Chlamydial Infections

Chlamydial Infection Among Adolescents and Adults

Chlamydial infection is the most frequently reported bacterial infectious disease in the United States, and prevalence is highest among persons aged ≤24 years (*141*,*784*). Multiple sequelae can result from *C. trachomatis* infection among women, the most serious of which include PID, ectopic pregnancy, and infertility. Certain women who receive a diagnosis of uncomplicated cervical infection already have subclinical upper genital tract infection.

Asymptomatic infection is common among both men and women. To detect chlamydial infection, health care providers frequently rely on screening tests. Annual screening of all sexually active women aged <25 years is recommended, as is screening of older women at increased risk for infection (e.g., women aged ≥25 years 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) (*149*). In a community-based cohort of female college students, incident chlamydial infection was also associated with BV and high-risk HPV infection (*785*). Although chlamydia incidence might be higher among certain women aged ≥25 years in certain communities, overall, the largest proportion of infection is among women aged <25 years (*141*).

Chlamydia screening programs have been demonstrated to reduce PID rates among women (*786*,*787*). Although evidence is insufficient to recommend routine screening for *C. trachomatis* among sexually active young men because of certain factors (i.e., feasibility, efficacy, and cost-effectiveness), screening of sexually active young men should be considered in clinical settings with a high prevalence of chlamydia (e.g., adolescent clinics, correctional facilities, or STD specialty clinics) or for populations with a high burden of infection (e.g., MSM) (*149*,*788*). Among women, the primary focus of chlamydia screening should be to detect and treat chlamydia, prevent complications, and test and treat their partners, whereas targeted chlamydia screening for men should be considered only when resources permit, prevalence is high, and such screening does not hinder chlamydia screening efforts for women (*789*–*791*). More frequent screening than annual for certain women (e.g., adolescents) or certain men (e.g., MSM) might be indicated on the basis of risk behaviors.

Diagnostic Considerations

For women, *C. trachomatis* urogenital infection can be diagnosed by vaginal or cervical swabs or first-void urine. For men, *C. trachomatis* urethral infection can be diagnosed by testing first-void urine or a urethral swab. NAATs are the most sensitive tests for these specimens and are the recommended test for detecting *C. trachomatis* infection (*553*). NAATs that are FDA cleared for use with vaginal swab specimens can be collected by a clinician or patient in a clinical setting. Patient-collected vaginal swab specimens are equivalent in sensitivity and specificity to those collected by a clinician using NAATs (*792*,*793*), and this screening strategy is highly acceptable among women (*794*,*795*). Optimal urogenital specimen types for chlamydia screening by using NAAT include first-catch urine (for men) and vaginal swabs (for women) (*553*). Recent studies have demonstrated that among men, NAAT performance on self-collected meatal swabs is comparable to patient-collected urine or provider-collected urethral swabs (*796*–*798*). Patient collection of a meatal swab for *C. trachomatis* testing might be a reasonable approach for men who are either unable to provide urine or prefer to collect their own meatal swab over providing urine. Previous evidence indicates that the liquid-based cytology specimens collected for Pap smears might be acceptable specimens for NAAT, although test sensitivity using these specimens might be lower than that associated with use of cervical or vaginal swab specimens (*799*); regardless, certain NAATs have been cleared by FDA for use on liquid-based cytology specimens.

Rectal and oropharyngeal *C. trachomatis* infection among persons engaging in receptive anal or oral intercourse can be diagnosed by testing at the anatomic exposure site. NAATs have been demonstrated to have improved sensitivity and specificity, compared with culture, for detecting *C. trachomatis* at rectal and oropharyngeal sites (*553*,*800*–*804*), and certain NAAT platforms have been cleared by FDA for these anatomic sites (*805*). Data indicate that NAAT performance on self-collected rectal swabs is comparable to clinician-collected rectal swabs, and this specimen collection strategy for rectal *C. trachomatis* screening is highly acceptable among men (*217*,*806*). Self-collected rectal swabs are a reasonable alternative to clinician-collected rectal swabs for *C. trachomatis* screening by NAAT, especially when clinicians are not available or when self-collection is preferred over clinician collection. Annual screening for rectal *C. trachomatis* infection should be performed among men who report sexual activity at the rectal site. Extragenital chlamydial testing at the rectal site can be considered for females on the basis of reported sexual behaviors and exposure through shared clinical decision-making by the patient and the provider. The majority of persons with *C. trachomatis* detected at oropharyngeal sites do not have oropharyngeal symptoms. The clinical significance of oropharyngeal *C. trachomatis* infection is unclear, and prevalence is low, even among populations at high risk. However, when gonorrhea testing is performed at the oropharyngeal site, chlamydia test results might be reported because certain NAATs detect both bacteria from a single specimen.

POC tests for *C. trachomatis* among asymptomatic persons can expedite treatment of infected persons and their sex partners. Among symptomatic patients, POC tests for *C. trachomatis* can optimize treatment by limiting unnecessary presumptive treatment at the time of clinical decision-making and improve antimicrobial stewardship. Thus, using a POC test will likely be a cost-effective diagnostic strategy for *C. trachomatis* infection (*807*). Newer NAAT-based POC tests have promising performance and are becoming commercially available (*807*–*809*).

Treatment

Treating persons with *C. trachomatis* prevents adverse reproductive health complications and continued sexual transmission. Furthermore, treating their sex partners can prevent reinfection and infection of other partners. Treating pregnant women usually prevents transmission of *C. trachomatis* to neonates during birth. Treatment should be provided promptly for all persons with chlamydial infection; treatment delays have been associated with complications (e.g., PID) in a limited proportion of women (*810*).

Recommended Regimens for Chlamydial Infection Among Adolescents and Adults

Doxycycline 100 mg orally 2 times/day for 7 days

Alternative Regimens

Azithromycin 1 g orally in a single dose
OR
Levofloxacin 500 mg orally once daily for 7 days

A meta-analysis and a Cochrane systematic review evaluated data from randomized clinical trials of azithromycin versus doxycycline for treating urogenital chlamydial infection determined that microbiologic treatment failure among men was higher for azithromycin than for doxycycline (*748*,*749*). Observational studies have also demonstrated that doxycycline is more efficacious for rectal *C. trachomatis* infection for men and women than azithromycin (*748*,*811*). A randomized trial for the treatment of rectal chlamydia infection among MSM reported microbiologic cure was 100% with doxycycline and 74% with azithromycin (*812*). A published review reported that *C. trachomatis* was detected at the anorectal site among 33%–83% of women who had urogenital *C. trachomatis* infection, and its detection was not associated with report of receptive anorectal sexual activity (*813*).

Although the clinical significance of oropharyngeal *C. trachomatis* infection is unclear and routine oropharyngeal screening is not recommended, oropharyngeal *C. trachomatis* can be sexually transmitted to genital sites (*211*,*814*); therefore, if *C. trachomatis* is identified from an oropharyngeal specimen while screening for pharyngeal gonorrhea, it should be treated. Evidence is limited regarding the efficacy of antimicrobial regimens for oropharyngeal chlamydia; however, a recently published observational study indicates doxycycline might be more efficacious than azithromycin for oropharyngeal chlamydia (*815*).

Available evidence supports that doxycycline is efficacious for *C. trachomatis* infections of urogenital, rectal, and oropharyngeal sites. Although azithromycin maintains high efficacy for urogenital *C. trachomatis* infection among women, concern exists regarding effectiveness of azithromycin for concomitant rectal *C. trachomatis* infection, which can occur commonly among women and cannot be predicted by reported sexual activity. Inadequately treated rectal *C. trachomatis* infection among women who have urogenital chlamydia can increase the risk for transmission and place women at risk for repeat urogenital *C. trachomatis* infection through autoinoculation from the anorectal site (*816*). Doxycycline is also available in a delayed-release 200-mg tablet formulation, which requires once-daily dosing for 7 days and is as effective as doxycycline 100 mg twice daily for 7 days for treating urogenital *C. trachomatis* infection in men and women. It is more costly but also has lower frequency of gastrointestinal side effects (*817*). Levofloxacin is an effective treatment alternative but is more expensive. Erythromycin is no longer recommended because of the frequency of gastrointestinal side effects, which can result in nonadherence. When nonadherence to doxycycline regimen is a substantial concern, azithromycin 1 g regimen is an alternative treatment option but might require posttreatment evaluation and testing because it has demonstrated lower treatment efficacy among persons with rectal infection.

Among persons receiving multidose regimens, medication should be dispensed with all doses involved, on-site and in the clinic, and the first dose should be directly observed. To maximize adherence with recommended therapies, on-site, directly observed single-dose therapy with azithromycin should always be available for persons for whom adherence with multiday dosing is a considerable concern.

Other Management Considerations

Doxy PEP as an STI Prevention Strategy – Guidelines on the use of doxycycline post-exposure prophylaxis (doxy PEP) to prevent some bacterial STIs.

To minimize disease transmission to sex partners, persons treated for chlamydia should be instructed to abstain from sexual intercourse for 7 days after single-dose therapy or until completion of a 7-day regimen and resolution of symptoms if present. To minimize risk for reinfection, patients also should be instructed to abstain from sexual intercourse until all of their sex partners have been treated. Persons who receive a diagnosis of chlamydia should be tested for HIV, gonorrhea, and syphilis. MSM who are HIV negative with a rectal chlamydia diagnosis should be offered HIV PrEP.

Follow-Up

Test of cure to detect therapeutic failure (i.e., repeat testing 4 weeks after completing therapy) is not advised for nonpregnant persons treated with the recommended or alternative regimens, unless therapeutic adherence is in question, symptoms persist, or reinfection is suspected. Moreover, using chlamydial NAATs at <4 weeks after completion of therapy is not recommended because the continued presence of nonviable organisms (*553*,*818*,*819*) can lead to false-positive results.

A high prevalence of *C. trachomatis* infection has been observed among women and men who were treated for chlamydial infection during the preceding months (*753*,*755*,*820–822*). The majority of posttreatment infections do not result from treatment failure but rather from reinfection caused by failure of sex partners to receive treatment or initiation of sexual activity with a new infected partner (*823*), indicating a need for improved education and treatment of sex partners. Repeat infections confer an elevated risk for PID and other complications among women. Men and women who have been treated for chlamydia should be retested approximately 3 months after treatment, regardless of whether they believe their sex partners were treated; scheduling the follow-up visit at the time of treatment is encouraged (*753*). If retesting at 3 months is not possible, clinicians should retest whenever persons next seek medical care <12 months after initial treatment.

Management of Sex Partners

Sex partners should be referred for evaluation, testing, and presumptive treatment if they had sexual contact with the partner during the 60 days preceding the patient's onset of symptoms or chlamydia diagnosis. Although the exposure intervals defining identification of sex partners at risk are based on limited data, the most recent sex partner should be evaluated and treated, even if the time of the last sexual contact was >60 days before symptom onset or diagnosis.

If health department partner management strategies (e.g., disease intervention specialists) are impractical or unavailable for persons with chlamydia, and if a provider is concerned that sex partners are unable to promptly access evaluation and treatment services, EPT should be considered as permitted by law (see Partner Services). Compared with standard patient referral of partners, this approach to therapy, which involves delivering the medication itself or a prescription by the patient or collaborating pharmacy, has been associated with decreased rates of persistent or recurrent chlamydia among women (*125–127*). Providers should provide patients with written educational materials to give to their partners about chlamydia, which should include notification that partners have been exposed and information about the importance of treatment. These materials also should inform partners about potential therapy-related allergies and adverse effects, along with symptoms indicative of complications (e.g., testicular pain among men and pelvic or abdominal pain among women). Educational materials for female partners should include information about the importance of seeking medical evaluation, especially if PID symptoms are present; undertreatment of PID among female partners and missed opportunities for diagnosing other STIs among women are concerning. MSM with chlamydia have a high risk for coexisting infections, especially undiagnosed HIV, among their partners and might have partners without HIV who could benefit from HIV PrEP. Data are also limited regarding effectiveness of EPT in reducing persistent or recurrent chlamydia among MSM (*123*,*133*,*134*); thus, shared clinical decision-making regarding EPT for MSM is recommended. Having partners accompany patients when they return for treatment is another strategy that has been used successfully for ensuring partner treatment (see Partner Services). To avoid reinfection, sex partners should be instructed to abstain from condomless sexual intercourse until they and their sex partners have been treated (i.e., after completion of a 7-day regimen) and any symptoms have resolved.

Special Considerations

Pregnancy

Clinical experience and published studies indicate that azithromycin is safe and effective during pregnancy (*824–826*). Doxycycline is contraindicated during the second and third trimesters of pregnancy because of risk for tooth discoloration. Human data reveal that levofloxacin presents a low risk to the fetus during pregnancy but has potential for toxicity during breastfeeding; however, data from animal studies increase concerns regarding cartilage damage to neonates (*431*).

Test of cure (i.e., repeat testing after completion of therapy) to document chlamydial eradication, preferably by NAAT, at approximately 4 weeks after therapy completion during pregnancy is recommended because severe sequelae can occur among mothers and neonates if the infection persists. In addition, all pregnant women who have chlamydial infection diagnosed should be retested 3 months after treatment. Detection of *C. trachomatis* infection during the third trimester is not uncommon among adolescent and young adult women, including those without *C. trachomatis* detected at the time of initial prenatal screening (*827*). Women aged <25 years and those at increased risk for chlamydia (i.e., 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) should be screened at the first prenatal visit and rescreened during the third trimester to prevent maternal postnatal complications and chlamydial infection in the infant (*149*).

Recommended Regimen for Chlamydial Infection During Pregnancy

Azithromycin 1 g orally in a single dose

Alternative Regimen

Amoxicillin 500 mg orally 3 times/day for 7 days

Because of concerns regarding chlamydia persistence after exposure to penicillin-class antibiotics that has been demonstrated in animal and in vitro studies, amoxicillin is listed as an alternative therapy for *C. trachomatis* for pregnant women (*828*,*829*). Erythromycin is no longer recommended because of the frequency of gastrointestinal side effects that can result in therapy nonadherence. In addition, systematic reviews and meta-analyses have noted an association with macrolide antimicrobials, especially erythromycin, during pregnancy and adverse child outcomes, indicating cautious use in pregnancy (*830–831*).

HIV Infection

Persons who have chlamydia and HIV infection should receive the same treatment regimen as those who do not have HIV.

Chlamydial Infection Among Neonates

Prenatal screening and treatment of pregnant women is the best method for preventing chlamydial infection among neonates. *C. trachomatis* infection of neonates results from perinatal exposure to the mother's infected cervix. Initial *C. trachomatis* neonatal infection involves the mucous membranes of the eye, oropharynx, urogenital tract, and rectum, although infection might be asymptomatic in these locations. Instead, *C. trachomatis* infection among neonates is most frequently recognized by conjunctivitis that develops 5–12 days after birth. *C. trachomatis* also can cause a subacute, afebrile pneumonia with onset at ages 1–3 months. Although *C. trachomatis* has been the most frequent identifiable infectious cause of ophthalmia neonatorum, neonatal chlamydial infections, including ophthalmia and pneumonia, have occurred less frequently since institution of widespread prenatal screening and treatment of pregnant women. Neonates born to mothers at high risk for chlamydial infection, with untreated chlamydia, or with no or unconfirmed prenatal care, are at high risk for infection. However, presumptive treatment of the neonate is not indicated because the efficacy of such treatment is unknown. Infants should be monitored to ensure prompt and age-appropriate treatment if symptoms develop. Processes should be in place to ensure communication between physicians and others caring for the mother and the newborn to ensure thorough monitoring of the newborn after birth.

Ophthalmia Neonatorum Caused by *C. trachomatis*

A chlamydial etiology should be considered for all infants aged ≤30 days who experience conjunctivitis, especially if the mother has a history of chlamydial infection. These infants should receive evaluation and age-appropriate care and treatment.

Preventing Ophthalmia Neonatorum Caused by *C. trachomatis*

Neonatal ocular prophylaxis with erythromycin, the only agent available in the United States for this purpose, is ineffective against chlamydial ophthalmia neonatorum (or pneumonia) (*833*). As an alternative, prevention efforts should focus on prenatal screening for *C. trachomatis,* including

- screening pregnant women at risk for *C. trachomatis* infection at the first prenatal visit (e.g., women aged <25 years and those aged ≥25 years 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);
- treating all pregnant women with *C. trachomatis* during pregnancy and performing a test of cure 4 weeks after treatment to verify chlamydial eradication; these women should also be retested 3 months after treatment and again in the third trimester or at time of delivery, and their partners should also be tested and treated;
- retesting pregnant women during the third trimester who initially tested negative but remained at increased risk for acquiring infection (e.g., women aged <25 years and those aged ≥25 years 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); and
- screening at delivery those pregnant women who were not screened for *C. trachomatis* during pregnancy if at risk or who had no prenatal care; physicians and others caring for the mother and the newborn should communicate to ensure follow-up on the results of laboratory tests performed at delivery, and if positive, prompt and age-appropriate treatment for the newborn and the mother.

Neonates born to mothers for whom prenatal chlamydia screening has been confirmed and the results are negative are not at high risk for infection.

Diagnostic Considerations

Sensitive and specific methods for diagnosing chlamydial ophthalmia in the neonate include both tissue culture and nonculture tests (e.g., DFA tests and NAATs). DFA is the only nonculture FDA-cleared test for detecting chlamydia from conjunctival swabs. NAATs are not cleared by FDA for detecting chlamydia from conjunctival swabs, and clinical laboratories should verify the procedure according to CLIA regulations. Specimens for culture isolation and nonculture tests

should be obtained from the everted eyelid by using a Dacron (DuPont)-tipped swab or the swab specified by the manufacturer's test kit; for culture and DFA, specimens must contain conjunctival cells, not exudate alone. Ocular specimens from neonates being evaluated for chlamydial conjunctivitis also should be tested for *N. gonorrhoeae* (see Ophthalmia Neonatorum Caused by *N. gonorrhoeae*).

Treatment

Recommended Regimen for Chlamydial Infection Among Neonates

Erythromycin base or **ethylsuccinate** 50 mg/kg body weight/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 among infants aged <6 weeks. Infants treated with either of these antimicrobials should be followed for IHPS signs and symptoms.

Although data regarding use of azithromycin for treating neonatal chlamydial infection are limited, available data demonstrate that a short therapy course might be effective (*834*). Topical antibiotic therapy alone is inadequate for treating ophthalmia neonatorum caused by chlamydia and is unnecessary when systemic treatment is administered.

Follow-Up

Because the efficacy of erythromycin treatment for ophthalmia neonatorum is approximately 80%, a second course of therapy might be required (*834*,*835*). Data regarding the efficacy of azithromycin for ophthalmia neonatorum are limited. Therefore, follow-up of infants is recommended to determine whether the initial treatment was effective. The possibility of concomitant chlamydial pneumonia should be considered (see Infant Pneumonia Caused by *C. trachomatis*).

Management of Mothers and Their Sex Partners

Mothers of infants who have ophthalmia caused by chlamydia and the sex partners of these women should be evaluated and presumptively treated for chlamydia (see Chlamydial Infection Among Adolescents and Adults).

Infant Pneumonia Caused by *C. trachomatis*

Chlamydial pneumonia among infants typically occurs at age 1–3 months and is a subacute pneumonia. Characteristic signs of chlamydial pneumonia among infants include a repetitive staccato cough with tachypnea and hyperinflation and bilateral diffuse infiltrates on a chest radiograph. In addition, peripheral eosinophilia (≥400 cells/mm^3) occurs frequently. Because clinical presentations differ, all infants aged 1–3 months suspected of having pneumonia, especially those whose mothers have a history of, are at risk for (e.g., aged <25 years and those aged ≥25 years 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), or suspected of having a chlamydial infection should be tested for *C. trachomatis* and treated if infected.

Diagnostic Considerations

Specimens for chlamydial testing should be collected from the nasopharynx. Tissue culture is the definitive standard diagnostic test for chlamydial pneumonia. Nonculture tests (e.g., DFA and NAAT) can be used. DFA is the only nonculture FDA-cleared test for detecting *C. trachomatis* from nasopharyngeal specimens; however, DFA of nasopharyngeal specimens has a lower sensitivity and specificity than culture. NAATs are not cleared by FDA for detecting chlamydia from nasopharyngeal specimens, and clinical laboratories should verify the procedure according to CLIA regulations (*553*). Tracheal aspirates and lung biopsy specimens, if collected, should be tested for *C. trachomatis*.

Treatment

Because test results for chlamydia often are unavailable at the time initial treatment decisions are being made, treatment for *C. trachomatis* pneumonia frequently is based on clinical and radiologic findings, age of the infant (i.e., 1–3 months), and risk for chlamydia in the mother (i.e., aged <25 years, history of chlamydial infection, multiple sex partners, a sex partner with a concurrent partner, or a sex partner with a history of an STI). In the absence of laboratory results in a situation with a high degree of suspicion of chlamydial infection and the mother is unlikely to return with the infant for follow-up, exposed infants can be presumptively treated with the shorter-course regimen of azithromycin 20 mg/kg body weight/day orally, 1 dose daily for 3 days.

Recommended Regimen for Chlamydial Pneumonia Among Infants

Erythromycin base or **ethylsuccinate** 50 mg/kg body weight/day orally divided into 4 doses daily for 14 days

Alternative Regimen

Azithromycin suspension 20 mg/kg body weight/day orally, 1 dose daily for 3 days

Follow-Up

Because erythromycin effectiveness in treating pneumonia caused by *C. trachomatis* is approximately 80%, a second course of therapy might be required [833]. Data regarding effectiveness of azithromycin in treating chlamydial pneumonia are limited. Follow-up of infants is recommended to determine if the pneumonia has resolved, although certain infants with chlamydial pneumonia continue to have abnormal pulmonary function tests later during childhood.

Management of Mothers and Their Sex Partners

Mothers of infants who have chlamydial pneumonia and the sex partners of these women should be evaluated, tested, and presumptively treated for chlamydia (see, Chlamydial Infection Among Adolescents and Adults).

Chlamydial Infections Among Infants and Children

Sexual abuse should be considered a cause of chlamydial infection among infants and children. However, perinatally transmitted *C. trachomatis* infection of the nasopharynx, urogenital tract, and rectum can persist for 2–3 years (see Sexual Assault or Abuse of Children).

Diagnostic Considerations

NAATs can be used to test vaginal and urine specimens from girls and urine in boys (see Sexual Assault or Abuse of Children). Data are lacking regarding use of NAATs for specimens from extragenital sites (rectum and pharynx) among boys and girls (*553*); other nonculture tests (e.g., DFA) are not recommended because of specificity concerns. Although data regarding NAATs for specimens from extragenital sites for children are more limited and performance is test dependent (*553*), no evidence supports that NAAT performance for detecting *C. trachomatis* for extragenital sites among children would differ from that among adults. Because of the implications of a diagnosis of *C. trachomatis* infection in a child, only CLIA-validated, FDA-cleared NAAT should be used for extragenital site specimens (*837*).

Recommended Regimens for Chlamydial Infection Among Infants and Children

For Infants and Children Who Weigh <45 kg: Erythromycin base or **ethylsuccinate** 50 mg/kg body weight/day orally divided into 4 doses daily for 14 days

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

For children weighing ≥45 kg but aged <8 years: Azithromycin 1 g orally in a single dose

For children aged ≥8 years: Azithromycin 1 g orally in a single dose

or

Doxycycline 100 mg orally 2 times/day for 7 days

Other Management Considerations

See Sexual Assault or Abuse of Children.

Follow-Up

A test of cure to detect therapeutic failure ensures treatment effectiveness and should be obtained at a follow-up visit approximately 4 weeks after treatment is completed.

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