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2024 GUIDELINES FOR SYPHILIS SCREENING, TESTING, AND TREATMENT

City of Lubbock TEXAS
PUBLIC HEALTH

Dear Healthcare Community of Lubbock:

Between 2018 and 2022, rates of syphilis increased 648% in Lubbock. Lubbock Public Health and the U.S. Centers for Disease Control and Prevention (CDC) are recommending that all sexually active adults in Lubbock be screened for syphilis. **Syphilis can cause blindness, deafness, and damage to almost every organ system, especially the cardiovascular and nervous systems.**

Syphilis can kill adults and lead to significant permanent health impacts for both adults and infants. **If a pregnant person is infected, the infant has a high chance of being stillborn, of dying near birth, or of having lifelong health problems.**

Newborn (aka. congenital) syphilis rates have increased 10-fold nationwide in the last 10 years. In 2022, 25% of the country's newborn syphilis cases came from Texas.
We know that it can be challenging to choose and interpret syphilis tests, then to determine treatment options in light of contradictory results, intermittent drug shortages, and penicillin allergies.
Screening, testing, and treatment recommendations for *Treponema pallidum* (syphilis) infections have changed over time, and we want to empower all community health providers in Lubbock to tackle syphilis with current information.

This toolkit is designed to help you find much of the information you need about syphilis screening, testing, treatment, and reporting in one convenient location. This includes recent federal guidance about point-of-care (POC) testing and doxycycline post-exposure prophylaxis ("Doxy PEP").

We urge all providers to **SCREEN, TEST, and TREAT** for syphilis in every possible healthcare encounter. Clinicians should **REPORT** cases (and probable cases) of Primary and Secondary syphilis within 1 day to the Health Department, and all other stages of syphilis and newborn (congenital) syphilis within 1 week.

For any questions or comments, please contact the STI department of Lubbock Public Health at 806-775-2933, publichealth@mylubbock.us.

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[1]Berns et al. UT Health Houston: School of Public Health. Congenital Syphilis: A Report to the Texas Research-toPolicy Collaboration Project. Feb 16, 2024. (https://sph.uth.edu/research/centers/dell/legislative-initiatives/docs/Congenital%20Syphilis022724%20update.pdf).

Contents

Screening | Screen patients to see if they need a current test.

Geography-based screening

The CDC states that the greatest syphilis risk for many sexually active people is the county in which they live. This is currently true for Lubbock County, and screening everyone based on geography can help to reduce bias and stigma and increase access to testing.

Given the rates of syphilis in Lubbock, even monogamous sexually active adults should be tested for syphilis at least once per CDC guidelines. Even patients who were previously sexually active (but are not currently) should be tested, if not tested after their last sex partner.

To reduce rates of congenital (newborn) syphilis, the CDC particularly recommends offering testing to all sexually active people aged 15-44.

Please discuss the importance of syphilis testing with patients during every healthcare encounter and add syphilis testing to your lab orders for all adults or youth who have been sexually active. For people at increased risk of infection or who may be lost to follow-up, rapid point-of-care (POC) tests are now available, but they have limitations. (More information is below, under "testing.")

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[2]*CDC. County-level Syphilis Rates to Direct Screening Efforts. (https://www.cdc.gov/nchhstp/syphilis-county-level/?CDC_AAref_Val=https://www.cdc.gov/nchhstp/atlas/syphilis)*

CDC Syphilis Screening Guidelines by Risk Group

Even though everyone in Lubbock should be tested because of our infection rates, certain risk groups might need more frequent testing. See the CDC"s screening guidelines below, with Lubbock County residents meeting the "geography" risk criteria. More recommendations follow the CDC table, below:

WOMEN	• Screen asymptomatic women at increased risk (history of incarceration or transactional sex work, geography, race/ethnicity) for syphilis infection.
PREGNANT WOMEN	• All pregnant women at the first prenatal visit. • Retest at 28 weeks gestations and at delivery if a increased risk due to geography or personal risk (substance use, STIs during pregnancy, multiple partners, a new partner, partner with STIs)
MEN WHO HAVE SEX WITH WOMEN	• Screen asymptomatic adults at increased risk (history of incarceration or transactional sex work, geography, race/ethnicity, and being a male younger than 29 years) for syphilis infection.
MEN WHO HAVE SEX WITH MEN	• At least annually for sexually active MSM • Every 3 to 6 months if at increased risk • Screen asymptomatic adults at increased risk (history of incarceration or transactional sex work, geography, race/ethnicity, and being a male younger than 29 years) for syphilis infection.
TRANSGENDER AND GENDER DIVERSE PEOPLE	• Consider screening at least annually based on reported sexual behaviors and exposure
PERSONS WITH HIV	• For sexually active individuals, screen at first HIV evaluation, and at least annually thereafter • More frequent screening might be appropriate depending on individual risk behaviors and the local epidemiology.

Source: CDC. STI Treatment Guidelines, 2021. Screening Recommendations and Considerations Referenced in Treatment Guidelines and Original Sources: By Disease. https://www.cdc.gov/std/treatment-guidelines/screening-recommendations.htm

Pregnant Women

Test when pregnancy is first identified in any setting. Texas law also requires retesting at 28 weeks of gestation and at delivery for all pregnancies, not just those at increased risk.

Men Who Have Sex With Men (MSM)

At least annually, if sexually active.
Every 3 to 6 months if at increased risk.

People who Use Drugs

Drug use (especially methamphetamine use) and injection drug use have also emerged as risk factors for infections among men who have sex with women (MSW) and women who have sex with men (heterosexual transmission). Rising rates among women who have sex with men can increase rates of congenital (newborn) syphilis.[3]

[3]*Kidd SE, Grey JA, Torrone EA, Weinstock HS. Increased Methamphetamine, Injection Drug, and Heroin Use Among Women and Heterosexual Men with Primary and Secondary Syphilis – United States, 2013–2017. MMWR Morb Mortal Wkly Rep 2019;68:144–148. DOI: http://dx.doi.org/10.15585/mmwr.mm6806a4*

Testing | Choosing and Interpreting Syphilis Tests

Syphilis testing can be complicated, but the CDC's 2024 testing algorithm (below) makes it a bit easier to understand which tests to order, and when. The testing guidelines distinguish between a "traditional" algorithm for testing versus a "reverse sequence" algorithm for blood testing, with similar tests but with different starting points for each algorithm.

Additionally, there are two FDA-authorized and CLIA-waived point-of-care (POC) rapid syphilis antibody tests for which the U.S. Department of Health and Human Services (HHS) issued guidance in June 2024. These are fingerstick blood tests.

When available, it is most accurate to combine more than one type of blood test, combined with a clinical examination and complete history, in order to help determine the presence and staging of syphilis infections.

If there are contradictory results between a treponemal and nontreponemal test (e.g. one is positive and one is negative), a second treponemal test of another type (e.g. a TPPA) is recommended.[4]

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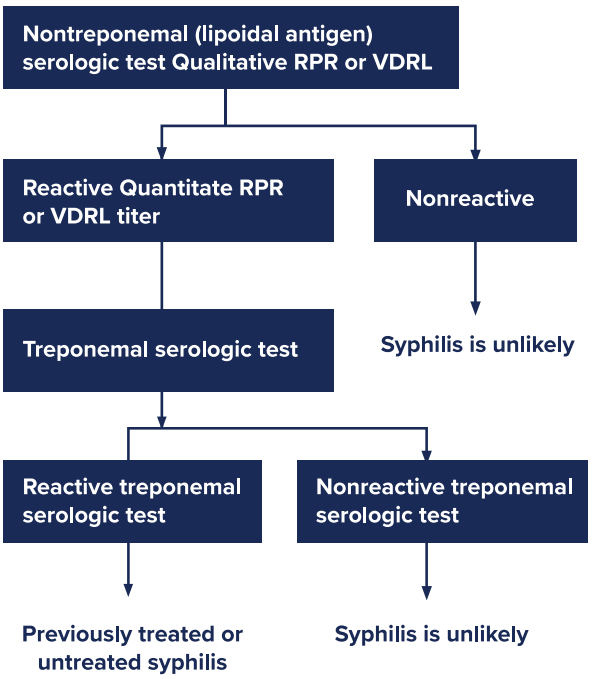
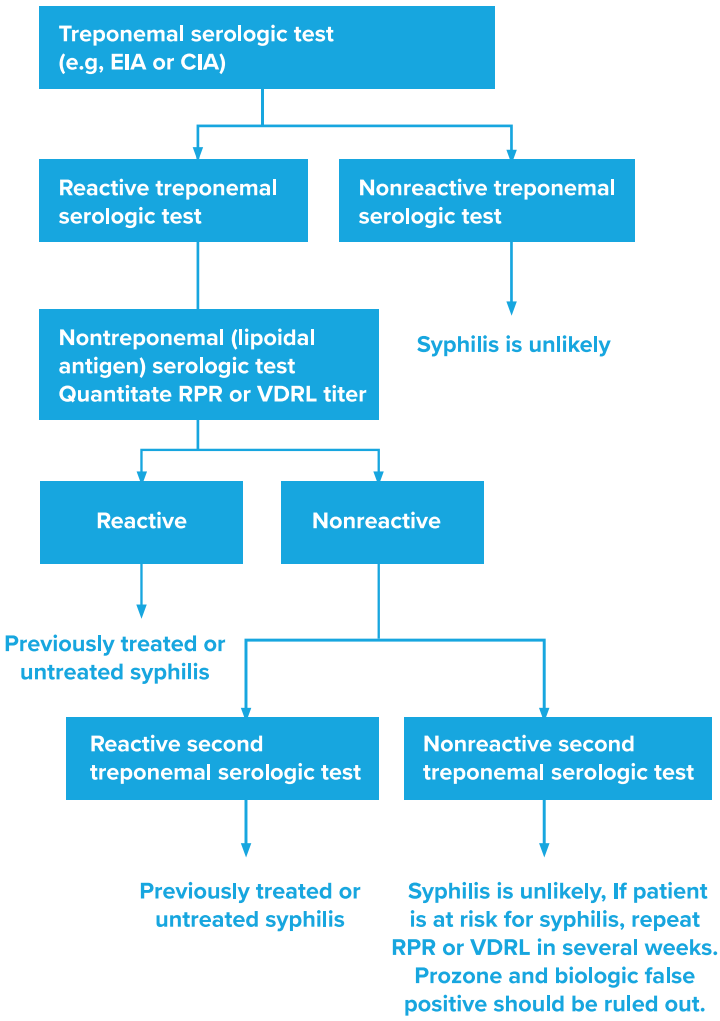
[4]Papp JR, Park IU, Fakile Y, Pereira L, Pillay A, Bolan GA. CDC Laboratory Recommendations for Syphilis Testing, United States, 2024. MMWR Recomm Rep 2024;73(No. RR-1):1–32. DOI: http://dx.doi.org/10.15585/mmwr.rr7301a1.

The CDC's 2024 Syphilis Testing Guidance Algorithms

TRADITIONAL ALGORITHM



REVERSE SEQUENCE ALGORITHM



(Source: Papp et al.)

Abbreviations: CIA = chemiluminescence immunoassay; EIA = enzyme immunoassay; RPR = rapid plasma reagin; TPPA Treponoma pallidum particle agglutination; VDRL = Venereal Disease Research Laboratory.

Traditional Algorithm (Starting with an RPR or VDRL)

Testing has traditionally started with a Qualitative RPR or VDRL blood test that reflexed to running Quantitative RPR or VDRL titers if the result was positive. These are referred to as nontreponemal (lipoidal antigen) tests.

RPRs or VDRLs are particularly helpful for people who have had a previous syphilis infection or there is a high suspicion of current infection, because the positive Qualitative titer result (positive or negative) will lead to a Quantitative titer result (e.g. 1:8 or 1:64) that can be used to guide treatment decisions and assess treatment efficacy. They are most accurate when combined with a medical history and physical examination.

Because the results take days to weeks to come back, RPR and VDRL are not always clinically useful for populations frequently lost to follow-up (such as people who lack insurance, people who use drugs, people who are undocumented, people with mental illness, and people with housing and transportation instability).

RPR and VDRL tests can be falsely negative early in the course of infection, and can also be falsely positive from factors not related to syphilis infections. That is why the traditional algorithm follows a positive nontreponemal (lipoidal antibody) test like the RPR or VDRL with a syphilis-specific antibody test (a treponemal test) like an EIA or a CIA, to verify that the cause of the positive nontreponemal antibody tests is syphilis infection, not something else.

False Negatives and False Positives

A 2019 study showed that 11% of 526,540 reactive nontreponemal tests were not associated with syphilis. In those cases, the tests were detecting antibodies to nontreponemal antigens generated by tissue damage from other diseases. Still, 89% of the reactive tests were associated with syphilis, implying that most nontreponemal tests detect antibodies triggered by *T. pallidum* antigens.
A nontreponemal (lipoidal antigen) test that is consistently reactive for conditions other than syphilis is referred to as a biologic false positive (BFP). Persons with antibodies that are reactive in the nontreponemal (lipoidal antigen) tests, but are nonreactive in a confirmatory treponemal test, are defined as "BFP reactors". Reactive nontreponemal (lipoidal antigen) tests attributable to BFP have been estimated to occur in 0.2%–0.8% of the population and are associated with medical conditions including malaria, leprosy, and HIV; recent vaccinations; autoimmune disorders; and injection drug use.

How to Interpret RPR and VDRL Quantitative Titers

Quantitative titers are reported as a ratio, reflecting how many times the sample was diluted and still had a positive result. For example, 1:2 is a sample that tested positive after being diluted 50%. If diluted again and still positive, that would be 1:4, then 1:8, 1:16, 1:32 and so on. A 1:128 result would be much higher titer than a 1:4, for example.

A four-fold increase or decrease in the value is considered clinically significant for treatment success or failure, so RPR or VDRL are best collected both before and after treatment.

For example, an increase from 1:8 to 1:32 could indicate treatment failure, or indicate a new infection in a previously-treated person. Similarly, a titer decrease from 1:64 to 1:16 would be considered an appropriate response to treatment, unless it subsequently rose again.

Although interpreted similarly, RPR and VDRL are different tests, and the results should not be compared to each other to determine new infection or treatment efficacy.
To compare tests to assess treatment response or new infection, the same type of test should be used on the same kind of specimen, ideally from the same lab.

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[5] *Papp et al.*
[6] *Papp et al.*

Need for Endpoint Titers

Results from any nontreponemal (lipoidal antigen) test should be reported as an endpoint titer by the lab, and not with greater or less than values, to allow for optimal clinical interpretation. Because certain automated RPR tests have a constrained serum dilution range, specimens should require reflex testing using a manual RPR procedure, to establish an endpoint titer at either the lower or upper bounds before reporting.

Without an endpoint titer, it is very difficult for clinicians to assess for reinfection or monitor treatment outcomes. The current testing guidelines recommend against nontreponemal (lipoidal) titer results containing mathematical symbols such as > or <.

Reverse Sequence Algorithm (Starting with Treponemal Antibodies)

Treponemal tests like EIA, CIA, and the point-of-care tests specifically target *T. pallidum* antigens. These tests were traditionally used to confirm that a reactive nontreponemal (lipoidal antigen) test was the result of syphilis infection (and not something else, as discussed above).

Because these antibodies persist after treatment, these results cannot be used to distinguish between a current infection or a previously treated infection, but they can be used as a rapid screening test if the likelihood of a previously treated infection is low.

Treponemal tests

Treponemal tests are clinically used to confirm results of reactive nontreponemal (lipoidal antigen) tests and evaluate patients with signs suggestive of syphilis in early primary infection when nontreponemal (lipoidal antigen) tests might not yet be reactive. If a treponemal test is positive, a nontreponemal test like an RPR or VDRL must be drawn to assess likelihood of current infection and the subsequent treatment response.

For discordant nontreponemal (lipoidal antigen) and treponemal test results (e.g. One test is positive and the other is negative.), an additional treponemal test is recommended using a different type of treponemal test assay and target (e.g., TP-PA).

Clinicians and state and local public health STD programs need nontreponemal (lipoidal antigen) test results coupled with treponemal test results for timely clinical management and public health reporting. The laboratory processing the initial screening test should ensure the second or third (if necessary) test results, especially if performed in a different laboratory, are linked with the screening test result when the report is sent to the ordering clinician and public health department.

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[7] *Papp et al.*

[8] *National Syphilis and Congenital Syphilis Syndemic Federal Task Force. Considerations for the Implementation of Point of Care (POC) Tests for Syphilis. May 2024. https://www.hhs.gov/sites/default/files/nscss-considerations-for-the-implementation-of-syphilis-poc-tests.pdf*

Point-of-Care (POC) Syphilis Testing

There are currently 2 FDA-authorized and CLIA-waived point-of-care (POC) tests for syphilis, the Syphilis Health Check Treponemal Antibody Test (SHC) and the ChemBio DPP HIV-Syphilis (ChemBio DPP) which detects both HIV and syphilis.

For these tests, a fingerstick test is performed on whole blood, providing antibody results in 10-15 minutes. This has the advantage of allowing for rapid treatment of infected people the same day. Because these tests detect antibodies that might be present from a previous syphilis infection, these tests are not appropriate for people with a known history of syphilis.

The National Syphilis and Congenital Syphilis Syndemic Federal Task Force published "Considerations for the Implementation of Point of Care (POC) Tests for Syphilis" through the U.S. Department of Health and Human Services (HHS) in June 2024.[8]

The Task Force states that laboratory-based testing is still the preferred option, especially for low-risk people and people with a history of syphilis. However, they state that even with the lower sensitivity and specificity of POC tests, POC tests can be valuable in settings where incidence of syphilis is high and access to healthcare is limited.

Specifically, the Taskforce recommends use of POC tests in populations who are experiencing high rates currently but have a historically low prevalence of infection, including:

- Pregnant people not engaged in prenatal care
- People using substances and not engaged in health care
- Cisgender women (especially of childbearing age)
- Persons identifying as American Indian or Alaskan Native (especially women)
- Black and Latino heterosexual people, especially non-Hispanic Black women (who have rates 8-10x higher than non-Hispanic White women in some parts of the country)
- People experiencing incarceration
- People living in geographic areas where syphilis is spreading rapidly

Some of the settings where the Task Force recommends using POC tests include:

- Correction facilities
- Emergency Departments
- Substance Use Treatment Programs
- Syringe Service and Harm Reduction Programs
- Outreach and community-based care events
- Rural communities
- Shelters

[8] *National Syphilis and Congenital Syphilis Syndemic Federal Task Force. Considerations for the Implementation of Point of Care (POC) Tests for Syphilis. May 2024. https://www.hhs.gov/sites/default/files/nscss-considerations-for-the-implementation-of-syphilis-poc-tests.pdf*

Because a positive result will need further testing (with a nontreponemal test and a lab-based treponemal test), as will a negative result with high clinical suspicion or contact history, staff performing POC tests need to have ready-available access to phlebotomists who can draw the needed labs and providers who can assess for clinical presentation and prescribe/administer treatment, or these people might also become lost to follow-up.

The Texas Department of State Health Services has staff training materials for using the SHC test at their website, updated in 2022.

Cerebrospinal Fluid (CSF) Testing, and Other Tissue Types

CSF collection is not indicated for every patient with syphilis. CSF laboratory anomalies can be common in early syphilis, but CSF examination is only indicated for people with tertiary syphilis or with syphilis and clinical neurologic findings such as:[9]

- Cognitive dysfunction
- Motor or sensory deficits
- Cranial nerve palsies
- Signs or symptoms of meningitis or stroke
- Vision: Ocular and syphilitic uveitis patients, only if clinical assessment shows cranial nerve abnormalities
- Hearing: Hearing loss and other otologic symptoms, only if clinical assessment shows cranial nerve abnormalities

The CDC's 2024 testing guidelines address other less common testing types, and the collection of other fluids and tissues than blood (e.g. lesion exudate, cerebrospinal fluid, placenta, umbilical cord and brain tissue).[10]

[9] *CDC. STI treatment Guidelines, 2021: Neurosyphilis, Ocular Syphilis, and Otosyphilis. https://www.cdc.gov/std/treatment-guidelines/neurosyphilis.htm*
[10] *Papp et al.*

Treatment | Correct Treatment at the Right Time

Standard Treatment for Primary and Secondary Syphilis

Penicillin is the mainstay of syphilis treatment, and there is no other recommended option for neurosyphilis, congenital (newborn) syphilis, or syphilis in pregnancy. Among non-pregnant adults, the standard treatment for primary or secondary syphilis infection is Benzathine penicillin G 2.4 million units given intramuscularly (IM) as a single dose.

Treatment for Neurosyphilis, Ocular Syphilis, or Otosyphilis

These infections are usually managed on an inpatient basis with intravenous (IV) aqueous crystalline penicillin G 18-24 million units per day for 10-14 days.

If compliance can be assured, an alternative 10-14 day regimen is procaine penicillin G 2.4 million units IM daily plus Probenecid 500 mg daily.[12]

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[12]*CDC. STI Treatment Guidelines, 2021. Neurosyphilis, Ocular Syphilis, and Otosyphilis. https://www.cdc.gov/std/treatment-guidelines/neurosyphilis.htm*

Treatment of Latent Syphilis

People who have positive syphilis seroreactivity and no other signs of primary, secondary or tertiary infection are said to have latent syphilis. Careful examination of all mucosal surfaces should be conducted to rule out primary or secondary syphilis.

People with latent syphilis are not contagious, and treatment is administered to prevent later sequelae of syphilis, not to prevent spread of the disease.[13]

Treatment for early (within 1 year) latent syphilis: 2.4 million units of benzathine penicillin G, given IM as a single dose. Treatment for late (over 1 year) latent syphilis: 7.2 million units benzathine penicillin G, administered as 3 doses of 2.4 million units each, given weekly for 3 weeks.

Treatment of Tertiary Syphilis

Tertiary syphilis refers to gummas, cardiovascular syphilis, people with psychiatric manifestations, or late neurosyphilis. Neurosyphilis is discussed separately, but people with gummas or cardiovascular manifestations of syphilis should receive 7.2 million units of benzathine penicillin G, given as 3 weekly divided doses of 2.4 million units each.[14]

Congenital (newborn) syphilis

Assessment, diagnosis and treatment of congenital syphilis can be complex. More information on diagnosis and treatment of congenital (newborn) syphilis can be found as part of the CDC's STI Treatment guidelines 2021, found here: **https://www.cdc.gov/std/treatment-guidelines/congenital-syphilis.htm** and here: **https://www.cdc.gov/syphilis/about/about-congenital-syphilis.html**

Serologic Response After Treatment

Clinical and serologic evaluation should be performed at 6 months and 12 months after treatment, or sooner if there is concern for repeat infection. If the patient's serologies don't show a 4-fold decrease, further neurological assessment and assessment for HIV infection are indicated. For people without titer reductions and no new exposures, CSF examination may be indicated, as the persistently high titers might be indicative of neurosyphilis.[15]

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[13]CDC. STI Treatment Guidelines, 2021. Latent syphilis. https://www.cdc.gov/std/treatment-guidelines/latent-syphilis.htm
[14]CDC. STI Treatment Guidelines, 2021. Tertiary syphilis. https://www.cdc.gov/std/treatment-guidelines/tertiary-syphilis.htm
[15]CDC. STI Treatment Guidelines, 2021.Primary and Secondary Syphilis Treatment. https://www.cdc.gov/std/treatment-guidelines/p-and-s-syphilis.htm

Ten to 20% of people with primary and secondary syphilis will not have a four-fold reduction in titers by 12 months follow-up. Some of the factors associated with being less likely to reduce 4-fold are:

- Diagnosis at a later stage (secondary or later)
- Initial titers being lower than 1:8
- Older age
- Being HIV positive

If retreatment is indicated, weekly IM injections of 2.4 million units of benzathine penicillin G for 3 weeks is recommended. Clinicians can consult with the STD Clinical Consultation Network for assistance with complex cases of titer interpretation (https://stdccn.org/render/Public).

Treatment for People Allergic to Penicillin

Penicillin is the only approved treatment for pregnant women, for neurosyphilis, and for congenital syphilis. People in these groups who are believed to be allergic to penicillin need to be desensitized and treated with Penicillin G.[16]

Other people with primary or secondary syphilis can be treated with doxycycline (100 mg orally, twice a day, for 14 days) or tetracycline (500 mg orally, 4 times a day, for 14 days). Doxycycline is better-tolerated, due to the gastrointestinal side effects of tetracycline.[17]

Azithromycin (e.g. 2 grams orally, as one dose) is not recommended for syphilis infections because of treatment failures and documented emerging drug resistance.

Recent research has shown syphilis isolates are now almost universally resistant to azithromycin.[18]

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[16]*Workowski et al.*
[17]*CDC. STI Treatment Guidelines, 2021.Primary and Secondary Syphilis Treatment. https://www.cdc.gov/std/treatment-guidelines/p-and-s-syphilis.htm*

Penicillin Shortages

Earlier this year, there was a shortage of benzathine penicillin ("Bicillin") in the United States. Because of shortages of Pfizer's Bicillin L-A®, the FDA temporarily allowed importation and use of Extencilline, an equivalent product used in other countries.

Effective June 10, 2024, Pfizer announced that they have an adequate supply of Bicillin L-A 2.4 million units/4ml. Pfizer recommends that providers call them directly with any supply issues at 844-646-4398 or email them at PISupplyContinuity@Pfizer.com.

In times of penicillin shortages, the CDC recommends that Bicillin be reserved for pregnant people and babies with congenital syphilis to preserve supplies, given that no treatment alternatives exist for pregnant women or for congenital syphilis.[19]

Doxycycline Post-Exposure Prophylaxis (aka. "Doxy PEP")

In June 2024, the CDC came out with a recommendation to utilize oral doxycycline 200 mg within 72 hours of sex to drastically reduce bacterial STIs (including gonorrhea, chlamydia, and syphilis) in certain populations. Currently, this recommendation only applies to men who have sex with men (MSM) and transgender women (TGW) who have had a bacterial STI within the last 12 months.

In three large randomized controlled trials, 200 mg of doxycycline taken within 72 hours after sex was shown to reduce syphilis and chlamydia infections by >70% and gonococcal infections by approximately 50%.[20]

[19]CDC. Clinical Reminders During Bicillin L-A Shortage. https://www.cdc.gov/sti/php/from-the-director/2023-07-20-mena-bicillin.html
[20] Bachmann LH, Barbee LA, Chan P, et al. CDC Clinical Guidelines on the Use of Doxycycline Postexposure Prophylaxis for Bacterial Sexually Transmitted Infection Prevention, United States, 2024. MMWR Recomm Rep 2024;73(No. RR-2):1–8. DOI: http://dx.doi.org/10.15585/mmwr.rr7302a1

Reporting | Using the STI Form in a Timely Way

Use Lubbock Public Health's STI reporting form found at the Health Department's Disease Surveillance page, here:

https://ci.lubbock.tx.us/departments/health-department/disease-surveillance

It is important to include any clinical information that was found upon examining the patient, any previous testing (if available), and good contact information for the patient.
Primary and secondary syphilis should be reported to Lubbock Public Health within 1 day.

Latent, tertiary, and congenital syphilis should be reported within 1 week.

Another Helpful Resource for Diagnosis

CDC's healthcare provider syphilis pocket guide:
https://www.cdc.gov/std/syphilis/syphilis-pocket-guide-final-508.pdf