalent serologic methods) and a reactive treponemal test (e.g., TP-PA, EIA, CIA or equivalent serologic methods) with both of the following:

- Clinical symptoms or signs that are consistent with neurosyphilis without other known causes for these clinical abnormalities, AND
- Elevated CSF protein (>50 mg/dL2) or leukocyte count (>5 WBC/mm3 CSF) in the absence of other known causes of these abnormalities.

Verified: a person with a reactive nontreponemal test (e.g., VDRL, RPR, or equivalent serologic methods) and a reactive treponemal test (e.g., TP-PA, EIA, CIA or equivalent serologic methods) with both of the following:

- Clinical symptoms or signs that are consistent with neurosyphilis without other known causes for these clinical abnormalities, AND
- A reactive VDRL in CSF in the absence of grossly bloody contamination of the CSF.

Ocular Manifestations:

Ocular manifestations (ocular syphilis) can occur at any stage of syphilis. If the patient has ocular manifestations of syphilis, the case should be reported with the appropriate stage of infection (as if ocular manifestations were not present) and ocular manifestations should be noted in the case report data.

Clinical description

Infection of any eye structure with *T. pallidum*, as evidenced by manifestations including posterior uveitis, panuveitis, anterior uveitis, optic neuropathy, and retinal vasculitis. Ocular syphilis may lead to decreased visual acuity including permanent blindness.

Classification of ocular manifestations (ocular syphilis)

Possible: a person with a reactive nontreponemal test (e.g., VDRL, RPR, or equivalent serologic methods) and a reactive treponemal test (e.g., TP-PA, EIA, CIA or equivalent serologic methods) and clinical symptoms or signs consistent with ocular syphilis without other known causes for these clinical abnormalities.

Likely: a person with a reactive nontreponemal test (e.g., VDRL, RPR, or equivalent serologic methods) and a reactive treponemal test (e.g., TP-PA, EIA, CIA or equivalent serologic methods) and both of the following:

- Clinical symptoms or signs consistent with ocular syphilis without other known causes for these clinical abnormalities, AND
- Findings on exam by an ophthalmologist that are consistent with ocular syphilis in the absence of other known causes for these abnormalities.

Verified: a person with a reactive nontreponemal test (e.g., VDRL, RPR, or equivalent serologic methods) and a reactive treponemal test (e.g., TP-PA, EIA, CIA or equivalent serologic methods) and both of the following:

- Clinical symptoms or signs consistent with ocular syphilis without other known causes for these clinical abnormalities, AND
- Demonstration of *T. pallidum* in aqueous or vitreous fluid by darkfield microscopy, or by PCR or equivalent direct molecular methods.

Otic Manifestations:

Otic manifestations can occur at any stage of syphilis. If the patient has otic manifestations of syphilis, the case should be reported with the appropriate stage of infection (as if otic manifestations were not present) and otic manifestations should be noted in the case report data.

Clinical description

Infection of the cochleovestibular system with *T. pallidum*, as evidenced by manifestations including sensorineural hearing loss, tinnitus, and vertigo.

Classification of otic manifestations (otosyphilis)

Possible: a person with a reactive nontreponemal test (e.g., VDRL, RPR, or equivalent serologic methods) and a reactive treponemal test (e.g., TP-PA, EIA, CIA or equivalent serologic methods) and clinical symptoms or signs consistent with otosyphilis without other known causes for these clinical abnormalities.

Likely: a person with a reactive nontreponemal test (e.g., VDRL, RPR, or equivalent serologic methods) and a reactive treponemal test (e.g., TP-PA, EIA, CIA or equivalent serologic methods) and both of the following:

• Clinical symptoms or signs consistent with otosyphilis without other known causes for these clinical abnormalities, AND

• Findings on exam by an otolaryngologist that are consistent with otosyphilis in the absence of other known causes for these abnormalities.

Verified: a person with a reactive nontreponemal test (e.g., VDRL, RPR, or equivalent serologic methods) and a reactive treponemal test (e.g., TP-PA, EIA, CIA or equivalent serologic methods) and both of the following:

- Clinical symptoms or signs consistent with otosyphilis without other known causes for these clinical abnormalities, AND
- Demonstration of *T. pallidum* in inner ear fluid by darkfield microscopy, or by PCR or equivalent direct molecular detection methods.

Late Clinical Manifestations:

Late clinical manifestations of syphilis usually develop only after a period of 15–30 years of untreated infection. Therefore, if the patient has late clinical manifestations of syphilis, the case should be reported with the appropriate stage of infection (for the vast majority of cases, unknown duration or late syphilis) and late clinical manifestations should be noted in the case report data.

Clinical description

Late clinical manifestations of syphilis (tertiary syphilis) may include inflammatory lesions of the cardiovascular system (e.g., aortitis, coronary vessel disease), skin (e.g., gummatous lesions), bone (e.g., osteitis), or other tissue. 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. In addition, certain neurologic manifestations (e.g., general paresis and tabes dorsalis) are also late clinical manifestations of syphilis.

Classification of late clinical manifestations of syphilis (tertiary syphilis)

Likely: a person with a reactive nontreponemal test (e.g., VDRL, RPR, or equivalent serologic methods) and a reactive treponemal test (e.g., TP-PA, EIA, CIA or equivalent serologic methods) with either of the following:

- Characteristic abnormalities or lesions of the cardiovascular system (e.g., aortitis, coronary vessel disease), skin (e.g., gummatous lesions), bone (e.g., osteitis), or other tissue, in the absence of other known causes of these abnormalities, OR
- Clinical signs and symptoms consistent with late neurologic manifestations of syphilis (e.g., general paresis, including dementia, or tabes dorsalis) in a case that meets the criteria for likely neurologic manifestations of syphilis (see above).

Verified: a person with a reactive nontreponemal test (e.g., VDRL, RPR, or equivalent serologic methods) and a reactive treponemal test (e.g., TP-PA, EIA, CIA or equivalent serologic methods) and either of the following:

Characteristic abnormalities or lesions of the cardiovascular system (e.g., aortitis, coronary vessel disease), skin (e.g., gummatous lesions), bone (e.g., osteitis), or other tissue in the absence of other known causes of these abnormalities, in combination with either demonstration of *T. pallidum* in late lesions by special stains or equivalent methods, or by PCR or equivalent direct molecular methods, or demonstration of pathologic changes that are consistent with *T. pallidum* infection on histologic examination of late lesions, OR

Clinical signs and symptoms consistent with late neurologic manifestations of syphilis (e.g., general paresis, including dementia, or tabes dorsalis) in a case that meets the criteria for verified neurologic manifestations of syphilis (see above).

Gonorrhea (Effective as of 1/2023)

Clinical description

Gonorrhea is a sexually transmitted infection caused by the bacterium *Neisseria gonorrhoeae*. Gonococcal infection can result in urethritis, epididymitis, cervicitis, acute salpingitis, proctitis, pharyngitis, or other syndromes when sexually transmitted; however, infections at the endocervix, pharynx, and rectum are often asymptomatic. Perinatal exposure to endocervical infection may result in gonococcal conjunctivitis in newborns. Disseminated gonococcal infection (DGI) is an additional syndrome caused by *Neisseria gonorrhoeae*.

DGI occurs when *Neisseria gonorrhoeae* from a mucosal site infection (urogenital, pharyngeal, rectal) invades the bloodstream and spreads to distant sites in the body. Clinical manifestations of DGI include petechial or pustular acral skin lesions, tenosynovitis, asymmetric polyarthralgia, bacteremia, oligoarticular septic arthritis, or, on rare occasions, endocarditis, osteomyelitis, or meningitis.

Laboratory criteria for diagnosis

Confirmatory laboratory evidence:

- Isolation of *Neisseria gonorrhoeae* by culture of a clinical specimen, minimally with isolation of typical gram-negative, oxidase-positive diplococci,
 OR
- Detection of *Neisseria gonorrhoeae* by nucleic acid amplification (e.g., Polymerase Chain Reaction [PCR]) or hybridization with a nucleic acid probe in a clinical specimen

Presumptive laboratory evidence:

• Observation of gram-negative intracellular diplococci in a urethral or an endocervical smear

Case classification

Probable: Meets presumptive laboratory evidence in the absence of confirmatory laboratory evidence.

Confirmed: Meets confirmatory laboratory evidence.

Classification of disseminated gonococcal infection (DGI)

Classification of Neisseria gonorrhoeae infection cases to identify DGI:

Verified: Isolation or detection of *Neisseria gonorrhoeae* from a disseminated site of infection (e.g., skin, synovial fluid, blood, or cerebrospinal fluid [CSF]) by culture or nucleic acid amplification test (NAAT).

Likely: Clinical manifestations of DGI without other known causes AND isolation or detection of *Neisseria gonorrhoeae* from a mucosal site of infection by culture or nucleic acid amplification test (NAAT).

Chlamydia trachomatis Infection (Effective as of 1/2022)

Clinical description

Chlamydia is a sexually transmitted infection that has a variable clinical course based on the serotype causing infection. Serovars D-K of C. trachomatis are the typical cause of chlamydial infections in the United States, and

infection with C. trachomatis can result in urethritis, epididymitis, cervicitis, acute salpingitis, or other syndromes when sexually transmitted; however, the infection is often asymptomatic. Perinatal infections may result in inclusion conjunctivitis and pneumonia in newborns. Other syndromes caused by C. trachomatis include LGV and trachoma.

LGV is a specific type of chlamydial infection, caused by the serovars L1, L2, and L3 of C. trachomatis. Symptomatic LGV can be divided into three stages. The primary stage can include a small ulcer or lesion at the site of inoculation (genital, rectal, or oral/oropharyngeal sites). The secondary stage can include a syndrome featuring cervical, inguinal, and/or femoral lymphadenopathy that may rupture or an anorectal syndrome featuring proctocolitis (including mucoid or hemorrhagic rectal discharge, anal pain, constipation, fever, and/or tenesmus). Late stage LGV typically involves sequelae, such as genital elephantiasis, lymph node scarring, chronic colorectal fistulas and strictures, perirectal abscesses, and/or anal fissures. LGV may also be asymptomatic.

Laboratory criteria for diagnosis

- Demonstration of *C. trachomatis* in a clinical specimen by detection of antigen or nucleic acid, **OR**
- Detection of LGV-specific antigen or nucleic acid in a clinical specimen, OR
- Isolation of *C. trachomatis* by culture

Case classification

Confirmed: a case that that meets laboratory evidence.

Chancroid (Effective as of 9/1996)

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 \geq 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.