

# 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.

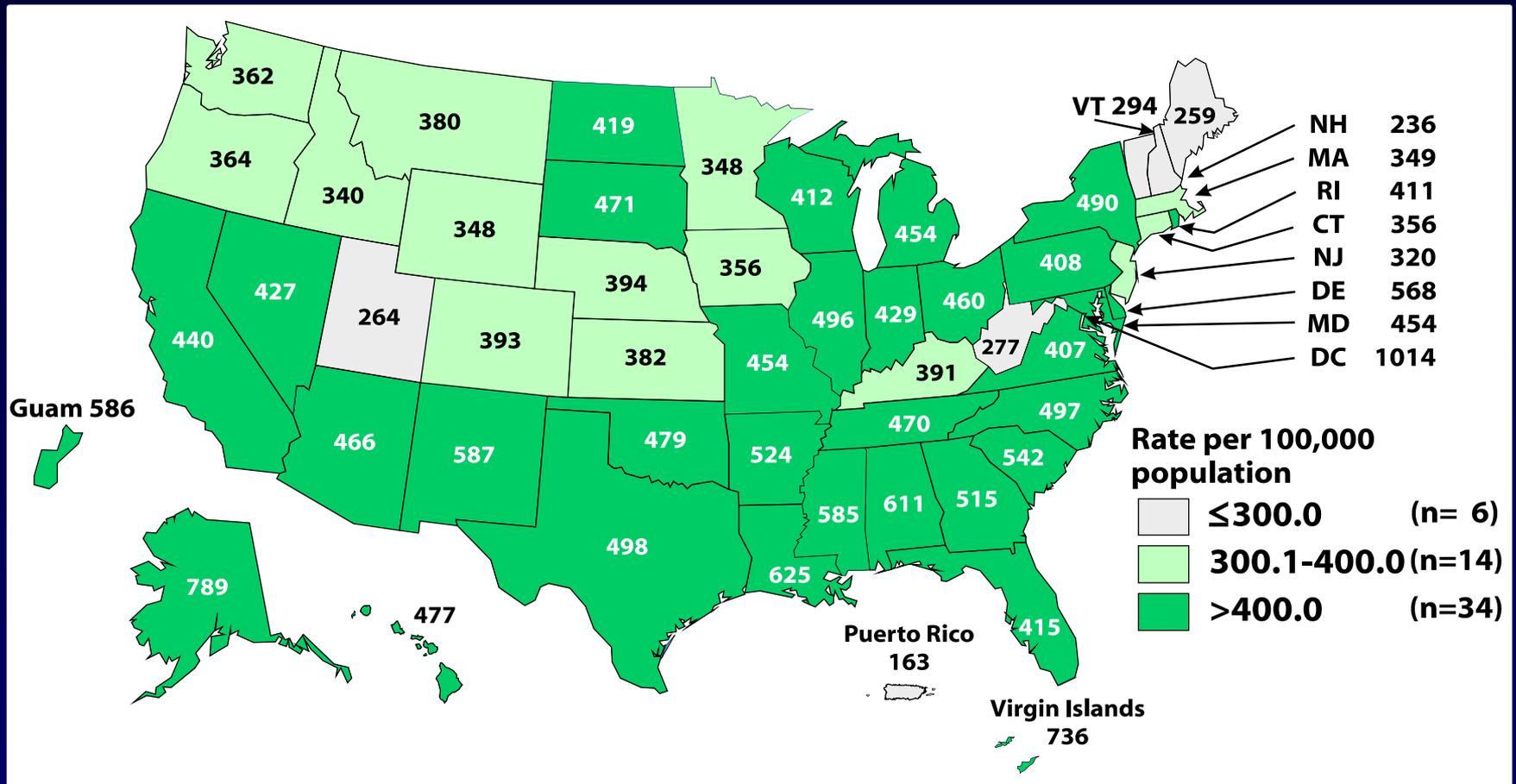
# Incidence and Cost

- Most frequently reported STI in the U.S.
- Estimated 2.9 million new infections in U.S. annually
- Estimated annual incidence of selected STIs:
  - Human Papillomavirus (HPV) — 14.1 million
  - Trichomoniasis — 1.1 million
  - Gonorrhea — 820,000
  - Herpes Simplex Virus (HSV) — 776,000
  - Syphilis — 55,400
- Direct and indirect annual costs total approximately \$2.4 billion

# National Chlamydia Surveillance Systems

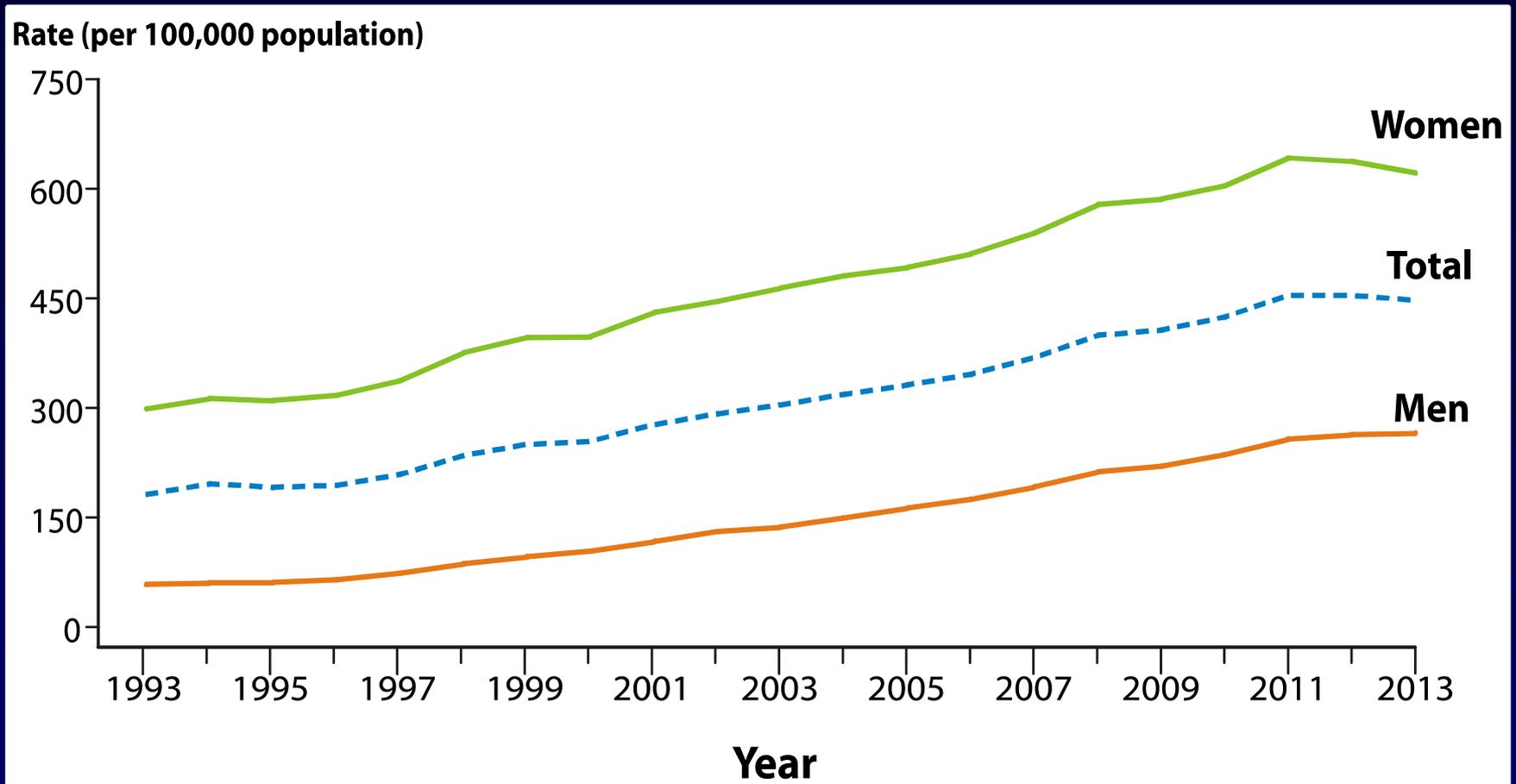
- Case Reporting
- National Prevalence Survey
- Prevalence Monitoring (positivity in sentinel clinics)

# Chlamydia—Rates of Reported Cases by State, United States and Outlying Areas, 2013



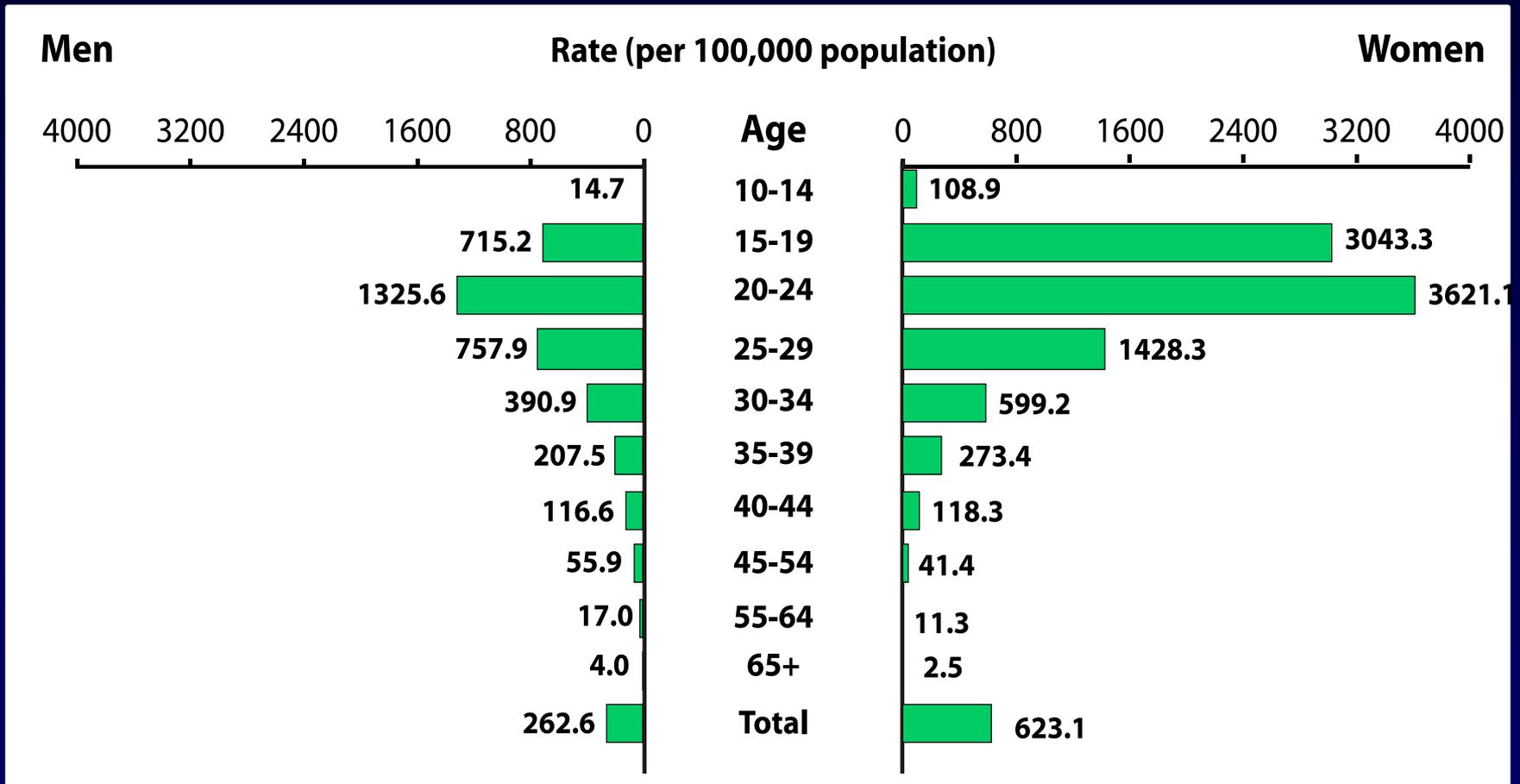
**NOTE:** The total rate of reported cases of chlamydia for the United States and outlying areas (Guam, Puerto Rico, and Virgin Islands) was 443.5 per 100,000 population.

# Chlamydia—Rates of Reported Cases by Sex, United States, 1993–2013

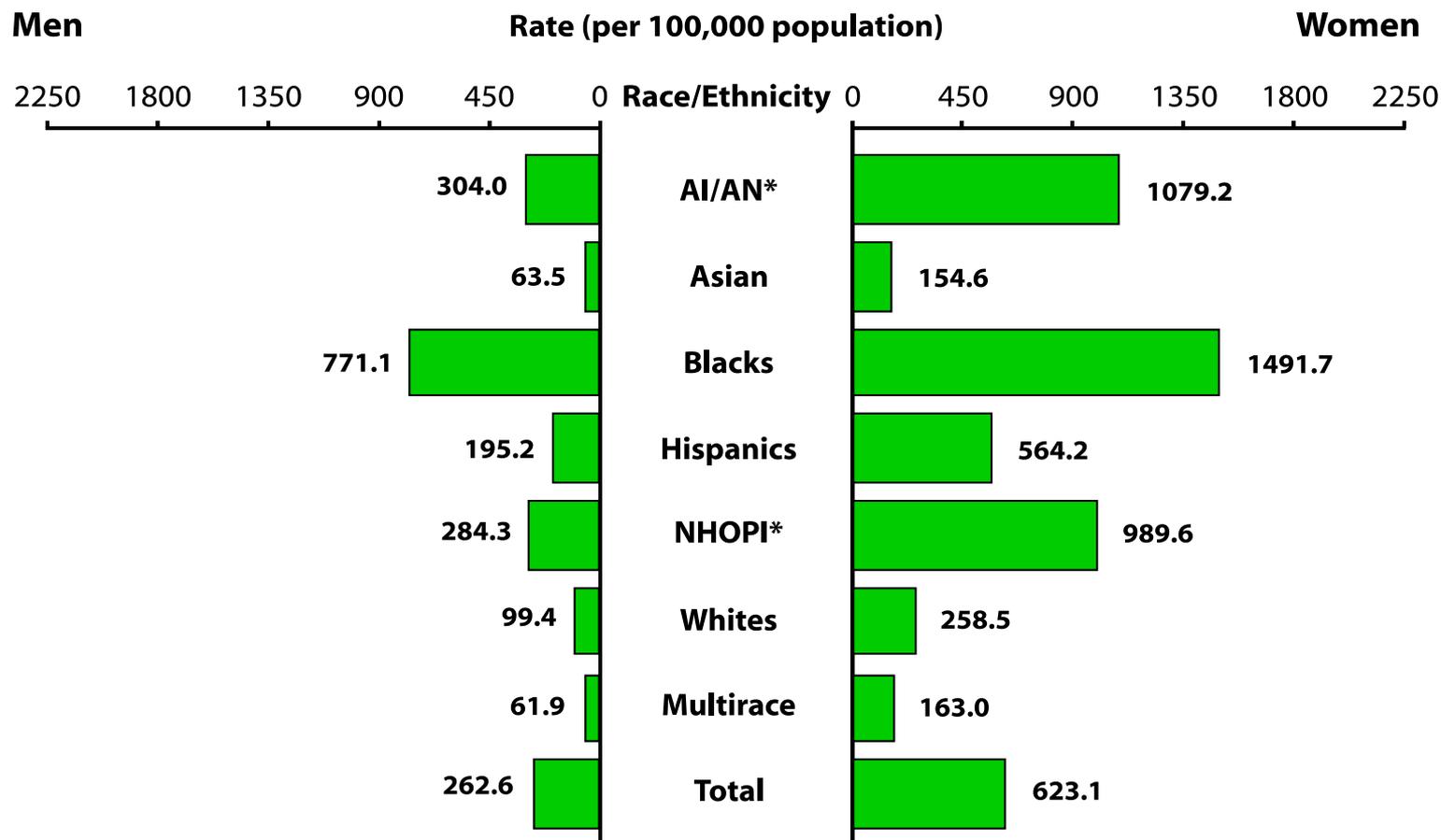


**NOTE:** As of January 2000, all 50 states and the District of Columbia have regulations that require the reporting of chlamydia cases.

# Chlamydia—Rates of Reported Cases by Age and Sex, United States, 2013



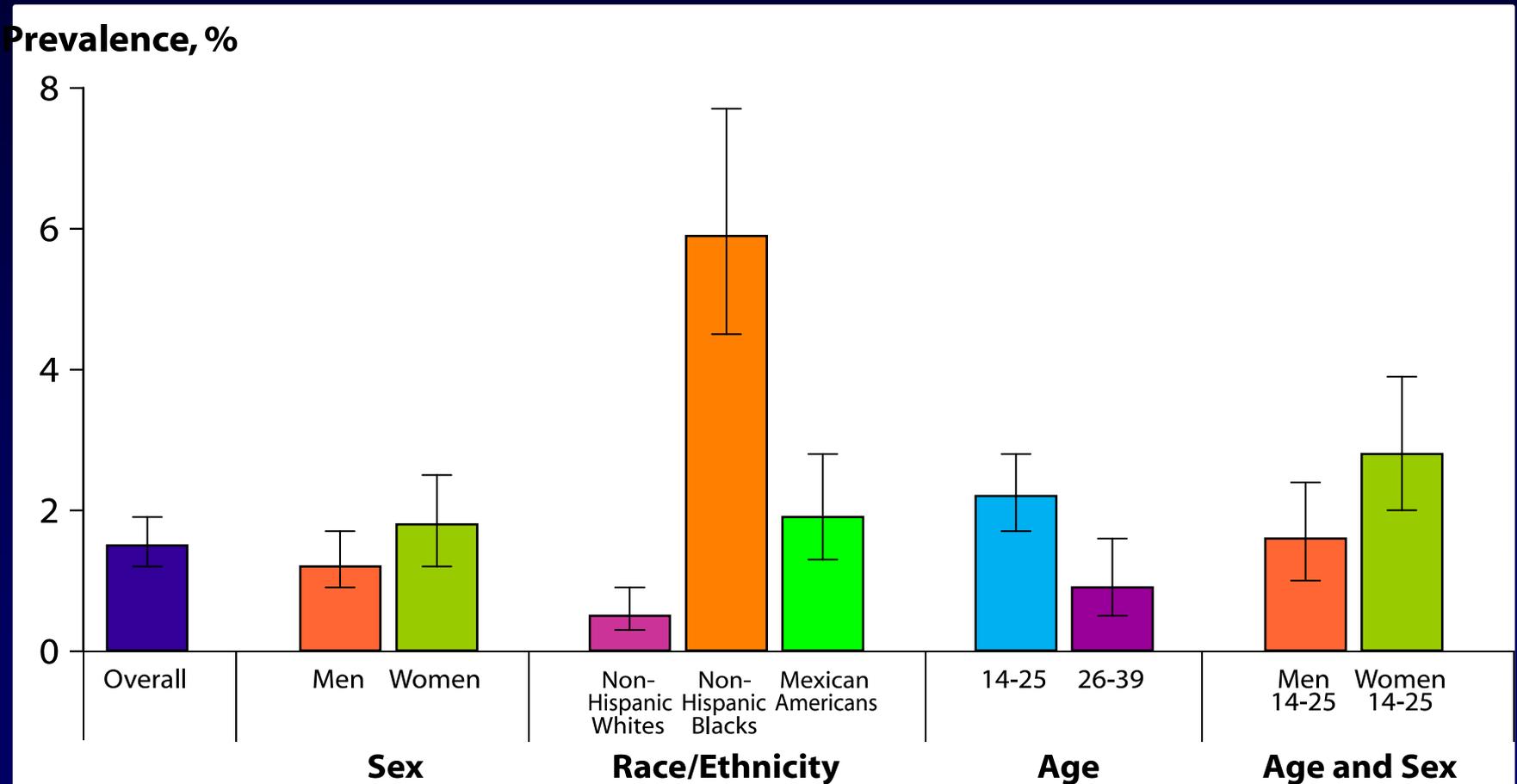
# Chlamydia—Rates of Reported Cases by Race/Ethnicity and Sex, United States, 2013



\*AI/AN = American Indians/Alaska Natives; NHOPI = Native Hawaiian and Other Pacific Islanders.

NOTE: Includes 47 states and the District of Columbia reporting race/ethnicity data in Office of Management and Budget compliant formats in 2013.

# Chlamydia—Prevalence Among Persons Aged 14–39 Years by Sex, Race/Ethnicity, or Age Group, National Health and Nutrition Examination Survey, 2005–2008



NOTE: Error bars indicate 95% confidence intervals.

## Screening Results: Women in Sentinel Clinics, 2009

- Positivity in selected female populations
  - Family planning clinics, 3.5%–15.5%
  - Youth detention facilities, 2%–36%
  - National job training recruits, 4%–19%

# Risk Factors

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

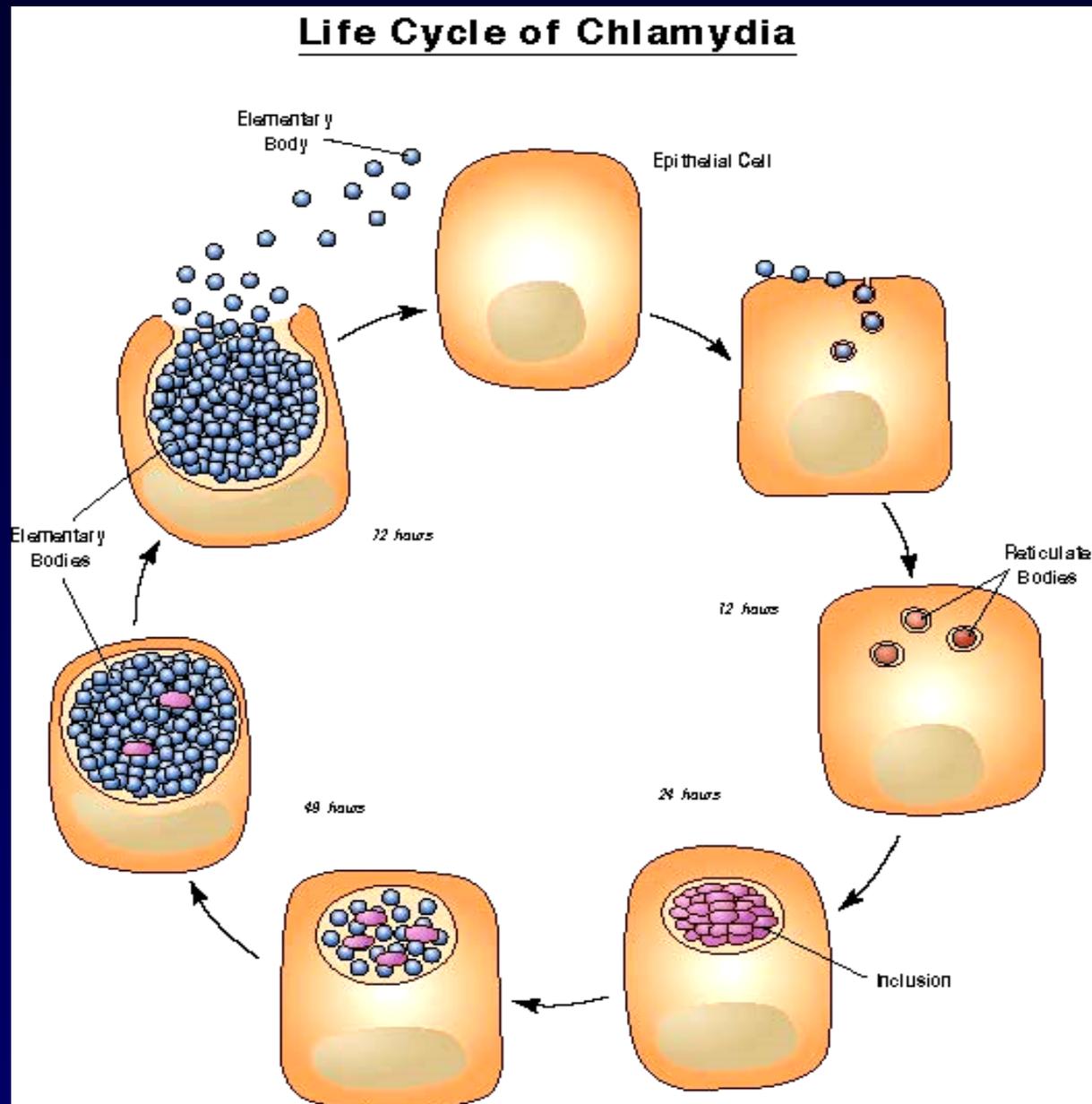
# Transmission

- Transmission is **sexual** or **vertical**
- Highly transmissible
  - > 50% of sexual partners acquire infection
  - 60%–70% of infants exposed during passage through birth canal acquire infection
- Incubation period 7–21 days
- Significant asymptomatic reservoir
- Reinfection is common

# 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 →	Urethritis Proctitis Conjunctivitis	Epididymitis Reactive arthritis (rare)	Infertility (rare) Chronic arthritis (rare)
Women →	Cervicitis Urethritis Proctitis Conjunctivitis	Endometritis Salpingitis Perihepatitis Reactive arthritis (rare)	Infertility Ectopic pregnancy Chronic pelvic pain Chronic arthritis (rare)
Infants →	Conjunctivitis Pneumonitis Pharyngitis Rhinitis	<b>Chronic lung            disease?</b>	Rare, if any 20

## *C. trachomatis* Infection in Men

- Urethritis—One cause of nongonococcal urethritis (NGU)
  - Majority (>50%) asymptomatic
  - Symptoms/signs if present: mucopurulent, mucoid or clear urethral discharge, dysuria
  - Incubation period unknown (probably 7–21 days in symptomatic infection)

# Nongonococcal Urethritis: Muroid Discharge



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

# *C. trachomatis* Complications in Men

- Epididymitis
- Reactive Arthritis

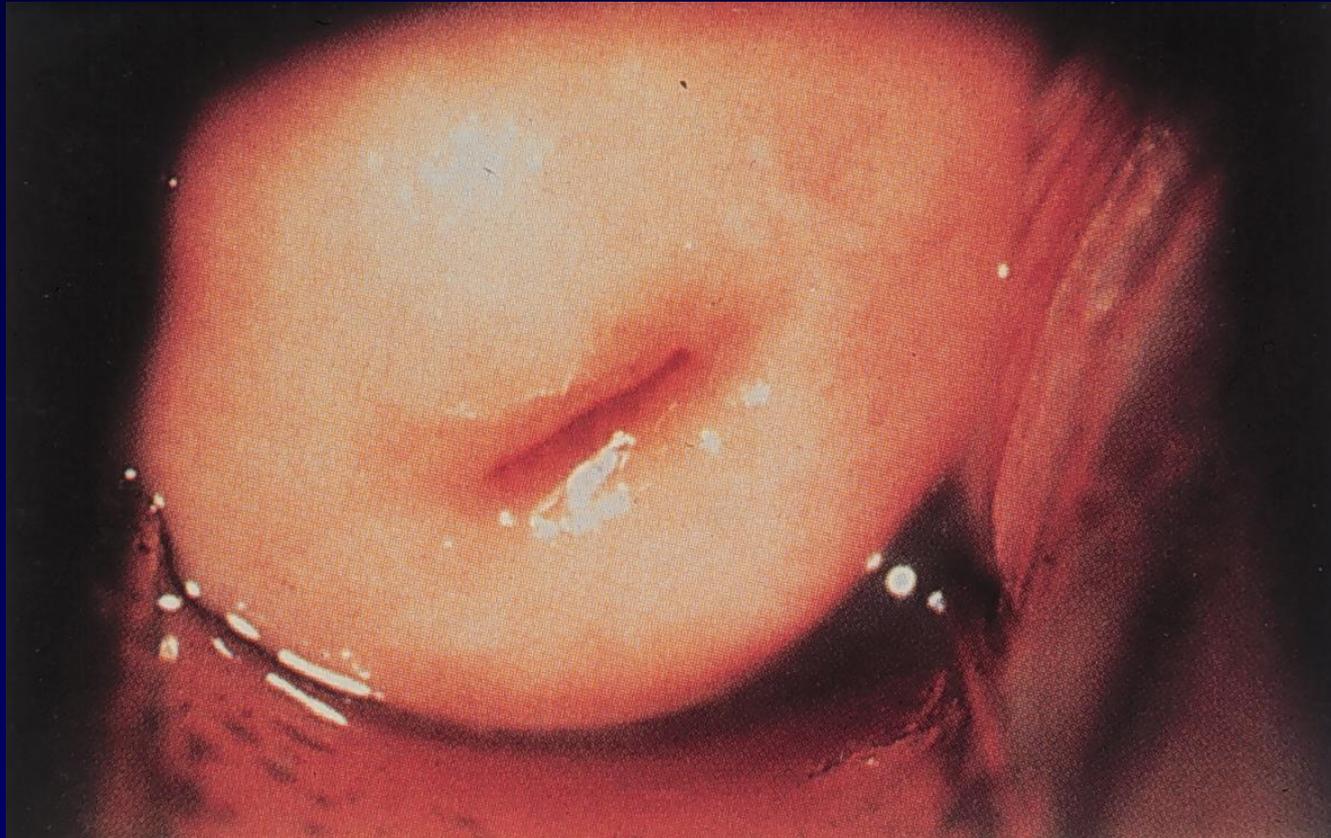
# Swollen or Tender Testicles (epididymitis)



# *C. trachomatis* Infections in Women

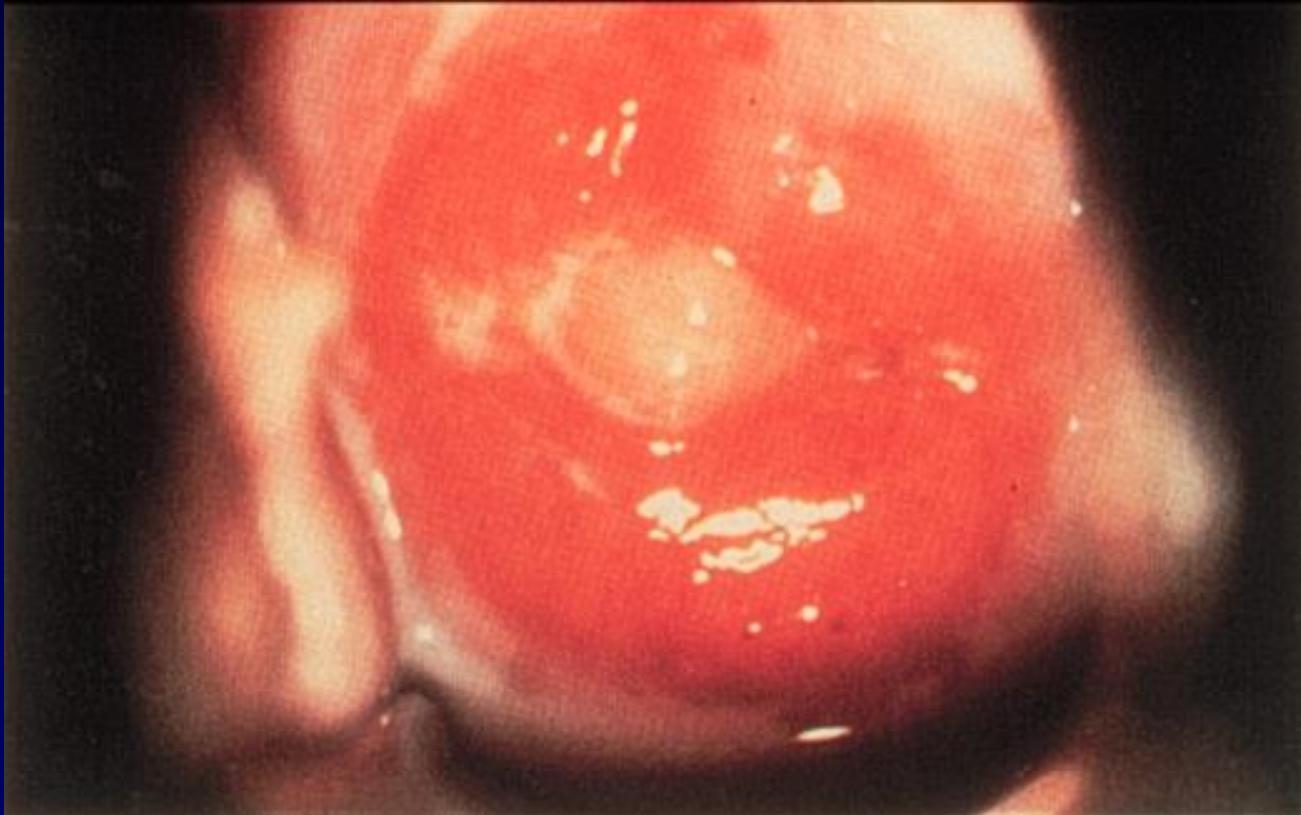
- Cervicitis
  - Majority are asymptomatic
  - Local signs of infection, when present, include
    - Mucopurulent endocervical discharge
    - Edematous cervix with erythema and friability
- Urethritis
  - Usually asymptomatic
  - Signs/symptoms, when present, include dysuria, frequency, “sterile” pyuria

# Normal Cervix



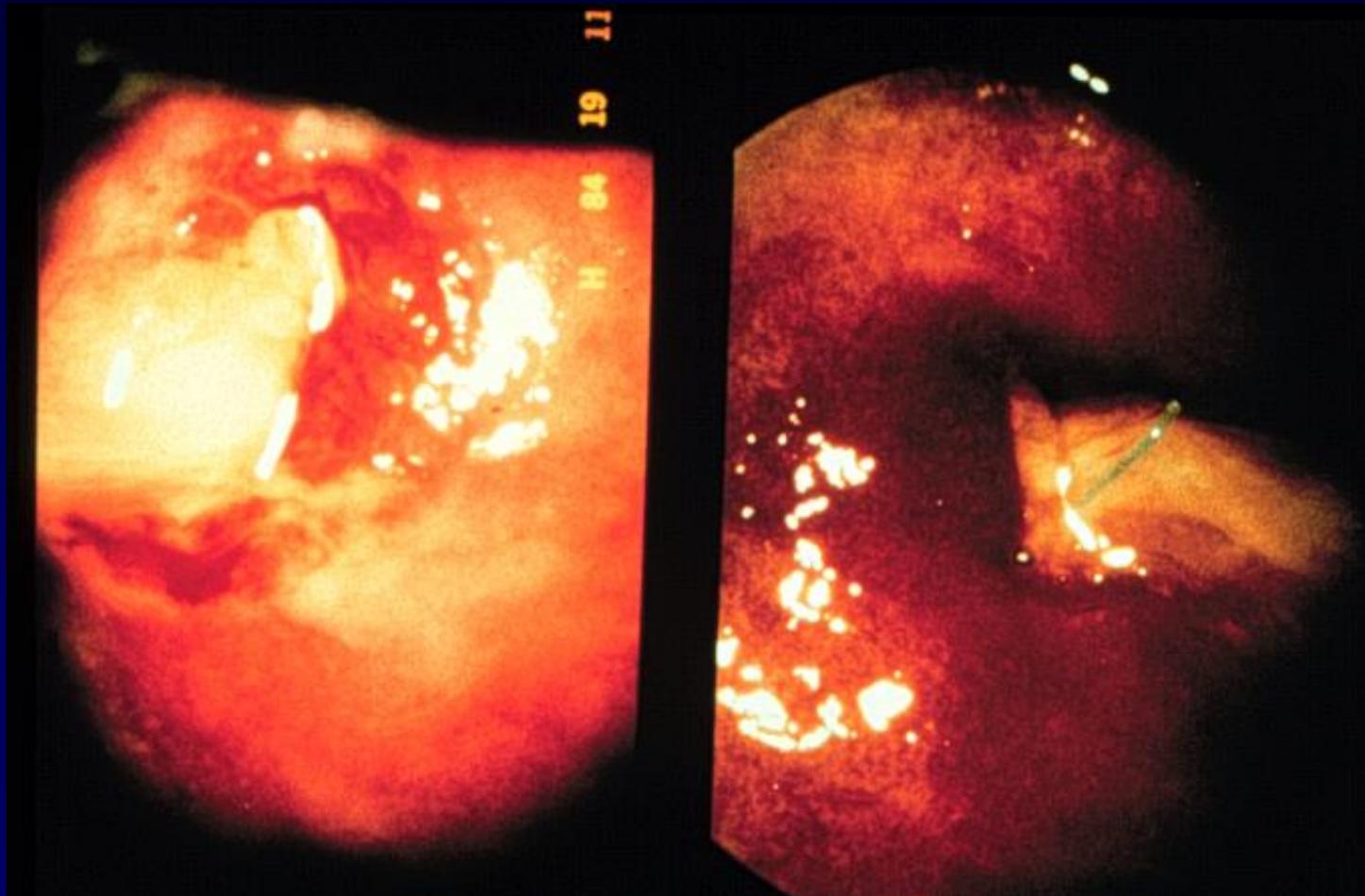
Source: STD/HIV Prevention Training Center at the University of Washington/Claire E. Stevens

# Chlamydial Cervicitis



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

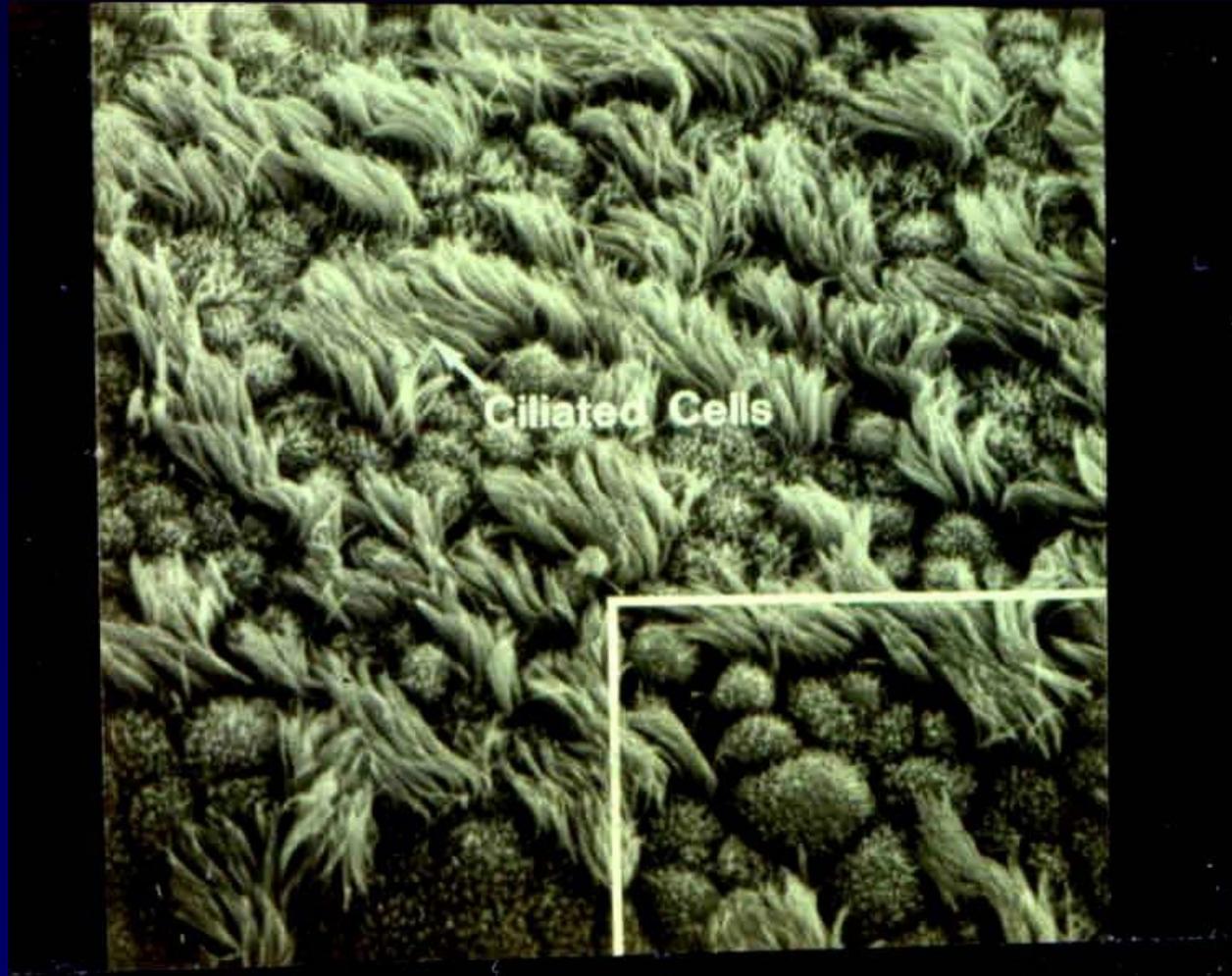
# Cervicitis



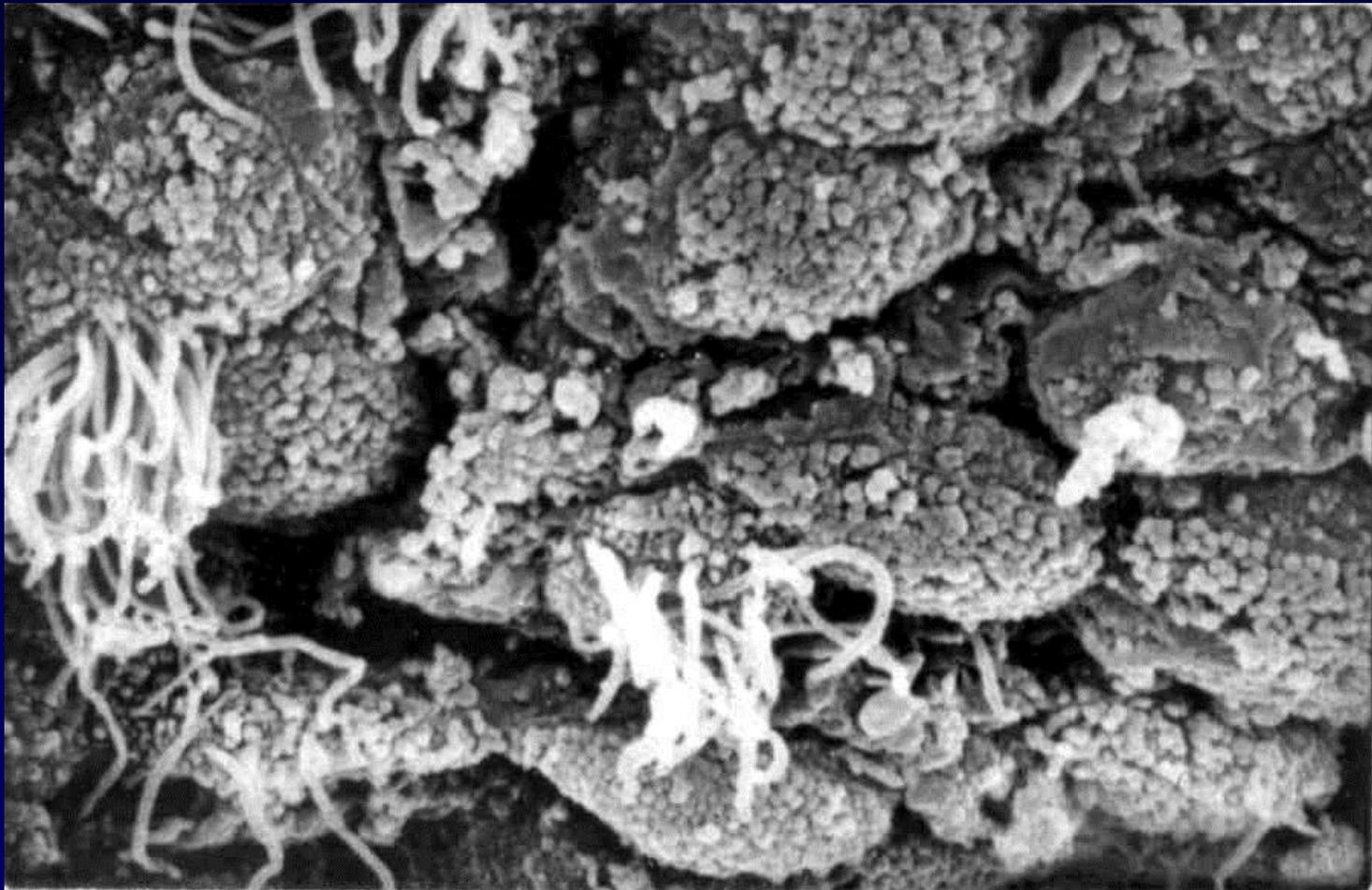
# *C. trachomatis* Complications in Women

- Pelvic Inflammatory Disease (PID)
  - Endometritis
  - Salpingitis
  - Tubo-ovarian abscess
  - Peritonitis
- Perihepatitis (Fitz-Hugh-Curtis Syndrome)
- Reactive arthritis

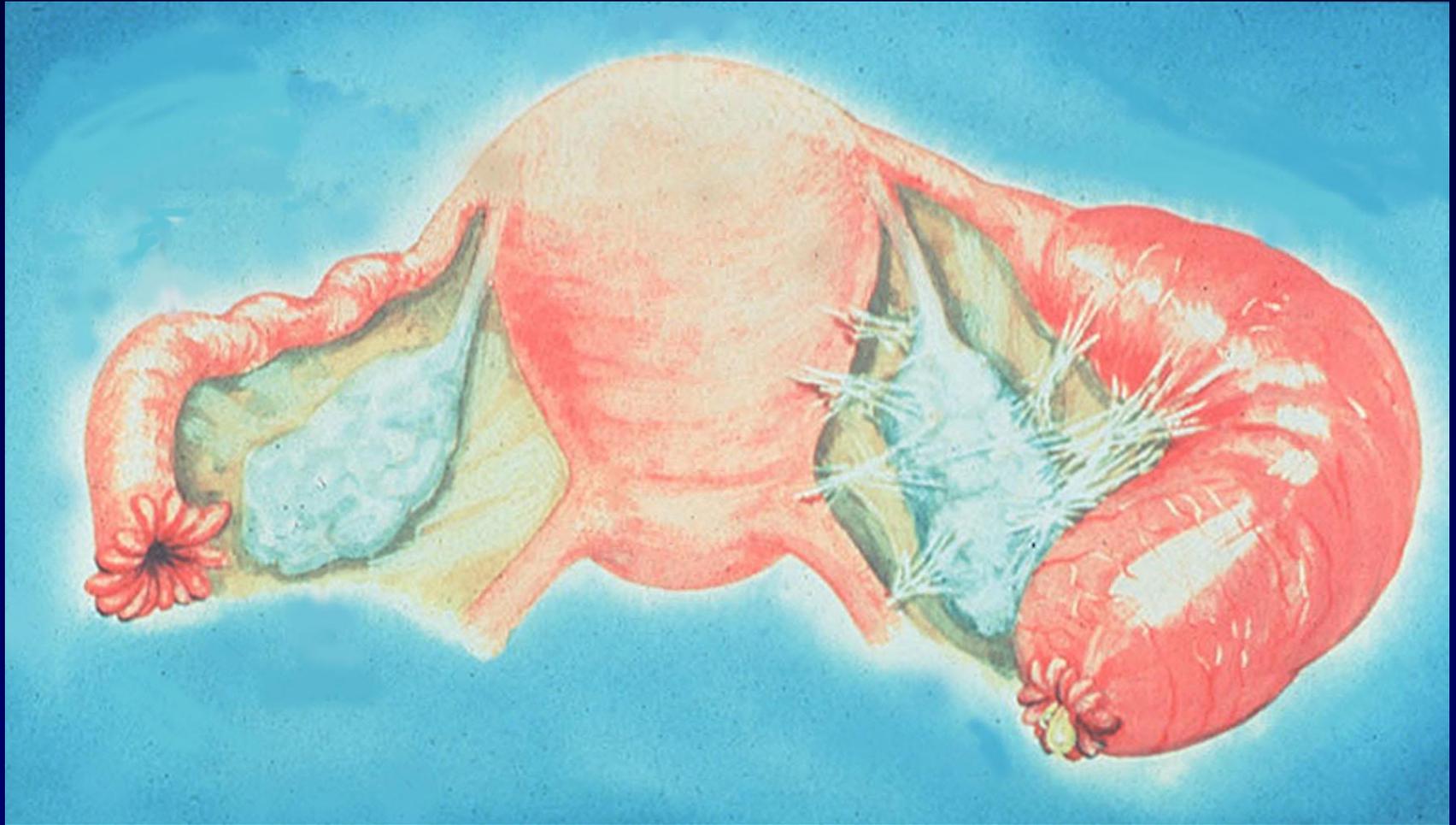
# Normal Human Fallopian Tube Tissue



# *C. trachomatis* Infection (PID)



# Acute Salpingitis



# *Other Less Common C. trachomatis* Syndromes Seen in Men or Women

- Non-LGV serovars
  - Conjunctivitis
  - Proctitis
  - Reactive arthritis
- LGV serovars
  - Lymphogranuloma venereum

# LGV Lymphadenopathy



# *C. trachomatis* Infections in Infants

- Perinatal clinical manifestations:
  - Inclusion conjunctivitis
  - Pneumonia

# *C. trachomatis* Infections in Children

- Preadolescent males and females
  - Urogenital infections
    - Usually asymptomatic
    - Vertical transmission
    - Sexual abuse

# Lesson IV: Diagnosis

# Chlamydia Diagnostics

- Preferred
  - Nucleic acid amplification tests (NAATs)
- Acceptable in limited circumstances
  - Culture
- Not recommended
  - Non-amplification tests
  - Serology

# NAATs

- NAATs amplify and detect organism-specific genomic or plasmid DNA or rRNA
- A number of NAATs are commercially available. They include
  - Abbott LCx
  - Artus/Qiagen RealArt PCR
  - Becton Dickinson BDProbe Tec®
  - Gen-Probe AmpCT, Aptima®
  - Roche Amplicor®
- Some can detect *C. trachomatis* and *N. gonorrhoeae* in the same specimen.
- Significantly more sensitive than other tests.

# NAATs (continued)

- FDA cleared
  - All NAATs
    - urethral swabs from men
    - cervical swabs for women
    - urine from men and women
  - Certain NAATs
    - vaginal swabs
- Not FDA cleared
  - Rectal
  - Pharyngeal
  - Some laboratories have met regulatory requirements

# Culture

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

# Non-Amplification Tests: Not Recommended

- Less expensive than culture or NAATs, but sensitivity only 50 – 75%
- 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 of LGV 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, or
- 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

# 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
  - Test of cure, by NAAT, 3 weeks after completion of therapy
  - Repeat testing for reinfection 3 months after completion of therapy
- Nonpregnant women and men
  - Repeat testing 3 months after treatment is recommended to detect re-infection with *C. trachomatis*
    - If not possible, then repeat testing should be performed at next presentation for care within 12 months
  - Test of cure (3 weeks after therapy) is not recommended, but can be considered when
    - compliance is in question,
    - symptoms persist,
    - re-infection is suspected, or
    - erythromycin is used.

# Lesson VI: Prevention

# Why Screen for Chlamydia?

- Most infections are asymptomatic
- Screening may reduce the incidence of PID by more than 50% and may decrease the prevalence of infection in the population

# Screening Recommendations: Nonpregnant Women

- Sexually-active women < age 25 years should be screened annually
- Women  $\geq 25$  years old should be screened if risk factors are present.
- Repeat testing of all women 3 months after treatment for *C. trachomatis* infection.
  - If not possible, then repeat testing should be performed at next presentation 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.

# Screening Recommendations: Men

- Screening of sexually-active young men should be considered in clinical settings with a high prevalence of chlamydia and when resources permit.
- Repeat testing is recommended for all men 3 months after treatment for *C. trachomatis* infection
  - If not possible, then repeat testing should be performed at next presentation for care within 12 months.

# 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.
- Expedited partner therapy (EPT) - Delivery of therapy to sex partners by heterosexual male or female patients (“patient-delivered partner therapy”) is an option in some jurisdictions

# Reporting

- Chlamydia is a reportable STD in all states.
- All clinicians and laboratories must 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 reinfection.
- 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 doxycycline or alternative 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
- 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

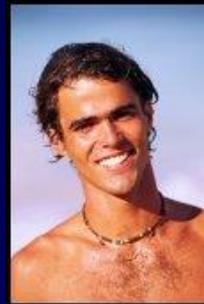
# Questions

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 3 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 3-month follow-up visit?