



Clinical Practice Alert

August 2022

Syphilis Screening, Diagnosis, and Treatment

Introduction

Rates of syphilis have been rising in the U.S., including in California, which has resulted in a corresponding rise in the rates of congenital syphilis (CS). Fifteen percent of women of childbearing age diagnosed with syphilis are pregnant. Statewide, CS cases increased more than 900 percent between 2012 and 2018. These trends mirror a sharp increase in all stages of syphilis among females, which increased more than 500 percent during the same period.

Note: This Clinical Practice Alert includes management of primary, secondary, and latent syphilis. It does not include screening and management of syphilis in people who are pregnant or the diagnosis and treatment of tertiary syphilis.

Questions and Answers



Who should be screened for syphilis?

The California Department of Public Health (CDPH) guidelines for “Syphilis Screening for All People Who Could Become Pregnant” include two new, important recommendations:

- All sexually active people who could become pregnant should receive at least one lifetime screen for syphilis, with additional screening for those at increased risk.
- All sexually active people who could become pregnant should be screened for syphilis at the time of each HIV test.

The U.S. Preventive Services Task Force (USPSTF)¹ and the CDPH recommendations define individuals who are at increased risk for syphilis infection as:

- MSM (men having sex with men), MSMW (a man who has sex with men and women) & TGW (transgender women): screen annually; more frequently if at increased risk
- Males younger than 29 years of age
- Recent incarceration or a sex partner who was recently incarcerated
- Individuals with a history of commercial sex work

- Having sex in exchange for resources, such as money or drugs
- Having sex under the influence of alcohol or drugs
- Methamphetamine use, intravenous drug use
- Homeless or unstable housing
- History of syphilis infection
- Diagnosis of another STI within the past 12 months
- Pelvic pain or a diagnosis of pelvic inflammatory disease (PID)
- Multiple sex partners
- Sex partners who are MSMW or who have other concurrent partners
- Regional variations (hot spots)
 - Living in a local health jurisdiction with high syphilis morbidity among females
 - Living in a local health jurisdiction with high-congenital syphilis morbidity
- HIV-seropositive (all genders): annually; more frequently if at increased risk
- Using HIV PrEP (all genders): every 3 months

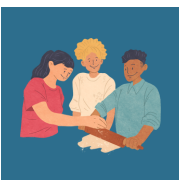
The Centers for Disease Control and Prevention (CDC) *Sexually Transmitted Infection (STI) Treatment Guidelines*, 2021² further recognize risk factors that are common to both HIV and syphilis, indicating people who could become pregnant seeking evaluation and treatment for STIs should be screened concurrently for HIV and syphilis.



Are there special situations to screen for syphilis in the context of family planning services?

Offer syphilis screening as a component of pre-pregnancy care to clients who:

- Are seen for advice about achieving pregnancy or basic infertility services
- Request removal of an intrauterine device (IUD) or contraceptive implant to become pregnant
- Request pregnancy testing (whether positive or negative)
- Disclose during reproductive intentions counseling that they would like to become pregnant immediately or in the next 12 months, or those who are ambivalent or indifferent to becoming pregnant



Who can consent to syphilis screening and diagnostic testing?

In California, all persons aged 12 years and older have a right to consent on their own to confidential STI prevention, testing, and treatment services, including syphilis-related care.



When should diagnostic testing be performed?

The disease is divided into stages based on clinical findings, which guide treatment and follow-up.

Persons with asymptomatic syphilis include those with incubating syphilis (before the signs of primary syphilis are present) and latent syphilis. Infection acquired within the preceding year is referred to as early latent syphilis and all other cases are late latent syphilis or syphilis of unknown duration. Incubating and latent infections are detected by serologic testing.

Physical signs of primary syphilis:

- Chancre at a site of sexual exposure. A typical chancre is a single painless ulcer with an indurated border and smooth base. However, primary syphilis occasionally may present with multiple and/or painful chancres.
 - In females, chancres can occur on the outer genitals: vulva, perineum, or anus, as well as inside the vaginal or anal canal.
 - In males, chancres usually occur on the penis, underneath the foreskin in uncircumcised males, the scrotum, on the anus, or inside the anal canal.
- In both females and males, chancres can appear within the mouth, on the tongue, or on the lip, and can also occur on the fingers.
- Localized, firm non-tender lymphadenopathy (enlarged lymph nodes).

Physical signs of secondary syphilis:

- Condyloma lata: large moist circular wart-like papules on anogenital skin
- Bilaterally symmetrical macular or papular, nonpruritic rash on body or extremities. May be present only on the palms and soles
- Patchy alopecia (hair loss) on scalp, eyebrows, or eyelashes
- Mucous patches in the mouth or on the cervix
- Single or multiple chancres
- Generalized non-tender lymphadenopathy
- Fever, malaise



Which laboratory tests should be done to detect syphilis?

- An initial nontreponemal test [Venereal Disease Research Laboratory (VDRL) or rapid plasma reagin (RPR) test]
- If positive, the lab will perform a reflex confirmatory treponemal antibody detection test [fluorescent treponemal antibody absorption (FTA-ABS) or Treponema pallidum particle agglutination (TPPA) test].
 - If positive, Syphilis test, non-treponemal antibody; *quantitative* is required for management.
 - When repeated, use only as necessary to confirm response to treatment; it should not be separately ordered with presumptive diagnosis codes.
- Handling and/or conveyance of blood specimen for transfer to lab, only if the provider is charged for conveyance.



What is the “traditional algorithm” of laboratory tests to detect syphilis?

- The initial test is a nontreponemal test [Venereal Disease Research Laboratory (VDRL) or rapid plasma reagin (RPR) test].
- If positive, the lab will perform a reflex confirmatory treponemal antibody detection test [fluorescent treponemal antibody absorption (FTA-ABS) or *Treponema pallidum* particle agglutination (TP-PA) test].
 - If positive, non-treponemal antibody; quantitative test is required for management.
 - When repeated later, use only as necessary to confirm response to treatment, it should not be ordered separately with presumptive diagnosis codes.
- Handling and/or conveyance of blood specimen for transfer to lab, only if the provider is charged for conveyance.



What is the "reverse sequence algorithm"?

Some labs have switched over to the reverse sequence algorithm. This provides more information about a syphilis diagnosis and is automated.

- The initial test is a treponemal antibody test: either an FTA-ABS, TP-PA, *T. pallidum* enzyme immunoassay (EIA), or chemiluminescence immunoassay (CLIA).
- If positive, the lab will reflex to a quantitative non-treponemal test (VDRL or RPR) quantitative.
- If both the initial and quantitative non-treponemal tests are positive, syphilis is diagnosed.
- If the initial treponemal test is positive but the quantitative non-treponemal test is negative, the lab will perform a second (but different) treponemal test.
 - If positive, past or present syphilis is diagnosed.
 - If there is an ulcer on exam or recent contact with a known case of syphilis, treat for early syphilis.
 - If there is no known history of syphilis, no recent known syphilis contacts, and no findings, treat for late latent syphilis.
 - If negative, probably the initial test was a false positive. However, if the client is at high risk for syphilis, repeat a treponemal test in 2-4 weeks, followed by a non-treponemal test if the treponemal test is positive.



Do syphilis cases have to be reported in California?

Syphilis is a reportable communicable disease in California. Laboratories routinely notify the CDPH of positive syphilis tests.³ CA Urgency Reporting Requirements [17 CCR§2500(h)(i)] requires report

of a clinical diagnosis of syphilis by electronic transmission (including FAX, telephone, or mail) within one working day of identification.⁴ This can be achieved by logging into the CalREDIE (California Reportable Disease Information Exchange) Provider Portal website at:

<https://www.cdph.ca.gov/Programs/CID/DCDC/Pages/CalREDIE-Provider-Portal.aspx>

The Provider Portal provides secure access for health care providers to electronically submit Confidential Morbidity Reports (CMRs), required by California Code of Regulations, directly to local Health Departments. CMRs received via the Provider Portal are available in real-time to local health staff for investigation and follow-up, thus reducing the burden of data entry at the local level and increasing the timeliness of reporting. The CMR form can be found at:

<https://www.cdph.ca.gov/CDPH%20Document%20Library/ControlledForms/cdph110a.pdf>



Which treatment regimens are recommended for syphilis?

Primary and Secondary Syphilis (including persons with HIV Infection) *and early latent syphilis*

- Benzathine penicillin G (Bicillin-LA) 2.4 million units IM in a single dose

To ensure appropriate treatment of all individuals diagnosed with syphilis, the CDPH encourages empirically treating persons who have a typical chancre (ulcer) or a preliminary positive syphilis test while awaiting confirmatory testing, especially if there is no history of previous syphilis and patient follow-up is uncertain.

Late Latent Syphilis or Latent Syphilis of Unknown Duration

- Benzathine penicillin G 7.2 million units in total, administered as three doses of 2.4 million units IM each at 1-week intervals



What about persons with penicillin allergy?

Primary and secondary syphilis; early latent syphilis

- Doxycycline 100 mg orally twice daily for 14 days

Late latent syphilis or syphilis of unknown duration

- Doxycycline 100 mg orally twice daily for 28 days

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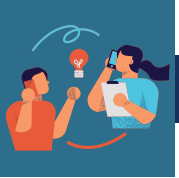
- If compliance with therapy or follow-up cannot be ensured, desensitization and treatment with benzathine penicillin is recommended by CDC. Treatment should be performed in consultation with an infectious disease specialist.
- Clinics diagnosing syphilis should have immediate access to Bicillin-LA to facilitate adequate and timely treatment.



What about treatment of sexual partners?

Sex partners of individuals with syphilis should be confidentially notified of their exposure and need for evaluation. In clients with:

- Primary syphilis: screen and treat partners within the past 3 months, plus duration of symptoms.
- Secondary syphilis: screen and treat partners within the past 6 months, plus duration of symptoms
- Early Latent Syphilis: screen and treat partners within the last year



How should people be followed up after treatment of syphilis?

Primary and secondary syphilis

- Repeat quantitative non-treponemal tests at 6 and 12 months. If the patient is a person with HIV infection, repeat RPR at 3, 6, 9, 12, and 24 months.

Latent syphilis

- Repeat quantitative non-treponemal serologic tests at 6, 12, and 24 months.
- VDRL and RPR are equally valid assays; however, quantitative results from the two tests cannot be compared directly with each other because the methods are different, and RPR titers frequently are slightly higher than VDRL titers.
- Patients with at least a fourfold increase in non-treponemal test titer persisting for >2 weeks likely experienced treatment failure or were re-infected.
- If titers increase fourfold, if an initially high titer (at least 1:32) fails to decline at least fourfold within 24 months, or if the patient develops signs or symptoms attributable to syphilis, they should be retreated and reevaluated for HIV infection.



When should clients be referred for management of syphilis?

- Immediately refer pregnant patients who may or will continue their pregnancy for prenatal care. The provider to whom the patient will be referred should be contacted so that the patient's evaluation and treatment can be expedited.
- For penicillin-allergy skin testing and desensitization, as necessary for some individuals with penicillin allergy.
- If signs or symptoms of neurologic, otologic or ophthalmic disease, refer to infectious disease specialist or to the local emergency department for immediate evaluation.
- All primary and secondary syphilis cases should be referred to the local health department's Communicable Disease Specialist or Disease Intervention Specialist for further counseling and sex partner referral.



Patient Education / Counseling

- Explain the significance of having syphilis and the importance of both partners treatment to prevent reinfection or infection of others.
- Clarify the fact that the patient's infection could have introduced by any current or past sexual partner and may have been acquired years ago (in the case of late latent syphilis or syphilis of unknown duration).
- Explain the need for examination and treatment of sex partners and avoidance of sex with untreated partners.
- Clarify the need for, and schedule, follow-up blood tests to ensure that the infection is cured.
- Instruct patient to return for reevaluation if symptoms persist.
- Inform the patient of the possibility of a Jarisch-Herxheimer reaction and what to do about it. The Jarisch-Herxheimer reaction is an acute febrile reaction due to release of bacterial-endotoxin like products following death of *T. pallidum* organisms after treatment. It may be accompanied by headache, myalgia, fever, or tachycardia. Patients should be counseled that the Jarisch-Herxheimer reaction does not reflect an allergic reaction to penicillin or other antibiotics. NSAIDs may be used to manage symptoms but are not known to prevent this reaction.
- Discuss prevention of future episodes: among persons who are sexually active, the best way to prevent syphilis is through consistent and correct use of condoms during all penile-vaginal sexual encounters.
- Assist patient in developing a personalized STI/HIV risk reduction plan.

Application of Family PACT Policies

For the complete text of the Family PACT policies and billing information for the ICD-10 codes that should be used when screening and treating syphilis for Family PACT clients, please refer to the [*Family PACT Policies, Procedures, and Billing Instructions Manual*](#).

References

1. US Preventive Services Task Force: Screening for Syphilis Infection in Nonpregnant Adults and Adolescents. US Preventive Services Task Force Recommendation Statement. JAMA. 2016;315(21):2321-2327.
 - On-line: USPSTF Final Recommendation Statement. Syphilis Infection in Nonpregnant Adults and Adolescents: Screening, 2016.
 - <https://www.uspreventiveservicestaskforce.org/uspstf/recommendation/syphilis-infection-nonpregnant-adults-adolescents-screening>
2. CDC Sexually Transmitted Infection Treatment Guidelines, 2021. <https://www.cdc.gov/std/treatment-guidelines/provider-resources.htm>
3. Expanded Syphilis Screening Recommendations for the Prevention of Congenital Syphilis Guidelines for California Medical Providers 2020. <https://www.cdph.ca.gov/Programs/CID/DCDC/Pages/STDs-ClinicalGuidelines.aspx>
4. Title 17, California Code of Regulations (CCR) §2500, §2593, §2641.5- 2643.20, and §2800-2812 Reportable Diseases and Conditions <https://www.cdph.ca.gov/Programs/CID/DCDC/CDPH%20Document%20Library/ReportableDiseases.pdf>