Gonococcal Infections

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Module 2: Self-Study Lessons
Lesson 2: Gonococcal Infections

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Introduction

Gonorrhea is the second most common notifiable sexually transmitted infection (STI) in the United States. 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 remained high in recent years, particularly among sexually active persons who are 20 to 29 years of age. 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.

Epidemiology in the United States

2023 Gonorrhea Surveillance Data

In 2023, a total of 601,319 cases of *Neisseria gonorrhoeae* (gonorrhea) were reported in the United States, making gonorrhea the second-highest reported bacterial STI (Figure 1).[1] 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, a significant increase from 2010 through 2021 and, most recently, a decrease in 2022 and 2023.[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 2023.[1]

- **Sex**: Since 2014, the rates of reported gonorrhea cases among males have been significantly higher than in females. In 2023, the gonorrhea rate (cases per 100,000 population) was 228.3 in males versus 130.7 in females.
- **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. The age group with the second-highest rate for males was individuals 25–29 years of age, and for females, it was individuals 15–19 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. The total number of gonorrhea cases was highest in Black people and next highest in White people.
- **Geographic Region**: The overall rate of gonorrhea cases in the United States was 179.5 per 100,000 people. The highest reported rates of gonorrhea were in the South. The five states with the highest rates in 2023 (in descending order) were Alaska, Louisiana, Georgia, South Dakota, and Mississippi; the gonorrhea rate in the District of Columbia was 853.3 per 100,000 population, which was higher than in any state.

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.[2][Q] Gonorrhea Rates in United States by Age Group

Gonococcal Antimicrobial Susceptibility

Antimicrobial resistance is an important consideration in the treatment of gonorrhea.[3,4,5] Much of the information regarding antimicrobial susceptibility of *N. gonorrhoeae* isolates in the United States has come from the Centers for Disease Control and Prevention (CDC) Gonococcal Isolate Surveillance Project (GISP).[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 an 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.[6] The following data summarizes data from the 2022 GISP (Figure 2).[6]

- **Azithromycin**: From 1998-2012, the percentage of isolates with reduced azithromycin susceptibility (MIC ≥2.0 µg/mL) was consistently less than 1%, but the resistance rates have consistently increased since then. During the 2018-2022 time period, 5.2% of the gonococcal isolates had an MIC ≥2.0 µg/mL.
- **Cefixime**: Since 2013, the percentage of gonococcal isolates with cefixime MICs ≥0.25 µg/mL has consistently been less than 1%. In 2022, there were 0.1% of gonococcal isolates with cefixime MICs ≥0.25 µg/mL.
- **Ceftriaxone**: Since 1998, the percentage of isolates with reduced ceftriaxone susceptibility (MIC ≥0.125 µg/mL) has remained less than 0.5%. During 2018-2022, the percentage of isolates with reduced susceptibility to ceftriaxone (MICs ≥0.125 µg/mL) was 0.1%. 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.[7]
- **Ciprofloxacin**: Fluoroquinolone-resistant *N. gonorrhoeae* is widely disseminated throughout the United States (and globally), and rates have steadily increased during the past decade. Since 2017, more than 30% of the GISP isolates showed resistance to ciprofloxacin.
- **Gentamicin**: From 2018-2022, more than 75% of the gonococcal isolates had a gentamicin MIC value of 8 µg/mL. In 2022, among all gonococcal isolates tested, 3.8% had an MIC of ≥16 µg/mL, and 0.2% had an MIC of ≥32 µg/mL. The criteria for gonococcal susceptibility to gentamicin have not been established. 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 32 µg/L or greater are resistant.[8,9]
- **Penicillin**: In 2022, resistance to penicillin (MIC ≥2.0 µg/mL) was detected in 10.7% of gonococcal isolates. Since 2006, the penicillin gonococcal resistance rates have consistently been greater than 10%.
- **Tetracycline**: In 2022, resistance to tetracycline (MIC ≥2.0 µg/mL) was detected in 20.2% of the gonococcal isolates. Since 2005, the tetracycline gonococcal resistance rates have consistently been greater than 15%.

[Q] Neisseria gonorrhoeae and Antimicrobial Resistance

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) with hair-like pilli extending from the surface outer membrane (Figure 3). 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 its surface pili, rendering it capable of infecting mucosal surfaces, such as the urogenital epithelium, oropharyngeal tract, and conjunctival tissue.[10,11] 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.[10,11,12] Infection with *N. gonorrhoeae* generates limited immunity, and thus, repeated infections can occur.[12]

[Q] Biology of Neisseria gonorrhoeae

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.[13]
- 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.[14]
- 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-penile contact (fellatio).[15,16] In addition, epidemiologic data have associated acquisition of pharyngeal gonorrhea with kissing and oral-anal contact.[17,18,19]
- Transmission of *N. gonorrhoeae* from the pharynx of a person with gonorrhea to the urethra (or a person without gonorrhea) can occur during fellatio.[20,21,22]
- 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 in men who have sex with men (MSM) who have rectal gonorrhea.[23] 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.[24]

[Q] Transmission of Neisseria gonorrhoeae

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). Untreated gonorrhea infection in women 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 within the window of time between acquisition and onset of symptoms.[25] Asymptomatic gonorrhea may act as a reservoir that perpetuates transmission in the community.[26] The typical symptoms of gonococcal urethritis, when present, include a purulent or mucopurulent urethral discharge (Figure 4), often accompanied by dysuria. Less often, the discharge is clear or cloudy. The incubation period ranges from 1–14 days, with most men becoming symptomatic within 2–5 days after exposure.[27]

Anorectal Infections

Anorectal infection most often occurs in men who have sex with men, with the 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.[28] 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, prostatitis, and rarely perirectal abscess.[Q] Symptoms of Gonorrhea in Men

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.[11,29] Clinically, examination of the cervix may show mucopurulent or purulent cervical discharge (Figure 5) and bleeding of the cervix with minimal contact.[29] The incubation period in women is variable, but symptoms, when they do occur, usually develop within 10 days of the exposure.[30] 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.[31] 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. gonorrhea m*ay 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 6).
- **Pelvic Inflammatory Disease**: 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.[32] In some women, PID may also be asymptomatic. Presumptive treatment for PID should be considered if one or more of the following 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 more often associated with chlamydial infection. Gonococcal perihepatitis is characterized by right upper quadrant pain and may be accompanied by abnormal liver function tests.[Q] Complications of Gonococcal Infection in Women

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.[33,34,35] 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.[17] Symptoms of pharyngeal gonococcal infection may include pharyngitis, tonsillitis, fever, and cervical adenitis; exudative pharyngitis is rare.[15,36]

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 7).[37] 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.[18,38] It occurs more often in women than in men, particularly during or shortly after menstruation and during pregnancy.[38] The risk of developing disseminated gonococcal infection is also increased in persons with terminal complement deficiency and in people receiving eculizumab, a medication that inhibits complement activation.[39] Disseminated gonococcal infection is often associated with strains that have a propensity to produce bacteremia without associated urogenital

symptoms.[40] To this end, disseminated gonococcal infection is frequently not suspected due to the minimal mucosal inflammation and lack of urogenital symptoms.[40] Clinical manifestations of disseminated gonococcal infection may include a combination of arthralgia, tenosynovitis, arthritis, skin lesions, hepatitis, myocarditis, endocarditis, and meningitis (Figure 8).[41,42]

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 sexually abused 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 the widespread use of nucleic acid amplification tests (NAATs).[43] Gram 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 Food and Drug Administration (FDA)-cleared for endocervical specimens from women, urethral specimens from men, and urine specimens from men and women.[43,44,45] Some NAATs are also cleared for vaginal swabs. Multiple NAATs are now FDA cleared for extragenital diagnostic testing of *N. gonorrhoeae* and *Chlamydia trachomatis* in rectal and pharyngeal samples.[46] 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

There are several point-of-care tests that can accurately diagnose gonococcal infections.

- **Binx Health**: 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.[47] This point-of-care test can be run on vaginal swabs obtained from women or on urine samples collected from men.[47] This assay can provide a result in approximately 30 minutes.[47] 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.[48] For gonorrhea, the sensitivity estimates were 100.0% in women and 97.3% in men; the specificity estimates were 99.9% for women and 100.0% for men.[48] In addition, the investigators found that self-obtained vaginal swabs in women performed equivalent to clinician-collected vaginal swabs.[48]
- **Visby Medical Sexual Health Test:** In March 2023, the FDA provided clearance and CLIA waiver for the second-generation Visby Medical point-of-care sexual health test. This CLIA-waived point-of-care PCR assay provides results within 30 minutes. This palm-sized device is for single use on a self-collected vaginal swab in women and can accurately detect *C. trachomatis*, *N. gonorrhoeae*, and *Trichomonas vaginalis*.[49] In an evaluation of 1,555 women presenting at clinical sites, the assay performed with a sensitivity of 97·4% and specificity of 99·4% for *N.gonorrhoeae*.[49]

At-Home Sample Collection for NAAT

In November 2023, the FDA granted marketing authorization for the first at-home sample collection kit (*Simple 2 Test*) for the diagnosis of urogenital chlamydia and gonorrhea in persons 18 years of age and older.[50,51] The collection kits include materials for persons to self-collect a vaginal swab or a penile urine sample to be shipped to a clinical laboratory to use the Aptima Combo 2 assay (NAAT).[52] The test is available over the counter for use without the supervision of a health care provider. In a cross-sectional study, investigators evaluated this test for the diagnosis of chlamydia and gonorrhea using vaginal swabs obtained from 1,258 women and urine samples collected from 1,797 men.[52] For gonorrhea diagnosis in women, the sensitivity and specificity estimates for vaginal swabs were 97.7% and 99.6%, respectively. For gonorrhea diagnosis in men, the sensitivity and specificity estimates for urine samples were 98.7% and 99.7% in men.[52] The presence of some brands of hand soap and hand sanitizer caused false-negative gonorrhea results in urine samples from men.

Gram Stain

The use of Gram stain is a nonculture test that can make a presumptive diagnosis of gonorrhea. In the clinical setting, a Gram stain to detect *N. gonorrhoeae* is most often performed on a male with purulent urethral discharge. A Gram stain on a specimen positive for *N. gonorrhoeae* shows polymorphonuclear leukocytes with intracellular gram-negative diplococci (Figure 9). A Gram stain, when using proper laboratory techniques, has greater than 95% sensitivity and greater than 99% specificity for diagnosing symptomatic male gonococcal urethritis.[43] Thus, the Gram stain is considered reliable both to diagnose and to exclude gonococcal urethritis in symptomatic men.[25] The sensitivity of a Gram stain is lower for males with asymptomatic urethral infection and thus not considered adequate to rule out infection in asymptomatic men.[25] Performing a Gram stain is not recommended on endocervical, pharyngeal, or rectal specimens due to poor sensitivity.[25]

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 Thayer-Martin media. At present, culture is primarily used for antimicrobial resistance surveillance.[25][Q] Diagnostic Tests for Gonorrhea

Diagnosis in Cases of Possible 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*.[25] 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 during the assault.[] In evaluating children with suspected sexual abuse, either culture or NAAT can be used to detect *N. gonorrhoeae*and *C. trachomatis*.[54] 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.[54] 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.[55] Further, it is important to ensure the results are appropriately interpreted. 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.[54] A Gram 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 obtained 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 and reduce the burden of disease in the community.[25,56] Testing samples should be obtained from the anatomic sites of sexual exposure. The following summarizes recommendations for gonorrhea screening in the 2021 STI Treatment Guidelines and [Guidelines] Doxy PEP Guidelines.[25,56,57]

Women [25]

- Routine screening for gonorrhea is recommended for all sexually active women younger than 25 years of age.
- Sexually active women who are 25 years of age 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 [58]

- 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 [56,59]

- 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).
- Retesting for gonorrhea should be done during the third trimester for women under 25 years of age or those with an increased risk of acquiring gonorrhea during the pregnancy.

Men Who Have Sex Only with Women [56]

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

Men Who Have Sex with Men [56,60]

- 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 of acquiring chlamydia, and persons who have multiple sex partners or their sex partners have multiple partners).

Persons with HIV [56]

- 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 Receiving HIV Preexposure Prophylaxis (HIV PrEP)

- Persons receiving HIV preexposure prophylaxis (HIV PrEP) should undergo routine gonorrhea screening at baseline. The frequency of gonorrhea screening for persons while they are receiving HIV PrEP varies as follows:
    - Every 3 months for MSM taking oral HIV PrEP (tenofovir DF-emtricitabine or tenofovir alafenamide-emtricitabine)
    - Every 4 months for MSM who are receiving long-acting injectable cabotegravir
    - Every 6 months for men who have sex with women and women who have sex with men (with any HIV PrEP)

Persons Receiving Doxycycline Postexposure Prophylaxis (Doxy PEP) [57]

- Persons starting on doxycycline postexposure prophylaxis (doxy PEP) should undergo routine gonorrhea screening at baseline.
- The frequency of gonorrhea screening for persons while they are continuing on doxy PEP should be every 3 to 6 months.

Persons in Correctional Facilities [61]

- 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.[Q] Routine Screening for Gonorrhea

Treatment

Treatment of Gonococcal Infections

The following summarizes gonococcal treatment recommendations in the 2021 STI Treatment Guidelines.[25] These recommendations depend on the site of the infection and whether chlamydia infection has been ruled out.[25]

Uncomplicated Infections of the Cervix, Urethra, and Rectum

For persons with uncomplicated gonococcal infections of the cervix, urethra, or rectum, the recommended treatment for persons who weigh less than 150 kg is a single intramuscular dose of ceftriaxone 500 mg; for persons who weigh 150 kg or more, the ceftriaxone dose should be increased to 1 gram.[25] If chlamydia infection has not been excluded, then treatment should include oral doxycycline 100 mg twice daily for 7 days (except for pregnant women).[25] For pregnant women, if chlamydia has not been excluded, oral azithromycin 1 gram should be used in place of doxycycline.[25] 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.[25]

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*

During pregnancy, oral azithromycin 1 gram in a single dose is recommended to treat chlamydia.
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.

Source: Workowski KA, Bachmann LH, Chan PA, et al. Sexually transmitted infections treatment guidelines, 2021. Gonococcal infections. MMWR Recomm Rep. 2021;70(No. RR-4):1-187. [2021 STI Treatment Guidelines]

[Q] Treatment of Gonococcal Urethritis

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 for pharyngeal gonorrhea for persons who weigh less than 150 kg is a single intramuscular dose of ceftriaxone 500 mg; for persons who weigh 150 kg or more, the ceftriaxone dose should be increased to 1 gram.[25] Note there are no reliable alternative regimens for the treatment of pharyngeal gonorrhea.[25] If chlamydia infection was also identified when the pharyngeal testing was performed, then treatment should include oral doxycycline 100 mg twice daily for 7 days (except for pregnant women).[25] If treatment for chlamydia pharyngeal infection is indicated and the patient is a woman who is pregnant, oral azithromycin (1 gram single-dose treatment) should be used in place of doxycycline. 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.[25]

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

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

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.

Source: Workowski KA, Bachmann LH, Chan PA, et al. Sexually transmitted infections treatment guidelines, 2021. Gonococcal infections. MMWR Recomm Rep. 2021;70(No. RR-4):1-187. [2021 STI Treatment Guidelines]

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.[62] Based on this study, the recommended treatment for gonococcal conjunctivitis is a single ceftriaxone 1-gram intramuscular dose.[25] In addition, a one-time lavage of the infected eye with saline should be considered.[25]

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

Recommended Regimen
Ceftriaxone *1 g IM in a single dose*

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

Source: Workowski KA, Bachmann LH, Chan PA, et al. Sexually transmitted infections treatment guidelines, 2021. Gonococcal infections. MMWR Recomm Rep. 2021;70(No. RR-4):1-187. [2021 STI Treatment Guidelines]

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.[25]

Disseminated Infection With Gonococcal-Related Arthritis and Arthritis-Dermatitis Syndrome

Disseminated gonococcal infection is often complicated by joint complications (e.g., polyarthralgia, tenosynovitis, or oligoarticular septic arthritis) and by dermatologic manifestations (e.g., pustular lesions and petechiae).[38,63,64] The following summarizes treatment of disseminated gonococcal infection, including with arthritis and/or dermatitis complications, consists of initial antimicrobial therapy with intramuscular or intravenous ceftriaxone 1 gram 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 the patient is clinically improved and antimicrobial sensitivity testing shows an effective oral choice.[25] If meningitis or endocarditis is diagnosed, then treatment should be changed to that recommended in the next section (Disseminated Infection with Meningitis and/or Endocarditis).[25]

Table 4. 2021 STI Treatment Guidelines: Gonococcal Infections Treatment of Disseminated Gonococcal Infection (DGI): Arthritis and Arthritis-Dermatitis Syndrome

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

Alternative Regimens

Cefotaxime *1 gram IV every 8 hours*
Note: If chlamydial infection has not been excluded, providers should treat for chlamydia with doxycycline 100 mg orally 2 times/day for 7 days.

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

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.

Source: Workowski KA, Bachmann LH, Chan PA, et al. Sexually transmitted infections treatment guidelines, 2021. Gonococcal infections. MMWR Recomm Rep. 2021;70(No. RR-4):1-187. [2021 STI Treatment Guidelines]

Disseminated Infection With Meningitis and/or Endocarditis

For persons diagnosed with DGI and meningitis, parenteral therapy requires a higher dose of ceftriaxone, and therapy should continue for at least 10 to 14 days; with endocarditis, parenteral therapy should be given for at least 4 weeks.[25]

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

Recommended Regimen
Ceftriaxone *1–2 g IV every 24 hours*
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.

Source: Workowski KA, Bachmann LH, Chan PA, et al. Sexually transmitted infections treatment guidelines, 2021. Gonococcal infections. MMWR Recomm Rep. 2021;70(No. RR-4):1-187. [2021 STI Treatment Guidelines]

Allergy to Penicillin 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-reported 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.[65] 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.[66] 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.[8,25,67] 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 an Ig-E mediated allergic reaction in the prior 10 years.

Gonococcal Infections in Pregnancy

Pregnant women with *N. gonorrhoeae* should be treated with a single intramuscular dose of ceftriaxone 500 mg, with the addition of a single dose of azithromycin 1.0 g orally if chlamydia infection is not ruled out.[3] Pregnant women 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.[Q] Treatment of Gonorrhea in Pregnancy

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 upward trend of MICs documented by the United States Gonococcal Isolate Surveillance Project (GISP) remains worrisome.[68,69,70,71] 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.[7] 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.[72,73,74,75]

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).[25] 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.[76,77,78] 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.[25] 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.[25] 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 with 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 result from reinfection.
- **Antimicrobial Options for Likely Treatment Failure**: For individuals considered to have a 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.
- **New FDA-Approved Therapies for *N. gonorrhoeae***: Two oral antimicrobials, gepotidacin and zoliflodacin, were recently FDA-approved for the treatment of uncomplicated gonorrhea in persons at least 12 years of age. In separate phase 3 trials, these antibiotics were shown to be non-inferior to ceftriaxone plus azithromycin.[79,80] Geptotidacin is administered as two oral 3 g doses, taken 12 hours apart. Zoliflodacin is taken as a single 3 g oral dose. The mechanism of action for both of these antimicrobials is inhibition of bacterial topoisomerase II (DNA gyrase) and topoisomerase IV. Zoliflodacin and gepotidacin were FDA approved for the treatment of gonorrhea after the release of the 2021 CDC STI treatment guidelines and therefore are not included as an option to treat gonorrhea in the current 2021 CDC STI treatment guidelines.

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.[25] 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.[25] 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.[25] Because nucleic acid tests frequently remain positive for 7–10 days after treatment, many experts recommend doing the follow-up test-of-cure on post-treatment day 14 (or as near to post-treatment day 14 as possible). 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.[56] 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.[25]

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 the 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.[25,81] 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.[25]

- **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, except for pregnant women; if there is concern regarding the partner taking multidose therapy for chlamydia, then azithromycin 1-gram orally as a single dose can be given.[25,82]
- **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 the 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).

Prevention

Doxycycline Post-Exposure Prophylaxis for Prevention of STIs

Doxycycline administered as 200 mg once within 72 hours after a condomless sexual encounter, can help prevent bacterial STIs, including chlamydia, syphilis, and gonorrhea. The use of doxycycline post-exposure prophylaxis (doxy PEP) has been shown to be effective for men who have sex with men in several randomized trials.[83,84,85] One clinical trial using doxy PEP for women in Africa has been completed, and it did not show benefit in reducing STIs.[86] In 2024, the CDC published *Clinical Guidelines on the Use of Doxycycline Post-exposure Prophylaxis for Bacterial STI Prevention*.[57] These guidelines do not recommend doxy PEP for women. The following will focus on the impact of doxy PEP on preventing gonococcal infections.

Doxycycline Post-Exposure Prophylaxis for Prevention of Gonorrhea

Data are mixed on the efficacy of doxy PEP for the prevention of gonococcal infections. In the DoxyPEP randomized trial in the United States, which was conducted in San Francisco and Seattle during 2020-2022, the use of doxy PEP, as compared to standard of care, led to an approximate 55% reduction in incident gonorrhea, including a major reduction in pharyngeal gonorrhea.[83] In addition, the quarterly incidence of new gonorrhea infections was significantly reduced in both main study arms—people without HIV who were receiving HIV PrEP and in those with HIV.[83] In the French IPERGAY-DoxyPEP study, which was conducted during 2015-2016, the use of doxy PEP among 232 MSM who were receiving HIV PrEP led to no significant changes in the occurrence of a new episode of gonorrhea, as compared to standard of care.[85] In another randomized trial involving MSM (the French ANRS DOXYVAC), there was moderate efficacy of doxy PEP against gonorrhea (33% reduction).[84] The most plausible reason for the discrepant findings between the United States and French trials is the difference in background prevalence of tetracycline resistance (roughly 27% in the United States versus 56% in France).[83,87] Given conflicting results thus far, more studies are needed regarding the efficacy of doxy PEP for the prevention of gonorrhea.

Meningococcal B Vaccine as Potential Prevention of Gonorrhea

Observational data have suggested reductions in gonorrhea among individuals who received outer membrane vesicle-based meningococcal vaccines, including the meningococcal group B vaccine/MenB-4C, a recombinant protein-based *Neisseria meningitidis* group B meningococcal vaccine that is licensed for use in the United States.[88,89,90] The 4C designation in the MenB-4C vaccine refers to the four main *N. meningitidis* recombinant antigens: Factor H-binding protein (FHbp), Neisserial adhesin A (NadA), Neisserial Heparin-Binding Antigen (NHBA), and Outer Membrane Vesicles (OMV).[91] Vaccine-related cross-protection against gonorrhea is thought to arise from the 80-90% genetic sequence homology between the *N. gonorrhoeae* proteins and the OMV and NHBA antigens in the MenB-4C vaccine.[92,93] The antigens in the other licensed meningococcal B vaccine (MenB-FHbp) do not provide cross-protection against *N. gonorrhoeae*.[94] Similarly, the meningococcal pentavalent vaccine (MenACWY-TT/MenB-FHbp) does not have cross-protection with *N. gonorrhoeae* since the Men B antigens used in this vaccine are MenB-FHbp.[94] The ANRS DOXYVAC trial randomized MSM taking HIV PrEP to assess whether 2 doses of MenB-4C vaccination, given 2 months apart, versus placebo, would reduce the incidence of gonorrhea in MSM, but there was not a statistically significant reduction in gonorrhea incidence.[84] Randomized trials using 4CMenB for the prevention of gonorrhea are ongoing, including the HPTN 107 study, a randomized, placebo-controlled multi-site trial among men and women considered disproportionately vulnerable to *N. gonorrhoeae* infection.

Summary Points

- In the United States, rates of gonococcal infection have increased overall since 2010. The age group with the highest gonorrhea rates is persons 20-24 years of age.
- Gonococcal antimicrobial resistance to ceftriaxone and cefixime remains low in the United States. Antimicrobial resistance to azithromycin has increased in recent years. Resistance rates are high with penicillin, tetracycline, and ciprofloxacin.
- 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 if there is a concern for antimicrobial-resistant gonococcal infection.
- 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 women, 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 the infection, the importance of partner notification, when they can resume sexual activity, and how they can reduce their risk of acquiring STIs in the future.

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Figures

Figure 1 Gonorrhea Reported Cases in the United States

Source: Centers for Disease Control and Prevention. *Sexually Transmitted Infections Surveillance*, 2023. Atlanta: U.S. Department of Health and Human Services; 2024.

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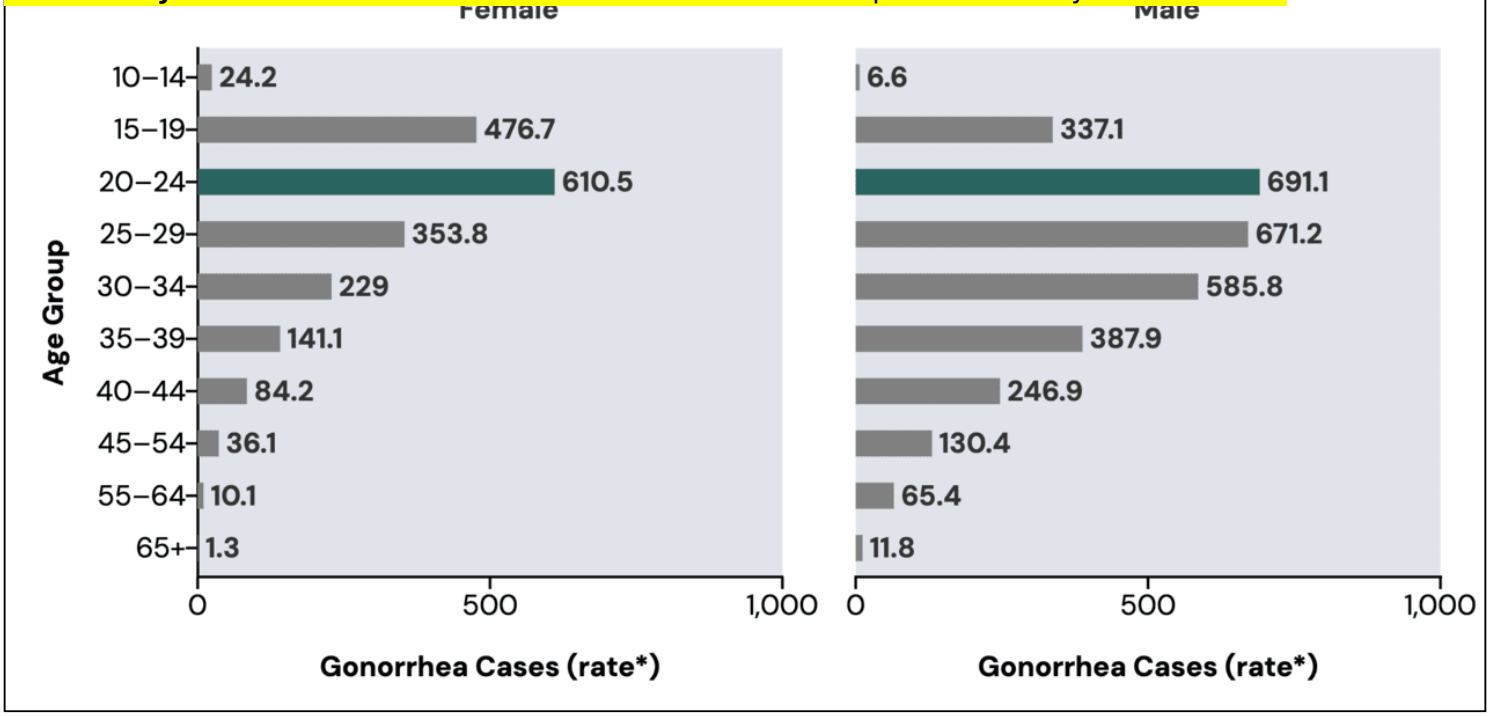


Figure 2 (Image Series) - Gonococcal Isolate Surveillance Project (GISP), GISP 2010-2022 (Image Series) - Figure 2 (Image Series) - Gonococcal Isolate Surveillance Project (GISP), GISP 2010-2022
Image 2A: Antimicrobial Drugs Used to Treat Gonorrhea, GISP 1988 through 2022

Abbreviations: GISP = Gonococcal Isolate Surveillance Project (GISP)
NOTE: In 2022, Cefixime 800 mg (0.1%) and Ceftriaxone 1 g (0.2%) each represented less than one percent of primary antimicrobial drugs used to treat gonorrhea among GISP participants and may not be visible in this figure.

Source: Centers for Disease Control and Prevention. Gonococcal Isolate Surveillance Project (GISP) Profiles, 2022.

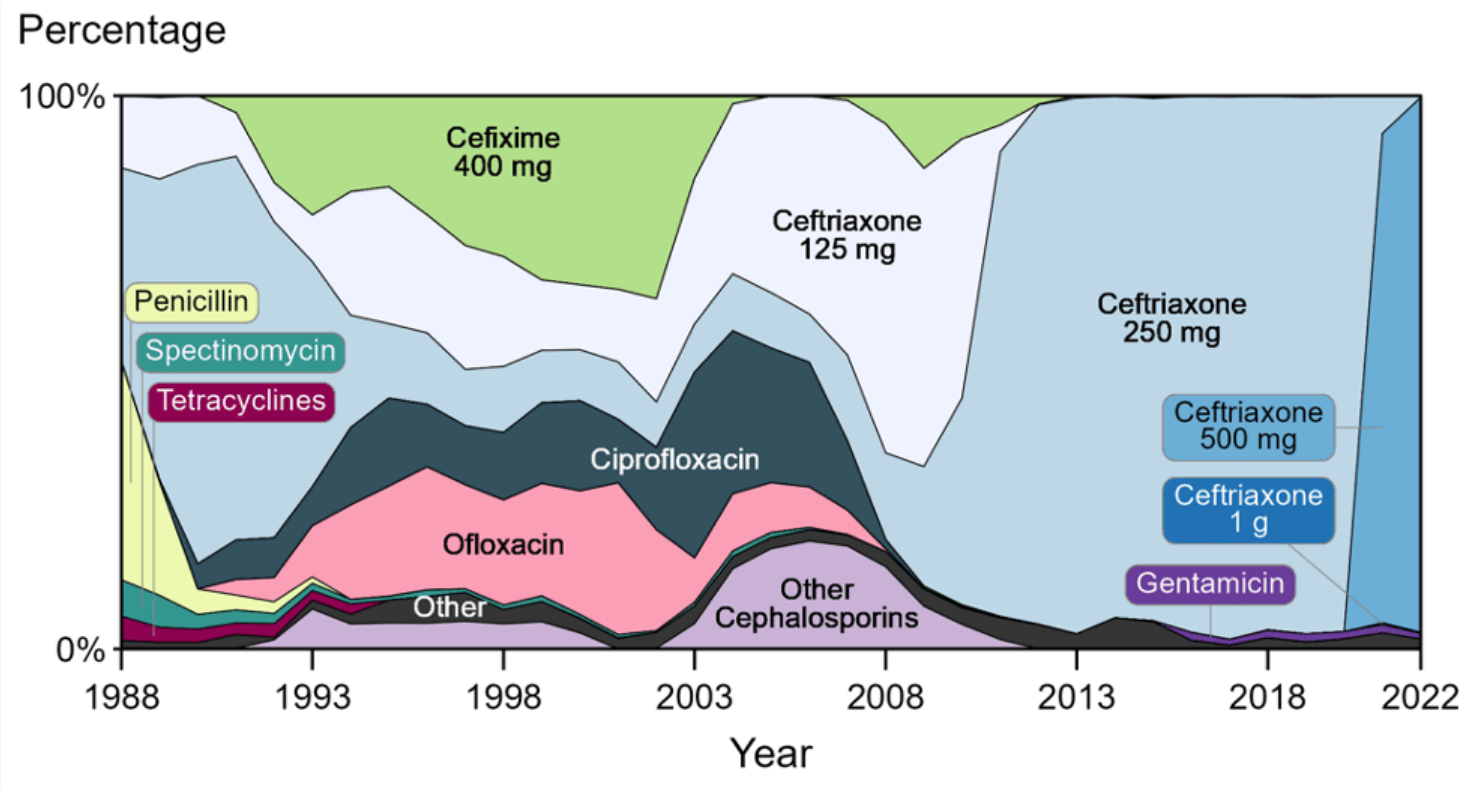


Figure 2 (Image Series) - Gonococcal Isolate Surveillance Project (GISP), GISP 2010-2022
Image 2B: *Neisseria gonorrhoeae*—Percentage of Isolates with Elevated MICs to Azithromycin, Cefixime, and Ceftriaxone

Abbreviations: GISP = Gonococcal Isolate Surveillance Project; MICs = minimum inhibitory concentrations; Elevated MICS = Azithromycin ≥2.0 µg/mL; Cefixime ≥0.25 µg/mL; Ceftriaxone ≥0.125 µg/mL

Source: Centers for Disease Control and Prevention. Gonococcal Isolate Surveillance Project (GISP) Profiles, 2022.

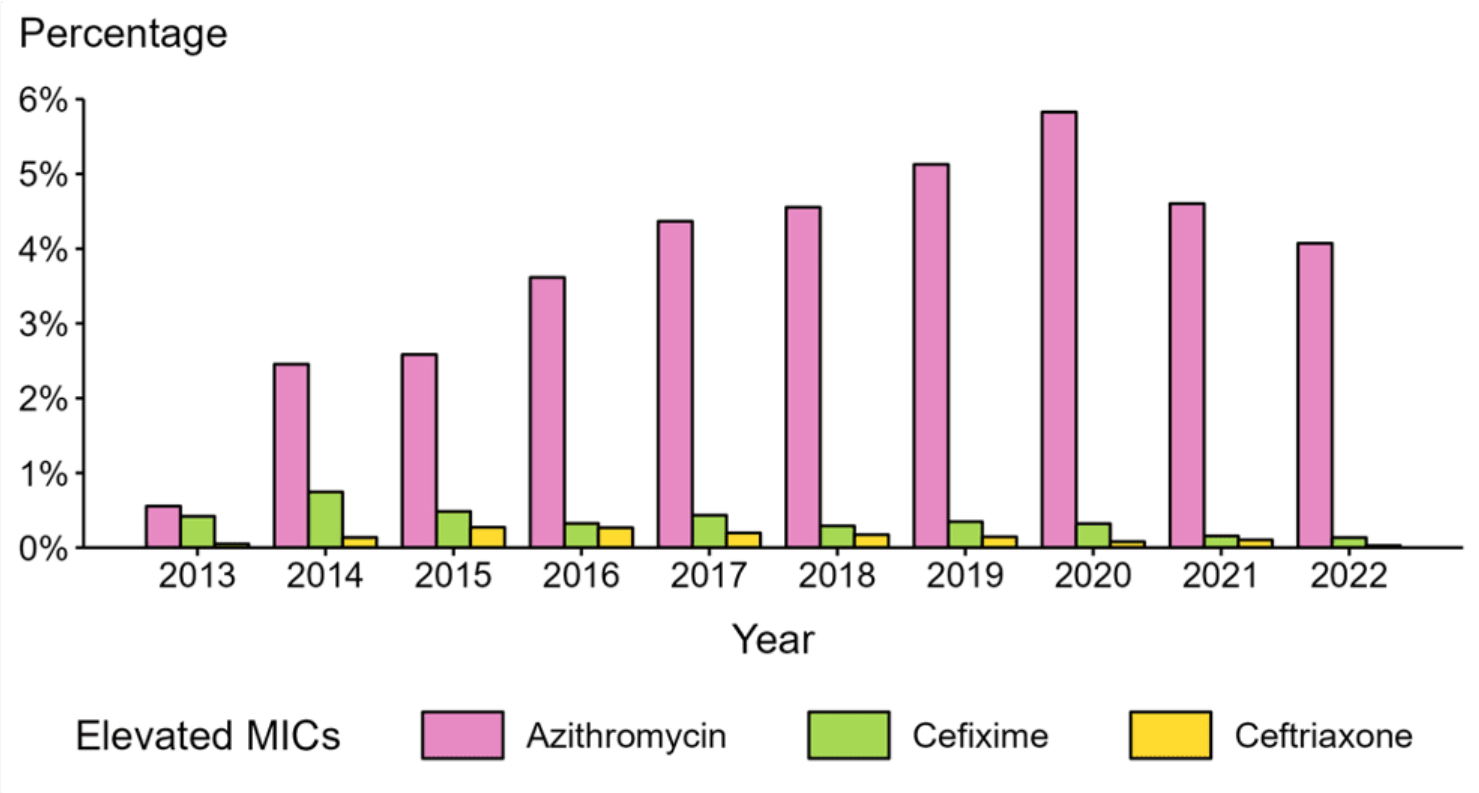


Figure 2 (Image Series) - Gonococcal Isolate Surveillance Project (GISP), GISP 2010-2022
Image 2C: Prevalence of Tetracycline, Penicillin, or Fluoroquinolone Resistance* or Elevated Cefixime, Ceftriaxone, or Azithromycin MICs^, by Year

Abbreviations: 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 = *Elevated MICs: Azithromycin: MIC ≥ 1.0 µg/mL (2000–2004); ≥ 2.0 µg/mL (2005–2022); Ceftriaxone: MIC ≥ 0.125 µg/mL; Cefixime: MIC ≥ 0.25 µg/mL

Source: Centers for Disease Control and Prevention. Gonococcal Isolate Surveillance Project (GISP) Profiles, 2022.

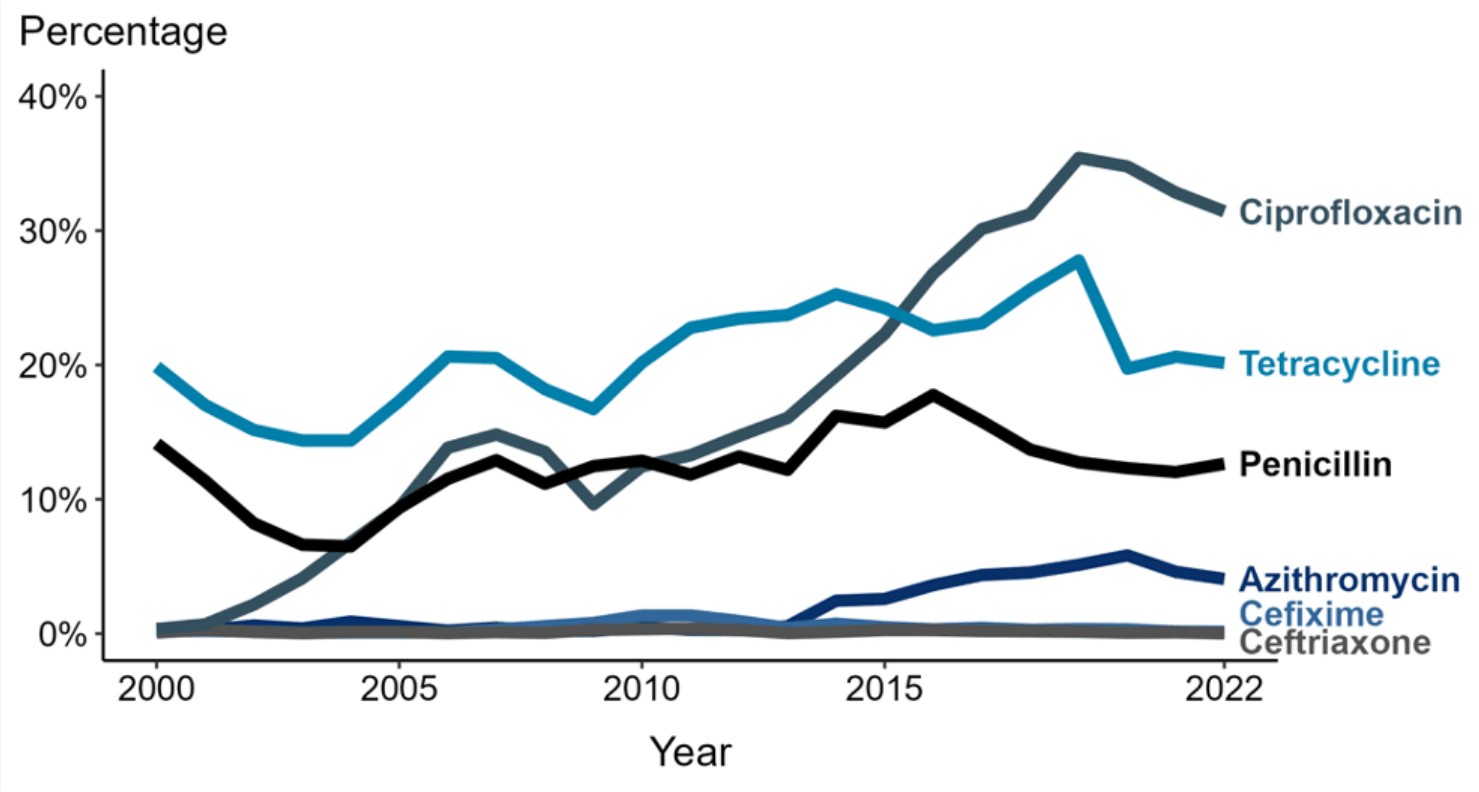


Figure 2 (Image Series) - Gonococcal Isolate Surveillance Project (GISP), GISP 2010-2022
Image 2D: *Neisseria gonorrhoeae*—Distribution of Gentamicin MICs by Year, 2018–2022

Abbreviations: MICs = minimum inhibitory concentrations
Note: Beginning 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.

Source: Centers for Disease Control and Prevention. Gonococcal Isolate Surveillance Project (GISP) Profiles, 2022.

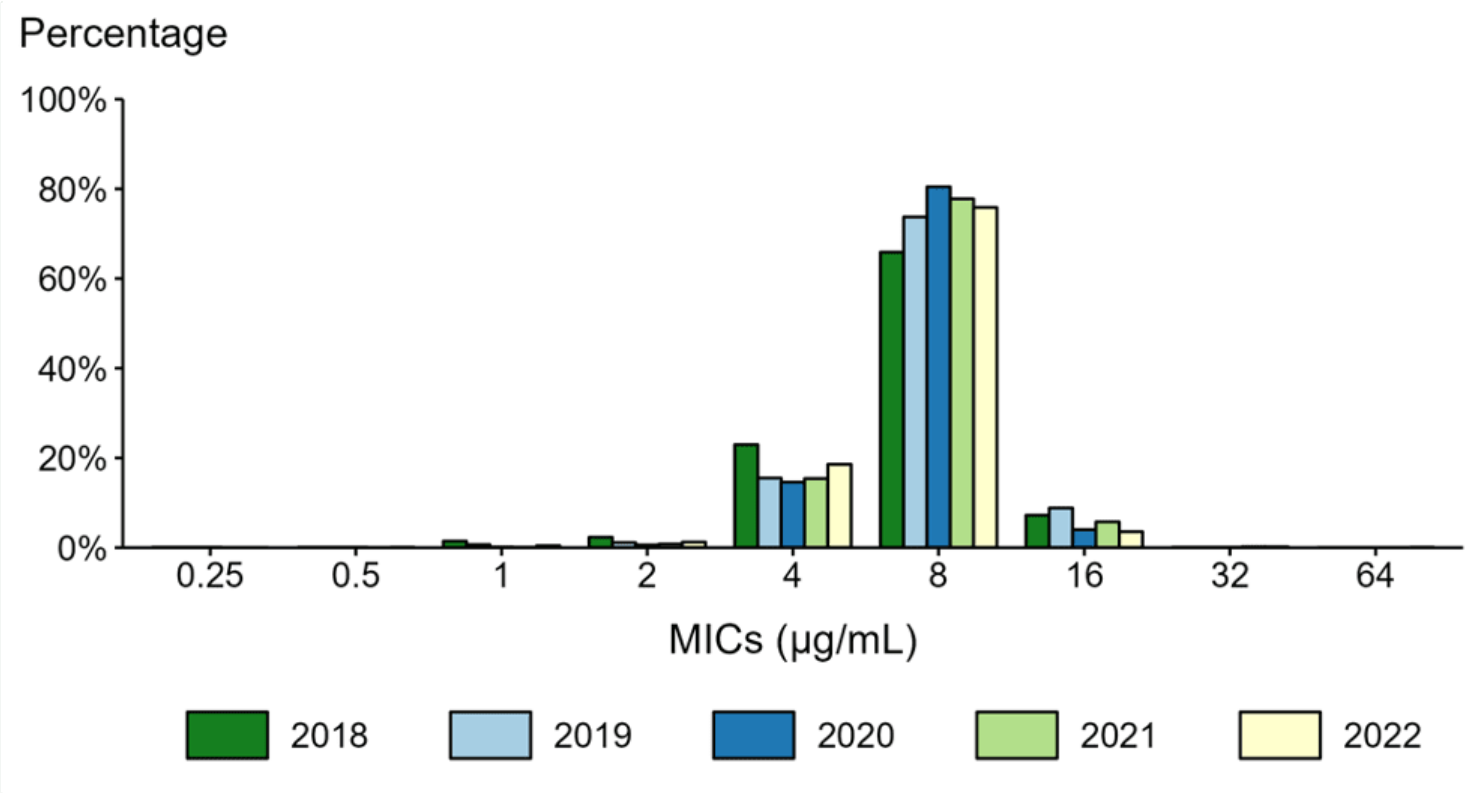


Figure 3 (Image Series) - *Neisseria gonorrhoeae* Diplococci (Image Series) - Figure 3 (Image Series) - *Neisseria gonorrhoeae* Diplococci
Image 3A: *Neisseria gonorrhoeae* and Binary Fission

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

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

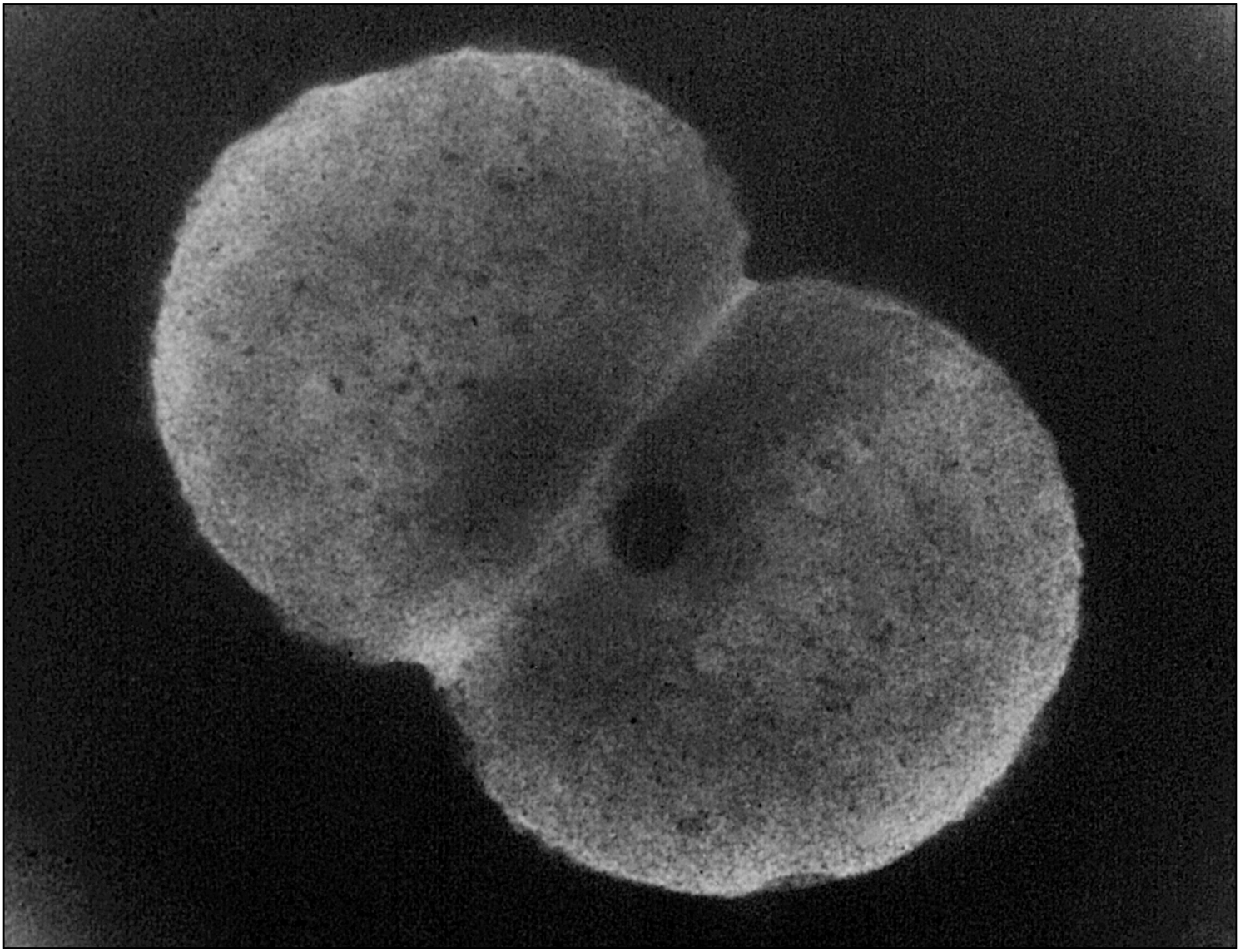


Figure 3 (Image Series) - *Neisseria gonorrhoeae* Diplococci
Image 3B: *Neisseria gonorrhoeae*

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 surface membrane; 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).

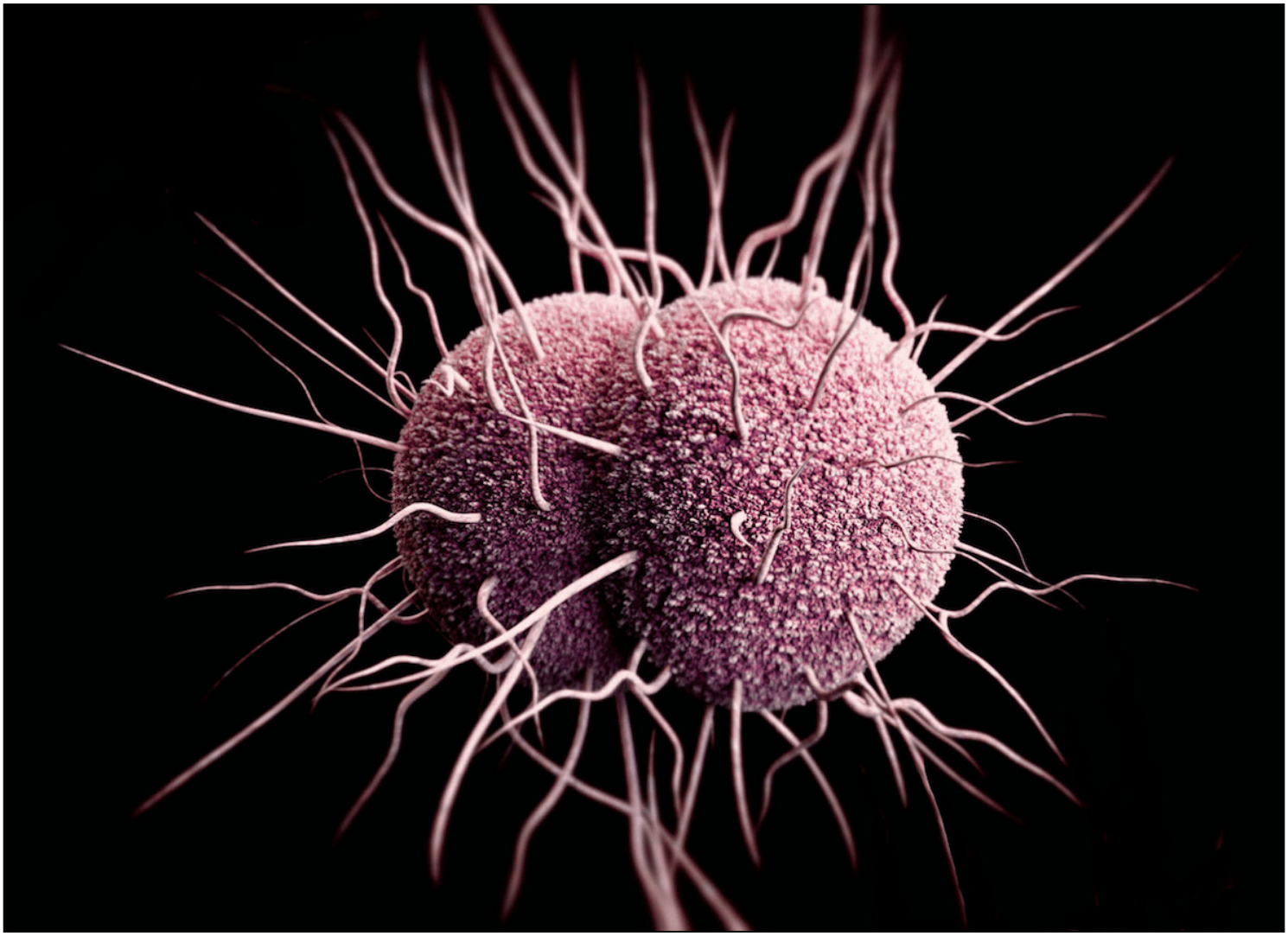


Figure 4 Purulent Urethral Discharge with Gonococcal Infection

Photograph from Negusse Ocbamichael, PA; Public Health—Seattle & King County Sexual Health Clinic



Figure 5 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

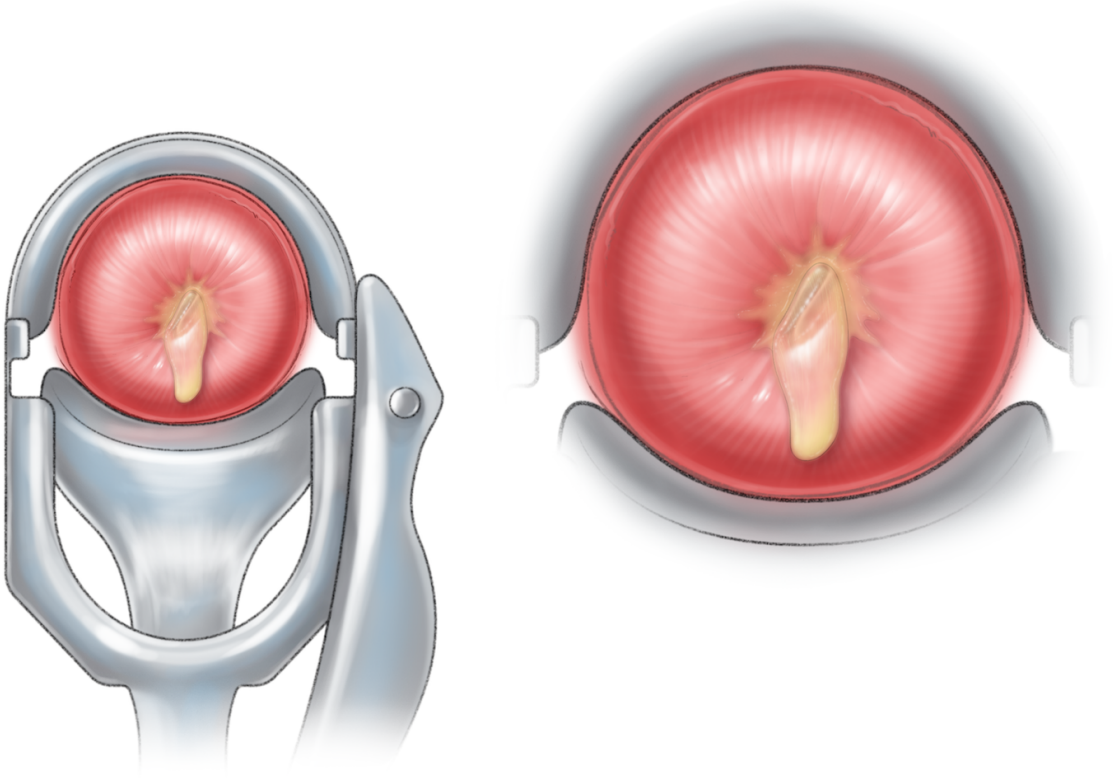


Figure 6 (Image Series) - Bartholin Glands, Bartholin Cyst, and Bartholin Abscess (Image Series) - Figure 6 (Image Series) - Bartholin Glands, Bartholin Cyst, and Bartholin Abscess
Image 6A: Bartholin Glands

The Bartholin glans are located on each side of the vaginal introitus, at approximately the 4 and 8 o'clock positions. Each gland is normally oval-shaped and less than 1 cm in diameter.

Illustration credit: Cognition Studio, Inc. and David H. Spach, MD

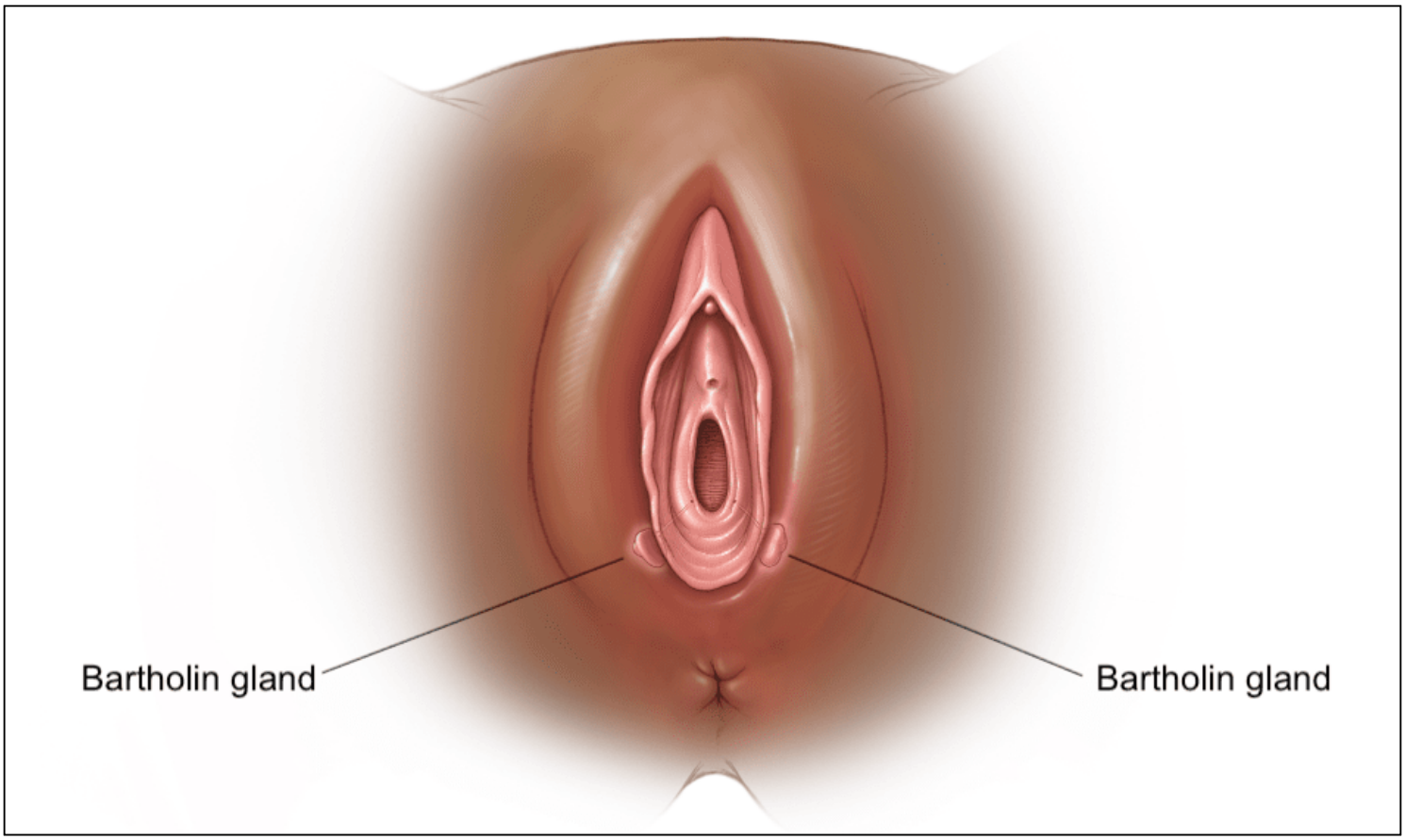


Figure 6 (Image Series) - Bartholin Glands, Bartholin Cyst, and Bartholin Abscess
Image 6B: Bartholin Cyst

This illustration shows a Bartholin cyst involving the patient’s right Bartholin gland. 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 credit: Cognition Studio, Inc. and David H. Spach, MD

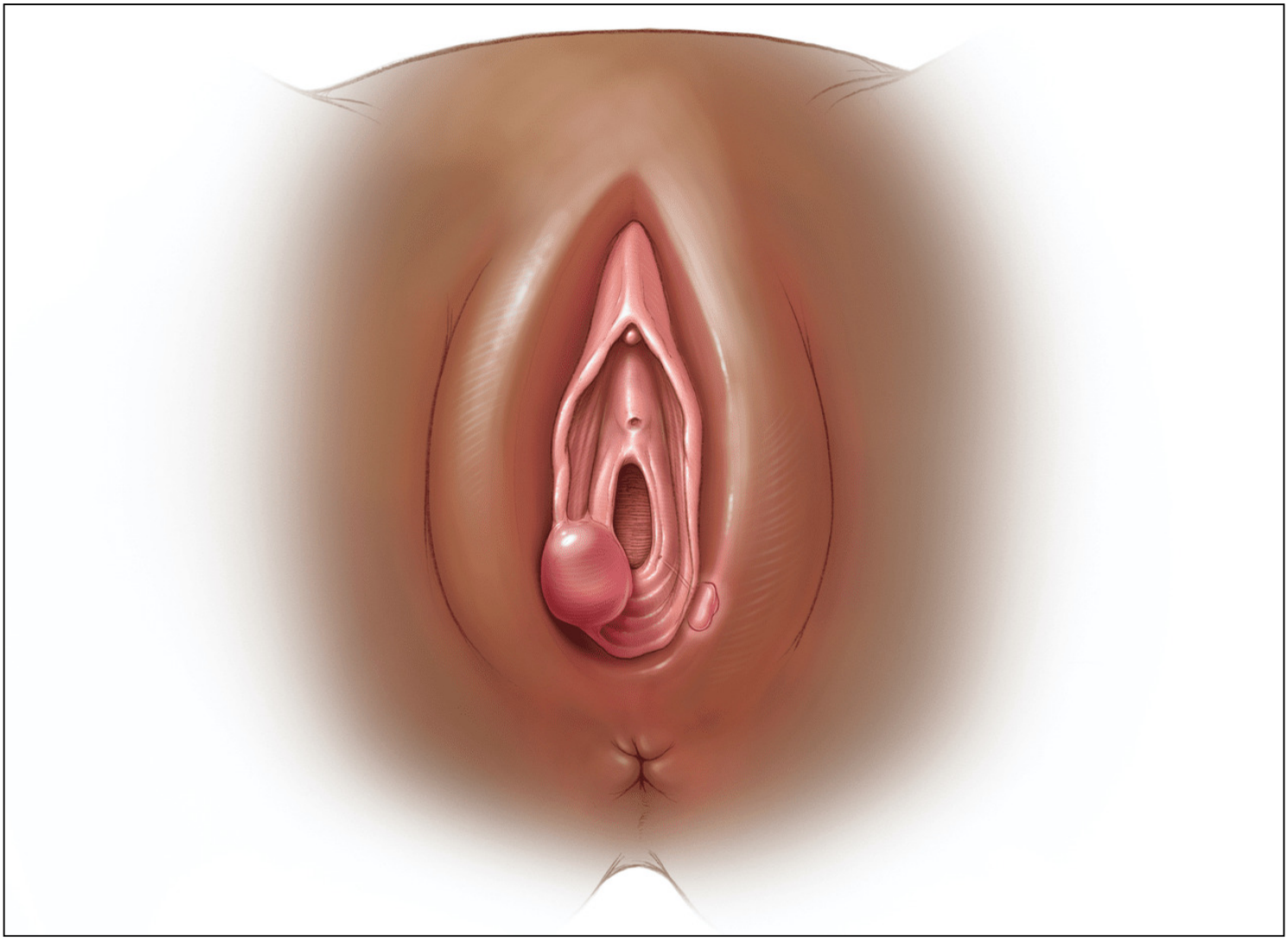


Figure 6 (Image Series) - Bartholin Glands, Bartholin Cyst, and Bartholin Abscess
Image 6C: Bartholin Abscess

This illustration shows Bartholin abscess involving the patient's right Bartholin gland. A Bartholin cyst can become infected and develop into a Bartholin abscess that is tense, painful, and filled with pus.

Illustration credit: Cognition Studio, Inc. and David H. Spach, MD

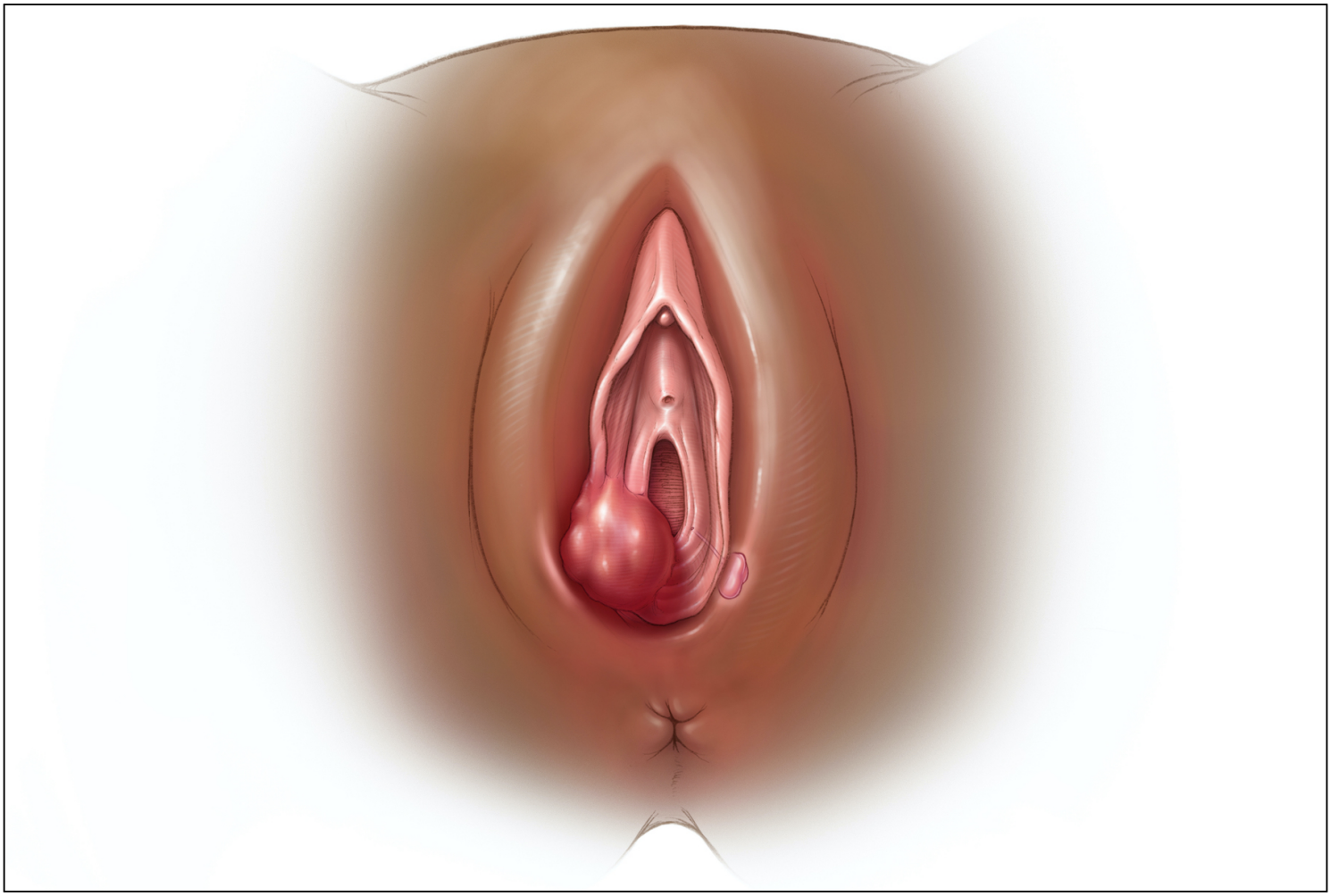


Figure 7 Gonococcal Conjunctivitis

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.

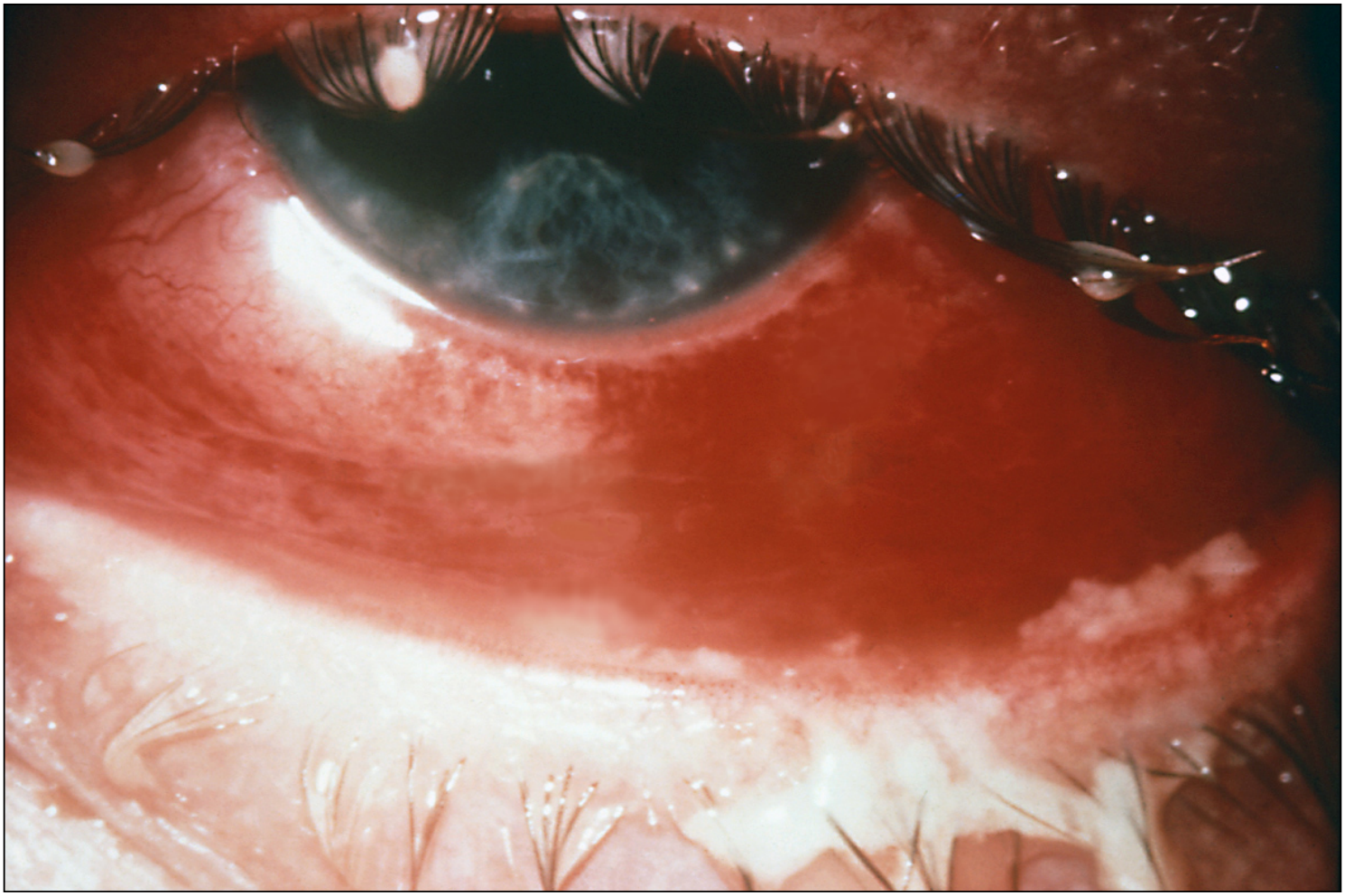


Figure 8 (Image Series) - Disseminated Gonococcal Infection (Image Series) - Figure 8 (Image Series) - Disseminated Gonococcal Infection
Image 8A: Disseminated Gonococcal Infection with Arthritis

Source: Centers for Disease Control and Prevention Public Health Image Library (Emory, Tom Sellers, 1963).



Figure 8 (Image Series) - Disseminated Gonococcal Infection
Image 8B: 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 9 Urethral Swab Gram Stain in a Patient with Gonorrhea

This Gram 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).

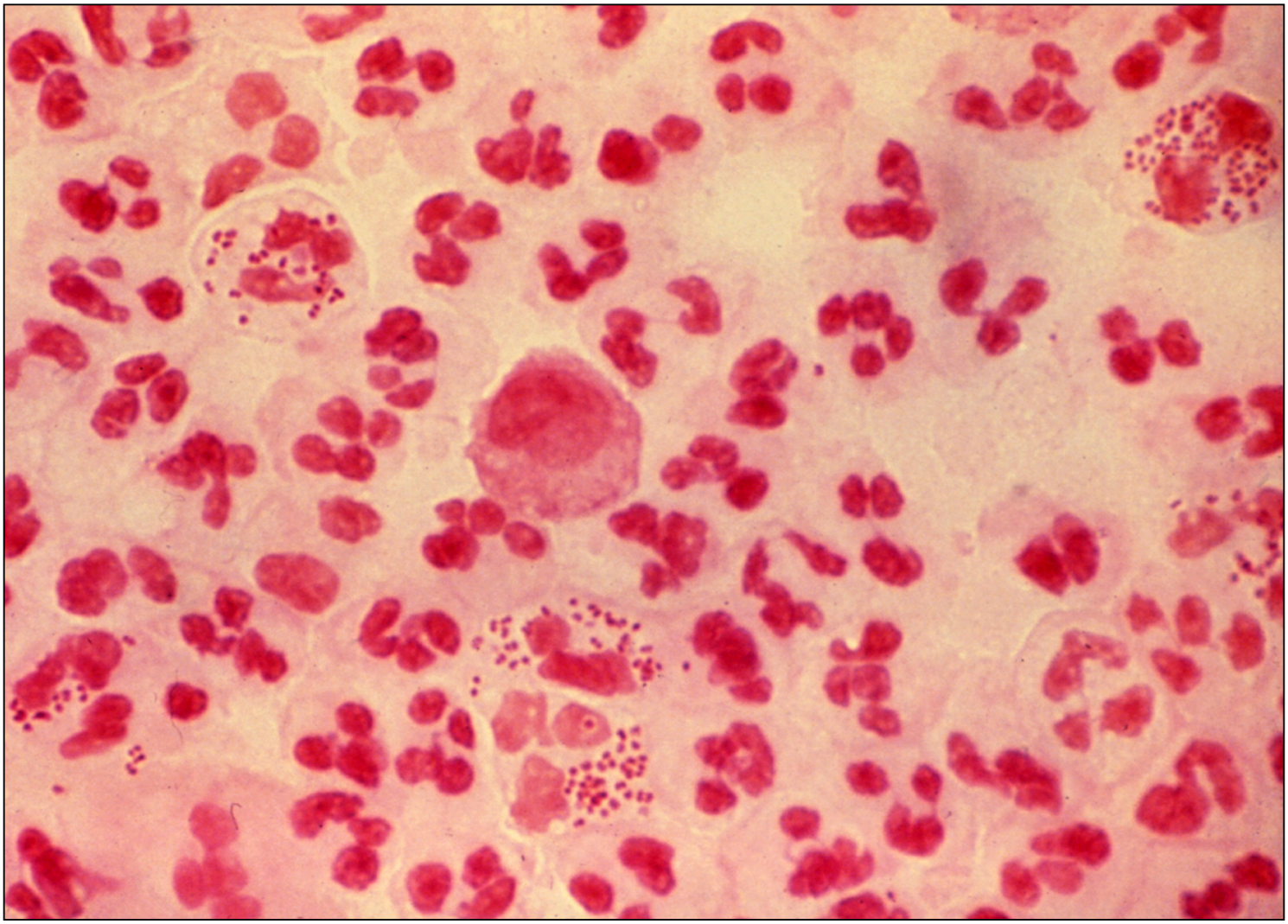


Table 1. 2021 STI Treatment Guidelines: Gonococcal Infections
Treatment of Uncomplicated Gonococcal Infection of the Cervix, Urethra, or Rectum

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

During pregnancy, oral azithromycin 1 gram in a single dose is recommended to treat chlamydia.
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.

Source: Workowski KA, Bachmann LH, Chan PA, et al. Sexually transmitted infections treatment guidelines, 2021. Gonococcal infections. MMWR Recomm Rep. 2021;70(No. RR-4):1-187. [2021 STI Treatment Guidelines]

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

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

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.

Source: Workowski KA, Bachmann LH, Chan PA, et al. Sexually transmitted infections treatment guidelines, 2021. Gonococcal infections. MMWR Recomm Rep. 2021;70(No. RR-4):1-187. [2021 STI Treatment Guidelines]

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

Recommended Regimen
Ceftriaxone *1 g IM in a single dose*

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

Source: Workowski KA, Bachmann LH, Chan PA, et al. Sexually transmitted infections treatment guidelines, 2021. Gonococcal infections. MMWR Recomm Rep. 2021;70(No. RR-4):1-187. [2021 STI Treatment Guidelines]

Table 4. 2021 STI Treatment Guidelines: Gonococcal Infections
Treatment of Disseminated Gonococcal Infection (DGI): Arthritis and Arthritis-Dermatitis Syndrome

Recommended Regimen

Ceftriaxone
1 g IM or IV every 24 hours

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

Alternative Regimens

Cefotaxime
1 gram IV every 8 hours

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

Alternative Regimens

Ceftizoxime
1 g IV every 8 hours

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

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.

Source: Workowski KA, Bachmann LH, Chan PA, et al. Sexually transmitted infections treatment guidelines, 2021. Gonococcal infections. MMWR Recomm Rep. 2021;70(No. RR-4):1-187. [2021 STI Treatment Guidelines]

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

Recommended Regimen
Ceftriaxone *1–2 g IV every 24 hours*
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.

Source: Workowski KA, Bachmann LH, Chan PA, et al. Sexually transmitted infections treatment guidelines, 2021. Gonococcal infections. MMWR Recomm Rep. 2021;70(No. RR-4):1-187. [2021 STI Treatment Guidelines]