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## Urethritis in Men and Women

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### Article info

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### Abstract

Urethritis is usually caused by sexually transmissible organisms. Sexually transmitted diseases (STDs) increase the risk of acquiring other STDs, which is why patients presenting with urethritis should generally be examined for other STDs as well, and examination and treatment of sexual partners are necessary. Standard diagnosis is made via stains of urethral swabs or urine, but modern microbiological diagnostic methods such as nucleic acid amplification techniques achieve higher diagnostic accuracy. In non-gonococcal urethritis, a causative organism can often not be isolated. Antibiotic treatment is usually based on current epidemiologic data.

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### 1. Introduction

Urethritis is characterized by urethral discharge, dysuria, and/or itching. The etiology can be infectious or noninfectious. Infectious urethritis is differentiated into gonococcal urethritis (the “classic” form of infective urethritis), caused by *Neisseria gonorrhoeae*, and non-gonococcal urethritis (NGU), which is most often caused by either *Chlamydia trachomatis* or *Mycoplasma genitalium* [1,2]. In addition, but distinctly less common, infectious NGU can also be caused by *Trichomonas vaginalis*, *Gardnerella vaginalis*, *Ureaplasma urealyticum*, herpes simplex virus (HSV), and adenoviruses [1,3].

### 2. Clinical picture

A urethral discharge that is putrid or watery, dysuria, and/or urethral or perimeatal irritation or itching characterize the clinical picture (Fig. 1). The onset may be insidious or sudden. Asymptomatic cases are common, accounting for approximately 30–50% of cases among men and more among women [4].

The clinical picture and macroscopic assessment of the urethral discharge do not allow a clear-cut diagnosis other than suspicion of urethritis. Therefore, the discharge must

be examined microscopically to establish the presence of inflammation. The microscopic and laboratory findings suggesting the presence of inflammation of the urethra are:

- A discharge on clinical examination;
- A high number of polymorphonuclear leucocytes in a Gram-stained smear of the discharge ( $\geq 2$  leucocytes per high-power field [1000 $\times$ ]);
- A high number of polymorphonuclear leucocytes in the sediment of first-void urine (stained or unstained;  $\geq 10$  leucocytes at 400 $\times$  magnification); and
- A positive leucocyte esterase test on urine dipstick (first-void portion).

### 3. Etiology and diagnosis of urethritis

The great majority of urethritis cases are caused by infective etiologies. Other noninfective causes are very rare (see below).

#### 3.1. *Neisseria gonorrhoeae*

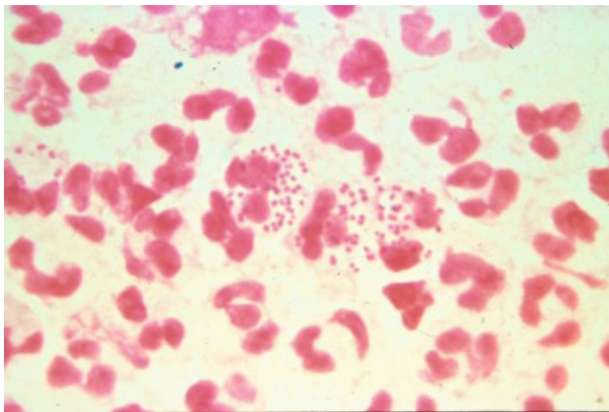
Gonococcal urethritis is the best known and clinically most obvious form of urethritis. It is caused by infection with *N. gonorrhoeae*, an intracellular, aerobic, oxidase-positive

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**Fig. 1 – Clinical picture of gonococcal urethritis with a putrid urethral discharge (courtesy of S. Schubert).**



**Fig. 2 – *Neisseria gonorrhoeae*: intracellular Gram-negative diplococci in a urethral smear.**

diplococcus (Fig. 2). Gonococci grow only on special culture media, such as chocolate agar and Thayer-Martin agar, with CO<sub>2</sub> enrichment. The incubation time is 2–7 d. Gonococcal urethritis used to be considered the classic form of urethritis. This is why classification of infectious urethritis still differentiates between gonococcal and non-gonococcal urethritis.

For a quick diagnosis, Gram staining of the urethral secretion should be performed (Fig. 2). This has sensitivity of 95% and specificity of 99.9% in men for diagnosis of gonococcal urethritis [5,6]. Alternatively, a simpler methylene blue/gentian violet stain can be used, which does not require heat fixation and performs similarly well [4].

### 3.2. Non-gonococcal urethritis

NGU be caused by a variety of organisms, most commonly *C. trachomatis*, *M. genitalium*, or *T. vaginalis*, less commonly *G. vaginalis* or *U. urealyticum*, and rarely by herpes simplex virus. However, despite advances in the diagnosis of NGU, determination of an identifiable pathogen is not possible in many cases (up to 50%) [7].

#### 3.2.1. Mycoplasmas

Mycoplasmas are the smallest free-living organisms. In the urogenital tract, *M. genitalium*, *U. urealyticum*, *U. parvum*,

and *M. hominis* can be differentiated, of which the two latter are discussed to be not pathogenic in humans. Mycoplasmas, in contrast to most other bacteria, do not have a cell wall and cannot be grown on standard media.

3.2.1.1. *M. genitalium*. *Mycoplasma* accounts for 10–35% of NGU cases, while its prevalence among healthy men and women is only approximately 1–3% [8]. It is easily transmitted by sexual contact. In women, *M. genitalium* is associated with urethritis, cervicitis, endometritis, pelvic inflammatory disease, and disorders of fertility (pre-term birth, spontaneous abortion, and tubal factor infertility).

In men, persistence after ineffective treatment may have important implications for greater susceptibility to HIV infection. *M. genitalium* is considered to be slightly less contagious during sexual contact than *C. trachomatis*. The incubation time is estimated to be 14 d.

The only useful method for diagnosis is NAT for urine samples or urethral, vaginal, or cervical swabs. Sexual contacts within the previous 3 mo should be examined. The high rate of resistance to primary treatment with macrolides is increasing, which is why a post-treatment reassessment is required.

3.2.1.2. *U. urealyticum*. There has been a great deal of disagreement about the role of the mycoplasma family member *Ureaplasma* in NGU. *Ureaplasma* can be isolated in urethral swabs from asymptomatic men in 30–40% of cases, but the association with NGU is controversial because older studies did not differentiate between *U. urealyticum* and *U. parvum*. While the latter is a nonpathogenic component of the urethral flora, *U. urealyticum* seems to be a likely cause of NGU, although probably in only a small number of cases [4,9]. This etiology should therefore be considered in men without other identifiable NGU etiologies.

#### 3.2.2. *C. trachomatis*

Chlamydiae are very old bacteria in terms of evolutionary development, and there are three species that are pathogenic in humans: *C. trachomatis*, *C. psittaci*, and *C. pneumoniae*. These are small Gram-negative bacteria that live as intracellular parasites, which is why they were originally thought to be large viruses [10]. Their intracellular existence predisposes to long-persisting infections. The primary target organs for *C. trachomatis* are the epithelium of the urethra in males and of the cervix in women, but the mucosa of the rectum and the conjunctiva can also be infected [11].

Some serotypes cause human trachoma in tropical climates, while serotypes D–K are sexually transmissible and are among the most common sexually transmitted diseases (STDs). The prevalence in the general population in the USA is 1.4% in men and 2.0% in women, but is higher in other countries [12].

Infections are often asymptomatic in women (70%), while most infections in men are symptomatic (70%) [11]. Chlamydia infections account for approximately 25–50% of all cases of male urethritis. In females, cervicitis and/or urethritis result from infections, and *C. trachomatis*

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