

What's New — October 2011 Update

Update for *Section II: Prevention*

- Patient education about the risk of acquiring syphilis and other STIs from unprotected sexual contact, including all sites of possible transmission, such as anus, cervix, vagina, urethra, and oropharynx

Update for *Section III: Screening and Reporting*

- Nontreponemal testing, such as the RPR or VDRL, for repeat screening in HIV-infected patients with a history of syphilis infection; the same nontreponemal reagin test should be used when performing repeat screening and when following response to treatment in these patients

Update for *Section V: Diagnosis*

- Lumbar puncture for HIV-infected patients with syphilis or history of syphilis in the following cases:
 - Neurologic or ophthalmologic signs or symptoms are present, including unexplained change in mental status
 - Evidence of treatment failure (as defined in Table 2 footnote)
 - Evidence of active tertiary syphilis (aortitis, gummas)
- Laboratory dilution and retesting of a negative nontreponemal sample when there is clinical suspicion for syphilis

Update for *Section VI: Treatment and Follow-Up*

- Treatment for primary syphilis in HIV-infected patients if they present with a chancre even in the setting of a preliminary negative nontreponemal screening test
- For penicillin-allergic, HIV-infected patients:
 - Clinician consultation with an expert in infectious diseases and close follow-up if non-penicillin regimens are used to treat syphilis
 - Penicillin desensitization followed by penicillin therapy for neurosyphilis and other forms of tertiary syphilis
 - Penicillin desensitization and treatment with penicillin, rather than use of alternate therapies, if adherence to therapy or close follow-up cannot be ensured

I. INTRODUCTION

Since 2001, rates of primary and secondary syphilis have increased annually in the United States,¹ especially among HIV-infected men who have sex with men (MSM).² In the setting of underlying HIV infection, atypical presentations of early syphilis, rapid progression to tertiary syphilis, treatment failures, and more frequent cases of neurosyphilis have been reported. Despite the number of reports of unusual features, the presentation and management of syphilis in the majority of patients co-infected with HIV is similar to that in non-HIV-infected patients.

II. PREVENTION

RECOMMENDATIONS:

Clinicians should counsel HIV-infected patients about the risk of acquiring syphilis and other STIs from unprotected sexual contact, including all sites of possible transmission, such as anus, cervix, vagina, urethra, and oropharynx. (AIII)

When HIV-infected patients are diagnosed with early syphilis (primary, secondary, or early latent), clinicians should intensify risk-reduction counseling, including discussions about the importance of condom use. (AIII)

Syphilis and other STIs are primarily transmitted by unprotected sexual contact involving genital, rectal, or oral mucosal surfaces. Patients should be counseled about the risk of acquiring syphilis at all sites of possible exposure. Oral sex is a route of transmission of syphilis that many individuals often do not consider.³

Genital ulcer disease has been associated with an increased risk of HIV transmission.⁴⁻⁶ Ulcers (HSV, syphilis, and chancroid) directly increase the likelihood that genital secretions will contain an infectious amount of HIV-1. This increases the potential for contact between HIV-1 in these secretions with genital mucosal cells receptive to HIV-1 infection. When genital ulcerative disease is present, clinicians should intensify risk-reduction counseling.

Clinicians who are uncomfortable discussing sexual behaviors and STI transmission risk can seek training to enhance their comfort level and to develop a nonjudgmental approach to educating patients about the importance of STI screening. For information regarding risk-reduction counseling related to sexual transmission, refer to the HIV Prevention

Guidelines: [Prevention with Positives: Integrating HIV Prevention into HIV Primary Care](#).

Training in STI prevention and counseling is also available through the [HIV Clinical Education Initiative](#) and the [Region II STD/HIV Prevention Training Center](#).

III. SCREENING AND REPORTING

RECOMMENDATIONS:

As part of the annual comprehensive physical examination, clinicians should examine all skin surfaces for lesions, especially in less visible areas such as the anus, cervix, vagina, urethra, and oropharynx, as well as under the foreskin in uncircumcised males. (AIII)

Clinicians should:

- Obtain serologic screening for syphilis at least annually for HIV-infected patients, and every 4 months for patients with continued high-risk behavior (AII)
- Obtain confirmatory testing if the initial screen is reactive (AII)
- Be familiar with their referring laboratory's syphilis screening algorithm (AIII)

Clinicians should perform a nontreponemal test, such as the RPR or VDRL, for repeat screening in HIV-infected patients with a history of syphilis infection; the same nontreponemal reagent test should be used when performing repeat screening and when following response to treatment in these patients. (AII)

In New York State, clinicians must report suspected or confirmed syphilis diagnoses to their local health department.

Serologic Tests Used for Syphilis Screening

Nontreponemal:

RPR, rapid plasma reagin

VDRL

Treponemal:

FTA-Abs, fluorescent treponemal antibody absorbed

TP-PA, *T. pallidum* particle agglutination

IgG, treponemal EIA/CIA test*

* Some clinical laboratories and blood banks use the treponemal IgG ELISA or EIA assay first, with confirmation by nontreponemal tests.

HIV-infected patients should be screened for syphilis at least once per year. Patients with continued high-risk behavior should be screened for syphilis every 4 months. Factors that may prompt more frequent screening include multiple or anonymous sex partners, past history of STIs, high prevalence of STIs in the area or patient population, life changes that may lead to risky behaviors, or sex or needle-sharing partners with any of these risks.

Because the chancres of primary syphilis are usually painless, it is important that the clinician perform a careful physical examination, especially in less visible areas such as the anus, cervix, vagina, urethra, and oropharynx, as well as under the foreskin in uncircumcised males.

Traditionally, the screening algorithm for syphilis has used a nontreponemal screening test (i.e., RPR or VDRL), followed by a confirmatory test for treponemal antigen (i.e., FTA-Abs or TP-PA). However, some municipalities with a high volume of syphilis testing, including some

laboratories in New York City, have begun to use a reverse-sequence screening algorithm with an automated treponemal EIA or CIA as the initial screening test, followed by confirmation with the nontreponemal RPR. When discordant results are provided by laboratories using the alternative algorithm (i.e., reactive EIA/ELISA with a non-reactive RPR), the CDC recommends a confirmatory TP-PA test to exclude very early syphilis or previously untreated syphilis infection.⁷ Information regarding a given laboratory's screening algorithm may not be immediately available. Clinicians should request information regarding the screening algorithm of their referring laboratory and be familiar with the testing sequence used.

For most individuals with a history of syphilis infection, the FTA-Abs, TP-PA, ELISA, and EIA tests remain positive for life, and some individuals previously treated for syphilis will continue to have a low positive serum RPR or VDRL (i.e., "serofast" syphilis). A 4-fold or greater increase in serum RPR or VDRL indicates treatment failure or re-infection with syphilis. The same nontreponemal reagin test should be used for both repeat screening and following the response to treatment in these patients.

Prompt reporting of suspected or confirmed syphilis is mandated under the New York State Sanitary Code (10NYCRR 2.10). The following cases should be reported by phone to the local health department:

- Any nontreponemal test $\geq 1:16$
- Any positive primary or secondary stage disease
- Any positive prenatal or delivery test, regardless of serum reagin level

All other cases may be reported by mail. The local health department may contact the patient for epidemiological investigation or to offer assistance with partner notification. More information regarding communicable disease reporting requirements is available at the following sites:

- New York State: www.health.state.ny.us/nysdoh/cdc/cdcrept.pdf
- New York City: www.nyc.gov/html/doh/html/hcp/hcp-reporting.shtml

Clinicians can contact local health departments to obtain previously reported nontreponemal and treponemal test results. See Appendix A for the contact information of the STI coordinator for each of the local health departments in New York State.

IV. PRESENTATION

Syphilis is classified into four stages: primary, secondary, latent, and tertiary. Lesions of *primary syphilis* usually develop following an incubation period of 10 to 90 days (usually 3 weeks). Primary lesions usually last 3 weeks and resolve without treatment. The onset of *secondary syphilis* occurs from 2 weeks to 6 months after the resolution of the primary stage (usually 4 weeks). Secondary symptoms usually last 4 weeks, and like primary symptoms, resolve without treatment. *Latent syphilis* may persist for up to 50 years after infection. Latent infection is divided into early latent (<1 year since infection) and late latent (≥ 1 year after infection). During early latent infection, relapse of secondary syphilis and subsequent transmission to sexual partners are possible. *Tertiary syphilis* refers to clinical manifestations occurring after the latent stage (range, 2-50 years after latency). Typically, tertiary syphilis is divided by organ system involvement into gummatous syphilis, cardiovascular syphilis, and neurologic syphilis.

Key Points:

- In the setting of HIV, syphilis may mimic other infections, including herpes and fungal rash, and non-infectious dermatologic conditions, such as psoriasis.
- Syphilitic gumma may present as a focal mass lesion.
- Frequency of clinical relapse after syphilis treatment may be higher in HIV-infected patients, particularly in patients with advanced HIV.

Most HIV-infected patients present similarly to non-HIV-infected patients, although some key features exist. Table 1 summarizes the usual clinical presentation of syphilis in the non-HIV-infected population and the reports of atypical manifestations described in HIV-infected individuals. Appendix B shows photographic examples of secondary syphilis in HIV-infected patients.

TABLE 1 DIFFERENCES IN CLINICAL PRESENTATION OF SYPHILIS IN PATIENTS WITH AND WITHOUT HIV INFECTION		
Stage	All Patients	Reported in HIV-Infected Patients⁸⁻²⁵
Primary	<ul style="list-style-type: none"> • Develops 10-90 days after exposure (usually 3 weeks) • Single chancre: painless, indurated ulcer with a clean base and smooth borders • Chancre persists 1-5 weeks (average, 3 weeks) and heals spontaneously, regardless of treatment • Painless, rubbery lymphadenopathy in some cases 	<ul style="list-style-type: none"> • Multiple chancres • Chancres that are larger, deeper, and resolve more slowly • Atypical chancres appearing as abrasions or fissures
Secondary	<ul style="list-style-type: none"> • Signs and symptoms occur 2 weeks to 6 months after resolution of primary syphilis (usually 4 weeks) • May include low-grade fever, adenopathy, headache, malaise, and rash • Common findings are macular-papular rash, involving palms and soles, mucous patches in the mouth, condyloma lata, and patchy alopecia (persists 2-6 weeks and heals spontaneously) • Uveitis, iritis, hepatitis, and nephrotic syndrome may occur 	<ul style="list-style-type: none"> • Coincident chancres with signs of secondary syphilis • Duration of rash may be slightly longer, and rash may be more widespread • Atypical skin rashes, including papular, nodular, ulceronodular (lues maligna) • Reports of ocular syphilis, mainly uveitis (found in 10% of patients with a positive CSF VDRL in one study); patients should receive treatment for neurosyphilis • Retinitis, papillitis, and cranial nerve abnormalities II, III, or V in association with syphilitic meningitis; patients should receive treatment for neurosyphilis

Table 1 continues

Table 1 continued

<p>Latent</p>	<ul style="list-style-type: none"> • In both HIV-infected and non-infected patients, latent infections are those that can be detected by serologic testing, but otherwise lack any other evidence of disease • Early latent syphilis refers to latent syphilis acquired within the preceding year. This diagnosis can be made if any of the following occur in the year preceding the evaluation: <ul style="list-style-type: none"> – Seroconversion was documented (i.e., documented nonreactive nontreponemal test within preceding 12 months) – Four-fold increase in nontreponemal serum reagin since the last adequately treated infection – A history of unequivocal symptoms of primary or secondary syphilis – Sex partner documented to have primary, secondary, or early latent syphilis • All other asymptomatic cases are either late latent syphilis or latent syphilis of unknown duration 	
<p>Tertiary Gummatous (late benign syphilis)</p>	<ul style="list-style-type: none"> • Occurs 1 to >40 years after infection (average, 4 to 10 years) • Gumma-indolent lesion that consists of a marked granulomatous response on histopathology • Occurs in any organ system • Rare in the antibiotic era 	<ul style="list-style-type: none"> • Several reports of gummas • One case of rapid progression to gumma within several months of a chancre • Located in multiple organ systems including the brain
<p>Cardio-vascular</p>	<ul style="list-style-type: none"> • Occurs after 15 to 30 years of latency • Pathologic lesion is endarteritis obliterans of vasa vasorum of the aorta • May result in aneurysms, coronary artery stenosis, or aortic regurgitation • Rare in the antibiotic era 	<ul style="list-style-type: none"> • Rare cases of rapidly developing aortitis reported
<p>Neurologic</p>	<ul style="list-style-type: none"> • Asymptomatic or symptomatic meningitis (early after infection) • Meningovascular syphilis presenting as cerebrovascular accident • Parenchymatous syphilis presenting as general paresis (>20 years after infection), or tabes dorsalis (15-20 years after infection) 	<ul style="list-style-type: none"> • Numerous case reports of neurologic syphilis • Progression to neurologic syphilis despite treatment of early syphilis • Reports of rapid progression to neurologic syphilis without long latency • Cases have occurred in patients with both normal and low CD4 counts • Clinical features include asymptomatic disease, meningitis, cranial nerve deficits, optic neuritis, myelitis, stroke, cerebral gummas

V. DIAGNOSIS

RECOMMENDATIONS:

Clinicians should include syphilis as part of the differential diagnosis for HIV-infected patients presenting with oral, genital, cervical, or anal lesions, as well as for patients presenting with rash, eye disease, or neurologic disease. Definitive diagnosis is made either by identification of the organism or serologically. (AIII)

Clinicians should perform a baseline neurologic examination for all HIV-infected patients diagnosed with syphilis and should educate patients about the signs and symptoms of neurosyphilis. (AIII)

When there is clinical suspicion for syphilis in an HIV-infected patient, but the nontreponemal test result is negative, clinicians should order laboratory dilution and retesting of the sample. (AII)

A. Identification of *T. pallidum* (Lesion-Based Testing)

Direct Fluorescent Antibody Test (DFA)

A direct fluorescent antibody test can be performed on lesion exudate or tissue specimen. There are no differences in test performance characteristics among HIV-infected and non-HIV-infected patients.

Darkfield Microscopy

Examination of exudate from an ulcer base or a mucocutaneous lesion under darkfield microscopy can identify the spirochete (*T. pallidum*). This test is invalid for oral samples and is typically available only in specialized centers (consult with your local health department for availability; see Appendix A). There are no differences in test performance characteristics among HIV-infected and non-HIV-infected patients.

Silver Stain

Spirochetes may be seen in biopsy specimens of suspicious lesions such as palmar macular rash or gummatous lesions. There are no differences in test performance characteristics among HIV-infected and non-HIV-infected patients.

B. Serology

A diagnosis of syphilis is possible with the use of two diagnostic tests: a nontreponemal reagent test and, if positive, a confirmatory specific treponemal antibody test. Some clinical laboratories and blood banks use treponemal syphilis IgG ELISA or EIA tests with verification by nontreponemal tests.

Key Points:

- Serologic test results are negative in patients with incubating syphilis.
- Serologic testing has limited sensitivity during the early primary stage of syphilis (i.e., within the first 10 days after the lesion appears). Use of lesion-based testing or presumptive diagnosis based on lesion appearance may be the only means of diagnosis.

Nontreponemal Tests

RPR (rapid plasma reagin) or VDRL (venereal disease research laboratory) are non-specific quantitative tests that result from the cross-reaction of human cardiolipin-lecithin in syphilis infection. The tests correlate with disease activity and are used to follow the clinical course and determine the effectiveness of treatment. If reactive during primary syphilis, the nontreponemal tests usually become positive approximately 7-10 days after the onset of the chancre. Because the nontreponemal tests are positive in only 80% of cases presenting with chancre (i.e., primary ulcer), patients presenting with chancre who test negative according to nontreponemal tests should receive treatment.

The sensitivity of these tests is near 100% during secondary syphilis. Serum reagin levels are typically low (<1:16) in primary syphilis and higher (>1:32) in secondary syphilis; serum reagin levels are variable thereafter and may serorevert to negative in approximately 25% of untreated patients (usually 2 years following the infection). Serum samples containing large amounts of nontreponemal reagin occasionally demonstrate a false-negative reaction, known as a prozone reaction.²⁶ When there is clinical suspicion for syphilis, but the nontreponemal test result is negative, clinicians should order laboratory dilution and retesting of the sample. Nontreponemal tests may be positive in the setting of medical conditions other than syphilis, including HIV infection, collagen vascular disease, narcotic drug use, advanced age, pregnancy, chronic liver disease, and some viral infections, such as Epstein-Barr virus, and other chronic inflammatory conditions (i.e., biological false-positive nontreponemal test).

Treponemal Tests

The FTA-Abs (fluorescent treponemal antibody test), TP-PA (*T. pallidum* particle agglutination), and syphilis IgG ELISA or EIA tests are treponemal assays that measure antibody to surface protein of *T. pallidum*. The treponemal tests are more specific than nontreponemal tests and become reactive approximately 7 to 10 days after the appearance of the chancre. A treponemal test should be explicitly ordered during primary infection. Treponemal tests do not correlate with disease activity and remain positive for life in approximately 80% of patients, even after effective treatment.

Considerations for serology in HIV-infected patients

Serologic test results for the majority of HIV-infected patients with syphilis are consistent with those seen in non-HIV-infected patients with syphilis; however, there have been reports of atypical serologies in patients co-infected with HIV as described below:

- HIV-infected patients may have false-positive nontreponemal reagin test results (RPR/VDRL). In one study, 4% of HIV-infected patients tested had false-positive RPR results²⁷
- Seroreactivity may be delayed or absent in HIV-infected patients. Rare cases have been reported of biopsy-proven secondary syphilis in HIV-infected patients with negative syphilis serologies²⁸
- HIV-infected patients may have higher mean serologic serum nontreponemal reagin levels than non-HIV-infected patients⁸
- Serum nontreponemal reagin levels may decline more slowly after treatment in HIV-infected patients than non-infected patients^{8,29,30}
- No correlation has been found between serologic response to therapy and CD4 count⁸
- Prozone reaction occurs more commonly in HIV-infected persons³¹

C. Diagnosis of Neurosyphilis

RECOMMENDATIONS:

Clinicians should include neurosyphilis in the differential diagnosis of all HIV-infected patients who present with neurologic symptoms. (AII)

Clinicians should perform a lumbar puncture in HIV-infected patients with syphilis or history of syphilis in the following cases (AII):

- **Neurologic or ophthalmologic signs or symptoms are present, including unexplained change in mental status**
- **Evidence of treatment failure** (as defined in Table 2 footnote)
- **Evidence of active tertiary syphilis (aortitis, gummas)**

The diagnosis of neurosyphilis requires examination of the CSF. Neurosyphilis is definitively diagnosed when a CSF VDRL is reactive. In patients who have serologic evidence of syphilis *and* CSF pleocytosis and/or elevated CSF protein, neurosyphilis can be presumptively diagnosed even when the CSF VDRL is non-reactive. Non-specific CSF abnormalities, such as pleocytosis or increased protein, may be found in HIV-infected patients due to the HIV infection itself or other HIV-associated conditions, making the results of CSF VDRL-negative examinations difficult to interpret. Due to the high sensitivity of FTA-Abs and TP-PA in CSF, negative FTA-Abs or TP-PA results may be useful to exclude the possibility of neurosyphilis.^{32,33}

Central nervous system involvement can occur at any stage of syphilis. Neurologic signs and symptoms, including, but not limited to, meningitis, ophthalmologic, or otologic abnormalities, warrant examination of the CSF, regardless of stage of syphilis. Patients may also present with change in mental status, such as the onset of acute psychiatric symptoms. Any evidence of tertiary syphilis or treatment failure is also an indication for CSF examination.

Detection of the organism in the CSF in early syphilis is not more common in HIV-infected patients, does not correlate with subsequent development of neurosyphilis, and is not linked to serologically defined treatment failure. For these reasons, most experts do not recommend routine CSF examination for HIV-infected patients with early syphilis who do not present with neurologic symptoms. Most reported cases of neurologic syphilis in HIV-infected patients have been in patients with high serum reagin levels ($\geq 1:32$)^{34,35}; therefore, some clinicians would perform early lumbar puncture in this setting rather than waiting 12 months to document a 4-fold decrease in serum reagin levels. Similarly, some clinicians would examine CSF in HIV-infected patients with previously treated syphilis who remain serofast with high serum reagin levels ($\geq 1:32$) after re-infection has been excluded. Consultation with an infectious diseases specialist is recommended when the diagnosis of neurosyphilis is being considered in patients with high serum reagin levels that fail to decline within the first 12 months or patients who were previously treated for syphilis and then present with high serum reagin levels (BIII).

One study examined CSF results in 326 patients with syphilis. HIV-infected patients with syphilis who had an RPR serum reagin level $\geq 1:32$ and a CD4 count < 350 cells/mm³ were more likely to have neurosyphilis.³⁴ Some experts recommend CSF examination for all HIV-infected patients with syphilis regardless of syphilis stage when serum RPR is $\geq 1:32$ or CD4 count is < 350 cells/mm³.

VI. TREATMENT AND FOLLOW-UP

RECOMMENDATIONS:

Clinicians should obtain baseline serum nontreponemal reagin level before or at the time of initial treatment for syphilis in order to monitor treatment response. (AI)

Clinicians should treat HIV-infected patients for primary syphilis if they present with a chancre even in the setting of a preliminary negative nontreponemal screening test. (AI)

Clinicians should use long-acting benzathine penicillin G as the preferred treatment for HIV-infected patients with syphilis. Clinicians should ensure that the proper formulations and dosages of penicillin are used. Preparations of long-acting benzathine penicillin G and dosing regimens vary by stage of syphilis and are outlined in Table 2. (AI)

Detailed treatment and follow-up recommendations for HIV-infected patients with syphilis are presented in Table 2. Penicillin is the drug of choice, and recommendations for treatment vary by stage. There are no differences in recommended penicillin regimens for HIV-infected patients compared with non-HIV-infected patients. There have been instances in which the incorrect pharmaceutical preparation of penicillin has been used; clinicians should ensure that long-acting benzathine penicillin G (i.e., Bicillin LA and *not* Bicillin CR) is ordered.

HIV-infected patients with syphilis should be followed closely. Follow-up is largely serologic and varies by stage (see Table 2).

A. Treating Syphilis in HIV-Infected Patients With Penicillin Allergy

RECOMMENDATIONS:

Clinicians should consult with an expert in infectious diseases and provide close follow-up if non-penicillin regimens are used to treat syphilis in penicillin-allergic, HIV-infected patients. (AIII)

Penicillin desensitization followed by penicillin therapy is the treatment of choice for neurosyphilis and other forms of tertiary syphilis. (AII)

Clinicians should desensitize penicillin-allergic, HIV-infected patients and treat with penicillin, rather than attempt alternate therapies, if adherence to therapy or close follow-up cannot be ensured. (AIII)

Alternate treatment options for HIV-infected patients with penicillin allergy have not been well studied. Non-penicillin therapies should be used with caution and only in consultation with an expert in infectious diseases. Such regimens require close clinical and serologic follow-up to identify treatment failure or relapse. If adherence to therapy or close follow-up cannot be ensured with alternative regimens, clinicians should desensitize and treat with penicillin.

Doxycycline (100 mg PO bid for 14 days) may be effective for early syphilis. If treatment failure occurs with doxycycline, patients should undergo desensitization to penicillin and penicillin treatment. Resistance and treatment failures have been documented with the use of azithromycin (2 g PO in a single dose) for early syphilis; this agent should be used with caution and only when treatment with penicillin or doxycycline is not feasible. Azithromycin should not be used in MSM or pregnant women.³⁶ Ceftriaxone has been used for treatment of latent and neurologic syphilis, but failures have been reported. No clear alternative regimens exist for tertiary forms of syphilis other than neurosyphilis.³⁷

B. Jarisch-Herxheimer Reaction

RECOMMENDATION:

Clinicians should inform patients about possible adverse reactions to syphilis treatment, including the Jarisch-Herxheimer reaction. (AIII)

The Jarisch-Herxheimer reaction, which is caused by the immunologic response to the destruction of the spirochete, can occur within the first 24 hours of syphilis therapy and may require acute management. This acute febrile reaction is frequently accompanied by headache, myalgia, and/or worsening of secondary syphilis rash, and occurs most often in patients with early syphilis. The Jarisch-Herxheimer reaction may induce early labor or cause fetal distress in pregnant women, but this concern should not prevent or delay therapy.

C. Treatment Failure

Treatment failure is defined by any of the following:

- 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 during the first 12 months of follow-up

RECOMMENDATIONS:

Clinicians should evaluate the CSF of HIV-infected patients who experience treatment failure. (AII)

According to the results of the CSF examination, the clinician should either re-treat with therapy for late latent syphilis or initiate parenteral therapy using a recommended regimen for neurosyphilis (see Table 2). (AIII) Consultation with an expert in STIs is indicated.

Treatment failure has been reported in HIV-infected patients at all stages of syphilis and with all of the recommended regimens. The use of ART to restore immune function may reduce treatment failure rates in HIV-infected patients with syphilis.³⁸

TABLE 2
RECOMMENDATIONS FOR THE TREATMENT AND FOLLOW-UP OF
SYPHILIS IN HIV-INFECTED PATIENTS

Stage	Treatment^a	Follow Up^b	Comments
Primary, secondary, or early latent	2.4 million units IM benzathine penicillin × 1 dose	3, 6, 9, 12, 24 months	
Late latent or unknown duration	2.4 million units IM benzathine penicillin per week × 3 weeks	3, 6, 9, 12, 24 months	– CSF examination recommended only if neurologic, ophthalmologic, or unexplained mental status changes ^c
Gummatous	2.4 million units IM benzathine penicillin per week × 3 weeks	3, 6, 9, 12, 24 months (no data on which to base this)	– CSF examination recommended ^c – Some experts recommend IV therapy as for neurosyphilis
Cardiovascular	2.4 million units IM benzathine penicillin per week × 3 weeks	3, 6, 9, 12, 24 months (no data on which to base this)	– CSF examination recommended ^c – IV therapy as for neurosyphilis recommended by some experts
Neurologic	Aqueous crystalline penicillin G 18-24 million units IV qd for 14 days	3, 6, 9, 12, 24 months Repeat CSF exam q 6 months until CSF cell count is normal	– 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 HIV-infected patients is unknown. Penicillin-allergic patients should be desensitized if possible. Alternate treatment regimens should only be used in consultation with an expert in infectious diseases and when close follow-up is ensured.

^b Follow-up should include a physical examination, neurologic examination, and repeat serologic testing. Treatment failure is defined as development of new clinical signs or symptoms, a 4-fold (2 reagin level) increase in nontreponemal serology (e.g., RPR 1:4 increases to 1:16), or a failure of nontreponemal serology to decline 4-fold (2 reagin levels) by 12 months (nontreponemal serology should decline more rapidly in patients with primary syphilis). Treatment failure in an HIV-infected patient warrants CSF examination, treatment based on results; consultation with an expert in STIs is indicated.

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

VII. MANAGEMENT OF PARTNERS

RECOMMENDATION:

Clinicians should consider both HIV and STI exposures to partners when HIV-infected patients present with a new STI. (AIII)

A. Management of HIV Exposure in Partners

RECOMMENDATIONS:

When HIV-infected patients present with a new STI, clinicians should offer assistance with notifying partners of both the potential HIV and STI exposures or should refer patients to other sources for partner notification assistance ([Partner Services](#) in New York State or [CNAP](#) in New York City). Partners without confirmed HIV infection should undergo HIV testing at baseline, 1, 3, and 6 months. Confirmatory testing according to New York State regulations must be performed to confirm HIV diagnoses.

Clinicians should educate patients with non-HIV-infected partners or partners of unknown HIV status to be vigilant for any post-exposure acute HIV symptoms in their partners, such as febrile illness accompanied by rash, lymphadenopathy, myalgias, and/or sore throat (see [Diagnosis and Management of Acute HIV Infection](#)). (AIII)

Partners who present within 36 hours of an HIV exposure should be evaluated as soon as possible for initiation of post-exposure prophylaxis therapy (see [HIV Prophylaxis Following Non-Occupational Exposure Including Sexual Assault](#)). (AII)

Presentation of a new STI in HIV-infected patients suggests exposure of both HIV and the STI to their partners. In this case, offering HIV non-occupational post-exposure prophylaxis (nPEP) to partners is usually not an option because the period prior to STI symptom onset is usually longer than the 36-hour window for initiating HIV nPEP. Therefore, sequential HIV testing of partners without confirmed HIV infection should be performed for early identification of potential HIV acquisition. However, if a patient with an HIV exposure does present within 36 hours, evaluation for nPEP should occur (see [HIV Prophylaxis Following Non-Occupational Exposure Including Sexual Assault](#)).

B. Management of Syphilis Exposure

RECOMMENDATIONS:

Clinicians must report all cases of syphilis infections to state and local public health authorities. Clinicians should educate patients with reportable illnesses in New York State about the potential for confidential follow-up from the New York State Department of Health.

Persons exposed sexually to a patient who has syphilis in any stage should be evaluated for oral, vaginal, penile, and anal lesions, and serology should be obtained. Clinicians should treat partners with a recommended regimen according to the following recommendations:

- *For persons who were exposed within the 90 days preceding the diagnosis of primary, secondary, or early latent syphilis in a sex partner:* these persons may be infected even if they are seronegative; therefore, such persons should be treated presumptively. (AII)
- *For persons who were exposed >90 days before the diagnosis of primary, secondary, or early latent syphilis in a sex partner:* treat presumptively if serologic test results are not available immediately and the opportunity for follow-up is uncertain. (AIII)
- *For long-term sex partners of patients who have latent syphilis:* evaluate clinically and serologically for syphilis and treat on the basis of the evaluation findings. (AIII)

Sexual transmission of *T. pallidum* occurs only when mucocutaneous syphilitic lesions are present; such manifestations are uncommon after the first year of infection.

VIII. HEALTHCARE WORKER EXPOSURE

Historically, many clinicians were taught that the skin lesions of secondary syphilis were “teeming with spirochetes.” However, the only lesions that actually appear to present any risk to the healthcare worker are those of the primary chancre or condylomata lata (secondary lesions involving the mucous membranes). Standard barrier precautions (i.e., gloves) should suffice in protecting the healthcare worker from transmission of syphilis from ulcerative lesions.

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APPENDIX A

STI Clinics in New York State

A list of STI clinics in New York State is available at:

http://www.nyhealth.gov/diseases/communicable/std/clinics/county_list.htm

APPENDIX B

PHOTOGRAPHIC EXAMPLES OF SECONDARY SYPHILIS IN HIV-INFECTED PATIENTS

(From the slide collection of The Ronald O. Perelman Department of Dermatology, New York University School of Medicine.)

Photographic examples of secondary syphilis in HIV-infected patients are available at:

<http://www.hivguidelines.org/clinical-guidelines/adults/management-of-stis-in-hiv-infected-patients/syphilis/#APPENDIX B - PHOTOGRAPHIC EXAMPLES OF SECONDARY SYPHILIS IN HIV-INFECTED PATIENTS>