CME CREDIT *EDUCATIONAL OBJECTIVE:* Readers will recognize and treat sexually transmitted diseases effectively

ROBYN NEBLETT FANFAIR, MD, MPH
Division of STD Prevention, National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention, US Centers for Disease Control and Prevention, Atlanta, GA

KIMBERLY A. WORKOWSKI, MD
Division of STD Prevention, National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention, US Centers for Disease Control and Prevention, Atlanta, GA; and Division of Infectious Diseases, Department of Medicine, Emory University School of Medicine, Atlanta, GA; Chairperson, Sexually Transmitted Diseases Treatment Guidelines, 2014

Clinical update in sexually transmitted diseases–2014

ABSTRACT

Sexually transmitted diseases (STDs) and their associated syndromes are extremely common in clinical practice. Early diagnosis, appropriate treatment, and partner management are important to ensure sexual, physical, and reproductive health in our patients.

KEY POINTS

Anyone can have an STD, although the prevalence is higher in some groups, such as younger sexually active people, certain racial and ethnic minorities, men who have sex with men, and people who engage in risky sexual behavior.

Preexposure vaccination is one of the most effective ways to prevent human papillomavirus, hepatitis A virus, and hepatitis B virus infections.

The risk of acquiring human immunodeficiency virus is two to five times higher if the patient has a genital ulcerative disease such as syphilis or herpes at the time of exposure.

Chlamydia trachomatis and *Neisseria gonorrhoeae* are major players in urethritis, cervicitis, and proctitis.

The most common conditions associated with vaginitis include bacterial vaginosis, trichomoniasis, and candidiasis.

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With nearly 20 million new infections annually, sexually transmitted diseases (STDs) are very common in the United States.[1,2] And with recent changes to the national health care landscape, including the passage of the Affordable Care Act and state budget cuts resulting in the closure of STD and human immunodeficiency virus (HIV) clinics, primary care providers can expect to encounter more patients with STDs.

For women and infants, STDs can have serious and long-term consequences, including infertility, facilitation of HIV infection, reproductive tract cancer, pelvic inflammatory disease, and poor perinatal outcomes.[2] STDs cost the US health care system nearly $16 billion every year.[3]

STD prevention and control strategies traditionally include surveillance, screening, behavioral interventions, treatment, and partner management.[4] This paper will review patient management by syndrome and provide guidance to clinicians to facilitate timely diagnosis and treatment, important components of any effective STD prevention strategy.

ANYONE CAN HAVE AN STD

STDs affect people of all races, ages, and sexual orientations. That said, some groups are at greater risk:

Adolescents and young adults. Persons ages 15 through 24 represent 25% of the sexually experienced population in the United States but account for nearly half of all incident STDs.[1]

Racial and ethnic minorities. STD disparities are one of the five greatest health disparities for African American communities.[4]

Drugs discussed in this paper

acyclovir (Zovirax)
azithromycin (Zithromax)
ceftriaxone (Rocephin)
clindamycin (Cleocin)
doxycycline (Vibramycin)
famciclovir (Famvir)
metronidazole (Flagyl)
moxifloxacin (Avelox)
penicillin G
tinidazole (Tindamax)
valacyclovir (Valtrex)

Men who have sex with men number approximately 2% to 4% of the US male population, yet account for approximately 70% of reported cases of primary and secondary syphilis and more than 50% of persons with HIV infection.[3,5,6]

HIGH-RISK BEHAVIOR AND SCREENING

A thorough sexual history will reveal behaviors that place a person at risk of infection. The US Preventive Services Task Force (USPSTF) defines high-risk sexual behavior as having multiple current partners, having a new partner, using condoms inconsistently, having sex while under the influence of alcohol or drugs, or exchanging sex for money or drugs.[7]

Everyone age 13 through 64 should be tested for HIV at least once

An effective strategy for obtaining a sexual history is the "five Ps"[8]:

- **Partners** (eg, Do you have sex with men, women, or both?)
- **Prevention of pregnancy** (eg, What are you doing to prevent pregnancy?)
- **Protection from STDs** (eg, What do you do to protect yourself from STDs?)
- **Practices** (eg, To understand your risks for STDs, I need to understand the kind of sex you have had recently.)
- **Past history of STDs** (eg, Have you ever had an STD?).[8]

The USPSTF and the US Centers for Disease Control and Prevention (CDC) recommend certain populations be screened for STDs.[7,8]

Everyone age 13 through 64 should be tested for HIV at least once, per CDC recommendation.[8]

Sexually active females up to age 24 should routinely be screened for chlamydia every year.[7,8]

Nonpregnant women at higher risk of infection should be screened for gonorrhea and syphilis.

Pregnant women, regardless of risk, should be screened for chlamydia, hepatitis B, HIV, and syphilis; pregnant women at higher risk of infection should also be screened for gonorrhea and hepatitis C.[7,9]

Men should be screened for HIV, and men at higher risk should also be screened for syphilis.[8]

Men who have sex with men should be screened at least annually for HIV and syphilis and undergo a test for urethral chlamydia and gonorrhea infection. Men who participate in receptive anal intercourse should be tested for rectal chlamydia and gonorrhea and, in those who participate in oral intercourse, for pharyngeal gonorrhea.[8]

PREVENTION

Vaccination against HPV, hepatitis A and B

Preexposure vaccination is one of the most effective ways to prevent human papillomavirus (HPV), hepatitis A, and hepatitis B infection.[10]

HPV vaccination. The Advisory Committee on Immunization Practices recommends routine HPV vaccination of female patients at age 11 or 12, or through age 26 if not previously vaccinated.[11,12] Routine vaccination is also recommended for males at age 11 or 12 and through age 21, if not previously vaccinated.[12] The upper age is extended through age 26 for men who have sex with men and for immunocompromised patients.[12]

Two HPV vaccines are available for females; one is quadrivalent and the other is bivalent. Both protect against two HPV types that cause cervical and other HPV-associated cancers.[11] The quadrivalent vaccine also protects against the two types that cause 90% of genital warts.[13] Only the quadrivalent vaccine is licensed for use in males.[12]

Hepatitis A and B vaccination. Hepatitis B vaccination is recommended for all unvaccinated, uninfected patients being evaluated for an STD.[8,14]

Vaccinating for hepatitis A and hepatitis B is important for men who have sex with men, who have a higher risk of acquiring and transmitting these infections.[15]

Other preventive practices

Male circumcision has been shown to reduce the risk of HIV infection, high-risk genital HPV infection, and genital herpes in

heterosexual men.[10,16,17]

Male condoms, when used consistently and correctly, can reduce the risk of chlamydia, gonorrhea, and trichomoniasis.[8] The risk of transmission of syphilis, genital HPV, and genital herpes can also be reduced by correctly and consistently using condoms when the infected area of exposure is covered.[8]

Microbiocides not recommended. Topical microbiocides do not have not enough evidence to recommend them for STD prevention. However, limited data suggest that tenofovir 1% vaginal gel may reduce the risk of acquiring genital herpes simplex virus type 2 (HSV-2) infection in women.[18,19]

GENITAL ULCERATIVE DISEASE: HERPES, SYPHILIS, OTHERS

The risk of acquiring HIV is two to five times higher if one is exposed to it when a genital ulcerative disease is present.[20,21]

In the United States, most cases of genital, anal, or perianal ulcers in sexually active persons are due to genital herpes or syphilis.[8] Other causes include chancroid, granuloma inguinale, lymphogranuloma venereum, and noninfectious causes.

Although the frequency of these conditions varies by geographic area and demographic profile, herpes is the most prevalent of them.[8] HSV-2 infection is one of the most prevalent STDs in the United States, with approximately 17% of all adolescents and adults infected,[1,22] and a much higher prevalence in persons who use drugs.[23]

A thorough medical history and physical examination should be conducted. In addition, an accurate diagnosis requires specific tests: syphilis serology, dark field microscopy (if available), and culture or polymerase chain reaction (PCR) testing for herpes.[8] A positive serologic test for HSV-1 or HSV-2 is enough to make the diagnosis in a patient whose symptoms suggest herpes, even if PCR and culture are negative.

GENITAL HERPES: MOSTLY ASYMPTOMATIC

Genital herpes is caused by HSV-1 or HSV-2. Of these, HSV-1 is on the rise, causing an increasing proportion of first episodes of genital herpes in some populations. It may now account for most new genital herpes infections in young women and in men who have sex with men.[8,24]

Most people infected with HSV-1 or HSV-2 have no symptoms or have subclinical disease. When symptoms do occur, one or more vesicles may appear on or around the genitals, rectum, or mouth. The average incubation period after exposure is 4 days (range 2–12).[25] The first episode of genital herpes is often associated with systemic symptoms (eg, fever, headache, myalgia, and malaise) and local symptoms (eg, dysuria, vaginal or urethral discharge, and inguinal adenopathy).[26,27]

Genital herpes often recurs, especially during the first year. Recurrences are less frequent with HSV-1 than with HSV-2.

Diagnosing genital herpes requires laboratory testing

Diagnosing genital herpes by clinical signs and symptoms is both insensitive and nonspecific. Therefore, laboratory testing should be performed for patients who present with genital ulcerative disease.

Several herpes vaccines have been tested, but an effective one remains elusive

Virologic tests. Viral culture and nucleic acid amplification methods, including PCR assays, are the preferred virologic tests for herpes.[8] Although viral culture is widely available, its sensitivity depends on the stage of the lesion and rapidly declines as lesions begin to heal. PCR assays are more sensitive than viral culture, can be done in automated systems, and are increasingly being used in clinical settings.[26] However, if the patient has no active lesions at the time of testing, failure to detect herpes by culture or PCR does not guarantee that the patient is not infected, as viral shedding is intermittent.

Serologic tests. Type-specific antibodies to HSV develop during the first several weeks following infection and persist indefinitely. Providers should specifically request serologic type-specific immunoglobulin G (IgG) assays. IgM testing for HSV should not be used, as IgM testing is not type-specific. Moreover, although some clinicians believe IgM is a good test for early infection because levels rise early and then decline, IgM may be positive during recurrent episodes.[8]

Both laboratory-based assays and point-of-care tests for HSV-2 are available. They are performed on capillary blood or serum and have sensitivities that range from 80% to 100% and specificities greater than 96%, compared with HSV-2 immunoblot and Western blot testing as the standard.[28,29]

False-negative results may be more frequent in the early stages of infection. HSV-2 antibody indicates anogenital infection, while HSV-1 antibody might also be due to orolabial infection, which is something to keep in mind in a patient without genital symptoms.[8]

Treatment can control herpes but not eradicate it

Several herpes vaccines have undergone clinical trials, but an effective one remains elusive.[30,31]

Antiviral therapy is used to control signs and symptoms of clinical disease but does not eradicate latent virus. For initial clinical episodes of genital herpes, the CDC recommends acyclovir, valacyclovir, or famciclovir for 7 to 10 days.[8] In patients with established genital herpes, daily suppressive antiviral therapy can reduce recurrences, subclinical shedding, and the likelihood of transmission to partners; famciclovir is somewhat less efficacious for suppressing viral shedding.[8]

Without active lesions, negative herpes culture or PCR does not guarantee absence of infection

A diagnosis of herpes can carry considerable stigma, which can substantially interfere with a patient's current and future relationships.[25,32,33] Sex partners of patients with genital herpes may benefit from evaluation and counseling. Clinicians should appreciate the psychological impact of a genital herpes diagnosis and address these concerns by providing education, counseling, and support while encouraging patients to recognize that herpes is a manageable condition.[34]

SYPHILIS IS INCREASING IN MEN WHO HAVE SEX WITH MEN

Since 2001, rates of syphilis, a systemic disease caused by *Treponema pallidum*, have been increasing in men who have sex with men.[3,35] As of 2011, this group accounts for approximately 72% of all cases of primary and secondary syphilis in the United States.[3]

Primary syphilis is characterized by a firm, painless chancre at the site of inoculation. The chancre lasts 3 to 6 weeks and heals regardless of treatment. However, if the infected person does not receive adequate treatment, the infection progresses to the secondary stage.[26]

Secondary syphilis typically starts with a nonpruritic rash, usually macular or papular, on the trunk and extremities, classically including the palms and soles. Other symptoms may include alopecia, lymphadenopathy, condylomata, and systemic symptoms.

Without treatment, the infection can progress to latent syphilis, which is further categorized as early (acquired during the preceding year), late latent, or of unknown duration.[26]

Practical diagnosis of syphilis relies on serologic testing

Definitive diagnosis of early syphilis requires dark field microscopy or PCR to detect *T pallidum* in lesion exudate or tissue.[8] However, because there are no commercially available tests for *T pallidum*, serologic testing is the mainstay.

Two types of serologic tests must be performed to diagnose syphilis: a nontreponemal test and a treponemal test.[8]

Nontreponemal tests:

- The Venereal Disease Research Laboratory (VDRL) test
- The rapid plasma reagin (RPR) test.

Treponemal tests:

- *T pallidum* passive particle agglutination (TP-PA) assay
- Fluorescent treponemal antibody absorbed (FTA-ABS) test
- Enzyme immunoassay (EIA)
- Chemiluminescence immunoassay (CIA).

Using only one type of serologic test is insufficient for diagnosis because each type has limitations, including the possibility of false-positive results.

Nontreponemal test results may correlate with disease activity, and results should be reported quantitatively; a four-fold change in titer, equivalent to a change of two dilutions, is needed to demonstrate a clinically significant difference between two nontreponemal test results using the same serologic test.[8]

Which order of testing for syphilis is best?

The CDC recommends that nontreponemal tests be used to screen for syphilis and treponemal tests be used to confirm the diagnosis.[36] This traditional algorithm performs well in identifying persons with active infection who require further evaluation and treatment, while minimizing false-positive results in low-prevalence populations.

However, some clinical laboratories have adopted the reverse sequence, using treponemal tests (usually an EIA or a CIA) to screen for syphilis, followed by a nontreponemal test to confirm active infection.[36–38] This reverse-sequence testing may result in overdiagnosis and overtreatment of syphilis in some clinical settings.[37] When reverse-sequence syphilis screening is used, the CDC recommends reflexively testing all sera that produce reactive EIA or CIA results with a quantitative nontreponemal test and reflexively testing sera with discordant results (ie, a reactive EIA or CIA and a nonreactive RPR or VDRL test) with a different treponemal test.[36]

Traditionally, the FTA-ABS test had been considered the gold standard treponemal test; however, it has lower specificity than other treponemal tests. Accordingly, TP-PA is the recommended confirmatory treponemal test.[8,39] False-negative results, although rare, may occur for biological or technical reasons, such as the prozone phenomenon, resulting in a missed diagnosis. The prozone phenomenon occurs when the antibody titer is high and antigen binding sites are saturated, preventing the cross-linking reaction between antigens and antibodies. In this instance, when syphilis is suspected clinically and the RPR assay is nonreactive, the clinician can request RPR testing at dilutions of sera, ie, diluting the patient's serum to bring the antibody concentration into the zone equivalence.[40]

Suspect neurosyphilis if neurologic symptoms arise

Central nervous system involvement can occur at any stage of syphilis. If clinical evidence of neurologic involvement (meningitis, stroke, cranial nerve dysfunction, or auditory or ophthalmic abnormalities) is observed in any patient with syphilis, regardless of stage, a cerebrospinal fluid examination should be performed.[8] Laboratory testing can support the diagnosis of neurosyphilis; however, no single laboratory test can be used to diagnose it.

Cerebrospinal fluid abnormalities (ie, mononuclear pleocytosis, increased protein) are common in patients with early syphilis even in the absence of clinical neurologic findings. There is no firm evidence to support diverging from recommended treatment for early syphilis in these patients.[35]

Cerebrospinal fluid examination is recommended for all patients with serologic evidence of syphilis infection and neurologic symptoms and for patients who do not achieve an adequate serologic decline with stage-appropriate treatment.[8]

Penicillin is still the mainstay of syphilis treatment

Penicillin is still the mainstay of syphilis treatment.

- Patients with early syphilis (primary, secondary, or early latent) should receive a single intramuscular dose of benzathine penicillin G (2.4 million units).[8,35]
- Patients with late latent syphilis should receive three intramuscular doses of benzathine penicillin G (2.4 million units each) at 1-week intervals.
- Neurosyphilis should be treated with aqueous crystalline penicillin G 18 to 24 million units daily for 10 to 14 days.[8]

Neurologic involvement can occur at any stage of syphilis

Doxycycline is the preferred alternative in nonpregnant patients who are allergic to penicillin. The dosage is 100 mg orally twice a day for 14 days (for primary, secondary, or early latent infections) or for 28 days (for late latent infections or those of unknown duration).[35,41]

Ceftriaxone (1–2 g daily) may be effective for treating early syphilis. However, data are limited, and the optimal dose and duration of therapy are not defined.[8,42]

Azithromycin in a single 2-g oral dose is effective for treating early syphilis. However, *T pallidum* chromosomal mutations associated with macrolide resistance are being detected.[35,43] In view of this, azithromycin should not be used in men who have sex with men or in pregnant women.

Follow-up of syphilis patients and partners

Close clinical and serologic follow-up is strongly advised in persons who receive an alternate regimen to evaluate for treatment failure.[8]

Sex partners of patients with primary syphilis should be considered at risk and given treatment if they had sexual contact with the patient within 3 months plus the duration of symptoms, within 6 months plus the duration of symptoms for those with secondary syphilis, or 1 year for patients with early latent syphilis.[8]

Serologic and clinical evaluation should be repeated at 6, 12, and 24 months after treatment. HIV-infected patients should receive closer follow-up, ie, at 3, 6, 9, 12, and 24 months. The same quantitative nontreponemal serologic test should be used at each visit, with at least a fourfold decrease in titer representing an appropriate serologic decline.

Failure to achieve an appropriate serologic decline in 6 to 12 months may represent treatment failure.[8] Optimal management in this instance is unclear; at a minimum, additional clinical and serologic follow-up should be performed.[8] If additional follow-up cannot be ensured, retreatment (weekly intramuscular injections of benzathine penicillin G 2.4 million units for 3 weeks) is recommended. Cerebrospinal fluid examination can be considered to exclude unrecognized neurosyphilis.[8]

Resistance to azithromycin appears to be emerging in *T pallidum*

URETHRITIS: GONORRHEA, CHLAMYDIA TOP THE LIST

Symptoms of urethritis can include dysuria, discharge (purulent or mucopurulent), and urethral pruritus.[26] However, asymptomatic infections are common.[8]

Several organisms are associated with infectious urethritis, including[26]:

- *Neisseria gonorrhoeae*
- *Chlamydia trachomatis*
- *Mycoplasma genitalium*
- *Trichomonas vaginalis*
- *Ureaplasma urealyticum*.

Diagnosing urethritis: Try to identify the agent

The clinician should attempt to obtain objective evidence of urethral inflammation. Urethral discharge should be examined with microscopy using Gram stain or methylene blue, or a first-void urine sample should be tested with microscopy and leukocyte esterase.[26] If clinic-based diagnostic testing is not available, testing for *N gonorrhoeae* and *C trachomatis* using nucleic acid amplification can identify additional infections.[8]

During the clinic visit, either Gram-stain microscopy of a urethral swab or microscopic examination of a first-catch urine sample may identify the causative agent. If gram-negative intracellular diplococci are seen on urethral smear, gonorrhea infection is diagnosed. Nongonococcal urethritis is diagnosed when microscopy or urinalysis displays evidence of inflammation (positive leukocyte esterase or at least 10 white blood cells per high-power field) without gram-negative intracellular diplococci.[8]

Testing should be performed to determine the specific cause of urethritis, because both chlamydia and gonorrhea are reportable diseases. Nucleic acid amplification tests are the most sensitive tests for *C trachomatis* and *N gonorrhoeae* and can be performed on urethral swabs or urine.[44] If clinic-based diagnostic tools are unavailable, patients should receive empiric treatment for chlamydia and gonorrhea.[8]

Treatment of urethritis, by organism

Urethral gonorrhea should be treated with dual therapy: ceftriaxone 250 mg in a single intramuscular dose and either azithromycin 1 g orally as a single dose or doxycycline 100 mg orally twice a day for 7 days. Oral cephalosporins are no longer recommended as first-line treatment of gonorrhea.[45]

Chlamydial urethritis is treated with azithromycin 1 g in a single oral dose or doxycycline 100 mg orally twice a day for 7 days. Although azithromycin provides the advantages of a single-dose regimen administered and directly observed by the provider, some evidence suggests that doxycycline may be more effective than azithromycin for symptomatic chlamydial urethritis.[46]

All sex partners within the preceding 60 days should be referred for evaluation, testing, and empiric treatment with a drug regimen effective against chlamydia (if nongonococcal urethritis or only C *trachomatis* was identified) and gon-

orrhea (if *N gonorrhoeae* was identified). When patients diagnosed with chlamydia or gonorrhea indicate that their partners are unlikely to seek evaluation, providers can offer patient-delivered partner therapy, a form of expedited partner therapy in which partners of infected persons are treated without previous medical evaluation. Providers should visit www.cdc.gov/std/ept for updated information for their individual jurisdiction, as expedited partner therapy is prohibited in some states. No studies have been published involving patient-delivered partner therapy for chlamydia or gonorrhea in men who have sex with men.[8]

Patients with recurrent or persistent urethritis can be retreated with the initial regimen if they did not comply with treatment or were reexposed to an untreated sex partner. However, persistent urethritis after doxycycline therapy may suggest the presence of doxycycline-resistant *M genitalium* or *U urealyticum*. *T vaginalis* may also cause urethritis in men. Diagnostic evaluation may include culture or nucleic acid amplification testing of a urethral swab or urine (ie, PCR [Amplicor] or transcription-mediated amplification).[8]

M *genitalium* or *U urealyticum* urethritis. Currently, no commercially available diagnostic test exists for *M genitalium* or *U urealyticum*, so clinicians must choose a treatment regimen on the basis of objective evidence of inflammation in the absence of an etiologic agent. If azithromycin was not given during the initial course, metronidazole 2 g orally or tinidazole 2 g orally in a single dose plus azithromycin 1 g orally should be considered.[8]

M genitalium is one of the most common pathogens in men with persistent urethritis, accounting for 15% to 25% of cases. Several studies have shown that moxifloxacin 400 mg orally daily for 7 days is effective against *M genitalium*.[46–48] Therefore, men for whom an initial regimen of azithromycin fails should be retreated with moxifloxacin 400 mg orally once daily for 7 days.

If men require treatment with a new antibiotic regimen for persistent urethritis and a sexually transmitted agent is the suspected cause, all partners in the past 60 days before the initial diagnosis and any interim partners should be referred for evaluation and appropriate treatment.

CERVICITIS: CHLAMYDIA, GONORRHEA, OTHERS

Cervicitis is frequently asymptomatic, but signs on pelvic examination may include purulent or mucopurulent endocervical exudate and sustained endocervical bleeding easily induced by passage of a cotton swab through the cervical os.[26]

In most cases, the pathogen cannot be identified.[49] When an organism is isolated, it is typically *C trachomatis* or *N gonorrhoeae*. Others that may cause cervicitis include the organisms responsible for bacterial vaginosis, *T vaginalis*, HSV, and possibly *M genitalium*.[50]

Diagnostic workup for cervicitis

Diagnostic workup for cervicitis should include microscopic evaluation of an endocervical specimen and testing for *C trachomatis* and *N gonorrhoeae*. A finding of leukorrhea (> 10 white blood cells per high-power field on microscopic examination of vaginal fluid) has been associated with chlamydial and gonococcal infection of the cervix.[8] In the absence of inflammatory vaginitis, leukorrhea might be a sensitive indicator of cervical inflammation, with a high negative predictive value.

Determine the specific cause of urethritis, because chlamydia and gonorrhea are reportable diseases

Nucleic acid amplification testing for *C trachomatis* and *N gonorrhoeae* can be performed on urine, endocervical, or vaginal swab specimens collected by the clinician or self-collected.[51] The performance of *C trachomatis* nucleic acid amplification testing on patient-collected vaginal swab specimens has similar sensitivity and specificity to those performed on cervical and first-void urine samples.[26,44,52]

Women with cervicitis also should be evaluated for bacterial vaginosis and trichomoniasis, and if the organisms that cause these conditions are detected, treatment is advised. Microscopy has a low sensitivity (approximately 50%) for detecting *T vaginalis*; if the organism is not identified, further testing such as culture may be performed to exclude it as the pathogen.

Women with cervicitis should also be evaluated for clinical signs of pelvic inflammatory disease, including uterine, adnexal, and cervical motion tenderness, and fever.

Cervicitis can be treated presumptively

Women with cervicitis who should receive presumptive therapy include those at higher risk of chlamydial infection (ie, those with new or multiple sex partners, those age 25 or younger, and those who engage in unprotected intercourse, especially if follow-up cannot be ensured).[8]

Recommended therapy is either azithromycin 1 g orally in a single dose or doxycycline 100 mg orally twice a day for 7 days. The clinician should consider dual therapy to cover gonorrhea if the prevalence of gonorrhea is more than 5% (ie, in younger patients).[8] If bacterial vaginosis or *T vaginalis* infection is diagnosed, these conditions should be treated at the time of clinical evaluation (see vaginitis section for more detail). For women in whom presumptive therapy is deferred, the results of diagnostic testing should guide appropriate treatment.

Repeat testing 3 to 6 months after treatment is recommended for all women diagnosed with chlamydia or gonorrhea,[53] and all sex partners in the past 60 days should be referred for evaluation and receive treatment for the STDs for which the index patient received treatment. In states where it is allowed, patient-delivered partner therapy should be considered if the patient indicates her partner is unlikely to seek medical evaluation.

The data are limited on how to manage recurrent bacterial vaginosis

VAGINITIS: NOT JUST YEAST

Women with vaginitis may present with complaints of discharge, pruritus, or a bad vaginal odor. A careful medical history, including information on sexual behaviors and vaginal hygiene practices (ie, douching), should be conducted in addition to physical examination and diagnostic testing.

The most common conditions associated with vaginitis are bacterial vaginosis, trichomoniasis, and candidiasis. However, vulvovaginal candidiasis, most often caused by *Candida albicans*, is not transmitted sexually and will not be reviewed further here. Although bacterial vaginosis is associated with known risk factors for STDs (eg, new or multiple sex partners), the cause of the microbial alteration that precipitates it is not known.[44] Co-infection with *T vaginalis* is extremely common.[54]

BACTERIAL VAGINOSIS: VERY COMMON

Bacterial vaginosis is the most common genital infection in reproductive-age women.[55] It is a polymicrobial syndrome in which anaerobic bacteria (*Prevotella* and *Mobiluncus* species), *Gardnerella vaginalis*, *Ureaplasma*, and *Mycoplasma* replace the normal vaginal flora.

Diagnosis of bacterial vaginosis

Bacterial vaginosis can be diagnosed by clinical criteria or Gram staining. Clinical diagnosis requires three of the following clinical criteria proposed by Amsel et al[56]:

- Clue cells
- Vaginal fluid pH > 4.5
- Fishy odor before or after addition of 10% potassium hydroxide
- Thin, homogeneous, white discharge that smoothly coats the vaginal walls.

The clinical utility of PCR for diagnosing *G vaginalis* remains unclear, and culture is not recommended because it has low specificity. Gram staining can be used to determine the concentration of lactobacilli, small gram-negative or variable rods (*G vaginalis* and anaerobic rods), and curved gram-negative rods (ie, *Mobiluncus* species).

Treatment of bacterial vaginosis: Metronidazole or clindamycin

Treatment is recommended to relieve vaginal symptoms, with the potential benefit of reducing the risk of acquiring chlamydia, gonorrhea, and HIV and other viral STDs.[8]

Recommended treatment is with metronidazole 500 mg orally twice a day for 7 days, metronidazole gel 0.75% vaginal suppository once a day for 5 days, or clindamycin cream 2% vaginal suppository once a day for 7 days.[44] A meta-analysis of several trials found that clindamycin and metronidazole have equivalent effectiveness for eradicating bacterial vaginosis symptoms.[57] Accordingly, providers can consider patient preference, co-infections, and possible side effects when selecting a regimen. Alternative regimens include tinidazole or clindamycin orally or in vaginal ovules.

Women should be advised to refrain from sexual intercourse during treatment. Routine treatment of male or female sexual partners is not warranted.

Bacterial vaginosis commonly recurs, and limited data exist regarding optimal management of recurrences. Using a different treatment regimen may be an option in patients who have a recurrence; however, re-treatment with the same topical regimen is an acceptable approach for treating recurrent bacterial vaginosis during the early stages of infection.[58] One study suggests that metronidazole for 7 days, followed by intravaginal boric acid for 21 days, and then, for those in remission, suppressive metronidazole gel for 16 weeks may be another option.[59] For women with multiple recurrences, metronidazole gel twice weekly for 4 to 6 months has been shown to reduce recurrences, although its benefit may not persist after it is stopped. The therapeutic role for probiotics remains unclear.[60]

TRICHOMONIASIS: TREAT PARTNERS

Although most women with trichomoniasis have few or no symptoms, some have vaginal discharge that may be diffuse, malodorous, and yellow-greenish, and some have vulvar irritation.

Diagnosis of trichomoniasis: Microscopy is first-line but insensitive

The most common method for diagnosing *T vaginalis* infection remains microscopic evaluation of wet preparations of genital secretions, because of its convenience and relatively low cost. This may demonstrate the motile, flagellated protozoa *T vaginalis* and many white blood cells. Slides of vaginal fluid specimens should be examined immediately after collection to maximize performance. Unfortunately, the sensitivity of wet preparation is 44% to 80% in vaginal specimens.[61]

Culture is still considered the gold standard for diagnosing trichomoniasis and, if available, should be performed when direct microscopy is unrevealing.

Point-of-care diagnostic tests for *T vaginalis* infection include the OSOM Trichomonas Rapid Test (Sekisui Diagnostics, San Diego, CA), which is an immunochromatographic capillary flow dipstick test, and the Affirm VPIII (Becton, Dickinson and Company, Franklin Lakes, NJ), a nucleic acid probe-hydridization test that identifies *T vaginalis*, G *vaginalis*, and C *albicans*.[44,62] Liquid-based Pap tests may demonstrate *T vaginalis*, although they should not be performed exclusively for this purpose. Among women, nucleic acid amplification tests may detect a prevalence three to five times higher than indicated by wet mount microscopy. The APTIMA *Trichomonas vaginalis* assay (Hologic Gen-Probe, San Diego, CA) was the most sensitive test for trichomonas detection in this study.[63]

Extragenital testing with nucleic acid amplification tests is not recommended for *T vaginalis*, as it remains unclear if the rectum can serve as a reservoir for infection, and *T vaginalis* has not been found to infect oral sites.[8]

Treatment of trichomoniasis: Metronidazole or tinidazole

Nitroimidazoles, ie, metronidazole and tinidazole, are the only class of drugs available to treat trichomoniasis. The recommended regimen is metronidazole or tinidazole 2 g orally in a single dose. Studies suggest that tinidazole may be superior to metronidazole, with higher cure rates due to its longer half-life and higher tissue concentrations.[64]

Low-level metronidazole resistance is estimated to occur in 2% to 5% of trichomoniasis infections[65]; high-level resistance occurs rarely. If a single dose of metronidazole 2 g fails to cure the infection and reinfection is ruled out, the patient should be treated with metronidazole 500 mg orally twice a day for 7 days. If this regimen is not effective, providers can consider tinidazole or metronidazole 2 g orally for 7 days.[44,62,64] Consultation and susceptibility testing for *T vaginalis* is available from the CDC if these alternative regimens are ineffective.

***T vaginalis* infection has a high rate of transmission to sexual partners**

T vaginalis infection has a high rate of transmission to sexual partners,[66] and all partners should be treated. Male sexual partners should be treated with metronidazole 500 mg twice a day orally for 7 days, tinidazole 2 g orally in a single dose, or tinidazole 500 mg twice a day for 7 days. Patient-delivered partner therapy may have a role in partner management for trichomoniasis.[67]

PROCTITIS: SUSPECT LYMPHOGRANULOMA VENEREUM

Acute proctitis in men and women who practice receptive anal intercourse is usually sexu-

ally acquired. The most common causative organisms are *N gonorrhoeae*, *C trachomatis* (serotypes associated with or not associated with lymphogranuloma venereum), and HSV; *T pallidum* is less common.[6,8] Co-infections are not uncommon in this setting.[6,9]

Symptoms of proctitis may include anal discharge, rectal ulcers and bleeding, anorectal pain, tenesmus, and constipation. Patients with lymphogranuloma venereum may also present with tender, fluctuant inguinal or femoral lymphadenopathy (buboes), or herpetiform genital ulcers or papules.

Diagnosis of proctitis

Clinical evaluation should include digital rectal examination and anoscopy (if possible) to look for abnormalities such as ulcerations, hemorrhoids, anal fissures, condylomas, strictures, exudate, and bleeding.

Appropriate diagnostic testing includes Gram staining and culture of discharge, herpes viral culture or PCR, and nucleic acid amplification testing for chlamydia and gonorrhea (in laboratories with Clinical Laboratory Improvement Amendments validation).[8]

Nucleic acid amplification tests detect *C trachomatis* serotypes L1–L3, responsible for lymphogranuloma venereum, and non-lymphogranuloma venereum serotypes A–K, but cannot distinguish between the two, whereas PCR-based genotyping can.[8,26] Although this distinction is important to ensure appropriate evaluation and management of sex partners, empiric treatment for lymphogranuloma venereum (doxycycline 100 mg orally twice a day for 21 days) should be provided to patients at high risk, including men who have sex with men and who have anorectal chlamydia, HIV infection, or bloody discharge and perianal or mucosal ulcers.[8]

Treatment of proctitis

Patients with painful perianal or mucosal ulceration should receive presumptive treatment for lymphogranuloma venereum and HSV while awaiting results of diagnostic testing. If rectal discharge is detected or Gram staining of anorectal secretions detects polymorphonuclear leukocytes, treatment should include ceftriaxone 250 mg intramuscularly and doxycycline 100 mg orally twice a day for 7 days.[8] Additional testing for syphilis and HIV should also be performed.

All sexual partners should be evaluated for any disease diagnosed in the index patient. ■

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***ADDRESS**: Robyn Neblett Fanfair, MD, MPH, Division of Sexually Transmitted Disease Prevention, National Center for HIV–AIDS, Viral Hepatitis, STD, and TB Prevention, Centers for Disease Control and Prevention, 1600 Clifton Road NE, MS E-02, Atlanta, GA 30333; e-mail: iyo5@cdc.gov*