

# Chlamydia

*Chlamydia trachomatis*

# 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 *Chlamydia trachomatis*.
3. Describe 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 chlamydial infection.
7. Describe public health measures for the prevention of chlamydial infection.

# Lessons

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

# Lesson I: Epidemiology: Disease in the U.S.

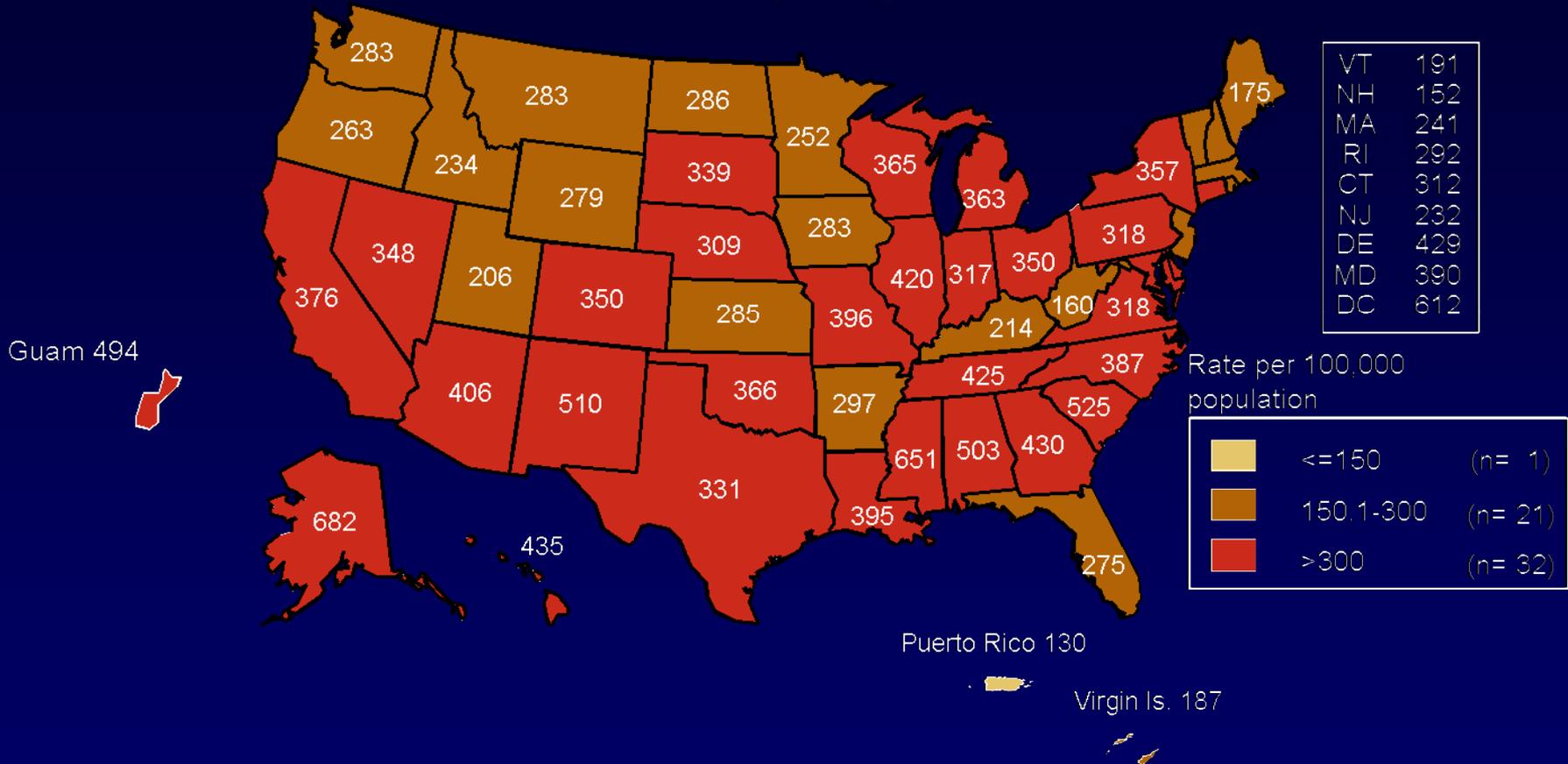
# Incidence and Cost

- Estimated 3 million new cases in U.S. annually
- Most frequently reported disease in U.S.
- Estimated annual incidence of selected STDs:
  - Trichomoniasis — 7.4 million
  - Human Papillomavirus (HPV) — 6.2 million
  - Herpes Simplex Virus (HSV) — 1.6 million
  - Gonorrhea — 718,000
  - Syphilis — 37,000
- Direct and indirect annual costs total approximately \$2.4 billion

# National Chlamydia Surveillance Systems

- Case Reporting
- National Prevalence Survey
- Prevalence Monitoring (sentinel clinics)

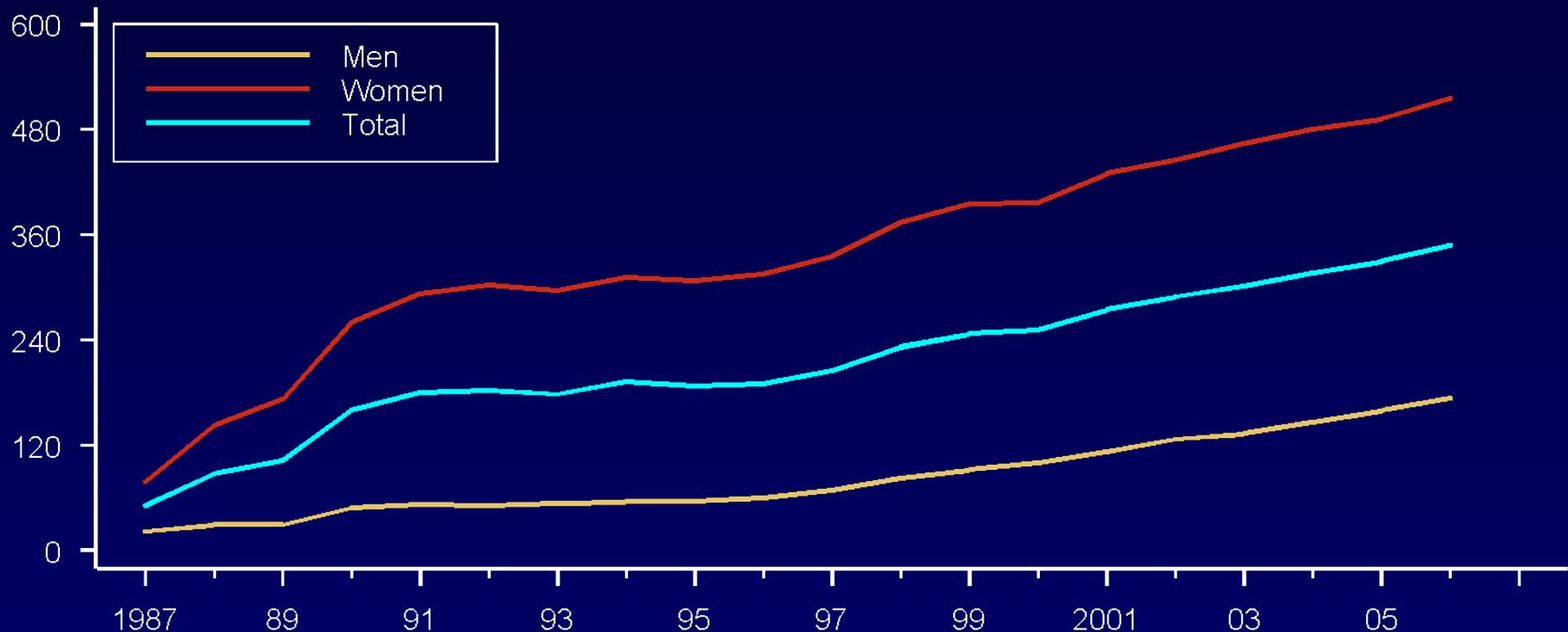
# Chlamydia — Reported rates by state: United States and outlying areas, 2006



Note: 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.

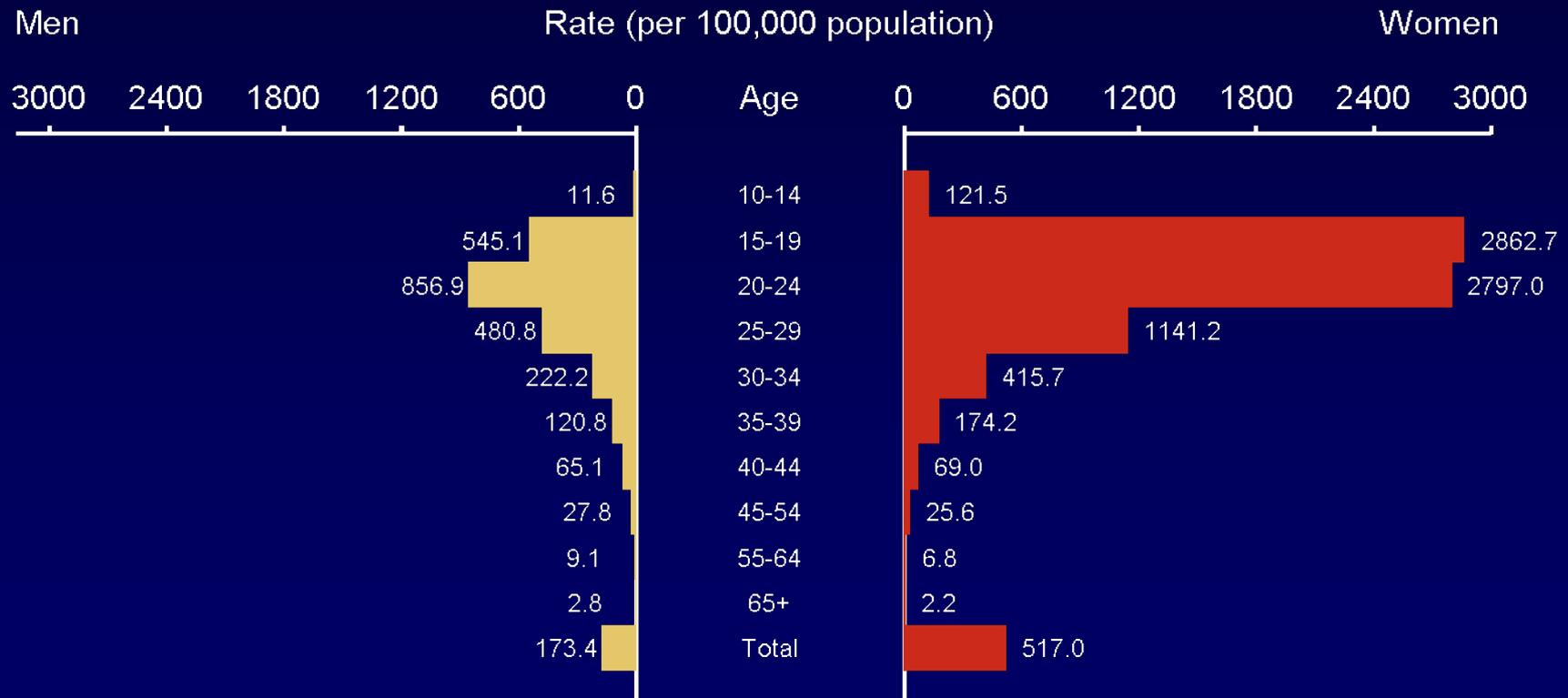
# Chlamydia — Reported rates: Total and by sex: United States, 1987–2006

Rate (per 100,000 population)

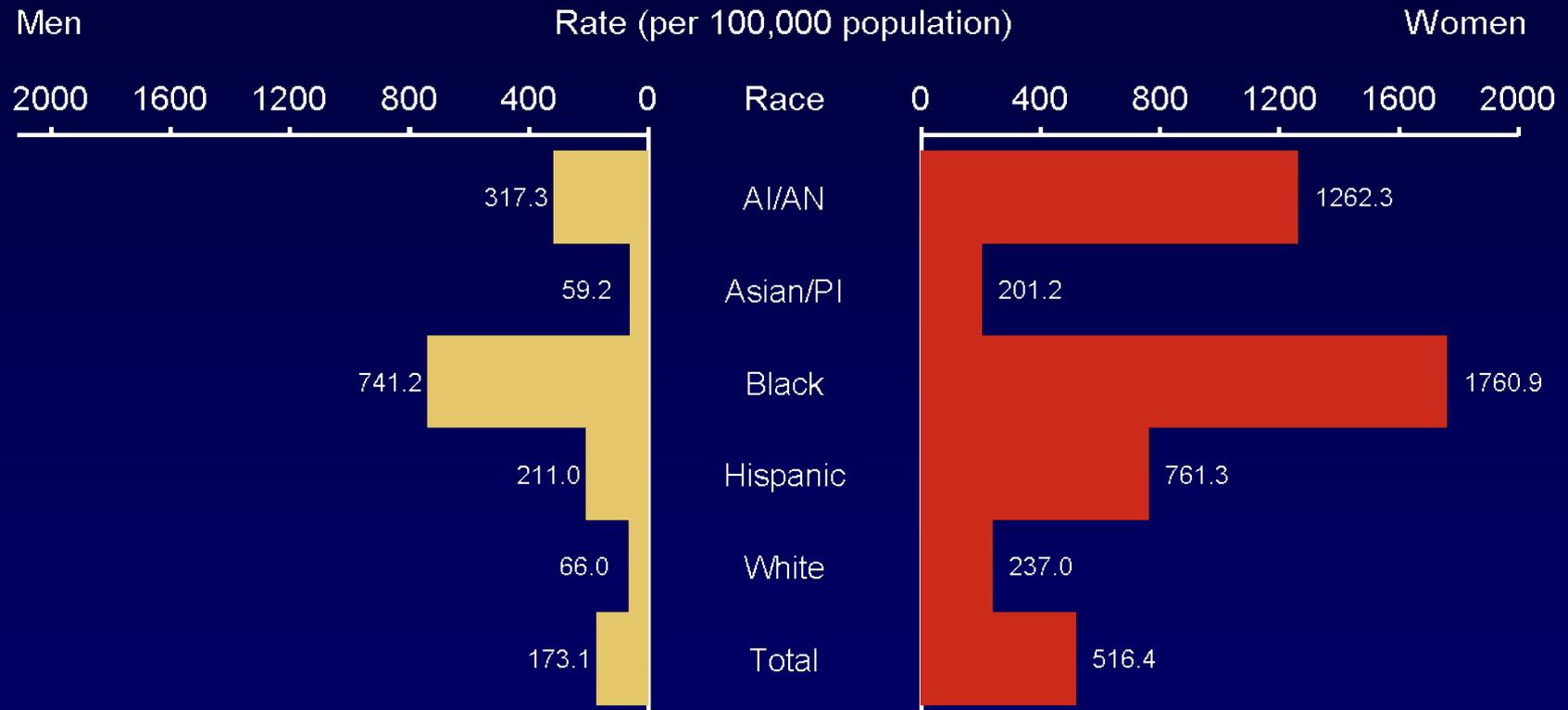


Note: As of January 2000, all 50 states and the District of Columbia had regulations requiring the reporting of chlamydia cases.

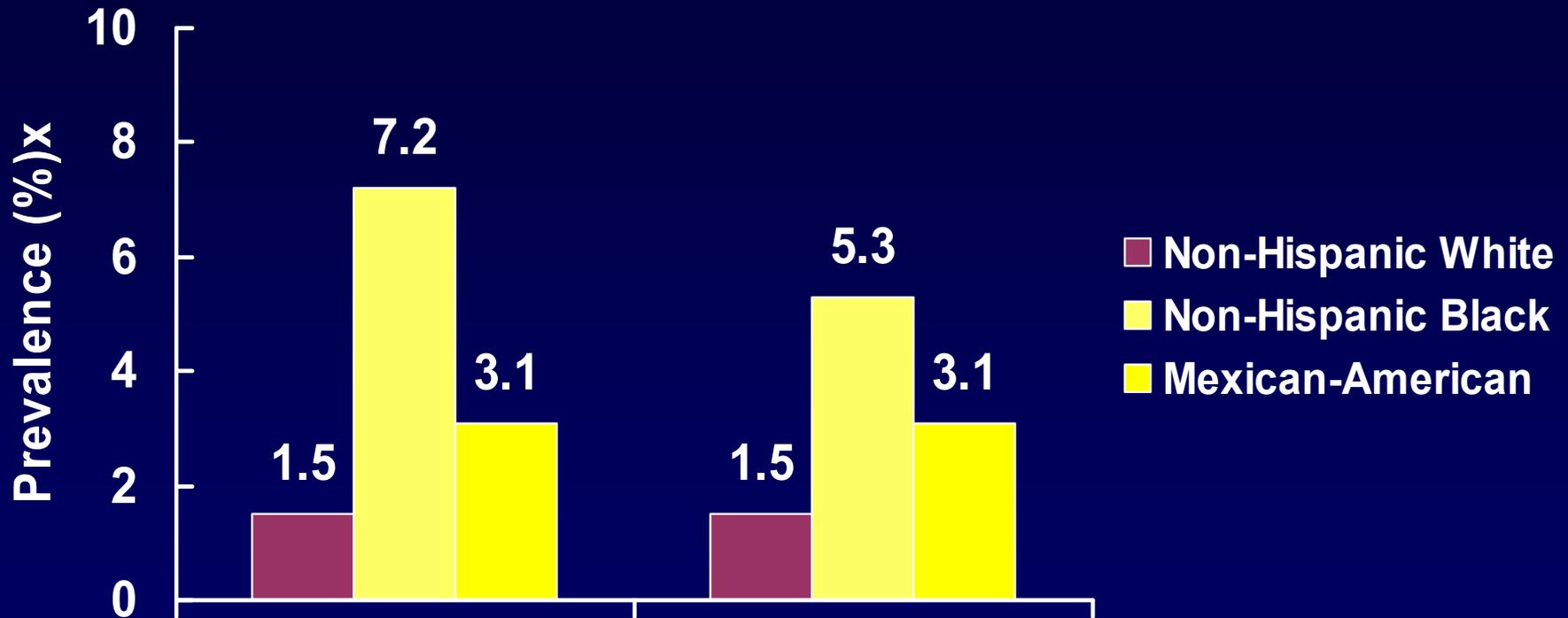
# Chlamydia — Reported rates by age- and sex: United States, 2006



# Chlamydia — Reported rates by race/ethnicity and sex: United States, 2006



# Chlamydia Prevalence Among Women and Men Aged 14-39 Years by Race/Ethnicity (NHANES)\*, 1999-2002

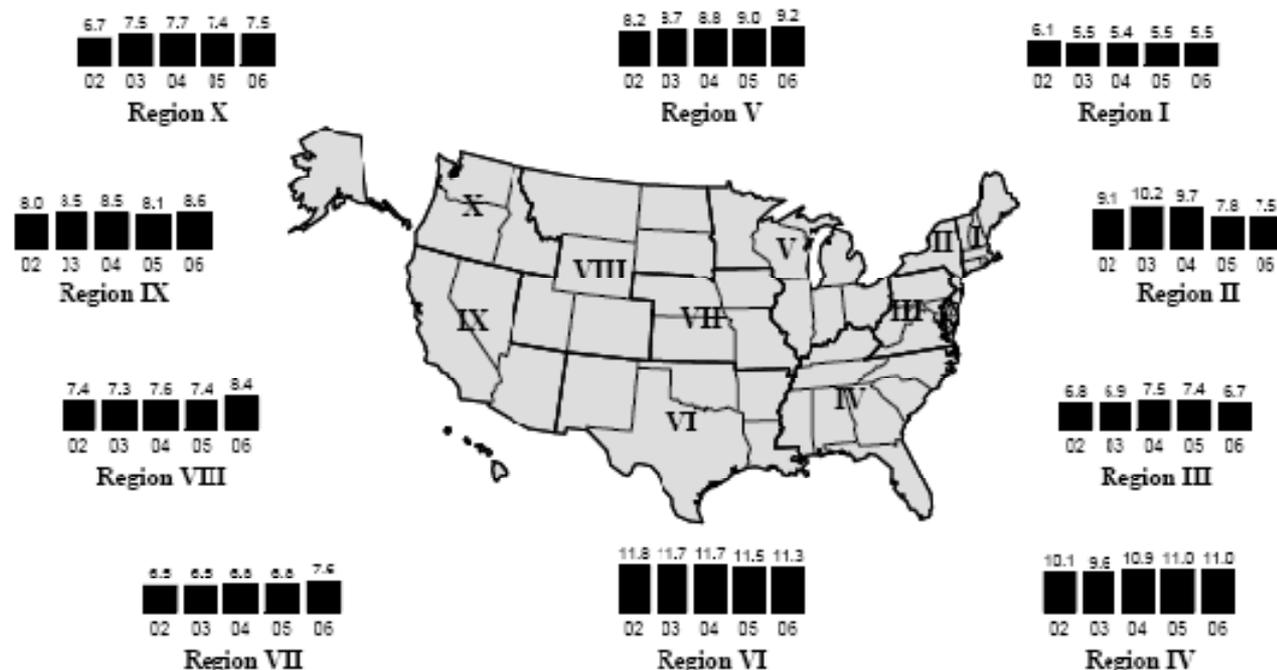


\*National Health and Nutrition Examination Survey

## Screening Results: Women in Sentinel Clinics

- Prevalence (approximate) in selected female populations:
  - Family planning clinics, 3%-14%
  - Indian Health Service, 7%-10%
  - Youth detention facilities, 6%-28%
  - National job training recruits, 4%-17%

**Figure 7. Chlamydia — Trends in positivity among 15- to 24-year-old women tested in family planning clinics by HHS region, 2002–2006**



Note: Trends adjusted for changes in laboratory test method and associated increases in test sensitivity.

SOURCE: Regional Infertility Prevention Projects, Office of Population Affairs, Local and State STD Control Programs; Centers for Disease Control and Prevention

# Risk Factors

- Adolescence
- New or multiple sex partners
- History of STD infection
- Presence of another STD
- Oral contraceptive user
- Lack of barrier contraception

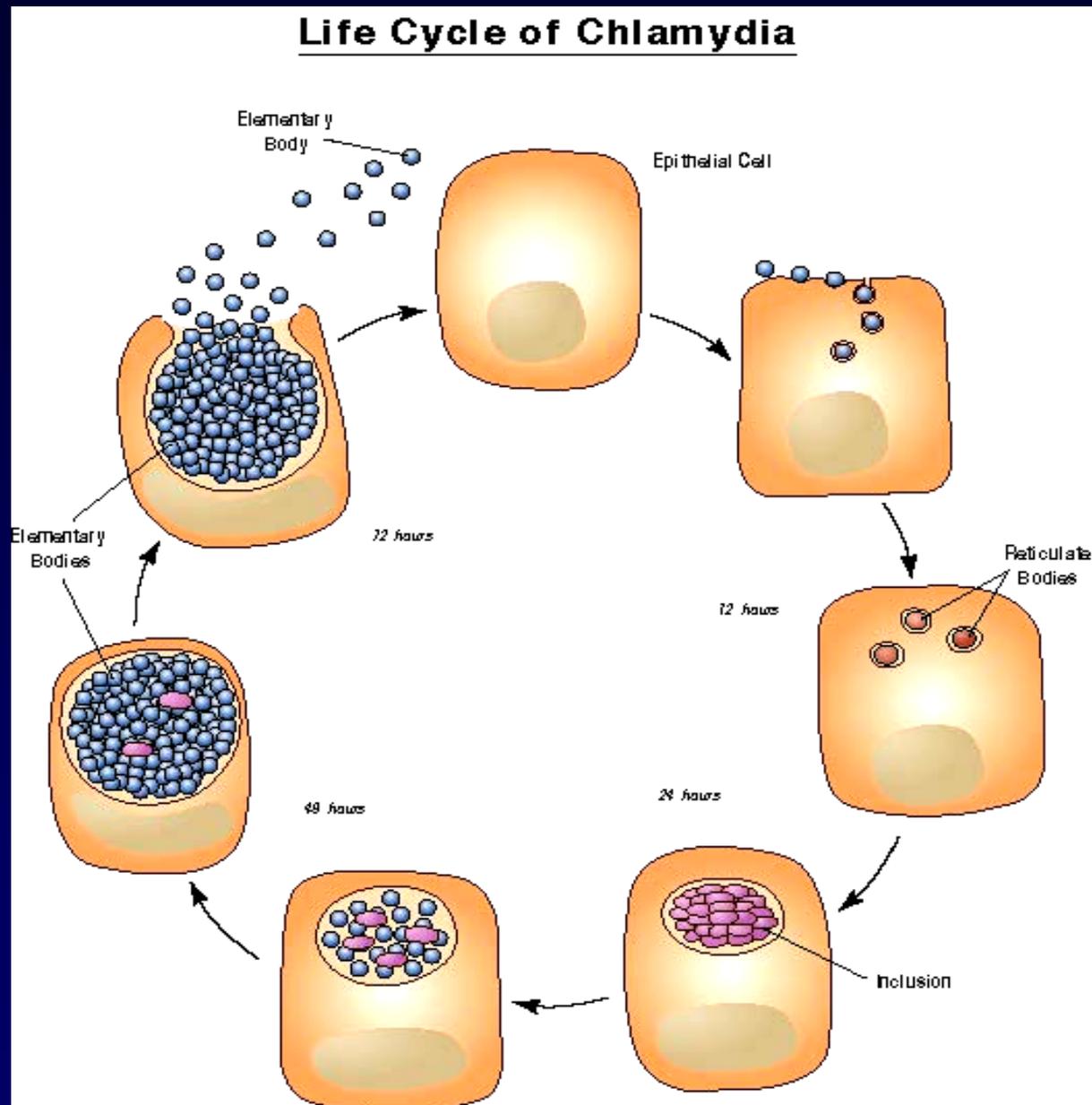
# Transmission

- Transmission is **sexual** or **vertical**
- Highly transmissible
- Incubation period 7-21 days
- Significant asymptomatic reservoir
- Re-infection is common
- Perinatal transmission results in neonatal conjunctivitis in 30%-50% of exposed babies

# Lesson II: Pathogenesis

# Microbiology

- Obligatory intracellular bacteria
- Infect columnar epithelial cells
- Survive by replication that results in the death of the cell
- Takes on two forms in its life cycle:
  - Elementary body (EB)
  - Reticulate body (RB)



# Chlamydiaceae Family

## (species that cause disease in humans)

Species	Disease
<i>C. trachomatis</i> 2 biovars, non-LGV LGV	Trachoma, NGU, MPC, PID, conjunctivitis, Infant pneumonia, LGV
<i>C. pneumoniae</i>	Pharyngitis, bronchitis, pneumonia
<i>C. psittaci</i>	Psittacosis

# Lesson III: Clinical Manifestations

# Clinical Syndromes Caused by *C. trachomatis*

	Local Infection	Complication	Sequelae
Men	Conjunctivitis Urethritis Proctitis	Epididymitis Reiter's syndrome (rare)	Infertility (rare) Chronic arthritis (rare)
Women	Conjunctivitis Urethritis Cervicitis Proctitis	Endometritis Salpingitis Perihepatitis Reiter's syndrome (rare)	Infertility Ectopic pregnancy Chronic pelvic pain Chronic arthritis (rare)
Infants	Conjunctivitis Pneumonitis Pharyngitis Rhinitis	Chronic lung disease?	Rare, if any

## *C. trachomatis* Infection in Men

- Urethritis—One cause of non-gonococcal urethritis (NGU)
  - Majority (>50%) asymptomatic
  - Symptoms/signs if present: mucopurulent, mucoid or clear urethral discharge, dysuria
  - Incubation period unknown (probably 5-10 days in symptomatic infection)

# Non-Gonococcal Urethritis: Mucoid Discharge



Source: Seattle STD/HIV Prevention Training Center at the University of Washington/UW HSCER Slide Bank

# *C. trachomatis* Complications in Men

- Epididymitis
- Reiter's Syndrome

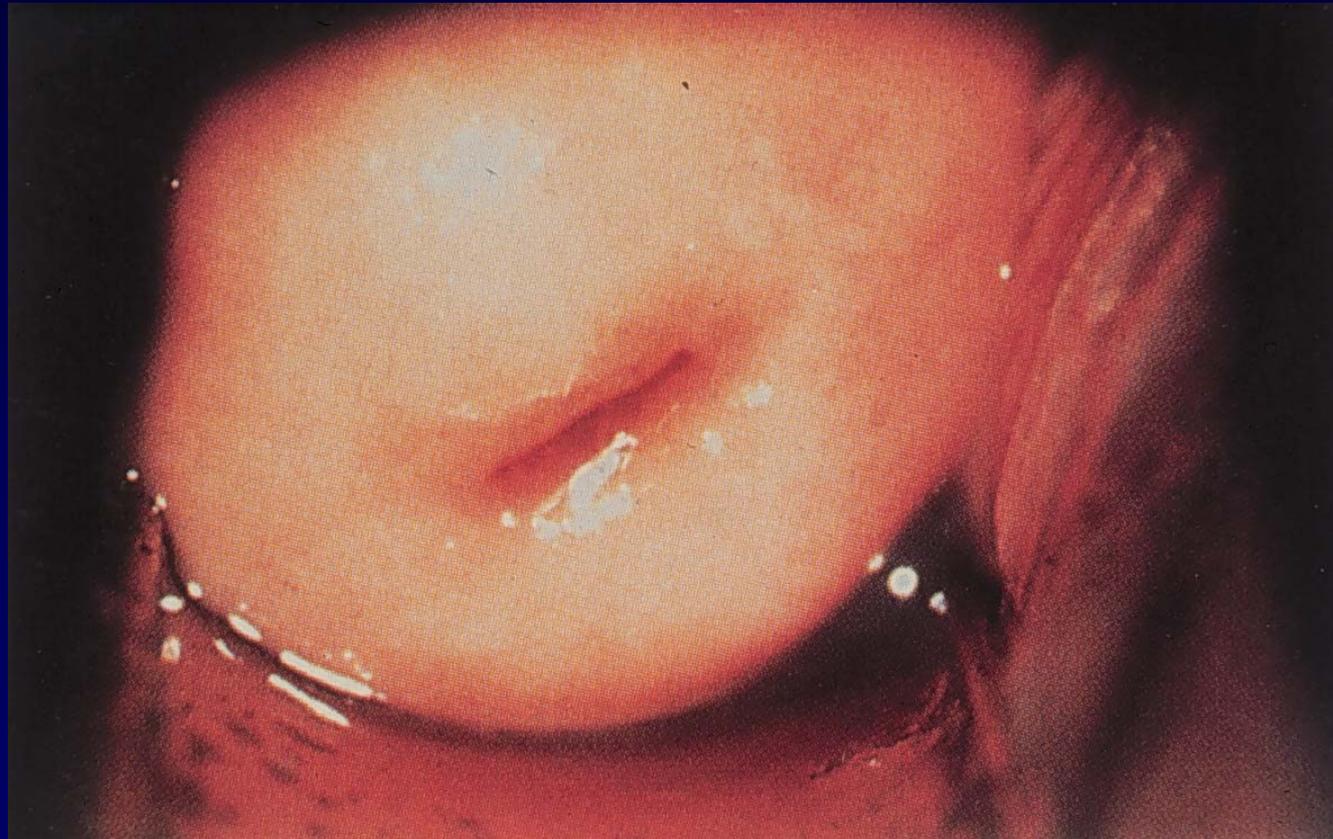
# Swollen or tender testicles (epididymitis)



# *C. trachomatis* Infections in Women

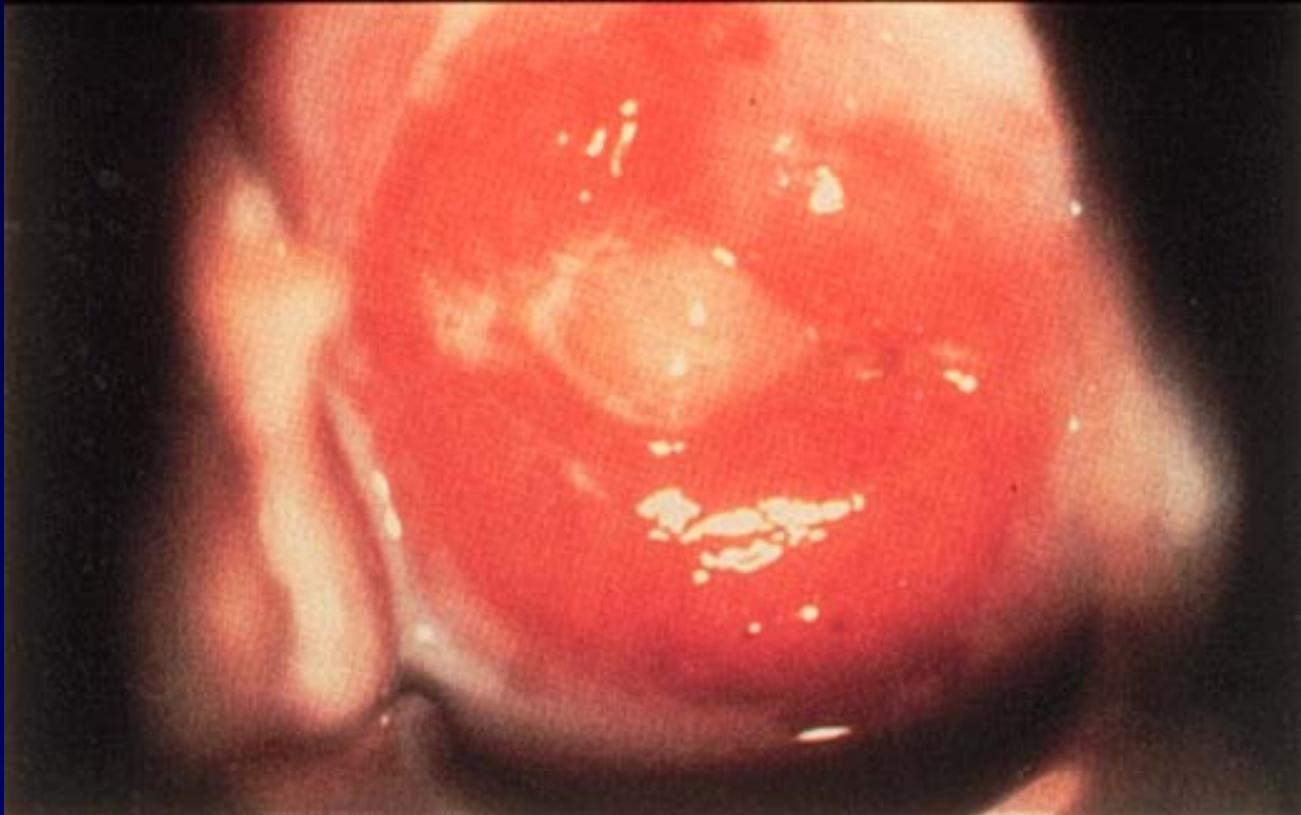
- Cervicitis
  - Majority are asymptomatic
  - Local signs of infection, when present, include:
    - Mucopurulent endocervical discharge
    - Edematous cervical ectopy with erythema and friability
- Urethritis
  - Usually asymptomatic
  - Signs/symptoms, when present, include dysuria, frequency, pyuria

# Normal Cervix



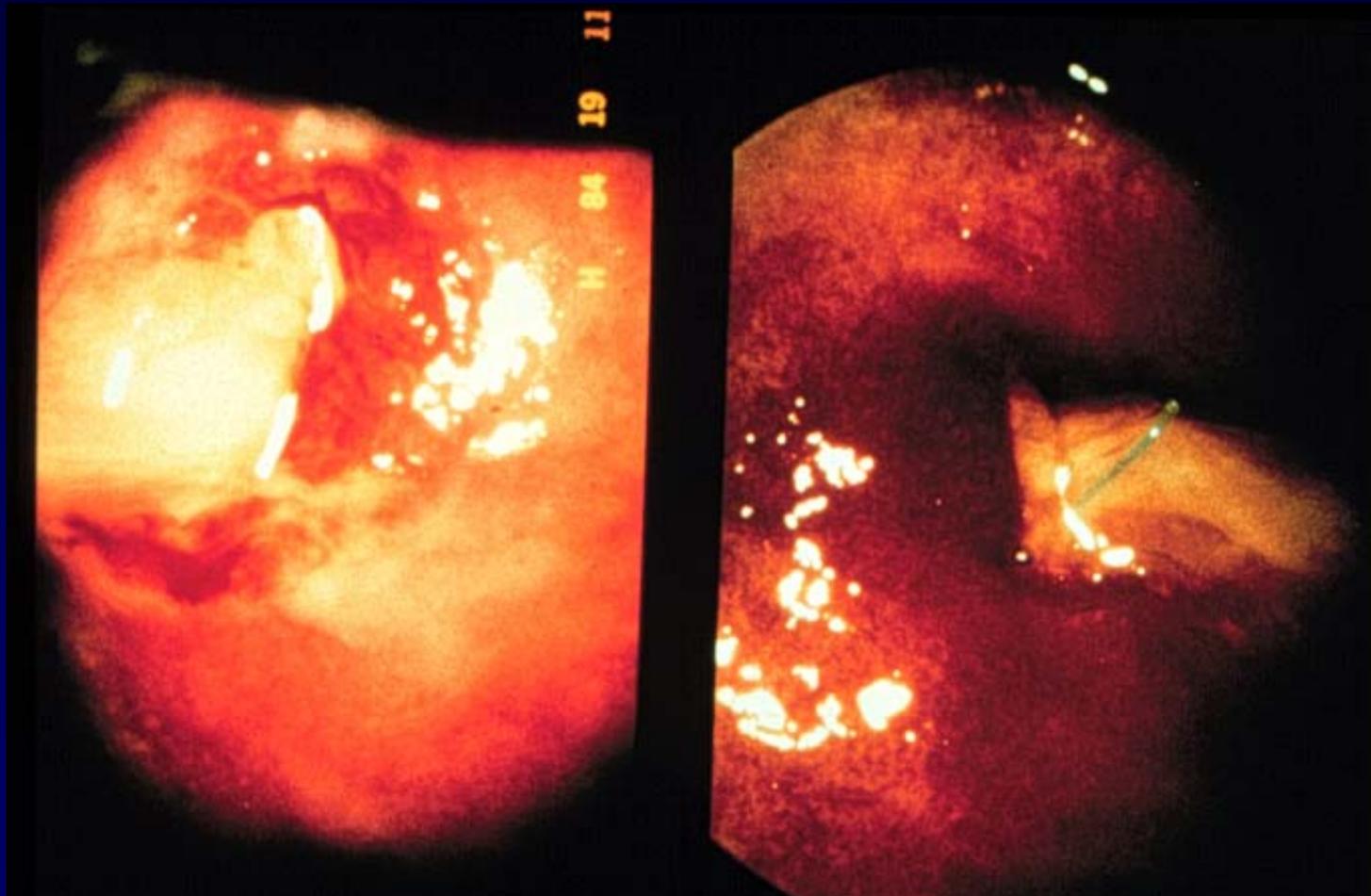
Source: STD/HIV Prevention Training Center at the University of Washington/Claire E. Stevens

# Chlamydial Cervicitis



*Source:* STD/HIV Prevention Training Center at the University of Washington/Connie Celum and Walter Stamm

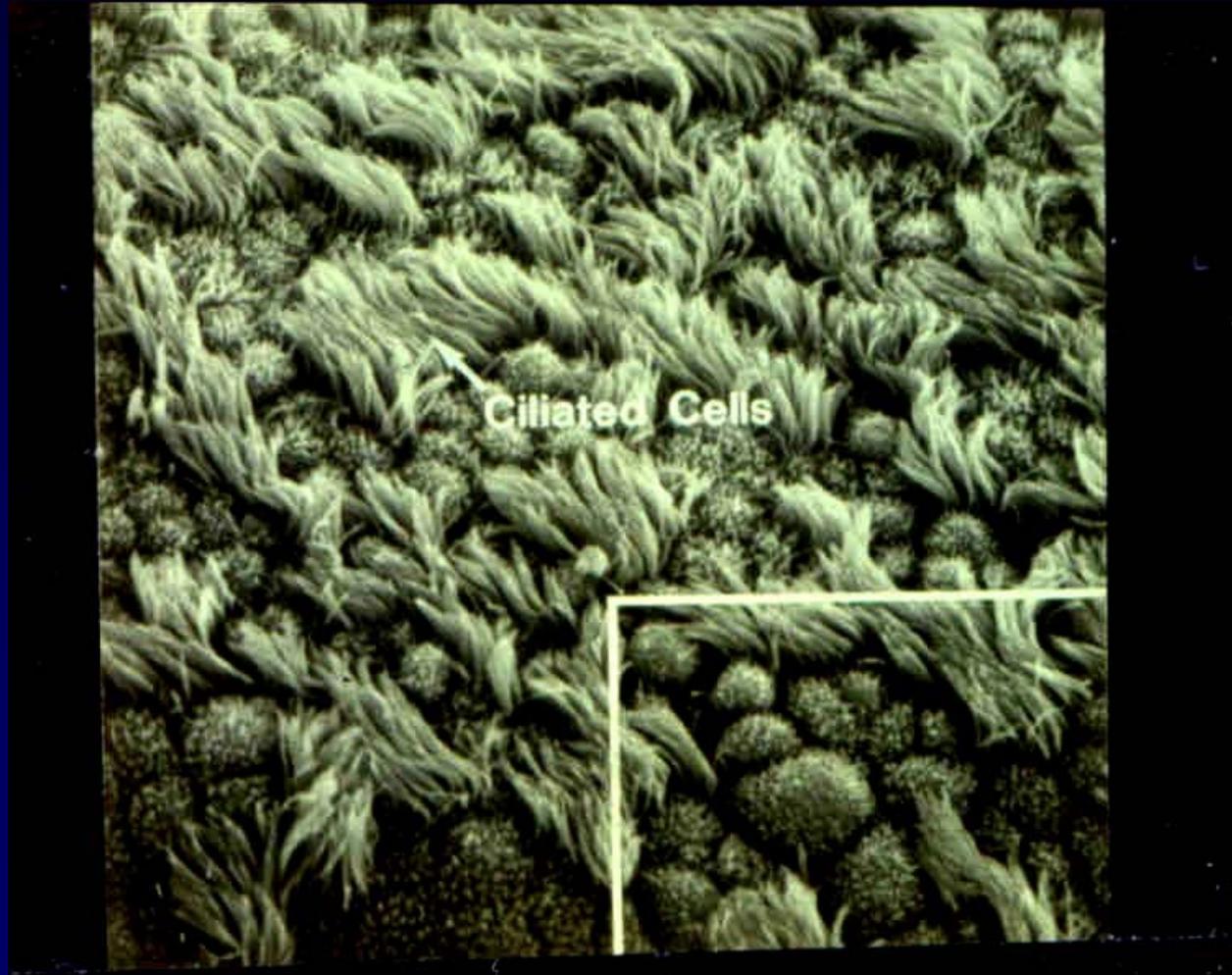
# Cervicitis



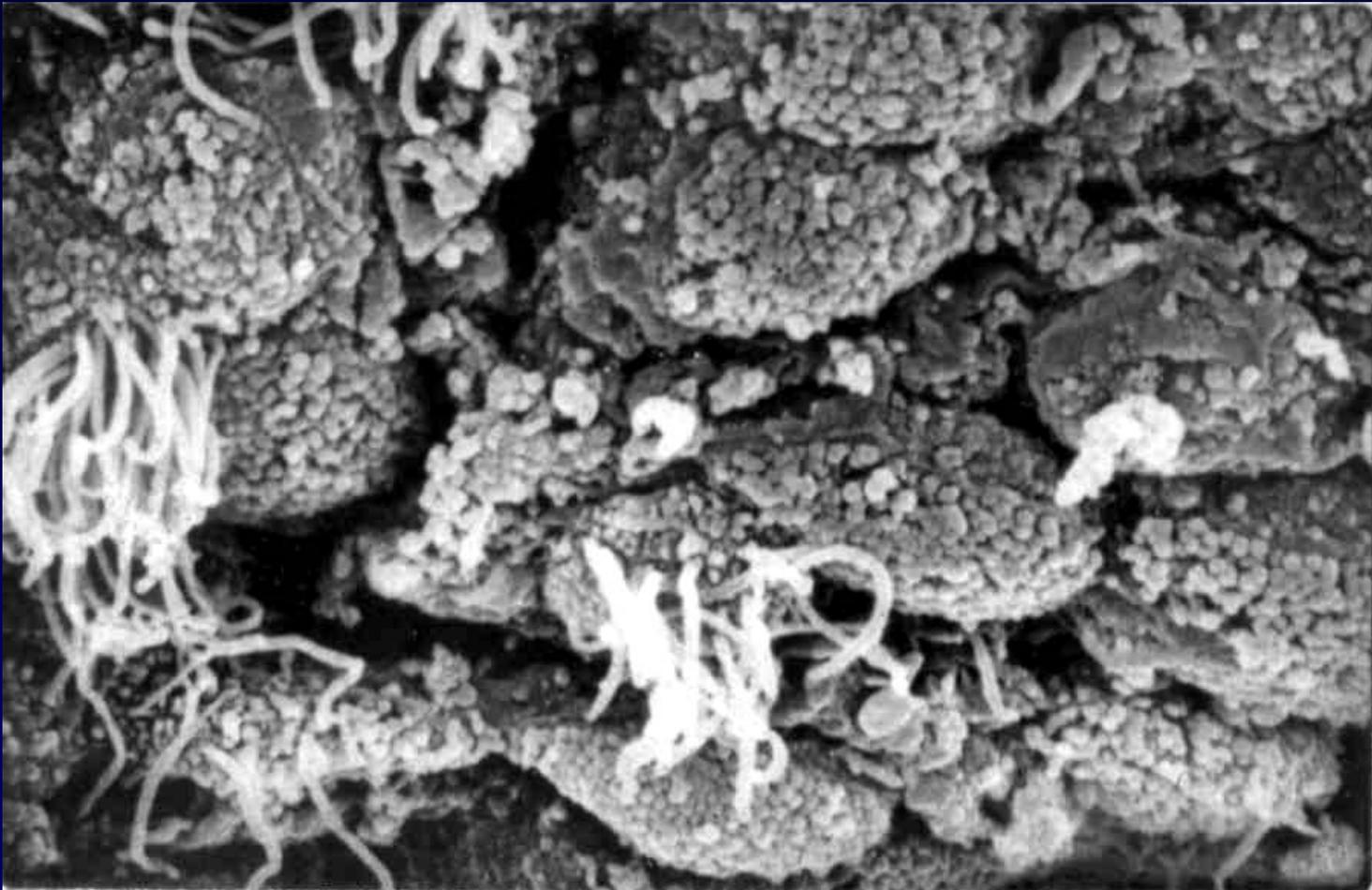
# *C. trachomatis* Complications in Women

- Pelvic Inflammatory Disease (PID)
  - Salpingitis
  - Endometritis
- Perihepatitis (Fitz-Hugh-Curtis Syndrome)
- Reiter's Syndrome

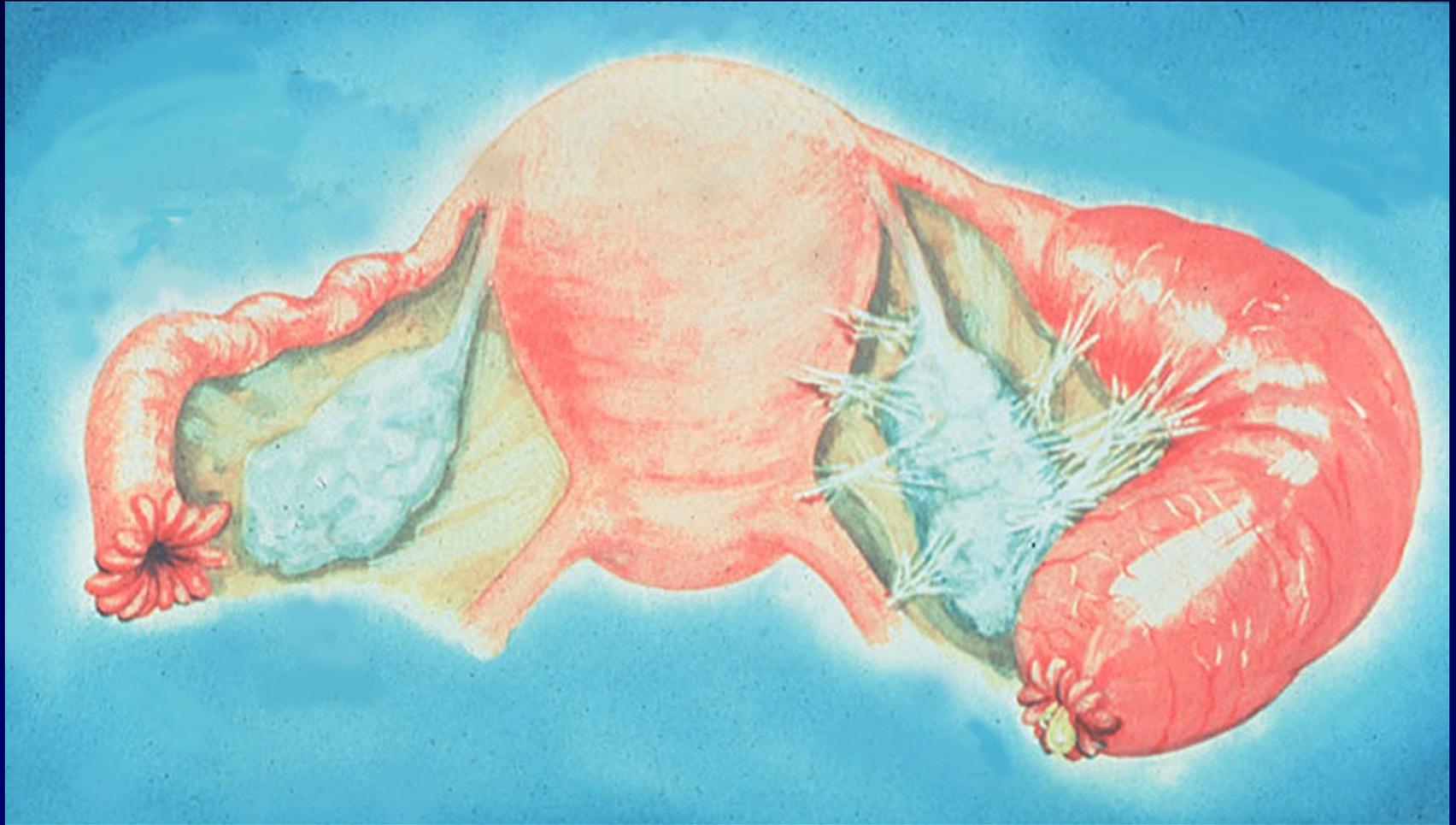
# Normal Human Fallopian Tube Tissue



# *C. trachomatis* Infection (PID)



# Acute Salpingitis



# *C. trachomatis* Syndromes Seen in Men or Women

- Non-LGV serovars
  - Conjunctivitis
  - Proctitis
  - Reiter's Syndrome
- LGV serovars
  - Lymphogranuloma venereum

# LGV Lymphadenopathy



# *C. trachomatis* Infections in Infants

- Perinatal clinical manifestations:
  - Inclusion conjunctivitis
  - Pneumonia

# *C. trachomatis* Infections in Children

- Pre-adolescent males and females:
  - Urogenital infections
    - Usually asymptomatic
    - Vertical transmission
    - Sexual abuse

# Lesson IV: Diagnosis

# Testing Technologies

- Culture
- Non-culture tests
  - Nucleic Acid Amplification Tests (NAATs)
  - Non-Amplification Tests
  - Serology

# Culture

- Historically the “gold standard”
- Variable sensitivity (50%-80%)
- High specificity
- Use in legal investigations
- Not suitable for widespread screening

# NAATs

- NAATs amplify and detect organism-specific genomic or plasmid DNA or rRNA
- Commercially available NAATs include:
  - Becton Dickinson BDProbe Tec®
  - Gen-Probe AmpCT, Aptima®
  - Roche Amplicor®
- Can detect *N. gonorrhoeae* in the same specimen
- Significantly more sensitivity than other tests

# NAATs (continued)

- FDA cleared for:
  - All NAATs
    - urethral swabs from men
    - cervical swabs
    - urine from men and women
  - Certain NAATs
    - vaginal swabs
- Non-FDA cleared for:
  - rectal
  - pharyngeal

(some laboratories have met regulatory requirements)

# Non-Amplification Tests

- Direct fluorescent antibody (DFA)
  - Detects intact bacteria with a fluorescent antibody
  - Variety of specimen sites
- Enzyme immunoassay (EIA)
  - Detects bacterial antigens with an enzyme-labeled antibody
- Nucleic acid hybridization (NA probe)
  - Detects specific DNA or RNA sequences of *C. trachomatis* and *N. gonorrhoeae*

# Serology

- Rarely used for uncomplicated infections
- Comparative data between types of serologic test are lacking
- Criteria used in LGV diagnosis
  - Complement fixation titers  $>1:64$  can support diagnosis in the appropriate clinical context
  - Serologic test interpretation for LGV is not standardized

# Lesson V: Patient Management

# Treatment of Uncomplicated Genital Chlamydial Infections

## **CDC-recommended regimens**

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

## **Alternative regimens**

- Erythromycin base 500 mg orally 4 times a day for 7 days, OR
- Erythromycin ethylsuccinate 800 mg orally 4 times a day for 7 days, OR
- Ofloxacin 300 mg orally twice a day for 7 days
- Levofloxacin 500 mg orally once a day for 7 days

# Treatment of Chlamydial Infection in Pregnant Women

## **CDC-recommended regimens**

- Azithromycin 1 g orally in a single dose, OR
- Amoxicillin 500 mg orally 3 times a day for 7 days

## **Alternative regimens**

- Erythromycin base 500 mg orally 4 times a day for 7 days, OR
- Erythromycin base 250 mg orally 4 times a day for 14 days, OR
- Erythromycin ethylsuccinate 800 mg orally 4 times a day for 7 days, OR
- Erythromycin ethylsuccinate 400 mg orally 4 times a day for 14 days, OR

# Treatment of Neonatal Conjunctivitis and/or Pneumonia

## **CDC-recommended regimen**

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

# Treatment of Chlamydial Infection in Children

## Children who weigh <45 kg:

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

## Children who weigh $\geq 45$ kg, but are <8 years of age:

- Azithromycin 1 g orally in a single dose

## Children $\geq 8$ years of age:

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

# Treatment of Lymphogranuloma Venereum (LGV)

## **CDC-recommended regimen**

- Doxycycline 100 mg orally twice a day for 21 days

## **Alternative regimen**

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

# Repeat Testing after Treatment

- Pregnant women
  - Repeat testing, preferably by NAAT, 3 weeks after completion of recommended therapy
- Non-pregnant women
  - Test of cure not recommended unless compliance is in question, symptoms persist, or re-infection is suspected
  - Repeat testing recommended 3-4 months after treatment, especially adolescents due to high prevalence of repeated infection
  - Screen at next health care visit

# Lesson VI: Prevention

# Why Screen for Chlamydia?

- Screening can reduce the incidence of PID by more than 50%.
- Most infections are asymptomatic.
- Screening decreases the prevalence of infection in the population and reduces the transmission of disease.

# Screening Recommendations: Non-pregnant Women

- Sexually active women age 25 years and under should be screened annually.
- Women >25 years old should be screened if risk factors are present.
- Repeat testing of all women 3-4 months after treatment for *C. trachomatis* infection, especially adolescents.
- Repeat testing of all women treated for *C. trachomatis* when they next present for care within 12 months.

# Screening Recommendations: Pregnant Women

- Screen all pregnant women at the first prenatal visit.
- Pregnant women aged <25 years and those at increased risk for chlamydia should be screened again in the third trimester.

# Partner Management

- Sex partners should be evaluated, tested, and treated if they had sexual contact with the patient during the 60 days preceding the onset of symptoms or diagnosis of chlamydia.
- 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.
- Delivery of therapy to sex partners by heterosexual male or female patients might be an option.

# Reporting

- Chlamydia is a reportable STD in all states.
- Report cases to the local or state STD program.

# Prevention Counseling

- Nature of the infection
  - Chlamydia is commonly asymptomatic in men and women.
  - In women, there is an increased risk of upper reproductive tract damage with re-infection.
- Transmission issues
  - Effective treatment of chlamydia may reduce HIV transmission and acquisition.
  - Abstain from sexual intercourse until partners are treated and for 7 days after a single dose of azithromycin or until completion of a 7-day regimen.

# Prevention Counseling (continued)

- Risk reduction

The clinician should:

- Assess the patient's behavior-change potential.
- Discuss prevention strategies (abstinence, monogamy, condoms, limit number of sex partners, etc.). Latex condoms, when used consistently and correctly, can reduce the risk of transmission of chlamydia.
- Develop individualized risk-reduction plans.

# Case Study



# History

- Suzy Jones: 17-year-old college student who presents to the Student Health Center 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

# Physical Exam

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

# Questions

1. What is the initial clinical diagnosis?
2. What is the most *likely* microbiologic diagnosis?
3. Which laboratory tests should be ordered or performed?
4. What is the appropriate treatment at the initial visit?

# Laboratory Results

- 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

# Questions

5. What is the final diagnosis?
6. What are the appropriate prevention and counseling messages for Suzy?
7. Who is responsible for reporting this case to the local health department?

# Partner Management

Suzy's sex partners from 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?

# Follow-Up

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

- Her 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?