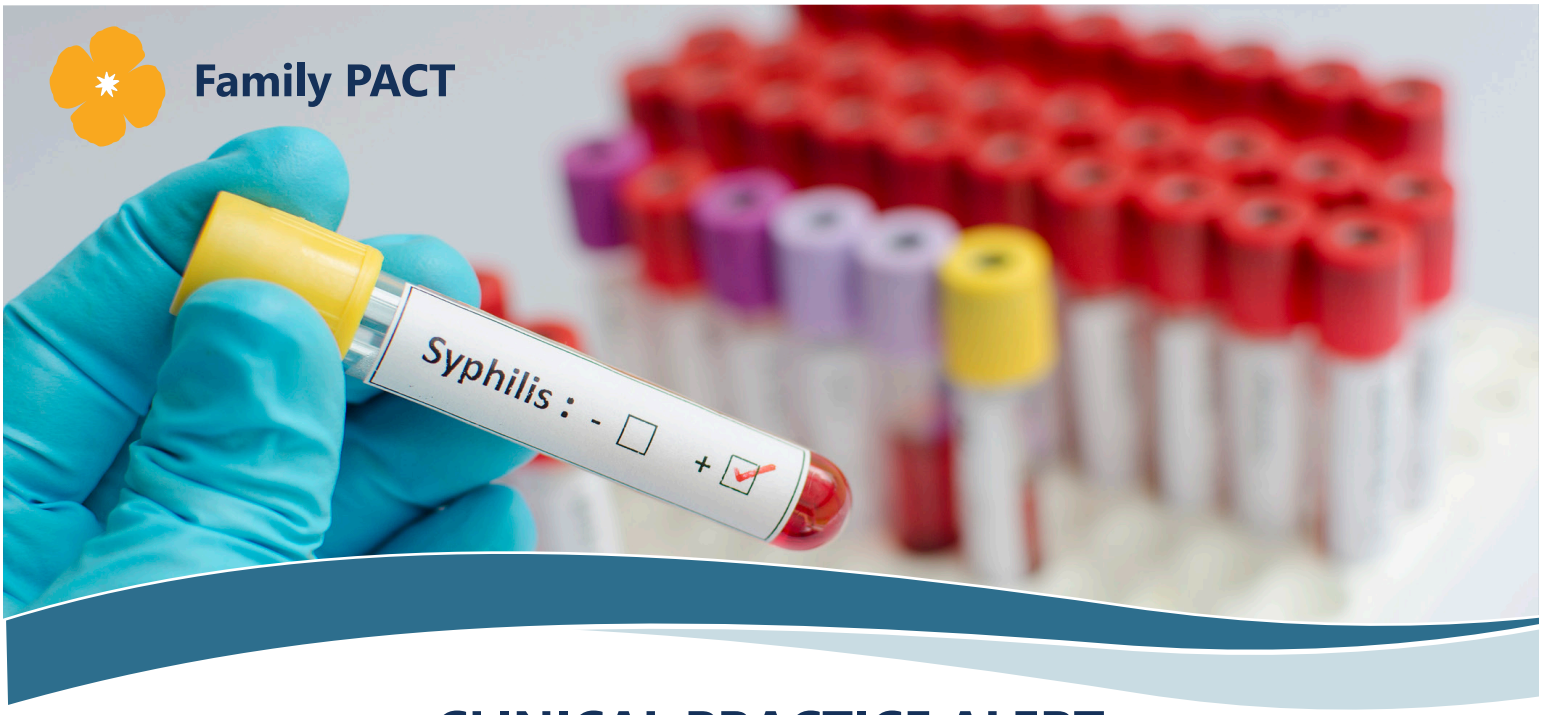

CLINICAL PRACTICE ALERT
SYPHILIS SCREENING, DIAGNOSIS, AND TREATMENT

Introduction

Rates of syphilis have been rising in the United States, including in California, which have resulted in a corresponding rise in the rates of congenital syphilis (CS). In 2021, seventeen percent of women of childbearing age diagnosed with syphilis were pregnant. In California, CS cases increased 1,500% between 2012 and 2021. These trends mirror a sharp increase in early syphilis among females, which increased more than 1,113% 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 individuals who are pregnant or the diagnosis and treatment of tertiary syphilis.

Key Syphilis Screening Recommendations

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 are ambivalent or indifferent to becoming pregnant

Questions and Answers

Who should be screened for syphilis?

The California Department of Public Health (CDPH) guidelines[1] for "Syphilis Screening for All People Who Could Become Pregnant" include two 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 United States Preventive Services Task Force (USPSTF)[2] and the CDPH recommendations define individuals who are at increased risk for syphilis infection as:

- Men who have sex with men (MSM), men who have sex with men and women (MSMW), and transgender women (TGW): 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 sexually transmitted infection (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
- HIV-seropositive (all genders): annually; more frequently if at increased risk
- Using HIV pre-exposure prophylaxis (PrEP) (all genders): every 3 months
- Regional variations (hot spots)
  - Living in a local health jurisdiction with high syphilis morbidity among females, including a local health jurisdiction with high-congenital syphilis morbidity
  - The Centers for Disease Control and Prevention (CDC) National Center for HIV, Viral Hepatitis, STD, and TB Prevention (NCHHSTP) Atlas tracks syphilis prevalence by U.S. County.
  - The CDC recommends offering syphilis screening to all sexually active people aged 15-44 years in counties with a rate of primary and secondary syphilis among women aged 15-44 years that is greater than 4.6 per 100,000.

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 five stages based on clinical findings, which guide treatment and follow-up, including incubating, primary, secondary, latent, and tertiary syphilis.

Individuals with asymptomatic syphilis include those with incubating syphilis (before the signs of primary syphilis are present) and latent syphilis. Asymptomatic infection acquired within the preceding year is referred to as early latent syphilis and all other asymptomatic cases are late latent syphilis or syphilis of unknown duration. Latent infections are detected by serologic screening. Serology tests may or may not detect incubating syphilis, depending on the timing of exposure and test sensitivity.

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

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 quantitative VDRL or RPR and a confirmatory treponemal antibody detection test. These include the fluorescent treponemal antibody absorption test (FTA-ABS), *Treponema pallidum* particle agglutination (TP-PA) test, and a newer enzyme immunoassay (EIA) test.

- If the confirmatory test is reactive, the client has a new (or old) syphilis infection.
- If non-reactive, syphilis is unlikely and the initial nontreponemal test may be a biologic false positive.

How is the reverse sequence algorithm different from the traditional algorithm?

Some labs have switched over to the reverse sequence algorithm, which is easier to perform and more accurate for the diagnosis of syphilis in someone without a prior history.

- 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 a quantitative non-treponemal test (VDRL or RPR). 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 negative, the initial test probably was a false positive. However, if the individual 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. California Urgency Reporting Requirements [17 CCR§2500(h)(i)] requires reports of a clinical diagnosis of syphilis by electronic transmission (including fax, telephone, or mail) within one working day of identification. This can be achieved by creating an account and logging into the California Reportable Disease Information Exchange (CalREDIE) Provider Portal.

The Provider Portal provides secure access for health care providers to electronically submit the Confidential Morbidity Report (CMR) form, required by the 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.

Which treatment regimens are recommended for syphilis[1,3]?

Primary and Secondary Syphilis (including individuals with HIV infection) and Early Latent Syphilis

- Benzathine penicillin G (Bicillin® L-A) 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 or a preliminary positive syphilis test while awaiting confirmatory testing, especially if there is no history of previous syphilis and client follow-up is uncertain.

Late Latent Syphilis or Latent Syphilis of Unknown Duration

- Benzathine penicillin G (Bicillin® L-A) 7.2 million units in total, administered as three doses of 2.4 million units IM each at 1-week intervals.

Are there alternatives when benzathine penicillin is not available or for individuals with penicillin allergy?

CDC guidelines recommend oral doxycycline, except in pregnant people with syphilis. The only acceptable treatment in pregnancy is benzathine penicillin.

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

NOTE: There has been a shortage of benzathine penicillin G (Bicillin® L-A) in the United States. The CDPH STD Control Branch recommends the following prioritization categories:

» Pregnant individuals with syphilis infection (or exposure) as well as for infants exposed to syphilis in utero.

» Individuals with contraindications to doxycycline (e.g., anaphylaxis, hemolytic anemia, Stevens-Johnson syndrome) or those who are unwilling or unable to use an extended 14–28-day course of doxycycline or tetracycline.

» Conserve Bicillin® L-A by using alternative drugs for the treatment of infectious diseases (e.g., streptococcal pharyngitis) where oral medications or other effective antimicrobials are available.

What about treatment of sexual partners?

Sex partners of individuals with syphilis should be confidentially notified of their exposure and need for evaluation. In individuals 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 individuals be followed up after treatment of syphilis?

Primary and Secondary Syphilis

» Repeat quantitative non-treponemal tests at 6 and 12 months. In individuals 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.

» Individuals with at least a fourfold increase in the 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 individual develops signs or symptoms attributable to syphilis, they should be retreated and reevaluated for HIV infection.

When should individuals be referred for management of syphilis?

- Unless you provide prenatal care, pregnant individuals with syphilis who may or will continue their pregnancy should be referred immediately for prenatal care, if possible, in order to maintain continuity of care during treatment and follow-up.[4] If not, treat the pregnant individual with benzathine penicillin in order to minimize the risk of the client being lost to follow-up and left untreated.
  - The provider to whom the individual will be referred for prenatal care should be contacted so that the individual's evaluation and treatment can be expedited.
- For penicillin-allergy skin testing and desensitization, as necessary for pregnant individuals with penicillin allergy.
- If signs or symptoms of neurologic, otologic or ophthalmic disease, refer to an infectious disease specialist or to the local emergency department for immediate evaluation.

NOTE: The Family PACT Program does not cover prenatal, perinatal care, or any services for pregnant individuals.

Client Education and 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 individual's infection could have been 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.

Instruct the client to return for reevaluation if symptoms persist.

Clarify the need for, and schedule follow-up blood tests to ensure that the infection is cured.

Inform the individual 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. Individuals should be counseled that the Jarisch-Herxheimer reaction does not reflect an allergic reaction to penicillin or other antibiotics. Non-steroidal anti-inflammatory drugs (NSAIDs) may be used to manage symptoms but are not known to prevent this reaction.

Assist the individual in developing a personalized STI/HIV risk reduction plan.

Discuss prevention of future episodes: among individuals who are sexually active, the best way to prevent syphilis is through consistent and correct use of condoms during all penile-vaginal sexual encounters.

Application of Family PACT Policies

For the complete text of the *Family PACT Standards*, official administrative practices, and billing information, please refer to the *Family PACT Policies, Procedures and Billing Instructions (PPBI)* manual.

References

1. 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.
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4. McDonald R, O'Callaghan K, Torrone E, et al. *Vital Signs*: Missed Opportunities for Preventing Congenital Syphilis — United States, 2022. *MMWR Morb Mortal Wkly Rep* 2023;72:1269–1274. DOI: http://dx.doi.org/10.15585/mmwr.mm7246e1.

Revised April 2024. For more information, visit: www.FamilyPACT.org.