Centers for Disease Control and Prevention
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Chlamydial Infections

Chlamydial Infections in Adolescents and Adults

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Chlamydial infection is the most frequently reported infectious disease in the United States, and prevalence is highest in persons aged ≤24 years (*118*). Several sequelae can result from *C. trachomatis* infection in women, the most serious of which include PID, ectopic pregnancy, and infertility. Some women who receive a diagnosis of uncomplicated cervical infection already have subclinical upper-reproductive–tract infection.

Asymptomatic infection is common among both men and women. To detect chlamydial infections, 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., those who have a new sex partner, more than one sex partner, a sex partner with concurrent partners, or a sex partner who has a sexually transmitted infection (*108*). Although CT incidence might be higher in some women aged ≥25 years in some communities, overall the largest burden of infection is among women aged <25 years.

Chlamydia screening programs have been demonstrated to reduce the rates of PID in women (*497,498*). Although evidence is insufficient to recommend routine screening for *C. trachomatis* in sexually active young men because of several factors (e.g., feasibility, efficacy, and cost-effectiveness), the screening of sexually active young men should be considered in clinical settings with a high prevalence of chlamydia (e.g., adolescent clinics, correctional facilities, and STD clinics) or in populations with high burden of infection (e.g., MSM) *(108,121)*. Among women, the primary focus of chlamydia screening efforts should be to detect chlamydia, prevent complications, and test and treat their partners, whereas targeted chlamydia screening in men should only be considered when resources permit, prevalence is high, and such screening does not hinder chlamydia screening efforts in women (*499,500*). More frequent screening for some women (e.g., adolescents) or certain men (e.g., MSM) might be indicated.

Diagnostic Considerations

C. trachomatis urogenital infection can be diagnosed in women by testing first-catch urine or collecting swab specimens from the endocervix or vagina. Diagnosis of *C. trachomatis* urethral infection in men can be made by testing a urethral swab or first-catch urine specimen. NAATs are the most sensitive tests for these specimens and therefore are recommended for detecting *C. trachomatis* infection (*394*). NAATs that are FDA-cleared for use with vaginal swab specimens can be collected by a provider or self-collected in a clinical setting. Self-collected vaginal swab specimens are equivalent in sensitivity and specificity to those collected by a clinician using NAATs (*501,502*), and women find this screening strategy highly acceptable (*503,504*). Optimal urogenital specimen types for chlamydia screening using NAAT include first catch-urine (men) and vaginal swabs (women) (*394*). Rectal and oropharyngeal *C. trachomatis* infection in persons engaging in receptive anal or oral intercourse can be diagnosed by testing at the anatomic site of exposure. NAATs are not FDA-cleared for use with rectal or oropharyngeal swab specimens. However, NAATs have been demonstrated to have improved sensitivity and specificity compared with culture for the detection of *C. trachomatis* at rectal sites (*505-507*) and at oropharyngeal sites among men (*505-508*). Some laboratories have established CLIA-defined performance specifications when evaluating rectal and oropharyngeal swab specimens for *C. trachomatis,* thereby allowing results to be used for clinical management. Most persons with *C. trachomatis* detected at oropharyngeal sites do not have oropharyngeal symptoms. However, when gonorrhea testing is performed at the oropharyngeal site, chlamydia test results might be reported as well because some NAATs detect both bacteria from a single specimen. Data indicate that performance of NAATs 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 (*509-511*). 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. Previous evidence suggests that the liquid-based cytology specimens collected for Pap smears might be acceptable specimens for NAAT testing, although test sensitivity using these specimens might be lower than that associated with use of cervical or vaginal swab specimens (*512*); regardless, certain NAATs have been FDA-cleared for use on liquid-based cytology specimens.

Treatment

Treating persons infected with *C. trachomatis* prevents adverse reproductive health complications and continued sexual transmission, and 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. Chlamydia treatment should be provided promptly for all persons testing positive for infection; treatment delays have been associated with complications (e.g., PID) in a limited proportion of women (*513*).

Recommended Regimens

Azithromycin 1 g orally in a single dose
OR

Doxycycline 100 mg orally twice a day for 7 days

Alternative Regimens
Erythromycin base 500 mg orally four times a day for 7 days OR
Erythromycin ethylsuccinate 800 mg orally four times a day for 7 days OR
Levofloxacin 500 mg orally once daily for 7 days OR
Ofloxacin 300 mg orally twice a day for 7 days

A meta-analysis of 12 randomized clinical trials of azithromycin versus doxycycline for the treatment of urogenital chlamydial infection demonstrated that the treatments were equally efficacious, with microbial cure rates of 97% and 98%, respectively (*514*). These studies were conducted primarily in populations with urethral and cervical infection in which follow-up was encouraged, adherence to a 7-day regimen was effective, and culture or EIA (rather than the more sensitive NAAT) was used for determining microbiological outcome. More recent retrospective studies have raised concern about the efficacy of azithromycin for rectal *C. trachomatis* infection (*515,516*), however, these studies have limitations, and prospective clinical trials comparing azithromycin versus doxycycline regimens for rectal *C. trachomatis* infection are needed.

Although the clinical significance of oropharyngeal *C. trachomatis* infection is unclear and routine oropharyngeal screening for CT is not recommended, available evidence suggests oropharyngeal *C. trachomatis* can be sexually transmitted to genital sites (*152,517*); therefore, detection of *C. trachomatis* from an oropharyngeal specimen should be treated with azithromycin or doxycycline. The efficacy of alternative antimicrobial regimens in resolving oropharyngeal chlamydia remains unknown.

In a double-blinded randomized control trial, a doxycycline delayed-release 200 mg tablet administered daily for 7 days was as effective as generic doxycycline 100 mg twice daily for 7 days for treatment of urogenital *C. trachomatis* infection in men and women and had a lower frequency of gastrointestinal side effects. However, this regimen is more costly than those that involve multiple daily doses (*518*). Delayed-release doxycycline (Doryx) 200 mg daily for 7 days might be an alternative regimen to the doxycycline 100 mg twice daily for 7 days for treatment of urogenital *C. trachomatis* infection. Erythromycin might be less efficacious than either azithromycin or doxycycline, mainly because of the frequent occurrence of gastrointestinal side effects that can lead to nonadherence with treatment. Levofloxacin and ofloxacin are effective treatment alternatives, but they are more expensive and offer no advantage in the dosage regimen. Other quinolones either are not reliably effective against chlamydial infection or have not been evaluated adequately.

Other Management Considerations

To maximize adherence with recommended therapies, onsite, directly observed single-dose therapy with azithromycin should always be available for persons for whom adherence with multiday dosing is a concern. In addition, for multidose regimens, the first dose should be dispensed on site and directly observed. 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 are treated. Persons who receive a diagnosis of chlamydia should be tested for HIV, GC, and syphilis.

Follow-Up

Test-of-cure to detect therapeutic failure (i.e., repeat testing 3–4 weeks after completing therapy) is not advised for persons treated with the recommended or alterative regimens, unless therapeutic adherence is in question, symptoms persist, or reinfection is suspected. Moreover, the use of chlamydial NAATs at <3 weeks after completion of therapy is not recommended because the continued presence of nonviable organisms (*394,395,519*) can lead to false-positive results.

A high prevalence of *C. trachomatis* infection has been observed in women and men who were treated for chlamydial infection during the preceding several months (*480,481,520-522*). Most post-treatment infections do not result from treatment failure, but rather from reinfection caused by failure of sex partners to receive treatment or the initiation of sexual activity with a new infected partner, indicating a need for improved education and treatment of sex partners. Repeat infections confer an elevated risk for PID and other complications in women. Men and women who have been treated for chlamydia should be retested approximately 3 months after treatment, regardless of whether they believe that their sex partners were treated (*480,481*). If retesting at 3 months is not possible, clinicians should retest whenever persons next present for medical care in the 12-month period following 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 defined for the identification of at-risk sex partners 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.

Among heterosexual patients, if health department partner management strategies (e.g., disease intervention specialists) are impractical or not available for persons with chlamydia and 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, has been associated with decreased rates of persistent or recurrent chlamydia (*93-95*). Providers should also provide patients with written educational materials to give to their partner(s) about chlamydia in general, to include notification that partner(s) 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 suggestive of complications (e.g., testicular pain in men and pelvic or abdominal pain in women). EPT is not routinely recommended for MSM with chlamydia because of a high risk for coexisting infections (especially undiagnosed HIV) among their partners, and because data are limited regarding the effectiveness of this approach in reducing persistent or recurrent chlamydia among MSM. Having partners accompany patients when they return for treatment is another strategy that has been used to ensure partner treatment (See Partner Services). To avoid reinfection, sex partners should be instructed to abstain from sexual intercourse until they and their sex partners have been adequately treated (i.e., for 7 days after a single-dose regimen or after completion of a 7-day regimen) and have resolved any symptoms.

Special Considerations

Pregnancy

Doxycycline is contraindicated in the second and third trimesters of pregnancy. Human data suggest ofloxacin and levofloxacin present a low risk to the fetus during pregnancy, with a potential for toxicity during breastfeeding; however, data from animal studies raise concerns about cartilage damage to neonates (*317*). Thus, alternative drugs should be used to treat chlamydia in pregnancy. Clinical experience and published studies suggest that azithromycin is safe and effective (*523-525*). Test-of-cure to document chlamydial eradication (preferably by NAAT) 3–4 weeks after completion of therapy is recommended because severe sequelae can occur in 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 at repeat screening during the third semester is not uncommon in adolescent and young adult women, including in those without *C. trachomatis* detected at the time of initial prenatal screening (*526,527*). Women aged <25 years and those at increased risk for chlamydia (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 a sexually transmitted infection) should be rescreened during the third trimester to prevent maternal postnatal complications and chlamydial infection in the infant (*108*).

Recommended Regimens
Azithromycin 1 g orally in a single dose
Alternative Regimens
Amoxicillin 500 mg orally three times a day for 7 days OR
Erythromycin base 500 mg orally four times a day for 7 days OR
Erythromycin base 250 mg orally four times a day for 14 days OR
Erythromycin ethylsuccinate 800 mg orally four times a day for 7 days OR
Erythromycin ethylsuccinate 400 mg orally four times a day for 14 days

Because of concerns about chlamydia persistence following exposure to penicillin-class antibiotics that has been demonstrated in animal and in vitro studies, amoxicillin is now considered an alternative therapy for *C. trachomatis* in pregnant women (*528,529*). The frequent gastrointestinal side effects associated with erythromycin can result in nonadherence with these alternative regimens. The lower dose 14-day erythromycin regimens can be considered if gastrointestinal tolerance is a concern. Erythromycin estolate is contraindicated during pregnancy because of drug-related hepatotoxicity.

HIV Infection

Persons who have chlamydia and HIV infection should receive the same treatment regimen as those who do not have HIV infection. For more information, see Chlamydia, Treatment.

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Chlamydial Infections 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. Although the efficacy of neonatal ocular prophylaxis with erythromycin ophthalmic ointments to prevent chlamydia ophthalmia is not clear, ocular prophylaxis with these agents prevents gonococcal ophthalmia and therefore should be administered (see Ophthalmia Neonatorum Caused by *N. gonnorrhoeae)*.

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 in 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 the institution of widespread prenatal screening and treatment of pregnant women.

Ophthalmia Neonatorum Caused by *C. trachomatis*

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

Diagnostic Considerations

Sensitive and specific methods used to diagnose chlamydial ophthalmia in the neonate include both tissue culture and nonculture tests (e.g., direct fluorescence antibody [DFA] tests and NAAT). DFA is the only nonculture FDA-cleared test for the detection of chlamydia from conjunctival swabs; NAATs are not FDA-cleared for the detection of chlamydia from conjunctival swabs, and clinical laboratories must verify the procedure according to CLIA regulations. Specimens for culture isolation and nonculture tests should be obtained from the everted eyelid using a dacron-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. gonnorrhoeae*).

Treatment of Ophthalmia Neonatorum

Recommended Regimen
Erythromycin base or ethylsuccinate 50 mg/kg/day orally divided into 4 doses daily for 14 days*
Alternative Regimen
Azithromycin suspension, 20 mg/kg/day orally, 1 dose daily for 3 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 signs and symptoms of IHPS.

Although data on the use of azithromycin for the treatment of neonatal chlamydia infection are limited, available data suggest a short course of therapy might be effective (*530*). Topical antibiotic therapy alone is inadequate for treatment for 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 (*531*). Data on the efficacy of azithromycin for ophthalmia neonatorum are limited. Therefore, follow-up of infants is recommended to determine whether 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. For more information, see Chlamydial Infection in Adolescents and Adults.

Infant Pneumonia Caused by *C. trachomatis*

Chlamydia pneumonia in infants typically occurs at 1–3 months and is a subacute pneumonia. Characteristic signs of chlamydial pneumonia in infants include 1) a repetitive staccato cough with tachypnea and 2) hyperinflation and bilateral diffuse infiltrates on a chest radiograph. In addition, peripheral eosinophilia (≥400 cells/mm3) occurs frequently. Because clinical presentations differ, all infants aged 1–3 months suspected of having pneumonia (especially those whose mothers have a history of 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 the detection of *C. trachomatis* from nasopharyngeal specimens, but DFA of nasopharyngeal specimens has a lower sensitivity and specificity than culture. NAATs are not FDA-cleared for the detection of chlamydia from nasopharyngeal specimens, and clinical laboratories must verify the procedure according to CLIA regulations (*394*). Tracheal aspirates and lung biopsy specimens, if collected, should be tested for *C. trachomatis*.

Treatment

Because test results for chlamydia often are not available at the time that initial treatment decisions must be made, treatment for *C. trachomatis* pneumonia must frequently be based on clinical and radiologic findings, age of the infant (i.e., 1–3 months), and risk of chlamydia in the mother (i.e., age <25, multiple partners, and history of chlamydial infection). The results of tests for chlamydial infection assist in the management of an infant's illness.

Recommended Regimen
Erythromycin base or ethylsuccinate 50 mg/kg/day orally divided into 4 doses daily for 14 days
Alternative Regimen

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

Follow-Up

Because the effectiveness of erythromycin in treating pneumonia caused by *C. trachomatis* is approximately 80%, a second course of therapy might be required (*532*). Data on the effectiveness of azithromycin in treating chlamydial pneumonia are limited. Follow-up of infants is recommended to determine whether the pneumonia has resolved, although some infants with chlamydial pneumonia continue to have abnormal pulmonary function tests later in childhood.

Management of Mothers and Their Sex Partners

Mothers of infants who have chlamydia pneumonia and the sex partners of these women should be evaluated, tested, and presumptively treated for chlamydia. For more information, see Chlamydial Infection in Adolescents and Adults.

Neonates Born to Mothers Who Have Chlamydial Infection

Neonates born to mothers who have untreated chlamydia are at high risk for infection; however, prophylactic antibiotic treatment is not indicated, as the efficacy of such treatment is unknown. Infants should be monitored to ensure appropriate treatment if symptoms develop.

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Chlamydial Infections Among Infants and Children

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

Diagnostic Considerations

NAAT can be used for vaginal and urine specimens from girls (see Sexual Assault or Abuse of Children), although data are insufficient to recommend the use of NAAT in boys. Data also are lacking regarding use of NAAT for specimens from extragenital sites (rectum and pharynx) in boys and girls (*394*); other nonculture tests (e.g., DFA) are not recommended because of specificity concerns. Culture is still the preferred method for detection of urogenital *C. trachomatis* in boys and at extragenital sites in boys and girls.

Recommended Regimen for Infants and Children Who Weigh <45 kg

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

Data are limited on the effectiveness and optimal dose of azithromycin for the treatment of chlamydial infection in infants and children who weigh <45 kg

Recommended Regimen for Children Who Weigh ≥45 kg but Who Are 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
OR

Doxycycline 100 mg orally twice a day for 7 days

Other Management Considerations

See Sexual Assault or Abuse of Children.

Follow-Up

A test-of-cure culture (repeat testing after completion of therapy) to detect therapeutic failure ensures treatment effectiveness. Therefore, this culture with should be obtained at a follow-up visit approximately 2 weeks after treatment is completed.

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