# Diagnosis and Treatment of Urethritis in Men

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**Symptoms of urethritis in men typically include urethral discharge, penile itching or tingling, and dysuria. A diagnosis can be made if at least one of the following is present: discharge, a positive result on a leukocyte esterase test in first-void urine, or at least 10 white blood cells per high-power field in urine sediment. The primary pathogens associated with urethritis are *Chlamydia trachomatis* and *Neisseria gonorrhoeae*. Racial disparities in the prevalence of sexually transmitted infections persist in the United States, with rates of gonorrhea 40 times higher in black adolescent males than in white adolescent males. Recent studies have focused on identifying causes of nongonococcal urethritis and developing testing for atypical organisms, such as *Mycoplasma genitalium* and *Ureaplasma* species. Less common pathogens identified in patients with urethritis include *Trichomonas* species, adenovirus, and herpes simplex virus. History and examination findings can help distinguish urethritis from other urogenital syndromes, such as epididymitis, orchitis, and prostatitis. The goals of treatment include alleviating symptoms; preventing complications in the patient and his sexual partners; reducing the transmission of coinfections (particularly human immunodeficiency virus); identifying and treating the patient's contacts; and encouraging behavioral changes that will reduce the risk of recurrence. The combination of azithromycin or doxycycline plus ceftriaxone or cefixime is considered first-line empiric therapy in patients with urethritis. Expedited partner treatment, which involves giving patients prescriptions for partners who have not been examined by the physician, is advocated by the Centers for Disease Control and Prevention and has been approved in many states. There is an association between urethritis and an increased human immunodeficiency virus concentration in semen. (*Am Fam Physician.* 2010;81(7):873-878, 879-880. Copyright © 2010 American Academy of Family Physicians.)**

▶ **Patient information:** A handout on urethritis, written by the author of this article, is provided on page 879.

The symptoms and management of urethritis in men are distinctly different from those in women. Although there are infectious and noninfectious etiologies, most studies have focused on urethritis as a sexually transmitted infection (STI). Because it is the most common STI in men, diagnosis and treatment remain clinical and public health priorities. The goals of treatment are to alleviate symptoms, prevent complications, reduce transmission of coinfections (particularly human immunodeficiency virus [HIV]), identify and treat contacts, and encourage behavioral changes to reduce the risk of recurrence.

## Nomenclature

Historically, the term urethritis was reserved for patients with urethral discharge. However, recent literature has demonstrated that STIs often occur in men without discharge, but with symptoms such as itching, tingling, or dysuria. STIs may also be asymptomatic.

The classification of urethritis as gonococcal or nongonococcal is based on the traditional Gram staining of urethral discharge for gram-negative diplococci. This terminology persists, although dual DNA-based testing for *Neisseria gonorrhoeae* and *Chlamydia trachomatis* infections is now recommended and has largely replaced Gram staining in primary care practice. Additionally, gonococcal and nongonococcal infections often coexist, further confounding these terms.

## Etiology

*C. trachomatis* and *N. gonorrhoeae* are the primary pathogens identified in men with urethritis. Chlamydia is the most commonly reported STI in the United States, with more than three times as many cases reported as gonorrhea.[1] A nationally representative sample found a 4 percent prevalence of chlamydia in young adults,[2] with an estimated 2.8 million cases in the United States each year, mostly asymptomatic.[3] Although chlamydia can cause complications in men, such as reactive arthritis with associated urethritis (formerly known as Reiter syndrome), this occurs in only about 1 percent of patients.[4] One large study found a slight increase in prostatitis and a fourfold risk of epididymitis following chlamydial infection,

**SORT: KEY RECOMMENDATIONS FOR PRACTICE**

| *Clinical recommendation* | *Evidence rating* | *References* | *Comments* |
|---|---|---|---|
| Men with urethral symptoms should be tested for *Chlamydia trachomatis* and *Neisseria gonorrhoeae*. | C | 2, 4, 6, 16 | Based on large population studies and expert guidelines |
| The combination of azithromycin (Zithromax) or doxycycline plus ceftriaxone (Rocephin) or cefixime (Suprax) is recommended as empiric treatment for urethritis. | C | 16, 19, 20 | Based on expert guidelines |
| Treatment of urethritis may reduce the transmission of human immunodeficiency virus. | C | 32, 33 | Based on limited studies |

*A = consistent, good-quality patient-oriented evidence; B = inconsistent or limited-quality patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to http://www.aafp.org/afpsort.xml.*

but no increase in subsequent male infertility.[5] One of the main goals of treatment is to identify and treat sexual partners to prevent disease transmission and sequelae, such as pelvic inflammatory disease.

The Centers for Disease Control and Prevention (CDC) estimates that more than 700,000 persons in the United States acquire gonorrhea each year.[3] Overall in the United States, the incidence of gonorrhea is decreasing, although there was a slight increase in cases reported in 2006 and 2007 before dropping again in 2008.[6] There is a marked racial disparity in the United States, with gonorrhea rates 40 times higher in 15- to 19-year-old black males than in white males of the same age.[7] Genital gonorrhea is rarely asymptomatic in men. The goals of treatment are to alleviate symptoms and reduce the spread of infection to sexual partners.

The role of *Mycoplasma genitalium* in nongonococcal urethritis has attracted much attention in the past decade. Numerous studies have concluded that *M. genitalium* is a common cause of nongonococcal urethritis and that eradication is associated with symptomatic improvement.[8-10] Although studies have shown that *Mycoplasma* species cause symptomatic infections more often than *Chlamydia*, it remains controversial whether mycoplasmal urethritis causes complications in men or significant morbidity in women.[11] Commercially available DNA-based tests with sensitivity of up to 97 percent have been developed but are not yet widely available. *M. genitalium* is a fastidious organism that is difficult to culture.[12]

A number of other pathogens have been implicated in nongonococcal urethritis. Like *Mycoplasma*, *Ureaplasma* species are common in men with urethral symptoms, but their exact role as a pathogen has not been completely defined.[13] *Trichomonas* species may also cause urethral symptoms in men but are difficult to detect.[14] Herpes simplex virus (HSV) should be considered, particularly in patients with recurrent symptoms or inflammation of the meatus. Adenovirus has also been established as a pathogen. Urethritis caused by HSV or adenovirus is associated with insertive oral sex among men who have sex with men.[15]

## Diagnosis

Men presenting with urethral symptoms should be examined for inguinal lymphadenopathy, ulcers, or urethral discharge. The urethra should be gently "milked" by serial palpation down the shaft of the penis toward the urethra. Any discharge should be tested according to the available laboratory methods for gonorrhea and chlamydia. Currently, urethritis is diagnosed by at least one of the following: the presence of urethral discharge, a positive leukocyte esterase test result in first-void urine, or at least 10 white blood cells per high-power field in first-void urine sediment.[16] If no discharge is present, first-void urine should be tested to document pyuria, and DNA-based testing should be ordered for chlamydia and gonorrhea. Palpation of the scrotum for evidence of epididymitis or orchitis is advised. A digital rectal examination of the prostate may be considered, especially in older patients or if rectal pain is reported. Testing and examination of other sites of sexual exposure (e.g., oropharynx, anus) should be considered if signs of inflammation are present. *Table 1* lists suggested diagnoses and management considerations for several urogenital syndromes.[14,16,17]

If a urinary tract infection is suggested by the history (e.g., severe dysuria, hematuria, nocturia, urgency, lack of sexual exposure), examination (e.g., lack of discharge), or laboratory results (e.g., nitrites present on urinalysis),

**Table 1. Clinical Clues in Men with Urogenital Syndromes**

| *History and examination findings* | *Suggested diagnoses* | *Management considerations* |
|---|---|---|
| Age older than 35 years | Urethritis or UTIs[16] caused by increased rates of gram-negative organisms | Consider 100 mg oral doxycycline twice a day for seven days, instead of azithromycin (Zithromax) |
| Age older than 35 years, severe dysuria, hematuria, nocturia, frequent urination, lack of sexual exposure, lack of discharge, positive nitrite result on urinalysis | UTI (leukocyte esterase and nitrite dipstick testing has sensitivity and specificity of 83 to 90 percent)[17] | Urine culture, oral fluoroquinolones, evaluate for prostatic hypertrophy, test of cure after completion of therapy |
| Anal sexual exposure, symptoms present | Gonorrhea | *Chlamydia* can be found in anus, but usually asymptomatic and no FDA-approved test |
| Fever, flank pain, white blood cells on urine microscopy | Pyelonephritis | Antibiotics directed against enteric bacteria, urine culture<br>May require parenteral treatment<br>Milder cases can be treated with oral fluoroquinolones |
| Genital ulcers | HSV (painful); syphilis (nonpainful); chancroid (painful) | Viral culture/DNA testing<br>Venereal Disease Research Laboratory or rapid plasma reagin tests |
| Inguinal lymphadenopathy | Nonspecific, suggests genital infection | Lymphadenopathy with painful ulcers suggests chancroid |
| Oropharyngeal exudates | Gonorrhea | Chlamydia rarely causes pharyngitis<br>Ceftriaxone (Rocephin) should be used instead of cefixime (Suprax) |
| Persistent, recurrent urethritis symptoms | Noninfectious causes; trichomoniasis[14] | Consider *Trichomonas* culture or empiric metronidazole (Flagyl) treatment<br>Avoid urethral irritants |
| Prostatic tenderness, boggy texture on palpation | Acute prostatitis | Prostatic massage contraindicated<br>May require parenteral treatment<br>Milder cases can be treated with same regimen as for epididymitis |
| Unilateral pain, tenderness or swelling of testes or epididymis | Epididymitis; orchitis | Rule out torsion<br>250 mg intramuscular ceftriaxone plus 100 mg oral doxycycline twice a day for 10 days[16] |
| Unprotected insertive anal intercourse in men who have sex with men | Usual organisms, plus enteric bacteria[16] | Consider 100 mg oral doxycycline twice a day for seven days instead of azithromycin |
| Unprotected insertive oral intercourse in men who have sex with men | Usual organisms, HSV, adenovirus[16] | Test results often negative |

*FDA = U.S. Food and Drug Administration; HSV = herpes simplex virus; UTI = urinary tract infection.*

*Information from references 14, 16, and 17.*

a midstream urine specimen should be obtained and treatment should be directed at urinary pathogens.[18]

If urethritis or STI risk factors are present, blood testing for syphilis, HIV, and hepatitis B should be offered because coinfection is common. Testing for urethral pathogens other than *N. gonorrhoeae* and *Chlamydia* is controversial, and is generally reserved for patients with resistant or recurrent unexplained symptoms. Testing and treatment recommendations from the CDC are shown in *Table 2*.[16]

It is common for all test results to be negative. Many patients with negative test results respond well to antimicrobial treatment, suggesting false-negative tests or the presence of unknown pathogens.[19] Noninfectious causes of urethritis are poorly defined in the medical literature.

**Table 2. Urethritis Testing and Treatment Guidelines**

| *Type of office visit* | *Testing* | *Treatment* |
|---|---|---|
| Initial visit or return visit with a new or untreated sexual partner | Gonorrhea or chlamydia testing from penile discharge or urine<br>Urinalysis with microscopy if no discharge present<br>Offer Venereal Disease Research Laboratory or rapid plasma reagin test<br>Human immunodeficiency virus and hepatitis B | Positive test results* or mucopurulent discharge<br>Empiric treatment† with 1 g oral azithromycin (Zithromax; single dose) or 100 mg oral doxycycline (twice a day for seven days), plus 125 mg intramuscular ceftriaxone (Rocephin) or 400 mg oral cefixime (Suprax)<br>Negative urine test results and no mucopurulent discharge<br>Defer treatment until results are available, unless patient is at high risk of sexually transmitted infections and is unlikely to return for treatment |
| Subsequent visit within three months, no new sexual partner | Same tests as above<br>Consider *Mycoplasma* or *Ureaplasma*‡ and *Trichomonas* cultures§ from urethra or urine | Azithromycin (500 mg orally once a day for five days), or doxycycline (100 mg orally twice a day for seven days) plus metronidazole (Flagyl; single 2-g dose orally) |

**—Positive leukocyte esterase test on first-void urine or at least 10 white blood cells per high-power field in first-void urine sediment.*
*†—If previous results or rapid tests identify gonorrhea or chlamydia, treat only for the causative organism.*
*‡—With polymerase chain reaction testing.*
*§—Wet mount for* Trichomonas *is not sensitive enough in men to be useful.*

*Information from reference 16.*

## Treatment

In patients with confirmed urethritis, concurrent treatment for gonorrhea and chlamydia is recommended unless test results are already known or rapid results can be obtained to narrow treatment. Current CDC recommendations for these infections are listed in *Table 2*.[16] The combination of a single 1-g dose of oral azithromycin (Zithromax) or 100 mg of oral doxycycline twice per day for seven days (for chlamydia) plus either 400 mg of oral cefixime (Suprax) or 125 mg of intramuscular ceftriaxone (Rocephin; for gonorrhea) is the primary treatment.[16] Because of increased resistance, fluoroquinolones are no longer recommended for empiric treatment of gonorrhea. Although fluoroquinolones may succeed if used inadvertently, a test of cure is suggested in these cases. In men with urethral symptoms but no objective signs or findings, treatment generally should be deferred until test results are available. Exceptions include patients at high risk of STIs who are unlikely to return for test results and treatment.

Men returning for evaluation of persistent or recurrent urethral symptoms can be challenging to diagnose and treat. Considerations include a recurrent infection, usually because of a lack of simultaneous treatment of partners or reinfection by a new partner; an untreated infection, such as *Mycoplasma*, *Ureaplasma*, *Trichomonas*, HSV, *Enterobacteriaceae*, or adenovirus; a resistant organism; or a noninfectious cause.

Azithromycin is the drug of choice for mycoplasmal, ureaplasmal, and chlamydial infections.[20] Azithromycin may also be effective in patients who test negative for these pathogens, with one Japanese study showing an 85 percent cure of signs and symptoms.[19] Emergence of azithromycin resistance in *Mycoplasma* has been demonstrated, leading to a suggestion of longer or alternative treatment for persistent cases.[21] In areas with a high prevalence of trichomoniasis, metronidazole (Flagyl) or tinidazole (Tindamax) may be added to usual regimens.[14]

If all infections have been ruled out, it is reasonable to suggest that patients use fragrance-free soaps, lubricants, and other products; increase water intake and avoid carbonated beverages; discontinue spermicide use; and decrease penile trauma through less frequent or less vigorous masturbation or intercourse.[22] Dietary interventions, although unproven, are consistent with recommendations for other inflammatory urogenital syndromes.[23] Men with urethritis secondary to an STI should be advised to abstain from sex for one week following initiation of therapy. Patient education should be aimed at awareness and reduction of risk factors for STIs.

### PARTNER NOTIFICATION AND TREATMENT

Family physicians have varying degrees of comfort with partner identification and notification methods.[24] Ideally, names and contact information of sexual partners are gathered immediately and referred to a health department, or the patient notifies the contacts directly. Some practices use a paper card that patients can give to their contacts. *Figure 1* shows a customizable sample of a notification card. Alternatively, InSPOT is a widely used, free electronic resource (http://www.inspot.org) that allows patients in some areas to send an anonymous e-mail notification to their sexual partners.[25]

**Important Health Notification**

**You may have been exposed to:**

❑ Gonorrhea ❑ HIV/AIDS
❑ Chlamydia ❑ Herpes
❑ Syphilis ❑ Other _____
❑ *Trichomonas*

*Please take this card to your family physician or health department for testing and treatment.*

**Figure 1.** Customizable sexual partner notification card for sexually transmitted infections. (HIV = human immunodeficiency virus.)

Expedited partner treatment is a CDC-recommended strategy for situations in which the patient's sexual partners are otherwise likely to go untreated.[26] In this approach, patients with STIs are given prescriptions or medications for partners who have not been evaluated by the physician. Among patients with urethritis, expedited partner treatment has been shown to decrease recurrence.[27] Although it is effective at increasing the treatment rates of partners, the legality of expedited partner treatment varies by state because it involves treating persons with whom the physician may have no existing relationship. *Table 3* shows the legal status of expedited partner treatment in each state.[28] The CDC provides additional details for each state at http://www.cdc.gov/std/EPT/legal/default.htm.

## Screening

The U.S. Preventive Services Task Force (USPSTF) has examined routine screening for chlamydia and gonorrhea in men. Because direct complications of chlamydial infections in men are uncommon, and because evidence has not shown that screening men leads to a decrease in adverse outcomes in women, the USPSTF concluded in 2007 that evidence was insufficient to recommend routine screening for chlamydia in men.[29] Asymptomatic gonorrheal infections are uncommon in men; this, combined with a relatively low prevalence in the general population, led to the USPSTF's 2005 recommendation against routine screening for gonorrheal infections in men at low risk of infection.[30]

The CDC recommends several annual screening tests for men who have sex with men.[31] These include urethral/urine DNA testing for gonorrhea and chlamydia in men who have had insertive intercourse during the preceding year; testing for rectal gonorrhea and chlamydia in men who have had receptive anal intercourse during the preceding year; and DNA swab or culture for pharyngeal gonorrhea in men who have had receptive oral intercourse during the preceding year. Testing for pharyngeal chlamydial infection is not recommended.

**Table 3. Legal Status of Expedited Partner Therapy**

| *Permissible* | *Potentially allowable* | *Prohibited* |
|---|---|---|
| Arizona | Alabama | Arkansas |
| California | Alaska | Florida |
| Colorado | Connecticut | Kentucky |
| Illinois | Delaware | Michigan |
| Iowa | District of Columbia | Ohio |
| Louisiana | Georgia | Oklahoma |
| Minnesota | Hawaii | South Carolina |
| Mississippi | Idaho | West Virginia |
| Nevada | Indiana | |
| New Hampshire | Kansas | |
| New Mexico | Maine | |
| New York | Maryland* | |
| North Carolina | Massachusetts | |
| North Dakota | Missouri | |
| Oregon | Montana | |
| Pennsylvania | Nebraska | |
| Tennessee | New Jersey | |
| Texas | Puerto Rico | |
| Utah | Rhode Island | |
| Vermont | South Dakota | |
| Washington | Virginia | |
| Wyoming | Wisconsin | |

**—Permissible in Baltimore, Md.*

*Adapted from Centers for Disease Control and Prevention. Legal status of expedited partner therapy (EPT). http://www.cdc.gov/std/EPT/legal/default.htm. Accessed February 15, 2010.*

## HIV Prevention

There is evidence that the intact urethral endothelium is an important barrier to infection. The disruption of this lining by urethritis may foster the spread of bloodborne pathogens. It has been demonstrated that men with urethritis who are HIV positive have higher HIV RNA titers in their semen than men without urethritis who are HIV positive.[32] Furthermore, treatment of urethritis leads to decreases in HIV-1 expression in semen.[33]

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