

Sexually Transmitted Infections



Source: Florida STD/HIV Prevention Training Center

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*

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

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.

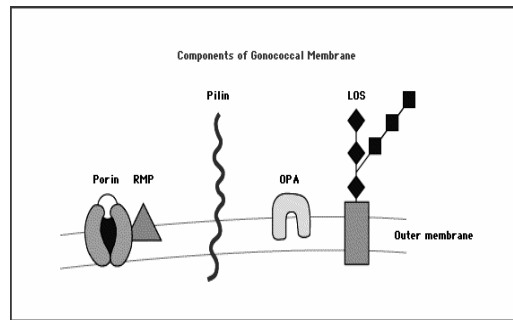
Urethritis

Gonorrhea
Chlamydia

Neisseria gonorrhoeae

- Gram negative diplococci, kidney-bean shaped
- Aerobic, non-motile, nonspore-forming
- Fastidious organisms requiring complex media and CO₂-enriched atmosphere for optimal growth
- Oxidase positive
- Ferments glucose only, vs. *N. meningitidis* which ferments glucose and maltose

Microbiology and Pathogenesis



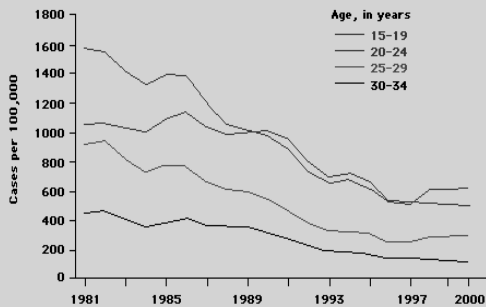
Immune evasion -- antigenic variation, phase variation, IgA protease

Epidemiology

- Second most commonly reported STD in the US
- 720,000 new infections annually in U.S.
- 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

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.**



Data from Centers for Disease Control and Prevention, Sexually Transmitted Disease Surveillance, 2000. Atlanta, GA: US Department of Health and Human Services, Centers for Disease Control and Prevention, September 2001.

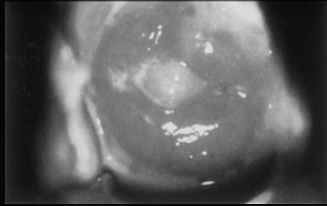
Normal cervix



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



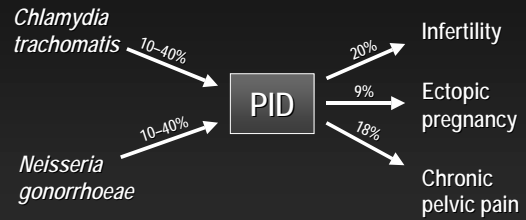
Mucopurulent Cervicitis



Source: Seattle STD/HIV Prevention Training Center



Fertility-Associated Complications of PID¹

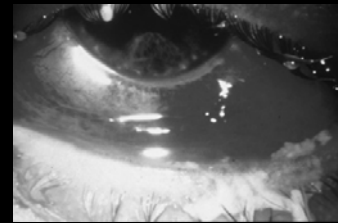


PID=pelvic inflammatory disease.

1. Hillis SD, et al. *N Engl J Med.* 1996;334:1399-1401.

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



Gonococcal ophthalmia



Pelvic Inflammatory Disease

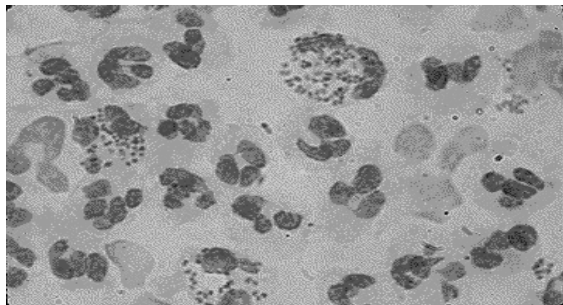


Source: Cincinnati STD/HIV Prevention Training Center



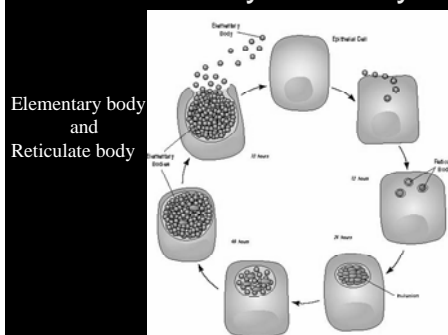
Diagnosis of gonococcal infections

- 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.

Chlamydia life cycle



Source: California STD/HIV Prevention Training Center



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)

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

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

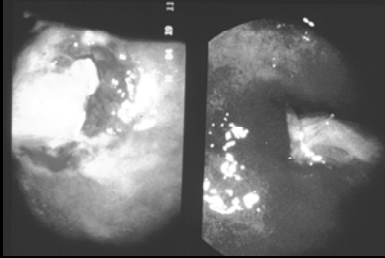
Nongonococcal Urethritis



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



Chlamydia Cervicitis

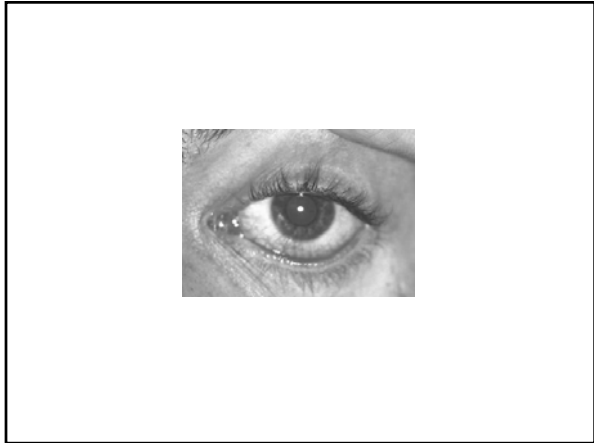


Source: St. Louis STD/HIV Prevention Training Center



Diagnosis of chlamydial infections

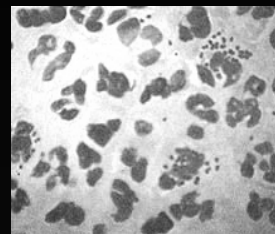
- Nucleic acid amplification tests
 - Tests of choice (90-98% sensitive and specific)
 - Urethral and cervical samples as well as urine and vaginal swabs
 - Combination assays for gc and chlamydia
- Cell culture
 - Not routinely used; less sensitive
- Serology for LGV



Source: Florida STD/HIV Prevention Training Center



Gonorrhea Gram Stain



Source: Cincinnati STD/HIV Prevention Training Center



Treatment

- Gonorrhea
 - Third generation cephalosporins
 - (single injection of ceftriaxone or single oral dose of cefixime)
 - Quinolones (single oral dose of cipro, but increasing resistance)
 - *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!



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

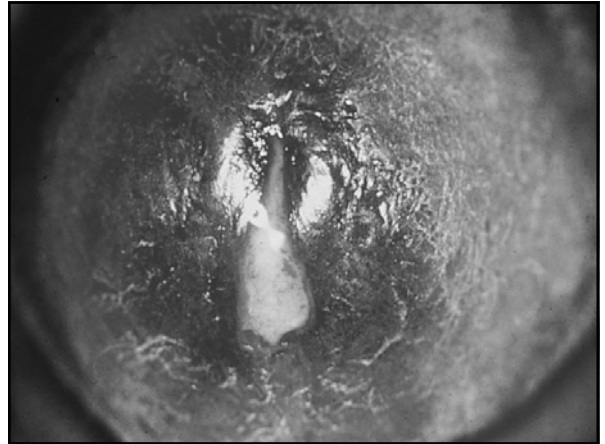
GC and Chlamydia -- Prevention

- Education regarding safer sex practices
- Aggressive detection and treatment
- Rigorous follow-up screening and treatment of sexual contacts
- *Screening of asymptomatic at-risk persons
 - Non-invasive techniques
- No vaccine available

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.



STD 101 for Clinicians

Drips

Normal cervix



Source: Claire E. Stevens, Seattle 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

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.

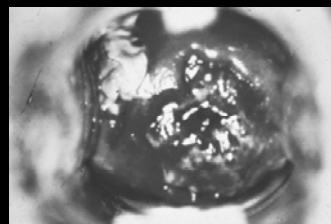
Temp. is 102. Her abdomen is soft with moderate bilateral lower abdominal tenderness. Pelvic exam reveals a yellow cervical discharge, cervical motion tenderness, and bilateral adnexal tenderness.



Lymphogranuloma Venereum



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National Center for
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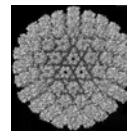
Clinical Scenario #4

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.

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

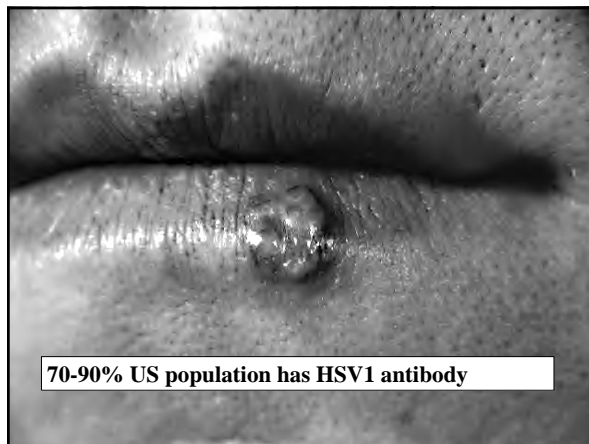


STD 101 for Clinicians



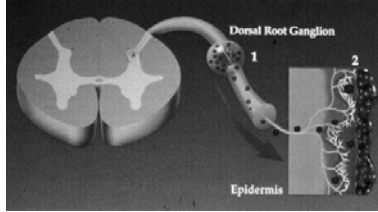
Source: Centers for Disease Control and Prevention

CDC
30
STD Prevention



70-90% US population has HSV1 antibody

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.

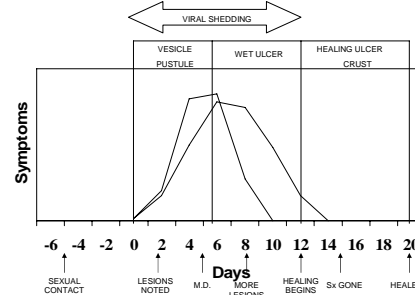
Herpes Simplex - Clinical

- 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

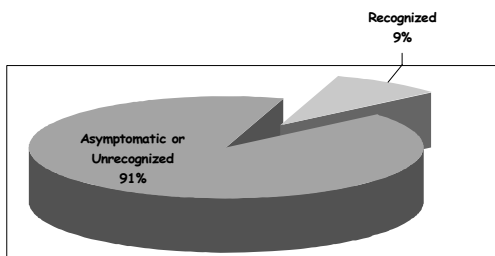
Epidemiology

- 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*

Primary HSV Infection - Clinical Course

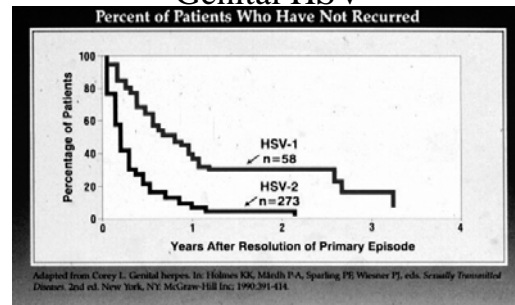


In Persons With HSV-2 Antibody:



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

Clinical Course of Recurrent Genital HSV



Adapted from Corey L. Genital herpes. In: Holmes KK, Månth P-A, Spang P, Wiesner P, eds. Sexually Transmitted Diseases. 2nd ed. New York, NY: McGraw-Hill Inc; 1990:391-414.

Genital Herpes Simplex



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



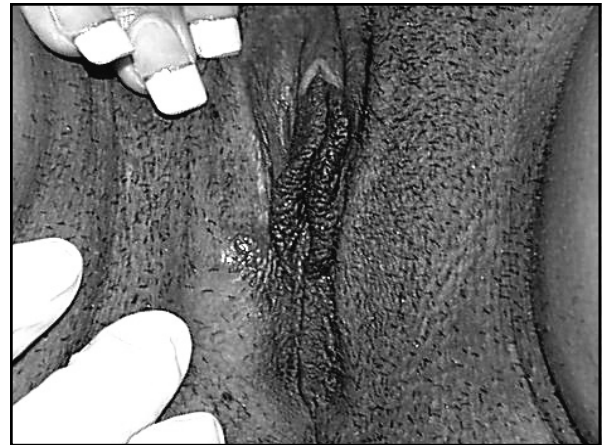
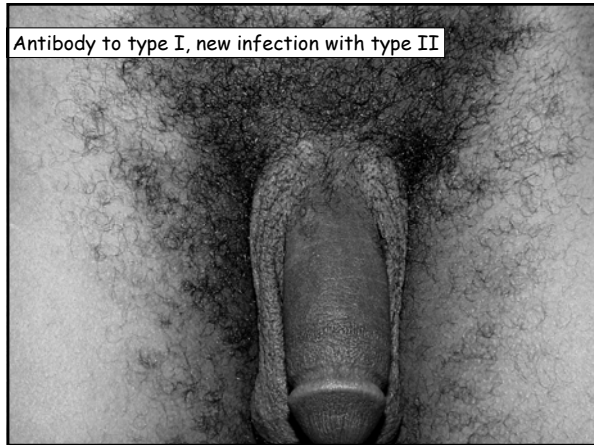
Genital Herpes Simplex



Source: Florida STD/HIV Prevention Training Center

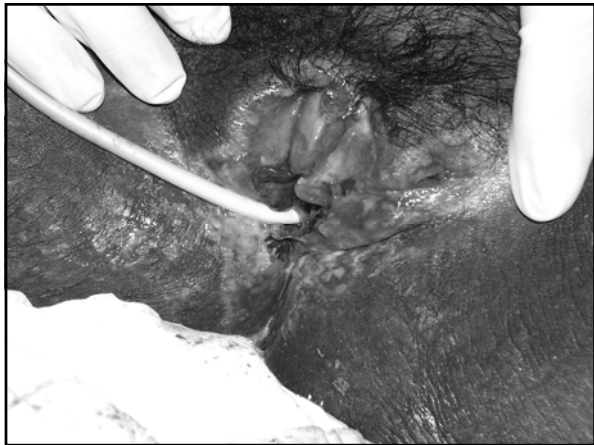


Antibody to type I, new infection with type II



Primary herpes, female





Patient Teaching Points

Watch the finger pointing....

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!

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

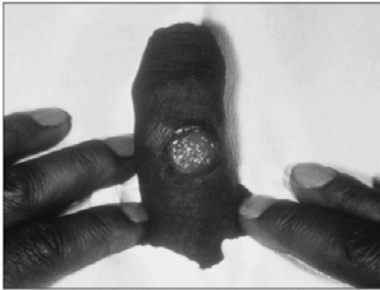
HSV – Treatment and Prevention

- 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

Haemophilus ducreyi - Chancroid

- Gram negative coccobacilli
- Common in Africa, uncommon in USA
 - major risk for acquisition of HIV
- Most cases in males
- Painful ulcer with ragged undermined edges and a gray or yellow exudate, usually a solitary lesion
- Bubo – expansive, tender lymph nodes, can become fluctuant and spontaneously drain
- Diagnosis – culture (fastidious) or visualization on an aspirate
- Treatment – macrolide, cephalosporin, or quinolone

Other causes of genital ulcers . . .



Chancroid Ulcer and Lymphadenitis



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Chancroid with Tissue Destruction



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Clinical Scenario #5

Keith, a 28 year-old HIV-infected man, presents with a several month history of penile lesions that he thinks might be warts. They are not painful, but have become bulky and uncomfortable as well as cosmetically distressing. He also reports anal itching.

He reports multiple sexual partners (men and women) in the past 3 years, but none in the past 2 months.

Granuloma Inguinale (Donovanosis)



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Calymmatobacterium granulomatis



Condyloma acuminata, penile

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Granuloma Inguinale



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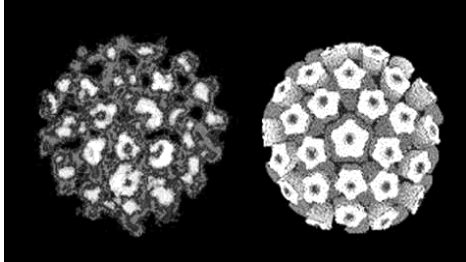


Condyloma acuminata, anal

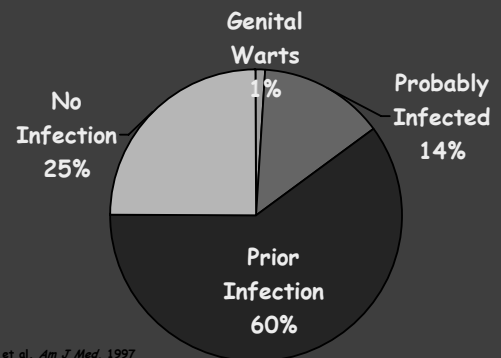
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Human Papilloma Virus



Estimated Prevalence of Genital HPV Among Sexually Active 15-49 year old Men and Women in the United States



Koutsky et al. *Am J Med*, 1997

HPV

- Most common viral STD in the U.S.
- Double stranded DNA viruses
- More than 100 types, more than 25 in genital tract
- Cause anogenital warts (condylomata acuminata)
 - HPV types 6 and 11, "low risk"
- Associated with anogenital malignancy including cervical, vaginal, vulvar, penile, and anal carcinoma
 - HPV types 16 and 18 unequivocally linked to cervical cancer
 - At least 15 types (31, 33, 35) "high-risk" for intraepithelial neoplasia (SIN or CIN)
- Concern is PERSISTENT infection with high-risk type



Condyloma acuminata, vulva

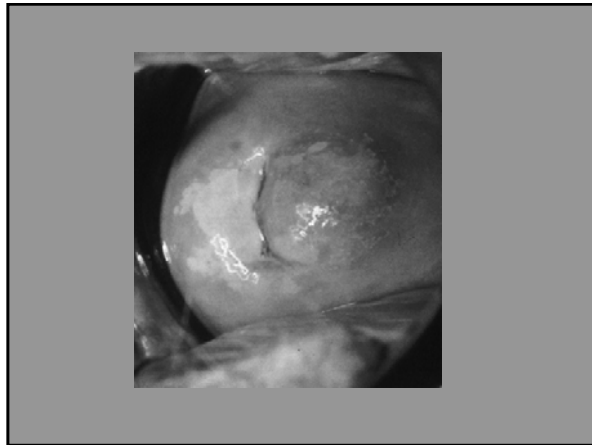
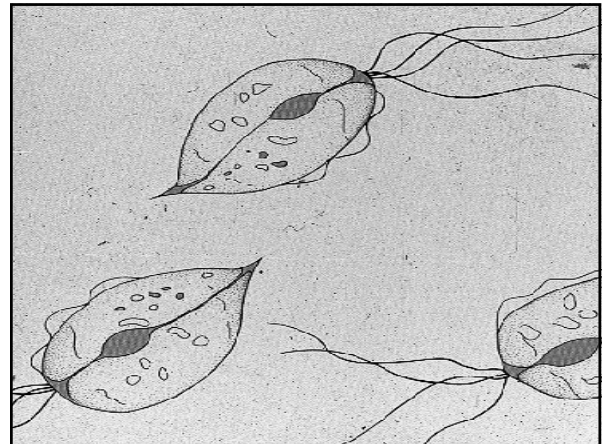
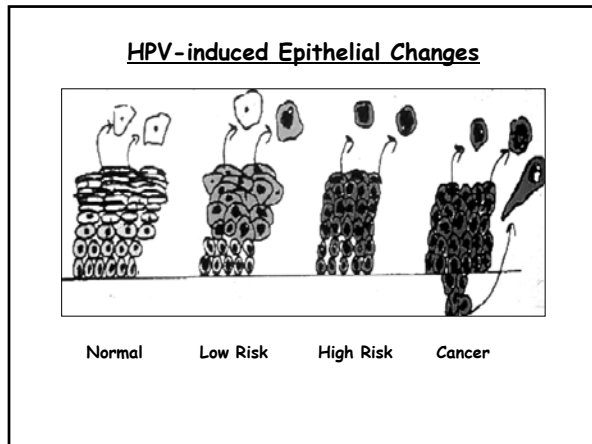
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HPV Epidemiology

- Estimated 6.2 million new infections each year in U.S. – very common, most are subclinical
- Spread by unprotected penetrative intercourse and close physical contact (role of condoms in prevention unclear)
- Risk increases with number of sexual partners, number of partners' partners, partners with genital warts, increased frequency of sex, other STDs
- Asymptomatic patients drive transmission
- Primary cause worldwide of cervical cancer*





"...the Neopolitans, and the rest of the Italians called it the French Disease, *Mal Francese*, alledging it was imported into Italy by the French when they attacked the kingdom of Naples in the year 1494; While the French, on the contrary, called it the Neopolitan or Italian Disease, *Mal de Naples*, because it was first caught by them in the Kingdom of Naples during the above mentioned expedition; The Germans too call it *Frantozen* or *Frantzozischen Pocken*, that is, *The French Disease* or *The French Pox*; and the English likewise call it by the same Name, because it was propagated in those nations by the French...

It was called by the Flemish and Dutch Spaanse Pocken; by the Portuguese, The Castilian Disease, by the East Endians and Japanese, The Disease of the Turks; by the Polanders, the Disease of the Germans; and last of all, by the Russians, the Disease of the Polanders...

-Astruc, 1754

HPV disease prevention

- Role of condoms in prevention unclear
- Regular Pap smears and follow-up/treatment of abnormal smears to prevent cervical cancer
- ?Screening anal Pap smears in men who engage in anal intercourse to prevent anal cancer
- Investigational HPV vaccines