



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 Program and Training 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 2006 CDC STD Treatment Guidelines

Information on the NNPTC can be Accessed at:
<http://depts.washington.edu/nnptc/index.html>

The 2006 CDC STD Treatment Guidelines Can be accessed or ordered online at:
<http://www.cdc.gov/std/treatment/>



March 2010

Centers for Disease Control and Prevention
Division of STD Prevention
Program and Training Branch
STDCurriculum@cdc.gov

CHLAMYDIA

Chlamydia trachomatis

[Slide 2]

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.

[Slide 3]

Lessons

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

[Slide 4]

Epidemiology: Disease in the U.S.

[Slide 5]

- A. Incidence: Estimated 3 million new cases in the U.S. annually (includes estimates of asymptomatic and unreported cases). Most commonly reported notifiable disease 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.

[Slide 6]

- A. National Chlamydia Surveillance Systems
 1. Case Reporting
 2. National Prevalence Survey
 3. Prevalence Monitoring-screening program sentinel sites

[Slide 7-10]

B. Graphs-Case Reporting

1. Slide 7: Chlamydia – Reported rates by state: United States and outlying areas
 - a) Chlamydia is reportable in all 50 states.
 - b) In 2006, the total rate of chlamydia for the United States and outlying areas (Guam, Puerto Rico and Virgin Islands) was 345.0 per 100,000 population.
2. Slide 8: Chlamydia – Reported rates by sex: United States and outlying areas
 - a) 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.
 - b) Increases are at least in part due to increased testing with more sensitive tests.
3. Slide 9: Chlamydia – Reported rates by age and sex: United States
 - a) Rates are highest among adolescents and young adults
 - b) Rates are higher among females than males in part due to screening in females and syndromic diagnosis of urethritis in males.
4. Slide 10: Chlamydia – Reported rates by race/ethnicity and sex: United States,
 - a) Racial and ethnic minorities continue to be disproportionately affected by sexually transmitted diseases in the United States.
 - b) These disparities may be, in part, because racial and ethnic minorities are more likely to seek care in public health clinics that report STDs more completely than private providers. However, this reporting bias does not fully explain these differences. Other contributing factors include limited access to quality health care, poverty, and higher prevalence of disease in these populations.
 - c) In 2006, the rate of chlamydia among African Americans was more than eight times higher than the rate among whites (1275.0 vs. 153.1 per 100,000 population), with approximately 46 percent of all chlamydia cases reported among African Americans. Additionally, the rates among American Indians/Alaska Natives (797.3 per 100,000) and Hispanics (477.0 per 100,000), were five times and three times higher than whites, respectively.
 - d) In 2006, chlamydia rates increased for all racial/ethnic groups, except for Asians/Pacific Islanders.

[Slide 11]

C. Graphs-National Prevalence Survey (National Health and Nutrition Examination Survey-NHANES)

1. Slide 11: Chlamydia -- NHANES Prevalence: gender and race/ethnicity.
 - a) African Americans disproportionately affected
 - b) 5 times higher than whites in a national population survey

[Slide 12-13]

D. Graphs-Prevalence Monitoring

1. Slide 12: Screening Results: Prevalence in selected populations
 - a) Family planning: 3%-14.2%
 - b) Indian Health Service: 7.4%-9.7%
 - c) Youth detention facilities: 6.3%-28.3%
 - d) National Job Training Program entrants: 4.4%-16.8%

2. Slide 13: Chlamydia-trends in positivity among 15- to 24-year old women tested in family planning clinics by HHS region, 2002-2006.
 - a) Chlamydia test positivity in regional Infertility Prevention Project family planning clinics has been relatively stable between 2002-2006.
 - b) Positivity
 - 1) Decreased in three regions,
 - 2) Remained unchanged in one region, and
 - 3) Increased in six regions.

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?*

[Slide 14]

A. Risk factors

1. Adolescence (especially females)
 - a) Risky behaviors contribute to susceptibility.
 - b) The presence of columnar epithelial cells on the ectocervix is called ectopy which is more susceptible to chlamydial infection. Ectopy is more common among adolescents.
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

[Slide 15]

B. Transmission

1. Transmission is sexual (genital) or vertical (perinatal).
2. *C. trachomatis* is highly transmissible (chlamydial infection rates in partners

- are > 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.

[Slide 16]

Pathogenesis

[Slide 17]

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).

[Slide 18]

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.

[Slide 19]

C. Taxonomy

Chlamydiaceae family—one genus *Chlamydia* containing three species that infect humans:

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

3. *C. psittaci* (Parrot fever)--causes pneumonia

[Slide 20]

Clinical Manifestations

[Slide 21]

- 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* cause the eye disease, trachoma, and lymphogranuloma venereum (LGV).

[Slide 22]

- 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 muco-purulent, mucoid or clear, 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.

[Slide 23]

Image: Non-gonococcal urethritis: mucoid discharge

[Slide 24]

2. Complications-are uncommon in men. If complications do occur, they may include the following.
 - 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 can also

- be caused by. Enterin organisms 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 (rare)
 - 1) Post inflammatory immune response following infection with *C. trachomatis*
 - 2) Predominantly affects males
 - 3) 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
 - 4) Chlamydial antigens and DNA present within joints
 - 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.

[Slide 25]

Image: Epididymitis

[Slide 26]

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%. Most cervical infections are without asymptomatic.
 - b) When present, signs and symptoms may be non-specific, such as spotting, or may include: mucopurulent endocervical discharge, edema, erythema, and friability (easily induced bleeding) within the endocervix or any zones of ectopy.
 - c) Other causes of mucopurulent cervicitis include *N. gonorrhoeae* and possibly *M. genitalium*. In the majority of cases of cervicitis, the cause is unknown.
 - d) The majority of women with *C. trachomatis* infections cannot be distinguished from uninfected women by clinical examination.
 - e) 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.

[Slide 27]

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.

[Slide 28]

Image: Chlamydial cervicitis

DISCUSSION QUESTION: Describe this cervix.

This slide shows a mucopurulent discharge coming from the os.

[Slide 29]

Image: Cervicitis

DISCUSSION QUESTION: Describe this cervix.

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

[Slide 30]

3. Complications in women

- a) Pelvic Inflammatory Disease (PID)– a subclinical to 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, or uterine or 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)

[Slide 31]

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).

[Slide 32]

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?*

[Slide 33]

Image: Acute salpingitis (inflammation of the fallopian tubes)

[Slide 34]

- 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, fever, tenesums, 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., although sporadic cases and outbreaks reported among MSM in Europe and 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) Rectal infection can lead to severe proctitis or proctocolitis (associated with rectal pain, mucoid or hemorrhagic discharge, fever, tenesums. Genital and lymph nodes specimens are tested for *C. trachomatis* by culture, direct immunofluorescence, or nucleic acid detection. Additional procedures are required to differentiate LGV from non LGV and trachomatis. Chlamydia section can support the diagnosis in the appropriate clinical content.
4. Reiter's syndrome (see male complications)

[Slide 35]

Image: LGV lymphadenopathy

[Slide 36]

E. Chlamydial infections in infants

- 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 or antibiotic ointments, 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.

[Slide 37]

- 2. Infections in children (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. Genital or rectal infection can persist for as long as 2 to 3 years and be the result of perinatally acquired infection.
 - 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, specimens for *C. trachomatis* cultures should be 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 sequence from the initial test is available.

[Slide 38]

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 15 years and represents a substantial improvement in sensitivity.

[Slide 39]

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

[Slide 40]

- 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 (cost and complexity)

[Slides 41-42]

- C. NAATs
 - a) Amplification tests
 - 1) Nucleic acid amplification tests (NAATs)
 - 2) Commercially available tests include: Becton Dickinson *BD ProbeTec*®; GenProbe *AmpCT*, *APTIMA*®; Roche *Amplicor*®
 - 3) Can detect *N. gonorrhoea* in some specimens
 - 4) Increases the sensitivity to >80%-90% for cervical and urethral swabs
 - 5) Specificity >99%
 - 6) Cleared for urine in men and women, urethral swabs in men and endocervical swabs in women and some tests are cleared for vaginal

swabs.

- 7) All can be used on first catch (10-15 cc) of urine specimens from men and women (recommended > 2 hours after last void).
- 8) Self-collected vaginal swabs may offer another sensitive specimen for NAAT testing, i.e., GenProbe Aptima.
- 9) Although the use for pharyngeal and rectal specimens is not FDA-cleared, some laboratories have completed the requirements to perform NAATs on these specimens.

[Slide 43]

D. Non-Amplification tests

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) 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

[Slide 44]

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 (can support the diagnosis in the appropriate clinical context)
 - 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).*

[Slide 45]

Patient Management

[Slide 46]

- 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 300 mg orally twice a day for 7 days, OR
 - d) Levofloxacin 500 mg orally once a day for 7 days

[Slide 47]

- B. Treatment of chlamydial infection in pregnant women
1. CDC-recommended regimens
 - a) Azithromycin 1 g orally in a single dose, OR
 - b) Amoxicillin 500 mg orally 3 times a day for 7 days
 2. Alternative regimens
 - a) Erythromycin base 500 mg orally 4 times a day for 7 days, OR
 - b) Erythromycin base 250 mg orally 4 times a day for 14 days, OR
 - c) Erythromycin ethylsuccinate 800 mg orally 4 times a day for 7 days, OR
 - d) Erythromycin ethylsuccinate 400 mg orally 4 times a day for 14 days, OR
 3. Erythromycin estolate, doxycycline, ofloxacin, and levofloxacin are contraindicated during pregnancy.

[Slide 48]

- 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.

[Slide 49]

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

[Slide 50]

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.

[Slide 51]

F. There has been no clinically significant emergence of drug resistance among *C. trachomatis* strains.

G. Repeat testing after treatment for a chlamydial infection NAAT

1. Pregnant women: repeat testing, preferably by culture, 3 weeks after completion of therapy
2. Repeat testing of all women 3-4 months after treatment for chlamydial infection.
3. Retest all women whenever they next seek medical care within the following 3-12 months after treatment for chlamydial infection.
4. Consider test of cure 3 weeks after completion of therapy any time erythromycin is used.

[Slide 52]
Prevention

[Slide 53]

- 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.

[Slides 54-55]

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, the U.S. Preventive Services Task Force (USPSTF), American Academy of Pediatrics, American College of Obstetricians and Gynecologists, and American Academy of Family Physicians.
 - 2) Women >25 years old should be screened if risk factors are present.
 - 3) Repeat testing of all women approximately 3-4 months after treatment of *C. trachomatis* infection (especially adolescents).
 - 4) Repeat screening of all women treated for *C. trachomatis* when they next present for care within 12 months.
 - b) For men
 - 1) Screening of sexually active young men should be considered in clinical settings with a high prevalence of chlamydia (e.g., adolescent clinics, correctional facilities, and STD clinics.)
 - 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.

[Slide 56]

- 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.
 2. 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.
 3. If concerns exist that sex partners will not seek evaluation and treatment, or if other management strategies are impractical or unsuccessful, then delivery of antibiotic therapy by heterosexual male or female patients to their partners

might be an option. Patient-delivered partner therapy is not routinely recommended for MSM because of high risk for coexisting infections.

[Slide 57]

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.

[Slides 58-59]

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

[Slide 60-61]

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

[Slide 62]

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.

[Slide 63]

Questions

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

Endocervicitis: The clinical diagnosis of endocervicitis 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 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 endocervicitis, no etiologic agent is found.

3. 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.
- *Chlamydia trachomatis* - A nucleic acid amplification test is the most sensitive test for detection.
- *Neisseria gonorrhoeae* - A nucleic acid amplification test is the most sensitive test for detection.
- 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.

4. 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 Cervicitis and the risk of Chlamydia and gonorrhea (age < 25yrs, partners, unprotected sex) 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.

[Slide 64]

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
- Pregnancy test: negative

[Slide 65]

5. What is the final diagnosis?

Chlamydial cervicitis. The positive NAAT confirms the diagnosis.

6. 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-test in 3-4 months, due to the high prevalence of repeat infection.

7. 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 66]

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

8. 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 67]

Follow-Up

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

4-Month Follow-Up

- A repeat chlamydia test was 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- 4months.

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 higher annual estimated incidence than chlamydia?
 - a) Gonorrhea
 - b) **HPV**
 - c) HSV
 - d) Syphilis
3. The reported rates of chlamydia are higher in women than in men. This could be due to which of the following:
 - a) Women are more symptomatic and access care more frequently.
 - 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 duration of infection.
 - 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 sub-acute or silent.**
14. Which of the following is a method to diagnose chlamydial infection?

- a) Nucleic acid (DNA, RNA) amplification technique
 - b) Cell culture techniques, using live cells
 - c) Antigen detection methods
 - d) **All of the above**
15. The laboratory test for *C. trachomatis* with the highest sensitivity is:
- a) **NAAT (nucleic acid amplification test)**
 - b) Culture
 - c) DFA (MicroTrak)
 - d) EIA (Chlamydiazyme)
16. The CDC-recommended treatment of choice for uncomplicated genital chlamydial infection is:
- a) Amoxicillin 500 mg orally 3 times a day for 7 days
 - b) Tetracycline 250 mg orally 4 times a day for 7 days
 - c) **Azithromycin 1 g orally in a single dose OR Doxycycline 100 mg orally twice a day for 7 days**
 - d) 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:
- a) **Azithromycin 1 g orally in a single dose OR Amoxicillin 500 mg orally 3 times daily for 7 days**
 - b) Tetracycline 250 mg orally 4 times a day for 7 days
 - c) Erythromycin 250mg orally 4 times a day for 14 days
 - d) 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?
- a) 3 days
 - b) **7 days**
 - c) 10 days
 - d) 14 days
19. The risk of transmitting or acquiring chlamydial infection can be reduced by which of the following methods:
- a) Abstinence
 - b) Reducing risky sexual behavior(s)
 - c) Consistent and correct use of latex condoms
 - d) **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?
- a) Only the most recent sex partner needs to be referred for treatment.
 - b) **All partners exposed in the last 60 days should be referred for treatment.**
 - c) 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 sexually active young men.**
 - d) Repeat testing of infected women approximately 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

1. Black CM, et al. Head to head multicenter comparison of DNA probe and nucleic acid amplification tests for *Chlamydia trachomatis* infection in women performed with an improved reference standard. J Clin Microbiol. 2002;40(10):3757-63. CCID, Centers for Disease Control & Prevention.
2. CDC. Expedited partner therapy in the management of sexually transmitted diseases. Atlanta, GA: US Department of Health and Human Services, 2006.
3. CDC. Sexually transmitted disease surveillance 2006 supplement, chlamydia prevalence monitoring project. Atlanta (GA): U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, December 2007. Available from URL: <http://www.cdc.gov/std/chlamydia2006/>.
4. CDC. Sexually transmitted diseases treatment guidelines 2006. MMWR 2006; 55(RR-11):38-42. Available from URL: <http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5511a1.htm>.
5. CDC. Screening tests to detect *Chlamydia trachomatis* and *Neisseria gonorrhoeae* Infections 2002. MMWR 2002; 51(No. RR-15) 1-38.
6. CDC. Recommendations for the prevention and management of *Chlamydia trachomatis* infection. MMWR 1993; 42(RR-12):1-39. Available from URL: <http://www.cdc.gov/mmwr/preview/mmwrhtml/00021622.htm>.
7. Cook RL et al. Systematic review: noninvasive testing for *Chlamydia trachomatis* and *Neisseria gonorrhoeae*. Ann Intern Med. 2005 Jun 7; 142(11):914-25.
8. Datta SD, Sternberg M, Johnson RE, et al. Gonorrhea and chlamydia in the United States among persons 14 to 39 years of age, 1999 to 2002. Ann Intern Med. 2007 Jul 17; 147(2):89-96.
9. Gaydos CA, Quinn TC, et al. Performance of the APTIMA Combo 2 assay for detection of *Chlamydia trachomatis* and *Neisseria gonorrhoeae* in female urine and endocervical swab specimens. J Clin Microbiol. 2003 Jan; 41(1):304-9.
10. Hadgu, A, Dendukuri N, Hilden J. Evaluation of nucleic acid amplification tests in the absence of a perfect gold-standard test: a review of the statistical and epidemiologic issues. Epidemiology. 2005 Sep; 16(5):604-12.
11. Hu D, Hook EW 3rd, Goldie SJ. Screening for *Chlamydia trachomatis* in women 15 to 29 years of age: a cost-effectiveness analysis. Ann Intern Med. 2004 Oct 5; 141(7): 501-13.
12. Hillis SD, Wasserheit JN. Prevention of pelvic inflammatory disease. N Engl J Med 1996; 334:1399-1401.
13. Lau CY, Qureshi Ak. Azithromycin versus doxycycline for genital chlamydial infections: a meta-analysis of randomized clinical trials. Sex Transm Dis. 2002 Sep; 29(9): 497-502.
14. Peterman TA, Tian LH, Metacalf CA, et al. High incidence of new sexually transmitted infections in the year following a sexually transmitted infection: a case for rescreening. Ann Intern Med. 2006 Oct 17; 145(8):564-72.]

15. Scholes D, Stergachis A, Heidrich FE, Andrilla H, Holmes KK, Stamm WE. Prevention of pelvic inflammatory disease by screening for cervical chlamydial infection. *N Engl J Med* 1996; 334:1362-66.
16. Stamm WE, et al. Azithromycin for empirical treatment of the nongonococcal urethritis syndrome in men. *JAMA* 1995; 274:545-41.
17. Stephens Rs. The cellular paradigm of chlamydial pathogenesis. *Trends Microbiol.* 2003 Jan; 11(1):44-51.
18. United States Preventive Services Task Force (USPSTF). Screening: chlamydial infection. Available from URL: <http://www.ahrq.gov/clinic/uspstf/uspSchlm.htm>.
19. Watson EJ, Templeton A, Russell I, et al. The accuracy and efficacy of screening tests for *Chlamydia trachomatis*: a systematic review. *J Med Microbiol.* 2002 Dec; 51(12):1021-31.
20. Weinstock H, Berman S, Cates W Jr. Sexually transmitted diseases among American youth: incidence and prevalence estimates, 2000. *Perspect Sex Repro Hlth* 2004; 36 (1): 6-10.
21. Wiesenfield HC, Hillier SL, Krohn MA, et al. Lower genital tract infection and endometritis: insight into subclinical pelvic inflammatory disease. *Obstet Gynecol.* 2002 Sep; 100(3): 456-63.

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. 2006 CDC STD Treatment Guidelines (including downloadable version for Palm devices): <http://www.cdc.gov/STD/treatment/>
4. STD information and referrals to STD clinics
 CDC-INFO
 1-800-CDC-INFO (800-232-4636)
 TTY: 1-888-232-6348
 In English, en Español
5. CDC National Prevention Information Network (NPIN): www.cdcnpin.org
6. American Social Health Association (ASHA): www.ashastd.org