

17-ID-11**Committee:** Infectious Disease**Title:** Update to Public Health Reporting and National Notification for Syphilis

I. Statement of the Problem

The current syphilis case definition was updated in 2013 and the congenital syphilis case definition was updated in 2014. Changes are needed to the syphilis case definition to ensure consistent accurate reporting of cases and the appropriate capture of clinical manifestations, especially neurologic and ocular manifestations.

II. Background and Justification

Background

Syphilis is a sexually transmitted disease (STD) caused by the bacterium *Treponema pallidum*. Syphilis is passed from person to person through direct contact with a syphilitic chancre. Chancres occur mainly on the external genitals, vagina, anus, or in the rectum but can also occur on the lips and in the mouth. Transmission of the organism occurs during vaginal, anal, or oral sex. Pregnant women with the disease can transmit it through the placenta to the fetus or at birth to the neonate. Many people infected with syphilis do not have any symptoms for years, yet remain at risk for late complications if they are not treated. Although transmission occurs from persons with chancres who are in the primary or secondary stage, many of these chancres are unrecognized. Thus, transmission may occur from persons who are unaware of their infection.

In the United States, testing for syphilis is currently being done using two algorithms. The traditional one has consisted of initial screening with an inexpensive nontreponemal test, followed by retesting reactive specimens with a more specific treponemal test. Quantitative nontreponemal tests are used to monitor responses to treatment or to indicate new infections. In the last 5–10 years, there has been an increase in the adoption of automated treponemal tests by laboratories which has resulted in the syphilis testing algorithm being reversed. Many laboratories now use an automated treponemal test as the initial screening test followed by a nontreponemal test. While this algorithm is more timely and cost effective for laboratories, it does have a ~14–40% false-positive rate with a second treponemal test often being used to help determine what clinical action should be taken.

Syphilis infections have continued to increase since their nadir in 2000–2001. Primary and secondary syphilis (the most infectious forms) had a rate of 2.1/100,000 (6,103 cases) in 2001; in 2015, this rate was 7.5/100,000 (23,872), the highest reported since 1994. While cases continue to occur primarily among males with men having sex with men being the primary risk factor, cases among women have also increased. Along with these dramatic increases in adult syphilis, congenital syphilis cases have also been increasing since 2012 with 487 cases reported in 2015 (12.4/100,000 live births). In addition, multiple jurisdictions have observed increases in ocular syphilis, a clinical manifestation that can occur at any stage of syphilis. However, at present, data on severe clinical manifestations such as ocular syphilis are not sufficiently captured in national syphilis case report data. Preliminary data for 2016 indicates an increase in syphilis infections of all stages, including congenital syphilis.

Justification

Updates to the case definition are needed to accurately capture all clinical manifestations of syphilis to accurately characterize the current epidemic and any future changes. Other changes to nomenclature are required to be able to more accurately describe the different stages of syphilis.

III. Statement of the desired action(s) to be taken

1. Utilize standard sources (e.g. reporting*) for case ascertainment for syphilis. Surveillance for syphilis should use the following recommended sources of data to the extent of coverage presented in Table III.

Table III. Recommended sources of data and extent of coverage for ascertainment of cases of syphilis.

Source of data for case ascertainment	Coverage	
	Population-wide	Sentinel sites
Clinician reporting	x	
Laboratory reporting	x	
Reporting by other entities (e.g., hospitals, veterinarians, pharmacies, poison centers)	x	X (STD Clinics)
Death certificates	x	
Hospital discharge or outpatient records	x	
Extracts from electronic medical records	x	
Telephone survey		
School-based survey		
Other _____		

2016 Template

2. Utilize standardized criteria for case identification and classification (Sections VI and VII) for syphilis and add syphilis to the *Nationally Notifiable Condition List*.

- 2a. Immediately notifiable, extremely urgent (within 4 hours)
- 2b. Immediately notifiable, urgent (within 24 hours)
- 2c. Routinely notifiable

CSTE recommends that all States and Territories enact laws (statue or rule/regulation as appropriate) to make this disease or condition reportable in their jurisdiction. Jurisdictions (e.g. States and Territories) conducting surveillance (according to these methods) should submit case notifications** to CDC.

Expectations for Message Mapping Guide (MMG) development for a newly notifiable condition: NNDSS is transitioning to HL7-based messages for case notifications; the specifications for these messages are presented in MMGs. When CSTE recommends that a new condition be made nationally notifiable, CDC must obtain OMB PRA approval prior to accepting case notifications for the new condition. Under anticipated timelines, notification using the Generic V2 MMG would support transmission of the basic demographic and epidemiologic information common to all cases and could begin with the new *MMWR* year following the CSTE annual conference. Input from CDC programs and CSTE would prioritize development of a disease-specific MMG for the new condition among other conditions waiting for MMGs.

3. CDC should publish data on syphilis as appropriate in *MMWR* and other venues (see Section IX).

CSTE recommends that all jurisdictions (e.g. States or Territories) with legal authority to conduct public health surveillance follow the recommended methods as outlined above.

Terminology:

* Reporting: process of a healthcare provider or other entity submitting a report (case information) of a condition under public health surveillance TO local or state public health.

**Notification: process of a local or state public health authority submitting a report (case information) of a condition on the Nationally Notifiable Condition List TO CDC.

CSTE requests that CDC adopt this revised, standardized reporting definition for syphilis, including the following changes:

1. Add data elements and guidance related to clinical manifestations of syphilis (i.e., ocular manifestation, otic manifestations, and late clinical manifestations) and their classification
2. Revise the nomenclature for some of the clinical stages of syphilis
3. Clarify language used in previous version of the case definitions

IV. Goals of Surveillance

To provide information on the temporal, geographic, and demographic occurrence of syphilis to facilitate its prevention and control.

V. Methods for Surveillance: Surveillance for syphilis should use the recommended sources of data and the extent of coverage listed in Table III.

Surveillance for Syphilis should use the recommended sources of data and the extent of coverage listed in Table III.

VI. Criteria for case identification

A. Narrative: A description of suggested criteria for case ascertainment of syphilis.

Report to public health authorities any of the following laboratory test results:

- Demonstration of *Treponema pallidum* in clinical specimens by darkfield microscopy
- Demonstration of *T. pallidum* in late lesions by special stains
- Reactive polymerase chain reaction (PCR) or equivalent direct molecular tests
- Reactive nontreponemal serologic tests:
 - Reactive Venereal Disease Research Laboratory [VDRL] serologic test
 - Reactive rapid plasma reagin [RPR] serologic test
 - Reactive results with equivalent serologic methods
- Reactive treponemal serologic tests:
 - Reactive *T. pallidum* particle agglutination [TP-PA] serologic test
 - Reactive treponemal enzyme immunoassay (EIA) serologic test
 - Reactive treponemal chemiluminescence immunoassay (CIA) serologic test
 - Reactive results with equivalent serologic methods
- Reactive Venereal Disease Research Laboratory [VDRL] in a specimen of cerebrospinal fluid

In addition, other laboratory test results associated with congenital syphilis:

- Demonstration of *T. pallidum* in lesions, body fluids, or neonatal nasal discharge by darkfield microscopy
- Demonstration of *T. pallidum* by polymerase chain reaction (PCR) or other equivalent direct molecular methods of lesions, neonatal nasal discharge, placenta, umbilical cord, or autopsy material
- Demonstration of *T. pallidum* by immunohistochemistry (IHC), or special stains (e.g., silver staining) of specimens from lesions, placenta, umbilical cord, or autopsy material

NOTE: Treponemal and/or nontreponemal tests are often performed to confirm or follow up a reactive serologic test for syphilis. All such confirmatory test results (both reactive and nonreactive) should be reported when available, but their availability should not delay report of an initial reactive serologic test result. All reactive results should be reported regardless of treatment status of the patient.

If associated with one or more of the above laboratory tests, report to public health authorities any of the following clinical presentations:

- Ulcerative lesion (e.g. chancre)
- Localized or diffuse mucocutaneous lesions (non-pruritic macular, maculopapular, papular or pustular lesions), generalized lymphadenopathy, mucous patches, condyloma lata, or alopecia (at least one of these is required)

Clinical findings associated with congenital syphilis:

- Evidence of congenital syphilis on physical examination

- Evidence of congenital syphilis on radiographs of long bones

Any of the following clinical presentations should be reported to public health authorities:

Clinical signs or symptoms and laboratory results that meet the likely or verified criteria for neurosyphilis, ocular syphilis, otosyphilis, or late clinical manifestations (tertiary) of syphilis

Report to public health authorities any of the following epidemiologic risk factors:

- In a potential case of congenital syphilis, an infant whose mother had untreated or inadequately treated syphilis at delivery, regardless of signs in the infant. (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.)

Report any death certificate that lists syphilis as a cause of death or a significant condition contributing to death.

B. Table of criteria to determine whether a case should be reported to public health authorities

Table VI-B. Table of criteria to determine whether a case should be reported to public health authorities.

Criterion	Syphilis		Congenital Syphilis
<i>Clinical presentation</i>			
Ulcerative lesion (e.g. chancre)		O	
Localized or diffuse mucocutaneous lesions (non-pruritic macular, maculopapular, papular or pustular lesions)		O	
Generalized lymphadenopathy		O	
Mucous patches		O	
Condyloma lata		O	
Alopecia		O	
Clinical signs or symptoms and laboratory results that meet the likely or verified criteria for neurologic, ocular, otic, or late clinical manifestations syphilis	S		
Evidence of congenital syphilis on physical examination			S
Evidence of congenital syphilis on radiographs of long bones			S
<i>Laboratory Findings</i>			
Demonstration of <i>Treponema pallidum</i> in clinical specimens by darkfield microscopy	S	O	
Demonstration of <i>T. pallidum</i> in late lesions by special stains	S	O	

Reactive polymerase chain reaction test (PCR) or equivalent direct molecular methods	S	O	
Reactive non-treponemal serologic test (Venereal Disease Research Laboratory [VDRL], rapid plasma reagin [RPR], or equivalent serologic methods)	S	O	S
Reactive treponemal serologic test (<i>T. pallidum</i> particle agglutination [TP-PA]), enzyme immunoassay [EIA], chemiluminescence immunoassay [CIA], or equivalent serologic methods)	S	O	S
Reactive Venereal Disease Research Laboratory [VDRL] test in a specimen of cerebrospinal fluid	S	O	S
Demonstration of <i>T. pallidum</i> in lesions, body fluids, or neonatal nasal discharge by darkfield microscopy			S
Reactive polymerase chain reaction (PCR) or other equivalent direct molecular methods of lesions, neonatal nasal discharge, placenta, umbilical cord or autopsy material			S
Demonstration of <i>T. pallidum</i> in lesions, placenta, umbilical cord, or autopsy material by immunohistochemistry, or special stains (silver staining)			S
<i>Epidemiological Risk Factors</i>			
An infant whose mother had untreated or inadequately treated syphilis at delivery, regardless of signs in the infant. (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.)			S
Any death certificate that lists syphilis as a cause of death or a significant condition contributing to death.	S		S

Notes:

S = This criterion alone is Sufficient to report a case.

N = All "N" criteria in the same column are Necessary to report a case.

O = At least one of these "O" (One or more) criteria in each category (e.g., clinical evidence and laboratory evidence) in the same column—in conjunction with all "N" criteria in the same column—is required to report a case.

* A requisition or order for any of the "S" laboratory tests is sufficient to meet the reporting criteria.

C. Disease-specific data elements

Disease-specific data elements to be included in the initial report are listed below.

Non-treponemal serologic test titer

Stage of syphilis

Pregnancy status

HIV Status

Gender of sex partners

Neurologic manifestations of syphilis

Ocular manifestations of syphilis

Otic manifestations of syphilis

Late manifestations of syphilis

NOTE: Public health authorities do not expect that an initial report will contain all the information necessary for case investigation and case classification. The disease-specific data elements listed here are meant to assist public health authorities in prioritizing case interviews.

VII. Case Definition for Case Classification

A. Narrative: Description of criteria to determine how a case should be classified.

Syphilis is a complex sexually transmitted disease that has a highly variable clinical course. Adherence to the following surveillance case definitions will facilitate understanding the epidemiology of this disease across the U.S. The following guidance is intended to be used for the purposes of syphilis surveillance, and is not intended to be used as a guide to the clinical management or public health management of syphilis cases.

- Syphilis, primary
- Syphilis, secondary
- Syphilis, early non-primary, non-secondary
- Syphilis, unknown duration or late
- Syphilis, congenital
- Syphilitic stillbirth

In addition to describing the case definitions, the following also provides guidance for reporting neurologic, ocular, otic, and late clinical manifestations of syphilis. Cases should be reported according to stage of infection, as defined below (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.

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

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).*

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 confirmatory laboratory criteria.

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

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 signs can include mucous patches, condyloma lata, and alopecia. The primary ulcerative lesion may still be present.*

Laboratory criteria

- 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), AND
- A reactive treponemal serologic test (*T. pallidum* particle agglutination [TP-PA], enzyme immunoassay [EIA], chemiluminescence immunoassay [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.

*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.

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

Confirmatory: N/A

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.

Epidemiologic 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.

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

Confirmed: N/A

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).

Confirmed: N/A

Comment:

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.

ADDITIONAL INFORMATION TO BE COLLECTED ON CLINICAL MANIFESTATIONS OF REPORTED SYPHILIS CASES

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)
- 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 cerebrospinal fluid (CSF) protein (>50 mg/dL²) or leukocyte count (>5 white blood cells/cubic millimeter 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 polymerase chain reaction (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 polymerase chain reaction (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 polymerase chain reaction (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).

Syphilis, Congenital

Clinical description

A condition caused by infection in utero with *Treponema 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 *Treponema pallidum* by:

- Darkfield microscopy of lesions, body fluids, or neonatal nasal discharge, or
- Polymerase chain reaction (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 (Venereal Disease Research Laboratory [VDRL], rapid plasma reagin [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 cerebrospinal fluid (CSF) venereal disease research laboratory test (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

Syphilitic Stillbirth

Clinical case definition

A fetal death that occurs after a 20-week gestation or in which the fetus weighs greater than 500 g 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.

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, 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.

B. Classification Tables

Table VII-B. Criteria for defining a case of syphilis.

Criterion	Confirmed			Probable						
	Primary	Secondary	Congenital	Primary	Secondary	Early, non-primary, non-secondary	Unknown Duration/Late			Congenital
Clinical presentation										
Ulcerative lesion (e.g. chancre)	N	O		N	O					
Localized or diffuse mucocutaneous lesions (non-pruritic macular, maculopapular, papular or pustular lesions)		O			O					
Generalized lymphadenopathy		O			O					
Mucous patches		O			O					
Condyloma lata		O			O					
Alopecia		O			O					
Syphilitic inflammatory lesions of the cardiovascular system, (e.g., aortitis, coronary vessel disease), skin (e.g., gummatous lesions), bone (e.g., osteitis) or other tissue or structure									N	
Clinical signs or symptoms and laboratory results that meet the likely or verified criteria for neurologic, ocular, otic, or late clinical manifestations syphilis									N	
Evidence of congenital syphilis on physical examination (see signs and stigmata, based upon age, detailed below)										O

An infant or child (aged less than 2 years) with signs such as hepatosplenomegaly, rash, condyloma lata, snuffles, jaundice (nonviral hepatitis), pseudoparalysis, anemia, or edema (nephrotic syndrome and/or malnutrition).												O
A child (aged more than 2 years) with stigmata of congenital syphilis (e.g., interstitial keratitis, nerve deafness, anterior bowing of shins, frontal bossing, mulberry molars, Hutchinson teeth, saddle nose, rhagades, or Clutton joints)												O
Evidence of congenital syphilis on radiographs of long bones (e.g., metaphyseal and epiphyseal changes)												O
No clinical signs or symptoms of primary or secondary syphilis						N	N	N	N	N		
Laboratory Findings												
Demonstration of <i>Treponema pallidum</i> in clinical specimens other than those from the oropharynx by darkfield microscopy	O	O										
Reactive polymerase chain reaction test (PCR) or equivalent direct molecular methods	O	O										
Reactive non-treponemal serologic test (Venereal Disease Research Laboratory [VDRL], rapid plasma reagin [RPR], or equivalent serologic methods)			O	N	N		N					
An infant or child with a reactive non-treponemal serologic test (Venereal Disease Research Laboratory [VDRL], rapid plasma reagin [RPR], or equivalent serologic methods)												N
Reactive Venereal Disease Research Laboratory [VDRL], rapid plasma reagin [RPR], or equivalent serologic test demonstrating a fourfold or greater increase in titer sustained >2 weeks							N		N			
Reactive Venereal Disease Research Laboratory [VDRL] test in a specimen of cerebrospinal fluid												O
Reactive treponemal serologic test (<i>T. pallidum</i> particle agglutination [TP-PA]), enzyme immunoassay [EIA], chemiluminescence immunoassay [CIA], or equivalent serologic methods)			O	N	N		N					

Elevated CSF protein or CSF leukocyte count in absence of other known cause												O
Demonstration of <i>T. pallidum</i> in late lesions by special stains												
Demonstration of <i>T. pallidum</i> by darkfield microscopy (of lesions, body fluids, or neonatal nasal discharge), or by polymerase chain reaction (PCR) or other equivalent direct molecular methods (of lesions, neonatal nasal discharge, placenta, umbilical cord, or autopsy material), or by immunohistochemistry (IHC) or other special stains (e.g. silver staining) (of lesions, placenta, umbilical cord, or autopsy material)			N									
Seroconversion or fourfold or greater increase in titer of a nontreponemal test during the previous 12 months sustained for >2 weeks							O	O				
Documented seroconversion of a treponemal test during the previous 12 months							O	O				
Epidemiological Risk Factors												
An infant whose mother had untreated or inadequately treated syphilis at delivery, regardless of signs in the infant. (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.)												O
A fetal death that occurs after a 20-week gestation or in which the fetus weighs greater than 500 g 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.)												S
History of syphilis diagnosis								N		N		
No evidence of having acquired disease within previous 12 months									N	N	N	
History of symptoms consistent with primary or secondary syphilis within the previous 12 months							O	O				
History of sexual exposure within the previous 12 months to a partner who had confirmed or probable primary or secondary syphilis or probable early non-primary, non-secondary syphilis (documented							O	O				

independently as duration less than 12 months)												
Only sexual contact (sexual debut) was within the last 12 months						O	O					
Criteria to distinguish a new case												
No history of syphilis diagnosis						N		N				

Notes:

*** When reporting neurosyphilis to CDC, the case should be reported as the stage of infection with “neurologic manifestations present” noted in the case report data.**

S = This criterion alone is Sufficient to classify a case.

N = All “N” criteria in the same column are Necessary to classify a case. A number following an “N” indicates that this criterion is only required for a specific disease/condition subtype (see below).

A = This criterion must be absent (i.e., NOT present) for the case to meet the classification criteria.

O = At least one of these “O” (One or more) criteria in each category (e.g., clinical evidence and laboratory evidence) in the same column—in conjunction with all “N” criteria in the same column—is required to classify a case. (These “O” criteria are alternatives, which means that a single column will have either no O criteria or multiple O criteria; no column should have only one O.) A number following an “O” indicates that this criterion is only required for a specific disease/condition subtype.

VIII. Period of Surveillance

Surveillance should be ongoing.

IX. Data sharing/release and print criteria

Notification to CDC of confirmed and probable cases of syphilis is recommended. De-identified data are provided by jurisdictions to CDC. Jurisdiction-specific case counts are reported weekly in the MMWR. Data are also analyzed and published in the CDC's annual *Sexually Transmitted Disease Surveillance*, in STD surveillance updates within the MMWR, and in peer-reviewed publications. Reports and publications are provided to jurisdictions, to other interested parties, and made available on the internet.

X. Revision History

Position Statement ID	Section of Document	Revision Description
13-ID-04	Section VII, A	Renamed "early latent", to "early non-primary, non-secondary"
13-ID-04	Section VII, A	Renamed "late latent" and "late with clinical manifestations" stages to "unknown duration or late"
13-ID-04	Section VII, A	New section on clinical manifestations of syphilis that includes neurosyphilis and late clinical manifestations and gives guidance on classification
13-ID-04	Section VII, Table VII-B	Changes to Section VII, A incorporated into the table
17-ID-11	Table VI-B, Section VII, Table VII-B	CSTE National Office made minor technical clarifications during post-conference technical review to align narrative sections and tables.

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XII. Coordination

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