Chlamydial Infections

Introduction

Chlamydia is the most common notifiable sexually transmitted infection (STI) in the United States. This infection, which is caused by the bacterium *Chlamydia trachomatis*, is transmitted primarily through sexual activity, and less often, through vertical transmission at birth. Rates of chlamydial infection are particularly high in sexually active young women. Most persons who acquire *C. trachomatis* remain asymptomatic or experience only mild symptoms, leading to a significant number of persons with undiagnosed and untreated chlamydia. Individuals with chlamydial infection can also develop a broad array of symptomatic clinical manifestations. Untreated genital chlamydia in women can lead to major health consequences, including pelvic inflammatory disease (PID), chronic pelvic pain, fallopian tube scarring, and infertility. Untreated rectal chlamydia in men who have sex with men (MSM) increases the risk of HIV acquisition. There are excellent diagnostics, treatment, and prevention strategies, if broadly used, that can markedly reduce transmission rates of and morbidity associated with *C. trachomatis* infection. In the following discussion, the terms “woman” or “women” are used to describe persons who have a female sex assigned at birth (persons with a cervix), including transgender men with cervix and gender diverse persons who have a cervix. Similarly, the terms “man” or “men” are used to describe persons who have male sex assigned a birth (persons with a penis), including transgender women with a penis and gender diverse persons who have a penis.
Epidemiology in the United States

2020 Chlamydia Surveillance Data

Chlamydia is the most common reportable bacterial STI in the United States, with approximately 1.6 million reported cases in 2020.[1] Since many persons with chlamydial infection may have minimal or no symptoms, the actual number of annual infections is significantly higher than the reported cases.[2] Overall, the number of reported chlamydia cases has significantly increased since reporting began in the 1980s (Figure 1); this increase likely reflects an increase in the number of infections, but enhanced screening with more sensitive diagnostic tests may also have contributed to higher numbers of reported cases in recent years.[1] From 2019 to 2020, there was a 13% decrease in reported cases of chlamydia in the United States, but this was unlikely due to a true reduction in new infections.[1] More likely, this decrease resulted from factors related to the COVID-19 pandemic, including less frequent accessing of medical care and reduced screening of asymptomatic persons.[1] The following summarizes several key epidemiologic features of chlamydial infections as reported for 2020 in the United States.[1]

- **Sex:** Rates of reported chlamydial infection have consistently been higher in women than in men; in 2020, the rate in women was 1.8 times higher than in men (616.5 versus 339.4 per 100,00 population) (Figure 2).
- **Age:** For both females and males, the highest rates (per 100,000 population) of chlamydial infection occurred among those 20 to 24 years of age; among females, the second highest rate was in persons 15 to 19 years of age, and for males, the second highest rate was for those 25 to 29 years of age (Figure 3).
- **Race/Ethnicity:** Rates of chlamydial infection were disproportionately higher among persons in certain racial and ethnic groups, with the highest rates among Black persons (Figure 4). Factors that may contribute to such inequities include differential access to quality health care, social and economic conditions, higher prevalence of disease in sexual networks, and differences in immunogenetic determinants that influence the immune response to chlamydia.
- **Region and State:** In recent years, the South has consistently had the highest rate (per 100,000 population) of chlamydial infections. In 2020, the five states with the highest rates (per 100,000 population) of reported chlamydia cases (in descending order) were Mississippi, Louisiana, Alaska, South Carolina, and North Carolina. Of note, the rate of reported cases (per 100,000 population) in Washington DC was markedly higher than any state (Figure 5).

Factors Associated with Acquisition of Chlamydia

Factors associated with the acquisition of chlamydial infection include a previous or coexisting STI, new or multiple sex partners, a new sex partner, more than one partner, a sex partner who is having sex with other partners at the same time, as sex partner who has an STI, inconsistent condom use, history of incarceration, and exchanging sex for money or drugs.[3] The presence of columnar epithelial cells on the ectocervix, referred to as ectopy, is a condition that may increase susceptibility to chlamydial infection.[4, 5] Adolescents and young adults are at increased risk for chlamydial infection for a combination of biological, behavioral, and cultural reasons, including difficulty accessing preventive health care services for STIs.[Q]

Impact

Untreated genital chlamydia infections can result in major complications for women, including pelvic inflammatory disease, chronic pelvic pain, fallopian tube scarring, and infertility.[6, 7] In the United States, for bacterial STIs, chlamydia has the highest lifetime direct medical cost (the total lifetime direct medical cost is calculated by multiplying the estimated number of incident infections in a year by the estimated lifetime cost per infection). In 2018, there were an estimated 2.35 million chlamydial infections acquired in the United States at an estimated total lifetime direct medical cost of $691.3 million.[8, 9] In addition, studies have
shown that rectal chlamydia infection in MSM increases the risk of HIV acquisition, which contributes to increases in the number of new HIV infections and subsequent HIV-related major lifetime medical costs. [10, 11]
Microbiology, Pathogenesis, and Transmission

Organism and Classification

*Chlamydia trachomatis* is an obligate intracellular bacterium with a cell wall and ribosomes similar to those of gram-negative organisms.[12] The *C. trachomatis* cell wall is unique in that it contains an outer lipopolysaccharide membrane, but it lacks peptidoglycan; within the cell wall, cysteine-rich proteins act as the functional peptidoglycan equivalent. The absence of peptidoglycan explains why the organism is not seen with standard Gram’s staining. *Chlamydia trachomatis* is a member of the *Chlamydiaceae* family. The genus Chlamydia includes three species that infect humans: *C. trachomatis*, *C. pneumoniae*, and *C. psittaci*.

**Chlamydia Serovars**

The species *C. trachomatis*, which exclusively infects humans, can cause (1) trachoma in persons of all ages, (2) anogenital infections, lymphogranuloma venereum (LGV), and conjunctivitis in adolescents and adults, and (3) conjunctivitis and pneumonia in neonates. The type of clinical infection caused by *C. trachomatis* is usually determined by the outer membrane protein A (OmpA—also known as the major outer membrane protein [MOMP]), which can be determined based on serology (OmpA serovar) or molecular methods (OmpA genotype); these techniques are not routinely used for clinical purposes.[13,14,15] Genital, rectal, oropharyngeal, and conjunctival infections are usually caused by *C. trachomatis* serovars D through K (as is conjunctivitis and pneumonia in neonates), chronic keratoconjunctivitis (trachoma) by serovars A-C, and lymphogranuloma venereum (LGV) by serovars L1-L3.[14,16] Although most *C. trachomatis* infections caused by OmpA types D through K in women and men are asymptomatic, clinical manifestations can develop with these OmpA types at any site of infection.

**Life Cycle**

*Chlamydia trachomatis* typically infects columnar epithelial cells at mucosal sites, often becoming a chronic infection that may last months or even longer than a year if untreated. *Chlamydia trachomatis* has a complex reproductive cycle, typically requiring 48 to 72 hours to complete.[16,17] The organisms replicate within a host cell, frequently causing eventual death of the host cell.[18] The life cycle of *C. trachomatis* involves five key steps (Figure 6):

1. The elementary body, a small, infectious, but nonreplicating particle found in secretions, attaches to and enters a host cell, such as an endocervical or urethral columnar epithelial cell. The contact with the host cell membrane causes the elementary body to induce its own endocytosis.
2. Within 8 hours, the now-intracellular elementary body interacts with glycogen and transforms into a reticulate body, which begins to multiply within an isolated intracellular structure referred to as an inclusion. The reticulate bodies are the noninfectious replicating form.
3. Within 48 hours, some reticulate bodies begin to reorganize back to elementary bodies.
4. Within 72 hours, most of the reticulate bodies have transitioned back to elementary bodies, and the inclusion either undergoes lysis at the host cell wall or the intact inclusion (containing numerous elementary bodies) is released into the extracellular space, a process called extrusion.
5. Regardless of whether the inclusion undergoes lysis or extrusion, the elementary bodies are released to infect adjacent cells or to be transmitted to and infect another person.

[Q] Chlamydia Microbiology Question

**Transmission**

Sexually-acquired *C. trachomatis* is highly transmissible—rates of *C. trachomatis* transmission between sex partners is approximately 55%, with a per-act transmission of urogenital infection of about 10%; transmission rates per sex act for rectal and oropharyngeal infection is unknown.[19] Sexual transmission rates per sex act
are thought to be slightly higher from men-to-women than from women-to-men, but given the number of asymptomatic carriers in the general population, estimates for the rate of transmission remain imprecise. Transmission of *C. trachomatis* can also occur from mother-to-infant via the infant’s contact with the mother’s genital tract during birth. Among mothers with untreated chlamydial infection, the rate of transmission to the neonate is estimated at about 50%.[20]
**Clinical Manifestations**

*Chlamydia trachomatis* can cause a range of clinical syndromes in adults, including cervicitis, urethritis, proctitis, and conjunctivitis. In persons who develop symptomatic infection, the incubation period for *C. trachomatis* infection is estimated to be 7 to 21 days.

**Urogenital Infections in Women**

Most women with urogenital chlamydial infection initially have no signs or symptoms, but may present later with a range of manifestations and complications, including cervicitis, urethritis, pelvic inflammatory disease (PID), perihepatitis, endometritis, salpingitis, or reactive arthritis.[2,21]

**Cervicitis**

The cervix is the site of infection in 75 to 80% of women with chlamydial infection and most women with cervical chlamydial infection are asymptomatic. When symptoms are present, they are often nonspecific, such as vague abdominal discomfort or spotting. Typically, the clinical examination of the cervix is normal in women with cervical chlamydial infection, but some may have findings that suggest cervicitis, such as mucopurulent endocervical discharge and spontaneous (or easily induced) endocervical bleeding.[22,23] Causes of mucopurulent cervicitis other than *C. trachomatis* include *Neisseria gonorrhoeae* and *Mycoplasma genitalium*.

**Urethritis**

Urethral infection with chlamydia in women is usually asymptomatic, but it may cause dysuria and urinary frequency, which can mimic acute cystitis.[24] Nearly all women with urethral chlamydial infection also have cervical infection.[24]

**Pelvic Inflammatory Disease**

Women with *C. trachomatis* infection can develop PID, which is a subclinical to acute clinical syndrome caused by the ascending spread of microorganisms from the cervix to the endometrium, fallopian tubes, ovaries, and contiguous structures (Figure 7).[21,25] Following untreated genital infection with *C. trachomatis*, PID develops in approximately 3% of women within 2 weeks and in 10% of women within 1 year.[26,27] Although most women with PID caused by *C. trachomatis* initially have a mild or subclinical illness, some present with lower abdominal pain and may have findings of cervical motion tenderness, with or without uterine or adnexal tenderness.[7,25] Chlamydia-associated PID can result in tubal scarring, which may lead to tubal factor infertility, increased risk for ectopic pregnancy, and chronic pelvic pain.[21,28] Among women treated for PID caused by chlamydia, approximately 20% become infertile, 30% develop chronic pain, and 1% have an ectopic pregnancy when they conceive.[29] The extensive long-term morbidity associated with chlamydial infection underscores the importance of aggressive prevention, screening, and treatment programs.[30,31]

**Perihepatitis (Fitz-Hugh-Curtis Syndrome)**

Untreated pelvic infection in women with *C. trachomatis* can infrequently cause inflammation of the liver capsule, which is commonly referred to as perihepatitis or the Fitz-Hugh-Curtis Syndrome.[32,33] Although perihepatitis was initially attributed only to gonococcal infection, it is now known to be more often associated with chlamydial infection. Perihepatitis is characterized by right upper quadrant pain, nausea, vomiting, and fever, which are generally accompanied by evidence of PID on physical examination.[34] [Q] Clinical Presentation of Chlamydial Cervicitis in Women

**Urogenital Infection in Men**
In men, *C. trachomatis* can cause an array of genitourinary clinical manifestations. Serious complications are uncommon in men, but they can manifest as epididymitis, reactive arthritis, proctitis, and proctocolitis.

**Urethritis**

The most common site for chlamydial infection in heterosexual men is the urethra. Although most men identified with urethral chlamydial infection have no symptoms, some will develop dysuria and urethral discharge, which is typically clear, mucoid, or mucopurulent; the clinical presentation is typically referred to as nongonococcal urethritis.[35] Although attempts to distinguish gonococcal urethritis from nongonococcal urethritis on clinical examination are not reliable, the discharge caused by *C. trachomatis* is usually less purulent than with gonococcal urethritis.

**Epididymitis**

In males, epididymitis is the most common local complication of urethral *C. trachomatis* infection, and persons with this complication typically develop unilateral scrotal pain, epididymal swelling, and tenderness.[36] For persons with epididymitis who have concomitant urethral discharge, most have at least 2 white blood cells per high power field on Gram’s staining of a urethral discharge specimen. Approximately 70% of sexually transmitted cases of epididymitis are due to *C. trachomatis*.[36]

**Manifestations Seen in Men or Women**

**Conjunctivitis**

Infection of the eye with *C. trachomatis* serovars D through K most often occurs in adults as a result of autoinoculation from genital tract secretions (hand to eye transmission).[37] This ocular disorder, which usually involves infection with *C. trachomatis* serovars D through K, manifests as chronic follicular conjunctivitis and is often referred to as adult inclusion conjunctivitis (Figure 8). The most common presentation is unilateral eye discomfort with hyperemia. Although these secretions may be mucopurulent, they are more often clear to cloudy.

**Oropharyngeal Infection**

In both men and women, oropharyngeal chlamydial infection is usually asymptomatic.[38] It can also present as acute tonsillitis, acute pharyngitis, or abnormal pharyngeal sensation syndrome. When clinical signs and symptoms are described, the presentation can range from minimally symptomatic disease (i.e. dry or pruritic throat) to exudative tonsillopharyngitis.[39]

**Rectal Infection**

Infection with *C. trachomatis* OmpA types D through K in the rectal region is usually asymptomatic. This infection can occur in men or women who engage in receptive anal intercourse. Among women, however, rates of rectal infection are substantial, even among those who do not have receptive anal intercourse; in these women, the rectal infection presumably occurs via autoinoculation from infected vaginal secretions.[40,41] Some men and women with rectal infection can develop proctitis or proctocolitis, which can manifest as rectal pain, mucoid or hemorrhagic discharge, fever, and/or tenesmus.[42,43] A clinical diagnosis can be supported via anoscopy findings (mucopurulent discharge, pain, and spontaneous or induced bleeding). Chronic infection can rarely cause scarring and fistula formation. Lymphogranuloma venereum (LGV), which is caused by *C. trachomatis* serovars L1, L2, or L3, more often presents as proctitis or proctocolitis, and additional diagnostic methods, such as LGV-specific molecular testing are required to differentiate LGV from non-LGV strains of *C. trachomatis*. These molecular tests, however, are not widely available and results do not return within a time frame that would alter the clinical management.[44,45]
Lymphogranuloma venereum (LGV)

Lymphogranuloma venereum is caused by *C. trachomatis* serovars L1, L2, or L3; it is an uncommon infection in the United States, but sporadic cases and outbreaks have been reported among MSM, many of whom have HIV. Rectal manifestations with LGV can include anorectal pain, purulent rectal discharge, rectal bleeding, tenesmus, diarrhea, and constipation, which is clinically diagnosed as proctitis. Although most cases of LGV in the United States are rectal infections, LGV can also cause inguinal lymphadenopathy characterized by multiple, unilateral, enlarged, matted, tender inguinal lymph nodes, termed “buboes” that may suppurate. Systemic signs and symptoms, such as fever, chills, or myalgia, also may be present with either rectal or inguinal manifestations. A self-limited genital ulcer sometimes occurs at the site of inoculation. Less often, oral ulceration can occur and may be associated with cervical adenopathy. Specimens from anogenital sites and lymph nodes can be obtained in an attempt to identify *C. trachomatis* by a nucleic acid amplification test (NAAT).

Reactive Arthritis

Reactive arthritis, previously referred to as Reiter’s syndrome, is a post-inflammatory autoimmune disease that can result from urogenital chlamydia infection. The characteristics of the syndrome include conjunctivitis, urethritis, oligoarthritis, skin lesions (keratoderma blennorrhagica), and circinate balanitis. This complication infrequently occurs, but when it does, the onset is typically 3 to 6 weeks after urogenital chlamydia infection, and it can occur even in persons who receive effective treatment for chlamydia infection. Reactive arthritis affects predominantly males, particularly those positive for HLA-B27, and it usually resolves within 3 to 6 months. Reactive arthritis may not respond to antimicrobial treatment, but symptoms usually respond to nonsteroidal antiinflammatory agents.

Chlamydial Infections in Infants and Children

Although chlamydial infections are now seen infrequently among infants and children in the United States, they must still be considered in the scenario of inadequate prenatal care. Among cases of perinatal chlamydial infection, the most common presentation is inclusion conjunctivitis, which occurs in about 25% of neonates born to mothers who have untreated cervical chlamydia infection. The second most common manifestation is neonatal pneumonia, and this occurs in only about 10 to 15% of infants of mothers who have untreated cervical chlamydia.

Conjunctivitis

For infants, conjunctivitis is the most common clinical condition resulting from perinatal transmission of chlamydia. Ocular infection with *C. trachomatis* results from exposure of the neonate to infected secretions from the mother's genital tract during birth, and the exposure may also involve mucous membranes of the oropharynx, urogenital tract, and rectum. Inclusion conjunctivitis occurs 5 to 14 days after delivery. The signs range from mild scant mucoid discharge to severe copious purulent discharge, chemosis, pseudomembrane formation, erythema, friability, and edema. Neonatal ocular prophylaxis with silver nitrate solution or antibiotic ointments for prevention of gonorrhea transmission does not prevent perinatal transmission of *C. trachomatis* from mother to infant. A chlamydial etiology should be considered for all infants aged 30 days or younger who have conjunctivitis.

Pneumonia

Chlamydial pneumonia in infants occurs 4 to 12 weeks after delivery. Notably, infection of the nasopharynx is thought to be a precursor condition that is usually asymptomatic, but can progress to pneumonia. The signs are cough, congestion, and tachypnea. Infants are usually afebrile, and rales are apparent with auscultation of the lungs.

Trachoma
Trachoma is the leading cause of preventable blindness in the world and is caused primarily by *C. trachomatis* serotypes A, B, Ba, and C.[47] Trachoma is found in select regions of the world, mostly in the Middle East and Southeast Asia. The disease is most often contracted person-to-person through hand (or fomite) contact with an infected eye, followed by autoinoculation. Most cases of trachoma occur in the setting of poor sanitary conditions and some cases result from fly transmission.[48] The process begins as follicular conjunctivitis, which, if untreated, progresses to an entropion wherein the eyelid turns inward and chronic eyelash abrasion results in opacification of the corneal surface over time. The disease is diagnosed clinically and treatment with single-dose azithromycin is usually effective. This disorder is not an STI, and it is not transmitted from mother-to-child during birth.

**Urogenital Infection**

Urogenital infections in preadolescent males and females are usually asymptomatic and can be the result of vertical transmission during the perinatal period.[2] Genital or rectal infection can persist for as long as 2 to 3 years, so infection in young children may be the result of perinatally-acquired infection. Sexual abuse is a major concern when chlamydia (or any STI) is detected in preadolescent males or females. The STI evaluation in a case of suspected abuse should be performed by, or in consultation with, an expert in the assessment of child sexual abuse. Only tests with high specificity should be used because of the legal and psychosocial consequences of a false-positive diagnosis.
Laboratory Diagnosis

The selection of a laboratory test to detect the presence of *C. trachomatis* is a critical component of disease management and prevention.[45] The testing technology has shifted from culture-based methods to molecular-based techniques and this represents a substantial improvement in test sensitivity and ease of specimen collection. The nucleic acid amplification tests (NAATs) are the preferred testing method for diagnosing chlamydial infections; this testing method is preferred due to high sensitivity, very high specificity, ability to use on multiple different types of clinical specimens, and ease of transport.[45]

Nucleic Acid Amplification Test (NAAT)

Nucleic acid amplification tests (NAATs) amplify nucleic acid sequences (either DNA or RNA) that are specific for the organism being detected. Similar to other nonculture tests, NAATs can detect replicating or nonviable organisms. Multiple commercially available NAATs are FDA-cleared as diagnostic tests for *C. trachomatis* on urine specimens from men and women, urethral secretions in men, and endocervical swabs in women; some tests are cleared for vaginal swabs.[2] In addition, in May 2019, the United States Food and Drug Administration (FDA) cleared two NAATs for diagnostic testing of chlamydia at extragenital sites (pharynx and rectum); the two tests are the Aptima Combo 2 Assay and the Xpert CT/NG.[49] For chlamydia testing in men, NAATs are highly sensitive for detecting *C. trachomatis* in either urethral secretions or a first-catch urine specimen, but most experts prefer using first-catch urine samples.[2,45] For women, vaginal swabs are preferred over urine samples since they are more sensitive than urine samples. Several studies have shown that self-collected vaginal swabs are preferred by women and perform equal to or better than clinician-collected vaginal swabs.[50,51,52,53,54] In addition, in men and women, self-collected rectal swabs for NAAT have also performed well.[55] Nucleic acid amplification tests do not distinguish non-LGV from LGV serovars.

Point-of-Care NAAT Testing

In March 2021, the FDA approved the first point-of-care NAAT (Binx Health IO CT/NG Assay) for the diagnosis of urogenital chlamydia and gonorrhea.[56] This point-of-care test can be run on vaginal swabs obtained from women or on urine samples collected from men.[56] This assay can provide a result in approximately 30 minutes.[56] 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.[57] For chlamydia, the sensitivity estimates were 96.1% in women and 92.5% in men; the specificity estimates were 99.1% for women and 99.3% for men.[57] In addition, the investigators found that self-obtained vaginal swabs in women performed equivalent to clinician-collected vaginal swabs.[57]

Non-amplification Molecular Tests

Molecular tests that do not use nucleic acid amplification encompass a variety of antigen detection and nucleic acid hybridization methods. These tests include enzyme-immunoassays (EIA), direct fluorescent antibody tests (DFA), and nucleic acid hybridization tests—a distinct non-NAAT methodology that can detect *C. trachomatis*-specific DNA or RNA sequences in ribosomal RNA, genomic DNA, or plasmid DNA. All have a significantly lower sensitivity (range 50% to 75%) than NAATs.[58] These non-amplification tests are rarely used in clinical practice, and they are classified as not recommended by the Centers for Disease Control and Prevention (CDC).[2]

Culture

Historically, cell culture to detect *C. trachomatis* was the most sensitive and specific method available to detect chlamydial infection. Cell culture, however, is technically complex, expensive, difficult to standardize, and has a lower sensitivity than amplification tests. In addition, performing *C. trachomatis* cell culture requires collection of *C. trachomatis* elementary bodies from relevant anatomical site(s) and use of stringent transport requirements. Because of their excellent sensitivity and specificity, NAATs have replaced the use of
culture in most clinical situations; the use of culture for *C. trachomatis* is primarily limited to evaluation of suspected cases of sexual abuse in children.

**Serology**

Serologic testing is rarely used in clinical practice to diagnose genital infections caused by *C. trachomatis* and chlamydia serologic tests do not reliably distinguish current from prior infection. Two main types of serologic tests are used for diagnosis: (1) chlamydia complement fixation test (CFT), which measures antibody against group-specific lipopolysaccharide antigen, and (2) microimmunofluorescence (MIF).[45]

**Diagnosing LGV**

Since routinely used NAATs for diagnosing chlamydial infections do not distinguish non-LGV strains of *C. trachomatis* from LGV strains, additional diagnostic methods, such as LGV-specific molecular testing with PCR genotyping, are required to make a laboratory diagnosis of LGV. These molecular tests, however, are not widely available and results do not return within a time frame that would alter clinical management.[44,45] In addition, chlamydia serologic testing is not recommended for diagnosing LGV.[59] Therefore, the diagnosis of LGV should be based on epidemiologic information, compatible clinical findings, and a positive *C. trachomatis* NAAT at the symptomatic anatomic site.[59]

**Diagnosing Ophthalmia Neonatorum in Neonates**

The diagnosis of chlamydial ophthalmia neonatorum should be suspected in any infant with conjunctivitis that occurs within 30 days after birth. Diagnostic testing for chlamydial ophthalmia neonatorum is unique in that DFA is the only nonculture, FDA-cleared test from conjunctival swabs. Nucleic acid amplification tests are not FDA cleared for this site, but local validation studies can be done to support its use. Culture can also be performed on the everted eyelid using a Dacron-tipped swab specified by the testing kit. The specimens must contain epithelial cells, not just the exudate.

**Diagnostic Evaluation of Suspected Sexual Abuse in Children**

In the routine workup of suspected sexual abuse in children, testing for *C. trachomatis* (and *Neisseria gonorrhoeae*) should be included.[60] Due to major legal implications involved in these cases, it is advised that clinical teams work with child advocacy centers prior to embarking on testing and evaluation. For this testing, culture or NAAT can be used, but with special considerations.[60] If a NAAT is used, there is the potential for false-positive results to occur; therefore, consultation with an expert should be part of this process.[60] In addition, because of the profound implications of making a diagnosis of an STI in a child, only Clinical Laboratory Improvement Amendment (CLIA)-validated, FDA-cleared NAATs should be used in this setting.[2] Further, all initial positive tests require confirmatory testing.[45,60] All specimens should be retained for additional confirmatory testing. Other nonculture tests, such as DFA, are not recommended in this setting because of poor specificity.

**Reporting Requirements**

Laws and regulations in all states require that persons diagnosed with chlamydia be reported to local public health authorities. Reporting can be done by medical providers, laboratories, or both.
Screening for Chlamydial Infection

Screening for chlamydial infection in asymptomatic persons has been found to significantly reduce the incidence of chlamydia–associated PID.[30,61,62] In general, routine screening for chlamydia should utilize NAAT as the diagnostic test; the United States Food and Drug Administration (FDA) has cleared NAATs for chlamydia testing on (1) male and female urine samples; (2) male and female rectal and throat samples; (3) clinician-collected endocervical, vaginal, and male urethral samples; and (4) self-collected vaginal swabs if obtained in a clinical setting. Data indicate that self-collected urine and rectal swabs are comparable to clinician-collected swabs and may even be preferable.[55,63] The following summarizes recommendations for chlamydial screening in the 2021 STI Treatment Guidelines.[2,64,65]

Women Who Have Sex with Men [3,64]

- All sexually active women younger than 25 years of age should undergo annual screening. The rationale for this recommendation is threefold: (1) the incidence of chlamydial infection is highest in women 15-25 years of age, (2) chlamydia infection is typically asymptomatic in women, and (3) untreated chlamydial infection in women can cause severe health and reproductive complications. For certain young women, particularly adolescents, more frequent screening (at 3- to 6-month intervals) may be indicated based on their sexual activity.
- Women 25 years of age and older should undergo annual screening if they are considered to have increased risk for chlamydia infection (e.g. those who have a new sex partner, more than one sex partner, a sex partner with concurrent partners, or a sex partner who has an STI).
- Screening for rectal chlamydia (based on history of receptive anal or oral sex) should be considered through a shared clinical decision-making process between the woman and the health care provider.

**Women Who Have Sex with Women [66]**

- Screening for chlamydial infection in sexually active women who have sex with women should be offered per the screening guidelines for sexually active women who have sex with men.

**Pregnant Women [64,67]**

- At the first prenatal visit, screen all pregnant women younger than 25 years of age.
- At the first prenatal visit, screen all pregnant women 25 years of age and older who have increased risk for chlamydia infection (e.g. those who have a new sex partner, more than one sex partner, a sex partner with concurrent partners, or a sex partner who has an STI).
- Retest for chlamydia infection during the third trimester in all women younger than 25 years of age and in women older than 25 years of age who have an increased risk of acquiring chlamydia infection (e.g. those who have a new sex partner, more than one sex partner, a sex partner with concurrent partners, or a sex partner who has an STI).
- Pregnant women diagnosed with chlamydia should have a test-of-cure 4 weeks after completing treatment and repeat testing for chlamydia within 3 months after completing treatment.

**Men Who Have Sex Only with Women [2,64]**

- Routine screening for chlamydial infection is not recommended for sexually active men who have sex only with women. The rationale for this recommendation is the low risk for chlamydial infection in men who have sex only with women, and the lack of data to show benefit of screening this population. Nevertheless, targeted screening for men should be considered if resources permit, the community prevalence is high, and such screening does not hinder chlamydia screening efforts for women.
- Screening can be considered in sexually active young men in high chlamydia prevalence settings, including adolescent clinics, correctional facilities, STI clinics, or sexual health clinics.
Men Who Have Sex with Men [64,68]

- All sexually active men who have sex with men should undergo screening at least annually.
- Screening should consist of testing urethral and rectal sites for those who report exposures at these sites during sexual activity, regardless of condom use during sexual activity. The preferred tests (self-collected or provider-collected) are urine NAAT and rectal NAAT.
- Routine testing of oropharyngeal testing for chlamydia infection is not recommended. For MSM, gonococcal screening of the oral pharynx is recommended; since some NAAT tests for gonorrhea can detect both *N. gonorrhoeae* and *C. trachomatis*, the results will be reported for both pathogens.
- More frequent screening at 3- to 6-month intervals is indicated for men who have sex with men if they have increased risk (e.g. persons taking HIV preexposure prophylaxis, individuals with HIV, persons with ongoing risk for acquiring chlamydia, and persons who have multiple sex partners or their sex partners have multiple partners).

Transgender and Gender Diverse Persons [64,69]

- Screening for chlamydial infection in transgender and gender diverse persons should be based on the person’s sexual practices, age, and genital anatomy. For example, if an individual is sexually active, younger than 25 years of age, has a cervix, and identifies as a transgender man or nonbinary, they should have annual chlamydial screening, similar to screening in cisgender women who have a cervix.
- Screening for transgender women who have undergone vaginoplasty surgery should include screening of the neovagina. The optimal method for neovagina chlamydial screening (vaginal swab versus urine) is not known.
- Screening for chlamydia infection in transgender men who have undergone metoidioplasty surgery (with urethral lengthening), but not vaginectomy, should utilize a vaginal swab to detect cervical infection due to the low yield of urine testing in this post-surgical setting.

Persons with HIV [64,70]

- Screening for chlamydial infection is recommended for persons with HIV who are sexually active; the screening should take place at the initial evaluation and at least annually thereafter.
- More frequent screening (e.g. every 3 to 6 months) may be indicated for persons with HIV based on risk activity, persons on HIV preexposure prophylaxis (PrEP), and local prevalence of specific STIs.
- Testing samples should be obtained from the anatomic sites of sexual exposure. Note that routine screening for oropharyngeal chlamydia infection is not recommended, but since some NAATs used for gonorrhea can detect both *N. gonorrhoeae* and *C. trachomatis*, screening for pharyngeal gonorrhea may also include results for chlamydia.

Correctional Facilities [71]

- Routine opt-out screening for chlamydial infection screening of all sites of sexual activity (pharyngeal, urethral or vaginal, and rectal) should be offered during intake (or within 48 hours of intake) at correctional facilities for all females 35 years of age and younger and all males younger than 30 years of age.\[Q\] Routine Screening for Chlamydia Infection
Treatment of Adolescents and Adults

General Approach

The treatment of all persons with chlamydial infection is of high priority for two important reasons: (1) to reduce the risk of adverse reproductive health complications and (2) to decrease the sexual transmission of *C. trachomatis* to others. In addition, treatment for chlamydial infection should occur without delay in order to minimize complications, particularly PID in women. The following summarizes recommendations in the 2021 STI Treatment Guidelines for the treatment of chlamydial infections.[2]

Adolescents and Adults with Urogenital Chlamydia Infections

The recommended treatment for nonpregnant adolescents and adults with uncomplicated chlamydial infections at urethral, cervical, rectal, and oropharyngeal sites is doxycycline 100 mg orally twice daily for 7 days; alternative options include azithromycin 1 gram orally in a single dose and levofloxacin 500 mg orally given daily for 7 days (Table 1).[2] In persons for whom adherence with doxycycline is a substantial concern, consideration can be given for using the alternative single-dose oral azithromycin regimen. The following outlines several reasons why doxycycline is now preferred over azithromycin for urogenital chlamydial infections.

- Two randomized, double-blind clinical trials have shown that a 7-day course of doxycycline is superior to single-dose azithromycin for the treatment of asymptomatic rectal chlamydial infections among MSM (Figure 10).[72,73] Several additional, nonrandomized studies have also shown that a 7-day course of doxycycline is superior to single-dose azithromycin for the treatment of rectal chlamydial infections among MSM.[74,75]
- Several studies have also shown that a significant number (33-83%) of women diagnosed with urogenital chlamydial infection also had *C. trachomatis* detected at the anorectal site, even though most did not report having receptive anal sex.[40]
- One prospective, open-label study in persons with pharyngeal chlamydia suggested better treatment responses with a 7-day course of doxycycline than with single-dose azithromycin.[76]
- Chlamydia treatment studies in women have been conflicting. Several randomized, controlled trials have shown equal efficacy with a 7-day course of doxycycline and single-dose azithromycin.[77,78] In an observational study that compared the effectiveness of azithromycin and doxycycline in uncomplicated rectal and vaginal chlamydial infections in women, microbiologic cure rates for vaginal infections were similar for the two regimens, but cure rates were much higher with doxycycline than azithromycin for rectal infections (Figure 11).[79]

Treatment of Chlamydial Infections During Pregnancy

The recommended regimen for the treatment of chlamydial infections in pregnant women is azithromycin 1 gram orally in a single dose; amoxicillin is the alternative medication.[2,80,81,82,83] (Table 2).[2] Doxycycline and levofloxacin are not recommended for the treatment of chlamydial infections in pregnancy.[2] Erythromycin is no longer recommended for the treatment of chlamydia during pregnancy due to gastrointestinal side effects that make adherence challenging for the mother during pregnancy. All pregnant women treated for chlamydial infection should have a test-of-cure performed 4 weeks after completing therapy and all should be retested 3 months after treatment for reinfection.[2]

Adults with Oropharyngeal Chlamydial Infections

The clinical significance of oropharyngeal *C. trachomatis* infection remains unclear, and routine screening for oropharyngeal *C. trachomatis* infection is not recommended. Nevertheless, since oropharyngeal *C. trachomatis* can be transmitted to genital sites of sex partners[84,85], detection of *C. trachomatis* from an
oropharyngeal sample warrants the same treatment as with urogenital chlamydial infection: doxycycline 100 mg orally twice daily for 7 days as the preferred regimen for nonpregnant adults and azithromycin 1 gram single dose orally preferred for pregnant persons.[2]

**Treatment for LGV**

The recommended treatment for *C. trachomatis* infections caused by LGV strains is oral doxycycline 100 mg twice daily for 21 days; note this treatment is significantly longer than the 7-day treatment for non-LGV chlamydia strains [Regimens] 2021 STI Treatment Guidelines: Diseases Characterized by Genital, Anal, or Perianal Ulcers: Lymphogranuloma Venereum.[2,59] The alternative LGV treatment regimens include oral azithromycin 1 gram weekly for 3 weeks or oral erythromycin base 500 mg four times daily for 21 days.[59] Since practical laboratory diagnostic methods are not available for making a timely diagnosis of LGV, the indication to provide LGV treatment (doxycycline 100 mg twice daily for 21 days) should be based on epidemiologic information, compatible clinical finding, and a positive *C. trachomatis* NAAT at the symptomatic anatomic site.[59] In addition, empiric therapy for LGV is indicated for persons in whom (1) symptoms or signs of proctocolitis (e.g. bloody discharge, tenesmus, or ulceration), (2) those with severe inguinal lymphadenopathy with bubo formation, especially if the individual reports recently having a genital ulcer, and (3) persons with a genital ulcer and other causes for the genital ulcer have been excluded.[59]

**Post-treatment Follow-Up and Retesting**

The CDC does not recommend routine test-of-cure after completing therapy for chlamydia in nonpregnant persons, but all females and males should return for follow-up and repeat testing approximately 3 months after receiving treatment for chlamydial infection, due to the substantial risk of reinfection during that 3-month period.[2,86,87] If an individual is treated for chlamydia and continues to have symptoms (or they have resolution and recurrence of symptoms), then reevaluation and retesting may be indicated. Repeat NAAT testing within the first 4 weeks after treatment of chlamydial infection is not recommended due to the high rates of false-positive test results from detection of residual noninfectious (dead or inactive) chlamydial organisms.[88,89] [Q] Follow-Up
Management of Sex Partners

Evaluation and Treatment of Sex Partners

For persons diagnosed with urogenital chlamydial infection, all sex partners with whom they had sexual contact during the 60 days preceding the onset of symptoms or chlamydia diagnosis should be referred for evaluation, testing, and presumptive treatment of chlamydia.\[2\] If no sex contacts have occurred in the 60 days before the diagnosis of chlamydia or onset of symptoms, then the most recent sex partner prior to that 60-day period should be evaluated and treated.\[2\] All sex contacts should have testing for STIs as part of the evaluation process. The sex contacts should receive presumptive treatment for chlamydia without waiting for their STI test results to ensure the treatment does not depend on an additional follow-up visit. The empiric treatment for nonpregnant sex contacts is oral doxycycline 100 mg twice daily for 7 days and for pregnant contacts it is azithromycin 1 gram orally as a single dose. The purpose of performing an evaluation for the contact, even if they will receive presumptive treatment, is to perform counseling and screening for other STIs, which may require treatment. For neonates or infants diagnosed with chlamydial infection, it is important that mothers and their sex partners undergo diagnostic evaluation and receive empiric treatment for chlamydial infection.\[Q\] Management of Sex Partners of Persons Diagnosed with Chlamydia

Use of Expedited Partner Therapy

Certain situations may arise in which sexual contacts are unable or unwilling to present for evaluation, testing, and treatment. In this scenario, there may be an option to provide expedited partner therapy (EPT)—a process whereby the patient diagnosed with chlamydia delivers treatment (or a prescription for treatment)—to the recent sex partner, without a medical provider examining the partner. This strategy has been demonstrated to decrease the rate of recurrent or persistent chlamydia infection.\[90, 91, 92\] There are concerns regarding the use of EPT for MSM, since, ideally, these individuals would get tested for other STIs, such as syphilis and HIV, during a clinic visit.\[2\] The use of EPT for MSM should therefore be performed on a shared-decision basis. Finally, 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.
Treatment of Neonates and Children

Infants Born to Mothers with Chlamydial Infection

When neonatal chlamydial infection occurs, it results from neonatal contact with a chlamydia-infected cervix during the birth process. Neonatal chlamydial infection most often manifests as conjunctivitis (ophthalmia neonatorum) that develops 5 to 12 days after birth or as a subacute, afebrile pneumonia with onset at ages 1 to 3 months. The erythromycin eye ointment that is routinely given to neonates at birth to prevent neonatal gonococcal ophthalmia neonatorum does not prevent neonatal chlamydial eye infection.[2] The most effective strategy for preventing perinatal chlamydia transmission is to screen pregnant women for chlamydial infection and promptly treat those women who test positive. Prophylactic antibiotic treatment is not recommended for infants who are born to mothers at high risk for chlamydia or who have untreated chlamydia. In this situation, the recommended approach is to monitor the infant for signs and symptoms of chlamydial infection and promptly evaluate and treat any documented infection in the neonate.[2]

Neonates with Ophthalmia Neonatorum

The recommended treatment regimen for the neonate with ophthalmia neonatorum is a 14-day course of oral erythromycin base or erythromycin ethylsuccinate (Table 4).[2] Data on oral azithromycin for the treatment of neonatal chlamydial infection are limited, but a small study suggested a short 3-day course of azithromycin may be effective.[93] The use of topical erythromycin alone is not effective for ophthalmia neonatorum, and it is not recommended for use in combination with oral antibiotics.[2] The use of a recommended or alternative therapy has an efficacy of only approximately 80% and some infants require treatment with a second course of antibiotics. Treatment with oral erythromycin or oral azithromycin in infants during the first 6 weeks of life has been associated with an increased risk of infantile hypertrophic pyloric stenosis.[94,95,96,97] Thus, all infants with chlamydial ophthalmia neonatorum should have close follow-up to determine the treatment response and to evaluate signs and symptoms of infantile hypertrophic pyloric stenosis.[96]

Infant Pneumonia

For infants with pneumonia caused by C. trachomatis, the recommended treatment is a 14-day regimen of oral erythromycin base or erythromycin ethylsuccinate; the alternative regimen is a 3-day course of oral azithromycin (Table 5).[2] The treatment for chlamydial pneumonia in neonates often occurs empirically, based on the infant's chest radiographic findings, the age of the infant, and the mother's epidemiologic risk for chlamydial infection.[2] In situations when presumptive therapy is used in a situation with a high degree of suspicion of chlamydial infection, and there is considerable concern that follow-up will not occur, the 3-day azithromycin alternative regimen can be used.[2]

Chlamydial Infections in Infants and Children

The treatment of infants and children with chlamydia is stratified into three groups: (1) younger than 8 years of age and weight less than 45 kg, (2) younger than 8 years of age and weight 45 kg or greater, and (3) age 8 or older (Table 6). In infants and children who weigh less than 45 kg, the preferred treatment of chlamydial infections is a 14-day course of oral erythromycin base or oral erythromycin ethylsuccinate.[2] For children younger than 8 years of age and weighing 45 kg or greater, the recommended regimen is single-dose oral azithromycin. Children older than 8 years of age should be treated with single-dose oral azithromycin or a 7-day course of oral doxycycline.[2] A follow-up visit with chlamydia test-of-cure is recommended approximately 4 weeks after completion of treatment to evaluate for treatment effectiveness.[2]

Management of Mothers and Their Sex Partners

For neonates or infants diagnosed with chlamydial infection, it is important that mothers and their sex partners undergo diagnostic evaluation and receive empiric treatment for chlamydial infection.[2][Q] Adverse
Counseling and Education

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

- **Resuming Sexual Activity**: Persons treated for chlamydial infection should receive instructions to abstain from sexual activity until all the following criteria are met: (1) they have completed a course of doxycycline or at least 7 days have elapsed since completing single-dose treatment with azithromycin, (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 completed a course of doxycycline or at least 7 days have elapsed since the partner was treated with azithromycin.

- **Partner Notification**: It is extremely important that persons treated for chlamydial 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 chlamydia.

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

- **Complications of Chlamydial Infection**: Even with appropriate antimicrobial treatment, chlamydial infection can have long-term sequelae in women, and to a lesser extent in men. Accordingly, basic counseling on chlamydial-associated potential complications should ideally be performed at the time of the initial diagnosis or, at the 3-month follow-up visit.

- **STI Prevention and Screening**: 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). In addition, clinicians should use any opportunity to highlight the high importance of routine chlamydia screening for those in whom it is indicated, especially for sexually active females 14 through 24 years of age.
Summary Points

- Chlamydia is the most common reportable bacterial sexually transmitted infection in the United States, with approximately 1.6 million cases reported in 2020.

- The highest rates of chlamydia infections in the United States are in females aged 15 to 24 years of age.

- *Chlamydia trachomatis* frequently causes asymptomatic infection; it can also cause a wide range of clinical manifestations, including cervicitis, urethritis, pelvic inflammatory disease, infertility, and pelvic pain in women, as well as urethritis and epididymitis in men.

- Less common manifestations in men and women may include conjunctivitis, oropharyngeal infection, proctitis or proctocolitis, and reactive arthritis.

- Infants born to mothers with untreated *C. trachomatis* infection may develop conjunctivitis, trachoma, pneumonia, and urogenital infection.

- Screening for chlamydia in asymptomatic persons significantly reduces the incidence of chlamydia-associated complications and is recommended in all sexually active women younger than 25 years of age, as well as in other persons at high risk of chlamydial infection.

- In most circumstances, the preferred method to diagnose chlamydia is a NAAT, which is FDA-cleared for chlamydia testing on (1) male and female urine samples; (2) male and female rectal and throat samples; (3) clinician-collected endocervical, vaginal, and male urethral samples, and (4) self-collected vaginal swabs if obtained in a clinical setting.

- For adults and adolescents, the recommended treatment for urogenital chlamydial infections in nonpregnant females and all males is a 7-day course of oral doxycycline 100 mg twice daily. The recommended treatment for pregnant females is 1 gram of oral azithromycin.

- The diagnosis of LGV should be based on epidemiologic information, compatible clinical finding, and a positive *C. trachomatis* NAAT at the symptomatic anatomic site. The recommended treatment for LGV is a 21-day course of oral doxycycline 100 mg twice daily.

- Recent sex partners of persons diagnosed with chlamydial infection should be referred for evaluation and presumptive treatment; expedited partner therapy should be considered in certain circumstances.
Citations


49. U.S. Food and Drug Administration. FDA clears first diagnostic tests for extragenital testing for chlamydia and gonorrhea. FDA news release. May 23, 2019. [U.S. FDA] -


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Charoenwatanachokchai A, Chitwarakorn A, Palanuvej T, Pakdeewong S, Khumhaeng M, Kreaurat M.


[PubMed Abstract] -

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[PubMed Abstract] -


Tipple C, Hill SC, Smith A. Is screening for pharyngeal Chlamydia trachomatis warranted in high-risk


Figures

Figure 1 Chlamydia trachomatis: Reported Cases in United States, 1984-2020

As shown, the number of reported cases of chlamydia in the United States has steadily increased from 1984 to 2020.

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

*per 100,000 population
The rate for cases of chlamydia was consistently higher in females than in males during 2012 to 2020.

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

*per 100,000 population


<table>
<thead>
<tr>
<th>Male Rate*</th>
<th>Age Group</th>
<th>Female Rate*</th>
</tr>
</thead>
<tbody>
<tr>
<td>5,000</td>
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<td>0</td>
</tr>
<tr>
<td>4,000</td>
<td>11.3</td>
<td>85.4</td>
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<tr>
<td>3,000</td>
<td>846.3</td>
<td>2,857.9</td>
</tr>
<tr>
<td>2,000</td>
<td>1,627.3</td>
<td>3,729.6</td>
</tr>
<tr>
<td>1,000</td>
<td>988.3</td>
<td>1,548.0</td>
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<tr>
<td></td>
<td>611.7</td>
<td>713.3</td>
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<tr>
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<tr>
<td></td>
<td>98.8</td>
<td>59.7</td>
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<tr>
<td></td>
<td>38.7</td>
<td>16.5</td>
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<tr>
<td></td>
<td>6.4</td>
<td>2.0</td>
</tr>
<tr>
<td></td>
<td>339.4</td>
<td>616.5</td>
</tr>
</tbody>
</table>

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

Figure 5 Chlamydia—Rates of Reported Cases by State, United States, 2020

Rates are cases per 100,000 persons


*Rate = per 100,000 population.
Figure 6 Life Cycle of Chlamydia

The elementary body attaches to and enters a host cell. The contact with the host cell membrane causes the elementary body to induce its own endocytosis. Within eight hours, the now-intracellular elementary body interacts with glycogen and transforms into a reticulate body, which begins to multiply within an isolated intracellular structure referred to as an inclusion. Within 48 hours, some reticulate bodies begin to reorganize back to elementary bodies. Within 72 hours, most of the reticulate bodies have transitioned back to elementary bodies and the inclusion either undergoes lysis at the host cell wall or the intact inclusion is released into the extracellular space. The elementary bodies are released to infect adjacent cells or to be transmitted to and infect another person.

Illustration by Jared Travnicek and David Ehlert, Cognition Studio
Figure 7 *Chlamydia trachomatis* and Ascension to the Upper Genital Tract in Women

Figure 8 Adult Chlamydial Inclusion Conjunctivitis-

This image reveals a close view of a patient’s left eye with the upper lid retracted in order to reveal the inflamed conjunctival membrane lining the inside of both the upper and lower lids. The conjunctivitis was caused by *Chlamydia trachomatis* infection.

Source: Centers for Disease Control and Prevention Public Health Image Library (Susan Lindsley, 1978).
Figure 9 Reiter's Syndrome and Circinate Balanitis

Source: photograph from Seattle & King County Sexual Health Clinic Clinic.
**Study Design: Rectal Treatment Study**

- **Background**: Multicenter, randomized, double-blind study in Australia comparing azithromycin to doxycycline in men with asymptomatic rectal chlamydial infection.

- **Inclusion Criteria (n = 625)**
  - Males age ≥16 years
  - Report sex with males in prior 12 months
  - Positive screening rectal chlamydial NAAT
  - Excluded if rectal symptoms present

- **Regimens (Oral)**
  - Azithromycin: 1 gram single dose
  - Doxycycline: 100 mg twice daily x 7 days

- **Outcomes**
  - Microbiologic cure by NAAT at 4 weeks

Figure 10 (Image Series) - Azithromycin versus Doxycycline in Asymptomatic Rectal Chlamydial Infections in Men who have Sex with Men

Image 10B: Results: Microbiologic Cure at 4 Weeks

Abbreviations: ITT = intent-to-treat

**Study Design: FEMCure**

- **Background:** Multicenter, observational study comparing azithromycin to doxycycline in women with uncomplicated rectal and vaginal chlamydial infection.

- **Inclusion Criteria (n = 416 analyzed)**
  - Rectal and vaginal (n = 319)
  - Vaginal only (n = 75)
  - Rectal only (n = 22)

- **Regimens**
  - Doxycycline for rectal CT+
  - Azithromycin for vaginal CT+, rectal (-), and rectal untested

- **Outcomes**
  - Microbiologic cure by NAAT at 4 weeks

Figure 11 (Image Series) - Azithromycin versus Doxycycline in Uncomplicated Rectal and Vaginal Chlamydial Infections in Women (FEMCure)

Image 11B: Results: Microbiologic Cure at 4 Weeks

Abbreviations: CT+ = Chlamydia trachomatis-positive

### Table 1. 2021 STI Treatment Guidelines: Chlamydial Infections
#### Treatment of Chlamydial Infections Among Adolescents and Adults

<table>
<thead>
<tr>
<th>Recommended Regimen</th>
<th>Doxycycline</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>100 mg orally twice a day for 7 days</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Alternative Regimens</th>
<th>Azithromycin</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>1 g orally in a single dose</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>Alternative Regimens</th>
<th>Levofloxacin</th>
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<tbody>
<tr>
<td></td>
<td>500 mg orally once daily for 7 days</td>
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</table>

Note: Doxycycline is also available in a more costly delayed-release 200-mg tablet formulation, which requires once-daily dosing for 7 days and is equally effective as doxycycline 100 mg twice daily for 7 days for treating urogenital chlamydial infection in men and women.

### Table 2. 2021 STI Treatment Guidelines: Chlamydial Infections
#### Treatment of Chlamydial Infections During Pregnancy

<table>
<thead>
<tr>
<th><strong>Recommended Regimen</strong></th>
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<tbody>
<tr>
<td><strong>Azithromycin</strong></td>
<td>1 g orally in a single dose</td>
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</table>

<table>
<thead>
<tr>
<th><strong>Alternative Regimen</strong></th>
<th></th>
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</thead>
<tbody>
<tr>
<td><strong>Amoxicillin</strong></td>
<td>500 mg orally three times a day for 7 days</td>
</tr>
</tbody>
</table>

Table 4. 2021 STI Treatment Guidelines: Chlamydial Infections
Treatment of Chlamydial Infection Among Neonates

<table>
<thead>
<tr>
<th>Recommended Regimens</th>
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</thead>
<tbody>
<tr>
<td><strong>Erythromycin base</strong></td>
</tr>
<tr>
<td>50 mg/kg/day orally divided into 4 doses daily for 14 days*</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Recommended Regimens</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Erythromycin ethylsuccinate</strong></td>
</tr>
<tr>
<td>50 mg/kg/day orally divided into 4 doses daily for 14 days*</td>
</tr>
</tbody>
</table>

*An association between oral erythromycin and azithromycin and infantile hypertrophic pyloric stenosis (IHPS) has been reported in infants aged <6 weeks. Infants treated with either of these antimicrobials should be followed for IHPS signs and symptoms.

### Table 5. 2021 STI Treatment Guidelines: Chlamydial Infections
#### Treatment of Chlamydial Pneumonia Among Infants

<table>
<thead>
<tr>
<th>Recommended Regimens</th>
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<tbody>
<tr>
<td><strong>Erythromycin base</strong></td>
<td></td>
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<tr>
<td>50 mg/kg/day orally divided into 4 doses daily for 14 days</td>
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<table>
<thead>
<tr>
<th>Recommended Regimens</th>
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<tbody>
<tr>
<td><strong>Erythromycin ethylsuccinate</strong></td>
<td></td>
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<tr>
<td>50 mg/kg/day orally divided into 4 doses daily for 14 days</td>
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<table>
<thead>
<tr>
<th>Alternative Regimen</th>
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<tbody>
<tr>
<td><strong>Azithromycin oral suspension</strong></td>
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<tr>
<td>20 mg/kg/day, 1 dose daily for 3 days</td>
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</table>

Table 6. 2021 STI Treatment Guidelines: Chlamydial Infections
Treatment of Chlamydial Infections Among Infants and Children

<table>
<thead>
<tr>
<th>Recommended Regimens for Infants and Children Who Weigh &lt;45 kg</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Erythromycin base</strong></td>
</tr>
<tr>
<td>50 mg/kg/day orally divided into 4 doses daily for 14 days</td>
</tr>
<tr>
<td>Note: Data are limited regarding the effectiveness and optimal dose of azithromycin for treating chlamydial infection among infants and children weighing &lt;45 kg</td>
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<table>
<thead>
<tr>
<th>Recommended Regimens for Infants and Children Who Weigh &lt;45 kg</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Erythromycin ethylsuccinate</strong></td>
</tr>
<tr>
<td>50 mg/kg/day orally divided into 4 doses daily for 14 days</td>
</tr>
<tr>
<td>Note: Data are limited regarding the effectiveness and optimal dose of azithromycin for treating chlamydial infection among infants and children weighing &lt;45 kg</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Recommended Regimen for Children Who Weigh ≥45 kg but Aged &lt;8 Years</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Azithromycin</strong></td>
</tr>
<tr>
<td>1 g orally in a single dose</td>
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</table>

<table>
<thead>
<tr>
<th>Recommended Regimens for Children Aged ≥8 years</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Azithromycin</strong></td>
</tr>
<tr>
<td>1 g orally in a single dose</td>
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</table>

<table>
<thead>
<tr>
<th>Recommended Regimens for Children Aged ≥8 years</th>
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</thead>
<tbody>
<tr>
<td><strong>Doxycycline</strong></td>
</tr>
<tr>
<td>100 mg orally twice a day for 7 days</td>
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</table>
