

# Manifestations of Gonorrhea and Chlamydial Infection

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**G**onorrhea and chlamydia are the 2 most commonly reported bacterial sexually transmitted diseases (STDs) in the United States.<sup>1</sup> Early diagnosis is an important challenge with both gonorrhea and chlamydia because most patients do not exhibit symptoms. *Neisseria gonorrhoeae* can infect mucosal surfaces, including the urethra, endocervix, pharynx, and rectum. Disseminated gonococcal infection can occur as well, leading to arthritis, tenosynovitis, and dermatitis. *Chlamydia trachomatis* infection in men can lead to urethritis, epididymitis, and prostatitis, while in women it can cause urethritis, cervicitis, and salpingitis. Women with *N. gonorrhoeae* and *C. trachomatis* are more often asymptomatic and therefore are more likely to develop complications from untreated infection, including pelvic inflammatory disease (PID), ectopic pregnancy, and infertility.<sup>2</sup> This article discusses the genitourinary and extragenital manifestations of *N. gonorrhoeae* and *C. trachomatis* infections and briefly outlines laboratory diagnosis and recommended treatment.

## EPIDEMIOLOGY

In the United States, chlamydial genital infection is the most frequently reported STD in the United States, followed by gonorrhea.<sup>1</sup> The prevalence of chlamydia and gonorrhea peaks during the late teenage years in women and during the early 20s in men.<sup>3-6</sup> Coinfection is common, with an overall prevalence of approximately 30%;<sup>5</sup> however, 1 study reported a prevalence of 46%.<sup>6</sup> There are substantial racial/ethnic disparities for both chlamydial and gonococcal infections—chlamydial infection is 6 times more common, and gonorrhea is 20 times more common among black young adults as compared with white young adults.<sup>5,7</sup>

Lymphogranuloma venereum (LGV) is an STD caused by *C. trachomatis* serovars L1, L2, or L3.<sup>8-10</sup> LGV is uncommon in the United States but is responsible for 10% of genital ulcer disease in tropical countries.<sup>8,10</sup> LGV is endemic in Southeast Asia, the Caribbean, Latin America, and regions of Africa.<sup>8,10</sup> The lack of a

## FEATURES OF GONORRHEA AND CHLAMYDIA

- Gonorrhea and chlamydia are the 2 most commonly reported bacterial sexually transmitted diseases.
- *Chlamydia trachomatis* infection is frequently asymptomatic in both men and women, whereas men with *Neisseria gonorrhoeae* infection typically experience symptoms.
- *N. gonorrhoeae* and *C. trachomatis* coinfection is common; therefore, all patients with gonorrhea should be empirically treated for chlamydia unless it has already been ruled out.
- Symptoms of gonorrhea and chlamydia are similar and include urethral discomfort and dysuria, with or without urethral discharge. Discharge associated with gonorrhea is usually purulent.
- Women are more likely to develop long-term complications from infection with chlamydia and gonorrhea, such as pelvic inflammatory disease, ectopic pregnancy, and infertility.

widely available specific diagnostic test has complicated the diagnosis of LGV;<sup>11</sup> therefore, the prevalence in the United States is likely underreported.

## GENITOURINARY MANIFESTATIONS

### Chlamydia

*C. trachomatis* infection is frequently asymptomatic in both men and women, but men are more likely to develop symptoms as compared with women.<sup>12</sup> The incubation period of *C. trachomatis* is 1 to 3 weeks.<sup>3</sup>

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Urogenital symptoms are caused by *C. trachomatis* serovars D through K.<sup>3</sup> Common symptoms of chlamydial infection in men include urethral pain and dysuria, a result of inflammation of the urethra (ie, urethritis). Infection with *C. trachomatis* alone, however, does not usually present with urethral discharge.<sup>12</sup> Infection can ascend into contiguous urogenital organs, leading to epididymitis and prostatitis. Untreated infection in men can also cause infertility and reactive arthritis.<sup>12</sup> In women, chlamydial infection can cause urethritis, cervicitis, and salpingitis. Because women with *C. trachomatis* infection are typically asymptomatic, they are more likely to develop complications from undiagnosed chlamydial infection, such as PID (a result of an ascending infection), infertility, or ectopic pregnancy.<sup>3</sup>

*C. trachomatis* (serovars D–K) can also cause infection of the rectum, resulting in mild proctitis (ie, inflammation of the rectal mucosa). This is most often found in men who have sex with men. The majority of patients are asymptomatic; however, patients may report rectal pain, discharge, tenesmus (ie, frequent or continuous urge to have a bowel movement), or constipation.<sup>13,14</sup>

The clinical course of LGV can be divided into 3 stages. LGV starts as a single, asymptomatic genital ulcer after an incubation period of 3 to 30 days.<sup>3,15</sup> Two to 12 weeks after initial exposure, a localized fluctuant inguinal adenopathy (buboes) and ulceration develop. The third stage involves scarring, strictures, and fistulas involving the inguinal glands, genitalia, anus, and rectum.<sup>15</sup> Diagnosis of LGV is based primarily on clinical findings, as the necessary testing for LGV is not routinely done.<sup>11,15</sup> LGV is an emerging cause of proctitis and proctocolitis (ie, inflammation extending into the sigmoid colon) in men who have sex with men.<sup>16</sup> Symptoms of proctocolitis include fever, anal pruritus, rectal pain, anal discharge, and tenesmus. Anal discharge may be purulent and blood-stained. Anorectal involvement can mimic Crohn's disease.<sup>15</sup>

### Gonorrhoea

Men with *N. gonorrhoeae* infection often experience symptoms. The incubation period is 3 to 5 days.<sup>17</sup> Urethritis is the most common genitourinary manifestation in men, resulting in urethral discomfort, dysuria, and purulent discharge (**Figure 1**).<sup>17</sup> In women, the cervix is typically the first site of *N. gonorrhoeae* infection. Women with *N. gonorrhoeae* infection are frequently asymptomatic, but if they do experience symptoms, the most common is vaginal discharge (typically purulent), which is a result of endocervicitis.

Similar to *C. trachomatis*, rectal infection with *N. gonorrhoeae* may occur through direct inoculation by receptive

anal intercourse and is typically seen in men who have sex with men but can be seen in women. Patients often do not experience symptoms (two thirds of patients), but anal pruritus, painless rectal discharge, and tenesmus may be seen.<sup>15</sup> Symptoms may arise 5 to 10 days after exposure.<sup>15</sup>

### Pelvic Inflammatory Disease

In women, the most common complication of untreated gonorrhoea or *Chlamydia* infection is PID, which occurs when infection in the lower genital tract spreads to the upper genital tract.<sup>18,19</sup> It is well established that aerobic and anaerobic organisms in addition to *N. gonorrhoeae* and *C. trachomatis* are implicated in PID.<sup>20</sup> It has been hypothesized that the ascending spread of sexually transmitted microorganisms facilitates access of normal vaginal flora into the upper genital tract, causing PID.<sup>20,21</sup>

Physical examination findings in a patient with PID include lower abdominal tenderness, adnexal tenderness, and cervical motion tenderness. Patients often complain of a purulent vaginal discharge. The clinical spectrum of PID ranges from silent to severe disease. In silent PID, the patient is asymptomatic but has evidence of infection with *C. trachomatis* on laboratory testing of a cervical specimen and tubal scarring. Patients with severe PID have fever, nausea, and vomiting and appear ill.<sup>19</sup> PID has major chronic sequelae, including chronic pelvic pain, infertility, and an increased risk of ectopic pregnancy.<sup>19</sup>

Pelvic ultrasound is warranted in patients who present with fever, purulent vaginal discharge, and adnexal tenderness. Ultrasound evaluation is helpful in evaluating for tubo-ovarian abscesses, which develop when bacteria collect within the fallopian tubes. On ultrasound, a tubo-ovarian abscess appears as a thin-walled cystic mass with air-fluid levels. A tubo-ovarian abscess should be considered in anyone with PID, especially patients with unilateral adnexal tenderness. Tubo-ovarian abscesses may require surgical intervention.

### EXTRAGENITAL MANIFESTATIONS

#### Pharyngitis

The pharynx is the most common site of gonococcal infection in men who have sex with men.<sup>13</sup> Gonococcal pharyngitis is most commonly acquired during orogenital contact during fellatio. It may present as exudative pharyngitis but is usually asymptomatic.<sup>22</sup> Fever and cervical lymphadenopathy are uncommon and manifest in less than 10% of patients with gonococcal pharyngitis.<sup>23</sup>

*C. trachomatis* can also cause pharyngitis, occurring



**Figure 1.** Purulent urethral discharge associated with chlamydial infection. (Reprinted with permission from Wolff K, Johnson RA, Suurmond D. Fitzpatrick's color atlas and synopsis of clinical dermatology. 5th ed. New York: McGraw-Hill Medical Publishing Division; 2005:907.)



**Figure 2.** Disseminated gonococcal infection. Note the hemorrhagic painful pustules. (Reprinted with permission from Wolff K, Johnson RA, Suurmond D. Fitzpatrick's color atlas and synopsis of clinical dermatology. 5th ed. New York: McGraw-Hill Medical Publishing Division; 2005:910.)

in 1.4% to 2.3% of patients presenting to STD clinics.<sup>13,24</sup> Like gonococcal pharyngitis, it is acquired during the practice of oral sex. It is not possible to identify patients with *C. trachomatis* pharyngitis by clinical signs and symptoms alone; thus, laboratory testing is needed to confirm this diagnosis.<sup>24</sup>

### Disseminated Gonococcal Infection

Disseminated gonococcal infection is caused by hematogenous dissemination of *N. gonorrhoeae* from the primary site. It can occur in both sexes but is seen more frequently in women, largely due to the fact that women with gonorrhea are often asymptomatic, allowing for dis-



**Figure 3.** Keratoderma blennorrhagica. (Reprinted with permission from Wolff K, Johnson RA, Suurmond D. Fitzpatrick's color atlas and synopsis of clinical dermatology. 5th ed. New York: McGraw-Hill Medical Publishing Division; 2005:427.)

semination before the patient experiences symptoms.<sup>25,26</sup> Pregnancy, menses, and terminal component complement deficiencies also increase the risk for disseminated gonococcal infection as a result of endometrial exposure of submucosal vessels to the infecting organisms.<sup>25-27</sup>

Disseminated gonococcal infection typically manifests as arthritis (may or may not be purulent), tenosynovitis, and dermatitis but can also present as perihepatitis. Rarely, endocarditis, meningitis, and osteomyelitis occur. Skin lesions appear initially as small vesicles that subsequently become pustules and develop a hemorrhagic base (Figure 2).<sup>28</sup> Gonococcal arthritis is asymmetric and migratory, can involve any joint, and is commonly associated with fever and chills. The knees, wrists, ankles, and finger joints are most commonly affected.<sup>25</sup> Tenosynovitis most often occurs in the hands, presenting as erythema and local tenderness along a tendon sheath.

### Fitz-Hugh-Curtis Syndrome

Acute perihepatitis (ie, Fitz-Hugh-Curtis syndrome) is a rare complication of PID and is thought to occur through direct extension of *N. gonorrhoeae* or *C. trachomatis* from the fallopian tube to the liver capsule and peritoneum along the paracolic gutters. The syndrome was first proposed by Curtis in 1930 and confirmed by Fitz-Hugh in 1934 after describing acute gonococcal peritonitis in the right upper quadrant with "violin-string adhesions" between the liver capsule and abdominal wall.<sup>29,30</sup> Fitz-Hugh-Curtis syndrome is a perihepatitis or inflammation of the liver capsule, in which patients present with sharp, pleuritic right upper quadrant pain.<sup>31</sup> The diagnosis of Fitz-Hugh-Curtis syndrome is made clinically in the setting of PID by eliminating other causes of right upper quadrant pain. Liver enzyme levels are usually

normal. Computed tomography of the abdomen may reveal hepatic capsular or pericapsular enhancement.<sup>32</sup> The only method of definitive diagnosis is laparoscopy with direct visualization of the liver capsule to identify adhesions between the liver and abdominal wall; however, laparoscopy is warranted only if symptoms do not resolve with treatment. The perihepatitis usually resolves with treatment of underlying PID. Laparoscopy is also used for lysis of adhesions.

### Reactive Arthritis (Reiter Syndrome)

The classic triad of arthritis, nongonococcal urethritis, and conjunctivitis (ie, formerly known as Reiter syndrome) was first described by Hans Reiter in 1916.<sup>33</sup> It is more common in men than women.<sup>34</sup> Infection with *C. trachomatis* causes a reactive nonpurulent arthritis, typically seen as an asymmetric oligoarthritis, predominantly in the lower extremity. The classic finding is swelling at the heels and/or sausage finger or toe caused by uniform inflammation. Dermatologic manifestations include keratoderma blennorrhagica, which begins as clear vesicles on an erythematous base that progress to macules, papules, and nodules, usually found on the soles of feet, palms of the hands, trunk, and scalp (Figure 3).

### DIAGNOSIS

*N. gonorrhoeae* is a gram-negative, intracellular, aerobic diplococcus. The diagnostic standard for diagnosis of gonorrhoea is culture using Thayer-Martin medium. Gram staining of endocervical and urethral specimens (in women and men, respectively) can also confirm the diagnosis by demonstrating the presence of typical gram-negative intracellular diplococci in neutrophils. DNA probes, which are labeled with an organism-specific chemiluminescent marker, are also frequently used and have similar diagnostic accuracy when compared with culture.<sup>35</sup> Gonococcal infection can also be detected with nucleic acid amplification tests; results are available within hours, but these tests are more expensive than culture. In men, polymerase chain reaction assay of urine samples may also be used, but it is important to utilize first void urine to increase the sensitivity and specificity of the test.<sup>17</sup>

In disseminated gonococcal infection, blood cultures are positive in approximately 30% of cases.<sup>25</sup> At least 2 sets of cultures should be obtained. Urethral or cervical culture with Thayer-Martin medium will be positive in 50% of patients with disseminated gonococcal infection.<sup>36</sup> Chocolate agar is used to grow gonococci from otherwise sterile sites.

*C. trachomatis* are obligate intracellular bacteria. As

previously mentioned, serovars D through K are associated with urogenital infection, while serovars L1, L2, and L3 are associated with LGV.<sup>37</sup> DNA probes hybridized to a specific sequence of chlamydial 16S rRNA are commonly used to detect chlamydial infection. Serologic tests for *C. trachomatis* do not provide a definitive diagnosis because they are not serovar-specific; however, these tests can be useful, with complement fixation titers greater than 1:64 supporting a diagnosis of LGV.<sup>11</sup> Very few laboratories have the capacity to sequence DNA to identify the L-serovars of *C. trachomatis* from anorectal specimens.<sup>11</sup>

### TREATMENT

Due to the increasing prevalence of fluoroquinolone resistance to *N. gonorrhoeae*, the Centers for Disease Control and Prevention (CDC) no longer recommends the use of fluoroquinolones for the treatment of gonococcal infections and associated conditions such as PID.<sup>38</sup> Consequently, only cephalosporins are recommended for the treatment of gonorrhoea.<sup>38</sup> For uncomplicated gonorrhoeal infection, the CDC recommends a 1-time intramuscular injection of ceftriaxone 125 mg. For PID and epididymitis, the dose of ceftriaxone is 250 mg intramuscularly. For chlamydial infection, the CDC recommends azithromycin 1 g orally or doxycycline 100 mg orally twice daily for 7 days.<sup>39</sup> A single 1-g oral dose of azithromycin is as effective as a standard 7-day course of doxycycline in achieving clinical cure.<sup>39</sup> Of note, patients with gonococcal infection should be treated for possible *C. trachomatis* coinfection if chlamydia has not been ruled out.<sup>38</sup>

The CDC recommends empiric treatment of PID in women at risk for STDs if adnexal tenderness or cervical motion tenderness are present and no other cause for the illness can be identified.<sup>40</sup> Inpatient management of PID requires parenteral therapy with cefotetan 2 g intravenously every 12 hours or cefoxitin 2 g intravenously every 6 hours plus doxycycline 100 mg intravenously every 12 hours. Inpatient management should be considered in pregnant patients or in those who have failed outpatient treatment, have a high fever, or have a tubo-ovarian abscess.<sup>18</sup>

For patients with reactive arthritis, the treatment of urethritis has not been shown to modify the course of the disease but is needed to eradicate infection with *C. trachomatis*.<sup>41,42</sup> Most patients have a self-limited course of arthritis and need only symptomatic treatment with nonsteroidal anti-inflammatory drugs. Patients with LGV should be treated with doxycycline 100 mg twice daily for 3 weeks.<sup>3</sup>

## PREVENTION

One of the best methods for preventing complications of gonorrhea and/or *Chlamydia* infection (eg, PID) is screening of sexually active adolescents and young adults.<sup>43</sup> Patient education is critical, emphasizing the use of condoms (barrier protection) during sexual activities. If the patient has been diagnosed with gonorrhea or chlamydia, all sexual contacts should be referred for testing and treatment. Testing for other STDs is also recommended. Patients should be advised to abstain from sexual intercourse until their treatment is completed and all partners have been evaluated and treated. The period of abstinence should be 7 days whether using a single-dose or 7-day regimen.<sup>2</sup> Patients should be counseled regarding the risk associated with other STDs and transmission of STDs.

## CONCLUSION

Chlamydial and gonococcal infections are important causes of PID, ectopic pregnancy, and infertility, and coinfection with both *N. gonorrhoeae* and *C. trachomatis* is common. Common pitfalls in management include failure to treat for coinfection, failure to instruct patients to refer partners for evaluation, and failure to instruct patients to abstain from sexual intercourse during treatment for 7 days.

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