

TREATMENT AND FOLLOW-UP, cont.

- Clinicians should obtain baseline and monthly assessment of serum nontreponemal reagin levels when treating syphilis in pregnant patients with HIV infection if the risk of syphilis reinfection is high. (AII)

TREATMENT OF SYPHILIS IN PENICILLIN-ALLERGIC PATIENTS

- Clinicians should administer desensitization therapy followed by penicillin therapy to treat penicillin-allergic patients who have neurosyphilis, other forms of tertiary syphilis, syphilis in pregnancy, or syphilis that cannot be treated by an alternative regimen. (AII)
- Clinicians should administer desensitization therapy for patients with HIV infection, followed by penicillin therapy, rather than attempt alternate therapies if adherence to therapy or close follow-up cannot be ensured. (AII)
- Clinicians should not prescribe azithromycin to treat syphilis in patients with HIV infection. (AII)

JARISCH-HERXHEIMER REACTION

- In women treated for syphilis infection during the second half of their pregnancy, clinicians should: 1) Obtain a fetal sonogram to evaluate for congenital syphilis, and 2) advise women who experience fever, contractions, or a decrease in fetal movements to seek immediate obstetric care. (AII)

TREATMENT FAILURE

- Clinicians should perform CSF examination for patients who experience treatment failure, and 1) initiate parenteral therapy using a recommended penicillin regimen for neurosyphilis if CSF test results are negative; and 2) treat using a recommended penicillin regimen for late latent syphilis if CSF test results are positive. (AII)
- Clinicians should test and treat patients who report exposure to syphilis according to the recommendations in Table 4: Standard Testing and Treatment of Sex Partners Exposed to Syphilis, below. (AII)
- When a patient with HIV infection is diagnosed with syphilis, clinicians should advise the patient to encourage sex partners to seek medical care for possible exposure to both HIV and syphilis and should inform the patient that NYSDOH Partner Services offers free, confidential partner notification assistance. (AIII)

Definition of treatment failure: In the absence of potential exposure for reinfection, treatment failure is defined by any of the following:

- Persistence or development of new clinical signs or symptoms potentially related to syphilis, such as rashes, ulcers, neurologic/ophthalmic signs or symptoms, or gummas.
- Four-fold increase in nontreponemal serology (e.g., RPR 1:4 increases to 1:16).
- Failure of the nontreponemal serology to decrease 4-fold within 12 to 24 months of treatment.

NEW YORK STATE REPORTING REQUIREMENTS:

- Clinicians must report all suspected or confirmed syphilis diagnoses to the local health department of the area where the patient resides according to New York State requirements.
- Medical providers must talk with HIV-infected individuals about their options for informing their sexual partners that they may have been exposed to HIV.

NEW YORK STATE: Prompt reporting of suspected or confirmed syphilis is mandated under the New York State Sanitary Code (10NYCRR 2.10). In NYS, syphilis cases should be reported by telephone to the local health department as follows: 1) Any positive primary or secondary stage disease; 2) Any positive prenatal or delivery test, regardless of serum reagin level; 3) Any nontreponemal test ≥1:16.

For more information about disease reporting in New York State, care providers should contact the local health department where the patient resides or the NYSDOH Bureau of Communicable Disease Control at 518-473-4439.

NEW YORK CITY: New York City's Health Code Article 11 requires that all cases of syphilis, including congenital, be reported promptly. In NYC, syphilis cases can be reported using the Universal Reporting Form, which can be submitted as follows: **Online** via NYC MED, **By fax:** call 866-692-3641 for the appropriate fax number, **By mail:** New York City Department of Health and Mental Hygiene, 42-09 28th Street, CN-22, Long Island City, NY 11101.



← Use this code with your phone's QR code reader to go directly to a mobile-friendly version of this guideline.

■ This 1/4-Folded Guide is a companion to the New York State Department of Health AIDS Institute guideline *Management of Syphilis in Patients with HIV*. Full guideline is available at hivguidelines.org.

- Penicillin is the only recommended treatment for all stages of syphilis in pregnant patients. (AII)
- Clinicians should use long-acting benzathine penicillin G as the recommended treatment for syphilis in patients with HIV infection. (AII)
- Because of the possibility of false-negative test results in primary syphilis, clinicians should presumptively treat patients at risk of syphilis who present with a lesion typical of a syphilitic chancre. (AIII)

TREATMENT AND FOLLOW-UP

- Evidence of active tertiary syphilis (aortitis, gummas). (AII)
- Evidence of treatment failure. (AII)
- That are not explained by another etiology. (AII)
- Neurologic, ophthalmologic, otic, or neuropsychiatric signs or symptoms following:
 - Clinicians should perform a lumbar puncture in patients with HIV infection who have syphilis or a history of syphilis when patients present with the following:
 - Clinicians should include neurosyphilis in the differential diagnosis of all patients with HIV infection who present with neurologic, ophthalmologic, otic, or neuropsychiatric signs or symptoms. (AII)
 - Clinicians should perform a lumbar puncture in patients with HIV infection who have syphilis or a history of syphilis when patients present with the following:
 - Clinicians should include neurosyphilis in the differential diagnosis of all patients with HIV infection who present with neurologic, ophthalmologic, otic, or neuropsychiatric signs or symptoms. (AII)

NEUROSYPHILIS:

- Clinicians should perform a nonreponemal test, such as the RPR or VDRL test, for repeat screening in patients who have a history of syphilis infection. (AI)
- Clinicians should perform a nonreponemal test, such as the RPR or the laboratory if the initial screen is reactive. (AI)
- Clinicians should ensure that two-stage syphilis testing is performed by Follow-Up of Syphilis in Patients with HIV Infection, below. (AII)
- Clinicians should perform a neurologic review of systems, including ophthalmologic and otic, for all patients with HIV infection who are diagnosed with syphilis and follow-up with further neurologic evaluation, as recommended in Table 3: Recommendations for Treatment and Follow-Up of Syphilis in Patients with HIV Infection, below. (AII)
- Clinicians should perform a neurologic review of systems, including in uncircumcised males. (AIII)
- For patients with HIV infection, clinicians should examine all skin and mucosal surfaces for lesions, especially less-visible areas, such as the anus, cervix, vagina, vulva, urethra, oropharynx, and under the foreskin.

PRESENTATION, DIAGNOSIS, AND REPORTING



MANAGEMENT OF SYPHILIS IN PATIENTS WITH HIV INFECTION GUIDELINE

TRANSMISSION AND PREVENTION

- Clinicians should inform patients with HIV infection about the risk of acquiring syphilis and other STIs from close physical contact with all sites of possible exposure, including the anus, cervix, vagina, urethra, tongue, oropharynx, or any other location where infectious lesions may be present. (AIII)

OBTAINING A SEXUAL HISTORY

- Clinicians should ask all patients about sexual behaviors and new sex partners at each routine monitoring visit to assess for risk behaviors that require repeat or ongoing. (AIII)

SCREENING FREQUENCY

- Clinicians should obtain serologic screening for syphilis at least annually for all patients with HIV infection. (AII)
- In response to the current epidemiology in NYS, clinicians should perform syphilis screening every 3 months (AIII) for HIV-infected MSM at highest risk of syphilis infection, including those who:
 - Report, or whose partners report, multiple or anonymous sex partners. (AIII)
 - Have been, or whose sex partners have been, diagnosed with or treated for a bacterial STI since the last evaluation. (AIII)
 - Engage, or whose sex partners may engage, in sexual activity at sex parties or other high-risk venues. (AIII)
 - Are involved, or whose sex partners may be involved, in transactional sex (e.g., sex workers and their clients). (AIII)
 - Report recreational substance use during sexual activity. (AIII)
 - Self-identify as at high risk of STIs. (AIII)

- Clinicians should obtain serologic screening for syphilis for pregnant patients with HIV infection at the first prenatal visit, during the third trimester (28–32 weeks gestation, and at delivery. (AII) *Continued on P.2 →*

KEY POINTS

Screening

- STI screening should be performed every 3 months for persons at high risk regardless of the frequency of their HIV monitoring visits.

Diagnosis

- Because the chancres of primary syphilis are usually painless and may go unnoticed by the patient, it is important that the clinician examine all skin and mucosal surfaces of patients during the annual comprehensive physical examination.
- Syphilis should be included as part of the differential diagnosis for patients presenting with oral, genital, cervical, or anal lesions; rash; eye disease or vision complaints; aortitis; or neurologic disease.
- Definitive diagnosis of syphilis is made either serologically or, if available, by identification of the causative organism.
- Serologic test results are negative in patients with incubating syphilis, and the sensitivity of serologic tests is approximately 80% during the early primary stage of syphilis (i.e., within the first 10 days after the lesion appears).

Difficulties with interpreting syphilis serologies

- All syphilis serologic tests may be falsely negative early in infection, including at the initial appearance of the syphilitic chancre.
- Serum samples containing large amounts of nontreponemal reagin rarely, but occasionally, demonstrate a false-negative reaction, known as a prozone reaction. When there is clinical suspicion of syphilis but the nontreponemal test result is negative, clinicians should order laboratory dilution and retesting of the sample.
- Treponemal tests rarely produce false-negative results; however, if clinical suspicion is high, an alternative treponemal test should be considered.

Treatment

- To avoid use of the incorrect pharmaceutical preparation of penicillin, clinicians should ensure that long-acting benzathine penicillin G (i.e., Bicillin LA and not Bicillin CR) is ordered.
- Treatment failure in a person with HIV infection warrants CSF examination and treatment based on test results.
- Early labor and fetal distress are associated with the Jarisch-Herxheimer reaction. Prompt medical care should be sought by women receiving syphilis treatment during their second half of pregnancy if they experience fever, contractions, or a decrease in fetal movements.

Partner Exposure

- When a patient with HIV infection is diagnosed with syphilis, the clinician should inform the patient about the implications of the diagnosis for his/her sex partner(s):
 - A new STI diagnosis signals that the patient was engaging in sexual behaviors that place sex partners at increased risk of acquiring HIV infection.
 - A sex partner may also have been exposed to syphilis and should be tested and evaluated for treatment.
 - The local health department may contact a sex partner confidentially about the potential exposure and treatment options.
 - Clinicians should provide patients with information and counseling about notifying partners, risk reduction, and safer sex practices.

STANDARD TESTING AND TREATMENT OF SEX PARTNERS EXPOSED TO SYPHILIS [adapted from CDC]

Timing of Partner Exposure	Testing	Treatment	Key Points
Within 90 days of the patient's diagnosis of primary, secondary, or early latent syphilis	Baseline testing	Presumptive (AII)	<ul style="list-style-type: none"> After initial infection, the incubation period of syphilis can last from 3 weeks to 3 months; therefore, sex partners who were exposed within 90 days of a patient's diagnosis of primary, secondary, or early latent syphilis may be infected (incubating infection) even if their serologic syphilis test is nonreactive. Sex partners who were exposed within 90 days of a patient's diagnosis of primary, secondary, or early latent syphilis should receive presumptive treatment. Baseline syphilis testing of sex partners treated presumptively should still be performed to ensure that, if positive, other individuals who may have been exposed are notified and treated.
>90 days before a patient's diagnosis of primary, secondary, or early latent syphilis	Baseline testing	Based on test results (AIII)	<ul style="list-style-type: none"> Sex partners may be treated presumptively if serologic test results are not available immediately and the opportunity for follow-up is unlikely.

SCREENING AND DIAGNOSTIC TESTS FOR SYPHILIS

Serologic Tests	Description
Nontreponemal: <ul style="list-style-type: none"> RPR VDRL 	<ul style="list-style-type: none"> Nonspecific quantitative tests May be negative in 15% to 25% of cases presenting with primary chancre Near 100% sensitivity during secondary syphilis May be positive in the setting of medical conditions other than syphilis, including HIV infection; collagen vascular diseases; narcotic drug use; advanced age; pregnancy; chronic liver disease; some viral infections, such as Epstein-Barr virus; and other chronic inflammatory conditions
Treponemal: <ul style="list-style-type: none"> FTA-Abs TP-PA ELISA EIA/CIA 	<ul style="list-style-type: none"> More specific than nontreponemal tests Measure antibody to surface protein of <i>T. pallidum</i> (antibodies will persist; they do not afford protective immunity and cannot be used to diagnose subsequent episodes or to monitor response to therapy) Become reactive approximately 7 to 10 days after the appearance of the chancre Rarely produce false-positive results
Lesion-Based Tests	Description
DFA	Performed on lesion exudate or tissue specimen
Darkfield microscopy	Performed on exudate from an ulcer base or a mucocutaneous lesion
Silver stain	Performed on biopsy specimens of suspicious lesions, such as palmar macular rash or gummatous lesions
PCR	Performed on specimens of lesions

• Some clinical laboratories and blood banks use the *T. pallidum* IgG + IgM ELISA or treponemal CIA/EIA assay first, followed by nontreponemal tests.
 • Lesion-based testing is used when serologic testing is nonreactive in the presence of a lesion.

RECOMMENDATIONS FOR TREATMENT AND FOLLOW-UP OF SYPHILIS IN PATIENTS WITH HIV INFECTION [a]

Stage	Treatment [b] (AII)	Follow-Up Intervals (AIII)	Comments
Primary, secondary	2.4 million units IM benzathine penicillin × 1 dose	3, 6, 9, 12, 24 months post-treatment	<ul style="list-style-type: none"> CSF examination recommended in the presence of neurologic, ophthalmologic, or otic changes or evidence of treatment failure [b]
Early latent		6, 12, 18, 24 months post-treatment	
Late latent or unknown duration	2.4 million units IM benzathine penicillin per week × 3 weeks	6, 12, 18, 24 months post-treatment [c]	<ul style="list-style-type: none"> CSF examination recommended in the presence of neurologic, ophthalmologic, or otic changes or evidence of treatment failure [b] CSF examination recommended Some experts recommend parenteral therapy as for neurosyphilis
Tertiary gummatous			
Tertiary cardiovascular			
Neurosyphilis	Aqueous crystalline penicillin G 18 to 24 million units IV daily for 10 to 14 days	3, 6, 9, 12, 24 months [e] post-treatment; repeat CSF examination every 6 months until CSF cell count is normal	<ul style="list-style-type: none"> CSF examination recommended in the presence of neurologic, ophthalmologic, or otic changes or evidence of treatment failure Some experts recommend 2.4 million units IM benzathine after parenteral penicillin to have total duration of therapy equal to that of late latent syphilis CSF abnormalities (elevated total protein and/or positive CSF VDRL) may persist for prolonged periods

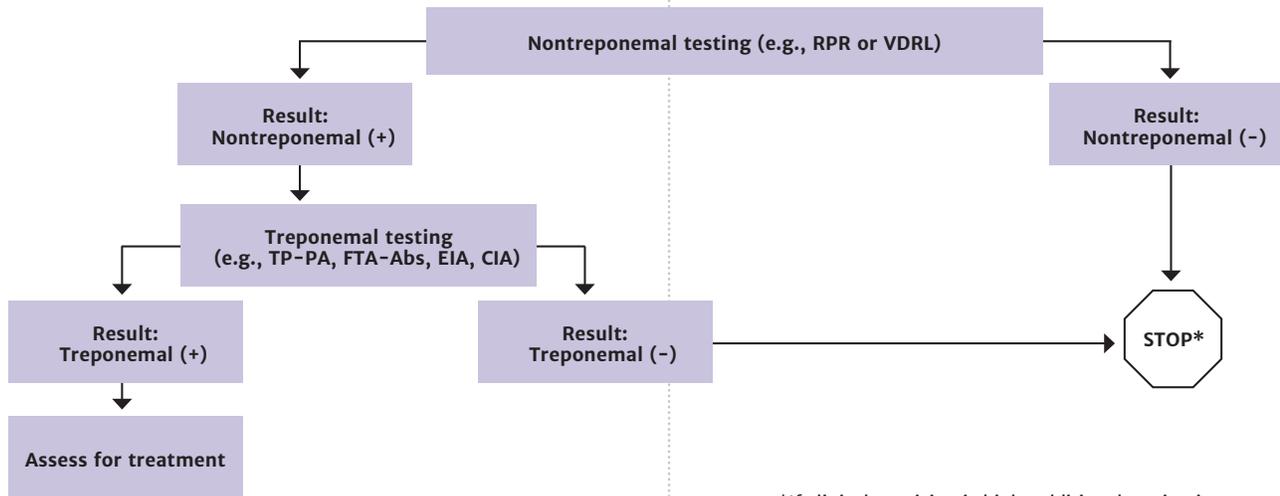
a. The efficacy of non-penicillin regimens in patients with HIV infection is unknown. Penicillin-allergic patients should be desensitized if possible. Close clinical and serologic follow-up is necessary when non-penicillin regimens are used to treat syphilis in patients with HIV infection.

b. CSF examination yielding pleocytosis, increased total protein, or positive VDRL may be consistent with neurosyphilis.

c. There are no published data to inform a recommendation regarding serologic follow-up in patients treated for tertiary syphilis. Because tertiary syphilis is a late complication of syphilis, occurring after the first year of infection, this committee recommends providers utilize the serologic follow-up schedule for late, latent syphilis (6, 12, 18, 24 month post-treatment).

d. There are limited data addressing serologic follow-up of patients treated for neurosyphilis. Because neurosyphilis may occur during all stages of syphilis, this committee recommends serologic follow-up for HIV co-infected patients treated for neurosyphilis at 3, 6, 9, 12, and 24 months post-treatment.

STANDARD PROTOCOL FOR SYPHILIS SCREENING AND DIAGNOSIS



ALTERNATIVE, REVERSE ALGORITHM FOR SYPHILIS SCREENING AND DIAGNOSIS

