Sexually Transmitted Infections

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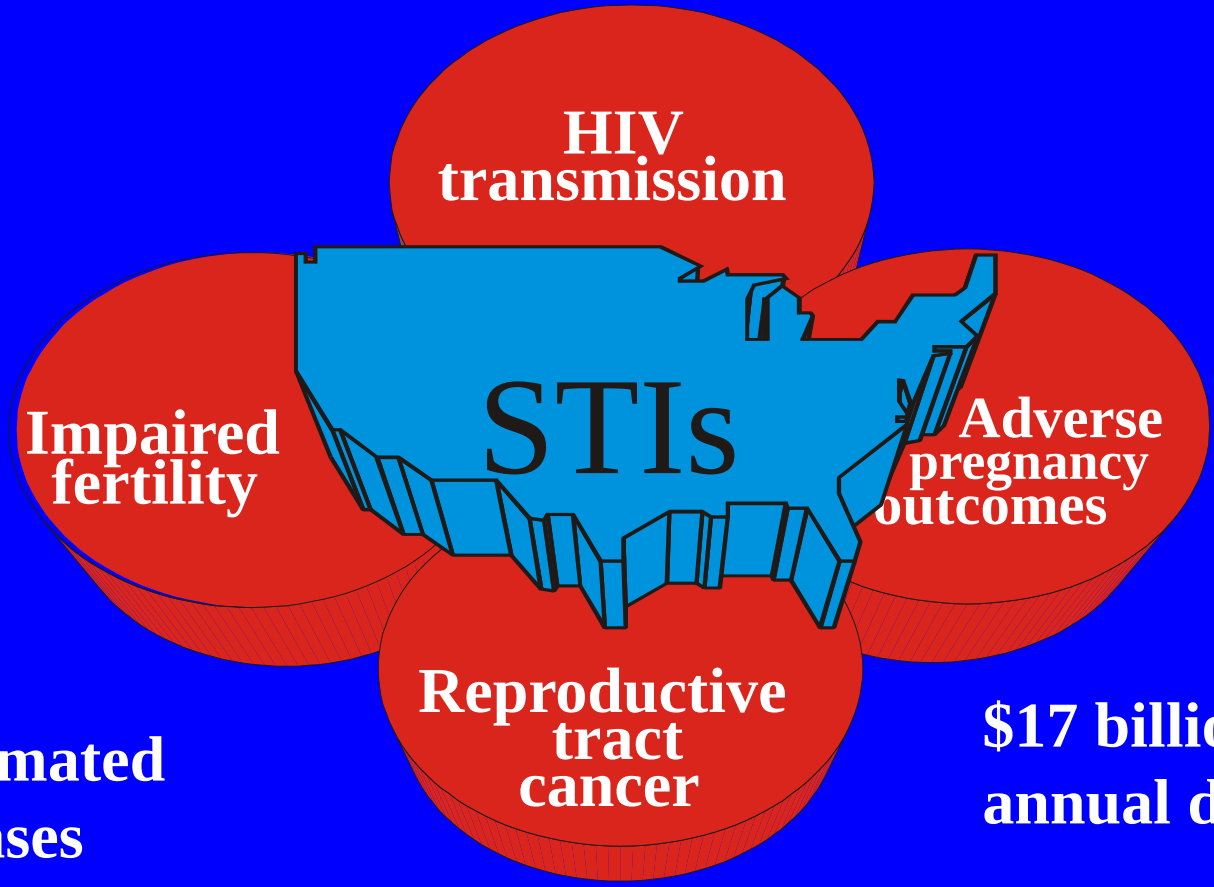
STIs and their Consequences



19 million estimated annual new cases

$17 billion estimated annual direct costs

CDC. STD *Surveillance 2010*. Atlanta: U.S.DHHS; 2012
Chesson HW, et al. Perspect Sex Reprod Health 36(1):11–9. 2004

STIs are Associated with Increased HIV Acquisition

-STDs can produce mucosa breaks & inflammation that attracts immune cells (HIV target)

Genital ulcers: herpes, syphilis

Inflammation: gonorrhea, non-gonococcal urethritis

-STDs increase amount of HIV shed at genital mucosa

Cervix, urethra, rectum

-Some STDs increase plasma HIV viral load

-STD treatment (gonorrhea, syphilis, and trichomoniasis) can reduce plasma & genital HIV

- Paz-Bailey *JID* 2009 & *CID* 2010; Dunne *JAIDS* 2008; Johnson *STD* 2008

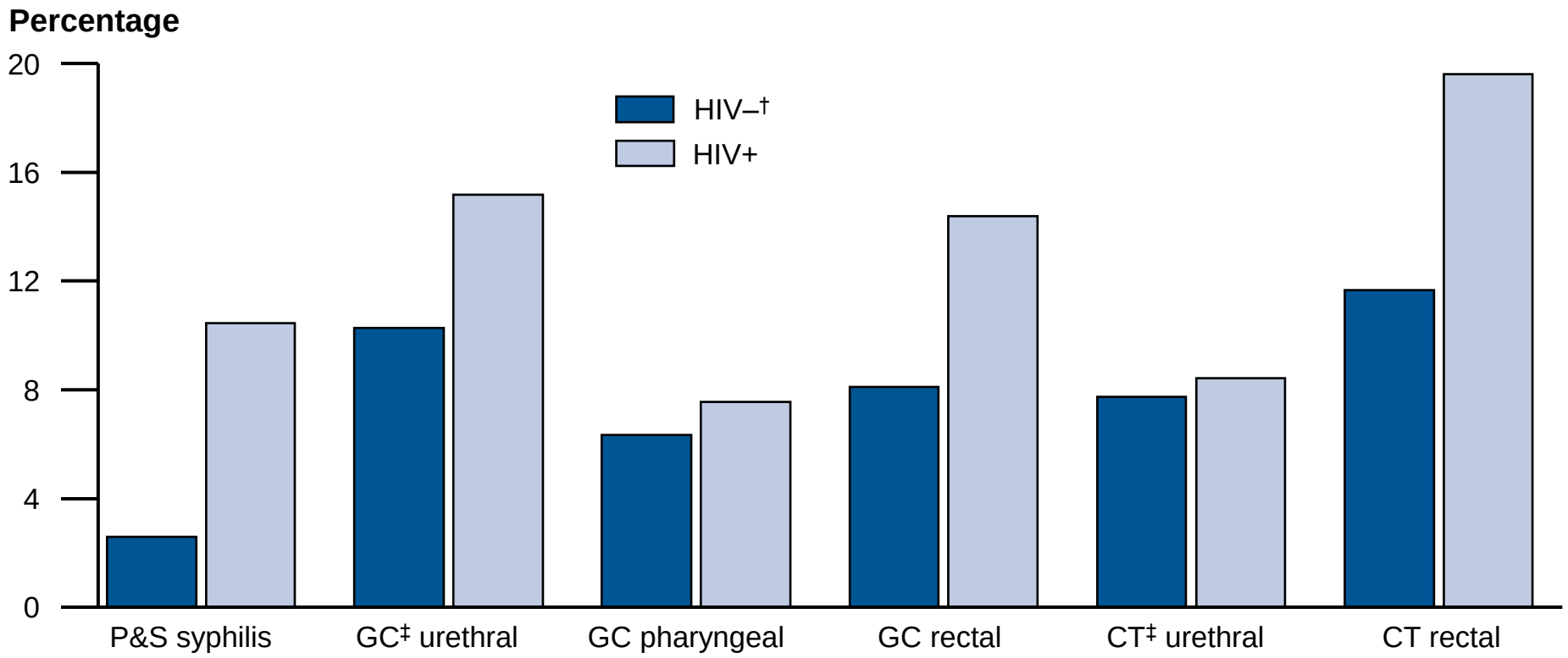
Populations at Greatest Risk for STIs

- Youth
  - 50% of STIs estimated to occur in 15-24 yr
- Men who have sex with men (MSM)
  - Account for 75% of syphilis cases in 2012
  - High rates of HIV co-infection
- Racial/ethnic minorities
  - STIs among highest racial /ethnic disparity

STI in MSM

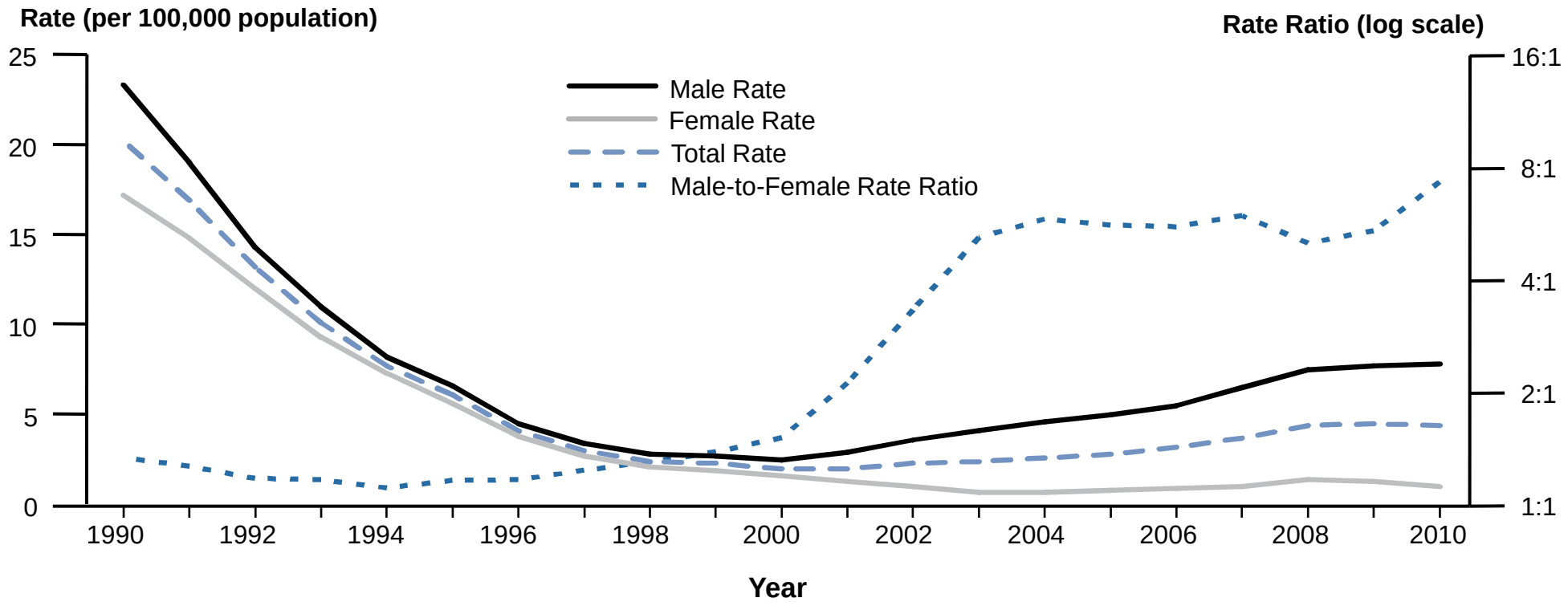
- STI risk higher in subgroups of MSM
  - Racial disparity
  - Methamphetamine,internet partnering
  - Syphilis, rectal chlamydia/gonorrhea, lymphogranuloma venereum, hepatitis C
- Changing attitudes
  - Unprotected oral sex perceived as low risk
    - 20% syphilis (MMWR 2004); fellatio only 5% CT/GC (Hourihan,2004)
  - Serosorting and seropositioning

STD Surveillance Network (SSuN)—Proportion of MSM* Attending STD Clinics with Primary and Secondary Syphilis, Gonorrhea or Chlamydia by HIV Status, 2010

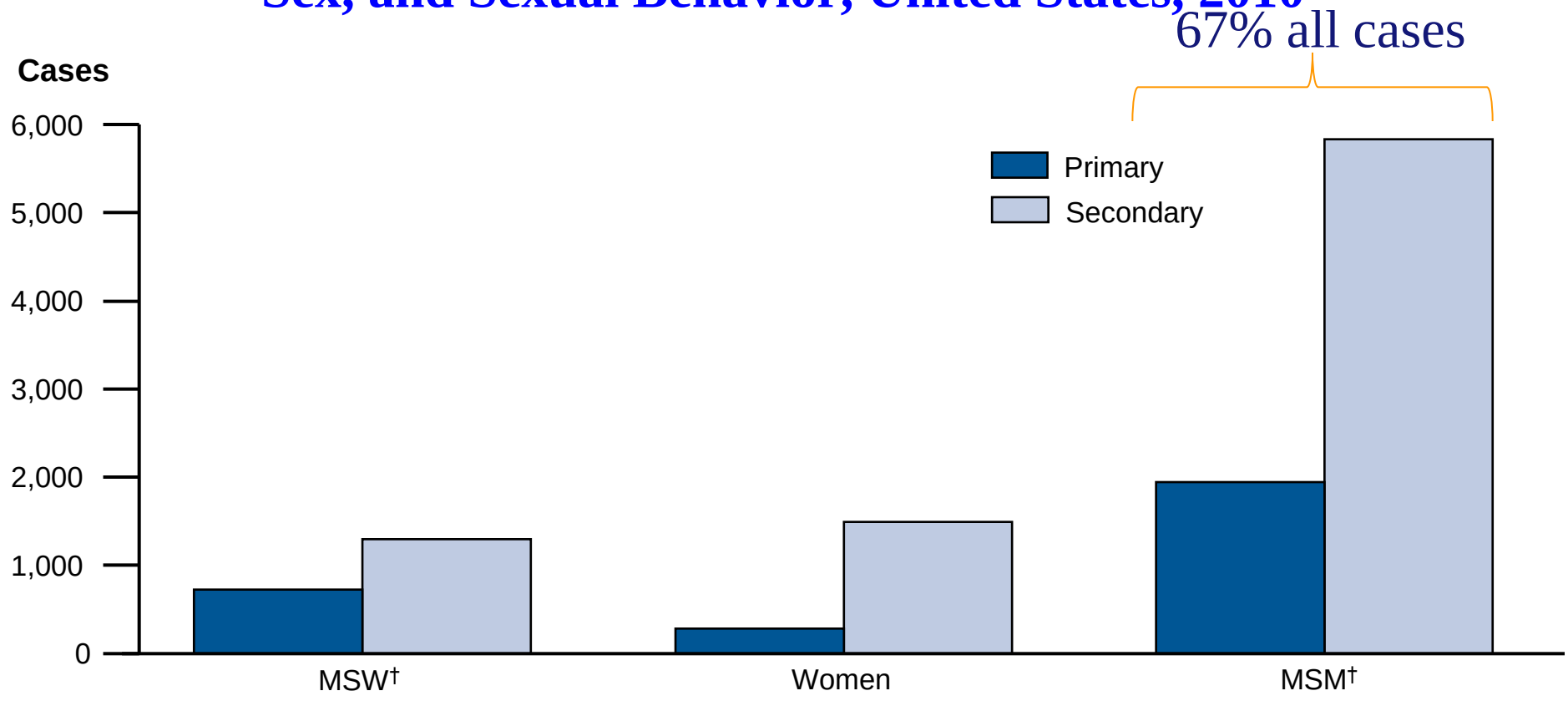


* MSM = men who have sex with men.
† HIV negative status includes persons of unknown status for this analysis.
‡ GC urethral and CT urethral include results from both urethral and urine specimens.

Primary and Secondary Syphilis—Rates by Sex and Male-to-Female Rate Ratios, United States, 1990–2010



Primary and Secondary Syphilis—Reported Cases* by Stage, Sex, and Sexual Behavior, United States, 2010

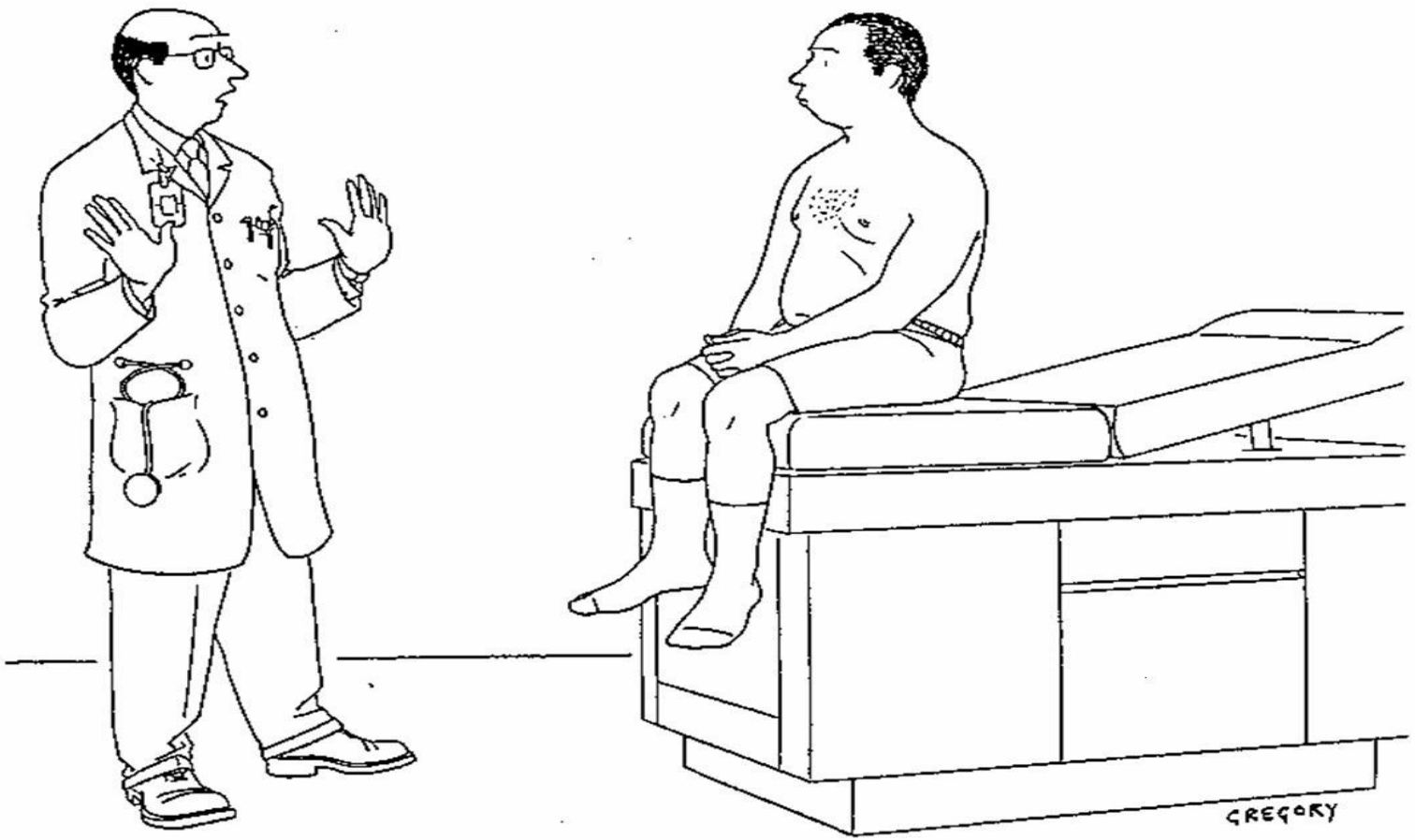


* Of the reported male cases of primary and secondary syphilis, 18.3% were missing sex of sex partner information.
† MSW = men who have sex with women only; MSM = men who have sex with men.

Routine Visit

- JM is 34 yo HIV+ man
  - CD4 470, VL <20
- Relationship problems with male partner, and reports “sex with other men” over past 2 mo
  - Receptive anal intercourse (protected)
  - Receptive oral intercourse (unprotected)

STD Screening: Requires asking



"Whoa—way too much information."

Ongoing Sexually Transmitted Disease Acquisition and Risk-Taking Behavior Among US HIV-Infected Patients in Primary Care: Implications for Prevention Interventions

Kenneth H. Mayer, MD, Timothy Bush, BA,† Keith Henry, MD,‡ Edgar T. Overton, MD,§ John Hammer, MD,¶ Jean Richardson, PhD,‖ Kathy Wood, RN, BSN,** Lois Conley, MPH,† John Papp, MSc, PhD,†† Angela M. Caliendo, MD, PhD,‡‡ Pragna Patel, MD, MPH,† and John T. Brooks, MD†; the SUN Investigators*

557 HIV-infected adults in primary care in 4 cities

Screened/treated for STI at enrollment and at 6 months

13% with STI at enrollment; 7% incident STI at 6 months

- Excluding trichomoniasis, 94% of incident STIs were in MSM
- Most common in men: rectal chlamydia, oropharyngeal gonorrhea
- Risks: polysubstance use, > 4 partners in 6 months

20% of MSM diagnosed with an STI by 6 months, most were asymptomatic

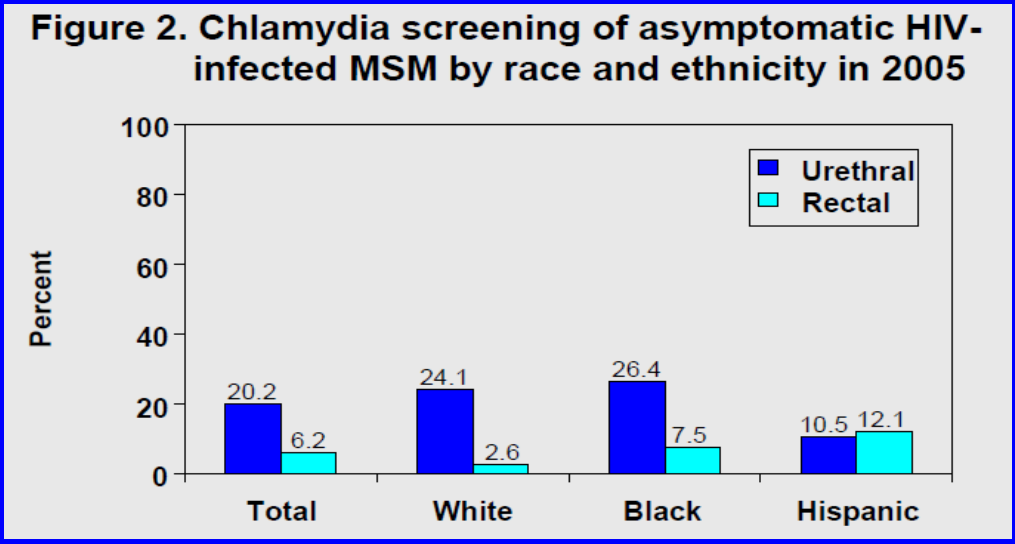
- Mayer et al. *Sex Transm Dis* 2012

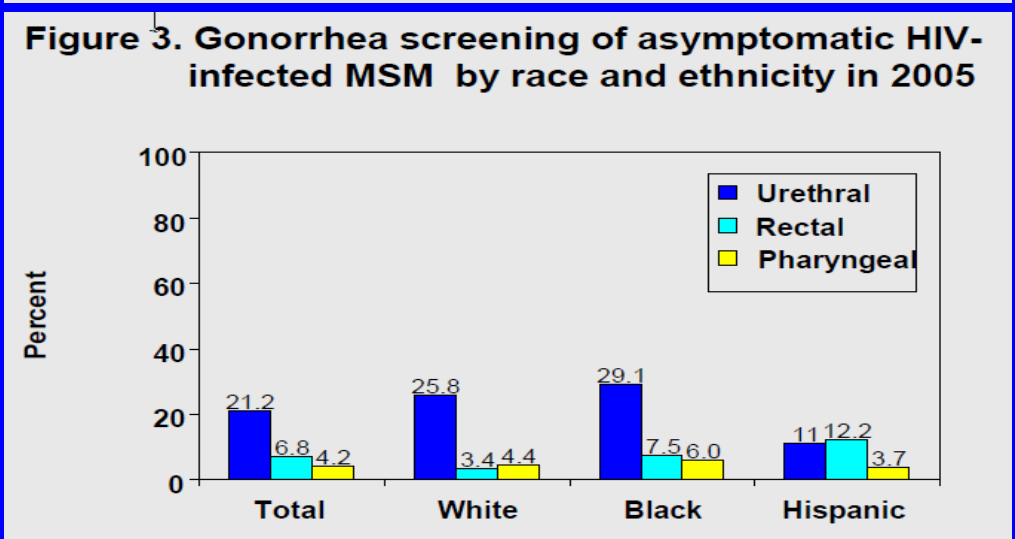
STI Screening

- Sexually active HIV+ men and women (annually)
  - Syphilis serology
  - GC/CT NAAT (vaginal swabs, urine, cervix, urethra)
  - Hepatitis serology A,B,C
- Women
  - Trichomonas (NAAT, in pouch media); Cervical pap test
- Receptive anal intercourse
  - CT/GC NAAT (lab validated) or culture
- Receptive oral intercourse
  - GC NAAT or culture

CDC STD Treatment Guidelines 2010; HIV OI Guidelines 2011

STD Screening HIV-Infected MSM





Mean visits: 8 (1-45)

Mean age: 41 years

42% non-Hispanic white
21% non-Hispanic black
33% Hispanic

35% privately insured
56% publicly insured
9% self-pay

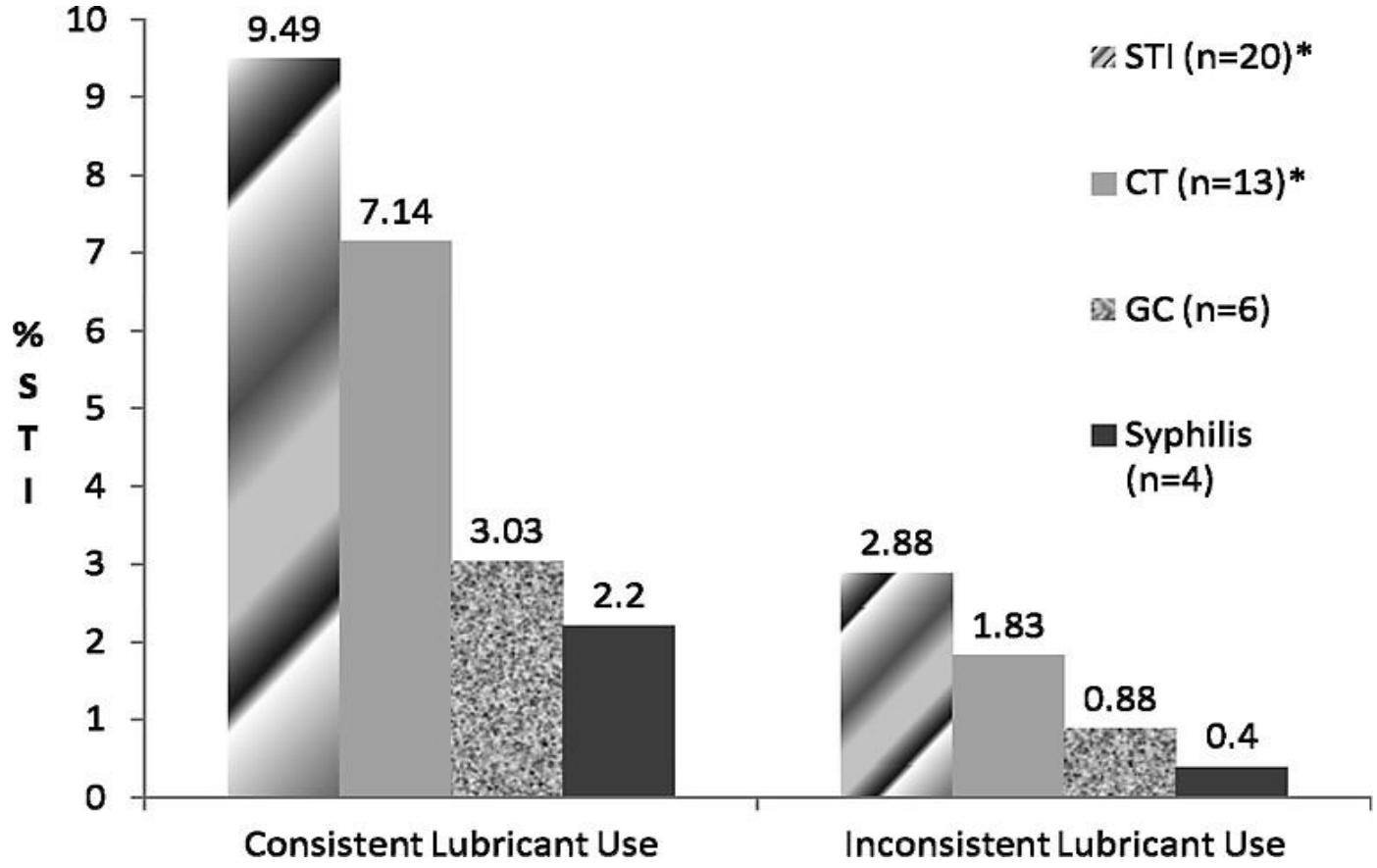
Hoover STD 2010

STI Screening

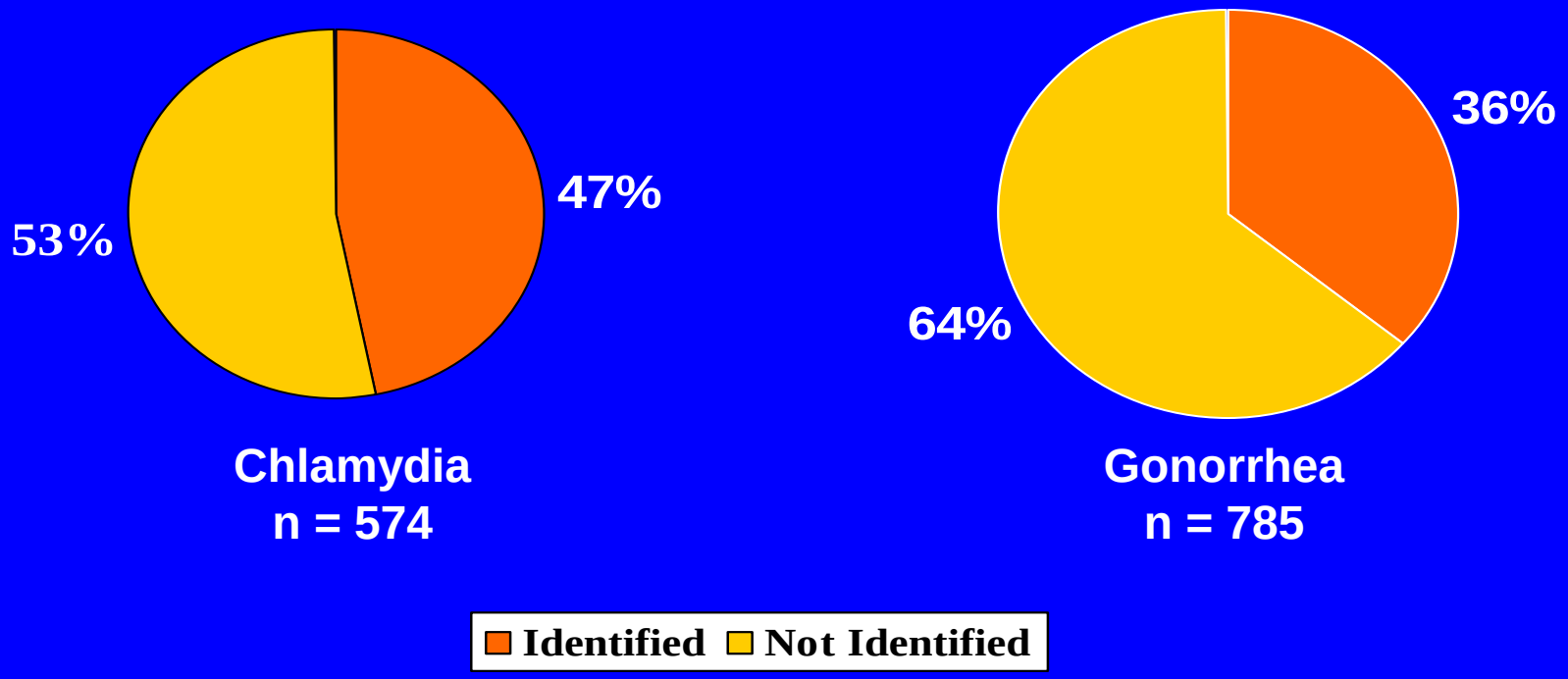
- Persons at higher risk screen at q3-6 mo intervals
  - Multiple or anonymous sex partners; history of STIs
  - Behaviors associated with transmission of HIV/STIs
  - Sex or needle sharing partner with any risk
  - High prevalence of STIs in area or population
- Objective marker of sexual activity
  - Certain STIs increase plasma VL and genital shedding
  - Treatment of specific STIs associated with reductions in HIV shedding

The Slippery Slope: Lubricant Use and Rectal Sexually Transmitted Infections: A Newly Identified Risk

Pamina M. Gorbach, DrPH,†** Robert E. Weiss, PhD,‖ Edward Fuchs, PA-C,‡ Robin A. Jeffries, MS,‖ Marjan Hezerah, PhD,§ Stephen Brown, MD,§ Alen Voskanian, MD,† Edward Robbie, MPH,* Peter Anton, MD,**†† and Ross D. Cranston, MD¶*

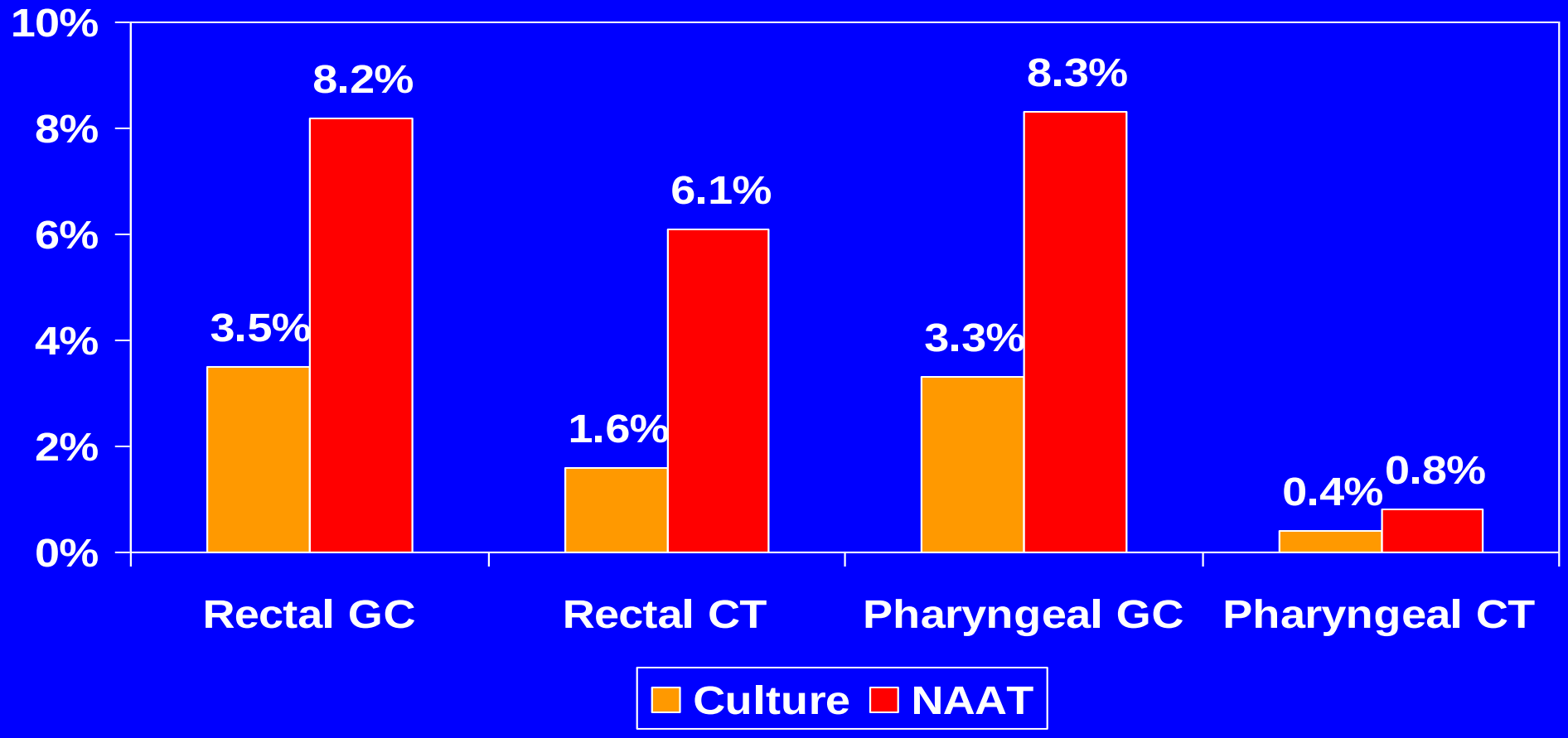


Proportion of chlamydial and gonococcal infections not identified if urine/urethral testing only



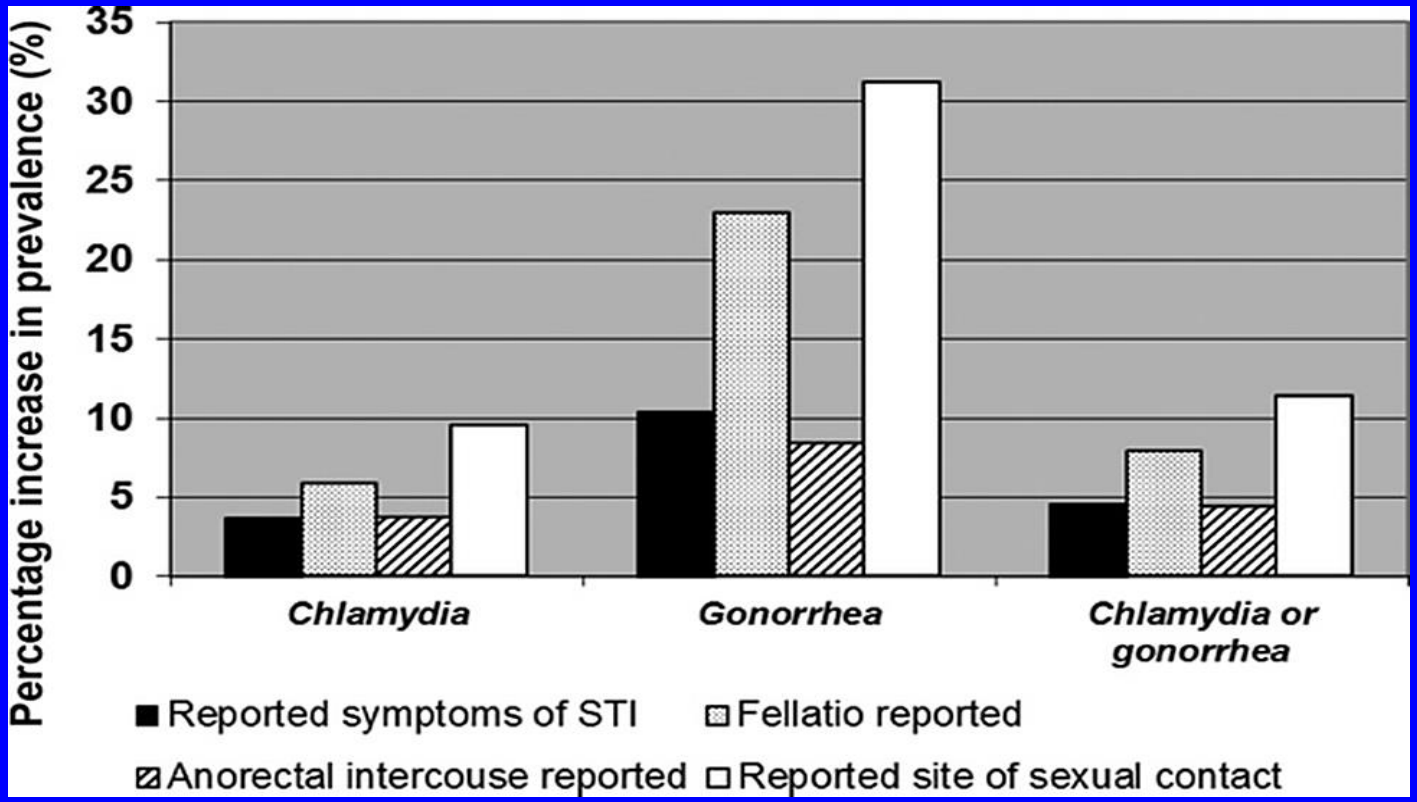
Kent et al. CID 2005

Nucleic Acid Amplification Tests Superior

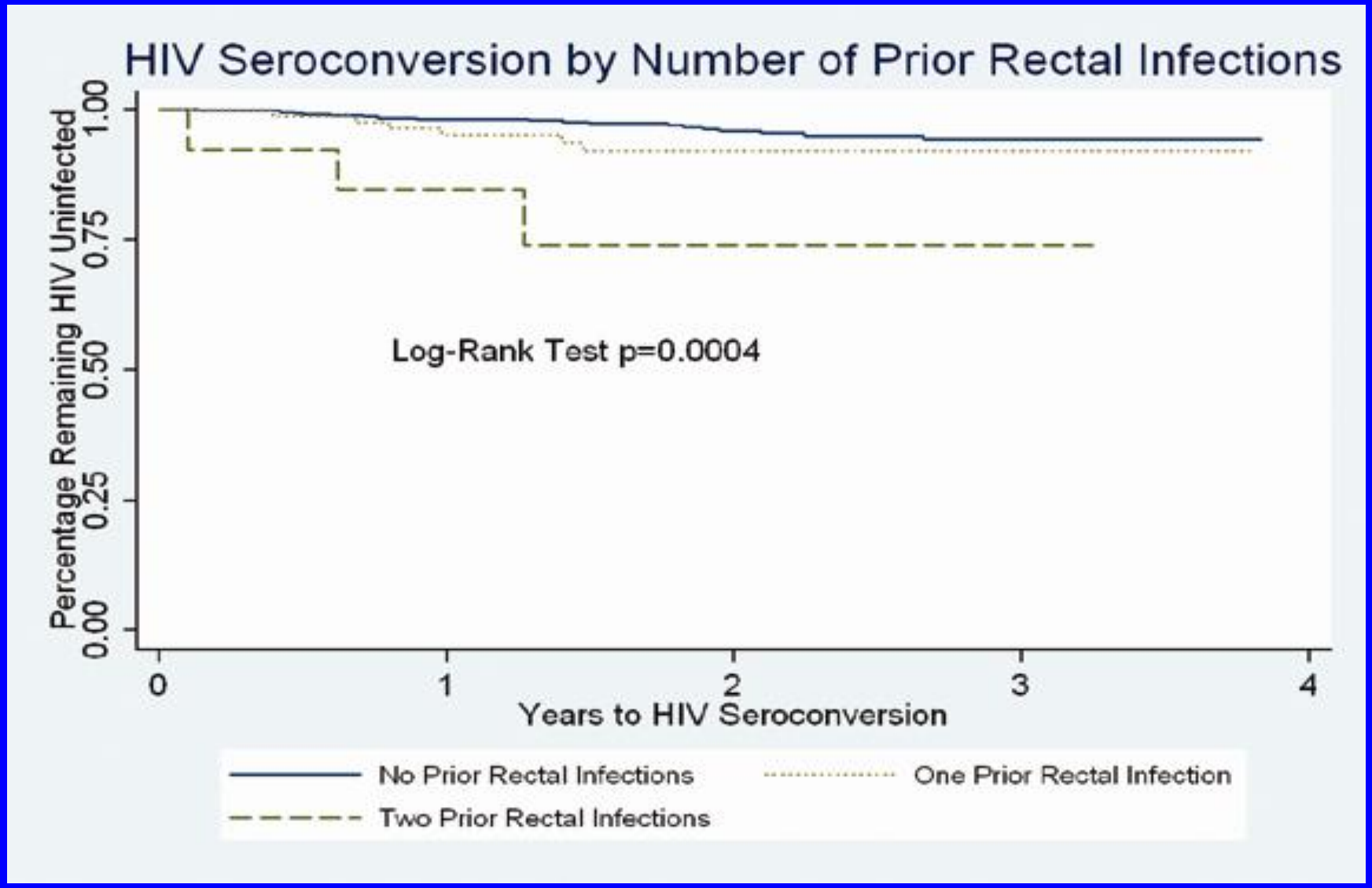


Schachter J. STD 2008

Prevalence of chlamydia and gonorrhea by screening of oropharynx and anorectum relative to endocervical testing alone in female STD attendees



Peters RP, Sex Transm Dis. 2011



Bernstein K, JAIDS 2010

San Francisco STD Clinic, 2003 – 2005

	Company-Specific Ordering Codes for Combined GC/CT Nucleic Acid Amplified Tests (NAATs)		Company-Specific Ordering Codes for CT test only
	LabCorp*	Quest*	LabCorp
Rectal	188672	16506	188706
Pharyngeal	188698	70051	188714
NAATs are offered at (or from) any location in the country with these two codes.			

For information on specimen collection and transportation, clinicians should contact the local reference laboratory representative.

CPT Billing Codes	
CT detection by NAAT	87491
GC detection by NAAT	87591

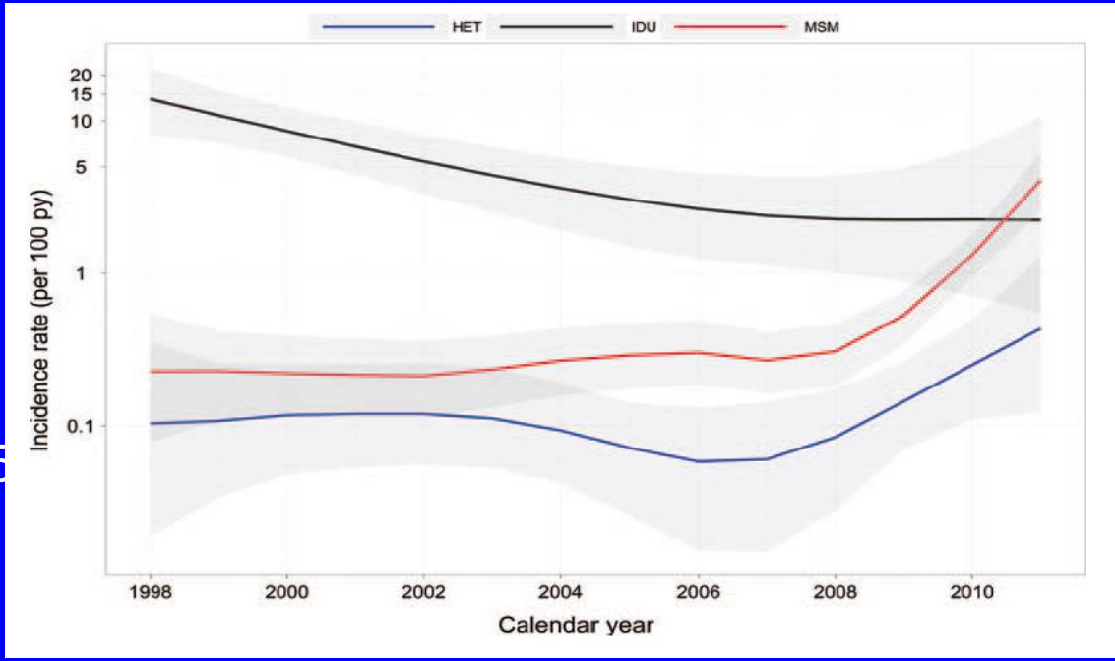
- *** Represent the largest laboratories nationally. Some private or public health laboratories have verified rectal and pharyngeal testing with NAATs.**

STI Screening
Hepatitis

- HbsAg testing to detect current infection
- Hepatitis A and B vaccination (nonimmune)
- HCV sexual transmission (HIV+ MSM)
  - HCV serology at initial visit
  - HCV RNA with unexplained ALT rise
  - Routine HCV testing
    - High risk sexual behavior or ulcerative STIs
  - Prevention (condoms) at sites of penetration

Hepatitis C Virus Infection in MSM

- Increasing incidence among MSM
- Risks:
  - Unprotected receptive anal intercourse; h/o syphilis
  - Rougher or poorly lubricated unprotected anal penetration, including fisting
- Screen if HIV+, IDU, and/or born 1945-65
- Acute infection may be HCV antibody negative (HCV RNA)

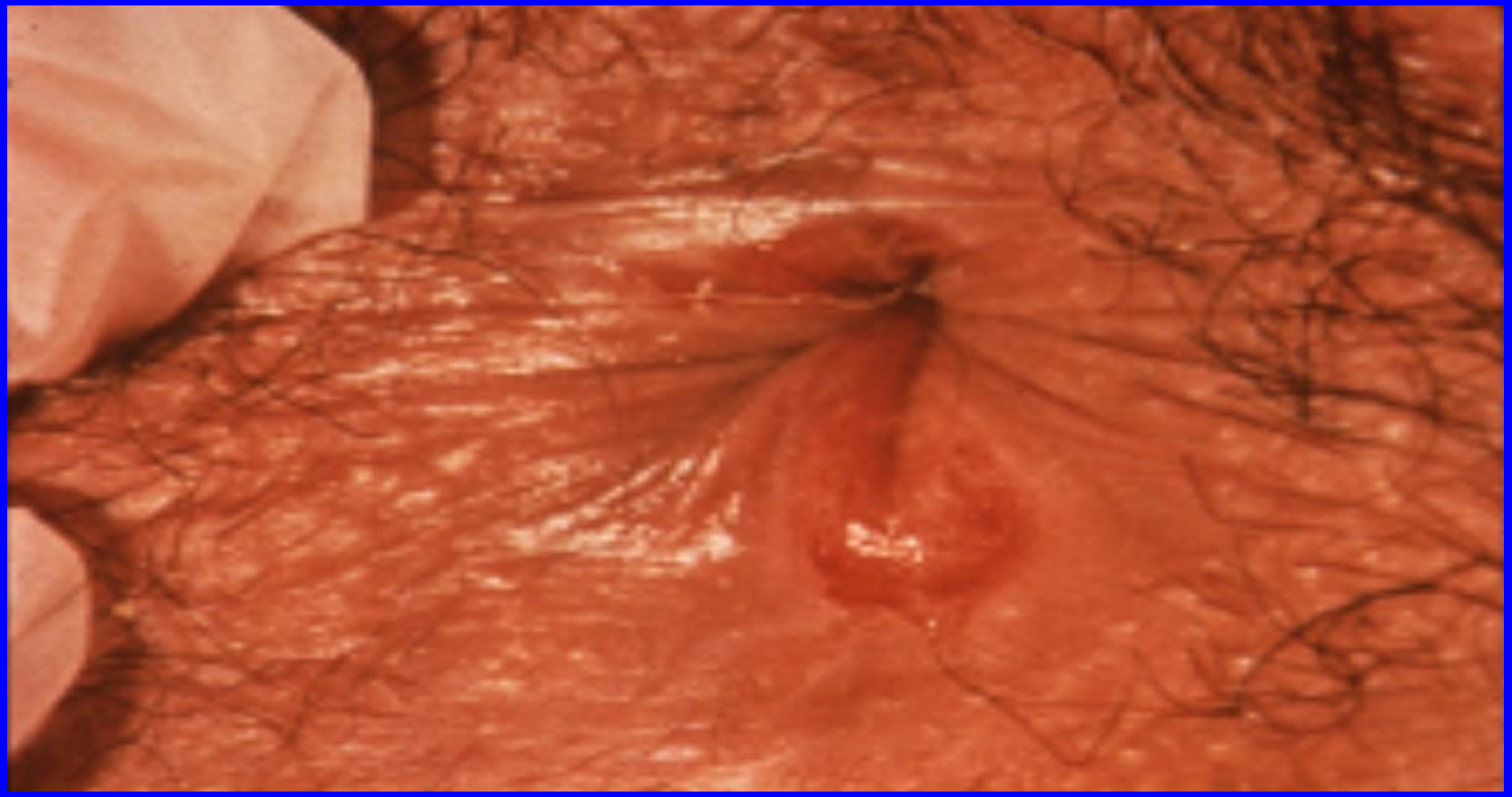


Vandeler, *Clin Infect Dis* 2012

Prevention Strategies

- High-intensity behavioral counseling
  - Partners, pregnancy, protection, practices, past STIs
- Pre-exposure vaccination (hepatitis A, B, HPV)
- Male latex condoms
  - Mucosal fluids (HIV, GC, CT, trichomonias)
- Avoid agents that disrupt anal/vaginal epithelium
  - N9 spermicide, hyperosmolar lubricants
- Male circumcision reduces risk of HPV, genital herpes (African heterosexuals)

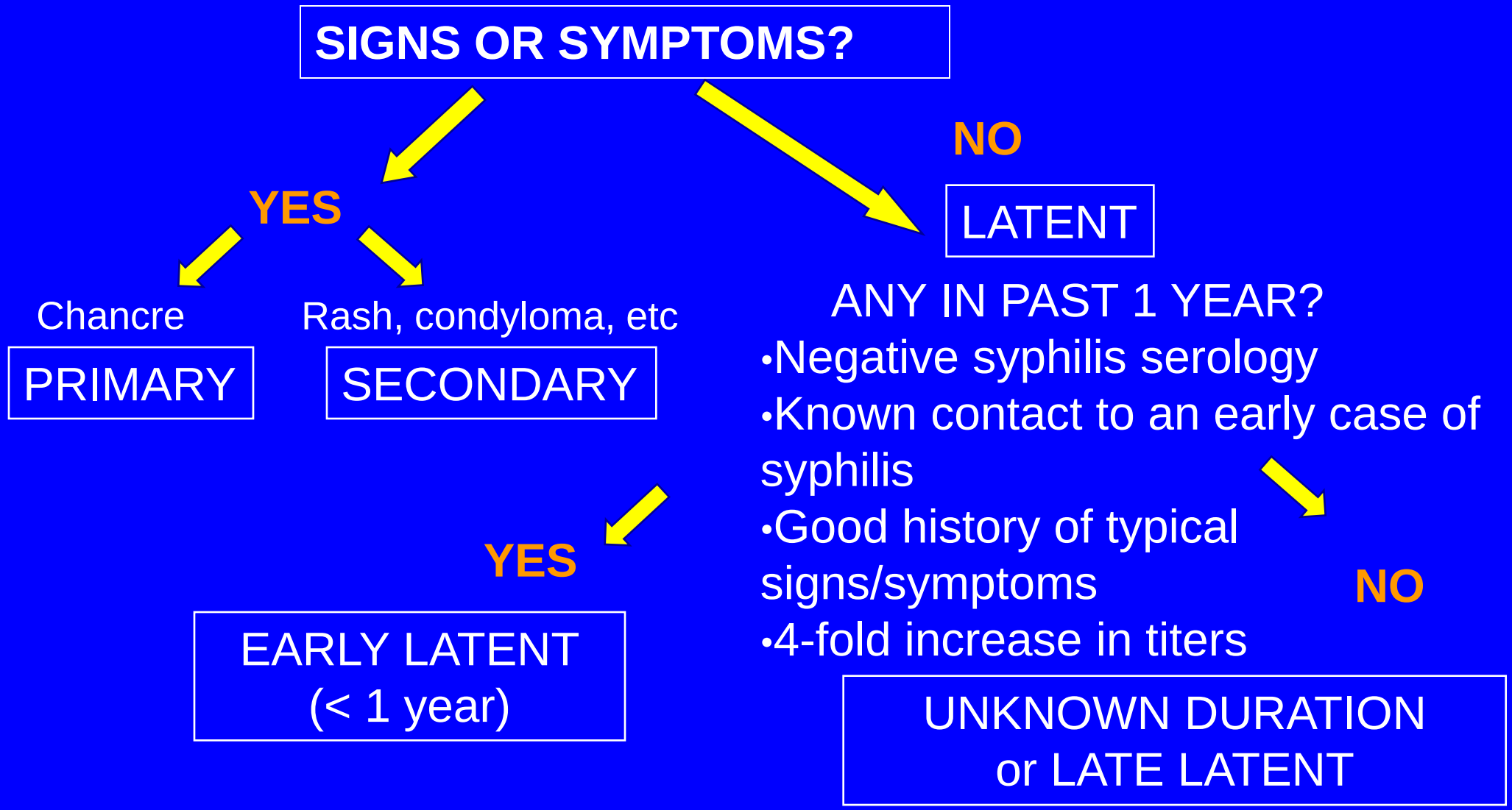
JM Physical Examination

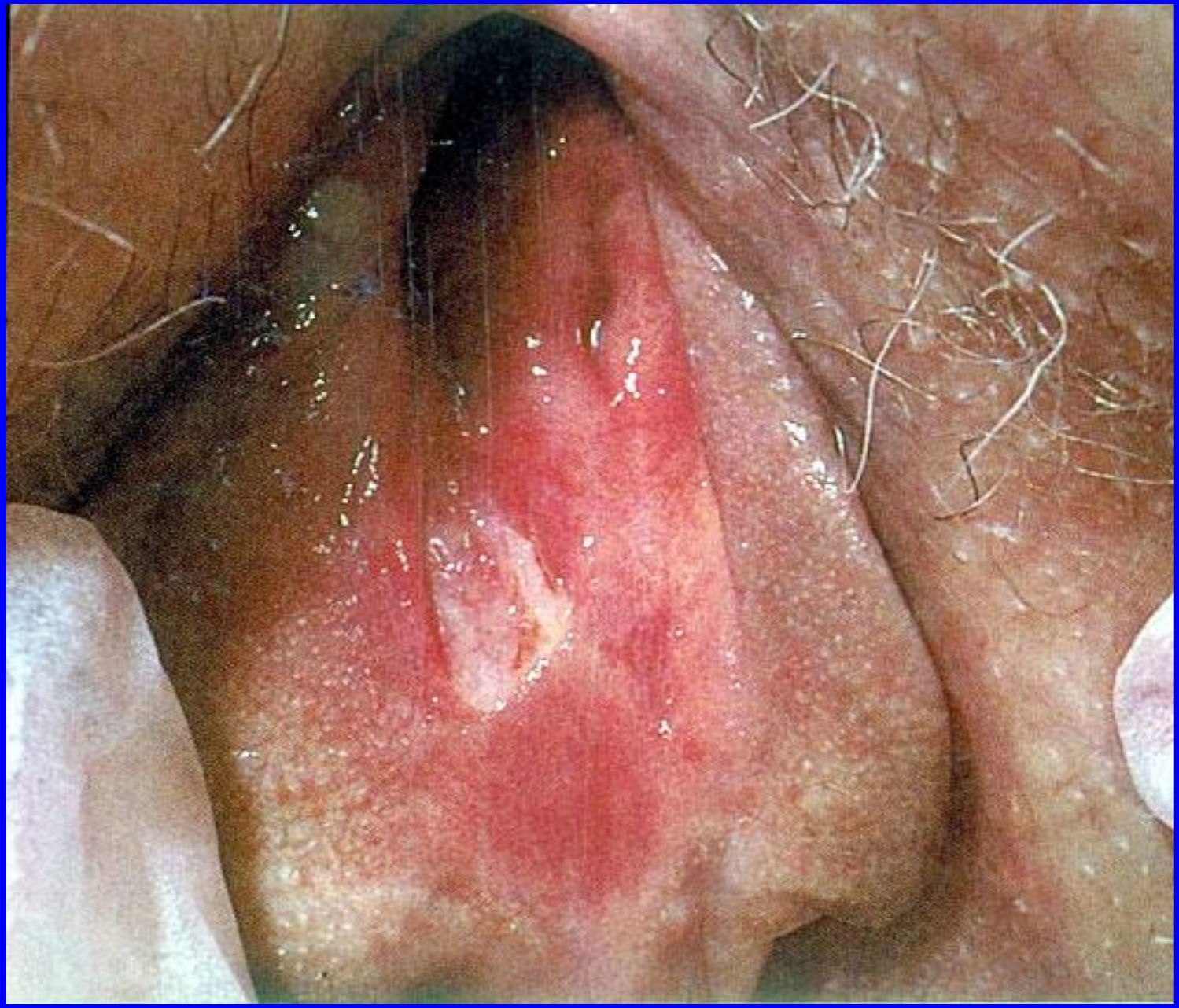


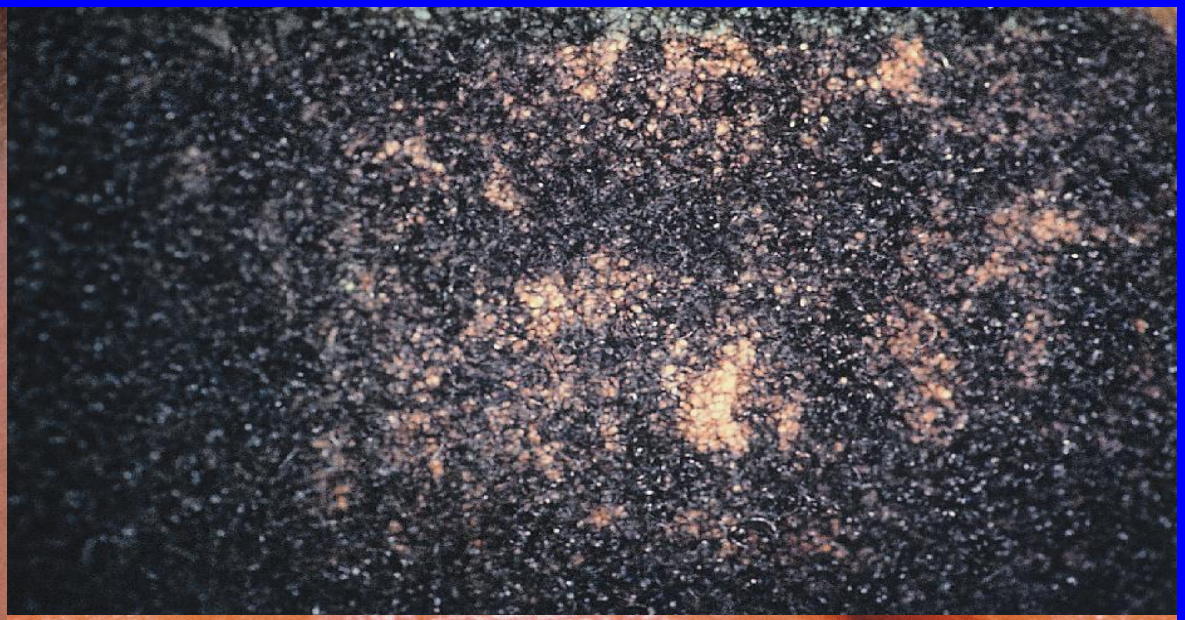
Genital, Perianal, Anal Ulcers

- History/exam often inaccurate
- HSV or syphilis most common
  - Serologic test for syphilis (darkfield or PCR)
  - HSV evaluation (culture, PCR)
  - Noninfectious (yeast, aphthi, drug eruption, psoriasis)
- Treat for diagnosis most likely
  - If primary syphilis is suspected, treat empirically
- Biopsy if uncertain

Syphilis Staging







Syphilis

- Management principles (HIV+)
  - Multiple/deep ulcers, primary/secondary, lues maligna
  - Uveitis, meningitis more common
  - Frequent clinical/serologic monitoring
- Definitive diagnosis for early syphilis
  - Darkfield microscopy or PCR
  - No commercially available *Tp* detection tests
- Nontreponemal/treponemal serologic testing
  - Reverse serologic screening (EIA/CIA)

Diagnostic tests for syphilis

Treponema pallidum **cannot be easily cultured**

Ideally, symptomatic syphilis would be diagnosed using direct detection methods

- Darkfield microscopy
- Polymerase chain reaction (PCR)
- Direct fluorescent antibody test for *T. pallidum* (DFA-TP)

Direct detection methods are not widely available

Syphilis is usually diagnosed with serologic tests

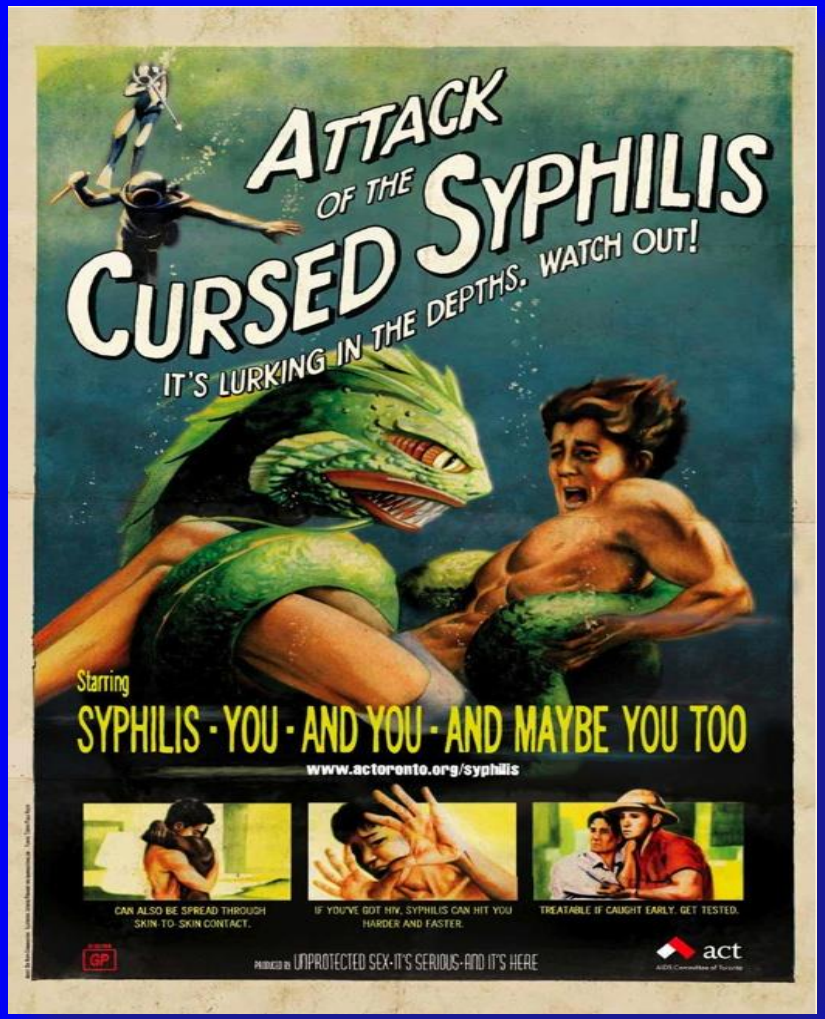
Syphilis Serology

Nontreponemal: VDRL & RPR

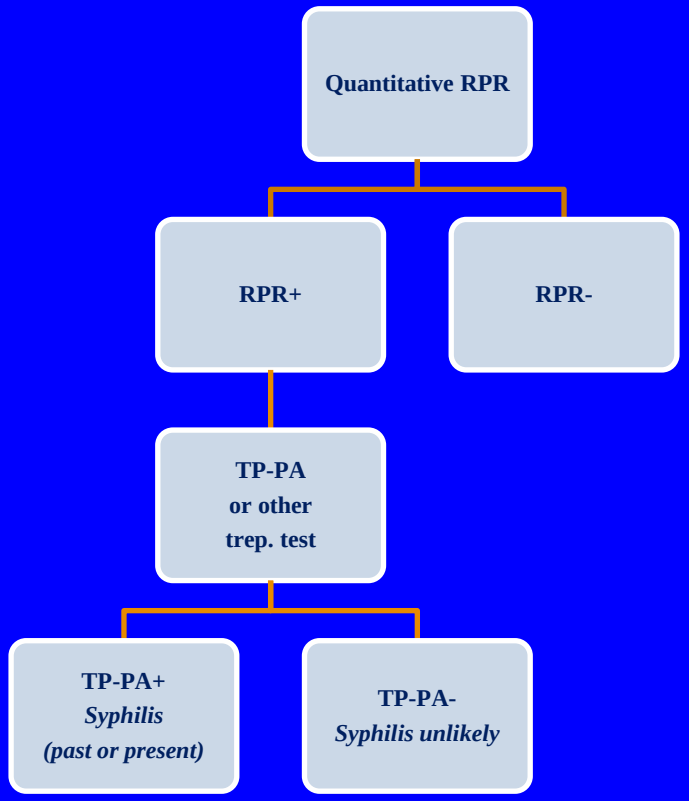
- Antibody to cardiolipin-lecithin-cholesterol antigen; not specific to *T. pallidum*
- Quantitative: titer measured
- Used to follow treatment response

Treponemal: TP-PA, FTA-ABS, EIA/CIA

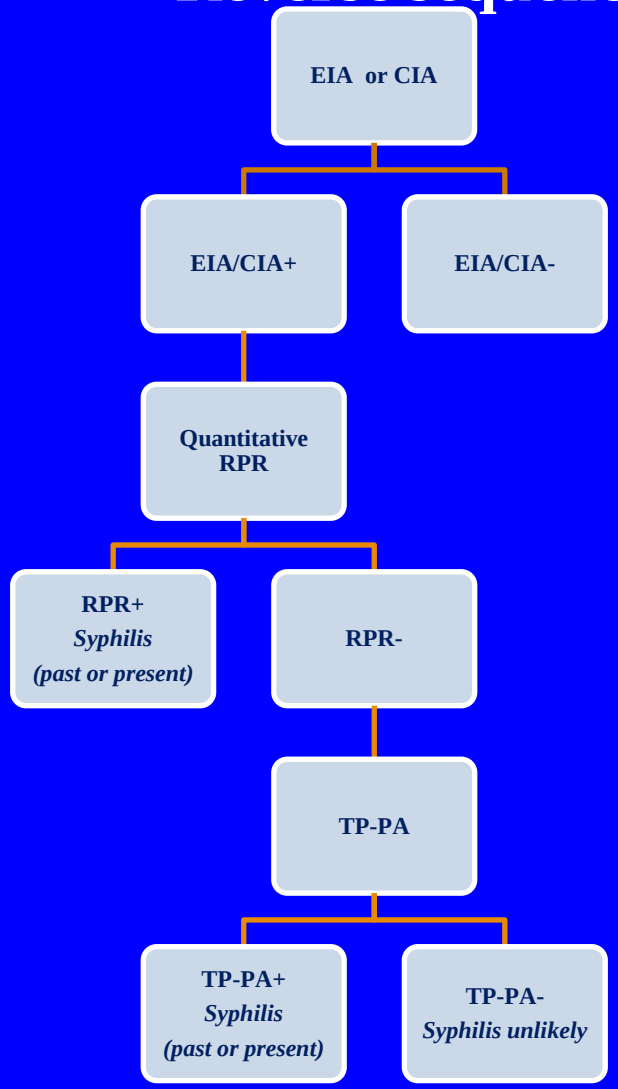
- Qualitative
- Confirmatory



Traditional



Reverse sequence



Which algorithm?

Traditional algorithm

- Detects active infection
- High rate of biologic false positives
  - Confirmation with treponemal test
    - Use of both tests results in a high positive predictive value
- Can miss early primary and treated infection

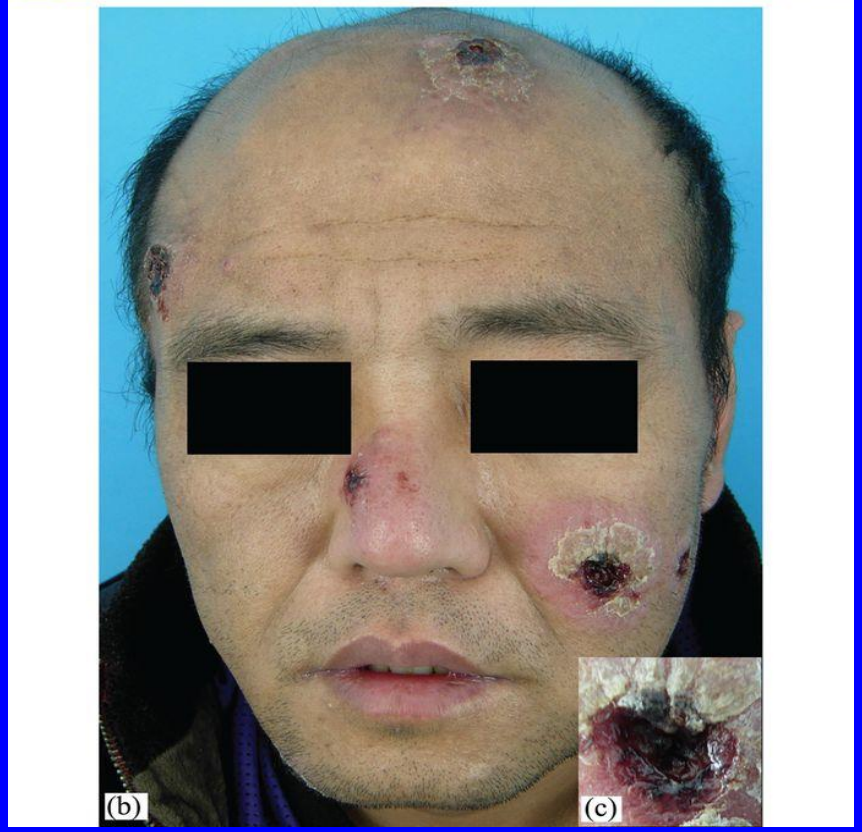
Reverse sequence algorithm

- Detects early primary and treated infection (may be missed with traditional screening)
- Nontreponemal test needed to detect active infection
- EIAs and CIAs nonspecific; FP results; varies by population

Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Weekly / Vol. 60 / No. 5
February 11, 2011

Discordant Results from Reverse Sequence Syphilis Screening — Five Laboratories, United States, 2006–2010

Population	Test	Total	Reactive EIA/CIA		Nonreactive RPR		Nonreactive confirmatory treponemal test*	
		N	n	% total	n	% EIA/CIA+	n	% RPR–
Overall	**Various**	**140,176**	**4,834**	**3.4**	**2,743**	**56.7**	**866**	**31.6**
Low prevalence (Kaiser x 3)	*Trep-Chek, LIAISON*, Trep-Sure	127,402	2,984	2.3	1,807	60.6	737	40.8
High prevalence (New York, Chicago)	Trep-Chek Trep-Sure	12,774	1,850	14.5	936	50.6	129	14.1



Syphilis in HIV: Manifestations May Be Protean, More Severe, and More Invasive

- Significant symptomatic neuroinvasive disease, especially auditory and ocular neuropathy (Li CID 2009)

Lues maligna in HIV+ man

Wang, Intl J STD AIDS 2012

Lues Maligna

Treatment Recommendations
Primary, Secondary, Early Latent

- Penicillin treatment of choice +/-HIV
  - Benzathine penicillin 2.4 mu IM x 1
- No benefit of additional therapy
  - Enhanced treatment (IM + oral)
- Penicillin alternatives
  - Doxycycline, ceftriaxone

What would you do?

- AC is 46 yo male
  - Truvada, Atazanavir, Norvir
  - CD4 220; VL undetectable
- RPR nonreactive 15 mo ago
- RPR 1:4 TPPA +
- Tinnitus x 2 mo

Syphilis
Evaluation of CNS Involvement

- Neurologic, ocular, auditory signs/sxs
- CNS invasion in early syphilis +/- HIV +/- neuro
  - Clinical significance unknown(protein, pleocytosis)
  - Neurosyphilis - combination of tests + clinical
- LP: neuro/ocular sx, serologic treatment failure, tertiary
  - Some studies - clinical and CSF consistent with NS
    - RPR $\geq$ 1:32 and/or CD4 $\leq$350
  - Unless neurologic sx, CSF exam has not been associated with improved clinical outcomes

CSF Findings

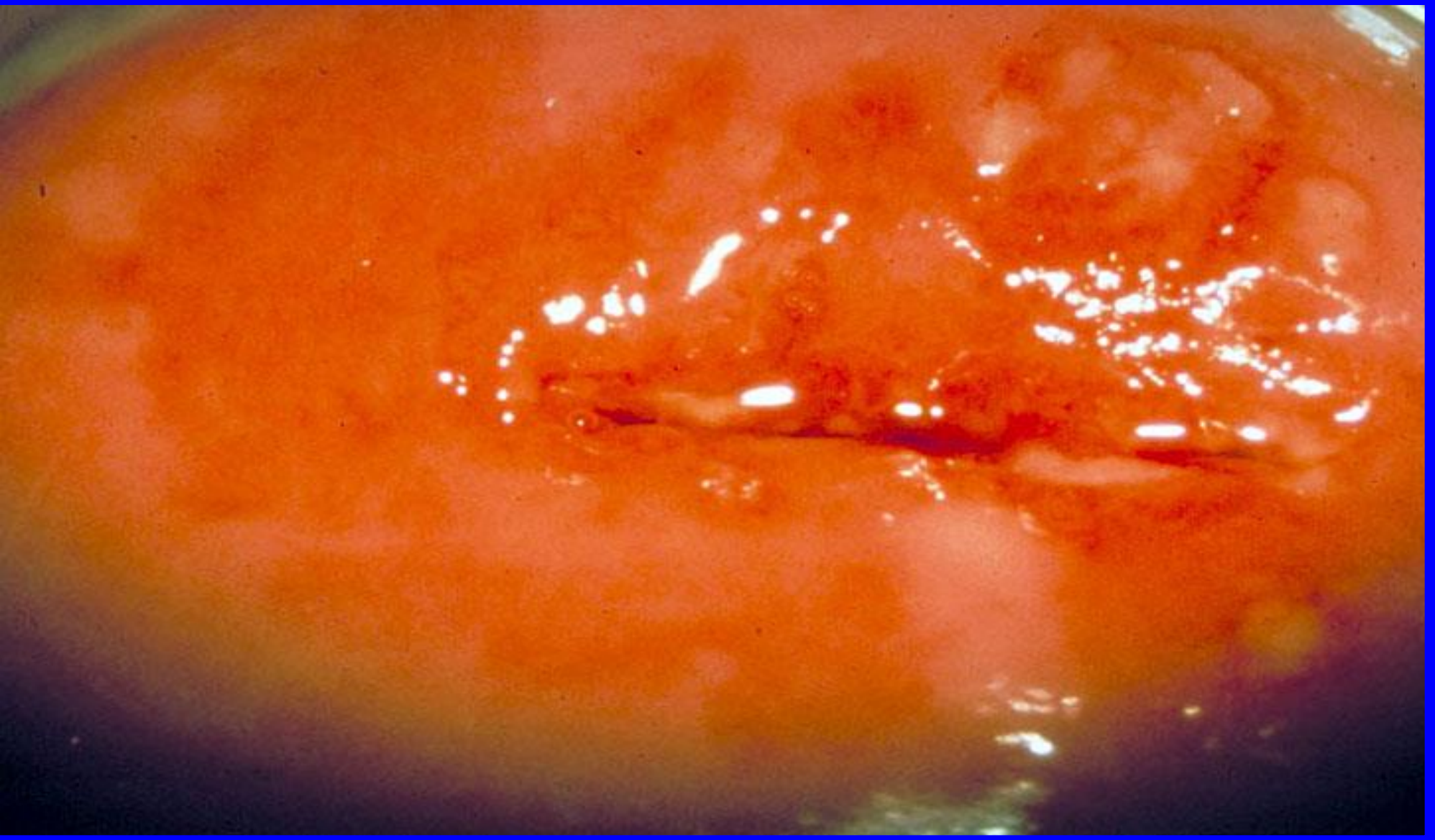
- CSF evaluation
  - VDRL neg, protein/glucose nl, WBC 25
- Does this patient have NS?
  - No single test is diagnostic for NS
  - CSF VDRL specific not sensitive
  - Clinical syndrome, reactive serology, elevated WBC
  - CSF WBCs > 5; higher threshold in HIV+ (>20)
  - Treated with Penicillin G IV 24 mu x 14 d

Monitoring

- Jarish-Herxheimer reaction (Yang *CID* 2010)
  - early syphilis, high nontreponemal titers, prior pcn tx
- IRIS uncommon
- ARVs
  - reduced risk of serologic tx failure
  - lower risk of neurosyphilis
  - CSF normalization with serum RPR decline

  (Marra 2008, Ghanem 2008)

33 yo HIV+ woman with vaginal discharge



Genital Herpes

- Most infections unrecognized
  - ~70% of HIV+ HSV-2 +
- Reactivation intermittent at mucosal surfaces
  - Increases HIV RNA; detection cell culture or PCR
- Type specific serology
  - Transmission risk to sex partners
  - Recurrent genital sx without dx
  - Atypical lesions

HSV2 Genital Shedding

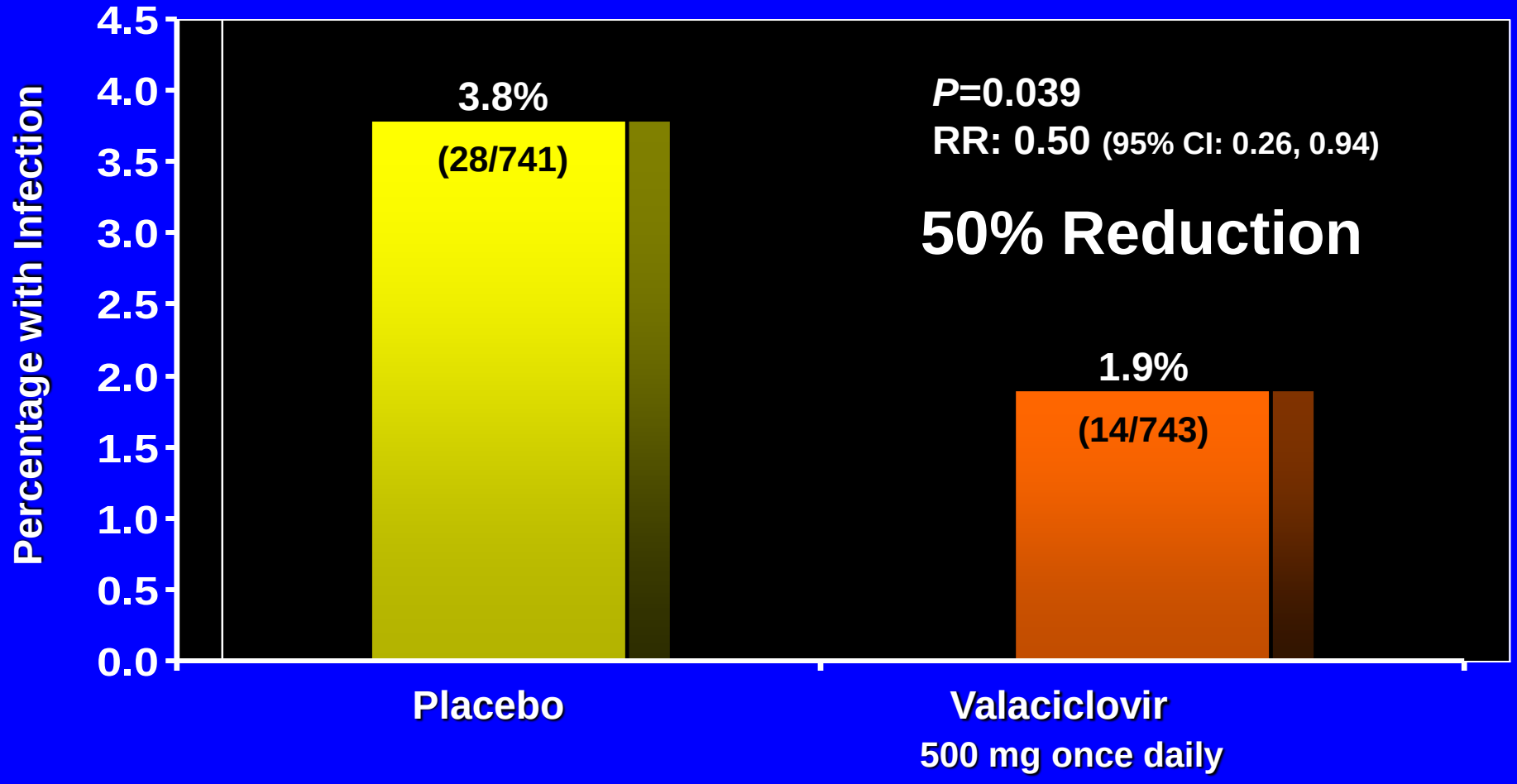
- 498 immunocompetent men and women with HSV2+
  (Tronstein, JAMA 2011;305(14):1441-9)
- Self collected genital swabs for 30 days

	Symptomatic	Asymptomatic	
HSV2 (% of days)	20%	10%	<.001
Subclinical shedding	13%	8.8%	<.001
HSV DNA	4.3 log	4.2 log	.27

HSV2/HIV Infection

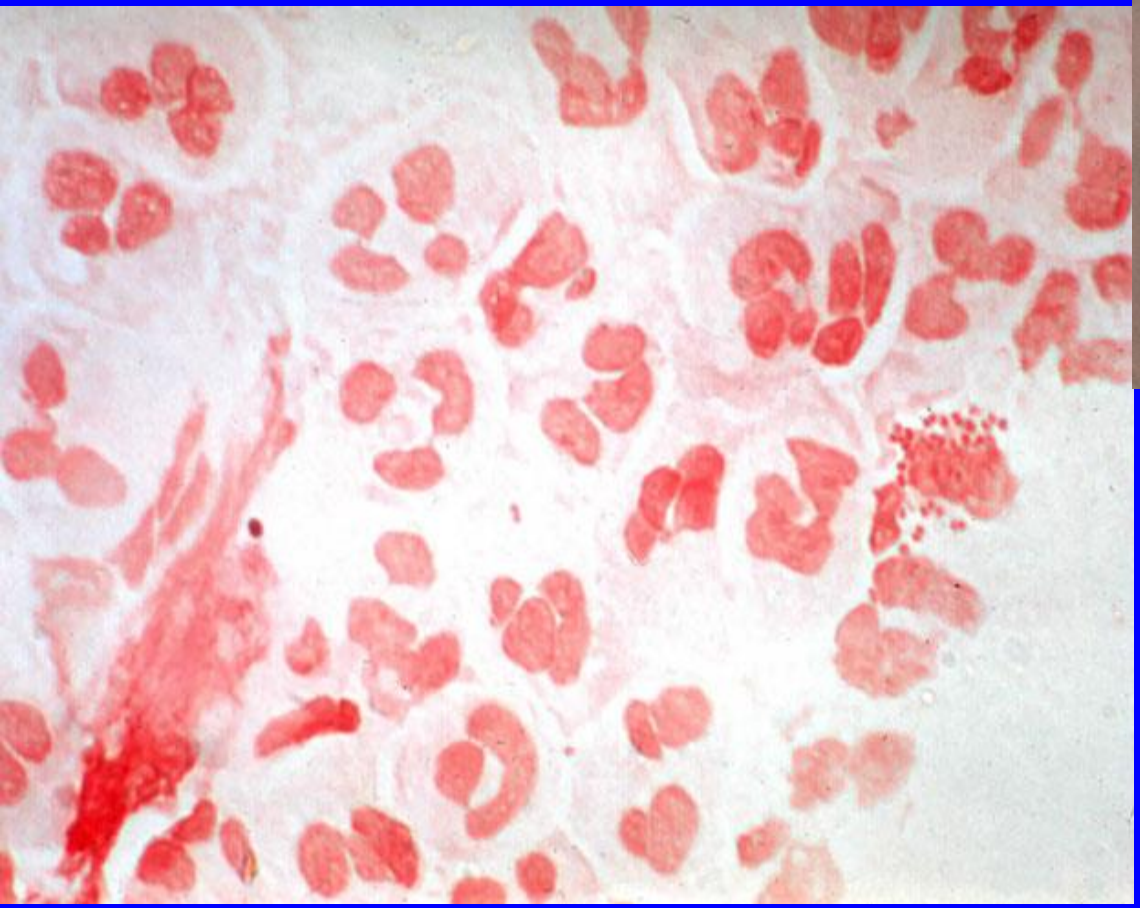
- Lesions may be severe, prolonged, atypical
- HSV shedding despite ARV
- IgM testing not recommended
- Antiviral efficacy (HIV-)
  - Famciclovir slightly less effective for suppression
  - Higher doses or prolonged duration (HIV+)
- Acyclovir resistance
  - Foscarnet, topical cidofovir or imiquimod
  - Suppressive tx (bone marrow transplant) less resistance

Efficacy of Oral Valacyclovir in Prevention of HSV-2 Transmission (Corey. NEJM 2004)




7 8 9 10 11 12 13 14 15 16 17 18 19 20 21

32 yo man complains of dysuria, urinary frequency and intermittent penile discharge



Urethritis

- GC (5-20%), CT (15-40%)
- Nongonoccocal urethritis (NGU)
  - *Mycoplasma genitalium* 5-25%
  - *Ureaplasma* 0-20%
  - *Trichomonas vaginalis* 5-20%
  - Primary infection HSV 15-30%
  - Adenovirus, enterics, Candida, anaerobes

Mycoplasma genitalium

- Small bacteria that lacks cell wall (gram stain neg)
- No commerically available diagnostic test
- Association with acute or persistent NGU
  - No role in male infertility
- Conflicting evidence in women: cervicitis, PID, infertility, ectopic pregnancy, birth outcomes
- Azithromycin superior to doxycycline for MG urethritis (Mena 2009)
  - Resistance to azithromycin (Jensen 2009)
- Moxifloxacin for persistent NGU
  - 400 mg daily x 7 d

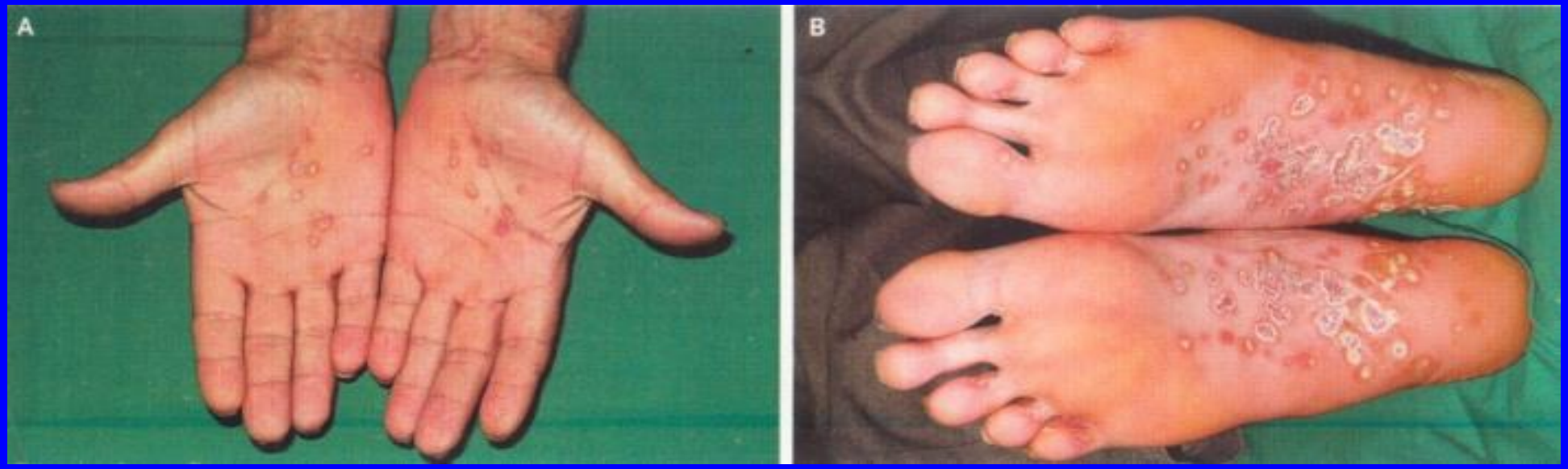
Urethritis

- Diagnosis
  - Gram stain (GC gram neg diplococci) or methylene blue
    or ≥2 WBCS/high powered field (NGU) [draft]
  - GC/CT nucleic acid amplification tests
- NGU Treatment

  - Azithromycin 1gm PO once

  - Doxycycline 100mg PO bid x 7 days
- Recurrent or persistent infection
  - retreat if non-compliant
  - Trichomonas
  - Resistant ureaplasma or mycoplasma

Patient returns 3 weeks after Appropriate Treatment

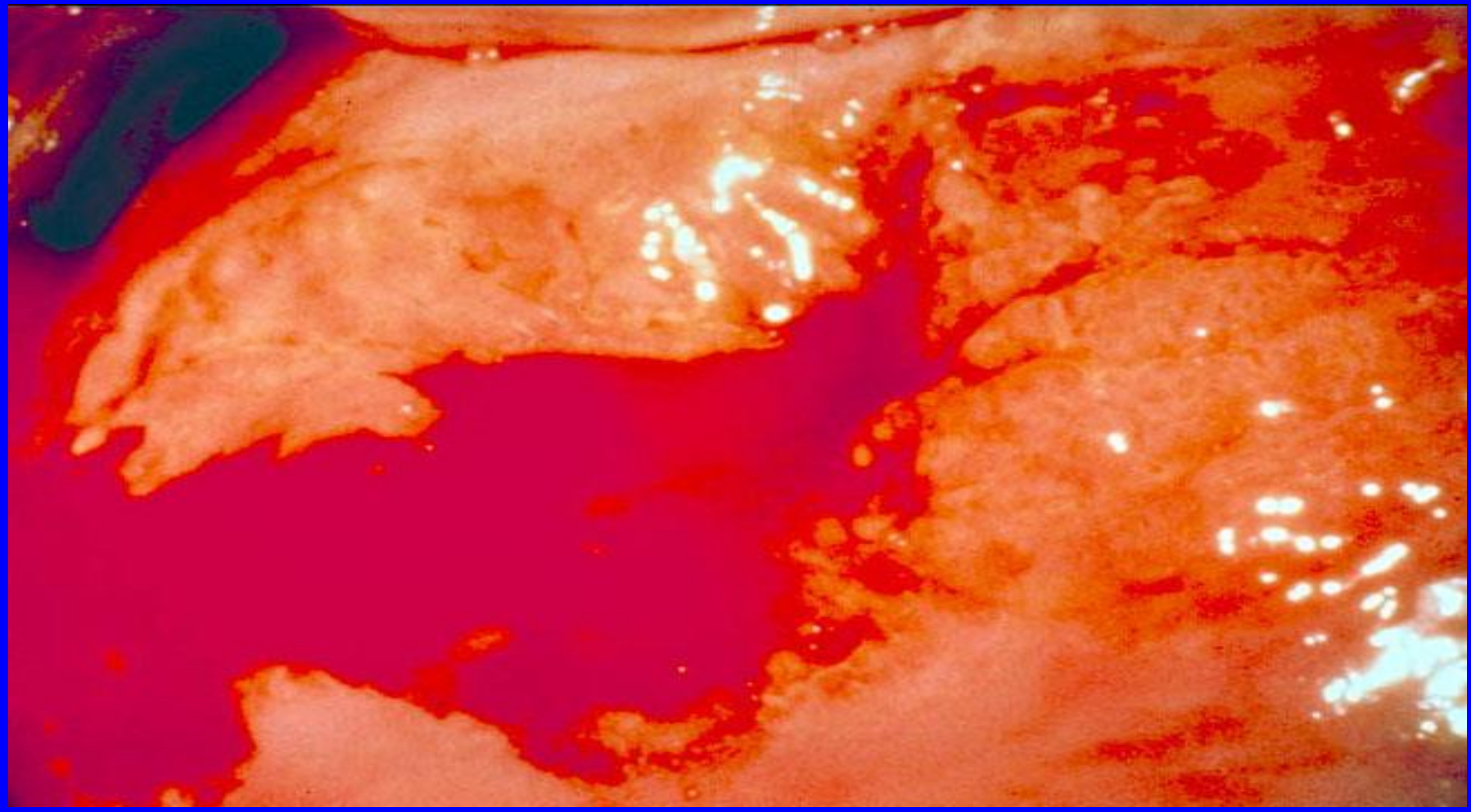


Keratoderma Blenorrhagica

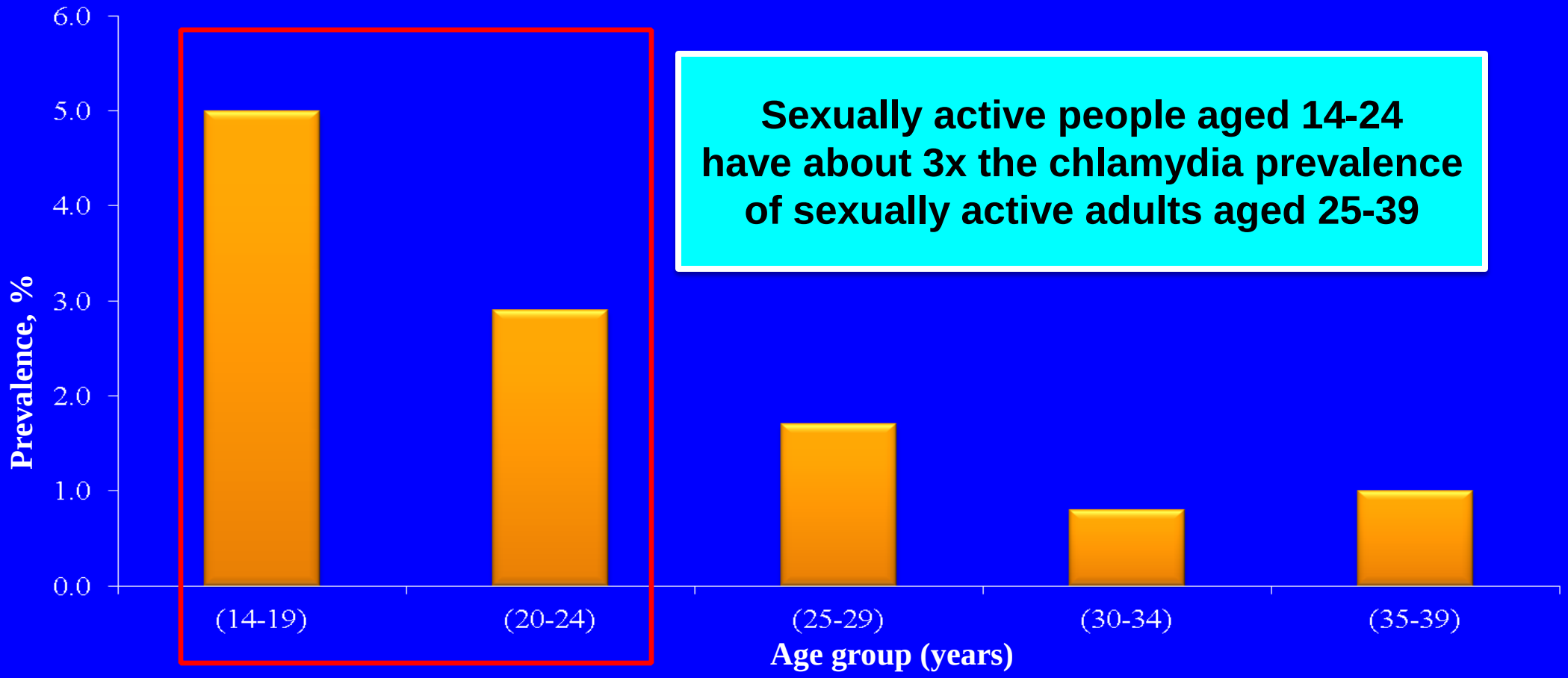
Cervicitis

- Frequently asymptomatic
  - purulent or mucopurulent endocervical exudate
  - easily induced endocervical bleeding
- Etiology: chlamydia, gonorrhea, trichomonas, herpes, bacterial vaginosis (BV)
- Dx: nucleic acid amplification test (gonorrhea, chlamydia, trichomoniasis) , wet mount/culture (Trichomonas, BV)
- Presumptive therapy:
  - azithromycin 1gm PO once OR
  - doxycycline 100 mg PO bid for 7d

Easily induced endocervical bleeding



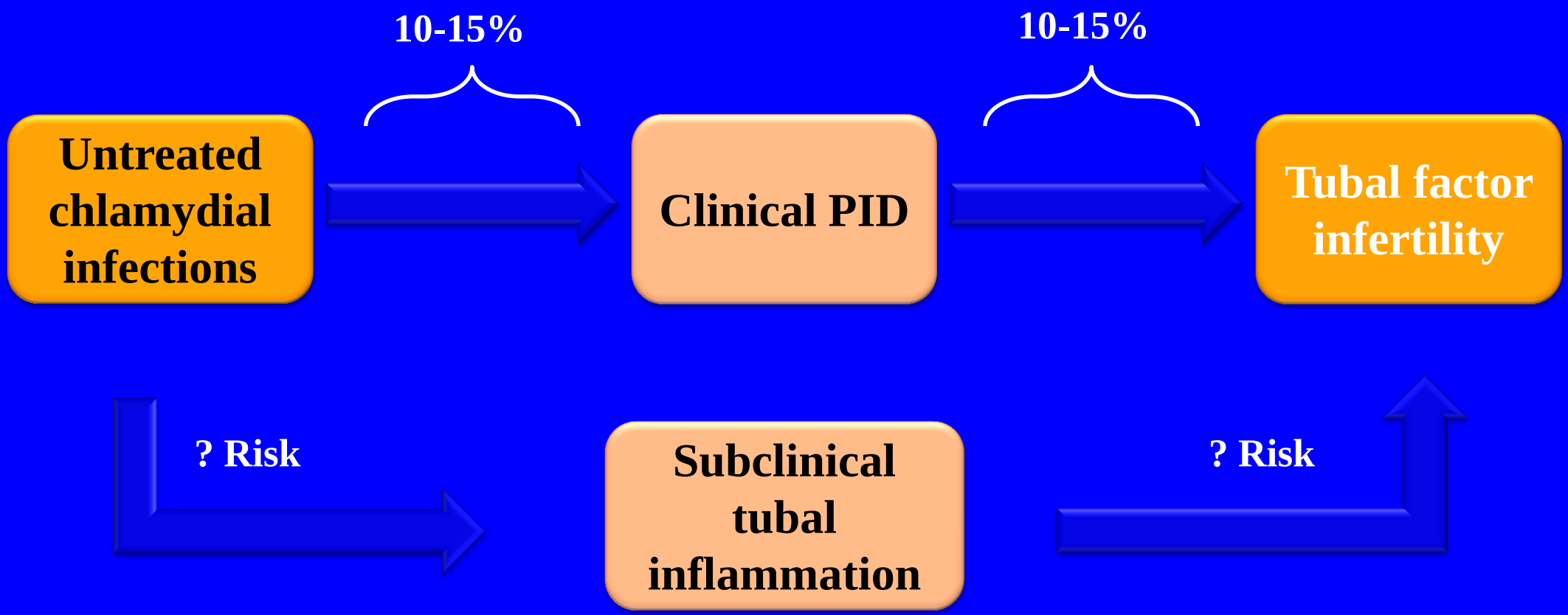
Burden of Infection Highest, Sexually Active Adolescents and Young Adults



Sexually active people aged 14-24 have about 3x the chlamydia prevalence of sexually active adults aged 25-39

NHANES, National Health and Nutrition Examination Survey, 1999-2008
Sexual activity ="yes" response to "Have you ever had sex?"
Sex = vaginal, anal, or oral sex

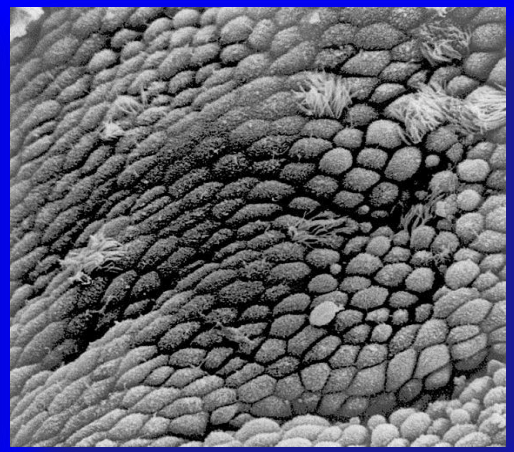
Risk for Sequelae in Women



Long-term Reproductive Complications

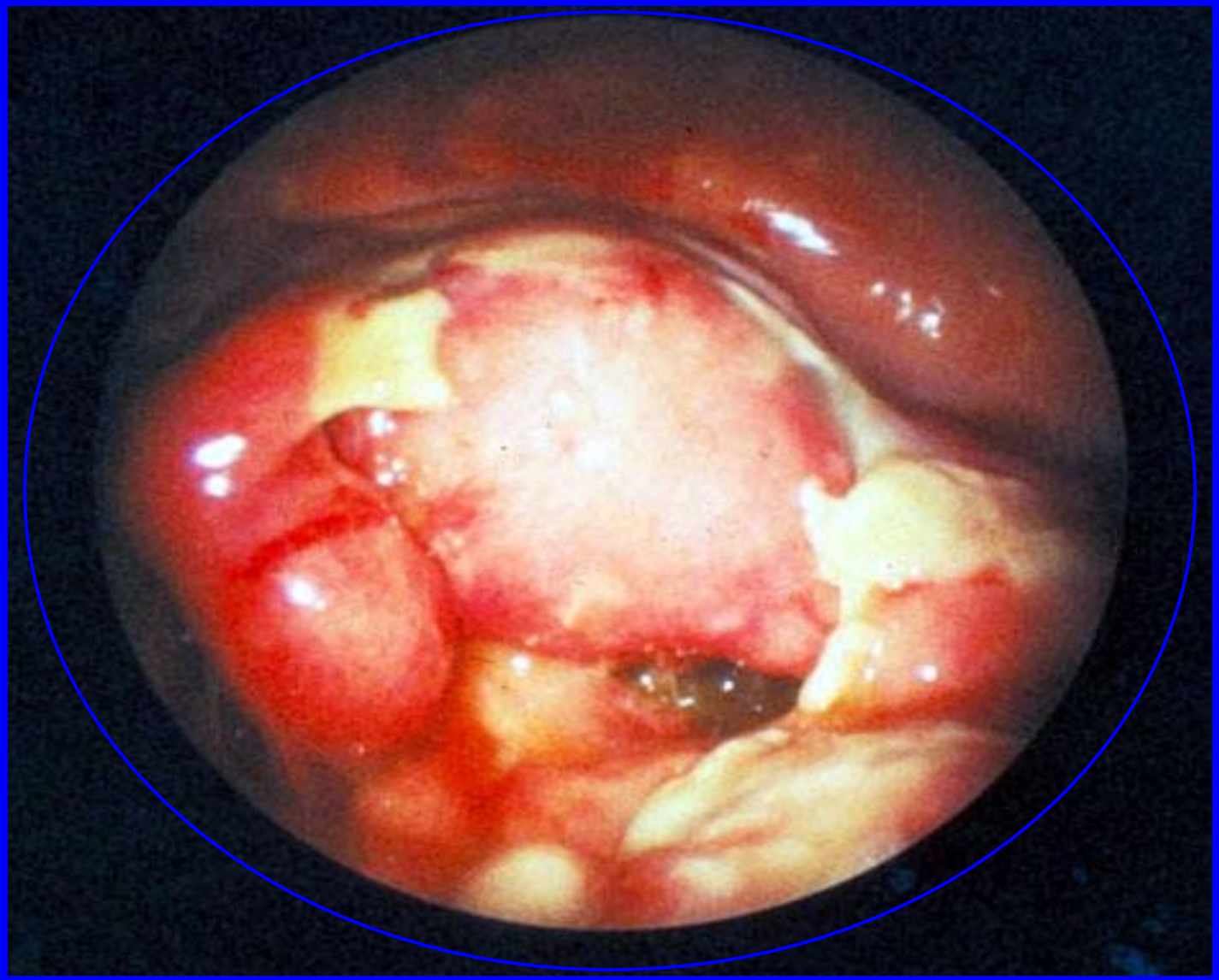
- Tubal inflammation can result in scarring, loss of function
- Long-term sequelae
  - Tubal factor infertility
  - Ectopic pregnancy
  - Chronic pelvic pain
- Tubal factor infertility

Normal tubal tissue, 1200x



Post-PID, 1200x

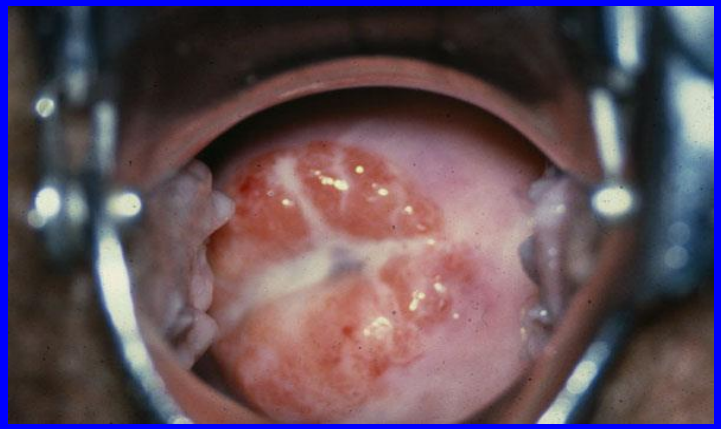
Chlamydia is the leading preventable cause of tubal factor infertility

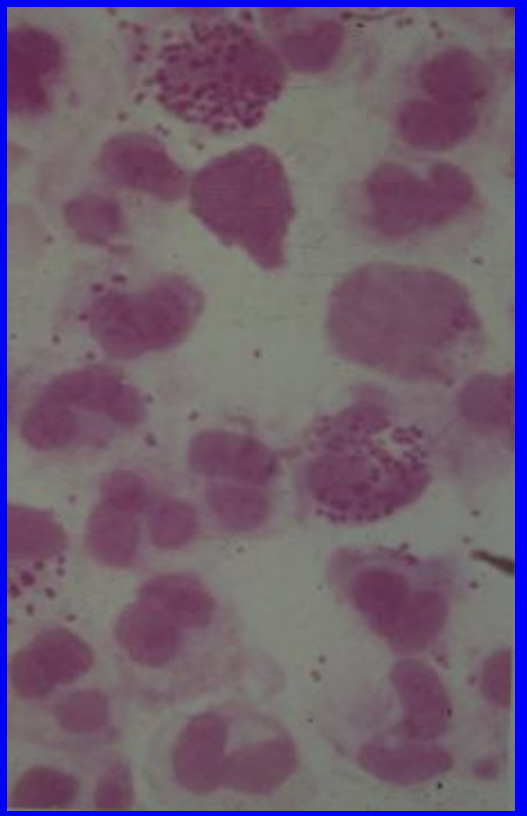


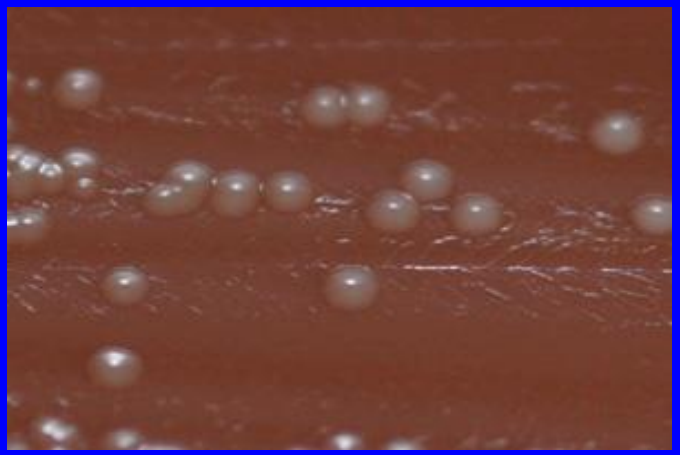
Chlamydia Screening

- Detect and prevent complications in women
  - Sexually active women ≤25/yr; > 25 risk factors; more frequent screening (sexual risk assessment)
- Selective male screening- adolescent clinics, corrections, national job training program, < 30 yrs, previous STI, military
- Retest women/men 3 mo post therapy
  - Third trimester of pregnancy

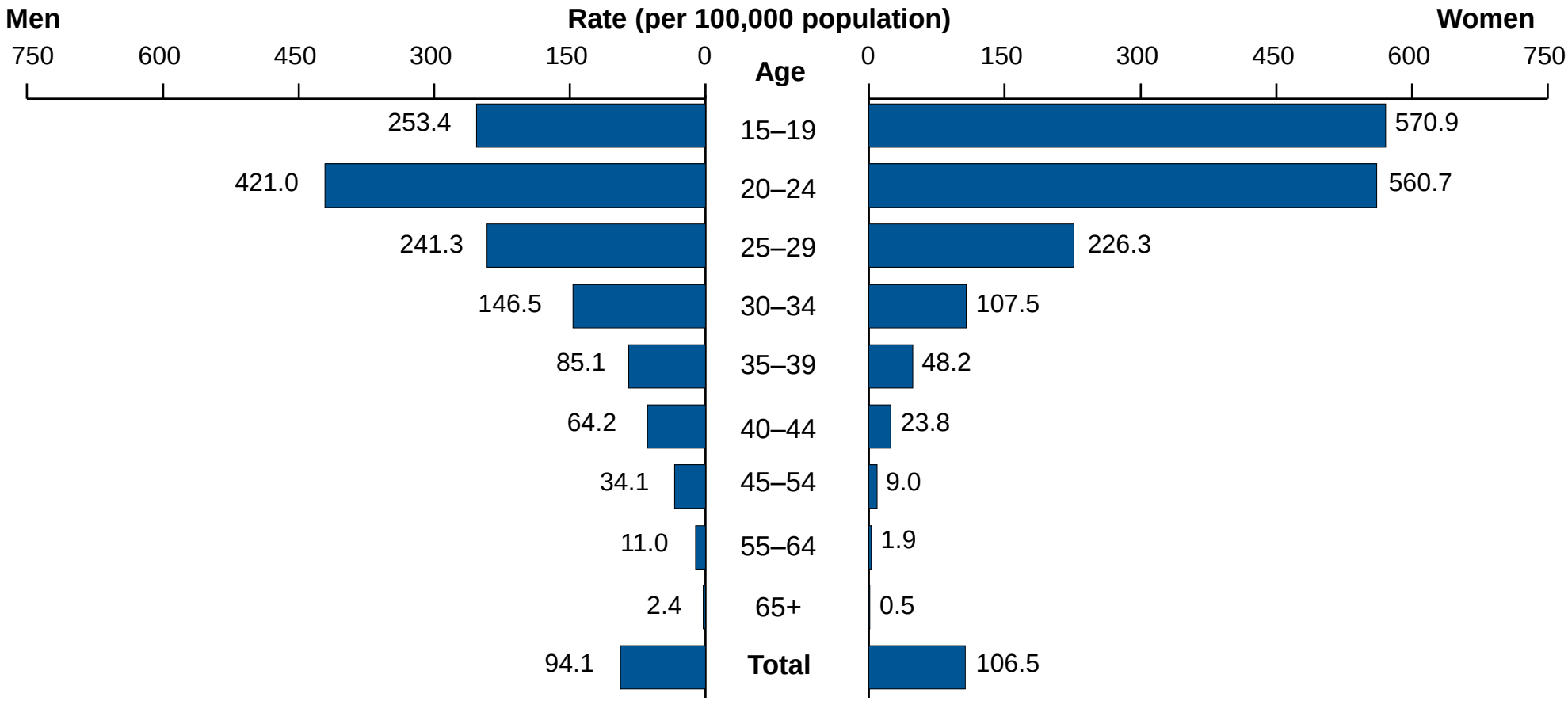
Gonorrhea: Mucosal and Systemic Disease







Gonorrhea—Rates by Age and Sex, United States, 2010



Gonorrhea

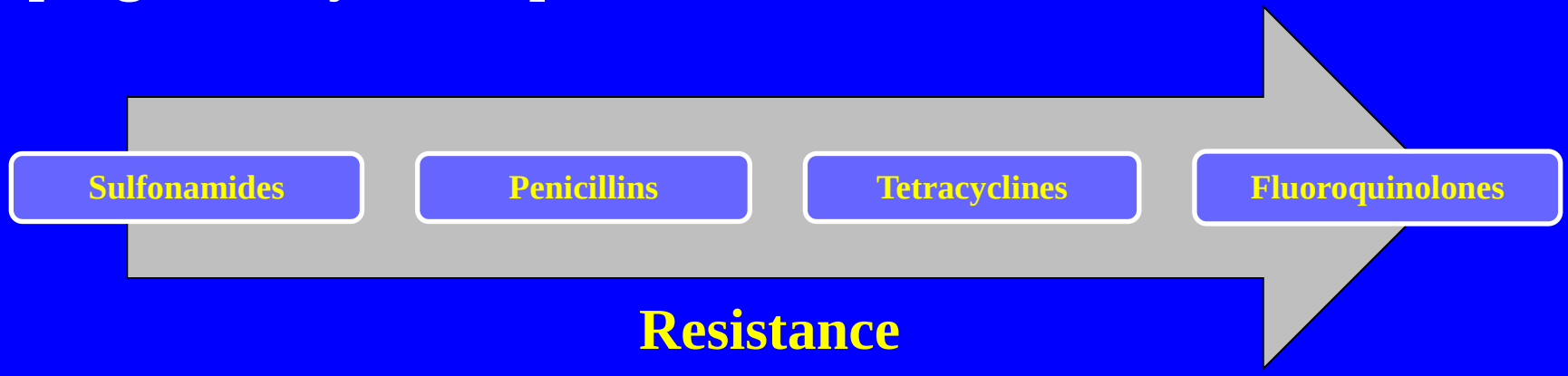
- Screen sexually active women at increased risk (USPSTF)
  - <25 years
  - Previous GC or other STDs
  - Commercial sex work
  - New or multiple partners
  - Inconsistent condom use
  - Drug use
- No screening in men or women at low risk of infection
- Nucleic acid amplification tests
  -vaginal swabs (women), urine (men); rectal/pharyngeal sites (MSM)
  -asymptomatic infection
- Retest women/men 3 mo after treatment

Neisseria gonorrhoeae
Antibiotic Resistance

Antibiotic resistance

- Undermines treatment success
- Heightens risk of complications
- Facilitates transmission

***Neisseria gonorrhoeae* (NG) has demonstrated ability to progressively develop antibiotic resistance**

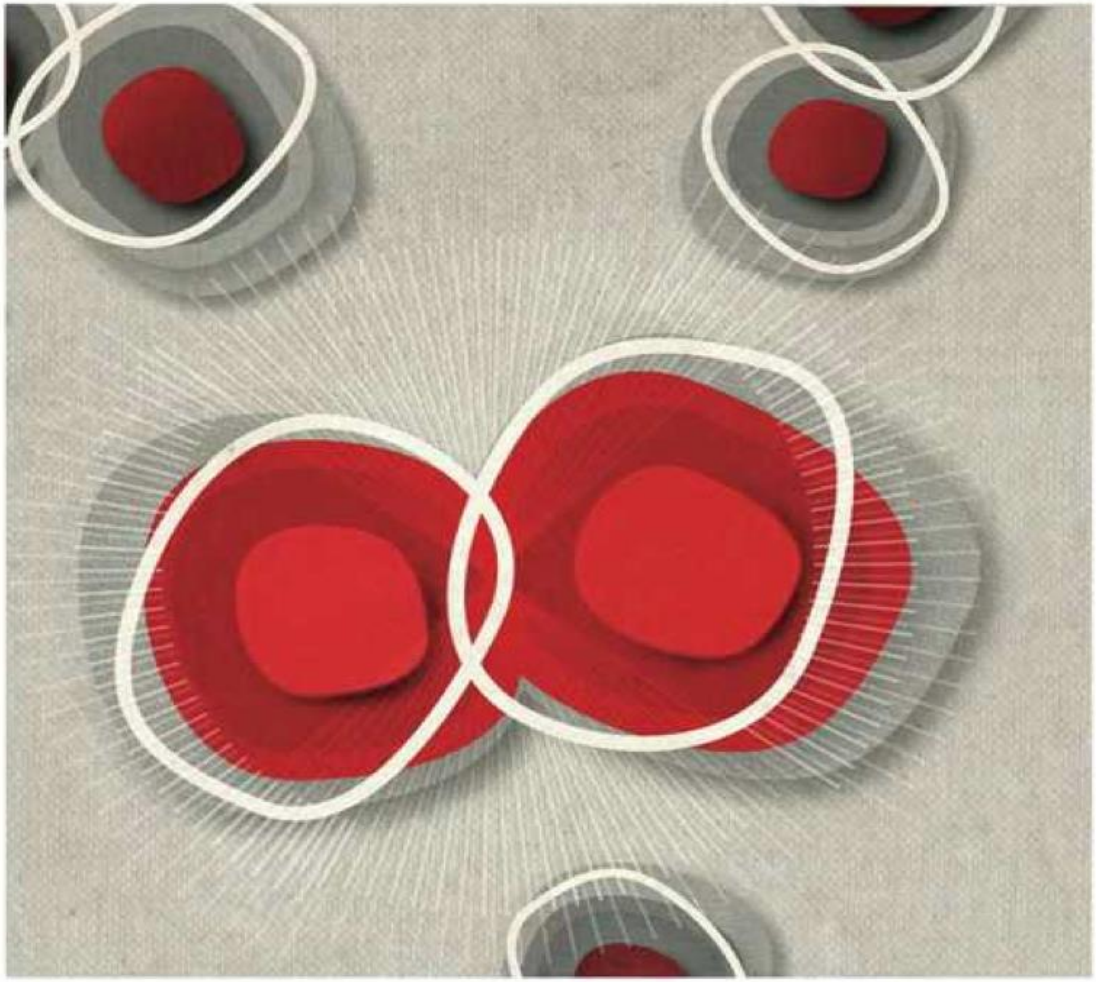


MEDICAL DISPATCHES

SEX AND THE SUPERBUG

The rise of drug-resistant gonorrhea.

BY JEROME GROOPMAN

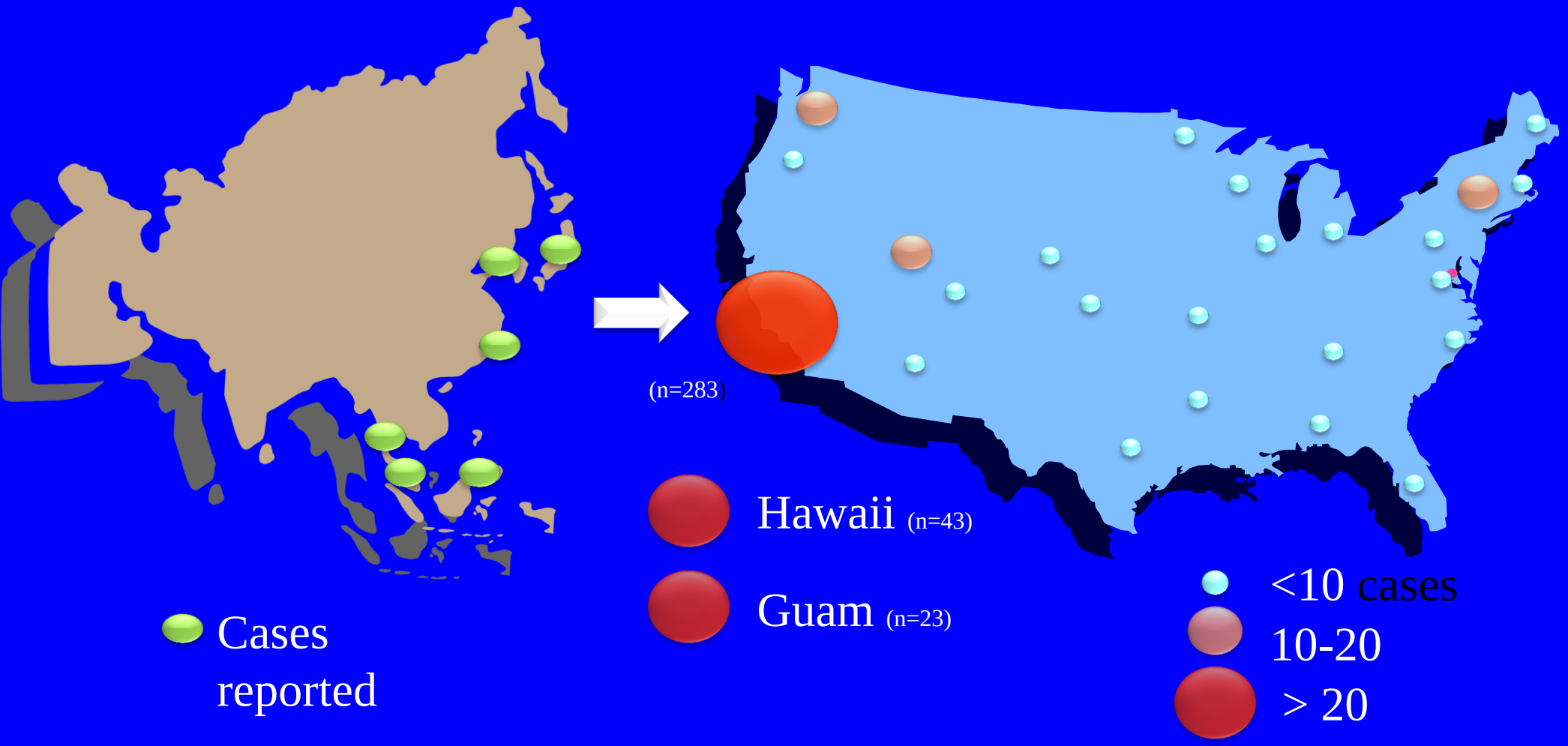


Gonorrhea mutates in the pharynx, making oral sex far more risky than people think.

The New Yorker, October 1, 2012

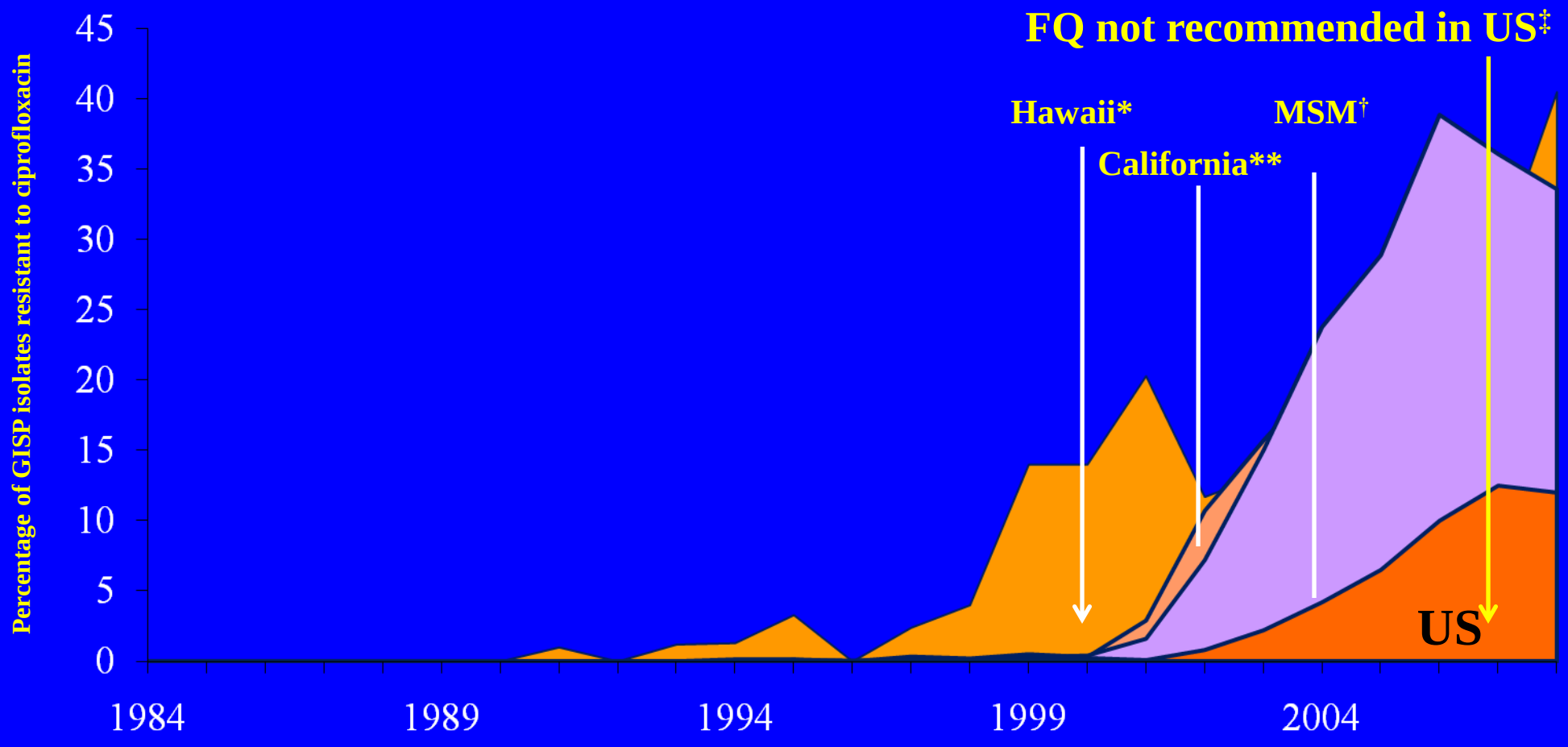
"Whatever freedoms were won during the sexual revolution, bacterial evolution promises soon to constrain."

Global Transmission of NG Resistance: Distribution of Reported PPNG Cases,1976–1979



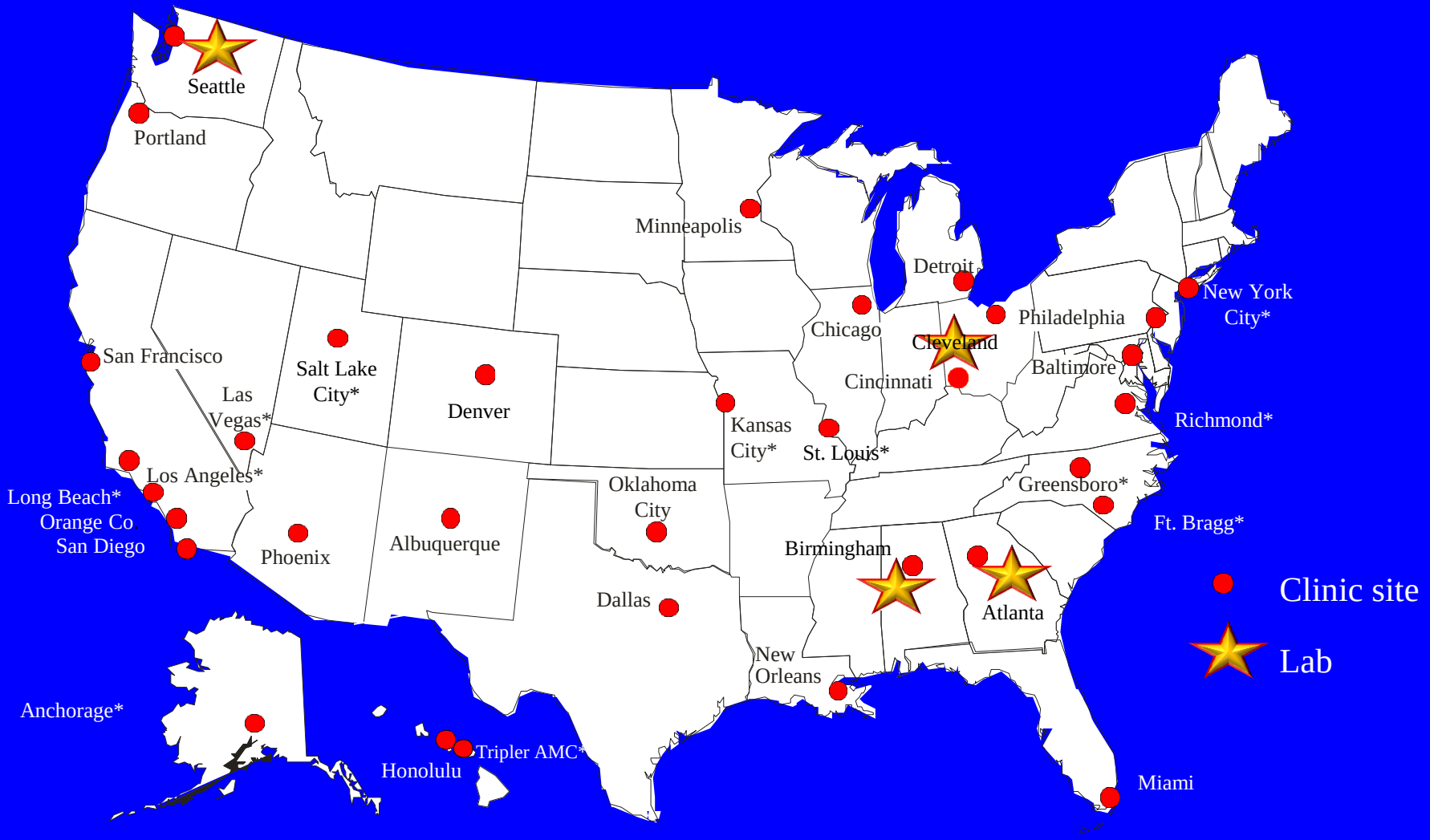
Perine et al, 1979

Emergence of Fluoroquinolone-resistant *N. gonorrhoeae* (QRNG), United States



* CDC, MMWR 2000; ** CDC, MMWR, 2002; † CDC, MMWR, 2004.; ‡ CDC, MMWR, 2007.

GISP Sentinel Surveillance



1986- present

International Emergence of *N. gonorrhoeae* with Decreased Susceptibility to Cephalosporins

Case reports of oral cephalosporin treatment failures

East Asia and Western Pacific, 2000-present

Europe, 2010-present

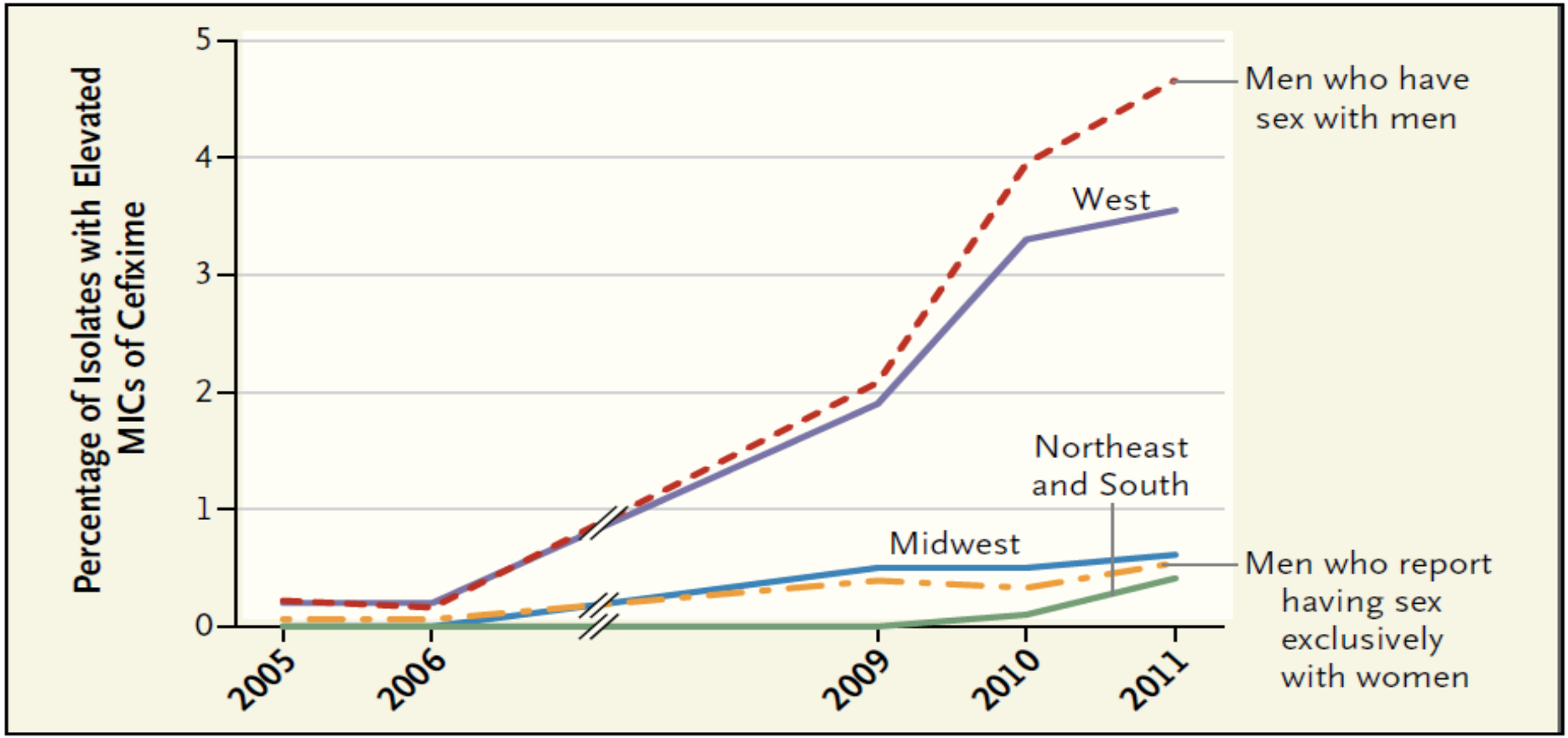
Increasing proportion of isolates with laboratory evidence of decreased susceptibility

Elevated Minimum Inhibitory Concentrations

Extended Spectrum Cephalosporin Resistance

H014 –Japanese CSW pharynx isolate with ceftriaxone MIC 2-4 (Ohnishi 2011)

F89- French MSM urethra isolate with cefixime MIC 4, ceftriaxone 1-2 (Unemo 2012)



Percentage of Isolates in Which Minimal Inhibitory Concentrations (MICs) of Cefixime Were 0.25 μg per Milliliter or Higher, 2005–2011.

Susceptibility to cefixime was not tested in 2007 or 2008. From the Gonococcal Isolate Surveillance Project.

Bolan GA . N Engl J Med. 2012 Feb 9;366(6): 485-7.

Anogenital GC Treatment

- Dual therapy
  - Ceftriaxone 250 mg IM
    - PLUS azithromycin 1 gm (preferred) or doxy 100 mg bid x 7
- Alternatives (test of cure)
  - Cefixime 400 mg PO
    - PLUS azithromycin 1 gm or doxy100 mg bid x 7
  - Azithromycin 2 g (pen allergy)
- Treatment Failure
  - ID consult, cx/susceptability, ceftriaxone 250 mg IM + 2 gm azi, test of cure at one wk, report!

Disseminated GC

- 1-3% with mucosal infection (culture of cervix, urethra, and rectum)
- Monoarticular septic arthritis
- Tenosynovitis/dermatitis
- Complement deficiency (C5-C8)

Chancroid (soft chancre)

- Causative agent is *Haemophilus ducreyi*
- Tender papule with erythema, becomes pustular then ulcerated
- Ulcers: **painful**, nonindurated, erythematous halo; single (men) or multiple (women)
- Tender regional LN +/- suppuration (50%)

Chancroidal Buboes

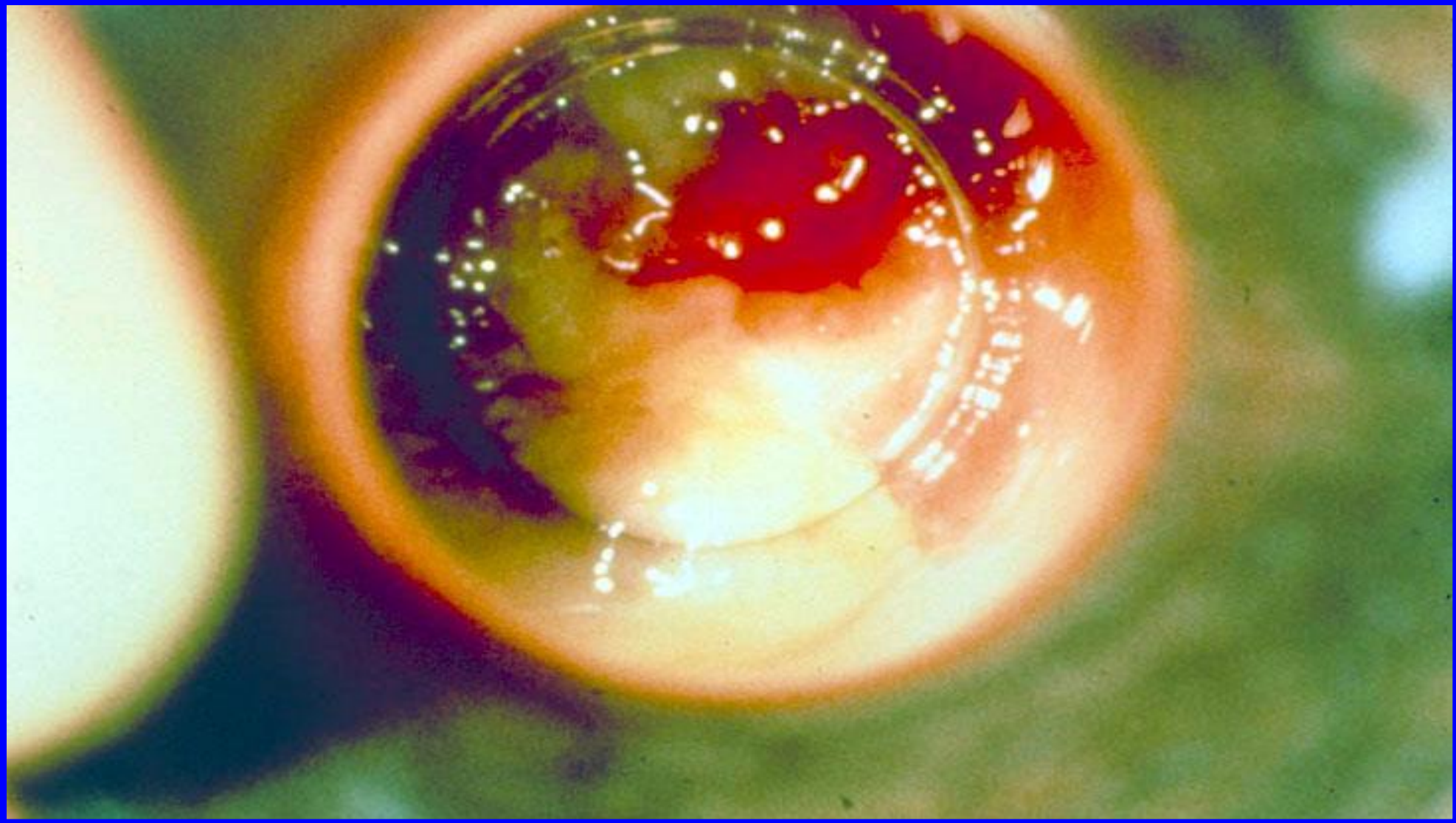
Chancroid: Diagnosis

- Painful genital ulcer & tender inguinal adenopathy
- Definitive - *H. ducreyi (*special culture media)
- Probable- painful genital ulcers, regional adenopathy, -herpes culture, -syphilis serology
- Nucleic acid amplification testing improves sensitivity

Chancroid: Treatment

- Azithromycin 1gm PO once
- Ceftriaxone 250mg IM once
- Ciprofloxacin 500mg bid for 3 days
- Erythromycin base 500mg tid for 7 days
- Treatment response may be delayed in HIV+

44 yo HIV+ man with rectal pain and bleeding

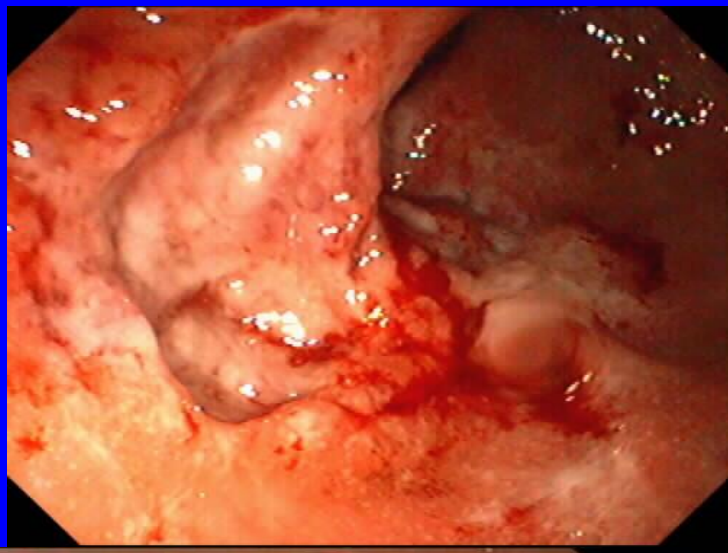


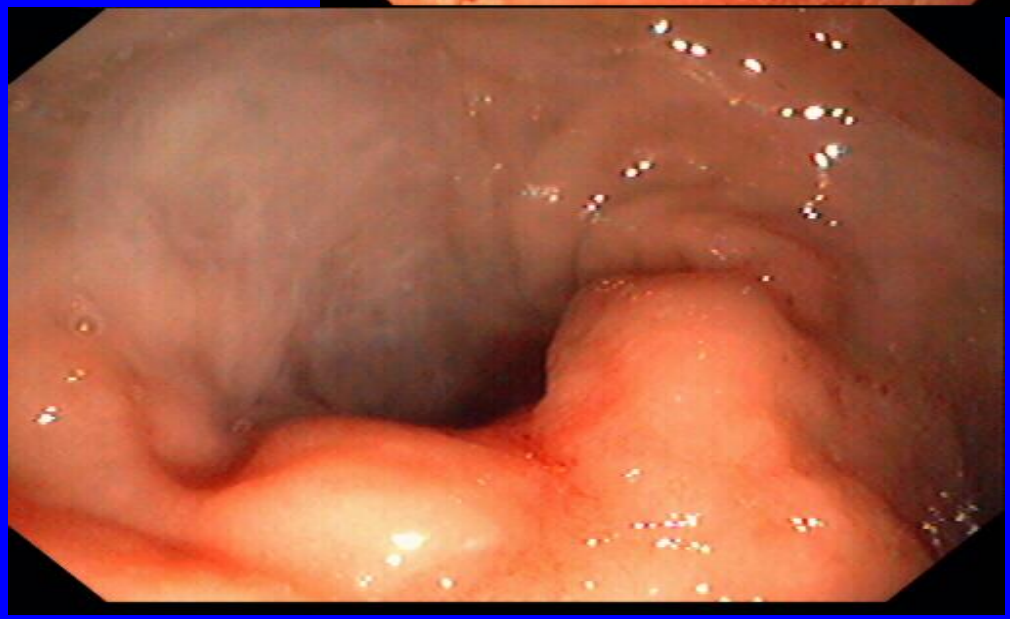
Sexually Transmitted GI Syndromes

- Proctitis
  - GC, CT, HSV, syphilis
- Proctocolitis
  - Camplyobacter, shigella, salmonella, *Entamoeba histolytica*, LGV
- Enteritis
  - Giardia
- Hepatitis A, B, C

LGV Proctitis

- CT serovar L2
- MSM or women with rectal IC
- Rectal ulcers or lesions
- Mucoid anal discharge
- Rectal bleeding
- Doxycycline 100 mg bid x 21 d





LGV inguinal syndrome

- Caused by *C.trachomatis* serovars L1, L2, or L3
- Herpetiform genital ulcers and/or papules
- Tender, fluctuant, inguinal lymphadenopathy (buboes)

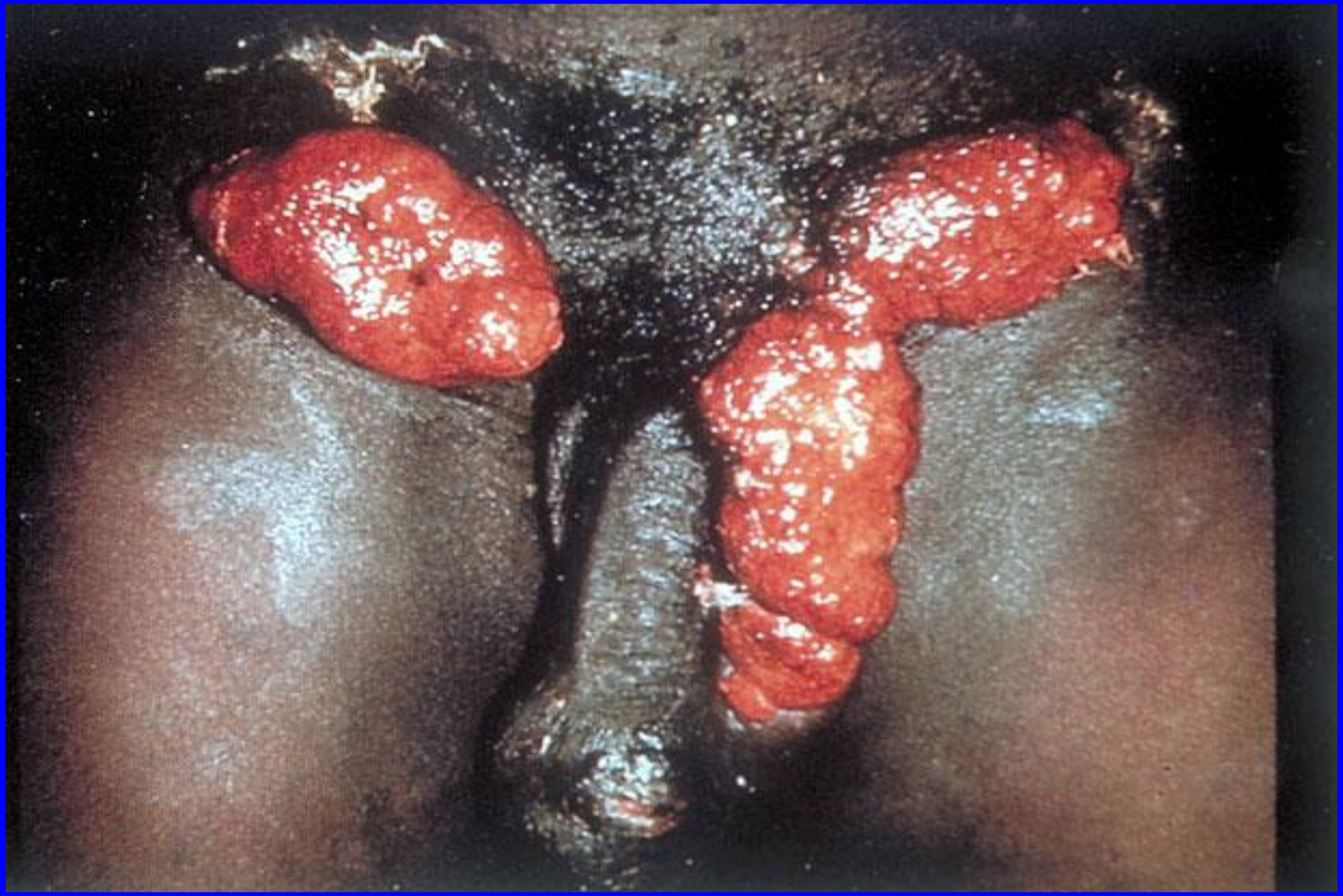
Genital Ulcer

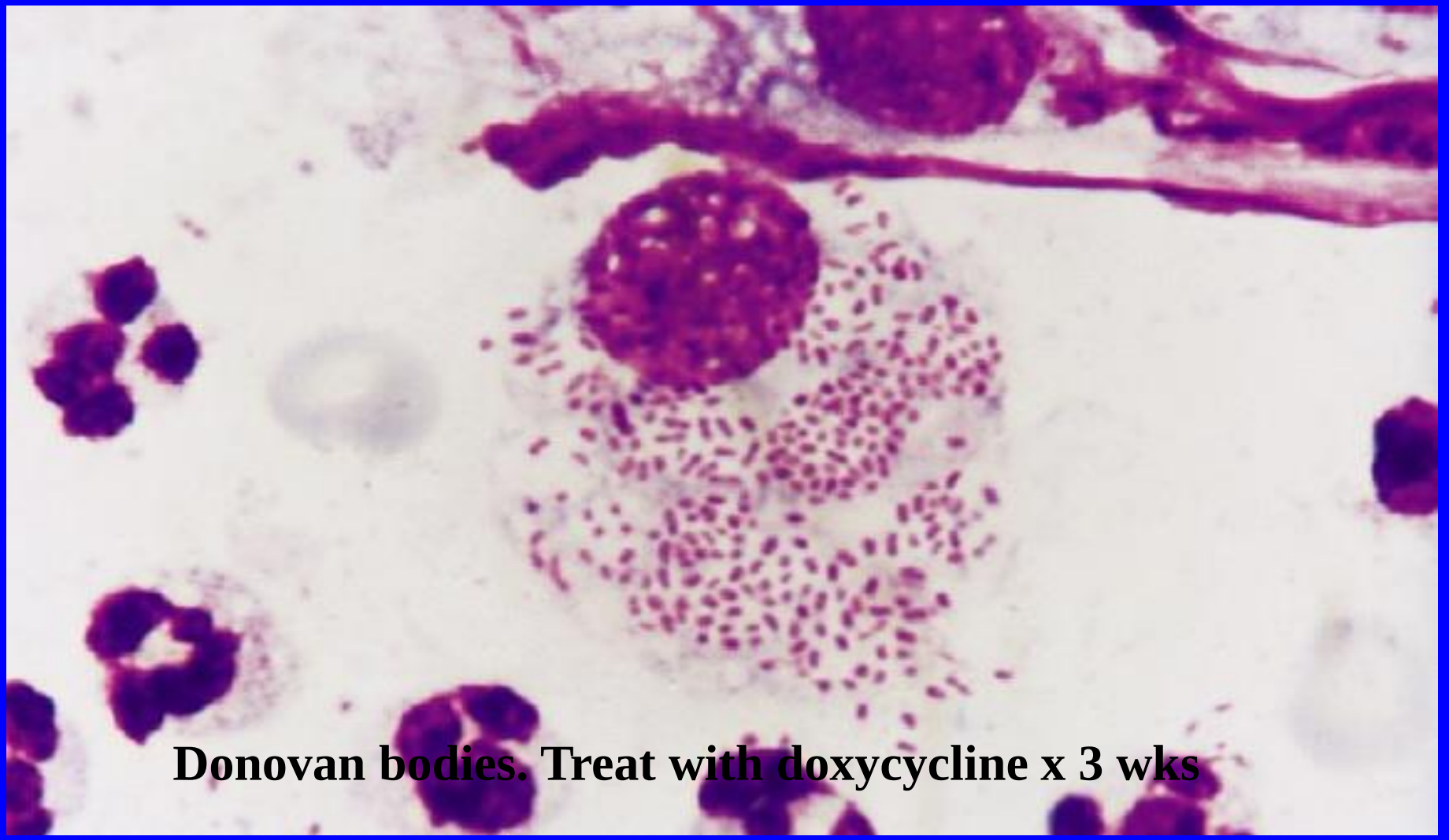
Buboes

Ulcerated bubo

Granuloma inguinale (Donovanosis)

- *Klebsiella granulomatis* (formerly *Calymmatobacterium ganulomatis*)
- India, the Caribbean, Papua New Guinea, & south Africa. Rare in USA
- Small **painless** papule – to form beefy-red granulomatous ulcer that bleeds easily
- Can spread subcutaneously. Elephantiasis of the external genitalia may occur



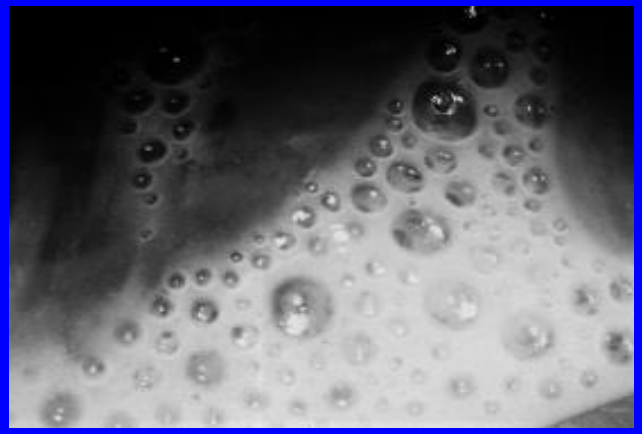


Donovan bodies. Treat with doxycycline x 3 wks


33 yo woman presents with
malodorous, vaginal discharge.
Trichomoniasis on wet mount.

Trichomoniasis

- Vagina, urethra, endocervix
- Sx- vaginal discharge, itching, odor, dysuria
- Elevated vaginal pH, amines
- Frothy discharge and strawberry cervix
- Men- NGU, symptomatic, chronic prostatitis



Trichomonas and Risk for HIV

	RR	P value
HIV Infected PN		
Plasma HIV copies.ml	2.89	<0.001
Condom Use in F/U	0.22	<0.001
HIV Uninfected PN		
Age, per 5 yr	0.82	0.006
HSV-2 + enrollment	2.14	0.012
GUD	2.65	0.004
Trichomonas	2.57	0.002
Cervicitis/vaginitis	3.63	0.005
Circumcision	0.53	0.37

Hughes et al. Determinants per-coital act HIV infectivity in African serodiscordant couples JID 2012;205:358-365. 86 transmissions; MTF 0.0019; FTM 0.0010

NAAT for Trich

- APTIMA TMA (Gen-Probe) (ATV)

	Sensitivity	Specificity
Wet mount	55	100
Culture	75	100
ATV vaginal swab	97	100
ATV cervical swab	90	100
ATV urine	88	100

Nye, AJOG 2009

Comparison of APTIMA *Trichomonas vaginalis* transcription-mediated amplification to wet mount microscopy, culture, and polymerase chain reaction for diagnosis of trichomoniasis in men and women

Melinda B. Nye, PhD; Jane R. Schwebke, MD; Barbara A. Body, PhD

Trichomoniasis – HIV

- Common STI among HIV+ women 10-30% (Magnus 2003, Niccolai 2000)- test at entry into care (in pouch, NAAT)
- Increased HIV vaginal shedding (Sorvillo 2201, John 2001, Tuomala 2003)
- Treatment reduces HIV vaginal shedding (Kissinger 2009, Wang 2001)
- Repeat infection higher
  - 13-36% HIV+ vs 7-8% HIV- (Kissinger 2008, Van der Pol 2005, Das 2005, Kissinger 2010)

Trichomoniasis Treatment

- ***Recommended Regimens***
  - Metronidazole 2 g orally in a single dose
  - Tinidazole 2 g orally in a single dose
- ***Alternative Regimen***
  - Metronidazole 500 mg orally twice a day for 7 days
- Studies supporting recommendations in HIV-

MTZ 2 gm vs Multidose Regimen

- HIV + women- routine pelvic exam (culture)
  - 16.9% + (n=480); 65% ARV
- Tx arms similar (age, cd4, race, VL, ARV, LTFU)
- PDPT to sexual partners; sexual exposure (ACASI)
- Repeat TV
  - TOC - 2gm (16.8%) vs multi (8.5%)
  - 3 mo – 2gm (24.1%) vs multi (11%)

Kissinger, AIDS 2010

BV influences response to *T. vaginalis* treatment in HIV-infected women

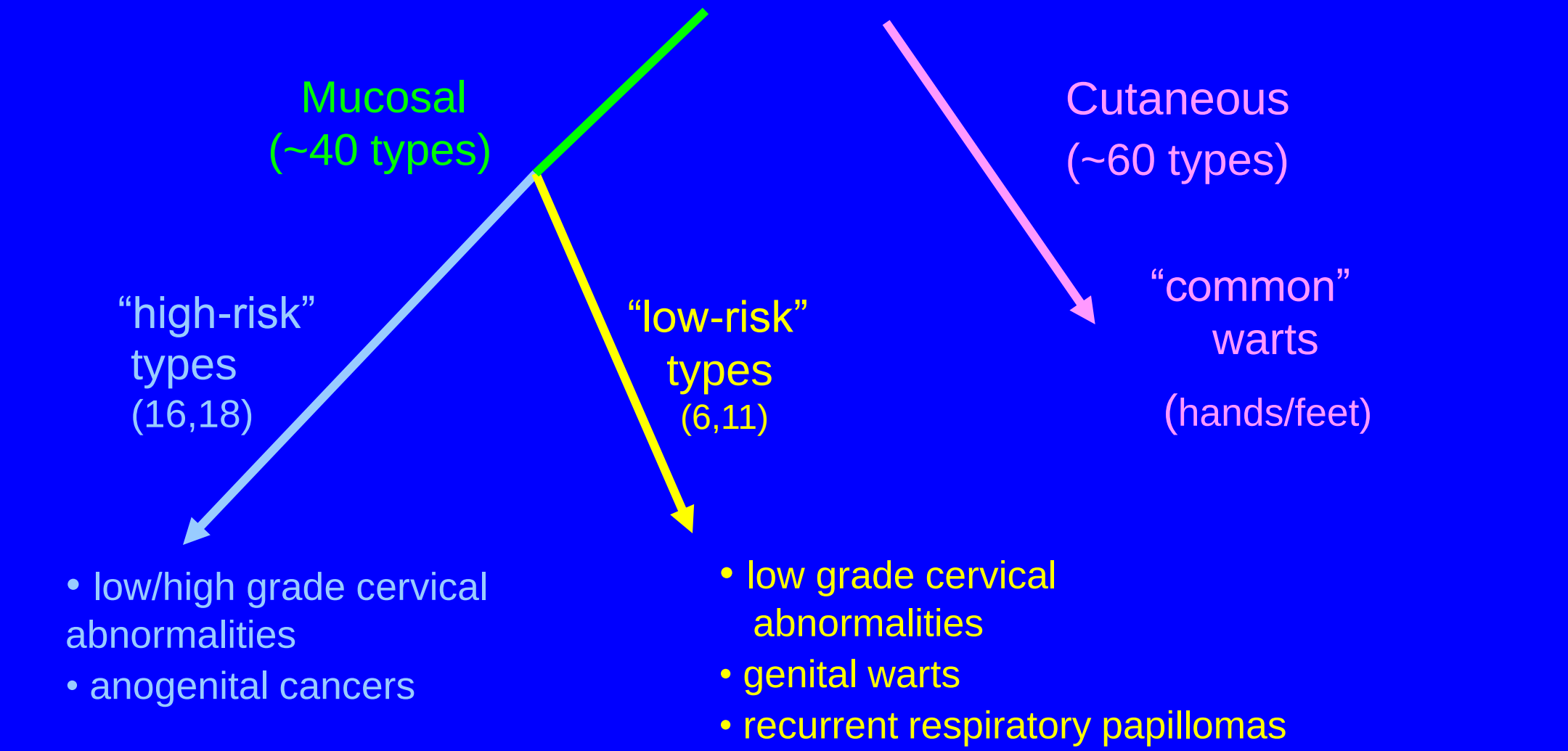
Gatski *et al.* STI 2011

- HIV+ women with BV were more likely to have *T. vaginalis* at test of cure RR 2.42 (95% CI 0.96, 6.07)
- Association between BV and trichomoniasis treatment response was seen in the single-dose arm only

HPV-Associated Disease in Males and Females

HPV-associated Disease	Males	Females
Genital precancers and cancers	penile, anal	cervical, vaginal, vulvar, anal
Oropharyngeal cancers	X	X
Recurrent respiratory papillomatosis	X	X
Anogenital warts	X	X

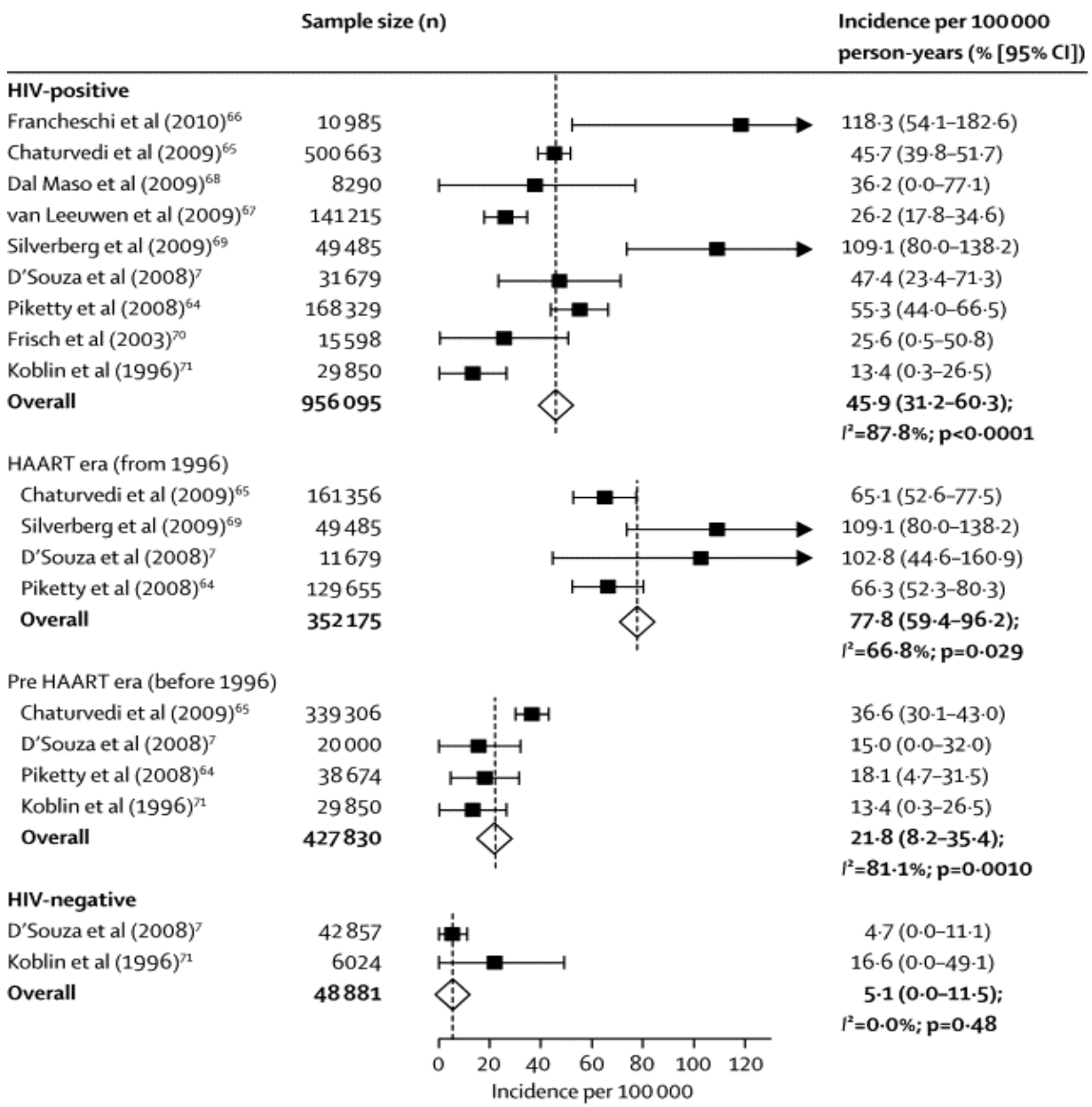
>100 HPV types



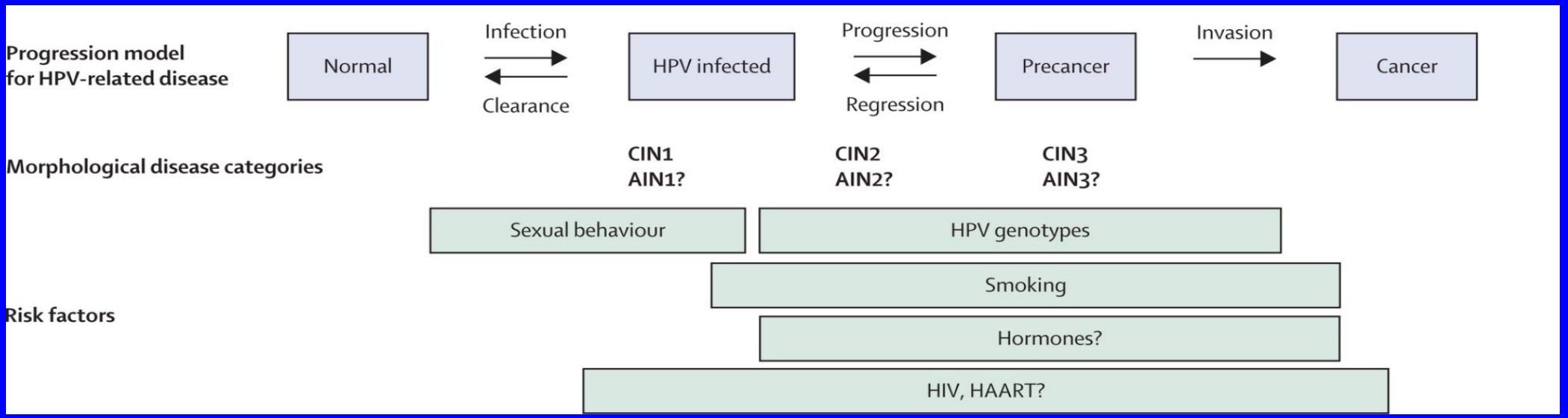
HPV/Genital Warts

- Counseling messages
  - Transmission –genital and oral (Dunne, CID 2011)
- HPV testing not recommended
  - Vaccinate or STI screen
- Genital warts treatment
  - Sinecatechins ointment (15%)
  - Vitiligo side effect of imiquimod
- Imiquimod cream for precancerous anal lesions (Fox, AIDS 2010)

Incidence of anal cancer in men who have sex with men, by HIV status



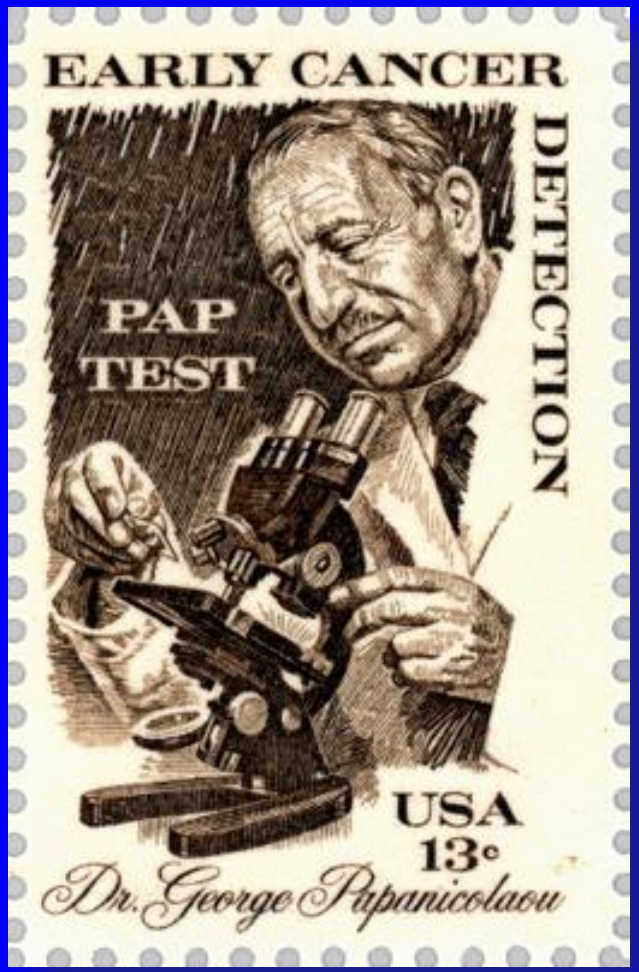
Summary



- Early natural history appears to be similar to cervix
- Biomarkers established for cervix also detect anal precancer
- Risk of invasion is not well understood; reports are mostly anecdotal and heterogeneous
- Systematic evaluations of treatment outcomes are needed

Screening for Anal Dysplasia and Cancer in MSM

- **CDC, HIVMA OI guidelines: *consider* anal Pap tests in MSM**
  - **Evidence is limited**
    - **Natural history**
    - **Reliability of screening methods**
    - **Safety and response to treatments**
    - **Programmatic support needed**
  - **Patients with abnormal results should be evaluated with high-resolution anoscopy (HRA)**
- **HPV DNA screening of rectum not recommended**



Human papillomavirus vaccines

	Bivalent (Cervarix)	**Quadrivalent** (Gardasil)
Manufacturer	**GlaxoSmithKline**	**Merck**
VLP Types	**16, 18**	**6, 11, 16, 18**
Schedule (IM)	**3 dose series** (0,1,6 mos)	**3 dose series** (0,2,6 mos)
Producer cells	***Baculovirus infected Trichoplusia ni* insect cell line**	***Saccharomyces cerevisiae* (yeast)**
Adjuvant	**AS04** **500 µg aluminum hydroxide** **50 µg 3-*O*-desacyl-4'- monophosphoryl lipid A**	**AAHS** **225 µg amorphous aluminum hydroxyphosphate sulfate**

HPV vaccines - efficacy trials

Females ~15-26 years

- Both vaccines: high efficacy against cervical precancers, CIN2+ (>94%)
- Quadrivalent vaccine: high efficacy against genital warts (>98%)

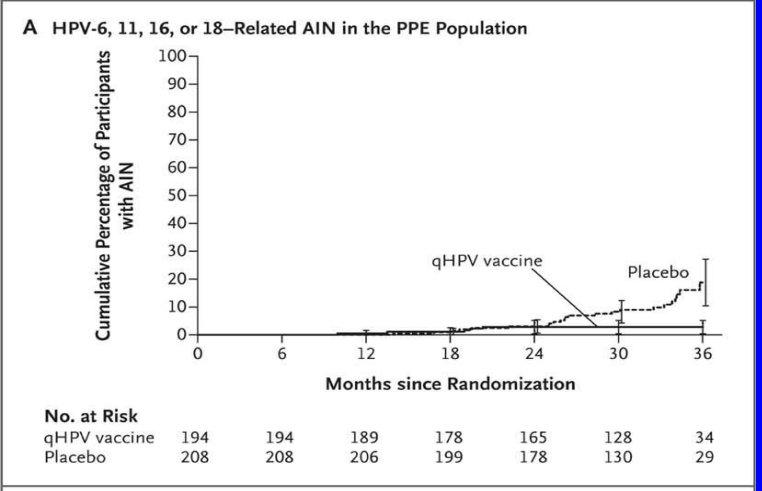
Females >25 years (mid adult women)

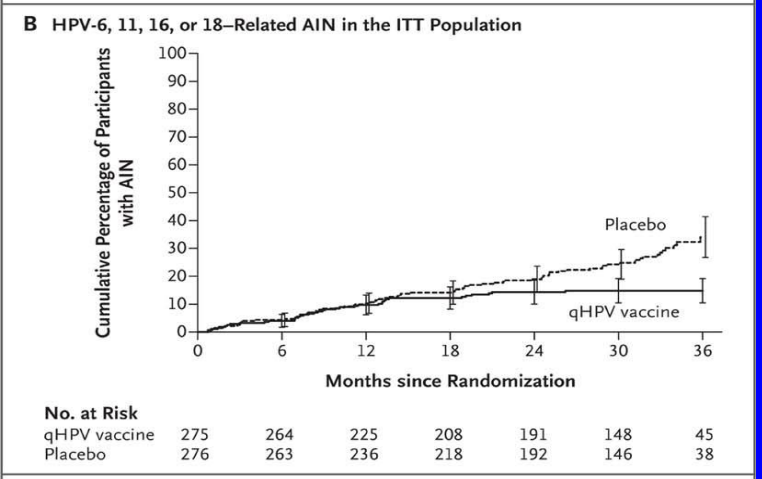
- Quadrivalent vaccine: high efficacy against infection and CIN
- Bivalent vaccine: data not yet published+

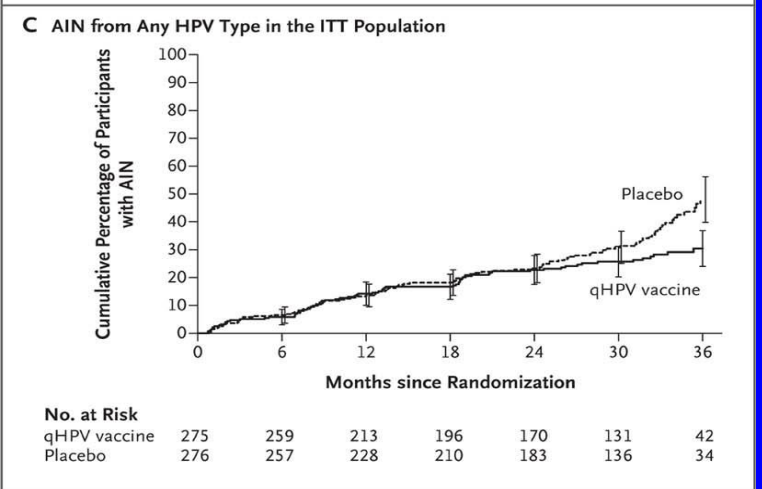
Males 16-26 years

- Quadrivalent vaccine: High efficacy against genital warts (89%) anal pre cancers, AIN2+ (75%)

Efficacy for per protocol populations; + data from bivalent vaccine in abstract only; CIN2+, cervical intraepithelial neoplasia grade 2 or higher, or adenocarcinoma in situ; AIN2+, anal intraepithelial neoplasia grade 2 or higher







HPV Immunization

- Recommended for men through 26 years of age
- Prevents AIN in MSM
- Prevents genital warts
- Safe in HIV+ (Wilkin 2010)
- Efficacy studies ongoing in HIV+

Cumulative % of Participants with HPV–Related AIN

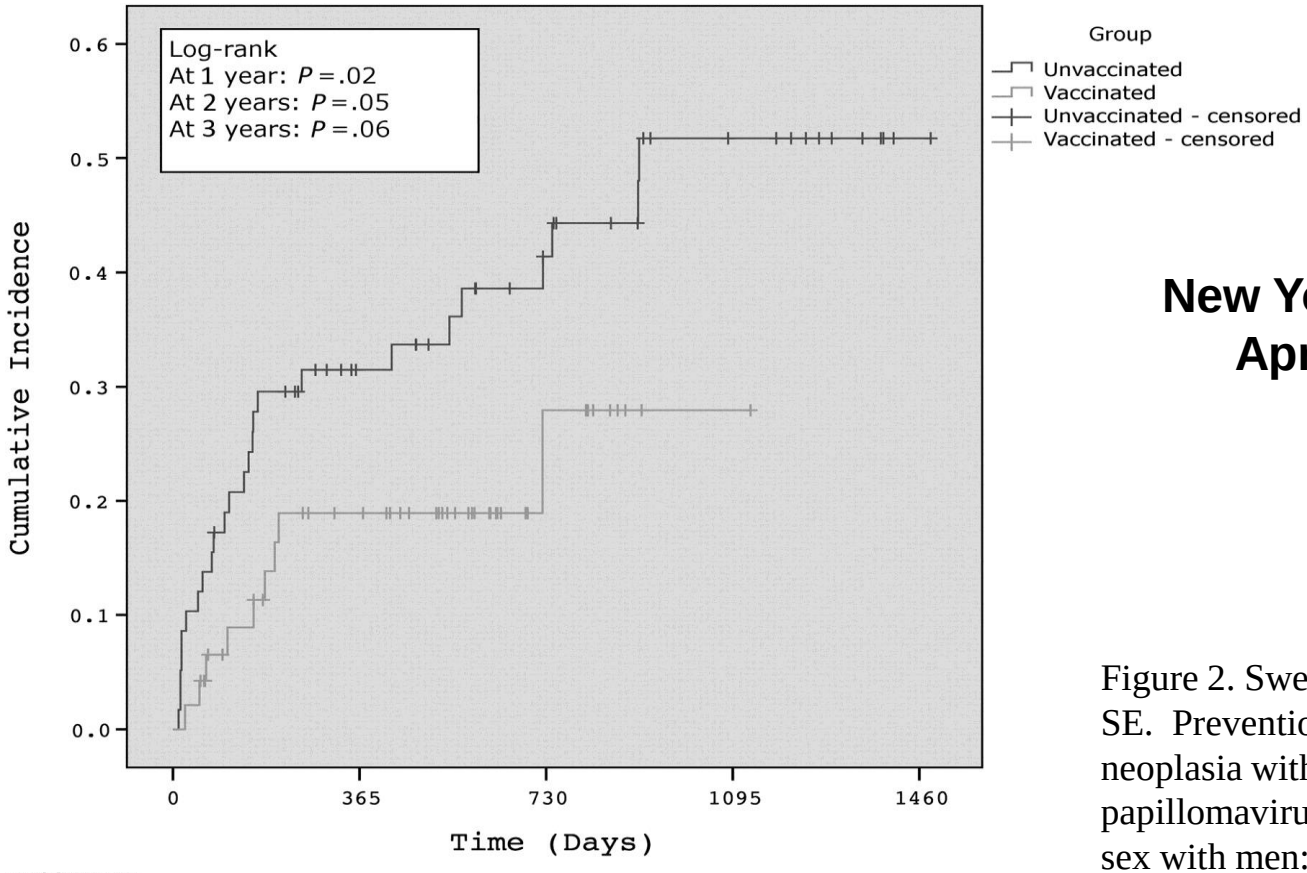
Palefsky JM et al. N Engl J Med 2011;365:1576-1585

HPV vaccine, completed trials in HIV+

Investigator/ Institution	Study Description	Population	Results
Myron Levine, et al PACTG	RCT of HPV4 compared to placebo, stratified evaluation based on immune status	Girls, Boys 7-12	6,11,16 100% 18 97%
Tim Wilkin, et al NIH	Safety and Immunogenicity of HPV4, CD4 >200 VL <200	Men >18 yrs	>98% all serotypes

~ 13 trials ongoing, most data on HPV4

Time to recurrence of high-grade anal neoplasia among vaccinated and unvaccinated oncogenic human papillomavirus–infected men who have sex with men with a history of high-grade anal neoplasia

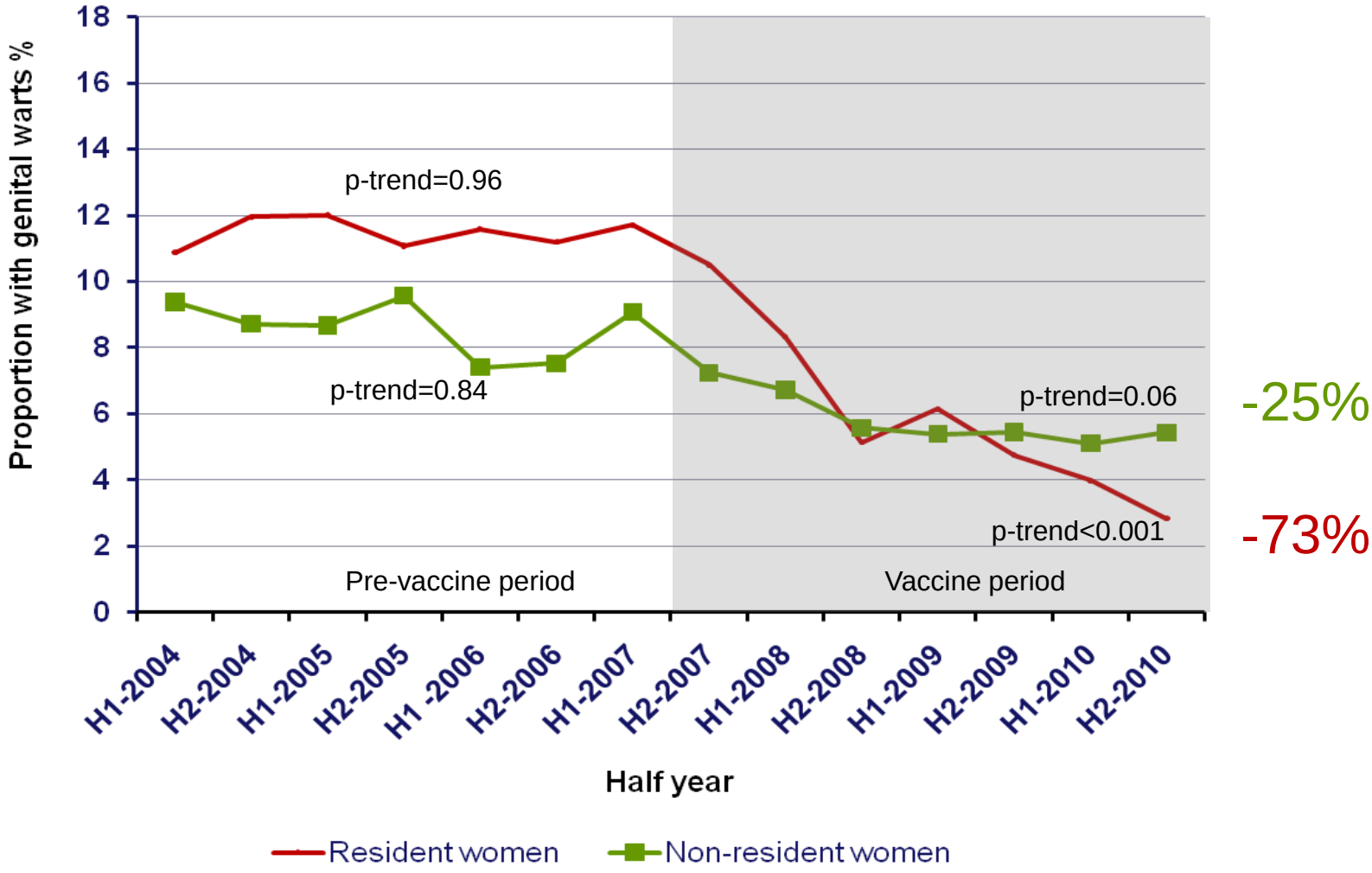


VACCINATED				
No. of cases	0	8	9	9
No. remaining	47	29	8	1
UNVACCINATED				
No. of cases	0	18	22	25
No. remaining	58	31	20	9

New York City, April 2007–April 2011 (n = 105).

Figure 2. Swedish KA, Factor SH, Goldstone SE. Prevention of recurrent high-grade anal neoplasia with quadrivalent human papillomavirus vaccination of men who have sex with men: a nonconcurrent cohort study. Clin Infect Dis. 2012 Apr; 54(7):891-8.

Proportion of eligible age women* with genital warts, by resident status, Australia, 2004-2010



* Eligible age - ≤26 years old in July 2007

Prevention Guidance

- Education/counseling to reduce risk of STI acquisition
- Detection of asymptomatic infection
- Effective diagnosis and treatment
- Evaluation, treatment, counseling of sexual partners
- Pre-exposure vaccination-hepatitis A, B, HPV

- Authoritative source
- Diagnostic evaluation, treatment regimens, prevention, vaccination strategies
- **www.cdc.gov/std**