Urethritis in adult males

Author: Laura H Bachmann, MD, MPH, FIDSA
Section Editor: Jeanne Marrazzo, MD, MPH, FACP, FIDSA
Deputy Editor: Allyson Bloom, MD

All topics are updated as new evidence becomes available and our peer review process is complete.

Literature review current through: Aug 2022. | **This topic last updated:** Oct 07, 2021.

INTRODUCTION

Urethritis, or inflammation of the urethra, is a common manifestation of sexually transmitted infections among males.

This topic addresses the clinical manifestations, diagnosis, and empiric treatment of urethritis. Details on the clinical manifestations, diagnosis, and treatment of specific pathogens that can cause urethritis are discussed elsewhere. (See "Epidemiology and pathogenesis of Neisseria gonorrhoeae infection" and "Treatment of uncomplicated Neisseria gonorrhoeae infections" and "Clinical manifestations and diagnosis of Chlamydia trachomatis infections" and "Treatment of Chlamydia trachomatis infection" and "Mycoplasma genitalium infection in males and females".)

The discussion in this topic is consistent with the 2021 Sexually Transmitted Infections Treatment Guidelines from the United States Centers for Disease Control and Prevention [1].

EPIDEMIOLOGY AND MICROBIOLOGY

Infectious urethritis is typically caused by a sexually transmitted pathogen; thus, most cases are seen in young, sexually active men.

Neisseria gonorrhoeae and *Chlamydia trachomatis* are commonly identified in cases of urethritis. *Mycoplasma genitalium* has also been strongly associated with urethritis.

Because *N. gonorrhoeae* is easily visualized on Gram stain, which has classically been the primary mode of evaluating urethral discharge in males, urethritis is traditionally classified as gonococcal versus nongonococcal in settings where microscopy is performed. While useful for clinical management, particularly as it relates to limiting unnecessary antibiotic exposure, the lack of available point-of-care microscopy in most settings renders this distinction less relevant.

Gonococcal urethritis — *N. gonorrhoeae* is a relatively common cause of urethritis in the United States and Europe, especially in urban areas and sexually transmitted infection (STI) clinics, although a large proportion of cases are diagnosed in private practices or health maintenance organizations [2].

In a study of 768 males screened for STIs at 11 different clinic settings in the United States in 2012, the prevalence of *N. gonorrhoeae* ranged from 21.6 percent among symptomatic to 1.4 percent among asymptomatic males [3]. The overall incidence of gonorrhea cases among males reported in the United States was 224.4 cases per 100,000 males in 2019, reflecting a 5.9 percent increase since 2018 and a 60.6 percent increase since 2015 [2]. These rate increases may be secondary to increased transmission, more comprehensive screening (ie, extragenital screening), or both [2]. However, incidence varies substantially by race and geographical region. As examples, gonorrhea rates are disproportionately higher among non-Hispanic Black males compared with non-Hispanic White males and are generally highest in the South compared with other regions in the country.

The burden of gonococcal urethritis may be even higher in certain regions of the developing world. As an example, in a study from South Africa, *N. gonorrhoeae* was detected in 62 percent of males with symptoms of urethritis [4].

Of note, coinfections with other sexually transmitted pathogens are common. In a study of more than 3800 heterosexual males and females attending an STI clinic, chlamydial coinfection was demonstrated in 20 percent of males and 42 percent of females with gonorrhea [5].

Neisseria meningitidis has also been reported as a cause of symptomatic urethritis clinically and microscopically similar to gonococcal urethritis in males [6-8]. In such cases, the source of the infection may be from asymptomatic carriage of the organism in the throat of an oral sex partner.

Nongonococcal urethritis — *C. trachomatis* is generally the most commonly identified cause of nongonococcal urethritis (NGU), with *M. genitalium* the second most common; however, almost half of all cases of NGU do not have a specific etiology identified.

In the United States, reported cases of *C. trachomatis* in males have increased every year between 2000 and 2019, with the exceptions of 2012 and 2013 [2]. The reported rate increased by 5.5 percent from 2018 to 2019. The increases may be due to increases in testing (including extragenital testing), increases in transmission, or both.

However, among NGU cases for which a pathogen is identified, the proportion caused by *C. trachomatis* may be decreasing [9]. Historically, *C. trachomatis* was estimated to be responsible for approximately 50 percent of cases of NGU [10], although other studies have reported that chlamydia accounts for only 15 to 30 percent of NGU cases [11-14]. This observation is likely a reflection of the use of a more diverse and sensitive set of diagnostic assays to detect other urethral pathogens, such as *M. genitalium* and *Trichomonas vaginalis*. *M. genitalium* is estimated to cause approximately 15 to 25 percent of NGU cases [1].

The proportion of cases of NGU attributable to different organisms varies by study and geographic region. A study of 329 males in Australia with symptoms of urethritis conducted between March 2004 and March 2005 detected *C. trachomatis* (20 percent), *M. genitalium* (9 percent), adenoviruses (4 percent), herpes simplex virus (HSV; 3 percent), and no pathogen (65 percent) [13]. In a trial of 305 males with symptomatic NGU in the United States conducted between November 2006 and April 2009, much higher prevalences were reported for *C. trachomatis* (43 percent), *M. genitalium* (31 percent), and *T. vaginalis* (13 percent) [15]. *T. vaginalis* is an important cause of NGU in heterosexual males in Africa, where the organism has been reported in up to 20 percent of cases [16-18].

Certain pathogens may be associated with specific demographic or behavioral features, and sexual practices may contribute to differences in causative agents of NGU in men who have sex with men (MSM) compared with MSW [19,20]. As examples, in the Australian study described above, HSV and adenovirus were detected more frequently among men who have sex with men and in association with a history of insertive oral sex [13,21]. In contrast, *C. trachomatis* and *M. genitalium* were associated with sex with women and unprotected vaginal sex. Insertive oral sex was also a significant risk factor in pathogen-negative NGU, suggesting that oropharyngeal microbiota may be a significant source of other bacterial and viral pathogens. Some studies suggest an association between NGU in men who have sex with women (MSW) and the bacteria associated with bacterial vaginosis [22].

Other organisms that can infrequently cause symptoms of urethritis include *Treponema pallidum*, as an endourethral syphilitic chancre may also lead to clinical urethritis, and *Haemophilus influenzae*, which may be transmitted through respiratory secretions from a carrier during oral sex [23,24]. The role of *Ureaplasma urealyticum* and *Ureaplasma parvum* as urethral pathogens is unclear since these organisms can also be found as commensals in hosts with no

evidence of disease. Several studies have identified an association between *Ureaplasma* spp and NGU [25-27], but others have not [13,28]. (See "Mycoplasma hominis and Ureaplasma infections", section on 'Nongonococcal urethritis'.)

CLINICAL MANIFESTATIONS

Dysuria, or discomfort with urination, is usually the chief complaint in males with urethritis and is reported in the majority of males with gonorrhea and over half of patients with nongonococcal urethritis (NGU) [29]. Other complaints include pruritus, burning, and discharge at the urethral meatus. Urethral discharge can range from mucoid or watery to frankly purulent and may be present throughout the day or may be scanty and only present on the first morning void. Some males notice grossly visible mucous threads in their morning urine stream. The incubation period is variable, but is typically four to seven days after exposure for gonococcal urethritis and five to eight days for NGU [30].

However, not all males with laboratory evidence of urethritis have symptoms. Five to 10 percent of cases of laboratory-documented gonococcal urethritis and up to 42 percent of males with NGU are asymptomatic [31,32].

On exam, discharge may be grossly evident or may only be detectable after gentle "stripping" or "milking" of the penis. The urethra can be milked from the base to the meatus by placing a gloved thumb along the ventral surface of the base of the penis and the forefinger on the dorsum, applying gentle pressure, and moving the hand slowly toward the meatus to expel any discharge for specimen collection [1,33]. The meatus may appear inflamed or edematous. Gram stain of the urethral discharge typically demonstrates an elevated number of polymorphonuclear leukocytes (picture 1). (See 'Gram stain of urethral sample' below.)

Certain clinical features can suggest distinct microbial etiologies; however, specific testing is required to identify the causative pathogen:

- An acute presentation of a frankly purulent urethral discharge is suggestive of, but not definitive for, gonorrhea.
- Patients with dysuria alone are more likely to have chlamydial infection.
- Dysuria that is accompanied by painful genital ulcers is most likely due to genital herpes simplex virus (HSV); patients with primary HSV infection may also complain of fever, tender local inguinal lymphadenopathy, and headache.

Nevertheless, the syndromes of gonococcal and nongonococcal urethritis often overlap and cannot be reliably distinguished only on clinical grounds. Additionally, urethritis due to HSV can present without evident ulceration. (See 'Determining the microbial etiology' below.)

A small minority of patients with urethritis, particularly due to *C. trachomatis*, may develop a reactive arthritis triad (formerly known as Reiter syndrome). This syndrome is discussed in detail elsewhere. (See "Reactive arthritis".)

The specific clinical manifestations of urethritis due to the various causative organisms are discussed in detail elsewhere. (See "Clinical manifestations and diagnosis of Chlamydia trachomatis infections", section on 'Urethritis' and "Mycoplasma genitalium infection in males and females", section on 'Nongonococcal urethritis in men' and "Mycoplasma hominis and Ureaplasma infections", section on 'Nongonococcal urethritis' and "Epidemiology, clinical manifestations, and diagnosis of genital herpes simplex virus infection", section on 'Clinical features' and "Clinical manifestations and diagnosis of Neisseria gonorrhoeae infection in adults and adolescents", section on 'Infection of the male urogenital tract'.)

DIAGNOSIS

Diagnostic criteria — The diagnosis of urethritis can be confirmed in a symptomatic male patient by the presence of one of the following findings [1]:

- Mucoid, mucopurulent, or purulent discharge on examination
- Any of the following urethral swab Gram stain findings suggestive of urethritis (a methylene blue or gentian violet [MB or GV] stain can alternatively be used):
  - ≥2 white blood cells (WBC) per oil immersion field in high prevalence settings (eg, sexually transmitted infection clinics)
  - ≥5 WBC per oil immersion field in lower prevalence settings (eg, family planning clinics)
  - Gram-negative diplococci visualized within WBC (on MB or GV stain, these appear dark purple), consistent with presumed gonococcal infection
- Positive leukocyte esterase ("dipstick") or the presence of ≥10 WBCs per high power field of the first-void or first-catch spun urine

If none of these findings are present, a presumptive or suspected diagnosis of urethritis can be made in sexually active males with suggestive symptoms. Many clinical sites may not have

ready access to Gram, MB, or GV staining or microscopy. In such settings, the presumptive diagnosis of urethritis can likewise be made based on the presence of symptoms, risk factors, or a positive leukocyte esterase on dipstick on first-voided urine. (See 'Diagnostic approach' below.)

When urethritis is suspected or confirmed, additional testing to identify the involved pathogen(s), ideally with nucleic acid amplification tests (NAATs), is warranted. (See 'Determining the microbial etiology' below.)

Gram stain of urethral sample — Gram stains performed on male urethral swabs can play an important role in defining nongonococcal urethritis (NGU) and guiding empiric therapy as a point-of-care test, especially in clinics dedicated to the management of sexually transmitted infections (STIs). A specimen for Gram stain can be collected from expressed urethral discharge or from inside the urethra. A swab should be inserted gently at least 2 cm into the urethra and rotated 360 degrees while making contact with the urethral mucosa, taking care not to force the tip past an obstruction. The swab can then be rolled across a clean microscope slide for air drying and Gram stain evaluation. (See "Approach to Gram stain and culture results in the microbiology laboratory", section on 'Procedure'.)

The Gram stain should be examined for the presence of WBCs (also specified as polymorphonuclear neutrophils [PMNs]) and any organisms. In the United States, the Centers for Disease Control and Prevention suggests using a lower threshold (≥2 WBC per high powered field [hpf]) for urethritis diagnosis in high prevalence settings (eg, sexually transmitted infection clinics) than low prevalence settings (≥5 WBC/hpf); the lower threshold is more sensitive for urethritis caused by *C. trachomatis* [1,34,35]. In a retrospective study that compared over 13,000 urethral Gram stain findings to NAAT results in males presenting with suspected urethritis, the rate of *C. trachomatis* positivity by NAAT increased with increasing number of WBC observed (5 percent for 0 WBC/hpf to 44 percent for 10 WBC/hpf) [35]. Using a threshold of 5 WBC/hpf would have missed 16 percent of males with *C. trachomatis*, whereas a threshold of 2 WBC/hpf misses only 7 percent. Of the males with *N. gonorrhoeae*, only 2 percent had <10 WBC/hpf. Guidelines from other locations may use different diagnostic criteria. As an example, European guidelines recommend a threshold of 5 WBC/hpf for the diagnosis of urethritis in all settings [36,37].

The presence of PMNs without any visible organisms is consistent with NGU (picture 1), whereas gonococcal urethritis may be diagnosed by the demonstration of gram-negative intracellular diplococci in the urethral exudate (picture 2).

Using an MB or GV stain can also identify WBC and gonococcal forms on urethral swab specimens and can be performed more rapidly than the Gram stain. Results correlate with

those of a Gram stain, although *N. gonorrhoeae* appear as dark purple on the MB or GV stain [38].

First-void urine — Urethritis is suggested by a positive leukocyte esterase on dipstick or the presence of ≥10 WBC/hpf on microscopy of first-void or first-catch spun urine. Inspection for WBCs can be performed by spinning 10 to 15 milliliters of urine and examining the sediment microscopically. This urine sample is also used for nucleic acid amplification testing for identification of the involved pathogen. (See 'Determining the microbial etiology' below.)

The optimal urine sample is the first-void urine, which refers to the initial portion of the first urinary stream after awakening, collected without pre-cleaning the urethral meatus. However, collection of the first-void urine at the point-of-care is impractical, so most practitioners request a first-catch urine, which refers to the initial portion of the urinary stream (generally the first 10 to 20 mL), collected without pre-cleaning the urethral meatus and ideally at least one hour after the previous micturition. Some small studies suggest that urine collected 20 minutes post-void has near-equivalent sensitivity for *C. trachomatis* by nucleic acid amplification testing as one hour post-void samples [39,40].

The volume of urine collected affects the sensitivity of NAAT-based diagnostic tests. In one study, a device that allowed collection of 4 to 5 mL of first-catch urine yielded a specimen with a sixfold higher *C. trachomatis* organism load by NAAT compared with urine collected in a 50-mL cup [41].

Diagnostic approach — Urethritis should be suspected in any sexually active man who presents with symptoms consistent with urethritis, in particular, dysuria, urethral pruritus, and/or urethral discharge (see 'Clinical manifestations' above). In general, the diagnosis and treatment of urethritis should occur at the time of the presenting visit. The approach to diagnosis depends on the availability of point-of-care testing, such as Gram or MB/GV stain of urethral discharge (algorithm 1).

If Gram stain (or MB or GV stain) is available, it should be performed first using a urethral swab specimen. Urine NAATs should still be performed for identification of specific organisms (eg, *N. gonorrhoeae* and *C. trachomatis*). (See 'Determining the microbial etiology' below.)

- If gram-negative (or deep purple on MB or GV stain) diplococci are visualized inside WBC (picture 2), the diagnosis of gonococcal urethritis is made, and individuals should be treated appropriately. (See 'Gonococcal urethritis' below and 'Determining the microbial etiology' below.)

- If ≥2 WBC/hpf (or ≥5 WBC/hpf in low prevalence settings) are seen but no intracellular diplococci are detected (picture 1), the presumptive diagnosis of nongonococcal urethritis is made, and individuals should be treated accordingly (see 'Nongonococcal urethritis' below). However, in situations where there is high suspicion for gonorrhea, such as possible contact with a patient with gonorrhea, extracellular diplococci, or epidemiologic factors associated with *N. gonorrhoeae* acquisition, we suggest that presumptive therapy for gonococcal urethritis be given rather than waiting for urine NAAT results. (See 'Gonococcal urethritis' below.)

- If <2 WBC/hpf (or <5 WBC/hpf in low prevalence settings) are seen, the suspicion is low for an STI, and it is appropriate to wait for results of NAAT testing if the patient agrees to follow up. The diagnosis of urethritis is made if a NAAT for one of the above organisms is positive.

If Gram, MB, or GV stain is not an available option at the presenting visit, diagnosis depends on the presence of at least one of the following objective findings of urethritis (mucopurulent discharge on exam, leukocyte esterase on dipstick, or ≥10 WBC on spun sediment of the first-void or first-catch urine). Urine NAATs should still be performed for specific identification of organisms (eg, *N. gonorrhoeae* and *C. trachomatis*). (See 'Determining the microbial etiology' below.)

- If any of these objective findings of urethritis are present, the presumptive diagnosis of urethritis can be made. These patients should be treated for urethritis with therapy that provides coverage for both gonococcal and chlamydial infections. If the presumptive diagnosis is made on the presence of urine leukocyte esterase or WBC alone, the possibility of urinary tract infection or prostatitis should also be considered, although this should not delay empiric therapy for urethritis among sexually active young males. (See 'Gonococcal urethritis' below and 'Differential diagnosis' below.)

- If none of these are present, the diagnosis is uncertain despite the presence of symptoms. For males who are at high risk for STIs (ie, more than one partner, age <25 years) **and** who are unlikely to return for follow-up, empiric treatment to cover both gonococcal and nongonococcal etiologies before availability of NAAT results is reasonable. Otherwise, treatment can be deferred and selected based on NAAT results. Among males without sexual risk factors, other causes of dysuria should be considered. (See 'Gonococcal urethritis' below and 'Differential diagnosis' below.)

The approach to males who present with recurrent or persistent symptoms after treatment for urethritis is discussed elsewhere. (See 'Recurrent or persistent symptoms' below.)

ADDITIONAL EVALUATION

Determining the microbial etiology — If urethritis is suspected or confirmed based on clinical findings, urethral Gram, methylene blue (MB), or gentian violet (GV) stain results, or the presence of urine leukocytes, testing for *N. gonorrhoeae* and *C. trachomatis* should be performed, typically with nucleic acid amplification testing (NAAT) of a first-catch urine (see 'First-void urine' above) [1]. In the United States, both chlamydia and gonorrhea are reportable diseases. Some UpToDate contributors also recommend testing for *M. genitalium* at the initial urethritis presentation. (See "Mycoplasma genitalium infection in males and females", section on 'Whom to test'.)

Testing for other possible pathogens, including *T. vaginalis*, depends on the local availability of sensitive diagnostic tests and the suspicion for involvement of these additional organisms based on epidemiology or clinical findings. (See "Trichomoniasis: Clinical manifestations and diagnosis", section on 'Diagnosis'.)

A specific microbial diagnosis should direct presumptive treatment of sex partner(s).

NAAT of a first-catch urine is highly sensitive and specific and is the test of choice for identification of pathogens most commonly associated with urethritis. Urine-based diagnostic testing also avoids the patient discomfort associated with urethral sampling, thereby potentially improving patient acceptance of diagnostic testing. Diagnostic testing for *N. gonorrhoeae*, *C. trachomatis*, and *M. genitalium* is discussed elsewhere. (See "Clinical manifestations and diagnosis of Neisseria gonorrhoeae infection in adults and adolescents", section on 'Nucleic acid amplification' and "Clinical manifestations and diagnosis of Chlamydia trachomatis infections", section on 'Diagnosis of chlamydial infections' and "Mycoplasma genitalium infection in males and females", section on 'Microbiologic testing'.)

A urethral Gram, MB, or GV stain that demonstrates intracellular diplococci is highly specific for gonococcal urethritis. However, there have been reports of *N. meningitidis* causing symptomatic urethritis and being initially mistaken for *N. gonorrhoeae* on Gram, MB, or GV stain [6,7,42]. In such cases, NAAT for *N. gonorrhoeae*, if performed, is negative. Definitive identification of *N. meningitidis* requires culture.

Even if intracellular diplococci are seen on Gram, MB, or GV stain and gonococcal urethritis is presumed, NAAT for *C. trachomatis* is still indicated because the two infections can coexist. When intracellular diplococci are not seen on Gram, MB, or GV stain or if staining of the urethral smear is not performed, testing for both *N. gonorrhoeae* and *C. trachomatis* is indicated.

NAAT is the only accurate diagnostic test for *M. genitalium* infections; in the United States, the first US Food and Drug Administration (FDA)-cleared test for this organism became available in January 2019 [43]. (See "Mycoplasma genitalium infection in males and females", section on 'Diagnosis'.)

The identification of *T. vaginalis* in the setting of urethritis is somewhat difficult. NAAT performed on urine or urethral specimens for *T. vaginalis* is the optimal diagnostic test, as it is highly sensitive (74 to 100 percent, depending on the specimen and reference standard) and specific (97 to 100 percent) [44]. If available, NAAT for *T. vaginalis* is useful when the local prevalence of the organism is high and among males with recurrent or persistent urethritis. However, NAAT is expensive, not FDA cleared in the United States for use on male urine, and may not be widely available; other diagnostic tests for *T. vaginalis* are less useful in males. Although wet mount preparations for trichomonads can be useful in females, microscopy is very insensitive in males [1]. Endourethral culture and cultures of the first-void urine sediment also have low sensitivity in males. (See "Trichomoniasis: Clinical manifestations and diagnosis", section on 'Diagnosis'.)

Culture, molecular, or serologic diagnostic testing for herpes simplex virus (HSV) and serologic diagnostic testing for syphilis are warranted in patients with symptoms of urethritis who also have urethral genital ulcers on exam, although HSV and syphilis are infrequently causes of urethritis. (See "Epidemiology, clinical manifestations, and diagnosis of genital herpes simplex virus infection", section on 'Diagnosis' and "Syphilis: Screening and diagnostic testing".)

Evaluation for complications and other sites of infection — Urethritis can occur in conjunction with other infectious processes of the lower urogenital tract, including epididymitis or prostatitis. Males with urethritis should be questioned about and evaluated for the presence of fever, testicular pain and swelling, obstructive urinary symptoms (dribbling or hesitancy), perineal or pelvic pain, which may suggest involvement of the epididymis or prostate. Gentle digital rectal exam is warranted in males who have symptoms suggestive of underlying prostatitis. (See "Acute bacterial prostatitis" and "Chronic bacterial prostatitis" and "Acute scrotal pain in adults", section on 'Acute epididymitis or epididymo-orchitis'.)

Additionally, other anatomical sites, such as the pharynx or rectum, may be affected by sexually transmitted infections, and pharyngitis, proctitis, or (more commonly) asymptomatic infection at these extragenital sites may accompany urethritis. Patients should be questioned about oral or rectal sexual exposures. NAAT is the test of choice at these sites, and the FDA cleared the first diagnostic tests for extragenital testing for chlamydia and gonorrhea in May 2019 [45]. The issue of screening for chlamydia and gonorrhea at extragenital sites is discussed in detail elsewhere. (See "Screening for sexually transmitted infections", section on 'Men who have sex

with men' and "Screening for sexually transmitted infections", section on 'Individuals seeking STI evaluation'.)

Screening for other sexually transmitted infections — Patients presenting with sexually transmitted infections or risk factors should also routinely be offered screening for syphilis and HIV infection. (See "Syphilis: Screening and diagnostic testing" and "Screening for sexually transmitted infections", section on 'Screening recommendations'.)

DIFFERENTIAL DIAGNOSIS

Other infectious diagnoses to consider among males presenting with dysuria include cystitis, epididymitis, and prostatitis. Clinical findings such as growth of uropathogens from urine culture or acute scrotal pain suggest these other processes. However, these conditions may also coexist with urethritis, so even if findings are consistent with one of these alternate diagnoses, the possibility of urethritis is not necessarily ruled out. These conditions are discussed in greater detail elsewhere. (See "Acute simple cystitis in adult males" and "Acute bacterial prostatitis" and "Chronic bacterial prostatitis" and "Acute scrotal pain in adults", section on 'Acute epididymitis or epididymo-orchitis'.)

Noninfectious etiologies may also lead to inflammation of the urethra. These include chemical irritation (eg, from spermicides and soaps) and repeated vigorous stripping of the urethra by the patient, which may occur during masturbation. While history may be able to identify such possibilities, the diagnosis of infectious urethritis should first be thoroughly evaluated and excluded.

MANAGEMENT

Initial therapy — The initial antimicrobial treatment of urethritis is typically empiric at the point-of-care and should be offered to males with suspected or confirmed urethritis. The regimen depends on the clinical evidence for gonococcal versus nongonococcal urethritis (NGU).

Gonococcal urethritis — In males with symptoms of urethritis who have microscopic evidence of gonococcal urethritis (ie, gram-negative or purple intracellular diplococci in the urethral exudate) or high clinical suspicion of gonococcal infection (eg, known or suspected *N. gonorrhoeae* exposure, extracellular diplococci, epidemiologic factors associated with *N. gonorrhoeae* acquisition), treatment for *N. gonorrhoeae* is indicated [1]. When microscopic

evaluation of urethral specimens is not available, sexually active males with urethritis should be empirically treated for gonococcal urethritis.

- The preferred regimen for gonococcal infections is a single intramuscular dose of ceftriaxone (500 mg for individuals <150 kg or 1 g for individuals ≥150 kg).
- If testing results for *C. trachomatis* are not available at the time of treatment, presumptive therapy for chlamydia coinfection is also indicated. In such cases, we suggest doxycycline 100 mg twice daily for seven days.

This approach is consistent with recommendations from the United States Centers for Disease Control and Prevention [1]. The rationale for these regimens is discussed elsewhere. (See "Treatment of uncomplicated Neisseria gonorrhoeae infections", section on 'Preferred regimen'.)

Of note, **oral** cephalosporins are not a recommended regimen for gonococcal infection because they do not provide as high, nor as sustained, bactericidal blood levels as ceftriaxone, and efficacy for pharyngeal infection is limited. Fluoroquinolones are also not recommended because of resistance. (See "Treatment of uncomplicated Neisseria gonorrhoeae infections", section on 'Cephalosporins' and "Treatment of uncomplicated Neisseria gonorrhoeae infections", section on 'Fluoroquinolones'.)

Urethritis caused by *N. meningitidis* is treated the same as gonococcal urethritis [1].

Nongonococcal urethritis

Empiric therapy — Empiric treatment of nongonococcal urethritis (NGU), in which Gram stain shows no gram-negative diplococci in WBC and clinical suspicion for *N. gonorrhoeae* is low, should be targeted against *C. trachomatis* as the most likely pathogen. Doxycycline (100 mg orally twice daily for seven days) is first-line treatment for chlamydia, and thus is first-line treatment for nongonococcal urethritis as well. If adherence to a multi-day regimen is a concern, azithromycin given as a single 1 g oral dose is an alternative; if adherence is not a concern but doxycycline cannot be used for other reasons, azithromycin 500 mg orally on day 1 followed by 250 mg orally daily for four days is an alternative and may be less associated with emergent macrolide resistance in *M. genitalium* than the single dose. Ideally, the full regimen should be dispensed on site and the first dose administered as directly observed therapy.

These recommendations are based on evidence suggesting greater microbial efficacy of doxycycline compared with azithromycin for *C. trachomatis* and concern that the single-dose azithromycin regimen could promote resistance in *M. genitalium* [1].

- Several studies have suggested that doxycycline results in higher microbiologic cure rates for *C. trachomatis* than azithromycin [15,46,47]. In a meta-analysis of nine trials comparing doxycycline for seven days with single-dose azithromycin in males with urogenital *C. trachomatis* infection, there were more microbiologic failures with azithromycin than doxycycline (81 versus 33 per 1000, relative risk [RR] 2.45, 95% CI 1.36-4.41) [47]. Clinical failure rates were similar (116 versus 123 per 1000, RR 0.94, 95% CI 0.43-2.05). (See "Treatment of Chlamydia trachomatis infection", section on 'Doxycycline as preferred agent'.)

- Although azithromycin-based regimens have resulted in higher microbiologic cure rates for *M. genitalium* and *U. urealyticum* than doxycycline [15,46], increasing resistance to azithromycin in *M. genitalium* has resulted in decreased reported cure rates over time [48]. Additionally, single-dose azithromycin is thought to have contributed to emergent resistance, as selection of treatment-associated mutations in *M. genitalium* isolates has been described following failure with that regimen [49]. Higher doses of azithromycin are associated with a lower rate of emergent resistance. (See "Mycoplasma genitalium infection in males and females", section on 'Impact of empiric syndromic therapy on M. genitalium'.)

Our treatment recommendations are consistent with guidelines from the Centers for Disease Control and Prevention in the United States [1]. Similarly, the International Union against Sexually Transmitted Infections in Europe explicitly favors doxycycline [36]. They also recommend a five-day dosing regimen of azithromycin rather than the single oral dose if azithromycin is administered. These issues are discussed in detail elsewhere. (See "Treatment of Chlamydia trachomatis infection", section on 'Doxycycline as preferred agent' and "Mycoplasma genitalium infection in males and females", section on 'Directed therapy of documented infection'.)

Directed therapy — Antimicrobial treatment can be directed towards a specific bacterial pathogen(s) if sensitive diagnostic testing is available to guide therapy. However, approximately a third of males with nongonococcal urethritis will have an unidentified etiology despite NAATs [13]. Directed therapy of specific organisms is discussed in detail separately.

- (See "Treatment of Chlamydia trachomatis infection", section on 'Antibiotic treatment of chlamydia'.)
- (See "Mycoplasma genitalium infection in males and females", section on 'Treatment'.)
- (See "Trichomoniasis: Treatment", section on 'Sex partners'.)

When in-person evaluation and treatment are not feasible during the COVID-19 pandemic — In the setting of the coronavirus disease 2019 (COVID-19) pandemic, opportunities for in-person evaluation and treatment may be limited. Sexually active patients who have clinical syndromes consistent with urethritis and cannot be directly evaluated should be presumptively treated with a regimen active against gonococcal urethritis, as detailed elsewhere. (See 'Gonococcal urethritis' above and "Treatment of uncomplicated Neisseria gonorrhoeae infections", section on 'Preferred regimen'.)

Preferred and alternative regimens for gonococcal infections include intramuscular antibiotics. If possible, clinicians should refer patients to other clinics or pharmacies that can administer the intramuscular dose. If this is not feasible, all-oral alternatives include cefixime 800 mg once or cefpodoxime 400 mg every 12 hours for two doses, each in addition to treatment for chlamydia (if it has not been ruled out) [50,51]. If cephalosporins cannot be given because of allergy or availability, azithromycin 2 g in a single dose is the alternative. These regimens can also be used for expedited partner therapy.

Because of decreased susceptibility to oral cephalosporins, these all-oral regimens are not as effective against gonococcal infection as those that include a parenteral cephalosporin (see "Treatment of uncomplicated Neisseria gonorrhoeae infections", section on 'Alternate regimens'). Patients who are treated presumptively with an all-oral regimen should be instructed to contact the clinician if symptoms do not improve within a week.

All patients who are treated presumptively for urethritis should be advised to return for comprehensive STI care and counseling once services are available.

Recurrent or persistent symptoms — Recurrent or persistent symptoms are common following therapy for urethritis. Possible causes include poor adherence to the regimen, reinfection, antimicrobial resistance (particularly in the case of *N. gonorrhoeae*), and involvement of other organisms inadequately treated by the empiric regimen (in particular, *M. genitalium* or in men who have sex with women [MSW], *Trichomonas*).

Males with persistent or recurrent symptoms of urethritis should be evaluated for objective evidence of urethritis (mucopurulent discharge on exam, leukocyte esterase positive urine, or ≥10 white blood cells [WBC] on spun sediment of the first-void or first-catch urine, and/or ≥2 to ≥5 WBC/high power field [hpf; depending on the prevalence of urethritis in the setting] on Gram, methylene blue [MB], or gentian violet [GV] stain of a urethral sample). Symptoms alone are not an indication for retreatment [1]. (See 'Diagnostic criteria' above.)

For males with objective evidence of persistent urethritis, we recommend repeat NAAT for *N. gonorrhoeae* and *C. trachomatis,* as well as testing for *M. genitalium* and *T. vaginalis* with urine-

based NAAT, if available. For males with prior gonococcal urethritis, a primary concern is the possibility of antimicrobial resistance and treatment failure. Evaluation and management for this is discussed elsewhere. (See "Treatment of uncomplicated Neisseria gonorrhoeae infections", section on 'Monitoring for and managing treatment failure'.)

In some cases, empiric therapy can be given while awaiting testing results. Males who were not adherent to the initial antibiotic course or were re-exposed to an untreated partner can be retreated with the same initial regimen. Men who have sex with women and who were adherent and not re-exposed can be presumptively treated for *T. vaginalis*; specific regimens are discussed elsewhere.

Otherwise, therapy should ideally be based on results of microbiologic testing. *M. genitalium* is a common cause of persistent nongonococcal urethritis. If testing for *M. genitalium* is unavailable, it is reasonable to empirically treat for this organism in males with persistent nongonococcal urethritis who have tested negative for other organisms. Treatment of *M. genitalium* is discussed in detail elsewhere. (See "Mycoplasma genitalium infection in males and females", section on 'Empiric M. genitalium therapy in select clinical treatment failure cases'.)

Herpes simplex virus (HSV) can also be a causative agent of persistent urethritis, although HSV is often distinguished from other pathogens by characteristic physical examination findings. Other causes of dysuria and noninfectious etiologies of symptoms of urethritis should also be considered. (See 'Differential diagnosis' above.)

COUNSELING AND FOLLOW UP

Sexual activity — In order to decrease the risk of transmission, males with infectious urethritis should be instructed to refrain from sexual activity for at least seven days following the initiation of therapy (including single-dose therapy) and until their symptoms have resolved. Recurrent and persistent symptoms should prompt reevaluation for possible reinfection, antimicrobial resistance, or the possible involvement of pathogens that were not covered by the empiric regimen. (See 'Recurrent or persistent symptoms' above.)

The National Coalition for Sexual Health published a provider's guide that offers strategies and tips on incorporating sexual health discussion into patient care [52].

Repeat testing — In males with confirmed gonorrhea, chlamydia, and trichomonas, repeat testing for these pathogens with nucleic acid amplification testing (NAAT) is warranted three months after treatment because there is a high rate of reinfection [1]. Repeat testing should be performed regardless of whether sex partners were treated.

Test of cure — A test of cure is a microbial diagnostic test (eg, culture or NAAT) that is performed one to three weeks following treatment, regardless of symptom resolution, to document eradication of the pathogen. In general, a test of cure is not necessary for males with urethritis treated with first-line regimens for *N. gonorrhoeae* or *C. trachomatis*. Test of cure following treatment for these pathogens is discussed in further detail elsewhere. (See "Treatment of uncomplicated Neisseria gonorrhoeae infections", section on 'Test of cure' and "Treatment of Chlamydia trachomatis infection", section on 'Test of cure for select patients'.)

PARTNER MANAGEMENT

All individuals who have had sexual contact with patients diagnosed with *N. gonorrhoeae*, *C. trachomatis*, or *T. vaginalis* within the 60 days prior to the diagnosis should be evaluated and presumptively treated. There are no formal recommendations regarding the management of sexual contacts with patients diagnosed with *M. genitalium*, but some UpToDate contributors suggest partner evaluation and treatment for this organism as well. (See "Mycoplasma genitalium infection in males and females", section on 'Whom to test'.)

If the patient's most recent sexual contact was greater than 60 days prior to diagnosis, the most recent sexual partner should be evaluated and treated. For partners of patients with urethritis but no identified pathogen, we suggest empiric therapy for chlamydia as well as testing and directed therapy for any pathogen identified. (See "Treatment of uncomplicated Neisseria gonorrhoeae infections", section on 'Management of sexual partners' and "Treatment of Chlamydia trachomatis infection", section on 'Management of sex partners'.)

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Sexually transmitted infections".)

INFORMATION FOR PATIENTS

UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more

sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

Basics topics (see "Patient education: Urethritis (The Basics)")

SUMMARY AND RECOMMENDATIONS

- **Causes** – Most cases of urethritis are seen in young, sexually active men. *Neisseria gonorrhoeae, Chlamydia trachomatis,* and *Mycoplasma genitalium* are the most commonly associated organisms. *Trichomonas vaginalis* and herpes simplex virus (HSV) are also recognized causes. (See 'Epidemiology and microbiology' above.)

- **Clinical manifestations** – Dysuria, or painful urination, is usually the chief complaint. Other complaints include pruritus, burning, and discharge at the urethral meatus. Acute onset of frankly purulent discharge suggests *N. gonorrhoeae*, dysuria alone suggests *C. trachomatis*, and painful genital ulcers suggest HSV. However, syndromes of gonococcal and nongonococcal urethritis cannot be reliably distinguished on clinical grounds only. (See 'Clinical manifestations' above.)

- **Diagnosis** – Urethritis should be suspected in any sexually active man with dysuria, urethral pruritus, and/or urethral discharge (algorithm 1). Any of the following confirms the diagnosis in a symptomatic male (see 'Diagnosis' above):

  - Mucoid, mucopurulent, or purulent urethral discharge on examination

  - Gram stain (or methylene blue [MB] or gentian violet [GV] stain) of a urethral swab demonstrating ≥2 white blood cells (WBC) per oil immersion field (or ≥5 WBC per oil immersion field in low prevalence settings); intracellular diplococci confirms gonococcal urethritis

  - Positive leukocyte esterase ("dipstick") or ≥10 WBC per high power field of first-void/first-catch spun urine

  If none are present or if point-of-care testing is unavailable, a presumptive diagnosis can be made in sexually active males with suggestive symptoms.

- **Additional microbiologic testing** – Testing for *N. gonorrhoeae* and *C. trachomatis*, ideally with nucleic acid amplification testing (NAAT) on first-void urine, is indicated for suspected or confirmed urethritis. Some UpToDate contributors also recommend NAAT for *M. genitalium* at initial presentation. (See 'Additional evaluation' above.)

- **Differential diagnosis** – Other infectious diagnoses to consider among males presenting with dysuria include cystitis, epididymitis, and prostatitis. Noninfectious etiologies that can lead to inflammation of the urethra include chemical irritation and repeated vigorous self-stripping of the urethra. (See 'Differential diagnosis' above.)

- **Initial therapy** – This is typically empiric at the point-of-care.

  - In males who have microscopic evidence of gonococcal urethritis (ie, gram-negative or purple intracellular diplococci) or high clinical suspicion of gonococcal urethritis, treatment is as outlined for uncomplicated gonococcal infections. This regimen consists of a single 500 mg intramuscular dose of ceftriaxone (or 1 g for individuals ≥150 kg) and, if it has not been ruled out at the time of treatment, presumptive treatment for chlamydia. (See 'Gonococcal urethritis' above and "Treatment of uncomplicated Neisseria gonorrhoeae infections", section on 'Preferred regimen'.)

  - For patients with nongonococcal urethritis (ie, no laboratory evidence of or suspicion for *N. gonorrhoeae*) we suggest doxycycline 100 mg orally twice daily for seven days (**Grade 2C**). Azithromycin (either as 500 mg orally on day one then 250 mg orally daily for four days or as a single 1 g dose) is an alternative, although the single-dose regimen is associated with lower *C. trachomatis* microbiologic cure rates than doxycycline and possibly contributes to emergent azithromycin resistance in *M. genitalium*. (See 'Empiric therapy' above.)

  If microbial diagnostic testing results are available prior to receipt of therapy, antimicrobial treatment can be directed towards the identified pathogen(s). (See 'Directed therapy' above.)

- **Recurrent or persistent symptoms** – Possible causes include poor adherence to the regimen, reinfection, antimicrobial resistance (particularly with *N. gonorrhoeae*), and involvement of other organisms inadequately treated by the empiric regimen (in particular, *M. genitalium* or, in men who have sex with women, *Trichomonas*). (See 'Recurrent or persistent symptoms' above.)

- **Counseling and follow-up** – Sexual activity should be avoided for at least seven days following the initiation of therapy. Males with documented *N. gonorrhoeae*, *C. trachomatis,*

or *T. vaginalis* infections should undergo repeat testing three months after treatment. Sexual contacts warrant evaluation and treatment for sexually transmitted pathogens identified in the index patient or, if no test results are available, treatment with the same empiric regimen. (See 'Counseling and follow up' above and 'Partner management' above.)

DISCLOSURE

The findings and conclusions in this topic are those of the author and do not necessarily represent the official position of the United States Centers for Disease Control and Prevention.

REFERENCES

1. Workowski KA, Bachmann LH, Chan PA, et al. Sexually Transmitted Infections Treatment Guidelines, 2021. MMWR Recomm Rep 2021; 70:1.
2. Centers for Disease Control and Prevention. Sexually Transmitted Disease Surveillance 2019. https://www.cdc.gov/std/statistics/2019/default.htm (Accessed on May 18, 2021).
3. Taylor SN, Liesenfeld O, Lillis RA, et al. Evaluation of the Roche cobas® CT/NG test for detection of Chlamydia trachomatis and Neisseria gonorrhoeae in male urine. Sex Transm Dis 2012; 39:543.
4. Black V, Magooa P, Radebe F, et al. The detection of urethritis pathogens among patients with the male urethritis syndrome, genital ulcer syndrome and HIV voluntary counselling and testing clients: should South Africa's syndromic management approach be revised? Sex Transm Infect 2008; 84:254.
5. Lyss SB, Kamb ML, Peterman TA, et al. Chlamydia trachomatis among patients infected with and treated for Neisseria gonorrhoeae in sexually transmitted disease clinics in the United States. Ann Intern Med 2003; 139:178.
6. Katz AR, Chasnoff R, Komeya A, Lee MV. Neisseria meningitidis urethritis: a case report highlighting clinical similarities to and epidemiological differences from gonococcal urethritis. Sex Transm Dis 2011; 38:439.
7. Bazan JA, Peterson AS, Kirkcaldy RD, et al. Notes from the Field: Increase in Neisseria meningitidis-Associated Urethritis Among Men at Two Sentinel Clinics - Columbus, Ohio, and Oakland County, Michigan, 2015. MMWR Morb Mortal Wkly Rep 2016; 65:550.

8. Bazan JA, Turner AN, Kirkcaldy RD, et al. Large Cluster of Neisseria meningitidis Urethritis in Columbus, Ohio, 2015. Clin Infect Dis 2017; 65:92.
9. Burstein GR, Zenilman JM. Nongonococcal urethritis--a new paradigm. Clin Infect Dis 1999; 28 Suppl 1:S66.
10. Stamm WE. Chlamydia trachomatis infections: progress and problems. J Infect Dis 1999; 179 Suppl 2:S380.
11. Gaydos C, Maldeis NE, Hardick A, et al. Mycoplasma genitalium compared to chlamydia, gonorrhoea and trichomonas as an aetiological agent of urethritis in men attending STD clinics. Sex Transm Infect 2009; 85:438.
12. Stamm WE, Hicks CB, Martin DH, et al. Azithromycin for empirical treatment of the nongonococcal urethritis syndrome in men. A randomized double-blind study. JAMA 1995; 274:545.
13. Bradshaw CS, Tabrizi SN, Read TR, et al. Etiologies of nongonococcal urethritis: bacteria, viruses, and the association with orogenital exposure. J Infect Dis 2006; 193:336.
14. Romanowski B, Talbot H, Stadnyk M, et al. Minocycline compared with doxycycline in the treatment of nongonococcal urethritis and mucopurulent cervicitis. Ann Intern Med 1993; 119:16.
15. Schwebke JR, Rompalo A, Taylor S, et al. Re-evaluating the treatment of nongonococcal urethritis: emphasizing emerging pathogens--a randomized clinical trial. Clin Infect Dis 2011; 52:163.
16. Watson-Jones D, Mugeye K, Mayaud P, et al. High prevalence of trichomoniasis in rural men in Mwanza, Tanzania: results from a population based study. Sex Transm Infect 2000; 76:355.
17. Hobbs MM, Kazembe P, Reed AW, et al. Trichomonas vaginalis as a cause of urethritis in Malawian men. Sex Transm Dis 1999; 26:381.
18. Price MA, Miller WC, Kaydos-Daniels SC, et al. Trichomoniasis in men and HIV infection: data from 2 outpatient clinics at Lilongwe Central Hospital, Malawi. J Infect Dis 2004; 190:1448.
19. Rane VS, Fairley CK, Weerakoon A, et al. Characteristics of acute nongonococcal urethritis in men differ by sexual preference. J Clin Microbiol 2014; 52:2971.
20. Rane VS, Fairley CK, Weerakoon A, et al. Predictors and Pathogens Among 4,326 Cases of Acute Non-Gonoccocal Urethritis. Sex Transm Infect 2013; 89:A53.
21. Handsfield HH. Nongonococcal urethritis: a few answers but mostly questions. J Infect Dis 2006; 193:333.

22. Manhart LE, Khosropour CM, Liu C, et al. Bacterial vaginosis-associated bacteria in men: association of Leptotrichia/Sneathia spp. with nongonococcal urethritis. Sex Transm Dis 2013; 40:944.
23. Ito S, Hatazaki K, Shimuta K, et al. Haemophilus influenzae Isolated From Men With Acute Urethritis: Its Pathogenic Roles, Responses to Antimicrobial Chemotherapies, and Antimicrobial Susceptibilities. Sex Transm Dis 2017; 44:205.
24. Ito S, Hanaoka N, Shimuta K, et al. Male non-gonococcal urethritis: From microbiological etiologies to demographic and clinical features. Int J Urol 2016; 23:325.
25. Yokoi S, Maeda S, Kubota Y, et al. The role of Mycoplasma genitalium and Ureaplasma urealyticum biovar 2 in postgonococcal urethritis. Clin Infect Dis 2007; 45:866.
26. Couldwell DL, Gidding HF, Freedman EV, et al. Ureaplasma urealyticum is significantly associated with non-gonococcal urethritis in heterosexual Sydney men. Int J STD AIDS 2010; 21:337.
27. Ondondo RO, Whittington WL, Astete SG, Totten PA. Differential association of ureaplasma species with non-gonococcal urethritis in heterosexual men. Sex Transm Infect 2010; 86:271.
28. Totten PA, Schwartz MA, Sjöström KE, et al. Association of Mycoplasma genitalium with nongonococcal urethritis in heterosexual men. J Infect Dis 2001; 183:269.
29. William M. McCormack. Urethritis. In: Mandell, Douglas, and Bennett's Principles and Practice of Infectious Disease, 7, Gerald L Mandell, John E. Bennet, and Raphael Dolin (Eds), Elsevier, 2010. Vol I, p.1485.
30. Schofield CB. Some factors affecting the incubation period and duration of symptoms of urethritis in men. Br J Vener Dis 1982; 58:184.
31. McNagny SE, Parker RM, Zenilman JM, Lewis JS. Urinary leukocyte esterase test: a screening method for the detection of asymptomatic chlamydial and gonococcal infections in men. J Infect Dis 1992; 165:573.
32. Kent CK, Chaw JK, Wong W, et al. Prevalence of rectal, urethral, and pharyngeal chlamydia and gonorrhea detected in 2 clinical settings among men who have sex with men: San Francisco, California, 2003. Clin Infect Dis 2005; 41:67.
33. McCormack W, Rein M. Urethritis. In: Principles and Practice of Infectious Diseases, Mandell, Douglas, and Bennett (Eds), 2006.
34. Orellana MA, Gómez-Lus ML, Lora D. Sensitivity of Gram stain in the diagnosis of urethritis in men. Sex Transm Infect 2012; 88:284.

35. Rietmeijer CA, Mettenbrink CJ. Recalibrating the Gram stain diagnosis of male urethritis in the era of nucleic acid amplification testing. Sex Transm Dis 2012; 39:18.
36. Horner PJ, Blee K, Falk L, et al. 2016 European guideline on the management of non-gonococcal urethritis. Int J STD AIDS 2016; 27:928.
37. Moi H, Hartgill U, Skullerud KH, et al. Microscopy of Stained Urethral Smear in Male Urethritis; Which Cutoff Should be Used? Sex Transm Dis 2017; 44:189.
38. Taylor SN, DiCarlo RP, Martin DH. Comparison of methylene blue/gentian violet stain to Gram's stain for the rapid diagnosis of gonococcal urethritis in men. Sex Transm Dis 2011; 38:995.
39. Mathew T, O'Mahony C, Mallinson H. Shortening the voiding interval for men having chlamydia nucleic acid amplification tests. Int J STD AIDS 2009; 20:752.
40. Kwan B, Ryder N, Knight V, et al. Sensitivity of 20-minute voiding intervals in men testing for Chlamydia trachomatis. Sex Transm Dis 2012; 39:405.
41. Wisniewski CA, White JA, Michel CE, et al. Optimal method of collection of first-void urine for diagnosis of Chlamydia trachomatis infection in men. J Clin Microbiol 2008; 46:1466.
42. Tzeng YL, Bazan JA, Turner AN, et al. Emergence of a new Neisseria meningitidis clonal complex 11 lineage 11.2 clade as an effective urogenital pathogen. Proc Natl Acad Sci U S A 2017; 114:4237.
43. US Food and Drug Administration. FDA News Release: FDA permits marketing of first test to aid in the diagnosis of a sexually-transmitted infection known as Mycoplasma genitalium. https://www.fda.gov/news-events/press-announcements/fda-permits-marketing-first-test-aid-diagnosis-sexually-transmitted-infection-known-mycoplasma (Accessed on October 16, 2019).
44. Bachmann LH, Hobbs MM, Seña AC, et al. Trichomonas vaginalis genital infections: progress and challenges. Clin Infect Dis 2011; 53 Suppl 3:S160.
45. US Food and Drug Administration. FDA News Release: FDA clears first diagnostic tests for extragenital testing for chlamydia and gonorrhea. https://www.fda.gov/news-events/press-announcements/fda-clears-first-diagnostic-tests-extragenital-testing-chlamydia-and-gonorrhea (Accessed on October 16, 2019).
46. Manhart LE, Gillespie CW, Lowens MS, et al. Standard treatment regimens for nongonococcal urethritis have similar but declining cure rates: a randomized controlled trial. Clin Infect Dis 2013; 56:934.
47. Páez-Canro C, Alzate JP, González LM, et al. Antibiotics for treating urogenital Chlamydia trachomatis infection in men and non-pregnant women. Cochrane Database Syst Rev 2019;

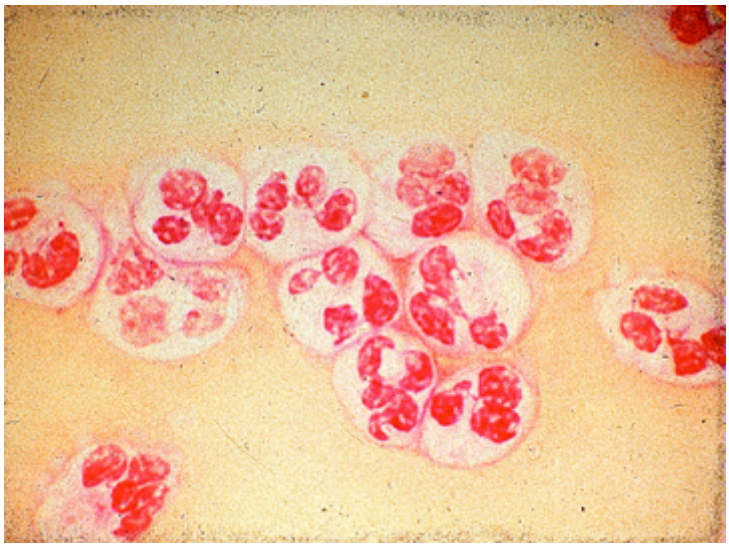
1:CD010871.

48. Lau A, Bradshaw CS, Lewis D, et al. The Efficacy of Azithromycin for the Treatment of Genital Mycoplasma genitalium: A Systematic Review and Meta-analysis. Clin Infect Dis 2015; 61:1389.
49. Jensen JS, Bradshaw CS, Tabrizi SN, et al. Azithromycin treatment failure in Mycoplasma genitalium-positive patients with nongonococcal urethritis is associated with induced macrolide resistance. Clin Infect Dis 2008; 47:1546.
50. Centers for Disease Control and Prevention. Dear Colleague Letter: Providing effective care and prevention when facility-based services and in-person patient-clinician contact is limite d. May 5, 2020. https://www.cdc.gov/std/dstdp/DCL-STDTreatment-COVID19-04062020.pdf (Accessed on July 21, 2020).
51. St Cyr S, Barbee L, Workowski KA, et al. Update to CDC's Treatment Guidelines for Gonococcal Infection, 2020. MMWR Morb Mortal Wkly Rep 2020; 69:1911.
52. National Coalition for Sexual Health. Sexual Health and Your Patients: A Provider's Guide. U pdated 2019. https://nationalcoalitionforsexualhealth.org/tools/for-healthcare-providers/se xual-health-and-your-patients-a-providers-guide (Accessed on October 31, 2019).

Topic 86698 Version 30.0

GRAPHICS

Gram stain of urethral discharge

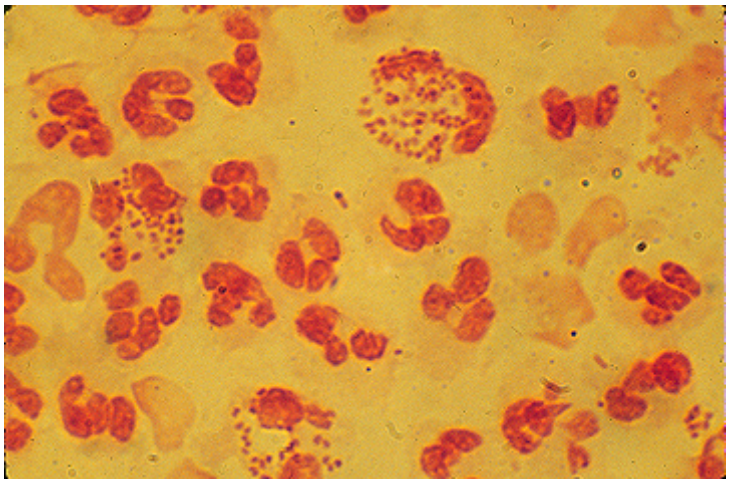


Polymorphonuclear leukocytes without intracellular pathogens are characteristic of the mucopurulent discharge seen in men with chlamydial infection.

Reproduced from the Centers for Disease Control and Prevention.

Graphic 56547 Version 2.0

Gram stain of gonococcus in urethral discharge



Gram stain of purulent exudate from the male urethra (x1000) shows polymorphonuclear leukocytes containing numerous intracellular gram-negative diplococci. As expected, *Neisseria gonorrhoeae* grew from this specimen.

Courtesy of Harriet Provine.

Graphic 50351 Version 3.0

Approach to the male patient with suspected urethritis

NAAT: nucleic acid amplification test; STI: sexually transmitted infection; WBC/hpf: white blood cells per high powered field.

* First-void urine refers to the initial portion of the first urine stream upon wakening. The more practical first-catch urine refers to the initial portion of the urine stream at least one hour after the most recent micturition. Both are collected without precleaning the urethral meatus, and the volume collected is limited to approximately 10 mL.

¶ Although urethritis is often treated empirically prior to the results of NAAT for specific organisms, this testing remains important for documentation of specific infections and facilitation of sex partner management. Some UpToDate authors also recommend NAAT for *Mycoplasma genitalium* at the initial presentation.

Δ A methylene blue or gentian violet stain is an alternative to the Gram stain and can be performed more rapidly.

◇ In areas of low prevalence of sexually transmitted infection (eg, in family planning clinics), a higher threshold of ≥5 WBC/hpf is used to make the diagnosis of urethritis.

Graphic 102369 Version 7.0

Contributor Disclosures

Laura H Bachmann, MD, MPH, FIDSA No relevant financial relationship(s) with ineligible companies to disclose. **Jeanne Marrazzo, MD, MPH, FACP, FIDSA** Equity Ownership/Stock Options: Osel Inc [Vaginal infections]. Grant/Research/Clinical Trial Support: BD Diagnostics [Vaginal infections, STI]. Consultant/Advisory Boards: Gilead [HIV];Merck [HIV]. All of the relevant financial relationships listed have been mitigated. **Allyson Bloom, MD** No relevant financial relationship(s) with ineligible companies to disclose.

Contributor disclosures are reviewed for conflicts of interest by the editorial group. When found, these are addressed by vetting through a multi-level review process, and through requirements for references to be provided to support the content. Appropriately referenced content is required of all authors and must conform to UpToDate standards of evidence.

Conflict of interest policy

→