Gonococcal Infections

Introduction

Gonorrhea is the second most common notifiable sexually transmitted infection in the United States and is a major public health problem. This infection is caused by the gram-negative bacterium *Neisseria gonorrhoeae*, and is transmitted through sexual activity or perinatally during vaginal delivery. Reported cases of gonorrhea have increased significantly in recent years, particularly among sexually active persons who are 20 to 29 years of age. Many individuals who acquire *N. gonorrhoeae* have no symptoms or minimal symptoms, and can unknowingly transmit this organism. The most common clinical sites for gonococcal infection are the urethra, cervix, pharynx, or rectum. In the modern era, there are excellent diagnostic tests for gonorrhea. Due to antimicrobial resistance concerns, the treatment recommendations for gonorrhea have recently changed. Aggressive screening and public health measures are needed to reduce *N. gonorrhoeae* transmission rates and thereby reverse the recent epidemiologic trend of increasing gonococcal infections in the United States. In the following discussion, the terms “woman” or “women” are used to describe persons who have a female sex assigned at birth (persons with a cervix), including transgender men with cervix and gender diverse persons who have a cervix. Similarly, the terms “man” or “men” are used to describe persons who have male sex assigned a birth (persons with a penis), including transgender women with a penis and gender diverse persons who have a penis.
Epidemiology in the United States

2020 Gonorrhea Surveillance Data

In 2020, a total of 677,769 cases of *Neisseria gonorrhoeae* (gonorrhea) were reported in the United States, making gonorrhea the second highest reported bacterial sexually transmitted infection (STI).[1] The reported number of gonorrhea cases probably substantially underestimates the actual total number of cases, which have been estimated in recent years at approximately 1,500,000 cases per year. Since reporting of gonorrhea began in the United States in the early 1940s, there have been several major trends—a steady rise in cases during the 1950s and 1960s, a peak in cases during the mid-1970s, a subsequent decline until a historic low in 2009, and, most recently, a significant increase from 2010 through 2020 (Figure 1).[1] There are significant differences in the incidence of gonorrhea based on sex, age, race/ethnicity, and region of residence.[1] The following summarizes several key epidemiologic features of gonococcal infections as reported in the United States for the year 2020.[1] Note: the Centers for Disease Control and Prevention (CDC) surveillance report provides data on gender that is based on sex assigned at birth (male and female) and therefore the terms male and female are used below.[1]

- **Sex:** The rate of reported gonorrhea cases among males was significantly higher than among females (238.5 versus 174.5 cases per 100,000 population). From 2012-2020, the gonorrhea rate among males increased 127%, while the rate among females increased 22% (Figure 2). The significant increase among males predominantly resulted from a marked increase in gonorrhea cases among men who have sex with men (MSM).
- **Age:** Based on age group, the highest rate of gonorrhea cases for both males and females occurred among persons 20 to 24 years of age (Figure 3). For females, the age group with the second highest rate was those 15 to 19 years of age. Among males, the age group with the second highest rate was in those 25 to 29 years of age.
- **Race/Ethnicity:** The gonorrhea rates (cases per 100,000 persons) among different racial/ethnic groups in the United States were highest among Black persons, with the next highest rates in American Indian/Alaska Native persons (Figure 4). These racial differences in rates of gonorrhea may result from the marked health disparities in the United States related to inequalities in income, education, and access to health care.[1,2,3]
- **Region and State:** The highest reported rates of gonorrhea were in the South and the Midwest. The five states with the highest rates in 2020 (in descending order) were Mississippi, Louisiana, South Carolina, Alabama, and Oklahoma; the gonorrhea rate in the District of Columbia (550 per 100,000 population) were higher than in any state (Figure 5).

Impact

Gonococcal infections are a significant public health problem in the United States. Based on the estimated incident cases among all ages in 2018, the total lifetime direct medical cost of gonorrhea in the United States was estimated at $271 million.[4]
Gonococcal Antimicrobial Susceptibility

Antimicrobial resistance is an important consideration in the treatment of gonorrhea.[5,6,7] Much of the information regarding antimicrobial susceptibility of *N. gonorrhoeae* isolates in the United States comes from the Centers for Disease Control and Prevention (CDC) Gonococcal Isolate Surveillance Project (GISP).[1,6] The higher the minimum inhibitory concentrations (MICs) in clinical isolates, the greater the antimicrobial concentration needed to inhibit the growth of *N. gonorrhoeae*. Increases above a defined cutoff indicate elevated risk of treatment failure or impending resistance, often referred to as “alert values”. The GISP tracks trends in antimicrobial susceptibility in the United States to seven antimicrobials that are currently or previously used for gonorrhea treatment: azithromycin, cefixime, ceftriaxone, ciprofloxacin, gentamicin, penicillin, and tetracycline (Figure 6).[1,6]

- **Azithromycin**: From 2010-2013, the percentage of isolates with reduced azithromycin susceptibility (MIC ≥2.0 μg/mL) was less than 1%, but during 2014 through 2020, the percentage of gonococcal isolates with reduced azithromycin susceptibility steadily increased to a level greater than 5%.[1] In 2020, among men who have sex with men, 9.2% of the isolates had elevated azithromycin MIC levels (compared to 4.3% among men who have sex with women only).[1]
- **Cefixime**: During 2010 through 2020, the proportion of *N. gonorrhoeae* isolates in the United States with reduced cefixime susceptibility (MIC ≥0.25 μg/mL) peaked in 2010 and 2011 at 1.4%.[1] From 2011-2020, the percentage of gonococcal isolates with cefixime MICs ≥0.25 μg/mL has consistently been less than 1%.[1]
- **Ceftriaxone**: During 2010 through 2020, the percentage of isolates with reduced ceftriaxone susceptibility (MIC ≥0.125 μg/mL) remained less than 0.5%.[1] In 2020, the percentage of isolates with reduced susceptibility to ceftriaxone (MICs ≥0.125 μg/mL) was 0.1%. In GISP, five isolates have been reported with a ceftriaxone MIC of ≥0.5 μg/mL.[1] In November 2019, the Southern Nevada Public Health Laboratory identified a clinical *N. gonorrhoeae* isolate with a confirmed ceftriaxone MIC of 1.0 μg/mL, which is the highest ceftriaxone MIC identified in GISP to date.[1,8]
- **Ciprofloxacin**: Fluoroquinolone-resistant *N. gonorrhoeae* is widely disseminated throughout the United States (and globally), and rates have steadily increased during the past decade. In 2020, resistance to ciprofloxacin was observed in 34.8% of the GISP isolates.[1]
- **Gentamicin**: From 2016-2020, most (range 65.9 to 80.5%) of the gonococcal isolates had a gentamicin MIC value of 8 μg/mL.[1] In 2020, among all gonococcal isolates tested, none had an MIC greater than 16 μg/mL.[1] Some experts have suggested gonococcal isolates with a gentamicin MIC of less than or equal to 4 μg/L are susceptible, those with an MIC of 8 to 16 μg/L have intermediate susceptibility, and those with an MIC greater than 16 μg/L are resistant.[9,10]
- **Penicillin**: In 2020, resistance to penicillin (MIC ≥2.0 μg/mL) was detected in 12.3% of gonococcal isolates.[1] Since 2010, the penicillin gonococcal resistance rates have consistently been greater than 10%.[1]
- **Tetracycline**: In 2020, resistance to tetracycline (MIC ≥2.0 μg/mL) was detected in 19.7% of the gonococcal isolates.[1] Since 2010, the tetracycline gonococcal resistance rates have consistently been greater than 15%.[1]
Microbiology, Pathogenesis, and Transmission

Organism

Gonorrhea is a common bacterial sexually transmitted disease caused by *N. gonorrhoeae*, a gram-negative bacterium that divides by binary fission and thus usually appears as pairs (diplococci) (Figure 7). Optimal growth of *N. gonorrhoeae* requires nutritional supplementation, such as with a Thayer-Martin media. *Neisseria gonorrhoeae* attaches to different types of epithelial cells via a number of structures located on its surface (Figure 8), rendering it capable of infecting mucosal surfaces, such as the urogenital epithelium, oropharyngeal tract, and conjunctival tissue.[11,12] This organism has a number of virulence factors, including type IV pili, lipooligosaccharide antigens, outer membrane porin protein (Por), opacity protein (Opa), and IgA protease, that collectively facilitate evasion of the host immune response.[11,12,13] Infection with *N. gonorrhoeae* generates limited immunity, and thus, repeated infections can occur.[13]

Transmission

Multiple factors have been identified that are associated with an increased risk for acquiring gonorrhea, including multiple or new sex partners, lack of consistent use of condoms, living in an urban area where gonorrhea prevalence is high, age younger than 30 years, and exchange of sex for drugs or money. The transmission of *N. gonorrhoeae* can occur in several ways:

- Transmission of *N. gonorrhoeae* from the urethra (in a person with gonorrhea) to the vagina (in a person without gonorrhea) occurs at a rate of approximately 50 to 70% per episode of vaginal intercourse that includes ejaculation; transmission of *N. gonorrhoeae* can occur from the urethra to the vagina without ejaculation, but at a lower rate.[14]
- Transmission of *N. gonorrhoeae* from the vagina (in a person with gonorrhea) to the urethra (in a person without gonorrhea) can occur during insertive vaginal intercourse, with an estimated rate of transmission of approximately 20% per episode of intercourse; the transmission rate increases to approximately 60 to 80% after four or more episodes of insertive vaginal intercourse.[15]
- Transmission of *N. gonorrhoeae* from the genital tract (of a person with gonorrhea) to the pharynx (of a person without gonorrhea) can occur via oral-genital contact; this is best documented with oral-genital contact (fellatio).[16,17] In addition, epidemiologic data have associated acquisition of pharyngeal gonorrhea with kissing and oral-anal contact.[18,19,20]
- Transmission of *N. gonorrhoeae* from the pharynx of a person with gonorrhea to the urethra (or a person without gonorrhea) can occur during fellatio.[21,22,23]
- Perinatal transmission (mother-to-infant) can occur during vaginal delivery when a mother with gonorrhea has not been treated during the perinatal period.
- Insertive and receptive rectal intercourse gonorrhea transmission rates have not been quantified, but rectal intercourse appears to be an efficient mode of transmission.
- Gonorrhea is associated with increased susceptibility to HIV acquisition, particularly rectal gonorrhea in men who have sex with men.[24] For men with HIV who are not taking suppressive antiretroviral therapy, urethral gonorrhea is associated with an increase in HIV transmission due to increased urethral HIV shedding.[25]
Clinical Manifestations

*Neisseria gonorrhoeae* infection can potentially cause an array of clinical syndromes, including urogenital, pharyngeal, and rectal infections in males and females, conjunctivitis in adults and neonates, and uncommonly, disseminated gonococcal infection (DGI). If untreated in females, gonorrhea can cause pelvic inflammatory disease (PID), tubal infertility, ectopic pregnancy, and chronic pelvic pain.

Genital Infection in Men

Urethritis

Urethritis is a common manifestation of gonorrhea in men. Most men develop overt, symptomatic urethritis, but some will develop asymptomatic (unrecognized) infection. Transmission can occur in the window of time after acquisition but prior to onset of symptoms.[26] Asymptomatic gonorrhea may act as a reservoir that perpetuates transmission in the community.[27] The typical symptoms of gonococcal urethritis, when present, include a purulent or mucopurulent urethral discharge (Figure 9), often accompanied by dysuria. The discharge may less often be clear or cloudy. The incubation period ranges from 1-14 days, with most men becoming symptomatic within 2-5 days after exposure (Figure 10).[28]

Anorectal Infections

Anorectal infection most often occurs in men who have sex with men, with acquisition of rectal *N. gonorrhoeae* occurring through receptive anal intercourse. Most men with anorectal gonococcal infection are asymptomatic, although proctitis can occur. Symptoms of proctitis include anal irritation, painful defecation, constipation, scant rectal bleeding, painless mucopurulent discharge, anal pruritus, and tenesmus.[29] When proctitis is suspected, an anoscopic examination is recommended to assess for inflammation and mucosal injury. The range of findings on anoscopy may include normal-appearing anorectal mucosa, purulent discharge, erythema, and easily induced anorectal bleeding.

Complications of Genital Infection in Men

Men with untreated gonococcal genital infection can develop epididymitis, with typical symptoms of unilateral testicular pain and swelling, and epididymal tenderness. Epididymitis is infrequent following gonococcal infection, but it is the most common local complication of gonorrhea infection in men. When it does occur, epididymitis is often associated with overt or subclinical urethritis. Urethral discharge may or may not be present. Other less common complications associated with gonococcal infection in men include inguinal lymphadenitis, penile edema, periurethral abscess or fistula, accessory gland infection ( Tyson's glands), balanitis, urethral stricture, and prostatitis, and rarely perirectal abscess.

Genital Infection in Women

Cervicitis

Most women with gonococcal infection of the cervix are asymptomatic, but when symptoms occur they may include nonspecific vaginal discharge, intermenstrual bleeding, dysuria, lower abdominal pain, and dyspareunia.[12,30] Clinically, examination of the cervix may show mucopurulent or purulent cervical discharge (Figure 11) and bleeding of the cervix with minimal contact.[30] The incubation period in women is variable, but symptoms, when they do occur, usually develop within 10 days of the exposure.[31] Approximately 80% of women with genital gonococcal infection have laboratory evidence of urethral infection (urethritis); dysuria may be present, but these women frequently do not have specific urethral symptoms.

Anorectal Infections

Anorectal gonococcal infection is uncommon in women, but it can occur via anal intercourse.[32] In addition,
anorectal infection has been reported in women with gonococcal cervicitis who do not acknowledge anal intercourse; presumably, in these women, the anorectal infection results from perineal contamination with infected cervical secretions.

Complications of Genital Infection in Women

There are several complications associated with gonorrhea in women:

- **Accessory (Bartholin) Gland Infections**: Infection with *N. gonorrhoea* may cause or contribute to an occlusion of the female sex accessory glands (Bartholin’s glands or Skene's glands); this obstruction typically manifests as a unilateral fluid-filled cyst on the labia (Bartholin cyst); infection of this cyst may result in the formation of a painful, tender abscess (Bartholin abscess) (Figure 12).

- **Pelvic Inflammatory Disease (PID)**: If cervical gonococcal infection ascends to the endometrium and/or fallopian tubes, PID may develop, typically causing symptoms that include lower abdominal pain, vaginal discharge, dyspareunia, intermenstrual bleeding, and fever.[33] In some women, PID may also be asymptomatic. Presumptive treatment for PID should be considered if one or more of the following minimum criteria are present on pelvic examination: uterine or adnexal tenderness or cervical motion tenderness. The long-term sequelae of untreated PID can include chronic pelvic pain, tubal infertility, and increased risk for ectopic pregnancy.

- **Perihepatitis (Fitz-Hugh-Curtis Syndrome)**: In situations where gonococcal infection ascends from the cervix, infection may produce inflammation of the liver capsule and the adjacent peritoneum. Most women with perihepatitis have associated PID, but perihepatitis can occur independently. Historically, perihepatitis was attributed only to gonococcal infection, but now it is often associated with chlamydial infection. Gonococcal perihepatitis is characterized by right upper quadrant pain and may be accompanied by abnormal liver function tests.

Additional Syndromes Seen in Men and Women

**Pharyngeal Infection**

Overall, most persons diagnosed with pharyngeal gonorrhea are asymptomatic or have a very mild sore throat.[34, 35, 36] In a longitudinal natural history study involving MSM, most of the men reported a sore throat at some time in the first 1 to 2 weeks after acquiring pharyngeal gonorrhea, followed by asymptomatic carriage for an average of approximately 4 months.[18] Symptoms of pharyngeal gonococcal infection may include pharyngitis, tonsillitis, fever, and cervical adenitis; exudative pharyngitis is rare.[16, 37]

**Ocular Infection**

Gonococcal infection of the eye, when it does occur, typically presents as conjunctivitis. Gonococcal conjunctivitis in adults most often results from autoinoculation in persons with genital gonococcal infection. Persons with gonococcal conjunctivitis may initially develop mild, nonpurulent conjunctivitis, that, if untreated, typically progresses to marked conjunctival redness, copious purulent discharge, and conjunctival edema (Figure 13).[38] Less often, ulcerative keratitis develops. Untreated gonococcal conjunctivitis can cause complications that may include corneal perforation, endophthalmitis, and blindness.

**Disseminated Gonococcal Infection**

Disseminated gonococcal infection is an uncommon, but potentially life-threatening systemic infection. Rates of disseminated gonococcal infection decreased during the period 1975-2008, but there have been several outbreaks in the United States in recent years.[19, 39] It occurs more often in women than in men, particularly during or shortly after menstruation and during pregnancy.[39] The risk of developing disseminated gonococcal infection is also increased in persons with terminal complement deficiency and in person receiving eculizumab, a medication that inhibits complement activation.[40] Disseminated gonococcal infection is often associated with strains that have a propensity to produce bacteremia without associated urogenital
symptoms. To this end, disseminated gonococcal infection is frequently not suspected due to the minimal mucosal inflammation and lack of urogenital symptoms. Clinical manifestations of disseminated gonococcal infection may include a combination of the following: skin lesions, arthralgia, tenosynovitis, arthritis (Figure 14), hepatitis, myocarditis, endocarditis, and meningitis.

**Infection in Children**

Perinatal infections most often occur during childbirth when the neonatal conjunctiva, pharynx, respiratory tract, or anal canal may become infected. Conjunctivitis (ophthalmia neonatorum) is preventable by ocular antimicrobial prophylaxis in the newborn. All cases of gonorrhea beyond the newborn period should be considered possible evidence of sexual abuse. Vulvovaginitis (not cervicitis) is the most common manifestation in prepubescent girls. Signs and symptoms may include vaginal discharge (often purulent or crusting), dysuria, odor, irritation, and pruritus. The anorectum and the pharynx are the most frequently infected sites in sexually abused boys; urethritis is less frequently seen. If specimens are to be collected, proper guidelines for collecting forensic evidence must be followed. When evaluating a child who has potentially suffered sexual abuse, the clinician should consult individual state laws concerning reporting and counseling.
Laboratory Diagnosis

The approach to diagnostic testing for *N. gonorrhoeae* has evolved from traditional cultivation to widespread use of nucleic acid amplification tests (NAATs).[42] Gram’s stain, another non-culture test, can be used if available for the diagnosis of urethral gonorrhea in symptomatic males. Culture is still recommended if antimicrobial resistance is a concern, especially in cases of suspected treatment failure.

Nucleic Acid Detection Tests

The NAATs used for detecting *N. gonorrhoeae* in the United States include polymerase chain reaction tests (Roche Amplicor and Cepheid GeneXpert CT/NG), transcription-mediated amplification (Gen-Probe Aptima), and strand displacement amplification (Becton-Dickinson BDProbeTec ET). Amplified tests are FDA-cleared for endocervical specimens from women, urethral specimens from men, and urine specimens from men and women.[42,43,44] Some NAATs are also cleared for vaginal swabs. In May 2019, the FDA cleared two NAATs (Aptima Combo 2 Assay and the Xpert CT/NG) for extragenital diagnostic testing of *N. gonorrhoeae* and *Chlamydia trachomatis* in rectal and pharyngeal samples.[45] Multiple studies have shown NAATs are the most sensitive test to detect *N. gonorrhoeae* infections. At present, antimicrobial susceptibility cannot be determined with NAATs, but research in this area is ongoing. In addition, the major limitation of NAATs is the potential for false-positive results due to remnant nucleic acids, either from contamination or dead organisms; this property limits the utility of NAATs for immediate post-treatment testing.

Point-of-Care NAAT Testing

In March 2021, the FDA approved the first point-of-care NAAT (Binx Health IO CT/NG Assay) for the diagnosis of urogenital chlamydia and gonorrhea.[46] This point-of-care test can be run on vaginal swabs obtained from women or on urine samples collected from men.[46] This assay can provide a result in approximately 30 minutes.[46] In a cross-sectional study, investigators evaluated this point-of-care NAAT for the diagnosis of chlamydia and gonorrhea using vaginal swabs obtained from 1,523 women and urine samples collected from 922 men.[47] For gonorrhea, the sensitivity estimates were 100.0% in women and 97.3% in men; the specificity estimates were 99.9% for women and 100.% for men.[47] In addition, the investigators found that self-obtained vaginal swabs in women performed equivalent to clinician-collected vaginal swabs.[47]

Gram’s Stain

The use of Gram's stain is a nonculture test that can make a presumptive diagnosis of gonorrhea. In the clinical setting, a Gram’s stain to detect *N. gonorrhoeae* is most often performed on a male with purulent urethral discharge. A Gram's stain on a specimen positive for *N. gonorrhoeae* shows polymorphonuclear leukocytes with intracellular gram-negative diplococci (Figure 16). A Gram’s stain, with proper laboratory technique, has greater than 95% sensitivity and greater than 99% specificity for diagnosing symptomatic male gonococcal urethritis.[42] Thus, the Gram’s stain is considered reliable both to diagnose and to exclude gonococcal urethritis in symptomatic men.[26] The sensitivity of a Gram’s stain is lower for males with asymptomatic urethral infection and thus not considered adequate to rule out infection in asymptomatic men.[26] Performing a Gram’s stain is not recommended on endocervical, pharyngeal, or rectal specimens due to poor sensitivity.[26]

Culture

Obtaining a bacterial culture is the historical standard for detecting *N. gonorrhoeae*. It has several advantages over nonculture tests, including low cost, use for a variety of specimen sites, and antimicrobial susceptibility testing if *N. gonorrhoeae* is isolated from the specimen. Despite having some advantages, culture is not as sensitive as NAAT and is more laboratory intensive, which has led to infrequent use in modern practice. Optimal growth of *N. gonorrhoeae* requires nutritional supplementation, such as with a Thayer-Martin media. At present, culture is primarily used for antimicrobial resistance surveillance.[26]
Diagnosis in Sexual Abuse/Assault

In cases of suspected sexual abuse or assault, the legal standard is to obtain culture samples combined with additional tests in an attempt to identify STIs, including *N. gonorrhoeae*. Due to the legal complexity of these cases, it is imperative that all positive specimens be retained for additional confirmatory testing. In adults, NAATs are preferred for the diagnostic evaluation of sexual assault regardless of whether penetration occurred with the assault. In evaluating children with suspected sexual abuse, either culture or NAAT can be used to detect *N. gonorrhoeae* and *C. trachomatis*. In this setting, making a diagnosis of an STI in a child has tremendous implications. When using a NAAT to detect *N. gonorrhoeae*, there is the possibility of cross-reaction with nongonococcal *Neisseria* species and other commensals. Accordingly, if a NAAT is used for evaluation, it is important to include expert consultation in this process and ensure that the NAAT has been Clinical Laboratory Improvement Amendments (CLIA)-validated and FDA-cleared. Further, it is important to and to ensure appropriate interpretation of results. Any initial testing on a specimen that generates a positive result should have confirmatory testing, either by retesting the original specimen or obtaining a new specimen from the same site from where the original sample was obtained. Gram's stain is inadequate for evaluating prepubertal children for gonorrhea and should not be used to diagnose or exclude gonorrhea.

Special Diagnostic Considerations with Disseminated Gonococcal Infection

When evaluating persons with suspected disseminated gonococcal infection, diagnostic testing should consist of (1) obtaining and ordering NAAT and culture for specimens from all applicable urogenital and extragenital mucosal sites, (2) ordering culture for all specimens obtained from disseminated sites of infection (e.g. skin, synovial fluid, blood, or cerebrospinal fluid), and (3) performing antimicrobial susceptibility testing on all *N. gonorrhoeae* isolates obtained in culture specimens.

Reporting Requirements

Laws and regulations in all states require clinicians, laboratories, or both to report persons diagnosed with gonorrhea to local public health authorities. Reporting can be done by medical providers, laboratories, or both.
Screening for Gonococcal Infection

Routine screening for gonococcal infection in persons at increased risk is recommended in order to decrease morbidity as well as to reduce the burden of disease in the community.[26,51] The following summarizes recommendations for gonorrhea screening in the 2021 STI Treatment Guidelines:[26,51,52]

Women [26]

- Routine screening for gonorrhea is recommended for all sexually active women younger than 25 years of age.
- Sexually active women age 25 years and older should have screening for gonorrhea if they are at increased risk (other STIs, a new sex partner, more than one sex partner, a sex partner with concurrent partners, a sex partner who has an STI, or a sex partner who is exchanging sex for money or drugs).
- Screening for pharyngeal and rectal gonorrhea screening can be considered in females based on reported sexual activities and exposure through shared clinical decision-making.

Women Who Have Sex with Women (WSW) and Women Who Have Sex with Women and Men (WSWM) [53]

- Gonorrhea screening recommendations for women who have sex only with women (WSW) and women who have sex with women and men (WSWM) are the same as outlined above for women who have sex with men.

Pregnant Women [51,54]

- Routine screening for gonorrhea should be performed on all pregnant women younger than 25 years of age and in older pregnant women if at increased risk for gonococcal infection (other STIs, a new sex partner, more than one sex partner, a sex partner with concurrent partners, a sex partner who has an STI, or a sex partner who is exchanging sex for money or drugs).
- Retest for gonorrhea should be done during the 3rd trimester for women under 25 years of age or those with increased risk for acquiring gonorrhea during the pregnancy.

Men Who Have Sex Only with Women [51]

- For men who have sex only with women, routine screening for gonococcal infection is not recommended.

Men Who Have Sex with Men (MSM) [51,55]

- All sexually active MSM should undergo screening for gonorrhea at least annually.
- Screening should consist of testing at sites of sexual contact (urethra, rectum, pharynx). The preferred tests (self-collected or provider-collected) are urine NAAT, rectal NAAT, and pharyngeal NAAT.
- More frequent screening at 3- to 6-month intervals is indicated for men who have sex with men if they have increased risk (e.g. persons taking HIV preexposure prophylaxis, individuals with HIV, persons with ongoing risk for acquiring chlamydia, and persons who have multiple sex partners or their sex partners have multiple partners).

Transgender and Gender Diverse Persons [51,56]

- Routine gonorrhea screening should be adapted based on the individual's anatomy. For example, all transgender men and gender diverse persons who have a cervix should have the same screening for
gonorrhea as cisgender women who have sex with men (e.g. routine screening if younger than age 25 years and screening for those 25 years of age and older if they have increased risk).

- Consider screening at the pharyngeal and rectal sites based on reported sexual activity and exposures.

**Persons with HIV [51]**

- All persons with HIV who are sexually active should have screening for gonorrhea at the initial HIV evaluation visit and at least annually thereafter.
- Some individuals may require more frequent screening depending on their sexual activity and local epidemiology for their region.

**Persons in Correctional Facilities [57]**

- Routine opt-out screening for gonococcal infection should be offered at intake upon entering a correctional facility for women 35 years of age and younger and for men younger than 30 years of age.
Treatment

Major Changes in Treatment of Gonococcal Infections

Recommendations for the treatment of gonorrhea have undergone recent major changes in the 2021 STI Treatment Guidelines.[5,26] The following summarizes several of these key new recommendations:[5,26]

- For the treatment of uncomplicated gonococcal infection of the cervix, urethra, or rectum in persons who weigh less than 150 kg, the single intramuscular ceftriaxone dose has been increased from 250 mg to 500 mg; for persons who weigh 150 kg or greater, the dose should be increased to 1 gram. The increased dose of ceftriaxone is recommended based on pharmacokinetic and pharmacodynamic data that show ceftriaxone concentrations at 24 hours with a 500 mg dose provides more reliable eradication of \( N. gonorrhoeae \) than with a 250 mg dose.[58,59] Further, because ceftriaxone produces variable levels in the pharynx, the 500 mg ceftriaxone dose should provide a more reliable treatment for pharyngeal gonorrhea.

- For persons with uncomplicated gonococcal infection of the cervix, urethra, or rectum in whom chlamydia infection has been ruled out, ceftriaxone monotherapy is recommended, which is in contrast to the prior recommendation to add azithromycin as dual therapy for all gonococcal infections.[51] The rationale for eliminating the routine use of azithromycin as dual therapy for the treatment of gonorrhea is twofold: (1) the concern for azithromycin causing antimicrobial resistance in commensal organisms and concurrent pathogens, and (2) the trend of increasing \( N. gonorrhoeae \) resistance to azithromycin.[1,60,61]

- For persons with gonococcal infection in whom chlamydia infection has not been excluded, oral doxycycline is added to ceftriaxone for the purpose of treating chlamydia (for nonpregnant persons). This new recommendation is based on emerging data suggesting better chlamydia treatment efficacy with doxycycline than with azithromycin, especially with rectal chlamydia.[62,63,64]

- For persons with pharyngeal gonococcal infection, a test-of-cure is recommended 7 to 14 days after treatment, regardless of the treatment regimen used.[5,26] The prior recommendation was to perform a test-of-cure after treatment of pharyngeal gonococcal infection only if an alternative regimen was used.

- The recommended expedited partner therapy (EPT) with a single oral dose of cefixime has increased from 400 mg to 800 mg and routine dual therapy with azithromycin is no longer recommended; if concurrent chlamydia was not excluded in the source individual who was diagnosed with gonorrhea, then the expedited partner therapy should include oral doxycycline 100 mg for 7 days (for nonpregnant persons).[26]

Uncomplicated Infections of the Cervix, Urethra, and Rectum

For persons with uncomplicated gonococcal infections of the cervix, urethra, or rectum, the recommended treatment is a single intramuscular dose of ceftriaxone 500 mg, with or without oral doxycycline 100 mg twice daily for 7 days depending on whether chlamydia infection has been excluded (Table 1).[5,26] For pregnant persons, if chlamydia has not been excluded, oral azithromycin 1 gram should be used in place of doxycycline.[26] If ceftriaxone is not available, the two options are (1) intramuscular gentamicin 240 mg plus oral azithromycin 2 grams or (2) oral cefixime 800 mg.[5]

Uncomplicated Infections of the Pharynx

Gonococcal infections of the pharynx are more difficult to eradicate than infections at urogenital and anorectal sites. The recommended treatment of pharyngeal gonorrhea is a single intramuscular dose of ceftriaxone 500 mg; if chlamydia infection was also identified when the pharyngeal testing was performed, then it should be treated with oral doxycycline 100 mg twice daily for 7 days (Table 2).[26] Concomitant treatment for pharyngeal chlamydial infection is not indicated if testing for pharyngeal chlamydia was not performed or if the testing for chlamydia was negative.[26] If treatment for chlamydia pharyngeal infection is
indicated and the person is pregnant, oral azithromycin 1 gram should be used in place of doxycycline. Note there are no reliable alternative regimens for the treatment of pharyngeal gonorrhea.[26]

**Conjunctivitis**

In the only published study of the treatment of gonococcal conjunctivitis among adults, all 12 study participants responded to a single 1 gram intramuscular injection of ceftriaxone.[65] Based on this study, the recommended treatment for gonococcal conjunctivitis is a single ceftriaxone 1 gram intramuscular dose (Table 3).[26] In addition, a one-time lavage of the infected eye with saline should be considered.[26]

**Disseminated Gonococcal Infection**

Persons with disseminated gonococcal infection (DGI) can develop severe sequelae and complications. Therefore, in addition to antimicrobial therapy, management should include hospitalization and consultation with an infectious diseases specialist.[26] The recommended initial antimicrobial therapy is ceftriaxone 1 gram intramuscularly or intravenously every 24 hours; if chlamydia has not been excluded, then treatment of chlamydia with doxycycline 100 mg twice daily should be given. The first dose of ceftriaxone should be given after promptly obtaining appropriate diagnostic samples. The duration of therapy for disseminated gonococcal infection with arthritis-dermatitis syndrome is at least 7 days, and the ceftriaxone can transition to oral therapy if antimicrobial sensitivity testing shows an effective oral choice (Table 4).[26] For persons diagnosed with DGI and meningitis, parenteral therapy should continue for 10 to 14 days; with endocarditis, parenteral therapy should be given for at least 4 weeks (Table 5).[26]

**Allergy to Penicillins or Cephalosporin**

For persons who report a penicillin or cephalosporin allergy, it is important to determine the severity of the reaction, if the reaction was consistent with an IgE-mediated reaction, and whether the reaction occurred within the prior 10 years. Among all persons who self-report a history of an allergic reaction to penicillin or another beta-lactam antibiotic, only 7.1% had a positive objective test that confirmed the penicillin allergy.[66] In addition, among persons with a history of penicillin allergy, fewer than 1.0% will have an allergic reaction to a third-generation cephalosporin, such as ceftriaxone or cefixime.[67] For persons who have a documented or strongly suspected IgE-mediated allergic reaction to penicillin or cephalosporins, one option is to administer dual treatment with a single dose of intramuscular gentamicin 240 mg plus a single dose of oral azithromycin 2 grams.[9,26,68] This regimen, however, is not recommended for the treatment of pharyngeal gonorrhea due to its low efficacy. Some individuals with a penicillin or cephalosporin allergy may require expert consultation with an allergy specialist, especially those with a history of Ig-E mediated allergic reaction in the prior 10 years.

**Gonococcal Infections in Pregnancy**

Pregnant persons with *N. gonorrhoeae* should be treated with a single intramuscular dose of ceftriaxone 500 mg, with the addition of azithromycin if chlamydia infection was not ruled out.[5] Pregnant persons should not be treated with any fluoroquinolone or tetracycline drugs. Because spectinomycin is not available in the United States, pregnant women who cannot tolerate a cephalosporin should be evaluated by an infectious diseases specialist.

**Management of Antibiotic-Resistant Gonorrhea**

Although there are no confirmed cases of treatment failure due to cephalosporin-resistant *N. gonorrhoeae* in the United States, the gradual upwards trend of MICs documented by the United States Gonococcal Isolate Surveillance Project (GISP) remains worrisome.[69,70,71,72] Criteria for resistance to cefixime and ceftriaxone have not been defined by the Clinical and Laboratory Standards Institute (CLSI), but isolates with cefixime or ceftriaxone MICs equal to or greater than 0.5 μg/mL are considered to have decreased
susceptibility. Only five isolates with ceftriaxone MIC equal to or greater than 0.5 μg/mL have been reported during the history of the GISP. In 2019, one isolate from Nevada was reported with a ceftriaxone MIC of 1.0 μg/mL.[8] Notably, isolates with high-level cefixime and ceftriaxone MICs (cefixime MICs 1.5 to 8 μg/mL and ceftriaxone MICs 1.5 to 4 μg/mL) have been identified in Japan, France, and Spain.[73,74,75,76]

Defining Gonococcal Treatment Failure

Cephalosporin treatment failure should be suspected in persons who meet the following criteria: (1) they have received appropriate treatment for gonorrhea; (2) they report no sexual contact during the post-treatment follow-up period; and (3) they remain symptomatic (symptoms do not resolve within 3 to 5 days of receiving treatment), or they have a positive test of cure (a positive culture greater than 72 hours after treatment or a positive NAAT greater than 7 days after treatment).[26] Risk factors for treatment failure due to resistant organisms include multiple prior treatment courses for gonorrhea, international travel, or pharyngeal disease.

Management of Suspected Gonococcal Treatment Failure

In the United States, gonococcal infections identified after treatment with ceftriaxone usually result from reinfection rather than treatment failure.[77,78,79] Persons with persistent infection following treatment and who deny any post-treatment sexual contact should undergo repeat testing and evaluation for *N. gonorrhoeae* infection that ideally includes culture evaluation.[26] Detection of *N. gonorrhoeae* infection in a person with suspected cephalosporin treatment failure should result in the following: (1) culture and susceptibility testing of all relevant clinical specimens; (2) guidance from expert opinion for clinical management (through the STD Clinical Consultation Network, a local STD/HIV Prevention Training Center clinical expert, the CDC, or an infectious diseases specialist); and (3) generation of a case report to the CDC through state and local public health authorities.[26] In cases of suspected cephalosporin treatment failure, isolates that grow *N. gonorrhoeae* should be saved and sent to the CDC through state public health laboratory mechanisms. Health departments should prioritize notification and culture evaluation for sex partner(s) of persons with *N. gonorrhoeae* infection who have suspected cephalosporin treatment failure and/or gonococcal isolates that demonstrate decreased susceptibility to cephalosporins.

- **Initial Approach to Suspected Treatment Failure:** Persons with suspected cephalosporin treatment failure should first receive retreatment and receive a single dose of intramuscular ceftriaxone 500 mg, with doxycycline if chlamydial infection exists. This initial approach is recommended in the United States because most suspected treatment failures actually result from reinfection.
- **Antimicrobial Options for Likely Treatment Failure:** For individuals considered to have high likelihood of true treatment failure, especially those with a documented elevated cephalosporin MIC for *N. gonorrhoeae*, the suggested option to consider is single-dose oral therapy with azithromycin 2 grams plus a single intramuscular injection of a 240 mg dose of gentamicin.
- **Investigational Therapy for *N. gonorrhoeae***: Several antimicrobials under investigation have shown promise in the treatment of gonorrhea in phase 2 trials, including single-dose oral gepotidacin and single-dose oral zoliflodacin.[80,81] These two agents are now under study in phase 3 trials, and both may have a future role in treating drug-resistant gonorrhea and gonorrhea in persons with serious penicillin or cephalosporin allergy. Two oral agents—solithromycin and delafloxacin—showed promising early results, but phase 3 studies have been disappointing, and these agents are not likely to have a clinical role in the treatment of gonorrhea.[82,83,84,85]

Follow-Up

Due to the significant risk of reinfection in persons diagnosed with gonorrhea, all persons diagnosed with gonorrhea should have repeat testing in 3 months at the anatomic site of exposure, regardless of whether they have symptoms; this is considered a test for reinfection, not a test-of-cure.[26] For persons with uncomplicated gonococcal infections of the cervix, urethra, or rectum, a routine test-of-cure at 7 to 14 days
post-treatment is not recommended. For persons with pharyngeal gonorrhea, however, a routine test-of-cure (using either culture or NAAT) is recommended 7 to 14 days after completing treatment, regardless of the treatment regimen. For these individuals, if the test-of-cure NAAT is positive, an effort should be made to perform a confirmatory culture before retreatment; all positive cultures for test-of-cure should undergo antimicrobial susceptibility testing. For persons with suspected cephalosporin-resistant gonorrhea who receive retreatment, a test-of-cure at relevant clinical sites should be obtained 7 to 14 days after retreatment; culture is the recommended test, preferably with simultaneous NAAT and susceptibility testing of *N. gonorrhoeae* if isolated.
Management of Sex Partners

Evaluation and Treatment of Sex Partners

All recent sex partners (within the 60 days preceding the onset of symptoms or gonorrhea diagnosis) should be referred for evaluation, testing, and presumptive treatment of gonorrhea. If the most recent contact with a sex partner occurred more than 60 days preceding onset of symptoms or gonorrhea diagnosis, that partner should be referred for evaluation and treatment. Sex partners who are treated should also be instructed to abstain from sexual activity for 7 days after they have completed antimicrobial treatment.

Expedited Partner Therapy

In settings where prompt referral and treatment are unavailable or impractical, medical providers can consider expedited partner therapy. This entails providing appropriate antibiotics as well as educational information for the partner. These written materials should include notification that partner(s) have been exposed, information about the importance of treatment, signs and symptoms of potential complications, as well as possible therapy-related allergic reactions and adverse effects.

- **Recommended Regimen:** The expedited partner therapy regimen for sex partners of patients with *N. gonorrhoeae* infection is oral cefixime 800 mg with delivery of the prescription to the partner by either the person diagnosed with gonorrhea, a disease investigation specialist, or a collaborating pharmacy as permitted by law; if concurrent chlamydia was not excluded in the source individual who was diagnosed with gonorrhea, then the expedited partner therapy should include oral doxycycline 100 mg for 7 days (for nonpregnant persons); if there is concern regarding the partner taking multidose therapy for chlamydia, then azithromycin 1 gram orally as a single dose can be given.

- **State-by-State Legal Status:** It is essential to check with one’s state health department to clarify the policies, as the use of expedited partner therapy is not legal in all states. The CDC maintains an updated information page, [Legal Status of Expedited Partner Therapy](#), that identifies the legal status of expedited partner therapy in each state in the United States, as well as providing links to each state for more detailed state policies.

- **Follow-Up After Expedited Partner Therapy:** Provision of expedited partner therapy alone is not sufficient, and each partner should ideally be seen in follow-up for repeat testing to check for reinfection. Although offering expedited partner therapy to female partners is acceptable, this approach may result in undertreatment of pelvic inflammatory disease.

- **Contraindications for Expedited Partner Therapy:** The use of expedited partner therapy for gonorrhea is contraindicated in a female partner who has current signs or symptoms that are suggestive of PID. Female partners who have current signs and symptoms suggestive of PID should undergo prompt evaluation by a health care provider. In addition, the use of expedited partner therapy should not be considered a routine partner management strategy in MSM with gonorrhea for several reasons, including the high risk for coexisting infections (especially HIV and syphilis), inadequate data regarding the efficacy of expedited partner therapy in this patient population, and concerns regarding the increased proportion of gonococcal isolates among MSM with reduced susceptibility to cefixime.
Counseling and Education

The following summarizes key counseling messages for persons diagnosed with gonococcal infection.

- **Resuming Sexual Activity**: Persons treated for gonococcal infection should receive instructions to abstain from sexual activity until all the following criteria are met: (1) at least 7 days have elapsed since completing treatment, (2) any genitourinary symptoms have resolved, and (3) if they are planning to resume sexual activity with a recent sex partner, the sex partner should have received appropriate treatment for gonorrhea and at least 7 days have elapsed since the partner was treated.

- **Partner Notification**: It is extremely important that persons treated for gonococcal infection understand the importance of partner notification (for all sex partners in the prior 60 days). Partner notification with evaluation and treatment can markedly reduce the spread of STIs in the community, and it also reduces the likelihood of reinfection for the person diagnosed with gonorrhea.

- **Follow-Up Testing**: It is important that all persons treated for gonorrhea have a follow-up visit in approximately 3 months for repeat STI testing. The purpose of this 3-month visit is to test for reinfection with gonorrhea, as well as to test for other STIs that could have been acquired in the 3-month post-treatment time frame.

- **STI Prevention**: At the time a person is receiving treatment for an STI, it is appropriate to provide counseling messages on how to prevent STIs in the future (e.g. limiting the number of sex partners and consistently using condoms).
Summary Points

- In the United States, rates of gonococcal infection have increased in recent years, especially among men who have sex with men. The age group with the highest gonorrhea rates is persons 20-24 years of age.
- Gonococcal antimicrobial resistance to ceftriaxone remains low in the United States. Antimicrobial resistance to azithromycin has increased in recent years.
- Gonorrhea is associated with increased susceptibility to HIV acquisition as well as an increased risk of HIV transmission.
- Neisseria gonorrhoeae can cause a wide array of urogenital, pharyngeal, and rectal symptoms as well as serious complications, such as pelvic inflammatory disease, tubal infertility, ectopic pregnancy, neonatal conjunctivitis, and rarely, disseminated infection.
- Screening for gonorrhea is recommended in sexually active women under 25 years of age and in other persons at increased risk of acquiring N. gonorrhoeae.
- The NAAT is the preferred test for screening and diagnosing gonorrhea in both men and women. Culture is now primarily used when the concern for antimicrobial resistance arises.
- Therapy with intramuscular ceftriaxone 500 mg is recommended in all persons (including pregnant women) with uncomplicated gonococcal infections of the cervix, urethra, rectum, or pharynx. If chlamydia infection has not been excluded, then concomitant treatment for chlamydia should be given with doxycycline 100 mg twice daily for 7 days; for pregnant individuals, a single 1-gram dose of oral azithromycin should be used instead of doxycycline to treat chlamydia.
- A test-of-cure is not routinely recommended after treatment of uncomplicated infections of the cervix, urethra, and rectum, but it should be performed in all persons at 7 to 14 days following the treatment of pharyngeal gonorrhea.
- Most cases of suspected treatment failures represent reinfection with N. gonorrhoeae, but if true cephalosporin treatment failure is suspected, clinicians should perform culture and sensitivity testing and seek expert consultation.
- Persons who are diagnosed with gonorrhea should receive counseling about the nature of infection, the importance of partner notification, when they can resume sexual activity, and how they can reduce their risk for acquiring STIs in the future.
Citations


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Figures

Figure 1 Gonorrhea—Reported Cases by Year, United States, 1941-2020

Figure 2 Gonorrhea—Rates of Reported Cases by Sex, United States, 2012-2020

Figure 3 Gonorrhea—Rates of Reported Cases by Sex and Age Group, United States, 2020


*Per 100,000 population
Figure 4 Gonorrhea—Rates of Reported Cases by Race/Ethnicity, 2020

Figure 5 Gonorrhea—Rates of Reported Cases by State, United States and Outlying Areas, 2020


*Rate = per 100,000 population.
Figure 6A: Antimicrobial Drugs Used to Treat Gonorrhea, GISP 1988 through 2020

NOTE: “Other” includes azithromycin 2g (0.3%), no therapy (0.1%), and other less frequently used drugs (0.8%). In 2020, 96.8% of GISP participants were treated with ceftriaxone 250 mg. Participants treated with gentamicin 240 mg increased from 0.2% in 2015 to 1.3% in 2020.

Figure 6 (Image Series) - Gonococcal Isolate Surveillance Project (GISP), GISP 2010-2020
Image 6B: *Neisseria gonorrhoeae*—Percentage of Isolates with Elevated MICs to Azithromycin, Cefixime, and Ceftriaxone

MICs = minimum inhibitory concentrations
Elevated MICs = Azithromycin $\geq 2.0 \mu g/mL$; Cefixime $\geq 0.25 \mu g/mL$; Ceftriaxone $\geq 0.125 \mu g/mL$
Abbreviations: MICs = minimum inhibitory concentrations; GISP = Gonococcal Isolate Surveillance Project

Figure 6 (Image Series) - Gonococcal Isolate Surveillance Project (GISP), GISP 2010-2020
Image 6C: Prevalence of Tetracycline, Penicillin, or Fluoroquinolone Resistance* or Elevated Cefixime, Ceftriaxone, or Azithromycin MICs^, by Year

MICs = minimum inhibitory concentrations
Resistance: Ciprofloxacin = MIC ≥ 1.0 µg/mL; Penicillin = MIC ≥ 2.0 µg/mL or Beta-lactamase positive; Tetracycline = MIC ≥ 2.0 µg/mL
^Elevated MICs = Azithromycin ≥ 2.0 µg/mL; Cefixime ≥ 0.25 µg/mL; Ceftriaxone ≥ 0.125 µg/mL

Figure 6 (Image Series) - Gonococcal Isolate Surveillance Project (GISP), GISP 2010-2020
Image 6D: Neisseria gonorrhoeae—Distribution of Gentamicin MICs by Year, 2015-2017

MICs = minimum inhibitory concentrations. In 2018, the antibiotic susceptibility testing range for gentamicin was expanded from MICs of 1 µg/mL–32 µg/mL in previous years to 0.25 µg/mL–64 µg/mL.

Figure 7 *Neisseria gonorrhoeae* and Binary Fission

Transmission electron micrograph (TEM) showing *Neisseria gonorrhoeae* undergoing binary fission.

Source: Centers for Disease Control and Prevention Public Health Image Library (Dr. Wiesner, 1972).
Figure 8 Neisseria gonorrhoeae

This illustration shows a three-dimensional computer-generated image of *Neisseria gonorrhoeae* diplococci. The illustration is an artistic recreation based on scanning electron microscopic (SEM) imagery. Note the hair-like appendages extending from the organisms’ exterior; these are type IV pili that promote motility and improve surface adherence.

Source: Centers for Disease Control and Prevention Public Health Image Library (Medical Illustration—James Archer, 2013).
Figure 9 Purulent Urethral Discharge with Gonococcal Infection

Photograph from Negusse Ocbamichael, PA; Public Health—Seattle & King County Sexual Health Clinic
Figure 10 Incubation Period with Gonococcal Urethritis

This graph illustrates the timing of onset of urethral symptoms in 44 men following exposure to *N. gonorrhoeae*.

**Figure 11 Cervicitis**

This illustration of a woman with cervicitis shows a light purulent discharge from the cervical os seen with a speculum examination (on left) and in close up (right).

Illustration by Jared Travnicek, Cognition Studio
A Bartholin cyst is a fluid-filled sac on the labial or vaginal wall; this cyst forms from the obstruction of the Bartholin's gland.

Illustration by Jared Travnicek, Cognition Studio
Figure 12 (Image Series) - Bartholin Cyst and Bartholin Abscess
Image 12B: Bartholin Abscess

A Bartholin cyst can become infected and develop into a sac that is tense, painful, and filled with pus.

Illustration by Jared Travnicek, Cognition Studio
Figure 13 Gonococcal Conjunctivitis

This photograph illustrates a severe case of gonococcal conjunctivitis. Note the purulent material on the upper and lower lids.

Source: Centers for Disease Control and Prevention Public Health Image Library. CDC, 1977.
Figure 14 Disseminated Gonococcal Infection with Skin Lesions

This patient had disseminated gonococcal infection including multiple cutaneous lesions on the feet (black arrows).

Source: Centers for Disease Control and Prevention Public Health Image Library (J. Pledger and Dr. S. E. Thompson, VDCD, 1979).
**Figure 15 Disseminated Gonococcal Infection with Arthritis**

This image taken from a woman with disseminated gonococcal infection and right elbow arthritis.

Source: Centers for Disease Control and Prevention Public Health Image Library (Emory, Tom Sellers, 1963).
Figure 16 Urethral Swab Gram's Stain in Patient with Gonorrhea

This Gram's stain of a smear of a urethral discharge in a man diagnosed with acute gonococcal urethritis.

Source: Centers for Disease Control and Prevention Public Health Image Library (Joe Miller, 1979).
Table 1. 2021 STI Treatment Guidelines: Gonococcal Infections
Treatment of Uncomplicated Gonococcal Infection of the Cervix, Urethra, or Rectum

| Recommended Regimen if Chlamydial Infection Excluded |
| Ceftriaxone | 500 mg* IM in a single dose for persons weighing <150 kg |
| **Note:** *For persons weighing ≥150 kg, ceftriaxone 1 g IM should be administered.* |

| Recommended Regimen if Chlamydial Infection Has Not Been Excluded |
| Ceftriaxone | 500 mg* IM in a single dose for persons weighing <150 kg |
| **+** Doxycycline | 100 mg orally twice daily for 7 days |
| **Note:** *For persons weighing ≥150 kg, ceftriaxone 1 g IM should be administered.* |

| Alternative Regimen if Ceftriaxone is Not Available |
| Gentamicin | 240 mg IM in a single dose |
| **+** Azithromycin | 2 g orally in a single dose |

| Alternative Regimen if Ceftriaxone is Not Available |
| Cefixime | 800 mg orally in a single dose |
| **Note:** If treating with cefixime, and chlamydial infection has not been excluded, providers should treat for chlamydia with doxycycline 100 mg orally twice daily for 7 days. During pregnancy, oral azithromycin 1 g in a single dose is recommended to treat chlamydia. |

### Table 2. 2021 STI Treatment Guidelines: Gonococcal Infections
#### Treatment of Uncomplicated Gonococcal Infection of the Pharynx

<table>
<thead>
<tr>
<th>Recommended Regimen</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ceftriaxone</strong></td>
<td></td>
</tr>
<tr>
<td>500 mg* IM in a single dose for persons weighing &lt;150 kg</td>
<td></td>
</tr>
<tr>
<td>If chlamydial infection is identified when pharyngeal gonorrhea testing is performed, treat with doxycycline 100 mg orally 2 times a day for 7 days; persons who are pregnant should receive azithromycin 1 g orally in a single dose (instead of doxycycline).</td>
<td></td>
</tr>
<tr>
<td>Note: *For persons weighing ≥150 kg, ceftriaxone 1 g IM should be administered.</td>
<td></td>
</tr>
</tbody>
</table>

No reliable alternative treatments are available for pharyngeal gonorrhea. For persons with a history of a beta-lactam allergy, a thorough assessment of the reaction is recommended. For persons with an anaphylactic or other severe reaction (e.g., Stevens Johnson syndrome) to ceftriaxone, consult an infectious disease specialist for an alternative treatment recommendation.

Table 3. 2021 STI Treatment Guidelines: Gonococcal Infections
Treatment of Gonococcal Conjunctivitis Among Adolescents and Adults

<table>
<thead>
<tr>
<th>Recommended Regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ceftriaxone</td>
</tr>
<tr>
<td>1 g IM in a single dose</td>
</tr>
</tbody>
</table>

Providers should consider one-time lavage of the infected eye with saline solution.

### Table 4. 2021 STI Treatment Guidelines: Gonococcal Infections

#### Treatment of Disseminated Gonococcal Infection (DGI): Arthritis and Arthritis-Dermatitis Syndrome

<table>
<thead>
<tr>
<th>Recommended Regimen</th>
<th>Ceftriaxone</th>
<th>1 g IM or IV every 24 hours</th>
</tr>
</thead>
<tbody>
<tr>
<td>Note: If chlamydial infection has not been excluded, providers should treat for chlamydia with doxycycline 100 mg orally 2 times/day for 7 days.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Alternative Regimens</th>
<th>Cefotaxime</th>
<th>1 gram IV every 8 hours</th>
</tr>
</thead>
<tbody>
<tr>
<td>Note: If chlamydial infection has not been excluded, providers should treat for chlamydia with doxycycline 100 mg orally 2 times/day for 7 days.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Alternative Regimens</th>
<th>Ceftizoxime</th>
<th>1 g IV every 8 hours</th>
</tr>
</thead>
<tbody>
<tr>
<td>Note: If chlamydial infection has not been excluded, providers should treat for chlamydia with doxycycline 100 mg orally 2 times/day for 7 days.</td>
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<td></td>
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</tbody>
</table>

When treating for the arthritis-dermatitis syndrome, the provider can switch to an oral agent guided by antimicrobial susceptibility testing 24–48 hours after substantial clinical improvement, for a total treatment course of at least 7 days.

Table 5. 2021 STI Treatment Guidelines: Gonococcal Infections
Treatment of Disseminated Gonococcal Infection: Meningitis and Endocarditis

<table>
<thead>
<tr>
<th>Recommended Regimen</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ceftriaxone</strong></td>
<td>1-2 g IV every 24 hours</td>
</tr>
</tbody>
</table>

Note: If chlamydial infection has not been excluded, providers should treat for chlamydia with doxycycline 100 mg orally 2 times a day for 7 days.

No recent studies have been published regarding treatment of DGI involving the CNS or cardiovascular system. The duration of treatment for DGI in these situations has not been systematically studied and should be determined in consultation with an infectious disease specialist. Treatment for DGI should be guided by the results of antimicrobial susceptibility testing. Length of treatment should be determined based on clinical presentation. Therapy for meningitis should be continued with recommended parenteral therapy for 10-14 days. Parenteral antimicrobial therapy for endocarditis should be administered for >4 weeks.
