

# Sexually Transmitted Infections

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Slides by

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## Sexually Transmitted Pathogens

- **Bacteria**

*Neisseria gonorrhoeae*  
*Chlamydia trachomatis*  
*Mycoplasma genitalium*  
*Ureaplasma urealyticum*  
*Treponema pallidum*  
*Gardnerella vaginalis*  
*Hemophilus ducreyi*  
*Calymmatobacterium granulomatis*  
*Shigella* spp.  
*Salmonella* spp.  
*Campylobacter* spp.

- **Viruses**

Herpes simplex  
Hepatitis A, B, C  
Cytomegalovirus  
Papillomavirus  
Molluscum contagiosum  
HIV

- **Fungi**

*Candida Albicans*(?)

- **Protozoa**

*Trichomonas vaginalis*  
*Entamoeba histolytica*  
*Giardia lamblia*

- **Ectoparasites**

*Phthirus pubis*  
*Sarcoptes scabiei*

## Clinical Scenario #1

Henry, a 22 year old man, comes to your office complaining of pain when he urinates for the past 3 days. This morning he noticed a “drip” from the tip of his penis.

He has had unprotected sex with four new female partners in the past 4 weeks, most recently 6 days ago.



## A few general points . . .

- Taking a sexual history
- Counseling on safer sexual behavior
- STD risk factors
- Multiple STDs may present together
- Always test for syphilis and HIV
- Single dose drug regimens are preferable
- Evaluate and treat sexual partners
- Follow local and state public health reporting laws
- Screen asymptomatic at-risk persons for STDs

## Urethritis

Gonorrhea

Chlamydia

## *Neisseria gonorrhoeae*

- Gram negative diplococci, kidney-bean shaped
- Aerobic, non-motile, nonspore-forming
- Fastidious organisms requiring complex media and CO<sub>2</sub>-enriched atmosphere for optimal growth
- Oxidase positive
- Ferments glucose only, vs. *N. meningitidis* which ferments glucose and maltose

## **Epidemiology**

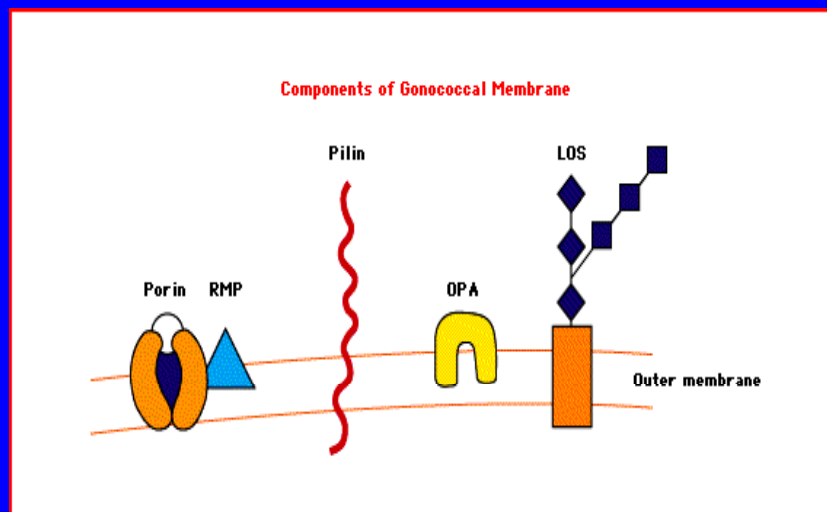
- Second most commonly reported STD in the US
- 356,000 cases reported in U.S. (2007)
- Peak incidence in the age group 15 to 24 years
- Transmitted by sexual contact – from infected urethral, cervical, rectal and pharyngeal surfaces
- Recurrent infection is common
- Major reservoir = asymptomatic infected persons
- 50% infected women are asymptomatic
- 95% men are initially symptomatic

## Gonorrhea — Rates: United States, 1941–2007 and the Healthy People 2010 target



Note: The Healthy People 2010 target for gonorrhea is 19.0 cases per 100,000 population.

## Microbiology and Pathogenesis



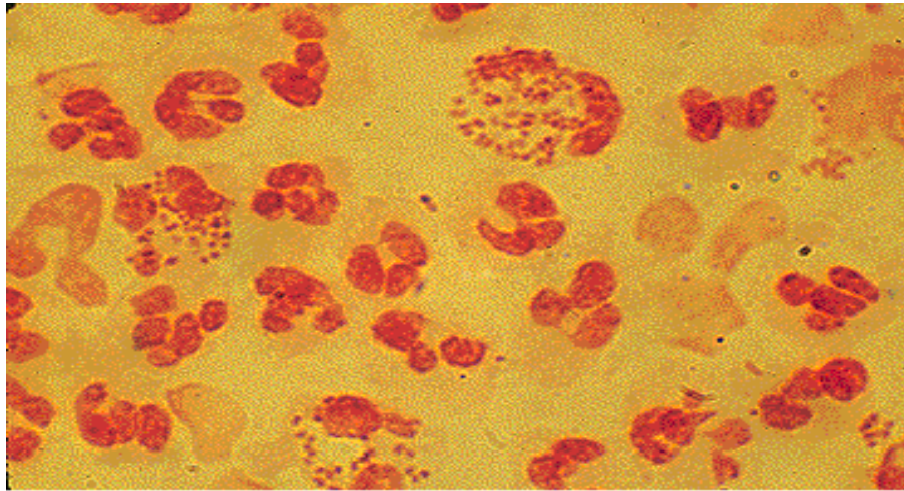
Immune evasion -- antigenic variation, phase variation, IgA protease

## Pathogenesis: GC

- Attachment
  - Pili (filamentous outer membrane appendages made of subunits e.g. pilin or pilE)
  - PilC proteins (PilC1 and PilC2 (assist in cell attachment)
  - Opa (opacity related proteins) Opa ligands bind to CD66 on epithelial cells
- Local invasion
  - endocytosis-porins (transmembrane channels and bind calmodulin which induces endocytosis, blunts WBC oxidative burst and blocks phagolysosomal fusion.
- Proliferation
  - both intracellular and in phagocytic vacuoles
- Dissemination- inhibiting normal immune response (complement)
  - Por A key for serum resistance (blocking of activated complement); block deposition of terminal complement on out membranes)
  - Antigenic and phase variation of Opa, Pil and LOS; IgA proteases; etc
  - Antibodies to reduction modifiable protein (Rmp)- block complement fixing anti-Por antibodies

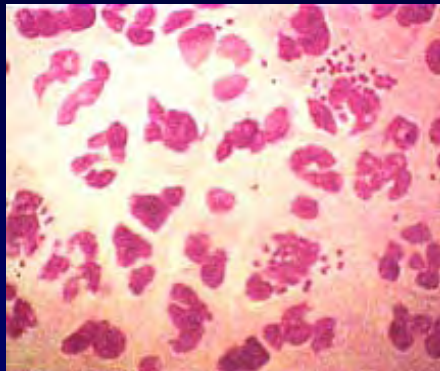
## Diagnosis of gonococcal infections

- Gram stain
  - Helpful for men with gc urethritis – Gram stain of urethral discharge showing intracellular Gram negative diplococci is > 90% sensitive and >98% specific in symptomatic men
  - Less reliable in women and asymptomatic men
- Culture
  - Urethral, cervical, rectal, pharyngeal specimens
  - Selective media (e.g., modified Thayer-Martin)
- Nucleic acid amplification assays



**Gonococcus in urethral discharge** Gram stain of purulent exudate from the male urethra (x1000) shows polymorphonuclear leukocytes containing numerous intracellular Gram negative diplococci. As expected, Neisseria gonorrhoeae grew from this specimen. Courtesy of Harriet Provine.

## Gonorrhea Gram Stain



## Clinical manifestations

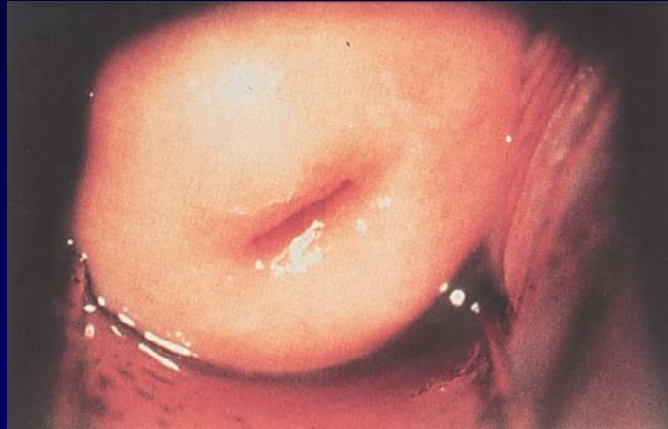
### Genital gonorrhea

- Incubation period = 2 to 5 days (can be 1 to 14)
- Men – primary site of infection is the urethra
- Symptoms: purulent urethral discharge & dysuria
- Women – endocervix primary site
- Symptoms: increased vaginal discharge, urinary frequency, dysuria, abdominal pain, vag bleeding
- \*\*Up to 30% of male and female patients with gonorrhea will also be infected with *Chlamydia trachomatis*. Patients diagnosed with gonorrhea are routinely treated for both pathogens.\*\*



Gonococcal ophthalmia

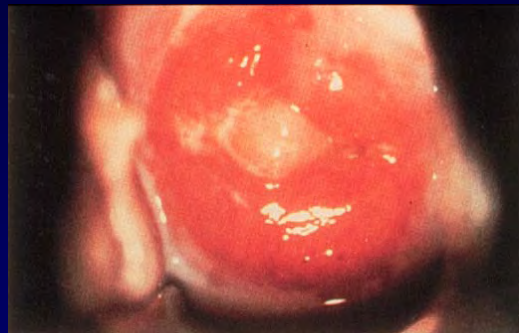
## Normal cervix



Source: Claire E. Stevens, Seattle STD/HIV Prevention Training Center



## Mucopurulent Cervicitis



Source: Seattle STD/HIV Prevention Training Center



## Other manifestations

- Epididymitis, Prostatitis
- Bartholin's gland abscess
- Pharyngeal infection
- Rectal infection (proctitis)
- Pelvic inflammatory disease\*\*
  - Endometritis, salpingitis, pelvic peritonitis
  - Tubo-ovarian abscess
  - Infertility\*\*, ectopic pregnancy
- Ophthalmia neonatorum
- Disseminated infection

## Disseminated gonococcal infection

- 1-3% of infected patients
- Associated with female sex and menstruation
- Deficiency in C5-C8 may increase susceptibility
- Symptoms: fever, skin lesions, tenosynovitis, migratory polyarthralgias, oligoarthritis
  - Overt septic arthritis in one or two joints may occur
  - Hepatitis, endocarditis, meningitis rarely
- Diagnosis:
  - Gram stain, culture, nucleic acid amplification

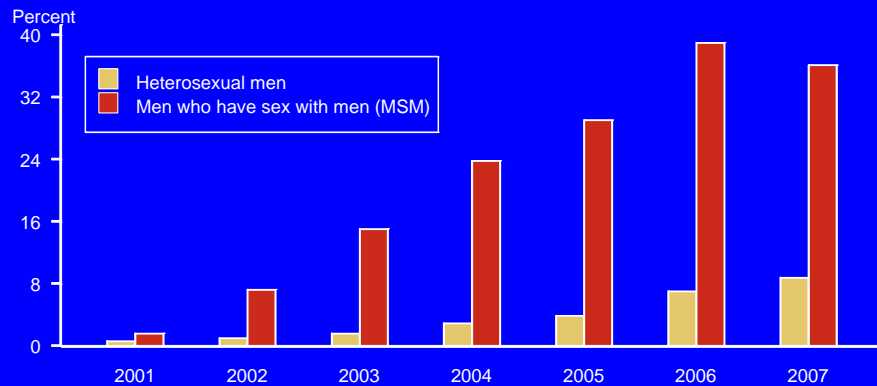




## Treatment

- Gonorrhea
  - Third generation cephalosporins
    - (single injection of ceftriaxone or single oral dose of cefixime)
  - Quinolones are no longer recommended
  - \*Presumptively treat for chlamydia\*
- Chlamydia
  - One dose of azithromycin (a macrolide) or a 7-day course of doxycycline (a tetracycline)
- PID – cover gc, chlamydia, anaerobes, GNRs, strep, and treat longer
- Evaluation and treatment of sexual partners!

Gonococcal Isolate Surveillance Project  
(GISP) — Percent of *Neisseria gonorrhoeae*  
isolates with resistance to ciprofloxacin by  
sexual behavior,  
2001–2007



## Clinical Scenario #2

Sarah, a 17 year-old high school student comes to your office saying, “My boyfriend Henry told me I need to get checked out for diseases.” A couple of weeks ago, her boyfriend of 3 months told her he had experienced pain with urination and had been treated with two antibiotics.

She has no symptoms. She has had two other male sexual partners in the past 6 months and does not use condoms.

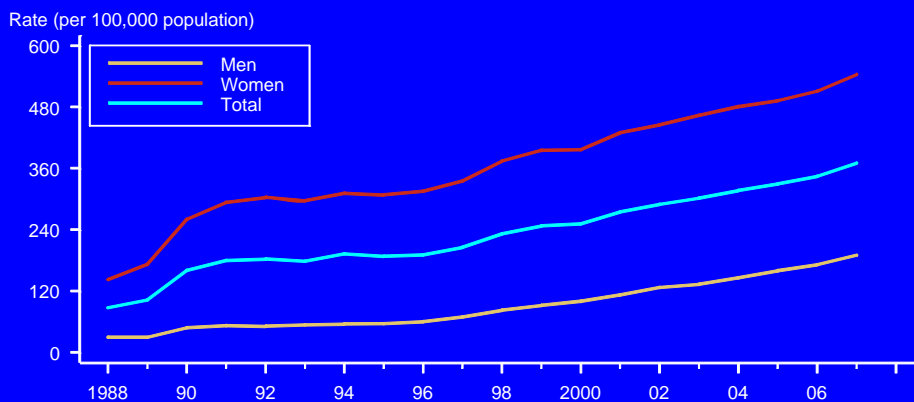
## *Chlamydia trachomatis*

- Obligate intracellular parasites
- Inner and outer membranes similar to Gram negative bacteria, but lack rigid peptidoglycan layer
- *Chlamydophila pneumoniae* and *Chlamydophila psittaci* also in family chlamydiaceae
- Serovars
  - A to C – endemic trachoma
  - D to K – genital tract infections
  - L1 to L3 – lymphogranuloma venereum (LGV)

## **Chlamydia Epidemiology**

- Most common sexually transmitted bacterial disease in U.S.
- 3 million Americans are infected each year, THE MAJORITY OF WHOM ARE ASYMPTOMATIC
- Prevalence: 3-5% of asymptomatic men and women in gen med clinics, to 15-20% of those seen in STD clinics
- Highest prevalence in sexually active adolescents

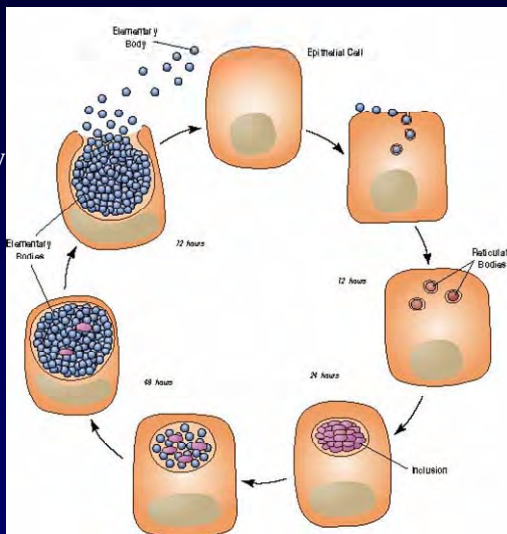
## Chlamydia — Rates: Total and by sex: United States, 1988–2007



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

## Chlamydia life cycle

Elementary body  
and  
Reticulate body



Source: California STD/HIV Prevention Training Center

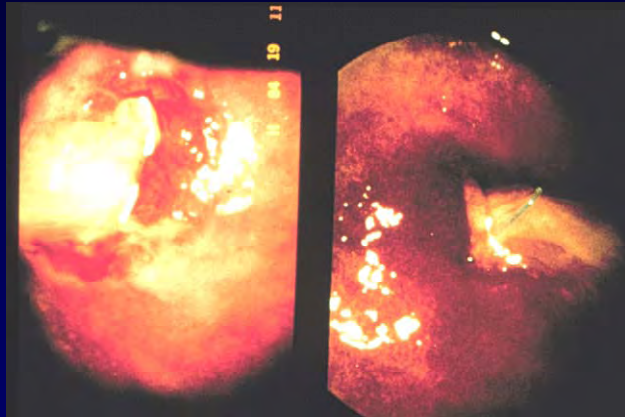
## Clinical manifestations -- Chlamydia

- Urethritis in men
  - Incubation period 7-21 days
  - “Nongonococcal urethritis (NGU)
  - As many as 25% men are asymptomatic
- Cervicitis and PID in women
  - The majority of women with cervicitis (80%) are asymptomatic and have normal cervical exam (complicates control of PID)
- Urethritis in women
- Epididymitis, prostatitis, proctitis, Reiter’s
- Newborn inclusion conjunctivitis

## Nongonococcal Urethritis



# Chlamydia Cervicitis



Source: St. Louis STD/HIV Prevention Training Center





## Diagnosis of chlamydial infections

- Nucleic acid amplification tests
  - Tests of choice (90-98% sensitive and specific)
  - Urethral and cervical samples as well as urine and vaginal swabs
  - Combination assays for gc and chlamydia
- Cell culture
  - Not routinely used; less sensitive
- Serology for LGV

Screening for GC and CT: nucleic acid amplification (NAAT) and nucleic acid hybridization tests - **site specific**

<u>Manufacturer</u>	<u>Test Name</u>	<u>Test Method</u>
<b>NAAT</b>		
Roche Diagnostics Corp.	Amplicor	Polymerase chain reaction (PCR)
Abbott Laboratories	LCx	Ligase chain reaction (LCR)
Becton, Dickinson & Co.	BDProbeTec ET	Strand displacement assay (SDA)
Gen-Probe, Inc.	APTIMA	Transcription-mediated amplification (TMA)
<b>Nucleic Acid Hybridization</b>		
Gen-Probe, Inc.	PACE-2	DNA hybridization
Digene Corporation	Hybrid Capture	RNA hybridization



Florida STD/HIV PREVENTION TRAINING CENTER

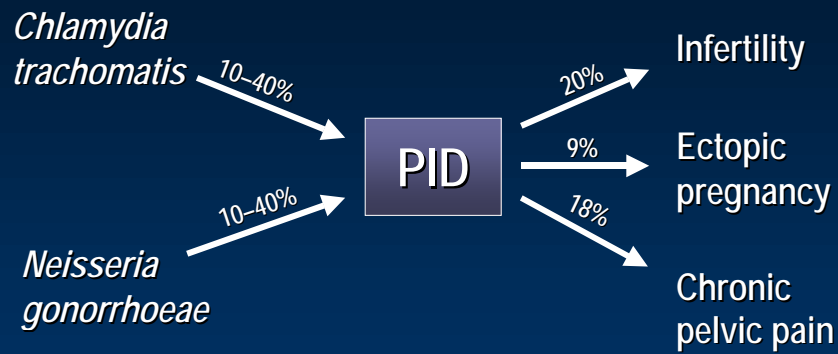
### Clinical Scenario #3

Jill, an 18-year-old woman presents with pelvic pain which has been worsening over the past week. She also complains of vaginal discharge and burning with urination. She is sexually active, has had 3 lifetime sexual partners, uses oral contraceptive pills, and does not regularly use condoms.

Temp. is 102. Her abdomen is soft with moderate bilateral lower abdominal tenderness. Pelvic exam reveals a yellow cervical discharge, cervical motion tenderness, and bilateral adnexal tenderness.



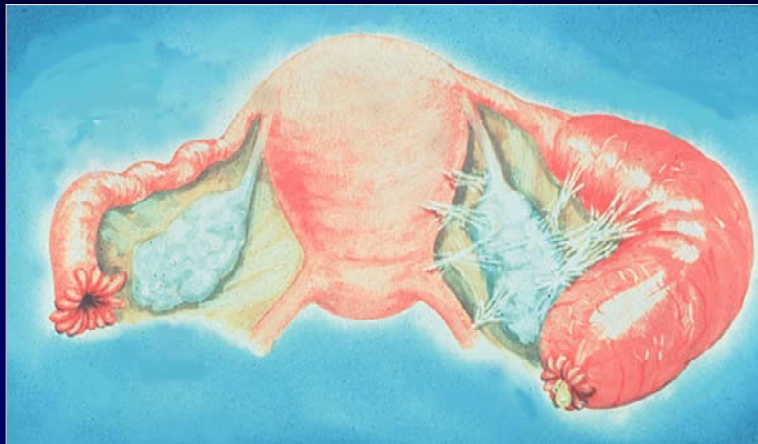
# Fertility-Associated Complications of PID<sup>1</sup>



PID=pelvic inflammatory disease.  
1. Hillis SD, et al. *N Engl J Med.* 1996;334:1399-1401.

STD 101 for Clinicians

## Pelvic Inflammatory Disease



Source: Cincinnati STD/HIV Prevention Training Center



## *Chlamydia trachomatis* - LGV

- Lymphogranuloma venereum - L serotypes
- Primary
  - painless genital lesion – papule or ulcer -- 3-30 days after exposure
- Secondary (days to weeks)
  - multilocular suppurative adenopathy; buboes
  - constitutional symptoms (fever, headache, myalgias)
  - proctocolitis if primary site was anal canal
- Late (months to years)
  - draining sinus tracts, urethral/rectal strictures, lymphatic obstruction, chronic hard inguinal masses

LGV Diagnosis: clinical\*,  
epidemiologic link, NAAT for CT,  
serology. PCR



**Lymphogranuloma Venereum**  
**Treatment: Doxycycline or erythromycin x**  
**21 days**



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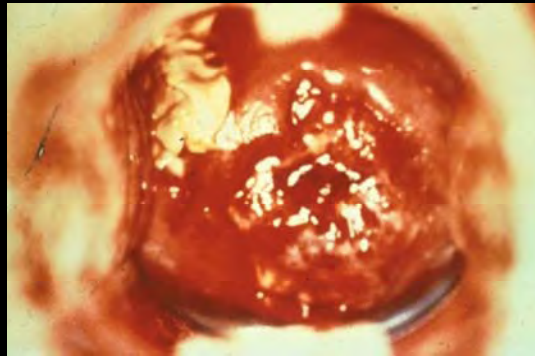
**Clinical Scenario #4**

Susan, a 32 year-old stockbroker, comes to your office for evaluation of genital ulcers. Five days ago she developed vaginal itching and discharge, dysuria, and fever and malaise. She thought she had a yeast infection and maybe was also “coming down with the flu.” However, 2 days ago she developed rather severe vaginal pain and noticed ulcers in her vulvar area which are tender to the touch.

She’s very upset because she thought she was in a monogamous relationship with a new partner for the past 3 months, and this partner denied any history of STDs.



Source: Centers for Disease Control and Prevention

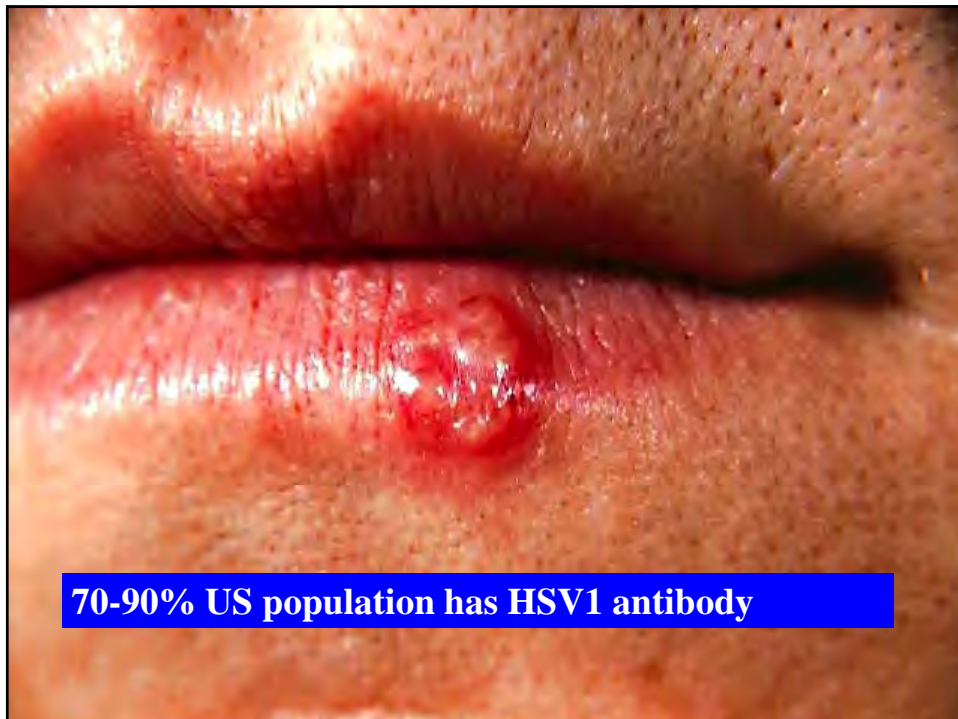
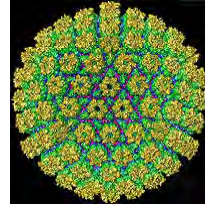


Division of  
STD  
Prevention

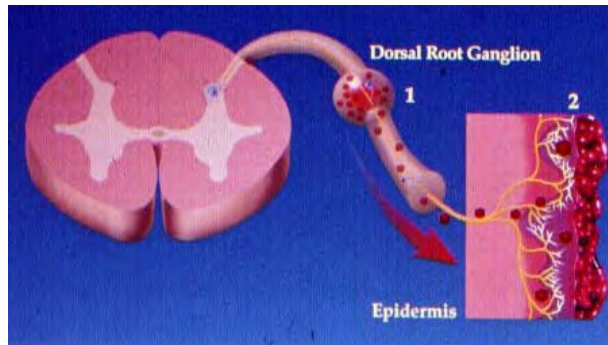


# Herpes Simplex

- Icosahedral DS DNA virus
- Causes ulcerative genital disease
- a recurrent, life-long viral infection
- Causes primary and recurrent infections
- HSV-1 more frequently causes orolabial lesions (gingivostomatitis) and keratitis, but can cause genital lesions which tend NOT to be recurrent
- HSV-2 the primary cause of recurrent genital lesions



## Pathogenesis of Reactivated Genital HSV Infection

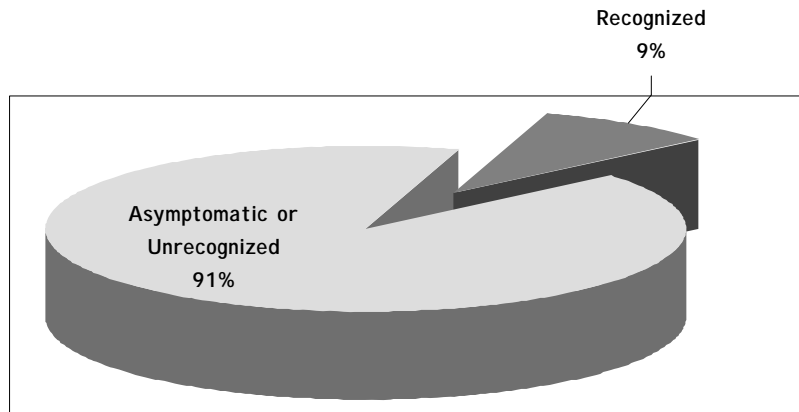


1. Reactivated HSV in ganglionic nerve cells produces recurrent disease via peripheral migration along axons to skin and mucous membranes
2. Reactivation results in recurrent mucocutaneous lesions and potential for transmission.

## Epidemiology

- Genital HSV affects 50,000,000 in the U.S.
- 1 in 4 persons over the age of 18 has HSV-2 antibodies, but most are unaware of this
- Many such persons have mild or unrecognized infections but shed virus intermittently in the genital tract, allowing transmission to others.
- HSV and all other genital ulcer diseases have been associated with increased transmission of HIV\*

## In Persons With HSV-2 Antibody:

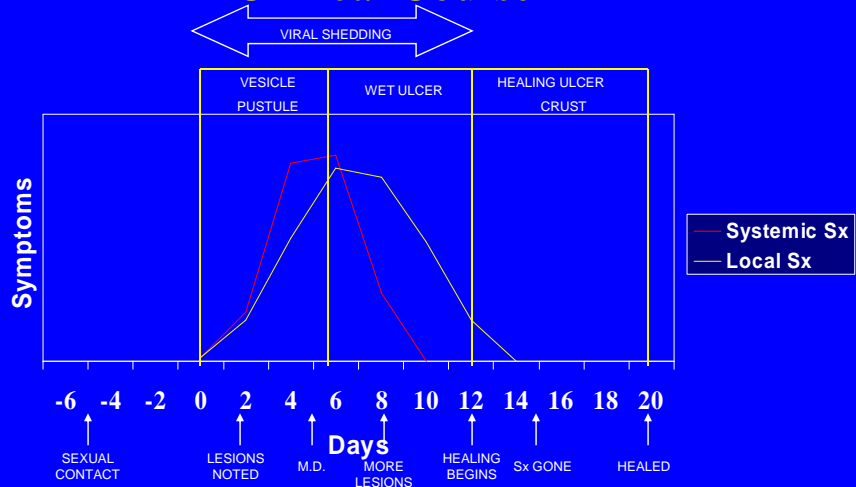


Most persons infected with HSV-2 have not been diagnosed. Asymptomatic viral shedding is responsible for much of the transmission.

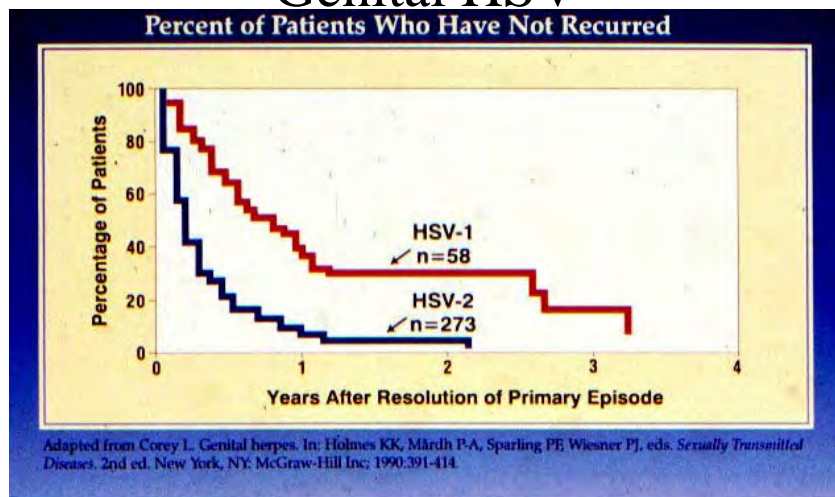
## Herpes Simplex - Clinical

- Primary infection
  - Women: painful vulvovaginitis, cervicitis (80%), urethritis (pain, itching, dysuria, vag discharge)
  - Men: painful balanitis, urethritis (pain, itch, dysuria)
  - Many have systemic symptoms (fever, HA, malaise)
  - Tender inguinal lymphadenopathy may develop
  - Painful fluid-filled vesicles that evolve into pustules and then shallow ulcers which crust
  - Duration of primary stage is 21 days
- Recurrence – in at least 70%
  - Milder, shorter and fewer, unilateral, prodrome
- Neonatal HSV infection

## Primary HSV Infection - Clinical Course



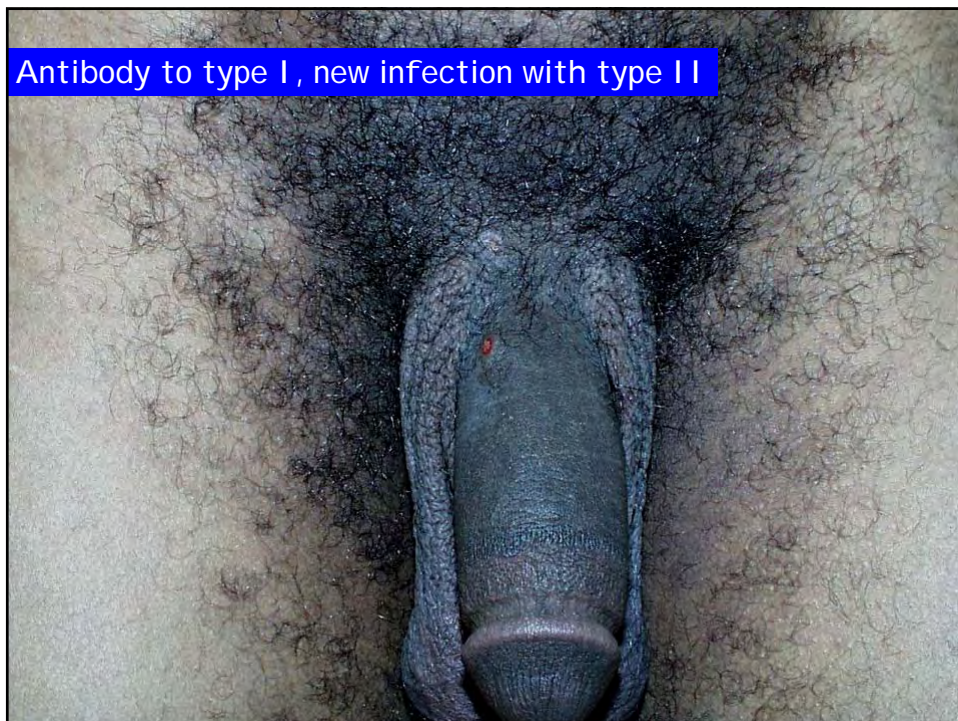
## Clinical Course of Recurrent Genital HSV



# Genital Herpes Simplex



Source: Diepgen TL, Yihune G et al. Dermatology Online Atlas





# Genital Herpes Simplex



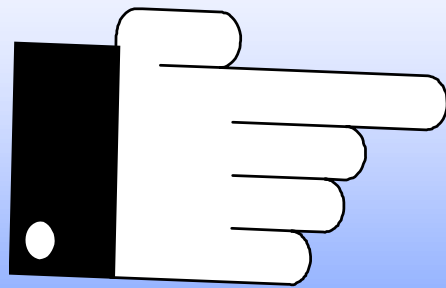
Source: Florida STD/HIV Prevention Training Center



## Herpes simplex -- Diagnosis

- Viral culture – better yield early in course
- Direct immunofluorescence
- Tzanck preparation – unreliable
- Detection of DNA (in situ hybridization or PCR)
- Serology
  - Newer tests based on glycoprotein G can differentiate between HSV-1 and HSV-2
- Rule out other causes of genital ulcers!

## Patient Teaching Points



Watch the finger pointing...

## Anecdotal Teaching Points

Your partner may have no idea they are infected

This may NOT be a new infection

Your partner should have a blood test to see if they have the infection

## HSV – Treatment and Prevention

- Treatment with acyclovir, famciclovir, or valacyclovir can decrease duration/severity but will not prevent recurrence
- Daily suppressive therapy can be used to reduce recurrences, reduce viral shedding, and perhaps to reduce transmission
- Evaluation of sex partners
- Condoms can reduce risk
- HSV vaccines in clinical trials

## Other causes of genital ulcers . . .



## *Haemophilus ducreyi* - Chancroid

- Gram negative coccobacilli
- Common in Africa, uncommon in USA
  - major risk for acquisition of HIV
- Most cases in males
- PAINFUL ulcer
  - ragged undermined edges and a gray or yellow exudate, usually a solitary lesion



## Chancroid Ulcer and Lymphadenitis

- Bubo – expansive, tender lymph nodes, can become fluctuant and spontaneously drain
- Diagnosis – culture (fastidious) or visualization on an aspirate
- Treatment – macrolide, cephalosporin, or quinolone



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## Chancroid with Tissue Destruction



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## Calymmatobacterium granulomatis

- Gram negative bacillus
- Uncommon in US, endemic in Papua New Guinea and parts of India, southern Africa, Caribbean, and South America
- PAINLESS subcutaneous nodule WITHOUT regional lymphadenopathy.
- DX: dark-staining Donovan bodies in a smear of the lesion or histologic study of the tissue (Wright's or Giemsa's).



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## Granuloma Inguinale



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Treatment: doxycycline x 21 days or till improved!!!  
alternatives azithromycin, ciprofloxacin, erythromycin or trimethoprim-sulfamethoxazole

