

Syphilis

Disease plan

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Utah Department of Health and Human Services: Syphilis

Last updated: 12/14/2023 by Nikki Baer

Questions about this disease plan?

Contact the Utah Department of Health and Human Services Office of Communicable Diseases: 801-538-6191.

Note: Utah DHHS acknowledges transgender and gender non-conforming/binary individuals. In this disease plan, "male" refers to individuals with male anatomy and "female" refers to individuals with female anatomy to coincide with language currently used by the CDC.

Syphilis critical clinician information

Clinical evidence

Signs/symptoms

- Primary syphilis: ulcerative lesion (chancre) that is usually firm, round, small, and painless
- Secondary syphilis: localized or diffuse mucocutaneous lesions (non-pruritic macular, maculopapular, papular, or pustular lesions), generalized lymphadenopathy, mucous patches, condyloma lata, and/or alopecia
- Neurosyphilis: cognitive dysfunction, motor or sensory deficits, cranial nerve palsies, or symptoms or signs of meningitis or stroke
- Ocular syphilis: posterior uveitis, panuveitis, anterior uveitis, optic neuropathy, and/or retinal vasculitis
- Otic manifestations: sensorineural hearing loss, tinnitus, and/or vertigo
- Late clinical manifestations (tertiary syphilis): inflammatory lesions of the cardiovascular system (aortitis, coronary vessel disease), skin (gummatous lesions), bone (osteitis), and/or other tissue. Certain neurological manifestations, including general paresis and tabes dorsalis
- Congenital: fetal death, hepatosplenomegaly, rash, condyloma lata, snuffles, jaundice (non-viral hepatitis), pseudo-paralysis, anemia, and/or edema (nephrotic syndrome and/or malnutrition)

Period of communicability

• The extent of communicability depends on the existence of infectious lesions (sores), which may or may not be visible

Incubation period

• The average time between infection with syphilis and the development of a painless lesion known as a chancre is 21 days, but can range from 10–90 days

Mode of transmission

- Sexual: person-to-person via vaginal, anal, or oral sex through direct contact with syphilis sores or lesions
- Vertical: from infected mother to the unborn baby via the bloodstream

Laboratory testing

- Darkfield microscopy
- Special stains (silver staining)
- Polymerase chain reaction (PCR) or equivalent direct molecular tests
- Nontreponemal serologic tests
 - Venereal disease research laboratory (VDRL)
 - Rapid plasma reagin (RPR)
- Treponemal serologic tests
 - Treponema pallidum particle agglutination (TP-PA)
 - Treponemal enzyme immunoassay (EIA)
 - Treponemal chemiluminescence immunoassay (CIA)

A positive treponemal and a positive nontreponemal test are required to confirm a syphilis infection.

Type of specimens

Blood
Cerebrospinal fluid (CSF)
• Specimens from lesions, neonatal nasal discharge, placenta, umbilical cord, or autopsy material
Treatment recommendations
Type of treatment
• Early syphilis: benzathine penicillin G—2.4 million units IM
 Doxycycline (100 mg BID x 14 days) may be used as an alternative
• Unknown duration or late syphilis: benzathine penicillin G—2.4 million units IM x 3 at weekly intervals
 Doxycycline (100 mg BID x 28 days) may be used as an alternative
• See complete <u>CDC guidelines</u> for treatment of pregnant women, children, congenital syphilis, and
clinical manifestations including neurosyphilis, ocular syphilis, and otic manifestations
Time period to treat
Early syphilis: single dose
Unknown duration or late syphilis: 3 doses each at 1 week intervals
Prophylaxis
All contacts of cases of early syphilis exposed within 90 days of examination should receive
treatment
Contact management
Isolation of case
• Cases should avoid sexual contact until at least 7 days since syphilis treatment is completed, all
mucosal and skin lesions have resolved, and their sex partners have been treated
Quarantine of contacts
Not applicable
Infection control procedures

• Standard body substance precautions in hospitals.

Why is syphilis important to public health?

Syphilis is a complex, sexually transmitted infection made up of several stages throughout the duration of infection. Untreated syphilis can cause clinical manifestations affecting the cardiovascular system, skin, bone, and other tissues. Neurological manifestations are also possible. A pregnant person who has syphilis can pass this infection to the infant *in utero*. If left untreated, severe birth defects and fetal death can occur.

Disease and epidemiology

Clinical description

Syphilis is a sexually transmitted infection (STI) caused by the bacterium *Treponema pallidum*. Acute infection is characterized clinically by a primary lesion (chancre) or a secondary rash involving skin and mucous membranes. Chronic infection is characterized by long periods of latency and late lesions of the skin, bone, viscera, central nervous system (CNS), and cardiovascular system.¹

Primary syphilis: the primary stage of syphilis begins with the eruption of a painless sore or chancre at the site of the infection. The average time between infection with syphilis and the development of a chancre is 21 days, but can range from 10–90 days. Chancres most frequently occur in the genital, oral, perineal, or anal area; however, any part of the body may be infected.²

Secondary syphilis: in the secondary stage, a disseminated skin rash and lesions of the mucous membranes are most common. Other symptoms include malaise, lymphadenopathy, mucous patches (elevated patches in the mouth or anus), condylomata lata (syphilitic wart-like lesions generally in the perineal and perirectal areas) and alopecia (patchy hair loss). The rash of secondary syphilis usually begins 4–10 weeks after the onset of the primary lesion (chancre).³

Early non-primary non-secondary syphilis: Without treatment, syphilis infection persists in the body even though symptoms resolve. This clinical latency can occur between the primary and secondary (P&S) stages, between secondary relapses, and after the secondary stage. People are classified as early non-primary non-secondary if they are free of primary and secondary symptoms at the time of diagnosis and at least one of the following is true:

- A documented negative test within the prior 12 months.
- In a previously treated person, a 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.
- Unequivocal symptoms of primary or secondary syphilis within the prior 12 months.

- Sexual contact in the prior 12 months with a partner who had untreated primary, secondary, or early non-primary non-secondary syphilis.
- The only possible exposure occurred during the previous 12 months (people whose first sexual experience was in the past 12 months).³

Unknown duration or late syphilis: a stage of infection in which the initial infection occurred more than 12 months before the diagnosis date, or in which there is insufficient evidence to conclude the infection was acquired during the previous 12 months.³

Congenital syphilis: a condition caused by an infection *in utero* with *T. pallidum*. A wide spectrum of severity exists, from infant death or stillbirth to infants born with no documented signs or symptoms. An infant or child (aged <2 years) may have signs such as hepatosplenomegaly, rash, condyloma lata, snuffles, jaundice (non-viral hepatitis), pseudoparalysis, anemia, or edema (nephrotic syndrome and/or malnutrition). A child older than 2 years may have abnormal tooth development (Hutchingson's teeth and mulberry molars), perforation of the hard palate, facial changes, ophthalmic disorders, bone abnormalities, and deafness.³

Syphilis stillbirth: a fetal death that occurs after a 20-week gestation, or in which the fetus weighs more than 500 g, and the mother had untreated or inadequately treated syphilis at delivery.⁴ Any person who delivers a stillborn infant after a 20-week gestation should be screened for syphilis to determine whether the fetus should be classified as a syphilis stillbirth.²

Neurological manifestations: these can occur at any stage of syphilis and include cognitive dysfunction, motor or sensory deficits, cranial nerve palsies, or signs/symptoms of meningitis or stroke.¹

Ocular manifestations: These can occur at any stage of syphilis and include posterior uveitis, panuveitis, anterior uveitis, optic neuropathy, and retinal vasculitis. Ocular syphilis may lead to decreased visual acuity including permanent blindness.¹

Otic manifestations: These can occur at any stage of syphilis and include sensorineural hearing loss, tinnitus, and vertigo.¹

Causative agent

Syphilis is caused by *T. pallidum*, a corkscrew shaped bacterium (spirochete).

Differential diagnosis

The differential diagnosis for primary syphilis includes chancroid, granuloma inguinale, trauma to the penis, genital herpes, lymphogranuloma venereum, malignancy, or a fixed drug eruption, which may cause lesions resembling a chancre. An important distinguishing feature is that a chancre is usually painless. The differential diagnosis for secondary syphilis lesions includes pityriasis rosea, which may closely resemble psoriasis, erythema multiforme, or a drug eruption.

Laboratory identification

- Direct methods of diagnosis through direct visualization or detection in clinical specimens⁴:
 - Demonstration of *T. pallidum* in clinical specimens by darkfield microscopy
 - Demonstration of *T. pallidum* in late lesions by special stains
 - Polymerase chain reaction (PCR) or equivalent direct molecular test.
- Nontreponemal serologic tests⁴:
 - Reactive Venereal Disease Research Laboratory (VDRL) serologic test
 - Reactive rapid plasma reagin (RPR) serologic test
 - Reactive results with equivalent serologic methods
- Treponemal serologic tests⁴:
 - 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 VDRL in a specimen of cerebrospinal fluid (CSF)⁴

In addition, other laboratory test results associated with congenital syphilis include⁴:

- Demonstration of *T. pallidum* in lesions, body fluids, or neonatal discharge by darkfield microscopy
- Demonstration of *T. pallidum* by 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 (silver staining) of specimens from lesions, placenta, umbilical cord, or autopsy material

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

Treatment

Penicillin G, administered parenterally, is the preferred drug for all stages of syphilis. Doxycycline can be used in nonpregnant patients in the instance of a penicillin allergy or when penicillin is not available.¹ Pregnant women who are allergic to penicillin should be desensitized and treated with penicillin G. In instances of a penicillin G shortage, this medication should be reserved for pregnant and immunocompromised individuals while all others should be treated with doxycycline. Patients who have been treated with a regimen other than penicillin G should receive close post-treatment monitoring to make sure treatment is successful. Additional alternative treatment regimens can be found in the <u>CDC STI Treatment Guidelines</u>.

Primary, secondary, or early non-primary non-secondary syphilis

Benzathine penicillin G: 2.4 million units IM in a single dose.

OR

Doxycycline: 100 mg twice daily for 14 days.

Unknown duration or late syphilis

Benzathine penicillin G: 7.2 million units total, administered as 3 doses of 2.4 million units IM each at 1 week intervals (intervals can extend up to 9 days for pregnant individuals and up to 10–14 days for non-pregnant individuals).

OR

Doxycycline: 100 mg twice daily for 28 days.

Clinical manifestations: Neurosyphilis and ocular syphilis

Aqueous crystalline penicillin G: 18–24 million units per day, administered as 3–4 million units IV every 4 hours or continuous infusion, for 10–14 days.

Congenital syphilis

Aqueous crystalline penicillin G: 100,000–150,000 units/kg/day, administered as 500,000 units/kg/dose IV every 12 hours during the first 7 days of life and every 8 hours thereafter for a total of 10 days.

OR

Procaine penicillin G: 50,000 units/kg/dose IM in a single daily dose for 10 days.

Case fatality

According to historical studies, 10–20% of untreated cases die from syphilis infection.^{5,6} However, due to high treatment rates, deaths caused by syphilis are rare in the U.S. and have been for several decades.⁶ Untreated syphilis in pregnant women results in infant death in up to 40% of cases.²

Reservoir

Humans are the only known natural hosts.

Transmission

Syphilis is transmitted by direct contact with a syphilitic sore or rash during vaginal, anal, or oral sex. Transmission may also occur across the placenta prior to birth. Transmission rarely occurs by blood transfusion or organ donation.⁷

Susceptibility

Susceptibility is universal, though people with untreated syphilis are thought to not be able to acquire a new, symptomatic syphilis infection.²

Incubation period

The incubation period of primary syphilis is 10-90 days, with a median incubation period of 21 days. The incubation period of tertiary syphilis is 10-30 years after initial infection.²

Period of communicability

Patients are most infectious during the primary and secondary stages of syphilis when symptoms, such as lesions or a rash, are present.³

Epidemiology

Syphilis is a complex, sexually transmitted infection made up of several stages throughout the duration of infection. Primary and secondary (P&S) syphilis represent symptomatic disease and indicate incident infection. Consequently, rates of P&S syphilis are used to monitor trends in disease. Reported national rates of syphilis reached record lows in 2000. Since then, rates have steadily increased almost every year, increasing 28.6% between 2020 and 2021.[§] Nationally, rates increased among both males and females. Rates of P&S syphilis increased in all racial/Hispanic ethnicity groups, with the greatest increases among non-Hispanic American Indian/Alaska Native people who had the highest P&S syphilis rate in 2021.[§] Congenital syphilis cases in the United States increased 755% during 2012–2021.[§] In 2022, a total of 3,761 cases of congenital syphilis were reported to CDC, including 231 (6%) stillbirths and 51 (1%) infant deaths.[§] Lack of timely testing and adequate treatment during pregnancy contributed to 88% of cases of congenital syphilis.[§]

Internal DHHS data show P&S syphilis rates in Utah continue to rise with a rate of 7.0 cases per 100,000 persons in 2022. This represents a 13% increase from the 2021 rate, and a 84% increase in the past 5 years. In 2022, 74% of P&S syphilis cases were in men who have sex with men and rates in males overall were significantly higher than in females. The highest rates were among people aged 25–34 which accounts for 35% of all cases. Racial and ethnic minorities continued to be disproportionately affected by syphilis in 2022 with the highest rates seen in people who are Black/African American (32.3), Native Hawaiian/Pacific Islander (22.5), American Indian/Alaska Native (19.1), and Hispanic persons (14.2).

In Utah, congenital syphilis cases continue to increase. Internal DHHS data show that in 2022, there were 7 cases and no stillbirths or infant deaths. Increases in congenital syphilis mirror trends observed in rates of primary and secondary syphilis cases in women of reproductive age,

which increased 210% during 2013–2022. Utah's congenital syphilis cases have been spread across the state. During the years of 2013–2022, Weber-Morgan Health Department reported 5 cases, Davis County Health Department reported 4 cases, Utah County Health Department reported 3 cases, and Salt Lake County Health Department and Southwest Utah Health Department each reported 1 case.

Public health control measures

Public health responsibility

- Investigate all suspect cases of disease and fill out and submit appropriate disease investigation forms.
- Provide education to the general public and clinicians about disease transmission and prevention.
- Identify disease clusters or outbreaks.
- Identify sources of exposure and stop further transmission.
- Provide/facilitate treatment for the patient and their partner(s).

Prevention

- Emphasis should be placed on early detection and effective treatment of patients who have transmissible syphilis and their contacts.
- Educate the community about general health promotion measures:
 - Provide sexual health education that teaches the importance of risk reduction measures including abstinence, reducing the number of sex partners, mutual monogamy, and condom use.
 - Protect the community and control STIs in sex workers and their clients.
 - Teach methods of personal prophylaxis to use before, during, and after exposure, especially the correct and consistent use of condoms.
- Provide healthcare facilities with education about early diagnosis and treatment:
 - Encourage providers to educate patients about symptoms of sexually transmitted infections, modes of transmission, reinfection, and the importance of notifying sexual partners.
 - Make these services culturally appropriate, readily accessible, and acceptable, regardless of economic status.
 - Implement repeated serological screening for syphilis within special populations who have known high incidence of STIs.
 - Implement serological screening for syphilis among all pregnant women at the first prenatal visit and again at 28 weeks gestation for those at high risk. High risk factors

include living in a community with high syphilis morbidity, drug misuse, an STI diagnosis during pregnancy, multiple partners, a new partner, or a partner with STIs.

- Screen any person who delivers a stillborn infant after 20 weeks gestation for syphilis.
- Exclude other STI infections, including HIV, through testing.
- Offer PrEP if HIV results are negative at the time of diagnosis.

Chemoprophylaxis

All contacts of cases of early syphilis exposed within 90 days of examination should receive treatment.

Vaccine

None.

Isolation and quarantine requirements

Isolation: Avoid sexual contact until at least 7 days since syphilis treatment is completed, all mucosal and skin lesions have resolved, and sex partners have been treated.³

Hospital: Standard body substance precautions.

Quarantine: Not applicable.

Case investigation

Reporting (CSTE position statement, 2017)

All cases of syphilis are reportable, even asymptomatic syphilis. Below is a table to determine whether a case should be reported to public health authorities¹⁰:

Note: The following section is copied directly from <u>CSTE position statement 17-ID-11¹⁰</u>

Criteria to determine whether a case should be reported to public health authorities (CSTE)

Criterion	Syp	hilis	Congenital syphilis	
Clinical presentation				
Ulcerative lesion (e.g., chancre)		0		
Localized or diffuse mucocutaneous lesions (non-pruritic macular,	0			
maculopapular, papular or pustular lesions)	0			
Generalized lymphadenopathy		0		
Mucous patches		0		
Condyloma lata		0		

Alopecia		0	
Clinical signs or symptoms and laboratory results that meet the			
likely or verified criteria for neurologic, ocular, otic, or late clinical	S		
manifestations syphilis			
Evidence of congenital syphilis on physical examination			S
Evidence of congenital syphilis on radiographs of long bones			S
Laboratory findings			
Demonstration of <i>T. pallidum</i> in clinical specimens by darkfield	c	0	
microscopy	2	0	
Demonstration of <i>T. pallidum</i> in late lesions by special stains	S	0	
Reactive PCR test or equivalent direct molecular methods	S	0	
Reactive nontreponemal serologic test (VDRL, RPR, or equivalent	6	0	c
serologic methods)	5	0	5
Reactive treponemal serologic test (TP-PA, EIA, CIA, or equivalent	c		c
serologic methods)	5	0	2
Reactive VDRL test in a specimen of cerebrospinal fluid	S	0	S
Demonstration of <i>T. pallidum</i> in lesions, body fluids, or neonatal			c
nasal discharge by darkfield microscopy			C C
Reactive PCR or other equivalent direct molecular methods of			
lesions, neonatal nasal discharge, placenta, umbilical cord, or			S
autopsy material			
Demonstration of <i>T. pallidum</i> in lesions, placenta, umbilical cord,			
or autopsy material by immunohistochemistry, or special stains			S
(silver staining)			
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,			S
in accordance with CDC treatment guidelines, appropriate for			
stage of infection, initiated 30 or more days before delivery.)			
Any death certificate that lists syphilis as a cause of death or a	S		S
significant condition contributing to death			

Notes:

S = These criterion alone are 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.

Case definition

Syphilis is a complex, sexually transmitted infection 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. Epidemiologists classify infections according to the following¹⁰:

Note: The following section is copied directly from <u>CSTE position statement 17-ID-11¹⁰</u>

Criteria for defining a case of syphilis (CSTE)

	Со	nfirm	ed				Prob	able			
Criterion	Primary	Secondary	Congenital	Primary	Secondary	Early	non-secondary		Unknown duration/late		Congenital
Clinical presentation											
Ulcerative lesion (e.g., chancre)	Ν	0		Ν	0						
Localized or diffuse											
mucocutaneous lesions											
(non-pruritic macular,		0			0						
maculopapular, papular or											
pustular lesions)											
Generalized lymphadenopathy		0			0						
Mucous patches		0			0						
Condyloma lata		0			0						
Alopecia		0			0						
Syphilitic inflammatory lesions of											
the cardiovascular system, (e.g.,											
aortitis, coronary vessel disease),										NI	
skin (e.g., gummatous lesions),										IN	
bone (e.g., osteitis) or other tissue											
or structure											
Clinical signs or symptoms and											
laboratory results that meet the										Ν	
likely or verified criteria for											

neurologic, ocular, otic, or late										
clinical manifestations syphilis										
Evidence of congenital syphilis on										
physical examination (see signs										0
and stigmata, based upon age,										Ū.
detailed below)										
An infant or child										
(aged <2 years) with signs such as										
hepatosplenomegaly, rash,										
condyloma lata, snuffles, jaundice										0
(nonviral hepatitis),										Ŭ
pseudoparalysis, anemia, or										
edema (nephrotic syndrome										
and/or malnutrition)										
A child (aged >2 years) with										
stigmata of congenital syphilis										
(e.g., interstitial keratitis, nerve										
deafness, anterior bowing of										0
shins, frontal bossing, mulberry										
molars, Hutchinson teeth, saddle										
nose, rhagades, or Clutton joints)										
Evidence of congenital syphilis on										
radiographs of long bones (e.g.,										0
metaphyseal and epiphyseal										0
changes)										
No clinical signs or symptoms of					NI	N	NI	N	N	
primary or secondary syphilis					IN	N	IN	N	N	
Laboratory findings										
Demonstration of <i>T. pallidum</i> in										
clinical specimens other than	0	0								
those from the orpharynx by	0	0								
darkfield microscopy										
Reactive PCR or equivalent direct	0	0								
molecular methods	0	0								
Reactive nontreponemal serologic										
test (VDRL, RPR, or equivalent			0	Ν	Ν		Ν			
serologic methods)										

An infant or child with a reactive									
nontreponemal serologic test									
(VDRL, RPR, or equivalent									Ν
serologic methods)									
Reactive VDRL, RPR, or equivalent									
serologic test demonstrating a									
fourfold or greater increase in						Ν		Ν	
titer sustained >2 weeks									
Reactive VDRL test in a specimen									0
of cerebrospinal fluid									
Reactive treponemal serologic test									
(TPPA, EIA, CIA, or equivalent			0	Ν	Ν		Ν		
serologic methods)									
Elevated CSF protein or CSF									
leukocyte count in absence of									0
other known cause									
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 PCR or other									
equivalent direct molecular									
methods (of lesions, neonatal									
nasal discharge, placenta,		NI							
umbilical cord, or autopsy		IN							
material), or by									
immunohistochemistry (IHC) or									
other special stains (e.g. silver									
staining) (of lesions, placenta,									
umbilical cord, or autopsy									
material)									
Seroconversion or fourfold or									
greater increase in titer of a									
nontreponemal test during the					0	0			
previous 12 months sustained for									
>2 weeks									

Documented seroconversion of a								
treponemal test during the			0	0				
previous 12 months								
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								0
completion of a penicillin-based								0
regimen, in accordance with CDC								
treatment guidelines, appropriate								
for stage of infection, initiated 30								
or more days before delivery.)								
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								ç
defined as completion of a								2
penicillin-based regimen, in								
accordance with CDC treatment								
guidelines, appropriate for stage								
of infection, initiated 30 or more								
days before delivery.)								
History of syphilis diagnosis				Ν		Ν		
No evidence of having acquired								
disease within previous 12					Ν	Ν	Ν	
months								
History of symptoms consistent								
with primary or secondary syphilis			0	0				
within the previous 12 months								
History of sexual exposure within								
the previous 12 months to a								
partner who had confirmed or				0				
probable primary or secondary			U	υ				
syphilis or probable early								
non-primary, non-secondary								

Syphilis: Utah public health disease investigation plan

syphilis (documented							
independently as duration less							
than 12 months)							
Only sexual contact (sexual debut)			0	•			
was within the last 12 months			0	0			
Criteria to distinguish a new case							
No history of syphilis diagnosis			Ν		Ν		

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 = These criterion alone are sufficient to classify a case.

N = All "N" criteria in the same column are necessary to classify a case.

O = At least one of these "O" 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.

Syphilis, primary

Note: The following section is copied directly from <u>CSTE position statement 17-ID-11¹⁰</u>

Clinical description

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

Laboratory criteria for diagnosis⁴

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 PCR or equivalent direct molecular methods in any clinical specimen.

Supportive:

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

Case classification⁴

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

Syphilis, secondary

Note: The following section is copied directly from <u>CSTE position statement 17-ID-11¹⁰</u>

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.

Because of the wide array of symptoms possibly indicating secondary syphilis, serologic tests for syphilis and a thorough sexual history and physical examination are crucial to determining if a case should be classified as secondary syphilis.

Laboratory criteria for diagnosis⁴

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 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 classification⁴

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

Note: The following section is copied directly from <u>CSTE position statement 17-ID-11¹⁰</u>

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 diagnosis⁴

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 criteria⁴

- 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 was within the previous 12 months (sexual debut)

Case classification⁴

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
- o Documented seroconversion of a treponemal test during the previous 12 months
- o A history of symptoms consistent with primary or secondary syphilis during the previous 12 months
- o Meets epidemiologic criteria

Confirmed: N/A

Syphilis, unknown duration or late

Note: The following section is copied directly from <u>CSTE position statement 17-ID-11¹⁰</u>

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 classification⁴

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

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

Syphilitic stillbirth

Note: The following section is copied directly from <u>CSTE position statement 17-ID-11¹⁰</u>

Clinical case definition⁴

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.

Syphilis, congenital

Note: The following section is copied directly from <u>CSTE position statement 17-ID-11¹⁰</u>

Clinical description

A condition caused by infection *in utero* with *T. pallidum*. A wide spectrum of severity exists, and only severe cases are clinically apparent at birth. An infant or child (aged <2 years) may have signs such as hepatosplenomegaly, rash, condyloma lata, snuffles, jaundice (non-viral hepatitis), pseudoparalysis, anemia, or edema (nephrotic syndrome and/or malnutrition). A child older than 2 years 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 diagnosis⁴

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 other special stains (e.g., silver staining) of specimens from lesions, placenta, umbilical cord, or autopsy material.

Case classification⁴

Probable:

- 1. a condition affecting an infant whose mother had untreated or inadequately treated syphilis at delivery, regardless of signs in the infant, **OR**
- 2. an infant or child who has a reactive nontreponemal test for syphilis (VDRL, RPR, or equivalent serologic methods) **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 VDRL test in a specimen of CSF
 - In a non-traumatic lumbar puncture, an elevated CSF protein or CSF leukocyte count (without other cause):
 - o Suggested parameters for abnormal CSF WBC and protein values:
 - During the first 30 days of life, a CSF WBC count of >15
 WBC/mm3 or a CSF protein >120 mg/dl is abnormal.
 - After the first 30 days of life, a CSF WBC count of >5 WBC/mm3 or a CSF protein >40 mg/dl is abnormal.

Confirmed: a case that is laboratory confirmed.

Comment⁴

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 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.

Clinical manifestations

Note: The following section is copied directly from <u>CSTE position statement 17-ID-11¹⁰</u>

Late clinical manifestations (tertiary syphilis)⁴

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

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 symptoms or signs 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 below).

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 below).

Neurologic manifestations⁴

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

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:

- 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, **AND**
- Clinical symptoms or signs that are consistent with neurosyphilis without other known causes for these clinical 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:

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

Ocular manifestations⁴

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

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 manifestations⁴

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

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.

Case investigation process

- Contact medical provider to gather patient demographics, clinical, and treatment information, as well as patient notification status.
- Fill out a morbidity form.
- Conduct a client interview.
- Fill out a client interview record on the original patient and contact records for identified contacts and suspected contacts.
- Conduct investigations on contacts and suspected contacts.
- Provide/facilitate treatment based on case definitions and follow-up for contacts.
- Re-interview client for additional contacts and suspected contacts.
- Complete interview record.

Outbreaks

A syphilis outbreak occurs when the observed rate of disease in a geographical area exceeds the normal (endemic) rate.

Case contact management

A fundamental feature of programs for syphilis control is patient interviews to identify sexual contacts from whom the infection was acquired, in addition to those who may have been infected by the patient.

- All sexual partners of cases of primary syphilis during the 3 months before onset of symptoms should be examined, tested, and treated.
- All sexual partners of cases of secondary syphilis during the 6 months before the onset of symptoms should be examined, tested, and treated.
- For early non-primary non-secondary syphilis, all sexual contacts within the last 12 months, or from the most recent negative test (if documented) during the preceding year, should be examined and tested.
- For unknown duration or late syphilis, all sexual contacts during the past 12 months, plus long-term partners and children of infected mothers should be examined and tested.
- All patients who have syphilis should be tested for HIV and other STIs.

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Version control

V.08.15 Updated epidemiological information, adding Utah-specific epidemiology. Updated the treatment section according to 2015 CDC treatment guidelines. Added minimum data set (MDS), added Table of contents, updated swim lanes.

V.12.15 Changed incubation period for secondary syphilis to 3–6 months from 3–12 months.

V.02.18 Critical clinician information and electronic laboratory reporting sections added to disease plan. Epidemiology section updated with current national and Utah-specific data. Content changes were made throughout the document (including the swim lanes) to align the disease plan definitions with the new CSTE syphilis case definitions. A summary of the changes is as follows:

- Changed early latent syphilis to early non-primary non-secondary syphilis.
- Combined late latent syphilis and late with clinical manifestations syphilis into a new stage, unknown duration or late.
- Included new clinical symptoms variables (to be answered for all stages of syphilis) and possible, likely, and verified responses are thoroughly defined.
 - o Neurologic symptoms
 - o Ocular symptoms
 - o Otic symptoms
 - o Late clinical symptoms
- Updated UT-NEDSS Minimum/Required Fields by Tab section.

V.12.23 Epidemiology section updated with current national and Utah-specific data. Made corrections and clarifications to case definition swim lanes. Added screening recommendation for pregnant people and people who have delivered a stillborn infant after 20 weeks of gestation. Added recommendation for using doxycycline as an alternative treatment. Added in text citations.

UT-NEDSS/EpiTrax minimum/required fields by tab

Morbidity event

(Primary, secondary, early non-primary nonsecondary, unknown duration or late)

Demographic

- Last name
- First name
- Street
- Unit number
- City
- State
- County
- ZIP code
- Date of birth
- Area code
- Phone number
- Birth sex
- Ethnicity
- Race
- Disposition (*if promoted contact*)
- Disposition date (if promoted contact)
- Contact type (*if promoted contact*)

Clinical

- Disease
- Date diagnosed
- Pregnant (if female)
- Expected delivery date (if pregnant)
- Treatment given
- Treatment (if treated)
- Date of treatment (*if treated*)
- Clinician last name
- Clinician area code
- Clinician phone
- Diagnostic facility
- Type of facility

- Method of case detection
- Symptoms observed or present
- Clinician observed symptoms
- Clinician observed symptom type (*if applicable*)
- Anatomic site of clinician observed lesions *(if applicable)*
- Patient observed symptoms
- Patient observed symptom type (if applicable)
- Anatomic site of patient observed lesions *(if applicable)*
- Neurological manifestations
- Ocular manifestations
- Otic manifestations
- Late clinical manifestations
- HIV status
- Previous STD diagnosis
- Ever tested for HIV?
- Most recent HIV test date (MM/YY) (*if tested*)

Laboratory

- Lab
- Test type
- Organism
- Test result
- Specimen source
- Collection date

Specimen source section

- Specimen source
- Collection date

Test type and quantitative result section

- Nontreponemal serologic test type
- Quantitative test result

Investigation

- Date case assigned
- Was the case interviewed?
 - o Interview date (if yes)
 - o Interview period (if yes)
 - o Reason not interviewed (if no)
- Date closed
- Is the patient MSM? (if male)
- Had sex with a male?
- Had sex with a female?
- Met sex partners via the Internet?
- Had sex with an anonymous partner?
- Had sex with a person known to be an IDU?
- Had sex while intoxicated/high on drugs?
- Exchanged drugs and/or money for sex?
- Been incarcerated?
- Engaged in IDU?
- Had sex with a person known MSM? *(if female)*
- Drug use?

Contact event

Demographic

- Contact name
- Contact address county (if known)
- Contact date of birth (if known)
- Contact birth sex (*if known*)
- Contact disposition
- Contact disposition date
- Contact type

Contacts

- Total number of sex partners during interview period
- Total number of sex partners in past 12 months

Reporting

• Date first reported to public health

Administrative

- State case status (completed by DHHS)
- Outbreak association

Clinical

- Contact lab collection date
- Contact lab test results
- Contact pregnant (*if known*)(*if female*)
- Contact expected delivery date (*if pregnant*)
- Contact treatment given (*if known*)
- Contact date of treatment (if treated)

Electronic laboratory reporting processing rules

Syphilis rules to enter laboratory test results

The following rules describe how laboratory results reported to public health should be added to new or existing events in UT-NEDSS/EpiTrax. These rules have been developed for the automated processing of electronic laboratory reports, although they apply to manual data entry, as well.

Test-specific rules

Test-specific rules describe what test type and test result combinations are allowed to create new morbidity events in UT-NEDSS/EpiTrax, and what test type and test result combinations are allowed to update existing events (morbidity or contact) in UT-NEDSS/EpiTrax.

Tost type	Tost rosult	Create a new event	Update an existing
Test type	rescresult	Create a new event	event
	Positive	Yes	Yes
PCR	Negative	No	Yes
	Equivocal	Yes	Yes
FTA (transportation	Positive	Yes	Yes
antibody tost)	Negative	No	Yes
antibudy test)	Equivocal	No	Yes
	Positive	Yes	Yes
lgG antibody	Negative	No	Yes
	Equivocal	No	Yes
	Positive	Yes	Yes
lgM antibody	Negative	No	Yes
	Equivocal	No	Yes
	Positive	Yes	Yes
VDRL	Negative	No	Yes
	Equivocal	No	Yes
	Positive	Yes	Yes
ТРРА	Negative	No	Yes
	Equivocal	No	Yes
	Positive	Yes	Yes
MHA-TP	Negative	No	Yes
	Equivocal	No	Yes
	Positive	Yes	Yes
Microscopy (darkfield)	Negative	No	Yes
	Equivocal	Yes	Yes

	0		
	Positive	Yes	Yes
Total antibody	Negative	No	Yes
	Equivocal	No	Yes
RPR	Positive	Yes	Yes
	Negative	No	Yes
	Equivocal	No	Yes
Mastara (immuna)	Positive	Yes	Yes
Western (immune) blot IgG	Negative	No	Yes
	Other	No	Yes

Whitelist rules

Whitelist rules describe how long an existing event can have new laboratory data appended to it. If a laboratory result falls outside the whitelist rules for an existing event, it should not be added to that event, and should be evaluated to determine if a new event (CMR) should be created.

Syphilis morbidity whitelist rule: Add to newest case.

Syphilis contact whitelist rule: If the specimen collection date of the laboratory result is one year or less after the event date of the contact event, the laboratory results should be added to the contact event.

Graylist rule

We often receive laboratory results through ELR that cannot create cases, but can be useful if a case is created in the future. These laboratory results go to the graylist. The graylist rule describes how long an existing event can have an old laboratory result appended to it.

Syphilis graylist rule: If the specimen collection date of the laboratory result is 365 days before to 7 days after the event date of the morbidity event, the laboratory result should be added to the morbidity event.

Other electronic laboratory processing rules

• If an existing event has a state case status of not a case, ELR will never add additional test results to that case. New labs will be evaluated to determine if a new CMR should be created.