



Ready-to-Use

STD Curriculum for Clinical Educators

Chlamydia Module

Target Audience - Faculty in clinical education programs, including those programs that train advanced practice nurses, physician assistants, and physicians

Contents - The following resources are provided in this module:

- **Faculty Notes** (Microsoft Word and Adobe Acrobat formats) - Includes notes that correspond to the slide presentation, a case study with discussion points, and test questions with answers
- **Slide Presentation** (Microsoft PowerPoint and Adobe Acrobat formats)
- **Student Handouts**
 - **Case Study** (Microsoft Word format)
 - **Test Questions** (Microsoft Word format)
 - **Slides Handout** (Adobe Acrobat format)
 - **Resources** (Microsoft Word format)

Suggested Time Allowance - The approximate time needed to present this module is 60-90 minutes.

These materials were developed by the Training and Health Communication Branch, Division of STD Prevention, CDC. They are based on the curriculum developed by the National Network of STD/HIV Prevention Training Centers (NNPTC) which includes recommendations from the 2002 CDC STD Treatment Guidelines.

Information on the NNPTC can be accessed at:

<http://www.stdhivpreventiontraining.org>

The 2002 CDC STD Treatment Guidelines can be accessed or ordered online at:

<http://www.cdc.gov/std/treatment/default.htm>



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CHLAMYDIA

Chlamydia trachomatis

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Learning Objectives

Upon completion of this content, the learner will be able to:

1. Describe the epidemiology of chlamydial infection in the U.S.
2. Describe the pathogenesis of *C. trachomatis*.
3. Discuss the clinical manifestations of chlamydial infection.
4. Identify common methods used in the diagnosis of chlamydial infection.
5. List CDC-recommended treatment regimens for chlamydial infection.
6. Summarize appropriate prevention counseling messages for patients with chlamydia.
7. Describe public health measures for the prevention of chlamydial infection.

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Lessons

- I. Epidemiology: Disease in the U.S.
- II. Pathogenesis
- III. Clinical manifestations
- IV. Diagnosis
- V. Patient management
- VI. Prevention

[Slide 4]

I. Epidemiology: Disease in the U.S.

[Slide 5]

- A. Incidence: Estimated 3 million cases in the U.S. annually (includes estimates of asymptomatic and unreported cases). Most commonly reported notifiable STD in the U.S.
 1. STDs with higher annual estimated incidence:
 - a) Human Papillomavirus (HPV) — 6.2 million
 - b) Trichomoniasis — 7.4 million
 2. STDs with lower annual estimated incidence:
 - a) Herpes Simplex Virus (HSV) — 1.6 million
 - b) Gonorrhea — 718,000
 - c) Syphilis — 37,000
 3. The direct and indirect annual costs of chlamydial infection, including costs of treating complications, total approximately \$2.4 billion.
 4. Chlamydia is reportable in all 50 states.
 5. The female and male rate differential is partly attributable to screening practices. With the availability of new (urine-based) screening methods, it is likely that reported incidence in males will increase.
 6. The prevalence of chlamydia is decreasing in selected areas with control programs that include clinic-based screening and treatment.

[Slides 6-8]

B. Graphs

1. Slide 6: Chlamydia -- rates by state: United States and outlying areas, 2003
2. Slide 7: Chlamydia -- rates by sex: United States and outlying areas, 1984-2003
3. Slide 8: Chlamydia -- age- and sex-specific rates: United States, 2003
 - a) Chlamydia rates by sex: reported rates may increase in males as a result of increased screening.
 - b) More sensitive tests are now available and may impact reported rates of chlamydia.

DISCUSSION QUESTION: *Based on these demographics, which population(s) should be screened to get the most out of limited public health funds? How might the use of more sensitive tests impact reported rates of chlamydia?*

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C. Prevalence in selected populations

1. Family planning: 3%-14.2%
2. Youth detention facilities: 6.3%-28.3%
3. National Job Training Program entrants: 4.4%-16.8%
4. Indian Health Service: 7.4%-9.7%

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D. Risk factors

1. Adolescence (especially females)
 - a) Cervical epithelial cells are developmentally immature (ectopy) making them more susceptible to infection.
 - b) Risky behaviors also contribute to susceptibility.
2. New or multiple sex partners
3. History of past STD infection
4. Presence of another STD
5. Oral contraceptive use (contributes to cervical ectopy)
6. Lack of barrier contraception

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E. Transmission

1. Transmission is sexual (genital) or vertical (perinatal).
2. *C. trachomatis* is highly transmissible (co-infection rates in partners > 50%).
3. Incubation period preceding symptomatic infection is thought to be 7-21 days.
4. Significant asymptomatic reservoir exists in the population.
5. Re-infection is common.
6. Perinatal transmission results in neonatal conjunctivitis in 30%-50% of exposed babies and pneumonia in 3%-16% of exposed babies.
7. Exact transmission rates unknown; transmission is thought to be more efficient from men to women.

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II. Pathogenesis

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A. Microbiology

1. *C. trachomatis* is an obligate intracellular bacterium with a Gram-negative-like cell wall.
2. *C. trachomatis* infects columnar epithelial cells of cervix or urethra--may become chronic.
3. *C. trachomatis* survives by replication that results in the death of the cell. (Alternative modes of replication and persistence of organisms are important research topics.)
4. Chlamydia life cycle is approximately 72 hours.
5. Chlamydia takes 2 forms in the cycle: elementary body (EB) and reticulate body (RB).

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B. Image: Chlamydia life cycle

1. The elementary body (EB) is a small, infectious particle found in secretions.
2. The EB attaches to and enters a cell, such as an endocervical or urethral cell, to replicate.
3. This process induces a strong immune response that can result in damage and scarring to the infected site.
4. Within 8 hours, the EB transforms into a reticulate body (RB), which begins to multiply within an isolated area called an inclusion.
5. Within 24 hours, some RBs change back to EBs. Eventually the cell wall bursts and the RBs are released to adjacent cells or transmitted to infect another partner.

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C. Taxonomy

Chlamydiaceae family—three genera that infect humans:

1. *C. trachomatis*--causes trachoma, genital infections, lymphogranuloma venereum (LGV), and conjunctivitis in adults, and conjunctivitis and pneumonia in infants
2. *C. psittaci* (Parrot fever)--causes pneumonia
3. *C. pneumoniae* --causes pharyngitis, bronchitis, and pneumonia

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III. Clinical Manifestations

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A. Table: Summary of common clinical syndromes caused by *C. trachomatis*

1. *C. trachomatis* causes urogenital infection in males and females, conjunctivitis in adults and neonates, and pneumonia in infants.
2. Distinct strains of *C. trachomatis* which are rare in the United States cause

the eye disease, trachoma, and the syndrome, lymphogranuloma venereum (LGV).

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B. Genital infection in men

1. Urethritis (inflammation of the urethra)
 - a) Most common site of infection in males
 - b) One cause of non-gonococcal urethritis (NGU)
 - c) Majority of infections (>50%) asymptomatic
 - d) Incubation period unknown (probably 5-10 days in symptomatic infection)
 - e) Signs/symptoms if present: dysuria, urethral discharge (clear or mucoid)
 - 1) Distinguishing gonococcal urethritis (GU) from NGU on clinical exam is not reliable—nor is it possible to distinguish *C. trachomatis*-positive NGU from *C. trachomatis*-negative NGU on clinical exam.
 - 2) The discharge from urethritis caused by *C. trachomatis* tends to be a mucoid or clear urethral discharge, rather than frankly purulent as in gonorrhea.
 - 3) A substantial minority of newly infected men remain asymptomatic or minimally symptomatic, which results in an accumulation of unrecognized infections in the male population.

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Image: Non-gonococcal urethritis: mucoid discharge

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2. Complications

- a) Epididymitis (inflammation of the epididymis)
 - 1) Infrequent but most common local complication of *C. trachomatis* infection in young males
 - 2) Bacterial etiology varies by sexual behavior and age
 - 3) Up to 70% of sexually transmitted cases are due to *C. trachomatis*; other cases are due to *N. gonorrhoeae*; some cases have both pathogens. The etiology varies by sexual behavior and age.
 - i) Sexually transmitted cases in young heterosexuals are usually caused by chlamydia or gonorrhea.
 - ii) Sexually transmitted cases in men who have sex with men are often caused by *E. coli* or gonorrhea.
 - iii) Can also be non-sexually transmitted, such as epididymitis caused by *E. coli* or pseudomonas in older men.
 - 4) Symptoms/signs: fever, epididymal/unilateral scrotal pain, swelling, tenderness, evidence of NGU on gram stain, epididymal tenderness/mass on exam
- b) Reiter's syndrome (rarely seen in women)
 - 1) Post inflammatory immune response following infection with *C. trachomatis*
 - 2) Characteristic manifestations of the syndrome include: conjunctivitis,

urethritis, oligoarthritis, and skin lesions (keratoderma blenorrhagica and circinate balanitis) occurring 3 to 6 weeks after genital chlamydial infection

- 3) Chlamydial antigens and DNA present within joints
- 4) Predominantly affects males
- 5) Symptoms usually respond to non-steroidal anti-inflammatory agents. Use of long-term antimicrobial treatment under study.
- 6) Most cases will spontaneously resolve within 2-6 months but can last more than one year.

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Image: Epididymitis

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C. Genital infections in women

1. Cervicitis (inflammation of the cervix)
 - a) The cervix is the most common site of infection in women--frequency of infection at cervical site: 75%-80%. 70% to 80% of cervical infections are without associated symptoms or signs.
 - b) When present, which is 30% of the time, signs and symptoms may be non-specific, such as spotting, or may include: mucopurulent cervicitis, including mucopurulent endocervical discharge, edema, erythema, and friability (easily induced bleeding) within the endocervix or any zones of ectopy.
 - c) The majority of women with *C. trachomatis* infections cannot be distinguished from uninfected women by clinical examination.
 - d) The Pap test is not a sensitive or specific indicator of chlamydial infection.
2. Urethritis (inflammation of the urethra)
 - a) Usually asymptomatic
 - b) 50% of women screened positive yield chlamydia from both urethra and cervical sites
 - c) May cause the "dysuria-pyuria" syndrome mimicking acute cystitis. Symptoms include dysuria and frequency, often seen in young women with a recent new sex partner.
 - d) On urinalysis, pyuria present but few bacteria.

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Image: Normal cervix

DISCUSSION QUESTION: Describe this cervix.

This is a slide of a normal healthy cervix. The os is small and oval or slit-like and the cervix is covered by squamous pink epithelium.

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Image: Chlamydial cervicitis

DISCUSSION QUESTION: Describe this cervix.

This slide shows a mucopurulent discharge coming from the os.

[Slide 25]

Image: Cervicitis

DISCUSSION QUESTION: Describe this cervix.

This slide shows cervical ectopy with a mucopurulent discharge at the os. This may be due to infection with *N. gonorrhoeae* or *C. trachomatis*, although tests often are negative for both. *Mycoplasma genitalium* is also strongly associated with mucopurulent cervicitis.

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3. Complications in women

- a) Pelvic Inflammatory Disease (PID)—an acute clinical syndrome associated with ascending spread of microorganisms from the vagina or cervix to the endometrium, fallopian tubes, ovaries, and contiguous structures.
 - 1) PID is defined as any combination of endometritis, salpingitis, tubo-ovarian abscess, or pelvic peritonitis.
 - 2) Signs and symptoms when present: lower abdominal pain, cervical motion tenderness, and uterine/adnexal tenderness on pelvic exam.
 - 3) A substantial proportion of chlamydia-associated PID is clinically silent, but still results in tubal scarring which may lead to infertility and ectopic pregnancy.
 - 4) It is estimated that up to 40% of women with untreated *C. trachomatis* infection will develop PID. Of those with PID, 20% will become infertile, 18% will experience debilitating chronic pelvic pain, and 9% will have a life-threatening ectopic pregnancy.
- b) Endometritis (inflammation of the endometrium)
- c) Salpingitis (inflammation of the fallopian tubes)
- d) Perihepatitis (Fitz-Hugh-Curtis syndrome)
 - 1) Inflammation of the liver capsule. Initially attributed to gonococcal infection but now more often (up to 70%) associated with chlamydial disease.
 - 2) Characterized by right upper quadrant pain, nausea, vomiting, fever
 - 3) Generally accompanied by signs of PID on a physical exam
- e) Reiter's syndrome (see male complications)

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Image: Normal human fallopian tube tissue

The Scanning Electron Micrograph (SEM) shows normal human fallopian tube epithelial tissue with healthy mucosal folds. The normal ciliated cell contains 250-300 cilia per individual cell (x1,500).

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Image: *C. trachomatis* infection (PID)

The Scanning Electron Micrograph (SEM) shows ciliated and secretory epithelial cells that appear to be breaking away from the normally intact mucosal surface. Large cracks appear on the mucosal surface. Note the sparse distribution of ciliated cell types in these diseased tissues (x 2,600). The lack of the ciliated cell type can impair fertilized ovum transport.

DISCUSSION QUESTION: *What could happen as a result of impaired ovum transport?*

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Image: Acute salpingitis (inflammation of the fallopian tubes)

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D. Syndromes seen in men or women

1. Conjunctivitis (inflammation of the conjunctiva)
 - a) In adults, it usually occurs as a result of autoinoculation from infected genitalia.
 - b) Signs/symptoms: unilateral eye discomfort, hyperemia, with non-purulent secretions
2. Proctitis (inflammation of the anus and rectum)
 - a) Signs/symptoms: rectal pain, discharge, abnormal anoscopy (mucopurulent discharge, pain, spontaneous or induced bleeding)
 - b) Infection is often seen in persons practicing receptive anal sex.
 - c) Rectal colonization of chlamydia in women can also be due to the spread of secretions from the cervix. This is seen in approximately 25%-30% of patients but generally doesn't lead to symptomatic disease.
3. Lymphogranuloma venereum (LGV)
 - a) Caused by LGV serovars (L1, L2, L3)--rarely seen in the U.S.
 - b) Sign/symptoms: Multiple, enlarged, matted, tender inguinal lymph nodes that may be suppurative and are usually bilateral. Generalized signs and symptoms such as fever, chills, meningismus, or myalgias may also be present. A self-limited genital lesion may occur at the site of inoculation.
 - c) The diagnosis of LGV is made serologically, by typing, or by nucleic acid (see diagnostic methods).
4. Reiter's syndrome (see male complications)

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Image: LGV lymphadenopathy

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E. Chlamydial infections in infants and children

1. Infants - most common clinical manifestations
 - a) Inclusion conjunctivitis (ophthalmia neonatorum)

- 1) Occurrence: 5-14 days after delivery
 - 2) Signs/symptoms: range from mild, with a scant mucoid discharge, to severe with copious purulent discharge, chemosis, and pseudomembrane formation, erythema, friability, or edema
 - 3) Neonatal ocular prophylaxis with silver nitrate, while effective for prevention of *N. gonorrhoeae*-induced conjunctivitis, is not effective in preventing conjunctivitis caused by *C. trachomatis*.
- b) Pneumonia
- 1) Occurrence: 4-12 weeks after delivery
 - 2) Signs/symptoms: cough and congestion, tachypnea, rales apparent with auscultation of the lungs, usually afebrile. Most affected infants have a history of conjunctivitis.

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2. Infections in pre-adolescent males and females
 - a) Most vaginal and rectal infections in boys and girls are asymptomatic.
 - b) Vertical transmission: Vaginal and rectal infection in young children can occur as a result of perinatal transmission. Colonization can persist for as long as 2 to 3 years and may not indicate sexual abuse or assault.
 - c) Sexual abuse
 - 1) If sexual abuse is suspected, the STD evaluation should be performed by, or in consultation with, an expert in the assessment of child sexual abuse.
 - 2) If STD testing is indicated, because of the legal and psychosocial consequences of a false-positive diagnosis, only tests with high specificities should be used.
 - 3) If sexual abuse is suspected, the CDC recommends performing cultures for *C. trachomatis* from specimens collected from the anus in both boys and girls and from the vagina in girls.
 - 4) Experts suggest that Nucleic Acid Amplification Tests (NAATs) may be an alternative ONLY if cultures are unavailable and if confirmation by a second FDA-approved NAAT that targets a different molecule from the initial test is available.

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IV. Laboratory Diagnosis

The selection of a laboratory test to detect the presence of *C. trachomatis* is a critical component of disease management and prevention. The diagnostic technology has changed significantly over the past 10 years and represents a substantial improvement in sensitivity.

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- A. Chlamydia diagnostics
 1. Culture
 2. Non-culture
 - a) Nucleic acid amplification tests (NAATs)

- b) Non-nucleic acid amplification tests (Non-NAATs)
- c) Serology

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B. Culture

- 1. Historically the “gold standard”
- 2. Variable sensitivity (50%-80%)
- 3. High specificity
- 4. Use in legal investigations
- 5. Approved for use in all anatomical sites
- 6. Not suitable for widespread screening

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C. NAATs

a) Amplified tests

- 1) Nucleic acid amplification tests (NAATs)
- 2) Commercially available tests include: Becton Dickinson *BD ProbeTec®*; GenProbe *AmpCT, APTIMA®*; Roche *Amplicor®*
- 3) Cleared for endocervical swabs in women, urethral swabs in men, and urine in men and women
- 4) Increases the sensitivity to >80%-90% for cervical and urethral swabs
- 5) Specificity >99%
- 6) All can be used on first catch (10-15 cc) of urine specimens from men and women (recommended > 2 hours after last void).
- 7) Self-collected vaginal swabs may offer another sensitive specimen for NAAT testing, i.e., GenProbe *Aptima*.

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D. Non-NAATs

- 1. Rely on detection of bacterial products (proteins, nucleic acid) in patient samples. Less expensive than culture or NAATs. A disadvantage is that they have sensitivities that range from 50% to 75%.
- 2. Non-culture, non-amplified tests
 - 1) Direct Fluorescent Antibody (DFA), e.g., *MicroTrak®*
 - i) Detects intact bacteria with a fluorescent antibody
 - ii) Can be used with a variety of specimen sites
 - iii) Stable transport
 - iv) Can be used to determine quality of endocervical specimens
 - v) Does not require live organisms—therefore, less expensive than culture
 - 2) Enzyme Immunoassay (EIA), e.g., *Chlamydiazyme®*
 - i) Detects bacterial antigens with an enzyme-labeled antibody
 - ii) Stable transport
 - 3) Nucleic acid hybridization (NA probe), e.g., GenProbe *Pace 2®*
 - i) Detects specific DNA or RNA sequences of *C. trachomatis* and/or *N. gonorrhoeae*

- ii) Stable transport
- iii) In general, performance characteristics similar to EIA

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E. Other tests

1. Serology

- a) Rarely used for uncomplicated genital infections
- b) For the diagnosis of LGV, complement-fixation test titers of 1:64 or greater (titers of >256 strongly support a diagnosis and titers of ≤ 32 rule it out)
- c) High background prevalence and infrequent rises and falls in IgG and IgM
- d) May be useful in selected tissue invasive infections (perihepatitis, LGV, PID, infant pneumonitis). Problems with specificity exist.

DISCUSSION: Review of terminology – sensitivity and specificity

Sensitivity

- *Likelihood a test will be positive when disease is present*
- *If 100 infected people are tested and test results are positive for 85, the sensitivity is 85% (85/100).*

Specificity

- *Likelihood a test will be negative when disease is not present*
- *If 100 non-infected people are tested and test results are negative for 99, the specificity is 99% (99/100).*

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V. Patient Management

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A. Treatment of uncomplicated genital chlamydial infections

1. CDC-recommended regimens

- a) Azithromycin, 1 g orally in a single dose, OR
- b) Doxycycline 100 mg orally twice daily for 7 days

2. Alternative regimens

- a) Erythromycin base 500 mg orally 4 times a day for 7 days, OR
- b) Erythromycin ethylsuccinate 800 mg orally 4 times a day for 7 days, OR
- c) Ofloxacin 400 mg orally twice a day for 7 days, OR
- d) Levofloxacin 500 mg orally once a day for 7 days

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B. Treatment of chlamydial infection in pregnant women

1. CDC-recommended regimens

- a) Erythromycin base 500 mg orally 4 times a day for 7 days, OR
- b) Amoxicillin 500 mg orally 3 times a day for 7 days

2. Alternative regimens

- a) Erythromycin base 250 mg orally 4 times a day for 14 days, OR
- b) Erythromycin ethylsuccinate 800 mg orally 4 times a day for 7 days, OR

- c) Erythromycin ethylsuccinate 400 mg orally 4 times a days for 14 days, OR
 - d) Azithromycin 1 g orally in a single dose*
- * Data are insufficient to recommend the routine use in pregnant women. However, clinical experience of some experts and preliminary data suggest that azithromycin is safe and effective.
- 3. Erythromycin estolate, doxycycline, and ofloxacin are contraindicated during pregnancy.

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C. Treatment of neonatal conjunctivitis and/or pneumonia

1. CDC-recommended regimen

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

** An association between oral erythromycin and infantile hypertrophic pyloric stenosis (IHPS) has been reported in infants less than 6 weeks of age who were treated with the drug. Infants treated with erythromycin should be followed for signs and symptoms of IHPS. Data on use of other macrolides (azithromycin and clarithromycin) for the treatment of neonatal chlamydia infection are limited. The results of one small study suggest that a short course of azithromycin, 20 mg/kg/day orally, 1 dose daily for 3 days may be effective.

- 2. The effectiveness of erythromycin in treating pneumonia is approximately 80%; a second course of therapy may be required.
- 3. Prophylactic antibiotic treatment for infants born to mothers who have an untreated chlamydial infection is not indicated. Infants should be monitored to ensure appropriate treatment if infection develops.

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D. Treatment of chlamydial infection in children

1. CDC-recommended regimens

- a) Children who weigh <45 kg:

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

- b) Children who weigh \geq 45 kg but are < 8 years of age:

- 1) Azithromycin 1 g orally in a single dose

- c) Children \geq 8 years of age:

- 1) Azithromycin 1 g orally in a single dose, OR
- 2) Doxycycline 100 mg orally twice a day for 7 days

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E. Treatment of lymphogranuloma venereum (LGV)

1. CDC-recommended regimen

- a) Doxycycline 100 mg orally twice a day for 21 days

2. Alternative regimen

- a) Erythromycin base 500 mg orally 4 times a day for 21 days

- 3. Some experts believe azithromycin 1 g orally once weekly for 3 weeks is

likely to be effective, although clinical data are lacking. The activity of azithromycin against *C. trachomatis* suggests that it may be effective in multiple doses.

- F. There has been no clinically significant emergence of drug resistance among *C. trachomatis* strains.
- G. Patients should be instructed to abstain from sexual intercourse until partners are cured and for 7 days after a single dose of azithromycin or until completion of a 7-day regimen.

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- H. Repeat testing after treatment for a chlamydial infection
 - 1. Pregnant women: repeat testing, preferably by culture, 3 weeks after completion of therapy
 - 2. Consider test of cure 3 weeks after completion of therapy any time erythromycin is used.
 - 3. Repeat screening of adolescent women 3-4 months after treatment for chlamydial infection.

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VI. Prevention

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- A. Screening (testing of asymptomatic individuals)--Why screen for chlamydia?
 - 1. Screening for chlamydia has been found to reduce the incidence of pelvic inflammatory disease in women, complications in the individual, and the burden of disease in the community. Screening can reduce the incidence of PID by more than 50%.
 - 2. Most infections are asymptomatic.
 - 3. Screening decreases the prevalence of infection in the population and reduces the transmission of disease.

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- 4. Screening recommendations
 - a) For non-pregnant women
 - 1) Universal screening of sexually active women age 25 and under should be done annually. Supported by the CDC and the U.S. Preventive Services Task Force (USPSTF).
 - 2) Women >25 years old should be screened if risk factors are present.
 - 3) Repeat screening of women 3-4 months after *C. trachomatis* infection (especially adolescents).
 - 4) Repeat screening of all women treated for *C. trachomatis* when they next present for care.
 - b) For men
 - 1) The role of routine chlamydia screening in sexually active men is currently under investigation.
 - c) For pregnant women

- 1) Screen all pregnant women at the first prenatal visit.
- 2) Screen women <25 years and those at increased risk again in the third trimester.

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B. Partner management

1. Sex partners should be evaluated, tested, and treated if they had sexual contact with the patient during the 60 days preceding the patient's onset of symptoms or diagnosis of chlamydia.
 - a) The most recent sex partner should be evaluated and treated even if the time of the last sexual contact was >60 days before symptom onset or diagnosis.

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C. Reporting

1. Laws and regulations in all states require that persons diagnosed with chlamydia are reported to public health authorities by clinicians, labs, or both.

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D. Patient counseling and education

1. Nature of the infection
 - a) Asymptomatic infection is common in both men and women.
 - b) There is an increased risk of upper tract damage with reinfection.
2. Transmission issues
 - a) Effective treatment of chlamydia may reduce HIV transmission and susceptibility.
 - b) Patients should be instructed to abstain from sexual intercourse until they and their sex partners have completed treatment for 7 days after a single dose of azithromycin or until completion of a 7-day regimen. Timely treatment of sex partners is essential for decreasing the risk for reinfected the index patient.
3. Risk reduction
The clinician should:
 - a) Assess the patient's behavior-change potential.
 - b) Discuss prevention strategies (abstinence, mutual monogamy with an uninfected partner, condoms, limit number of sex partners, etc.). Latex condoms, when used consistently and correctly, can reduce the risk of transmission of chlamydia.
 - c) Develop individualized risk-reduction plans.

CASE STUDY

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Suzy Jones is a 17-year-old college student who presents to the Student Health Center seeking advice about contraception.

History

- 17-year old white female
- College student
- Seeking advice about contraception
- Shy talking about her sexual practices
- Has never had a pelvic exam
- Has had 2 sex partners in past 6 months
- Does not use condoms or any other contraceptives
- Her periods have been regular, but she has recently noted some spotting between periods. Last menstrual period was 4 weeks ago.
- Denies vaginal discharge, dyspareunia, genital lesions or sores

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Physical Exam

- Vital signs: blood pressure 118/68, pulse 74, respiration 18, temperature 37.1° C
- Breast, thyroid, and abdominal exam within normal limits
- The genital exam reveals normal vulva, and vagina.
- The cervix appears inflamed, bleeds easily, with a purulent discharge coming from the cervical os.
- The bimanual exam is normal without cervical motion pain, uterine or adnexal tenderness.

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1. Based on Suzy's history and physical exam, what is the initial clinical diagnosis?

Mucopurulent cervicitis (MPC). The clinical diagnosis of MPC is made when a purulent or mucopurulent exudate is seen coming from the endocervical canal, or on a swab placed in the endocervix (swab test). Some experts also make the diagnosis of cervicitis based on cervical friability, or easily induced bleeding.

2. What are the *possible* etiologic agents associated with the clinical findings?

Correct responses include the following:

- *Chlamydia trachomatis*, which can cause endocervicitis.
- *Neisseria gonorrhoeae*, which can cause endocervicitis.
- Herpes simplex virus (HSV), which can cause an ectocervicitis characterized by cervical friability.

- *Trichomonas vaginalis*, which can cause ectocervicitis, but is often also associated with a diffuse, malodorous, yellow-green discharge with vulvar itching.
- In 30%-40% of cases of MPC, no organism is identified.

3. What is the most *likely* microbiologic diagnosis?

Based on the patient's age and the overall epidemiology of STDs, chlamydia and gonorrhea are the most likely diagnoses.

HSV and trichomonas tend to cause an ectocervicitis instead of a purulent endocervical exudate. Also, trichomoniasis is usually accompanied by a copious vaginal discharge and vaginal irritation. Herpetic cervicitis is often accompanied by ulcerations on other parts of the genital tract. In many cases of MPC, no etiologic agent is found.

4. Which laboratory tests should be ordered or performed?

Appropriate laboratory tests include the following:

- A pregnancy test - Irregular bleeding can also be caused by pregnancy.
- A sensitive test for *Chlamydia trachomatis* - A culture, nucleic acid amplification test, or non-NAAT test for *C. trachomatis* is appropriate.
- A sensitive test for *Neisseria gonorrhoeae* - A culture, nucleic acid amplification test, or a non-NAAT test for *N. gonorrhoea* is appropriate.
- Syphilis screen with RPR or VDRL - The history of risky sexual behavior is an indication for syphilis screening.
- Saline wet mount, pH, and KOH preparation of vaginal secretions - A microscopic examination of vaginal secretions can rule out the presence of a coexisting infection.
- Counseling and testing for HIV - The history of risky sexual behavior is an indication for offering HIV testing.
- Pap test - The Pap smear collected when there is an active cervical infection is likely to show some abnormalities, such as atypical squamous cells of unknown significance (ASC-US). Also, inflammation due to the infection may mask the presence of dysplasia. However, if follow-up is not certain, it may be prudent to collect a Pap smear at the initial visit instead of scheduling at a later date.

[Slide 60]

Laboratory

The test results are back from the laboratory.

Laboratory Test Results for Suzy Jones

- NAAT for *Chlamydia trachomatis*: positive
- NAAT for *Neisseria gonorrhoeae*: negative
- RPR: negative
- Wet mount: pH 4.2, no clue cells or trichomonads but numerous WBCs
- KOH preparation: negative for "whiff test"
- HIV antibody test: negative

- Pap smear: ASC-US
- Pregnancy test: negative

[Slide 61]

5. What is the final diagnosis?

Chlamydial cervicitis. The positive NAAT confirms the diagnosis.

6. What is the appropriate treatment at the initial visit?

The patient should be treated at the initial visit with **Azithromycin 1 g orally in a single dose** and **Cefixime 400 mg orally in a single dose** (if available) or **Ceftriaxone 125 mg IM in a single dose**. Because of the presence of MPC and the epidemiology of chlamydia and gonorrhea, CDC recommends that the patient should be treated empirically for gonorrhea and chlamydia at the initial visit. Doxycycline 100 mg orally twice a day for 7 days is an alternative recommended therapy for chlamydia. Azithromycin is more expensive than doxycycline but has the advantage of its single dose and directly observed therapy when patient adherence is in question.

7. What are the appropriate prevention and counseling messages for Suzy?

Appropriate prevention and counseling messages include the following:

- Suzy should refer her sex partners for evaluation, testing, and treatment.
- Chlamydia is often asymptomatic in men and women. Sequelae that can result from *C. trachomatis* infection in women include pelvic inflammatory disease (PID), ectopic pregnancy, and infertility.
- Effective treatment of chlamydia may reduce HIV transmission and susceptibility.
- Suzy should abstain from intercourse until she and her sex partners have completed treatment for 7 days after a single dose of azithromycin or until completion of an alternative 7-day regimen.
- Discuss individual risk-reduction and prevention strategies, including abstinence, monogamy with an uninfected partner, and condoms.
- Condoms, when used consistently and correctly, can reduce the risk of chlamydia transmission.
- If a hormonal contraceptive method (i.e., birth control pills, Depo-Provera) is prescribed, inform the patient that these methods of birth control offer no protection from STDs and HIV infection.
- Return to the clinic for re-screening in 4 months.

8. Who is responsible for reporting this case to the local health department?

Depending on local requirements, the health care provider, the laboratory, or both are responsible for reporting the case. Chlamydia is a reportable STD in all 50 states. In most areas, both the provider and the laboratory are required to report chlamydia cases to the local health department. Check with your local health department for details on reporting requirements in your area.

The CDC Division of STD Prevention website contains a link to state and some local health departments: http://www.cdc.gov/nchstp/dstd/Public_Health_dept.htm

[Slide 62]

Partner Management

Suzy has had 3 sex partners in the past year:

- John – Last sexual exposure 5 weeks ago
- Tom – Last sexual exposure 7 months ago
- Michael – Last sexual exposure 2 weeks ago

9. Which sex partners should be evaluated, tested, and treated?

John and **Michael** should be evaluated, tested, and treated. Treatment of sex partners is critical to avoid reinfection. Sex partners within the last 60 days should be evaluated, tested, and treated. If the patient with chlamydia has not had sex within 60 days, then treatment of the most recent sex partner is indicated. Chlamydial infection in men is most often asymptomatic.

Partner delivered therapy is an option in some areas. Check with your local health department to see if it is appropriate in your area.

[Slide 63]

Follow-Up

Suzy returned for a follow-up visit at 4 months.

4-Month Follow-Up

- Suzy returned for her repeat Pap test, which came back normal.
- A repeat chlamydia test returned positive.
- Suzy stated that her partner, Michael, went to get tested, but the test result was negative so he was not treated.

9. What is the appropriate treatment at the 4-month follow-up visit?

Azithromycin 1 g orally in a single dose. The patient should be retreated for chlamydia with Azithromycin 1 g orally in a single dose. She should be counseled to ensure that she does not resume sexual activity until all her partners are evaluated and treated. She should also return for chlamydia screening in 3-4 months.

TEST QUESTIONS

1. What is the most commonly reported notifiable STD in the United States?
 - a) Human Papillomavirus (HPV)
 - b) **Chlamydia**
 - c) Herpes Simplex Virus (HSV)
 - d) Gonorrhea
2. Which of the following STDs has a lower annual estimated incidence than chlamydia?
 - a) HPV
 - b) Trichomoniasis
 - c) **HSV**
 - d) PID
3. The reported rates of chlamydia are higher in women than in men. This could be due to which of the following:
 - a) Men are less susceptible to *C. trachomatis* infection.
 - b) Men are less likely to exchange sex for drugs.
 - c) **Women are screened for chlamydia more often than men.**
 - d) The bacteria are increasing in drug resistance; hence, the disease is more difficult to treat.
4. The pathogenesis of chlamydia includes which of the following?
 - a) The reticulate body becomes an elementary body.
 - b) The reticulate body enters vaginal cells.
 - c) **The elementary body enters the endocervical cells to replicate.**
 - d) There is no permanent damage to the cells which are invaded.
5. All of the following statements are true of *C. trachomatis* except:
 - a) *C. trachomatis* is an obligatory intracellular organism.
 - b) *C. trachomatis* organisms survive by replication that results in death of the cell they enter.
 - c) **The life cycle of *C. trachomatis* is 6 hours.**
 - d) The elementary body is the infectious particle of *C. trachomatis*.
6. Chlamydia causes mucosal infection of which type of cell?
 - a) **Columnar**
 - b) Squamous
 - c) Glandular
 - d) Keratinized
7. Which of the following best describes the clinical signs/symptoms of chlamydial urethral infection in men?
 - a) Yellow discharge from penis
 - b) Dysuria

- c) Scrotal pain
 - d) **Most men screened are asymptomatic.**
8. If symptomatic in men, the most common symptom of *C. trachomatis* infection is:
- a) Scrotal pain
 - b) Penile pain
 - c) **Urethral discharge**
 - d) Reiter's syndrome
9. Which of the following is true regarding chlamydial infection in men?
- a) **Epididymitis is a complication of untreated *C. trachomatis* infection.**
 - b) Epididymitis is always the result of a sexually transmitted infection.
 - c) Men almost always experience symptoms.
 - d) Chlamydial urethritis (or NGU) can be reliably distinguished clinically from gonococcal urethritis by its association with a clear urethral discharge (in contrast to gonorrhea's thicker yellow discharge).
10. Which of the following is NOT one of the characteristic symptoms of Reiter's syndrome?
- a) **Prostatitis**
 - b) Urethritis
 - c) Conjunctivitis
 - d) Oligoarthritis
11. Which of the following best describes the clinical signs/symptoms of chlamydial infection in women?
- a) Most women complain of a discharge.
 - b) Most women complain of urinary symptoms.
 - c) Clinical signs/symptoms depend on the strain of chlamydia.
 - d) **Most women are asymptomatic.**
12. Complications of untreated chlamydial infection in women include all of the following except:
- a) Perihepatitis
 - b) Salpingitis
 - c) Endometritis
 - d) **Gastritis**
13. Which of the following statements is true about *C. trachomatis* in women?
- a) The majority of women are symptomatic.
 - b) The majority of women with infection can be identified by clinical examination.
 - c) The most frequent sequella of untreated disease is having a life-threatening ectopic pregnancy.
 - d) **Chlamydia-associated PID is clinically milder than PID associated with gonorrhea.**

14. Which of the following is a method to diagnose chlamydial infection?
- Nucleic acid (DNA, RNA) amplification technique
 - Cell culture techniques, using live cells
 - Antigen detection methods
 - All of the above**
15. The laboratory test for *C. trachomatis* with the highest sensitivity is:
- NAAT (nucleic acid amplification test)**
 - Culture
 - DFA (MicroTrak)
 - EIA (Chlamydiazyme)
16. The CDC-recommended treatment of choice for uncomplicated genital chlamydial infection is:
- Amoxicillin 500 mg orally 3 times a day for 7 days
 - Tetracycline 250 mg orally 4 times a day for 7 days
 - Azithromycin 1 g orally in a single dose OR Doxycycline 100 mg orally twice a day for 7 days**
 - Erythromycin 250 mg orally 4 times a day for 14 days
17. The CDC-recommended treatment of choice for uncomplicated genital chlamydial infection in pregnant women is:
- Erythromycin base 500 mg orally 4 times a day for 7 days OR Amoxicillin 500 mg orally 3 times daily for 7 days**
 - Tetracycline 250 mg orally 4 times a day for 7 days
 - Erythromycin 250mg orally 4 times a day for 14 days
 - Ofloxacin 300 mg orally twice a day for 7 days
18. Patients and their partners who undergo the recommended treatment should wait how long before resuming intercourse?
- 3 days
 - 7 days**
 - 10 days
 - 14 days
19. The risk of transmitting or acquiring chlamydial infection can be reduced by which of the following methods:
- Abstinence
 - Changing risky sexual behavior(s)
 - Consistent and correct use of latex condoms
 - All of the above can help reduce the risk of chlamydial infection.**
20. Which of the following is true for sex partners of a patient diagnosed with chlamydia?
- Only the most recent sex partner needs to be referred for treatment.
 - All partners exposed in the last 60 days should be referred for treatment.**
 - Only symptomatic partners need to be referred for treatment.

- d) No partners need to be referred since chlamydia is not efficiently transmitted.
21. Which of the following is NOT a CDC recommendation for chlamydia screening?
- a) Screen all sexually active women age 25 years and under annually.
 - b) Women > 25 years should be screened if risk factors are present.
 - c) **Screen all male adolescents.**
 - d) Repeat screening of adolescent women 3-4 months after treatment.
22. In which state is chlamydia not reportable?
- a) **Chlamydia is reportable in all states.**
 - b) Alabama
 - c) Oregon
 - d) Idaho
23. Who is responsible for reporting a case of chlamydia to the local health department?
- a) The laboratory
 - b) The health care provider
 - c) None of the above—chlamydia is not reportable in most states
 - d) **Depending on the state, the laboratory, the health care provider, or both.**

RESOURCES

Publications

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Websites and Other Resources

1. CDC, Division of STD Prevention: www.cdc.gov/std
2. National Network of STD/HIV Prevention Training Centers: <http://depts.washington.edu/nnptc/>
3. 2002 CDC STD Treatment Guidelines (including downloadable version for Palm devices): <http://www.cdc.gov/STD/treatment/>
4. CDC National STD Hotline: 800-227-8922 or 800-342-2437
 - a. En Español: 800-344-7432
 - b. TTY for the Deaf and Hard of Hearing: 800-243-7889
5. CDC National Prevention Information Network (NPIN): www.cdcnpin.org
6. American Social Health Association (ASHA): www.ashastd.org