

Syphilis

Investigative Guidelines

April 2019

1. DISEASE REPORTING

1.1 Purpose of Reporting and Surveillance

1. To assess trends in disease patterns, understand the impact of syphilis, and better target population-level disease prevention efforts.
2. To assure adequate treatment for infected individuals, curtail infectiousness, and prevent complications (e.g., neurologic manifestations, cardiovascular disease).
3. To prevent transmission by identifying, informing, and referring to treatment recent sexual contacts of reported cases, and screening others at risk.
4. To prevent congenital syphilis by screening and treating infected pregnant women.

1.2 Legal Reporting Requirements

1. Health care providers must report a case or suspected case of syphilis within one working day to the Local Public Health Authority (LPHA) (OAR 333-018-0015).
2. Laboratories must report all positive syphilis test results to the LPHA of the county where the individual resides within one working day from the time of positive result.

1.3 Local Public Health Authority Investigation Responsibilities

1. Begin follow-up case investigation within two working days of receiving the case report.
2. Report all presumptive and confirmed cases to the Public Health Division HIV/STD/TB (HST) Program through the Oregon Public Health Epidemiology User System (Orpheus) by the end of the calendar week of initial provider or laboratory report.

2. DISEASE AND EPIDEMIOLOGY

2.1 Etiologic Agent

Treponema pallidum bacterium

2.2 Description of Illness

Syphilis is a complex, systemic, sexually transmitted infection that has a highly variable clinical course. Untreated, it progresses through stages that are often separated by long periods of latency. Case definitions and laboratory criteria for staging are presented in §3.1-§3.9.

1. **Primary** - The first stage after an incubation period of 10–90 days (average 21 days). This stage is characterized by a primary lesion (chancre) that is typically concave with a raised border. The chancre is usually painless and appears at the site of bacterial entry, generally the genitalia or anus. Lymphadenopathy often develops in proximity to the primary lesion. The chancre heals spontaneously

SYPHILIS

within 1-6 weeks (3 weeks average). Treponemal and nontreponemal tests may be negative when a primary syphilis ulcer first appears. A person is highly infectious during this stage.

2. Secondary - Secondary syphilis signs and symptoms generally appear 4-8 weeks after onset of the primary lesion. These include a generalized body rash, lymphadenopathy, mucous patches, alopecia, and malaise. Secondary symptoms typically persist for 1–6 weeks. Treponemal and nontreponemal tests are both usually reactive during this stage.
3. Latent syphilis is divided into two stages: early non-primary non-secondary and unknown duration or late. Treponemal and nontreponemal tests are both generally reactive in these stages, though nontreponemal tests may be non-reactive in up to one-third of people.
 - A. Early Non-Primary Non-Secondary - This stage applies when an individual is asymptomatic and the earliest date of infection or exposure can be determined to have occurred within a year of diagnosis. In some instances, earliest date of infection can be inferred from a documented negative serologic test result before the current diagnosis, or from onset of documented signs of primary or secondary syphilis.
 - B. Unknown Duration or Late - This stage applies when an individual is asymptomatic and either the time of infection cannot be determined with certainty or the infection occurred more than 12 months prior to diagnosis. If the case remains untreated, late syphilis can persist for the remainder of the person's life.
4. Clinical Manifestations of Syphilis - Neurologic, ocular, or otic manifestations (neurosyphilis, ocular syphilis, or otosyphilis) can occur during any stage and should be reported along with the appropriate stage.
 - A. Neurologic manifestations (neurosyphilis) - Infection of the central nervous system with *T. pallidum*, evidenced by manifestations including syphilitic meningitis, meningovascular syphilis, general paresis including dementia, and tabes dorsalis.
 - B. Ocular manifestations (ocular syphilis) - Infection of the eye with *T. pallidum*, evidenced by manifestations including posterior uveitis, panuveitis, anterior uveitis, optic neuropathy, and retinal vasculitis.
 - C. Otic manifestations (otosyphilis) - Infection of the cochlea and vestibule of the ear with *T. pallidum*, as evidenced by manifestations including sensorineural hearing loss, tinnitus, and vertigo.
 - D. Late clinical manifestations (tertiary syphilis) - Late clinical manifestations occur only many years after infection. Approximately 30–40% of untreated persons may develop late clinical manifestations. Manifestations may include inflammatory lesions of the cardiovascular system, skin, and bone. Neurological effects such as general paresis and tabes dorsalis are also late clinical manifestations of syphilis.
5. Congenital Syphilis - Congenital syphilis occurs when *T. pallidum* is transmitted from a pregnant woman with syphilis to the fetus. Transmission can occur during any trimester and any stage of syphilis, but the risk is higher when a pregnant woman is in the primary or secondary stage. Congenital syphilis can cause miscarriage or stillbirth and may cause infant death due to complications associated with pre-term delivery or generalized systemic disease. Other effects of congenital syphilis include brain or nerve involvement, blindness, deafness,

SYPHILIS

bone deformities, and liver and kidney damage. A CDC Congenital Syphilis Case Investigation and Report form must be completed for all cases in which maternal, infant, or syphilitic stillbirth criteria are met.

2.3 Serologic Tests for Syphilis

Traditional and reverse screening algorithms for syphilis are presented in Appendix A. See the [OHA STD Program](#) and [National STD Curriculum](#) sites for syphilis test interpretation resources.

1. Nontreponemal tests detect antibodies not specific for syphilis. These tests will typically be reactive by 21 days after infection but may be negative during very early primary syphilis.

Nontreponemal tests include:

- Rapid plasma reagin (RPR) test - most common nontreponemal test
- Venereal disease research laboratory (VDRL) test - more commonly used to test cerebrospinal fluid in diagnosing neurosyphilis and congenital syphilis

A reactive result should be reported quantitatively as a titer, or dilution (e.g., 1:2, 1:16, 1:32). This ratio represents the number of times a patient's blood serum was diluted until no antibodies could be detected. A titer of 1:2, for example, indicates a low concentration of antibodies in the serum, as none were detected after only two dilutions. On the other hand, a titer of 1:128 indicates a higher concentration of antibodies as eight dilutions were needed to reach the point at which none were detected in the serum. Nontreponemal tests usually become nonreactive after treatment, but a low titer may persist for life. Only titers of the same type of nontreponemal test should be compared in determining treatment response (e.g., an RPR titer should only be compared with an RPR titer).

2. Treponemal tests detect antibodies specific for syphilis. These tests will typically be reactive by 21 days after infection and earlier than nontreponemal tests but may be negative during very early primary syphilis. Treponemal tests usually remain positive for life, even after treatment. Results should be reported qualitatively. If a numerical value is reported with a reactive result, this value should not factor into patient assessment or treatment.

Examples of treponemal tests include:

- Enzyme or chemiluminescence immunoassays (EIA/CIA)
- Fluorescent treponemal antibody absorption test (FTA)
- *Treponema pallidum* particle agglutination assay (TP-PA)
- Microhemagglutination assay for antibodies to *Treponema pallidum* (MHA-TPA)

2.4 Laboratory Services at the Oregon State Public Health Laboratory (OSPHL)

The OSPHL conducts serologic testing using a nontreponemal RPR test and a treponemal CIA test (Syph-TP). If the RPR screen and treponemal Syph-TP test produce discrepant results, the treponemal FTA-ABS test is run as a secondary reflex "tiebreaker" test. Please refer to the OSPHL Lab Test Menu for all specific instructions to properly collect, store, and transport specimens, available at www.healthoregon.org/labtests.

2.5 Reservoirs

Humans

SYPHILIS

2.6 Sources and Modes of Transmission

Sexual - Syphilis is infectious in the primary and secondary stages and almost always transmitted through direct contact with infectious exudates from moist lesions and with mucous membranes of infected people during sexual intercourse.

Infectious syphilis disproportionately occurs among men who have sex with men. Cases among women are often linked epidemiologically to a male sex partner who also has sex with men.

Vertical - Transmitted from mother to fetus in utero or during delivery.

2.7 Incubation Period

10 to 90 days (average 21 days)

2.8 Period of Communicability

Infections are communicable to sex partners during the primary and secondary stages through direct physical contact with lesions or rash. In secondary syphilis, mucous patches and condyloma lata are believed to be more infectious than dry rashes.

Pregnant women can pass the infection to the fetus during any stage of infection.

2.9 Treatment

Since titers can rise rapidly in early syphilis, a baseline quantitative nontreponemal test should be collected no more than a few days before treatment is initiated so that treatment response is determined accurately.

If there are neurologic, ocular, or otic manifestations of syphilis, a cerebrospinal fluid (CSF) analysis should be performed to determine if intravenous therapy is needed.

First-line and preferred alternative regimens are outlined below. See the [CDC 2015 STD Treatment Guidelines](#) for additional information.

PRIMARY, SECONDARY, and EARLY NON-PRIMARY NON-SECONDARY SYPHILIS

Recommended Regimen—Adults

Benzathine penicillin G, 2.4 million units intramuscularly in a single dose

Alternative Regimens—Adults with Penicillin Allergy

Pregnant women should be desensitized and treated with penicillin only

Doxycycline 100 mg orally twice daily for 14 days

OR

Skin testing for penicillin allergy and desensitization

Recommended Regimen—Infants and Children

Benzathine penicillin G, 50,000 units/kg intramuscularly, up to the adult dose of 2.4 million units in a single dose

SYPHILIS

UNKNOWN DURATION or LATE SYPHILIS

Recommended Regimen—Adults

Benzathine penicillin G 7.2 million units total intramuscularly as three doses of 2.4 million units each at one-week intervals

Alternative Regimens—Adults with Penicillin Allergy

Pregnant women should be desensitized and treated with penicillin only

Doxycycline 100 mg orally twice daily for 28 days

OR

Skin testing for penicillin allergy and desensitization

Recommended Regimen—Infants and Children

Benzathine penicillin G 50,000 units/kg intramuscularly as 3 doses up to the adult dose of 2.4 million units each at 1-week intervals (total 150,000 units/kg up to the adult total dose of 7.2 million units)

NEUROSYPHILIS

Recommended Regimen—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

Alternative Regimen—Neurosyphilis and Ocular Syphilis

Procaine penicillin G 2.4 million units intramuscularly once daily

PLUS

Probenecid 500 mg orally four times a day, both for 10-14 days

For patients with clinical manifestations of neurosyphilis, ocular syphilis, or otosyphilis in the unknown duration or late stage of syphilis, consider administering benzathine penicillin G intramuscularly once weekly for three weeks after completion of the intravenous regimen to provide an equivalent total duration of therapy.

SYPHILIS

CONGENITAL SYPHILIS – Pregnant Women

There is no recommended alternative to penicillin for the treatment of syphilis during pregnancy. Pregnant women with syphilis who report a penicillin allergy should be desensitized and treated with penicillin.

Treatment of syphilis during pregnancy should be with a penicillin regimen appropriate for the stage of syphilis. The Oregon Health Authority recommendations for treatment of syphilis in pregnancy are shown in Table 1. In early syphilis (primary, secondary, and early non-primary non-secondary stages), the recommendation is for two doses of penicillin administered one week apart, based on data showing that two doses may be more effective than a single dose at preventing congenital syphilis and other adverse fetal outcomes. As HIV infection is a risk factor for treatment failure, HIV-positive pregnant women with early syphilis should receive at least two doses, if not three. In late syphilis or syphilis of unknown duration, all women should receive three weekly doses of penicillin. Any missed dose warrants repeating therapy from the start.

Table 1. Treatment Recommendations for Pregnant Women with Syphilis

Stage	Treatment	Treatment for HIV-Positive Women
Primary	Benzathine penicillin G 2.4 million units intramuscularly (IM) x 2	Administer at least two doses of benzathine penicillin G 2.4 million units IM and strongly consider three doses
Secondary		
Early non-primary non-secondary		
Unknown duration or late syphilis	Benzathine penicillin G 2.4 million units intramuscularly (IM) weekly x 3	
Neurosyphilis/ocular syphilis/otosyphilis	Penicillin 4 million units intravenously every 4 hours for 10-14 days	

SYPHILIS

CONGENITAL SYPHILIS – Infants

Treatment of infants is based on CDC categories of congenital syphilis (CS) that differ from the case classification definitions (§3.9). An infant may meet the criteria for treatment as outlined in the CDC 2015 STD Treatment Guidelines, without meeting the surveillance case definition of congenital syphilis. Refer to the [CDC 2015 STD Treatment Guidelines](#) for more details.

Maternal treatment consistent with the CDC 2015 STD Treatment Guidelines, rather than the Oregon Health Authority recommendations (Table 1), should be considered appropriate when determining an infant's CS classification for treatment purposes (outlined below).

Proven or Highly Probable CS

An infant with:

- An abnormal physical examination consistent with congenital syphilis, **OR**
- A serum quantitative nontreponemal serologic titer that is fourfold higher than the mother's titer, **OR**
- A positive darkfield test or PCR of lesions or body fluid

Recommended Treatment

Aqueous crystalline penicillin G 100,000–150,000 units/kg/day administered as 50,000 units/kg/dose intravenously every 12 hours during 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

Possible CS

An infant with a normal physical examination and a serum quantitative nontreponemal serologic titer equal to or less than fourfold the maternal titer and one of the following:

- Mother was inadequately treated, not treated, or has no documentation of having received treatment, **OR**
- Mother was treated with a regimen other than benzathine penicillin G, **OR**
- Mother received recommended treatment <4 weeks before delivery

Recommended Treatment

Aqueous crystalline penicillin G 100,000–150,000 units/kg/day administered as 50,000 units/kg/dose intravenously every 12 hours during 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 intramuscularly in a single daily dose for 10 days **OR**

Benzathine penicillin G 50,000 units/kg/dose intramuscularly in a single dose

Less Likely CS

An infant with a normal physical examination and a serum quantitative nontreponemal serologic titer \leq fourfold the maternal titer and both of the following are true:

SYPHILIS

- Mother was treated during pregnancy, treatment was appropriate for the stage, and treatment was administered >4 weeks before delivery, **AND**
- Mother has no evidence of reinfection or relapse

Recommended Treatment

Benzathine penicillin G 50,000 units/kg/dose intramuscularly in a single dose

Unlikely CS

An infant with a normal physical examination and a serum quantitative nontreponemal serologic titer equal to or less than fourfold the maternal titer and both of the following are true:

- Mother's treatment was adequate before pregnancy, **AND**
- Mother's nontreponemal serologic titer remained low and stable before and during pregnancy and at delivery

Recommended Treatment

No treatment is required. Infants with reactive nontreponemal tests should be followed to ensure the test returns to negative. Benzathine penicillin G 50,000 units/kg/dose intramuscularly in a single dose may be considered, particularly if the infant had a reactive nontreponemal test and may be lost to follow-up.

2.10 Assessing for Other Sexually Transmitted Infections and Prevention

All patients diagnosed with syphilis should be offered testing for HIV, hepatitis C, gonorrhea, and chlamydia. All patients with syphilis should be offered pre-exposure prophylaxis (PrEP) for the prevention of HIV infection.

3. CASE DEFINITIONS, DIAGNOSIS, AND LABORATORY SERVICES

3.1 Primary Syphilis

1. Clinical Description
Stage characterized by one or more ulcers (chancres)
2. Laboratory Criteria
 - A. Confirmatory: Demonstration of *T. pallidum* by darkfield microscopy or polymerase chain reaction or equivalent direct molecular methods
 - B. Supportive
 - i. A reactive nontreponemal test (e.g., RPR, VDRL) **OR**
 - ii. A reactive treponemal test (e.g., TPPA, EIA, CIA)
3. Case Classification
 - A. Confirmed: A case that meets the clinical description of primary syphilis and the confirmatory laboratory criteria
 - B. Presumptive: A case that meets the clinical description of primary syphilis and the supportive laboratory criteria

3.2 Secondary Syphilis

1. Clinical Description
Stage caused by *T. pallidum* and characterized by localized or diffuse mucocutaneous rash often with generalized lymphadenopathy. Other signs may

SYPHILIS

include mucous patches, condyloma lata, and alopecia. The primary ulcer may still be present.

2. Laboratory Criteria
 - A. Confirmatory: Demonstration of *T. pallidum* by darkfield microscopy or polymerase chain reaction or equivalent direct molecular methods
 - B. Supportive
 - i. A reactive nontreponemal test (e.g., RPR, VDRL) **AND**
 - ii. A reactive treponemal test (e.g., TPPA, EIA, CIA)
3. Case Classification
 - A. Confirmed: A case that meets the clinical description of secondary syphilis and the confirmed laboratory criteria
 - B. Presumptive: A case that meets the clinical description of secondary syphilis and the supportive laboratory criteria

3.3 Early Non-Primary Non-Secondary Syphilis

1. Clinical Description

Stage caused by *T. pallidum* in which initial infection occurred within the previous 12 months and there are no signs or symptoms of primary or secondary syphilis
2. Laboratory Criteria

Supportive: A current nontreponemal test titer demonstrating fourfold or greater increase from the last nontreponemal test titer, unless there is evidence that the increase was not sustained for more than two weeks
3. Class Classification
 - A. Cannot be confirmed
 - B. Presumptive: A person with no clinical signs or symptoms of primary or secondary syphilis who has one of the following:
 - i. No prior history of syphilis **AND** a current reactive nontreponemal test (e.g., RPR, VDRL) **AND** a current reactive treponemal test (e.g., TPPA, EIA, CIA) **OR**
 - ii. 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 of the following criteria:
 - o Documented seroconversion or fourfold or greater increase in titer of a nontreponemal test during the previous 12 months, unless there is evidence that the increase was not sustained for more than two 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:
 - a. 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)
 - b. Only sexual contact was within the previous 12 months

3.4 Unknown Duration or Late Syphilis

1. Clinical Description

SYPHILIS

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

2. Laboratory Criteria

None

3. Case Classification

A. Cannot be confirmed

B. Presumptive: A person with no clinical signs or symptoms of primary or secondary syphilis who has one of the following:

- i. No prior history of syphilis AND a current reactive nontreponemal test (e.g., RPR, VDRL) AND a current reactive treponemal test (e.g., TPPA, EIA, CIA)
OR
- ii. 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 more than two weeks **OR**
- iii. Clinical signs or symptoms and laboratory results that meet the likely or verified criteria for neurologic, ocular, otic, or late clinical manifestations of syphilis

3.5 Neurologic Manifestations

Neurosyphilis can occur at any stage of syphilis. The case should be reported with the appropriate stage of infection and neurological manifestations, if present, should be noted in the case report.

1. 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

2. Classification of Neurologic Manifestations

A. Possible: A person with a reactive nontreponemal test AND a reactive treponemal test AND clinical symptoms or signs that are consistent with neurosyphilis without other known causes

B. Likely: A person with a reactive nontreponemal test AND a reactive treponemal test with both of the following:

- i. Clinical symptoms or signs that are consistent with neurosyphilis without other known causes of these abnormalities, **AND**
- ii. Elevated cerebrospinal fluid (CSF) protein (>50 mg/dl²) or white blood cell (WBC) count (>5 WBC/mm³) in the absence of other known causes of these abnormalities

C. Verified: A person with a reactive nontreponemal test and a reactive treponemal test with both of the following:

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

SYPHILIS

3.6 Ocular Manifestations

Ocular syphilis can occur at any stage of syphilis. The case should be reported with the appropriate stage of infection and ocular manifestations, if present, should be noted in the case report.

1. 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.

2. Classification of Ocular Manifestations

- A. Possible: A person with a reactive nontreponemal test and a reactive treponemal test and clinical symptoms or signs consistent with ocular syphilis without other known causes
- B. Likely: A person with a reactive nontreponemal test and a reactive treponemal test and both of the following:
 - i. Clinical symptoms or signs consistent with ocular syphilis without other known causes, **AND**
 - ii. Findings on exam by an ophthalmologist that are consistent with ocular syphilis in the absence of other known causes
- C. Verified: A person with a reactive nontreponemal test and a reactive treponemal test and both of the following:
 - i. Clinical symptoms or signs consistent with ocular syphilis without other known causes, **AND**
 - ii. Demonstration of *T. pallidum* in aqueous or vitreous fluid by darkfield microscopy, or by polymerase chain reaction or other equivalent direct molecular methods

3.7 Otic Manifestations

Otosyphilis can occur at any stage of syphilis. The case should be reported with the appropriate stage of infection and otic manifestations, if present, should be noted in the case report.

1. Clinical Description

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

2. Classification of Otic Manifestations

- A. Possible: A person with a reactive nontreponemal test and a reactive treponemal test and clinical symptoms or signs consistent with otosyphilis without other known causes
- B. Likely: A person with a reactive nontreponemal test and a reactive treponemal test and both of the following:
 - i. Clinical symptoms or signs consistent with otosyphilis without other known causes, **AND**
 - ii. Findings on exam by an otolaryngologist that are consistent with otosyphilis in the absence of other known causes
- C. Verified: A person with a reactive nontreponemal test and a reactive treponemal test and both of the following:
 - i. Clinical symptoms or signs consistent with otosyphilis without other known causes, **AND**

SYPHILIS

- ii. Demonstration of *T. pallidum* in inner ear fluid by darkfield microscopy, or by polymerase chain reaction or other equivalent direct molecular methods

3.8 Late Clinical Manifestations

Late clinical manifestations of syphilis (tertiary syphilis) usually develop only after a period of 15-30 years of untreated infection. The case should be reported with the appropriate stage of infection (unknown duration or late syphilis in most cases) and late clinical manifestations, if present, should be noted in the case report.

1. Clinical Description

Late clinical manifestations of 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 and organs may be involved. Certain neurologic manifestations (e.g., general paresis and tabes dorsalis) are also late clinical manifestations of syphilis.

2. Classification of Late Clinical Manifestations of Syphilis

A. Likely: A person with a reactive nontreponemal test and a reactive treponemal test with either of the following:

- i. 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, **OR**
- ii. 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

B. Verified: A person with a reactive nontreponemal test and a reactive treponemal test and either of the following:

- i. 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, in combination with either demonstration of *T. pallidum* in late lesions by special stains or equivalent methods, or by polymerase chain reaction or equivalent direct molecular methods, or demonstration of pathologic changes that are consistent with *T. pallidum* infection on histologic examination of late lesions, **OR**
- ii. 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

3.9 Congenital Syphilis

1. Clinical Description

A condition caused by infection in utero with *T. pallidum*. A wide spectrum of severity exists, from inapparent infection to severe cases that are clinically apparent at birth. An infant or child <2 years old may have signs such as hepatosplenomegaly, rash, condyloma lata, snuffles, jaundice, pseudoparalysis, anemia, or edema.

For CDC reporting purposes, congenital syphilis includes cases of congenitally acquired syphilis among infants and children as well as syphilitic stillbirths. A syphilitic stillbirth is defined as a fetal death that occurs after 20 weeks of pregnancy or in which the fetus weighs greater than 500 g and the mother had untreated or inadequately treated syphilis at delivery.

2. Laboratory Criteria

SYPHILIS

- A. Demonstration of *T. pallidum* by darkfield microscopy of lesions, body fluids, or neonatal nasal discharge, **OR**
 - B. Polymerase chain reaction or other equivalent direct molecular methods of lesions, neonatal nasal discharge, placenta, umbilical cord, or autopsy material, **OR**
 - C. Immunohistochemistry or special stains of specimens from lesions, placenta, umbilical cord, or autopsy material
3. Case Classification
- A. Confirmed: A case that is laboratory confirmed by methods listed above
 - B. Presumptive:
 - i. A condition affecting an infant whose mother did not receive adequate treatment, defined as completion of stage-appropriate treatment initiated 30 or more days before delivery, regardless of signs in the infant, **OR**
 - ii. An infant or child who has a reactive nontreponemal test (e.g., RPR, VDRL) **AND** any one of the following:
 - o Evidence of congenital syphilis on physical exam
 - o Evidence of congenital syphilis on radiographs of long bones
 - o Reactive cerebrospinal fluid (CSF) VDRL test
 - o Elevated CSF white blood cell (WBC) count or protein (suggested abnormal values):
 - a. During the first 30 days of life, a CSF WBC count of >15 WBC/mm³ or a CSF protein >120 mg/dl
 - b. 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

At present, an infant titer that is fourfold higher than the maternal titer is not a condition included in the case definition. However, this finding might impact treatment decisions for the infant (§2.9).

4. ROUTINE CASE INVESTIGATION

4.1 Provider Interview

Contact the health care provider to verify treatment and complete missing, unclear, or erroneous elements of the initial case report. Inform the provider that a public health professional will contact the case-patient (hereafter referred to as “case” or “client”) directly for an interview. The provider interview can be conducted by phone or the provider can be sent a query letter to return by fax to the LPHA.

4.2 Case Reporting

1. When a lab and/or provider report of syphilis is received, the LPHA will follow the steps outlined in Table 2 for the applicable scenario.
As a reminder, new labs should not be added to reactor cases.

SYPHILIS

Table 2. Orpheus Documentation Scenarios Based on Syphilis History

Scenario	Investigate Syphilis History	Orpheus Documentation
No Orpheus Syphilis Case Record within Your Jurisdiction	N/A	Proceed with Orpheus documentation for new case.
Existing Orpheus Syphilis Case Record	Determine if new report indicates current infection or is related to previous infection (see §3)	<p>If report indicates current infection, proceed with Orpheus documentation for new case.</p> <p>If report is related to previous infection, add lab to most recent syphilis case record.</p>
Case May Have Syphilis History in a Different Jurisdiction	<p>Click “View Syphilis Case History” in Orpheus person record to view patient’s statewide syphilis records. (If no cases appear, there is no documented syphilis history in Oregon.)</p> <p>Determine if new lab report indicates current infection or is related to previous infection (see §3)</p>	<p>If report indicates current infection, proceed with Orpheus documentation for new case.</p> <p>If report is related to previous infection, add lab to most recent syphilis case record.</p>
Case Reports Prior Syphilis Diagnosis/ Treatment Outside Oregon	<p>Determine state(s) in which patient was diagnosed/ treated. Additional information (city/jurisdiction, provider, approximate dates of service) may be helpful. Contact OHA STD Program via phone or Orpheus note to request out-of-state records.</p> <p>Please do not contact another state health department directly unless an intercounty or interstate agreement is in place.</p>	STD Program will add out-of-state records to Orpheus case record and notify Oregon county with jurisdiction.

2. Case Interview

An interview should be attempted for all confirmed or presumptive cases of early syphilis (primary, secondary, early non-primary non-secondary stages). In-person interviews are the preferred methodology; however, telephone and other methods are also acceptable. If the client cannot be reached by traditional methods (e.g., phone, mailed letters, field or clinic-based visit), consider using technology-based tools. Use of texting, internet, and mobile apps to contact

SYPHILIS

patients should first be approved by LPHA management. Client privacy must be assured and maintained throughout the case investigation and interview.

All attempts to contact the client should be documented in Orpheus in real time when possible, or on the day of the attempt at minimum.

Consult with the LPHA administrator and/or STD program manager regarding investigation of cases involving individuals younger than 13 years old.

3. Orpheus Documentation

Enter information collected from the client into the appropriate areas of the Orpheus case report interface. This includes the basic case information column (client name/case number, disease type, staging/status information, client demographics [including pregnancy status, if applicable], ordering provider, local epi, and reason for exam), in addition to tabs labeled "Risks," "Clinical," and "Contacts."

If the client provides personal (non-clinical) information such as demographic or sexual exposure history that contradicts information collected from the provider report/interview, overwrite the provider response with the client response and make a note of the change in the "Notes" tab of the Orpheus case report.

▪ Contacts Tab:

Record information about contacts directly into the "Contacts" tab and related sub-tabs of the case entry interface. Use the "+ Contact" button on the "Contacts" tab of the Orpheus case report to add each new contact. This list should include all named contacts within the appropriate interview period, including those from whom the client might have acquired infection and others whom the client might have exposed. If you have decided to collect information about associates and sex partners named by others, record their information here too. Record the type of contact (see Appendix B) in the field labeled "Referral basis." Record the date and final disposition (see Appendix B) of your efforts in the "Contacts" tab of the case entry form. If there are multiple contacts, be sure that the name of the partner for whom you wish to enter information has been selected in the "Contacts" tab before entering data in any of the sub-tabs.

i. "Demographics" and "Notes" sub-tabs:

Enter partner information in the "Demographics" sub-tab of the "Contacts" tab. The "Notes" text box is embedded within the "Demographics" sub-tab.

Record the date and outcome of each attempt to interview each partner and record this information in the "Notes" sub-tab of the "Contacts" tab of the Orpheus case entry interface, along with any other useful information.

ii. "Exposure" sub-tab:

Record the date of the first sexual encounter between this partner and the client and the date of the most recent encounter in the "Exposure" sub-tab of the "Contacts" tab. Record the outcome of efforts to contact the partner in the exposure sub-tab.

iii. "Labs/Treatment" sub-tab:

Record the dates and results of any laboratory tests conducted and the dates and details of any presumptive treatment or treatment of laboratory-confirmed infection in the "Labs/Treatment" sub-tab.

SYPHILIS

4.3 Managing Sexual Partners

1. Partner Notification

All sex partners of the case within the appropriate interview period for the stage of syphilis (Table 2) should be examined, tested, and treated. To avert severe health outcomes such as congenital syphilis, prioritize male partners of female cases and female partners of male cases. Partners exposed within three weeks of the case interview should be treated preventively as serologic tests will not reliably be reactive in this time frame. Other partners should be treated preventively if they are likely to be difficult to contact or unlikely to return for results and treatment. If a patient has not had sex within the interview period, the most recent partner should be examined, tested, and treated, if indicated. Long-term sex partners of cases with late syphilis should be offered testing.

Table 3. Interview Period by Stage

Stage	Interview Period
Primary	90 days before date of onset of primary lesion through date of treatment
Secondary	6.5 months before date of onset of secondary symptoms through date of treatment
Early Non-Primary Non-Secondary	1 year before start of treatment

If the client prefers to notify and refer the partner, the LPHA should verify that the partner has been examined or treated. If the partner's treatment cannot be verified within a reasonable time frame (2–5 days), the LPHA should attempt to notify and refer the partner for examination and treatment.

If the LPHA is handling notification, named partners should be contacted within two working days of the initial case interview by phone, field visit, or other method, and referred to the LPHA or another health care provider for evaluation, testing, and treatment. Generally, LPHA staff should try to contact the partner three times before determining that the partner cannot be located. Attempts should be made to contact the partner on alternate days and times of day. When possible, alternate contact methods should also be tried. For example, if calls and texts have not been successful, a field visit should be considered. For information about technology-based STD/HIV partner services, consult the CDC report [Introducing Technology into Partner Services: A Toolkit for Programs](#).

2. Orpheus Documentation

When a partner is reached, all personal information reported by the provider should be confirmed and any outstanding information (indicated by the "Contacts" tab of the Orpheus case entry form) should be collected. The date and outcome of every attempt to interview each partner should be documented. The dates and results of any laboratory tests and the dates and details of any treatment should also be documented. When partner notification and treatment have been completed, the date and outcome (disposition) of the efforts should be documented and any additional pertinent information should also be recorded. Contact type codes and disposition codes are presented in Appendix B.

SYPHILIS

4.4 Out-of-Jurisdiction Cases/Contacts

Jurisdiction for a case belongs to the LPHA for a patient's county of residence. If the LPHA that received the initial report discovers that the case resides in a different county, the LPHA may transfer the case to the LPHA with jurisdiction via Orpheus by updating the home address in the case record and marking it for transfer when prompted by Orpheus.

If the patient identifies a partner who lives outside of the local health jurisdiction, the contact may be transferred to the appropriate jurisdiction via Orpheus by entering the contact's address and marking it for transfer when prompted by Orpheus. For partners residing out of state, LPHA staff should provide the state STD Program (971.673.0153) with the relevant information for necessary follow-up.

5. CONTROLLING FURTHER SPREAD

5.1 Education

Patients with early syphilis (primary, secondary or early non-primary non-secondary) should be advised to complete all recommended treatment, avoid sex until treatment has been completed and any sores or rashes have resolved, avoid sex with untreated sex partners until they too have been treated and their sores or rashes have resolved, and use condoms to reduce the risk of acquiring sexually transmitted infections in the future.

All patients with syphilis should be offered pre-exposure prophylaxis (PrEP) for the prevention of HIV infection.

5.2 Case Follow-up

Every individual with a reported case of syphilis should be advised to seek medical attention for persistent symptoms and to have a repeat nontreponemal test (typically RPR) at 6- and 12-months post-treatment and again at 24 months if treated for unknown duration or late syphilis. Follow-up testing at more frequent intervals may be appropriate if the case is at high risk of re-infection. See §6.1 & §6.2 for recommended follow-up testing intervals for pregnant women and individuals with HIV.

Re-treatment should be initiated if a case exhibits persistent or recurrent signs or symptoms or sustains a fourfold increase in nontreponemal test titer compared with titer at the time of treatment. Such cases should also undergo a cerebrospinal fluid evaluation and be evaluated for HIV infection.

Failure of nontreponemal test titers to decline fourfold within 6–12 months after therapy may be indicative of treatment failure, though some people with successful treatment will not exhibit the two-dilution decline in titer. If titers do not decline, patients should receive additional clinical and serologic follow-up, and consideration should be given to cerebrospinal fluid examination and re-treatment.

6. MANAGING SPECIAL SITUATIONS

6.1 Missed Treatment Doses

Treatment of unknown duration or late syphilis requires three doses of benzathine penicillin at one-week intervals. If the patient does not return for the next dose within seven days, the need to restart the treatment regimen will depend on the number of

SYPHILIS

days that elapse between injections. An interval of 10-14 days between doses of benzathine penicillin G may be acceptable, though 7-9 days is more optimal.

6.2 Co-infection with HIV

All persons with syphilis should be tested for HIV and other STDs, including gonorrhea and chlamydia.

Though uncommon, unusual serologic responses have been observed among HIV-positive persons with syphilis. These include higher-than-expected serologic titers, false negative serologic tests, and delayed appearance of antibodies.

Compared with HIV-negative individuals with syphilis, HIV-positive individuals with syphilis are at increased risk for neurologic complications. Ocular syphilis is reported frequently among individuals with HIV. Cerebrospinal fluid examination is not necessary in individuals with HIV and syphilis unless neurologic symptoms are present.

HIV-positive individuals with syphilis should be treated with the same regimens recommended for HIV-negative individuals. Treatment failure in HIV-positive individuals with syphilis should be managed in the same manner as treatment failure in HIV-negative individuals.

More frequent follow-up is recommended for HIV-positive individuals with syphilis. Titers should be collected at 3, 6, 9, 12 and 24 months after syphilis treatment.

6.3 Congenital Syphilis

1. Management of Syphilis in Pregnancy

Women should be linked to prenatal care as early in pregnancy as possible to ensure prompt and appropriate syphilis and treatment.

Syphilis testing is strongly recommended for all pregnant women at the following intervals: the first prenatal visit, the beginning of the third trimester (28–32 weeks), and at delivery. Since a nontreponemal test (RPR) may take up to 12 weeks to become reactive after exposure, strongly consider also screening women at the post-partum visit.

Pregnant women with a reactive RPR test should have confirmatory testing with a treponemal test. Treatment should not be delayed while awaiting the treponemal result if there is any concern that the patient will not return for treatment. Women with a reactive treponemal test and non-reactive RPR should be considered currently infected unless there is documentation of adequate treatment with a subsequent decline in nontreponemal serologic titers.

After completion of treatment, pregnant women should have monthly follow-up of RPR titers to evaluate the effectiveness of treatment. Most women will deliver before their serologic response to treatment can be assessed definitively. Thus, neonatal evaluation for congenital syphilis is crucial to ensuring timely appropriate therapy for baby.

2. Orpheus Documentation

During pregnancy collect and report the following:

- Stage of infection
- Syphilis treatment given during pregnancy
- Results of the first prenatal and third trimester screenings and any prior RPR tests, including negative results
- Ultrasound findings if syphilis was diagnosed after 20 weeks

SYPHILIS

- Expected due date, obstetric history, and trimester of first prenatal visit and of syphilis treatment
- HIV status

At *delivery* collect and report the following:

- Maternal RPR and infant RPR results at delivery
- Additional infant testing as indicated (§3.9)
- Maternal treatment and infant treatment, if applicable
- Hospital records

Additionally, add the infant as a contact to the mother to link the case records. Any documents regarding the maternal or infant cases should be uploaded to the appropriate Orpheus record. The CDC congenital syphilis report form should be uploaded to the infant's case record once completed.

6.4 Jarisch-Herxheimer Reaction

The Jarisch-Herxheimer reaction is an acute febrile reaction often accompanied by headache, myalgia, and other symptoms that usually occurs within the first 24 hours after initiation of treatment. It occurs most frequently among patients with early syphilis, presumably because bacterial burdens are higher during these stages. Non-steroidal anti-inflammatories or antipyretics can be taken to manage symptoms.

In pregnant women, the Jarisch-Herxheimer reaction might precipitate premature labor or fetal distress, but treatment should not be delayed or avoided. Women should seek obstetric care if they note fever, contractions, or decreased fetal movement.

6.5 Outbreak Situations

Contact the STD Program to discuss possible actions if a higher than usual number of early syphilis cases (primary, secondary, and early non-primary non-secondary stages) occur and are clustered in time and place.

7. APPLICABLE RULES

7.1 Reporting

OAR 333-018-0000 through 333-018-0020

7.2 Investigation

OAR 333-019-0000 and 333-019-0002

8. REFERENCES

1. Alexander JM, Sheffield JS, Sanchez PJ, Mayfield J, Wendel GD. Efficacy of treatment for syphilis in pregnancy. *Obstet Gynecol.* 1999;93(1):5–8.
2. Andrade R, Rodriguez-Barradas MC, Yasukawa K, Villarreal E, Ross M, Serpa JA. Single dose versus three doses of intramuscular benzathine penicillin for early syphilis in HIV: a randomized clinical trial. *Clin Infect Dis.* 2017;64(6):759–764.
3. Centers for Disease Control and Prevention. 2015 STD Treatment Guidelines. Available at www.cdc.gov/std/tg2015/default.htm.
4. Centers for Disease Control and Prevention. Syphilis (*Treponema pallidum*) 2018 Case Definition. Available at <https://www.cdc.gov/nndss/conditions/syphilis/case-definition/2018/>.

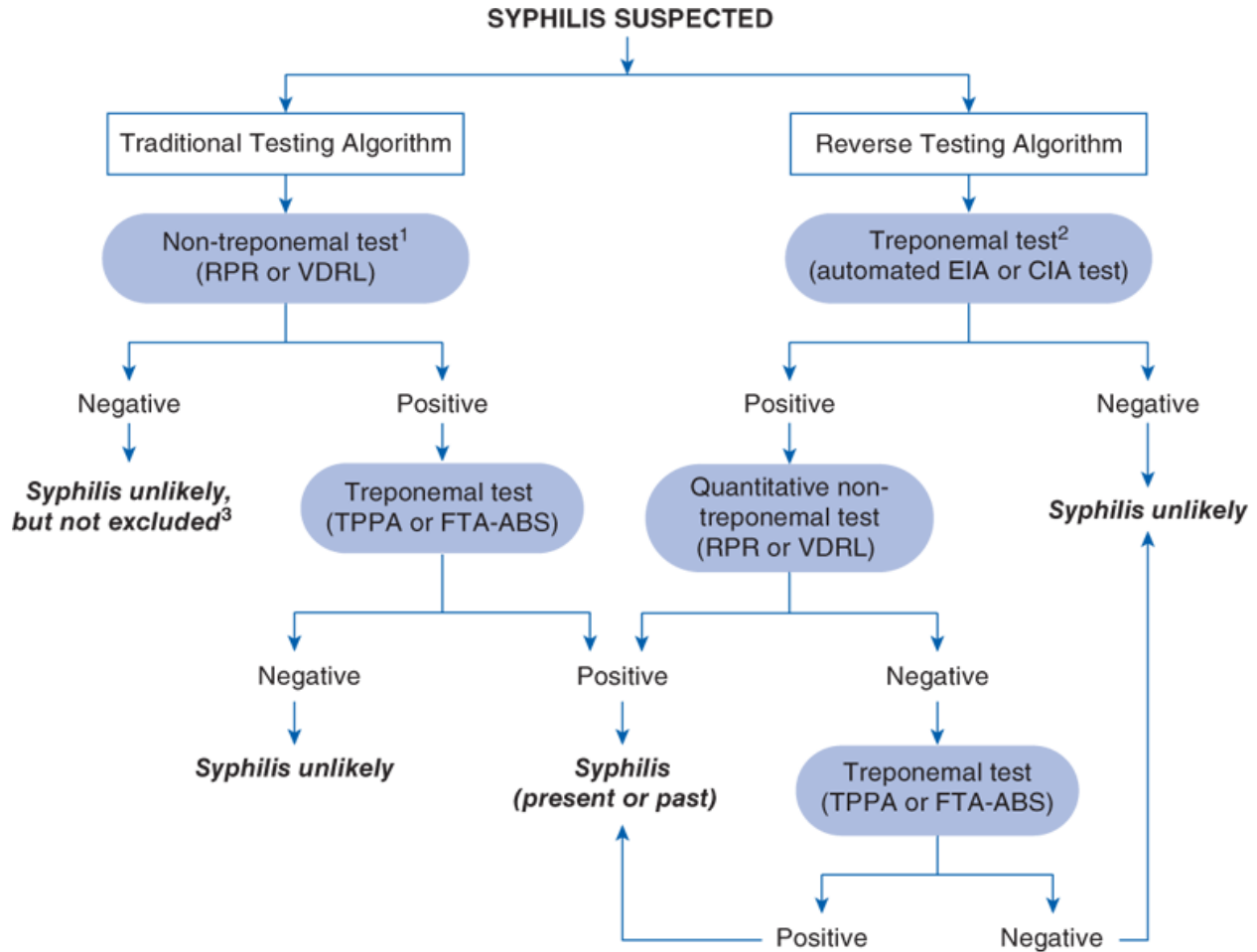
SYPHILIS

5. Donders GG, Desmyter J, Hooft P, Dewet GH. Apparent failure of one injection of benzathine penicillin G for syphilis during pregnancy in human immunodeficiency virus-seronegative African women. *Sex Transm Dis.* 1997;24(2):94–101.
6. Ganesan A, Mesner O, Okulicz JF, et al. A single dose of benzathine penicillin G is as effective as multiple doses of benzathine penicillin G for the treatment of HIV-infected persons with early syphilis. *Clin Infect Dis.* 2015;60(4):653–660.
7. Yang CJ, Lee NY, Chen TC, et al. One dose versus three weekly doses of benzathine penicillin G for patients co-infected with HIV and early syphilis: a multicenter, prospective observational study. *PLoS One.* 2014;9(10):e109667. Published 2014 Oct 6. doi:10.1371/journal.pone.0109667.

SYPHILIS

APPENDIX A

Syphilis Screening Algorithms



¹Non-treponemal tests measure levels of IgG and IgM antibodies produced by the host in response to lipids (mostly cardiolipin) released from damaged host cells associated with *T pallidum* infection.

²Treponemal tests detect either IgG or IgM antibodies produced by the host in response to specific *T pallidum* antigens; the tests use either whole cells or antigens derived from cells of *T pallidum*.

³RPR- or VDRL-based screening may miss some cases of early untreated, previously treated, and late latent syphilis. If clinically indicated, a treponemal test should be performed.

Source: Nicoll D, Lu CM, McPhee SJ. Guide to Diagnostic Tests, Seventh Edition.
www.accessmedicine.com Copyright ©McGraw-Hill Education. All rights reserved.

APPENDIX B
Contact Type and Disposition Codes

Table B1. Contact Type Codes

CONTACT TYPE	DISPOSITION CODE	USE
PARTNERS	P-1	Sex partner
	P-2	Needle partner
	P-3	Sex and needle partner
SOCIAL CONTACTS	S-1	Named by this case patient; has symptoms suggestive of disease
	S-2	Named by this case patient; is a sex partner of <i>another</i> person who is known to be infected
	S-3	Named by this case patient; needs exam; not S-2 or S-3
ASSOCIATES	A-1	Named by someone who is not infected; has symptoms suggestive of disease
	A-2	Named by someone who is not infected; is a sex partner of someone who is infected
	A-3	Named by someone who is not infected; could benefit from exam; not A-2 or A3

SYPHILIS

APPENDIX B (Continued)

Contact Type and Disposition Codes

Table B4. Disposition Codes for Partners and Associates

DISPOSITION CODE	USE
A - Preventive Therapy	Sex partner or associate of case, treated, no treponemal or nontreponemal test available
B - Refused Preventive Therapy	Sex partner or associate of case, refused treatment, no treponemal or nontreponemal test available
C - Infected, Brought to Treatment	Sex partner or associate meets probable or confirmed case definition (any stage), treated
D - Infected, Not Treated	Sex partner or associate meets probable or confirmed case definition (any stage), not treated (e.g. refused, lost to follow-up)
E - Previously Treated for this Infection	Sex partner or associate meets probable or confirmed case definition (any stage), treated by another healthcare provider prior to interview
F - Not Infected	Serologic tests results available for sex partner or associate and not consistent with probable or confirmed case definition (any stage)
G - Insufficient Information to Begin Investigation	Named suspect or associate without sufficient available information (such as telephone, address, or email) to attempt to contact
H - Unable to locate	Attempted but unable to locate sex partner or associate
J - Located, Refused Examination	Successfully located sex partner or associate, but refused testing or treatment
K - Out of Jurisdiction	Sex partner or associate resides in another state, country or county.
L - Other	Outcome of attempt to locate other than listed elsewhere in table.
M - Reverse Contact Link	Sex partner or associate also meets probable or confirmed case definition (any stage) and is likely source to current case. In this circumstance laboratory and treatment outcome is stored with the sex partner or associate's case information. This code is used to avoid "double counting" partners who are "reciprocally listed" on cases for which they were the source.