

Diagnosis and Treatment of *Neisseria gonorrhoeae* Infections

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The most common site of *Neisseria gonorrhoeae* infection is the urogenital tract. Men with this infection may experience dysuria with penile discharge, and women may have mild vaginal mucopurulent discharge, severe pelvic pain, or no symptoms. Other *N. gonorrhoeae* infections include anorectal, conjunctival, pharyngeal, and ovarian/uterine. Infections that occur in the neonatal period may cause ophthalmia neonatorum. If left untreated, *N. gonorrhoeae* infections can disseminate to other areas of the body, which commonly causes synovium and skin infections. Disseminated gonococcal infection presents as a few skin lesions that are limited to the extremities. These lesions start as papules and progress into bullae, petechiae, and necrotic lesions. The most commonly infected joints include wrists, ankles, and the joints of the hands and feet. Urogenital *N. gonorrhoeae* infections can be diagnosed using culture or nonculture (e.g., the nucleic acid amplification test) techniques. When multiple sites are potentially infected, culture is the only approved diagnostic test. Treatments for uncomplicated urogenital, anorectal, or pharyngeal gonococcal infections include cephalosporins and fluoroquinolones. Fluoroquinolones should not be used in patients who live in or may have contracted gonorrhea in Asia, the Pacific islands, or California, or in men who have sex with men. Gonorrhea infection should prompt physicians to test for other sexually transmitted diseases, including human immunodeficiency virus. (Am Fam Physician 2006;73:1779-84, 1786. Copyright © 2006 American Academy of Family Physicians.)

► Patient information:

A handout on gonorrhea, written by the author of this article, is provided on page 1786.

Most rectal gonococcal infections are subclinical, but symptoms can include anal pruritus and mucopurulent discharge.

N*eisseria gonorrhoeae* infections may present as a broad range of symptoms and can affect urogenital, anorectal, pharyngeal, and conjunctival areas. Severe cases can lead to disseminated gonococcal infections, endocarditis, and meningitis; and in women, to pelvic inflammatory disease (PID).

Two methods for detecting *N. gonorrhoeae* are culture and nonculture tests. Culture techniques are considered the tests of choice; but nonculture techniques, which are less labor-intensive and are similar in accuracy to cultures, have replaced culture techniques in some instances. The newest nonculture technique is the nucleic acid amplification test. This test has good sensitivity (92 to 96 percent) and specificity (94 to 99 percent) compared with cultures.¹

Urogenital Infections

The most common site of *N. gonorrhoeae* infection is the urogenital tract. In women it can infect the endocervix and, if an ascending infection develops, it can cause PID. Men may develop urethritis and, occasionally, epididymitis.

FEMALE INFECTIONS

In women, common symptoms include odorless vaginal discharge; vaginal bleeding, particularly after intercourse; and dyspareunia. Many women have no symptoms, however.² Physical findings in women include cervicitis with mucopurulent drainage from the os. The cervix tends to bleed easily when rubbed with a cotton-tipped swab. Gonorrhea infections do not cause vaginitis, but other concomitant infections may produce vaginal findings.

Ten to 20 percent of women with gonorrhea develop ascending infection that causes acute salpingitis with or without endometritis, also known as PID.² Presentations may range from no symptoms to severe abdominal pain with a high fever. PID can negatively affect fertility, causing infertility in 15 percent of patients²; 50 percent of patients who have three or more episodes of PID develop infertility.²

The Centers for Disease Control and Prevention (CDC) recommends that physicians maintain a low threshold for diagnosing PID because of significant negative sequelae associated with this infection.² The CDC currently recommends empiric treatment of PID in women with uterine and adnexal

SORT: KEY RECOMMENDATIONS FOR PRACTICE

<i>Clinical recommendation</i>	<i>Evidence rating</i>	<i>References</i>
Uncomplicated gonococcal infections of the cervix, urethra, or rectum should be treated with a single 125-mg dose of ceftriaxone (Rocephin) administered intramuscularly.	C	2
Oral regimens to treat pelvic inflammatory disease should continue for 14 days.	C	2
Women younger than 25 years who are sexually active should be screened annually for gonococcal infections.	B	2, 12
Fluoroquinolones should not be used to treat gonorrhea in men who have sex with men.	C	8

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 more information about the SORT evidence rating system, see page 1687 or <http://www.aafp.org/afpsort.xml>.

tenderness or cervical motion tenderness if they are at risk of sexually transmitted diseases (STDs) and no other causes can be identified.² Table 1² includes the CDC's criteria for diagnosing PID.

In women with urogenital disease, the nucleic acid amplification test can detect gonorrhea by endocervical or urine sample. Urine samples have a lower sensitivity and,

therefore, a higher chance of false negatives than do endocervical samples.¹

MALE INFECTIONS

Unlike women, men with urogenital infections are usually symptomatic. The normal incubation period is two to six days after exposure. Symptoms include purulent penile discharge and dysuria. The discharge may present at the meatus, which may be erythematous. Discharge may be expressed by milking the penis.

N. gonorrhoeae may also cause epididymitis, which can present as unilateral testicular pain without discharge or dysuria. The patient may or may not have a fever. On examination, the epididymis is swollen and tender to palpation.

Culture or nonculture techniques can diagnose urogenital gonorrhea in men.¹ If the sample is obtained using a urethral swab, the physician should milk the penis first. Nucleic acid amplification tests using urine samples provide similar results to that of the urethral swab technique.¹

Anorectal Infections

Gonorrhea infections in the rectal area are most common in women and in men who have sex with men (MSM). Perianal contamination from a cervical infection or a direct infection from anal intercourse can cause anorectal infections in women. In MSM, the infection is caused by direct exposure through anal intercourse. Most rectal gonococcal infections are subclinical. If present, symptoms can include anal pruritus and mucopurulent discharge, usually with

TABLE 1
Diagnostic Criteria for PID

Minimal criteria

Cervical motion tenderness
Uterine or adnexal tenderness

Additional criteria*

Abnormal cervical or vaginal mucopurulent discharge
Elevated C-reactive protein level
Elevated erythrocyte sedimentation rate
History of gonorrhea or chlamydia infection
Oral temperature greater than 101°F (38.3°C)
White blood cells present on saline preparation of vaginal secretions

Specific criteria

Evidence of endometritis on endometrial biopsy
Laparoscopic abnormalities consistent with PID
Transvaginal ultrasonography or magnetic resonance imaging shows thickened, fluid-filled tubes with or without free pelvic fluid or tubo-ovarian complex.

PID = pelvic inflammatory disease.

*—Additional criteria may be used to enhance the specificity of minimal criteria.

Information from reference 2.

a bowel movement. Rectal pain, tenesmus, and bleeding are more common in MSM. Severe gonococcal rectal infections may be difficult to differentiate from inflammatory bowel disease.

Although data suggest that nucleic acid amplification tests can detect rectal gonorrhea infections,³ the CDC recommends the culture technique for a diagnosis.² However, one study⁴ showed a high prevalence (7 percent) of asymptomatic rectal gonorrhea in MSM; therefore, it may be beneficial to screen these patients using nucleic acid amplification tests.

Pharyngeal Infections

Pharyngeal infections caused by *N. gonorrhoeae* usually occur after orogenital exposure; symptoms are mild or absent. On physical examination, the pharynx may be erythematous or have exudates. Anterior cervical lymphadenopathy also may be present. Most cases of pharyngeal infection will spontaneously resolve with no treatment and usually do not cause adverse sequelae. Treatment should be initiated, however, to reduce the potential for spreading the infection.² The CDC currently recommends cultures to test patients who have suspected pharyngeal gonorrhea.²

Infections in Children

There are two distinct categories of gonococcal infections in children. During the neonatal period and the first year of life, gonorrhea infections can cause neonatal conjunctivitis (ophthalmia neonatorum); pharyngitis; rectal infections; and, in rare cases, pneumonia. These infections most commonly develop within two to five days after birth, because the neonate is exposed to infected cervical exudates during delivery. Almost all new gonococcal infections in children older than one year are caused by sexual abuse.

OPHTHALMIA NEONATORUM

N. gonorrhoeae is not the most common cause of ophthalmia neonatorum. However, identifying and treating gonorrhea-related ophthalmia neonatorum is important because, if left untreated, it can cause perforation of

the globe of the eye and blindness. Infants at risk of gonococcal conjunctivitis are those who did not receive prophylaxis for ophthalmia neonatorum, those whose mothers had no prenatal care, and those whose mothers have a history of STDs or substance abuse. Common findings include inflammation of the conjunctiva and mucopurulent discharge from the eye.

Testing neonates who have ophthalmia neonatorum for *N. gonorrhoeae* should begin with a Gram stain of the conjunctival exudates. If intracellular gram-negative diplococci are present, *N. gonorrhoeae* infection is presumed and treatment should be initiated. Gonococcal cultures should confirm the diagnosis.²

SEXUAL ABUSE

Preadolescent children most commonly contract gonococcal infections through sexual abuse.² The common presentation is a girl with vaginitis symptoms. Pharyngeal and rectal infections also may be present, but they are usually asymptomatic.

A culture method should be used to test children for *N. gonorrhoeae*.² Nonculture techniques should not be used alone because the U.S. Food and Drug Administration has not approved them for use in children. Specimens from the vagina, pharynx, urethra, or rectum should be used to isolate *N. gonorrhoeae*.

Disseminated Infection

Disseminated infection is rare but can occur in 1 to 3 percent of adults who have gonorrhea.² Septic emboli can cause polyarticular tenosynovitis and dermatitis in these patients.² Symptoms of disseminated infection can range from slight joint pain, a few skin lesions, and no fever to overt polyarthritis and a high fever. Patients with disseminated gonorrhea usually have no urogenital symptoms.

The skin lesions typically are few and are limited to the extremities; they start as papules and progress into hemorrhagic pustules. Bullae, petechiae, or necrotic lesions also may be present. The skin lesions usually

Many experts advocate empiric treatment for chlamydia when treating patients with gonorrhea.

are resolved if the gonorrhea continues to disseminate. Skin lesions and blood cultures usually are negative for *N. gonorrhoeae*.

The joints most commonly affected by disseminated gonorrhea are the wrists, ankles, and the joints of the hands and feet. The axial skeleton rarely is involved. Initial aspiration of the joint may be negative for infection. If untreated, however, the patient will develop septic arthritis, which will most likely involve elbows, wrists, knees, or ankles. The joints will be swollen and warm, and a joint aspira-

tion will detect more than 40,000 leukocytes per mm³ (40 × 10⁹ per L) and contain gram-negative intracellular diplococci. Fluid cultures usually do not grow the organism.²

Disseminated gonorrhea also may present as bacterial endocarditis, meningitis, and myocarditis, although the incidences of these presentations have declined with the advent of antibiotic therapy.

Treatment

The CDC's treatment guidelines for uncomplicated gonococcal infections are included in Table 2.² Despite findings that fluoroquinolones have similar cure rates as ceftriaxone (Rocephin),⁵ *N. gonorrhoeae* has become increasingly resistant to fluoroquinolones in some geographic areas. Therefore, the CDC advises against using fluoroquinolones to treat gonorrhea infection in patients who live or may have acquired infection in Asia, the Pacific islands (including Hawaii), and California.² The CDC recently noted a substantial increase in fluoroquinolone-resistant *N. gonorrhoeae* in MSM, and it no longer recommends fluoroquinolones as first-line treatment in these patients.⁶ England, Wales, and Canada also have reported fluoroquinolone-resistant *N. gonorrhoeae*.^{7,8}

PID can be treated on an outpatient basis if the patient does not meet hospitalization criteria (Table 3).² Outpatient treatment may include either of two equally effective oral regimens.² If parenteral antibiotic therapy is indicated, the preferred therapy is cefotetan (Cefotan), 2 g intravenously every 12 hours, or cefoxitin (Mefoxin), 2 g intravenously every six hours, plus doxycycline (Vibramycin), 100 mg orally or intravenously every 12 hours. Doxycycline is best administered orally because intravenous doxycycline can be painful and can adversely affect veins.² Table 4 includes CDC treatment guidelines for PID.²

Pharyngeal gonococcal infections are more difficult to treat than urogenital or anorectal infections because few antibiotic regimens can reliably cure this infection. The CDC recommends ceftriaxone in a single 125-mg dose intramuscularly or ciprofloxacin (Cipro) in a single 500-mg dose orally,

TABLE 2
Treatment Guidelines for Uncomplicated Gonococcal Infections*

- Cefixime (Suprax), 400 mg orally†
- Ceftriaxone (Rocephin), 125 mg intramuscularly
- Ciprofloxacin (Cipro), 500 mg orally
- Levofloxacin (Levaquin), 250 mg orally
- Ofloxacin (Floxin), 400 mg orally

NOTE: All medications are administered as a single dose; fluoroquinolones should not be used in geographic areas of high resistance or in men who have sex with men.

*—Cervical, urethral, rectal.

†—This medication has been unavailable at times.

Information from reference 2.

TABLE 3
Criteria for Hospitalizing Patients with PID

- Patient does not respond to oral antimicrobial therapy.
- Patient is pregnant.
- Patient has severe illness, nausea and vomiting, or high fever.
- Surgical emergencies (e.g., appendicitis) cannot be excluded.
- Patient has a tubo-ovarian abscess.
- Patient is unable to follow or tolerate an outpatient oral drug regimen.

PID = pelvic inflammatory disease.

Information from reference 2.

TABLE 4
Treatment Guidelines for Patients with PID

Parenteral regimen

Cefotetan (Cefotan), 2 g IV every 12 hours
Cefoxitin (Mefoxin), 2 g IV every six hours

plus

Doxycycline (Vibramycin), 100 mg orally
or IV every 12 hours

Oral regimen A

Ofloxacin (Floxin), 400 mg orally twice per day
Levofloxacin (Levaquin), 500 mg once per day
with or without

Metronidazole (Flagyl), 500 mg orally twice
per day

Oral regimen B

Ceftriaxone (Rocephin), single 250-mg dose IM
Cefoxitin, single 2-g dose IM administered
concurrently with probenecid (Benemid),
single 1-g dose orally

plus

Doxycycline, 100 mg orally twice per day
with or without

Metronidazole, 500 mg twice per day

*PID = pelvic inflammatory disease; IV = intravenously;
IM = intramuscularly.*

*NOTE: Parenteral regimen may be discontinued 24 hours
after clinical improvement. Duration of oral regimens
is 14 days.*

Information from reference 2.

because these regimens have been shown to effectively treat pharyngeal gonorrhea.² If resistance to fluoroquinolone is a concern, ceftriaxone is the treatment of choice.

Children with ophthalmia neonatorum or suspected gonococcal infection should be treated with ceftriaxone in a single 25- or 50-mg per kg dose intravenously or intramuscularly.² Total dosage should not exceed 125 mg. Fluoroquinolones should be avoided in children who weigh less than 99 lb (45 kg), because they are at risk of articular cartilage damage.²

Patients with suspected disseminated gonococcal infection should be hospitalized initially.² The evaluation should include examining for clinical signs of endocarditis and meningitis. The CDC recommends

TABLE 5
Treatment Guidelines for Disseminated Gonococcal Infections

Recommended parenteral regimen

Ceftriaxone (Rocephin), 1 g IV or IM every
24 hours

Alternative parenteral regimens

Cefotaxime (Claforan), 1 g IV every eight hours
Ciprofloxacin (Cipro), 400 mg IV every 12 hours
Levofloxacin (Levaquin), 250 mg IV once per day
Ofloxacin (Floxin), 400 mg IV every 12 hours
Spectinomycin (Trobicin), 2 g IM every 12 hours

Oral regimen*

Cefixime (Suprax), 400 mg twice per day
Ciprofloxacin, 500 mg twice per day
Levofloxacin, 500 mg once per day
Ofloxacin, 400 mg twice per day

IV = intravenously; IM = intramuscularly.

**—Oral therapy should be initiated 24 to 48 hours
after the patient begins to improve and should con-
tinue for at least one week.*

Information from reference 2.

ceftriaxone, 1 g intravenously or intramuscularly every 24 hours, for patients with disseminated infections.² Parenteral antibiotics should be continued for 24 to 48 hours after clinical improvement begins and then oral regimens should begin.²

Fluoroquinolones and tetracyclines are contraindicated for pregnant women.² If the patient cannot tolerate cephalosporins, the alternative therapy is spectinomycin (Trobicin), 2 g intramuscularly every 12 hours. Both of these regimens have similar cure rates.⁹ *Table 5* includes CDC treatment guidelines for disseminated gonococcal infections.²

Concomitant STDs

Ten to 30 percent of patients with gonorrhea will have a concomitant chlamydia infection; therefore, many experts advocate empirically treating chlamydia when treating patients with gonorrhea.¹⁰ The CDC recommends azithromycin (Zithromax) in a single 1-g dose orally, or doxycycline, 100 mg twice a day for seven days, for patients with

uncomplicated infections of the cervix, urethra, and rectum and possible concomitant chlamydia infections.²

Physicians should strongly consider testing patients who have confirmed gonococcal infections for other STDs, including human immunodeficiency virus, using CDC guidelines for STD testing and treatment, which are available online at <http://www.cdc.gov/std/treatment/>.² Unfortunately, compliance with these guidelines is low. In one study¹¹ of an emergency department, compliance ranged from 14 to 79 percent with respect to history taking, physical examination, diagnostic testing, treatment, and counseling about safe sex. Less than one third of patients included in this study received CDC-recommended antibiotics.

Screening

According to the CDC, all sexually active women younger than 25 years should be screened annually for gonorrhea. Women 25 years of age or older should be screened annually if they have a new sexual partner or a history of multiple partners.² The U.S. Preventive Services Task Force (USPSTF) recommends that all sexually active women, including those who are pregnant, receive routine screening if they are at increased risk of infection.¹² Risk factors include age younger than 25 years, history of an STD, new or multiple sexual partners, inconsistent condom use, and history of prostitution or drug use.¹² The CDC and the USPSTF do not recommend routine screening for men because they usually are symptomatic.^{2,12}

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REFERENCES

1. Cook RL, Hutchinson SL, Ostergaard L, Braithwaite RS, Ness RB. Systematic review: noninvasive testing for *Chlamydia trachomatis* and *Neisseria gonorrhoeae*. *Ann Intern Med* 2005;142:914-25.
2. Workowski KA, Levine WC. Sexually transmitted diseases treatment guidelines 2002. Centers for Disease Control and Prevention. *MMWR Recomm Rep* 2002;51(RR-6):1-78. Accessed online September 14, 2005, at: <http://www.cdc.gov/std/treatment/>.
3. Koumans EH, Johnson RE, Knapp JS, St Louis ME. Laboratory testing for *Neisseria gonorrhoeae* by recently introduced nonculture tests: a performance review with clinical and public health considerations. *Clin Infect Dis* 1998;27:1171-80.
4. Young H, Manavi K, McMillian A. Evaluation of ligase chain reaction for the non-cultural detection of rectal and pharyngeal gonorrhea in men who have sex with men. *Sex Transm Infect* 2003;79:484-6.
5. Hook EW 3d, Jones RB, Martin DH, Bolan GA, Mroczkowski TF, Neumann TM, et al. Comparison of ciprofloxacin and ceftriaxone as single-dose therapy for uncomplicated gonorrhea in women. *Antimicrob Agents Chemother* 1993;37:1670-3.
6. Centers for Disease Control and Prevention. Increases in fluoroquinolone-resistant *Neisseria gonorrhoeae* among men who have sex with men — United States, 2003, and revised recommendations for gonorrhea treatment, 2004. *MMWR Morb Mortal Wkly Rep* 2004;53:335-8.
7. Fenton KA, Ison C, Johnson AP, Rudd E, Soltani M, Martin I, et al., for the GRASP collaboration. Ciprofloxacin resistance in *Neisseria gonorrhoeae* in England and Wales in 2002. *Lancet* 2003;361:1867-9.
8. Sarwal S, Wong T, Sevigny C, Ng LK. Increasing incidence of ciprofloxacin-resistant *Neisseria gonorrhoeae* infection in Canada. *CMAJ* 2003;168:872-3.
9. Brocklehurst P. Antibiotics for gonorrhoea in pregnancy. *Cochrane Database Syst Rev* 2002;(2):CD000098.
10. Lyss SB, Kamb ML, Peterman TA, Moran JS, Newman DR, Bolan G, et al, for the Project RESPECT Study Group. Chlamydia trachomatis among patients infected with and treated for *Neisseria gonorrhoeae* in sexually transmitted disease clinics in the United States. *Ann Intern Med* 2003;139:178-85.
11. Kane BG, Degutis LC, Sayward HK, D'Onofrio G. Compliance with the Centers for Disease Control and Prevention recommendations for the diagnosis and treatment of sexually transmitted diseases. *Acad Emerg Med* 2004;11:371-7.
12. U.S. Preventive Services Task Force. Screening for gonorrhea: recommendation statement. AHRQ Publication No. 05-0579-A. Rockville, Md.: Agency for Healthcare Research and Quality, May 2005. Accessed online June 7, 2005, at: <http://www.ahrq.gov/clinic/uspstf05/gonorrhea/gonrs.htm>.