

# **Common Sexually Transmitted Diseases: STD 101 for Clinicians**

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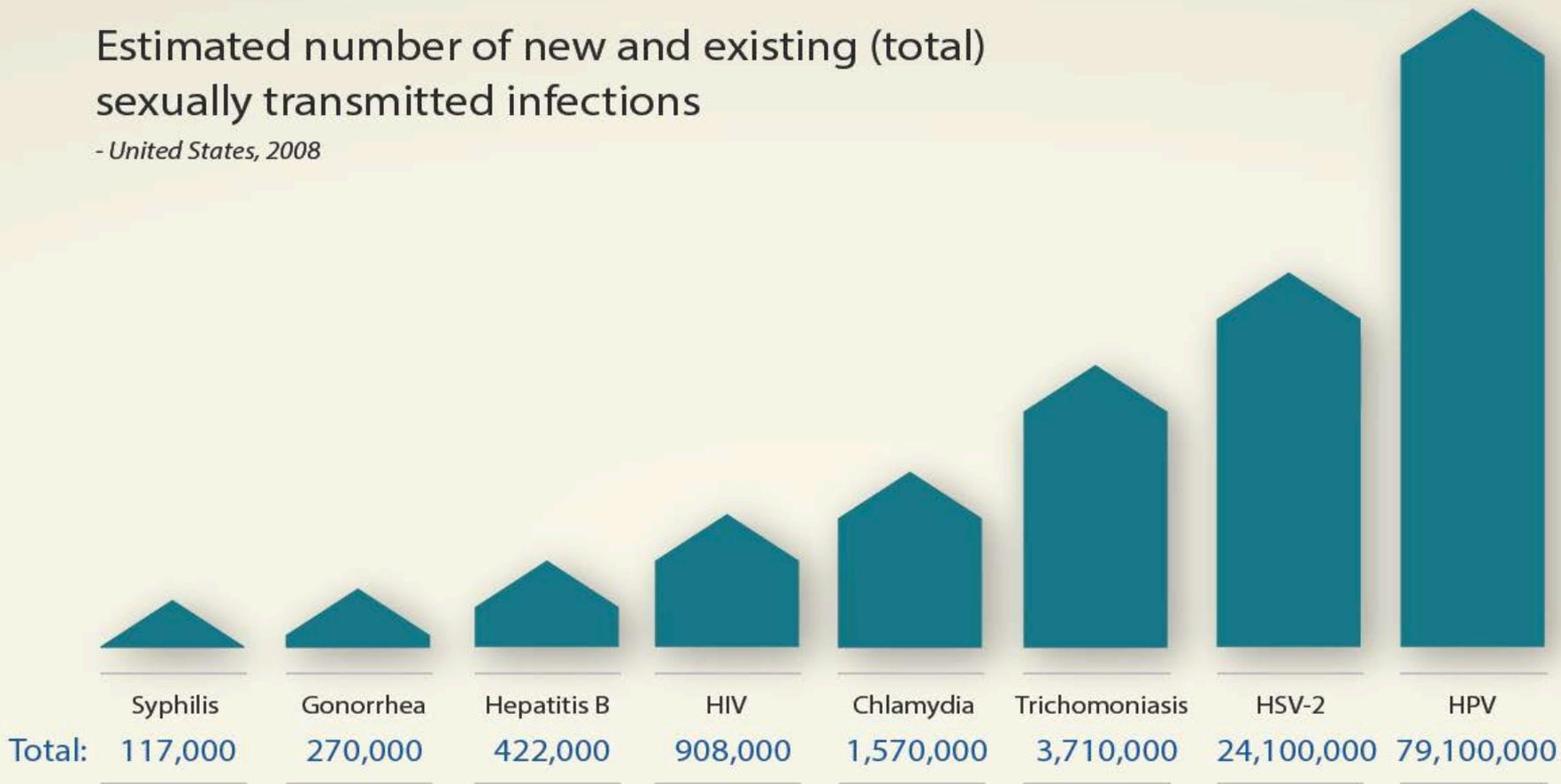
# Topics

- **Background Information**
- **“Sores”**
- **“Drips”**

# Background Information

# Estimated number of new and existing (total) sexually transmitted infections

- United States, 2008



50,627,400



59,569,500

**TOTAL: 110,197,000**

*Gender totals do not equal overall total, due to rounding*

# STIs Facilitate HIV Transmission

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- **Disruption of epithelial/mucosal barriers**
- **Increase the number of HIV target cells in the genital tract**
- **Increase expression of HIV co-receptors**
- **Induce secretion of cytokines (increase HIV shedding)**
- **HIV alters natural history of some STIs**



Fleming DT and Wasserheit JN. From Epidemiological Synergy to public health policy and practice: the contribution of other sexually transmitted diseases to sexual transmission of HIV infection. *Sex Transm Inf* 1999;75:3-17.

Slide courtesy of AL/NC STD/HIV Prevention Training Center

# Where are Americans most likely to go for STD care?

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- 1. Emergency room**
- 2. Family planning clinic**
- 3. Private provider\***
- 4. STD clinic**

# Where Do People Go for STD Treatment?

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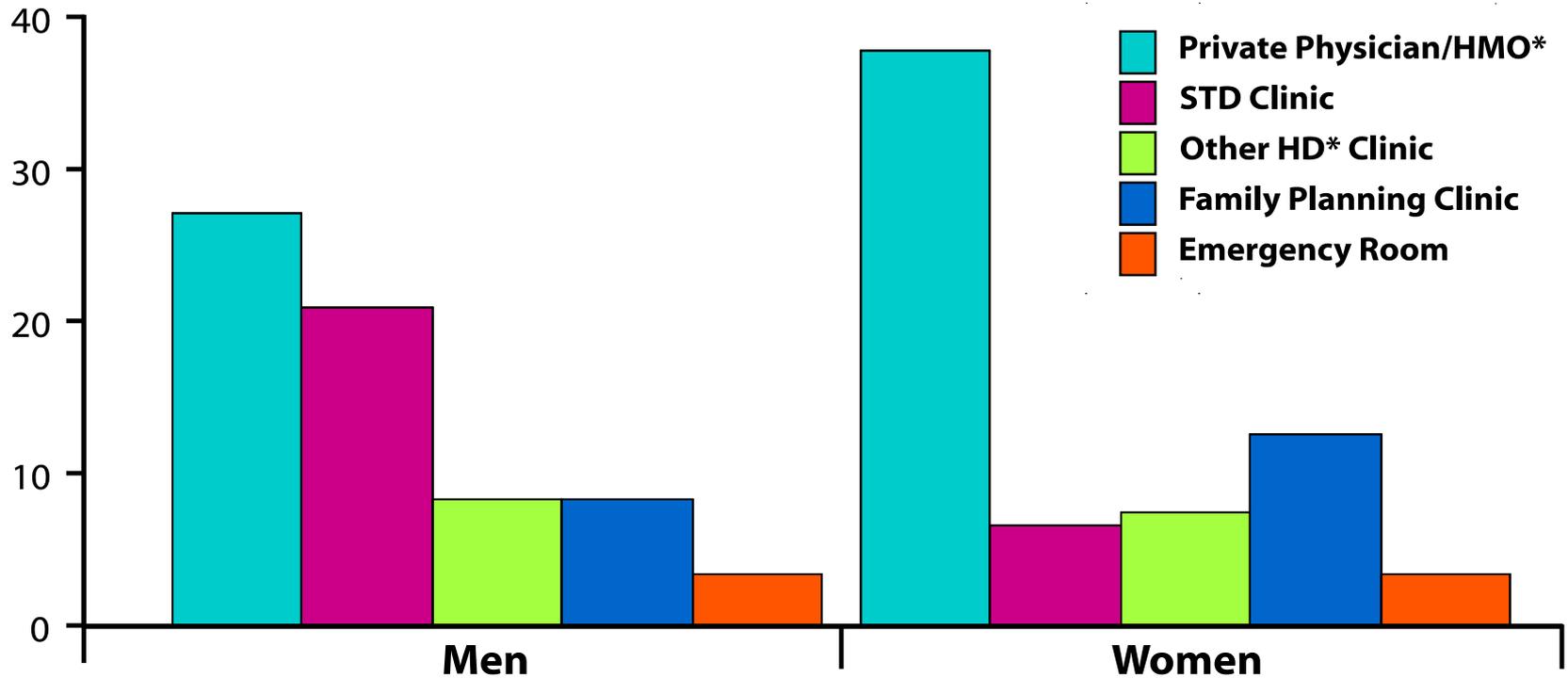
- **Population-based estimates from National Health and Social Life Survey**

<b>Private provider</b>	<b>59%</b>
<b>Other clinic</b>	<b>15%</b>
<b>Emergency room</b>	<b>10%</b>
<b>STD clinic</b>	<b>9%</b>
<b>Family planning clinic</b>	<b>7%</b>

*Source: Brackbill et al. Where do people go for treatment of sexually transmitted diseases? Family Planning Perspectives. 31(1):10-5, 1999*

# Chlamydia—Percentage of Reported Cases by Sex and Selected Reporting Sources, United States, 2012

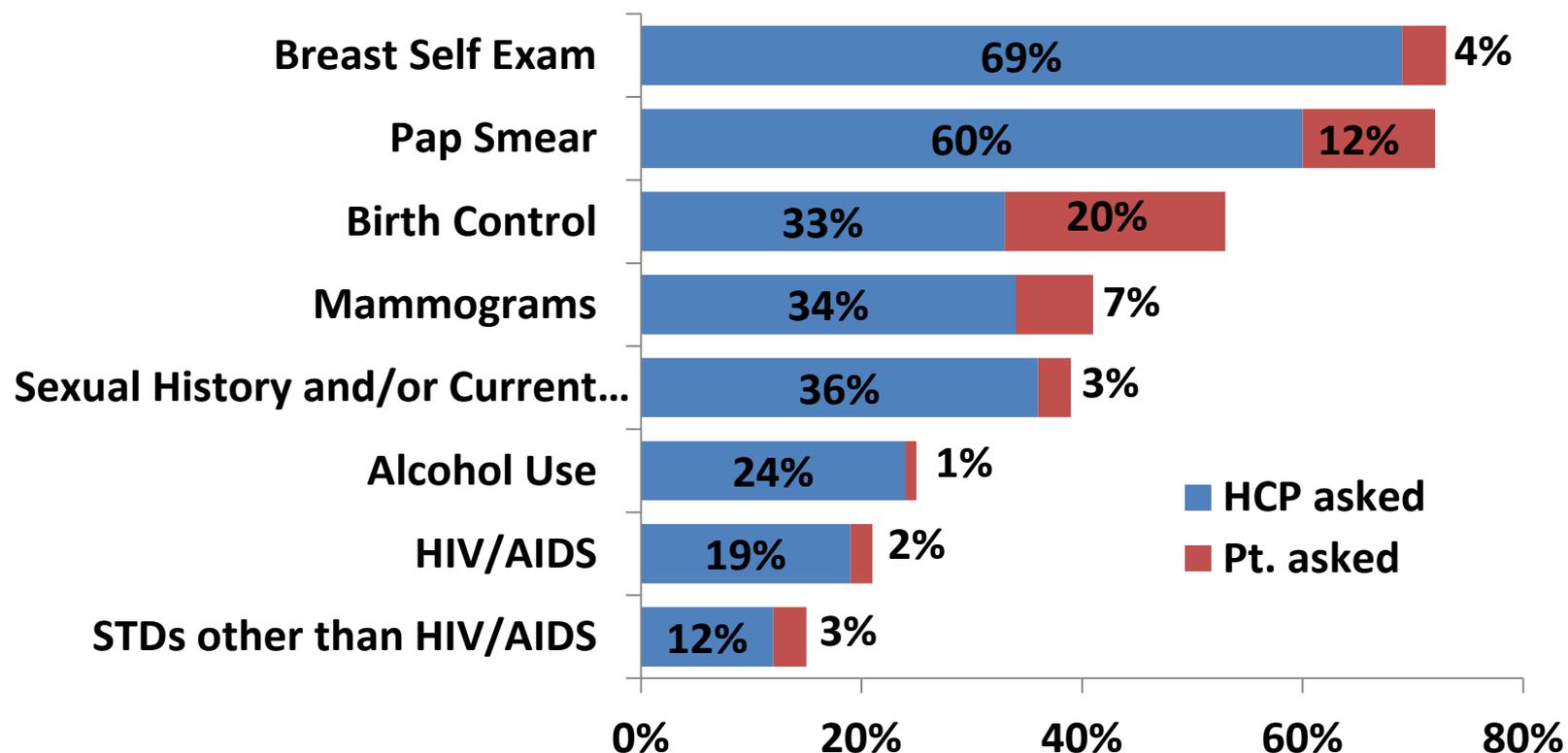
Percentage



\*HMO=health maintenance organization; HD=health department

**NOTE:** Of all cases, 11.4% had a missing or unknown reporting source. Among cases with a known reporting source, the categories presented represent 69.8% of cases; 30.2% were reported from sources other than those shown.

## Percent\* of Women Who Said Topic Was Discussed During First Visit With New Gynecological or Obstetrical Doctor/Health Care Professional



\* Percentages may not total to 100% because of rounding or respondents answering “Don’t know” to the question “Who initiated this conversation?”

Source: Kaiser Family Foundation/Glamour National Survey on STDs, 1997

# STDs of Concern

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- **“Sores” (ulcers)**
  - Syphilis
  - Genital herpes (HSV-2, HSV-1)
  - Others uncommon in the U.S.
    - Lymphogranuloma venereum
    - Chancroid
    - Granuloma inguinale

# STDs of Concern (continued)

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- **“Drips” (discharges)**
  - Gonorrhea
  - Chlamydia
  - Nongonococcal urethritis / mucopurulent cervicitis
  - Trichomonas vaginitis / urethritis
  - Candidiasis (not an STD)
  - Bacterial vaginosis (sexually associated)
- **Other major concerns**
  - Genital HPV (especially type 16, 18) and Cervical/Anal/Oral Cancer

**A 30 yr old black male presents with the following physical finding...**



Source: AL/NC STD/HIV Prevention Training Center

# What is the most likely diagnosis?

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1. Herpes simplex virus
2. Syphilis
3. Zipper cut
4. Granuloma inguinale
5. Additional testing is necessary\*

# **“Sores”**

**Syphilis**

**Genital Herpes (HSV-2, HSV-1)**

# Does It Hurt?

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- **Painful**
  - Chancroid
  - Genital herpes simplex
- **Painless**
  - Syphilis
  - Lymphogranuloma venereum
  - Granuloma inguinale

# Primary Syphilis – Clinical Manifestations

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- **Incubation: 10-90 days (average 3 weeks)**
- **Chancre**
  - **Early: macule/papule → erodes**
  - **Late: clean based, painless, indurated ulcer with smooth firm borders**
  - **Unnoticed in 15-30% of patients**
  - **Resolves in 1-5 weeks**
  - **HIGHLY INFECTIOUS**

# Primary Syphilis Chancre



# Primary Syphilis



Source: Centers for Disease Control and Prevention

# Secondary Syphilis - Clinical Manifestations

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- Represents hematogenous dissemination of spirochetes
- Usually 2-8 weeks after chancre appears
- Findings:
  - rash - whole body (includes palms/soles)
  - mucous patches
  - condylomata lata - HIGHLY INFECTIOUS
  - constitutional symptoms
- Sn/Sx resolve in 2-10 weeks

# Secondary Syphilis Rash



Source: Florida STD/HIV Prevention Training Center

# Secondary Syphilis: Generalized Body Rash



Source: CDC/NCHSTP/Division of STD Prevention, STD Clinical Slides

# Secondary Syphilis Rash



Source: Florida STD/HIV Prevention Training Center

# Secondary Syphilis Rash



Source: Cincinnati STD/HIV Prevention Training Center

# Secondary Syphilis



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

# Secondary Syphilis – Condylomata Lata



Source: Florida STD/HIV Prevention Training Center

# Early Syphilis – Diagnosis and Treatment

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## Diagnosis:

Clinical presentation

Darkfield

Serology

## Treatment:

Benzathine PCN G 2.4 million units x 1

# Genital Herpes Simplex - Clinical Manifestations

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- **Transmission through direct contact – usually during asymptomatic shedding**
- **Primary infection commonly asymptomatic; symptomatic cases sometimes severe, prolonged, systemic manifestations**
- **Vesicles ⇒ painful ulcerations ⇒ crusting**
- **Recurrence a potential**

# HSV-2 Infection: Who knows it?

	<b>% Seropositive for HSV-2</b>	<b>% Reporting history of genital herpes</b>	<b>Sensitivity</b>
<b>NHANES III</b>	<b>21.9</b>	<b>2.6</b>	<b>9.2</b>
<b>Black</b>			<b>3.7</b>
<b>Hispanic</b>			<b>3.8</b>
<b>White</b>			<b>12.2</b>
<b>Suburban MD Office</b>	<b>25.5</b>	<b>4.3</b>	<b>11.9</b>
<b>Project Respect</b>	<b>41</b>	<b>5</b>	<b>12</b>
<b>JCDH STD-males</b>	<b>45</b>	<b>6</b>	<b>36</b> <b>(3 questions)</b>

Fleming et al. NEJM 1997; 337:1105. Gottlieb et al. JID 2002; 186:1381-89. Leone P et al. Sex Transm Dis. 2004; 31(5): 311-316. Sizemore et al, Sex Trans Inf, 2005;81:303-5.

# HSV: Diagnosis and Treatment

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## Diagnosis:

PCR

Culture

Serology (Type-specific; Western blot)

## Treatment:

Acyclovir

Valacyclovir

Famciclovir

# Genital Herpes Simplex



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

# Genital Herpes Simplex



Source: CDC/NCHSTP/Division of STD, STD Clinical Slides

# Genital Herpes Simplex in Females



Source: Centers for Disease Control and Prevention

# Genital Herpes Simplex



Source: Florida STD/HIV Prevention Training Center

# Acyclovir Resistant HSV

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Source: AL/NC STD/HIV Prevention Training Center

# Case

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- **35yo HIV+ white man presents to urgent care with a 1 week history of yellow penile discharge and mild dysuria.**
- **No testicular pain, frequency, rash, lesion**
- **No gram stain available.**
- **Treated empirically with azithromycin 1gm po x 1**

# **“Drips”**

**Gonorrhea**

**Nongonococcal urethritis**

**Chlamydia**

**Mucopurulent cervicitis**

**Trichomonas vaginitis and urethritis**

**Bacterial vaginosis**

# Gonorrhea - Clinical Manifestations

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- **Urethritis - male**
  - Incubation: 1-14 d (usually 2-5 d)
  - Sx: Dysuria and urethral discharge (5% asymptomatic)
  - Complications
  
- **Urogenital infection - female**
  - Endocervical canal primary site
  - 70-90% also colonize urethra
  - Incubation: unclear; sx usually in 10 d
  - Sx: majority asymptomatic; may have vaginal discharge, dysuria, urination, labial pain/swelling, abdominal pain
  - Complications

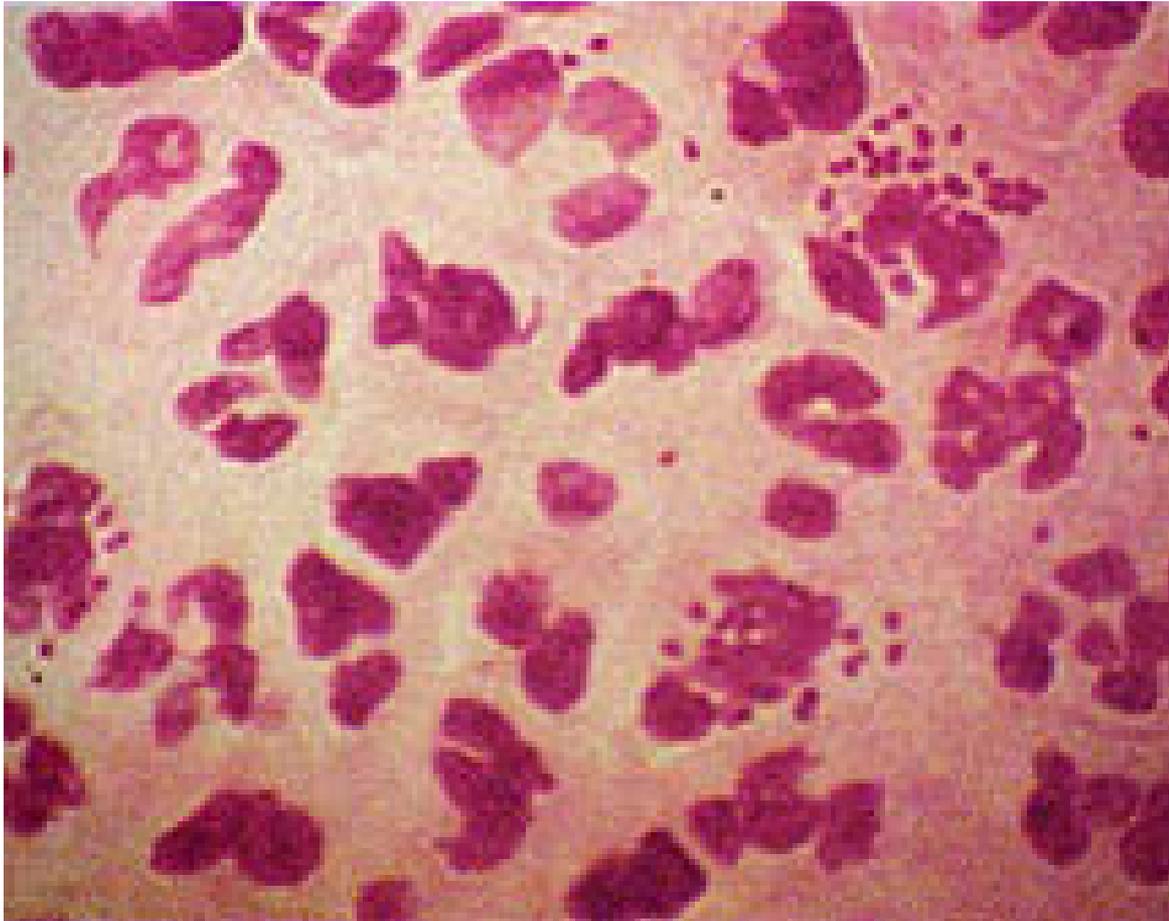
**Extra-genital infection mostly asymptomatic!!**

# Gonorrhea



Source: Florida STD/HIV Prevention Training Center

# Gonorrhea Gram Stain



Source: Cincinnati STD/HIV Prevention Training Center

# Nongonococcal Urethritis



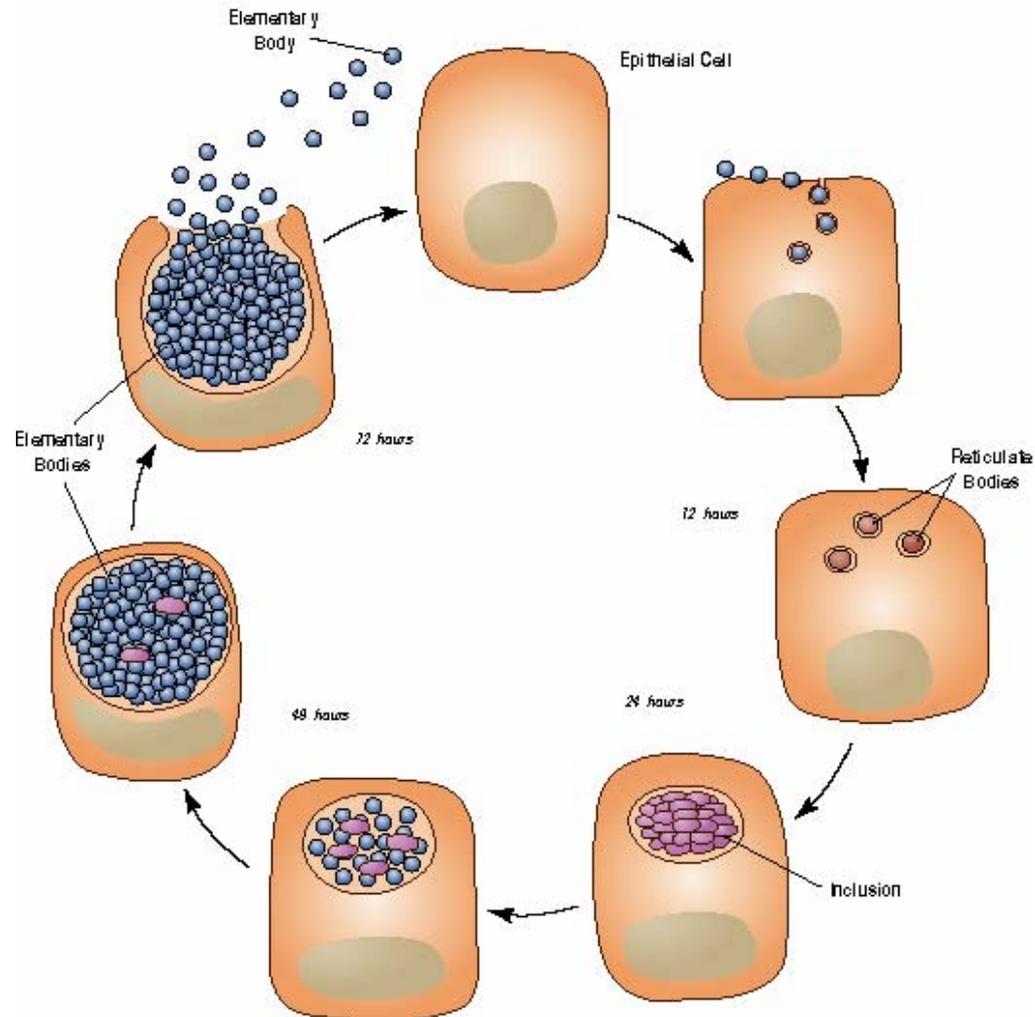
Source: Diepgen TL, Yihune G et al. Dermatology Online Atlas

# Nongonococcal Urethritis

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- Etiology:
  - 20-40% *C. trachomatis*
  - 20-30% genital mycoplasmas (*Mycoplasma genitalium*, *Ureaplasma urealyticum*)
  - Occasional *Trichomonas vaginalis*, HSV
  - Unknown in ~50% cases
- Sx: Mild dysuria, mucoid discharge
- Dx: Urethral smear  $\geq 5$  PMNs/OI field  
Urine microscopic  $\geq 10$  PMNs/HPF  
Leukocyte esterase (+)

# Chlamydia Life Cycle



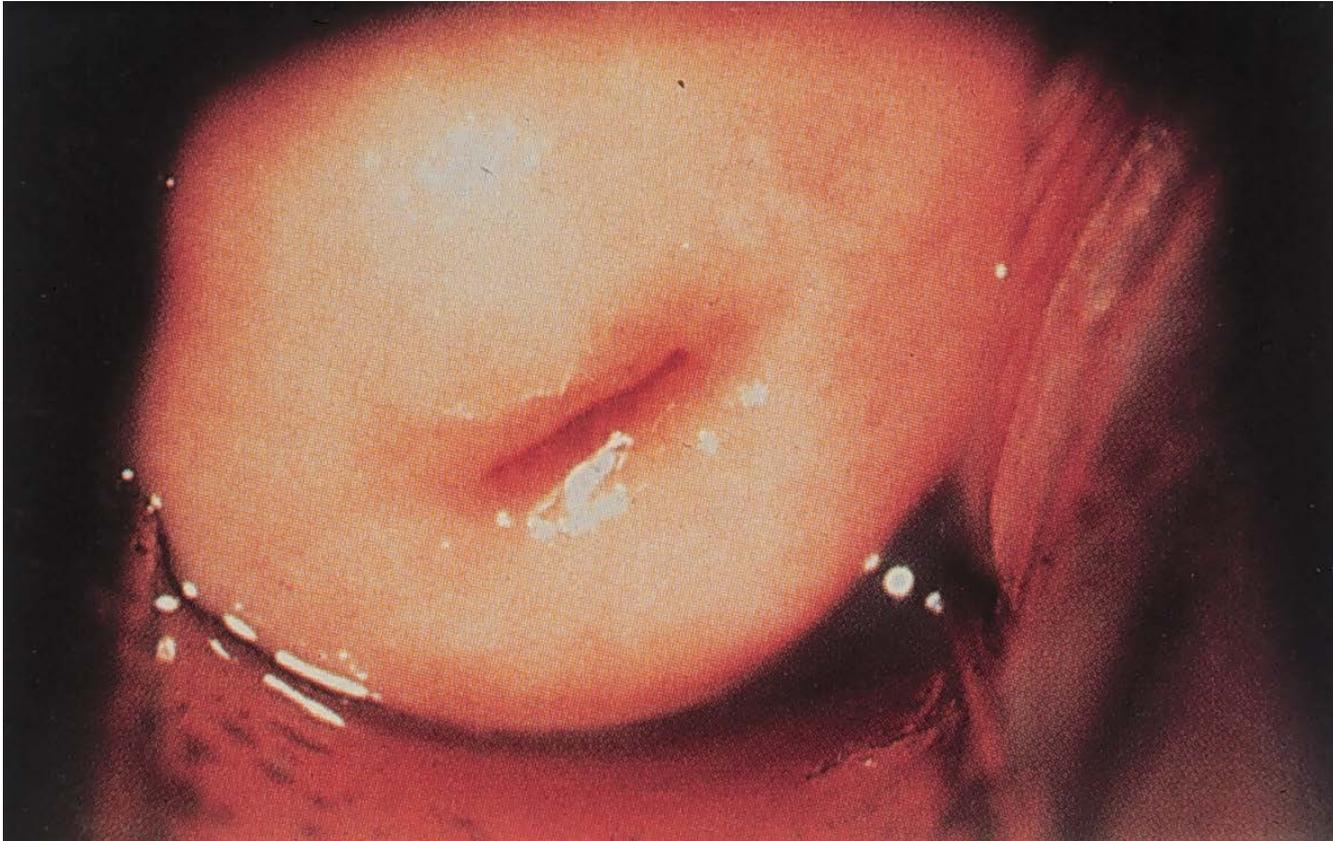
Source: California STD/HIV Prevention Training Center

# *Chlamydia trachomatis*

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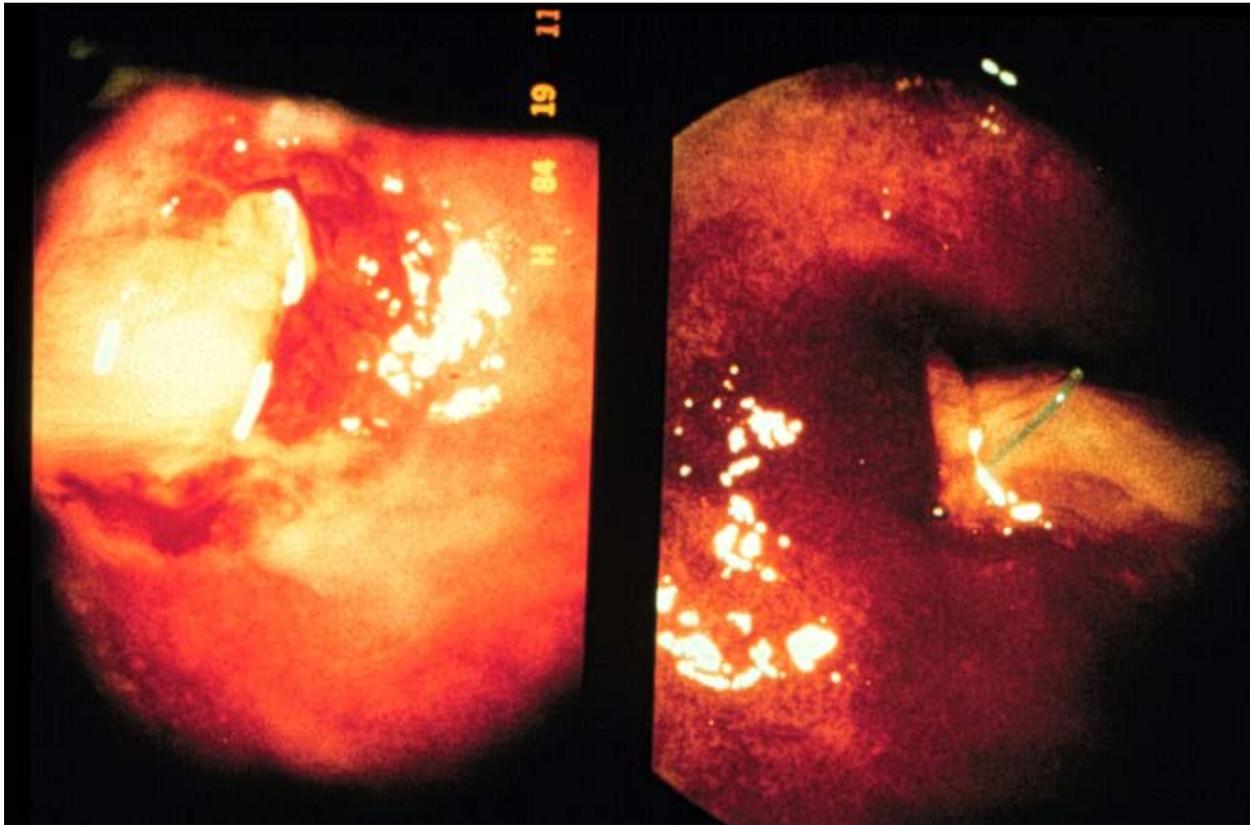
- **Clinical Manifestations:**
  - Mostly asymptomatic
  - cervicitis, urethritis, proctitis, lymphogranuloma venereum, and pelvic inflammatory disease
- **Complications: Potential to transmit to newborn during delivery**
  - Conjunctivitis, pneumonia

# Normal Cervix



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

# Chlamydia Cervicitis



Source: St. Louis STD/HIV Prevention Training Center

# Laboratory Testing: CT and GC

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- **Gram stain (gonorrhea)**
- **Culture**
- **Non-culture non-amplified tests**
- **Commercially available NAATs include:**
  - Becton Dickinson *BDProbeTec*<sup>®</sup>
  - Gen-Probe *AmpCT, Aptima*<sup>®</sup>
  - Roche *Amplicor*<sup>®</sup>
- **Specimen types: urine, cervical, urethral, vaginal, liquid PAP (not as sensitive)**
- **Serology (CT in setting of LGV)**

# 2010 CDC STD Treatment Guidelines: Gonorrhea

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- **Recommended**
  - **Ceftriaxone 250 mg IM x 1**
  - PLUS**
  - **Azithromycin 1gm PO x 1 Or**
  - **Doxycycline 100mg PO BID x 7d**

# 2010 CDC STD Treatment Guidelines

## Chlamydia/NGU

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### Recommended:

**Azithromycin 1gm po x 1 Or**

**Doxycycline 100mg po BID x 7d**

### Alternative:

**Erythromycin base 500mg po QID x 7d Or**

**Erythromycin EES 800mg po QID x 7d Or**

**Levofloxacin 500mg po qd x 7d Or**

**Ofloxacin 300mg po BID x 7d**

# Pelvic Inflammatory Disease (PID)

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- **10%-20% women with GC develop PID**
- **In Europe and North America, higher proportion of *C. trachomatis* than *N. gonorrhoeae* in women with symptoms of PID**
- **CDC minimal criteria**
  - **Uterine tenderness, adnexal tenderness +/- cervical motion tenderness**
- **Other symptoms include**
  - **endocervical discharge, fever, lower abdominal pain**
- **Complications:**
  - **Infertility: 15%-24% with 1 episode PID secondary to gonorrhea or chlamydia**
  - **7X risk of ectopic pregnancy with 1 episode PID**
  - **chronic pelvic pain in 18%**

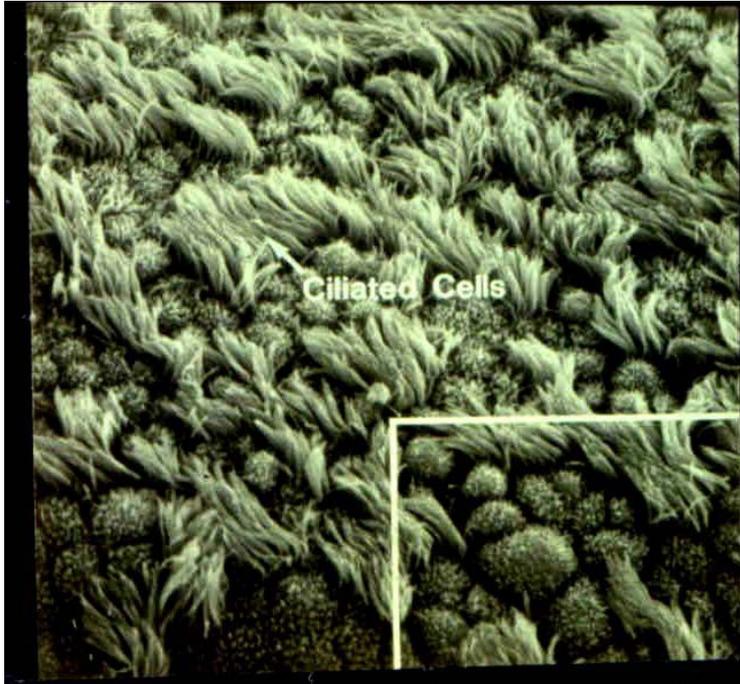
# Pelvic Inflammatory Disease



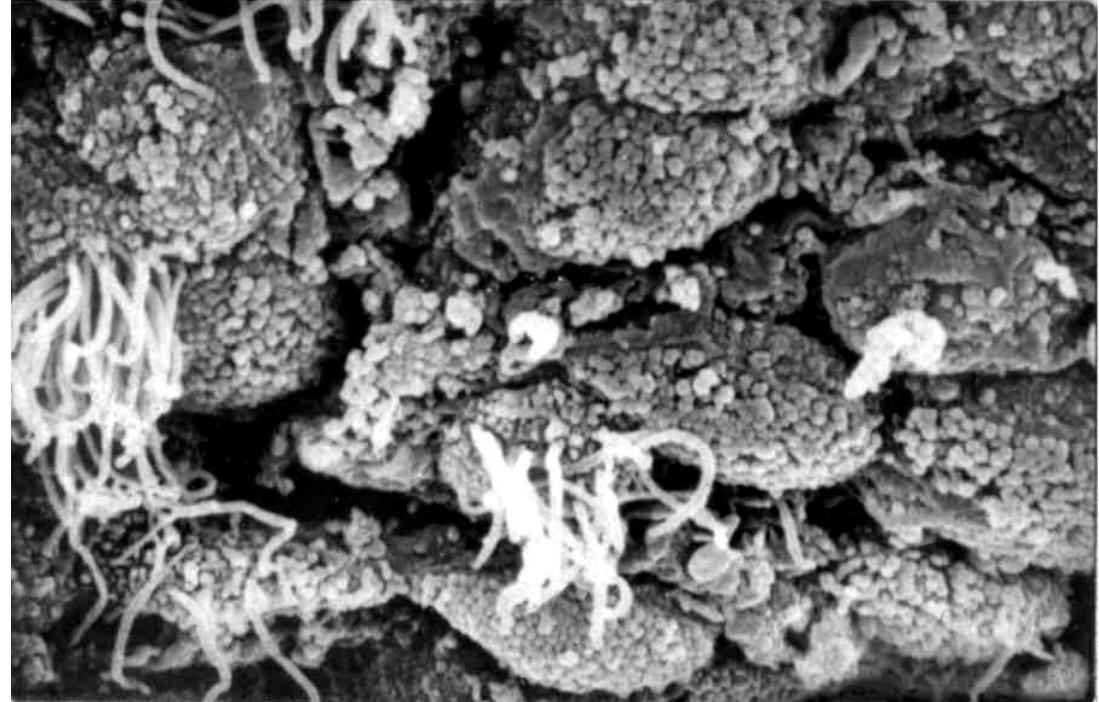
Source: Cincinnati STD/HIV Prevention Training Center

# *C. trachomatis* Infection (PID)

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Normal Human  
Fallopian Tube Tissue



PID Infection

Source: Patton, D.L. University of Washington, Seattle, Washington

# 2010 CDC STD Treatment Guidelines: PID Outpatient Treatment

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**Ceftriaxone 250mg IM x 1 PLUS doxycycline 100mg po BID x 14d +/- metronidazole 500mg po BID x 14d**

**Cefoxitin 2g IM x 1 and probenecid 1g po x 1 PLUS doxycycline 100mg po BID x 14d +/- metronidazole 500mg po BID x 14 d**

**Other parenteral third generation cephalosporin PLUS doxycycline 100mg po BID x 14d +/- metronidazole 500mg po BID x 14d**

# TV Incidence and Prevalence

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- Sexually transmitted parasite
- 248 million new cases world-wide in 2005 (WHO 2011)
- Estimated prevalence in US:
  - 3.1% in the general female population (2001-4)
    - Prevalence increases with age
    - Highest rates in AA (13.3%; 95%CI 10-17.7%)
    - Symptoms not predictive
  - 8.7% women from 21 states undergoing testing for GC/CT (N=7593)
  - 2.5-23.2% of adolescents
  - 8.6-38% of drug users

Sutton et al. Clin Infect Dis 2007; Van der Pol et al JID 2005; Miller et al Sex Transm Dis 2005; Plitt et al Sex Transm Dis 2005; Forhan et al Pediatrics 2009; Miller et al JID 2008; Ginocchio et al Jclin Microbiol 2012

# Clinical Manifestations of *T. vaginalis*

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**MOST TRICHOMONAL INFECTIONS ARE ASYMPTOMATIC!!!**

<b>Diagnostic test</b>	<b>Technique</b>	<b>Time to result</b>	<b>Specimen</b>	<b>Sensitivity</b>	<b>Specificity</b>
<b>Wet Mount</b>	<b>Vag swab with saline microscopy</b>	<b>Minutes, in office</b>	<b>Vag swab</b>	<b>35-82%</b>	<b>99.6-100%</b>
<b>Culture</b>	<b>Media: Diamond's, Trichosel, InPouch TV</b>	<b>24-120h; send out</b>	<b>Vag swab, urethral swab, urine, semen</b>	<b>F:75-87% M: 28.6-48%</b>	<b>100%</b>
<b>APTIMA Trichomonas (GenProbe)</b>	<b>NAAT – TMA to detect species specific 16S rRNA</b>	<b>Hours; send out</b>	<b>Vag swab (F) Urine (F) ThinPrep (F) Urethral swab (M) Urine (M)</b>	<b>96.6-98.4% 87.5% 96-100% 95.2% 73.8%</b>	<b>98-100% 100% 98.8-99.9% 96.5% 98.4%</b>
<b>Affirm VPIII (BD Diagnostics)</b>	<b>Direct specimen nucleic acid probe assay</b>	<b>45 min; send out or equipped office</b>	<b>Vag swab</b>	<b>83-90.5%</b>	<b>99.8-100%</b>
<b>OSOM Trichomonas rapid test (Genzyme Diagnostics)</b>	<b>Immunochromatographic capillary flow assay with murine monoclonal antibody</b>	<b>10 min; in office</b>	<b>Vag swab</b>	<b>82-94.7%</b>	<b>98.8-100%</b>

Adapted from Miller and Nyirjesy, Curr Infect Dis Rep 2011 13:595-603;Schwebke JCM Dec 2011

# 2010 CDC STD Treatment Guidelines:

## *Trichomonas vaginalis*

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### Recommended:

- Metronidazole 2gm PO x 1 dose Or
- Tinidazole 2gm PO x 1 dose

### Alternative:

- Metronidazole 500mg PO BID x 7d\*

\*Consider as preferred in HIV-infected women

# Bacterial Vaginosis

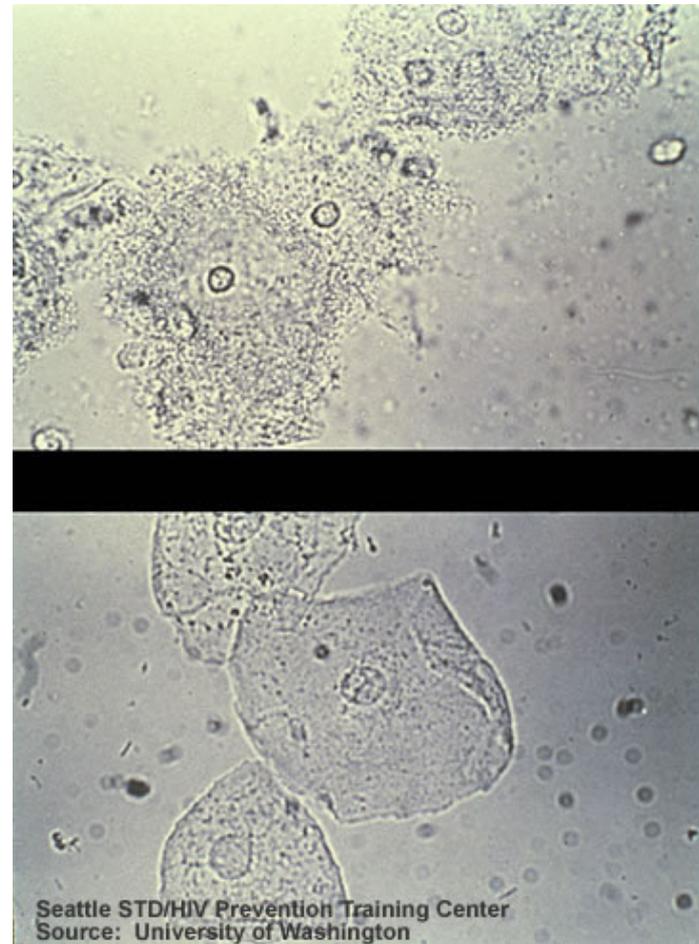
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- Polymicrobial clinical syndrome characterized by loss of H<sub>2</sub>O<sub>2</sub>-producing *Lactobacillus* sp.
- Most common cause of vaginitis/osis
- Prevalence varies by population:
  - 5%-25% among college students; 12%-61% among STD patients
- Complications:
  - Premature rupture of membranes, premature delivery, low birth-weight delivery, acquisition of HIV, development of PID, post-operative infections after gynecological procedures

# Bacterial Vaginosis

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- **50% asymptomatic**
- **Signs/symptoms when present:**
  - malodorous (fishy smelling) vaginal discharge
- **Diagnosis:**
  - Amsel Criteria, vaginal Gram stain, rapid tests



**Indication to treat BV:  
Symptoms!**

# Bacterial Vaginosis Treatment

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## CDC-recommended regimens:

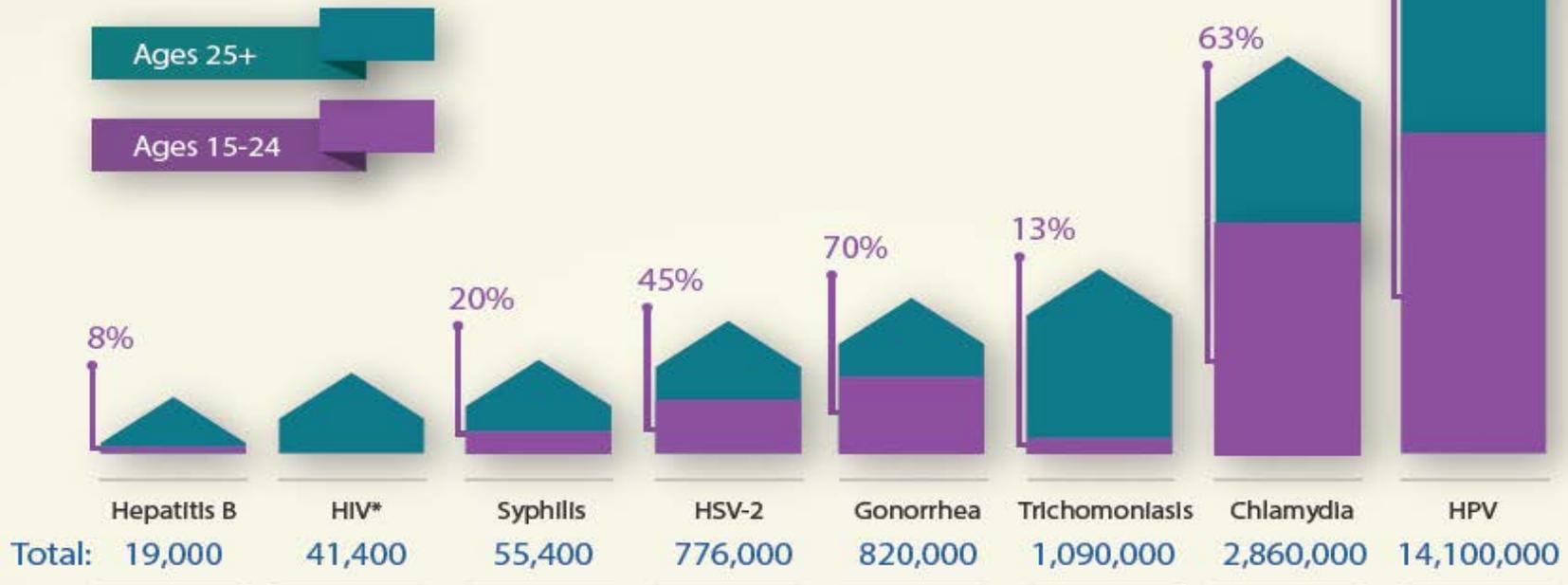
- **Metronidazole 500 mg orally twice a day for 7 days**
- **Metronidazole gel 0.75%, one full applicator (5 grams) intravaginally, once a day for 5 days**
- **Clindamycin cream 2%, one full applicator (5 grams) intravaginally at bedtime for 7 days**

## Alternative regimens:

- **Tinidazole 2gm po qd x 2 days**
- **Tinidazole 1gm po qd x 5 days**
- **Clindamycin 300 mg orally twice a day for 7 days**
- **Clindamycin ovules 100 g intravaginally once at bedtime for 3 days**

# Estimated number of new sexually transmitted infections

- United States, 2008



Young people (15-24) represent 50% of all new STIs

**TOTAL: 19,738,800**

*\*HIV Incidence not calculated by age in this analysis*

*Bars are for illustration only; not to scale, due to wide range in numbers of infections*

# HPV: Epidemiology

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- **Among sexually active women\*:**
  - **>50% have been infected with one or more genital types**
  - **15% have current infection**
    - **50-75% of these are high-risk**
    - **1% have genital warts**
- **Prospective study of young women#**
  - **36mo incidence rate of 43%**
- **NHANES survey – 26.8% women 14-59 with detectable HPV DNA (vaginal swabs)**

\*Koutsky. Am J Med 1997; Koutsky et al. Sex Trans Dis 1999. Svare et al JID 1997, Wideroff et al JID 1996;

\*#Ho et al. NEJM. 1998

# HPV

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- **Transmission: skin-to-skin contact**
- **High-risk (16, 18 etc) vs low-risk (6, 11 etc) types**
  - Low-risk types: genital warts
  - High-risk HPV infection is causally associated with cervical cancer and other anogenital squamous cell cancers (e.g. anal, penile, vulvar, vaginal)
- **Diagnosis: Clinical exam, cytology, nucleic acid amplification methods (in conjunction with cytology for high-risk HPV types)**
- **Treatment: Topical and destructive modalities**

# HPV-Associated Cervical Cancer

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- **528,000 cases of cervical cancer in 2012 world-wide**
- **In US, rates down but still 11,818 cases and 3,939 deaths from cervical cancer in 2010**

[http://www.wcrf.org/cancer\\_statistics/data\\_specific\\_cancers/cervical\\_cancer\\_statistics.p](http://www.wcrf.org/cancer_statistics/data_specific_cancers/cervical_cancer_statistics.p)  
hp accessed 6/1/2014

<http://www.cdc.gov/cancer/cervical/statistics> accessed 6/1/2014

# Anal Cancer Statistics

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- **New anal cancer cases in U.S. (2013): 7060**
- **Deaths from anal cancer in U.S. (2013): 880**
- **0.4% of all cancers diagnosed in the U.S. in 2013**
- **Anal Cancer rates have increased by ~2%/yr since the 1970's**
- **Incidence of SCCA among men in general population (~0.8/100K) vs HIV-infected MSM (~70/100K)**

NCI 2013; Chiao EY. Clin Infect Dis 2006;43:223-33

<http://www.cancer.org/acs/groups/content/@epidemiologysurveillance/documents/document/acspc-037124.pdf>

<http://seer.cancer.gov/statfacts/html/anus.htm>

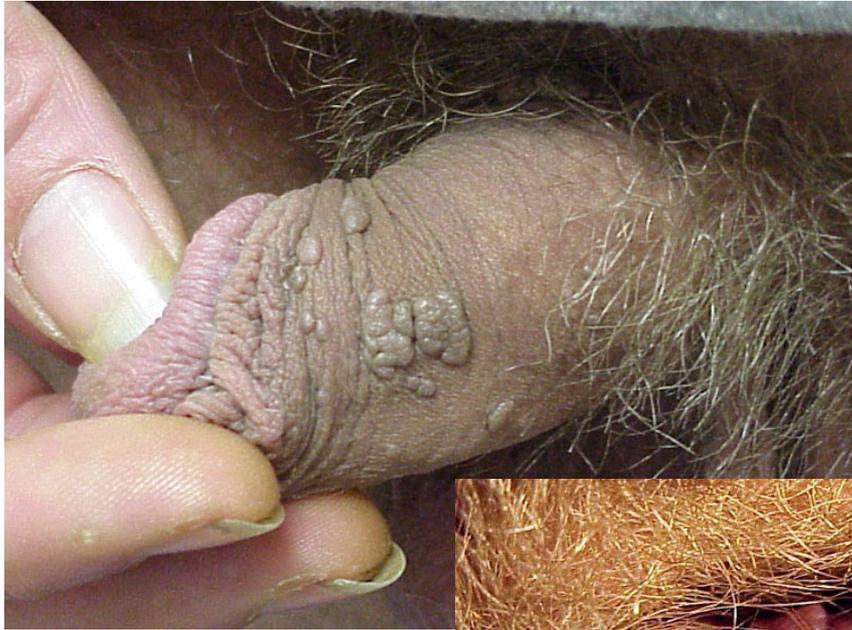
# Perianal Warts

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Source: Cincinnati STD/HIV Prevention Training Center

# HPV Penile Warts



Source: Cincinnati STD/HIV Prevention Training Center

# Intra-meatal Wart of the Penis (and Gonorrhea)

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Source: Florida STD/HIV Prevention Training Center

# HPV Warts on the Thigh

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Source: Cincinnati STD/HIV Prevention Training Center

# Oral Viral Lesions

## Human Papilloma Virus (HPV)

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Source: AL/NC STD/HIV Prevention Training Center

# HPV: Prevention

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- **Non-vaccine modalities:**
  - Decrease number of partners
  - Condoms
    - 70% reduction in newly sexually active college women when partners consistently used condoms
    - Shown to reduce incident infection, associated with lower rate of cervical cancer and associated with regression of HPV-related cervical and penile lesions
  - Microbicides
  - Treatment of warts
- **Smoking cessation**

# HPV Vaccines - Females

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## **Cervarix™ – GSK**

- **HPV 16 and 18**
- **0, 1, 6mo dosing**
- **Females 10-25yrs**
- **Approved 10/09**

## **Giardasil™ - Merck**

- **HPV types 6,11,16,18**
- **0, 2, 6mo dosing**
- **Females 9-26yrs**
- **Approved 6/06**

**Efficacy approximately 100% against precancerous lesions caused by specific types in the vaccine!**

# Gardasil for Males

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- **Initial study demonstrated 90+% efficacy for preventing external lesions caused by HPV types 6, 11, 16 and 18 in men 16-26y**
- **FDA approved (10/09) for males 9-26 for prevention of genital warts**

# **Gardasil for Anal Cancer Prevention**

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- **HPV associated with approximately 90% of anal cancer**
- **Vaccine approved for new indication  
December 22, 2010**
- **Males and females 9-26 years of age**
- **Prevention of anal cancer and associated precancerous lesions caused by HPV types 6, 11, 16, 18**

# Questions?

**Special Thanks to Dr. John Toney, MD  
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presentation**