Chlamydia

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Chlamydia

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IMPORTANT POINTS

1. **Epidemiologic studies have revealed that *Chlamydia pneumoniae* is a fairly common cause of infection in school-age children and young adults; along with *Mycoplasma pneumoniae*, it probably is the most common cause of community-acquired pneumonia in this age group.**
2. **Topical treatment of inclusion conjunctivitis is not recommended, primarily because of failure to eliminate concurrent nasopharyngeal carriage.**
3. **Ocular prophylaxis generally is not effective against neonatal *C trachomatis* conjunctivitis, even when erythromycin or tetracycline ointments are used.**
4. **Most chlamydial genital tract infections are asymptomatic.**
5. **Clinical conditions in which the likelihood of a chlamydial infection is high enough to warrant empiric therapy are: nongonococcal urethritis in heterosexual men, epididymitis in men younger than 35 years of age, gonococcal infection in either men or women, and pelvic inflammatory disease in women.**

The genus *Chlamydia* is divided into three species: *C psittaci*, *C pneumoniae*, and *C trachomatis*. *C psittaci* is responsible for psittacosis, an infection contracted by humans from infected birds, that is characterized by interstitial pneumonitis. The patient may have complaints of fever, headache, malaise, and nausea. It should be suspected in any patient who has atypical pneumonia and contact with birds. *C pneumoniae* causes pneumonia, pharyngitis, and bronchitis in humans. Epidemiologic studies have revealed that *C pneumoniae* is a relatively common cause of infection in school-age children and young adults; along with *Mycoplasma*, it is probably the most common cause of community-acquired pneumonia in this age group. As with disease due to *M pneumoniae*, a prodrome of headache and abdominal symptoms often is described, and pharyngitis and bronchospasm are common.

C trachomatis is associated with a spectrum of diseases. The species contains up to 15 serologically distinct variants known as serovars. Serovars A, B, Ba, and C cause ocular trachoma, a major source of blindness in many developing countries that is the most common cause of preventable blindness in the world. Serovars L1, L2, and L3 are associated with lymphogranuloma venereum, a sexually transmitted disease that is rare in the United States, but still is prevalent in many developing countries. Serovars D through K produce infection of the genital tract—urethritis and epididymitis in the male, cervicitis and salpingitis in the female. These are the most prevalent chlamydial diseases and are seen with high frequency in the United States. Major complications of genital tract disease include acute pelvic inflammatory disease, ectopic pregnancy, infertility, and infant pneumonia and conjunctivitis. These diseases comprise the primary focus of this review.

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Pathogen

Chlamydiae are obligatory intracellular bacterial parasites that exhibit a unique developmental cycle, with morphologically distinct infectious and reproductive forms. The extracellular infectious form, the elementary body, attaches to a susceptible epithelial cell and is ingested. Within an endocytotic vesicle, the elementary body reorganizes into the replicative form, the reticulate body. As the reticulate body divides, it fills the endosome, now a cytoplasmic inclusion, with its progeny. After 48 hours, multiplication ceases and nucleoid condensation occurs as the reticulate bodies transform to new infectious elementary bodies. The elementary bodies then are released from the cell by cytolysis or by a process of exocytosis or extrusion of the entire inclusion that leaves the host cell intact. Thus, chlamydiae are uniquely adapted to survival in the host. The elementary body survives adverse environmental features, is infectious, and induces its own phagocytosis. Once inside the cell, the elementary body prevents fusion of the phagosome and lysosomes, protecting itself from enzymatic destruction. Hiding from host attack by antibody or cell-mediated defenses, reticulate bodies successfully parasitize the host cell, divide, and multiply.

Pathogenesis

The mechanisms by which *C trachomatis* induces inflammation and tissue destruction have not been defined. Histopathology reveals that primary infection is characterized by an acute inflammatory response with a marked influx of polymorphonuclear neutrophils, especially early in infection. Chronic inflammatory cells, such as lymphocytes and plasma cells, also participate in the primary immune response, but they appear later, concomitant with the resolution of infection. In ocular and genital infections, large numbers of plasma cells may be present; in infant pneumonia, eosinophils and neutrophils predominate. A predominant acute inflammatory response has been reported in animal models of primary chlamydial infection. Of special note is the occurrence of genital tract tubal dilatation in some animals consequent to primary infection. Thus, at least one mechanism of tissue damage appears to involve the acute inflammatory process that results from an initial chlamydial insult.

Natural infection with *C trachomatis* appears to confer little protec-

tion against reinfection; that which is conferred is short-lived. Recurrent infections with chlamydiae result in a vigorous chronic inflammatory cellular response and an acceleration of scarring and tissue damage. A delayed-type hypersensitivity response to chlamydial antigens is believed to be important in the development of chlamydial disease, especially with chronic or repeated infections. There is a great potential for chronic, untreated infections because most chlamydial genital tract infections are asymptomatic and, therefore, are likely to be undiagnosed and untreated. The potential role of reinfection in chlamydial disease was recognized initially during human trachoma vaccine trials in which volunteers were immunized and subsequently challenged with live organisms. Limited strain-specific protection against infection was seen, but when infection did occur after immunization, the resulting disease was more severe.

Clinical Aspects

C trachomatis infections can be divided into four clinical categories: 1) classic ocular trachoma, 2) lymphogranuloma venereum, 3) other oculogenital disease in adolescents and adults, and 4) diseases of infancy.

Genital tract infection with *C trachomatis* is the most prevalent of these diseases. Cervical chlamydial infection has been reported in 2% to 30% of pregnant women. If a woman has active chlamydial infection during pregnancy, her infant is likely to acquire the infection during parturition and develop inclusion conjunctivitis, pneumonia, or both.

Disease in Infants and Children

SYMPTOMS AND SIGNS

C trachomatis is the most common cause of ophthalmia neonatorum, which is the primary clinical manifestation of neonatal chlamydial infection. The infant usually acquires infection during passage through an infected birth canal, although an occasional infant born by cesarean delivery acquires infection. Between 22% and 44% of infants born to *Chlamydia*-positive mothers develop conjunctivitis. The usual incubation period is 5 to 14 days after birth, but it may occur earlier with premature rupture of membranes. Chlamydial infection should be considered a cause of neonatal conjunctivitis through the first 30 days of life. At least 50% of infants who have chlamydial conjunctivitis have concurrent infection in the nasopharynx.

Typically, a watery ocular discharge appears, which becomes progressively purulent. The eyelids swell, and the conjunctivae become injected and swollen (Fig. 1). If the condition is not treated, lymphoid follicles and a pseudomembranous conjunctivitis can develop and persist for weeks or months. Scars and pannus formation are rare. Neovascularization of the cornea that results from repeated infection in classic trachoma does not occur with neonatal disease. This conjunctivitis must be distinguished from that produced by pyogenic bacteria, particularly *Neisseria gonorrhoeae*. Gonococcal ophthalmia usually occurs earlier, approximately 2 to 5 days after birth, although there may be overlap in age at onset. Gonococcal conjunctivitis usually is more rapidly progressive than that due to *C trachomatis*.

Approximately 10% to 20% of infants born to infected mothers develop pneumonia due to *C trachomatis*. Infected infants usually become symptomatic prior to 2 months of age, with an insidious development of nasal obstruction and/or discharge, tachypnea, and cough. Characteristically, the infants are symptomatic for 3 or more weeks prior to presentation. Most are only moderately ill and are afebrile. Approximately 50% of affected infants will have a history of conjunctivitis. Auscultation reveals scattered rales; wheezing is uncommon. The most consistent radiographic finding is hyperinflation accompanied by bilateral diffuse interstitial infiltrates (Fig. 2). Possible laboratory findings include

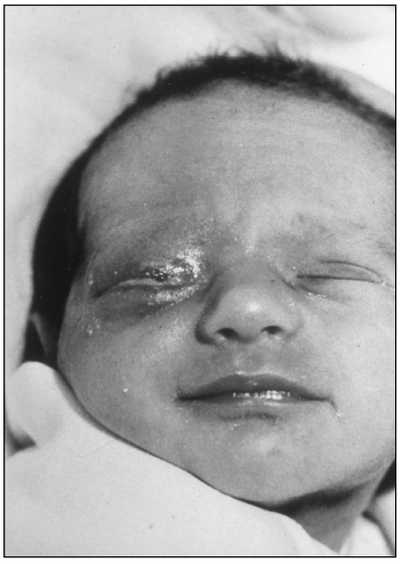

FIGURE 1. A 2-week-old infant who has chlamydial conjunctivitis. Note the erythematous and swollen conjunctiva with purulent exudate in the right eye.

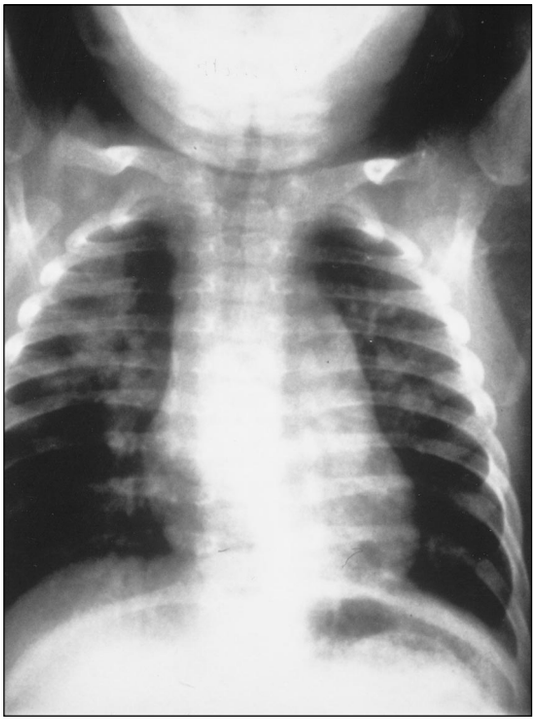

FIGURE 2. Findings on chest radiography of a 6-week-old infant who has chlamydial pneumonia include hyperexpansion and bilateral diffuse interstitial infiltrates, with some alveolar densities in both upper lobes.

a distinctive peripheral eosinophilia (>400 cells/L), arterial hypoxemia, and elevated serum immunoglobulin levels. In very young infants, infection may be more severe, leading to apnea or respiratory failure. Untreated disease has a protracted course lasting weeks to months. Long-term follow-up of children who had chlamydial pneumonia in the first 6 months of life has demonstrated a higher-than-normal frequency of reactive airway disease. Thus, long-term respiratory sequelae may be significant.

Infants born to *Chlamydia*-positive mothers also may become infected in the rectum and urogenital tract. These infections generally are asymptomatic and may persist for up to 3 years. Consequently, differentiating infection acquired perinatally from infection due to sexual abuse can be particularly difficult in young children.

DIAGNOSIS

The best indication of *C trachomatis* infection is isolation of the bacterium from cultures of conjunctiva or nasopharynx. Culture means isolation of the organism in tissue culture with confirmation by visual identification of the characteristic inclusions on fluorescent antibody staining. Care should be taken in obtaining culture specimens to ascertain that cells and not just discharge are collected. Dacron® polyester-tipped swabs that have either wire or plastic shafts are preferred; cotton-tipped swabs and wooden shafts are inhibitory to the organism.

Several nonculture methods for diagnosis of chlamydial conjunctivitis have received approval, including enzyme immunoassays and direct fluorescent antibody tests, which detect chlamydial antigen in a specimen. On conjunctival specimens, these tests have greater than 90% sensitivity and greater than 95% specificity compared with culture results. For infants who have conjunctivitis, it is important to test ocular exudate for *N gonorrhoeae* by Gram stain and culture. Unfortunately, nonculture methods of detection are not as effective with specimens from the nasopharynx, so culture of the organism from a nasopharyngeal swab should be used for the diagnosis of chlamydial pneumonia. An acute microimmunofluorescence serum titer of *Chlamydia*-specific immunoglobulin M (IgM) of 1:32 or greater is diagnostic for pneumonia in children. The microimmunofluorescence test is species-specific and -sensitive, but it is available only at a limited number of clinical laboratories.

Because of false-positive results, nonculture antigen detection tests should not be used to diagnose chlamydial infection in situations that have legal implications (eg, rape or sexual abuse). Cell culture is the only approved method for diagnosing rectal and genital chlamydial infections in prepubertal children.

TREATMENT AND PREVENTION

Topical treatment of inclusion conjunctivitis is not recommended primarily because of failure to eliminate concurrent nasopharyngeal infection. Recommended therapy for conjunctivitis or pneumonia is oral erythromycin 50 mg/kg per day in four divided doses for 10 to 14 days (Table 1). The failure rate is approximately 20%, and a second course of therapy may be required. Problems

TABLE 1. Treatment of *Chlamydia trachomatis* Infection

Uncomplicated genital infection in children 8 years of age or older, adolescents, adult men, and adult nonpregnant women
Recommended regimens
Doxycycline 100 mg orally two times a day for 7 days OR Azithromycin 1 g orally in a single dose
Alternative regimens
Ofloxacin* 300 mg orally two times a day for 7 days OR Erythromycin base 50 mg/kg/day (maximum dose, 500 mg) orally four times a day for 7 days OR Erythromycin ethylsuccinate 800 mg orally four times a day for 7 days
Uncomplicated genital infection among children younger than 8 years
Erythromycin ethylsuccinate 50 mg/kg/day (maximum dose, 500 mg) orally in four divided doses for 10 to 14 days
Uncomplicated genital infection in pregnant women
Recommended regimen
Erythromycin base 500 mg orally four times a day for 7 days
Alternative regimens
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
If the patient cannot tolerate erythromycin
Amoxicillin 500 mg orally three times a day for 7 to 10 days
Infants who have conjunctivitis
Erythromycin ethylsuccinate 50 mg/kg/day (maximum dose, 500 mg) orally in four divided doses for 10 to 14 days
Infants who have pneumonia
Erythromycin ethylsuccinate 50 mg/kg/day (maximum dose, 500 mg) orally in four divided doses for 14 days
Ofloxacin and other quinolone antibiotics are contraindicated for pregnant and lactating women and for children and adolescents younger than 18 years.

with compliance and tolerance are frequent. Oral sulfonamides may be used after the immediate newborn period for infants who do not tolerate erythromycin. Studies of azithromycin suspension, a potentially useful alternative, are underway in children.

Ocular prophylaxis is generally not effective against *C trachomatis* infection, even when erythromycin or tetracycline ointments are used. A 2.5% ophthalmic solution of povidone-iodine may have greater efficacy and fewer side effects than erythromycin or silver nitrate as prophylaxis against ophthalmia neonatorum. Thus, the only means of preventing neonatal infection is through screening and treatment of pregnant women and their sexual partners. Both parents of infected infants should be evaluated and treated for chlamydial infection. Infants born to mothers known to have untreated chlamydial infection should be evaluated and treated with oral erythromycin for 14 days.

Genital and Ocular Disease of Adolescents and Adults

EPIDEMIOLOGY

The Centers for Disease Control and Prevention has estimated that there are 4 million new *C trachomatis* infections annually in the United States. Many men and most women infected with *C trachomatis* are either asymptomatic or minimally symptomatic, and presentation for diagnosis is a result of screening or symptoms developing in a contact. This is in contrast to gonococcal infections, in which most infected individuals develop symptoms and present acutely for care. *C trachomatis* is the single most frequently identifiable cause of nongonococcal urethritis in men. The organism also can be recovered from approximately 20% of men who have gonococcal urethritis. Risk factors for chlamydial urethritis in men include age younger than 20 years, African-American descent, and heterosexual orientation. Approximately 10% of sexually active asymptomatic men are infected. Based on selective screening of target populations of sexually active women, the proportion infected ranges from 8% to 40%, with a median of about 15%. In the United States, higher prevalence rates in sexually active individuals have been associated with younger age, African-American descent, low socioeconomic status, and oral contraceptive use. Oral contraceptives may be simply a surrogate marker for sexual activity or they may increase susceptibility or ease of detection because of an increase in cervical ectopy, which can lead to an increase in exposed susceptible cells.

SYMPTOMS AND SIGNS

C trachomatis causes urethritis and epididymitis in males and mucopurulent cervicitis and pelvic inflammatory disease in females. The incubation period for symptomatic disease is 7 to 14 days. Males who have nongonococcal urethritis present with dysuria and urethral discharge that tends to be white, gray, or sometimes clear. It generally is less purulent and less profuse than the discharge observed with gonococcal urethritis. There is sufficient overlap between the symptoms and signs of gonococcal and chlamydial urethritis to make a reliable distinction impossible based solely on clinical evidence. The presence of four or more neutrophils per oil-immersion field in a Gram stain of an endourethral smear or more than 10 neutrophils per high-power field in the sediment of a first-voided urine specimen are evidence of urethritis, as is a positive urine leukocyte esterase test.

C trachomatis and *N gonorrhoeae* are the most frequent causes of epididymitis in men younger than age 35; urethritis also is usually present. Chlamydial epididymitis often is associated with oligospermia in the acute phase, but long-term follow-up has not been performed, and it is uncertain whether future fertility is impaired.

Although asymptomatic rectal carriage of *C trachomatis* occurs in both infants and adults, *C trachomatis* is a fairly common cause of proctitis and proctocolitis in homosexual men. If the infection is due to a lymphogranuloma venereum strain, as occurs in developing countries, a severe proctocolitis may develop that may be difficult to differentiate clinically and histopathologically from Crohn disease.

Approximately 1% of men presenting with nongonococcal urethritis develop an acute aseptic arthritis syndrome referred to as sexually reactive arthritis. It appears to be an immune-mediated inflammatory response to an infection that occurs at a site distant from the primary infection. One third of cases have the full complex of Reiter syndrome, consisting of the triad of arthritis, nonbacterial urethritis, and conjunctivitis. Most patients carry the histocompatibility antigen HLA-B27.

Approximately 70% of women infected with *C trachomatis* are asymptomatic or have mild symptoms such as vaginal discharge, vaginal spotting, mild abdominal pain, or dysuria. On examination the cervix may appear normal or exhibit edema, erythema, and hypertrophy, with a mucopurulent discharge from the os. Endocervicitis is the most common clinical manifestation of chlamydial infection in sexually active female adolescents.

Some women develop ascending infection of the genital tract that results in endometritis (infection of the uterine tissues) and salpingitis (infection of the fallopian tubes) (Fig. 3). Studies from Sweden and the United States indicate that approximately one in four patients admitted to the hospital with acute salpingitis has an upper genital tract infection caused by *C trachomatis* that is confirmed by isolation of the organism from the fallopian tubes. Why ascending infection develops in some women who have cervical infections is not known. Salpingitis may be 10 times more likely in a sexually active 15-year-old girl than in a sexually active 25-year-old woman. The definition of "pelvic inflammatory disease" is a sexually transmitted infection that ascends from the vagina and cervix to involve the uterus, ovaries, and peritoneal tissues as well as the fallopian tubes. Lower abdominal pain, usually bilateral, is the most common presenting symptom. Pain may be associated with an abnormal vaginal discharge, abnormal uterine bleeding, dysuria, dyspareunia, nausea, vomiting, fever, or other constitutional symptoms.

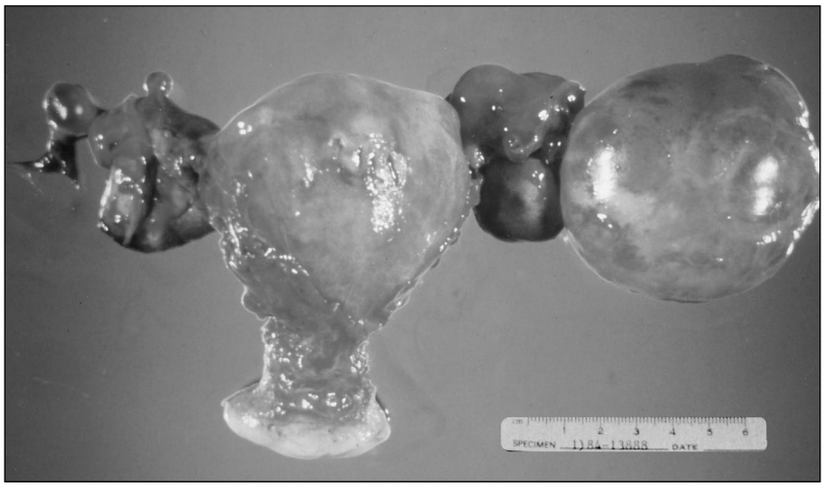

FIGURE 3. Uterus and oviducts from patient who was infertile and had a history of pelvic inflammatory disease. Note the oviductal scarring and fibrosis and the marked unilateral hydrosalpinx.

It is more commonly present in a subclinical form that lacks the typical acute symptoms, but continues to lead to the associated long-term sequelae of infertility and ectopic pregnancy. The most important causative organisms are *C trachomatis* and *N gonorrhoeae*; well over half of cases are caused by one or both of these pathogens. When women infected with both *C trachomatis* and *N gonorrhoeae* were treated with antibiotics active only against *N gonorrhoeae*, 6 of 20 (30%) developed evidence of upper genital tract infection. Other microorganisms implicated in pelvic inflammatory disease include bacteria found in the abnormal vaginal flora of women who have bacterial vaginosis, such as *Bacteroides* sp, anaerobic cocci, *Mycoplasma hominis*, and *Ureaplasma urealyticum*. *Escherichia coli* and other enteric organisms also have been found.

The spectrum of pelvic inflammatory disease associated with *C trachomatis* infection ranges from acute, severe disease with perihepatitis and ascites to asymptomatic or "silent" disease. Women who have chlamydial salpingitis are more likely to experience a chronic, subacute course with a longer duration of abdominal pain before seeking medical care than their counterparts who have gonococcal or nongonococcal-nonchlamydial salpingitis. Yet, they have as much or more tubal inflammation evident on laparoscopy.

Adolescent and adult patients who have genital tract disease presumably may autoinoculate their eyes, leading to inclusion conjunctivitis. The patient presents with an acute follicular conjunctivitis, often with the sensation of a foreign body in the eye. Hyperemia and mucoid discharge are replaced by purulent discharge, then by lymphoid follicle formation with epithelial keratitis. The infection usually resolves without complications; if untreated, however, the condition may persist for months, and scarring may occur. Although as many as 9% of patients who have keratoconjuctivitis and are 16 to 20 years of age have chlamydial ocular infection, eye involvement is seen in fewer than 1% of patients who have proven genital tract infection.

DIAGNOSIS

Although the specificity of culture approaches 100%, under optimal conditions the sensitivity of culture is estimated at 70% to 90%, even in experienced laboratories. Several nonculture tests for the detection of chlamydiae are available commercially. The tests are based on antigen detection by direct fluorescent antibody staining or by enzyme immunoassay or on detection of chlamydial ribosomal RNA by hybridization with a DNA probe. In addition, amplification tests based on the detection of chlamydial DNA using polymerase or ligase chain reactions have become available. Studies suggest that these may be more sensitive than culture and as specific. Moreover, they apparently detect *C trachomatis* in urine with a sensitivity comparable to that obtained with urogenital swab specimens and may make noninvasive testing for chlamydial infections possible. Quality assurance is essential to the performance of any test, especially the nonculture techniques in which false-positive tests can lead to adverse psychosocial outcomes for the patient and partner. Therefore, it is essential for the clinician to know the performance capabilities of both the test and the laboratory.

When a patient is part of a high prevalence population, it is acceptable to use a nonculture method to diagnose an endocervical infection in a woman and a urethral infection in a man. The test result should be verified if the patient is in a low prevalence population or in any circumstance where adverse social or legal effects would result from misdiagnosis.

Serologic testing is not helpful for the diagnosis of chlamydial infection in adolescents or adults. Because most infections are asymptomatic, it is difficult to demonstrate either a seroconversion or a rise in titers. Tests that demonstrate current presence of the organism should be used for diagnosis. Serosurveys of sexually active adult populations have found a prevalence of antichlamydial antibody in more than 20% of individuals.

TREATMENT AND PREVENTION

Antibiotics that have activity against *Chlamydia* include the tetracyclines, macrolides and related compounds, rifampin, and some of the fluoroquinolones. Although chlamydiae lack peptidoglycan, ampicillin and penicillin have some activity; cephalosporins and aminoglycosides do not. Antimicrobial resistance is not a problem.

The recommended regimen for the treatment of uncomplicated urethral, endocervical, or rectal infections in adolescent and adult men and nonpregnant women is doxycycline 100 mg orally twice

daily for 7 days. Alternative 7-day regimens include ofloxacin, erythromycin ethylsuccinate, or erythromycin base for 7 days. Single-dose therapy with azithromycin 1 g orally in a single dose (Table 1) is an attractive alternative. Compliance with 7- to 14-day regimens is a problem. The rate of compliance with a 7-day course of therapy is probably lowest among patients who have asymptomatic chlamydial infections and are identified by routine screening programs or on the basis of an infection in their sexual partners. Unfortunately, these patients are at risk for serious long-term sequelae. Asymptomatic men probably play a major role in the dissemination of the organism and, in part, account for its high prevalence in the population. Single-dose azithromycin treatment ensures a 100% rate of compliance.

Children younger than 8 years should be treated with erythromycin ethylsuccinate 50 mg/kg per day in four divided doses orally (maximum dose, 500 mg) for 10 to 14 days. Pregnant women unable to tolerate erythromycin base at the standard dose of 500 mg four times a day for 7 days can be treated with 250 mg four times a day for 14 days or amoxicillin 500 mg orally three times a day for 7 to 10 days. Doxycycline is contraindicated, and azithromycin has not been approved in pregnancy.

Clinical conditions in which the likelihood of a chlamydial infection is high enough to warrant empiric therapy include nongonococcal urethritis in heterosexual men, epididymitis in men younger than 35 years, gonococcal infection in either men or women, and pelvic inflammatory disease in women. Treatment should include the patient and any sexual partners. A patient who has the clinical diagnosis of mucopurulent cervicitis can be treated while diagnostic testing is being performed, or treatment can await the results of diagnostic tests.

Treatment of pelvic inflammatory disease always should include therapy directed against *C trachomatis*, *N gonorrhoeae*, and anaerobic bacteria. Recommended regimens include cefoxitin or cefotetan along with doxycycline, with the latter continued for a total of 14 days or clindamycin and an aminoglycoside, again followed by doxycycline to complete a total of 14 days of therapy (Table 2). An alternative to administration of doxycycline is to continue clindamycin orally at a dose of 450 mg four times a day to complete 14 days. Outpatient regimens include initial single-dose, intramuscular therapy with ceftriaxone 250 mg or another third-generation cephalosporin or cefoxitin 2 g intramuscularly plus probenicid 1 g orally in a single dose concurrently; all again are followed with 14 days of doxycycline. Alternative regimens include ofloxacin for 14 days plus clindamycin or metronidazole for 14 days. Patients who do not respond to outpatient therapy within 72 hours should be hospitalized for further diagnostic evaluation and parenteral therapy.

Although there are few clinical studies, doxycycline and erythromycin both seem effective for the treatment of adult inclusion conjunc-

TABLE 2. Treatment of Pelvic Inflammatory Disease

Inpatient treatment

Regimen A

Cefoxitin[a] 2 g IV q 6 h
PLUS Doxycycline[b] 100 mg IV or PO q 12 h
OR
Cefotetan 2 g IV q 12 h
PLUS Doxycycline[b] 100 mg IV or PO q 12 h
Either regimen is continued for at least 48 hours after the patient's condition improves, after which doxycycline[b] 100 mg orally two times a day is continued for a total of 14 days

Regimen B

Clindamycin 900 mg IV q 8 h
PLUS
Gentamycin 2 mg/kg loading dose IV or IM followed by 1.5 mg/kg q 8 h
This regimen is continued for at least 48 hours after the patient's condition improves, after which doxycycline[b] 100 mg PO two times a day *or* clindamycin 450 mg PO four times a day is given for a total of 14 days

Outpatient treatment[c]

Regimen A

Cofoxitin 2 g IV PLUS probenecid 1 g PO in a single dose concurrently
PLUS Doxycycline[b] 100 mg bid for 14 days
OR
Ceftriaxone 250 mg IM in a single dose
PLUS Doxycycline[b] 100 mg bid for 14 days
OR
Another third-generation cephalosporin (eg, cefotaxime, ceftizoxime)
PLUS Doxycycline[b] 100 mg bid for 14 days

Regimen B

Ofloxacin[d] 400 mg PO bid for 14 days
PLUS EITHER
Clindamycin 450 mg PO qid
OR
Metronidazole 500 mg orally bid for 14 days

[a] ***Ceftizoxime, ceftriaxone, and cefotaxime may be used at appropriate dosages. However, clinical data are limited, and these drugs are less active against anaerobic bacteria than are cefoxitin or cefotetan.***
[b] ***Erythromycin should be substituted for doxycycline for children younger than 9 years.***
[c] ***Patients who do not respond to outpatient therapy within 72 hours should be hospitalized for further diagnostic evaluation and parenteral therapy.***
[d] ***Ofloxacin and other quinolone antibiotics are contraindicated for pregnant and lactating women and for children and adolescents younger than 18 years.***

tivitis when given for 2 to 3 weeks.

Programs that appear effective in reducing transmission of *C trachomatis* include screening of high-risk populations for asymptomatic infections and notifying and treating partners. The feasibility of using noninvasive screening (ie, urine testing) in sexually active young men is being evaluated. Circumstances that suggest screening a woman for *C trachomatis* infection include: admission to a detention facility, presentation for an induced abortion, and diagnosis of mucopurulent cervicitis. Women who are younger than 20 years of age and sexually active; those who are 20 to 24 years of age and who either admit inconsistent use of barrier contraceptives or have had a new or more than one sex partner in the preceding 3 months; and those older than 24 years of age who have both of the previously noted risk factors have an increased risk for chlamydial infection and should be screened for *C trachomatis* during routine pelvic examination. Studies have shown that the incidence of pelvic inflammatory disease can be reduced significantly by identifying, testing, and treating women at increased risk for cervical chlamydial infection.

COMPLICATIONS AND PROGNOSIS

Permanent tubal dysfunction causing infertility can follow acute salpingitis. Infertility rates of 8% after a single episode of pelvic inflammatory disease, 19.5% after two episodes, and 40% after three or more episodes have been reported. Up to 70% of women who are infertile because of obstructed fallopian tubes have serum antibodies to chlamydiae. In contrast, fewer than 25% of women who are infertile for other reasons have such antibodies. Studies have found that 30% to 80% of women who experience infertility related to obstructed fallopian tubes had no history of clinically recognized disease. Similar data link silent disease to ectopic pregnancy. In one study, serologic evidence of a previous chlamydial infection was associated with twice the risk of ectopic pregnancy. The epidemics of infertility and ectopic pregnancy are the result of the current prevalence of pelvic inflammatory disease. Better diagnostic techniques and treatments that can prevent the long-term sequelae of this disease need to be developed.

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PIR QUIZ

6. Among school-age children and young adults, the two *most common* causes of community acquired pneumonia are *Chlamydia pneumoniae* and:
   A. *Aspergillus fumigatus.*
   B. *Moraxella catarrhalis.*
   C. *Mycoplasma pneumoniae.*
   D. *Pneumocystic carinii.*
   E. *Streptococcus pneumoniae.*

7. The treatment of *choice* for inclusion conjunctivitis of the newborn caused by *Chlamydia* is:
   A. Oral erythromycin.
   B. Oral sulfonamide.
   C. Topical povidone-iodine.
   D. Topical silver nitrate.
   E. Topical tetracycline.

8. The percentage of infants born to *Chlamydia*-positive mothers who develop conjunctivitis is *closest* to:
   A. 5%.
   B. 33%.
   C. 50%.
   D. 66%.
   E. 95%.

9. Most men and women who have a chlamydial infection are asymptomatic. However, when a discharge is present, the *best* description of the urethral dscharge seen in men infected with *C trachomatis* is:
   A. Foul-smelling and greenish.
   B. Mucoid and yellowish.
   C. Profuse and bloody.
   D. Purulent and rust-colored.
   E. Thin and whitish.

10. Among the following, the *best* antibiotic for a pregnant woman who has an uncomplicated chlamydial infection of the genital tract is:
    A. Amoxicillin.
    B. Azithromycin.
    C. Doxycycline.
    D. Erythromycin.
    E. Ofloxacin.

Chlamydia

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