Chlamydial Infections

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Module 2: Self-Study Lessons
Lesson 1: Chlamydial Infections

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Introduction

Chlamydia is the most common notifiable sexually transmitted infection (STI) in the United States.[1] This infection, which is caused by the bacterium *Chlamydia trachomatis*, is transmitted primarily through sexual activity. 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. Individuals with chlamydial infection can develop a broad array of symptomatic clinical manifestations. Untreated genital chlamydial infection in women can lead to major health consequences, including pelvic inflammatory disease (PID), chronic pelvic pain, fallopian tube scarring, and infertility. There are excellent diagnostics, treatment, and prevention strategies, if broadly used, that can markedly reduce transmission rates and morbidity associated with *C. trachomatis* infection.

Epidemiology in the United States

2023 Chlamydia Surveillance Data

Chlamydia is the most common reportable bacterial STI in the United States, with 1,648,568 reported cases in 2023 (Figure 1).[1] Since many persons with chlamydial infection may have minimal or no symptoms (and are not tested for *C. trachomatis*), the actual number of annual infections is significantly higher than the reported cases.[1] Overall, the number of reported chlamydia cases significantly increased from the 1980s to 2019 but leveled off in recent years.[1] The following summarizes several key epidemiologic features of chlamydial infections as reported for 2022 in the United States.[1]

- **Sex**: The chlamydial infection rate in women was 1.7 times higher than in men (610.7 versus 368.3 per 100,00 population). During the last 10 years, chlamydia infection rates have consistently been higher in women than in men.
- **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.
- **Race/Ethnicity**: Rates of chlamydial infection were highest among Black/African American persons and second-highest rate among American Indian/Alaskan Native individuals.
- **Geographic Regions and State**: The Southern United States had the highest rate (per 100,000 population) of chlamydial infections. Across all 50 states, the five states with the highest rates (per 100,000 population) of reported chlamydia cases (in descending order) were Louisiana, Mississippi, Alaska, Alabama, and Georgia. Of note, the rate of reported cases (per 100,000 population) in Washington DC was markedly higher than in any state.

Factors Associated with the Acquisition of *C. Trachomatis*

Factors associated with the acquisition of chlamydial infection include a previous or coexisting STI, a new sex partner, multiple sex partners, a sex partner who has an STI, inconsistent condom use, a history of incarceration, and a history of transactional sex (e.g., exchanging sex for money, drugs, or basic needs).[2] The presence of columnar epithelial cells on the ectocervix, referred to as ectopy, which commonly occurs in individuals of reproductive age, is a condition that may increase susceptibility to chlamydial infection.[3,4] 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] Chlamydia Epidemiology in U.S.

Impact

Untreated genital chlamydia infections can result in major complications for women, including pelvic inflammatory disease, chronic pelvic pain, fallopian tube scarring, and infertility.[5,6] 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.[7,8] In addition, studies have shown that rectal chlamydia infection in men who have sex with men (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.[9,10]

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.[11] 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 a standard Gram stain. *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 distinct infections in different populations, including (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 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.[12,13,14] 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 through C, and lymphogranuloma venereum (LGV) by serovars L1, L2, or L3.[13,15] 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 infects columnar epithelial cells at mucosal sites, often becoming a chronic infection that may last months or even longer than a year if untreated.[16] *Chlamydia trachomatis* has a complex replicative cycle, typically requiring 48 to 72 hours to complete.[15,17] 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 2):

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

Chlamydia trachomatis is highly transmissible via sexual contact. The overall rate of *C. trachomatis* transmission between sex partners is approximately 55%, with a per-act transmission of urogenital infection

of about 10%. The transmission rate 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 rates 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 20-50%.[20,21,22]

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.[23,24]

Cervicitis and Urethritis

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, women with cervical chlamydial infection have a normal-appearing cervix on clinical examination, but some may have findings that suggest cervicitis, such as mucopurulent endocervical discharge (originating from the cervical os) and spontaneous (or easily induced) endocervical bleeding (Figure 3).[25,26] Urethral infection with chlamydia in women is usually asymptomatic, but it may cause dysuria and urinary frequency, which can mimic acute cystitis.[27] Nearly all women with urethral chlamydial infection also have cervical infection.[27]

Pelvic Inflammatory Disease

Women with *C. trachomatis* infection can develop pelvic inflammatory disease (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 4).[23,28] 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.[29,30] 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.[6,28] Chlamydia-associated PID can result in tubal scarring, which may lead to tubal factor infertility, increased risk for ectopic pregnancy, and chronic pelvic pain.[23,31] 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.[32] The extensive long-term morbidity associated with chlamydial infection underscores the importance of aggressive prevention, screening, and treatment programs.[33,34]

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 (Figure 5).[35,36] 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.[37] [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 and reactive arthritis.

Urethritis

The most common site for chlamydial infection in men who have sex with women 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.[38] Although attempts to distinguish gonococcal urethritis from nongonococcal urethritis on clinical examination are not reliable, the discharge caused by *C. trachomatis* is usually less severe and with less purulence 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 (Figure 6).[39] Although urethritis is usually also present in men with epididymitis, the absence of urethritis does not rule out *C. trachomatis* or *N. gonorrhoeae* as a cause of epididymitis. Approximately 70% of sexually transmitted cases of epididymitis are due to *C. trachomatis*.[39][Q] Clinical Presentation of Chlamydial Urethritis in Men

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).[40] 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 7). 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.[41] 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 (e.g., dry or pruritic throat) to exudative tonsillopharyngitis.[42]

Rectal Infection

Infection with *C. trachomatis* OmpA types D through K in the rectum 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.[43,44] Some men or women with rectal infection can develop proctitis or proctocolitis, which can manifest as rectal pain, mucoid or hemorrhagic discharge, fever, and/or tenesmus.[45,46] 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. 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 timeframe that would alter clinical management.[47,48]

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 or proctocolitis.[46,49] Although most cases of LGV in the United States are rectal infections, urogenital LGV can also occur and often causes inguinal lymphadenopathy characterized by multiple, unilateral, markedly enlarged, matted, tender inguinal lymph nodes, termed “buboes” that may suppurate.[46,49] In LGV rectal infection, the LGV-associated buboes often cannot be appreciated on physical examination as the infected tissues drain to the internal iliac lymph nodes, which are deep in the pelvis. Systemic signs and symptoms, such as fever, chills, or myalgia, also may be present with either rectal or inguinal manifestations.[47] 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. Asymptomatic infection with LGV serovars may also occur—in a cohort of 192 MSM in Austria who tested positive for serovar L1, L2, or L3 *C*. *trachomatis* and 45% were asymptomatic.[50] 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 (Reiter’s Syndrome)

Reactive arthritis, previously referred to as Reiter’s syndrome, is a post-inflammatory autoimmune disease that can result from urogenital *C*. *trachomatis* infection. The characteristics of the syndrome include conjunctivitis, urethritis, oligoarthritis, skin lesions (keratoderma blennorrhagica), and circinate balanitis (Figure 8). This complication infrequently occurs, but when it does, the onset is typically 3 to 6 weeks after urogenital *C*. *trachomatis* infection, and it can occur even in persons who receive effective treatment for chlamydial infection. Reactive arthritis predominantly affects 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 anti-inflammatory agents; in rare circumstances, immunomodulatory agents may be needed to treat reactive arthritis.

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 *C*. *trachomatis* 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 *C*. *trachomatis*. This is often referred to as ophthalmia neonatorum. 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. Note that neonatal conjunctivitis (ophthalmia neonatorum) is not the same disorder as trachoma.

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, which is not an STI, is the leading cause of preventable infectious blindness in the world and is caused primarily by non-genital *C. trachomatis* serovars A, B, Ba, and C.[51] Trachoma is found in select regions of the world, mostly in South America, Sub-Saharan Africa, and Southeast Asia. The disease is most often transmitted person-to-person through hand or fomite (i.e., flies) contact with an infected eye, followed by autoinoculation. Most cases of trachoma occur in children living in communities with poor sanitary conditions, and some cases result from fly transmission.[52] The process begins as follicular conjunctivitis, which, if untreated, progresses to 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. In communities with a high trachoma prevalence (greater than 10%), community-wide mass drug administration of azithromycin to decrease the prevalence of *C. trachomatis* infection is recommended by the World Health Organization (WHO). The WHO recommends a multifaceted approach to trachoma treatment referred to as SAFE (Surgery for trichiasis, Antibiotics, Facial cleanliness [to discourage flies and person-to-person spread], and Environmental improvements [like installing toilets to prevent open defecation, which attracts flies]). Trachoma is not transmitted from mother to child during birth and is not the same as neonatal conjunctivitis (ophthalmia neonatorum).

Urogenital Infection

Urogenital *C. trachomatis* infections in preadolescent males and females are usually asymptomatic and can be the result of vertical transmission during the perinatal period.[24] 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 *C. trachomatis* (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.[48] The testing technology has shifted from culture-based methods to molecular-based techniques, representing a substantial improvement in test sensitivity and ease of specimen collection. Nucleic acid amplification tests (NAATs) are the preferred 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.[48]

Nucleic Acid Amplification Test (NAAT)

Nucleic acid amplification tests (NAATs) amplify nucleic acid sequences (either DNA or RNA) that are specific to 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.[24] 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.[53] For *C. trachomatis* 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.[24,48] 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.[54,55,56,57,58] In addition, in men and women, self-collected rectal swabs for NAAT have also performed well.[59] Nucleic acid amplification tests do not distinguish non-LGV from LGV serovars.

Point-of-Care NAAT Testing

There are several point-of care tests that can accurately detect C. trachomatis.

- **Binx Health CT/NG Assay**: 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.[60] This point-of-care test can be run on vaginal swabs obtained from women or on urine samples collected from men.[60] This assay can provide a result in approximately 30 minutes.[60] 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.[61] 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.[61] In addition, the investigators found that self-obtained vaginal swabs in women were equivalent to clinician-collected vaginal swabs.[61]
- **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*, *Neisseria gonorrhoeae* and *Trichomonas vaginalis*.[62] In an evaluation of 1,555 women presenting at clinical sites, the test had a sensitivity of 97·6% and specificity of 98·3% for the detection of *C. trachomatis*.[62]

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.[63] 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).[64] The test is available over the counter for use without the supervision of a health care provider. For diagnosing chlamydia in women, the sensitivity and specificity estimates were 97.2% and 98.5%; for the diagnosis of chlamydia in men, the sensitivity and specificity estimates were 95.2% and 99.7%.[64]

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 (EIAs), direct fluorescent antibody tests (DFAs), 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.[65] 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).[24]

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 the 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 the 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 antibodies against group-specific lipopolysaccharide antigen, and (2) microimmunofluorescence (MIF).[48]

Diagnosing Lymphogranuloma Venereum

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.[47,48] In addition, chlamydia serologic testing is not recommended for diagnosing LGV.[66] 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.[66]

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 *N. gonorrhoeae*) should be included.[67] Due to the 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.[67] 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.[67] In addition,

because of the profound implications of making an STI diagnosis in a child, only Clinical Laboratory Improvement Amendment (CLIA)-validated, FDA-cleared NAATs should be used in this setting.[24] Further, all initial positive tests require confirmatory testing.[48,67] 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.

[Q] Laboratory Diagnostic Methods

Screening for Chlamydial Infection

Screening for chlamydial infection in asymptomatic persons has been found to significantly reduce the incidence of chlamydia–associated PID.[33,68,69] 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.[59,70] 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 NAATs used for gonorrhea detect both *N. gonorrhoeae* and *C. trachomatis*, screening for pharyngeal gonorrhea may also include results for chlamydia. The following summarizes the recommendations for chlamydial screening in the 2021 STI Treatment Guidelines and [Guidelines] Doxy PEP Guidelines.[24,71,72]

Women Who Have Sex with Men [2,72]

- 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 chlamydial 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 a 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 [73]

- 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 [72,74]

- 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 chlamydial 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 chlamydial infection during the third trimester in all women younger than 25 years of age and women 25 years of age and older who have an increased risk of acquiring chlamydial 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 [24,72]

- 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 [72,75]

- 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).

Persons with HIV [72,76]

- 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 sexual activity, and local prevalence of specific STIs, and receipt of doxycycline postexposure prophylaxis (doxy PEP).

Persons Receiving HIV Preexposure Prophylaxis (HIV PrEP)

- Persons receiving HIV preexposure prophylaxis (PrEP) should undergo routine chlamydia screening. The frequency of chlamydia screening for persons receiving HIV PrEP varies as follows:
    - Every 3 months for MSM
    - Every 6 months for men who have sex with women and women who have sex with men

Persons Receiving Doxycycline Postexposure Prophylaxis (Doxy PEP) [71]

- Persons starting on doxy PEP should undergo routine chlamydia screening at baseline.
- The frequency of chlamydia screening for persons while they are taking doxy PEP should be every 3 to 6 months.

Correctional Facilities [77]

- Routine opt-out screening for chlamydial infection screening of all sites of sexual activity (pharyngeal, urethral, vaginal, 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 to minimize complications, particularly PID in women. The following summarizes recommendations in the 2021 STI Treatment Guidelines for the treatment of chlamydial infections.[24]

Adolescents and Adults with Urogenital Chlamydial Infections

The recommended treatment for adolescents and adults (except pregnant women) 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 or levofloxacin 500 mg orally given daily for 7 days.[24] In persons for whom doxycycline adherence is a substantial concern, consideration can be given to using the alternative single-dose oral azithromycin regimen.

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

Recommended Regimen
Doxycycline *100 mg orally twice a day for 7 days*

Alternative Regimens
Azithromycin *1 g orally in a single dose*

Alternative Regimens
Levofloxacin *500 mg orally once daily for 7 days*

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.

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

Key Chlamydia Treatment Studies

The following outlines several studies that highlight why doxycycline is now preferred over azithromycin for sexually-transmitted 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 9).[78,79] 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.[80,81]
- 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.[43]
- 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.[82]
- Chlamydia treatment studies in women have been conflicting. Several randomized, controlled trials have shown equal efficacy for urogenital chlamydia with a 7-day course of doxycycline and single-dose azithromycin.[83,84] 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 10).[85] [Q] Treatment of Urogenital Chlamydia Infection in Adults

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.[24,86,87,88,89] Doxycycline and levofloxacin are not recommended for the treatment of chlamydial infections in pregnancy.[24] 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.[24]

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

Recommended Regimen
Azithromycin *1 g orally in a single dose*

Alternative Regimen
Amoxicillin *500 mg orally three times a day for 7 days*

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

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[90,91], 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, except for pregnant women who should receive azithromycin 1 gram single dose orally.[24]

Treatment for Lymphogranuloma Venereum

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 *C. trachomatis* strains.[24,66] In a cohort of 58 MSM with rectal LGV in Italy, 76% of whom were symptomatic, clinical and microbiologic cure was 100% whether 7 or 21 days of doxycycline were used, suggesting that a 7-day course of doxycycline may be as effective as a 21-day course for the treatment of LGV.[92] 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.[66] 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.[66] In addition, empiric therapy for LGV is indicated for persons with (1) symptoms or signs of proctocolitis (e.g., bloody discharge, tenesmus, or ulceration), (2) severe inguinal lymphadenopathy with bubo formation, especially if the individual reports recently having a genital ulcer, and (3) a genital ulcer and other causes for the genital ulcer have been excluded.[66]

Table 3. 2021 STI Treatment Guidelines: Diseases Characterized by Genital, Anal, or Perianal Ulcers
Lymphogranuloma Venereum

Recommended for Lymphogranuloma Venereum
Doxycycline *100 mg orally twice daily for 21 days*

Alternative for Lymphogranuloma Venereum
Azithromycin *1 g orally once weekly for 3 weeks** *Because this regimen has not been validated, a test-of-cure with *C. trachomatis* NAAT 4 weeks after completion of treatment can be considered.

Alternative for Lymphogranuloma Venereum
Erythromycin base *500 mg orally four times a day for 21 days*

Source: Workowski KA, Bachmann LH, Chan PA, et al. Sexually transmitted infections treatment guidelines, 2021. Diseases characterized by genital, anal, or perianal ulcers: lymphogranuloma venereum (LGV). MMWR Recomm Rep. 2021;70(No. RR-4):1-187. [2021 STI Treatment Guidelines]

Post-treatment Follow-Up and Retesting

The CDC does not recommend routine test-of-cure after completing therapy for chlamydia, except after treatment of pregnant women. All persons treated for chlamydia should return for follow-up and repeat testing approximately 3 months after treatment, due to the substantial risk of reinfection during that 3-month period.[24,93,94] 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.[95,96] [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.[24] 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.[24] 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. These recommendations are the same for a sex contact of a person diagnosed with an LGV strain. The purpose of performing an evaluation for the contact, even when presumptive treatment will be given, 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.[97,98,99] 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.[24] The use of EPT for MSM should, therefore, be provided on a shared-decision basis. Finally, expedited partner therapy is not fully permissible 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 *C. trachomatis*-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.[24] 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.[24]

Neonates with Ophthalmia Neonatorum

The recommended treatment regimen for neonates with ophthalmia neonatorum is a 14-day course of oral erythromycin base or erythromycin ethylsuccinate.[24] Data on oral azithromycin for the treatment of neonatal chlamydial infection are limited, but a small study suggested a short three-day course of azithromycin may be effective.[100] The use of topical erythromycin alone is not effective for ophthalmia neonatorum, and it is not recommended for use in combination with oral antibiotics.[24] 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.[101,102,103,104] 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.[103]

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

Recommended Regimens
Erythromycin base *50 mg/kg/day orally divided into 4 doses daily for 14 days**

Recommended Regimens
Erythromycin ethylsuccinate *50 mg/kg/day orally divided into 4 doses daily for 14 days**

*An association between oral erythromycin and azithromycin and infantile hypertrophic pyloric stenosis (IHPS) has been reported in infants aged

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 timeframe.
- **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 potential complications associated with chlamydial infection should ideally be performed at the time of the initial diagnosis and/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 15 through 24 years of age.

Prevention

Doxycycline PostExposure Prophylaxis for Prevention of STIs

Doxycycline, when administered as a single-dose 200 mg postexposure prophylaxis (within 72 hours after a condomless sexual encounter), can help prevent bacterial STIs, including chlamydia, syphilis, and gonorrhea. Several randomized trials have shown that doxycycline postexposure prophylaxis (doxy PEP) reduces rates of STIs for men who have sex with men.[105,106,107] One clinical trial using doxy PEP for women in Africa has been completed, and it did not show benefit in reducing STIs.[108] In 2024, the CDC published *Clinical Guidelines on the Use of Doxycycline Post-exposure Prophylaxis for Bacterial STI Prevention*.[71] These guidelines do not recommend doxy PEP use in women. The following will focus on the impact of doxy PEP on preventing chlamydial infections.

Doxycycline Postexposure Prophylaxis for Prevention of Chlamydia

The use of doxy PEP in MSM is very effective at preventing chlamydial infection, with roughly a 70% reduction. In the DoxyPEP randomized trial conducted in San Francisco and Seattle, the quarterly incidence of new chlamydial infections in the doxy PEP arms was 1.4% in people without HIV and 3.9% in people with HIV, compared to 12.1% and 14.8%, respectively, in the standard of care arm.[107] The use of doxy PEP resulted in a reduction of chlamydial infections of 88% in those without HIV and 74% in those with HIV.[107] In the French ANRS DOXYVAC randomized trial, among MSM taking HIV PrEP, the incidence (per 100 person-years) of first-episode of chlamydia was 5.9 in the doxy PEP arm compared to 42.1 in the standard of care arm.[106] Similarly, in the French IPERGAY-DoxyPEP study, the use of doxy PEP among 232 MSM taking HIV PrEP led to a 71% relative risk reduction in the occurrence of chlamydia.[105] Implementation of doxy PEP in clinical practice in San Francisco during a 10-month period starting in 2022 resulted in a 51% reduction of chlamydia cases among these groups when compared to expected case numbers over that period.[109]

Summary Points

- Chlamydia is the most common reportable bacterial sexually transmitted infection in the United States, with approximately 1.65 million cases reported in 2023.
- The highest rates of chlamydial infections in the United States are in females 20 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, 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 findings, 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. All females and males should return for follow-up and repeat testing approximately 3 months after treatment.

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Figures

Figure 1 Chlamydia Reported Cases in the United States

Source: Centers for Disease Control and Prevention. *Sexually Transmitted Disease Surveillance, 2022*. Atlanta: U.S. Department of Health and Human Services; April 2024.

This is a dynamic visualization. Please visit our website to experience this dynamic content.

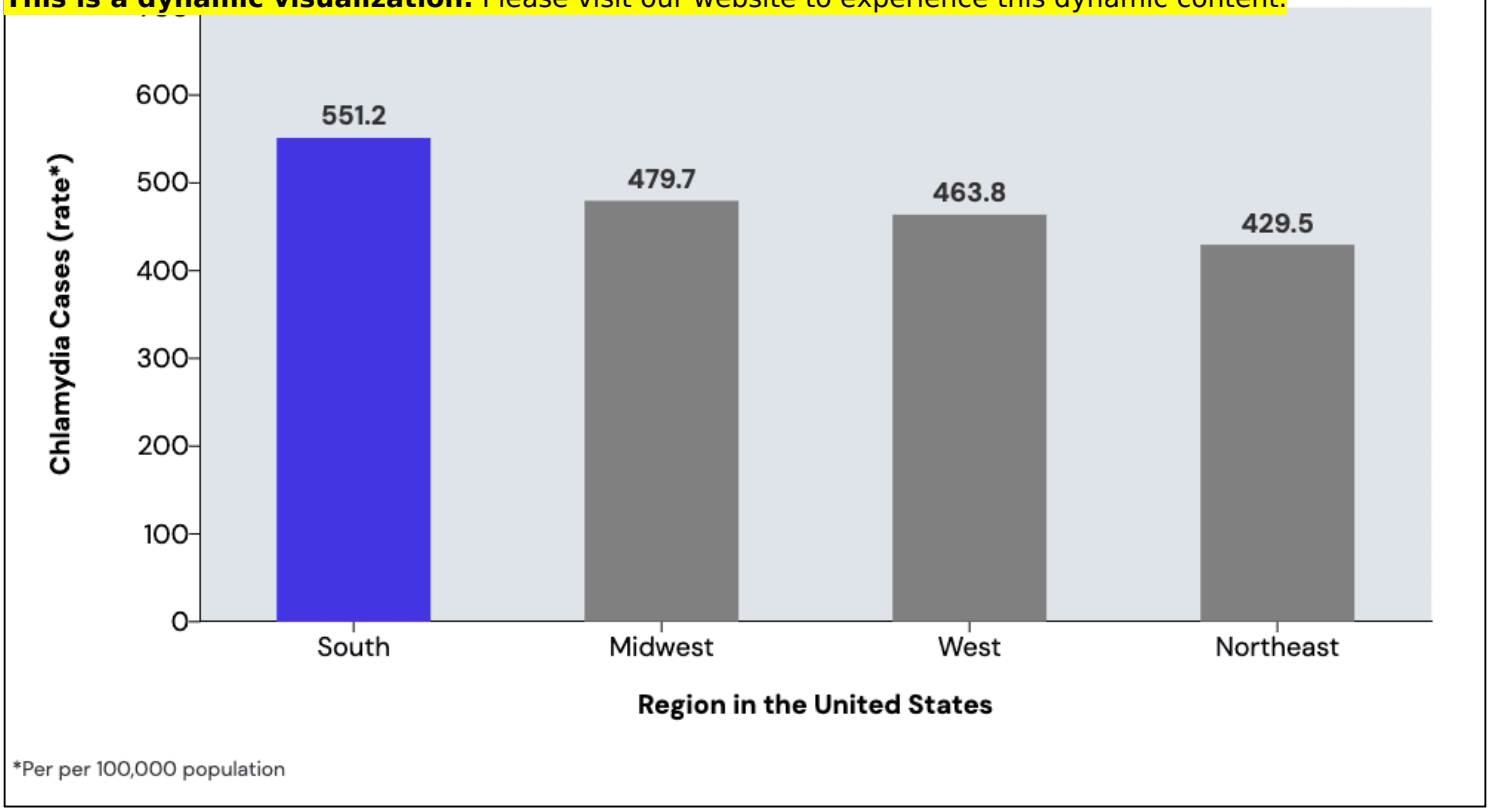

Figure 2 Chlamydia Life Cycle

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

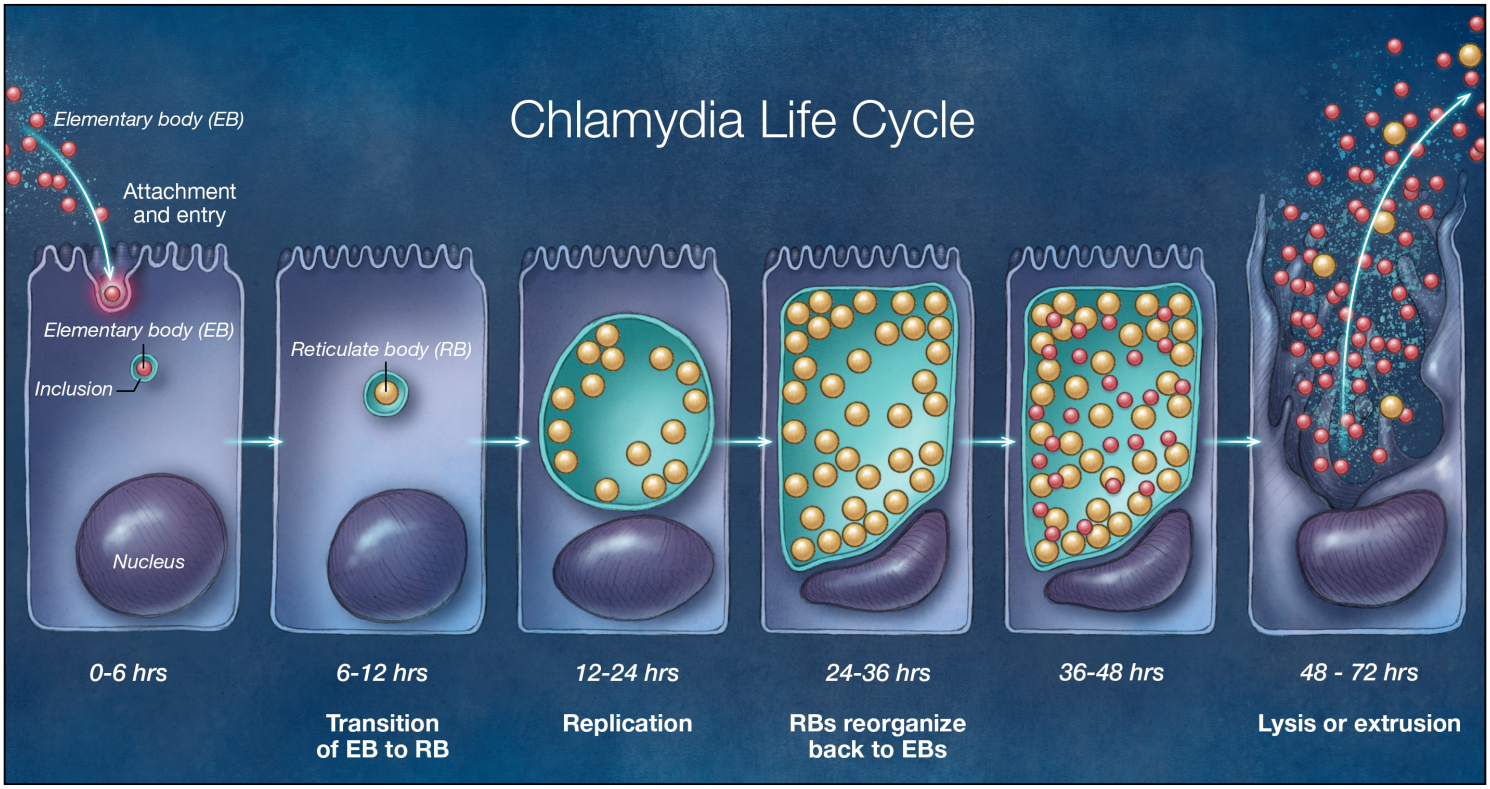

Figure 3 (Image Series) - Cervicitis Caused by Chlamydial Infection (Image Series) - Figure 3 (Image Series) - Cervicitis Caused by Chlamydial Infection
Image 3A: Cervicitis with Endocervical Discharge

Source: Cognition Studio, Inc. and David H. Spach, MD

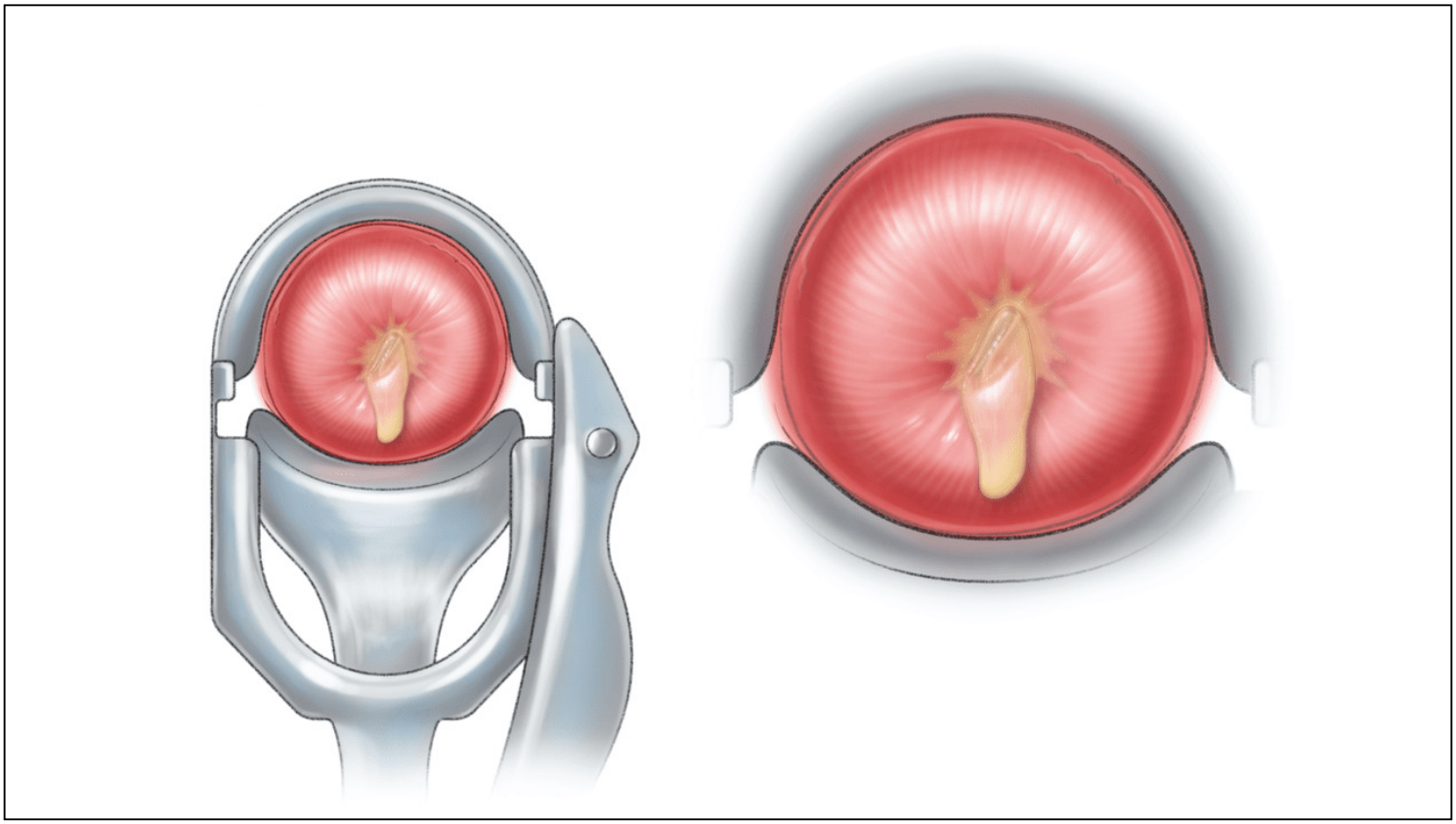

Figure 3 (Image Series) - Cervicitis Caused by Chlamydial Infection
Image 3B: Cervicitis and Endocervical Bleeding After Insertion of Swab in Cervical Os

Source: Cognition Studio, Inc. and David H. Spach, MD

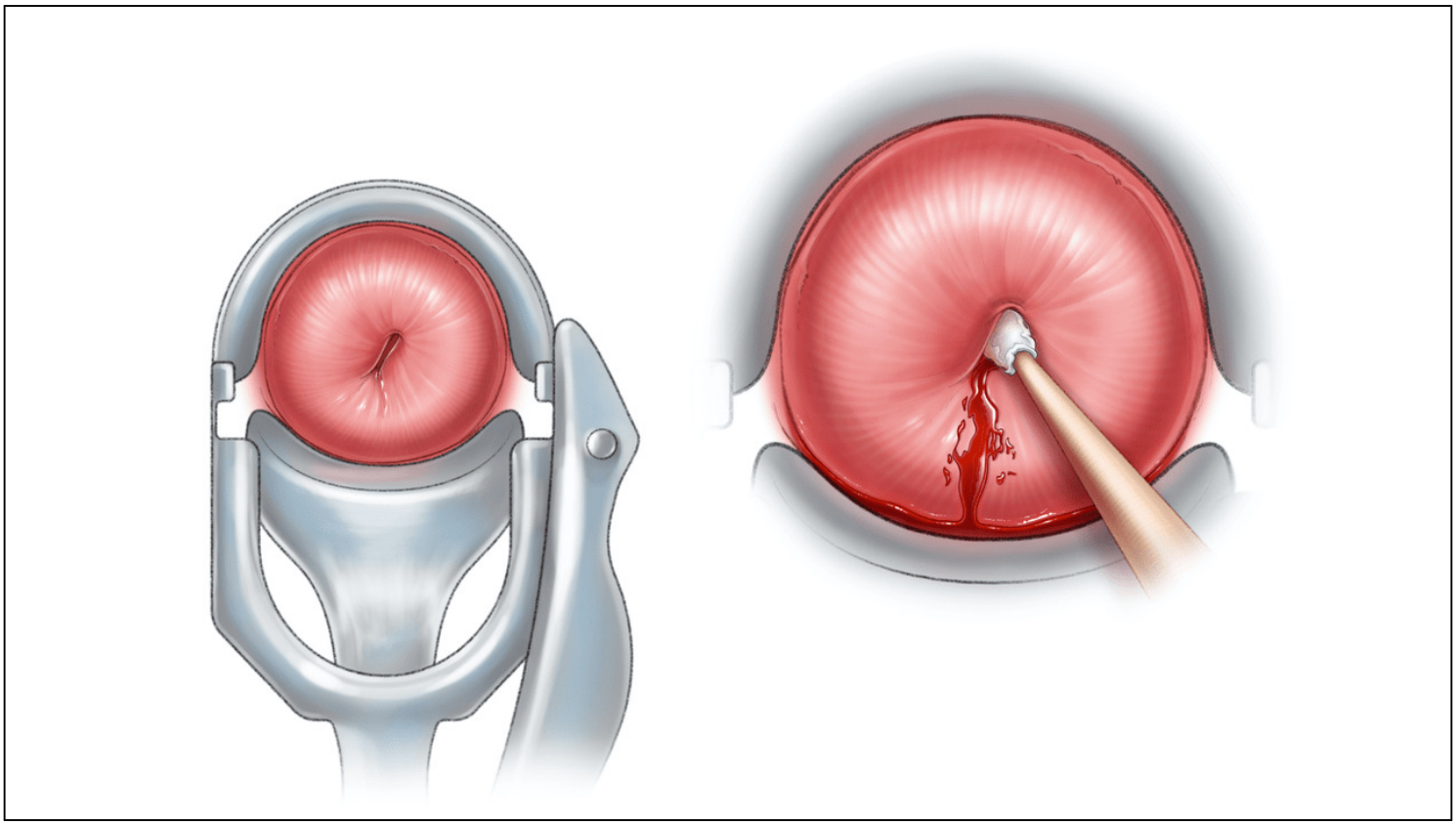

Figure 3 (Image Series) - Cervicitis Caused by Chlamydial Infection
Image 3C: Cervicitis with Endocervical Discharge, Friable Cervix, and Bleeding

Source: Cognition Studio, Inc. and David H. Spach, MD

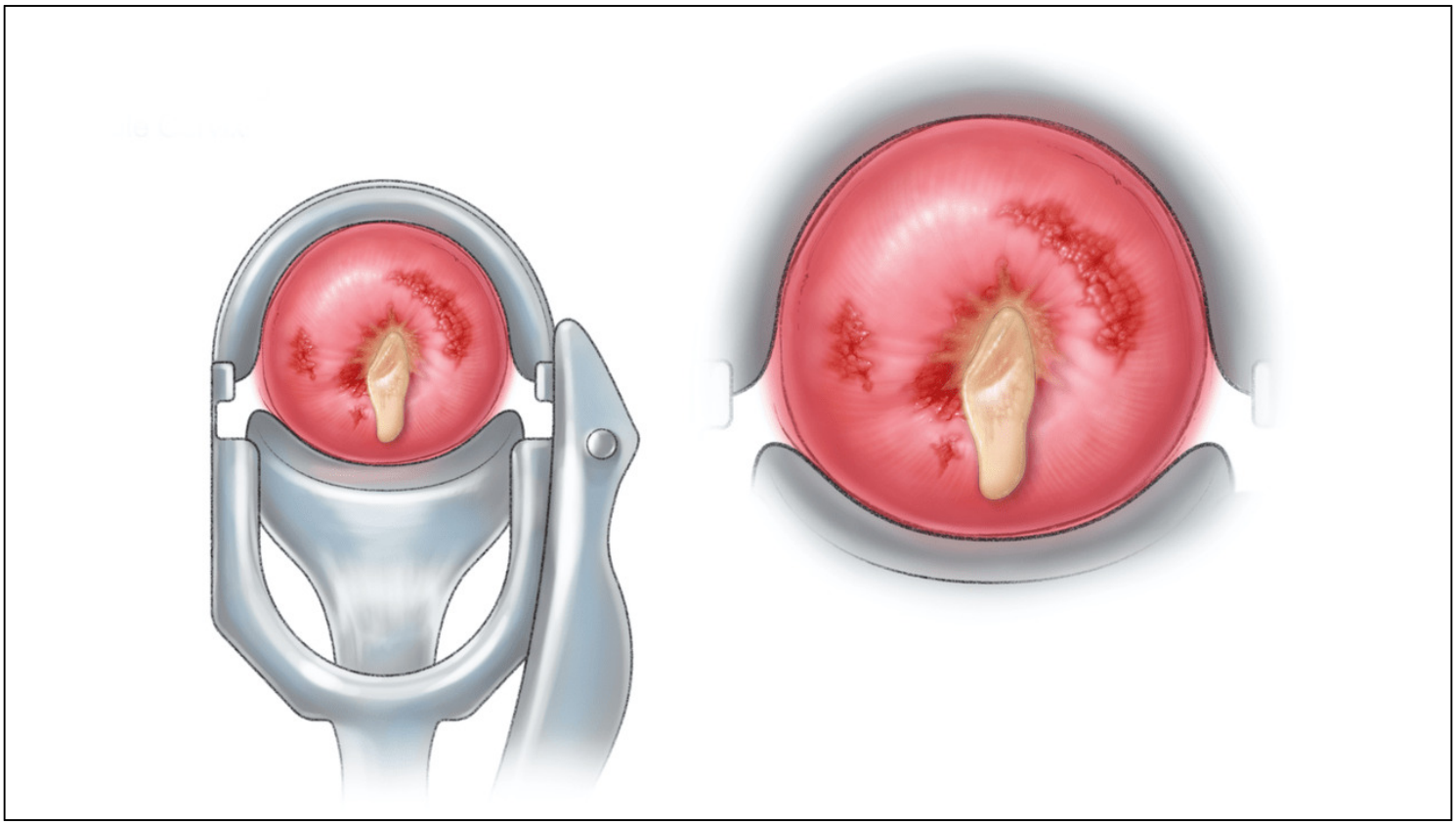

Figure 4 (Image Series) - *Chlamydia trachomatis* and Pelvic Inflammatory Disease (Image Series) - Figure 4 (Image Series) - *Chlamydia trachomatis* and Pelvic Inflammatory Disease
Image 4A: *Chlamydia trachomatis* and Ascending Infection in Women

Source: Cognition Studio, Inc. and David H. Spach, MD

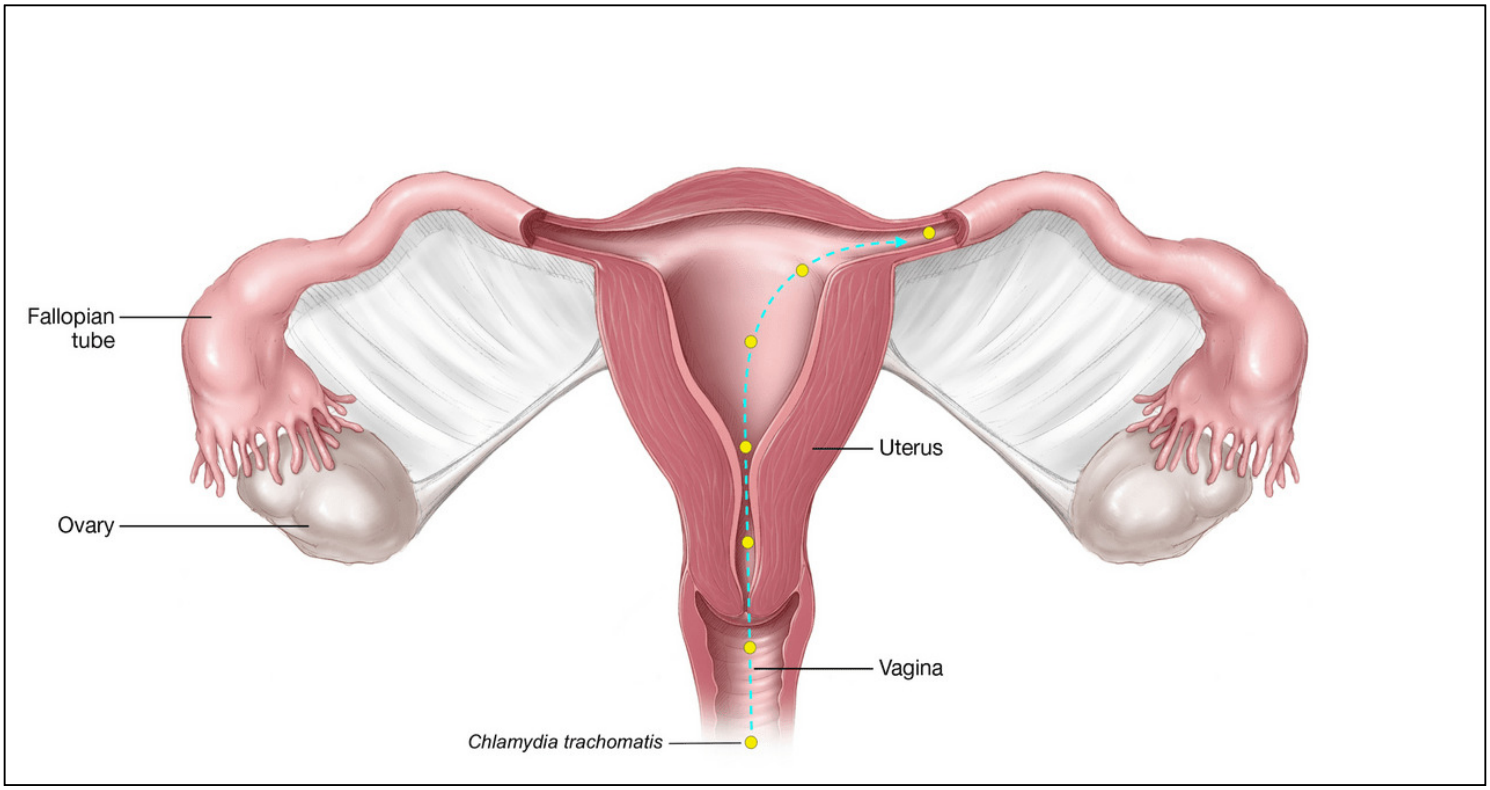

Figure 4 (Image Series) - *Chlamydia trachomatis* and Pelvic Inflammatory Disease
Image 4B: Pelvic Inflammatory Disease and Left-Sided Salpingitis

Source: Cognition Studio, Inc. and David H. Spach, MD

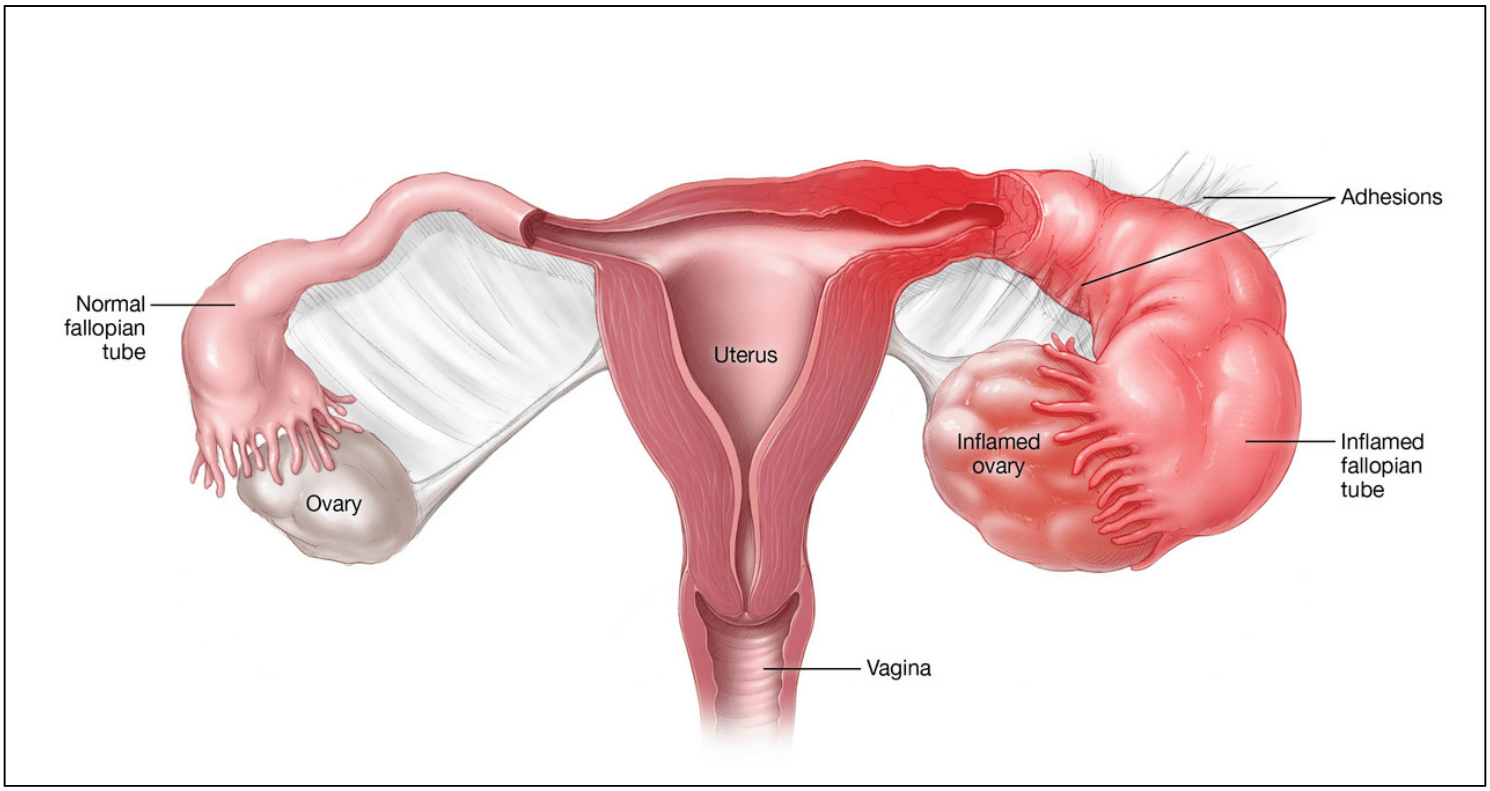

Figure 5 Fitz-Hugh-Curtis Syndrome

Source: Cognition Studio, Inc. and David H. Spach, MD

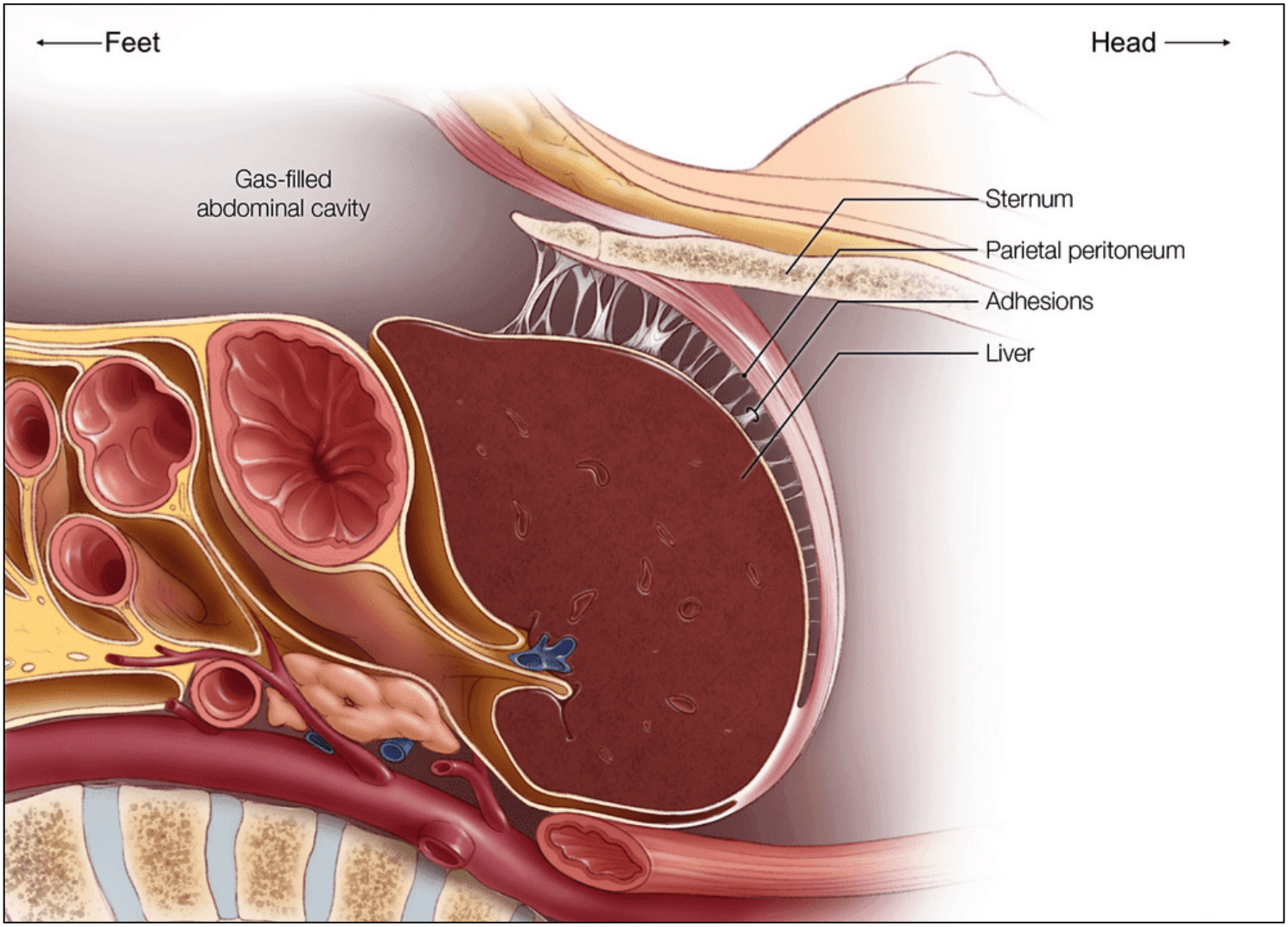

Figure 6 Left-Sided Epididymitis

This illustration shows a man with left-sided epididymitis, with characteristic findings that include swelling, erythema, and tenderness.

Source: Cognition Studio, Inc. and David H. Spach, MD

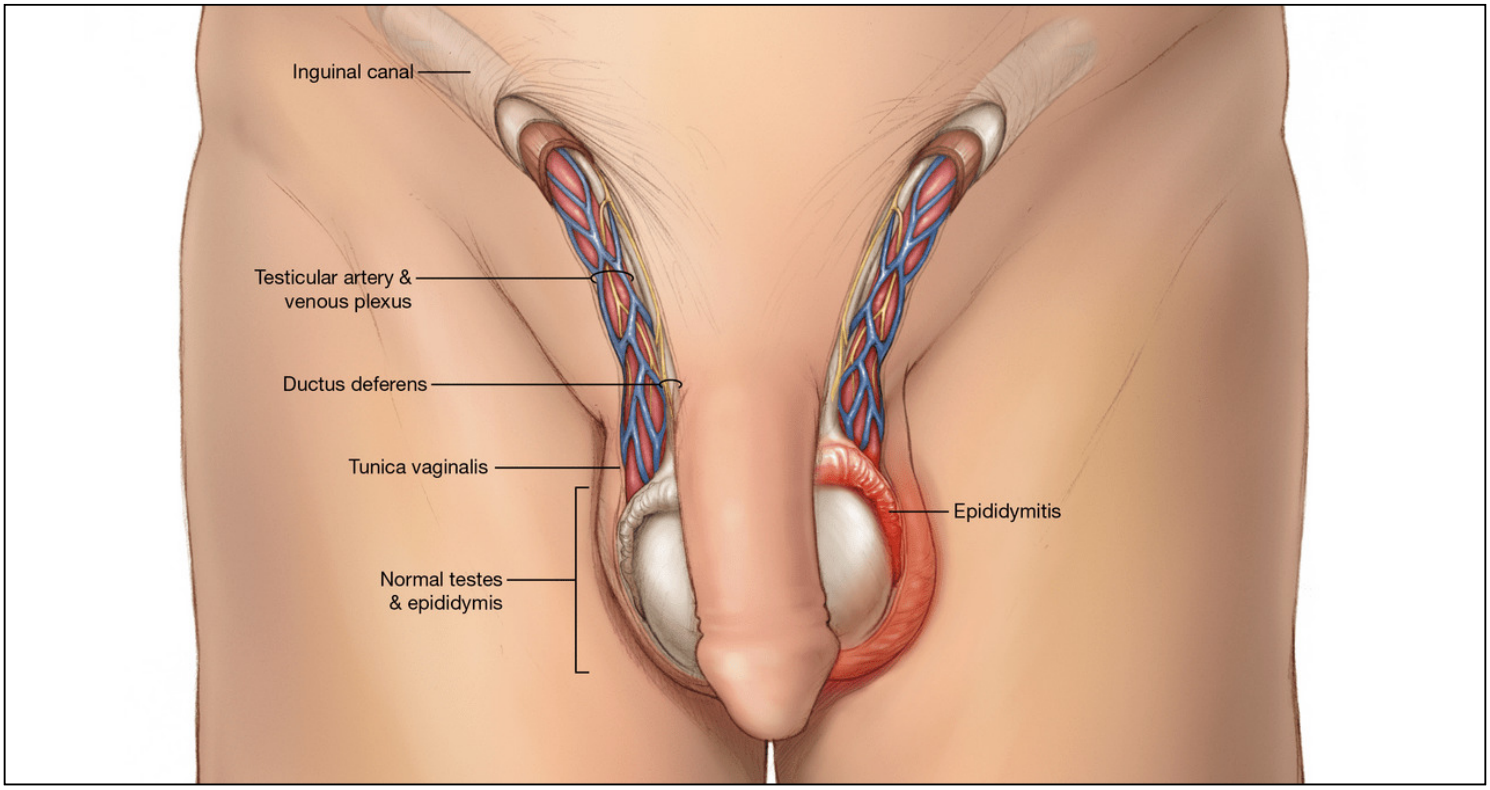

Figure 7 Adult Chlamydial Inclusion Conjunctivitis-

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).

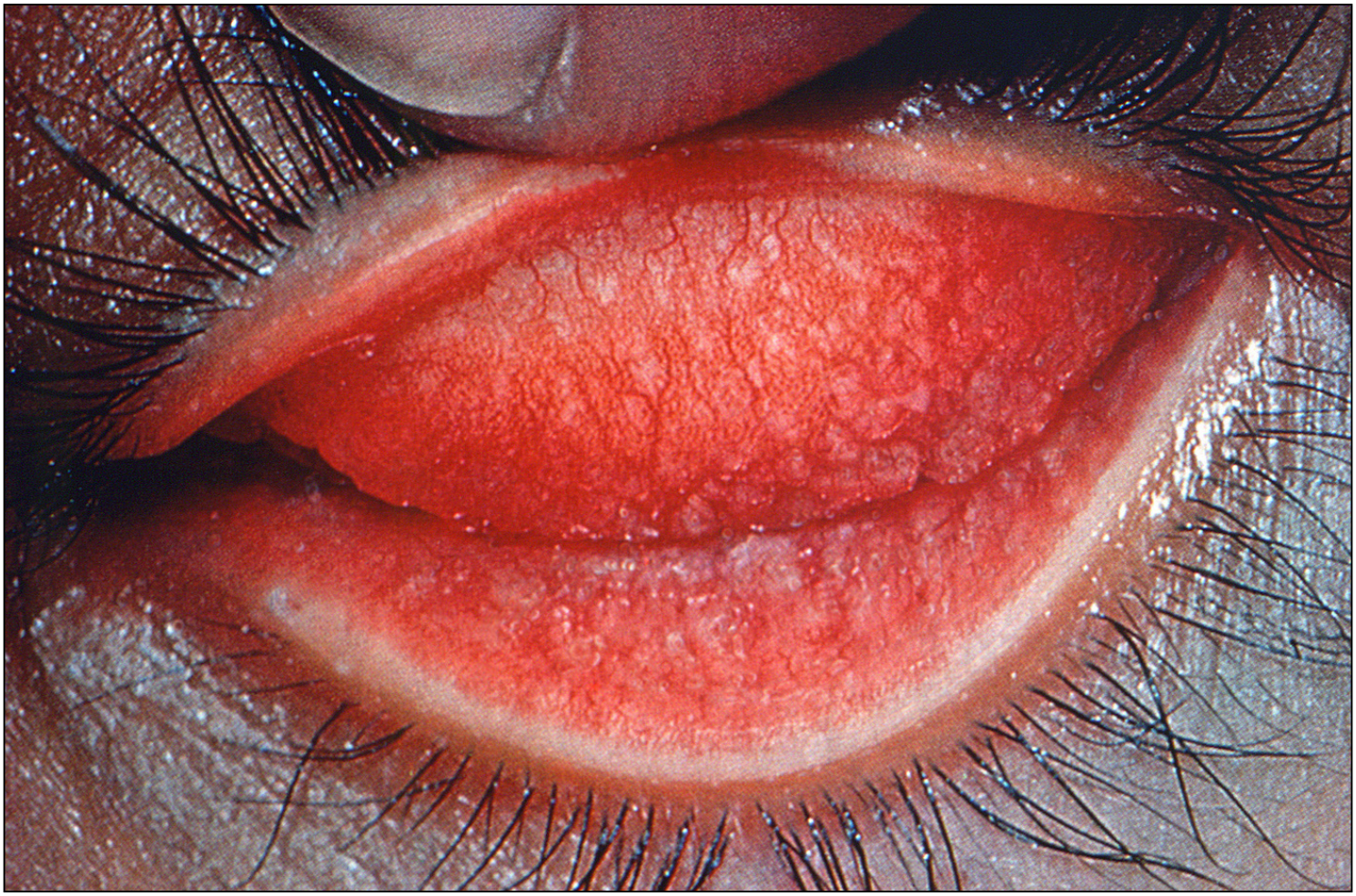

Figure 8 Reiter's Syndrome and Circinate Balanitis

Source: photograph from Seattle & King County Sexual Health Clinic Clinic.

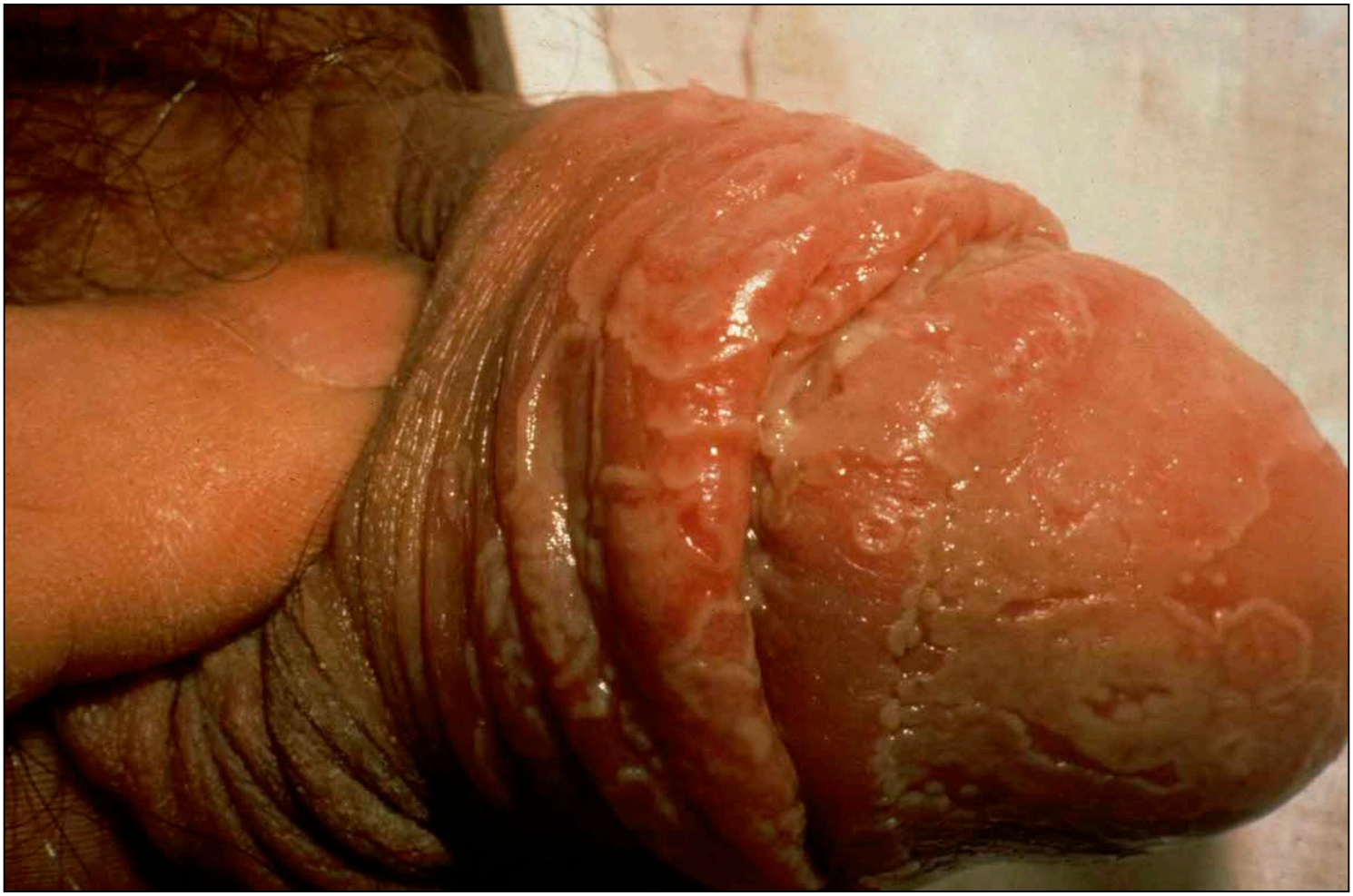

Figure 9 (Image Series) - Azithromycin versus Doxycycline in Asymptomatic Rectal Chlamydial Infections in Men who have Sex with Men (Image Series) - Figure 9 (Image Series) - Azithromycin versus Doxycycline in Asymptomatic Rectal Chlamydial Infections in Men who have Sex with Men

Image 9A: Study Design

Abbreviations: NAAT = nucleic acid amplification test

Source: Lau A, Kong FYS, Fairley CK, et al. Azithromycin or doxycycline for asymptomatic rectal *Chlamydia trachomatis*. N Engl J Med. 2021;384:2418-27.

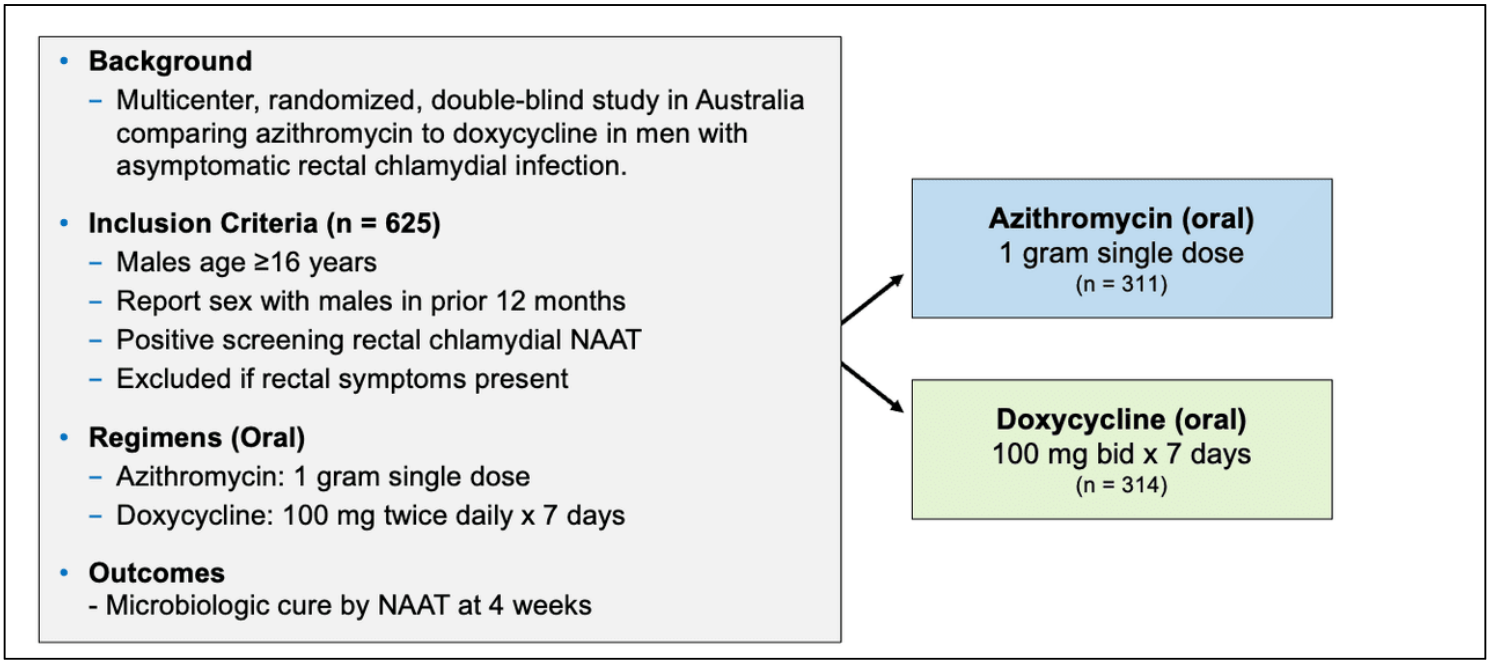

Figure 9 (Image Series) - Azithromycin versus Doxycycline in Asymptomatic Rectal Chlamydial Infections in Men who have Sex with Men
Image 9B: Results: Microbiologic Cure at 4 Weeks

Abbreviations: ITT = intent-to-treat

Source: Lau A, Kong FYS, Fairley CK, et al. Azithromycin or doxycycline for asymptomatic rectal *Chlamydia trachomatis*. N Engl J Med. 2021;384:2418-27.

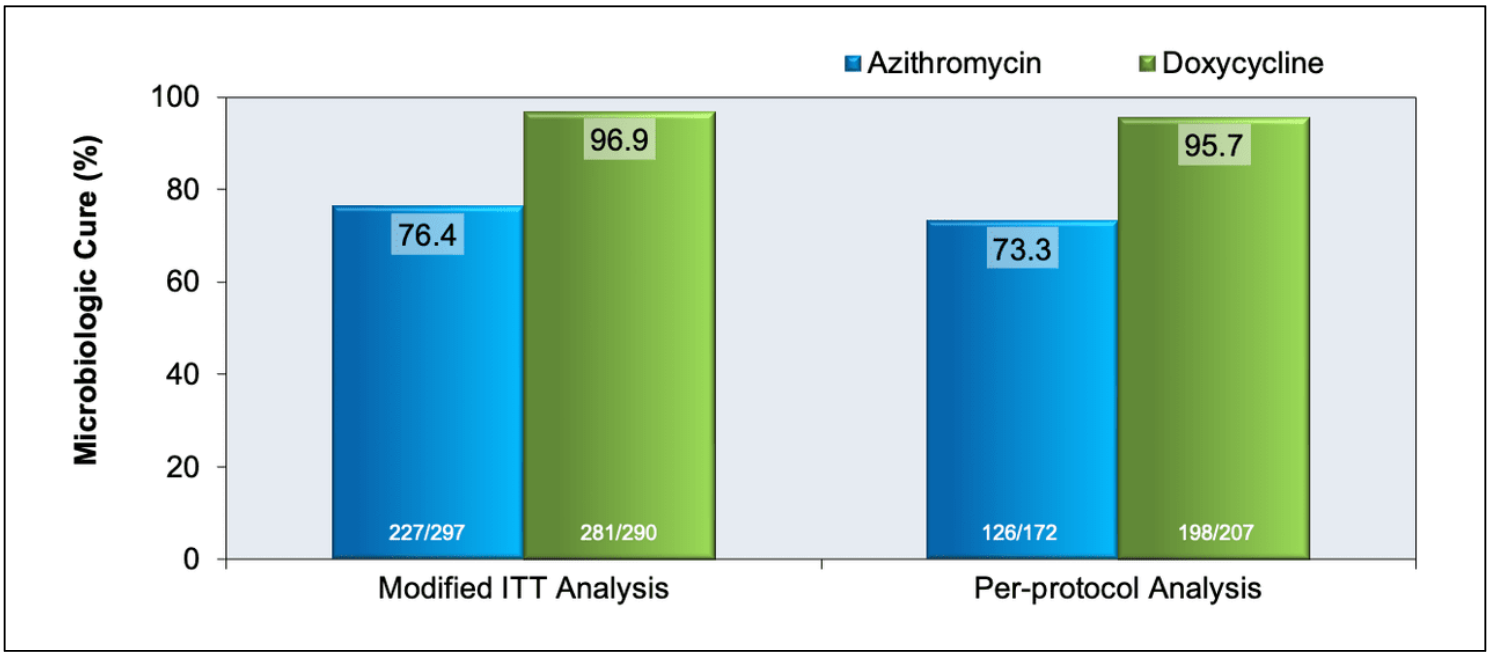

Figure 10 (Image Series) - Azithromycin versus Doxycycline in Uncomplicated Rectal and Vaginal Chlamydial Infections in Women (FEMCure) (Image Series) - Figure 10 (Image Series) - Azithromycin versus Doxycycline in Uncomplicated Rectal and Vaginal Chlamydial Infections in Women (FEMCure)
Image 10A: Study Design

Abbreviations: NAAT = nucleic acid amplification test

Source: Dukers-Muijrers NHTM, Wolffs PFG, De Vries H, et al. Treatment effectiveness of azithromycin and doxycycline in uncomplicated rectal and vaginal *Chlamydia trachomatis* infections in women: a multicenter observational study (FemCure). Clin Infect Dis. 2019;69:1946-54.

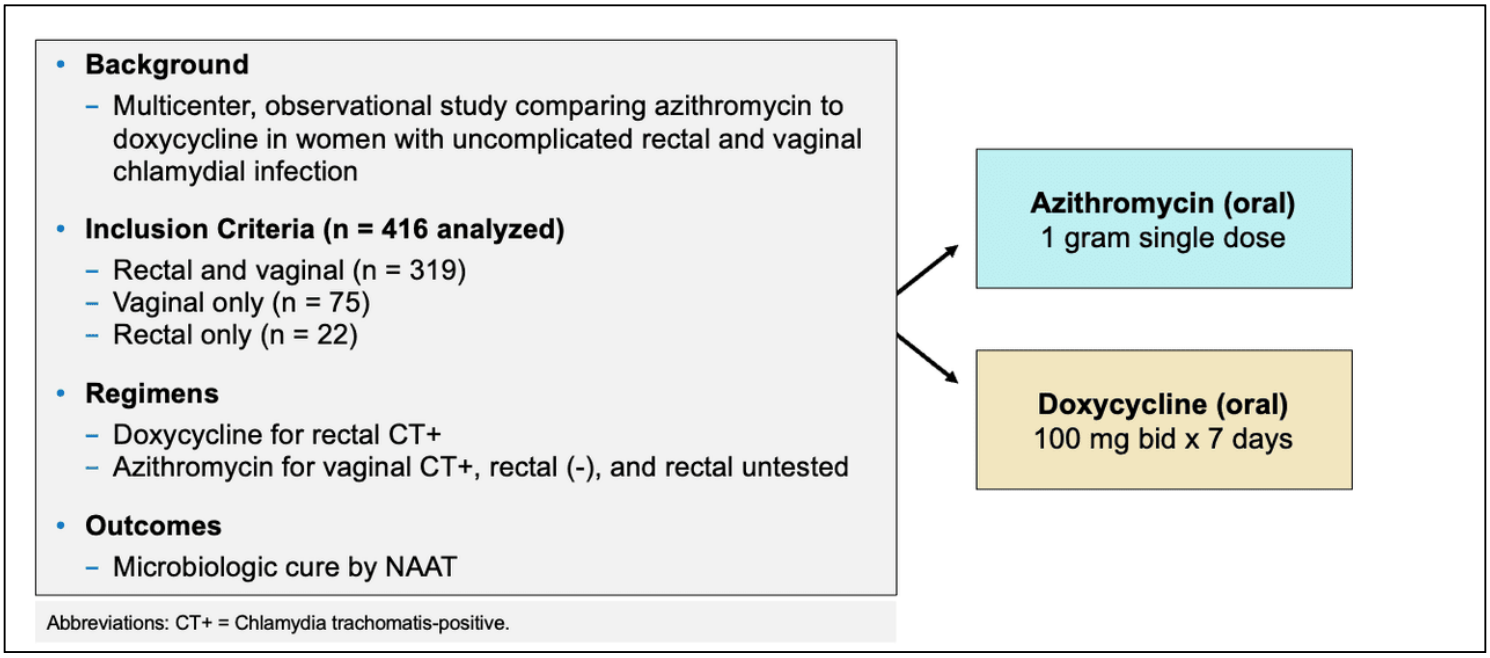

Figure 10 (Image Series) - Azithromycin versus Doxycycline in Uncomplicated Rectal and Vaginal Chlamydial Infections in Women (FEMCure)
Image 10B: Results: Microbiologic Cure at 4 Weeks

Abbreviations: CT+ = *Chlamydia trachomatis*-positive

Source: Dukers-Muijrers NHTM, Wolffs PFG, De Vries H, et al. Treatment effectiveness of azithromycin and doxycycline in uncomplicated rectal and vaginal *Chlamydia trachomatis* infections in women: a multicenter observational study (FemCure). Clin Infect Dis. 2019;69:1946-54.

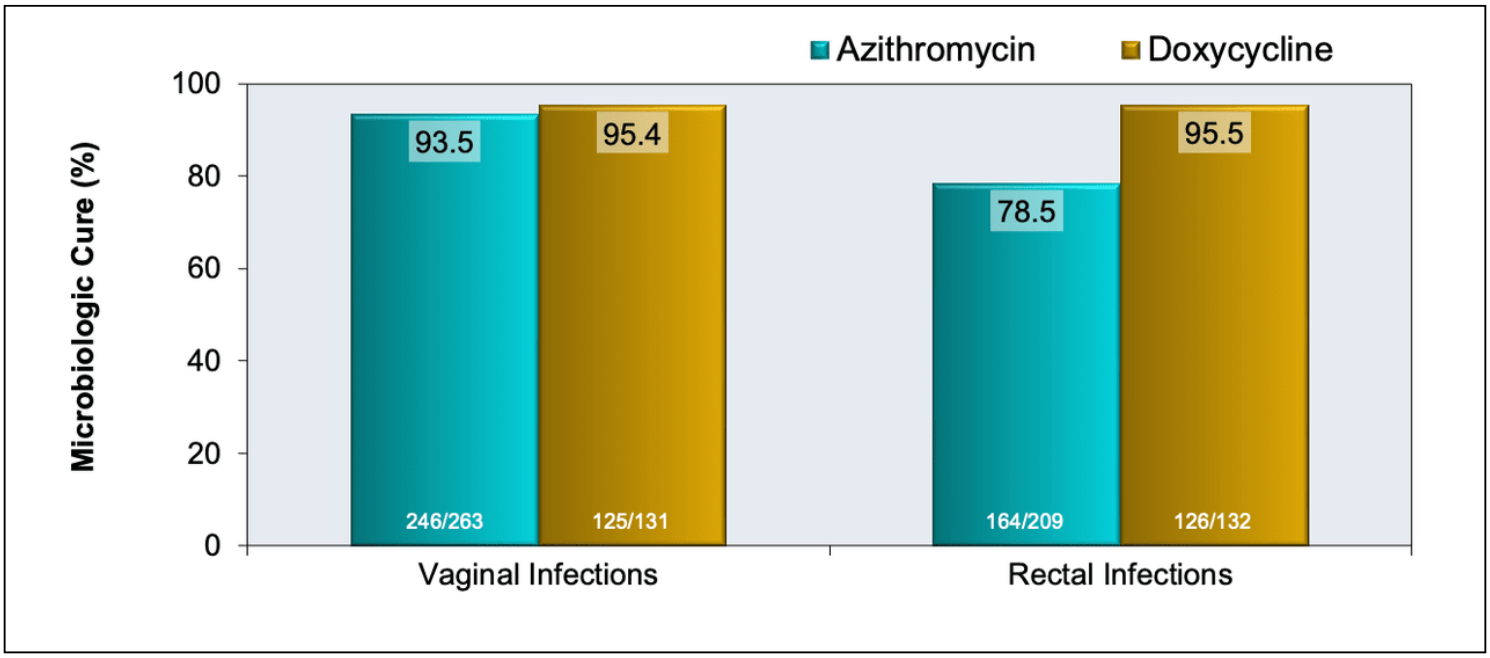

Table 1. 2021 STI Treatment Guidelines: Chlamydial Infections
Treatment of Chlamydial Infections Among Adolescents and Adults

Recommended Regimen
Doxycycline *100 mg orally twice a day for 7 days*

Alternative Regimens
Azithromycin *1 g orally in a single dose*

Alternative Regimens
Levofloxacin *500 mg orally once daily for 7 days*

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.

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

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

Recommended Regimen
Azithromycin *1 g orally in a single dose*

Alternative Regimen
Amoxicillin *500 mg orally three times a day for 7 days*

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

Table 3. 2021 STI Treatment Guidelines: Diseases Characterized by Genital, Anal, or Perianal Ulcers
Lymphogranuloma Venereum

Recommended for Lymphogranuloma Venereum

Doxycycline
100 mg orally twice daily for 21 days

Alternative for Lymphogranuloma Venereum

Azithromycin
*1 g orally once weekly for 3 weeks**

*Because this regimen has not been validated, a test-of-cure with *C. trachomatis* NAAT 4 weeks after completion of treatment can be considered.

Alternative for Lymphogranuloma Venereum

Erythromycin base
500 mg orally four times a day for 21 days

Source: Workowski KA, Bachmann LH, Chan PA, et al. Sexually transmitted infections treatment guidelines, 2021. Diseases characterized by genital, anal, or perianal ulcers: lymphogranuloma venereum (LGV). MMWR Recomm Rep. 2021;70(No. RR-4):1-187. [2021 STI Treatment Guidelines]

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

Recommended Regimens
Erythromycin base *50 mg/kg/day orally divided into 4 doses daily for 14 days**

Recommended Regimens
Erythromycin ethylsuccinate *50 mg/kg/day orally divided into 4 doses daily for 14 days**

*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.

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

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

Recommended Regimens

Erythromycin base
50 mg/kg/day orally divided into 4 doses daily for 14 days

Recommended Regimens

Erythromycin ethylsuccinate
50 mg/kg/day orally divided into 4 doses daily for 14 days

Alternative Regimen

Azithromycin oral suspension
20 mg/kg/day, 1 dose daily for 3 days

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

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

Recommended Regimens for Infants and Children Who Weigh <45 kg

Erythromycin base
50 mg/kg/day orally divided into 4 doses daily for 14 days

Note: Data are limited regarding the effectiveness and optimal dose of azithromycin for treating chlamydial infection among infants and children weighing <45 kg

Recommended Regimens for Infants and Children Who Weigh <45 kg

Erythromycin ethylsuccinate
50 mg/kg/day orally divided into 4 doses daily for 14 days

Note: Data are limited regarding the effectiveness and optimal dose of azithromycin for treating chlamydial infection among infants and children weighing <45 kg

Recommended Regimen for Children Who Weigh ≥45 kg but Aged <8 Years

Azithromycin
1 g orally in a single dose

Recommended Regimens for Children Aged ≥8 years

Azithromycin
1 g orally in a single dose

Recommended Regimens for Children Aged ≥8 years

Doxycycline
100 mg orally twice a day for 7 days

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