

Syphilis

Investigative Guidelines

August 2023

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.

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 skin ulcer 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 painless chancre BUT multiple chancres are common and can be painful (multiple chancres on genitals are often misdiagnosed as herpes simplex virus [HSV] infection)

- **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 only one type of lesion is associated with primary syphilis (chancre), 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 characteristic secondary rash appears on the hands and feet, and often the torso
 - Other secondary lesions may include:
 - Mucous patches in the mouth or genital area
 - Condyloma lata 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)

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- 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.

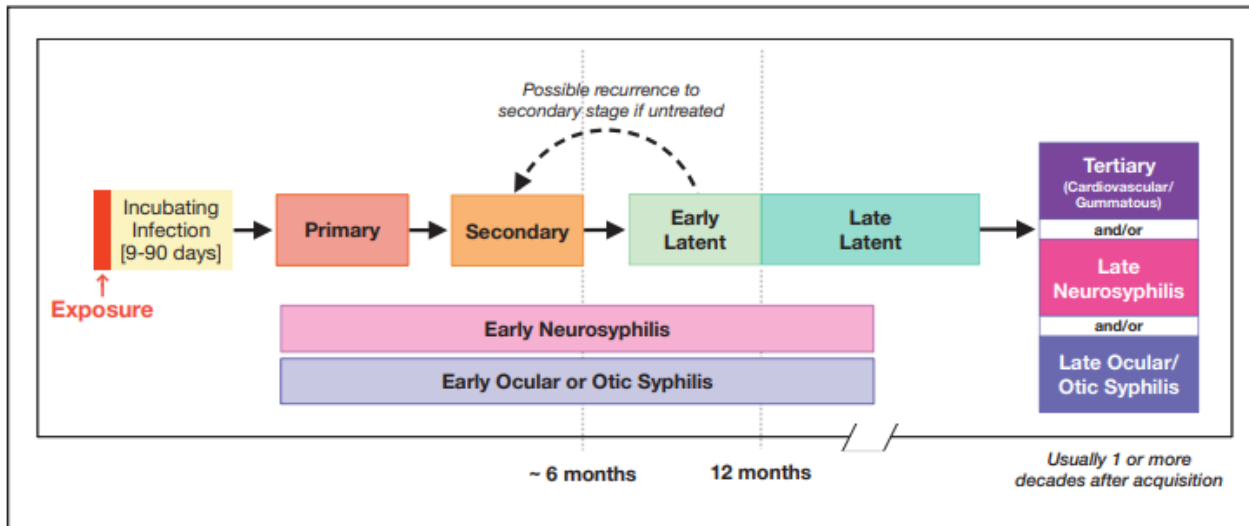
- **Neurosyphilis** can manifest as meningitis or stroke, cognitive dysfunction, motor or sensory deficits, and/or cranial nerve palsies
- **Ocular syphilis** can involve any eye structure but usually manifests as panuveitis or posterior uveitis
 - May cause permanent vision loss
 - Occurs with or without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

See **Figure 1** for a graphical summary of the natural history of syphilis.

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) 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) 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](#) and the [Is it Really a Penicillin Allergy?](#) fact sheet for guidance on evaluating a reported penicillin allergy.

- 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.
 - For people without pregnancy capacity, it is not necessary to restart treatment if intervals between doses are outside this range.
 - For non-pregnant people with pregnancy capacity, adherence to the 6–9-day interval is strongly encouraged to reduce the risk of congenital syphilis in a future pregnancy.
- **For pregnant patients 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. 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 Ootosyphilis	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 2 grams IV daily for 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 2018 Syphilis Surveillance Case Definition](#) page for more information on the stages below.⁵ The [CDC adult syphilis surveillance staging flowchart](#) (see Appendix A) is a useful tool for determining surveillance stage.

Since RPR testing is the most common form of nontreponemal testing, the terms “nontreponemal serologic testing” and “RPR” are used interchangeably throughout this section.

3.1.1 Primary Syphilis

1. Clinical Description
 - Stage characterized by one or more chancres
2. Laboratory Criteria
 - Confirmatory: *T. pallidum* by darkfield microscopy (only available at Multnomah Co. Health Department) or PCR or equivalent direct molecular methods
 - Supportive: Reactive serologic test for syphilis (RPR or treponemal test)
3. Case Classification
 - **Confirmed (rare):** Clinically compatible case with evidence of *T. pallidum* by darkfield microscopy or PCR or equivalent direct molecular methods
 - Confirmed criteria is NOT met by biopsy results or staining done with samples taken from lesions. If a darkfield exam (which does not involve staining) is not done, then a case is not confirmed.

- **Presumptive:** Clinically compatible case (must have chancre(s)) with at least one reactive serologic test (RPR or treponemal test)

3.1.2 Secondary Syphilis

1. Clinical Description
 - Stage characterized by a localized or diffuse rash. Other signs may include mucous patches, condyloma lata, and alopecia.
 - Secondary lesions may develop before primary chancres have fully resolved. If both primary and secondary signs are present, this is staged as secondary syphilis.
2. Laboratory Criteria
 - Confirmatory: *T. pallidum* by darkfield microscopy (only available at Multnomah Co. Health Department) or PCR or equivalent direct molecular methods
 - Supportive: Reactive RPR and reactive treponemal test
3. Case Classification
 - **Confirmed (rare):** Clinically compatible case with evidence of *T. pallidum* by darkfield microscopy or PCR or equivalent direct molecular methods
 - Confirmed criteria is NOT met by biopsy results or staining done with samples taken from lesions. If a darkfield exam (which does not involve staining) is not done, then a case is not confirmed.
 - **Presumptive:** Clinically compatible case (must have rash, mucous patches, condyloma lata, or alopecia) with reactive RPR **and** reactive treponemal test

3.1.3 Early Non-Primary Non-Secondary Syphilis

1. Clinical Description
 - Stage in which initial infection occurred within the previous 12 months and there are no signs or symptoms of primary or secondary syphilis
2. Laboratory Criteria
 - No past diagnosis of syphilis, and a reactive RPR and treponemal test **OR**
 - History of syphilis treatment, and a current RPR titer showing a fourfold or greater increase from the last titer (unless the increase was not sustained for >2 weeks). Refer to **Figure 2** for examples of increases in titers.
3. Case Classification
 - **Confirmed:** Cannot be confirmed. Can only be classified as presumptive.
 - **Presumptive:** No clinical signs or symptoms of primary or secondary syphilis and evidence of acquiring the infection within the previous 12 months based on one or more of the following:
 - Documented RPR seroconversion or at least a fourfold increase in titer in the past 12 months (unless the increase was not sustained for >2 weeks)
 - Documented treponemal test seroconversion in the past 12 months
 - History of symptoms consistent with primary or secondary syphilis in the past 12 months

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- History of sexual exposure to a partner in 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)
- Only sexual contact ever was in the past 12 months

3.1.4 Unknown Duration or Late Syphilis

1. Clinical Description

- Stage in which there are no signs or symptoms of primary or secondary syphilis and a) initial infection occurred >12 months ago or b) there is not enough evidence to prove the infection was acquired in the past 12 months

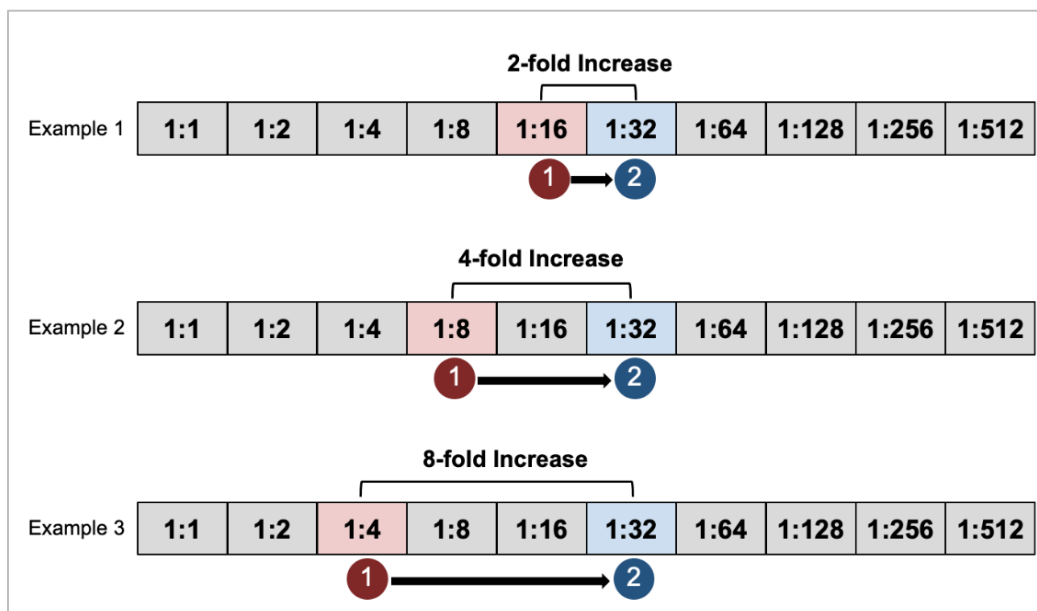
2. Laboratory Criteria

- No past diagnosis of syphilis, and a reactive RPR and treponemal test
OR
- History of syphilis treatment, and a current RPR titer showing a fourfold or greater increase from the last titer (unless the increase was not sustained for >2 weeks). Refer to **Figure 2** for examples of increases in titers.
OR
- Likely or verified neurologic, ocular, otic, or late clinical manifestations without a current RPR titer showing a fourfold or greater increase

3. Case Classification

- **Confirmed:** Cannot be confirmed. Can only be classified as presumptive.
- **Presumptive:** No clinical signs or symptoms of primary or secondary syphilis, no evidence of having acquired the disease in the past 12 months, and meets laboratory criteria

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](#).

3.2 Syphilis Complications

See the [CDC 2018 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. Clinical Description

- Infection of the central nervous system with *T. pallidum*, as shown by manifestations including cranial nerve dysfunction, meningitis, meningovascular syphilis, stroke, altered mental status, tabes dorsalis, and general paresis
- 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. Classification of Neurologic Manifestations

- **Possible:** Reactive RPR and treponemal test **AND** clinical symptoms or signs consistent with neurosyphilis without other known causes
- **Likely:** Reactive RPR and treponemal test with both of the following:
 - Clinical symptoms or signs consistent with neurosyphilis without other known causes of these abnormalities,
AND
 - Elevated cerebrospinal fluid (CSF) protein (>50 mg/dl²) or white blood cell (WBC) count (>5 WBC/mm³) without other known causes
- **Verified:** Reactive RPR and treponemal test with both of the following:
 - Clinical symptoms or signs that are consistent with neurosyphilis without other known causes
AND
 - A reactive CSF VDRL in the absence of grossly bloody contamination, defined as a red blood cell (RBC) concentration of over 6000 per cubic millimeter in the CSF

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. Ocular syphilis is an emergency—permanent vision loss can occur if not treated promptly.

1. Clinical Description

- Infection of any eye structure with *T. pallidum*, as shown by manifestations including posterior uveitis, panuveitis, anterior uveitis, optic neuropathy, retinal vasculitis, and interstitial keratitis
- 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. Classification of Ocular Manifestations

- **Possible:** Reactive RPR and treponemal test **AND** clinical symptoms or signs consistent with ocular syphilis without other known causes
- **Likely:** Reactive RPR and treponemal test with both of the following:
 - Clinical symptoms or signs consistent with ocular syphilis without other known causes of these abnormalities,**AND**
 - Findings on exam by an ophthalmologist that are consistent with ocular syphilis without other known causes
- **Verified (rare):** Reactive RPR and treponemal test with both of the following:
 - Clinical symptoms or signs that are consistent with ocular syphilis without other known causes**AND**
 - *T. pallidum* in eye fluid by darkfield microscopy or PCR

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. Otosyphilis is an emergency—permanent hearing loss can occur if not treated promptly.

1. Clinical Description

- Infection of the cochleovestibular system with *T. pallidum*, as shown by manifestations including sensorineural hearing loss, tinnitus, and vertigo
- Symptoms include hearing loss; tinnitus (ringing, buzzing, roaring, or hissing in the ears); balance difficulties; and dizziness or vertigo

2. Classification of Otic Manifestations

- **Possible:** Reactive RPR and treponemal test **AND** clinical symptoms or signs consistent with otosyphilis without other known causes
- **Likely:** Reactive RPR and treponemal test with both of the following:
 - Clinical symptoms or signs consistent with otosyphilis without other known causes of these abnormalities,**AND**
 - Findings on exam by an otolaryngologist that are consistent with otosyphilis without other known causes
- **Verified (rare):** Reactive RPR and treponemal test with both of the following:

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- Clinical symptoms or signs that are consistent with otosyphilis without other known causes

AND

- *T. pallidum* in inner ear fluid by darkfield microscopy or PCR

3.2.4 Late Clinical Manifestations (extremely rare)

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

1. Clinical Description

- Late clinical manifestations of syphilis may include inflammatory lesions of the cardiovascular system, skin, bone, or other tissue

2. Classification of Late Clinical Manifestations of Syphilis

- **Possible:** Not an option for late clinical manifestations
- **Likely:** Reactive RPR and treponemal test with either of the following:
 - Characteristic abnormalities or lesions of the cardiovascular system, skin, bone, or other tissue, without other known causes

OR

- Clinical signs and symptoms consistent with late neurologic manifestations of syphilis and either elevated CSF protein (>50 mg/dl²) or CSF WBC count (>5 WBC/mm³) without other known causes

- **Verified:** Reactive RPR and treponemal test and either of the following:
 - Characteristic abnormalities or lesions of the cardiovascular system, skin, bone, or other tissue without other known causes, in combination with either *T. pallidum* by special stains or PCR, or pathologic changes that are consistent with *T. pallidum* infection on histologic examination

OR

- Clinical signs and symptoms consistent with late neurologic manifestations of syphilis and a reactive CSF VDRL

3.3 Diagnosis

3.3.1 Direct Detection of *T. Pallidum*

Darkfield microscopy and molecular tests (e.g., PCR) for detecting *T. pallidum* directly from of lesion fluid or tissue are the definitive methods for immediate diagnosis of primary or secondary syphilis.

The only darkfield microscope currently in use in Oregon is at the Multnomah County Health Department.

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
<i>What are the common test names?</i>	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); <i>Treponema pallidum</i> 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.
<i>Is the test specific to syphilis?</i>	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 <i>T. pallidum</i> .
<i>Is the test qualitative or quantitative?</i>	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 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+), it should be ignored.

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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.

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.

No matter which screening algorithm is followed, a second treponemal test may be necessary if the first treponemal test result is equivocal/indeterminate.

If the reverse screening algorithm is followed, a second treponemal test may be necessary.

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 QI RPR Ser Titr RPR Titer
	VDRL	VDRL Ser QI VDRL Quantitative

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Treponemal Tests (qualitative only)	FTA	FTA-ABS T pallidum Ab Ser QI IF
	TPPA	TPPA TP-PA T pallidum Ab Particle Agglutination
	EIA/CIA*	Syphilis TP T pallidum Ab Ser QI T pallidum Ab Ser QI IA T pallidum IgG+IgM Ser QI 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 ($\geq 1:16$)
 - 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 preferable but interviews by phone 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:
 - [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 non-reactive 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 Bicillin L-A 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 PEP (DoxyPEP) and HIV pre- and post-exposure prophylaxis (PrEP and PEP)
 - Transgender women and gay, bisexual, and other men who have sex with men, on diagnosis of chlamydia, should be offered doxycycline postexposure prophylaxis for bacterial sexually transmitted infections (doxyPEP). Providers should use their clinical judgement and shared decision-making to inform use of doxyPEP with populations that are not part of CDC recommendations. See the [CDC doxyPEP guidelines](#) for more information.
 - 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

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.

Syphilis IG

- 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 (Bicillin L-A) 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 (Bicillin L-A) 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	3 months 6 months 9 months
	12 months	12 months 24 months
Late or Unknown Duration	6 months	6 months
	12 months	12 months 18 months
	24 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?

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- Yes. Primary syphilis is the only stage that does not require both a reactive RPR and a reactive treponemal test. 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 a chancre is not present, then this is not a primary case (see §3.1.1). Consult the [CDC adult syphilis surveillance staging flowchart](#) to determine the 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?
 - Most likely. However, the surveillance case definition for secondary syphilis requires a reactive treponemal test. 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, 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 Bicillin L-A doses even if the early non-primary non-secondary case definition is met since clinical and surveillance staging can differ.

TREATMENT

1. A patient was accidentally treated with only 1.2 million units of benzathine penicillin G (Bicillin L-A). 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 Bicillin L-A 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 Bicillin L-A should be considered since doxycycline regimens are difficult to complete. See §5.2 for additional recommendations.

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), and fluorescent treponemal antibody absorption (FTA-ABS) 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 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>
3. Oregon Revised Statutes. Chapter 433 Disease and Condition Control.
https://www.oregonlegislature.gov/bills_laws/ors/ors433.html
4. CDC Sexually Transmitted Infections Treatment Guidelines, 2021.
<https://www.cdc.gov/std/treatment-guidelines/default.htm>
5. CDC National Notifiable Diseases Surveillance System (NNDSS) Syphilis (*Treponema pallidum*) 2018 Case Definition. <https://ndc.services.cdc.gov/case-definitions/syphilis-2018/>

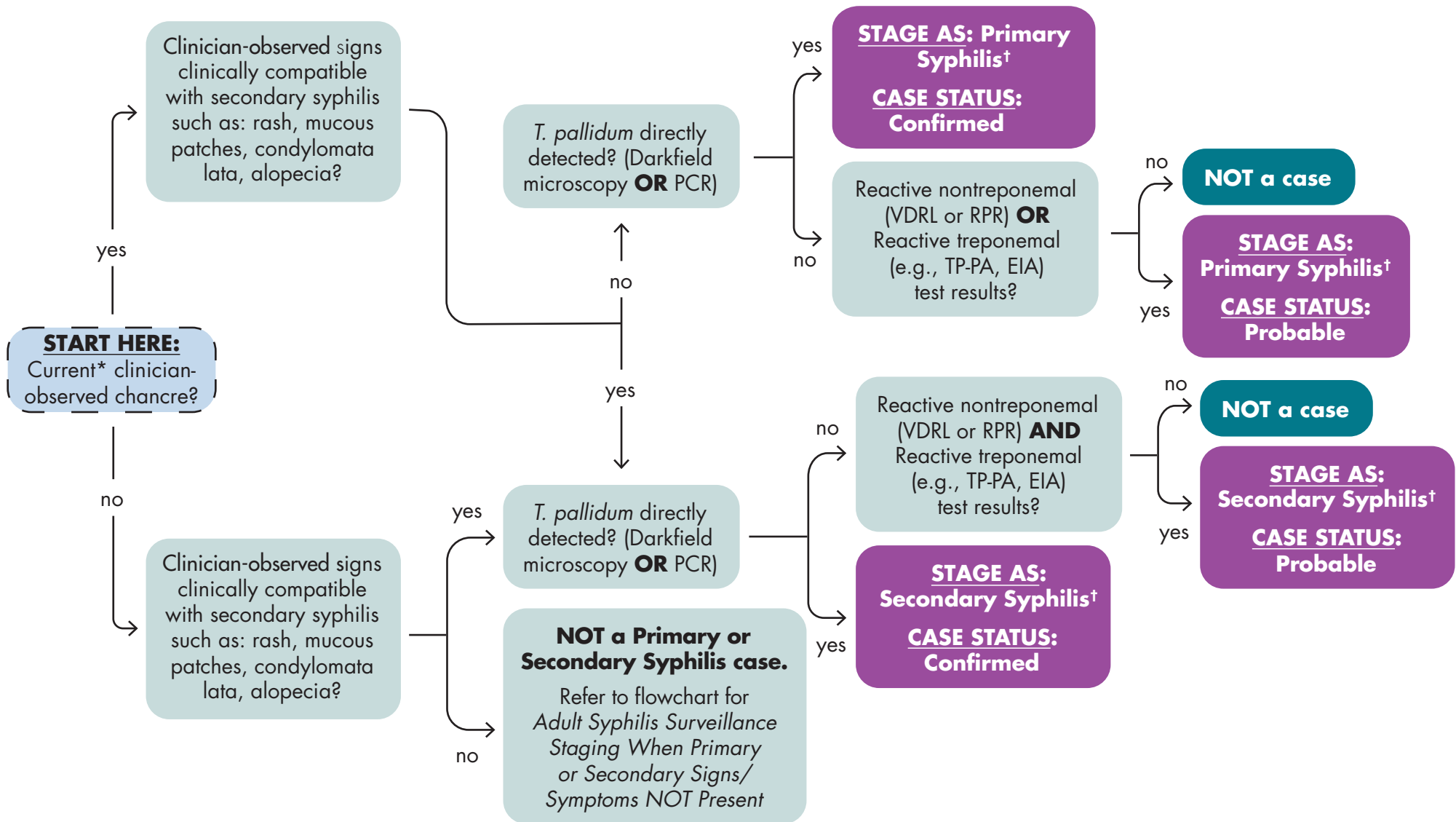
UPDATE LOG

July 2023. Extensively rewritten and reformatted. (Garai, Gonzalez Pena, Menza)
August 2024. Broken links and appendices updated. Confirmatory criteria and direct detection methods in §3 updated. Education on DoxyPEP added. (Garai)

Appendix A

ADULT SYPHILIS SURVEILLANCE STAGING WHEN PRIMARY OR SECONDARY SYPHILIS SIGNS/SYMPTOMS ARE PRESENT

(Not to be used as guidance for treatment)



*Current refers to the anchoring date of the original diagnosis, such as at time of original clinical diagnosis or positive screening test.

†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,” “Possible,” or “Unknown.” Late clinical manifestations of syphilis are classified separately as “No,” “Verified,” “Likely,” or “Unknown.” For assistance with classification of these manifestations, please see clinical manifestations algorithms.

ACRONYMS: *T. pallidum* = *Treponema pallidum*; PCR = polymerase chain reaction; VDRL = Venereal Disease Research Laboratory; RPR = rapid plasma reagin; TP-PA = *Treponema pallidum* particle agglutination; EIA = enzyme immunoassay

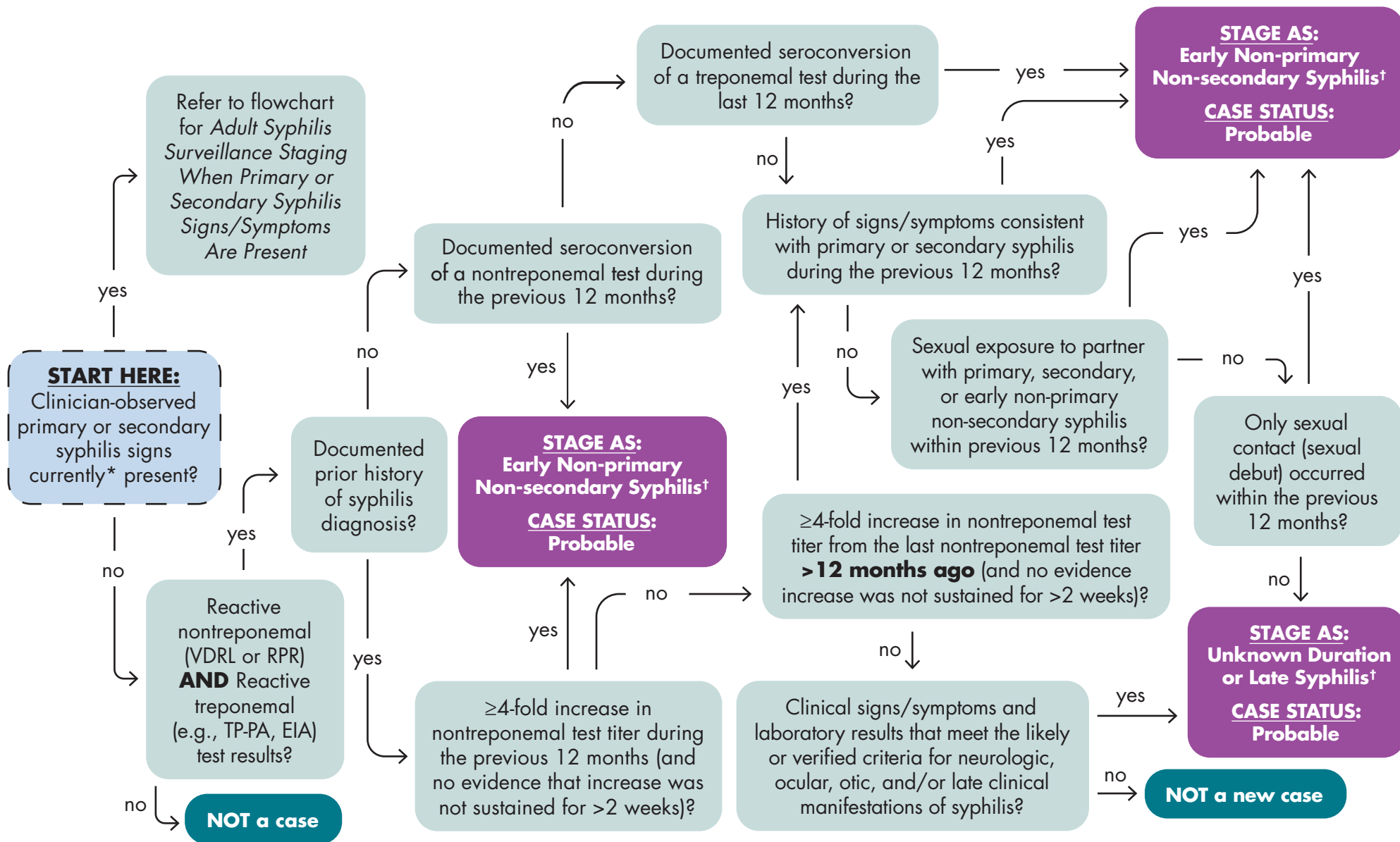
RESOURCES: [Syphilis case definitions](#); [Syphilis treatment guidelines](#); [Partner services](#)



Updated 6/1/2023

ADULT SYPHILIS SURVEILLANCE STAGING WHEN PRIMARY OR SECONDARY SIGNS/SYMPTOMS NOT PRESENT

(Not to be used as guidance for treatment)



*Current refers to the anchoring date of the original diagnosis, such as at time of original clinical diagnosis or positive screening test.

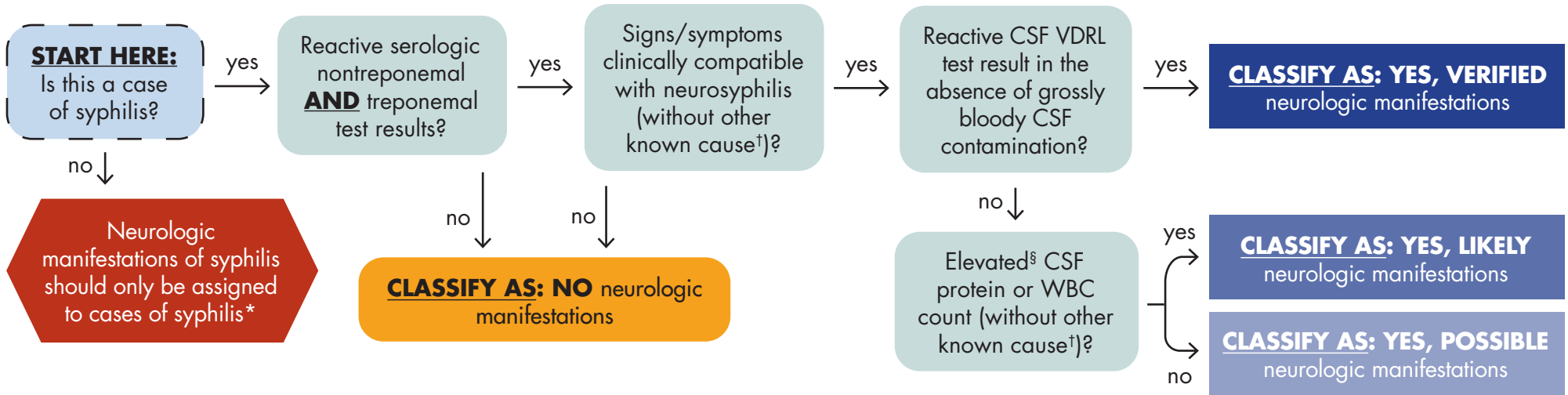
†Neurologic, ocular, and otic manifestations of syphilis can occur at any stage. After assigning syphilis stage, assess all cases for these clinical manifestations and classify separately as “No,” “Verified,” “Likely,” “Possible,” or “Unknown.” Late clinical manifestations of syphilis are classified separately as “No,” “Verified,” “Likely,” or “Unknown.” For assistance with classification of these manifestations, please see clinical manifestations algorithms.

ACRONYMS: VDRL = Venereal Disease Research Laboratory; RPR = rapid plasma reagin; TP-PA = *Treponema pallidum* particle agglutination; EIA = enzyme immunoassay.

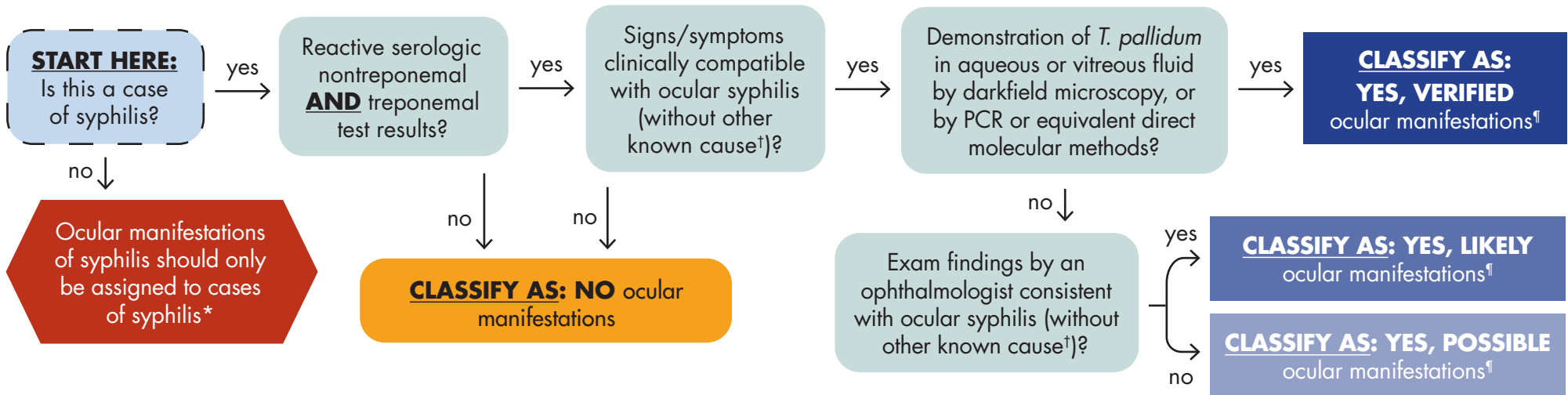
RESOURCES: [Syphilis case definitions](#); [Syphilis treatment guidelines](#); [Partner services](#)



SURVEILLANCE CLASSIFICATION OF **NEUROLOGIC** MANIFESTATIONS OF SYPHILIS *(Not to be used as guidance for treatment)*



SURVEILLANCE CLASSIFICATION OF **OCULAR** MANIFESTATIONS OF SYPHILIS *(Not to be used as guidance for treatment)*



*Any case with clinical signs/symptoms and laboratory results that meet the likely or verified criteria for neurologic, ocular, otic, or late clinical manifestations of syphilis and that has no evidence of having acquired the disease within the preceding 12 months meets the Council of State and Territorial Epidemiologists case definition for unknown duration or late syphilis.

[†]Clinician input may be needed to rule out other possible causes.

[§]The Council of State and Territorial Epidemiologists case definition for neurologic manifestations of syphilis defines elevated CSF protein as >50 mg/dL and elevated CSF WBC count as >5 WBCs/mm³. Additional guidance for interpretation of CSF results is available in [CDC's STI Treatment Guidelines](#).

[¶]Because ocular manifestations are considered signs/symptoms clinically compatible with neurosyphilis, cases classified as having ocular manifestations should also be classified as having neurologic manifestations.

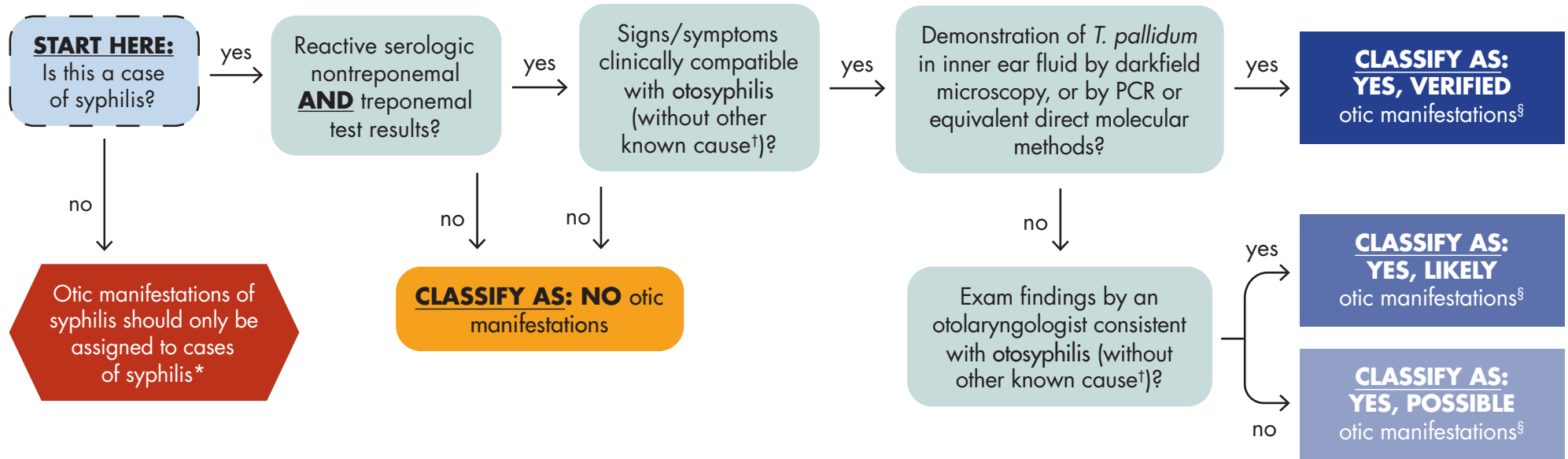
ACRONYMS: CSF = cerebrospinal fluid; VDRL = Venereal Disease Research Laboratory; WBC = white blood cell; *T. pallidum* = *Treponema pallidum*; PCR = polymerase chain reaction

RESOURCES: [Syphilis case definitions](#); [Syphilis treatment guidelines](#); [Partner services](#)



Updated 5/23/2023

SURVEILLANCE CLASSIFICATION OF **OTIC** MANIFESTATIONS OF SYPHILIS *(Not to be used as guidance for treatment)*



*Any case with clinical signs/symptoms and laboratory results that meet the likely or verified criteria for neurologic, ocular, otic, or late clinical manifestations of syphilis and that has no evidence of having acquired the disease within the preceding 12 months meets the Council of State and Territorial Epidemiologists case definition for unknown duration or late syphilis.

†Clinician input may be needed to rule out other possible causes.

§Because otic manifestations are considered signs/symptoms clinically compatible with neurosyphilis, cases classified as having otic manifestations should also be classified as having neurologic manifestations.

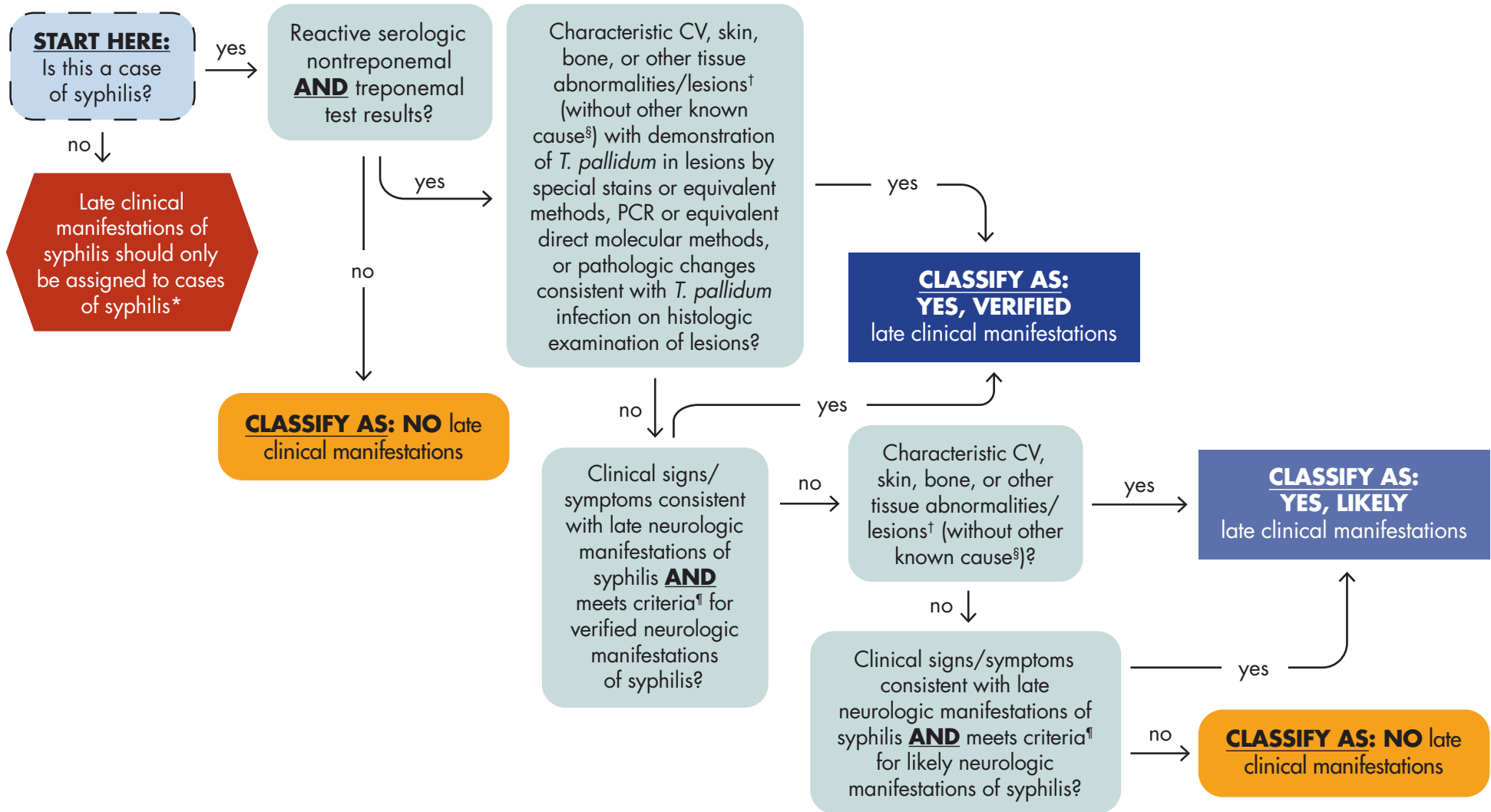
ACRONYMS: *T. pallidum* = *Treponema pallidum*; PCR = polymerase chain reaction

RESOURCES: [Syphilis case definitions](#); [Syphilis treatment guidelines](#); [Partner services](#)



Updated 5/23/2023

SURVEILLANCE CLASSIFICATION OF LATE CLINICAL MANIFESTATIONS OF SYPHILIS *(Not to be used as guidance for treatment)*



*Any case with clinical signs/symptoms and laboratory results that meet the likely or verified criteria for neurologic, ocular, otic, or late clinical manifestations of syphilis and that has no evidence of having acquired the disease within the preceding 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 neurologic manifestations classification algorithm for additional assistance.

ACRONYMS: CV = cardiovascular; *T. pallidum* = *Treponema pallidum*; PCR = polymerase chain reaction

RESOURCES: [Syphilis case definitions](#); [Syphilis treatment guidelines](#); [Partner services](#)



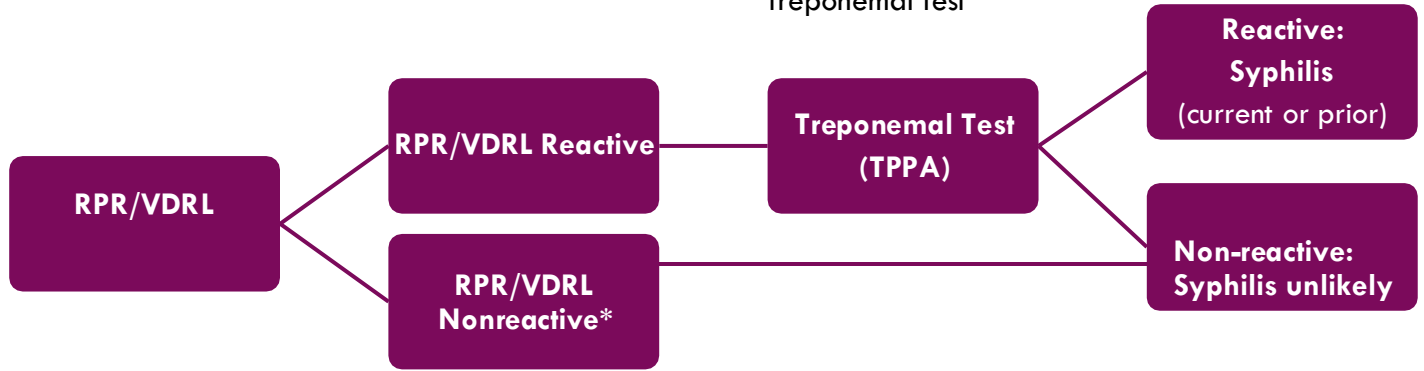
Appendix B

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	<ol style="list-style-type: none"> No syphilis Early/incubating syphilis (too early to be detected by serology) 	<ul style="list-style-type: none"> 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	<ol style="list-style-type: none"> Prior treated syphilis Untreated syphilis 	<ul style="list-style-type: none"> 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	<ol style="list-style-type: none"> False positive RPR or VDRL 	<ul style="list-style-type: none"> 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	<ol style="list-style-type: none"> Current syphilis Treated syphilis with residual/persistent RPR/VDRL titer 	<ul style="list-style-type: none"> 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 at least twice during pregnancy: once at either confirmation of pregnancy or at the first pre-natal encounter, and again during the third trimester (ideally between 28-32 weeks). Patients should also be screened at delivery, except those at low risk who have a documented negative screen in the third trimester. See <https://www.cdph.ca.gov/Programs/CID/DCDC/Pages/California-STI-Screening-Recommendations.aspx%20As%20of%20April%202024>. As of April 2024, the American College of Obstetrics and Gynecology 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.

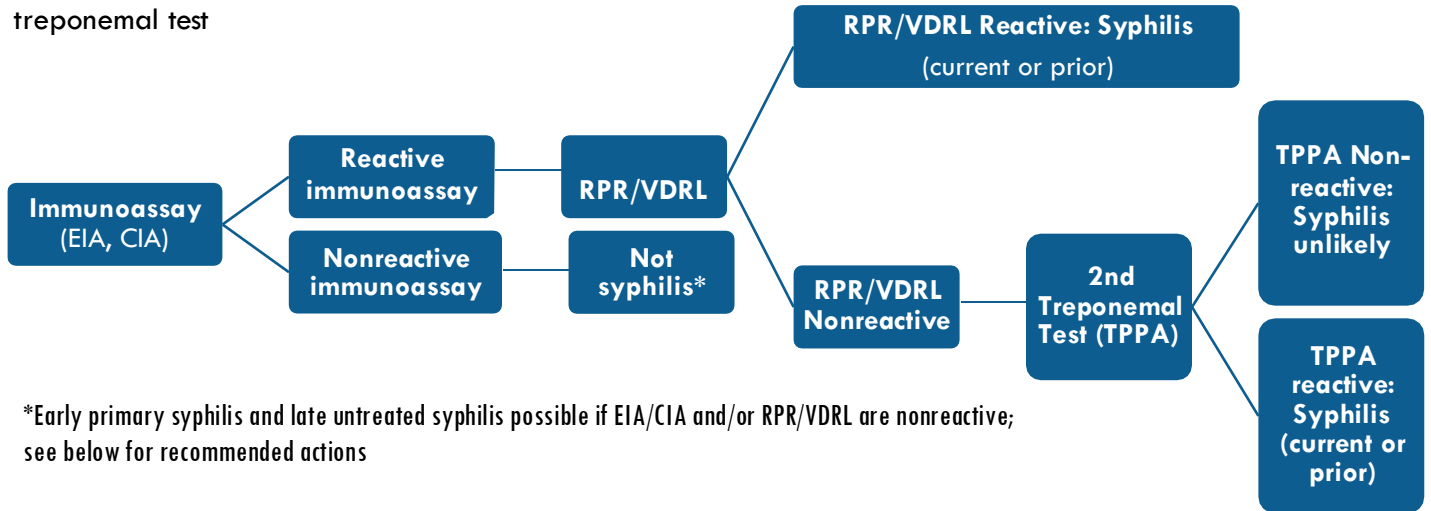
Clinical Interpretation of Syphilis Screening Algorithms

Testing: Reverse Algorithm^a

1. Screen with immunoassay treponemal test

2. Confirm reactive immunoassay test with non-treponemal test

3. Clarify discordant EIA/CIA and RPR/VDRL results with second treponemal test



*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

Immunoassay (CIA or EIA)	RPR/VDRL	TPPA	Possible Interpretations	Recommended Actions
Non-reactive	Non-reactive or not done	Non-reactive or not done	<ol style="list-style-type: none"> Syphilis unlikely Early/incubating syphilis (too early to be detected by serology) 	<ul style="list-style-type: none"> 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	<ol style="list-style-type: none"> False positive immunoassay Early/incubating syphilis Latent or prior syphilis (treated or untreated) 	<ul style="list-style-type: none"> 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	<ol style="list-style-type: none"> Latent or prior syphilis (treated or untreated) Early syphilis (prior to RPR/VDRL seroconversion) 	<ul style="list-style-type: none"> 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	<ol style="list-style-type: none"> Current syphilis Prior syphilis (treated or untreated) 	<ul style="list-style-type: none"> 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 at least twice during pregnancy: once at either confirmation of pregnancy or at the first pre-natal encounter, and again during the third trimester (ideally between 28-32 weeks). Patients should also be screened at delivery, except those at low risk who have a documented negative screen in the third trimester. See <https://www.cdph.ca.gov/Programs/CID/DCDC/Pages/California-STI-Screening-Recommendations.aspx%20As%20of%20April%202024>. As of April 2024, the American College of Obstetrics and Gynecology 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.