Chlamydia Trachomatis Infections: Screening, Diagnosis, and Management

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***Chlamydia trachomatis* is a gram-negative bacterium that infects the columnar epithelium of the cervix, urethra, and rectum, as well as nongenital sites such as the lungs and eyes. The bacterium is the cause of the most frequently reported sexually transmitted disease in the United States, which is responsible for more than 1 million infections annually. Most persons with this infection are asymptomatic. Untreated infection can result in serious complications such as pelvic inflammatory disease, infertility, and ectopic pregnancy in women, and epididymitis and orchitis in men. Men and women can experience chlamydia-induced reactive arthritis. Treatment of uncomplicated cases should include azithromycin or doxycycline. Screening is recommended in all women younger than 25 years, in all pregnant women, and in women who are at increased risk of infection. Screening is not currently recommended in men. In neonates and infants, the bacterium can cause conjunctivitis and pneumonia. Adults may also experience conjunctivitis caused by chlamydia. Trachoma is a recurrent ocular infection caused by chlamydia and is endemic in the developing world. (*Am Fam Physician*. 2012;86(12):1127-1132. Copyright © 2012 American Academy of Family Physicians.)**

▶ **Patient information:** A handout on this topic is available at http://familydoctor.org/familydoctor/en/diseases-conditions/chlamydia.html.

Chlamydia trachomatis is a gram-negative bacterium that infects the columnar epithelium of the cervix, urethra, and rectum, as well as nongenital sites. The bacterium is the cause of the most frequently reported sexually transmitted disease in the United States,[1] and is the leading cause of infectious blindness in the world.[2] According to the Centers for Disease Control and Prevention (CDC) in 2009, the rate of sexually transmitted chlamydia infections in the United States was 426 cases per population of 100,000, which represents a 24 percent increase in the rate of infection since 2006.[3] More recent data from 2010 indicates that 1,307,893 chlamydia infections were reported to the CDC from all 50 states and the District of Columbia.[4] The CDC estimates that there are 2.8 million chlamydia cases in the United States annually—more than twice the number actually reported.[5] This is an increase of 5 percent over the past year, and 27 percent from four years ago.[5] From 2000 to 2010, the chlamydia screening rate among young women nearly doubled, from 25 to 48 percent.[5]

Genitourinary Infections

Genitourinary infection affects primarily young adults and persons with multiple sex partners.[6] Women carry a disproportionate burden: CDC statistics show that the overall rate of infection was almost three times higher among women than men,[7] although this may be because of existing screening programs for women. Approximately 79 percent of the U.S. health costs for chlamydia infections can be attributed to women.[8]

Young women 15 to 19 years of age carry the highest incidence of disease, followed by women 20 to 24 years of age. Although chlamydia is common in all races, blacks, American Indians/Alaska Natives, and Hispanic women are disproportionately affected. Other groups at higher risk include adolescents and men who have sex with men.[8]

According to the CDC, chlamydia infection rates in men are also increasing, and at a faster rate than in women. Between 2005 and 2009, the reported infection rate for men rose from 159.4 to 219.3 cases per 100,000 males, a 37.6 percent increase.[7] During the same period, the rate of infection among women increased 29.3 percent.[7]

Prevalence rates among men vary depending on the subgroups screened. One study reported a prevalence of 3.7 percent in men 18 to 26 years of age.[9] Other studies report an overall prevalence among asymptomatic men in the United States of between 6 and 7 percent, and as much as 18 to 20 percent in men attending

SORT: KEY RECOMMENDATIONS FOR PRACTICE

Clinical recommendation	*Evidence rating*	*References*
Nucleic acid amplification tests are the most sensitive tests for detecting chlamydia infection, and may be performed on endocervical, urethral, vaginal, pharyngeal, rectal, or urine samples.	C	13
Azithromycin (Zithromax) or doxycycline should be used for the treatment of uncomplicated genitourinary chlamydia infection in men and women.	A	15
Azithromycin or amoxicillin should be used as first-line treatment of genitourinary chlamydia infection in pregnant women.	A	16
The USPSTF recommends screening for chlamydia infection in all sexually active nonpregnant women 24 years and younger, and all nonpregnant women 25 years and older who are at increased risk.	A	24
The USPSTF concludes there is insufficient evidence to recommend for or against the screening of men for chlamydia infection.	C	24
Although the CDC recommends screening for chlamydia infection in all pregnant women, the USPSTF recommends routine screening only in all pregnant women 24 years and younger, and in pregnant women 25 years and older who are at increased risk.	B	1, 24
Some experts recommend screening certain groups of high-risk men (e.g., men who have sex with men) for rectal chlamydia infection.	C	1, 11

CDC = Centers for Disease Control and Prevention; USPSTF = U.S. Preventive Services Task Force.

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, go to http://www.aafp.org/afpsort.xml.

inner-city primary care clinics.[10] In select groups, such as men who have sex with men, rates of rectal infections were found to be high.[11] Risk factors for men and women include lack of condom use, lower socioeconomic status, living in an urban area, and having multiple sex partners.

PRESENTATION

Most persons who are infected with *C. trachomatis* are asymptomatic. However, when symptoms of infection are present, in women they most commonly include abnormal vaginal discharge, vaginal bleeding (including bleeding after intercourse), and dysuria.[12] On physical examination, mucopurulent or purulent discharge from the endocervical canal and cervical friability are common. In men, symptoms may include penile discharge, pruritus, and dysuria. However, in one study, only 2 to 4 percent of infected men reported any symptoms.[10]

***Chlamydia trachomatis* is the cause of the most frequently reported sexually transmitted disease in the United States.**

Persons who have receptive anal intercourse can acquire a rectal infection, which can present as pain, discharge, or bleeding. Those engaging in oral sex can acquire a pharyngeal infection from an infected partner.

DIAGNOSIS

Nucleic acid amplification tests (NAATs) are the most sensitive tests for detecting chlamydia and gonococcal infections.[13] NAATs can be performed on endocervical, urethral, vaginal, pharyngeal, rectal, or urine samples (first-void is preferred).[13] The accuracy of NAATs on urine samples has been found to be nearly identical to that of samples obtained directly from the cervix or urethra.[13] On wet mount, a finding of leukorrhea (more than 10 white blood cells per high-power field on microscopic examination of vaginal fluid) has been associated with chlamydia and gonococcal infections of the cervix.[1] Oropharyngeal and rectal swabs may be obtained in persons who engage in receptive oral or anal intercourse.[13]

Point-of-care testing at a physician's office is recommended, although increasingly, researchers have begun to evaluate commercially available mail-in kits. To date, commercial kits have not been shown to be reliable, and have lower sensitivity and specificity than NAATs.[14]

TREATMENT

Uncomplicated genitourinary chlamydia infection should be treated with azithromycin (Zithromax; 1 g, single dose) or doxycycline (100 mg twice daily for seven days; *Table 1* [1,15-22]). Studies indicate that both treatments are equally effective.[15] Although dual therapy to cover gonorrhea and chlamydia is recommended when patients are diagnosed with gonorrhea, additional coverage for gonorrhea is not required with the diagnosis of chlamydia alone.[1]

Alternative regimens for uncomplicated chlamydia infection include erythromycin (500 mg four times daily for seven days), erythromycin ethylsuccinate (800 mg four times daily for seven days), levofloxacin (Levaquin; 500 mg once daily for seven days), or ofloxacin (Floxin; 300 mg twice daily or 600 mg once daily for seven days).[1] Erythromycin is reported to have higher occurrences of gastrointestinal adverse effects.[15]

Table 1. Treatment Recommendations for Chlamydia-Induced Infections

Condition	*Recommended oral treatments*
Uncomplicated genitourinary infection[15]	Azithromycin (Zithromax), 1 g (single dose) *or* Doxycycline, 100 mg twice daily for seven days Alternatives: Erythromycin, 500 mg four times daily for seven days Erythromycin ethylsuccinate, 800 mg four times daily for seven days Levofloxacin (Levaquin), 500 mg once daily for seven days Ofloxacin (Floxin), 300 mg twice daily (or 600 mg once daily) for seven days
Infection during pregnancy[1,16]	Azithromycin, 1 g (single dose) *or* Amoxicillin, 500 mg three times daily for seven days Alternatives: Erythromycin, 500 mg four times daily for seven days, or 250 mg four times daily for 14 days Erythromycin ethylsuccinate, 800 mg four times daily for seven days, or 400 mg four times daily for 14 days
Chronic reactive arthritis[17,18]	Doxycycline, 100 mg twice daily, plus rifampin, 300 mg once daily for six months *or* Azithromycin, 500 mg once daily for five days, then 500 mg twice weekly, plus rifampin, 300 mg once daily for six months
Lymphogranuloma venereum[1]	Doxycycline, 100 mg twice daily for 21 days Alternatives: Erythromycin, 500 mg four times daily for 21 days Azithromycin, 1 g once weekly for three weeks
Neonatal pulmonary infection[19]	Erythromycin or erythromycin ethylsuccinate, 50 mg per kg daily in four divided doses for 14 days
Ocular infection: ophthalmia neonatorum[19]	Erythromycin or erythromycin ethylsuccinate, 50 mg per kg daily in four divided doses for 14 days
Adult-inclusion conjunctivitis[20,21]	Doxycycline, 100 mg twice daily for one to three weeks *or* Erythromycin, 250 mg four times daily for one to three weeks
Trachoma[22]	Azithromycin, 1 g (single dose) *or* Doxycycline, 100 mg twice daily for 21 days

Information from references 1, and 12 through 19.

Pregnant women may be treated with azithromycin (1 g, single dose) or amoxicillin (500 mg three times daily for seven days). Alternative regimens include erythromycin (500 mg four times daily for seven days or 250 mg four times daily for 14 days) and erythromycin ethylsuccinate (800 mg four times daily for seven days or 400 mg four times daily for 14 days). Although all three medications show similar effectiveness, a recent review indicates that azithromycin may have fewer adverse effects when compared with erythromycin or amoxicillin in pregnant women.[16]

Test of cure is recommended three to four weeks after completion of treatment in pregnant women only. If chlamydia is detected during the first trimester, repeat testing for reinfection should also be performed within three to six months, or in the third trimester.[1] Men and nonpregnant women should be retested at three months. If this is not possible, clinicians should retest the patient to screen for reinfection when he or she next presents for medical care within 12 months after treatment.[1]

Partners should be notified of infection and treated appropriately. Studies indicate that expedited partner therapy (partners treated without medical consultation) may improve clinical and behavioral outcomes pertaining to partner management among heterosexual men and women with chlamydia infection.[23] Partners should be referred for evaluation, testing, and treatment if they engaged in sexual contact within 60 days before a diagnosis was made or at the onset of symptoms.[1] Patients should also be instructed to abstain from sexual intercourse until seven days after a single-dose regimen or after completion of a multiple-dose regimen, and after their partner has also completed treatment.[1] Patients infected with human immunodeficiency virus (HIV) should be treated using the same regimens recommended for those who are HIV-negative *(Table 2)*.[1] As of January 2000, all 50 states and the District of Columbia require chlamydia cases be reported to state or local health departments.

SCREENING FOR GENITOURINARY CHLAMYDIA

Currently, the U.S. Preventive Services Task Force recommends routine screening in all sexually active women 24 years and younger, and in women 25 years and older who are at increased risk because of having multiple partners or a new sex partner.[24] Because of the high risk of intrauterine and postnatal complications if left untreated, all pregnant women at increased risk should be routinely screened for chlamydia during

Table 2. Management Recommendations for Genitourinary Chlamydia Infection

Make diagnosis via specimen collection (i.e., urine, urethra, endocervix, pharynx, rectum, or vagina), using a nucleic acid amplification test.
All pregnant women infected with chlamydia should be retested three to four weeks after completing treatment.
Test of cure is not advised for nonpregnant patients who finished one of the recommended courses of treatment.
Repeat testing for reinfection of men and women who were recently infected is recommended at three months after completion of treatment, or within the first year following treatment.
Sex partners should be referred for evaluation, testing, and treatment if they engaged in sexual contact within 60 days before a diagnosis was made or at the onset of symptoms.
Advise patients to abstain from sexual contact until they and their sex partners have finished one of the recommended treatments, and for seven days afterward.

Information from reference 1.

the first prenatal visit.[1] Additionally, any pregnant woman undergoing termination of pregnancy should be tested for chlamydia infection.[25]

There is insufficient evidence to recommend screening in men, although a small number of studies suggest that screening high-risk groups may be useful and cost-effective.[24,26-29] Per the CDC, 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, sexually transmitted disease clinics), and in certain groups (e.g., men who have sex with men). In men who have sex with men, some experts recommend screening for rectal infections (a rectal swab in those who have had receptive anal intercourse during the preceding year).[1,11] The CDC includes chlamydia screening with a urine test among the list of annual tests for all men who have had insertive intercourse within the previous 12 months.[1] Testing for *C. trachomatis* pharyngeal infection is not recommended in men who have had receptive oral intercourse.

PREVENTION

There are a number of ways to prevent, or at least significantly reduce, the incidence of genitourinary chlamydia infection. The most definitive methods of prevention are practicing abstinence and being in a long-term, mutually monogamous relationship. Patients should be encouraged to avoid high-risk behaviors such as having unprotected sex or multiple sex partners. In addition, the correct and consistent use of condoms has been shown to reduce the risk of transmission of sexually transmitted diseases. For adolescents who are considered high risk, specific education about the transmission of disease through unprotected vaginal, anal, or oral sex is warranted.[1]

COMPLICATIONS

The health consequences for women who are infected with chlamydia may be substantial and life-threatening. Chlamydia infections put women at an increased risk of developing pelvic inflammatory disease, infertility, or perihepatitis (Fitz-Hugh-Curtis syndrome). Additional negative outcomes include chronic pelvic pain and ectopic pregnancy.

Infection during pregnancy increases the risk of poor outcomes for the fetus. Complications may include miscarriage, premature rupture of membranes, preterm labor, low birth weight, and infant death.[30]

In men, consequences may include epididymo-orchitis, resulting in infertility.[31] A chlamydia infection may also increase a person's susceptibility to HIV, if exposed.[32] For men and women who are already co-infected with HIV, a concurrent chlamydia infection may increase shedding of the virus.[31] Some studies have also documented an association between co-infection, human papillomavirus, and the subsequent development of cervical cancer, although the association is not definitive.[33]

Reactive arthritis (Reiter syndrome), a triad of aseptic arthritis, nongonococcal urethritis, and conjunctivitis, can also occur. Chlamydia-induced reactive arthritis is believed to be underdiagnosed, and emerging data suggest that asymptomatic chlamydia infections may be a common cause.[17] Studies suggest that prolonged antimicrobial therapy, up to six months of combination antibiotics, may be effective.[18]

LYMPHOGRANULOMA VENEREUM

Another sexually transmitted infection caused by *C. trachomatis* (a different serovar) is lymphogranuloma venereum (LGV). It generally presents as a unilateral, tender inguinal or femoral node, and may include a genital ulcer or papule. Anal exposure may result in proctocolitis, rectal discharge, pain, constipation, or tenesmus.[1] If left untreated, it may lead to chronic symptoms, including fistulas and strictures. Diagnosis is based on clinical symptoms and a genital lesion swab or lymph node sample, similar to those used to diagnose the more typical *C. trachomatis* genitourinary infection. Molecular identification may be needed to differentiate LGV from non-LGV *C. trachomatis*. Doxycycline (100 mg twice daily for 21 days) is the preferred treatment. An alternative treatment regimen includes erythromycin (500 mg four times daily for 21 days); azithromycin (1 g once weekly for three weeks) may also be used.[1]

Pulmonary Infection

C. trachomatis is thought to cause about 12,000 cases of neonatal pneumonia per year in the United States.[34,35] Fewer than 10 percent of neonates born to women with active chlamydia infection during labor develop chlamydia pneumonia.[34,35] *C. trachomatis* pneumonia usually manifests one to three months following birth, and should be suspected in a child who has tachypnea and a staccato cough (short bursts of cough) without a fever. Chest radiography may reveal hyperinflation and bilateral diffuse infiltrates, and blood work frequently reveals eosinophilia (400 or more cells per mm^3).[19] In addition, specimens should be collected from the nasopharynx. For neonates who have a lung infection, erythromycin (base or ethylsuccinate, 50 mg per kg daily divided into four doses for 14 days) is the treatment of choice. Follow-up is recommended, and a second course of antibiotics may be required.[19]

Ocular Infection

Ocular *C. trachomatis* infection occurs in three distinct disease patterns: ophthalmia neonatorum/neonatal conjunctivitis, adult inclusion conjunctivitis, and trachoma. Physicians treating immigrant and refugee populations, or those practicing internationally, may encounter chronic trachoma cases and should be familiar with its presentation and management.

OPHTHALMIA NEONATORUM/NEONATAL CONJUNCTIVITIS

This infection is transmitted vaginally from an infected mother, and can present within the first 15 days of life. One-third of neonates exposed to the pathogen during delivery may be affected.[19] Symptoms include conjunctival injection, various degrees of ocular discharge, and swollen eyelids. The diagnostic standard is to culture a conjunctival swab from an everted eyelid, using a Dacron swab or another swab specified for this culture. The culture must contain epithelial cells; exudates are not sufficient.[19]

The recommended treatment is oral erythromycin base or ethylsuccinate (50 mg per kg daily in four divided doses for 14 days).[19] Prophylaxis with silver nitrate solution or antibiotic ointments does not prevent vertical perinatal transmission of *C. trachomatis*, but it will prevent ocular gonococcal infection and should therefore be administered.[1]

ADULT INCLUSION CONJUNCTIVITIS

This acute mucopurulent conjunctival infection is associated with concomitant genitourinary tract chlamydia infection. If the diagnosis is suspected, a specimen from an everted lid collected using a Dacron swab should be sent for culture. Special culture media are required. Treatment consists of doxycycline (100 mg twice daily for one to three weeks) or erythromycin (250 mg four times daily for one to three weeks).[20] According to one study, a single 1-g dose of azithromycin may be just as effective.[21]

TRACHOMA

Trachoma is a chronic or recurrent ocular infection that leads to scarring of the eyelids. This scarring often inverts the eyelids, causing abnormal positioning of the eyelashes that can scratch and damage the bulbar conjunctiva. Trachoma is the primary source of infectious blindness in the world, affecting primarily the rural poor in Asia and Africa.[36] The initial infection is usually contracted outside of the neonatal period. It is easily spread via direct contact, poor hygiene, and flies. Although it has been eradicated in the United States, physicians may encounter cases in immigrants from endemic areas or during global health work.

Treatment has focused primarily on antibiotics *(Table 1*[1,15-22]*)*. Although the World Health Organization has instituted its SAFE (surgery, antibiotics, facial cleanliness, and environmental improvement) program, the large heterogeneity of studies has not clearly identified which of these modalities are most effective at stemming the disease.[22,37] Topical treatment is not effective. Mass community treatment, in which all members of a community receive antibiotics, has been found to be effective for up to two years following treatment, but recurrence and scarring remain problematic.[38]

Data Sources: We performed a Clinical Query PubMed search using the search terms *Chlamydia trachomatis* with limits including: humans, clinical trial, meta-analysis, practice guideline, randomized controlled trial, review, English, and being published within the past five years. The choice of authorship of this review also coincided with the publication of the Centers for Disease Control and Prevention's Sexually Transmitted Diseases: Treatment Guidelines, 2010. Articles referenced in this review were considered. We searched Dynamed, Essential Evidence Plus, the Cochrane Database of Systematic Reviews, the National Guideline Clearinghouse, the Institute for Clinical Systems Improvement, and the U.S. Preventive Services Task Force using the same search terms. Search date: December 16, 2010.

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Author disclosure: No relevant financial affiliations to disclose.

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