

Chapter 2

URETHRITIS IN MALES

ETIOLOGY

Urethritis is the most frequent STD syndrome seen in men. Customarily, clinicians categorize urethritis into gonococcal and nongonococcal etiologies. The relative frequency of nongonococcal urethritis (NGU) and gonococcal urethritis varies by population studied, but overall, more cases of NGU than gonococcal urethritis are now being seen in the United States. Up to one-fourth of heterosexual men with gonorrhea also have simultaneous *Chlamydia trachomatis* (CT) infections.

C. trachomatis causes 20 to 40% of cases of NGU, and some studies indicate that *Mycoplasma genitalium* and *Ureaplasma urealyticum* may cause an additional 10 to 20%. The remaining cases probably result from sexually transmitted pathogens, but their precise etiology remains unclear. Occasionally, urethritis results from infection with *Trichomonas vaginalis*, adenovirus or herpes simplex virus. Most patients with urethritis due to genital herpes infection will have obvious herpetic penile lesions, and many with urethritis due to *T. vaginalis* will have sex partners with trichomonal vaginitis.

INCUBATION PERIOD

Gonorrhea usually develops 2 to 6 days after exposure to *Neisseria gonorrhoeae* (GC), whereas NGU generally develops between 1 and 5 weeks after infection, with a peak around 2 weeks.



Nongonococcal urethritis (mucoid discharge) [1]

CLINICAL MANIFESTATIONS

Both gonococcal and nongonococcal urethritis typically cause urethral discharge, dysuria, or urethral itching. Three-quarters of men with gonococcal urethritis have purulent urethral discharge, and three-quarters of men with chlamydial or culture-negative NGU have clear or mucoid discharge. A significant proportion of men with urethral chlamydial infections are asymptomatic; conversely, most urethral gonococcal infections are symptomatic.



Gonococcal urethritis (purulent discharge) [2]

DIAGNOSIS

The diagnostic approach to men with urethritis begins by distinguishing those patients who have urethral discharge on examination from those who do not (see Figure 2-1). It should be emphasized that clinical features alone do not reliably differentiate between gonococcal and nongonococcal urethritis. For

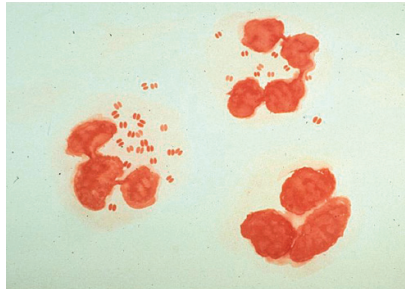
this reason, diagnosis and treatment should be based on the results of a urethral Gram stain and appropriate cultures or tests.

Document Urethritis

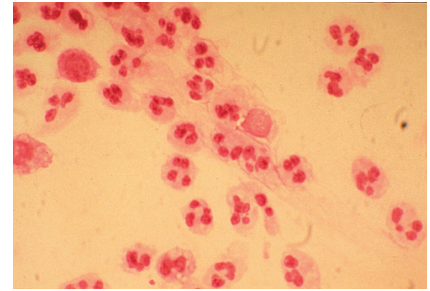
by the presence of at least *two* of the following three features:

1. Symptoms: history of urethral discharge and/or dysuria
2. Examination: presence of purulent, mucopurulent, or mucoid urethral discharge
3. Laboratory: (any one of following is sufficient)

- urethral Gram-stained smear showing ≥ 5 PMNs/1000X field in areas of maximal cellular concentration
- urinalysis showing ≥ 10 PMNs/400X field in centrifuged sediment
- positive urine leukocyte esterase test



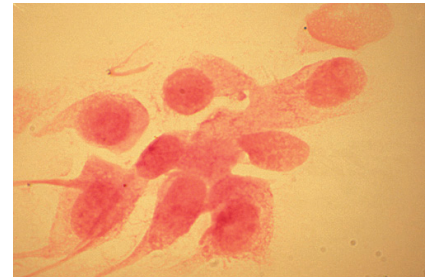
Intacellular Gram-negative diplococci (GNDC) in urethral Gram stain [3]



Urethral Gram stain with >5 PMNs per high power field (nongonococcal urethritis) [4]



Lesion of disseminated gonococcal infection [5]



Normal urethral cells on Gram stain [6]

Patients with symptoms of urethritis, but without a visible discharge on exam or laboratory evidence of urethritis, should be reexamined within 7 days when they have not urinated for 4 to 8 hours. If only one diagnostic criterion is met on reexamination, obtain the first 5 to 10 ml of voided urine, centrifuge, and examine the sediment microscopically: ≥ 10 PMNs/400X field confirms urethritis.

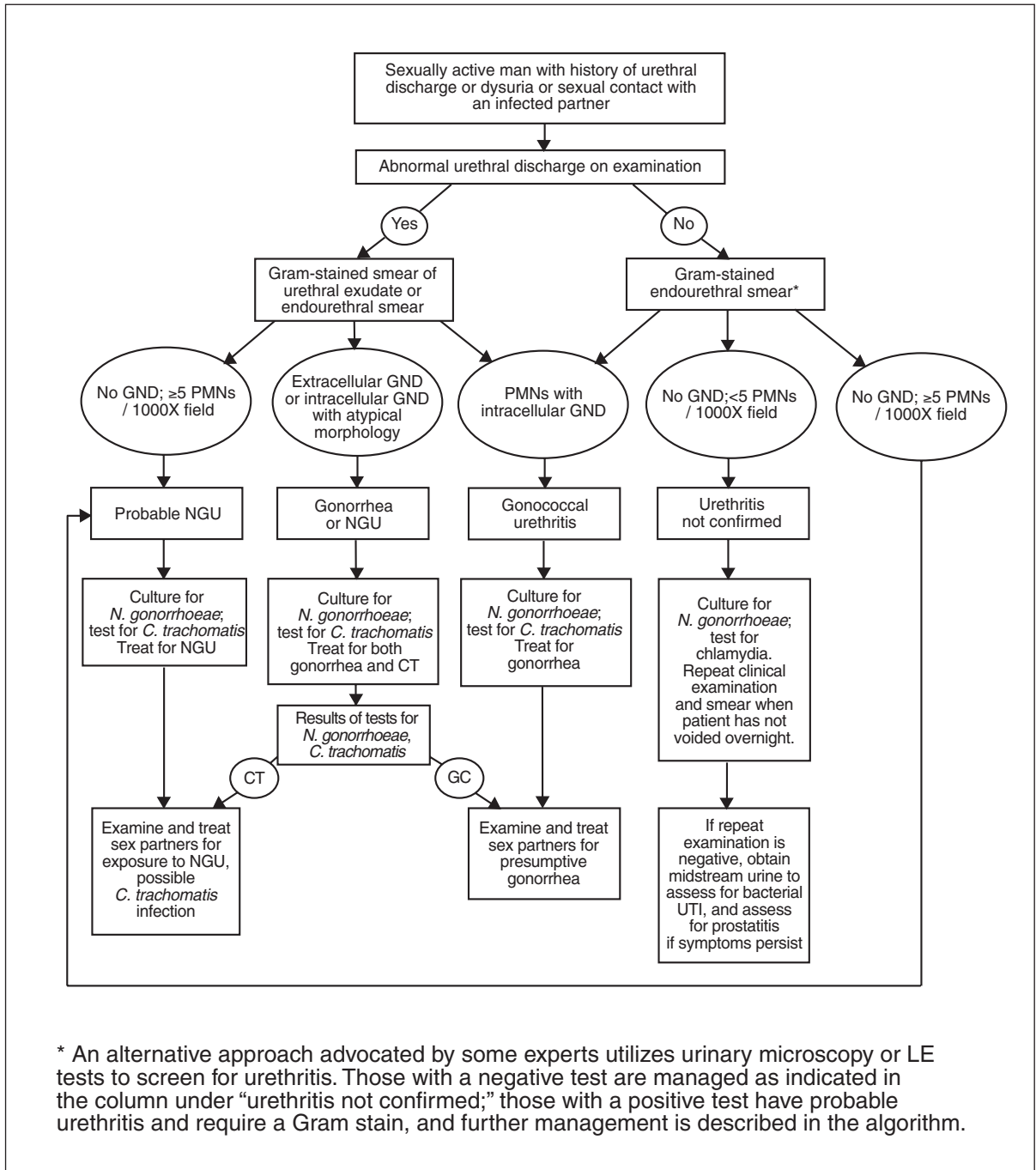
A urethral Gram-stained smear showing ≥ 5 PMNs/1000X field is suggestive of urethritis, even in the absence of other criteria.

Exclude Gonorrhea

1. Gram-stained smear of urethral exudate
 - negative for intracellular Gram-negative diplococci (IGND)
2. Confirmed by negative culture for *N. gonorrhoeae* (GC)

Test for Chlamydia

Obtain urethral specimen for *C. trachomatis* (CT) antigen-detection or DNA test, culture, or NAAT (LCR, PCR).



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Figure 2-1
Management of a male with possible urethritis.

TREATMENT

For a more detailed discussion of these regimens and other treatment considerations, please refer to the CDC STD Treatment Guidelines at <http://www.cdc.gov/std/treatment/>.

Gonococcal Urethritis **Uncomplicated anogenital gonorrhea**

Any of the following:

- Cefixime 400 mg PO (single dose) or 400 mg by suspension (200 mg / 5 ml)
- Ceftriaxone 125 mg IM (single dose)

Note:

1. Doxycycline is also provided with any of the above treatments for empirical treatment of possible coexisting *C. trachomatis* infection. Alternatively, azithromycin 1 gm PO single dose can be used instead of doxycycline for treatment of possible co-existing chlamydial infection.
2. The tablet formulation of Cefixime is currently not available in the United States. The liquid formulation of Cefixime is still available though not feasible or available in most clinics.

Alternative regimens

- Spectinomycin 2 g in a single intramuscular (IM) dose
- Single-dose cephalosporin regimens

Spectinomycin is currently not available in the United States. Other single-dose cephalosporin therapies that are considered alternative treatment regimens for uncomplicated urogenital and anorectal gonococcal infections include ceftizoxime 500 mg IM; or cefoxitin 2 g IM, administered with probenecid 1 g orally; or cefotaxime 500 mg IM. Some evidence indicates that cefpodoxime 400 mg and cefuroxime axetil 1 g might be oral alternatives..

Nongonococcal Urethritis **Recommended regimens**

Either of the following:

- Azithromycin 1 g orally in a single dose,
- Doxycycline 100 mg orally twice a day for 7 days

Alternative regimens

Any of the following:

- Erythromycin base 500 mg orally four times a day for 7 days,
- Erythromycin ethylsuccinate 800 mg orally four times a day for 7 days,
- Ofloxacin 300 mg twice a day for 7 days
- Levofloxacin 500 mg once daily for 7 days

Immediate treatment failure

(persistent urethritis while on therapy or recrudescence immediately after completion of treatment)

1. Confirm urethritis by examination and laboratory.
2. Obtain urethral wet prep and culture for trichomonas.
3. Pending results of trichomonas culture:
 - Treat with erythromycin if doxycycline was used initially
 - Erythromycin stearate or base 500 mg qid for 7 days
4. Treat with metronidazole 2 gm PO single dose (microscopy of first-void urine or urethral swabs shows trichomonads or if trichomonas culture is positive, or empirically if culture is unavailable)
 - Treat with doxycycline if erythromycin was used initially
 - Doxycycline 100 mg bid for 7 days

Recurrence of urethritis

(within 6 weeks, following apparent resolution)

1. Evaluate to confirm the diagnosis of urethritis.
2. Confirm that the treatment was followed and whether or not the patient had sexual activity before he or his partner were fully treated. If the patient has been noncompliant or has been exposed to an untreated partner, retreat with the original regimen.
3. Retreat with Metronidazole 2 g orally in a single dose, plus Erythromycin base 500 mg orally four times a day for 7 days, or Erythromycin ethylsuccinate 800 mg orally four times a day for 7 days.

FOLLOW-UP**Initial or isolated episode****Patients with gonococcal urethritis**

A test-of-cure is recommended only for patients with a known resistant strain of GC or for those with persistent symptoms.

Men with NGU

Request a return after 7 to 14 days only if symptoms persist or recur.

Persistent or recurrent NGU

Request that patients return prn for persistent or recurrent symptoms.

Consider referral to a urologist or other specialist.

Confirmed cases

of gonorrhea and chlamydia should be reported to the state/local health department (To locate health department STD programs, visit <http://www.ncsddc.org/programsites.htm>).

MANAGEMENT OF SEX PARTNERS**All contacts within the previous 4 weeks,**

and any other contacts suggested by the epidemiologic history:

1. Perform routine STD examination.
2. Regular partners and source contacts
 - of gonorrhea:
Treat with cefixime 400 mg PO (or other single dose regimen listed above) and provide doxycycline for possible coexisting *C. trachomatis* infection.
 - of chlamydia urethritis or CT-NGU:
Treat with doxycycline, ofloxacin or azithromycin.
When practical, use the same regimen used for the patient, unless contraindicated because of pregnancy or drug intolerance.
3. Casual contacts:
Individualize treatment, depending on the clinical examination, epidemiologic setting (for example, suspected source vs. spread contact), and results of gonorrhea and chlamydia tests.
Do not dispense antibiotics or prescriptions for contacts who are not examined, except in special circumstances.

Contacts of men with recurrent NGU

The need and value of treatment are unknown. Individualize the approach on the basis of available clinical, epidemiological, and microbiological data.

SEQUELAE

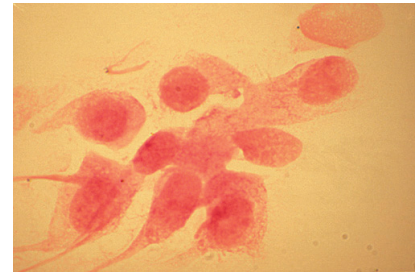
With the advent of antibiotics, complications as a result of gonococcal urethritis, such as locally invasive infection, urethral strictures, or disseminated gonococcal infection are now rare. NGU is generally a self-limited disease and, even without therapy, clinical consequences are minimal. Epididymitis can develop in up to 2% of cases, and conjunctivitis occasionally occurs. Reiter's syndrome may result from untreated chlamydial urethritis in genetically predisposed individuals. The psychological impact of persistent urethritis or frequent recurrences can be great.

LABORATORY SCREENING FOR URETHRITIS IN ASYMPTOMATIC MEN

A urethral Gram stain and cultures for chlamydia and gonorrhea should be obtained from heterosexual men who are seen in high-risk settings such as an STD clinic and who have no history of urethral symptoms or signs and no history of contact with an infected partner. An example of columnar epithelial cells obtained from an endourethral swab from an asymptomatic man is shown to the right; the presence of columnar epithelial cells indicates that the swab specimen has been obtained adequately to test for *C. trachomatis*. Some of these men will have asymptomatic gonorrhea or NGU as evidenced by persistent urethral leukocytosis, pyuria (as measured by urine microscopy or LE test), and/or a positive test for chlamydia or gonorrhea.



Lesion of disseminated gonococcal infection [5]



Normal urethral cells on Gram stain [6]