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

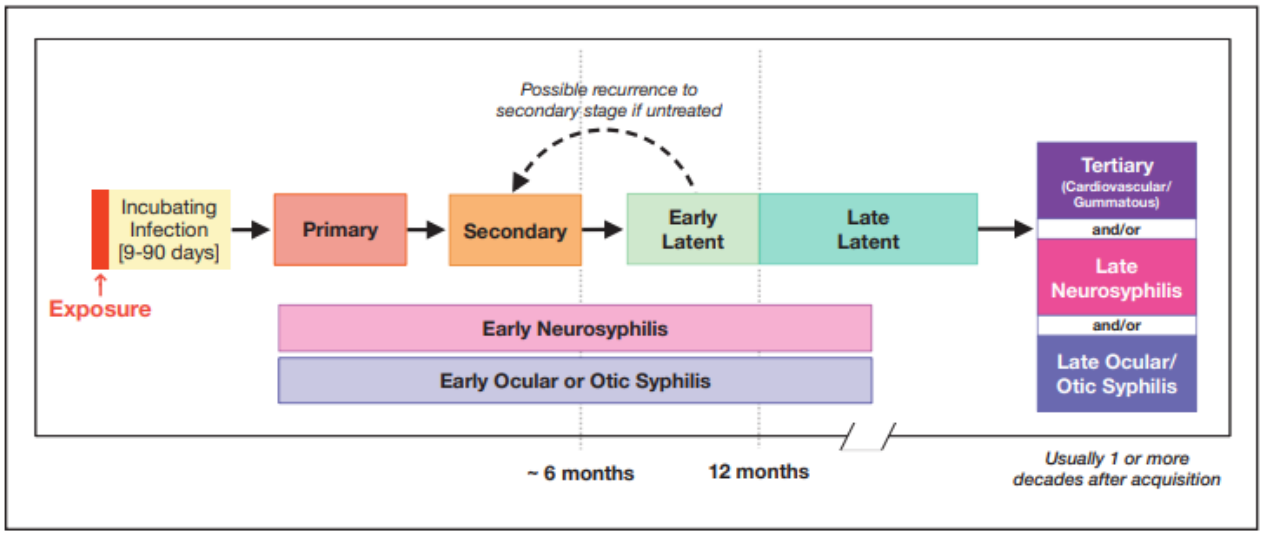
Neurosyphilis, Ocular Syphilis, and Otic Syphilis: clinical manifestations that can occur during any stage.

- **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

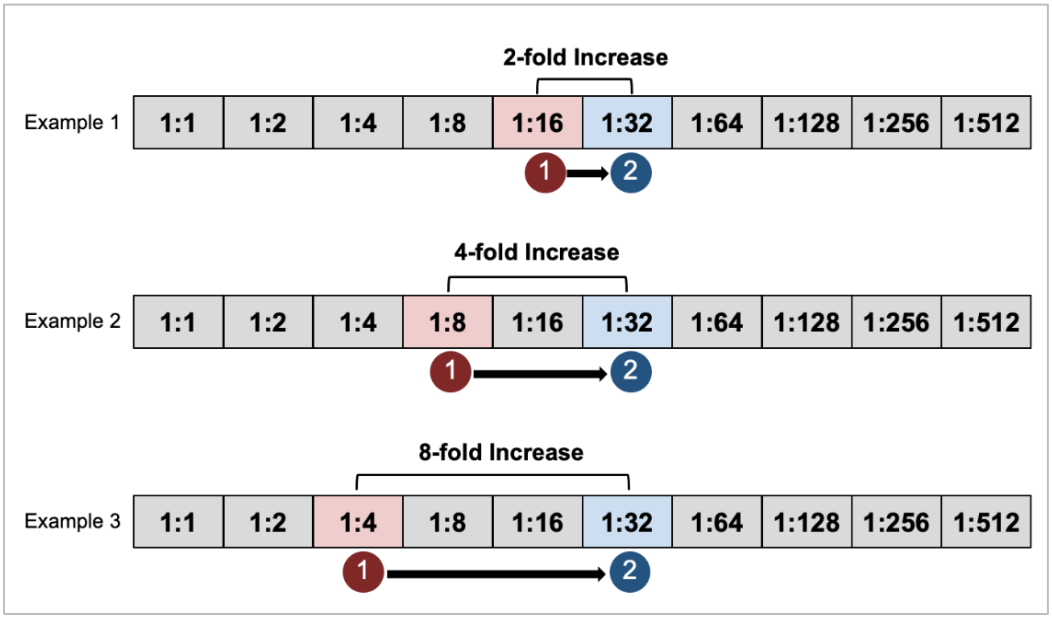
3.1.4 Unknown Duration or Late Syphilis

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

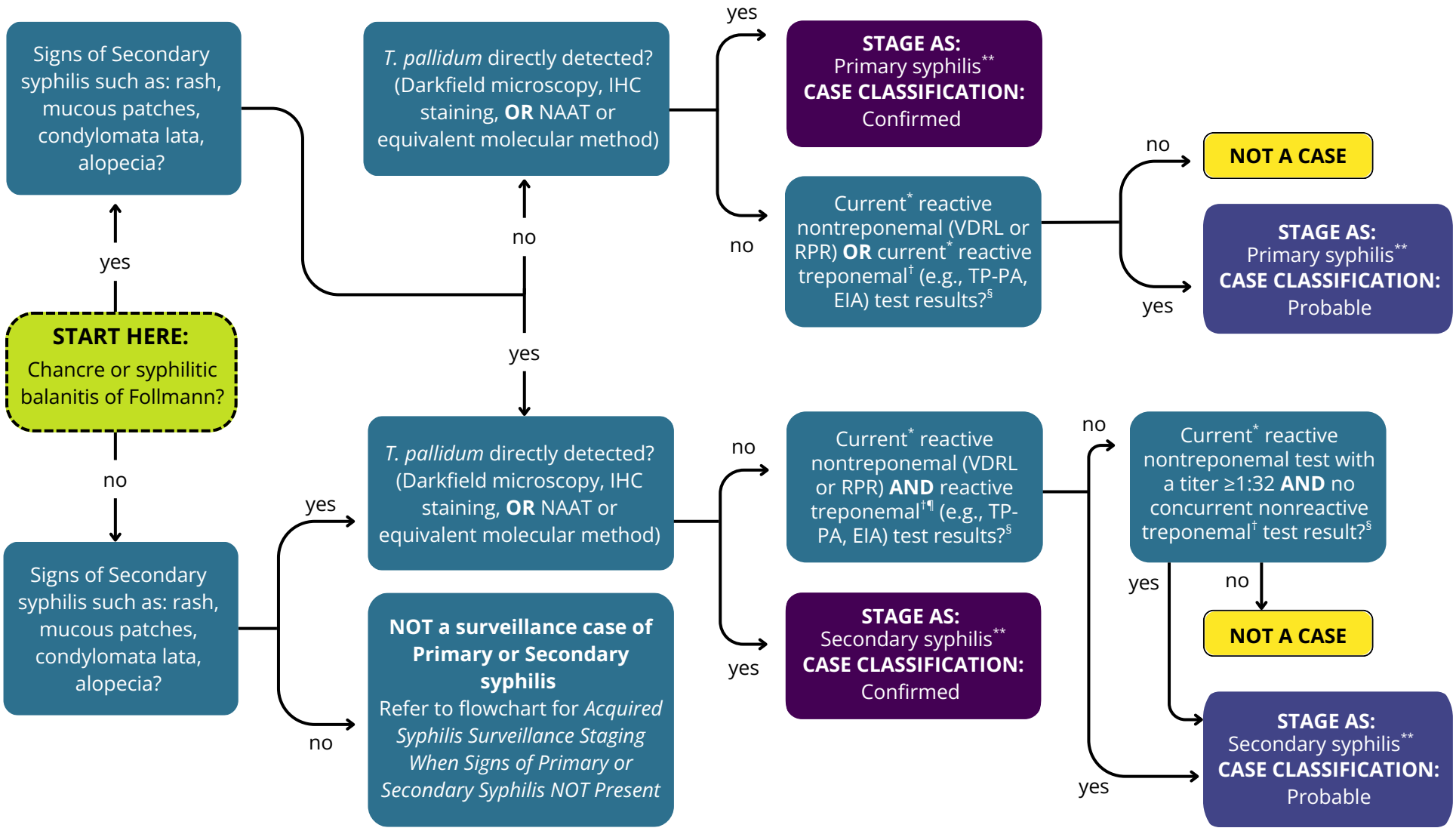
UPDATE LOG

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



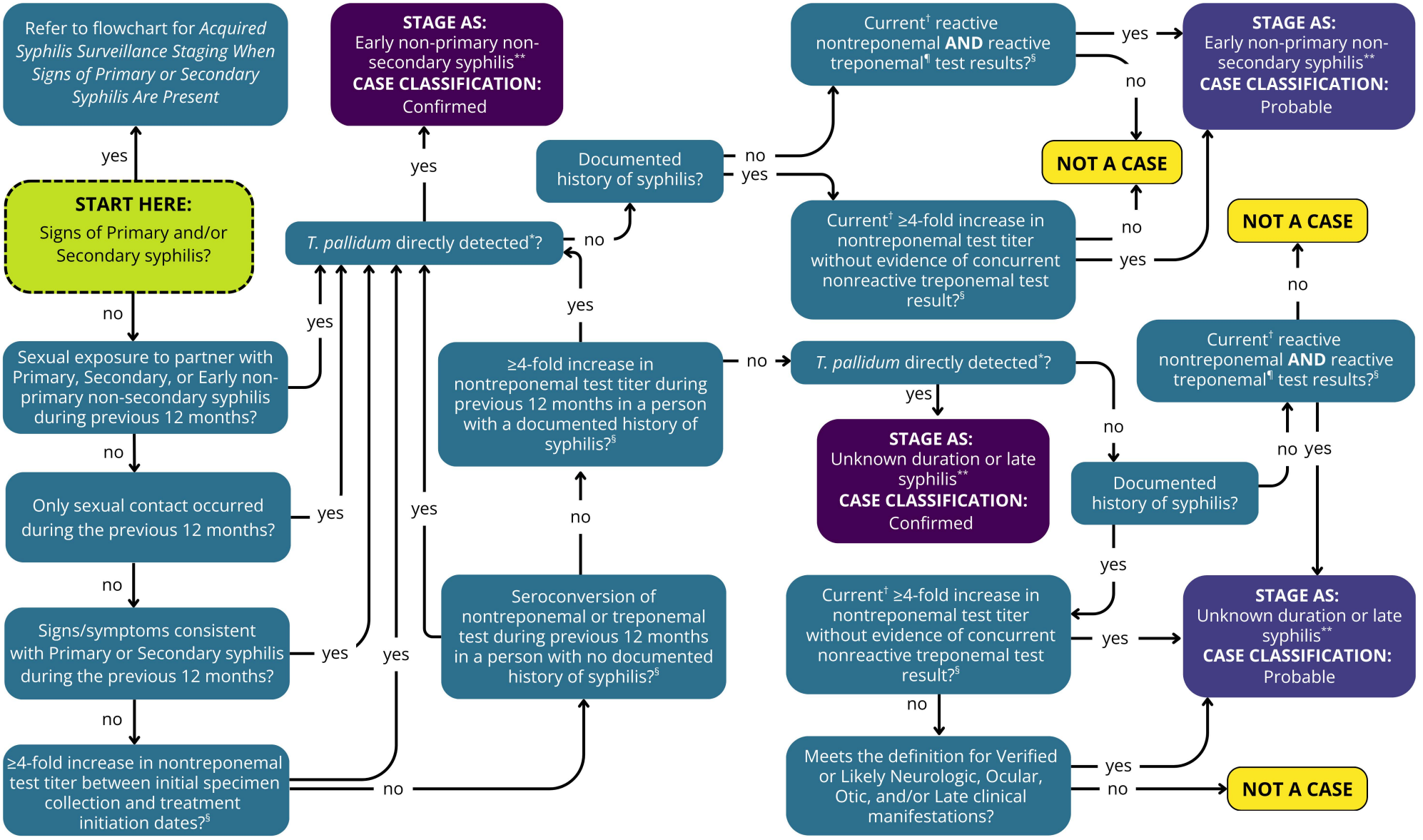
* Current refers to a test performed in the context of this index presentation.
† A reactive laboratory-based or point-of-care treponemal test result can be used to satisfy this requirement.
§ When nontreponemal and treponemal tests are mentioned in this algorithm, this refers to results from blood-based 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



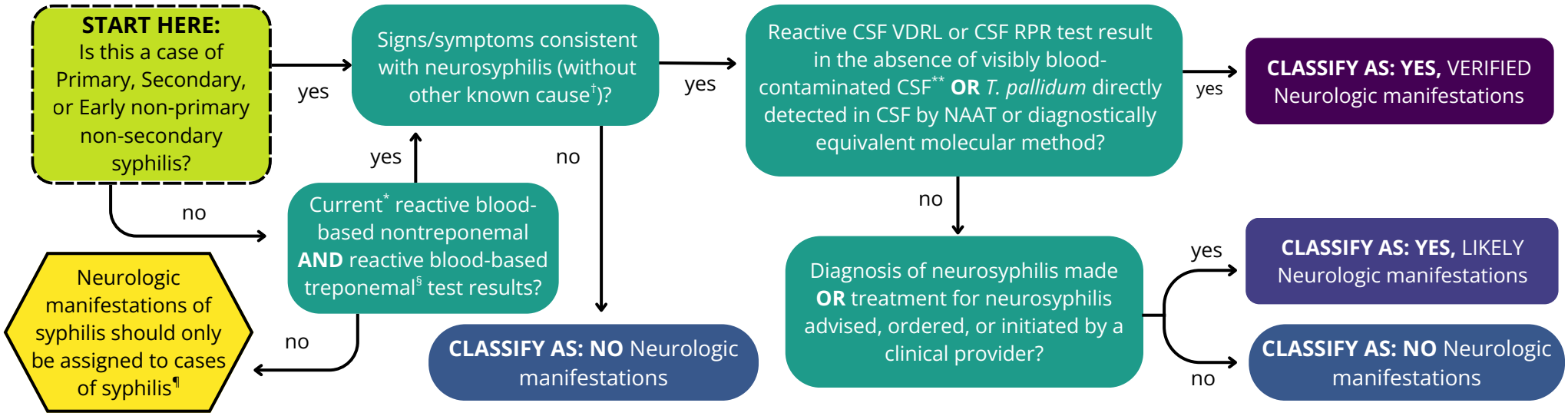
* Direct detection methods for cases of Early non-primary non-secondary syphilis may include nucleic acid amplification testing or a diagnostically equivalent molecular method. Direct detection methods for cases of Unknown duration or late syphilis may include nucleic acid amplification testing or a 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

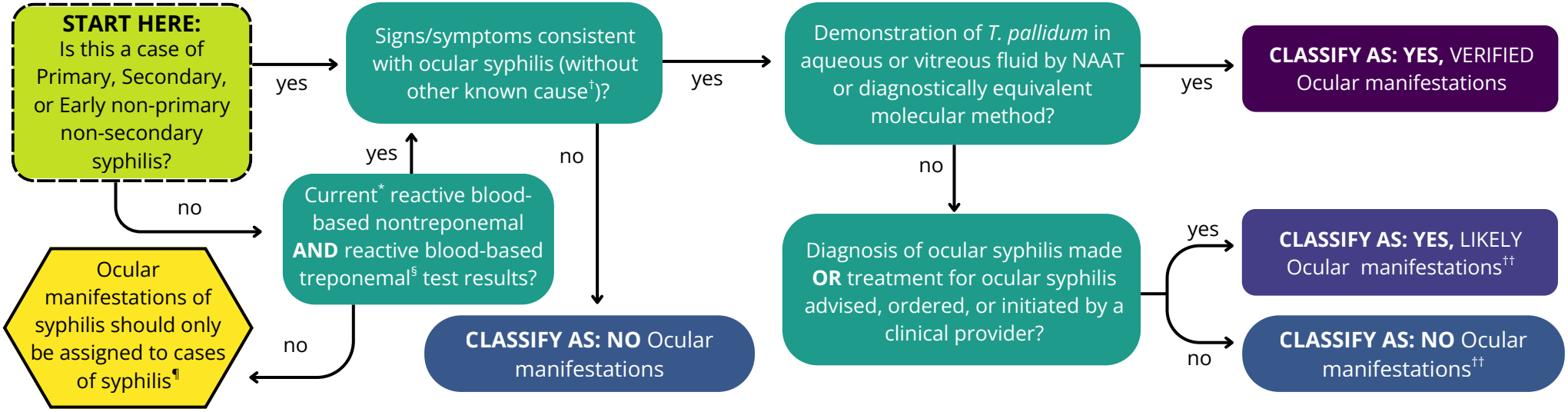
SURVEILLANCE CLASSIFICATION OF NEUROLOGIC MANIFESTATIONS OF SYPHILIS

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

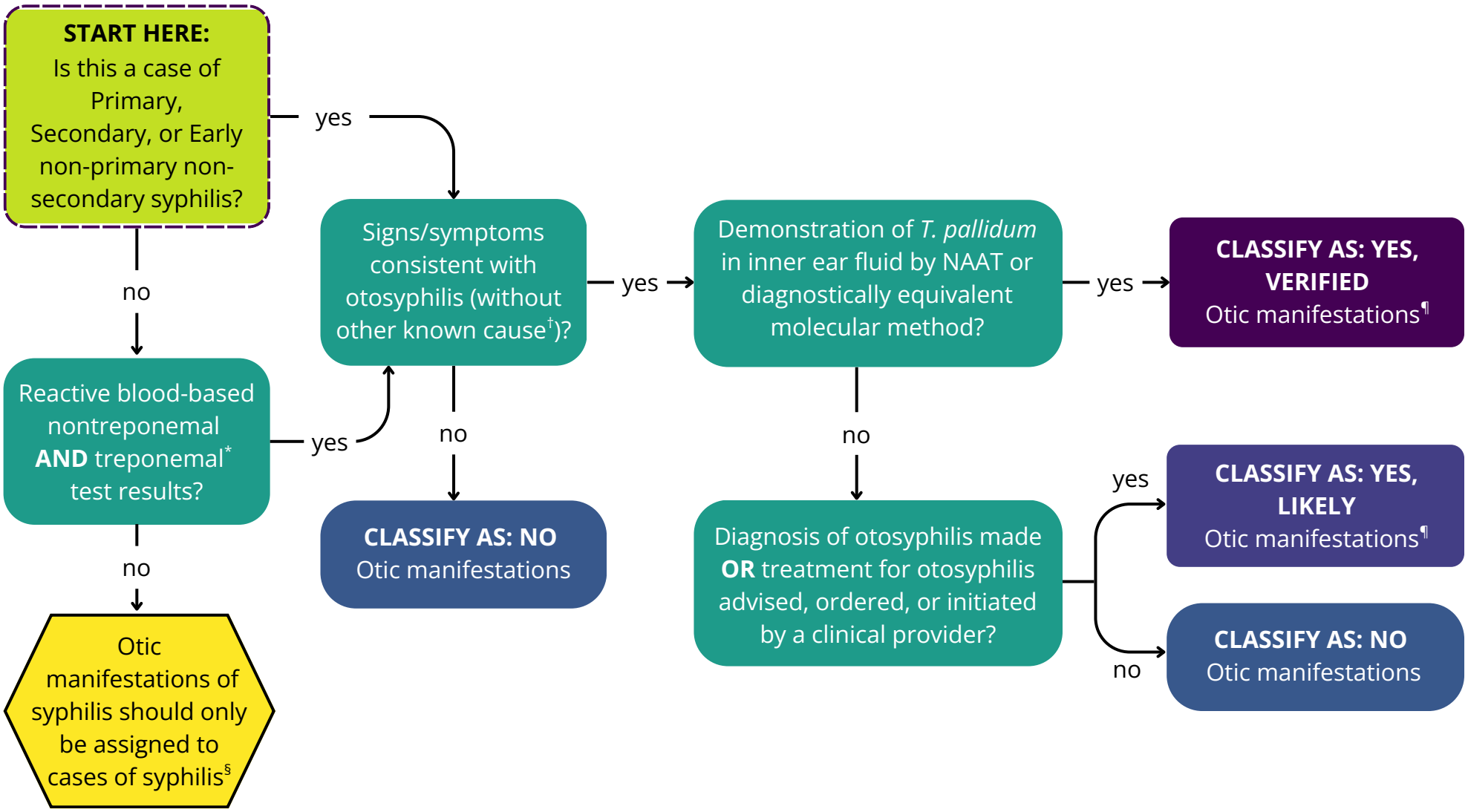


* Current refers to a test performed in the context of this index presentation.
† Clinician input may be needed to rule out other possible causes.
§ A reactive laboratory-based or point-of-care treponemal test result can be used to satisfy this requirement. Current or historical reactive treponemal antibody 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



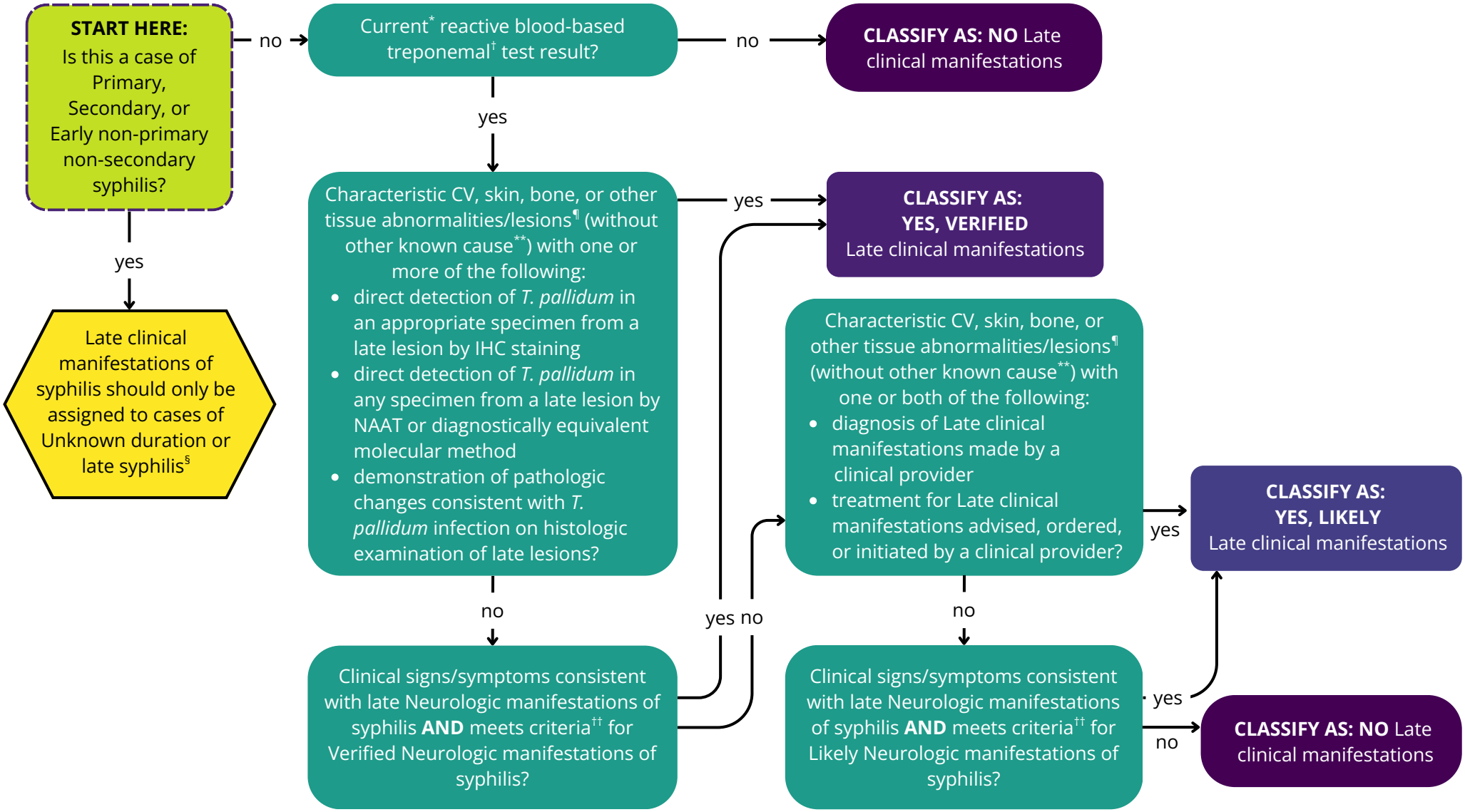
* A reactive laboratory-based or point-of-care treponemal test result can be used to satisfy this requirement. Current or historical reactive treponemal antibody tests can be used to satisfy this criterion.
† Clinician input may be needed to rule out other possible causes.
§ Any previously unreported 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**"

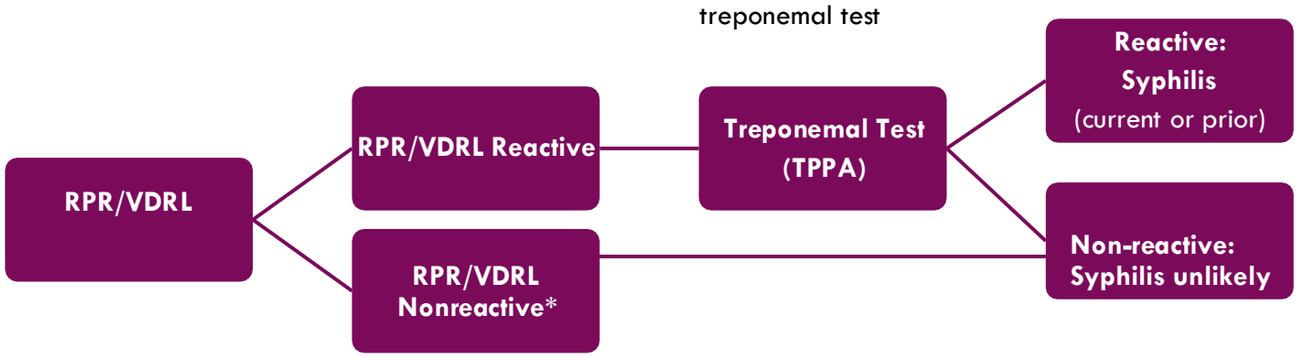
Appendix B

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.

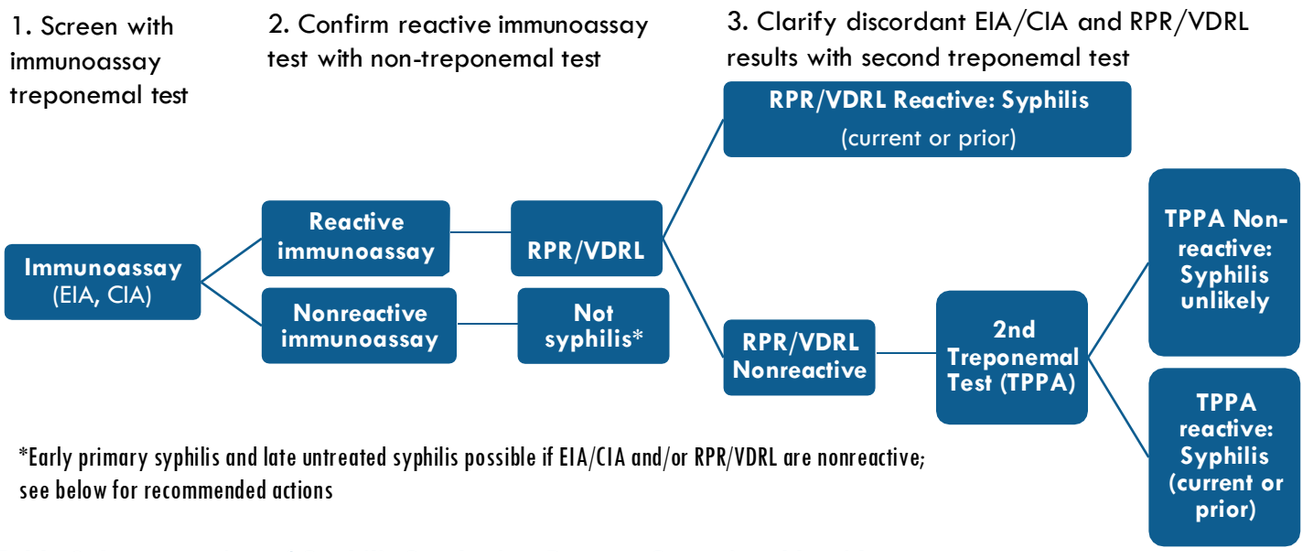
[b] False positives can be seen in pregnancy and/ in patients with autoimmune diseases, Lyme disease, certain viral infections (including HIV), injection drug use, and other conditions.

[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.