

Sexually Transmitted Infections

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Module 4: [Co-Occurring Conditions](#)
Lesson 4: [Sexually Transmitted Infections](#)

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Overview

Background

Sexually transmitted diseases (STDs) incorporate a variety of clinical syndromes caused by sexually transmitted infections (STIs) that may be acquired and transmitted through sexual activity.[1] Among persons with HIV (and those at increased risk of acquiring HIV), the diagnosis and treatment of STIs is important for three main reasons: (1) STIs are common, (2) HIV can potentially impact the severity and response to treatment of STIs, and (3) development of STIs can impact the acquisition and transmission of HIV.[2,3,4,5] Despite education and prevention efforts, national trends indicate a rising incidence of several STIs, especially among men with HIV who have sex with men.[6] Clinicians providing care to persons with HIV play a crucial role in STD prevention through regular risk assessment and counseling, immunization for vaccine-preventable STIs, routine screening, diagnosis and treatment of STIs, and partner services. This Topic Review will explore screening, diagnosis, and treatment strategies for the most common and important STIs that occur among persons with HIV; the recommendations herein are based primarily on the 2021 STI Treatment Guidelines.[1]

Screening for STIs in Persons Living with HIV

In order to adequately address the ongoing burden of STIs in persons with HIV, it is critical to implement routine screening strategies and follow evidence-based treatment guidelines (in coordination with state and local health departments). The highest priority for screening is to test for common curable STIs, including chlamydia, gonorrhea, and syphilis, in men and women, as well as trichomoniasis in women. In sexually active persons with HIV, screening for these STIs should be performed at the initial evaluation and then at least annually thereafter. More frequent screening may be appropriate depending on individual risk behaviors (e.g., history of STIs, exchanging sex for money or drugs, engaging in sex with a new sex partner, more than one sex partner, a sex partner with concurrent partners, or a sex partner who has a sexually transmitted infection) and local epidemiology of specific STIs. The following table outlines the 2021 STI Treatment Guidelines recommendations for STI screening in persons with HIV.[1]

Table 1.	
STI Screening Recommendations in Persons with HIV	
STI	Screening Indications and Frequency
Chlamydia	<ul style="list-style-type: none">For sexually active individuals, screen at first HIV evaluation, and at least annually thereafter

STI	Screening Indications and Frequency
	<ul style="list-style-type: none"> • More frequent screening might be appropriate depending on individual risk behaviors and the local epidemiology
Gonorrhea	<ul style="list-style-type: none"> • 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
Syphilis	<ul style="list-style-type: none"> • 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
Herpes	<ul style="list-style-type: none"> • Type-specific herpes simplex virus (HSV) serologic screening for HSV-2 should be considered for persons presenting for an STI evaluation (especially for those persons with multiple sex partners)
Trichomoniasis	<ul style="list-style-type: none"> • Recommended for sexually active women at entry to care and at least annually thereafter
HPV, Cervical Cancer	<ul style="list-style-type: none"> • Sexually active women with HIV who are at least 21 years of age should undergo cervical cancer screening at initial entry to HIV care and again 12 months later. • Annual Pap testing is recommended in women with HIV younger than 30 years of age, but if 3 consecutive annual screens are normal, Pap tests can be performed every 3 years. • Women with HIV who are 30 years of age and older should have either (1) cervical cancer screening by Pap testing alone or (2) Pap testing plus simultaneous HPV co-testing. If Pap testing alone is used, it should be performed at baseline and every 12 months; if the results of 3 consecutive Pap tests are normal, then follow-up testing can occur every 3 years. If Pap and HPV co-testing is performed and both are negative, follow-up screening can be performed in 3 years. • Cervical cancer screening should continue throughout the life in women with HIV.
Anal Cancer	<ul style="list-style-type: none"> • Digital anorectal rectal exam • Screen men who have sex with men with HIV who are 35 years of age and older and screen all others with HIV who are 45 years of age and older. Specific screening recommendations depend on availability of high resolution anoscopy (HRA).
Hepatitis B	<ul style="list-style-type: none"> • At the initial evaluation, test for hepatitis B

STI	Screening Indications and Frequency
Screening	surface antigen (HBsAg), antibody to hepatitis B core (anti-HBc), and hepatitis B surface antibody (anti-HBs)
Hepatitis C Screening	<ul style="list-style-type: none">• At the initial evaluation, perform serologic testing for antibody to HCV (anti-HCV), with reflex to HCV RNA for all positive anti-HCV tests• Annual HCV serologic testing in men who have sex with men• For persons with prior spontaneous or treatment clearance of HCV, screening should be conducted with HCV RNA
NOTE: This table is modified from recommendations in the Centers for Disease Control 2021 Sexually Transmitted Infections Treatment Guidelines and the Panel on Opportunistic Infections in Adults and Adolescents with HIV Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents with HIV.	

Source:

- Panel on Opportunistic Infections in Adults and Adolescents with HIV. Guidelines for the prevention and treatment of opportunistic infections in adults and adolescents with HIV: recommendations from the Centers for Disease Control and Prevention, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America. Human papillomavirus disease. July 9, 2024. [[HIV.gov](#)]
- Workowski KA, Bachmann LH, Chan PA, et al. Sexually transmitted infections treatment guidelines, 2021. Screening Recommendations and Considerations Referenced in Treatment Guidelines and Original Sources. MMWR Recomm Rep. 2021;70(No. RR-4):1-187. [[2021 STI Treatment Guidelines](#)]

Gonococcal Infections

Introduction

Gonorrhea is the second most common bacterial STI in the United States, with 710,151 cases reported in the United States in 2021.[6] Gonorrhea is most often diagnosed in younger adults, especially individuals 20 to 29 years of age (Figure 1).[6] The causative agent is *Neisseria gonorrhoeae*, a gram-negative intracellular diplococcus. Treatment of gonorrhea has been complicated by resistance among *N. gonorrhoeae* isolates to fluoroquinolones, azithromycin, and some cephalosporins.[6,7] Surveillance from the Centers for Disease Control and Prevention (CDC) Gonococcal Isolate Surveillance Project (GISP) has provided ongoing gonococcal resistance data in the United States, and these data help guide treatment recommendations.[6]

Clinical Manifestations

Similar to *C. trachomatis*, *N. gonorrhoeae* can cause a wide range of clinical manifestations, including urethritis, cervicitis, pelvic inflammatory disease, epididymitis, proctitis, prostatitis, pharyngitis, and neonatal infection. In addition, disseminated gonococcal infection can cause petechial or pustular skin rash, septic arthritis, tenosynovitis, and occasionally perihepatitis, endocarditis, and meningitis. Urethral infection is typically symptomatic, but pharyngeal and anorectal infection with *N. gonorrhoeae* often occurs without causing symptoms.

Screening Recommendations

Available data suggest that inflammatory sexually transmitted infections enhance transmission of HIV,[8,9] so routine screening and treatment of gonorrhea may indirectly reduce the risk of HIV transmission to sex partners. It is important to note that persons can have *N. gonorrhoeae* and have minimal or no symptoms. The 2021 STI Treatment Guidelines recommend the following for gonorrhea screening in persons with HIV:[10,11]

- Screen all sexually active persons for urogenital gonorrhea infection at baseline and at least annually thereafter, with the frequency depending on the presence of ongoing risk factors and the prevalence of sexually transmitted infections in the community.
- Screen all men who have sex with men at all anatomic sites of exposure every 3 to 6 months; sites of exposure may include screening for urethral, rectal, and pharyngeal gonorrhea.

Laboratory Diagnosis

The nucleic acid amplification tests (NAATs) are the preferred diagnostic tests for *Neisseria gonorrhoeae*, primarily due to superior sensitivity when compared with culture.[1,12] There are several NAATs that have FDA clearance for diagnostic testing of gonorrhea and chlamydia in genital samples, including endocervical and vaginal swab specimens from women, urethral specimens from men, and urine specimens from men and women.[10,12] As of May 23, 2019, the FDA has also cleared two NAATs for diagnostic testing of gonorrhea and chlamydia at extragenital sites (pharynx and rectum); the two tests are the Aptima Combo 2 Assay and the Xpert CT/NG.[13] In March 2021, the FDA cleared a point-of-care NAAT test that can detect *N. gonorrhoeae* and *C. trachomatis* using female vaginal swabs and male urine specimens.

- **Testing for Gonorrhea in Women:** The recommended sample type for detecting *N. gonorrhoeae* urogenital infections in women is a self- or clinician-collected vaginal swab, which has a greater than 95% sensitivity and specificity.[12,14] Self-collected vaginal swab specimens perform as well as clinician-collected samples for other approved specimens using NAATs.[12,14,15,16] Instructions should be provided to women performing self-collection vaginal swabs. In addition, a clinician-collected endocervical sample is also acceptable if a pelvic examination is indicated. Collecting a first-catch urine sample is also an option for screening in women, but this strategy detects approximately

10% fewer cases of *N. gonorrhoeae* infection compared with vaginal or endocervical swabs.[12] Use of Gram's stain is not recommended for making a diagnosis of gonorrhea on an endocervical or pharyngeal swab sample.[10] Routine screening of extragenital sites (rectum or pharynx) is not recommended for women at this time.[10]

- **Testing for Gonorrhea in Men:** For men, the recommended sample type for detecting *N. gonorrhoeae* urethral infection is a first-catch urine NAAT.[10,12] The sensitivity of NAAT is superior to culture.[10,12] Of note, a Gram's stain of a urethral specimen demonstrating the presence of leukocytes with intracellular gram-negative diplococci is highly specific for *N. gonorrhoeae* urethral infection, but should not be used to rule out *N. gonorrhoeae* infection due to lower sensitivity.[10] For men who have receptive anal or oral intercourse, self-collected or provider-collected swabs of the rectum and pharynx can be used for gonorrhea screening using NAAT testing. Specimen collection instructions should be provided to persons obtaining self-collected rectal or pharyngeal samples.[17] Performing Gram's stain is not recommended for pharyngeal or rectal specimens.

Treatment

The following summarizes recommendations in the 2021 STI Treatment Guidelines for the treatment of individuals with gonococcal infections; the treatment is the same for persons with or without HIV.[10]

- **Treatment of Uncomplicated Gonococcal Infection of Cervix, Urethra, or Rectum:** For uncomplicated gonococcal infections of the cervix, urethra, or rectum, the recommended regimen is ceftriaxone 500 mg given as a single intramuscular dose, with or without doxycycline 100 mg orally twice daily for 7 days, depending on whether chlamydia infection has been ruled out. For persons who weigh 150 kg or more, the ceftriaxone dose is 1 g as a single intramuscular dose. If ceftriaxone is not available, the two options are (1) gentamicin 240 mg given as a single intramuscular injection plus oral azithromycin 2 g or (2) cefixime 800 mg orally in a single dose. If chlamydia has not been ruled out, then doxycycline 100 mg orally twice daily for 7 days should be added to these alternative options. If Chlamydia treatment is needed and the patient is a pregnant woman, azithromycin 1 g orally as a single oral dose is recommended instead of doxycycline, due to concerns that tetracyclines may negatively affect fetal tooth and bone development.

2021 STI Treatment Guidelines: Gonococcal Infections

Table 2. Treatment of Uncomplicated Gonococcal Infection of the Cervix, Urethra, or Rectum

Recommended **Regimen if Chlamydial Infection Excluded**

Ceftriaxone

Ceftriaxone

Tradename:Rocephin

500 mg* IM in a single dose for persons weighing <150 kg

Note: *For persons weighing ≥150 kg, ceftriaxone 1 g IM should be administered.

Recommended **Regimen if Chlamydial Infection Has Not Been Excluded**

Ceftriaxone

Ceftriaxone

Tradename:Rocephin

500 mg* IM in a single dose for persons weighing <150 kg

Doxycycline

Doxycycline

Tradename:Doryx, Vibramycin

100 mg orally twice daily for 7 days+

During pregnancy, oral azithromycin 1 gram in a single dose is recommended to treat chlamydia.

Note: *For persons weighing ≥ 150 kg, ceftriaxone 1 g IM should be administered.

Alternative **Regimen if Ceftriaxone is Not Available**

Gentamicin

Gentamicin

Tradename:Garamycin

240 mg IM in a single dose

Azithromycin

Azithromycin

Tradename:Zithromax

2 g orally in a single dose+

Alternative **Regimen if Ceftriaxone is Not Available**

Cefixime

Cefixime

Tradename: Suprax

800 mg orally in a single dose

Note: If treating with cefixime, and chlamydial infection has not been excluded, providers should treat for chlamydia with doxycycline 100 mg orally twice daily for 7 days. During pregnancy, oral azithromycin 1 g in a single dose is recommended to treat chlamydia.

Source: Workowski KA, Bachmann LH, Chan PA, et al. Sexually transmitted infections treatment guidelines, 2021. Gonococcal infections. MMWR Recomm Rep. 2021;70(No. RR-4):1-187. [[2021 STI Treatment Guidelines](#)]

Courtesy of [National STD Curriculum](#).

- **Treatment of Uncomplicated Gonococcal Infection of the Pharynx:** For uncomplicated gonococcal infections of the pharynx, the same treatment regimen is recommended as for treatment for infection of the cervix, urethra, or rectum, except that alternative regimens are not an option and a test-of-cure (using either culture or NAAT) should be performed 7 to 14 days after treatment, regardless of the treatment regimen; the rationale for this recommendation is that *N. gonorrhoeae* is more difficult to eradicate in the oropharynx than at urogenital sites. Note that test-of-cure can be performed with NAAT or culture, but false-positive rates are significant at day 7 with NAAT due to residual bacterial DNA fragments. Thus, a positive NAAT test-of-cure should ideally be followed by culture to confirm active gonococcal infection prior to retreatment.

2021 STI Treatment Guidelines: Gonococcal Infections

Table 3. Treatment of Uncomplicated Gonococcal Infection of the Pharynx

Recommended **Regimen**

Ceftriaxone

Ceftriaxone

Tradename:Rocephin

500 mg* IM in a single dose for persons weighing <150 kg

If chlamydial infection is identified when pharyngeal gonorrhea testing is performed, treat with doxycycline 100 mg orally 2 times a day for 7 days; pregnant women should receive azithromycin 1 g orally in a single dose (instead of doxycycline).

Note: *For persons weighing ≥ 150 kg, ceftriaxone 1 g IM should be administered.

No reliable alternative treatments are available for pharyngeal gonorrhea. For persons with a history of a beta-lactam allergy, a thorough assessment of the reaction is recommended. For persons with an anaphylactic or other severe reaction (e.g., Stevens Johnson syndrome) to ceftriaxone, consult an infectious disease specialist for an alternative treatment recommendation.

Source: Workowski KA, Bachmann LH, Chan PA, et al. Sexually transmitted infections treatment guidelines, 2021. Gonococcal infections. MMWR Recomm Rep. 2021;70(No. RR-4):1-187. [[2021 STI Treatment Guidelines](#)]

Courtesy of [National STD Curriculum](#).

- **Persons with Penicillin Allergy:** The management of persons with penicillin allergy is complicated since fewer than 10% of persons who self-report a penicillin allergy have a positive skin test with penicillin allergy testing. In addition, fewer than 1.0% of persons with penicillin allergy will have an allergic reaction to a third-generation cephalosporin, such as ceftriaxone or cefixime. Thus, most persons with a penicillin allergy can receive ceftriaxone therapy for the treatment of gonorrhea. For individuals with a history of a severe penicillin allergy, the best option is dual therapy with gentamicin 240 mg as a single intramuscular dose plus azithromycin 2 g orally as a single dose, but note that a large randomized clinical trial demonstrated gentamicin is significantly less effective than ceftriaxone plus azithromycin for curing rectal and pharyngeal gonococcal infections.[18]
- **Resumption of Sexual Activity:** Persons diagnosed with gonorrhea should refrain from sexual intercourse for at least 7 days after receiving treatment. In addition, they should not resume sexual activity until all symptoms related to the gonococcal infection have resolved and their sex partners have received treatment for gonorrhea.
- **Management of Sex Partners:** All recent sex partners of persons diagnosed with gonorrhea should be referred for evaluation, testing, and presumptive treatment for gonorrhea; if the person diagnosed with gonorrhea did not have chlamydia excluded, then the sex partner should also receive treatment for chlamydia. In this context, “recent” is defined as sexual contact within the 60 days preceding onset of symptoms or gonorrhea diagnosis. If there were no sexual contacts in the prior 60 days, then the most recent sex partner should receive evaluation and treatment.
- **Follow-Up Testing:** Retesting in 3 months is indicated for all persons diagnosed with gonorrhea because of high reinfection rates. Routine test-of-cure is not recommended for persons diagnosed with gonorrhea from the cervix, urethra, or rectum. All persons diagnosed with pharyngeal gonorrhea should have a routine test-of-cure 7 to 14 days after completing treatment, regardless of the treatment regimen. If NAAT is used for follow-up test-of-cure, there are significant false-positive results on day 7 due to residual bacterial DNA fragments; the rate of these false-positive tests is lower if the NAAT is performed on posttreatment days 10 to 14.

Chlamydial Infections

Introduction

Chlamydia trachomatis, an intracellular bacteria, is the most commonly reported STI in the United States, with 1,644,416 reported cases in 2021.[6] Among the reported cases, based on sex assigned at birth, 64% were females; the highest rates are in females under the age of 25 years, particularly females 20 to 24 years of age (Figure 2).[6] Asymptomatic chlamydia is common among both women and men, and coinfection with *C. trachomatis* often occurs in persons diagnosed with gonococcal infection, especially among men who have sex with men.[19]

Clinical Manifestations

Although often asymptomatic, infection with *C. trachomatis* can cause a wide range of clinical manifestations, including cervicitis, urethritis, epididymitis, proctitis, prostatitis, pelvic inflammatory disease, and neonatal infection.[20] *Chlamydia trachomatis* is the most common cause of nongonococcal urethritis and cervicitis. Chlamydia infections can cause serious complications, especially in women, including pelvic inflammatory disease, ectopic pregnancy, and infertility.

Screening Recommendations

Screening asymptomatic women for chlamydia has been proven to lower both overall chlamydial infection rates and the rate of pelvic inflammatory disease.[20] Available data also suggest that persons with HIV who have inflammatory STIs have an increased risk of transmitting HIV, primarily through increased shedding of HIV in the genital tract,[8,9] so routine screening for chlamydia may indirectly reduce the risk of HIV transmission to sex partners. Screening samples for chlamydia should be obtained from all anatomical sites of exposure during sexual activity. The following summarizes recommendations for chlamydia screening in people with HIV.[20]

- Screen all sexually active individuals for urogenital chlamydia at baseline and at least annually thereafter, depending on the presence of ongoing risk factors and the prevalence of STIs in the community.
- Screen all men who have sex with men for chlamydia on entry to care and then every 3 to 6 months if they are sexually active. More frequent screening may be indicated based on the presence of ongoing risk of acquiring STIs and the prevalence and incidence of STIs in the community.
- Routine screening for oropharyngeal chlamydia is not currently recommended, as the clinical significance and transmission risk of chlamydia detected in the oropharynx is not well understood. However, since most commercially available nucleic acid amplification tests (NAATs) are a combination assay that will detect both *N. gonorrhoeae* and *C. trachomatis* from a single specimen, the test results may automatically report the presence of *C. trachomatis*, even if chlamydia oropharyngeal testing was not ordered.
- Routine screening for extragenital chlamydia is not currently recommended in asymptomatic women. Based on shared clinical decision-making between women with HIV and their providers, rectal chlamydia infection screening can be performed in women who have receptive anal intercourse.
- All pregnant women who are younger than 25 years of age should undergo screening for chlamydia infection at the first prenatal visit and again during the third trimester—in order to prevent fetal complications due to chlamydia. These screening recommendations also apply to pregnant women older than 25 years of age who are at increased risk of acquiring chlamydia, including women with new or multiple sex partners, a sex partner who concurrently has other sex partners, or a sex partner who has an STI.

Laboratory Diagnosis

Nucleic acid amplification tests (NAATs)

Nucleic acid amplification tests are the preferred method of testing for *C. trachomatis* due to improved sensitivity and specificity compared to culture.^[20] There are multiple NAATs that have FDA clearance for diagnostic testing of chlamydia and gonorrhea in genital samples, including with endocervical swabs, vaginal swabs, urethral swabs, and urine.^[12] As of May 23, 2019, the FDA has also cleared two NAATs for diagnostic testing of chlamydia and gonorrhea at extragenital sites (pharynx and rectum; the two tests are the Aptima Combo 2 Assay and the Xpert CT/NG).^[13] In March 2021, the FDA cleared a point-of-care NAAT test that can detect *N. gonorrhoeae* and *C. trachomatis* using female vaginal swabs and male urine specimens. The samples can be self-collected or clinician-collected: studies conducted in women and men have shown that patient-collected swabs have similar specificity and sensitivity when compared to clinician-collected specimens and are highly acceptable to the patient.^[17,21,22,23,24,25] Further, providing access to self-testing for extragenital infections has been shown to increase screening rates and be highly acceptable to patients.^[17,21,22,26]

- **Testing for Chlamydia in Women:** The optimal NAAT specimen types for detecting *C. trachomatis* urogenital infections in women are vaginal swabs. Alternatively, endocervical or first-catch urine samples perform well as screening tests in women, though up to 10% fewer *C. trachomatis* infections may be detected using a urine sample compared with vaginal or endocervical swabs.^[12,27] For women with a history of receptive anal intercourse, if the decision is made to do a NAAT test to detect rectal chlamydia infection, a rectal specimen should be collected.
- **Testing for Chlamydia in Men:** In men, the recommended sample type for detecting urogenital *C. trachomatis* infection with a NAAT is a first-catch urine specimen.^[12] When screening for chlamydia or gonococcal infections at other sites of exposure, such as the rectum and oropharynx, NAATs are more sensitive and specific than culture.^[12]

Treatment

The following summarizes recommendations in the 2021 STI Treatment Guidelines for the treatment of individuals with urogenital chlamydial infections; the treatment is the same for persons with or without HIV.^[20] Persons with HIV should receive the same treatment for urogenital chlamydia as those without HIV.^[20]

- **Uncomplicated Urogenital Chlamydial Infections:** The recommended treatment for uncomplicated genitourinary or rectal chlamydia in nonpregnant adults is doxycycline 100 mg orally twice a day for 7 days. Alternative, less preferable regimens include azithromycin 1 gram orally as a single dose or levofloxacin 500 mg orally once daily for 7 days. The recommendation to have doxycycline as the preferred treatment for chlamydia is based on two randomized, double-blind clinical trials that showed a 7-day course of doxycycline was superior to single-dose azithromycin for the treatment of asymptomatic rectal chlamydial infections among men who have sex with men.^[28,29] Studies performed in the general population have shown similar efficacy with azithromycin and doxycycline for urogenital chlamydia infections.^[29,30]

2021 STI Treatment Guidelines: Chlamydial Infections

Table 4. Treatment of Chlamydial Infections Among Adolescents and Adults

Recommended Regimen

Doxycycline

Doxycycline

Tradename:Doryx, Vibramycin

100 mg orally twice a day for 7 days

Alternative **Regimens**

Azithromycin

Azithromycin

Tradename:Zithromax

1 g orally in a single dose

Alternative **Regimens**

Levofloxacin

Levofloxacin

Tradename:Levaquin

500 mg orally once daily for 7 days

Note: Doxycycline is also available in a more costly delayed-release 200-mg tablet formulation, which requires once-daily dosing for 7 days and is equally effective as doxycycline 100 mg twice daily for 7 days for treating urogenital chlamydial infection in men and women.

Source: Workowski KA, Bachmann LH, Chan PA, et al. Sexually transmitted infections treatment guidelines, 2021. Chlamydial infections. MMWR Recomm Rep. 2021;70(No. RR-4):1-187. [[2021 STI Treatment Guidelines](#)]

Courtesy of [National STD Curriculum](#).

- **Chlamydial Infection During Pregnancy:** Azithromycin 1 g orally in a single dose is the preferred treatment during pregnancy; the alternative regimen in pregnancy is amoxicillin 500 mg orally three times daily for 7 days. Doxycycline is not recommended for the treatment of chlamydial infection during pregnancy due to its negative effects on fetal tooth and bone development.
- **Resumption of Sexual Activity:** Persons diagnosed with chlamydia should refrain from sexual intercourse for at least 7 days after receiving a single-dose regimen or after completion of a 7-day regimen. In addition, they should not resume sexual activity until all symptoms related to chlamydia have resolved and their sex partners have received treatment for chlamydia.
- **Management of Sex Partners:** All recent sex partners of persons diagnosed with chlamydia should be contacted and referred for evaluation, testing, and presumptive treatment of chlamydia. In this context, “recent” is defined as sex contact within the 60 days preceding onset of symptoms or chlamydia diagnosis. If no sexual contact has occurred in the 60 days before the diagnosis of chlamydia or onset of symptoms, then the most recent sex partner prior to that 60-day period should be evaluated and presumptively treated for chlamydial infection.
- **Follow-Up:** Routine test-of-cure after completing therapy for chlamydia is not recommended in nonpregnant individuals, but all persons diagnosed with chlamydia should return for repeat testing in approximately 3 months due to the substantial risk of reinfection during the period following initial diagnosis and treatment of chlamydia. All women treated for chlamydial infection during pregnancy should have a test-of-cure performed 4 weeks after completing therapy, as well as repeat testing 3 months after treatment to test for reinfection.
- **Oropharyngeal Chlamydia Infections:** Although routine screening for oropharyngeal chlamydial infection is not recommended, the detection of *C. trachomatis* may be reported when using a NAAT to screen for *N. gonorrhoeae* in the oropharynx. Since available evidence suggests oropharyngeal *C. trachomatis* can be sexually transmitted to genital sites of sex partners, detection of *C. trachomatis* detected from an oropharyngeal specimen warrants treatment with doxycycline in nonpregnant adults and azithromycin in pregnant women.[[20](#),[31](#),[32](#),[33](#)]

Lymphogranuloma Venereum

Introduction

Lymphogranuloma venereum (LGV) is a chronic infection caused by *C. trachomatis* serovars L1, L2, or L3. These serovars are considered more virulent and invasive compared with other *C. trachomatis* serovars. Although LGV was previously uncommon outside tropical regions, recent data suggest rising rates of LGV in the United States and Europe, particularly among men who have sex with men (MSM), many of whom are people with HIV.[[34,35,36,37](#)]

Clinical Manifestations

The classic description of LGV consists of unilateral tender inguinal or femoral lymphadenopathy, typically following a transient, self-limited genital ulcer or papule at the site of inoculation that often goes unnoticed. In the United States, recent outbreaks and sporadic cases of LGV among men who have sex with men (with high rates of HIV) have predominantly manifested as proctocolitis, with clinical findings that include anal ulcers, anal pain or pruritus, mucoid or hemorrhagic rectal discharge, tenesmus, and fever.[[38,39](#)] This LGV-related proctocolitis can be confused with inflammatory bowel disease or other ulcerative STIs such as genital herpes or mpox. If not treated early, LGV proctocolitis can progress to chronic colorectal fistulas and strictures.[[37,38](#)]

Laboratory Diagnosis

In general, the diagnosis of LGV is made based on clinical suspicion, local epidemiologic data, and a positive NAAT for *C. trachomatis*. With suspected LGV, it is important to exclude other etiologies for proctocolitis, inguinal adenopathy, or genital or rectal ulcers. When LGV is clinically suspected, relevant clinical samples should be sent for *C. trachomatis* NAAT.[[12,13](#)] Note that commercially available NAATs do not distinguish which *C. trachomatis* LGV serovars from non-LGV serovars. Real-time quadriplex PCR-based assay tests have been developed that can distinguish LGV from non-LGV *C. trachomatis*, but these tests are not widely available, and results do not return within a time frame to impact clinical management.[[38,39,40](#)]

Treatment

Presumptive treatment for LGV should be provided prior to the return of lab testing in persons presenting with a clinical syndrome suggestive of LGV, especially in persons who have a compatible clinical syndrome and a positive NAAT. The following summarizes the 2021 STI Treatment Guidelines recommendation for the treatment for LGV.[[39](#)]

- **Recommended Treatment of LGV in Persons with HIV:** The recommended treatment of LGV is the same in nonpregnant persons with and without HIV and consists of doxycycline 100 mg orally twice daily for 21 days. In persons with HIV, the treatment response may be delayed and longer courses of therapy may be necessary in some circumstances. For pregnant women, there are limited data, but most experts would recommend using oral azithromycin 1 gram once weekly for 3 weeks.

2021 STI Treatment Guidelines: Diseases Characterized by Genital, Anal, or Perianal Ulcers

Table 5. Lymphogranuloma Venereum

Recommended for Lymphogranuloma Venereum

Doxycycline

Doxycycline

Tradename:Doryx, Vibramycin

100 mg orally twice daily for 21 days

Alternative for Lymphogranuloma Venereum

Azithromycin

Azithromycin

Tradename:Zithromax

1 g orally once weekly for 3 weeks*

*Because this regimen has not been validated, a test-of-cure with *C. trachomatis* NAAT 4 weeks after completion of treatment can be considered.

Alternative for Lymphogranuloma Venereum

Erythromycin base

Erythromycin base

Tradename:Eryc

500 mg orally four times a day for 21 days

Source: Workowski KA, Bachmann LH, Chan PA, et al. Sexually transmitted infections treatment guidelines, 2021. Diseases characterized by genital, anal, or perianal ulcers: lymphogranuloma venereum (LGV). MMWR Recomm Rep. 2021;70(No. RR-4):1-187. [[2021 STI Treatment Guidelines](#)]

Courtesy of [National STD Curriculum](#).

- **Management of Sex Partners:** All recent (within 60 days) sex partners of persons diagnosed with LGV should be referred for evaluation, testing, and presumptive treatment of chlamydia.[39] If the sex partner does not have any signs or symptoms that suggest a diagnosis of LGV, then treatment consists of a standard chlamydia regimen (doxycycline 100 mg orally twice a day for 7 days for nonpregnant persons and azithromycin 1 g orally in a single dose for pregnant women). If the sex partner has signs or symptoms that suggest a diagnosis of LGV, they should receive the extended 3-week treatment course.
- **Follow-Up:** Routine test-of-cure after completing therapy for LGV is not recommended in nonpregnant individuals, but all persons diagnosed with chlamydia, including LGV, should return for repeat testing in approximately 3 months due to the substantial risk of reinfection during the period following initial diagnosis and treatment of chlamydia. All pregnant women treated for LGV should have a test-of-cure performed 4 weeks after the initial positive chlamydia NAAT test.[39]

Syphilis

Introduction

Syphilis is a systemic infection caused by the spirochete *Treponema pallidum*, referred to as “the great imitator” for its variable clinical manifestations. The natural history of untreated syphilis includes a wide range of complications and overlapping disease stages. Although the rate of syphilis cases declined in the United States in the 1990s, it has increased since 2001 ([Figure 3](#)).^[6] The increase in syphilis cases has been most pronounced in men, especially among men who have sex with men, but major increases have also occurred in women in recent years.^[6] In addition, there were 2,855 cases of congenital syphilis in the United States in 2021, which is a dramatic increase from the 362 cases in 2013.^[6] Coinfection with HIV is common in persons diagnosed with primary and secondary syphilis.^[6] Among cases of primary and secondary syphilis in the United States in 2021 for which information about HIV status was known, the percentage of HIV coinfection was 44.8% among men who have sex with men, 7.2% of men who have sex with women, and 4.1% of women.^[6] Syphilis is associated with an increased risk of sexual acquisition and transmission of HIV.^[6,41]

Clinical Manifestations and Stages of Syphilis

Individuals with HIV typically experience the same stages and physical manifestations of syphilis as persons without HIV, although the stages are more likely to overlap, and the symptoms may be more severe.

- **Primary Syphilis:** The manifestation of primary syphilis, if it occurs, is usually within 4 to 8 weeks after an exposure. The most common manifestation of primary syphilis is a firm, painless genital or oral ulcer, which is referred to as a chancre. Persons with HIV who develop primary syphilis may have larger, more numerous chancres that take longer to heal during primary syphilis.^[41] If primary syphilis goes untreated, 60 to 90% of persons will develop secondary syphilis (usually within 2 to 8 weeks).
- **Secondary Syphilis:** Secondary syphilis can occur following primary syphilis, but it can also develop in someone who does not have a clinically evident chancre. The manifestations of secondary syphilis often include a diffuse maculopapular rash on the trunk and extremities (which may involve the palms and soles); flat, mucoid wart-like plaques (condylomata lata) in the folds of the anus and genitals that are often mistaken for anogenital warts; patchy alopecia; and lymphadenopathy ([Figure 4](#)).^[41,42,43]
- **Latent Syphilis:** Asymptomatic persons who have a positive serologic test for syphilis without a history of prior syphilis or previous treatment are considered to have latent syphilis. Latent syphilis acquired within the preceding year is called early latent syphilis; all other cases of latent syphilis are either late latent syphilis or latent syphilis of unknown duration. The diagnosis of early latent syphilis may be made in persons who meet one of the following three criteria: (1) a documented seroconversion or a fourfold or greater increase in titer on a nontreponemal test within the past year, (2) a history of unequivocal symptoms of primary or secondary syphilis within the past year, or (3) a sexual encounter with a partner known to have primary, secondary, or early latent syphilis within the past year. Distinguishing early latent syphilis from late latent syphilis is important since they require different treatment regimens.
- **Tertiary Syphilis:** Tertiary syphilis develops in up to 25% of untreated syphilis and occurs between 1 and 30 years after the initial *T. pallidum* infection, with multiple possible manifestations, including cardiovascular, neurologic, and cutaneous disease.
- **Neurosyphilis, Ocular Syphilis, and Ootosyphilis:** The development of neurosyphilis, ocular syphilis, and otosyphilis can occur at any stage of *T. pallidum* infection. Persons with HIV and neurosyphilis can present with a myriad of manifestations, including headache, cranial nerve dysfunction, auditory and visual disturbances, altered mental status, stroke, visual deficits, and loss of vibration sense. The risk of developing neurosyphilis is increased in persons with HIV who have low CD4 counts and high HIV RNA levels.^[44,45,46] Persons with HIV are more likely to develop uveitis and meningitis compared to persons without HIV.^[41] Ocular syphilis and otosyphilis can develop

independently of neurosyphilis. People with ocular syphilis most often present with uveitis, but any portion of the eye can be involved; those with otosyphilis most often present with hearing loss.[43]

Screening Recommendations

All sexually active persons with HIV should be screened for syphilis upon initiation of HIV care and at least annually thereafter; more frequent screening is indicated for those with multiple partners, a history of condomless intercourse, a history of sex in conjunction with illicit drug use, or methamphetamine use.[11,12,43]

Laboratory Diagnosis

Two categories of serologic tests are required for the presumptive diagnosis of syphilis: (1) nontreponemal tests (e.g. Rapid Plasma Reagin [RPR] and Venereal Diseases Research Laboratory [VDRL]) and (2) treponemal tests (e.g. fluorescent treponemal antibody absorbed [FTA-ABS] tests, the *T. pallidum* particle agglutination [TP-PA] assay, various enzyme immunoassays [EIAs], and chemiluminescence assays). The use of one test is insufficient for the diagnosis of syphilis due to the limitations of each type of test, so an individual with a positive nontreponemal test should have confirmatory testing with a treponemal-specific test to confirm the diagnosis of syphilis, and vice versa. When serologic findings do not correlate with symptoms of early syphilis, other tests (e.g. darkfield microscopy, biopsy with silver staining, and PCR) should be considered.[43] Although the VDRL and RPR are equally valid assays, quantitative results from the two tests cannot be compared directly because RPR titers are frequently slightly higher than VDRL titers.

Traditional and Reverse Sequence Syphilis Testing Algorithms

Syphilis screening algorithms are typically characterized as either a traditional screening sequence or a reverse screening sequence (Figure 5).[43,47] The traditional syphilis screening algorithm has consisted of initial screening with a nontreponemal test followed by confirmatory testing of a positive screen with a treponemal test.[43,47,48] For economical and efficiency reasons, many clinical laboratories now use automated treponemal tests, such as EIAs or chemiluminescence Immunoassays, as the initial screening test for syphilis, with follow-up testing of positive tests using nontreponemal tests; this order in testing is often referred to as reverse sequence testing.[49] The treponemal tests will identify persons with untreated syphilis, as well as persons who were previously treated for syphilis (since treponemal tests tend to stay positive for life). Thus, if a person has a positive treponemal EIA test, a nontreponemal test (with a titer) should then be performed reflexively by the laboratory to guide management decisions. If the initial treponemal test is positive and the confirmatory nontreponemal test is negative (discordant results), a second and different treponemal test should be reflexively performed to help determine on a case-by-case basis whether this is a false-positive test result, early infection, or remote infection (treated or untreated).[49]

Evaluation for Neurosyphilis

Persons with syphilis who have new neurologic signs or symptoms should undergo lumbar puncture and cerebrospinal fluid (CSF) examination, regardless of syphilis stage or HIV status.[43] Common neurosyphilis manifestations include altered mental status, cranial nerve abnormalities, stroke, meningitis, or loss of vibratory sensation.[43] Persons with ocular syphilis or otosyphilis do not require CSF examination, unless they have concomitant neurologic symptoms or signs. No single laboratory test can be used to definitively diagnose neurosyphilis in all settings. For example, an elevated CSF white blood count or protein level supports a diagnosis of neurosyphilis, but analysis of CSF cell count is complicated in persons with HIV, as they may have mild mononuclear pleocytosis (and elevated protein levels) due to HIV alone.[43] Nontreponemal tests (RPR, VDRL) are highly specific for neurosyphilis whereas treponemal tests (FTA-ABS) of the CSF are highly sensitive. A positive CSF VDRL, in the absence of heavy contamination of the CSF with blood, strongly supports a diagnosis of neurosyphilis, whereas a negative CSF FTA-ABS makes the diagnosis of neurosyphilis highly unlikely. If neurosyphilis is suspected, but CSF VDRL is negative, obtaining a

treponemal test (FTA-ABS) of the CSF can be considered.[[43,50,51](#)]

Treatment

The following summarizes treatment of syphilis in persons with HIV based on the stage and type of syphilis diagnosed

2021 STI Treatment Guidelines: Syphilis

Table 6. Treatment of Syphilis Among Persons with HIV Infection

Recommended **Regimen for Treatment of Primary and Secondary Syphilis**

Benzathine penicillin G

Benzathine penicillin G

Tradename: Bicillin-LA

2.4 million units IM in a single dose

Note: Available data demonstrate that additional doses of benzathine penicillin G, amoxicillin, or other antibiotics in primary and secondary syphilis among persons with HIV infection do not result in enhanced efficacy.

Recommended **Regimen for Treatment of Early Latent Syphilis**

Benzathine penicillin G

Benzathine penicillin G

Tradename: Bicillin-LA

2.4 million units IM in a single dose

Recommended **Regimen for Treatment of Late Latent or Latent Syphilis of Unknown Duration**

Benzathine penicillin G

Benzathine penicillin G

Tradename: Bicillin-LA

7.2 million units total, administered as 3 doses of 2.4 million units IM each at 1-week intervals

Recommended **Regimen for Treatment of Neurosyphilis, Ocular Syphilis, and Otic Syphilis**

Aqueous crystalline penicillin G

Aqueous crystalline penicillin G

Tradename: Pfizerpen

18-24 million units per day, administered as 3-4 million units IV every 4 hours or continuous infusion, for 10-14 days

Note: The durations of the recommended and alternative regimens for neurosyphilis are shorter than the duration of the regimen used for latent syphilis. Therefore, benzathine penicillin, 2.4 million units IM once per week for up to 3 weeks, can be considered after completion of these neurosyphilis treatment regimens to provide a comparable total duration of therapy.

Alternative **Regimen for Treatment of Neurosyphilis, Ocular Syphilis, and Otic Syphilis**

Procaine penicillin G

Procaine penicillin G

Tradename:

2.4 million units IM once daily for 10-14 days

Probenecid

Probenecid

Tradename:

500 mg orally four times a day for 10–14 days+

If compliance with therapy can be ensured, this alternative regimen might be considered.

Note: The durations of the recommended and alternative regimens for neurosyphilis are shorter than the duration of the regimen used for latent syphilis. Therefore, benzathine penicillin G, 2.4 million units IM once per week for up to 3 weeks, can be considered after completion of these neurosyphilis treatment regimens to provide a comparable total duration of therapy.

Source: Workowski KA, Bachmann LH, Chan PA, et al. Sexually transmitted infections treatment guidelines, 2021. Syphilis. MMWR Recomm Rep. 2021;70(No. RR-4):1-187. [[2021 STI Treatment Guidelines](#)]

Courtesy of [National STD Curriculum](#).
.[43]

- **Early Syphilis (including primary, secondary, and early latent syphilis):** Treatment of early syphilis (primary, secondary, and early latent) requires a single intramuscular dose of benzathine penicillin G 2.4 million units.[43,52] Studies have demonstrated that enhancing therapy (e.g., adding additional doses of penicillin or other antibiotics) for early syphilis does not improve outcomes.[47] Doxycycline 100 mg orally twice daily for 14 days is considered an alternative for the treatment of early syphilis, but only for nonpregnant persons who have a penicillin allergy. In addition, doxycycline can be used for nonpregnant people if penicillin is not available due to shortages. Penicillin is the only known antimicrobial agent that has been shown to be effective in preventing maternal to fetal transmission of syphilis, so pregnant women with syphilis, including those with penicillin allergy, must undergo penicillin desensitization and receive treatment with penicillin.
- **Late Latent Syphilis or Syphilis of Unknown Duration:** The treatment of late latent syphilis (or latent syphilis of unknown duration) requires three injections of benzathine penicillin G 2.4 million units intramuscularly given at weekly intervals. Doxycycline 100 mg orally twice daily for 28 days is considered an alternative for the treatment of late latent syphilis, but only for nonpregnant individuals who have penicillin allergy (or if penicillin is not available due to shortages). Pregnant women with syphilis, including those who have a penicillin allergy, must undergo penicillin desensitization and receive treatment with penicillin.
- **Neurosyphilis, Ocular Syphilis, and Ootosyphilis:** The recommended treatment for neurosyphilis, ocular syphilis, and otosyphilis consists of aqueous crystalline penicillin G 18 to 24 million units per day (administered as 3 to 4 million units intravenously every 4 hours or via continuous infusion) for 10 to 14 days. An alternative treatment regimen for neurosyphilis is procaine penicillin 2.4 million units intramuscularly once daily plus probenecid 500 mg orally four times daily for 10- to 14 days. To provide a similar total duration of neurosyphilis treatment regimen as with late latent syphilis without neurologic involvement, some experts also give intramuscular benzathine penicillin G 2.4 million units once weekly for 1 to 3 weeks after completing the 10 to 14 day treatment regimen. Treatment of neurosyphilis, ocular syphilis, or otosyphilis with agents other than penicillin is not optimal, but limited data suggest ceftriaxone 1-2 g intravenously or intramuscularly daily for 10 to 14 days may be an option in some penicillin-allergic individuals, depending on their penicillin allergy. For pregnant women with neurosyphilis and a penicillin allergy, ceftriaxone should not be used; in such cases, penicillin desensitization is indicated.

PostTreatment Follow-Up

Persons with HIV who receive treatment for syphilis should have close follow-up to monitor signs, symptoms,

and serologic changes in nontreponemal titers (VDRL or RPR) that indicate possible treatment failure or reinfection. The serologic changes in nontreponemal titers are described as a quantitative fold increase or decrease, based on the comparison of baseline and follow-up nontreponemal titers.^[43] Most persons with syphilis will have reactive treponemal tests for the remainder of their lives, regardless of treatment or disease activity. Thus, treponemal tests should not be used to assess treatment response and usually are not helpful for future evaluation. The following summarizes recommendations for follow-up clinical and nontreponemal serologic monitoring after treatment of syphilis in people with HIV.^[43]

- **Recommended Monitoring:** After treatment for primary or secondary syphilis, repeat clinical and nontreponemal serologic testing at 3, 6, 9, 12, and 24 months should be performed. After treatment for latent syphilis (early or late) without neurologic involvement, follow-up nontreponemal testing should be performed at 6, 12, 18, and 24 months. Individuals taking antiretroviral therapy and who are treated for neurosyphilis, ocular syphilis, or otosyphilis do not need routine follow-up CSF examinations as part of their follow-up, as long as they continue to have good clinical and serologic responses after treatment. For persons not taking antiretroviral therapy (or those with poor clinical or serologic response), consideration should be given to include lumbar puncture and CSF examination as part of the follow-up; in this situation, the CSF is usually evaluated every 6 months until the CSF white blood cell count returns to normal. If the white blood cell count has not decreased in 6 months or abnormalities persist at 2 years, retreatment should be considered.
- **Adequate Serologic Response:** Individuals who achieve at least a 4-fold decline in nontreponemal titers within 24 months after treatment are considered to have achieved an adequate serologic response. This is sometimes referred to as serologic cure or serologic response.
- **Lack of Seroreversion:** In some instances, individuals achieve a 4-fold or greater decline in nontreponemal titers within 24 months after treatment, but they have persistently reactive nontreponemal titers; this situation is usually referred to as lack of seroreversion or serofast. There is no evidence that providing additional antibiotics changes outcomes in this situation. Therefore, in the absence of clinical manifestations that suggest treatment failure or new syphilis infection, additional antibiotic treatment of syphilis is not recommended in this setting.
- **Inadequate Serologic Response:** For individuals who fail to achieve at least a posttreatment 4-fold decline in nontreponemal titers within 24 months, the optimal management is unknown. The evaluation of these individuals should include, at a minimum, a neurologic examination and annual clinical follow-up that includes repeated syphilis serologic studies. Syphilis retreatment is recommended when follow-up cannot be ensured or if the person initially had a high titer (greater than 1:32) that did not decrease at least 4-fold in the 24-month posttreatment period; if no neurologic manifestations are present, then the recommended retreatment regimen should consist of weekly intramuscular injections of benzathine penicillin G 2.4 million units for 3 weeks. If neurologic manifestations are present, then evaluation with lumbar puncture and CSF is indicated, with treatment guided by the CSF results.
- **Probable Reinfection or Treatment Failure:** Reinfection or treatment failure is likely if any of the following occur: (1) syphilis-related signs or symptoms persist or recur, (2) the person experiences new signs or symptoms attributable to primary or secondary syphilis, or (3) repeated serologic testing shows a sustained 4-fold (or greater) increase in nontreponemal titer that persists for longer than 2 weeks. If reinfection or treatment failure is likely, evaluation for neurosyphilis with lumbar puncture and CSF evaluation is recommended if (1) new neurologic manifestations are present or (2) the individual has not had any recent sexual exposures (in the prior 6 months in persons treated for primary or secondary syphilis and the prior 12 months for persons treated for latent and other stages of syphilis). For persons who undergo lumbar puncture with CSF evaluation, the treatment is then guided based on the CSF results. In the setting where reinfection or treatment failure is likely, and neurosyphilis has been ruled out (clinically or with CSF results), then the retreatment regimen should be based on the syphilis stage at prior diagnosis. For example, a person previously diagnosed with primary or secondary syphilis should receive retreatment with one dose of intramuscular benzathine penicillin G 2.4 million units, whereas all others should receive retreatment with three doses of intramuscular benzathine penicillin G 2.4 million units given weekly for 3 weeks.

Chancroid

Introduction

Chancroid is a relatively common cause of sexually transmitted genital ulcer disease in parts of Africa and the Caribbean and is caused by a small gram-negative rod, *Haemophilus ducreyi*; the disease is endemic mostly in regions of the world with resource-poor health infrastructure and high HIV prevalence.[\[53\]](#) In the United States, chancroid rarely occurs, which creates challenges for recognition and diagnosis of this infection. In 2021, three cases of chancroid were reported in the United States.[\[6\]](#) Like other sexually transmitted genital ulcer diseases, chancroid may increase the risk of HIV transmission and acquisition.[\[53,54,55\]](#) Chancroid in persons with HIV requires close monitoring due to more severe manifestations, higher rates of treatment failure, and delayed healing times.

Clinical Manifestations

Individuals with chancroid often present with one or more painful genital ulcers with yellow or gray exudate, as well as tender inguinal lymph nodes that can progress to fluctuant buboes. In persons with HIV, extragenital involvement of the thighs, anus, abdomen, hands, breast, mouth, and feet can also occur.[\[53\]](#)

Laboratory Diagnosis

A definitive diagnosis of chancroid is made by culturing *H. ducreyi* on specialized culture media, which is neither widely available nor sensitive for detection of the infection.[\[55,56\]](#) In addition, there are no FDA-approved PCR tests available for *H. ducreyi* (though some laboratories have developed and validated their own PCR tests). A “probable” diagnosis of chancroid can be made in a person who has (1) one or more deep and painful genital ulcers, (2) tender suppurative inguinal lymphadenopathy, (3) negative testing for syphilis, and (4) negative testing for genital herpes.[\[55\]](#)

Treatment

Based on limited available data, persons with HIV should receive the same treatment for chancroid as those without HIV, but treatment failures and delayed healing of ulcers have been reported in individuals with HIV.[\[55\]](#) The following summarizes key recommendations for the treatment of chancroid.[\[55\]](#)

- **Treatment Options:** The recommended treatment options for chancroid include azithromycin 1 g orally in a single dose; ceftriaxone 250 mg intramuscularly in a single dose; ciprofloxacin 500 mg orally twice daily for 3 days; or erythromycin base 500 mg orally three times daily for 7 days

2021 STI Treatment Guidelines: Diseases Characterized by Genital, Anal, or Perianal Ulcers

Table 7. Chancroid

Recommended for Chancroid

Azithromycin

Azithromycin

Tradename: Zithromax

1g orally in a single dose

Recommended for Chancroid

Ceftriaxone

Ceftriaxone

Tradename: Rocephin

250 mg IM in a single dose

Recommended for Chancroid

Ciprofloxacin

Ciprofloxacin

Tradename: Cipro, Cipro XR

500 mg orally twice a day for 3 days

Recommended for Chancroid

Erythromycin base

Erythromycin base

Tradename: Eryc

500 mg orally three times a day for 7 days

Azithromycin and ceftriaxone offer the advantage of single-dose therapy. Worldwide, several isolates with intermediate resistance to either ciprofloxacin or erythromycin have been reported. However, because cultures are not routinely performed, data are limited regarding the current prevalence of *Haemophilus ducreyi* antimicrobial resistance.

Source: Workowski KA, Bachmann LH, Chan PA, et al. Sexually transmitted infections treatment guidelines, 2021. Diseases characterized by genital, anal, or perianal ulcers: chancroid. MMWR Recomm Rep. 2021;70(No. RR-4):1-187. [[2021 STI Treatment Guidelines](#)]

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- **Evaluation of Treatment Response:** Persons diagnosed with chancroid should be reevaluated 3 to 7 days after initiating treatment to ensure clinical and symptomatic improvement. In the absence of evidence of any improvement by 3 to 7 days, alternative diagnoses and antimicrobial resistance should be considered. Persons with HIV should receive very close follow-up after treatment of chancroid, and they may require repeated or longer courses of therapy.
- **Management of Sex Partners:** All very recent sex partners of persons diagnosed with chancroid should be referred for evaluation, testing, and presumptive treatment of chancroid. In this context, “very recent” is defined as sexual contact within the 10 days preceding the onset of symptoms.

Genital Herpes

Introduction

Infections with herpes simplex virus (HSV) frequently occur in persons with HIV; approximately 60% of persons with HIV are seropositive for HSV-2 and more than 95% test seropositive for either HSV-1 or HSV-2.[57,58] Recurrent HSV is a chronic infection characterized by periodic reactivation, during which shedding from orolabial and genital mucosal surfaces is increased; shedding can occur even in asymptomatic individuals, and HSV shedding also persists despite highly active antiretroviral therapy among persons coinfecting with HSV and HIV.[59,60,61,62] Persons with HIV, when compared to persons without HIV, tend to have more severe and chronic HSV lesions and more asymptomatic shedding of HSV-2 in the genital tract.[60] Furthermore, HSV-2 reactivation, including asymptomatic shedding without clinically apparent lesions, has been shown to increase the rates of HIV transcription, resulting in increased HIV RNA levels in both plasma and genital tissues, but these changes are negligible in persons on potent antiretroviral therapy.[63,64,65]

Clinical Manifestations

Infection with HSV-1 most often manifests with lesions of the mouth and/or lips, whereas HSV-2 more commonly causes genital lesions. Nevertheless, HSV-1 and HSV-2 can cause lesions anywhere on the body and are indistinguishable from a clinical perspective. Regardless of the site, persons with genital HSV typically experience a sensory prodrome followed by evolution of the lesion(s) from papule to vesicle to crusting stage.[58] Ulcers caused by HSV tend to be painful, erythematous, and have “punched out” borders (Figure 6). Genital HSV lesions may be present on the penis, scrotum, perianal region, and gluteal cleft (Figure 7). If untreated, most persons have symptoms that persist for 5 to 10 days; anti-herpes therapy initiated at onset of the prodrome can shorten the symptomatic period or even abort the outbreak. Individuals with a CD4 count less than 100 cells/mm³ may have deep, extensive and non-healing ulcers, and are more likely to develop acyclovir-resistant HSV if they receive multiple courses of herpes treatment.[58,66,67] In addition, persons who have just started effective antiretroviral therapy may develop unusual ulcerative lesions as a manifestation of immune reconstitution syndrome.[60]

Laboratory Diagnosis

The diagnosis of HSV can be difficult on a clinical basis alone, and lesions can mimic other infections. The diagnosis of genital herpes, therefore, should be pursued through laboratory testing.[68] Herpes simplex virus testing with a NAAT, including DNA PCR, is the most sensitive method and preferred test for establishing the diagnosis;[68,69,70] viral culture and antigen detection are also an option, though less preferable.[71,72] When obtaining clinical samples, the base of the lesion should be scraped to ensure an adequate number of cells are obtained. Serologic testing is available using type-specific serologic tests that are based on antigens specific for HSV-1 (gG1) and HSV-2 (gG2); these tests can reliably distinguish antibodies to HSV-2 from antibodies to HSV-1.[68] Type-specific serologic testing, if performed, should utilize a two-step process with an initial screening test and a confirmatory second test (for samples positive on the initial test).[68]

Screening Recommendations

Serologic screening for HSV-1 and HSV-2 infection is not indicated for the general population, but based on the interactions between HIV and HSV-2 and the availability of effective suppressive anti-HSV-2 therapy, some experts recommend performing serologic testing for persons with HIV at baseline to identify prior herpes infection.[58,68,73]

Treatment

Therapy for Episodic Genital Herpes

Since persons with HIV often have more severe, prolonged cases of orolabial, genital, and perianal HSV infections compared to those without HIV, the recommended treatment for episodic genital herpes in persons with HIV is a 5-to 10-day course of acyclovir, valacyclovir, or famciclovir; intravenous acyclovir may rarely be required for severe mucocutaneous disease.[\[58,68\]](#)

2021 STI Treatment Guidelines: Genital Herpes
Table 8. Episodic Therapy for Recurrent Genital Herpes Among Persons with HIV*

Recommended **Regimens**

Acyclovir

Acyclovir

Tradename:Zovirax

400 mg orally three times a day for 5–10 days

Recommended **Regimens**

Famciclovir

Famciclovir

Tradename:Famvir

500 mg orally twice a day for 5–10 days

Recommended **Regimens**

Valacyclovir

Valacyclovir

Tradename:Valtrex

1 g orally twice a day for 5–10 days

*For severe HSV disease, initiating therapy with acyclovir 5–10 mg/kg IV every 8 hours might be necessary.

Source: Workowski KA, Bachmann LH, Chan PA, et al. Sexually transmitted infections treatment guidelines, 2021. Diseases characterized by genital, anal, or perianal ulcers: genital herpes. MMWR Recomm Rep. 2021;70(No. RR-4):1-187. [[2021 STI Treatment Guidelines](#)]

Courtesy of [National STD Curriculum](#).

Suppressive Therapy for HSV

For persons with HIV who have severe recurrent HSV outbreaks or who want to decrease the frequency of outbreaks, chronic suppressive therapy with valacyclovir, famciclovir, or acyclovir can be effective. Decisions regarding the use of suppressive therapy should be made without regard to the individual's CD4 cell count or changes in CD4 cell count. The recommended daily suppressive therapies for persons with HIV include acyclovir, valacyclovir, and famciclovir.[[68](#)] Numerous studies have shown that suppressive therapy of HSV-2 reduces HIV-1 levels in both the plasma and genital tract.[[60,74,75](#)] In a study conducted in Africa that enrolled HIV-1-serodiscordant couples, investigators examined the impact of acyclovir suppressive therapy on HIV transmission for partners who were HSV-2 and HIV-1 positive but not taking antiretroviral therapy at the time of enrollment.[[76](#)] Although acyclovir decreased the HIV-1 plasma RNA levels, it did not reduce the risk of HIV transmission.[[76](#)] Daily suppressive valacyclovir has been shown to reduce HSV-2 transmission in studies involving heterosexual HSV-serodifferent couples who are not infected with HIV,[[77](#)] but similar findings were not observed when using twice-daily acyclovir suppressive therapy in persons with HIV.[[78](#)]

Acyclovir-Resistant HSV

Reports have documented rates of resistance to acyclovir in up to 5% of persons with HIV and HSV coinfection,[[66](#)] but in recent years, resistance rates have declined. Acyclovir resistance is associated with advanced immunosuppression and frequent use of anti-HSV drugs; repeated episodic therapy poses a greater risk than suppressive therapy. Immunosuppressed individuals with HIV and herpes infection may develop slowly expanding, large ulcerated lesions ([Figure 8](#)).[[79,80,81](#)] Clinicians should suspect acyclovir resistance when there is no clinical improvement after 7 to 10 days of appropriate HSV treatment. In this situation, a sample from the lesion should be sent for viral culture, with drug susceptibility testing if HSV is isolated. The most common mechanism of acyclovir resistance is absent or decreased production by HSV of the enzyme thymidine kinase (TK- and TK-partial mutants), an enzyme required for the initial step in the triphosphorylation of acyclovir.[[81](#)] The preferred treatment for acyclovir-resistant HSV is intravenous foscarnet, but this medication can cause significant adverse effects, including renal and electrolyte abnormalities.[[58,79,82](#)] Alternative therapies include topical ophthalmic trifluridine, topical or intravenous cidofovir, and topical imiquimod 5% cream; the topical therapies typically require 21 to 28 days before an adequate response occurs.[[58](#)] ([Table 10](#))

Human Papillomavirus and Anogenital Warts

Introduction

Anogenital warts, also called condyloma acuminata, are the most common viral STD and are caused by various strains of human papillomavirus (HPV), which is a small double-stranded DNA virus that can be categorized into cutaneous and mucosal groups. Most sexually active adults will acquire HPV infection at some point in their lives, and in most cases, the virus is cleared spontaneously. More than 100 types of HPV have been identified, and a subset (e.g., HPV 16 and 18) has oncogenic potential. Nononcogenic subtypes 6 and 11 cause most genital warts. Men and women with HIV have increased prevalence, greater severity, and persistence of HPV infection.[83,84] In addition, among individuals with HIV, anogenital warts may also be more recalcitrant to therapy due to deficient cell-mediated immunity, particularly in those with advanced immunosuppression.[85,86] Although effective antiretroviral therapy has not been proven to reduce the risk of developing anogenital warts, higher CD4 counts and lower HIV RNA levels seem to independently reduce the risk of developing clinically evident warts.[87] Among men with HIV who have sex with men, younger age and lower HIV RNA have been associated with higher rates of HPV clearance.[88]

Clinical Manifestations

Typical condyloma acuminata are flesh-colored and can range from smooth, flattened lesions to verrucous papules (Figure 9).[86] Most persons with HIV are asymptomatic when initial lesions develop, but some with extensive or multiple lesions may complain of pain, burning, or pruritus. Anogenital warts can appear at multiple sites along the anogenital tract, particularly around the introitus in women, beneath the foreskin of the uncircumcised penis, and on the shaft of the penis in circumcised men.

Screening Recommendations

Use of HPV testing, which detects viral nucleic acid (DNA or RNA) or capsid protein, is recommended as an adjuvant to Pap smears for cervical cancer screening in women aged 30 and older, regardless of HIV status, but should not be used for cervical cancer screening in women younger than age 30, in men, or in individuals with genital warts (or their partners).[85,86] For women younger than age 30 or men who have sex with men (any age), HPV testing is not recommended due to the relatively high prevalence of HPV infection in these populations.[85,86,89] For a full discussion of cervical cancer screening in women and anal cancer screening in men, refer to the [Cancer Screening Section](#) in the topic review on Primary Care Management.

Laboratory Diagnosis

The diagnosis of condyloma acuminata is typically made by visual inspection and can be confirmed by biopsy.[86] For lesions that are large, atypical, or refractory to therapy, biopsy with histologic examination is recommended. Persons with external (anal mucosal) warts often have internal warts on the rectal mucosa and thus should have a digital examination or anoscopy. Persons with anal warts should also have a screening test for syphilis because condylomata lata, a manifestation of secondary syphilis, can mimic genital warts caused by HPV. For diagnosing genital warts, the routine use of HPV DNA testing or clinical application of 3 to 5% acetic acid onto affected areas is not recommended.[90]

Treatment

The goals of treating warts are amelioration of symptoms (including cosmetic concerns) and removal of the warts; it is unclear whether wart removal reduces future transmission of HPV to sex partners, and there is no evidence that the presence of genital warts (or their treatment) has any effect on cervical cancer risk in women.[90] Compared to persons without HIV, those with HIV have more treatment-refractory warts and may experience more frequent recurrences.[86] Unfortunately, antiretroviral therapy does not appear to reduce the incidence or prevalence of genital warts, and HPV-related genital and oral disease may persist for years

through mechanisms of immune reconstitution; oral HPV warts may actually increase after introduction of antiretroviral therapy.[\[91,92\]](#) Treatment options can be categorized into patient-applied or provider-applied modalities, and they include chemical or physical destruction, immunologic therapy, and surgical therapy; the recommendations for treatment of anogenital warts are the same for persons with or without HIV.[\[90\]](#)

- Patient-applied options include imiquimod 3.75% cream, imiquimod 5% cream, podofilox 0.5% solution or gel, or sinecatechins 15% ointment.
- Provider-administered treatment options include cryotherapy with liquid nitrogen or cryoprobe, surgical removal, or trichloroacetic acid or bichloroacetic acid 80 to 90% solution.
- Regardless of the treatment method, recurrence rates are high, especially in the first three months after treatment.
- Treatment of internal anogenital warts (meatus, urethral, vaginal, and cervical) is more complicated than external warts and ideally should consist of management by or consultation with a specialist or medical provider who has experience with treating internal anogenital warts.[\[90\]](#)

2021 STI Treatment Guidelines: Anogenital Warts
Table 11. Treatment of Internal Anogenital Warts

Internal anogenital warts include urethral meatus, vaginal, cervical, or intra-anal warts. Management of cervical warts or intra-anal warts should include consultation with a specialist.

Recommended **for Urethral Meatus Warts**

Cryotherapy with liquid nitrogen

Cryotherapy with liquid nitrogen

Tradename:

Health care providers must be trained on the proper use of cryotherapy because over- and under-treatment can result in complications or low efficacy.

Recommended **for Urethral Meatus Warts**

Surgical removal

Surgical removal

Tradename:

Recommended **for Vaginal Warts**

Cryotherapy with liquid nitrogen

Cryotherapy with liquid nitrogen

Tradename:

Note: The use of a cryoprobe in the vagina is NOT recommended because of the risk for vaginal perforation and fistula formation.

Recommended **for Vaginal Warts**

Surgical removal

Surgical removal

Tradename:

Recommended **for Vaginal Warts**

Trichloroacetic acid (TCA) or Bichloroacetic acid (BCA) 80-90% solution

Trichloroacetic acid (TCA) or Bichloroacetic acid (BCA) 80-90% solution

Tradename:

A small amount should be applied only to the warts

Recommended **for Cervical Warts**

Cryotherapy with liquid nitrogen

Cryotherapy with liquid nitrogen

Tradename:

Management of cervical warts should include consultation with a specialist. For women who have exophytic cervical warts, a biopsy evaluation to exclude high-grade SIL must be performed before treatment is initiated.

Recommended **for Cervical Warts**

Surgical removal

Surgical removal

Tradename:

Management of cervical warts should include consultation with a specialist. For women who have exophytic cervical warts, a biopsy evaluation to exclude high-grade SIL must be performed before treatment is initiated.

Recommended **for Cervical Warts**

Trichloroacetic acid (TCA) or Bichloroacetic acid (BCA) 80-90% solution

Trichloroacetic acid (TCA) or Bichloroacetic acid (BCA) 80-90% solution

Tradename:

A small amount should be applied only to the warts.

Management of cervical warts should include consultation with a specialist. For women who have exophytic cervical warts, a biopsy evaluation to exclude high-grade SIL must be performed before treatment is initiated.

Recommended **for Intra-anal Warts**

Cryotherapy with liquid nitrogen

Cryotherapy with liquid nitrogen

Tradename:

Management of intra-anal warts should include consultation with a specialist. Health care providers must be trained on the proper use of cryotherapy because over- and under-treatment can result in complications or low efficacy.

Recommended **for Intra-anal Warts**

Surgical removal

Surgical removal

Tradename:

Management of intra-anal warts should include consultation with a specialist.

Recommended **for Intra-anal Warts**

Trichloroacetic acid (TCA) or Bichloroacetic acid (BCA) 80-90% solution

Trichloroacetic acid (TCA) or Bichloroacetic acid (BCA) 80-90% solution

Tradename:

A small amount should be applied only to the warts.

Management of intra-anal warts should include consultation with a specialist.

Source: Workowski KA, Bachmann LH, Chan PA, et al. Sexually transmitted infections treatment guidelines, 2021. Human papillomavirus (HPV) infection: anogenital warts. MMWR Recomm Rep. 2021;70(No. RR-4):1-187. [[2021 STI Treatment Guidelines](#)]

Courtesy of [National STD Curriculum](#).

Prevention

In the United States, the 9-valent human papillomavirus (9vHPV) vaccine is the only HPV vaccine that is currently manufactured. The 9vHPV vaccine is FDA-approved for females and males 9 through 45 years of age.[[93](#)] The 9-valent HPV vaccine includes seven HPV types protective against cancer (HPV types 16, 18, 31, 33, 45, 52, and 58) and two that protect against HPV-associated warts (HPV types 6 and 11).[[94](#)] For persons with HIV, the 9vHPV is recommended for all males and females aged 13 through 26; the 3-dose vaccine schedule should be used for all persons with HIV, regardless of age.[[86,94,95](#)] The HPV vaccine is not recommended for persons with HIV who are 27 to 45 years of age or older, but it can be considered with a shared clinical decision-making approach in certain situations where HPV vaccination might be of benefit, such as in persons with minimal prior HPV exposure.[[86,96](#)] For additional details on recommendations for the use of the HPV vaccine in persons with HIV, see the [Human Papillomavirus Vaccine](#) section in the topic review on Immunizations in Module 2.

Trichomoniasis

Introduction

Trichomoniasis is the most common nonviral STI worldwide and is caused by the protozoan pathogen *Trichomonas vaginalis*. In the United States, the prevalence of *T. vaginalis* infection among women with HIV is high, with estimates of up to 53%.[\[97\]](#) The epidemiology of *T. vaginalis* among men with HIV is less well characterized, in part because guidelines do not recommend routine screening for *T. vaginalis* in men.[\[48,98,99\]](#) Infection with *T. vaginalis* has been shown to increase HIV transmission risk among both men and women with HIV,[\[48,100\]](#) as well as to increase the risk of HIV acquisition among women.[\[101\]](#)

Clinical Manifestations

Trichomoniasis is usually asymptomatic or minimally symptomatic in most women and men. Women with symptomatic trichomonas typically present with diffuse, malodorous, yellow-green discharge and associated vulvar irritation, whereas men may present with symptoms of urethritis.[\[97,102,103\]](#) Trichomoniasis may increase the risk of pelvic inflammatory disease in women with HIV.

Screening Recommendations

Women with HIV should be screened for trichomoniasis at entry to care and at least annually thereafter.[\[97,104\]](#) Currently, there are no guidelines that recommend screening men for infection with *T. vaginalis*.

Laboratory Diagnosis

Multiple sensitive and specific NAAT assays for the detection of *T. vaginalis* are commercially available and FDA-cleared for use in women, including testing on vaginal, endocervical, or urine specimens. If NAAT is unavailable, the diagnosis in women can be made by microscopy of vaginal secretions (wet mount) or by culture, but the sensitivity is much lower with these methods than with NAAT.[\[105\]](#) For men, NAAT for *T. vaginalis* can be used for urethral swabs and urine samples (as long as validated per Clinical Laboratory Improvement Amendments [CLIA] regulations), but one study showed much higher sensitivity with urethral (penile-meatal) swabs.[\[106\]](#) Use of a wet mount is not a sensitive test for detecting *T. vaginalis* in men and should not be used; the optimal site and specimen for culture in men is unknown.

Treatment

- **Treatment of Trichomoniasis in Women:** The recommended treatment for trichomoniasis in women with HIV is metronidazole 500 mg orally twice daily for 7 days.[\[48,97\]](#) The recommendation to use the 7-day course of metronidazole in women with HIV is based on a randomized controlled trial of women with trichomoniasis and HIV that found single-dose therapy with metronidazole 2 g was less effective than a 7-day metronidazole course, based on reevaluation 1 to 2 weeks after treatment and 3 months after treatment.[\[107\]](#) The 2021 STI Treatment Guidelines do not recommend using alternative regimens to treat trichomoniasis in women with HIV.[\[97\]](#)
- **Treatment of Trichomoniasis in Men:** The 2021 STI Treatment Guidelines do not provide specific recommendations for the treatment of trichomoniasis for men with HIV. The recommended treatment of trichomoniasis in men without HIV is oral metronidazole 2 g in a single dose, and the alternative is tinidazole 2 g in a single dose.[\[97\]](#) No trials have yet examined the efficacy of single-dose therapy with metronidazole (or tinidazole) compared to multi-dose metronidazole therapy for trichomoniasis in men with HIV. Rescreening 3 months after treatment for trichomoniasis is not recommended for men with HIV.[\[97,104\]](#)
- **Management of Sex Partners:** Any current sex partners of individuals diagnosed with trichomoniasis should be referred for presumptive treatment. Furthermore, all individuals who are

diagnosed or being treated for trichomoniasis should be counseled to abstain from sexual activity until they and their partners have completed a course of treatment and all have symptom resolution.[\[97\]](#)

- **Follow Up:** Due to significant risk of reinfection, sexually active women should be retested 3 months after treatment for trichomoniasis, regardless of whether their sex partners have also been treated.[\[97\]](#)

Additional Topics

Cervicitis

Cervicitis can result from common STDs, including gonorrhea, chlamydia, trichomoniasis, and genital herpes. The diagnosis and treatment of cervicitis in women with HIV is the same as in those without HIV. Treatment of cervicitis in women with HIV has additional importance since cervicitis increases HIV genital shedding and may increase the risk of HIV transmission to sexual partners.[\[108\]](#) Evolving drug resistance is a significant threat to the treatment of *N. gonorrhoeae* and *T. vaginalis*, and there are case reports of azithromycin-resistant *C. trachomatis*, but there have not been any cases of confirmed *in vivo* resistance in *C. trachomatis* to either azithromycin or doxycycline.[\[109\]](#)

- **Recommended Treatment:** The recommended empiric treatment of cervicitis consists of doxycycline 100 mg orally twice daily for 7 days; concurrent treatment for gonococcal infection with a single dose of intramuscular ceftriaxone 500 mg should be provided if (1) the person is at risk for gonorrhea (age younger than 25 years, a new sex partner, a sex partner with concurrent partners, or a sex partner who has an STI) or lives in a community where the prevalence of gonorrhea is high, (2) follow-up cannot be ensured, or (3) testing with a NAAT for gonorrhea is not done.[\[108\]](#) The alternative to doxycycline is azithromycin 1 g orally as a single dose. In women with persistent cervicitis, if reinfection is ruled out and treatment failure is considered improbable, it is reasonable to consider alternative diagnoses, keeping in mind that no etiologic agent is found in more than half of all cases of cervicitis.[\[108,110\]](#) Repeating initial therapy, or treating with a longer course of standard therapy has not been established to improve response rates in persistent cervicitis.

Urethritis

Urethritis is characterized by dysuria, urethral pruritus, and urethral discharge (mucoid, mucopurulent, or purulent).[\[108\]](#) For individuals with symptoms compatible with urethritis, any one of the following criteria is sufficient to make a diagnosis of urethritis: (1) mucopurulent discharge, or (2) Gram's stain of a urethral smear sample that shows 2 or more leukocytes per high-power field (oil immersion), or (3) a first-void urine sample that is positive for leukocyte esterase test or has 10 or more leukocytes per high-power field on microscopic examination of the urine sediment.[\[108,111\]](#) All persons with urethritis should have an evaluation for *N. gonorrhoeae* and *C. trachomatis*. The urine nucleic acid amplification test (NAAT) has the highest sensitivity and specificity for diagnosis of these organisms and therefore is the preferred diagnostic test. Gonococcal urethritis can be diagnosed if the Gram's stain of a urethral smear reveals leukocytes with gram-negative intracellular diplococci. Urethritis without evidence of gram-negative intracellular diplococci is considered to be nongonococcal urethritis (NGU).

- **Recommended Treatment:** Empiric treatment for urethritis should have efficacy against both gonorrhea and chlamydia; the preferred regimen is ceftriaxone 500 mg as a single intramuscular dose plus doxycycline 100 mg orally twice daily for 7 days.[\[108\]](#) If gonorrhea is deemed unlikely based on a negative point of care test (no evidence of intracellular diplococci on Gram's stain, methylene blue, or gentian violet stain), then doxycycline alone is recommended. The alternative to doxycycline is azithromycin 1 g orally in a single dose or azithromycin 500 mg on day 1, followed by 250 mg daily for 4 days.

Persistent Urethritis

Persons with recurrent or persistent symptoms of urethritis following appropriate therapy for nongonococcal urethritis should be reevaluated; this is particularly important for persons with HIV, as nongonococcal urethritis may increase the risk of HIV transmission to sex partners.[\[108\]](#) Possible causes for persistent symptoms despite appropriate antibiotic therapy include reinfection, lack of adherence to initial course of treatment, infection with a resistant organism, or infection with a secondary pathogen; several studies found

that *Mycoplasma genitalium* was the most common cause of persistent urethritis, especially in persons who fail doxycycline therapy.[112,113]

- **Recommended Treatment:** For persons who did not comply with their initial treatment or had reexposure to an untreated sex partner, the same regimen they initially received can be used for retreatment. If a person was compliant with the initial regimen and reexposure did not occur, then retreatment should consist of moxifloxacin 400 mg orally once daily for 7 days.[108] In areas of high prevalence of *Trichomonas vaginalis*, men who have sex with women and have persistent urethritis should be treated with either metronidazole 2 g orally in a single dose or tinidazole 2 g orally in a single dose; in addition, for men initially treated with doxycycline, retreatment should include azithromycin 1 g orally in a single dose.[108] The diagnosis of prostatitis should be considered in men with persistent urethritis symptoms.

Epididymitis

Treatment of uncomplicated epididymitis is the same in all men regardless of HIV status and should be aimed at the most likely organisms. Men younger than age 35 typically have epididymitis secondary to *Chlamydia trachomatis* and *N. gonorrhoeae* infection, whereas men older than age 35 years are at increased risk for non-sexually transmitted epididymitis that is associated with urinary tract instrumentation or surgery. Men who practice insertive anal intercourse are also at risk for developing epididymitis from enteric organisms, such as *Escherichia coli*. In men with HIV, several organisms have been identified that can rarely cause epididymitis, including cytomegalovirus, *Salmonella*, *Toxoplasma gondii*, *Ureaplasma urealyticum*, *Corynebacterium* sp., *Mycobacterium* sp., and *Mima polymorpha*, fungal infections, and mycobacteria.[114]

- **Recommended Treatment:** The treatment for acute epididymitis is stratified based on three likely scenarios: (1) acute epididymitis most likely caused by chlamydia or gonorrhea, (2) acute epididymitis most likely caused by chlamydia, gonorrhea, or enteric organisms (men who practice insertive anal sex), or (3) acute epididymitis most likely caused by enteric organisms only.[114] In persons at risk for enteric organisms, levofloxacin should be given in addition to treatment for sexually transmitted *C. trachomatis* and *N. gonorrhoeae*. [114,115,116]

2021 STI Treatment Guidelines: Epididymitis
Table 12. Treatment of Epididymitis

Recommended **for acute epididymitis most likely caused by chlamydia or gonorrhea**

Ceftriaxone

Ceftriaxone

Tradename:Rocephin

500 mg* IM in a single dose for persons weighing <150 kg

Doxycycline

Doxycycline

Tradename: Doryx, Vibramycin

100 mg orally 2 times/day for 10 days+

Note: *For persons weighing ≥ 150 kg, ceftriaxone 1 g IM should be administered.

Recommended **for acute epididymitis most likely caused by chlamydia, gonorrhea, or enteric organisms (men who practice insertive anal sex)**

Ceftriaxone

Ceftriaxone

Tradename: Rocephin

500 mg* IM in a single dose for persons weighing < 150 kg

Levofloxacin

Levofloxacin

Tradename: Levaquin

500 mg orally once daily for 10 days+

Note: *For persons weighing ≥ 150 kg, ceftriaxone 1 g IM should be administered.

Recommended **for acute epididymitis most likely caused by enteric organisms only**

Levofloxacin

Levofloxacin

Tradename: Levaquin

500 mg orally once daily for 10 days

Source: Workowski KA, Bachmann LH, Chan PA, et al. Sexually transmitted infections treatment guidelines, 2021. Epididymitis. MMWR Recomm Rep. 2021;70(No. RR-4):1-187. [[2021 STI Treatment Guidelines](#)]

Courtesy of [National STD Curriculum](#).

Proctitis

The most common infectious etiologies of proctitis are *C. trachomatis* (including subtypes that cause LGV), *N. gonorrhoeae*, *T. pallidum*, and herpes simplex virus.[117] Diagnosis should be made by visual inspection (via anoscopy or sigmoidoscopy), Gram's staining of a smear of anorectal exudate or secretions, stool examination, and culture.

- **Recommended Treatment:** For persons with anorectal exudate identified by clinical examination or by detection of polymorphonuclear leukocytes on a Gram's stain smear of anorectal secretions, presumptive therapy for proctitis should be administered.[117] The recommended initial empiric therapy for acute proctitis should include treatment for *C. trachomatis* and *N. gonorrhoeae* with ceftriaxone 500 mg in a single intramuscular dose plus doxycycline 100 mg orally twice a day for 7 days.[117] Note that for persons who have symptoms consistent with LGV (bloody rectal discharge, perianal or mucosal ulcers, or tenesmus) in conjunction with a positive rectal chlamydia test, the duration of doxycycline therapy should be extended to 21 days to treat LGV.[117] In addition, the initial empiric treatment should also include an oral antiviral (acyclovir, famciclovir, or valacyclovir) to treat genital herpes if painful perianal ulcers are present or mucosal ulcers are detected on anoscopy.[117] The treatment regimen should be expanded or modified based on testing results.

Mycoplasma genitalium

Recently, increasing attention has been given to *Mycoplasma genitalium* as a possible cause for persistent or recurrent cervicitis and urethritis. In January 2019, the FDA authorized the use and marketing of the Aptima *Mycoplasma genitalium* Assay for diagnosing *M. genitalium*; this assay, which is a NAAT, is the first FDA-approved diagnostic test for *M. genitalium*. The sensitivity for this test is approximately 90% in vaginal, male urethral, and male urine samples. The sensitivity was relatively lower in female urine (77.8%) and endocervical samples (81.5%). The specificity of this test was very high, ranging from 97.8 to 99.6%, depending on the sample and the study.[118]

- **Recommended Treatment:** The recommended therapy for *M. genitalium* requires a two-stage antimicrobial approach, and the regimen selected depends on whether *M. genitalium* antimicrobial resistance testing is available.[118]
 - If resistance testing is available and *M. genitalium* is macrolide sensitive, then the recommended treatment is doxycycline 100 mg orally twice daily for 7 days, followed by azithromycin 1 g orally as an initial dose, followed by 500 mg orally daily for 3 additional days (2.5 grams total of azithromycin).
 - If *M. genitalium* is resistant to macrolides (or resistance testing is not available or not used), the recommended treatment is doxycycline 100 mg orally twice daily for 7 days, followed by moxifloxacin 400 mg orally once daily for 7 days.[118] The up-front empiric use of doxycycline in these regimens is to reduce the bacterial pathogen burden to minimize the risk of developing *M. genitalium* resistance to moxifloxacin.[118]

Summary Points

- Multiple studies document synergy between HIV and sexually transmitted diseases: HIV can increase the incidence, severity, and persistence of many infections, and STDs can increase the risk of sexual acquisition of HIV and enhance the transmission of HIV.
- Men and women with HIV should have screening for chlamydia, gonorrhea, and syphilis at baseline and periodically thereafter, depending on ongoing risk factors. Women with HIV should also be tested for trichomoniasis at baseline and periodically thereafter.
- The recommended treatment regimen for gonococcal infections is a single dose of intramuscular ceftriaxone 500 mg (in persons less than 150 kg), with or without oral doxycycline 100 mg twice daily for 7 days, depending on whether chlamydia infection has been ruled out. Pregnant women should receive a single 1 g oral dose of azithromycin instead of doxycycline.
- The recommended treatment for chlamydia in nonpregnant adults with HIV is doxycycline 100 mg orally twice daily for 7 days; during pregnancy, azithromycin 1 g orally in a single dose is recommended.
- Lymphogranuloma venereum, an infection caused by *C. trachomatis* serovars L1, L2, L3, is characterized by painful inguinal adenopathy or proctitis. The recommended treatment of LGV in nonpregnant persons with HIV is doxycycline 100 mg orally twice daily for 21 days.
- Treatment for syphilis depends on the stage of infection and whether neurosyphilis is suspected or documented. Individuals with HIV who are treated for syphilis require serologic follow-up for at least 24 months after completion of therapy.
- For treatment of trichomoniasis in women with HIV, a 7-day course of oral metronidazole 500 mg twice daily is recommended, whereas in men, a single 2 g dose of metronidazole is recommended.
- Chancroid infection is rare in the United States, and treatment experience is limited in persons with HIV; among individuals with HIV, the disease course with chancroid tends to be more severe and prolonged, and treatment failure rates are higher.
- Individuals with HIV tend to have more severe and chronic herpes simplex lesions, and more asymptomatic shedding of HSV-2 in the genital tract compared to persons without HIV; suppressive therapy with valacyclovir, acyclovir, or famciclovir, should be considered in persons with HIV.
- Genital warts caused by human papillomaviruses are common among individuals with HIV. Treatment is aimed at ameliorating symptoms, and the 9-valent HPV vaccine includes the HPV subtypes 6 and 11, which cause approximately 90% of genital warts.

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Figures

Figure 1 Gonorrhea-Rates of Reported Cases by Age Group, United States, 2021

Source: Centers for Disease Control and Prevention. Sexually Transmitted Disease Surveillance 2021. Gonorrhea. Atlanta: U.S. Department of Health and Human Services; April 2023.

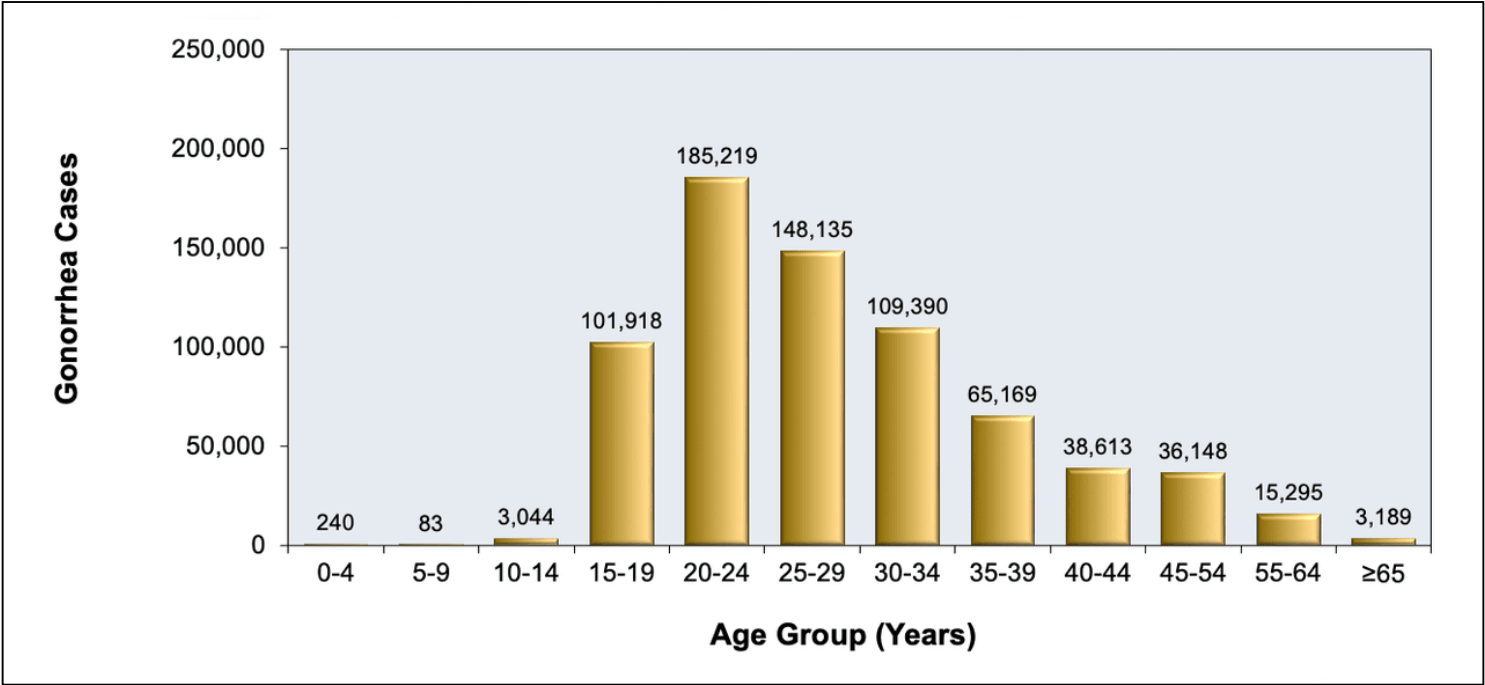


Figure 2 Chlamydia—Rates of Reported Cases by Sex and Age Group, United States, 2021

Source: Centers for Disease Control and Prevention. Sexually Transmitted Disease Surveillance 2021. Gonorrhea. Atlanta: U.S. Department of Health and Human Services; April 2023.

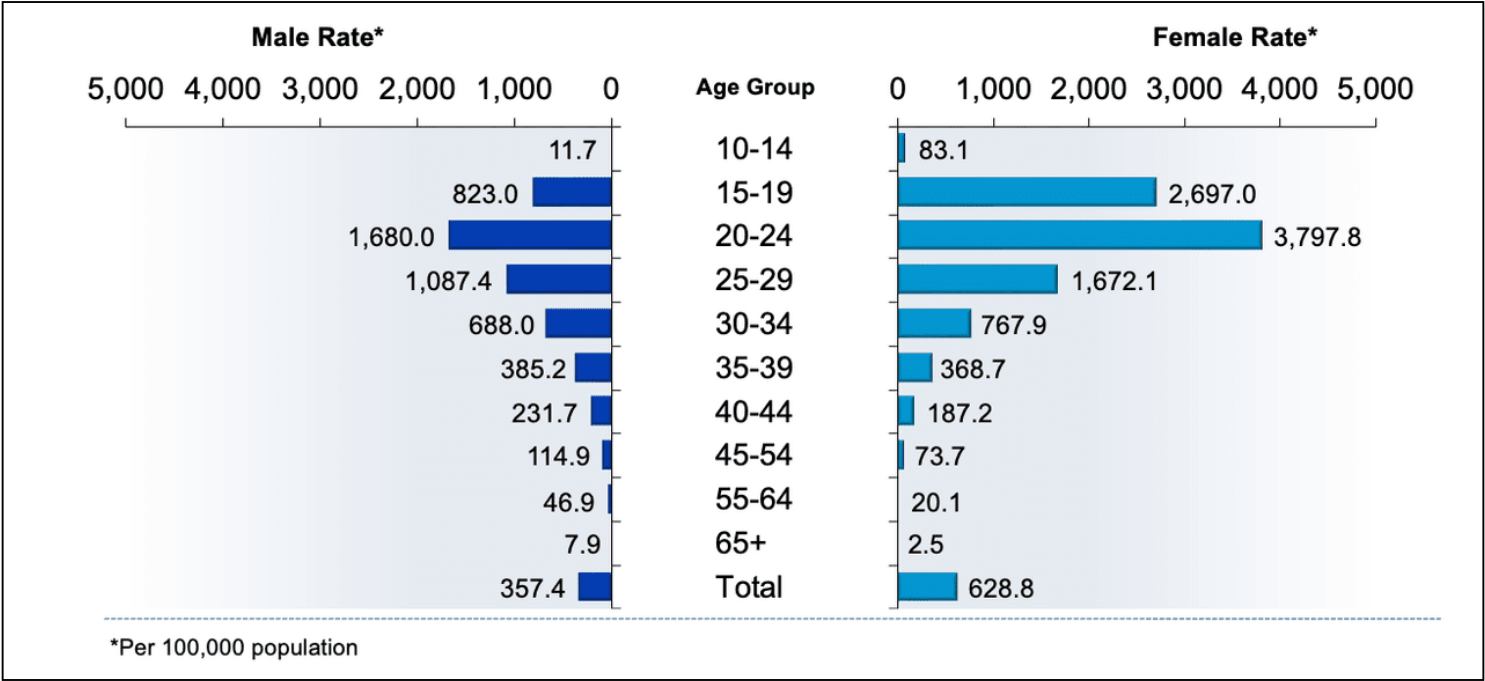


Figure 3 Syphilis Cases, All Stages of Infection, United States, 2000-2021

Source: Centers for Disease Control and Prevention. Sexually Transmitted Disease Surveillance 2021. Gonorrhea. Atlanta: U.S. Department of Health and Human Services; April 2023.

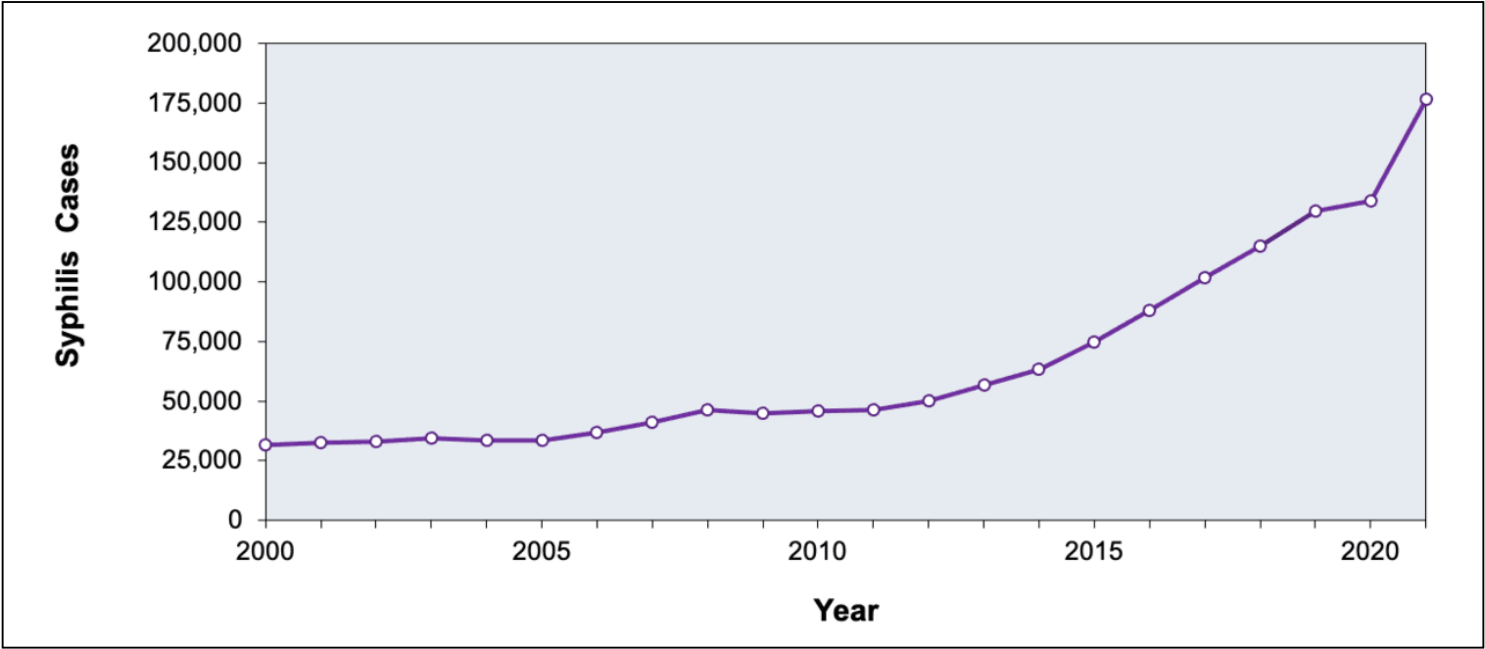


Figure 4 (Image Series) - Secondary Syphilis (Image Series) - Figure 4 (Image Series) - Secondary Syphilis
Image 4A: Diffuse Erythematous Maculopapular Lesions in Man with HIV and Secondary Syphilis

Photograph credit: David H. Spach, MD



Figure 4 (Image Series) - Secondary Syphilis
Image 4B: Secondary Syphilis: Diffuse Erythematous Maculopapular Lesions

Photograph credit: David H. Spach, MD

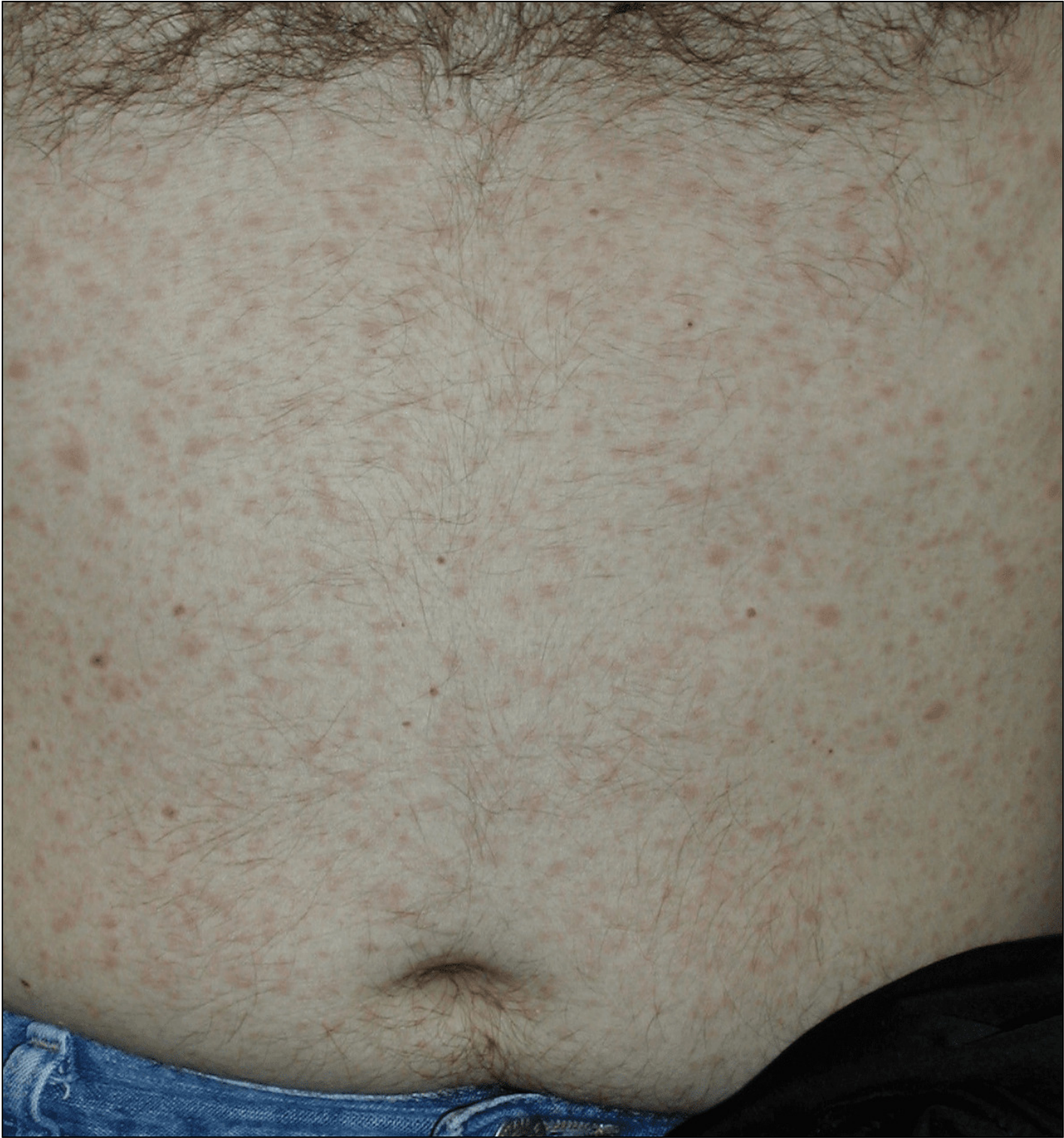


Figure 4 (Image Series) - Secondary Syphilis
Image 4C: Secondary Syphilis: Papular Lesions on Abdomen

Photograph credit: Negusse Ocbamichael, PA; Public Health—Seattle & King County Sexual Health Clinic



Figure 4 (Image Series) - Secondary Syphilis
Image 4D: Secondary Syphilis: Papular Lesions on Hand

Photograph credit: David H. Spach, MD



Figure 5 (Image Series) - Syphilis Serologic Screening (Image Series) - Figure 5 (Image Series) - Syphilis Serologic Screening
Image 5A: Traditional Sequence Algorithm

The traditional (standard) serologic screening sequence algorithm uses a quantitative nontreponemal test (RPR or VDRL) for screening followed by a treponemal test for confirmation of positive screening tests. Abbreviations: RPR = rapid plasma reagin; VDRL = Venereal Disease Research Laboratory; TP-PA = *Treponema pallidum* particle agglutination.

Source: Centers for Disease Control and Prevention (CDC). Discordant results from reverse sequence syphilis screening--five laboratories, United States, 2006-2010. MMWR Morb Mortal Wkly Rep. 2011;60:133-7.

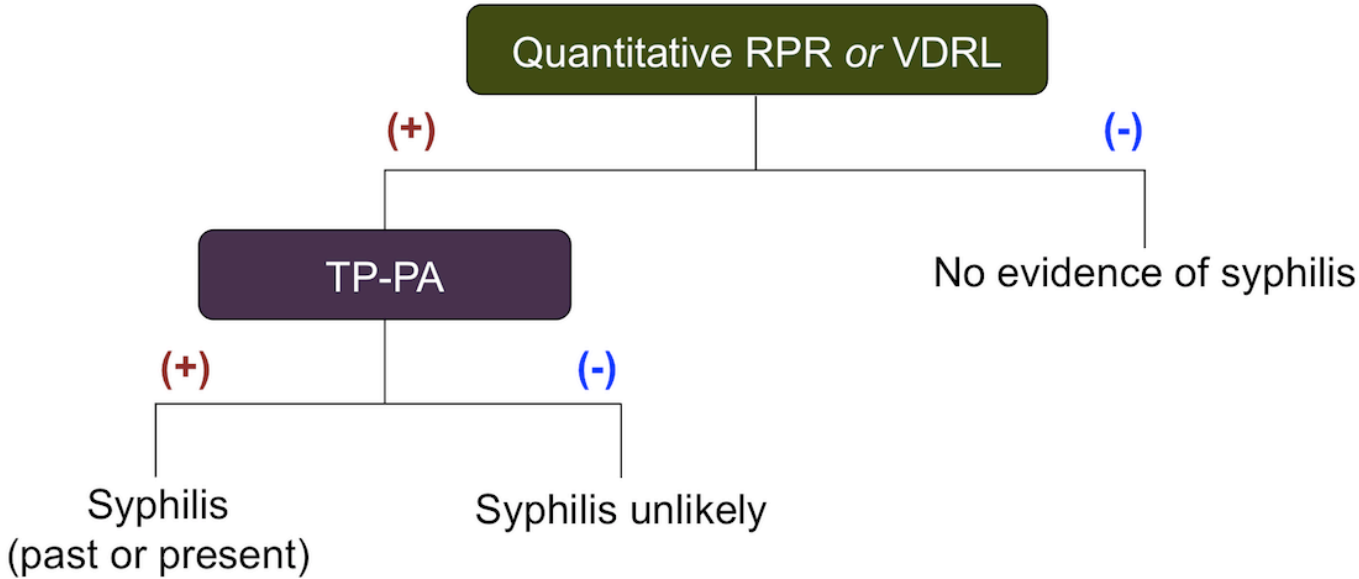


Figure 5 (Image Series) - Syphilis Serologic Screening
Image 5B: Reverse Sequence Algorithm

The reverse serologic screening algorithm uses an initial treponemal test for screening, followed by a nontreponemal test confirmation. A specimen with reactive EIA/CIA results should be tested reflexively with a quantitative nontreponemal test (RPR or VDRL). Abbreviations: EIA = enzyme immunoassay; CIA = chemiluminescence immunoassays; RPR = rapid plasma reagin; VDRL = Venereal Disease Research Laboratory; TP-PA = *Treponema pallidum* particle agglutination.

Source: Centers for Disease Control and Prevention (CDC). Discordant results from reverse sequence syphilis screening--five laboratories, United States, 2006-2010. MMWR Morb Mortal Wkly Rep. 2011;60:133-7.

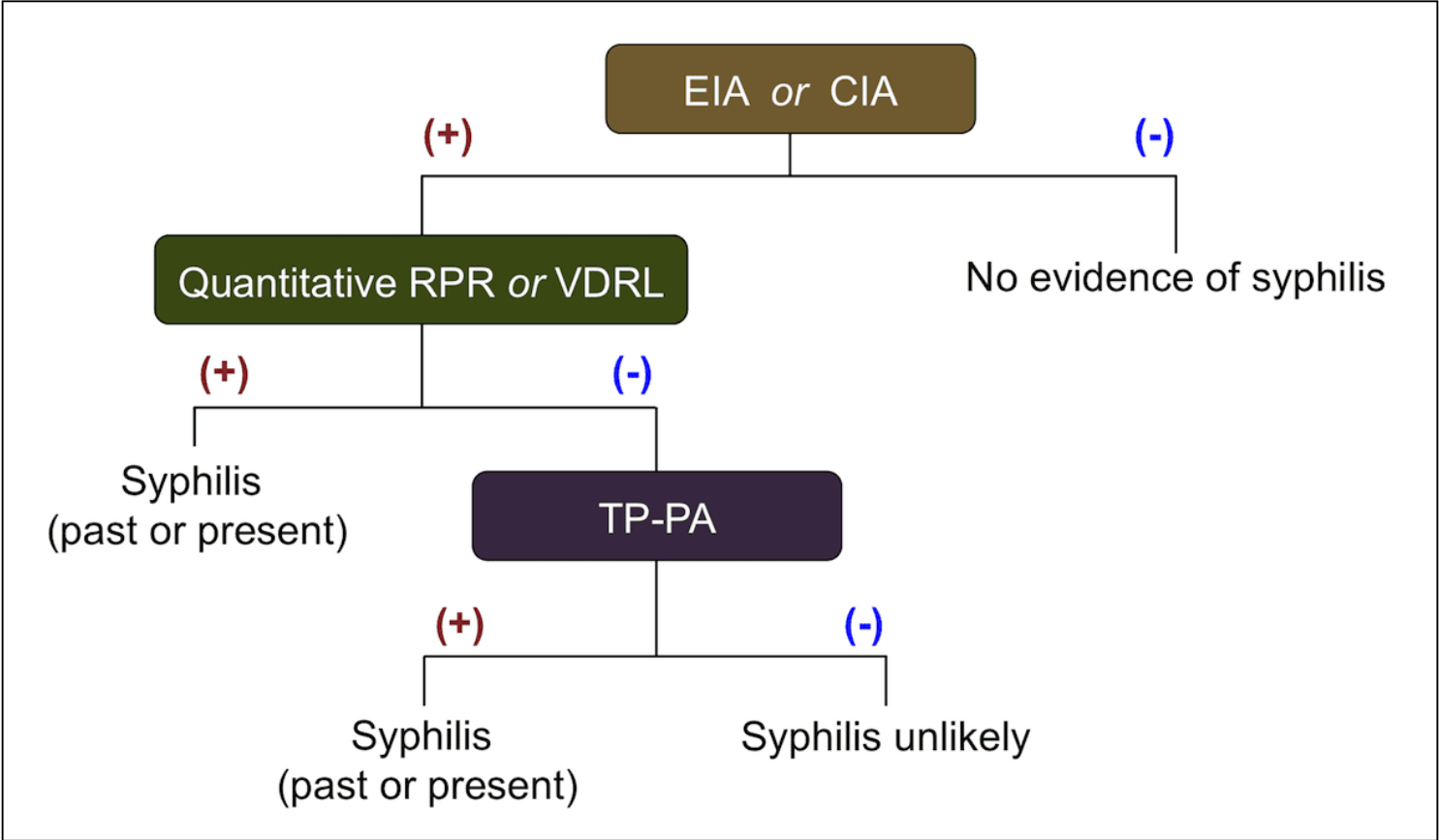


Figure 6 Multiple Ulcerated Lesions on the Scrotum of a Man with HIV and CD4 Count Less than 50 cells/mm³

Chronic ulcerative lesions caused by herpes simplex virus infection are much more common in persons with HIV if they have a CD4 count less than 100 cells/mm³

Photograph from David H. Spach, MD



Figure 7 HSV Lesion in Gluteal Cleft

The black arrow denotes the ulcerated lesion with exudate in the gluteal cleft.

Photograph from David H. Spach, MD



Figure 8 Acyclovir-Resistant HSV Lesion in Gluteal Fold

This man with advanced HIV developed a slowly expanding ulcerating lesion in the upper region of the gluteal cleft.



Figure 9 Multiple Warts on Shaft of Penis in Man with HIV

Photograph from David H. Spach, MD

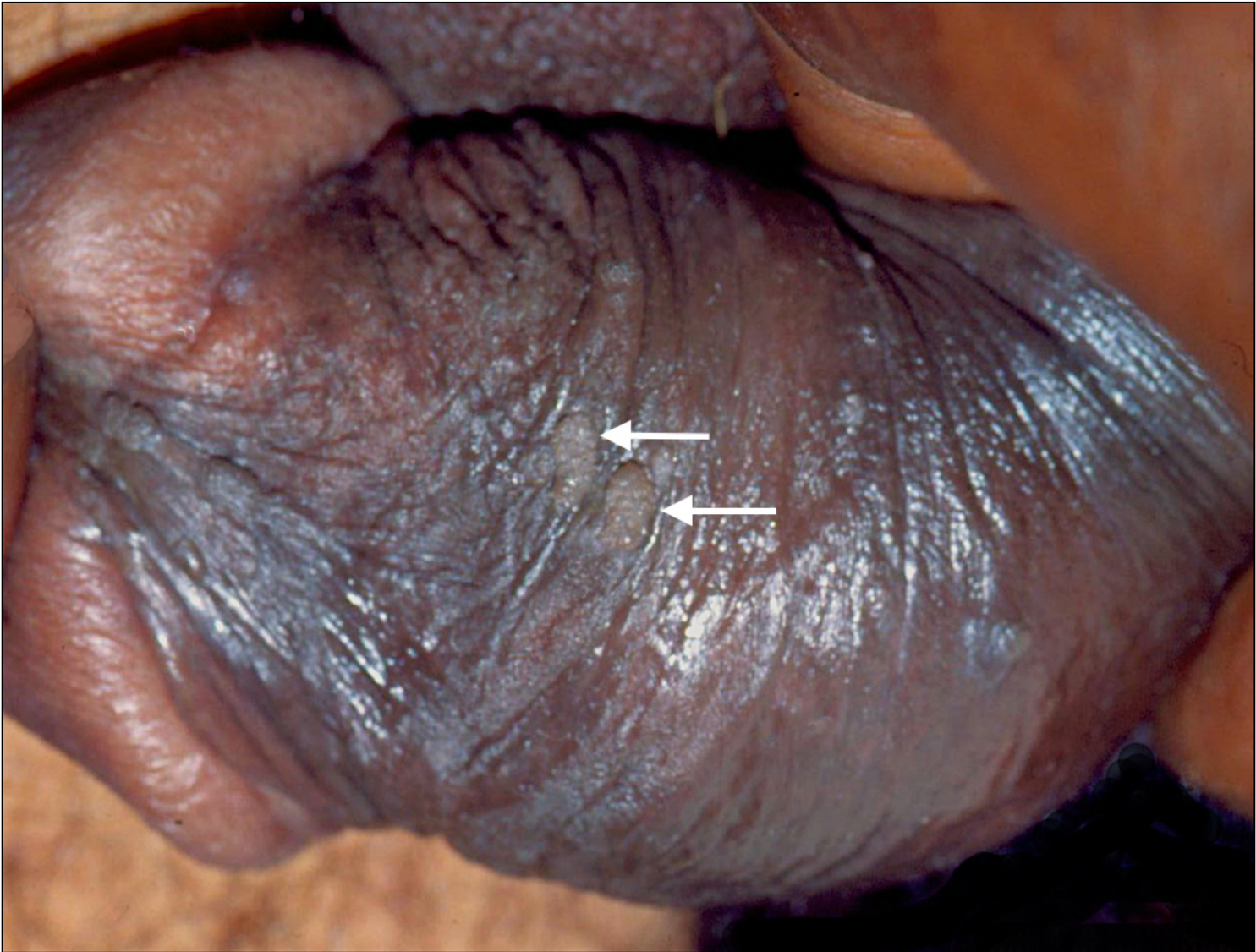


Table 1.

STI Screening Recommendations in Persons with HIV

STI	Screening Indications and Frequency
Chlamydia	<ul style="list-style-type: none"> • 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
Gonorrhea	<ul style="list-style-type: none"> • 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
Syphilis	<ul style="list-style-type: none"> • 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
Herpes	<ul style="list-style-type: none"> • Type-specific herpes simplex virus (HSV) serologic screening for HSV-2 should be considered for persons presenting for an STI evaluation (especially for those persons with multiple sex partners)
Trichomoniasis	<ul style="list-style-type: none"> • Recommended for sexually active women at entry to care and at least annually thereafter
HPV, Cervical Cancer	<ul style="list-style-type: none"> • Sexually active women with HIV who are at least 21 years of age should undergo cervical cancer screening at initial entry to HIV care and again 12 months later. • Annual Pap testing is recommended in women with HIV younger than 30 years of age, but if 3 consecutive annual screens are normal, Pap tests can be performed every 3 years. • Women with HIV who are 30 years of age and older should have either (1) cervical cancer screening by Pap testing alone or (2) Pap testing plus simultaneous HPV co-testing. If Pap testing alone is used, it should be performed at baseline and every 12 months; if the results of 3 consecutive Pap tests are normal, then follow-up testing can occur every 3 years. If Pap and HPV co-testing is performed and both are negative, follow-up screening can be performed in 3 years. • Cervical cancer screening should continue throughout the life in women with HIV.
Anal Cancer	<ul style="list-style-type: none"> • Digital anorectal rectal exam • Screen men who have sex with men with HIV

STI	Screening Indications and Frequency
	who are 35 years of age and older and screen all others with HIV who are 45 years of age and older. Specific screening recommendations depend on availability of high resolution anoscopy (HRA).
Hepatitis B Screening	<ul style="list-style-type: none"> At the initial evaluation, test for hepatitis B surface antigen (HBsAg), antibody to hepatitis B core (anti-HBc), and hepatitis B surface antibody (anti-HBs)
Hepatitis C Screening	<ul style="list-style-type: none"> At the initial evaluation, perform serologic testing for antibody to HCV (anti-HCV), with reflex to HCV RNA for all positive anti-HCV tests Annual HCV serologic testing in men who have sex with men For persons with prior spontaneous or treatment clearance of HCV, screening should be conducted with HCV RNA
NOTE: This table is modified from recommendations in the Centers for Disease Control 2021 Sexually Transmitted Infections Treatment Guidelines and the Panel on Opportunistic Infections in Adults and Adolescents with HIV Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents with HIV.	

Source:

- Panel on Opportunistic Infections in Adults and Adolescents with HIV. Guidelines for the prevention and treatment of opportunistic infections in adults and adolescents with HIV: recommendations from the Centers for Disease Control and Prevention, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America. Human papillomavirus disease. July 9, 2024. [[HIV.gov](https://www.hiv.gov)]
- Workowski KA, Bachmann LH, Chan PA, et al. Sexually transmitted infections treatment guidelines, 2021. Screening Recommendations and Considerations Referenced in Treatment Guidelines and Original Sources. MMWR Recomm Rep. 2021;70(No. RR-4):1-187. [[2021 STI Treatment Guidelines](#)]

Table 10. Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents with HIV

Treatment of Acyclovir-Resistant Mucocutaneous HSV Infection

Preferred Therapy

- Foscarnet 80–120 mg/kg/day IV in 2–3 divided doses until clinical response (AI)

Alternative Therapy (Duration: 21–28 days or longer, based on clinical response) (CIII):

- Topical trifluridine, *or*
- Topical cidofovir 1% gel, *or*
- Topical imiquimod 5% cream three times/week, *or*
- IV cidofovir 5 mg/kg IV once weekly
- Topical foscarnet 1% five times a day

Note

- Topical formulations of trifluridine and cidofovir are not commercially available
- Extemporaneous compounding of topical products can be prepared using trifluridine ophthalmic solution and the IV formulation of cidofovir.
- An expanded access program of oral pritelivir is now available for immunocompromised patients with acyclovir-resistant HSV infection; for more information see [AiCuris Pritelivir Early Access website](#).

HSV = herpes simplex virus; IV = intravenously

Rating System for Prevention and Treatment Recommendations

- Strength of Recommendation: A = Strong; B = Moderate; C = Optional
- Quality of Evidence for the Recommendation: I = One or more randomized trials with clinical outcomes and/or validated laboratory endpoints; II = One or more well-designed, non-randomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion

Source:

- Panel on Opportunistic Infections in Adults and Adolescents with HIV. Guidelines for the prevention and treatment of opportunistic infections in adults and adolescents with HIV: recommendations from the Centers for Disease Control and Prevention, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America. Herpes simplex virus. Last updated: May 26, 2020. [[HIV.gov](#)]

