CITY OF MILWAUKEE
HEALTH DEPARTMENT

Syphilis

Frequently Asked Questions (FAQs)

Prepared by
Caitlyn Stockhausen, Aziza Carter,
Heather Paradis, Jessica Dalby

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INTRODUCTION

This document is intended to provide information to medical providers, local and tribal health departments, and other public health entities regarding syphilis. Pursuant to Wis. Admin Code. § DHS 145.04(3)(b) and Wis. Stat. § 252.05, syphilis is a reportable sexually transmitted infection (STI). Sexual contact, including anal sex, vaginal sex, and oral sex, with an infected partner may lead to the contraction of syphilis. Though typically easily treated, undiagnosed syphilis may lead to significant impacts on health. Untreated syphilis may also be transmitted from an infected individual to the child they are carrying during pregnancy or childbirth. The contraction of syphilis and related health outcomes may be easily prevented through use of condoms and routine screening. Early detection of syphilis is key to prevention of further transmission among sexually active individuals.

The City of Milwaukee Health Department is committed to addressing the rise in syphilis cases. New diagnoses are increasing among women, individuals who exchange sex for money or drugs, and injection drug users. In the City of Milwaukee, the non-Hispanic Black population experiences the heaviest burden of infection demonstrating a significant racial inequity in sexual and reproductive health outcomes. We seek collaboration with others to combat this new epidemic.

Quick Access Guide

Test Abbreviations and Acronyms
CLIA or CIA- Chemiluminescence immunoassays (treponemal test)
EIA - Enzyme immunoassay (treponemal test)
FTA-ABS - Fluorescent treponemal antibody absorption (treponemal test)
MHA_TP - Microhemagglutination assay for antibodies to T. pallidum (treponemal test)
RPR – Rapid plasma reagin (nontreponemal test)
TPA (IGG or IGG/IGM)– Treponema pallidum antibody (treponemal test)
TPHA - T. pallidum hemagglutination assay (treponemal test)
TP-PA or TPPA - Treponema pallidum particle agglutination assay (treponemal test)
VDRL - Venereal disease research laboratory (nontreponemal test)

What testing is recommended for syphilis diagnosis?

A diagnosis of syphilis requires both treponemal and non-treponemal testing. There are 2 main screening methods for syphilis (see below). Check with your lab to see which method your clinic uses.

1. **Traditional sequencing algorithm**: Start with quantitative nontreponemal test (RPR or VDRL). If RPR/VDRL is reactive, confirmation is needed with a treponemal test (e.g. TPPA or FTA-ABS). If both the RPR and treponemal tests are reactive, the patient has syphilis.

2. **Reverse sequencing algorithm**: Start with a screening treponemal test (TPA IGG/IGM, EIA, CIA, etc). If the screening treponemal test is reactive, a quantitative nontreponemal test (RPR or VDRL) should be completed.
    a. If the screening treponemal test and RPR are in agreement (reactive), the patient has syphilis
    b. If the screening treponemal test and RPR are discordant (treponemal reactive and RPR/VDRL nonreactive) a second treponemal test should be ordered which should be different from the screening treponemal test. TP-PA is the preferred second treponemal test.
        i. If the second treponemal test is reactive, the patient has syphilis
        ii. If the second treponemal is nonreactive, this patient does not have syphilis

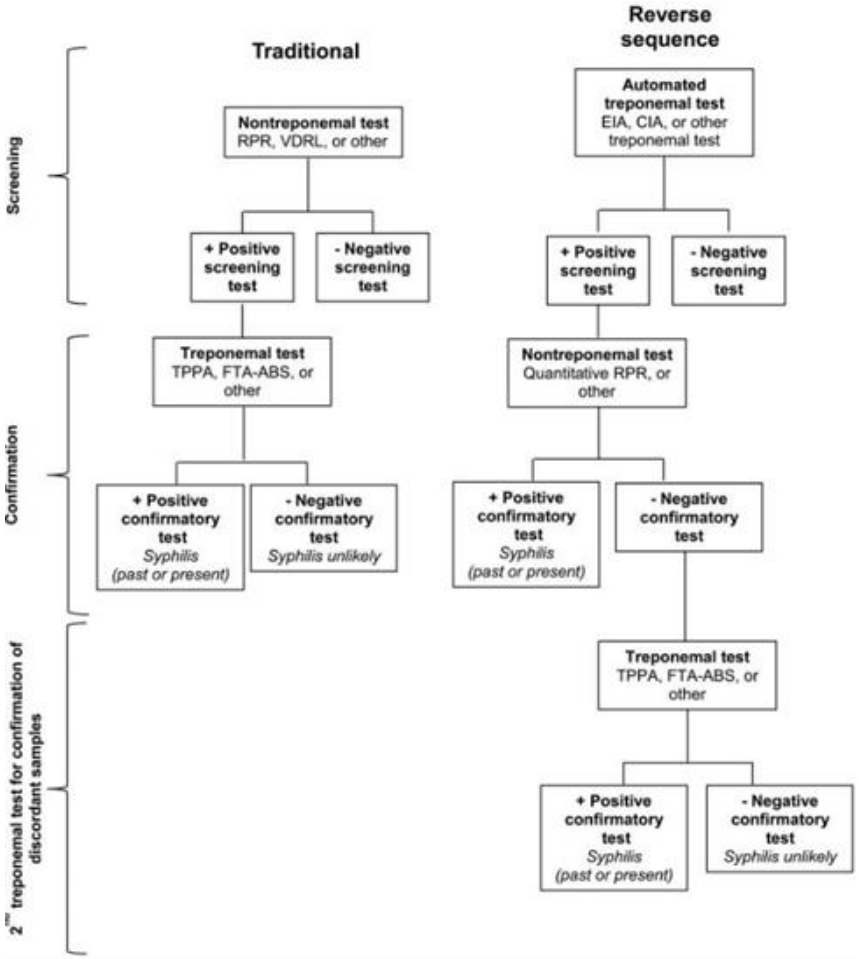


Figure 1. Screening for Syphilis in Nonpregnant Adolescents and Adults: Systematic Review to Update the 2004 U.S. Preventive Services Task Force Recommendation. Cantor A, Nelson HD, Daeges M, et al. Available here.

How can I report syphilis testing/treatment electronically to the Health Department?

Pursuant to Wis. Admin Code. § DHS 145.04(3)(b) and Wis. Stat. § 252.05 providers are required by law to submit syphilis diagnosis and treatment.

Positive test results, symptoms, and treatment information can be reported electronically through Wisconsin Electronic Disease Surveillance System (WEDSS). If you are interested in gaining access to WEDSS for electronic reporting please email DHSWEDSS@wi.gov. Many labs automatically report reactive syphilis test results. Contact your lab's client services for more information on laboratory reporting.

Do I need to do an exam?

Yes! A thorough physical examination is a crucial component of accurate syphilis diagnosis and treatment. Local Health Departments rely on providers to perform a thorough exam and report on observed symptomology. A screening neurologic examination should also be completed to rule out neurosyphilis.

What should I do if a patient is reporting exposure or re-exposure to syphilis?

All patients reporting exposure to syphilis should have a thorough exam and serologic testing for syphilis.

Empiric treatment with 2.4 MU Bicillin-LA should be provided to patients who were exposed to early syphilis within the last 90 days regardless of serologic test results. Empiric treatment is also recommended if exposure was >90 days prior if patient is exhibiting syphilitic symptoms or if serologic tests results are not immediately available and follow-up is uncertain.

Re-exposure and reinfection are common in high morbidity areas. If a patient or DIS reports re-exposure, the RPR should be repeated and patient should be empirically treated if the exposure was within the last 90 days.

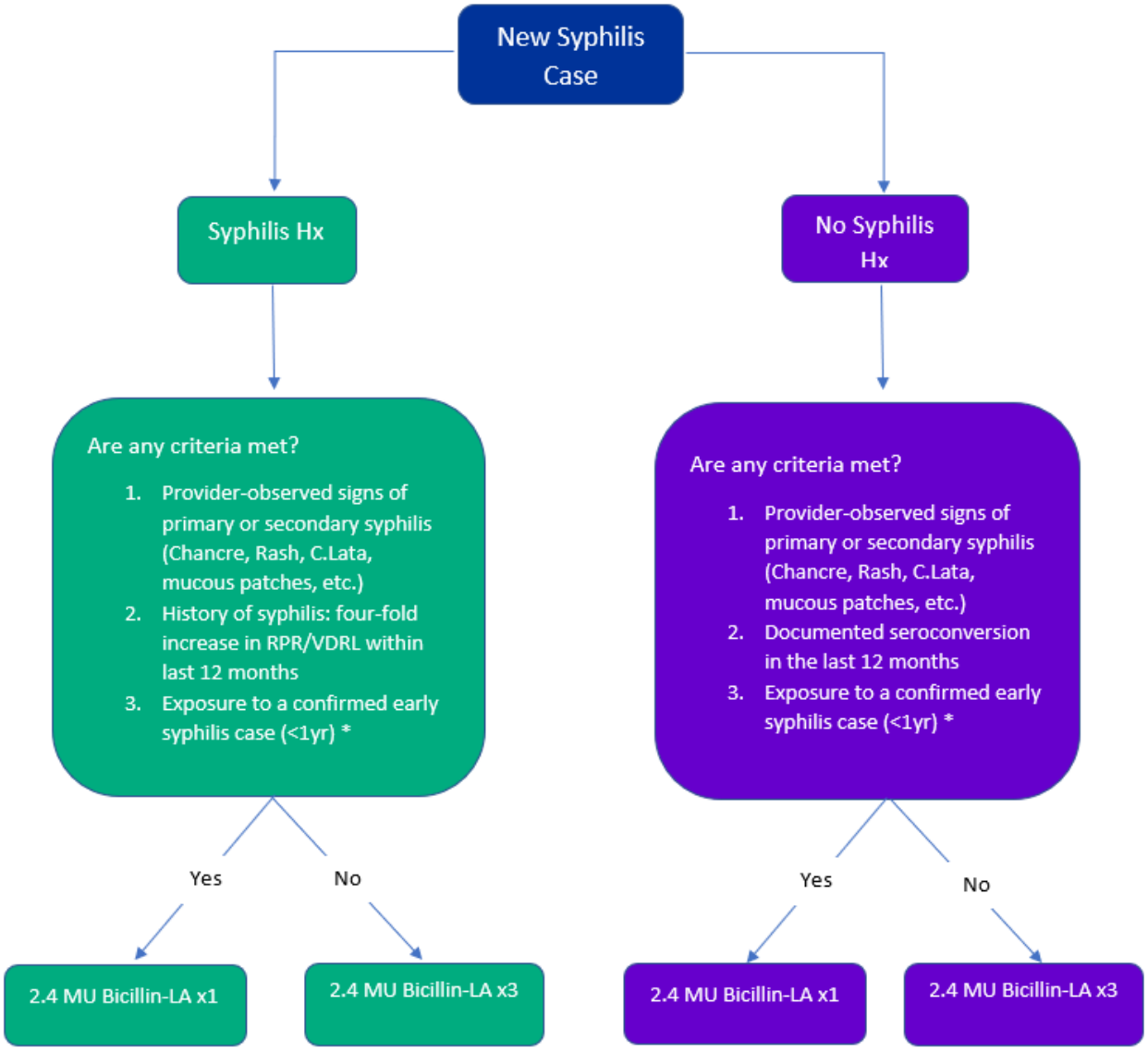
What else should I test for?

Gonorrhea, Chlamydia and HIV testing should be performed for patients diagnosed with or exposed to syphilis.

How to choose between BICx1 and BICx3

Conservative management is recommended with syphilis treatment. BICx3 is recommended unless one of the following criteria is verified:

1. Provider-observed syphilitic signs
2. Nonreactive syphilis testing in the last 12 months (nonreactive RPR valid only if current RPR is reactive)
3. Exposure to a confirmed early case of syphilis (consult local health department Disease Intervention Specialist for confirmation)



*Exposure to early case of syphilis must be verified by Local Health Department before criteria are met for treatment with BICx1

What is the minimum and maximum time period between doses of Bicillin-LA?

Best practice is to maintain as close to 7 days between doses of Bicillin-LA as possible for adequate treatment of syphilis. However, this is not always feasible.

Non-pregnant Patients

- Minimum: 5 days between doses
- Maximum: 14 days between doses

Pregnant Patients

- Minimum: 5 days between doses
- Maximum: 9 days between doses

What is the treatment for latent syphilis?

Latent syphilis occurs at various points during the course of a syphilis infection when there are no syphilitic symptoms present. This can occur during incubation, between primary and secondary syphilis, and after secondary syphilis.

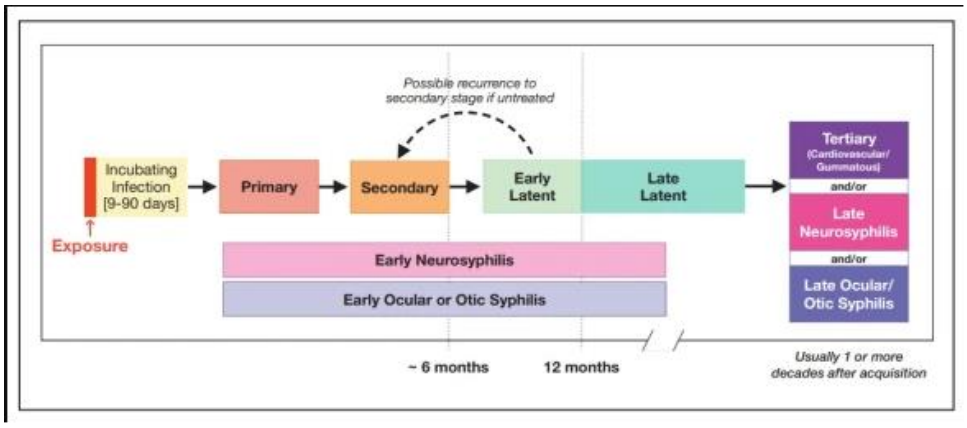
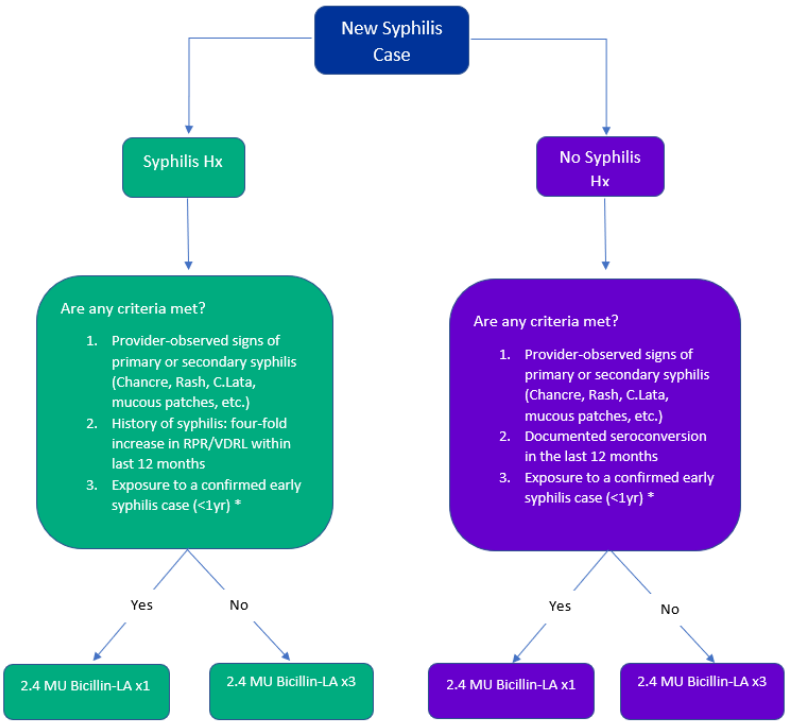


Figure 3. NYC Department of Health and Mental Hygiene, and the NYC STD Prevention Training Center. The Diagnosis and Management of Syphilis: An Update and Review. March 2019.

Treatment for latent syphilis is dependent on when the patient acquired the infection.
2.4 MU Bicillin-LA x1 is adequate treatment for Early Non-Primary, Non-Secondary Syphilis or Early Latent Syphilis which was acquired within the last 12 months where the patient has no current symptoms and one of the following:

a. Nonreactive syphilis testing in the last year (nonreactive RPR valid only if current RPR is reactive) for patients without a syphilis history
b. Fourfold increase in titer within the last 12 months for patients with a syphilis history
c. Exposure to a confirmed early case of syphilis (consult local health department Disease Intervention Specialist for confirmation)

2.4 MU Bicillin-LA x3 is adequate treatment for Syphilis of Unknown Duration or Late in which there are no symptoms and the criteria for Early Non-Primary Non-Secondary Syphilis are not met.



*Exposure to early case of syphilis must be verified by Local Health Department before criteria are met for treatment with BICx1

When is doxycycline an appropriate alternative?

Benzathine penicillin G (Bicillin-LA) is the recommended treatment for uncomplicated syphilis and **the only appropriate treatment for syphilis in pregnant individuals.**

Doxycycline 100 mg BID for 14 days for primary, secondary, and early syphilis (<1 year) or 28 days for unknown duration infection (>1 year) is an acceptable alternative for nonpregnant patients with a penicillin allergy*.

The effectiveness of alternatives to penicillin in treating syphilis is not well documented and adherence is a concern given the frequency and duration of the antibiotic course as well as possible side effects. If adherence is a concern, referral to an allergist is recommended for allergy testing and desensitization.

*While up to 10% of patients report a penicillin allergy, <1% of patients are truly penicillin allergic. The 2021 CDC STI guidelines have detailed guidance for managing patients with reported penicillin allergy. For patients with low risk history as outlined in the guidelines, consider an oral amoxicillin challenge to facilitate preferred treatment with Bicillin-LA.

When should I retest my patient who was adequately treated for syphilis?

Follow up quantitative nontreponemal tests (RPR or VDRL) should be repeated at 6, 12, and 24 months for patients who are not living with HIV. Closer follow-up may be beneficial if there are concerns about re-exposure, doxycycline compliance, or treatment failure.

Patients living with HIV should have follow-up quantitative nontreponemal testing at 3, 6, 9, 12 and 24 months

When should I test a pregnant woman?

All women living in Milwaukee County should be tested for syphilis:

1. At their first prenatal visit or at the time of pregnancy diagnosis
2. In the third trimester between 28-32 weeks
3. At delivery

MHD has noted several cases of missed opportunities to prevent congenital syphilis when testing was not done at third trimester and delivery.

What are the treatment recommendations for pregnant women?

Milwaukee Health Department recommends 2 doses of Bicillin-LA 2.4 MU spaced 7 days apart for early syphilis (<12 months) and 3 doses of Bicillin-LA 2.4 MU spaced 7 days apart for syphilis of unknown duration.
Per CDC, syphilis in pregnancy is recommended to be treated based on the stage of infection; however, there is some evidence to support an additional dose of 2.4 MU Bicillin-LA for early syphilis.

In pregnancy, the treatment course should be restarted if >9 days lapse between injections.

What testing and treatment is recommended in a newborn when the mother has a history of syphilis?

Newborns should have a quantitative non-treponemal test (RPR) performed after birth to compare to maternal levels.

Do not test cord blood. Do not perform treponemal testing as passive maternal antibody transfer is expected and persists up to 15 months of age. Additional work-up depends on maternal diagnosis, timeliness of treatment, suspicion for congenital syphilis and planned treatment of newborn. Please refer to the 2021 CDC STI guidelines for Congenital Syphilis.

When is a neurologic evaluation, including lumbar puncture, needed?

Central Nervous System involvement can occur at any stage of syphilis. Neurosyphilis can present with otic, ophthalmic, or neurologic changes. It is important to recognize neurosyphilis as adequate treatment involves a 10-14 day course typically using intravenous aqueous crystalline penicillin G.

A neurologic examination and review of otic, ophthalmic and neurologic symptoms should be completed for all patients diagnosed with syphilis. Any patient with clinical findings of neurologic involvement should have a lumbar puncture to evaluate CSF. If a patient with syphilis has isolated ocular symptoms without cranial nerve deficit or other neurologic impairment, they should have a complete ophthalmologic exam, but do not require a lumbar puncture prior to treatment for neurosyphilis. Those patients with cranial nerve dysfunction or other neurologic abnormalities, should have a lumbar puncture for CSF evaluation. Similarly, isolated otologic symptoms do not require lumbar puncture, but should be managed in collaboration with an otolaryngologist and treated as neurosyphilis.

For a patient who has been previously treated for syphilis, how do I know if the patient is reinfected?

Symptoms of primary or secondary syphilis (oral/genital lesions, rashes, alopecia, etc.)

Fourfold increase in the nontreponemal titer, compared to prior titer measured after adequate treatment, sustained for greater than 2 weeks.

How do I confirm patient is not infected/false-positive?

With a traditional sequencing algorithm (nontreponemal RPR/VDRL reflexing to treponemal test), a patient with a reactive RPR/VDRL and a nonreactive treponemal test would be considered not infected if there are no known exposures or symptoms. Testing can be repeated in 1 month if there is concern for early infection.

With a reverse sequencing algorithm (treponemal test reflexing to a nontreponemal RPR/VDRL), a patient with a reactive initial treponemal test would need a nonreactive RPR **and** nonreactive second treponemal test* to be considered not infected assuming there are no known exposures or symptoms. Testing can be repeated in 1 month if there is concern for early infection.

***The second treponemal test must be a different type of treponemal test from the first.**
TP-PA is recommended.

What if the patient's titer increased from baseline, but the patient denies any sexual activity and there are no signs or symptoms?

There are many factors that can impact the titer results of patients.

If there is no risk reported by the patient and no clinical indication of reinfection, repeat the nontreponemal test within 2 weeks of the prior test. If the fourfold increase is not sustained, additional treatment is not indicated.

For questions about syphilis diagnosis, including access to first-line treatment options, contact your local health department!

Milwaukee Health Department
Keenan Health Center, Sexual and Reproductive Health Program
3200 N 36th Street
Milwaukee, WI 53216

Disease Intervention Specialist Line: 414-286-5526

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milwaukee.gov/health