

Diagnosis and Treatment of *Chlamydia trachomatis* Infection

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Chlamydia trachomatis infection most commonly affects the urogenital tract. In men, the infection usually is symptomatic, with dysuria and a discharge from the penis. Untreated chlamydial infection in men can spread to the epididymis. Most women with chlamydial infection have minimal or no symptoms, but some develop pelvic inflammatory disease. Chlamydial infection in newborns can cause ophthalmia neonatorum. Chlamydial pneumonia can occur at one to three months of age, manifesting as a protracted onset of staccato cough, usually without wheezing or fever. Treatment options for uncomplicated urogenital infections include a single 1-g dose of azithromycin orally, or doxycycline at a dosage of 100 mg orally twice per day for seven days. The recommended treatment during pregnancy is erythromycin base or amoxicillin. The Centers for Disease Control and Prevention and the U.S. Preventive Services Task Force recommend screening for chlamydial infection in women at increased risk of infection and in all women younger than 25 years. (*Am Fam Physician* 2006;73:1411-6. Copyright © 2006 American Academy of Family Physicians.)

The incidence of chlamydial infection in women increased dramatically between 1987 and 2003, from 79 to 467 per 100,000.¹ In part, this may be attributed to increased screening and improved reporting, but the burden of the disease still is significant. The most common site of *Chlamydia trachomatis* infection is the urogenital tract, and severity ranges from asymptomatic to life-threatening.

Urogenital Infection in Women

In women, chlamydial infection of the lower genital tract occurs in the endocervix. It can cause an odorless, mucoid vaginal discharge, typically with no external pruritus, although many women have minimal or no symptoms.² An ascending infection can result in pelvic inflammatory disease (PID).

Physical findings of urogenital chlamydial infection in women include cervicitis with a yellow or cloudy mucoid discharge from the os. The cervix tends to bleed easily when rubbed with a polyester swab or scraped with a spatula. Chlamydial infection cannot be distinguished from other urogenital infections by symptoms alone. Clinical microscopy and the amine test

(i.e., significant odor release on addition of potassium hydroxide to vaginal secretions) can be used to help differentiate chlamydial infection from other lower genital tract infections such as urinary tract infection, bacterial vaginosis, and trichomoniasis.³ In addition, chlamydial infection in the lower genital tract does not cause vaginitis; thus, if vaginal findings are present, they usually indicate a different diagnosis or a coinfection.

Some women with *C. trachomatis* infection develop urethritis; symptoms may consist of dysuria without frequency or urgency. A urethral discharge can be elicited by compressing the urethra during the pelvic examination. Urinalysis usually will show more than five white blood cells per high-powered field, but urethral cultures generally are negative.

Women with chlamydial infection in the lower genital tract may develop an ascending infection that causes acute salpingitis with or without endometritis, also known as PID. Symptoms tend to have a subacute onset and usually develop during menses or in the first two weeks of the menstrual cycle.² Symptoms range from absent to severe abdominal pain with high fever and include dyspareunia, prolonged menses, and intramenstrual bleeding. Twenty percent of

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SORT: KEY RECOMMENDATIONS FOR PRACTICE

<i>Clinical recommendation</i>	<i>Evidence rating</i>	<i>References</i>
Azithromycin (Zithromax) or doxycycline (Vibramycin) is recommended for the treatment of uncomplicated genitourinary chlamydial infection.	A	2, 6
Amoxicillin is recommended for the treatment of chlamydial infection in women who are pregnant.	A	2, 7, 8
Patients who are pregnant should be tested for cure three weeks after treatment for chlamydial infection.	C	2
Women with chlamydial infection should be rescreened for infection three to four months after completion of antibiotic therapy.	C	2
All women who are 25 years or younger or at increased risk of sexually transmitted diseases should be screened for chlamydial infection annually.	A	2, 13, 14

A = consistent, good-quality patient-oriented evidence; B = inconsistent or limited-quality patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, see page 1313 or <http://www.aafp.org/afpsort.xml>.

women who develop PID become infertile, 18 percent develop chronic pelvic pain, and 9 percent have a tubal pregnancy.² The Centers for Disease Control and Prevention (CDC) recommends that physicians maintain a low threshold for diagnosing PID and that empiric treatment be initiated in women at risk of sexually transmitted disease (STD) who have uterine, adnexal, or cervical motion tenderness with no other identifiable cause.²

Culture techniques are the preferred method for detecting *C. trachomatis* infection, but they have been replaced in some instances by nonculture techniques. The newest nonculture technique is the nucleic acid amplification test, of which there are several. These tests have good sensitivity (85 percent) and specificity (94 to 99.5 percent) for endocervical and urethral samples when compared with urethral cultures.⁴ In women with urogenital disease, nucleic acid amplification tests can be used with an endocervical sample or a urine specimen to diagnose chlamydia.

The CDC recommends that anyone who is tested for chlamydial infection also should be tested for gonorrhea.² This recommendation was supported by a study⁵ in which

20 percent of men and 42 percent of women with gonorrhea also were found to be infected with *C. trachomatis*.

Urogenital Infection in Men

In men, chlamydial infection of the lower genital tract causes urethritis and, on occasion, epididymitis. Urethritis is secondary to *C. trachomatis* infection in approximately 15 to 55 percent of men, although the prevalence is lower among older men.² Symptoms, if present, include a mild to moderate, clear to white urethral discharge. This is best observed in the morning, before the patient voids. To observe the discharge, the penis may need to be milked by applying pressure from the base of the penis to the glans.

The diagnosis of nongonococcal urethritis can be confirmed by the presence of a mucopurulent discharge from the penis, a Gram stain of the discharge with more than five white blood cells per oil-immersion field, and no intracellular gram-negative diplococci.² A positive result on a leukocyte esterase test of first-void urine or a microscopic examination of first-void urine showing 10 or more white blood cells per high-powered field also confirms the diagnosis of urethritis.

For diagnosis of *C. trachomatis* infection in men with suspected urethritis, the nucleic acid amplification technique to detect

In one study, 20 percent of men and 42 percent of women with gonorrhea also had chlamydial infection.

chlamydial and gonococcal infections is best (see Urogenital Infection in Women).⁴ Empiric treatment should be considered for patients who are at high risk of being lost to follow-up.

Untreated chlamydial infection can spread to the epididymis. Patients usually have unilateral testicular pain with scrotal erythema, tenderness, or swelling over the epididymis. Men 35 years or younger who have epididymitis are more likely to have *C. trachomatis* as the etiologic agent than are older men.

Reiter Syndrome

A rare complication of untreated chlamydial infection is the development of Reiter syndrome, a reactive arthritis that includes the triad of urethritis (sometimes cervicitis in women), conjunctivitis, and painless mucocutaneous lesions. Reactive arthritis develops in a small percentage of individuals with chlamydial infection. Women can develop reactive arthritis, but the male-to-female ratio is 5:1. The arthritis begins one to three weeks after the onset of chlamydial infection. The joint involvement is asymmetric, with multiple affected joints and a predilection for the lower extremities. The mucocutaneous lesions are papulosquamous eruptions that tend to occur on the palms of the hands and the soles of the feet. The initial episode usually lasts for three to four months, but in rare cases the synovitis may last about one year.

Treatment of Urogenital Infection

The treatment of *C. trachomatis* infection depends on the site of the infection, the age of the patient, and whether the infection is complicated or uncomplicated. Treatment also differs during pregnancy.

UNCOMPLICATED INFECTION

For uncomplicated genitourinary chlamydial infection, the CDC recommends 1 g azithromycin (Zithromax) orally in a single dose, or 100 mg doxycycline (Vibramycin) orally twice per day for seven days (Table 1).² These regimens have similar cure rates and adverse effect profiles,⁶ although a benefit of azithromycin is that physicians can administer the

dose in the office. If patients vomit the dose of azithromycin within one to two hours of taking the medication, an alternative treatment should be considered (Table 1).²

Follow-up of patients with urethritis is necessary only if symptoms persist or recur after completion of the antibiotic course. If symptoms suggest recurrent or persistent urethritis, the CDC recommends treatment with 2 g metronidazole (Flagyl) orally in a single dose plus 500 mg erythromycin base orally four times per day for seven days, or 800 mg erythromycin ethylsuccinate orally four times per day for seven days.² This recommendation is to provide treatment for other bacterial causes of urethritis.

Patients should be advised to abstain from sexual intercourse for seven days after treatment initiation. In addition, physicians should obtain exposure information for the preceding 60 days and consider screening for other STDs such as human immunodeficiency virus (HIV).²

The CDC does not recommend repeat testing for chlamydia after completion of the antibiotic course unless the patient has persistent symptoms or is pregnant.² Because reinfection is a common problem, the CDC recommends that women with chlamydial infection should be rescreened three to four months after antibiotic completion. Women who present within 12 months after the

TABLE 1
CDC-Recommended Regimens for Uncomplicated Urogenital Chlamydial Infection in Adults

Recommended

Azithromycin (Zithromax) 1 g orally in a single dose
Doxycycline (Vibramycin) 100 mg orally twice per day

Alternatives

Erythromycin base 500 mg orally four times per day
Erythromycin ethylsuccinate 800 mg orally four times per day
Ofloxacin (Floxin) 300 mg twice per day
Levofloxacin (Levaquin) 500 mg once per day

NOTE: All regimens except azithromycin are for a total of seven days.

CDC = Centers for Disease Control and Prevention.

Information from reference 2.

TABLE 2
CDC-Recommended Regimens for Treatment of PID

Oral

Ofloxacin (Floxin) 400 mg orally twice daily for 14 days or levofloxacin (Levaquin) 500 mg orally once daily for 14 days; *with or without* metronidazole (Flagyl) 500 mg orally twice daily for 14 days

Alternative:

Ceftriaxone (Rocephin) 250 mg IM in a single dose or cefoxitin (Mefoxin) 2 g IM in a single dose with concurrent probenecid (Benemid) 1 g orally in single dose or other parenteral third-generation cephalosporin; *plus* doxycycline (Vibramycin) 100 mg orally twice daily for 14 days *with or without* metronidazole 500 mg orally twice daily for 14 days

Parenteral

Cefotetan (Cefotan) 2 g IV every 12 hours or cefoxitin 2 g IV every six hours; *plus* doxycycline 100 mg orally or IV every 12 hours

Alternatives:

Clindamycin (Cleocin) 900 mg IV every eight hours; *plus* gentamicin loading dose IV or IM (2 mg per kg) followed by a maintenance dose (1.5 mg per kg) every eight hours (single daily dosing may be substituted)

Ofloxacin 400 mg IV every 12 hours or levofloxacin 500 mg IV once daily; *with or without* metronidazole 500 mg IV every eight hours

Ampicillin/sulbactam (Unasyn) 3 g IV every six hours; *plus* doxycycline 100 mg orally or IV every 12 hours

NOTE: Doxycycline should be given orally whenever possible because it causes sclerosis and obliteration of venous access when given IV.

CDC = Centers for Disease Control and Prevention; PID = pelvic inflammatory disease; IM = intramuscular; IV = intravenous.

Information from reference 2.

TABLE 3
CDC-Recommended Regimens for Treatment of Chlamydial Infection in Pregnant Women

Recommended

Erythromycin base 500 mg orally four times per day for seven days

Amoxicillin 500 mg orally three times per day for seven days

Alternatives

Erythromycin base 250 mg orally four times per day for 14 days

Erythromycin ethylsuccinate 800 mg orally four times per day for seven days

Erythromycin ethylsuccinate 400 mg four times per day for 14 days

Azithromycin (Zithromax) 1 g orally in a single dose

CDC = Centers for Disease Control and Prevention.

Information from reference 2.

initial infection and have not been screened should be reassessed for infection regardless of whether the patient believes her sex partner was treated or not.²

PELVIC INFLAMMATORY DISEASE

PID usually can be treated on an outpatient basis. Hospitalization is required if a patient is pregnant; has severe illness, nausea and vomiting, or high fever; has tubo-ovarian abscess; is unable to follow or tolerate the outpatient oral regimen; or has disease that has been unresponsive to oral therapy. Hospitalization also is indicated if surgical emergencies cannot be excluded.² The CDC-recommended options for the treatment of PID are listed in *Table 2*.²

TREATMENT DURING PREGNANCY

Doxycycline and ofloxacin (Floxin) are contraindicated during pregnancy; therefore, the CDC recommends erythromycin base or amoxicillin for the treatment of chlamydial infection in pregnant women (*Table 3*).² Amoxicillin is more effective and tends to have fewer side effects than erythromycin in the treatment of antenatal chlamydial infection, and thus is better tolerated.^{7,8} Preliminary data suggest that azithromycin is a safe and effective alternative.²

Testing for cure is indicated in patients who are pregnant and should be performed three weeks after completion of treatment.² Culture is the preferred technique.² If risk of reexposure is high, screening should be repeated throughout the pregnancy.

Chlamydial Infection in Children

Exposure to *C. trachomatis* during delivery can cause ophthalmia neonatorum (conjunctivitis) in neonates or chlamydial pneumonia at one to three months of age.

OPHTHALMIA NEONATORUM

Ophthalmia neonatorum usually occurs within five to 12 days of birth but can develop at any time up to one month of age.² It may cause swelling in one or both eyes with mucopurulent drainage. Prophylaxis with silver nitrate or antimicrobial ointment, which reduces the risk of gonococcal

infection in neonates, does not reduce the risk of chlamydial infection.

Testing for chlamydial infection in neonates can be by culture or nonculture techniques. The eyelid should be everted and the sample obtained from the inner aspect of the eyelid. Sampling the exudates is not adequate because this technique increases the risk of a false-negative test.

Ophthalmia neonatorum can be treated with erythromycin base or ethylsuccinate at a dosage of 50 mg per kg per day orally, divided into four doses per day for 14 days.² The cure rate for both options is only 80 percent, so a second course of therapy may be necessary. Topical treatment is ineffective for ophthalmia neonatorum and should not be used even in conjunction with systemic treatment.

CHLAMYDIAL PNEUMONIA

Symptoms of chlamydial pneumonia typically have a protracted onset and include a staccato cough, usually without wheezing or temperature elevation.² Findings on chest radiograph include hyperinflation and diffuse bilateral infiltrates; peripheral eosinophilia may be present.

Testing can be performed on a sample obtained from the nasopharynx. Nonculture techniques may be used, but they are less sensitive and specific for nasopharyngeal specimens than for ocular specimens. If tracheal aspirates or lung biopsies are being collected for pneumonia in infants one to three months of age, the samples should be tested for *C. trachomatis*.²

Like ophthalmia neonatorum, pneumonia secondary to *C. trachomatis* is treated with erythromycin base or ethylsuccinate at a dosage of 50 mg per kg per day orally, divided into four doses per day for 14 days.² As with ophthalmic infection, a second course of therapy may be necessary.

Prevention

The CDC guidelines for the prevention and control of STDs are based on five major concepts (Table 4).² Primary prevention starts with changing sexual behaviors that increase the risk of contracting STDs.² Secondary

TABLE 4

Concepts for Prevention of STDs

Education and counseling on safer sexual behavior in persons at risk
Identification of asymptomatic infected persons and of symptomatic persons unlikely to seek diagnostic and treatment services
Effective diagnosis and treatment of infected persons
Evaluation, treatment, and counseling of sex partners of persons infected with an STD
Pre-exposure immunizations for vaccine-preventable STDs

STD = sexually transmitted disease.

Information from reference 2.

prevention consists of standardized detection and treatment of STDs.^{9,10}

STD prevention messages should be individually tailored and based on stages of patient development and understanding of sexual issues; these messages should be delivered nonjudgmentally.¹¹ Physicians should address misconceptions about STDs among adolescents and young adults (e.g., that virgins cannot become infected). Performing counseling and discussing behavioral interventions have been shown to reduce the likelihood of STDs and reduce risky sexual behavior.¹²

The CDC recommends annual screening for chlamydial infection in all sexually active women 24 years and younger and in women older than 24 years who are at risk of STDs (e.g., have a new sex partner, have a history of multiple sex partners).² The U.S. Preventive Services Task Force (USPSTF) strongly recommends that all women 25 years and younger receive routine screening for chlamydia.¹³ Screening for chlamydial infection is not recommended for men, including those who have sex with other men.^{14,15} The USPSTF has found insufficient evidence to recommend for or against routine screening of asymptomatic men.¹³

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