Syphilis
Investigative Guidelines
September 2026

1. DISEASE REPORTING

1.1 Purpose of Reporting and Surveillance

1. Identify cases of syphilis and prevent transmission
2. Ensure adequate treatment and follow-up for individuals with syphilis
3. Ensure appropriate management, including screening and presumptive treatment, of sexual contacts
4. Describe the epidemiology of syphilis in Oregon

1.2 Laboratory and Physician Reporting Requirements

1. Licensed laboratories must report all positive test results indicating syphilis infection to the Local Public Health Authority (LPHA) within one working day (OAR 333-018-0000; 333-018-0015)[1]
2. Clinicians must report lab-confirmed and clinically suspect cases of syphilis to the LPHA within one working day (OAR 333-018-0000; 333-018-0015)[1]
3. Health care providers, health care facilities, and licensed laboratories shall cooperate with public health authorities in the investigation and control of syphilis infections (OAR 333-019-0002)[2]

1.3 Local Public Health Authority Reporting and Follow-up Responsibilities

1. LPHA must begin follow-up case investigation within two working days of receiving the initial provider or laboratory report.
2. LPHA must report all cases to the OHA STD Program through the Oregon Public Health Epidemiology User System (Orpheus) by the end of the calendar week of initial provider or lab report (OAR 333-018-0020)[1]
3. LPHA must conduct case investigations and manage sexual contacts by following procedures outlined in these Investigative Guidelines (OAR 333-019-0000, ORS 433.006)[2,3]

2. DISEASE AND EPIDEMIOLOGY

2.1 Etiologic Agent

The etiologic agent in syphilis is *Treponema pallidum* subspecies *pallidum*, a spirochete (corkscrew-shaped) bacterium.

Of all the subspecies of *T. pallidum*, only *T. pallidum* subsp. *pallidum* is transmitted routinely by sexual contact. The other *T. pallidum* subspecies are transmitted non-sexually (e.g., yaws, pinta).

2.2 Description of Illness

Syphilis is called “the great imitator” because many of the signs and symptoms mimic those of other diseases. If untreated, syphilis infection progresses through stages that are often separated by periods without any symptoms (latency). Neurosyphilis, ocular syphilis, and otosyphilis can occur at any stage of infection. See **Figure 1** for a graphical summary of the natural history of syphilis.

During the incubation period, before clinical signs or symptoms appear, *T. pallidum* can spread to the circulatory, lymphatic, and central nervous systems.

Early Syphilis: clinical manifestations mainly involve the skin and mucosal surfaces, although secondary syphilis often has systemic manifestations.

- **Primary syphilis**
  - A chancre is the defining feature of primary syphilis. A chancre is a small round or oval ulcerated lesion with a smooth base and firm raised borders that appears where *T. pallidum* entered the body:
    - Most commonly appear on the penis, labia, perianal area, or mouth
    - May go unnoticed, especially if located inside the vagina, foreskin, or rectum
    - Resolve spontaneously within a few weeks, even without treatment
  - Classic primary syphilis is defined by a single chancre BUT multiple chancres are common and can be painful (multiple chancres on genitals are often misdiagnosed as herpes simplex virus [HSV] infection)
  - Syphilitic balanitis of Follmann (SBF, or Follmann balanitis) is a rare manifestation of primary syphilis thought to be present in less than 0.5% of cases of primary syphilis. SBF typically involves balanitis (inflammation of the glans penis) or balanoposthitis (inflammation of the glans penis and foreskin) with inguinal lymphadenopathy and may present with or without chancres
- **Secondary syphilis**
  - Skin and mucous membrane lesions are the defining feature of secondary syphilis. A lesion is an area of abnormal tissue anywhere in or on the body. While chancres are the only type of lesion associated with primary syphilis, different lesions are found in secondary syphilis:
    - Rashes can appear anywhere on the body, vary widely in appearance, and do not usually cause itching. The classic secondary rash appears on the palms of hands and soles of feet and often the torso
    - Other secondary lesions may include:

        - Mucous patches in the mouth or genital area
        - Condyloma lata, usually in the genital or rectal area
        - Alopecia
    - Symptoms generally appear about 4 to 10 weeks after the onset of the primary chancre (chancres may still be present when secondary symptoms develop)
    - Widespread dissemination of *T. pallidum* throughout the body via the bloodstream causes fever, headaches, muscle aches, malaise, and lymphadenopathy
    - Even without treatment, lesions and symptoms typically resolve spontaneously within a few weeks, but can persist for months
    - If untreated, secondary symptoms can reappear after a latency period

Latent Syphilis: characterized by the persistence of *T. pallidum* in the body without clinical signs or symptoms.

- **Early non-primary non-secondary (early latent) stage**:
    - Occurs when an individual is asymptomatic and there is evidence that the infection was acquired in the 12 months prior to diagnosis
    - Can occur between the primary and secondary stages, after the secondary stage, or between secondary relapses
- **Late or unknown duration (late latent) stage**:
    - Occurs when an individual is asymptomatic and the infection was acquired more than 12 months prior to diagnosis **OR** the time of infection cannot be determined with certainty

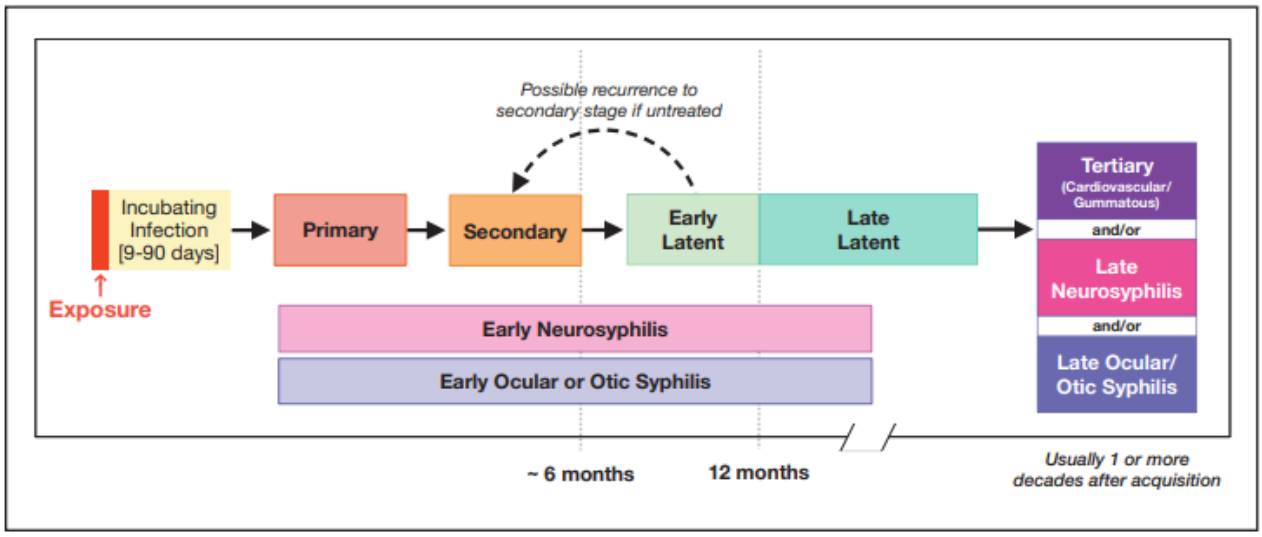
Neurosyphilis, Ocular Syphilis, and Otic Syphilis: clinical manifestations that can occur during any stage.

- **Neurosyphilis** can manifest as meningitis or stroke, cognitive dysfunction, motor or sensory deficits, and/or cranial nerve palsies
- **Ocular syphilis** can involve any eye structure but usually manifests as panuveitis or posterior uveitis
    - May cause permanent vision loss
    - Occurs with or without neurosyphilis
- **Otosyphilis** can manifest as hearing loss, tinnitus, and/or vertigo
    - May cause permanent hearing loss
    - Occurs with or without neurosyphilis

Late Clinical Manifestations (Tertiary Syphilis)

- Usually only develop after 15–30 years of untreated infection
- Can affect virtually any organ system including the cardiovascular system, central nervous system, and skin.

Figure 1. The Natural History of Untreated Syphilis



Source: New York City Department of Health and Mental Hygiene, and the New York City STD Prevention Training Center. The Diagnosis and Management of Syphilis: An Update and Review. March 2019. Available at www.nycptc.org

2.3 Reservoirs

Humans are the only reservoir for *T. pallidum*.

2.4 Modes of Transmission

Sexual transmission:

- *T. pallidum* enters the body via skin and mucous membranes through abrasions during sexual contact
- Persons are infectious throughout the primary and secondary stages, when lesions are present
- Usually results from contact with genital mucous membranes, but it can also occur from contact with the mouth, rectum, and cutaneous lesions

Vertical transmission:

- Results in fetal infection
- Occurs primarily via transplacental passage of *T. pallidum*
- Can occur during any stage of syphilis
- Can also occur if a newborn has contact with genital syphilis lesions at the time of delivery

Other forms of syphilis transmission are rare. Transfusion-associated syphilis has been virtually eliminated in the United States and transmission through needle-sharing is infrequent.

2.5 Incubation Period

The earliest sign of syphilis, a primary chancre, usually appears about 2 to 3 weeks after *T. pallidum* infection. Blood tests usually detect infection within 21 days of exposure but may take up to 6 weeks to show seroconversion.

2.6 Period of Communicability

Syphilis is spread by sexual contact—it is not spread through casual contact such as shaking hands. A person acquires syphilis when their mucous membranes (vulva, vagina, penis, anus, mouth) come into contact with bacteria-rich lesions (chancres, rash, condyloma lata, or mucous patches). These bacteria-rich lesions occur in primary and secondary syphilis and may not be visible.

2.7 Treatment

See the CDC 2021 STI Treatment Guidelines for detailed treatment information.[4] Refer to **Table 1** for treatment recommendations for syphilis in non-pregnant adults. Refer to **Table 2** for treatment recommendations for neurosyphilis, ocular syphilis, and otosyphilis. Refer to the Syphilis in Pregnancy and Congenital Syphilis Investigative Guidelines for treatment recommendations for pregnant people and infants/children.

Table 1. Treatment Recommendations for Syphilis in Non-Pregnant Adults

Stages	Recommended Regimen	Alternative Regimen if True Penicillin Allergy*
Primary, Secondary, and Early Non-Primary Non-Secondary	Benzathine penicillin G (Bicillin L-A or equivalent products like Lentocilin and Extencilline†) 2.4 million units IM in a single dose	Doxycycline 100 mg orally twice daily for 14 days **OR** Skin testing for penicillin allergy and desensitization
Unknown Duration or Late	Benzathine penicillin G (Bicillin L-A or equivalent imported products like Lentocilin and Extencilline) 7.2 million units total IM as three doses of 2.4 million units each at 7-day intervals	Doxycycline 100 mg orally twice daily for 28 days **OR** Skin testing for penicillin allergy and desensitization

* Approximately 10% of all U.S. patients report having a penicillin allergy. However, less than 1% of the population is truly allergic to penicillin. Refer to the CDC 2021 STI Treatment Guidelines section on managing persons who have a history of penicillin allergy.

† During recent Bicillin L-A shortages, the U.S. Food and Drug Administration has allowed the temporary importation of benzathine penicillin G products such as Lentocilin and Extencilline. These are therapeutically equivalent to Bicillin L-A (i.e., dosing, treatment regimens, and follow-up monitoring are the same) though injection preparation/administration and allergy considerations may differ.

- For unknown duration or late syphilis, the optimal interval between benzathine penicillin G doses is 7 days; an interval of 6-9 days is acceptable. Per the CDC STI Treatment Guidelines, clinical experience indicates that an interval of 10–14 days between doses might be acceptable before restarting the sequence of injections.

- **For pregnant patients with unknown duration or late syphilis, the Bicillin L-A dosing interval is critical. A 7-day interval is ideal and a 6-9 day interval is acceptable. If any doses are given outside this interval, the treatment series must be restarted. Refer to the Syphilis in Pregnancy Investigative Guidelines for further guidance on treatment in pregnancy.**

Table 2. Treatment Recommendations for Clinical Manifestations of Syphilis

Clinical Manifestations	Recommended Regimen
Neurosyphilis, Ocular Syphilis, or Otosyphilis	Aqueous crystalline penicillin G 18-24 million units per day, administered as 3-4 million units intravenously every 4 hours or continuous infusion, for 10-14 days

- Ceftriaxone 1–2 g daily either IM or IV for 10–14 days is an alternative regimen for non-pregnant patients. Ceftriaxone is not a CDC-recommended first-line therapy but may be appropriate for patients who:
  - Are not comfortable with an infusion pump **OR**
  - Cannot administer treatment at home due to unstable/unsafe housing

3. CASE DEFINITIONS, DIAGNOSIS, AND LABORATORY SERVICES

3.1 Syphilis Stages

See the CDC Syphilis 2026 Case Definition page for more information on the stages below.[5]

Given the complexity of the syphilis surveillance case definition, public health professionals are strongly encouraged to use the CDC surveillance flowcharts for syphilis stages and clinical manifestations (see Appendix A) instead of or alongside this section to determine the appropriate surveillance stage. The information in this section and the flowcharts is identical, but the flowcharts are much easier to follow.

3.1.1 Primary Syphilis

1. Clinical Description
   - In the absence of a more likely alternative diagnosis, meets at least one of the following signs:
     - One or more ulcerative lesions (chancres) **OR**
     - Syphilitic balanitis of Follmann—a rare sign of primary syphilis involving inflammation of the glans penis (balanitis), foreskin (posthitis), or both (balanoposthitis)
2. Laboratory Criteria
   - Confirmatory: Meets at least one of the following criteria:

    - Direct detection of *T. pallidum* by darkfield microscopy in a specimen that was both not obtained from the throat and not potentially contaminated by stool **OR**
    - Direct detection of *T. pallidum* by immunohistochemistry (IHC) staining in a specimen that was both not obtained from the throat and not potentially contaminated by stool **OR**
    - Direct detection of *T. pallidum* by nucleic acid amplification test (NAAT) or a diagnostically equivalent molecular method in any specimen
  - Presumptive: Meets at least one of the following criteria:
    - A current (performed in the context of this clinical evaluation) reactive blood-based nontreponemal antibody test **OR**
    - A current (performed in the context of this clinical evaluation) reactive blood-based treponemal antibody test
3. Case Classification
  - **Confirmed (rare):** Clinically compatible case with evidence of *T. pallidum* by a confirmatory direct detection method
  - **Presumptive:** Clinically compatible case with at least one reactive blood-based test

3.1.2 Secondary Syphilis

1. Clinical Description:
  - In the absence of a more likely alternative diagnosis, meets at least one of the following signs:
    - Localized or diffuse body rash classically described as copper-colored lesions that can be any combination of macular (flat), papular (raised), squamous (scaly), or pustular in appearance and typically involve the chest, back, palms of the hands, and/or soles of the feet **OR**
    - Mucous patches **OR**
    - Condyloma lata **OR**
    - Patchy alopecia often described as moth-eaten in appearance
2. Laboratory Criteria
  - Confirmatory: Meets at least one of the following criteria:
    - Direct detection of *T. pallidum* by darkfield microscopy in a specimen that was both not obtained from the throat and not potentially contaminated by stool **OR**
    - Direct detection of *T. pallidum* by immunohistochemistry (IHC) staining in a specimen that was both not obtained from the throat and not potentially contaminated by stool **OR**
    - Direct detection of *T. pallidum* by nucleic acid amplification test (NAAT) or a diagnostically equivalent molecular method in any specimen
  - Presumptive:
    - A current (performed in the context of this clinical evaluation) reactive blood-based nontreponemal antibody test **AND**

    - A reactive blood-based treponemal antibody test (current or historical)
- Supportive:
    - A current (performed in the context of this clinical evaluation) reactive blood-based nontreponemal antibody test with a titer ≥1:32 **AND**
    - No evidence of a concurrent nonreactive blood-based treponemal antibody test

3. Case Classification
    - **Confirmed (rare):** Clinically compatible case with evidence of *T. pallidum* by a confirmatory direct detection method
    - **Presumptive:** Clinically compatible case with **either** reactive nontreponemal and treponemal antibody tests **or** a titer ≥1:32 with no evidence of a nonreactive treponemal antibody test

3.1.3 Early Non-Primary Non-Secondary Syphilis

Stage of infection with *T. pallidum* in which there is evidence that the infection occurred within the previous 12 months AND there are no signs or symptoms of primary or secondary syphilis

1. Clinical Description
    - Documented history of syphilis, usually defined as evidence that the person was previously diagnosed and treated for syphilis AND a previous nontreponemal test titer is available
2. Laboratory Criteria
    - Confirmatory:
        - Direct detection of *T. pallidum* by nucleic acid amplification test (NAAT) or a diagnostically equivalent molecular method in any specimen
    - Presumptive:
        - A current (performed in the context of this clinical evaluation) reactive blood-based nontreponemal antibody test **AND**
        - A reactive blood-based treponemal antibody test (current or historical)
    - Supportive:
        - A current (performed in the context of this clinical evaluation) reactive blood-based nontreponemal antibody test **AND**
        - No evidence of a concurrent nonreactive blood-based treponemal antibody test
3. Evidence of Infection Acquired During Previous 12 Months:
    - No documented history of syphilis AND has evidence of seroconversion of a blood-based nontreponemal antibody or treponemal antibody test in a specimen collected during the previous 12 months **OR**
    - Documented history of syphilis AND has evidence of a current titer demonstrating a fourfold or greater increase in a specimen collected during the previous 12 months (see **Figure 2**) **OR**

- Signs/symptoms consistent with primary or secondary syphilis during the previous 12 months **OR**
- Fourfold or greater increase in titer from a specimen collected between the initial specimen collection date and the treatment initiation date (see **Figure 2**) **OR**
- Sexual exposure to a partner during the past 12 months who had primary, secondary, or early non-primary non-secondary syphilis (partner's stage must be documented in medical records and/or Orpheus) **OR**
- Only sexual contact ever was during the past 12 months

4. Case Classification
   - **Confirmed (rare):** Meets confirmatory laboratory evidence AND meets evidence of infection acquired in previous 12 months
   - **Presumptive:**
     - No documented history of syphilis AND meets *presumptive* laboratory evidence AND meets evidence of infection acquired in previous 12 months **OR**
     - Documented history of syphilis AND meets *supportive* laboratory evidence AND meets evidence of infection acquired in previous 12 months

3.1.4 Unknown Duration or Late Syphilis

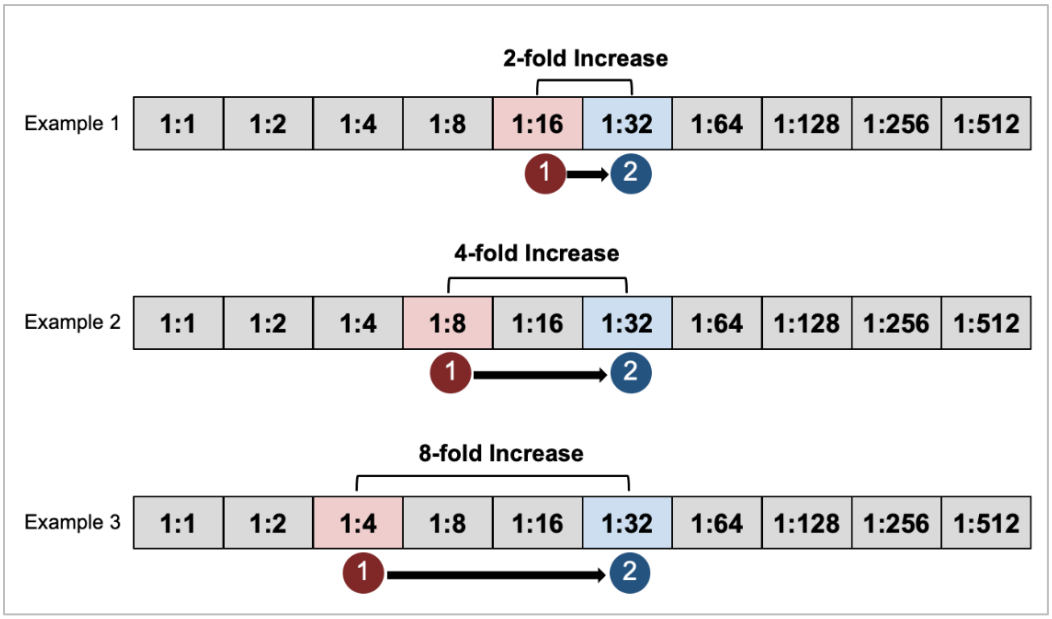
Stage of infection with *T. pallidum* in which the infection occurred more than 12 months prior or there is insufficient evidence to conclude the infection was acquired within the previous 12 months AND there are no signs or symptoms of primary or secondary syphilis

1. Clinical Description
   - Documented history of syphilis, usually defined as evidence that the person was previously diagnosed and treated for syphilis AND a previous nontreponemal test titer is available
2. Laboratory Criteria
   - Confirmatory:
     - Direct detection of *T. pallidum* by immunohistochemistry (IHC) staining in a specimen that was both not obtained from the throat and not potentially contaminated by stool **OR**
     - Direct detection of *T. pallidum* by nucleic acid amplification test (NAAT) or a diagnostically equivalent molecular method in any specimen
   - Presumptive:
     - A current (performed in the context of this clinical evaluation) reactive blood-based nontreponemal antibody test **AND**
     - A reactive blood-based treponemal antibody test (current or historical)
   - Supportive:
     - A current (performed in the context of this clinical evaluation) reactive blood-based nontreponemal antibody test **AND**

- No evidence of a concurrent nonreactive blood-based treponemal antibody test

3. Case Classification
   - **Confirmed (rare):** No evidence of having acquired the infection within the preceding 12 months AND meets confirmatory laboratory evidence
   - **Presumptive:**
     - No documented history of syphilis AND meets *presumptive* laboratory evidence AND no evidence of having acquired the infection within the preceding 12 months (see *Evidence of Infection Acquired During Previous 12 Months* in §3.1.3) **OR**
     - Documented history of syphilis AND meets *supportive* laboratory evidence AND no evidence of having acquired the infection within the preceding 12 months (see *Evidence of Infection Acquired During Previous 12 Months* in §3.1.3) **OR**
     - Does not otherwise meet the case definition for any other stage of syphilis as described above AND no evidence of having acquired the infection within the preceding 12 months (see *Evidence of Infection Acquired During Previous 12 Months* in §3.1.3) AND meets the definition for likely or verified neurologic, ocular, otic, or late clinical manifestations of syphilis

Figure 2. Examples of Increases in Nontreponemal Titers†*



* This graphic shows three examples of increases in nontreponemal titers when comparing two tests. Test number 1 is represented as red and test number 2 as blue. Illustration by David H. Spach, MD. Figure from National STD Curriculum Syphilis Quick Reference.

† For surveillance purposes, among people with a history of syphilis who were treated and then have a nonreactive nontreponemal test result, a fourfold or greater increase in titer is defined as a change from a nonreactive result to a reactive result with a titer of 1:4 or greater.

3.2 Syphilis Complications

See the CDC 2026 Syphilis Surveillance Case Definition for more information on the manifestations below. Note that for Orpheus documentation of these conditions, LPHA staff are only expected to select the criteria that are met—it is not necessary to know the classification category (i.e., Likely or Verified). Refer to the Syphilis Case Report and Data Entry Manual for guidance on Orpheus documentation.

3.2.1 Neurologic Manifestations

Neurosyphilis can occur at any stage of syphilis. A case should be staged appropriately and neurological manifestations, if present, should be documented in the case record.

1. Neurologic Clinical Criteria
   - Has clinical signs/symptoms consistent with infection of the central nervous system with *T. pallidum*, as shown by manifestations including syphilitic meningitis, meningovascular syphilis, tabes dorsalis, or general paresis, without other clear causes for these clinical abnormalities
   - Symptoms include: severe headache; muscle weakness or paralysis; numbness; changes in mental status (trouble focusing, confusion, personality changes); and dementia (problems with memory, thinking, and/or making decisions)
2. Neurologic Laboratory Criteria
   - A reactive CSF VDRL or CSF RPR test in the absence of visibly blood-contaminated CSF (defined as CSF red blood cell count of ≥500 RBCs/µL or, in the absence of a CSF RBC count, CSF described as bloody in appearance) **OR**
   - Direct detection of *T. pallidum* in CSF by nucleic acid amplification test (NAAT) or a diagnostically equivalent molecular method
3. Classification of Neurologic Manifestations
   - **Likely:**
     - Meets the case definition for primary, secondary, or early non-primary non-secondary syphilis AND meets neurologic clinical criteria AND a diagnosis of neurosyphilis was made by a clinical provider or treatment for neurosyphilis was advised, ordered, or initiated by a clinical provider **OR**
     - Has a reactive blood-based treponemal antibody test result (current or historical) AND a current (performed in the context of this clinical evaluation) reactive blood-based nontreponemal antibody test AND meets neurologic clinical criteria AND a diagnosis of neurosyphilis was made by a clinical provider or treatment for neurosyphilis was advised, ordered, or initiated by a clinical provider
   - **Verified:**
     - Meets the case definition for primary, secondary, or early non-primary non-secondary syphilis AND meets neurologic clinical criteria AND meets neurologic laboratory criteria **OR**

- Has a reactive blood-based treponemal antibody test result (current or historical) AND a current (performed in the context of this clinical evaluation) reactive blood-based nontreponemal antibody test AND meets neurologic clinical criteria AND meets neurologic laboratory criteria

3.2.2 Ocular Manifestations

Ocular syphilis can occur at any stage of syphilis. A case should be staged appropriately and ocular manifestations, if present, should be documented in the case record.

1. Ocular Clinical Criteria
   - Has clinical signs/symptoms consistent with infection of any eye structure with *T. pallidum*, as shown by manifestations including posterior uveitis, panuveitis, anterior uveitis, conjunctivitis, optic neuropathy, retinal vasculitis, and interstitial keratitis, without other clear causes for these clinical abnormalities. **Ocular syphilis may lead to permanent decreases in vision, including permanent blindness.**
   - Symptoms include: eye pain or redness, light sensitivity, floating spots in the field of vision (“floaters”), and changes in vision (blurry vision or vision loss)
2. Ocular Laboratory Criteria
   - Direct detection of *T. pallidum* in aqueous or vitreous fluid by nucleic acid amplification test (NAAT) or diagnostically equivalent molecular method
3. Classification of Ocular Manifestations
   - **Likely:**
     - Meets the case definition for primary, secondary, or early non-primary non-secondary syphilis AND meets ocular clinical criteria AND a diagnosis of ocular syphilis was made by a clinical provider or treatment for ocular syphilis was advised, ordered, or initiated by a clinical provider **OR**
     - Has a reactive blood-based treponemal antibody test result (current or historical) AND a current (performed in the context of this clinical evaluation) reactive blood-based nontreponemal antibody test AND meets ocular clinical criteria AND a diagnosis of ocular syphilis was made by a clinical provider or treatment for ocular syphilis was advised, ordered, or initiated by a clinical provider
   - **Verified:**
     - Meets the case definition for primary, secondary, or early non-primary non-secondary syphilis AND meets ocular clinical criteria AND meets ocular laboratory criteria **OR**
     - Has a reactive blood-based treponemal antibody test result (current or historical) AND a current (performed in the context of this clinical evaluation) reactive blood-based nontreponemal antibody test AND meets ocular clinical criteria AND meets ocular laboratory criteria

3.2.3 Otic Manifestations

Otosyphilis can occur at any stage of syphilis. A case should be staged appropriately and otic manifestations, if present, should be documented in the case record.

1. Otic Clinical Criteria
   - Has clinical signs/symptoms consistent with infection of the cochleovestibular system with *T. pallidum*, as shown by manifestations including tinnitus, vertigo, and sensorineural or conductive hearing loss that can be permanent, without other clear causes for these clinical abnormalities
   - Symptoms include hearing loss; tinnitus (ringing, buzzing, roaring, or hissing in the ears); balance difficulties; and dizziness or vertigo
2. Otic Laboratory Criteria
   - Direct detection of *T. pallidum* in inner ear fluid by nucleic acid amplification test (NAAT) or diagnostically equivalent molecular method
3. Classification of Otic Manifestations
   - **Likely:**
     - Meets the case definition for primary, secondary, or early non-primary non-secondary syphilis AND meets otic clinical criteria AND a diagnosis of otosyphilis was made by a clinical provider or treatment for otosyphilis was advised, ordered, or initiated by a clinical provider **OR**
     - Has a reactive blood-based treponemal antibody test result (current or historical) AND a current (performed in the context of this clinical evaluation) reactive blood-based nontreponemal antibody test AND meets otic clinical criteria AND a diagnosis of otosyphilis was made by a clinical provider or treatment for otosyphilis was advised, ordered, or initiated by a clinical provider
   - **Verified:**
     - Meets the case definition for primary, secondary, or early non-primary non-secondary syphilis AND meets otic clinical criteria AND meets otic laboratory criteria **OR**
     - Has a reactive blood-based treponemal antibody test result (current or historical) AND a current (performed in the context of this clinical evaluation) reactive blood-based nontreponemal antibody test AND meets otic clinical criteria AND meets otic laboratory criteria

3.2.4 Late Clinical Manifestations (extremely rare)

Late clinical manifestations of syphilis (tertiary syphilis) usually develop only after a period of 10 or more 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 documented in the case report.

1. Late Clinical Criteria
   - In the absence of other clear causes for the clinical abnormalities—characteristic abnormalities or inflammatory lesions of the cardiovascular

system (e.g., aortitis, coronary vessel disease), skin (gummatous lesions), bone (osteitis), or other tissues/structures (e.g., upper and lower respiratory tracts, mouth, eye, abdominal organs, reproductive organs, lymph nodes, central nervous system, and skeletal muscle)

2. Late Clinical Laboratory Criteria
   - Direct detection of *T. pallidum* by immunohistochemistry (IHC) staining in a specimen from a late lesion that was both not obtained from the throat and not potentially contaminated by stool **OR**
   - Direct detection of *T. pallidum* by nucleic acid amplification test (NAAT) or a diagnostically equivalent molecular method in any specimen from a late lesion **OR**
   - Demonstration of pathologic changes that are consistent with *T. pallidum* infection on histologic examination of late lesions
3. Classification of Late Clinical Manifestations of Syphilis
   - **Likely:**
     - Has a current (performed in the context of this clinical evaluation) reactive blood-based nontreponemal antibody test AND meets late clinical criteria AND a diagnosis of late clinical manifestations was made by a clinical provider or treatment for late clinical manifestations was advised, ordered, or initiated by a clinical provider **OR**
     - Clinical signs/symptoms consistent with late neurologic manifestations of syphilis (i.e., general paresis or tabes dorsalis) in a case that meets the criteria for likely neurologic manifestations of syphilis (see §3.2.1)
   - **Verified:**
     - Has a current (performed in the context of this clinical evaluation) reactive blood-based treponemal antibody test AND meets late clinical criteria AND meets late clinical laboratory criteria **OR**
     - Clinical signs and symptoms consistent with late neurologic manifestations of syphilis (i.e., general paresis or tabes dorsalis) in a case that meets the criteria for verified neurologic manifestations of syphilis (see §3.2.1)

3.3 Diagnosis

3.3.1 Direct Detection of *T. Pallidum*

The syphilis surveillance case definition lists multiple test types in the laboratory criteria sections. The inclusion of direct detection tests for *T. pallidum* in the syphilis surveillance case definition is intended to ensure that results of these tests can be utilized for staging surveillance cases of syphilis when they are available. However, including these methods was not intended to suggest that they are “preferred” over more traditional laboratory diagnostics for syphilis, such as serologic testing. Most syphilis surveillance cases will continue to be classified as Presumptive cases given the currently limited availability of direct detection testing in the United States. Additional information about direct

detection methods for the diagnosis of syphilis is available in the CDC Laboratory Recommendations for Syphilis Testing.

3.3.2 Serological Tests for Syphilis

Refer to **Table 3** for information and frequently asked questions about nontreponemal and treponemal serological tests for syphilis. The California PTC Clinical Interpretation of Syphilis Screening Algorithms Resource for Local Health Jurisdictions (see Appendix B) includes descriptions of the traditional and reverse syphilis screening algorithms and results.

Table 3. Frequently Asked Questions about Nontreponemal and Treponemal Tests

FAQs	***Nontreponemal Tests***	***Treponemal Tests***
What are the common test names?	The two nontreponemal tests are the rapid plasma reagin (RPR) and the VDRL. The RPR is the most common nontreponemal serological (blood) test. The VDRL is mainly used for CSF testing. Refer to **Table 4** for examples of syphilis test names on lab reports.	There are several types of treponemal tests, including enzyme or chemiluminescence immunoassays (EIA/CIA); *Treponema pallidum* particle agglutination assay (TP-PA); and fluorescent treponemal antibody absorption test (FTA). Refer to **Table 4** for examples of syphilis test names on lab reports.
Is the test specific to syphilis?	No. “Nontreponemal” means the antibodies detected by these tests are not responding to treponemal bacteria. Biologic false positive results can be due to many causes, such as pregnancy, autoimmune diseases, and HIV.	Yes. Treponemal tests detect antibodies specific to *T. pallidum*.
Is the test qualitative or quantitative?	Both. An initial nontreponemal result is qualitative. If reactive, it reflexes to a quantitative result known as a titer. The titer is the measurement of antibodies through diluting a person’s blood to determine the highest dilution at which a reactive result (agglutination/flocculation) is still produced. A 1:2 titer indicates a low	Treponemal test results are qualitative. If a numerical value is reported with a reactive result (e.g., FTA 4+), the number should be ignored. If *only* a numerical value is reported, there should be a comment/note on the ELR or lab report advising how to interpret the value qualitatively.

	concentration of antibodies, as none were detected after only two dilutions. A 1:128 titer indicates a high concentration of antibodies, as none were detected after eight dilutions.	
How soon does the test become positive?	Nontreponemal tests will typically be reactive by 21 days after infection.	Treponemal tests will typically be reactive by 21 days after infection. EIA/CIA and TP-PA tests may become positive sooner than nontreponemal tests.
Can the test be used to monitor for treatment response and reinfection?	Yes. A baseline titer should be done on or as close to the day of treatment initiation as possible so that treatment response can be determined accurately. Only titers of the same nontreponemal test type should be compared.	No. Treponemal tests remain positive for life, even after treatment. They are not useful for monitoring treatment response or diagnosing a new infection in anyone with syphilis history.
Does the test become negative after treatment?	Nontreponemal tests often become negative after treatment, but it is also common for a low titer to persist for life (known as serofast state). Even without treatment, titers drop over time. A negative nontreponemal test result is not a goal of treatment.	No. See above.
How should equivocal/indeterminate results be handled?	If the traditional screening algorithm is followed, an equivocal/indeterminate RPR result should be followed by a treponemal test. If the reverse screening algorithm is followed, a second treponemal test may be necessary.	No matter which screening algorithm is followed, a second treponemal test may be necessary if the first treponemal test result is equivocal/indeterminate.

Table 4. Examples of Syphilis Test Names on Lab Reports

	Test Type	Examples of Test Names on Lab Reports
Nontreponemal Tests (qualitative and quantitative)	RPR	RPR Ser Ql RPR Ser Titr RPR Titer
	VDRL	VDRL Ser Ql VDRL Quantitative
Treponemal Tests (qualitative only)	FTA	FTA-ABS T pallidum Ab Ser Ql IF
	TPPA	TPPA TP-PA T pallidum Ab Particle Agglutination
	EIA/CIA*	Syphilis TP T pallidum Ab Ser Ql T pallidum Ab Ser Ql IA T pallidum IgG+IgM Ser Ql IA Treponemal AB IgG Treponemal AB TOT

* If labs with the same specimen date include two EIA/CIA tests with different names, label the first Trep AB 1 and the second Trep AB 2 in Orpheus. Refer to the Syphilis Case Report and Data Entry Manual for guidance.

3.4 Services Available at Oregon State Public Health Laboratory (OSPHL)

The OSPHL conducts serologic syphilis screening using a treponemal CIA test (Syph-TP) that reflexes to an RPR. If these produce conflicting results, the TP-PA test is run as a reflex "tiebreaker" treponemal test. For patients with a history of syphilis and a recently documented (within past year) positive treponemal test, an "RPR only" should be ordered. For a visual representation of the OSPHL testing algorithm, refer to the Syphilis Testing Algorithm (pdf). Refer to the OSPHL Lab Test Menu, available at www.healthoregon.org/labtests, for additional information.

4. CASE INVESTIGATION

4.1 Provider Records

- Review medical records for the visits associated with syphilis lab results to obtain clinical, treatment, and risk information
- If electronic health records are not accessible, contact the provider by phone, fax, or query letter to request the necessary information
- If appropriate, inform the provider that a public health professional will contact the patient to discuss the syphilis diagnosis
- Refer to the STD Program's Syphilis Case Report and Data Entry Manual for guidance on entering data in Orpheus

4.2 Case Interview

4.2.1 Cases Prioritized for Investigation

An interview should be attempted for the following cases:

- All primary, secondary, and early non-primary non-secondary cases
- All cases involving pregnant and pregnancy-capable individuals regardless of stage. Refer to the Syphilis in Pregnancy Investigative Guidelines for guidance on investigations in pregnancy.
- Late or unknown duration syphilis cases that are suspicious for early syphilis should be investigated per LPHA protocol. Many factors can suggest early infection, including:
  - High titer (≥1:16)
  - Recent exposure to syphilis of unknown stage or suspected early syphilis
  - Concurrent/recent diagnosis of another STD

4.2.2 Interview Methods

- In-person interviews are best when possible. Interviews by phone, web-based questionnaire, and other methods are also acceptable.
- If the client cannot be reached by traditional methods (e.g., calls, texts, mailed letters, field or clinic-based visit), consider using technology-based tools such as social media sites and mobile apps to contact cases. Any method should be used in accordance with LPHA policies.
- Try contacting a case at least three times before closing the investigation
  - Attempts should be made on alternate days and times of day
  - Refer to §4.4 for resources that can assist with locating individuals.
- Maintain client privacy throughout the case investigation and interview
- Document all attempts to contact the client in real time when possible, or on the day of each attempt at minimum

4.2.3 Interview Exceptions

- The importance of an interview may be outweighed by a person's physical or mental health needs or other issues
- LPHAs can decide that an interview is not indicated and document the reason in the case record
- Examples of interview exceptions include:
  - If syphilis testing is done following sexual assault or during hospitalization for a serious medical condition that is not STD-related
  - If a case involves a person younger than 13 years old
    - Consult a supervisor about how to proceed
    - Case investigators are mandatory reporters required by law to report suspected child abuse (ORS 419B.005)
- If an interview is not conducted, obtain necessary information from the electronic health record

4.3 Management of Partners

4.3.1 Interview Periods

- Sexual contacts of a person diagnosed with primary, secondary, or early non-primary non-secondary syphilis are at high risk of acquiring the infection
- Interview periods help identify partners at risk of infection. The interview period is the time from the earliest date the case could have been infected to the date of treatment.
- Refer to **Table 5** for interview periods based on the case's stage ("case" refers to a person with presumptive or confirmed syphilis)
- All partners within the appropriate interview period should be confidentially notified of the exposure and need for evaluation
- Prioritize identifying partners when congenital syphilis is a risk (i.e., case or any partners are pregnant or pregnancy-capable)
- If a case has not had sex within the interview period, the most recent contact should be tested and presumptively treated if follow-up is uncertain

Table 5. Interview Periods by Stage

Stage	Interview Period
Primary	90 days before date of onset of primary chancre 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

4.3.2 Partner Notification

- **If LPHA is handling notification:**
  - Contact named partners within two working days of the initial case interview and refer for evaluation, testing, and treatment
  - If partners cannot be reached by traditional methods (e.g., calls, texts, mailed letters, field or clinic-based visit), consider using technology-based tools such as social media sites and mobile apps to contact cases. Any method should be used in accordance with LPHA policies.
  - Try to contact partners at least three times
    - Attempts should be made on alternate days and times of day
    - Refer to §4.4 for resources that can assist with locating individuals
- **If the case chooses to notify partners:**
  - Advise the case that LPHA staff can help arrange partner testing/treatment and encourage the case to share the staff's contact information with partners
  - If possible, contact the case again to offer LPHA notification and treatment referral if partner treatment cannot be verified within a reasonable time frame (2–5 days)

4.3.3 Partner Testing/Treatment

- Partners from **within 90 days** before case's diagnosis (or onset of symptoms) of early syphilis (primary, secondary, early non-primary non-secondary syphilis):
  - Test and presumptively treat for early syphilis
  - Contacts to late or unknown duration syphilis cases that are suspicious for early infection should also be tested and presumptively treated
- Partners from **>90 days** before case's diagnosis (or onset of symptoms) of early syphilis (primary, secondary, early non-primary non-secondary syphilis):
  - Test and presumptively treat for early syphilis if follow-up is uncertain
    - If positive: stage based on clinical and serologic evaluation and treat (if not treated presumptively)
    - If negative: no treatment is needed
- Long-term partners of a case diagnosed with late/unknown duration syphilis should be evaluated for syphilis and treated based on the clinical and serological findings

4.4 Requesting Locating Searches and Out-of-State Records

1. **Locating Searches**
   If LPHA staff and the provider cannot locate a case or contact using the available contact information, there are two useful resources available:
   - Request that State STD Program staff conduct an Accurint search for the person's current/recent addresses and phone numbers
     - Searches are prioritized for the following:
       - Early syphilis cases
       - Pregnant cases/contacts
       - Cases with unknown pregnancy status
   - Search Orestar to find mailing and residential addresses for Oregon residents
   - Search sites with correctional/judicial information:
     - Victim Information System in Oregon (VISOR) to see if a person is currently in a correctional facility or has been recently released
     - Oregon Department of Corrections to see if a person is in an Oregon state prison
     - Oregon Judicial Department to find information on court records, community supervision, name changes, etc.
2. **Out-of-State Records**
   - Out-of-state syphilis records should mainly be requested to:
     - Determine whether there is a new infection based on a comparison of the current and previous titers **OR**
     - Obtain documentation of past syphilis care for persons who are pregnant or pregnancy-capable
   - Clinical management should not be delayed while waiting on out-of-state records, especially if there is a risk of loss to follow-up
     - In many cases, records do not exist or are incomplete
   - Records should not be requested for persons without pregnancy capacity with a current titer 1:2 or lower

- A fourfold increase could not have occurred (a change from nonreactive to 1:2 is not considered a fourfold increase)
- It is only necessary for public health to review past treatment for pregnant and pregnancy-capable individuals, not for all people with syphilis history outside Oregon
- LPHAs have discretion to request records in this scenario if there is a compelling clinical need (e.g., clinical manifestations of syphilis)

4.5 Case/Contact Transfers and Other Orpheus Issues

Refer to the STD Program's Syphilis Case Report and Data Entry Manual for guidance on Orpheus-specific issues including transferring cases/contacts to other Oregon jurisdictions or out of state.

5. CONTROLLING FURTHER SPREAD

5.1 Education

- Persons diagnosed with early syphilis (primary, secondary, or early non-primary non-secondary stages) should be advised to:
  - Complete treatment
  - Avoid all types of sex until treatment has been completed (either benzathine penicillin G or doxycycline) and any skin lesions have resolved.
  - Avoid all types of sex with untreated partners until they have been treated and their skin lesions have resolved
- Other key education messages for people at risk of acquiring syphilis and other STIs:
  - Use condoms as often as possible
  - Get checked for HIV and other STIs
  - Talk to partners about testing
  - Know about STI post-exposure prophylaxis (Doxy PEP) and HIV pre- and post-exposure prophylaxis (PrEP and PEP)
    - Review current OHA Doxy PEP recommendations to determine eligible patient populations
    - PrEP education and referrals should be provided to anyone diagnosed with or at risk for syphilis. Refer to the OHA PrEP & PEP page for additional information
    - Visit the AETC site for a list of DoxyPEP and PrEP providers in Oregon
  - Talk with a provider about contraceptive options if not currently seeking pregnancy
  - Utilize syringe service programs (for those using/injecting drugs)
  - Stay up to date on vaccinations as appropriate, including for HPV and hepatitis A and B

5.2 Recommendations for Clinical Follow-Up

- **Primary, Secondary, and Early Non-Primary Non-Secondary Syphilis**
  - If signs/symptoms persist/return or titer increases fourfold or more:
    - Reinfection is most likely. Repeat treatment for early syphilis and retest for HIV.
    - If the person has neurological symptoms or had no sexual exposure in the prior 3-6 months, conduct CSF exam and retest for HIV.
  - If titer does not decrease fourfold within 12 months:
    - Evaluate for neurosyphilis and retest for HIV
    - Consider treating with benzathine penicillin G 2.4 million units for 3 weeks or treat for neurosyphilis if indicated
- **Late or Unknown Duration Syphilis**
  - If primary or secondary signs/symptoms occur or titer increases at least fourfold:
    - Reinfection is most likely. Treat based on stage and retest for HIV.
    - If the person has neurological symptoms or had no sexual exposure in the prior 12 months, conduct CSF exam and retest for HIV.
  - If titer does not decrease fourfold within 24 months:
    - Evaluate for neurosyphilis and retest for HIV
    - Consider retreating with benzathine penicillin G 2.4 million units for 3 weeks or treat for neurosyphilis if indicated

See **Table 6** for the recommended frequency of titer monitoring by stage of infection.

Table 6. Recommended Follow-Up of Treated Syphilis Cases

Stage of Infection	**Follow-Up RPR titers**	
	HIV Negative	HIV Positive
Primary, Secondary, Early Non-Primary Non-Secondary	6 months 12 months	3 months 6 months 9 months 12 months 24 months
Late or Unknown Duration	6 months 12 months 24 months	6 months 12 months 18 months 24 months

6. MANAGING SPECIAL SITUATIONS

6.1 Syphilis Case has Multiple Reportable Infections

- Check in Orpheus to see if a person diagnosed with syphilis has any other new reportable infections, especially other STI or HIV (may depend on Orpheus disease group access)
- Coordinate case investigations to reduce duplication and communication with case:
  - Combine questions for all infections in one interview session rather than having multiple people contact the case to ask different questions
  - Obtain partner information based on interview periods for each STI/HIV

6.2 Jarisch-Herxheimer Reaction

- The Jarisch-Herxheimer reaction is a flu-like reaction involving fever, headache, and muscle aches, that can occur after initiation of syphilis treatment
  - The reaction usually begins within 2 hours of treatment initiation, peaks at approximately 8 hours, and resolves in 24-36 hours
  - In most cases no treatment is required
- It is a reaction to the rapid killing of *T. pallidum* bacteria and is **not** an allergic reaction to syphilis treatment
- It occurs most often in early syphilis, likely because bacterial loads are higher during these stages
- Refer to the Syphilis in Pregnancy Investigative Guidelines for guidance on the Jarisch-Herxheimer reaction in pregnancy

6.3 Syphilis among Persons Living with HIV (PLWH)

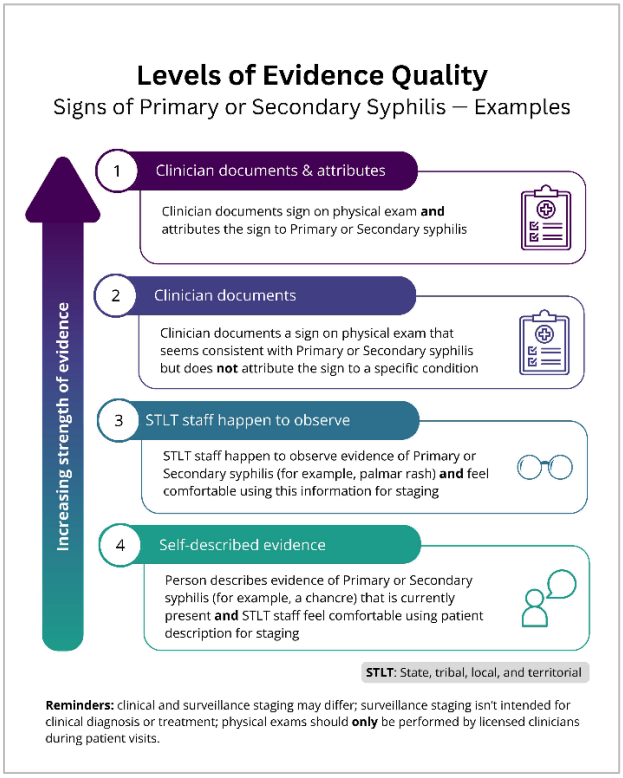
- Persons with syphilis who also have an HIV diagnosis and are not on antiretroviral therapy should be immediately linked to HIV care
  - Contact the OHA HIV Surveillance Program for assistance with these HIV cases
- Unusual syphilis test results can occur among PLWH but are rare
  - Post-treatment titers may be higher than expected (high serofast) or fluctuate
  - False-negative tests and delayed seroreactivity (detectable immune response to syphilis) have also been seen
- Treatment for all stages and for neuro/ocular/otic syphilis is the same regardless of HIV status
- All persons with HIV and syphilis coinfection should receive a careful neurologic, ocular, and otic examination
  - PLWH who have early syphilis might be at increased risk for neurologic complications
  - Ocular syphilis has been reported more frequently among PLWH

7. FAQ

STAGING

1. A patient who was treated for syphilis in the past now has primary symptoms, but their titer hasn't increased fourfold above their last titer. Is this a case?
   - Yes, this is a new case. Symptoms matter more than the titer in deciding whether it is a case—if someone previously treated for syphilis now has primary or secondary symptoms, then it is a new case no matter the current titer. See §3.1.
2. A patient with no syphilis history has primary chancres. The treponemal test is reactive but the RPR is negative. Is this a case?
   - Yes. If a primary chancre is present and at least one syphilis test is reactive, then the criteria for presumptive primary syphilis are met. See §3.1.1.
3. A patient requested syphilis testing following a "recent exposure" per the visit notes. They have a reactive treponemal test and RPR titer 1:16. They reported no syphilis signs/symptoms, and none were noted on exam. The provider diagnosed this as "primary syphilis." Should I stage it as primary since that's what the provider said?
   - No. Surveillance staging must be consistent with the CDC syphilis surveillance case definition and is separate from clinical staging. This is how we ensure that a primary syphilis case reported in Oregon is the same as a primary syphilis case reported in all other states. If primary signs/symptoms are not present, then this is not a primary case (see §3.1.1). Consult the CDC adult syphilis surveillance staging flowchart to determine appropriate stage.
4. A patient with no syphilis history has secondary signs/symptoms. The ED provider only ordered an RPR, which is reactive with a 1:8 titer. Is this a case?
   - Maybe. If the patient has not yet been treated, then another blood draw can be done at time of treatment. If a treponemal test is not done and the titer is <1:32, then this will be a "No Case" in Orpheus. See §3.1.2.
5. An asymptomatic case said they have a partner who had syphilis recently. The partner might have had a sore on their penis. Can I stage my case as early non-primary non-secondary since it sounds like this recent partner has early syphilis?
   - The partner needs to have a documented case of early syphilis to meet the criteria for this stage. If the partner has an early syphilis case documented in medical records or Orpheus, then your case can be staged as early non-primary non-secondary. If there is no documentation of the partner's early syphilis, then this stage's criteria is not met. See §3.1.3. Note that a provider may choose to treat with three benzathine penicillin G doses even if the early non-primary non-secondary case definition is met since clinical and surveillance staging can differ.
6. Do primary/secondary signs need to be clinically observed? Or can staging be based on a person with syphilis just reporting primary/secondary signs?
   - There are different levels of evidence for meeting the clinical criteria for primary or secondary syphilis. See **Figure 3** below from the CDC Syphilis Surveillance Technical Resources job aid, which covers this topic in more depth.

Figure 3. Levels of Evidence for Meeting the Clinical Criteria for Primary or Secondary Syphilis



TREATMENT

1. A patient was accidentally treated with only 1.2 million units of benzathine penicillin G. Do they need to return for a full dose?
   - The other half of the dose should be given within 7 days. If the patient can't return until more than 7 days later, they should then be given the full 2.4 million units. Consult the STD Program if this scenario occurs with a pregnant patient.
2. A patient has an RPR titer 1:4, a positive treponemal test, and no syphilis signs/symptoms. They have syphilis history, but there is no documentation of previous titers or treatment and the patient can't remember being treated. What should be done?
   - The most cautious approach is to stage and treat as though there is no syphilis history. This person would be staged as late/unknown duration and treated with three benzathine penicillin G doses unless they meet criteria for early non-primary non-secondary syphilis (see §3.1.3). For pregnant and pregnancy-capable people especially, this cautious approach is necessary to reduce the risk of congenital syphilis.
3. We received new labs for a case reported a year ago in which no treatment is documented. Should we add these labs to the existing case record, or create a new record?
   - This needs to be decided on a case-by-case basis. Factors to consider include whether current signs/symptoms are present and how the current titer compares to the previous titer. It is also important to determine if treatment was eventually obtained after the initial case investigation concluded. If treatment was not

completed, the current titer is less than fourfold the previous titer, and there are no current signs/symptoms, then the new labs can be added to the existing case record. If the current provider is unaware that treatment was not completed and does not plan to treat, they should be advised of the need for treatment completion.

FOLLOW-UP

1. A patient was appropriately treated <12 months ago and their titer hasn't dropped fourfold yet. They don't have any syphilis symptoms. Does anything need to be done?
   - No. It can take up to 12 months for the titer to drop fourfold in primary and secondary cases, and up to 24 months in unknown duration or late cases. See §5.2.
2. A patient was appropriately treated for early syphilis over 12 months ago, but the high baseline titer has not dropped and they are asymptomatic. How should this be managed?
   - This patient should be evaluated for reinfection, HIV infection, and neurosyphilis. If doxycycline was prescribed for the initial infection, retreatment with benzathine penicillin G should be considered since doxycycline regimens are difficult to complete. See §5.2 for additional recommendations.
3. A person with syphilis history whose last RPR was nonreactive now has an RPR titer of 1:2. Is this a fourfold increase?
   - For people with a history of syphilis who were treated and then have a nonreactive nontreponemal test result, a fourfold or greater increase in titer is defined as a change from a nonreactive result to a reactive result with a titer of 1:4 or greater.

GLOSSARY

CSF: Cerebrospinal fluid. CSF testing can indicate whether there is central nervous system involvement in a syphilis infection.

CBC: Complete Blood Count. A complete blood count is a set of tests that provide information about the cells in a person's blood. The CBC indicates the counts of white blood cells, red blood cells, and platelets, and the hemoglobin and hematocrit.

Early syphilis: Any of the stages that occur in the first 12 months of infection: primary, secondary, and early non-primary non-secondary syphilis.

IM: Intramuscular. An IM injection delivers medication, such as benzathine penicillin G for syphilis, into a muscle.

PCR: Polymerase chain reaction test is a laboratory technique for rapidly producing (amplifying) many copies of a specific segment of genetic material, e.g., *T. pallidum* DNA in syphilis.

RPR: Rapid plasma reagin test is a nontreponemal test. Unlike treponemal tests, the RPR measures antibodies that are not specific to *T. pallidum* bacteria and may be reactive due to conditions other than syphilis, including pregnancy.

Treponemal test: Treponemal tests measure antibodies directed against *T. pallidum* bacteria. Treponemal blood-based tests include enzyme immunoassays (EIAs) and chemiluminescence immunoassays (CIAs), *T. pallidum* particle agglutination (TP-PA),

fluorescent treponemal antibody absorption (FTA-ABS) tests, and point-of-care and self-test treponemal antibody tests. These qualitative tests usually remain reactive for life, regardless of treatment.

VDRL: Venereal Disease Research Laboratory test is a nontreponemal test that can be done on blood and CSF. Mostly used in CSF testing in congenital syphilis and neurosyphilis evaluations. The RPR is the more commonly used nontreponemal blood-based test.

REFERENCES

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4. CDC Sexually Transmitted Infections Treatment Guidelines, 2021. https://www.cdc.gov/std/treatment-guidelines/default.htm
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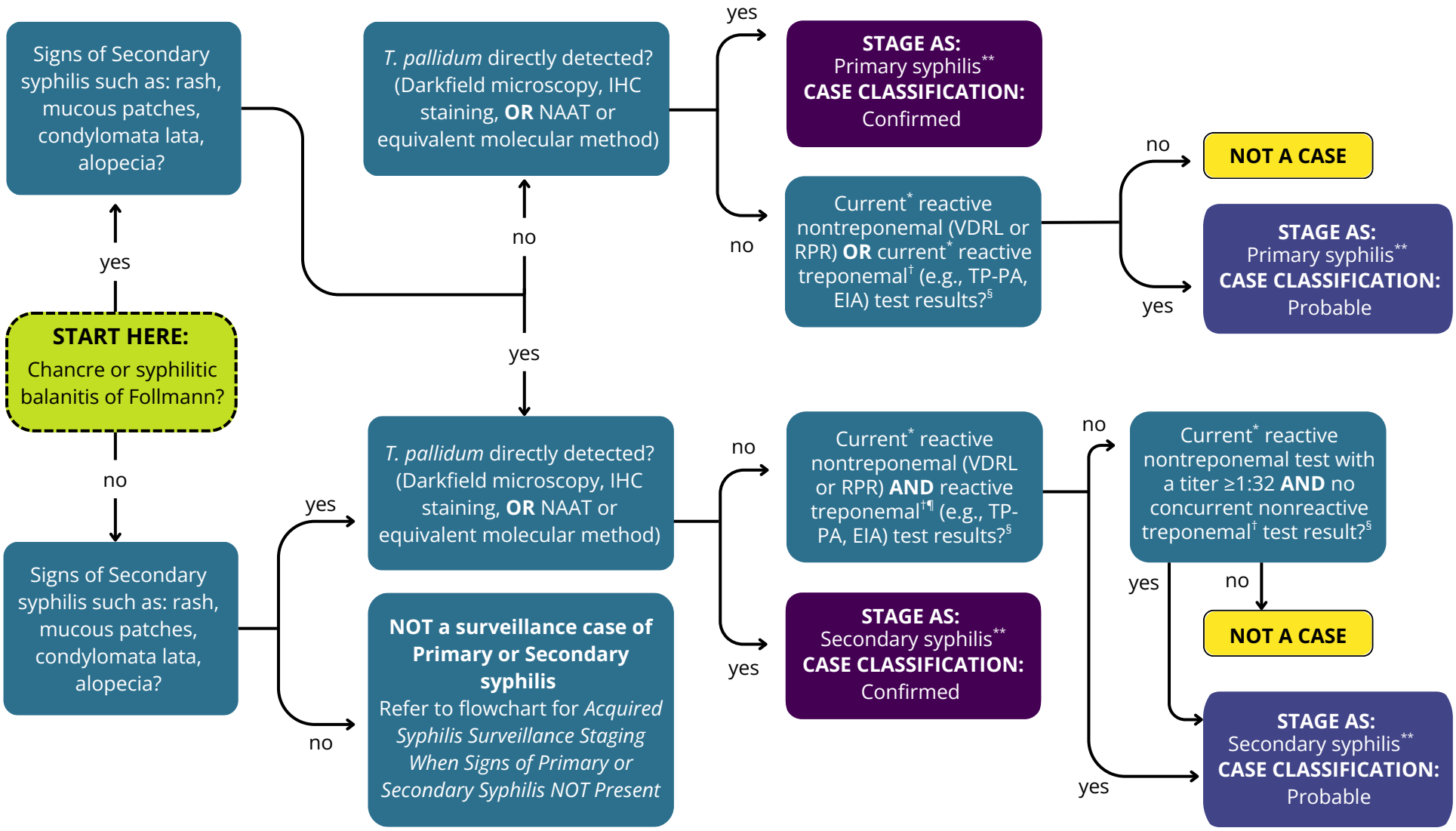
UPDATE LOG

July 2023. First draft. (Jillian Garai, Yuritzy Gonzalez Pena, Timothy Menza)
August 2024. Broken links and appendices updated. Confirmatory criteria and direct detection methods in §3 updated. Education on DoxyPEP added. (Garai)
September 2026. Surveillance case definition updated in accordance with 2025 CSTE syphilis position statement and 2026 CDC syphilis case definition. Treatment updated to include benzathine penicillin G products that are approved for temporary importation by the FDA during Bicillin L-A shortages. Other edits made throughout to align with current surveillance case definition. (Garai)

Appendix A

ACQUIRED SYPHILIS SURVEILLANCE STAGING WHEN SIGNS OF PRIMARY OR SECONDARY SYPHILIS ARE PRESENT

This tool should not be used for clinical decision-making and does not supersede the syphilis surveillance case definition



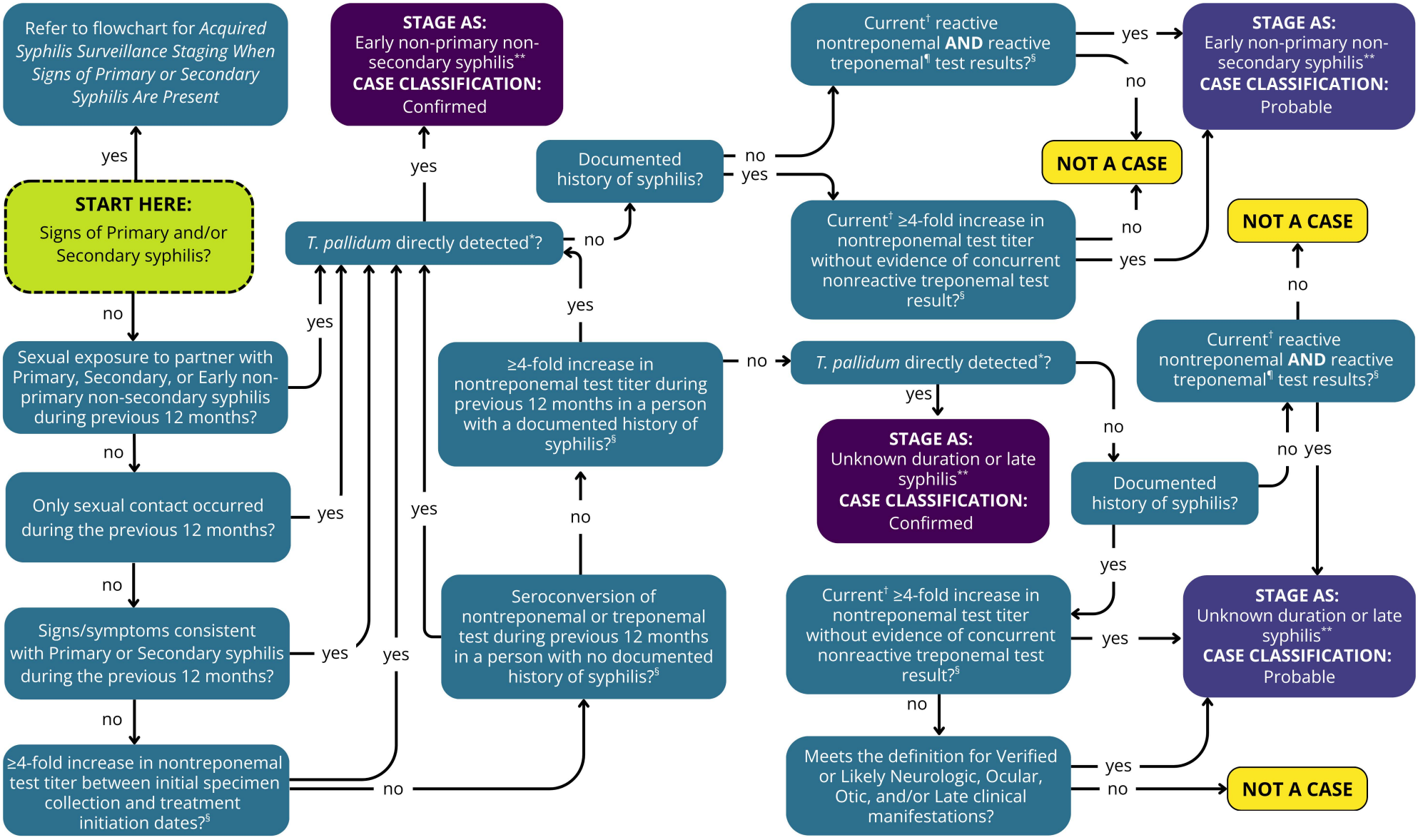
* Current refers to a test performed in the context of this index presentation.
† A reactive laboratory-based or point-of-care treponemal test result can be used to satisfy this requirement.
§ When nontreponemal and treponemal tests are mentioned in this algorithm, this refers to results from blood-based testing only.
¶ Current or historical reactive treponemal antibody tests can be used to satisfy this criterion.
** Neurologic, Ocular, and Otic manifestations of syphilis can occur at any stage. After assigning syphilis stage, assess all cases for these clinical manifestations and classify separately as "No," "Verified," "Likely," or "Unknown." Late clinical manifestations of syphilis are classified separately as "Verified," "Likely," "No," or "Unknown". Because Late clinical manifestations of syphilis (tertiary syphilis) usually only develop after >10 years of untreated syphilitic infection, these manifestations should only be included with cases of Unknown duration or late syphilis. For assistance with classification of these manifestations, please see clinical manifestations algorithms.

ACRONYMS: EIA = enzyme immunoassay; IHC = immunohistochemistry; NAAT = nucleic acid amplification test; RPR = rapid plasma reagin; *T. pallidum* = *Treponema pallidum*; TP-PA = *Treponema pallidum* particle agglutination; VDRL = Venereal Disease Research Laboratory **RESOURCES:** Case Definitions; Treatment Guidelines; Partner Services

Last updated 12/15/2025

ACQUIRED SYPHILIS SURVEILLANCE STAGING WHEN SIGNS OF PRIMARY OR SECONDARY SYPHILIS NOT PRESENT

This tool should not be used for clinical decision-making and does not supersede the syphilis surveillance case definition



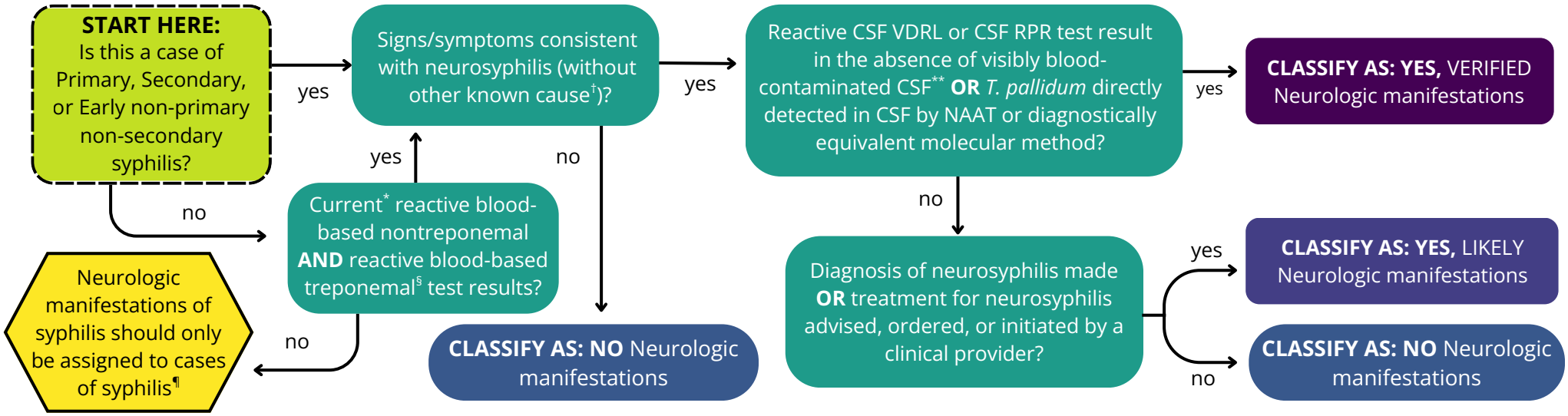
* Direct detection methods for cases of Early non-primary non-secondary syphilis may include nucleic acid amplification testing or a diagnostically equivalent molecular method. Direct detection methods for cases of Unknown duration or late syphilis may include nucleic acid amplification testing or a diagnostically equivalent molecular method or immunohistochemistry staining of an appropriate specimen.
† Current refers to a test performed in the context of this index presentation.
§ When nontreponemal and treponemal tests are mentioned in this algorithm, this refers to results from blood-based testing only.
¶ A reactive laboratory-based or point-of-care treponemal test result can be used to satisfy this requirement. Current or historical reactive treponemal antibody tests can be used to satisfy this criterion.
** Neurologic, Ocular, and Otic manifestations of syphilis can occur at any stage. After assigning syphilis stage, assess all cases for these clinical manifestations and classify separately as "Verified," "Likely," "No," or "Unknown." Late clinical manifestations of syphilis are classified separately as "Verified," "Likely," "No," or "Unknown." Because Late clinical manifestations of syphilis (tertiary syphilis) usually only develop after >10 years of untreated syphilitic infection, these manifestations should only be included with cases of Unknown duration or late syphilis. For assistance with classification of these manifestations, please see clinical manifestations algorithms.

ACRONYMS: *T. pallidum* = *Treponema pallidum* **RESOURCES:** Case Definitions; Treatment Guidelines; Partner Services

Last updated 5/13/2026

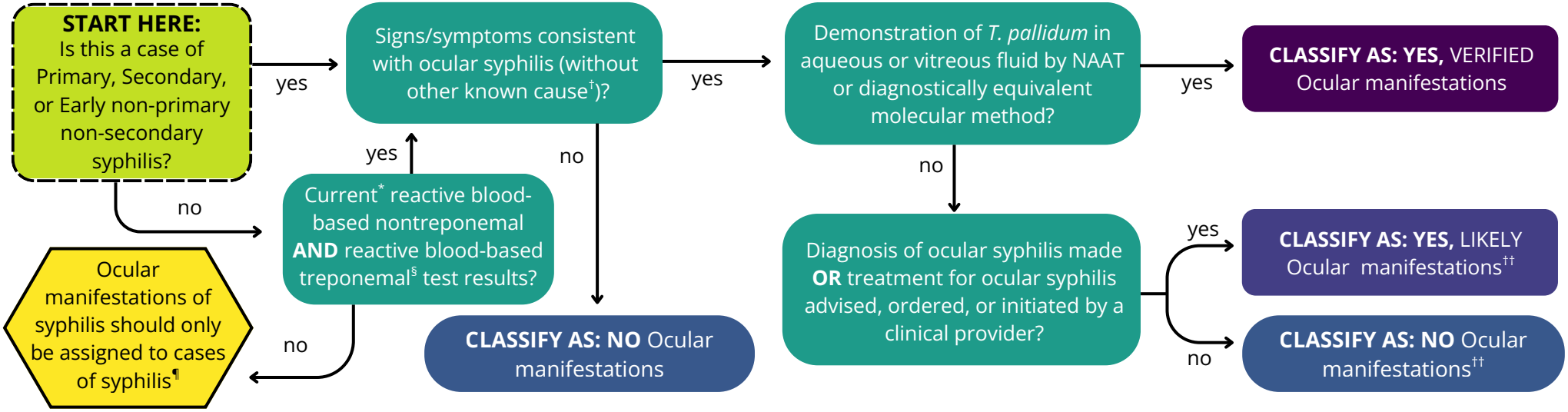
SURVEILLANCE CLASSIFICATION OF NEUROLOGIC MANIFESTATIONS OF SYPHILIS

This tool should not be used for clinical decision-making and does not supersede the syphilis surveillance case definition



SURVEILLANCE CLASSIFICATION OF OCULAR MANIFESTATIONS OF SYPHILIS

This tool should not be used for clinical decision-making and does not supersede the syphilis surveillance case definition

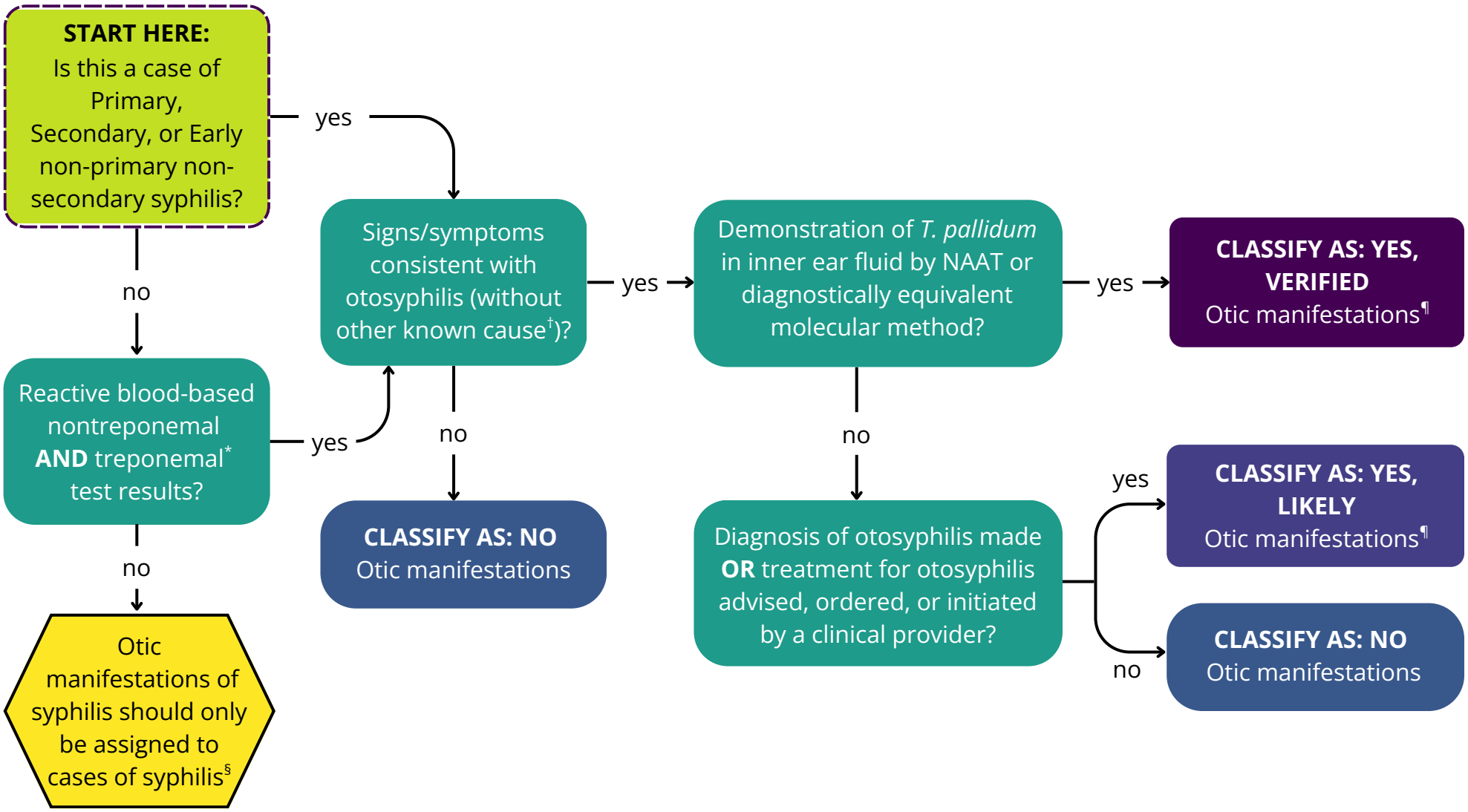


* Current refers to a test performed in the context of this index presentation.
† Clinician input may be needed to rule out other possible causes.
§ A reactive laboratory-based or point-of-care treponemal test result can be used to satisfy this requirement. Current or historical reactive treponemal antibody tests can be used to satisfy this criterion.
¶ Any previously unreported case of syphilis that meets the Likely or Verified criteria for Neurologic, Ocular, Otic, or Late clinical manifestations of syphilis and that has no evidence of having acquired the infection during the previous 12 months meets the Council of State and Territorial Epidemiologists case definition for Unknown duration or late syphilis.
** Visibly blood-contaminated CSF is defined as a CSF RBC count of ≥ 500 RBCs/µL or, in the absence of an available CSF RBC count, CSF that is described as bloody in appearance in a medical record.
†† For surveillance purposes, Ocular manifestations of syphilis are considered signs/symptoms consistent with neurosyphilis, so cases classified as having Ocular manifestations should also be classified as having Neurologic manifestations if they meet the definition for Verified or Likely Neurologic manifestations. For example, diagnosis or treatment of ocular syphilis is equivalent to diagnosis or treatment of neurosyphilis for surveillance.
ACRONYMS: CSF = cerebrospinal fluid; NAAT = nucleic acid amplification test; RBC = red blood cell; RPR = rapid plasma reagin; VDRL = Venereal Disease Research Laboratory; *T. pallidum* = *Treponema pallidum*; µL = microliter
RESOURCES: Case Definitions; Treatment Guidelines; Partner Services

Last updated 12/15/2025

SURVEILLANCE CLASSIFICATION OF OTIC MANIFESTATIONS OF SYPHILIS

This tool should not be used for clinical decision-making and does not supersede the syphilis surveillance case definition



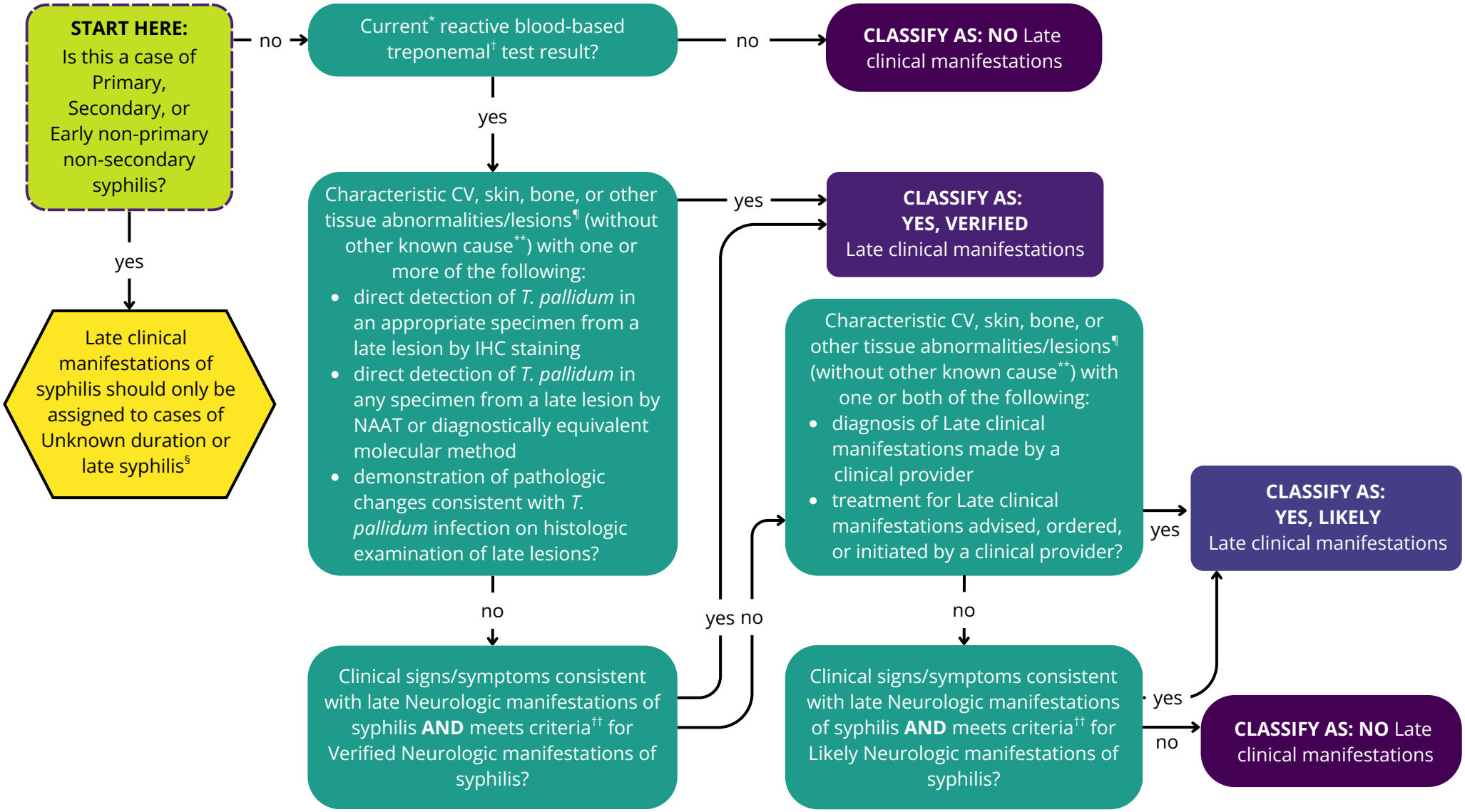
* A reactive laboratory-based or point-of-care treponemal test result can be used to satisfy this requirement. Current or historical reactive treponemal antibody tests can be used to satisfy this criterion.
† Clinician input may be needed to rule out other possible causes.
§ Any previously unreported case of syphilis that meets the Likely or Verified criteria for Neurologic, Ocular, Otic, or Late clinical manifestations of syphilis and that has no evidence of having acquired the infection during the previous 12 months meets the Council of State and Territorial Epidemiologists case definition for Unknown duration or late syphilis.
¶ For surveillance purposes, Otic manifestations of syphilis are considered signs/symptoms consistent with neurosyphilis, so cases classified as having Otic manifestations should also be classified as having Neurologic manifestations if they meet the definition for Verified or Likely Neurologic manifestations. For example, diagnosis or treatment of otosyphilis is equivalent to diagnosis or treatment of neurosyphilis for surveillance.

ACRONYMS: NAAT = nucleic acid amplification test; *T. pallidum* = *Treponema pallidum* **RESOURCES:** Case Definitions; Treatment Guidelines; Partner Services

Last updated 12/15/2025

SURVEILLANCE CLASSIFICATION OF LATE CLINICAL MANIFESTATIONS OF SYPHILIS

This tool should not be used for clinical decision-making and does not supersede the syphilis surveillance case definition



* Current refers to a test performed in the context of this index presentation.
† A reactive laboratory-based or point-of-care treponemal test result can be used to satisfy this requirement.
§ Any previously unreported case of syphilis that meets the likely or verified criteria for Neurologic, Ocular, Otic, or Late clinical manifestations of syphilis and that has no evidence of having acquired the infection during the previous 12 months meets the Council of State and Territorial Epidemiologists case definition for Unknown duration or late syphilis.
¶ Additional information about characteristic lesions associated with Late clinical manifestations of syphilis is available in CDC's STI Treatment Guidelines.
** Clinician input may be needed to rule out other possible causes.
†† Please see syphilis surveillance case definitions and the *Surveillance Classification of Neurologic Manifestations of Syphilis* algorithm for additional assistance.
ACRONYMS: CV = cardiovascular; IHC = immunohistochemistry; NAAT = nucleic acid amplification test; *T. pallidum* = *Treponema pallidum*
RESOURCES: Case Definitions; Treatment Guidelines; Partner Services

Last updated 12/15/2025

Version notes

Note: This document is a "living document," and updates will be made as needed. When updates are made, the "Last updated" date will be modified in the edited section to reflect the date the updates were made.

Version 2025_v1 – initial version drafted & released in December 2025

Version 2026_v1.1 – "yes" arrow added connecting the "Meets the definition for Verified or Likely Neurologic, Ocular, Otic, and/or Late clinical manifestations?" and "**STAGE AS:** Unknown duration or late syphilis; **CASE CLASSIFICATION:** Probable" boxes in the bottom right corner of the algorithm entitled "**ACQUIRED SYPHILIS SURVEILLANCE STAGING WHEN SIGNS OF PRIMARY OR SECONDARY SYPHILIS NOT PRESENT**"

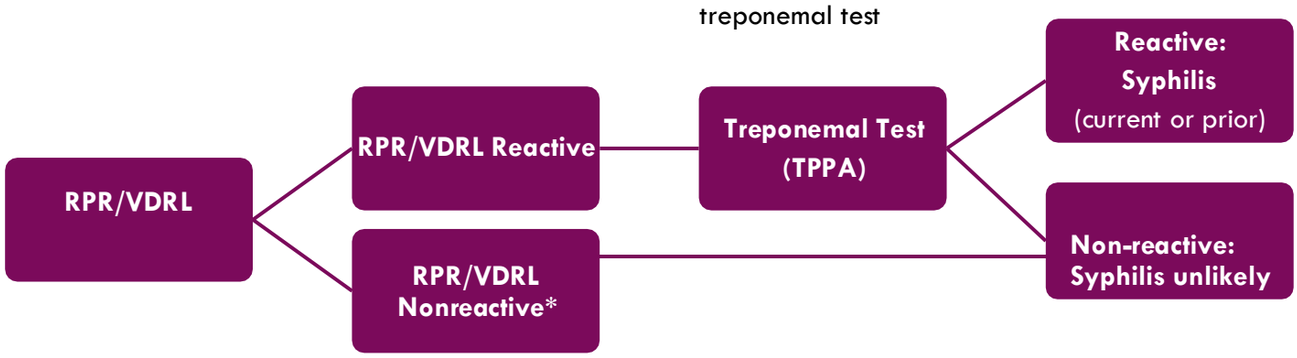
Appendix B

Clinical Interpretation of Syphilis Screening Algorithms

Testing: Traditional Algorithm[a]

1. Screen with non-treponemal test (RPR/VDRL)

2. Confirm reactive non-treponemal test with treponemal test



*Early primary syphilis and late untreated syphilis possible if RPR/VDRL are nonreactive; see below for recommended actions

Table 1: Interpretation of Syphilis Serologies, Traditional Algorithm

Non-Treponemal (RPR/VDRL)	Treponemal (TPPA)	Possible Interpretations	Recommended Actions
Nonreactive	Nonreactive or not done	1. No syphilis 2. Early/incubating syphilis (too early to be detected by serology)	▪ If syphilis unlikely, no further action needed. ▪ If early syphilis suspected, consider ordering a treponemal test (if not done initially) and repeating an RPR/VDRL in 1-2 weeks; if either test is reactive, treat for syphilis. ▪ If concerned for early syphilis (e.g., chancre present or known exposure) treat presumptively. If treating presumptively, repeat RPR/VDRL on day of treatment and, if nonreactive, again in 2-4 weeks to assess for seroconversion.
	Reactive	1. Prior treated syphilis 2. Untreated syphilis	▪ Treponemal tests (e.g., TPPA) often stay reactive for life; if patient has a history of adequate treatment for syphilis & no new exposures/ symptoms, no further action needed. ▪ If early syphilis suspected (e.g., chancre present or known exposure), treat presumptively according to stage. If treating presumptively, repeat RPR/VDRL on day of treatment and, if nonreactive, again in 2-4 weeks to assess for seroconversion. ▪ If no signs or symptoms, order a second treponemal test (e.g., EIA or CIA); see table 2 for recommendations based on results.
Reactive	Nonreactive	1. False positive RPR or VDRL	▪ Likely false positive (not syphilis).[b] ▪ In pregnancy or in patients at high risk for syphilis, consider rescreening with serologic testing in 2-4 weeks – if unchanged, no action needed.[c]
	Reactive	1. Current syphilis 2. Treated syphilis with residual/ persistent RPR/VDRL titer	▪ If RPR/VDRL is newly reactive, stage and treat. ▪ If previously treated and sustained (≥2 weeks) 4-fold rise in RPR/VDRL titer, manage as treatment failure versus re-infection.[d] ▪ Note that RPR/VDRL may still be reactive after treatment; if there is a fourfold decline within 12-24 months, treatment is considered to have been adequate even if RPR/VDRL remains reactive. ▪ Some treated patients may have a persistent low level RPR/VDRL titer for a prolonged period; re-treatment is not necessary in the absence of new exposures or symptoms.

[a] The traditional algorithm starts with a non-treponemal test (RPR or VDRL) which, if reactive, is followed by a confirmatory treponemal test (TPPA). In interpreting serologies, it is helpful to know which testing algorithm (traditional vs reverse) is being used in your lab.

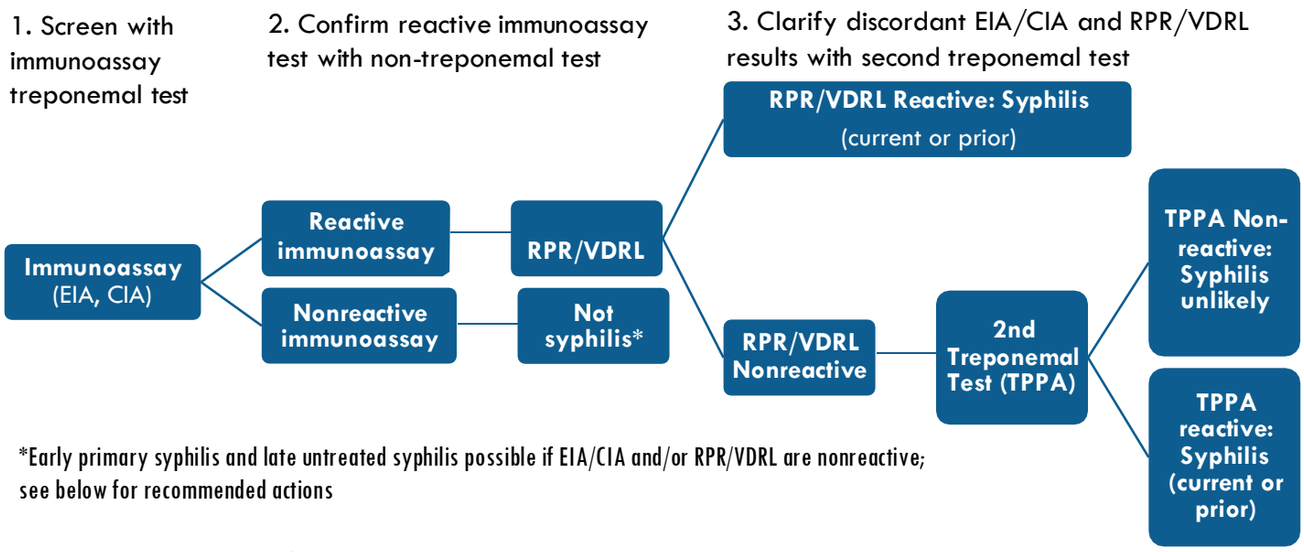
[b] False positives can be seen in pregnancy and/ in patients with autoimmune diseases, Lyme disease, certain viral infections (including HIV), injection drug use, and other conditions.

[c] In California, all pregnant people should be screened for syphilis three times during pregnancy: (1) at confirmation of pregnancy or first prenatal encounter, (2) early in the third trimester (at approximately 28 weeks gestation or as soon as possible thereafter), and (3) at delivery. The American College of Obstetrics and Gynecology also recommends screening all pregnant patients universally for syphilis three times: once at the first prenatal care visit, again during the third trimester, and again at birth.

[d] For patients determined to have new syphilis or treatment failure, refer to the Centers for Disease Control STD treatment guidelines at https://www.cdc.gov/std/treatment-guidelines/syphilis.htm for treatment and follow up recommendations.

Clinical Interpretation of Syphilis Screening Algorithms

Testing: Reverse Algorithm[a]



*Early primary syphilis and late untreated syphilis possible if EIA/CIA and/or RPR/VDRL are nonreactive; see below for recommended actions

Table 2: Interpretation of Syphilis Serologies, Reverse Screening Algorithm

Immuno-assay (CIA or EIA)	RPR/ VDRL	TPPA	Possible Interpretations	Recommended Actions
Non-reactive	Non-reactive or not done	Non-reactive or not done	1. Syphilis unlikely 2. Early/incubating syphilis (too early to be detected by serology)	▪ If syphilis unlikely, no further action needed. ▪ If immunoassay nonreactive but high clinical suspicion (such as a chancre or known exposure), treat presumptively for early syphilis. If treating presumptively, obtain RPR/VDRL on day of treatment and, if nonreactive, again in 2-4 weeks to assess for seroconversion.
Reactive	Non-reactive	Non-reactive or not done	1. False positive immunoassay 2. Early/incubating syphilis 3. Latent or prior syphilis (treated or untreated)	▪ If no signs/symptoms and low risk for syphilis, most likely a false positive immunoassay.[b] No further action needed. ▪ If concerned for early infection or in pregnant patients, re-screen in 2-4 weeks.[c] ▪ If signs/symptoms or contact to syphilis, treat presumptively. Repeat RPR/VDRL on day of treatment and, if nonreactive, again in 2-4 weeks to assess for seroconversion.
		Reactive	1. Latent or prior syphilis (treated or untreated) 2. Early syphilis (prior to RPR/VDRL seroconversion)	▪ No further action needed if patient treated appropriately for syphilis in past, assuming no new exposures/symptoms and a negative clinical exam. ▪ If no symptoms and no known prior adequate treatment, treat presumptively for latent syphilis. ▪ If early syphilis suspected (symptoms or known exposure), treat presumptively. Obtain RPR/VDRL on day of treatment. If nonreactive, repeat in 2-4 weeks to assess for seroconversion.
	Reactive	Not done or Reactive	1. Current syphilis 2. Prior syphilis (treated or untreated)	▪ If RPR/VDRL is newly reactive, stage and treat. ▪ If previously treated and sustained (≥2 weeks) 4-fold rise in RPR/VDRL titer, manage as treatment failure versus re-infection.[d] ▪ If known prior adequate treatment for stage of infection and RPR/VDRL declining appropriately (i.e., a fourfold decline within 12-24 months), no further action needed. ▪ Some treated patients may have a persistent low level RPR/VDRL titer for a prolonged period; re-treatment is not necessary in the absence of new exposures or symptoms.

[a] The reverse algorithm starts with an immunoassay detecting syphilis antibodies which, if reactive, is followed by an RPR/VDRL. If there is a discrepancy between the immunoassay and RPR (one reactive, one nonreactive), a treponemal test (TPPA) serves as the tie-breaker. In interpreting serologies, it is helpful to know which testing algorithm (traditional vs reverse) is being used in your lab.

[b] False positive immunoassays can occur with Lyme disease or non-syphilis treponemal infections.

[c] In California, all pregnant people should be screened for syphilis three times during pregnancy: (1) at confirmation of pregnancy or first prenatal encounter, (2) early in the third trimester (at approximately 28 weeks gestation or as soon as possible thereafter), and (3) at delivery. The American College of Obstetrics and Gynecology also recommends screening all pregnant patients universally for syphilis three times: once at the first prenatal care visit, again during the third trimester, and again at birth.

[d] For patients determined to have new syphilis or treatment failure, refer to the Centers for Disease Control STD treatment guidelines at https://www.cdc.gov/std/treatment-guidelines/syphilis.htm for treatment and follow up recommendations.

Syphilis in Pregnancy

Investigative Guidelines
September 2026

1. DISEASE REPORTING

1.1 Purpose of Reporting and Surveillance

1. Identify cases of syphilis in pregnancy and prevent vertical transmission
2. Ensure adequate treatment and follow-up for pregnant people with syphilis and the infant
3. Ensure appropriate management, including screening and presumptive treatment, of sexual contacts
4. Describe the epidemiology of syphilis in pregnancy in Oregon

1.2 Laboratory and Physician Reporting Requirements

1. Licensed laboratories must report all positive test results indicating syphilis infection to the Local Public Health Authority within one working day (OAR 333-018-0000; 333-018-0015)[1]
2. Clinicians must report lab-confirmed and clinically suspect cases of syphilis to the Local Public Health Authority within one working day (OAR 333-018-0000; 333-018-0015)[1]
   - Oregon Revised Statute (ORS) 433.017 requires individuals attending a pregnant patient to collect or order the collection of a blood specimen for submission to a licensed laboratory to test for syphilis and selected other infections, unless the pregnant patient declines testing (OAR 333-019-0036)[2,3]
   - Oregon Health Authority recommends that all pregnant people be tested for syphilis three times: 1) at the first prenatal visit or presentation to care, 2) at 28 weeks' gestation, and 3) at delivery
3. Health care providers, health care facilities, and licensed laboratories shall cooperate with public health authorities in the investigation and control of syphilis infections (OAR 333-019-0002)[3]

1.3 Local Public Health Authority Reporting and Follow-up Responsibilities

1. LPHA must begin follow-up case investigation within two working days of receiving the initial provider or laboratory report
2. LPHA must report all cases to the OHA STD Program through the Oregon Public Health Epidemiology User System (Orpheus) by the end of the calendar week of initial provider or laboratory report (OAR 333-018-0020)[1]

3. LPHA must conduct case investigations and manage sexual contacts by following procedures outlined in these Investigative Guidelines (ORS 433.006, OAR 333-019-0000)[2,3]

2. DISEASE AND EPIDEMIOLOGY

2.1 Etiologic Agent

The etiologic agent in syphilis is *Treponema pallidum* subspecies *pallidum*, a spirochete (corkscrew-shaped) bacterium.

Of all the subspecies of *T. pallidum*, only *T. pallidum* subsp. *pallidum* is transmitted routinely by sexual contact. The other *T. pallidum* subspecies are transmitted non-sexually (e.g., yaws, pinta).

2.2 Description of Illness

Syphilis is called “the great imitator” because many of the signs and symptoms mimic those of other diseases. If untreated, syphilis infection progresses through stages that are often separated by periods without any symptoms (latency). Neurosyphilis, ocular syphilis, and otosyphilis can occur at any stage of infection. See **Figure 1** for a graphical summary of the natural history of syphilis.

During the incubation period, before clinical signs or symptoms appear, *T. pallidum* can spread to the circulatory, lymphatic, and central nervous systems.

Early Syphilis: clinical manifestations mainly involve the skin and mucosal surfaces, although secondary syphilis often has systemic manifestations.

- **Primary syphilis**
  - A chancre is the defining feature of primary syphilis. A chancre is a small round or oval ulcerated lesion with a smooth base and firm raised borders that appears where *T. pallidum* entered the body:
    - Most commonly appear on the penis, labia, perianal area, or mouth
    - May go unnoticed, especially if located inside the vagina, foreskin, or rectum
    - Resolve spontaneously within a few weeks, even without treatment
  - Classic primary syphilis is defined by a single chancre BUT multiple chancres are common and can be painful (multiple chancres on genitals are often misdiagnosed as herpes simplex virus [HSV] infection)
  - Syphilitic balanitis of Follmann (SBF, or Follmann balanitis) is a rare manifestation of primary syphilis thought to be present in less than 0.5% of cases of primary syphilis. SBF typically involves balanitis (inflammation of the glans penis) or balanoposthitis (inflammation of the glans penis and foreskin) with inguinal lymphadenopathy and may present with or without chancres
- **Secondary syphilis**

    - Skin and mucous membrane lesions are the defining feature of secondary syphilis. A lesion is an area of abnormal tissue anywhere in or on the body. While chancres are the only type of lesion associated with primary syphilis, different lesions are found in secondary syphilis:
        - Rashes can appear anywhere on the body, vary widely in appearance, and do not usually cause itching. The classic secondary rash appears on the palms of hands and soles of feet and often the torso
        - Other secondary lesions may include:
            - Mucous patches in the mouth or genital area
            - Condyloma lata, usually in the genital or rectal area
            - Alopecia
    - Symptoms generally appear about 4 to 10 weeks after the onset of the primary chancre (chancres may still be present when secondary symptoms develop)
    - Widespread dissemination of *T. pallidum* throughout the body via the bloodstream causes fever, headaches, muscle aches, malaise, and lymphadenopathy
    - Even without treatment, lesions and symptoms typically resolve spontaneously within a few weeks, but can persist for months
    - If untreated, secondary symptoms can reappear after a latency period

Latent Syphilis: characterized by the persistence of *T. pallidum* in the body without clinical signs or symptoms.

- **Early non-primary non-secondary (early latent) stage**:
    - Occurs when an individual is asymptomatic and there is evidence that the infection was acquired in the 12 months prior to diagnosis
    - Can occur between the primary and secondary stages, after the secondary stage, or between secondary relapses
- **Late or unknown duration (late latent) stage**:
    - Occurs when an individual is asymptomatic and the infection was acquired more than 12 months prior to diagnosis **OR** the time of infection cannot be determined with certainty

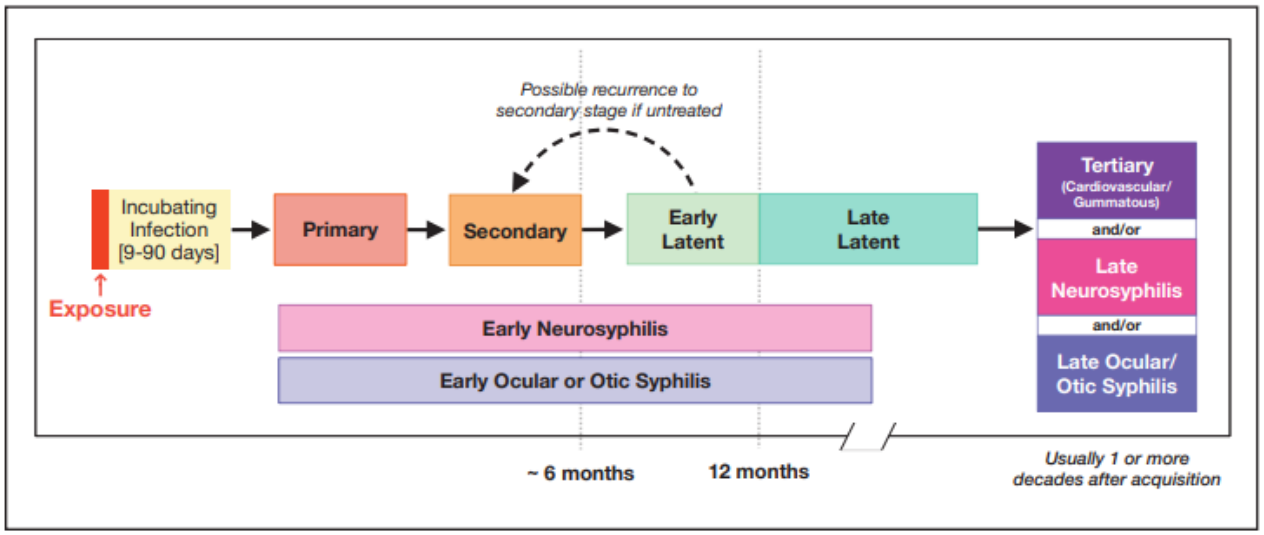
Neurosyphilis, Ocular Syphilis, and Otic Syphilis: clinical manifestations that can occur during any stage.

- **Neurosyphilis** can manifest as meningitis or stroke, cognitive dysfunction, motor or sensory deficits, and/or cranial nerve palsies
- **Ocular syphilis** can involve any eye structure but usually manifests as panuveitis or posterior uveitis
    - May cause permanent vision loss
    - Occurs with or without neurosyphilis
- **Otosyphilis** can manifest as hearing loss, tinnitus, and/or vertigo
    - May cause permanent hearing loss
    - Occurs with or without neurosyphilis

Late Clinical Manifestations (Tertiary Syphilis)

- Usually only develop after 15–30 years of untreated infection
- Can affect virtually any organ system including the cardiovascular system, central nervous system, and skin

Figure 1. The Natural History of Untreated Syphilis



Source: New York City Department of Health and Mental Hygiene, and the New York City STD Prevention Training Center. The Diagnosis and Management of Syphilis: An Update and Review. March 2019. Available at www.nycptc.org

2.3 Reservoirs

Humans

2.4 Modes of Transmission

Sexual transmission:

- *T. pallidum* enters the body via skin and mucous membranes through abrasions during sexual contact
- Persons are infectious throughout the primary and secondary stages, when lesions are present
- Usually results from contact with genital mucous membranes, but it can also occur from contact with the mouth, rectum, and cutaneous lesions

Vertical transmission:

- Results in fetal infection
- Occurs primarily via transplacental passage of *T. pallidum*
- Can occur during any stage of syphilis
- Can also occur on contact with genital syphilis lesions at the time of delivery

Other forms of syphilis transmission are rare. Transfusion-associated syphilis has been virtually eliminated in the United States and transmission through needle-sharing is infrequent.

2.5 Incubation Period

The earliest sign of syphilis, a primary chancre, usually appears about 2 to 3 weeks after *T. pallidum* infection. Blood tests usually detect infection within 21 days of exposure but may take up to 6 weeks to show seroconversion.

2.6 Period of Communicability

Syphilis is spread by sexual contact—it is not spread through casual contact such as shaking hands. A person acquires syphilis when their mucous membranes (vulva, vagina, penis, anus, mouth) come into contact with bacteria-rich lesions (chancres, rash, condyloma lata, or mucous patches). These bacteria-rich lesions occur in primary and secondary syphilis and may not be visible.

3. CASE DEFINITIONS, DIAGNOSIS, AND LABORATORY SERVICES—FOR PUBLIC HEALTH STAFF

3.1 Syphilis Stages

See the CDC Syphilis 2026 Case Definition page for more information on the stages below.[4]

Given the complexity of the syphilis surveillance case definition, public health professionals are strongly encouraged to use the CDC surveillance flowcharts for syphilis stages and clinical manifestations (see Appendix A) instead of or alongside this section to determine the appropriate surveillance stage. The information in this section and the flowcharts is identical, but the flowcharts are much easier to follow.

3.1.1 Primary Syphilis

1. Clinical Description
   - In the absence of a more likely alternative diagnosis, meets at least one of the following signs:
     - One or more ulcerative lesions (chancres) **OR**
     - Syphilitic balanitis of Follmann—a rare sign of primary syphilis involving inflammation of the glans penis (balanitis), foreskin (posthitis), or both (balanoposthitis)
2. Laboratory Criteria
   - Confirmatory: Meets at least one of the following criteria:
     - Direct detection of *T. pallidum* by darkfield microscopy in a specimen that was both not obtained from the throat and not potentially contaminated by stool **OR**

    - Direct detection of *T. pallidum* by immunohistochemistry (IHC) staining in a specimen that was both not obtained from the throat and not potentially contaminated by stool **OR**
    - Direct detection of *T. pallidum* by nucleic acid amplification test (NAAT) or a diagnostically equivalent molecular method in any specimen
- Presumptive: Meets at least one of the following criteria:
    - A current (performed in the context of this clinical evaluation) reactive blood-based nontreponemal antibody test **OR**
    - A current (performed in the context of this clinical evaluation) reactive blood-based treponemal antibody test

3. Case Classification
    - **Confirmed (rare):** Clinically compatible case with evidence of *T. pallidum* by a confirmatory direct detection method
    - **Presumptive:** Clinically compatible with at least one reactive blood-based test

3.1.2 Secondary Syphilis

1. Clinical Description
    - In the absence of a more likely alternative diagnosis, meets at least one of the following signs:
        - Localized or diffuse body rash classically described as copper-colored lesions that can be any combination of macular (flat), papular (raised), squamous (scaly), or pustular in appearance and typically involve the chest, back, palms of the hands, and/or soles of the feet **OR**
        - Mucous patches **OR**
        - Condyloma lata **OR**
        - Patchy alopecia often described as moth-eaten in appearance
2. Laboratory Criteria
    - Confirmatory: Meets at least one of the following criteria:
        - Direct detection of *T. pallidum* by darkfield microscopy in a specimen that was both not obtained from the throat and not potentially contaminated by stool **OR**
        - Direct detection of *T. pallidum* by immunohistochemistry (IHC) staining in a specimen that was both not obtained from the throat and not potentially contaminated by stool **OR**
        - Direct detection of *T. pallidum* by nucleic acid amplification test (NAAT) or a diagnostically equivalent molecular method in any specimen
    - Presumptive:
        - A current (performed in the context of this clinical evaluation) reactive blood-based nontreponemal antibody test **AND**
        - A reactive blood-based treponemal antibody test (current or historical)
    - Supportive:

    - A current (performed in the context of this clinical evaluation) reactive blood-based nontreponemal antibody test with a titer ≥1:32 **AND**
    - No evidence of a concurrent nonreactive blood-based treponemal antibody test

3. Case Classification
    - **Confirmed (rare):** Clinically compatible case with evidence of *T. pallidum* by a confirmatory direct detection method
    - **Presumptive:** Clinically compatible case with **either** reactive nontreponemal and treponemal antibody tests **or** a titer ≥1:32 with no evidence of a nonreactive treponemal antibody test

3.1.3 Early Non-Primary Non-Secondary Syphilis

Stage of infection with *T. pallidum* in which there is evidence that the infection occurred within the previous 12 months AND there are no signs or symptoms of primary or secondary syphilis

1. Clinical Description
    - Documented history of syphilis, usually defined as evidence that the person was previously diagnosed and treated for syphilis AND a previous nontreponemal test titer is available
2. Laboratory Criteria
    - Confirmatory:
        - Direct detection of *T. pallidum* by nucleic acid amplification test (NAAT) or a diagnostically equivalent molecular method in any specimen
    - Presumptive:
        - A current (performed in the context of this clinical evaluation) reactive blood-based nontreponemal antibody test **AND**
        - A reactive blood-based treponemal antibody test (current or historical)
    - Supportive:
        - A current (performed in the context of this clinical evaluation) reactive blood-based nontreponemal antibody test **AND**
        - No evidence of a concurrent nonreactive blood-based treponemal antibody test
3. Evidence of Infection Acquired During Previous 12 Months:
    - No documented history of syphilis AND has evidence of seroconversion of a blood-based nontreponemal antibody or treponemal antibody test in a specimen collected during the previous 12 months **OR**
    - Documented history of syphilis AND has evidence of a current titer demonstrating a fourfold or greater increase in a specimen collected during the previous 12 months (see **Figure 2**) **OR**
    - Signs/symptoms consistent with primary or secondary syphilis during the previous 12 months **OR**

- Fourfold or greater increase in titer from a specimen collected between the initial specimen collection date and the treatment initiation date (see **Figure 2**) **OR**
- Sexual exposure to a partner during the past 12 months who had primary, secondary, or early non-primary non-secondary syphilis (partner's stage must be documented in medical records and/or Orpheus) **OR**
- Only sexual contact ever was during the past 12 months

4. Case Classification
   - **Confirmed (rare):** Meets confirmatory laboratory evidence AND meets evidence of infection acquired in previous 12 months
   - **Presumptive:**
     - No documented history of syphilis AND meets *presumptive* laboratory evidence AND meets evidence of infection acquired in previous 12 months **OR**
     - Documented history of syphilis AND meets *supportive* laboratory evidence AND meets evidence of infection acquired in previous 12 months

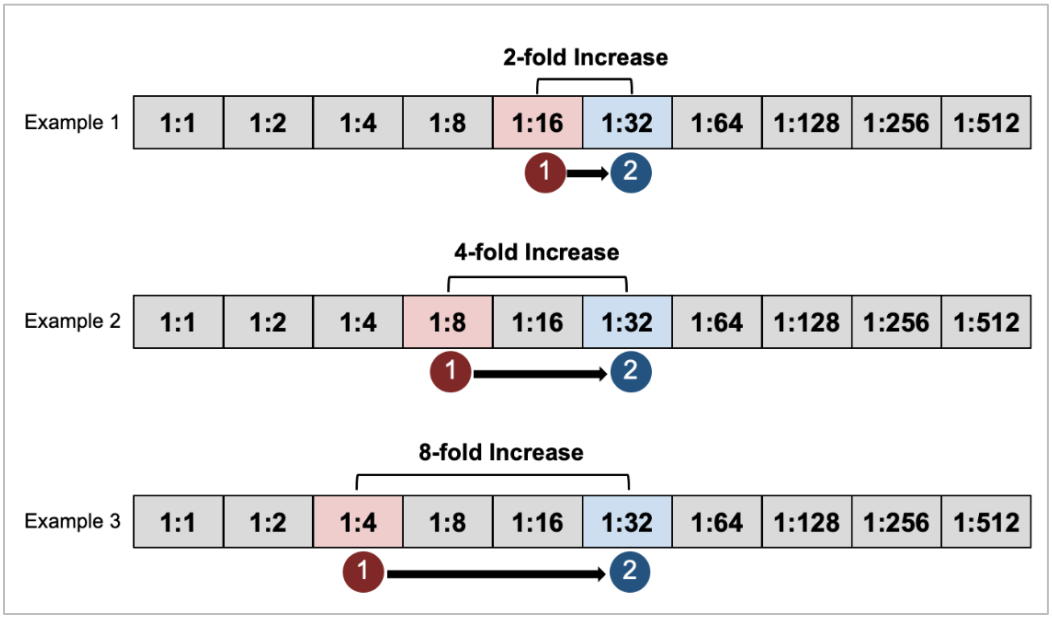
3.1.4 Unknown Duration or Late Syphilis

Stage of infection with *T. pallidum* in which the infection occurred more than 12 months prior or there is insufficient evidence to conclude the infection was acquired within the previous 12 months AND there are no signs or symptoms of primary or secondary syphilis

1. Clinical Description
   - Documented history of syphilis, usually defined as evidence that the person was previously diagnosed and treated for syphilis AND a previous nontreponemal test titer is available
2. Laboratory Criteria
   - Confirmatory:
     - Direct detection of *T. pallidum* by immunohistochemistry (IHC) staining in a specimen that was both not obtained from the throat and not potentially contaminated by stool **OR**
     - Direct detection of *T. pallidum* by nucleic acid amplification test (NAAT) or a diagnostically equivalent molecular method in any specimen
   - Presumptive:
     - A current (performed in the context of this clinical evaluation) reactive blood-based nontreponemal antibody test **AND**
     - A reactive blood-based treponemal antibody test (current or historical)
   - Supportive:
     - A current (performed in the context of this clinical evaluation) reactive blood-based nontreponemal antibody test **AND**
     - No evidence of a concurrent nonreactive blood-based treponemal antibody test
3. Case Classification

- **Confirmed (rare):** No evidence of having acquired the infection within the preceding 12 months AND meets confirmatory laboratory evidence
- **Presumptive:**
  - No documented history of syphilis AND meets *presumptive* laboratory evidence AND no evidence of having acquired the infection within the preceding 12 months (see *Evidence of Infection Acquired During Previous 12 Months* in §3.1.3) **OR**
  - Documented history of syphilis AND meets *supportive* laboratory evidence AND no evidence of having acquired the infection within the preceding 12 months (see *Evidence of Infection Acquired During Previous 12 Months* in §3.1.3) **OR**
  - Does not otherwise meet the case definition for any other stage of syphilis as described above AND no evidence of having acquired the infection within the preceding 12 months (see *Evidence of Infection Acquired During Previous 12 Months* in §3.1.3) AND meets the definition for likely or verified neurologic, ocular, otic, or late clinical manifestations of syphilis

*Figure 2. Examples of Increases in Nontreponemal Titers**



* This graphic shows three examples of increases in nontreponemal titers when comparing two tests. Test number 1 is represented as red and test number 2 as blue. Illustration by David H. Spach, MD. Figure from National STD Curriculum Syphilis Quick Reference.

† For surveillance purposes, among people with a history of syphilis who were treated and then have a nonreactive nontreponemal test result, a fourfold or greater increase in titer is defined as a change from a nonreactive result to a reactive result with a titer of 1:4 or greater.

3.2 Syphilis Complications

See the CDC 2026 Syphilis Surveillance Case Definition page for more information on the manifestations below. Note that for Orpheus documentation of these conditions, LPHA staff are only expected to select the criteria that are

met—it is not necessary to know the classification category (e.g., possible, likely, or verified). Refer to the Syphilis Case Report and Data Entry Manual for guidance on Orpheus documentation.

3.2.1 Neurologic Manifestations

Neurosyphilis can occur at any stage of syphilis. A case should be staged appropriately and neurological manifestations, if present, should be documented in the case record.

1. Neurologic Clinical Criteria
   - Has clinical signs/symptoms consistent with infection of the central nervous system with *T. pallidum*, as shown by manifestations including syphilitic meningitis, meningovascular syphilis, tabes dorsalis, or general paresis, without other clear causes for these clinical abnormalities
   - Symptoms include: severe headache; muscle weakness or paralysis; numbness; changes in mental status (trouble focusing, confusion, personality changes); and dementia (problems with memory, thinking, and/or making decisions)
2. Neurologic Laboratory Criteria
   - A reactive CSF VDRL or CSF RPR test in the absence of visibly blood-contaminated CSF (CSF red blood cell count of ≥500 RBCs/µL or, in the absence of a CSF RBC count, CSF described as bloody in appearance) **OR**
   - Direct detection of *T. pallidum* in CSF by nucleic acid amplification test (NAAT) or a diagnostically equivalent molecular method
3. Classification of Neurologic Manifestations
   - **Likely:**
     - Meets the case definition for primary, secondary, or early non-primary non-secondary syphilis AND meets neurologic clinical criteria AND a diagnosis of neurosyphilis was made by a clinical provider or treatment for neurosyphilis was advised, ordered, or initiated by a clinical provider **OR**
     - Has a reactive blood-based treponemal antibody test result (current or historical) AND a current (performed in the context of this clinical evaluation) reactive blood-based nontreponemal antibody test AND meets neurologic clinical criteria AND a diagnosis of neurosyphilis was made by a clinical provider or treatment for neurosyphilis was advised, ordered, or initiated by a clinical provider
   - **Verified:**
     - Meets the case definition for primary, secondary, or early non-primary non-secondary syphilis AND meets neurologic clinical criteria AND meets neurologic laboratory criteria **OR**
     - Has a reactive blood-based treponemal antibody test result (current or historical) AND a current (performed in the context of this clinical evaluation) reactive blood-based nontreponemal antibody test AND meets neurologic clinical criteria AND meets neurologic laboratory criteria

3.2.2 Ocular Manifestations

Ocular syphilis can occur at any stage of syphilis. A case should be staged appropriately and ocular manifestations, if present, should be documented in the case record.

1. Ocular Clinical Criteria
    - Has clinical signs/symptoms consistent with infection of any eye structure with *T. pallidum*, as shown by manifestations including posterior uveitis, panuveitis, anterior uveitis, conjunctivitis, optic neuropathy, retinal vasculitis, and interstitial keratitis, without other clear causes for these clinical abnormalities. **Ocular syphilis may lead to permanent decreases in vision, including permanent blindness.**
    - Symptoms include: eye pain or redness, light sensitivity, floating spots in the field of vision (“floaters”), and changes in vision (blurry vision or vision loss)
2. Ocular Laboratory Criteria
    - Direct detection of *T. pallidum* in aqueous or vitreous fluid by nucleic acid amplification test (NAAT) or diagnostically equivalent molecular method
3. Classification of Ocular Manifestations
    - **Likely:**
        - Meets the case definition for primary, secondary, or early non-primary non-secondary syphilis AND meets ocular clinical criteria AND a diagnosis of ocular syphilis was made by a clinical provider or treatment for ocular syphilis was advised, ordered, or initiated by a clinical provider **OR**
        - Has a reactive blood-based treponemal antibody test result (current or historical) AND a current (performed in the context of this clinical evaluation) reactive blood-based nontreponemal antibody test AND meets ocular clinical criteria AND a diagnosis of ocular syphilis was made by a clinical provider or treatment for ocular syphilis was advised, ordered, or initiated by a clinical provider
    - **Verified:**
        - Meets the case definition for primary, secondary, or early non-primary non-secondary syphilis AND meets ocular clinical criteria AND meets ocular laboratory criteria **OR**
        - Has a reactive blood-based treponemal antibody test result (current or historical) AND a current (performed in the context of this clinical evaluation) reactive blood-based nontreponemal antibody test AND meets ocular clinical criteria AND meets ocular laboratory criteria

3.2.3 Otic Manifestations

Otosyphilis can occur at any stage of syphilis. A case should be staged appropriately and otic manifestations, if present, should be documented in the case record.

1. Otic Clinical Criteria
    - Has clinical signs/symptoms consistent with infection of the cochleovestibular system with *T. pallidum*, as shown by manifestations

including tinnitus, vertigo, and sensorineural or conductive hearing loss that can be permanent, without other clear causes for these clinical abnormalities
    - Symptoms include hearing loss; tinnitus (ringing, buzzing, roaring, or hissing in the ears); balance difficulties; and dizziness or vertigo
2. Otic Laboratory Criteria
    - Direct detection of *T. pallidum* in inner ear fluid by nucleic acid amplification test (NAAT) or diagnostically equivalent molecular method
3. Classification of Otic Manifestations
    - **Likely:**
        - Meets the case definition for primary, secondary, or early non-primary non-secondary syphilis AND meets otic clinical criteria AND a diagnosis of otosyphilis was made by a clinical provider or treatment for otosyphilis was advised, ordered, or initiated by a clinical provider **OR**
        - Has a reactive blood-based treponemal antibody test result (current or historical) AND a current (performed in the context of this clinical evaluation) reactive blood-based nontreponemal antibody test AND meets otic clinical criteria AND a diagnosis of otosyphilis was made by a clinical provider or treatment for otosyphilis was advised, ordered, or initiated by a clinical provider
    - **Verified:**
        - Meets the case definition for primary, secondary, or early non-primary non-secondary syphilis AND meets otic clinical criteria AND meets otic laboratory criteria **OR**
        - Has a reactive blood-based treponemal antibody test result (current or historical) AND a current (performed in the context of this clinical evaluation) reactive blood-based nontreponemal antibody test AND meets otic clinical criteria AND meets otic laboratory criteria

3.2.4 Late Clinical Manifestations (extremely rare)

Late clinical manifestations of syphilis (tertiary syphilis) usually develop only after a period of 10 or more 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 documented in the case report.

1. Late Clinical Criteria
    - In the absence of other clear causes for the clinical abnormalities—characteristic abnormalities or inflammatory lesions of the cardiovascular system (e.g., aortitis, coronary vessel disease), skin (gummatous lesions), bone (osteitis), or other tissues/structures (e.g., upper and lower respiratory tracts, mouth, eye, abdominal organs, reproductive organs, lymph nodes, central nervous system, and skeletal muscle)
2. Late Clinical Laboratory Criteria

a. Direct detection of *T. pallidum* by immunohistochemistry (IHC) staining in a specimen from a late lesion that was both not obtained from the throat and not potentially contaminated by stool **OR**
b. Direct detection of *T. pallidum* by nucleic acid amplification test (NAAT) or a diagnostically equivalent molecular method in any specimen from a late lesion **OR**
c. Demonstration of pathologic changes that are consistent with *T. pallidum* infection on histologic examination of late lesions

3. Classification of Late Clinical Manifestations of Syphilis
   - **Likely:**
     - Has a current (performed in the context of this clinical evaluation) reactive blood-based nontreponemal antibody test AND meets late clinical criteria AND a diagnosis of late clinical manifestations was made by a clinical provider or treatment for late clinical manifestations was advised, ordered, or initiated by a clinical provider **OR**
     - Clinical signs/symptoms consistent with late neurologic manifestations of syphilis (i.e., general paresis or tabes dorsalis) in a case that meets the criteria for likely neurologic manifestations of syphilis (see §3.2.1)
   - **Verified:**
     - Has a current (performed in the context of this clinical evaluation) reactive blood-based treponemal antibody test AND meets late clinical criteria AND meets late clinical laboratory criteria **OR**
     - Clinical signs and symptoms consistent with late neurologic manifestations of syphilis (i.e., general paresis or tabes dorsalis) in a case that meets the criteria for verified neurologic manifestations of syphilis (see §3.2.1)

3.3 Diagnosis

3.3.1 Direct Detection of *T. Pallidum*

The syphilis surveillance case definition lists multiple test types in the laboratory criteria sections. The inclusion of direct detection tests for *T. pallidum* in the syphilis surveillance case definition is intended to ensure that results of these tests can be utilized for staging surveillance cases of syphilis when they are available. However, including these methods was not intended to suggest that they are “preferred” over more traditional laboratory diagnostics for syphilis, such as serologic testing. Most syphilis surveillance cases will continue to be classified as Presumptive cases given the currently limited availability of direct detection testing in the United States. Additional information about direct detection methods for the diagnosis of syphilis is available in the CDC Laboratory Recommendations for Syphilis Testing.

3.3.2 Serological Tests for Syphilis

Refer to **Table 1** for information and frequently asked questions about nontreponemal and treponemal serological tests for syphilis. The California PTC Clinical Interpretation of Syphilis Screening Algorithms Resource for Local Health Jurisdictions (see Appendix B) includes descriptions of the traditional and reverse syphilis screening algorithms and results.

Table 1. Frequently Asked Questions about Nontreponemal and Treponemal Tests

FAQ	***Nontreponemal Tests***	***Treponemal Tests***
What are the common test names?	The two nontreponemal tests are the rapid plasma reagin (RPR) and the VDRL. The RPR is the most common nontreponemal serological (blood) test. The VDRL is mainly used for CSF testing. Refer to **Table 2** for examples of syphilis test names on lab reports.	There are several types of treponemal tests, including enzyme or chemiluminescence immunoassays (EIA/CIA); *Treponema pallidum* particle agglutination assay (TP-PA); and fluorescent treponemal antibody absorption test (FTA). Refer to **Table 2** for examples of syphilis test names on lab reports.
Is the test specific to syphilis?	No. “Nontreponemal” means the antibodies detected by these tests are not responding to treponemal bacteria. Biologic false positive results can be due to many causes, such as pregnancy, autoimmune diseases, and HIV.	Yes. Treponemal tests detect antibodies specific to *T. pallidum*.
Is the test qualitative or quantitative?	Both. An initial nontreponemal result is qualitative. If reactive, it reflexes to a quantitative result known as a titer. The titer is the measurement of antibodies through diluting a person’s blood to determine the highest dilution at which a reactive result is still produced. A 1:2 titer indicates a low concentration of antibodies, as none were detected after only two dilutions. A 1:128 titer indicates a high concentration of antibodies, as none were detected after eight dilutions.	Treponemal test results are qualitative. If a numerical value is reported with a reactive result (e.g., FTA 4+), the number should be ignored. If only a numerical value is reported, there should be a comment/note on the ELR or lab report advising how to interpret the value qualitatively.
How soon does the test become positive?	Nontreponemal tests will typically be reactive by 21 days after infection.	Treponemal tests will typically be reactive by 21 days after infection. EIA/CIA and TP-PA tests may become positive sooner than nontreponemal tests.
Can the test be used to monitor for treatment	Yes. A baseline titer should be done on or as close to the day of	No. Treponemal tests usually remain positive for life, even after

response and reinfection?	treatment initiation as possible so that treatment response can be determined accurately. Only titers of the same nontreponemal test type should be compared.	treatment. They are not useful for monitoring treatment response or diagnosing a new infection in anyone with syphilis history.
Does the test become negative after treatment?	Nontreponemal tests often become negative after treatment, but it is also common for a low titer to persist for life (known as serofast state). Even without treatment, titers drop over time. A negative nontreponemal test result is not a goal of treatment.	No. See above.
How should equivocal/indeterminate results be handled?	If the traditional screening algorithm is followed, an equivocal/indeterminate RPR result should be followed by a treponemal test. If the reverse screening algorithm is followed, a second treponemal test may be necessary.	No matter which screening algorithm is used, a second treponemal test may be necessary if the first treponemal test result is equivocal/indeterminate.

Table 2. Examples of Syphilis Test Names on Lab Reports

	Test Type	**Examples of Test Names on Lab Reports**
Nontreponemal Tests (qualitative and quantitative)	RPR	RPR Ser Ql RPR Ser Titr RPR Titer
	VDRL	VDRL Ser Ql VDRL Quantitative
Treponemal Tests (qualitative only)	FTA	FTA-ABS T pallidum Ab Ser Ql IF
	TPPA	TPPA TP-PA T pallidum Ab Particle Agglutination
	EIA/CIA*	Syphilis TP T pallidum Ab Ser Ql T pallidum Ab Ser Ql IA T pallidum IgG+IgM Ser Ql IA Treponemal AB IgG Treponemal AB TOT

* If labs with the same specimen date include two EIA/CIA tests with different names, label the first *Trep AB 1* and the second *Trep AB 2* in Orpheus. Refer to the Syphilis Case Report and Data Entry Manual for guidance.

3.4 Services Available at Oregon State Public Health Laboratory (OSPHL)

The OSPHL conducts serologic syphilis screening using a treponemal CIA test (Syph-TP) that reflexes to an RPR. If these produce conflicting results, the TP-PA test is run as a reflex "tiebreaker" treponemal test. For patients with a history of syphilis and a recently documented (within past year) positive treponemal test, an "RPR only" should be ordered. For a visual representation of the OSPHL testing algorithm, refer to the Syphilis Testing Algorithm (pdf). Refer to the OSPHL Lab Test Menu, available at www.healthoregon.org/labtests, for additional information.

4. CASE INVESTIGATION—FOR PUBLIC HEALTH STAFF

4.1 Provider Records

- Review medical records for the visits associated with syphilis lab results to obtain clinical, treatment, and risk information
- If electronic health records are not accessible, contact the provider by phone, fax, or query letter to request the necessary information
- If appropriate, inform the provider that a public health professional will contact the patient to discuss the syphilis diagnosis
- Refer to the STD Program's Syphilis Case Report and Data Entry Manual for guidance on entering data in Orpheus

4.2 Case Interview

- All pregnant cases should be investigated and interviewed regardless of stage
- Cases with two reactive treponemal tests and a non-reactive RPR and no primary signs should be investigated (no interview needed) even though the syphilis surveillance case definition is not met—treatment for late/unknown duration syphilis is strongly recommended if there is no documentation of past adequate treatment.
- Interview methods:
  - In-person interviews are best when possible. Interviews by phone, web-based questionnaire, and other methods are also acceptable.
  - If the client cannot be reached by traditional methods (e.g., calls, texts, mailed letters, field or clinic-based visit), consider using technology-based tools such as social media sites and mobile apps to contact cases. Any method should be used in accordance with LPHA policies.
  - Refer to §4.4 for resources that can assist with locating individuals
  - Maintain client privacy throughout the case investigation and interview
  - Document all attempts to contact the client in real time when possible, or on the day of each attempt at minimum

4.3 Management of Partners

4.3.1 Interview Periods

- Sexual contacts of a person diagnosed with primary, secondary, or early non-primary non-secondary syphilis are at high risk of acquiring the infection
- Interview periods help identify partners at risk of infection. The interview period is the time from the earliest date the case could have been infected to the date of treatment.
- Refer to **Table 3** for interview periods based on the case's stage ("case" refers to a person with presumptive or confirmed syphilis)
- All partners within the appropriate interview period should be confidentially notified of the exposure and need for evaluation
- If a case has not had sex within the interview period, the most recent contact should be tested and presumptively treated if follow-up is uncertain

Table 3. Interview Periods by Stage

Stage	Interview Period
Primary	90 days before date of onset of primary chancre 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

4.3.2 Partner Notification

Partner treatment is key to preventing reinfection in pregnancy. All partners who pose a risk of reinfection during the pregnancy need to be identified and contacted so that they can be tested and presumptively treated.

- **If LPHA is handling notification:**
  - Contact named partners within two working days of the initial case interview and refer for evaluation, testing, and treatment
  - If partners cannot be reached by traditional methods (e.g., calls, texts, mailed letters, field or clinic-based visit), consider using technology-based tools such as social media sites and mobile apps to contact cases. Any method should be used in accordance with LPHA policies.
  - Try to contact partners at least three times
    - Attempts should be made on alternate days and times of day
    - Refer to §4.4 for resources that can assist with locating individuals
- **If the case chooses to notify partners:**
  - Advise the case that LPHA staff can help arrange partner testing/treatment and encourage the case to share the staff's contact information with partners
  - If possible, contact the case again to offer LPHA notification and treatment referral if partner treatment cannot be verified within a reasonable time frame (2–5 days)

4.3.3 Partner Testing/Treatment

- Partners from **within 90 days** before case's diagnosis (or onset of symptoms) of early syphilis (primary, secondary, early non-primary non-secondary syphilis):
  - Test and presumptively treat for early syphilis
  - Contacts to late or unknown duration syphilis cases that are suspicious for early infection should also be tested and presumptively treated
- Partners from **>90 days** before case's diagnosis (or onset of symptoms) of early syphilis (primary, secondary, early non-primary non-secondary syphilis):
  - Test and presumptively treat for early syphilis if follow-up is uncertain
    - If positive: stage based on clinical and serologic evaluation and treat (if not treated presumptively)
    - If negative: no treatment is needed
- Long-term partners of a case diagnosed with late/unknown duration syphilis should be evaluated for syphilis and treated based on the clinical and serological findings

4.4 Requesting Locating Searches and Out-of-State Records

1. **Locating Searches**
   If LPHA staff and the provider cannot locate a case or contact using the available contact information, there are useful resources available:
   - Request that State STD Program staff conduct an Accurint search for the person's current/recent addresses and phone numbers
     - Searches are prioritized for the following:
       - Early syphilis cases
       - Pregnant cases/contacts
       - Cases with unknown pregnancy status
   - Search Orestar to find mailing and residential addresses for Oregon residents
   - Search sites with correctional/judicial information:
     - Victim Information System in Oregon (VISOR) to see if a person is currently in a correctional facility or has been recently released
     - Oregon Department of Corrections to see if a person is in an Oregon state prison
     - Oregon Judicial Department to find information on court records, community supervision, name changes, etc.
2. **Out-of-State Records**
   - Out-of-state syphilis records should mainly be requested to:
     - Determine whether there is a new infection based on a comparison of the current and previous titers **OR**
     - Obtain documentation of past syphilis care for persons who are pregnant or pregnancy-capable
   - Clinical management should not be delayed while waiting on out-of-state records, especially if there is a risk of loss to follow-up
     - In many cases, records do not exist or are incomplete

4.5 Case/Contact Transfers and Other Orpheus Issues

Refer to the STD Program's Syphilis Case Report and Data Entry Manual for guidance on Orpheus-specific issues including transferring cases/contacts to other Oregon jurisdictions or out of state.

5. CLINICAL MANAGEMENT—FOR MEDICAL PROVIDERS

Through proper management of pregnant people and partners with syphilis, congenital syphilis can be prevented. Among pregnant people with syphilis who deliver after 20 weeks' gestation, maternal treatment with penicillin is 98% effective at preventing congenital syphilis. See the CDC 2021 STI Treatment Guidelines for detailed clinical recommendations.[5]

The OHA/AETC Prenatal Syphilis Screening, Staging, and Management Pocket Guide is a helpful tool summarizing clinical recommendations.

Since the RPR test is the most common blood-based nontreponemal antibody test, the terms "nontreponemal antibody test" and "RPR" are used interchangeably throughout this section.

5.1 Serologic Screening

- Screen all pregnant people three times in pregnancy, regardless of perceived risk:
  1. At the first prenatal visit or presentation to care
  2. At 28 weeks' gestation
  3. At delivery
- To diagnose syphilis, order a syphilis screening cascade:
  - Traditional algorithm: RPR with reflex to titer and treponemal test
  - Reverse algorithm: Treponemal test with reflex to RPR and titer

5.1.1 Interpreting Screening Algorithm Results (Note: if the initial test for either algorithm is negative, no further testing will be done)

Reactive treponemal test and reactive RPR and no documented syphilis history: Stage and treat with the appropriate penicillin-based regimen. See §5.2.

Reactive treponemal test and reactive RPR and documented history of syphilis diagnosis and treatment:

- Determine whether additional treatment is needed. If past treatment information is not readily available, treatment should be initiated while waiting for records. See §4.4 for information on requesting out-of-state records.
  - If previous treatment prior to or earlier in pregnancy was inadequate (not completed, not appropriate for stage, or not a CDC-recommended regimen): Treat with the penicillin-based regimen appropriate for the current stage of infection.

- If the current RPR titer is a fourfold or higher increase over previous titer or syphilis symptoms are present: Treat with the penicillin-based regimen appropriate for the current stage of infection.

Reactive treponemal test and nonreactive RPR: A second treponemal test (different from the first) is needed.

- **If second treponemal test is negative:** Initial reactive treponemal test is most likely a false positive. Manage as follows:
  - The provider should consider ordering repeat testing within 4 weeks to monitor for seroconversion. If both the RPR and second treponemal test remain negative, no treatment is necessary.
  - If follow-up is not likely, pregnant people with an isolated reactive treponemal test and without a history of treated syphilis should be treated with benzathine penicillin G 2.4 million units for presumptive early syphilis.
- **If second treponemal test is positive:** Either an old infection or a very early infection. If primary syphilis signs are present at time of testing, treat with the appropriate CDC-recommended regimen. If asymptomatic, proceed as follows:
  - If documentation of past completion of CDC-recommended treatment appropriate for stage: no further treatment needed.
  - If previous treatment prior was inadequate (not completed, not appropriate for stage, or not a CDC-recommended regimen): treat with the penicillin-based regimen appropriate for the current stage of infection.
  - If no documentation of treatment, or past treatment was inadequate, treat for late/unknown duration syphilis.

Reactive RPR and nonreactive treponemal test: Determine need for follow-up based on titer:

- If the RPR titer is <1:4, recommend repeat testing in one month to rule out incubating syphilis. If primary syphilis symptoms are present at time of testing, treat with benzathine penicillin G 2.4 million units.
- If the RPR titer is ≥1:4, further investigation is needed to determine risk of syphilis versus biological false positive.
  - If primary symptoms are present at the time of testing, treat with benzathine penicillin G 2.4 million units.
  - If no symptoms are present, repeat testing in one month is recommended to rule out incubating syphilis.

5.2 Treatment in Pregnancy

See the CDC 2021 STI Treatment Guidelines for detailed treatment information.[5] Refer to **Table 4** for treatment recommendations for syphilis in pregnancy.

- Penicillin G is the only effective antibiotic for treating fetal infection and preventing congenital syphilis
  - During recent Bicillin L-A shortages, the U.S. Food and Drug Administration has allowed the temporary importation of benzathine penicillin G products such as Lentocilin and

Extencilline. These are therapeutically equivalent to Bicillin L-A (i.e., dosing, treatment regimens, and follow-up monitoring are the same) though injection preparation/administration and allergy considerations may differ.
    - The Society for Maternal-Fetal Medicine supports the use of Extencilline and Lentocilin for the treatment of patients with syphilis in pregnancy *when Bicillin L-A is unavailable*. Clinical sites should contact their local and/or state health department to obtain Bicillin L-A for pregnant patients before resorting to using drugs approved by the FDA for temporary importation.
- For pregnant people with primary, secondary, or early non-primary non-secondary syphilis, a second dose of benzathine penicillin G 2.4 million units IM can be administered 1 week after the initial dose for additional protection. *This is not required.*
- **For pregnant people with unknown duration or late syphilis, the dosing interval is critical. A 7-day interval is ideal and a 6-9 day interval is acceptable. If any doses are given outside this interval, the treatment series must be restarted.** For example, if the third dose is given 10 days after the second dose, the three-dose regimen should be restarted (in this scenario, the third dose can be considered the first dose of the restarted series).

Table 4. Treatment Recommendations for Syphilis in Pregnancy

Stages	Recommended Regimen	If Penicillin Allergy*
Primary, Secondary, and Early Non-Primary Non-Secondary	Benzathine penicillin G (Bicillin L-A) 2.4 million units IM in a single dose	Skin testing for penicillin allergy and desensitization (urgent)
Unknown Duration or Late	Benzathine penicillin G (Bicillin L-A) 7.2 million units total IM as three doses of 2.4 million units each at 7-day intervals	Skin testing for penicillin allergy and desensitization (urgent)

* Approximately 10% of all U.S. patients report having a penicillin allergy. However, less than 1% of the population is truly allergic to penicillin. Refer to the CDC 2021 STI Treatment Guidelines section on managing persons who have a history of penicillin allergy.

Refer to **Table 5** for treatment recommendations for neurosyphilis, ocular syphilis, and otosyphilis in pregnant adults.

Table 5. Treatment Recommendations for Clinical Manifestations of Syphilis in Pregnancy

Clinical Manifestations	Recommended Regimen	If Penicillin Allergy

Neurosyphilis, Ocular Syphilis, or Otosyphilis	Aqueous crystalline penicillin G 18-24 million units per day, administered as 3-4 million units intravenously every 4 hours or continuous infusion, for 10-14 days	Skin testing for penicillin allergy and desensitization (urgent)

5.3 Sonographic Screening

When syphilis is diagnosed after 20 weeks' gestation, clinical management should include a sonographic fetal evaluation for congenital syphilis. This evaluation should not delay syphilis treatment.

5.4 Titer Monitoring in Pregnancy

- The main reason to check titers following syphilis treatment in pregnancy is to monitor for reinfection. Reinfection is indicated by a fourfold or higher increase in titer and/or syphilis signs/symptoms.
- A fourfold decrease in titer is unlikely before delivery following treatment during pregnancy. Titers should not be done with the expectation of achieving a fourfold decrease in titer or a nonreactive RPR before delivery.
- Titer monitoring in pregnancy:
  - **Diagnosed and treated at or before 24 weeks' gestation:**
    - Titers should NOT be repeated sooner than 8 weeks after treatment initiation. Titers can increase immediately after treatment, likely related to the treatment response. Unless primary or secondary signs appear, a follow-up titer should not be done until at least 8 weeks after treatment initiation.
    - A titer should be repeated at delivery.
    - Additional titers can be done if there are untreated partners who pose a continuing risk of reinfection during the pregnancy and/or if primary or secondary signs appear. Refer to §4.3 for guidance regarding management of sexual contacts to prevent reinfection.
  - **Diagnosed and treated after 24 weeks' gestation:**
    - A titer should be repeated at delivery.
    - There is little benefit to checking a titer following treatment and before delivery unless primary or secondary signs/symptoms are present or there are untreated partners who pose a continuing risk of reinfection during the pregnancy.
- See the Syphilis Investigative Guidelines for titer monitoring recommendations for non-pregnant adults.

6. CONTROLLING FURTHER SPREAD

6.1 Education

- Pregnant people diagnosed with syphilis should be advised to:
  - Complete treatment

    - Avoid all types of sex until treatment has been completed and any primary or secondary syphilis lesions have resolved.
    - Avoid all types of sex with untreated partners until the partners have been treated and any primary or secondary syphilis lesions have resolved
- Other key education messages for people at risk of acquiring syphilis and other STIs:
    - Use condoms as often as possible
    - Get checked for HIV and other STIs
    - Talk to partners about testing
    - Know about HIV pre- and post-exposure prophylaxis (PrEP and PEP)
        - PrEP education and referrals should be provided to anyone diagnosed with or at risk for syphilis. Refer to the OHA PrEP & PEP page for additional information.
        - Visit the AETC site for a list of PrEP providers in Oregon and southwest Washington State
    - Talk with a provider about contraceptive options if not currently seeking pregnancy
    - Utilize syringe service programs (for those using/injecting drugs)
    - Stay up to date on vaccinations as appropriate, including for HPV and hepatitis A and B

7. MANAGING SPECIAL SITUATIONS

7.1 Syphilis Case has Multiple Reportable Infections

- Check in Orpheus to see if a pregnant person diagnosed with syphilis has any other new reportable infections, especially other STI or HIV (may depend on Orpheus disease group access)
- Coordinate case investigations to reduce duplication and communication with case:
    - Combine questions for all infections in one interview session rather than having multiple people contact the case to ask different questions
    - Obtain partner information based on interview periods for each STI/HIV

7.2 Jarisch-Herxheimer Reaction

- The Jarisch-Herxheimer reaction is a flu-like reaction involving fever, headache, and muscle aches, that can occur after initiation of syphilis treatment
    - The reaction usually begins within 2 hours of treatment initiation, peaks at approximately 8 hours, and resolves in 24-36 hours
    - In most cases no treatment is required
- It is a reaction to the rapid killing of *T. pallidum* bacteria and is **not** an allergic reaction to syphilis treatment
- It occurs most often in early syphilis, likely because bacterial loads are higher during these stages

- Patients treated during the second half of pregnancy should be advised to seek obstetric care after treatment if they notice fever, contractions, or decreased fetal movement

7.3 Syphilis among Pregnant Persons Living with HIV (PLWH)

- Pregnant persons with syphilis who also have an HIV diagnosis and are not on antiretroviral therapy should be immediately linked to HIV care
  - Contact the OHA HIV Surveillance Program for assistance with these HIV cases
- Unusual syphilis test results can occur among PLWH but are rare
  - Post-treatment titers may be higher than expected (high serofast) or fluctuate
  - False-negative tests and delayed seroreactivity (detectable immune response to syphilis) have also been seen
- Treatment for all stages and for neuro/ocular/otic syphilis is the same regardless of HIV status
- All persons with HIV and syphilis coinfection should receive a careful neurologic, ocular, and otic examination
  - PLWH who have early syphilis might be at increased risk for neurologic complications
  - Ocular syphilis has been reported more frequently among PLWH

GLOSSARY

CSF: Cerebrospinal fluid. CSF testing can indicate whether there is central nervous system involvement in a syphilis infection.

Early syphilis: Any of the stages that occur in the first 12 months of infection: primary, secondary, and early non-primary non-secondary syphilis.

IM: Intramuscular. An IM injection delivers medication, such as benzathine penicillin G for syphilis, into a muscle.

PCR: Polymerase chain reaction test is a laboratory technique for rapidly producing (amplifying) many copies of a specific segment of genetic material, e.g., *T. pallidum* DNA in syphilis.

RPR: Rapid Plasma Reagin test is a nontreponemal serologic (blood) test. Unlike treponemal tests, the RPR measures antibodies that are not specific for *T. pallidum* bacteria and may be reactive due to conditions other than syphilis, including pregnancy.

Treponemal test: Treponemal tests measure antibodies directed against *T. pallidum* bacteria. Treponemal serologic (blood) tests include enzyme immunoassays (EIAs) and chemiluminescence immunoassays (CIAs), *T. pallidum* particle agglutination (TP-PA), fluorescent treponemal antibody absorption (FTA-ABS) tests, and point-of-care and self-test treponemal antibody tests. These qualitative tests usually remain reactive for life, regardless of treatment.

VDRL: Venereal Disease Research Laboratory test is a nontreponemal test that can be done on blood and CSF. Mostly used in CSF testing in congenital syphilis and neurosyphilis evaluations. The RPR is the more common nontreponemal serologic (blood) test in Oregon.

REFERENCES

1. Oregon Administrative Rules. Oregon Health Authority Chapter 333 Public Health Division, Division 18 Disease Reporting. https://secure.sos.state.or.us/oard/viewSingleRule.action?ruleVrsnRsn=292908
2. Oregon Revised Statutes. Chapter 433 Disease and Condition Control. https://www.oregonlegislature.gov/bills_laws/ors/ors433.html
3. Oregon Administrative Rules. Oregon Health Authority Public Health Division Chapter 333 Division 19 Investigation and Control of Diseases: General Powers and Responsibilities. https://secure.sos.state.or.us/oard/viewSingleRule.action?ruleVrsnRsn=292879
4. CDC Syphilis (*Treponema pallidum*) 2026 Case Definition. https://ndc.services.cdc.gov/case-definitions/syphilis-treponema-pallidum-2/
5. CDC Sexually Transmitted Infections Treatment Guidelines, 2021. https://www.cdc.gov/std/treatment-guidelines/default.htm

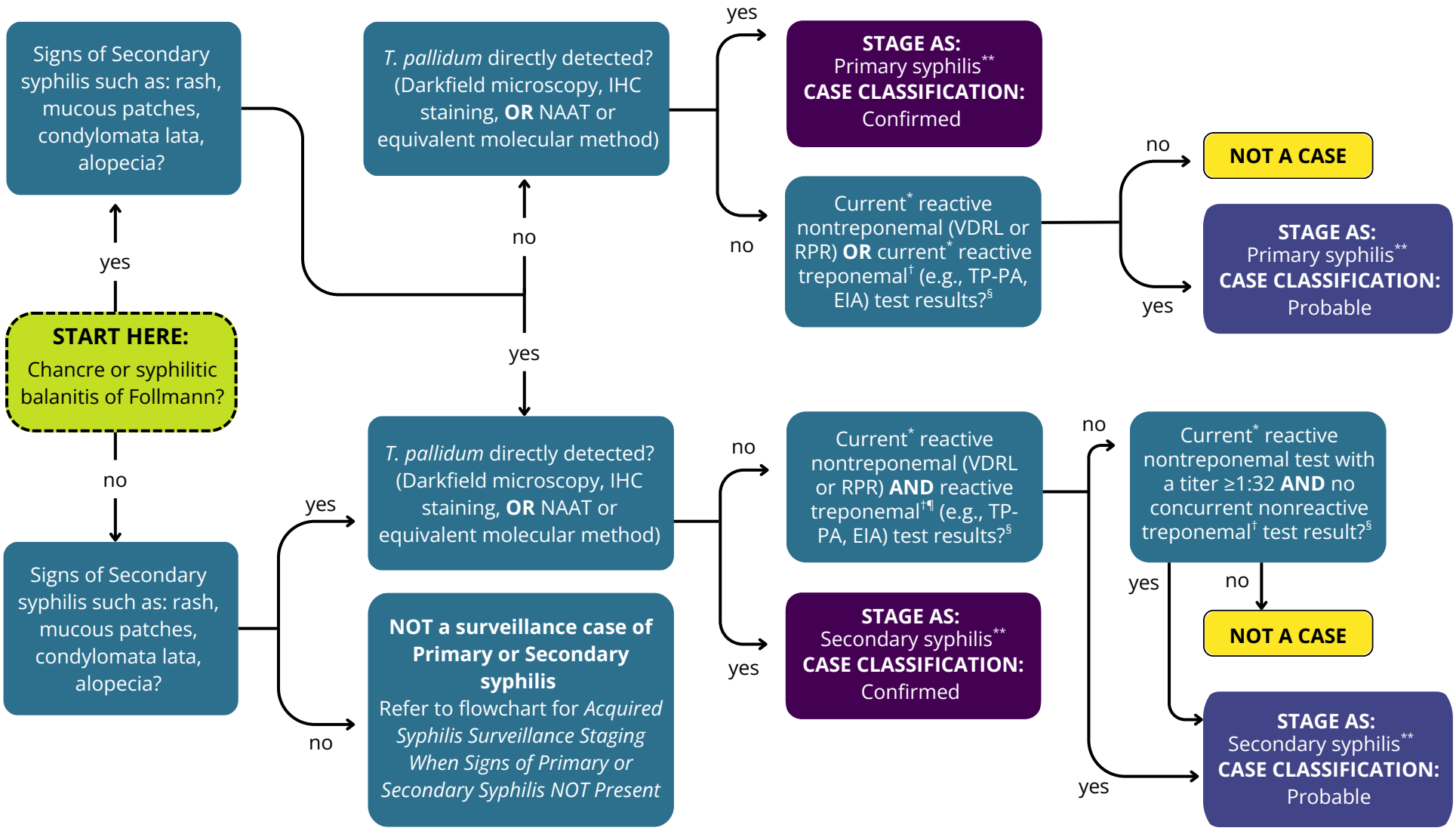
UPDATE LOG

July 2023. First draft. (Jillian Garai, Yuritzy Gonzalez Pena, Timothy Menza)
August 2024. Broken links and appendices updated. Confirmatory criteria and direct detection methods in §3 updated. Education on DoxyPEP added. (Garai)
July 2026. Surveillance case definition updated in accordance with 2025 CSTE syphilis position statement and 2026 CDC syphilis case definition. Treatment updated to include benzathine penicillin G products that are approved for temporary importation by the FDA during Bicillin L-A shortages. Other edits made throughout to align with current surveillance case definition. (Garai)

Appendix A

ACQUIRED SYPHILIS SURVEILLANCE STAGING WHEN SIGNS OF PRIMARY OR SECONDARY SYPHILIS ARE PRESENT

This tool should not be used for clinical decision-making and does not supersede the syphilis surveillance case definition



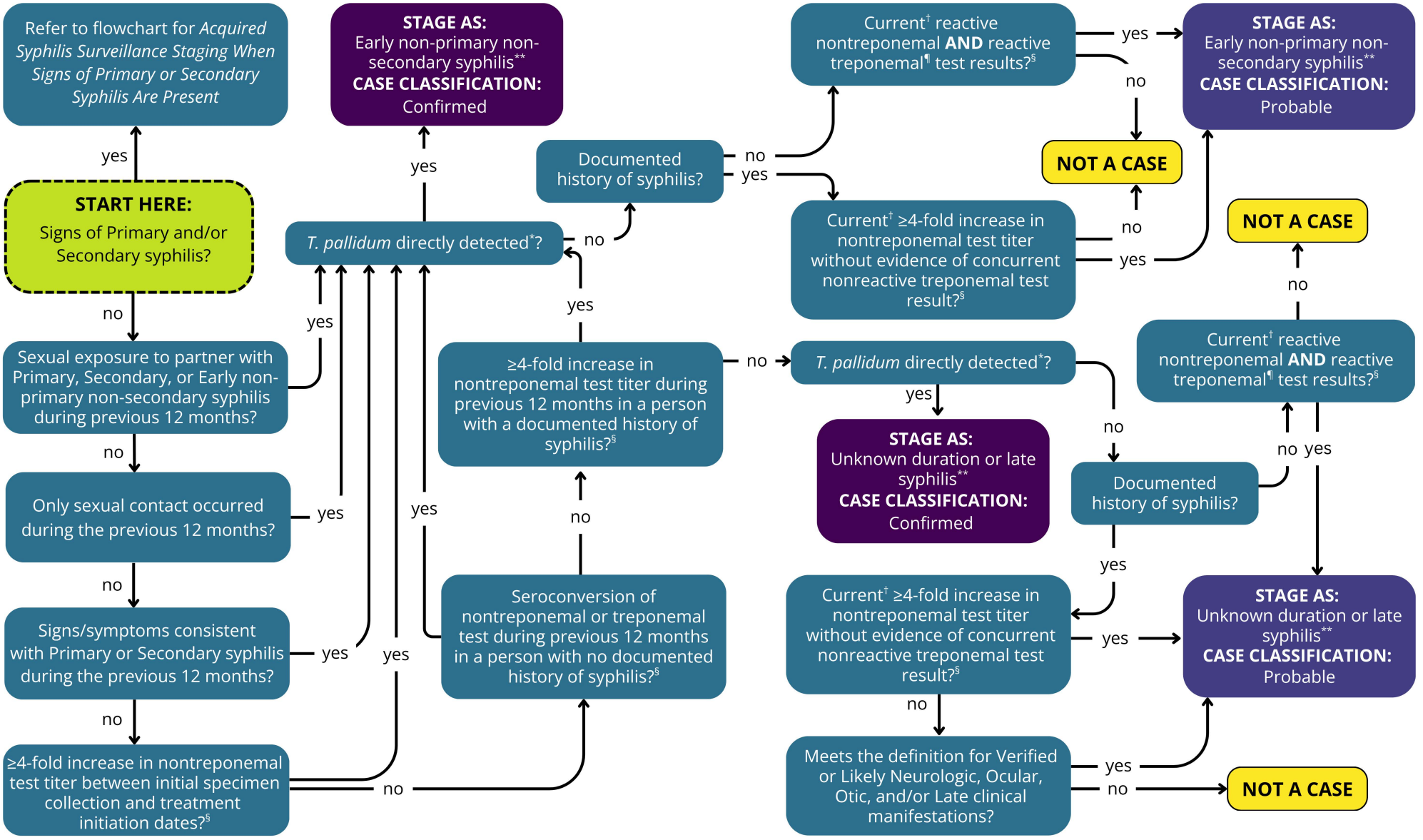
* Current refers to a test performed in the context of this index presentation.
† A reactive laboratory-based or point-of-care treponemal test result can be used to satisfy this requirement.
§ When nontreponemal and treponemal tests are mentioned in this algorithm, this refers to results from blood-based testing only.
¶ Current or historical reactive treponemal antibody tests can be used to satisfy this criterion.
** Neurologic, Ocular, and Otic manifestations of syphilis can occur at any stage. After assigning syphilis stage, assess all cases for these clinical manifestations and classify separately as "No," "Verified," "Likely," or "Unknown." Late clinical manifestations of syphilis are classified separately as "Verified," "Likely," "No," or "Unknown". Because Late clinical manifestations of syphilis (tertiary syphilis) usually only develop after >10 years of untreated syphilitic infection, these manifestations should only be included with cases of Unknown duration or late syphilis. For assistance with classification of these manifestations, please see clinical manifestations algorithms.

ACRONYMS: EIA = enzyme immunoassay; IHC = immunohistochemistry; NAAT = nucleic acid amplification test; RPR = rapid plasma reagin; *T. pallidum* = *Treponema pallidum*; TP-PA = *Treponema pallidum* particle agglutination; VDRL = Venereal Disease Research Laboratory **RESOURCES:** Case Definitions; Treatment Guidelines; Partner Services

Last updated 12/15/2025

ACQUIRED SYPHILIS SURVEILLANCE STAGING WHEN SIGNS OF PRIMARY OR SECONDARY SYPHILIS NOT PRESENT

This tool should not be used for clinical decision-making and does not supersede the syphilis surveillance case definition



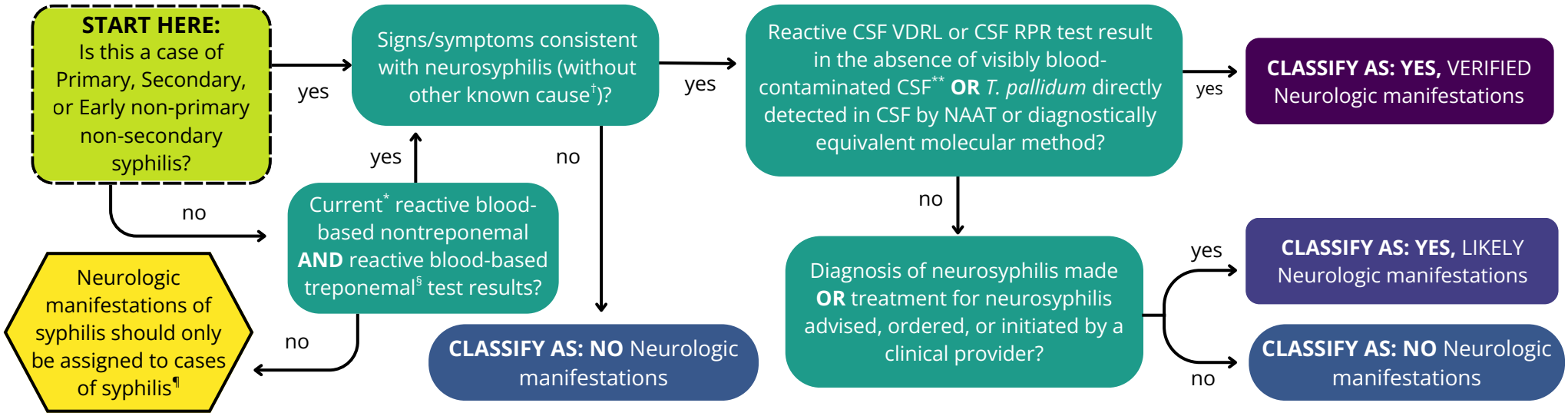
* Direct detection methods for cases of Early non-primary non-secondary syphilis may include nucleic acid amplification testing or a diagnostically equivalent molecular method. Direct detection methods for cases of Unknown duration or late syphilis may include nucleic acid amplification testing or a diagnostically equivalent molecular method or immunohistochemistry staining of an appropriate specimen.
† Current refers to a test performed in the context of this index presentation.
§ When nontreponemal and treponemal tests are mentioned in this algorithm, this refers to results from blood-based testing only.
¶ A reactive laboratory-based or point-of-care treponemal test result can be used to satisfy this requirement. Current or historical reactive treponemal antibody tests can be used to satisfy this criterion.
** Neurologic, Ocular, and Otic manifestations of syphilis can occur at any stage. After assigning syphilis stage, assess all cases for these clinical manifestations and classify separately as "Verified," "Likely," "No," or "Unknown." Late clinical manifestations of syphilis are classified separately as "Verified," "Likely," "No," or "Unknown." Because Late clinical manifestations of syphilis (tertiary syphilis) usually only develop after >10 years of untreated syphilitic infection, these manifestations should only be included with cases of Unknown duration or late syphilis. For assistance with classification of these manifestations, please see clinical manifestations algorithms.

ACRONYMS: *T. pallidum* = *Treponema pallidum* **RESOURCES:** Case Definitions; Treatment Guidelines; Partner Services

Last updated 5/13/2026

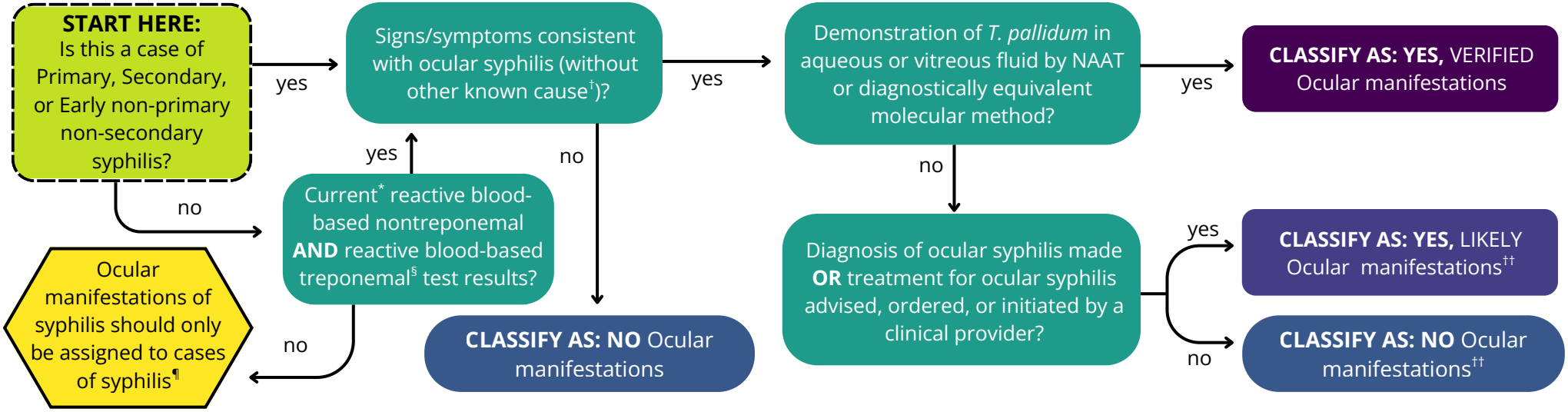
SURVEILLANCE CLASSIFICATION OF NEUROLOGIC MANIFESTATIONS OF SYPHILIS

This tool should not be used for clinical decision-making and does not supersede the syphilis surveillance case definition



SURVEILLANCE CLASSIFICATION OF OCULAR MANIFESTATIONS OF SYPHILIS

This tool should not be used for clinical decision-making and does not supersede the syphilis surveillance case definition

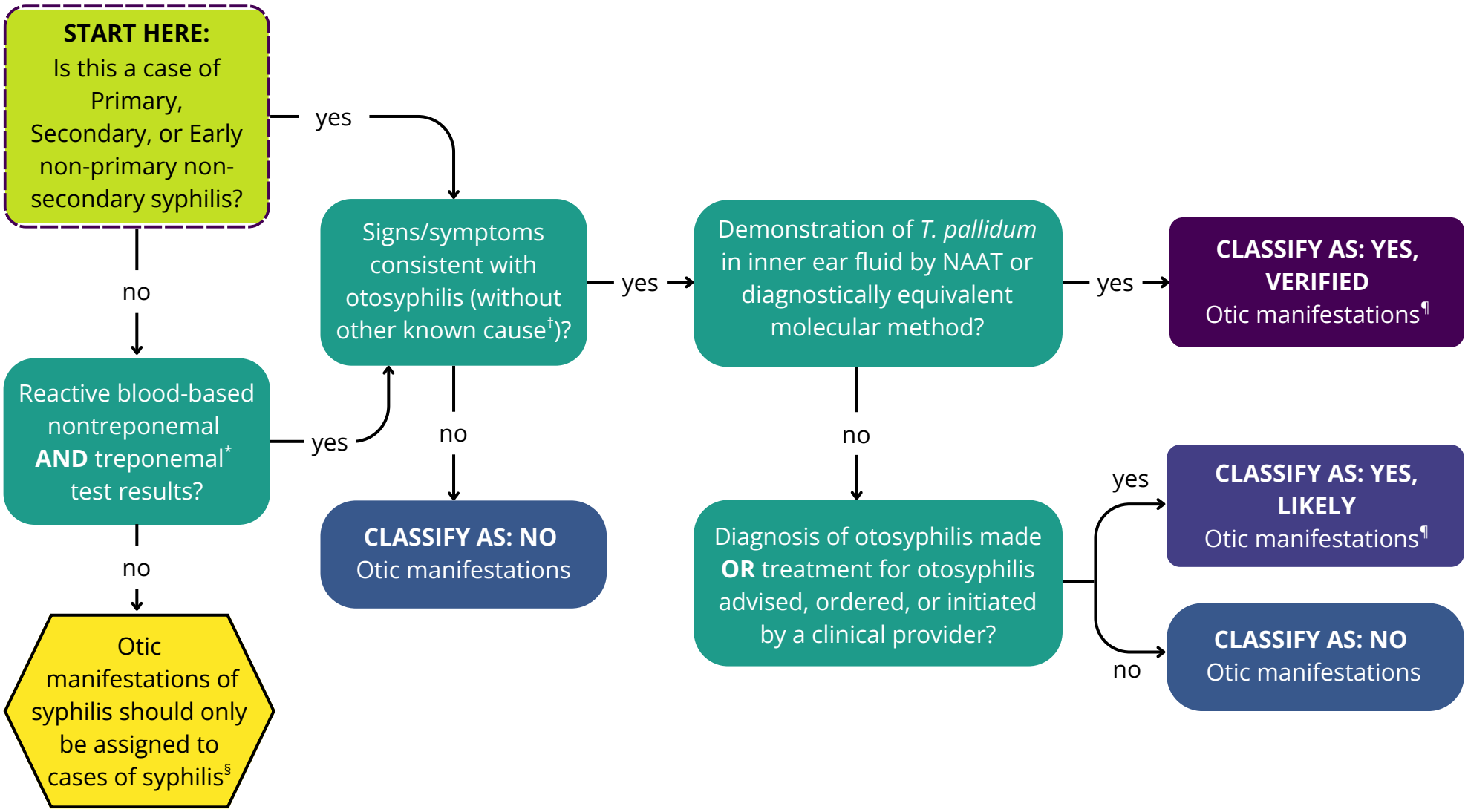


* Current refers to a test performed in the context of this index presentation.
† Clinician input may be needed to rule out other possible causes.
§ A reactive laboratory-based or point-of-care treponemal test result can be used to satisfy this requirement. Current or historical reactive treponemal antibody tests can be used to satisfy this criterion.
¶ Any previously unreported case of syphilis that meets the Likely or Verified criteria for Neurologic, Ocular, Otic, or Late clinical manifestations of syphilis and that has no evidence of having acquired the infection during the previous 12 months meets the Council of State and Territorial Epidemiologists case definition for Unknown duration or late syphilis.
** Visibly blood-contaminated CSF is defined as a CSF RBC count of ≥ 500 RBCs/µL or, in the absence of an available CSF RBC count, CSF that is described as bloody in appearance in a medical record.
†† For surveillance purposes, Ocular manifestations of syphilis are considered signs/symptoms consistent with neurosyphilis, so cases classified as having Ocular manifestations should also be classified as having Neurologic manifestations if they meet the definition for Verified or Likely Neurologic manifestations. For example, diagnosis or treatment of ocular syphilis is equivalent to diagnosis or treatment of neurosyphilis for surveillance.
ACRONYMS: CSF = cerebrospinal fluid; NAAT = nucleic acid amplification test; RBC = red blood cell; RPR = rapid plasma reagin; VDRL = Venereal Disease Research Laboratory; *T. pallidum* = *Treponema pallidum*; µL = microliter
RESOURCES: Case Definitions; Treatment Guidelines; Partner Services

Last updated 12/15/2025

SURVEILLANCE CLASSIFICATION OF OTIC MANIFESTATIONS OF SYPHILIS

This tool should not be used for clinical decision-making and does not supersede the syphilis surveillance case definition



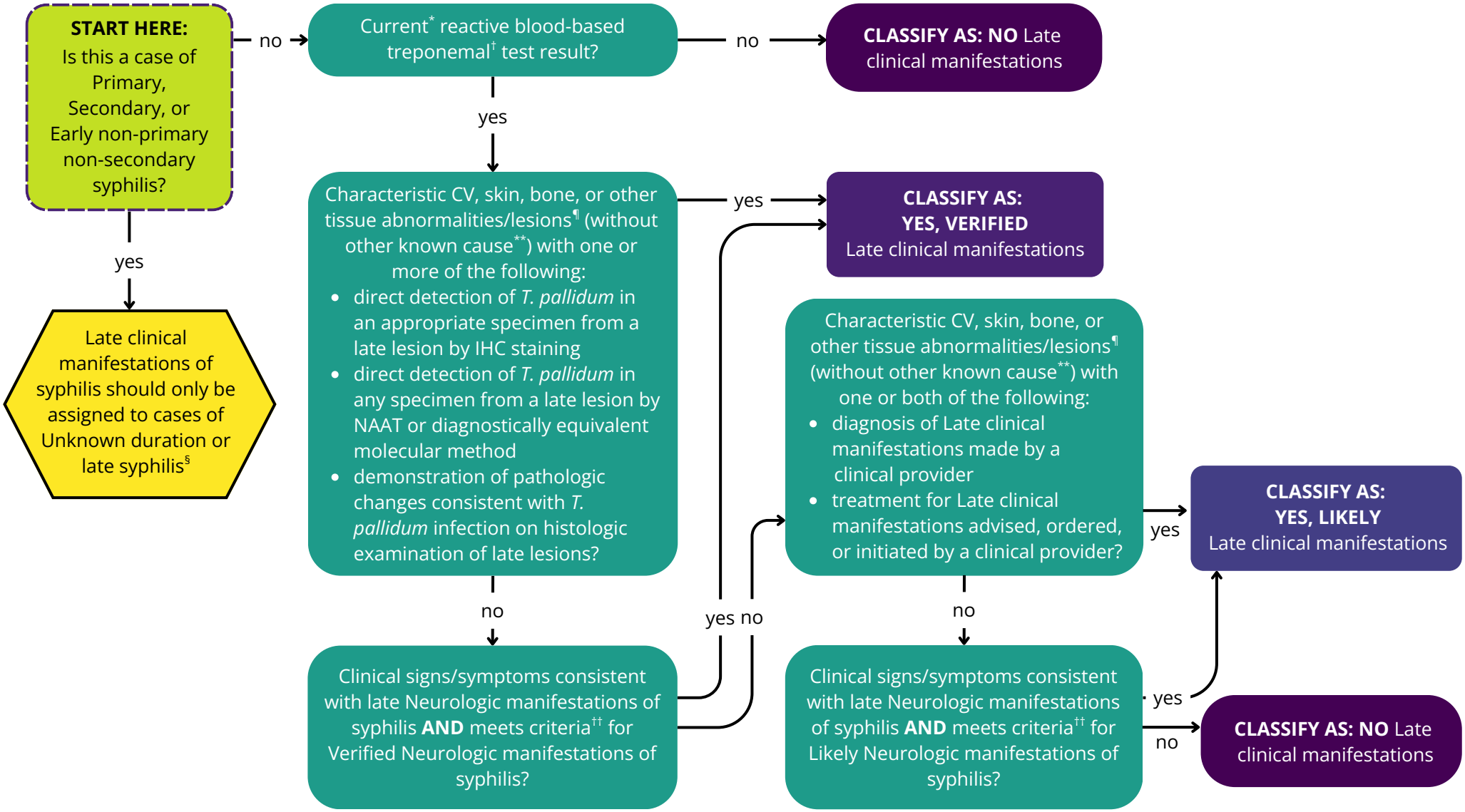
* A reactive laboratory-based or point-of-care treponemal test result can be used to satisfy this requirement. Current or historical reactive treponemal antibody tests can be used to satisfy this criterion.
† Clinician input may be needed to rule out other possible causes.
§ Any previously unreported case of syphilis that meets the Likely or Verified criteria for Neurologic, Ocular, Otic, or Late clinical manifestations of syphilis and that has no evidence of having acquired the infection during the previous 12 months meets the Council of State and Territorial Epidemiologists case definition for Unknown duration or late syphilis.
¶ For surveillance purposes, Otic manifestations of syphilis are considered signs/symptoms consistent with neurosyphilis, so cases classified as having Otic manifestations should also be classified as having Neurologic manifestations if they meet the definition for Verified or Likely Neurologic manifestations. For example, diagnosis or treatment of otosyphilis is equivalent to diagnosis or treatment of neurosyphilis for surveillance.

ACRONYMS: NAAT = nucleic acid amplification test; *T. pallidum* = *Treponema pallidum* **RESOURCES:** Case Definitions; Treatment Guidelines; Partner Services

Last updated 12/15/2025

SURVEILLANCE CLASSIFICATION OF LATE CLINICAL MANIFESTATIONS OF SYPHILIS

This tool should not be used for clinical decision-making and does not supersede the syphilis surveillance case definition



* Current refers to a test performed in the context of this index presentation.
† A reactive laboratory-based or point-of-care treponemal test result can be used to satisfy this requirement.
§ Any previously unreported case of syphilis that meets the likely or verified criteria for Neurologic, Ocular, Otic, or Late clinical manifestations of syphilis and that has no evidence of having acquired the infection during the previous 12 months meets the Council of State and Territorial Epidemiologists case definition for Unknown duration or late syphilis.
¶ Additional information about characteristic lesions associated with Late clinical manifestations of syphilis is available in CDC's STI Treatment Guidelines.
** Clinician input may be needed to rule out other possible causes.
†† Please see syphilis surveillance case definitions and the *Surveillance Classification of Neurologic Manifestations of Syphilis* algorithm for additional assistance.
ACRONYMS: CV = cardiovascular; IHC = immunohistochemistry; NAAT = nucleic acid amplification test; *T. pallidum* = *Treponema pallidum*
RESOURCES: Case Definitions; Treatment Guidelines; Partner Services

Last updated 12/15/2025

Version notes

Note: This document is a "living document," and updates will be made as needed. When updates are made, the "Last updated" date will be modified in the edited section to reflect the date the updates were made.

Version 2025_v1 – initial version drafted & released in December 2025

Version 2026_v1.1 – "yes" arrow added connecting the "Meets the definition for Verified or Likely Neurologic, Ocular, Otic, and/or Late clinical manifestations?" and "**STAGE AS:** Unknown duration or late syphilis; **CASE CLASSIFICATION:** Probable" boxes in the bottom right corner of the algorithm entitled "**ACQUIRED SYPHILIS SURVEILLANCE STAGING WHEN SIGNS OF PRIMARY OR SECONDARY SYPHILIS NOT PRESENT**"

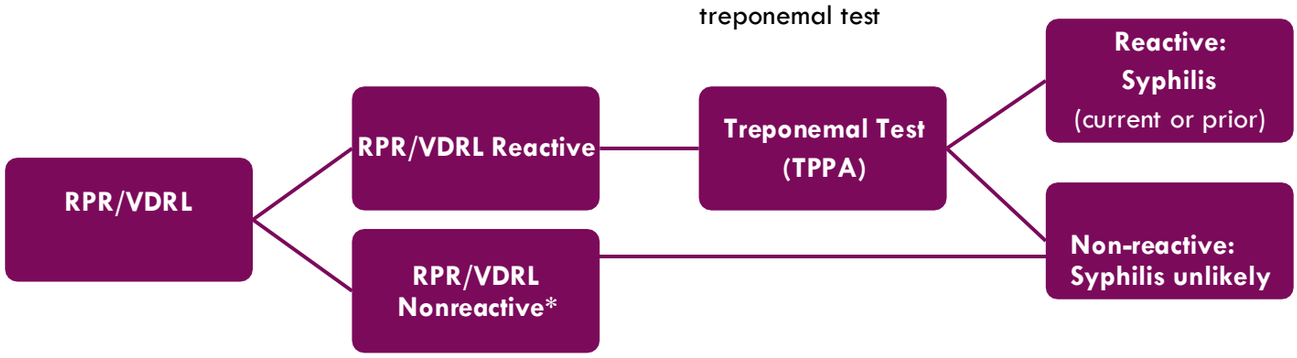
Appendix B

Clinical Interpretation of Syphilis Screening Algorithms

Testing: Traditional Algorithm[a]

1. Screen with non-treponemal test (RPR/VDRL)

2. Confirm reactive non-treponemal test with treponemal test



*Early primary syphilis and late untreated syphilis possible if RPR/VDRL are nonreactive; see below for recommended actions

Table 1: Interpretation of Syphilis Serologies, Traditional Algorithm

Non-Treponemal (RPR/VDRL)	Treponemal (TPPA)	Possible Interpretations	Recommended Actions
Nonreactive	Nonreactive or not done	1. No syphilis 2. Early/incubating syphilis (too early to be detected by serology)	▪ If syphilis unlikely, no further action needed. ▪ If early syphilis suspected, consider ordering a treponemal test (if not done initially) and repeating an RPR/VDRL in 1-2 weeks; if either test is reactive, treat for syphilis. ▪ If concerned for early syphilis (e.g., chancre present or known exposure) treat presumptively. If treating presumptively, repeat RPR/VDRL on day of treatment and, if nonreactive, again in 2-4 weeks to assess for seroconversion.
	Reactive	1. Prior treated syphilis 2. Untreated syphilis	▪ Treponemal tests (e.g., TPPA) often stay reactive for life; if patient has a history of adequate treatment for syphilis & no new exposures/ symptoms, no further action needed. ▪ If early syphilis suspected (e.g., chancre present or known exposure), treat presumptively according to stage. If treating presumptively, repeat RPR/VDRL on day of treatment and, if nonreactive, again in 2-4 weeks to assess for seroconversion. ▪ If no signs or symptoms, order a second treponemal test (e.g., EIA or CIA); see table 2 for recommendations based on results.
Reactive	Nonreactive	1. False positive RPR or VDRL	▪ Likely false positive (not syphilis).[b] ▪ In pregnancy or in patients at high risk for syphilis, consider rescreening with serologic testing in 2-4 weeks – if unchanged, no action needed.[c]
	Reactive	1. Current syphilis 2. Treated syphilis with residual/ persistent RPR/VDRL titer	▪ If RPR/VDRL is newly reactive, stage and treat. ▪ If previously treated and sustained (≥2 weeks) 4-fold rise in RPR/VDRL titer, manage as treatment failure versus re-infection.[d] ▪ Note that RPR/VDRL may still be reactive after treatment; if there is a fourfold decline within 12-24 months, treatment is considered to have been adequate even if RPR/VDRL remains reactive. ▪ Some treated patients may have a persistent low level RPR/VDRL titer for a prolonged period; re-treatment is not necessary in the absence of new exposures or symptoms.

[a] The traditional algorithm starts with a non-treponemal test (RPR or VDRL) which, if reactive, is followed by a confirmatory treponemal test (TPPA). In interpreting serologies, it is helpful to know which testing algorithm (traditional vs reverse) is being used in your lab.

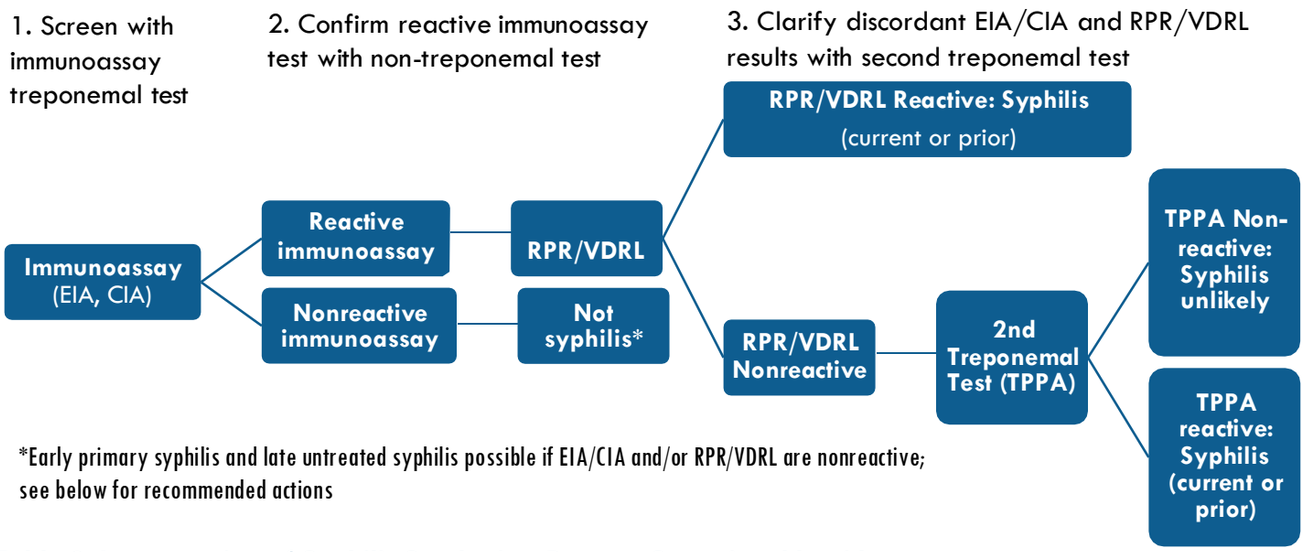
[b] False positives can be seen in pregnancy and/ in patients with autoimmune diseases, Lyme disease, certain viral infections (including HIV), injection drug use, and other conditions.

[c] In California, all pregnant people should be screened for syphilis three times during pregnancy: (1) at confirmation of pregnancy or first prenatal encounter, (2) early in the third trimester (at approximately 28 weeks gestation or as soon as possible thereafter), and (3) at delivery. The American College of Obstetrics and Gynecology also recommends screening all pregnant patients universally for syphilis three times: once at the first prenatal care visit, again during the third trimester, and again at birth.

[d] For patients determined to have new syphilis or treatment failure, refer to the Centers for Disease Control STD treatment guidelines at https://www.cdc.gov/std/treatment-guidelines/syphilis.htm for treatment and follow up recommendations.

Clinical Interpretation of Syphilis Screening Algorithms

Testing: Reverse Algorithm[a]



*Early primary syphilis and late untreated syphilis possible if EIA/CIA and/or RPR/VDRL are nonreactive; see below for recommended actions

Table 2: Interpretation of Syphilis Serologies, Reverse Screening Algorithm

Immuno-assay (CIA or EIA)	RPR/ VDRL	TPPA	Possible Interpretations	Recommended Actions
Non-reactive	Non-reactive or not done	Non-reactive or not done	1. Syphilis unlikely 2. Early/incubating syphilis (too early to be detected by serology)	▪ If syphilis unlikely, no further action needed. ▪ If immunoassay nonreactive but high clinical suspicion (such as a chancre or known exposure), treat presumptively for early syphilis. If treating presumptively, obtain RPR/VDRL on day of treatment and, if nonreactive, again in 2-4 weeks to assess for seroconversion.
Reactive	Non-reactive	Non-reactive or not done	1. False positive immunoassay 2. Early/incubating syphilis 3. Latent or prior syphilis (treated or untreated)	▪ If no signs/symptoms and low risk for syphilis, most likely a false positive immunoassay.[b] No further action needed. ▪ If concerned for early infection or in pregnant patients, re-screen in 2-4 weeks.[c] ▪ If signs/symptoms or contact to syphilis, treat presumptively. Repeat RPR/VDRL on day of treatment and, if nonreactive, again in 2-4 weeks to assess for seroconversion.
		Reactive	1. Latent or prior syphilis (treated or untreated) 2. Early syphilis (prior to RPR/VDRL seroconversion)	▪ No further action needed if patient treated appropriately for syphilis in past, assuming no new exposures/symptoms and a negative clinical exam. ▪ If no symptoms and no known prior adequate treatment, treat presumptively for latent syphilis. ▪ If early syphilis suspected (symptoms or known exposure), treat presumptively. Obtain RPR/VDRL on day of treatment. If nonreactive, repeat in 2-4 weeks to assess for seroconversion.
	Reactive	Not done or Reactive	1. Current syphilis 2. Prior syphilis (treated or untreated)	▪ If RPR/VDRL is newly reactive, stage and treat. ▪ If previously treated and sustained (≥2 weeks) 4-fold rise in RPR/VDRL titer, manage as treatment failure versus re-infection.[d] ▪ If known prior adequate treatment for stage of infection and RPR/VDRL declining appropriately (i.e., a fourfold decline within 12-24 months), no further action needed. ▪ Some treated patients may have a persistent low level RPR/VDRL titer for a prolonged period; re-treatment is not necessary in the absence of new exposures or symptoms.

[a] The reverse algorithm starts with an immunoassay detecting syphilis antibodies which, if reactive, is followed by an RPR/VDRL. If there is a discrepancy between the immunoassay and RPR (one reactive, one nonreactive), a treponemal test (TPPA) serves as the tie-breaker. In interpreting serologies, it is helpful to know which testing algorithm (traditional vs reverse) is being used in your lab.

[b] False positive immunoassays can occur with Lyme disease or non-syphilis treponemal infections.

[c] In California, all pregnant people should be screened for syphilis three times during pregnancy: (1) at confirmation of pregnancy or first prenatal encounter, (2) early in the third trimester (at approximately 28 weeks gestation or as soon as possible thereafter), and (3) at delivery. The American College of Obstetrics and Gynecology also recommends screening all pregnant patients universally for syphilis three times: once at the first prenatal care visit, again during the third trimester, and again at birth.

[d] For patients determined to have new syphilis or treatment failure, refer to the Centers for Disease Control STD treatment guidelines at https://www.cdc.gov/std/treatment-guidelines/syphilis.htm for treatment and follow up recommendations.

Congenital Syphilis
Investigative Guidelines
September 2026

1. DISEASE REPORTING

1.1 Purpose of Reporting and Surveillance

1. Identify cases of syphilis in pregnancy and prevent vertical transmission
2. Ensure adequate treatment and follow-up for pregnant people with syphilis and the infant
3. Ensure appropriate management, including screening and presumptive treatment, of sexual contacts of pregnant people with syphilis
4. Describe the epidemiology of congenital syphilis in Oregon

1.2 Laboratory and Physician Reporting Requirements

1. Licensed laboratories must report all positive test results indicating syphilis infection to the Local Public Health Authority within one working day (OAR 333-018-0000; 333-018-0015)[1]
2. Clinicians must report lab-confirmed and clinically suspect cases of syphilis to the Local Public Health Authority within one working day (OAR 333-018-0000; 333-018-0015)[1]
   - Oregon Revised Statute (ORS) 433.017 requires individuals attending a pregnant patient to collect or order the collection of a blood specimen for submission to a licensed laboratory to test for syphilis and selected other infections, unless the pregnant patient declines testing (OAR 333-019-0036)[2,3]
   - Oregon Health Authority recommends that all pregnant people be tested for syphilis three times: 1) at the first prenatal visit or presentation to care, 2) at 28 weeks' gestation, and 3) at delivery
3. Health care providers, health care facilities, and licensed laboratories shall cooperate with public health authorities in the investigation and control of syphilis infections (OAR 333-019-0002)[3]

1.3 Local Public Health Authority Reporting and Follow-up Responsibilities

1. LPHA must begin follow-up case investigation within two working days of receiving the initial provider or laboratory report
2. LPHA must report all congenital syphilis cases (including syphilitic stillbirths) to the OHA STD Program through the Oregon Public Health Epidemiology User System (Orpheus) by the end of the calendar week of initial provider or laboratory report (OAR 333-018-0020)[1]

3. LPHA must conduct case investigations and manage sexual contacts by following procedures outlined in these Investigative Guidelines (ORS 433.006, OAR 333-019-0000)[2,3]

2. THE DISEASE AND ITS EPIDEMIOLOGY

2.1 Etiologic Agent

The etiologic agent in syphilis is Treponema pallidum subspecies pallidum, a spirochete (corkscrew-shaped) bacterium.

Of all the subspecies of *T. pallidum*, only *T. pallidum* subsp*. pallidum* is transmitted routinely by sexual contact. The other *T. pallidum* subspecies are transmitted non-sexually (e.g., yaws, pinta).

2.2 Description of Illness

An infection of a stillbirth, infant or child <2 years old, or older child with *T. pallidum* contracted via transplacental transmission or, more rarely, exposure to genital lesions during birth. Congenital syphilis is commonly asymptomatic but may present with early or late signs and symptoms which are often non-specific.

2.3 Reservoirs

Humans

2.4 Modes of Transmission

- Primarily occurs via transplacental passage of *T*. *pallidum* during any stage of syphilis
- More rarely, can also occur on contact with genital lesions during birth

2.5 Incubation Period

Symptoms of congenital syphilis may not appear until several weeks or months after birth and, in some cases, may take years to appear. Early congenital syphilis typically manifests within the first 3 months of life. In late congenital syphilis, symptoms do not usually become apparent until two to five years of age.

2.6 Period of Communicability

Congenital syphilis risk is related to the syphilis stage during pregnancy, with the highest risk occurring during the primary and secondary stages:

- Untreated primary or secondary syphilis in pregnancy results in a 25% risk of stillbirth, a 14% risk of neonatal death, a 41% risk of a live infant with congenital syphilis, and a 20% chance of a non-infected infant
- Untreated late syphilis in pregnancy results in a 12% risk of stillbirth, a 9% risk of neonatal death, a 2% risk of giving birth to an infant with congenital syphilis, and a 77% chance of a non-infected infant[4]

3. CASE DEFINITIONS—FOR PUBLIC HEALTH STAFF

Public health staff determine whether the congenital syphilis surveillance case definition is met. Clinicians consult appropriate guidelines and use clinical judgement in evaluating and treating infants of people with syphilis in pregnancy. The CDC clinical scenarios (§4) do not perfectly align with the CDC congenital syphilis surveillance case definition.

3.1 Congenital Syphilis

See the CDC 2026 Syphilis Surveillance Case Definition page for further information on congenital syphilis case criteria and diagnosis.[5]

Given the complexity of the syphilis surveillance case definition, public health professionals are strongly encouraged to use the CDC Congenital Syphilis Surveillance Case Assessment Navigator (see Appendix A) instead of or alongside this section to determine whether the congenital syphilis surveillance case definition is met. The information in this section and the flowcharts is identical, but the flowcharts are much easier to follow.

3.1.1 Congenital Syphilis

1. Clinical Description
   - **Early Congenital Syphilis (infant or child <2 years old):** Manifestations can include rhinitis (“snuffles”), osteochondritis or periostitis, enlarged liver and spleen, nonimmune hydrops or edema, conjugated or direct hyperbilirubinemia, cholestatic jaundice, skin rashes, or nonspecific signs/symptoms
   - **Late Congenital Syphilis (child ≥2 years old):** Manifestations can include saddle nose, tibial thickening (“saber shins”), joint swelling (“Clutton joints”), perforation of hard palate, abnormal tooth development (“Hutchinson teeth” or “mulberry molars”), corneal inflammation, or brain and nerve problems causing blindness and deafness
   - **Syphilitic Stillbirth:** Fetal death that occurs at or after a 20-week gestation or in which the fetus weighs ≥350 grams and the birthing person had untreated or inadequately treated syphilis at delivery
     - Inadequate treatment consists of any nonpenicillin therapy; penicillin therapy initiated <30 days before delivery; incomplete therapy or dosing intervals outside of 6-9 days for treatment of late/unknown duration syphilis
2. Laboratory Criteria
   - Confirmatory: Meets at least one of the following criteria in an appropriate specimen:
     - Direct detection of *T. pallidum* by darkfield microscopy in a specimen that was both not obtained from the throat and not potentially contaminated by stool **OR**
     - Direct detection of *T. pallidum* by immunohistochemistry (IHC) staining in a specimen that was both not obtained from the oropharynx and not potentially contaminated by stool **OR**

    - Direct detection of *T. pallidum* by nucleic acid amplification test (NAAT) or a diagnostically equivalent molecular method in any specimen
  - Presumptive
    - A current (performed in the context of this clinical evaluation) reactive blood-based nontreponemal antibody test collected from an infant or child
  - Supportive Laboratory/Radiographic Evidence: Meets at least one of the following criteria in an infant or child, with no other identifiable causes for these abnormalities:
    - In a lumbar puncture without visibly blood-contaminated CSF (defined as CSF red blood cell count of ≥500 RBCs/μL or, in the absence of a CSF RBC count, CSF described as bloody in appearance), a reactive CSF VDRL test or an elevated CSF white blood cell (WBC) count **OR**
    - A blood-based nontreponemal antibody test titer at least fourfold higher than the maternal blood-based nontreponemal antibody test titer in specimens collected within 7 days of birth **OR**
    - Evidence on radiographs of long bone abnormalities consistent with congenital syphilis
3. Epidemiologic Linkage Criteria
  - A stillborn infant, liveborn infant, or child born to a person with untreated or inadequately treated syphilis at delivery
    - Inadequate treatment in pregnancy is anything other than completion of a recommended regimen, in accordance with CDC STI Treatment Guidelines or equivalent CDC clinical management guidelines, initiated 30 or more days before delivery.
    - Inadequate treatment for a non-pregnant person with childbearing capacity is any treatment given that differs from the recommended or alternative treatments listed in the CDC STI Treatment Guidelines or equivalent CDC clinical management guidelines.
4. Vital Records Criteria
  - A fetal death in which syphilis is specified on the Report of Fetal Death as the cause of, or a condition contributing to, fetal death
5. Case Classification
  - **Confirmed:**
    - A liveborn infant or child who meets confirmatory laboratory evidence AND the suspected or most likely source of infection is *in utero* **OR**
    - A fetal death that occurs at or after a 20-week gestation or in which the fetus weighs ≥350 g AND meets confirmatory laboratory evidence
  - **Presumptive:**
    - A liveborn infant or child born to a person with untreated or inadequately treated syphilis at delivery **OR**

- A liveborn infant or child who meets presumptive laboratory evidence AND the suspected or most likely source of infection is *in utero* AND meets either clinical criteria or supportive laboratory/radiographic evidence **OR**
- A fetal death that occurs at or after a 20-week gestation or in which the fetus weighs ≥350 g AND either is born to a person with untreated or inadequately treated syphilis at delivery or meets vital records criteria

4. CLINICAL MANAGEMENT—FOR MEDICAL PROVIDERS

The information in this section is adapted from the CDC 2021 STI Treatment Guidelines, which outline infant evaluation and treatment based on specific clinical scenarios.[6]

When a baby is born to a person with syphilis, the priority is to determine which clinical scenario applies. Clinicians consult appropriate guidelines and use clinical judgement in evaluating and treating infants of people with syphilis in pregnancy. Public health staff determine whether the congenital syphilis surveillance case definition is met (§3.2). The CDC clinical scenarios do not perfectly align with the CDC congenital syphilis surveillance case definition.

Serologic RPR testing should be performed on the infant's serum. Umbilical cord blood can become contaminated with maternal blood and yield a false-positive result and Wharton's jelly within the umbilical cord can yield a false-negative result.

Treponemal testing on the infant's serum is not recommended because it is difficult to interpret, as passively transferred maternal antibodies can persist for >15 months.

4.1 Management of Infants Aged <1 Month

Infants exposed to syphilis in utero should be examined for signs of congenital syphilis. Pathologic examination of the placenta or umbilical cord using IHC staining or PCR testing should be considered, including in cases of stillbirth.

Diagnosis of congenital syphilis can be difficult. Maternal nontreponemal and treponemal antibodies can be transferred through the placenta to the fetus, complicating the interpretation of reactive serologic tests for infants. Treatment decisions frequently must be made based on identification of maternal syphilis; adequacy of maternal treatment; clinical, laboratory, or radiographic evidence of syphilis in the infant; and comparison of maternal and infant titers at birth.

4.1.1 Infant Evaluation and Treatment: if maternal reactive RPR and treponemal tests in pregnancy and reactive RPR at delivery (including for cases diagnosed at delivery)

The OHA/AETC Congenital Syphilis Evaluation and Treatment Pocket Guide (see Appendix B) is a helpful flowchart for determining which clinical scenario below applies if the birthing person had reactive nontreponemal and treponemal

antibody tests in pregnancy and a reactive nontreponemal antibody test at delivery (including for cases diagnosed at delivery).

Scenario 1: Confirmed Proven or Highly Likely Congenital Syphilis

Infant with:

- Abnormal physical exam consistent with congenital syphilis **OR**
- RPR titer that is fourfold or greater higher than the maternal titer at delivery **OR**
- Positive darkfield test or PCR of placenta, cord, lesions or body fluids or a positive silver stain of the placenta or cord

Recommended Evaluation:

- CSF analysis for VDRL, white blood cell count, and protein
- Complete blood count (CBC) and differential and platelet count
- Long-bone X-rays
- Other tests as clinically indicated (e.g., chest X-ray, liver function tests, ophthalmologic exam)

Recommended Treatment:

- Aqueous crystalline penicillin G 100,000–150,000 units/kg body weight/day, administered as 50,000 units/kg body weight/dose by IV every 12 hours during the first 7 days of life and every 8 hours thereafter for a total of 10 days

Scenario 2: Possible Congenital Syphilis

Infant with a normal physical exam **AND** an RPR titer ≤fourfold of the maternal titer at delivery **AND** one of the following:

- Inadequate or no maternal treatment or no documentation of treatment
- Maternal treatment with non-penicillin G regimen
- Maternal treatment was **initiated** <30 days before delivery

Recommended Evaluation:

- CSF analysis for VDRL, white blood cell count, and protein
- Complete blood count (CBC) and differential and platelet count
- Long-bone X-rays

Recommended Treatment:

- Aqueous crystalline penicillin G 100,000–150,000 units/kg body weight/day, administered as 50,000 units/kg body weight/dose by IV every 12 hours during the first 7 days of life and every 8 hours thereafter for a total of 10 days *if any part of the evaluation is abnormal or not performed, the CSF is grossly contaminated, or follow-up as described in §4.2.3 is uncertain.*

OR

- Benzathine penicillin G 50,000 units/kg body weight/dose IM in a single dose *if all the recommended evaluation is performed, all results are available and normal, and follow-up as described in §4.2.3 is certain.*

Additional Considerations:

Infants born to birthing people with untreated early syphilis at the time of delivery may not have a reactive RPR and may have a normal clinical and laboratory evaluation. In this setting, the infant may have incubating or very early syphilis that is not yet clinically apparent. Therefore, even if follow-up as described in §4.3.2 is certain, infants should be treated with the 10-day regimen.

Scenario 3: Congenital Syphilis Less Likely

Infant with a normal physical exam **AND** an RPR titer ≤fourfold of the maternal titer at delivery **AND** both of the following are true:

- Birthing person was treated during pregnancy, treatment was appropriate for the syphilis stage, and the treatment regimen was initiated ≥30 days before delivery
- There is no evidence of maternal reinfection (i.e., no symptoms and titer has not increased fourfold or more)

Recommended Evaluation: None

Recommended Treatment:

- Benzathine penicillin G 50,000 units/kg body weight/dose IM in a single dose
- If follow-up is certain and maternal RPR titers decreased at least fourfold after therapy for early syphilis or remained stable for low-titer, latent syphilis (e.g., RPR<1:4), close RPR follow-up every 2-3 months for 6 months can be pursued instead of treatment.

Scenario 4: Congenital Syphilis Unlikely

Infant with a normal physical exam and an RPR titer ≤fourfold of the maternal titer at delivery **AND** both of the following are true:

- Maternal treatment was adequate before pregnancy
- Maternal RPR titers remained low and stable before and during pregnancy and at delivery

Recommended Evaluation: None

Recommended Treatment:

- No treatment required
- Benzathine penicillin G 50,000 units/kg body weight as a single IM injection should be considered if follow-up is uncertain and the infant has a reactive RPR

4.1.2 Infant Evaluation and Treatment: maternal reactive treponemal tests and a nonreactive RPR

1. **Reactive maternal treponemal tests with a nonreactive RPR during pregnancy:**
   - Congenital syphilis is highly unlikely for infants born to people with a nonreactive RPR after adequate treatment for syphilis during pregnancy or documentation of adequate treatment before pregnancy (with no evidence of reinfection)

- If the maternal RPR remains nonreactive at delivery and the infant has a normal physical examination and nonreactive RPR, manage like *Scenario 4: Congenital Syphilis Unlikely* scenario above. Benzathine penicillin G 50,000 units/kg body weight as a single IM injection might be considered if syphilis exposure is possible within 1 month before delivery and follow-up is uncertain.

2. **One reactive maternal treponemal test (e.g., EIA reactive, RPR nonreactive, TP-PA nonreactive) during pregnancy:**
   - Congenital syphilis is unlikely for infants born to people screened with the reverse sequence algorithm with an isolated reactive maternal treponemal test
   - If the infant has a normal physical examination and the risk for maternal syphilis is low, no evaluation and treatment are recommended for the infant
   - If maternal syphilis exposure is possible or unknown, repeat testing within 1 month is recommended to evaluate for early infection
3. **Reactive maternal treponemal test at delivery and no previous syphilis history or testing:**
   - Confirmatory testing is needed
   - If late or no prenatal care, the infant should be evaluated and treated with a 10-day course of penicillin as recommended in *Scenario 1: Confirmed Proven or Highly Likely Congenital Syphilis* above unless/until maternal syphilis is ruled out

4.1.3 Infant Follow-Up

- All infants with a reactive RPR at birth should receive thorough follow-up examinations and RPR testing every 2–3 months until the test becomes nonreactive*. Treponemal tests should not be used to evaluate infant infection status or treatment response*—these results are qualitative and passive transfer of maternal treponemal antibodies might persist for >15 months.
  - Treated infants who have persistent RPR titers by age 6–12 months should be reevaluated through CSF examination and managed in consultation with an expert. Retreatment with a 10-day course of a penicillin G regimen might be indicated.
  - For infants who were not treated because congenital syphilis was considered less likely or unlikely, RPR titers should decrease by age 3 months and be nonreactive by age 6 months, indicating that the reactive test result was caused by passive transfer of maternal antibodies
    - If the RPR is nonreactive at age 6 months, no further evaluation or treatment is needed
    - If the RPR is still reactive at age 6 months, the infant is likely infected and should be treated
- Infants with a negative RPR at birth born to people with a reactive RPR at delivery should be retested at age 3 months to rule out incubating congenital syphilis

- Infants whose initial CSF evaluations are abnormal do not need repeat lumbar puncture unless they exhibit persistent RPR titers at age 6–12 months. Persistent RPR titers and CSF abnormalities should be managed in consultation with an expert.

4.2 Management of Infants and Children Aged ≥1 Month

- Infants and children aged ≥1 month with reactive RPR and/or treponemal tests for syphilis should be examined thoroughly and have maternal serology and records reviewed to assess whether they have congenital or acquired syphilis
  - In the case of extremely early or incubating syphilis at the time of delivery, all maternal serologic tests might have been negative
  - Any infant or child at risk for congenital syphilis should receive a full evaluation and testing for HIV infection
- International adoptee, immigrant, or refugee children from countries where treponemal infections (e.g., yaws or pinta) are endemic might have reactive RPR and treponemal tests, which cannot distinguish between syphilis and other subspecies of *T. pallidum*. These children might also have syphilis and should be evaluated for congenital syphilis.

Recommended Evaluation:

- CSF analysis for VDRL, white blood cell count, and protein
- Complete blood count (CBC) and differential and platelet count
- Other tests as clinically indicated (e.g., chest X-ray, liver function tests, ophthalmologic exam)

Recommended Treatment:

- Aqueous crystalline penicillin G 200,000–300,000 units/kg body weight by IV, administered as 50,000 units/kg body weight every 4–6 hours for 10 days
- If there are no clinical manifestations of congenital syphilis and the evaluation is normal, treatment with up to 3 weekly doses of benzathine penicillin G 50,000 units/kg body weight IM can be considered
- These treatment regimens should also be adequate for children who might have other treponemal infections

Follow-up:

- Thorough follow-up examinations and RPR testing of infants/children treated for congenital syphilis after the first 30 days of life should be performed every 3 months until the test becomes nonreactive or the titer has decreased fourfold. *Treponemal tests should not be used to evaluate infant infection status or treatment response*—these results are qualitative and passive transfer of maternal treponemal antibodies might persist for >15 months.
- The titer response after therapy might be slower than for infants aged <1 month
- If titers increase at any point for >2 weeks or do not decrease fourfold after 12–18 months, the infant or child should be evaluated (e.g., CSF

examination), treated with a 10-day course of parenteral penicillin G, and managed in consultation with an expert.

- Infants/children whose initial CSF evaluations are abnormal do not need repeat lumbar puncture unless their RPR titers do not decrease fourfold after 12–18 months. After 18 months of follow-up, abnormal CSF results that persist and cannot be attributed to other ongoing illness indicate that retreatment is needed for possible neurosyphilis and should be managed in consultation with an expert.

5. MANAGING SPECIAL SITUATIONS

5.1 Infants Placed in Oregon Department of Human Services (DHS) Custody

When an infant is classified as a CS case and/or has a reactive RPR at birth, and is placed in ODHS custody:

- The county investigating the CS case should attempt to obtain information about where in Oregon the child will be residing and contact information for the child's pediatrician if known
- The county investigating the CS case should then notify the county where the child is residing so that the county of residence can monitor infants with a reactive RPR at birth for testing every 2–3 months until the RPR becomes nonreactive

GLOSSARY

CSF: Cerebrospinal fluid. CSF testing can indicate whether there is central nervous system involvement in a syphilis infection.

CBC: Complete Blood Count. A complete blood count is a set of tests that provide information about the cells in a person's blood. The CBC indicates the counts of white blood cells, red blood cells, and platelets, and the hemoglobin and hematocrit.

Early syphilis: Any of the stages that occur in the first 12 months of infection: primary, secondary, and early non-primary non-secondary syphilis.

IM: Intramuscular. An IM injection delivers medication, such as benzathine penicillin G for syphilis, into a muscle.

PCR: Polymerase chain reaction test is a laboratory technique for rapidly producing (amplifying) many copies of a specific segment of genetic material, e.g., *T. pallidum* DNA in syphilis.

RPR: Rapid plasma reagin test is a nontreponemal serologic (blood) test. Unlike treponemal tests, the RPR measures antibodies that are not specific for *T. pallidum* bacteria and may be reactive due to conditions other than syphilis, including pregnancy.

Treponemal test: Treponemal tests measure antibodies directed against T. pallidum bacteria. Treponemal serologic (blood) tests include enzyme immunoassays (EIAs) and chemiluminescence immunoassays (CIAs), T. pallidum particle agglutination (TP-PA),

fluorescent treponemal antibody absorption (FTA-ABS) tests, and point-of-care and self-test treponemal antibody tests. These qualitative tests usually remain reactive for life, regardless of treatment, following a syphilis infection.

VDRL: Venereal Disease Research Laboratory test is a nontreponemal test that can be done on blood and CSF. Mostly used in CSF testing in congenital syphilis and neurosyphilis evaluations. The RPR is the more common nontreponemal serologic (blood) test in Oregon.

REFERENCES

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UPDATE LOG

July 2023. First draft. (Jillian Garai, Yuritzy Gonzalez Pena, Timothy Menza)
July 2026. Surveillance case definition updated in accordance with 2025 CSTE syphilis position statement and 2026 CDC syphilis case definition. Other edits made throughout to align with current surveillance case definition. (Garai)

Appendix A

2026 Congenital Syphilis Surveillance Case Definition

The Centers for Disease Control (CDC), Division of STD Prevention (DSTDP), Surveillance and Data Science Branch developed this document as a technical resource for State, Tribal, Local, and Territorial (STLT) health departments that submit syphilis case data to CDC through National Notifiable Diseases Surveillance System for national surveillance. It is intended for recipients of PS19-1901 (Strengthening STD Prevention and Control for Health Departments) and PS23-2302 (Accelerating the Prevention and Control of HIV, Viral Hepatitis, STDs, and TB in the U.S.-Affiliated Pacific Islands). This document provides technical resources to support syphilis surveillance strategies described in those NOFOs. It does not introduce new NOFO requirements or represent official CDC recommendations. References to non-CDC websites do not constitute or imply endorsement.

DRAFT: 04.2026

Use this resource to assess whether a stillborn, infant, or child meets the Congenital Syphilis surveillance case definition and to classify a case as Probable or Confirmed.

This resource supports determination of

- Whether exposure to *Treponemal pallidum* (syphilis) occured during pregnancy or at delivery
- Whether Congenital syphilis was prevented by adequate treatment before delivery

Important information

- A stillborn, infant, or child can meet the surveillance case definition **even without signs or symptoms.**
- Surveillance and clinical case determination usually agree, but not always.
- The Congenital syphilis surveillance case definition is intentionally broad (sensitive).
- Most Congenital syphilis surveillance cases are **Probable**. **Confirmed** cases are uncommon.

Before you begin, gather available information, typically

- Maternal syphilis testing, diagnosis, and treatment history, and birth outcome
- Stillborn, infant, or child information: laboratory results, gestational age and/or weight, and clinical findings, if available

How to use this resource

STEP 1. Identify the proximate maternal infection

Identify the maternal infection closest in time (proximate) to the pregnancy or delivery using the Identifying the Proximate Maternal Infection flowchart.

Tip: Use the proximate maternal infection identified in STEP 1 to evaluate epidemiologic linkage in STEP 2.

STEP 2. Determine the case classification

Use the flowchart that matches the birth outcome **(stillborn** or **liveborn)** to determine whether the case meets the Congenital syphilis surveillance case definition and whether it is classified as a **Probable case**, **Confirmed case**, or **Not a case**:

- Flowchart: Case Classification for a **Stillborn**
- Flowchart: Case Classification for a **Liveborn** Infant or Child

NOTE: This document includes hyperlinks that connect within the document as well as links to external resources.
RESOURCES: 2026 Congenital syphilis surveillance case definition

Use this worksheet to record information as you work through the Congenital syphilis surveillance flowcharts.

Record IDs

Local use

STEP 1. Identify the proximate maternal infection

Proximate maternal infection

- ☐ **NO** surveillance evidence of a proximate maternal infection
- ☐ **YES,** proximate maternal infection identified

If yes, *record the promixmate maternal infection information from STEP 1 flowchart:*

Diagnosis[1] date: _____ Surveillance stage: _____

- ☐ Before this pregnancy
- ☐ During this pregnancy
- ☐ At delivery
- ☐ After delivery

STEP 2. Determine the case classification

Vital status

- ☐ Stillborn (fetal death)
- ☐ Liveborn - born alive, living
- ☐ Liveborn - born alive, then died

Case classification

- ☐ Confirmed case
- ☐ Probable case
- ☐ Not a case

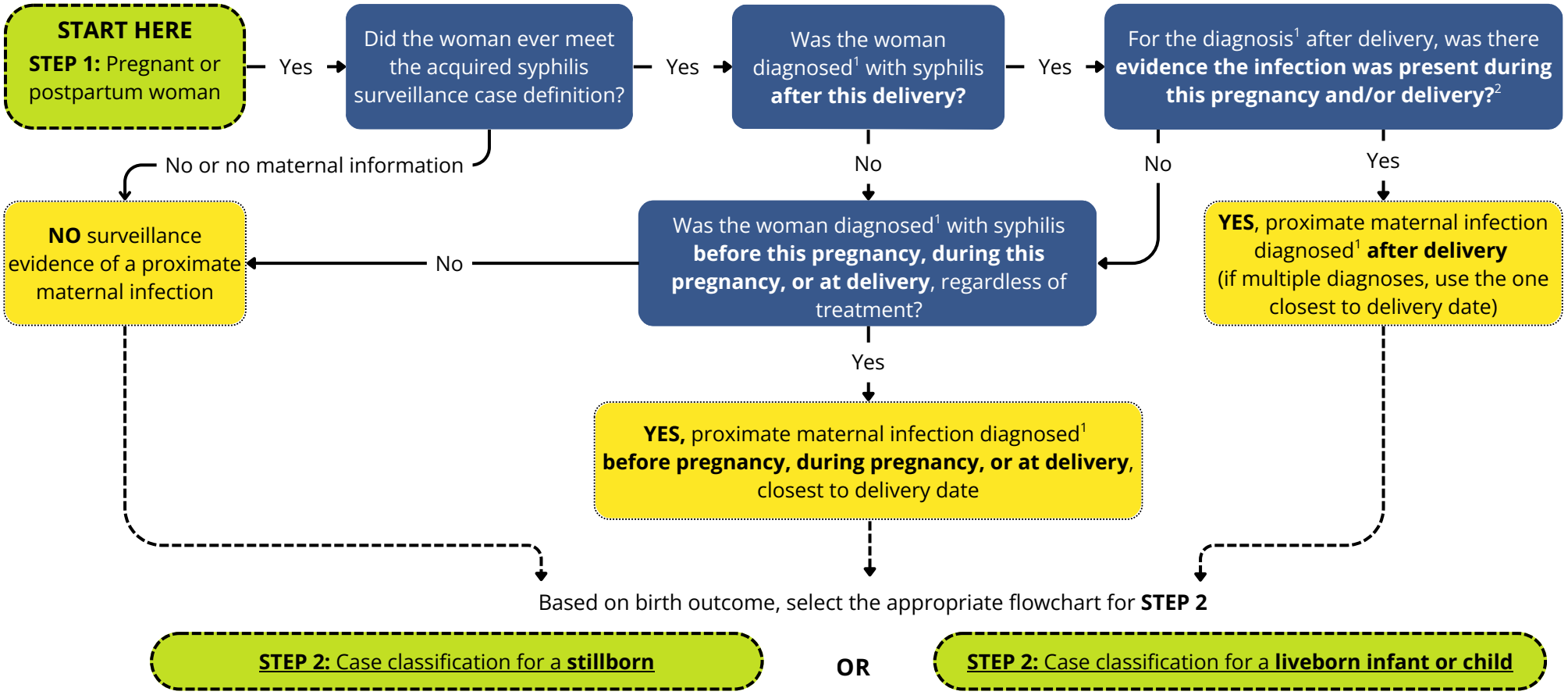
Notes

[1] Diagnosed means the woman met the surveillance case definition for acquired syphilis. The diagnosis date is usually based on the specimen collection date for the specimen(s) that led to case classification.
NOTE: This worksheet can be completed electronically as a fillable PDF; it may also be printed for handwritten use.

Use this flowchart to identify the maternal syphilitic infection that may have exposed the stillborn, infant, or child to *T. pallidum* (syphilis) in utero or at delivery. This step is required before using the case classification flowcharts.

Note: The proximate maternal infection may be diagnosed before pregnancy, during pregnancy, at delivery, or after delivery. It may be the first infection or a reinfection, and it may be any surveillance stage. Treatment does not determine which infection is proximate. An infection can be proximate whether it was untreated, adequately treated, or inadequately treated. Treatment status is assessed later when applying epidemiologic linkage criteria. Identifying the proximate maternal infection alone does not meet the epidemiologic linkage criteria.

Once the proximate maternal infection has been identified in STEP 1, use the STEP 2 Congenital syphilis flowcharts to determine whether the stillborn, infant, or child meets the surveillance case definition for Congenital syphilis.



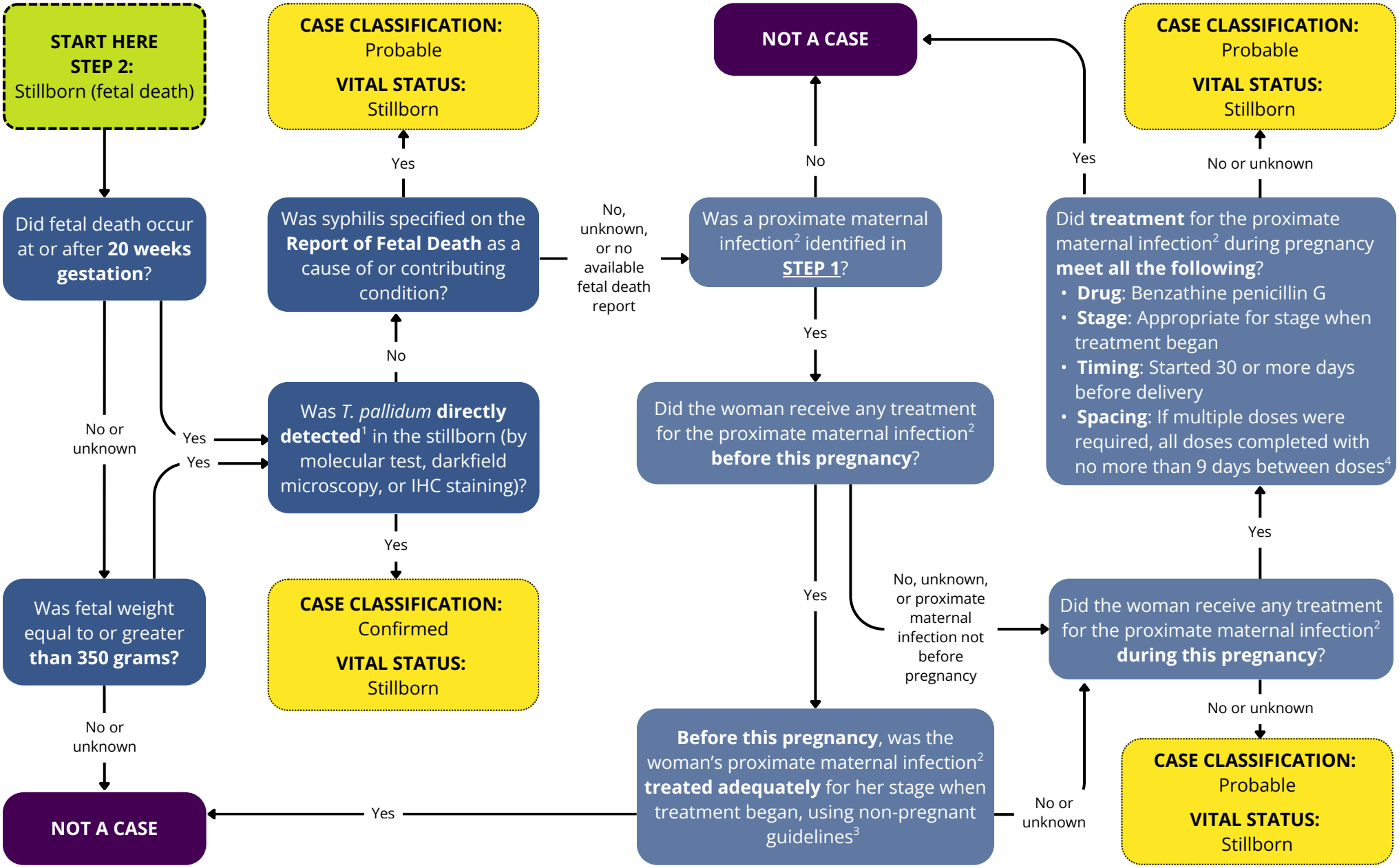
[1] Diagnosed means the woman met the surveillance case definition for acquired syphilis. The diagnosis date is usually based on the specimen collection date for the specimen(s) that led to case classification.
[2] Examples include, but are not limited to, the postpartum woman met the acquired syphilis surveillance case definition within 10 days of delivery (minimum incubation period) or had signs and/or symptoms of syphilis during pregnancy or at delivery. These examples do not cover every situation. Use all available information to decide whether she was infected before delivery, including possible exposure and other relevant clinical, laboratory, and epidemiologic information.

ACRONYMS: *T. pallidum* = *Treponema pallidum*
RESOURCES: 2026 Congenital syphilis surveillance case definition

STEP 2

Congenital Syphilis Surveillance Case Assessment Navigator (CS-SCAN): Case Classification for a **Stillborn**

This resource is based on the **2026** Congenital syphilis surveillance case definition and is not intended for clinical decision-making or to replace the syphilis surveillance case definition.



[1] Appropriate specimens are described in the CDC Laboratory Recommendations for Syphilis Testing. For example: molecular tests - lesion swabs, neonatal nasal discharge, neonatal blood or serum, autopsy material; darkfield - moist lesions, neonatal nasal discharge; IHC staining - brain, placenta, umbilical cord, lesion tissue. Specimens for darkfield and IHC staining cannot come from the oropharynx (mouth or throat) and cannot be potentially contaminated by stool (for example, specimen from the rectum or anus).

[2] A proximate maternal infection is the syphilitic infection closest to delivery that was present during this pregnancy or at delivery and could have exposed the stillborn to *T. pallidum* in utero or at delivery if not adequately treated before delivery. The proximate maternal infection may be identified before, at, or after this delivery. See STEP 1: Identifying the Proximate Maternal Infection flowchart.

[3] See CDC STI Treatment Guidelines for recommended treatment.

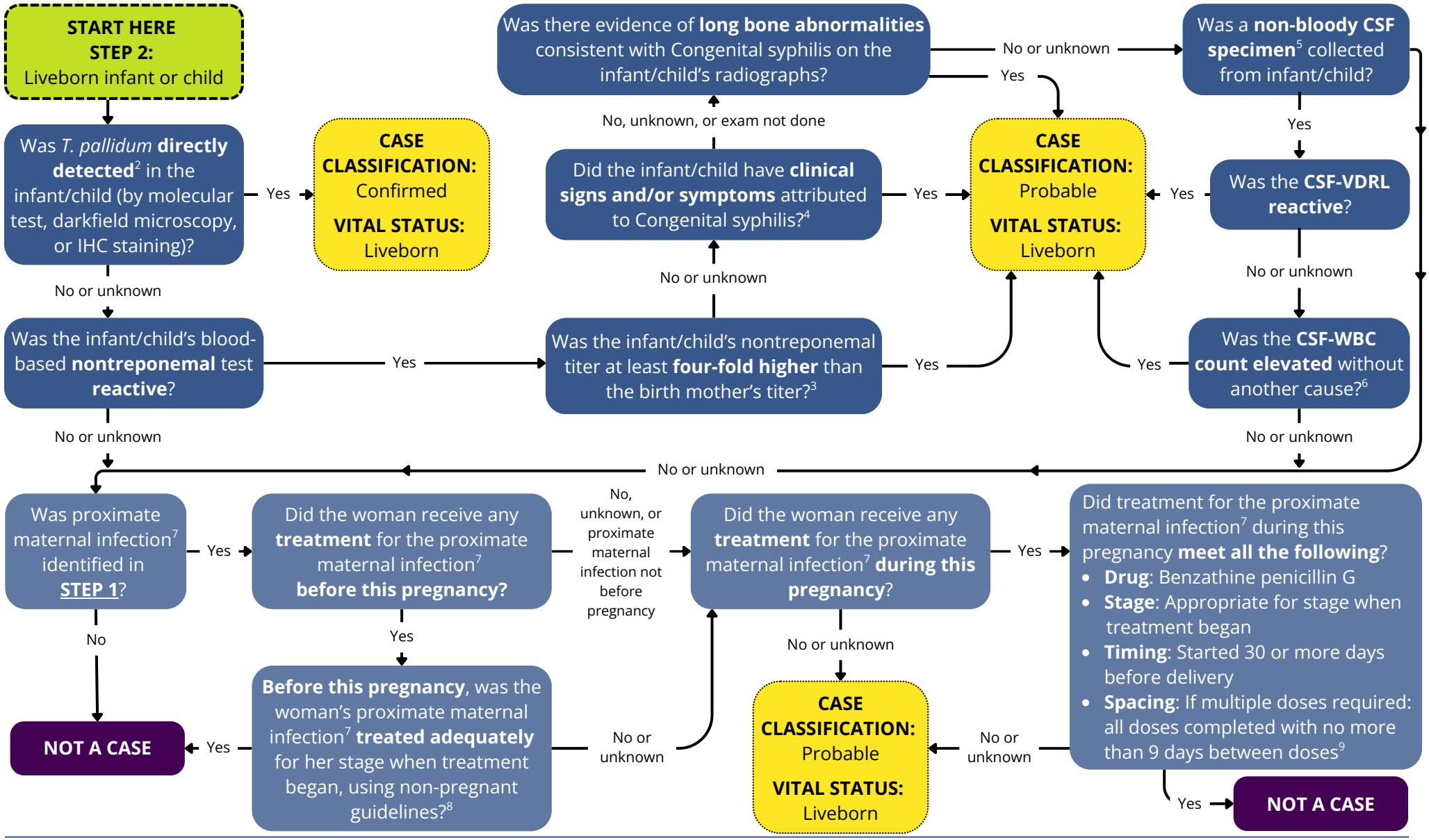
[4] CDC STI Treatment Guidelines do not define a minimum number of days between doses. Use local program guidance for the minimum interval.

ACRONYMS: IHC = Immunohistochemistry; *T. pallidum* = *Treponema pallidum*

RESOURCES: 2026 Congenital syphilis surveillance case definition

STEP 2 **Congenital Syphilis Surveillance Case Assessment Navigator (CS-SCAN)**: Case Classification for a **Liveborn** Infant or Child[1]

This resource is based on the **2026** Congenital syphilis surveillance case definition and is not intended for clinical decision-making or to replace the syphilis surveillance case definition.



[1] To classify as a Congenital syphilis surveillance case, the most likely source of syphilis exposure must be in utero or at delivery. If another source is more likely, use the acquired syphilis surveillance case definition.

[2] Appropriate specimens are described in the CDC Laboratory Recommendations for Syphilis Testing. For example: molecular tests - lesion swabs, neonatal nasal discharge, neonatal blood or serum, autopsy material; darkfield - moist lesions, neonatal nasal discharge; IHC staining - brain, placenta, umbilical cord, lesion tissue. Specimens for darkfield and IHC staining cannot come from the oropharynx (mouth or throat) and cannot be potentially contaminated by stool (for example, specimen from the rectum or anus).

[3] Compare maternal and infant blood-based titers from specimens collected within 7 days of birth and of each other.

[4] Signs and symptoms in infants or children are often non-specific and should be linked to congenital syphilis only if no more likely cause is present.

[5] CSF specimen must not be visibly bloody, defined as 500 or more RBCs per microliter. If RBCs are not available, the CSF should not be described as bloody in the medical record. If the CSF specimen is visibly contaminated, the result cannot be used for surveillance.

[6] Whenever possible, the treating clinician should interpret the results. For abnormal CSF WBC counts, refer to the latest CDC STI Treatment Guidelines.

[7] A proximate maternal infection is the syphilitic infection closest to delivery that was present during this pregnancy or at delivery and could have exposed the liveborn infant or child to *T. pallidum* in utero or at delivery if not adequately treated before delivery. The proximate maternal infection may be identified before, at, or after this delivery. See STEP 1: Identifying the Proximate Maternal Infection flowchart.

[8] See CDC STI Treatment Guidelines for recommended treatment.

[9] CDC STI Treatment Guidelines do not define a minimum number of days between doses. Use local program guidance for the minimum interval.

ACRONYMS: CSF = Cerebrospinal fluid; IHC = Immunohistochemistry; RBC = Red blood cell; *T. pallidum* = *Treponema pallidum*; WBC = White blood cell **RESOURCES**: 2026 Congenital syphilis surveillance case definition

Appendix B

CONGENITAL SYPHILIS (CS)

Evaluation and treatment of infants (<30 days old) exposed to syphilis in utero*

Start

INFANTS AND BIRTHING PARENT (e.g., mother) SHOULD HAVE SERUM RPR TITER DRAWN AT DELIVERY

Infant and Maternal Criteria

Infant Criteria:
- CS findings on physical exam
- Infant titer ≥fourfold higher than mother's titer
- + darkfield or PCR of placenta, cord, lesions, or body fluid
- + silver stain of placenta or cord

No to all

Maternal Criteria:
- Not treated
- Inadequately treated§
- Treatment undocumented
- Treated with a non-penicillin G regimen
- Initiated treatment <30 days before delivery

No to all

Additional Maternal Criteria:
- Adequately treated with penicillin G regimen appropriate for stage, initiated ≥30 days before delivery

AND

- No concern for reinfection or treatment failure

Yes to any

Scenario 1: Proven or Highly Probable CS

Yes to any

Scenario 2: Possible CS ||

Yes to both

Scenario 3: Less Likely CS

Infant Evaluation

- **CSF analysis†** VDRL, cell count, and protein
- **Complete blood count (CBC),** differential, and platelet count
- **Long-bone radiographs**
- **Tests as clinically indicated by signs on physical exam**

- **CSF analysis†** VDRL, cell count, and protein
- **CBC,** differential, and platelet count
- **Long-bone radiographs**

No additional infant evaluation

Review Maternal Titers & Stage:
- ≥4 fold decrease in titer after treatment for early syphilis

OR

- Stable titer for low-titer, latent syphilis (RPR < 1:4)

Any abnormalities, results not available, *OR* follow-up¶ uncertain

No abnormalities *AND* follow-up¶ certain

No to both *OR* follow-up¶ uncertain

Yes to either *AND* follow-up¶ certain

Infant Treatment

Aqueous crystalline penicillin G‡
100,000–150,000 units/kg/day, administered as 50,000 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

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

No treatment indicated
with close serologic follow-up of infant every 2-3 months for 6 months

* Scenario 4: CS Unlikely is not shown. This scenario covers infants with normal physical exam and RPR titer ≤fourfold of the maternal titer at delivery, and the mother was adequately treated prior to becoming pregnant and sustained RPR titers ≤1:4 throughout pregnancy.

† CSF test results obtained during the neonatal period can be difficult to interpret; normal values differ by gestational age.

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

§ Adequate treatment for syphilis in a pregnant person refers to the appropriate penicillin regimen recommended by the CDC initiated at least 30 days prior to delivery.

|| Evaluation is not necessary if a 10-day course of parenteral therapy is administered, although such evaluations might be useful. If the neonate's nontreponemal test is nonreactive and the mother's risk for untreated syphilis is low, a single IM dose of benzathine penicillin G (BPG) can be considered without evaluation.

¶ All neonates with reactive nontreponemal tests should receive careful follow-up examinations and serologic testing (i.e., a nontreponemal test) every 2–3 months until the test becomes nonreactive. Neonates with a negative nontreponemal test at birth whose mothers were seroreactive at delivery should be retested at 3 months to rule out serologically negative incubating congenital syphilis at the time of birth.

FOR MORE INFORMATION ABOUT SCENARIO 4 MANAGEMENT, TREATMENT OF SYPHILIS IN PREGNANCY, NEONATAL CSF INTERPRETATION, AND CS INFANT FOLLOW-UP, PLEASE REFER TO THE CDC 2021 STI TREATMENT GUIDELINES.

Oregon Health Authority

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