Chlamydia Infections in Children and Adolescents

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Educational Gaps

1. The need for annual screening for chlamydia in sexually active adolescents and young adults is underrecognized because this infection is asymptomatic in most females (75%) and males (50%).
2. Difficulty in diagnosis arises from the range of possible symptoms at presentation of symptomatic infections and the type of testing that can be used in each situation.

Objectives

After completing this article the reader should be able to:

1. Recognize the spectrum of clinical manifestations of chlamydia infection in neonates, children, and adolescents.
2. Discuss the appropriate use of culture and nonculture diagnostic tests for chlamydia infections in various age groups.
3. List the current recommendations for screening and treatment of chlamydia infections.

Case Study

A 17-year-old girl presents with prolonged menstrual bleeding associated with severe menstrual cramping pain. Her menarche was at age 13 years. Subsequent menstrual cycles were monthly, lasting 5 days, with average flow associated with mild to moderate pain relieved by over-the-counter pain medications. The current cycle began a month ago and is associated with severe lower abdominal pain. She admits to sexual activity with one partner and uses condoms intermittently. On examination she is afebrile and in discomfort, with a heart rate of 120 beats per minute. She does not appear anemic and has good capillary refill. She has diffuse abdominal pain with significant tenderness in both the right lower and upper quadrants.

Introduction

Chlamydiae are small obligate, gram-negative, intracellular bacteria that contain both DNA and RNA and were formerly considered to be viruses. There are 3 species that are pathogenic to humans: *Chlamydia trachomatis*, *Chlamydophilia pneumoniae*, and *Chlamydophilia psittaci*. They fall within 2 genera in the family Chlamydiaceae. *C trachomatis* is in the genera *Chlamydia*, and *C pneumoniae* and *C psittaci* are in the genera *Chlamydophilia*. *C trachomatis* can cause conjunctivitis, pneumonia, and urogenital infections. *C pneumoniae* can cause sinusitis, bronchitis, pneumonia, and possibly atherosclerosis. *C psittaci* can cause pneumonia (psittacosis).

The organism has 2 distinct phases in its developmental cycle: an extracellular, nonreplicating, infectious phase and an obligate intracellular, replicating, noninfectious stage. In the infectious stage, an elementary body attaches to the target cell membranes and then enters the cell via a phagosome. Reorganization into a metabolically active reticulocyte body is followed by repeated cycles of binary fission and secondary differentiation. Newly formed elementary bodies are then released, beginning another infectious cycle. The life

Abbreviations

CDC: Centers for Disease Control and Prevention
FDA: Food and Drug Administration
HIV: human immunodeficiency virus
LGV: lymphogranuloma venereum
MIF: microimmunofluorescent
MSM: men who have sex with men
NAAT: nucleic acid amplification tests
PID: pelvic inflammatory disease
STI: sexually transmitted infection

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cycle of chlamydia is prolonged (48-72 hours), unlike other bacteria (20 minutes), and this accounts for the characteristic prolonged and, most often, subclinical infection. There is no lasting immunity developed after one infection and thus no protection from further infections.

C trachomatis

C trachomatis is divided into 3 biovars: trachoma, lymphogranuloma venereum (LGV), and mouse pneumonitis. The biovars trachoma and LGV infect human epithelial cells and include 18 serovars (equivalent to serotypes) that have different tissue tropisms and disease severity. The A, B, Ba, and C serotypes cause trachoma; D, Da, E, F, G, H, I, Ia, J, and K serotypes are responsible for oculogenital infections (conjunctivitis in children and adults, pneumonia in children, and infections of the urogenital system); and the L1, L2, L2A, and L3 serotypes of the LGV biotype cause genital ulcers.

Trachoma

C trachomatis (biovar trachoma, serotypes A, B, Ba, and C) cause the ocular disease trachoma, which is still the major cause of preventable blindness worldwide. (1) It spreads as a result of poor hygiene from contact with the secretions from the infected eyes, (eg, through towels or fingers) and by eye-seeking flies. The World Health Organization in 2011 estimated that trachoma affects approximately 21.4 million people of whom approximately 2.2 million are visually impaired and 1.2 million are blind. Trachoma rarely occurs in the United States but continues to be hyperendemic in many of the poorest and most remote rural areas of the world with limited access to water and health care, as seen in Asia, Africa, the Middle East, Central and South America, and Australia. In these hyperendemic areas, the active disease is most common in preschool children, with prevalence rates as high as 60% to 90%. Repeated infections lead to sequelae that most often appear in young adulthood and middle-aged persons. Children who have severe or persistent disease remain a reservoir of infection in their families; thus, women who are in long-term, close contact with them are more likely to be infected and develop blindness than men. The organism causes an inclusion conjunctivitis that proceeds to more severe inflammation and scarring, which causes an in-turning of the eyelashes (trichiasis). This leads to further damage with corneal ulceration, scarring, opacifications, and loss of vision. Diagnosis is made on clinical grounds. Treatment involves prolonged topical antibiotic eye ointments or oral antibiotics. Under the leadership of the World Health Organization, a global initiative to eliminate trachoma, entitled GET 2020, was launched in 1997. (2) Their strategy, termed SAFE, involves lid surgery (S), antibiotics to treat the community pool of infection (A), facial cleanliness (F), and environmental changes (E).

Oculogenital Infections

Epidemiology

The serotypes that cause oculogenital infections (biovar trachoma, serotypes D, Da, E, F, G, H, I, Ia, J, and K), unlike those that cause trachoma, are usually sexually transmitted. *C trachomatis* is the most prevalent bacterial sexually transmitted infection (STI) in the United States, with a total of 1,307,893 infections reported to the Centers for Disease Control and Prevention (CDC) from 50 states and the District of Columbia in 2010. (3) It is a notifiable disease, and improvement in screening has accounted for a continued increase in reported cases during the last 20 years. The highest rates are in the South, followed by the Midwest, Northeast, and West. Estimates by race/ethnicity indicate that the rates among African Americans are 8 times that of whites, followed by American Indians/Alaska Natives (4.3 times) and Hispanics (2.7 times the rate in whites). The rate of chlamydia infection among women in 2010 was 2½ times that in men, suggesting lower rates of screening and reporting in men and among the sex partners of women infected with chlamydia. Most infections occur in 2 age groups—those 15 to 19 years old (3378.2 cases per 100,000 females) and those 20 to 24 years old (3407.9 cases per 100,000 females)—even though these groups represent only 25% of the sexually experienced population. Risk factors for acquisition include a combination of biological and behavioral factors.

Clinical Presentations

In pregnant women, infection with *C trachomatis* may pose a risk to the fetus, newborn (vertical transmission), and mother herself. Infection may induce a miscarriage, premature birth, low birth weight, and perinatal infection. It may also result in postpartum and postabortal endometritis. Although the newborn is usually infected while coming through the birth canal (50%-75%), there have been reports of infection in infants born by caesarean section. (4) Neonatal infections include conjunctivitis, pharyngitis, pneumonia, and, less often, asymptomatic colonization of the vagina and rectum that can persist for as long as 18 months. (5)(6) In the United States, systematic screening and treatment of *C trachomatis* in

pregnant women has markedly decreased the rate of perinatally acquired infections.

The most common presentation that occurs in a quarter to half of infected neonates is conjunctivitis. It starts 5 to 14 days after delivery but occasionally as late as 6 weeks as a watery discharge that progresses to becoming mucopurulent along with hyperemia and edema of the conjunctiva and eyelid swelling. This inclusion conjunctivitis may be accompanied by rhinitis and/or otitis media. Routine prophylactic topical treatment for *Neisseria gonorrhoeae* ophthalmia does not prevent this infection. Gonococcal ophthalmia usually occurs within 2 to 5 days of birth and progresses more rapidly. However, these 2 infections may be indistinguishable. If left untreated, chlamydial infection can progress to corneal and conjunctival scarring. The mother and her sexual partner need to be tested and treated for chlamydia.

Neonatal pneumonia is the second most common perinatal infection, occurring in 5% to 20% of those born to an infected mother, and usually presents 3 to 19 weeks after birth. The presentation is usually subacute with rhinorrhea, congestion with obstruction of the nares, followed by tachypnea and a pertussis-like (nonproductive staccato) cough with rales but rarely with any wheezing on auscultation. Approximately half of these infants will have had conjunctivitis. Chest radiography reveals hyperinflation with bilateral interstitial or patchy infiltrates. Laboratory testing reveals an eosinophilia (eosinophil count >400 /μL [0.40 $\times$ 10^9/L]) and elevated levels of serum immunoglobulins. Preterm infants may become symptomatic earlier, occasionally as early as 48 hours after birth, presenting with a respiratory distress syndrome picture often complicated by apneic episodes.

After infancy, *C trachomatis* infection is most often acquired through contact with infected genital secretions with an incubation period estimated between 7 and 21 days. *C trachomatis* in humans has a tissue tropism for columnar and transitional epithelium. In prepubertal girls, the vagina is lined with columnar epithelium and is the site of infection in the genital tract, presenting clinically with a purulent vaginal discharge. Evaluation for sexual abuse should be undertaken and a report made to Child Protective Services, remembering that asymptomatic colonization of the birth canal can persist and may be a confounding variable. During puberty, the vaginal epithelium changes from columnar to stratified squamous epithelium. In early puberty, the junction of these 2 epithelial elements is on the ectocervix, and the presence of exposed columnar epithelium on the ectocervix is a biological risk factor for acquiring chlamydia and may account for the high prevalence of infection at this age. The role of local immunity in protection after initial infections is being investigated. As the cervix grows and matures, the junction or transitional zone moves to the external os. Chlamydial infection in postpubertal females is a cervicitis not a vaginitis but also presents with vaginal discharge. A speculum examination may reveal a mucopurulent discharge at the external os, coming from the endocervical canal, along with an inflammed cervix, which may be easily induced to bleed when obtaining specimens for testing, referred to as friability. However, there may be no clinical findings associated with a positive test result. In approximately 10% to 15% of untreated women, the infection spreads upward from the cervix to the upper genital tract, causing pelvic inflammatory disease (PID), with occasional further spread along the right peritoneal gutter to the capsule of the liver, causing perihepatitis (Fitz-Hugh-Curtis syndrome). This infection may present with right upper quadrant pain without lower abdominal pain; the diagnosis will be missed if not considered in sexually active females. Untreated PID increases the risk of future infertility, chronic pelvic pain, and ectopic pregnancies. Occasionally, PID may present as nonpainful, prolonged, or irregular menstrual bleeding from endometritis. The spread of the chlamydia organism from the cervix to the upper genital tract is facilitated by the loss of the cervical mucous plug with the onset of menstruation, openings in the endometrium during menstrual shedding, and the attachment of chlamydia to sperm. The resultant inflammation of the endometrium may present with irregular, prolonged, and occasionally painful menstrual flow as with the girl described in the case study. Women infected with chlamydia have a 3- to 5-fold increased risk of acquiring human immunodeficiency virus (HIV), and testing for other infections, including HIV and syphilis, should be considered based on the clinical presentation.

The urethra may be infected in both males and females. Symptomatic women present with dysuria, frequency, and pyuria, with a negative urine culture result considered indicative of acute urethral syndrome. Infection may spread to the paraurethral or Skene glands and the Bartholin or greater vestibular glands. On examination, the urethral orifice may be inflammed with a mucopurulent discharge visible or that can be expressed from the urethra. The Bartholin duct opening is near the junction of the upper two-thirds and lower third of the medial surface of the labia majora. A blocked duct results in development of local pain and swelling and may progress to abscess formation that requires incision and drainage. Recurrent infection will need marsupialization of the gland. In symptomatic men, the combination of dysuria and

discharge is indicative of urethritis. The discharge is usually scant and watery or mucoid. Occasionally, penile itching and tingling may occur without a discharge; urinary frequency, dysuria, painful micturition, and occasionally hematuria and hematospermia may also be present. Chlamydia contributes to male infertility because organisms attached to sperm cause a marked decrease in sperm motility and viability.

Chlamydia can infect the rectum in men and women, either directly (through receptive anal sex) or possibly via spread from the cervix and vagina in a woman with cervical chlamydial infection. Infection at this site is often asymptomatic but may present with rectal pain, discharge, and/or bleeding and is referred to as proctitis.

Pharyngeal infection in both sexes may occur from oral sex with an infected partner and is usually asymptomatic. *C trachomatis* is not considered an important pathogen for pharyngitis. In men who have sex with men (MSM), chlamydia can be transmitted by oral or anal sex. Among those screened for rectal chlamydial infection, positivity has ranged from 3.0% to 10.5%, and among those screened for pharyngeal chlamydial infection, positivity has ranged from 0.5% to 2.3%. (7)

Infection in the urogenital system can be autoinoculated into the eyes, causing conjunctivitis. It commonly infects one eye and has a subacute course that lasts several days to weeks. Symptoms include photophobia with redness of the eye, a mucopurulent discharge, and severe eyelid swelling.

Urogenital *C trachomatis* infection may also be associated with Reiter syndrome, now referred to as reactive arthritis and characterized by conjunctivitis, urethritis, and arthritis. This condition in the pediatric age group usually follows gastrointestinal infection with *Campylobacter*, *Shigella*, *Salmonella*, or *Yersinia*. When it occurs with chlamydia infection, it is more commonly seen in males in the 20- to 40-year age group, and 75% of these individuals are HLA B27 antigen positive. Symptoms are milder in women. Other manifestations may include skin disease (keratoderma blennorrhagicum), development of brittle nails, cardiac disease, ulceration of mucous membranes, sacroiliitis, and enthesitis. Treatment requires that the organism be detected and treated with antimicrobials. Arthritis is treated with nonsteroidal anti-inflammatory agents. Management of eye findings include appropriate local and systemic agents and should preferably be undertaken by an ophthalmologist.

PREVENTION. In addition to abstinence education, adolescents should be instructed in the proper use of male latex condoms. When used consistently and correctly, the risk of getting or giving chlamydia is reduced. Addressing behavioral risk factors is also important. These risk factors include young age at initiation of intercourse, multiple sexual partners, having an older partner (>2 years older), lack of condom use, and substance use at the time of sexual activity. The younger the age of sexual debut, the greater the likelihood of having multiple sexual partners in the adolescent years. Therefore, early education to delay the onset of sexual activity and encourage long-term mutually monogamous relationships, along with use of condoms and getting screened at recommended intervals, are important preventive measures. In addition, physicians need an understanding of the existing barriers to implementing prevention strategies: lack of knowledge about the need for screening and fears related to disclosure of sexual activity because of the societal stigma related to STIs and concerns regarding confidentiality. (Of note, the current preferred term is *STI* and not *sexually transmitted disease*, although published guidelines still use the term *sexually transmitted disease*.) When adolescents seek care, however, many health care practitioners fail to take a sexual history and offer chlamydia screening. All 50 states and the District of Columbia currently allow minors to seek care for STI diagnosis and treatment without parental consent; maintaining confidentiality in the billing and insurance claims process however is challenging. The American Academy of Pediatrics and the Society for Adolescent Health and Medicine have developed coding and billing tools to maximize practitioner reimbursement while minimizing potential disclosure of confidential services through health plan billing statements.

Most STIs with *C trachomatis* are asymptomatic in both sexes, with estimates of up to 80% in women and 75% of men. This pool of asymptomatic infection contributes to the high rates of transmission and subsequent infection and makes the need for screening asymptomatic adolescents so important. Current screening frequency recommendations by the CDC and the US Preventive Services Task Force call for screening of all sexually active, asymptomatic, nonpregnant females 25 years and younger at least yearly and twice yearly in higher-risk populations. (8)(9) Risk factors should be assessed in sexually active females to help decide the frequency of testing (eg, screening may be needed more frequently in those with multiple sexual partners). The CDC recommends that all pregnant women should be screened for chlamydia at their first prenatal visit and for those younger than 25 years again in their third trimester. They also recommend additional testing 3 weeks and 3 months after completion of therapy.

There are no recommendations at this time to screen sexually active young men for *C trachomatis*. High-risk behavior, however, should prompt screening. MSM should be screened yearly for rectal gonorrhea and chlamydia or more frequently, depending on behavior, along with screening for pharyngeal gonorrhea for those who have receptive oral intercourse. More frequent screening is required for those with multiple or anonymous partners and if sex occurs along with the use of illicit drugs.

DIAGNOSTIC TESTING. A number of diagnostic tests are available for detection of chlamydia, and the choice depends on (1) the reason for needing a diagnosis (ie, screening and treatment in adolescents and adults or as part of an evaluation for child abuse), (2) the site of testing (eg, rectum vs cervix), and (3) the type of chlamydia being tested (eg, different biovars as with *C trachomatis* or *C pneumoniae*).

Screening of the asymptomatic adolescent for STIs no longer requires the use of a speculum examination to obtain a cervical specimen in females or a urethral swab in males. Newer tests use nucleic acid amplification of DNA or RNA from *C trachomatis* and are more sensitive than culture, as well as specific, and currently are the method of choice for screening. Because they are not cultures they do not require viable organisms, and their increased sensitivity is attributable to their ability to produce a positive signal from as little as a single copy of the target DNA or RNA. Commercially available tests differ in the amplification method and the target nucleic acid sequences used. The 3 types of tests used include polymerase chain reaction (Amplicor; Roche Molecular Diagnostics, Pleasantville, CA), strand displacement amplification (ProbeTec; Becton Dickinson, Franklin Lakes, NJ), and transcription-mediated amplification (Aptima C2; GenProbe, San Diego, CA). Polymerase chain reaction and strand displacement amplification are DNA amplification assays, and transcription-mediated amplification is an RNA amplification assay. All 3 assays have Food and Drug Administration (FDA) approval for use on genital sites (cervix, vagina, and urethra) and urine from adolescents and adults. Vaginal swabs can be collected by the patient or clinician. An advantage of the vaginal transcription-mediated amplification–nucleic acid amplification test (NAAT) is that results are not affected by the presence of menstrual blood. The other 2 tests for DNA amplification cannot be used in a menstruating female. The use of urine specimens has eliminated the need to collect urethral swabs in males and can be used in menstruating females. These changes should not be interpreted as a reason not to perform a pelvic examination in symptomatic females because many conditions could be missed without such an examination. For those who test positive for chlamydia, screening for other STIs should be considered.

In cases of suspected sexual abuse, testing is for the *C trachomatis* serovars that cause oculogenital disease. Diagnostic tests in suspected sexual abuse cases are undertaken for 2 purposes: treating patients and reporting to the legal system. It is important to use a diagnostic test that is considered the gold standard for the evidence to be admissible for any court proceedings. Until recently, cultures for *C trachomatis* were necessary for all such cases. These specimens have to be collected using a Dacron, rayon, or cotton-tipped swab on plastic or aluminum and never with a wood cotton-tipped swab. Although 100% specific, the sensitivity of culture is estimated at 50% to 80%; in part, this is due to a sampling issue. Excess mucus needs to be removed from the surface of the cervix before collection of the specimen to ensure collection of endocervical cells in postpubertal females. For testing purposes in suspected cases of abuse, although specimens for culture from the vagina in females, urethra in males, rectum, and pharynx are required for *N gonorrhea*, specimens for chlamydia culture are not needed from the urethra or pharynx in prepubertal children because the yield is low and, with a urethral specimen, does not justify the discomfort that would ensue. Nonculture tests were previously not recommended for diagnosis of an STI in cases of abuse. However, the CDC has now sanctioned the use of urine NAATs for screening in girls. (8)(10) No data are available regarding the use of NAATs in boys or for extragenital specimens (eg, those obtained from the rectum) in boys and girls. A positive result with the use of NAAT has to be confirmed before establishing the diagnosis and starting treatment. Although most often this requires a culture, some states allow confirmation by use of another type of NAAT. Transcription-mediated amplification (Aptima 2) offers an alternate target confirmation method, but data are limited with use of this procedure as a confirmatory test. Other options include sending a blinded specimen to a reference or alternate laboratory for confirmation or use of a second alternate-technology commercial NAAT. All specimens collected for forensics should be retained for purposes of additional testing in accordance with local policies and procedures.

The nonamplification antigen detection tests are specific but not as sensitive as NAATs. These tests include direct fluorescent antibody testing that detects intact bacteria with a fluorescent antibody and enzyme immunoassay that detects bacterial antigens with an enzyme-labeled

antibody. Genetic probe methods use nucleic acid hybridization to detect specific DNA or RNA sequences of *C trachomatis*. They require invasive testing using a direct swab from the cervix or urethra, and their sensitivity is also not as high as NAAT. The main advantage of these nonamplification tests are their low cost, but because NAATs have become more cost-competitive and have higher sensitivity, they are the preferred diagnostic test method.

Most available tests, including NAATs, are not cleared by the FDA for use with swabs from extragenital sites (ie, pharynx or rectum) in those practicing receptive anal or oral intercourse or for conjunctival specimens from infants with suspected *C trachomatis* conjunctivitis. Similarly, it is not available for tracheal aspirates or lung biopsy specimens for those with suspected pneumonia. Although published evaluations for NAAT with use of these specimens are limited, the sensitivity and specificity are probably at least as high as those for culture. Although chlamydial culture can be used, it is not widely available for specimens from these sites. Some commercial laboratories have validated the NAAT on rectal and pharyngeal swabs and demonstrated improved sensitivity and specificity compared with cultures. FDA-approved nonamplification direct detection methods have become less available in these situations.

The usefulness of serologic tests depends on the infecting serovars, site of infection, duration of disease, and previous exposure to chlamydial antigens. Serologic tests for *C trachomatis* have limited sensitivity and specificity and are seldom used to diagnose active, superficial genital tract infections; rather, testing is performed by molecular methods as discussed above. In children with pneumonia, an acute microimmunofluorescent (MIF) serum titer of *C trachomatis* specific IgM of 1:32 or greater is diagnostic. Diagnosis of LGV is supported by a positive result on a complement fixation test for chlamydia (ie, titer >1:64) or a high MIF titer (typically >1:128) for *C trachomatis,* but these results are not confirmatory.

Tests of cure are not recommended, except in pregnant women, those with persistent symptoms, or those who remain symptomatic because of inadequate treatment. This recommendation is based on the fact that the medications used are highly effective and achieve a cure in most patients. If the patient and partner were treated appropriately, a positive test result would imply treatment failure, which would need to be reported to the health department and further treatment performed in consultation with a specialist. If needed, a test of cure should not be performed earlier than 3 weeks after treatment because NAATs are sensitive and results will remain positive in the presence of dead organisms. A positive result on follow-up testing is usually considered to be a subsequent infection rather than failure of treatment and often is the result of subsequent infection from an untreated partner. So, although not routinely recommended, it may be prudent to recheck females who are at risk for subsequent infection, preferably waiting 3 months after treatment or at the next encounter. Periodic additional testing is important in pregnant women to prevent the infant from being put at risk for infection at birth.

TREATMENT. The purpose of treatment is to resolve symptoms, prevent spread within the patient with its attendant complications, and decrease the risk of transmission to others (ie, sexual partners or infants at delivery). Testing for syphilis, HIV, and other STIs should be considered based on the patient's clinical presentation. A positive result for *C trachomatis* needs to be reported to the public health department. Lastly, evaluation and treatment of sexual partners within the previous 60 days should be undertaken. In symptomatic patients, treatment should ideally await laboratory confirmation of an infectious agent because a specific diagnosis helps with reporting to the health department, partner notification, and improved compliance with treatment, especially by the partner. However, empiric treatment is recommended in high-risk patients who are unlikely to return for follow-up evaluations. Such empiric therapy should cover the common pathogens *N gonorrhoeae* and *C trachomatis* and preferably be administered as a single-dose medication for each to improve compliance. If possible, therapy should be observed to ensure compliance. Patients infected with *N gonorrhea* are frequently coinfected with *C trachomatis*, which has led to the recommendation that patients treated for gonorrhea also be routinely treated with a regimen that is effective against uncomplicated genital *C trachomatis* infection. However, in patients with *C trachomatis* infection, the recommended therapy does not include simultaneous treatment for *N gonorrhea*.

A single dose of 1 gram of azithromycin is the recommended first line of treatment for asymptomatic *C trachomatis* in both females and males and for urethritis and cervicitis. (8) Although doxycycline is effective therapy for *C trachomatis* infections and is lower in cost, it involves a 7-day course of therapy and is considered the second line of treatment in males and nonpregnant females because compliance may be an issue. Alternate regimens include erythromycin and quinolones, but these have more adverse effects, are costly, and require a week of therapy. To prevent transmission and subsequent

infection of partners, those treated should be instructed to abstain from sexual intercourse for a week after single-dose treatment or until completion of a 7-day treatment regimen, provided they are asymptomatic.

When cervical infection ascends to cause upper genital tract infection, treatment will depend on how early the infection is detected and how severe the symptoms are. Mild infections can be treated with ceftriaxone, 250 mg in a single dose intramuscularly, along with doxycycline, 100 mg orally twice daily for 14 days, with or without metronidazole, 500 mg orally twice daily for 14 days, for improved anaerobic coverage. For inpatient therapy, the recommended parenteral regimen includes cefoxitin, 2 g intravenously every 6 hours, along with doxycycline, 100 mg orally every 12 hours, and then switching to oral treatment with doxycycline when clinically improved, with or without the addition of metronidazole for improved anaerobic coverage in the dose of 500 mg orally twice daily for 14 days. Alternate regimens can be found on the CDC website. (8)

The CDC recommends treating proctitis and epididymitis empirically for both *C trachomatis* and *N gonorrhea* with doxycycline, 100 mg twice daily for 7 days, and ceftriaxone, 250 mg once intramuscularly, before the results of diagnostic tests return because patients will have a more rapid resolution of symptoms. Patients with severe proctitis may have LGV, which will require a 3-week course of doxycycline. The efficacy of treatment in oropharyngeal chlamydia infections is unclear. Most experts recommend treatment as for genital chlamydia infections.

In neonatal conjunctivitis, topical antibiotic therapy is inadequate for treatment, and the recommendation is for erythromycin base or ethylsuccinate, 50 mg/kg/d orally divided into 4 doses for 14 days. (8) These infants should be followed up to observe for signs and symptoms of infantile hypertrophic pyloric stenosis, the development of which has been associated with the use of oral erythromycin before 6 weeks of age. In addition, because the efficacy rate is 80%, they should be observed for resolution of symptoms because a second course of medications may be required. After the neonatal period, for those who cannot tolerate this medication, oral sulfonamides may be used. The same regimen is recommended by the CDC for chlamydial infection in prepubertal children younger than 8 years for pneumonia and genital infections. For those older than 8 years, azithromycin and doxycycline in adult doses may be used.

Expedited Partner Therapy

To increase the percentage of partners treated and reduce subsequent infection and transmission rates, a strategy termed *expedited partner therapy* has been proposed and should be considered when other strategies for management are impractical or likely to be unsuccessful. Treatment is provided without examination by giving a prescription or the antibiotic to the index patient or by calling in a prescription directly for the partner. Instructions to abstain from sexual activity until treatment is completed should be given. This method has been reported to be effective in ensuring male partner treatment and reducing repeat infection among females. (11) This approach is endorsed by the CDC and other medical organizations. The lost opportunity for screening and counseling and the risk for adverse events related to the antibiotics are limitations of this approach. The legal status of expedited partner therapy is state specific, and options can be found on the CDC website.

LGV

C trachomatis (biovar LGV, serotypes L1, L2, L2A, and L3) is also an STI that occurs sporadically in the United States (300-500 cases per year) but is more prevalent in South America, Asia, and Africa and has more recently emerged as a cause of outbreaks of proctitis among MSM worldwide. The infection starts with an ulcer that is transient and often missed. The usual presentation is with unilateral inguinal and/or femoral adenopathy. The presence of the groove sign with nodes above and below the inguinal ligament is helpful for a clinical diagnosis. Rectal exposure can result in proctocolitis. Laboratory diagnosis involves serologic testing, for which interpretation of the results is not standardized for LGV, as discussed previously. To diagnose LGV, a complement fixation titer greater than 1:64 or a titer greater than 1:128 on MIF is considered supportive given an appropriate clinical context but not confirmatory. Treatment is with doxycycline, 100 mg orally twice a day for 21 days. Erythromycin is an alternate regimen for 21 days.

C pneumoniae

This organism infects the respiratory tract epithelium, causing upper respiratory tract infections, including otitis media, sinusitis, acute bronchitis, atypical pneumonia, and community-acquired pneumonia. The organism can result in an illness with a prolonged cough that resembles pertussis. The community-acquired pneumonia may be indistinguishable from that caused by mycoplasma pneumonia or influenza. There is some evidence that it may cause pericarditis and asthma, but the role of this organism in most nonrespiratory conditions

(eg, Kawasaki disease, reactive arthritis, or chronic fatigue syndrome) has not been confirmed in case-control studies.

Infections occur most commonly in late winter and early spring in school-aged children (5–15 years old) in the developed world but can occur in both younger and older age groups in developing countries. The organism can survive on environmental surfaces, and direct inoculation is the proposed mode of clinical transmission. Asymptomatic infections are common, and symptomatic infections can vary from mild to severe. Even mild symptoms may be associated with radiographic findings of pneumonia that include bilateral nodular or ground-glass infiltrate and occasional unilateral findings. Diagnostic testing remains a challenge. Culture of the organism is difficult, and identification by isolation or polymerase chain reaction testing does not confirm the diagnosis because of prolonged asymptomatic shedding. Currently, the only endorsed method of testing is by serologic testing using the MIF method. IgM titers increase 2 to 3 weeks after the onset of illness and may not reach a peak until 6 to 8 weeks after the onset. An IgM titer of at least 1:16 or a 4-fold increase in IgG using paired acute- and convalescent-phase sera have been used for diagnosis. (6)

A high percentage of children will have their clinical symptoms resolve without treatment. *C pneumoniae* is susceptible to macrolides, ketolides, tetracycline, and most fluoroquinolones but not ciprofloxacin. Treatment regimens include the following: erythromycin, 40 to 50 mg/kg/d divided 4 times daily for 14 days; clarithromycin, 15 mg/kg/d divided twice daily for 7 to 14 days; azithromycin, 10 mg/kg on day 1 followed by 5 mg/kg/d from days 2 to 5; or doxycycline for those older than 8 years, 4 mg/kg/d divided twice daily for 14 to 21 days.

C psittaci Infection

C psittaci causes an infection previously referred to as parrot fever because the infection passed from its reservoir in birds in the order Psittaciformes (eg, parrots, parakeets, and macaws) to humans working in close contact with infected birds. However, other types of birds may also serve as reservoirs, and most of them are asymptomatic. Thus, this infection would be more appropriately termed *ornithosis* and not *psittacosis*. Although a reportable disease, fewer than 50 cases a year have been reported since 1996. Difficulty with diagnosis and underreporting may account for the small number of cases. The incubation period is 5 to 14 days or longer, and the infection, which is nonseasonal, presents with the abrupt onset of fever, chills, headache, muscle aches, and a dry cough. On examination there may be a rash and splenomegaly and on rare occasions evidence of keratoconjunctivitis, encephalitis, myocarditis, hepatitis, and arthritis. Chest radiography reveals interstitial infiltrates. Diagnosis requires a 4-fold increase between acute and convalescent antibody titers, with MIF being the preferred assay to distinguish between *C psittaci* and *C pneumoniae* infections. The treatment is the same for both infections.

Summary

- *Chlamydia trachomatis* is the cause of the most common, reportable, sexually transmitted bacterial infection in the United States.
- Most infections are asymptomatic and occur in those younger than 25 years.
- A high clinical index of suspicion for chlamydial infection (eg, pelvic inflammatory disease or epididymitis) and prompt treatment are necessary to resolve symptoms, prevent attendant complications, and prevent transmission to sexual partners.
- Chlamydia is easily diagnosed and treated. Nucleic acid amplification tests are the preferred diagnostic tests because of their superior sensitivity, and they can be performed on easily collected specimens, such as urine or vaginal swabs. Highly efficacious treatment options include single-dose oral azithromycin or a 1-week course of doxycycline.
- The cornerstone of chlamydia prevention is screening young females for infection because most of the reproductive complications of chlamydia occur in females.
- On the basis of strong research evidence, the US Preventive Services Task Force recommends screening for chlamydial infection for all sexually active nonpregnant females 24 years and younger and for older nonpregnant females who are at increased risk. (9)
- On the basis of strong research evidence, the US Preventive Services Task Force concludes that current evidence is insufficient to assess the balance of benefits and harms of screening for chlamydial infection for men. (9)

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PIR Quiz Requirements

To successfully complete 2014 *Pediatrics in Review* articles for AMA PRA Category 1 Credit, learners must demonstrate a minimum performance level of 60% or higher on this assessment, which measures achievement of the educational purpose and/or objectives of this activity. If you score less than 60% on the assessment, you will be given additional opportunities to answer questions until an overall 60% or greater score is achieved. NOTE: Learners can take *Pediatrics in Review* quizzes and claim credit online only at: http://pedsinreview.org.

1. You are seeing a 9-week-old male infant in your office for cough and poor feeding. The infant was seen 4 days ago with cough and rhinorrhea. Today the infant has a dry cough, nasal congestion, rhinorrhea, and mild tachypnea. The right eye is also injected, and the mother tells you the infant had some purulent discharge from the eye that started yesterday. Chest radiography is performed, which reveals mild hyperinflation and some patchy infiltrates. You are suspicious for *Chlamydia trachomatis* pneumonia and conjunctivitis. Of the following, the best treatment regimen should include:
   A. Ethylsuccinate, 50 mg/kg/d orally divided into 4 doses for 14 days.
   B. Erythromycin ophthalmic ointment in the eyes twice daily for 14 days.
   C. Doxycycline, 100 mg orally twice a day for 21 days.
   D. Azithromycin, 1 g orally given once.
   E. Amoxicillin, 80 to 90 mg/kg/d orally divided into 3 doses for 14 days.

2. A 7-year-old girl is being seen in the clinic for suspected sexual abuse. The recommended test to initially evaluate for *C trachomatis* infection is:
   A. Culture of cervical mucus.
   B. Vaginal transcription-mediated amplification–nucleic acid amplification test.
   C. Urethral culture.
   D. Urine nucleic acid amplification tests.
   E. Direct fluorescent antibody testing.

3. Which of the following statements is TRUE regarding the current recommendations for screening adolescents for chlamydia:
   A. All adolescent nonpregnant females 20 years and younger should be screened yearly.
   B. All sexually active asymptomatic nonpregnant females 25 years and younger should be screened at least yearly and twice yearly in higher-risk populations.
   C. All sexually active males and females 25 years and younger should be screened twice yearly regardless of sexual history.
   D. All adolescents older than 12 years should be screened for chlamydia yearly.
   E. Screening for chlamydia should begin at age 18 years in females regardless of sexual history.

4. In adults and adolescents, *C trachomatis* biovars are associated with a range of clinical manifestations worldwide, including:
   A. Exudative pharyngitis.
   B. Bacterial meningitis.
   C. Osteomyelitis.
   D. Laryngotracheitis.
   E. Chronic conjunctivitis.

5. You are seeing a sexually active 16-year-old girl in your office for vaginal discharge. She reports 2 male partners in the past year and says she uses condoms intermittently. On examination, she has mild lower abdominal tenderness on palpation, and there is mucopurulent discharge at the external os of the cervix. You send the discharge for culture but decide to treat her empirically because she has missed several appointments in the past. You best choice in management is:
   A. Ceftriaxone, 250 mg in a single dose intramuscularly, plus doxycycline, 100 mg orally twice daily for 14 days.
   B. Ceftriaxone, 250 mg in a single dose intramuscularly alone.
   C. Metronidazole, 500 mg orally twice daily for 14 days.
   D. Metronidazole, 500 mg orally twice daily for 14 days, plus doxycycline, 100 mg orally twice daily for 14 days.
   E. Azithromycin, 500 mg daily for 5 days.

Parent Resources From the AAP at HealthyChildren.org

- http://www.healthychildren.org/English/health-issues/conditions/sexually-transmitted/Pages/Chlamydia.aspx (English only)
- http://www.healthychildren.org/English/health-issues/conditions/chest-lungs/Pages/Chlamydia-pneumoniae-Infections.aspx
- Spanish: http://www.healthychildren.org/spanish/health-issues/conditions/chest-lungs/paginas/chlamydia-pneumoniae-infections.aspx
- http://www.healthychildren.org/English/health-issues/conditions/sexually-transmitted/Pages/Types-of-Sexually-Transmitted-Infections.aspx
- Spanish: http://www.healthychildren.org/spanish/health-issues/conditions/sexually-transmitted/paginas/types-of-sexually-transmitted-infections.aspx

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