Official websites use .gov A .gov website belongs to an official government organization in the United States. Secure .gov websites use HTTPS A lock ( ) or https:// means you've safely connected to the .gov website. Share sensitive information only on official, secure websites. Urethritis, as characterized by urethral inflammation, can result from either infectious or noninfectious conditions. Symptoms, if present, include dysuria, urethral pruritis, and mucoid, mucopurulent, or purulent discharge. Signs of urethral discharge on examination can also be present among persons without symptoms. Although N. gonorrhoeae and C. trachomatis are well established as clinically important infectious causes of urethritis, M. genitalium has been strongly associated with urethritis and, less commonly, prostatitis (691–697). If POC diagnostic tools (e.g., Gram, methylene blue [MB], or gentian violet [GV] stain microscopy) are unavailable, drug regimens effective against both gonorrhea and chlamydia should be administered. Further testing to determine the specific etiology is recommended for preventing complications, reinfection, and transmission because a specific diagnosis might improve treatment compliance, delivery of risk-reduction interventions, and partner services. Both chlamydia and gonorrhea are reportable to health departments. NAATs are preferred for detecting C. trachomatis and N. gonorrhoeae, and urine is the preferred specimen for males (553). NAAT-based tests for diagnosing T. vaginalis among men with urethritis have not been cleared by FDA; however, laboratories have performed the CLIA-compliant validation studies (698) needed to provide such testing. Multiple organisms can cause infectious urethritis. The presence of gram-negative intracellular diplococci (GNID) or purple intracellular diplococci (MB or GV) on urethral smear is indicative of presumed gonococcal infection, which is frequently accompanied by chlamydial infection. Nongonococcal urethritis (NGU), which is diagnosed when microscopy of urethral secretions indicate inflammation without GNID or MB or GV purple intracellular diplococci, is caused by C. trachomatis in 15%–40% of cases; however, prevalence varies by age group, with a lower proportion of disease occurring

among older men (699). Documentation of chlamydial infection as NGU etiology is essential because of the need for partner referral for evaluation and treatment to prevent complications of chlamydia, especially for female partners. Complications of C. trachomatis–associated NGU among males include epididymitis, prostatitis, and reactive arthritis. M. genitalium is associated with symptoms of urethritis and urethral inflammation and accounts for 15%–25% of NGU cases in the United States (691–693,696,697,700). Among men with symptoms of urethritis, M. genitalium was detected in 11% of those with urethritis in Australia (701), 12%–15% in the United Kingdom (702–704), 15% in South Africa (696), 19% in China (705), 21% in Korea, 22% in Japan (706), and 28.7% in the United States (range: 20.4%–38.8%) (697). Data are inconsistent regarding other Mycoplasma and Ureaplasma species as etiologic agents of urethritis (707). The majority of men with Ureaplasma infections do not have overt disease unless a high organism load is present. T. vaginalis can cause urethritis among heterosexual men; however, the prevalence varies substantially by U.S. geographic region, age, and sexual behavior and within specific populations. Studies among men with and without overt urethritis in developed countries document relatively low rates of T. vaginalis in the Netherlands (0.5%) (708), Japan (1.3%) (706,709), the United States (2.4%) (710), and the United Kingdom (3.6%) (703). Studies in other countries have documented higher rates, such as in Croatia (8.2%) (711) and Zimbabwe (8.4%) (712), particularly among symptomatic patients. Neisseria meningitidis can colonize mucosal surfaces and cause urethritis (713). Urogenital N. meningitidis rates and duration of carriage, prevalence of asymptomatic and symptomatic infection, and modes of transmission have not been systematically described; however, studies indicate that N. meningitidis can be transmitted through oral-penile contact (i.e., fellatio) (714–716). N. meningitidis has similar colony morphology appearance on culture and cannot be distinguished from N. gonorrhoeae on Gram stain. Identification of N. meningitidis as the etiologic agent with presumed gonococcal urethritis on the

basis of Gram stain but negative NAAT for gonorrhea requires a confirmation by culture. Meningococcal urethritis is treated with the same antimicrobial regimens as gonococcal urethritis. Although evidence is limited regarding the risk for sexual transmission or recurrent infections with meningococcal urethritis, treatment of sex partners of patients with meningococcal urethritis with the same antimicrobial regimens as for exposure to gonococcal infection can be considered. No indication exists for treating persons with N. meningitidis identified in their oropharynx when not also associated with symptomatic urethritis. In other instances, NGU can be caused by HSV, Epstein-Barr virus, and adenovirus (699) acquired by fellatio (i.e., oral-penile contact). In a retrospective review of 80 cases of HSV urethritis in Australia (717), the majority of infections were associated with HSV-1 with clinical findings of meatitis (62%), genital ulceration (37%), and dysuria (20%). Adenovirus can present with dysuria, meatal inflammation, and conjunctivitis (718). Enteric bacteria have been identified as an uncommon cause of NGU and might be associated with insertive anal intercourse (699). Other bacterial pathogens have been implicated as potential causes of clinical urethritis, either in clustered case series or as sporadic cases such as Haemophilus influenzae and Haemophilus parainfluenzae (719–723). Haemophilus was identified in 12.6% of cases among 413 men (mostly MSM reporting insertive oral sex) (724), and high rates of azithromycin resistance (39.5%) were identified among Haemophilus urethritis patients (725). Individual case reports have linked NGU to multiple bacterial species, including Corynebacterium propinquum (726), Kurthia gibsonii (727), Corynebacterium glucuronolyticum (728,729), Corynebacterium striatrium (730), Aerococcus urinae (731), and Neisseria elongata (732). Diagnostic testing and treatment for less-common organisms are reserved for situations in which these infections are suspected (e.g., sexual partner with trichomoniasis, urethral lesions, or severe dysuria and meatitis) or when NGU is not responsive to recommended therapy. Even in settings that provide comprehensive diagnostic testing, etiology can remain obscure in half of cases.

Idiopathic NGU was reported in 772 (59%) of 1,295 first presentations of NGU among men seeking sexual health services in Australia (701). In a case-control study of 211 men with NGU symptoms in Denmark, no identifiable pathogen was identified in 24% of acute cases and 33% of chronic cases (733). NGU's importance if not caused by a defined pathogen is uncertain; neither complications (e.g., urethral stricture or epididymitis) nor adverse outcomes among sex partners have been identified in these cases. Associations between NGU and insertive anal and oral exposure have been reported (734), as have higher rates of BV-associated Leptotrichia or Sneathia species among heterosexual men with urethritis (735). These studies increase concern for possible undetected infectious rectal or vaginal pathogens, or alternatively, a transient reactive dysbiosis after exposure to a new microbiome or even a noninfectious reactive etiology (736). Clinicians should attempt to obtain objective evidence of urethral inflammation. If POC diagnostic tests (e.g., Gram stain or MB or GV microscopy) are unavailable, urethritis can be documented on the basis of any of the following signs or laboratory tests: Men evaluated in settings in which Gram stain or MB or GV smear is unavailable who meet at least one criterion for urethritis (i.e., urethral discharge, positive leukocyte esterase test on first void urine, or microscopic examination of first-void urine sediment with ≥10 WBCs/HPF) should be tested for C. trachomatis and N. gonorrhoeae by NAATs and treated with regimens effective against gonorrhea and chlamydia. If symptoms are present but no evidence of urethral inflammation is present, NAATs for C. trachomatis and N. gonorrhoeae might identify infections (739). Persons with chlamydia or gonorrhea should receive recommended treatment, and sex partners should be referred for evaluation and treatment. If none of these clinical criteria are present, empiric treatment of men with symptoms of urethritis is recommended only for those at high risk for infection who are unlikely to return for a follow-up evaluation or test results. Such men should be treated with drug regimens effective against gonorrhea and chlamydia. NGU is a nonspecific diagnosis that can

have various infectious etiologies. C. trachomatis has been well established as an NGU etiology; however, prevalence varies across populations and accounts for <50% of overall cases (712,740–742). M. genitalium is estimated to account for 10%–25% of cases (696,697,701,703,704,706,733,743), and T. vaginalis for 1%–8% of cases depending on population and location (703,706,708,710,712). Other etiologies include different bacteria, such as Haemophilus species (724,725), N. meningitidis (713,716), HSV (706,717), and adenovirus (744). However, even when extensive testing is performed, no pathogens are identified in approximately half of cases (701,733). Clinical presentation can include urethral discharge, irritation, dysuria, or meatal pruritus (697,743,745). NGU is confirmed for symptomatic men when diagnostic evaluation of urethral secretions indicates inflammation, without evidence of diplococci by Gram, MB, or GV smear on microscopy (712,746,747). Visible discharge or secretions can be collected by a swab without inserting it into the urethra; if no visible secretions, the swab can be inserted into the urethral meatus and rotated, making contact with the urethral wall before removal. If microscopy is unavailable, urine testing for leukocyte esterase can be performed on first-void urine, and microscopic examination of sediment from a spun first-void urine demonstrating ≥10 WBCs/HPF has a high negative predictive value. All men who have suspected or confirmed NGU should be tested for chlamydia and gonorrhea by using NAATs. A specific diagnosis can potentially reduce complications, reinfection, and transmission. M. genitalium testing should be performed for men who have persistent or recurrent symptoms after initial empiric treatment. Testing for T. vaginalis should be considered in areas or among populations with high prevalence, in cases where a partner is known to be infected, or for men who have persistent or recurrent symptoms after initial empiric treatment. Ideally, treatment should be pathogen based; however, diagnostic information might not be immediately available. Presumptive treatment should be initiated at NGU diagnosis. Doxycycline is highly effective for chlamydial urethral infections and is also effective for chlamydial

infections of the rectum; it also has some activity against M. genitalium. In contrast, reports have increased of azithromycin treatment failures for chlamydial infection (748,749), and the incidence of macrolide resistance in M. genitalium also has been rapidly rising (697,702,705,750,751). Pharmacokinetic data indicate that changing azithromycin dosing from a single-dose strategy to a multiday strategy might protect against inducing resistance in M. genitalium infections (745,752) (see Mycoplasma genitalium). Doxycycline 100 mg orally 2 times/day for 7 days Azithromycin 1 g, orally in a single dose

OR

Azithromycin 500 mg orally in a single dose; then 250 mg orally daily for 4 days To maximize compliance with recommended therapies, medications should be dispensed on-site at the clinic, and, regardless of the number of doses involved in the regimen, the first dose should be directly observed. Erythromycin is no longer recommended for NGU because of its gastrointestinal side effects and dosing frequency. Levofloxacin is no longer recommended for NGU because of its inferior efficacy, especially for M. genitalium. To minimize transmission and reinfections, men treated for NGU should be instructed to abstain from sexual intercourse until they and their partners have been treated (i.e., until completion of a 7-day regimen and symptoms have resolved or for 7 days after single-dose therapy). Men with NGU should be tested for HIV and syphilis. Men should be provided their testing results obtained as part of the NGU evaluation. Those with a specific diagnosis of chlamydia, gonorrhea, or trichomoniasis should be offered partner services and instructed to return 3 months after treatment for repeat testing because of high rates of reinfection, regardless of whether their sex partners were treated (136,137,753,754) (see Chlamydial Infections; Gonococcal Infections; Trichomoniasis). If symptoms persist or recur after therapy completion, men should be instructed to return for reevaluation and should be tested for M. genitalium and T. vaginalis. Symptoms alone, without documentation of signs or laboratory evidence of

urethral inflammation, are insufficient basis for retreatment. Providers should be alert to the possible diagnosis of chronic prostatitis or chronic pelvic pain syndrome in men experiencing persistent perineal, penile, or pelvic pain or discomfort; voiding symptoms; pain during or after ejaculation; or new-onset premature ejaculation lasting for >3 months. Men with persistent pain should be referred to a urologist with expertise in pelvic pain disorders. All sex partners of men with NGU within the preceding 60 days should be referred for evaluation and testing and presumptive treatment with a drug regimen effective against chlamydia. All partners should be evaluated and treated according to the management section for their respective pathogen; EPT could be an alternate approach if a partner is unable to access timely care. To avoid reinfection, sex partners should abstain from sexual intercourse until they and their partners are treated. The objective diagnosis of persistent or recurrent NGU should be made before considering additional antimicrobial therapy. Symptomatic recurrent or persistent urethritis might be caused by treatment failure or reinfection after successful treatment. Among men who have persistent symptoms after treatment without objective signs of urethral inflammation, the value of extending the duration of antimicrobials has not been demonstrated. Treatment failure for chlamydial urethritis has been estimated at 6%–12% (755). The most common cause of persistent or recurrent NGU is M. genitalium, especially after doxycycline therapy (756,757). Treatment failure for M. genitalium is harder to determine because certain men achieve clinical cure (i.e., resolution of symptoms) but can still have detectable M. genitalium in urethral specimens (758). The initial step in recurrent urethritis is assessing compliance with treatment or potential reexposure to an untreated sex partner (697,743). If the patient did not comply with the treatment regimen or was reexposed to an untreated partner, retreatment with the initial regimen can be considered. If therapy was appropriately completed and no reexposure occurred, therapy is dependent on the initial treatment regimen. Ideally, diagnostic testing among men with recurrent or

persistent symptoms, including those with gonorrhea, chlamydia, M. genitalium, and trichomoniasis, can be used to guide further management decisions. T. vaginalis is also known to cause urethritis among men who have sex with women. In areas where T. vaginalis is prevalent, men who have sex with women with persistent or recurrent urethritis should be tested for T. vaginalis and presumptively treated with metronidazole 2 g orally in a single dose or tinidazole 2 g orally in a single dose; their partners should be referred for evaluation and treatment, if needed. If T. vaginalis is unlikely (MSM with NGU or negative T. vaginalis NAAT), men with recurrent NGU should be tested for M. genitalium by using an FDA-cleared NAAT. Treatment for M. genitalium includes a two-stage approach, ideally using resistance-guided therapy. If M. genitalium resistance testing is available it should be performed, and the results should be used to guide therapy (see Mycoplasma genitalium). If M. genitalium resistance testing is not available, doxycycline 100 mg orally 2 times/day for 7 days followed by moxifloxacin 400 mg orally once daily for 7 days should be used. The rationale for this approach is that although not curative, doxycycline decreases the M. genitalium bacterial load, thereby increasing likelihood of moxifloxacin success (759). Higher doses of azithromycin have not been effective for M. genitalium after azithromycin treatment failures. Men with persistent or recurrent NGU after treatment for M. genitalium or T. vaginalis should be referred to an infectious disease or urology specialist. NGU might facilitate HIV transmission (760). Persons with NGU and HIV infection should receive the same treatment regimen as those who do not have HIV. Two major diagnostic signs characterize cervicitis: 1) a purulent or mucopurulent endocervical exudate visible in the endocervical canal or on an endocervical swab specimen (commonly referred to as mucopurulent cervicitis), and 2) sustained endocervical bleeding easily induced by gentle passage of a cotton swab through the cervical os. Either or both signs might be present. Cervicitis frequently is asymptomatic; however, certain women might report an abnormal vaginal discharge and intermenstrual vaginal bleeding (e.g., especially after

sexual intercourse). The criterion of using an increased number of WBCs on endocervical Gram stain in the diagnosis of cervicitis has not been standardized; it is not sensitive, has a low positive predictive value for C. trachomatis and N. gonorrhoeae infections, and is not available in most clinical settings (297,761). Leukorrhea, defined as >10 WBCs/HPF on microscopic examination of vaginal fluid, might be a sensitive indicator of cervical inflammation with a high negative predictive value (i.e., cervicitis is unlikely in the absence of leukorrhea) (762,763). Finally, although the presence of gram-negative intracellular diplococci on Gram stain of endocervical exudate might be specific for diagnosing gonococcal cervical infection when evaluated by an experienced laboratorian, it is not a sensitive indicator of infection (764). C. trachomatis or N. gonorrhoeae is the most common etiology of cervicitis defined by diagnostic testing. Trichomoniasis, genital herpes (especially primary HSV-2 infection), or M. genitalium (761,765–768) also have been associated with cervicitis. However, in many cases of cervicitis, no organism is isolated, especially among women at relatively low risk for recent acquisition of these STIs (e.g., women aged >30 years) (769). Limited data indicate that BV and frequent douching might cause cervicitis (770–772). The majority of persistent cases of cervicitis are not caused by reinfection with C. trachomatis or N. gonorrhoeae; other factors might be involved (e.g., persistent abnormality of vaginal flora, M. genitalium, douching or exposure to other types of chemical irritants, dysplasia, or idiopathic inflammation in the zone of ectopy). Available data do not indicate an association between group B streptococcus colonization and cervicitis (773,774). No specific evidence exists for a role for Ureaplasma parvum or Ureaplasma urealyticum in cervicitis (707,761,765,775,776). Because cervicitis might be a sign of upper genital tract infection (e.g., endometritis), women should be assessed for signs of PID and tested for C. trachomatis and N. gonorrhoeae with NAAT on vaginal, cervical, or urine samples (553) (see Chlamydial Infections; Gonococcal Infections). Women with cervicitis also should be evaluated for concomitant BV and trichomoniasis. Because

sensitivity of microscopy for detecting T. vaginalis is relatively low (approximately 50%), symptomatic women with cervicitis and negative wet-mount microscopy for trichomonads should receive further testing (i.e., NAAT, culture, or other FDA-cleared diagnostic test) (see Trichomoniasis). Testing for M. genitalium with the FDA-cleared NAAT can be considered. Although HSV-2 infection has been associated with cervicitis, the utility of specific testing (i.e., PCR or culture) for HSV-2 is unknown. Testing for U. parvum, U. urealyticum, Mycoplasma hominis, or genital culture for group B streptococcus is not recommended. Multiple factors should affect the decision to provide presumptive therapy for cervicitis. Presumptive treatment with antimicrobials for C. trachomatis and N. gonorrhoeae should be provided for women at increased risk (e.g., those aged <25 years and women with a new sex partner, a sex partner with concurrent partners, or a sex partner who has an STI), if follow-up cannot be ensured, or if testing with NAAT is not possible. Trichomoniasis and BV should be treated if detected (see Bacterial Vaginosis; Trichomoniasis). For women at lower risk for STIs, deferring treatment until results of diagnostic tests are available is an option. If treatment is deferred and C. trachomatis and N. gonorrhoeae NAATs are negative, a follow-up visit to determine whether the cervicitis has resolved can be considered. Doxycycline 100 mg orally 2 times/day for 7 days * Consider concurrent treatment for gonococcal infection if the patient is at risk for gonorrhea or lives in a community where the prevalence of gonorrhea is high (see Gonococcal Infections). Azithromycin 1 g orally in a single dose To minimize transmission and reinfection, women treated for cervicitis should be instructed to abstain from sexual intercourse until they and their partners have been treated (i.e., until completion of a 7-day regimen or for 7 days after single-dose therapy) and symptoms have resolved. Women who receive a cervicitis diagnosis should be tested for syphilis and HIV in addition to other recommended diagnostic tests. Women receiving treatment should return to their provider for a follow-up visit to determine whether cervicitis has resolved. For women who are

untreated, a follow-up visit gives providers an opportunity to communicate test results obtained as part of the cervicitis evaluation. Providers should treat on the basis of any positive test results and determine whether cervicitis has resolved. Women with a specific diagnosis of chlamydia, gonorrhea, or trichomoniasis should be offered partner services and instructed to return in 3 months after treatment for repeat testing because of high rates of reinfection, regardless of whether their sex partners were treated (753). If symptoms persist or recur, women should be instructed to return for reevaluation. Management of sex partners of women treated for cervicitis should be tailored for the specific infection identified or suspected. All sex partners during the previous 60 days should be referred for evaluation, testing, and presumptive treatment if chlamydia, gonorrhea, or trichomoniasis was identified. EPT and other effective partner referral strategies are alternative approaches for treating male partners of women who have chlamydial or gonococcal infection (125–127) (see Partner Services). To avoid reinfection, sex partners should abstain from sexual intercourse until they and their partners are treated. Women with persistent or recurrent cervicitis despite antimicrobial therapy should be reevaluated for possible reexposure or treatment failure. If relapse or reinfection with a specific infection has been excluded, BV is not present, and sex partners have been evaluated and treated, management options for persistent cervicitis are undefined. In addition, the usefulness of repeated or prolonged administration of antimicrobial therapy for persistent symptomatic cervicitis remains unknown. The etiology of persistent cervicitis, including the potential role of M. genitalium (777), is unclear. M. genitalium might be considered for cases of cervicitis that persist after azithromycin or doxycycline therapy in which reexposure to an infected partner or medical nonadherence is unlikely. Among women with persistent cervicitis who were previously treated with doxycycline or azithromycin, testing for M. genitalium can be considered and treatment initiated on the basis of results of diagnostic testing (318) (see Mycoplasma genitalium). For women with persistent

symptoms that are clearly attributable to cervicitis, referral to a gynecologic specialist can be considered for evaluation of noninfectious causes (e.g., cervical dysplasia or polyps) (778). Women with cervicitis and HIV infection should receive the same treatment regimen as those who do not have HIV. Cervicitis can increase cervical HIV shedding, and treatment reduces HIV shedding from the cervix and thereby might reduce HIV transmission to susceptible sex partners (779–783). Diagnosis and treatment of cervicitis for pregnant women should follow treatment recommendations for chlamydia and gonorrhea (see Chlamydial Infections, Special Considerations, Pregnancy; Gonococcal Infections, Special Considerations, Pregnancy). According to U.S. Medical Eligibility Criteria for Contraceptive Use, 2016, leaving an IUD in place during treatment for cervicitis is advisable (58). However, current recommendations specify that an IUD should not be placed if active cervicitis is diagnosed (59). Next