

STDs in the HIV-infected Population

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Objectives

- **As a result of participating in this activity, participants will be able to:**
 - **Utilize the sexual history assessment to apply appropriate STD diagnostic testing strategies for HIV-infected individuals in your practice.**
 - **Consistently elicit a comprehensive sexual history and incorporate prevention messages into the context of HIV care for your patients.**

Off-Label Disclosure

- This presentation will include discussion of the following non-FDA-approved or investigational uses of products/devices:
- Oral and rectal testing for *N. gonorrhoeae* and *C. trachomatis* with:
 - Gen-Probe APTIMA Combo 2®
 - BDProbeTec™ ET
 - Roche COBAS® PCR
- Testing for *T. vaginalis* utilizing:
 - Gen-Probe APTIMA Combo 2®
 - Roche COBAS® Amplicor PCR

Sena et al. AIDS Patient Care 2008; 22(12): 955-963

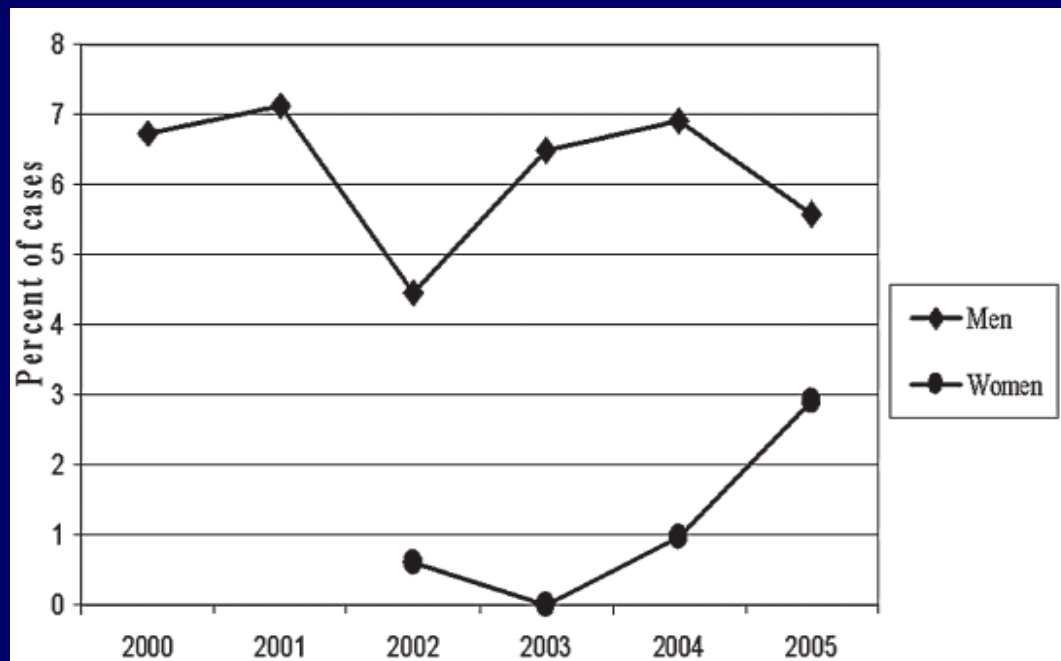


FIG. 1. Proportion of newly diagnosed HIV-positive men and women 18–30 years of age coinfected with early syphilis in North Carolina, 2000–2005.

CDC

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MMWR

Weekly

October 29, 2004 / 53(42);985-988

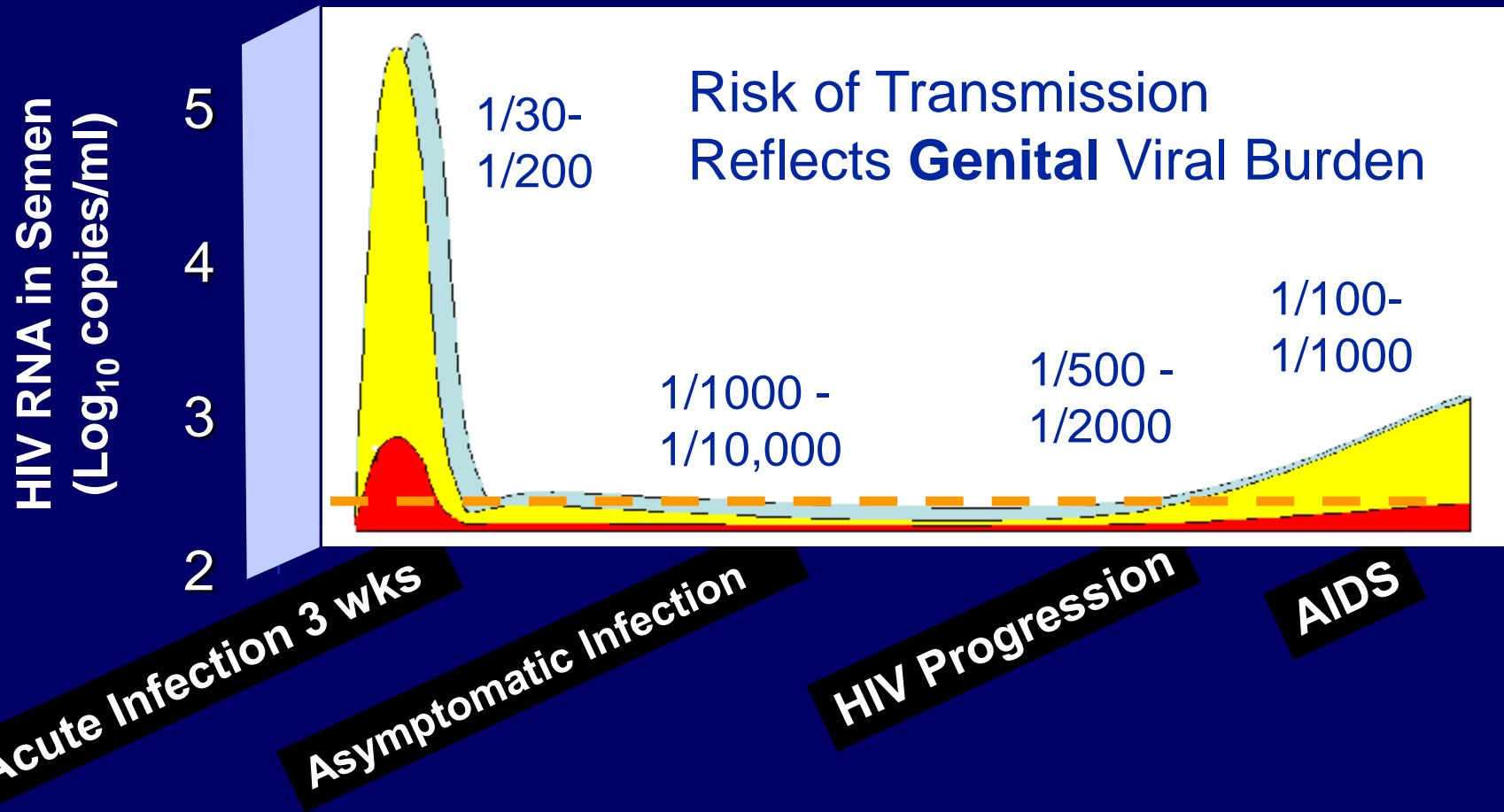
**Lymphogranuloma Venereum Among Men
Who Have Sex with Men --- Netherlands, 2003-
-2004**

STIs Facilitate HIV Transmission

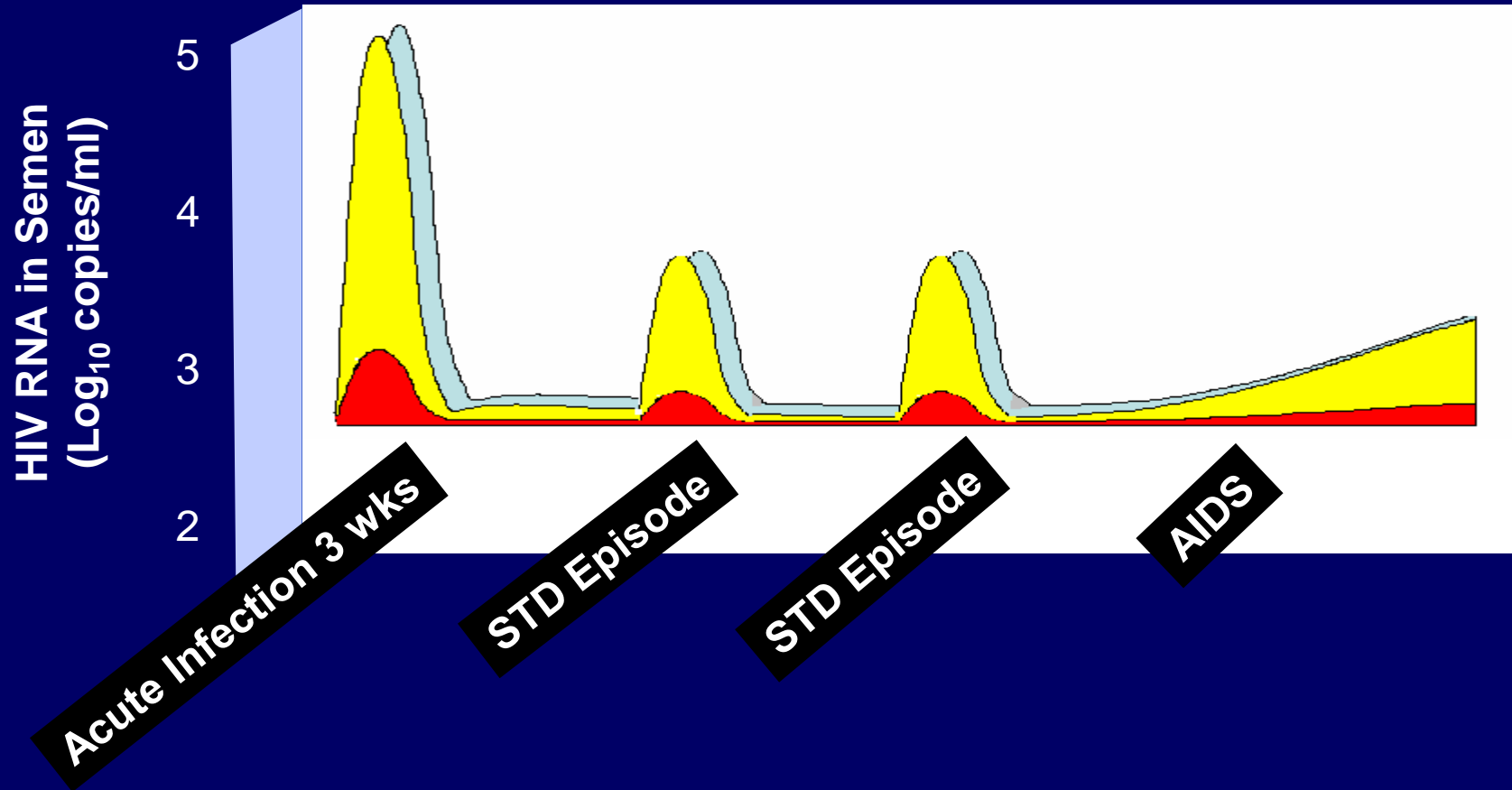
- Disruption of epithelial/mucosal barriers
- Increase the number of HIV target cells in the genital tract
- Increase expression of HIV co-receptors
- Induce secretion of cytokines (increase HIV shedding)
- HIV alters natural history of some STIs



Sexual Transmission of HIV



Acute HIV and STD Episodes



Cohen MS and Pilcher CD. Amplified HIV transmission and new approaches to HIV prevention. *J Infect Dis.* 2005;191:1391-3.

Case #1

- **33yo WF for initial visit to establish HIV care. No sexual activity for 6 months. Sex with men only. Oral, vaginal and anal exposure.**
- **No symptoms**
- **What is standard of care in terms of STI screening?**

Screening Methods

- **Screening for behavioral risk factors**
- **Screening for clinical risk factors**
 - **Diagnostic testing based on STI symptoms**
 - **Screening based on risk estimation**
- **Combination approach optimal**

CDC. Incorporating HIV prevention into the medical care of persons living with HIV: recommendations of CDC, the Health Resources and Services Administration, the National Institutes of Health and the HIV Medicine Association of the Infectious Diseases Society of America. *MMWR* 2003; 52(RR-12)

Screening for Behavioral Risks

- You won't know if you don't ask!
- Screening questions can be either open-ended or directed
- Provider comfort with subject matter key
- Many patients appreciate being asked!
- Risk is not static
- Partner's risk should be considered

Important Behaviors to Address

- Have they engaged in any type of sexual activity?
- Number, gender, type and HIV status of sexual partners
- Types of sexual activity (oral, vaginal, anal)
- Use of barrier methods (condoms, dental dams)
- Barriers to safer sexual practices

Laboratory Screening Strategies to Detect Asymptomatic STIs

For all patients

- Syphilis serology
- Gonorrhea and chlamydial urogenital specimen
- Other exposed sites as indicated

For women (in addition to routine cervical cancer screening)

- Wet mount examination or culture for *Trichomonas vaginalis*

Laboratory Testing: CT and GC

- **Culture**
- **Non-culture tests**
 - **Nucleic Acid Amplification Tests (NAATs)**
 - **Non-Nucleic Acid Amplification Tests (Non-NAATs)**
 - **Serology (CT in setting of LGV)**

NAATS

- NAATs amplify and detect organism-specific genomic or plasmid DNA or rRNA
- FDA cleared for urethral swabs from men/women, cervical swabs from women, and urine from both
- Commercially available NAATs include:
 - Becton Dickinson *BDProbeTec*®
 - Gen-Probe *AmpCT, Aptima*®
 - Roche *Amplicor*®
- Significantly more sensitive than other tests

Where do you test?

Self-reported Sites of Exposure (N=169)

Rectal, throat and genital	56 (33.1%)
Rectal and throat	19 (11.2%)
Rectal and genital	5 (3.0%)
Throat and genital	59 (34.9%)
Rectum only	3 (1.8%)
Throat only	11 (6.5%)
Genital only	16 (9.5%)

NAATS for oral testing

- **Oral GC testing:**
 - Culture (se – 50%-65%; sp – 99.0 - 99.4%)
 - NAATS (se – 83.6-100%; sp -94.2-98.6%)
 - Gen-Probe APTIMA Combo 2®
 - BDProbeTec™ ET
- **PCR not sufficiently specific for use at the oral site**

Gonococcal Infection by Site

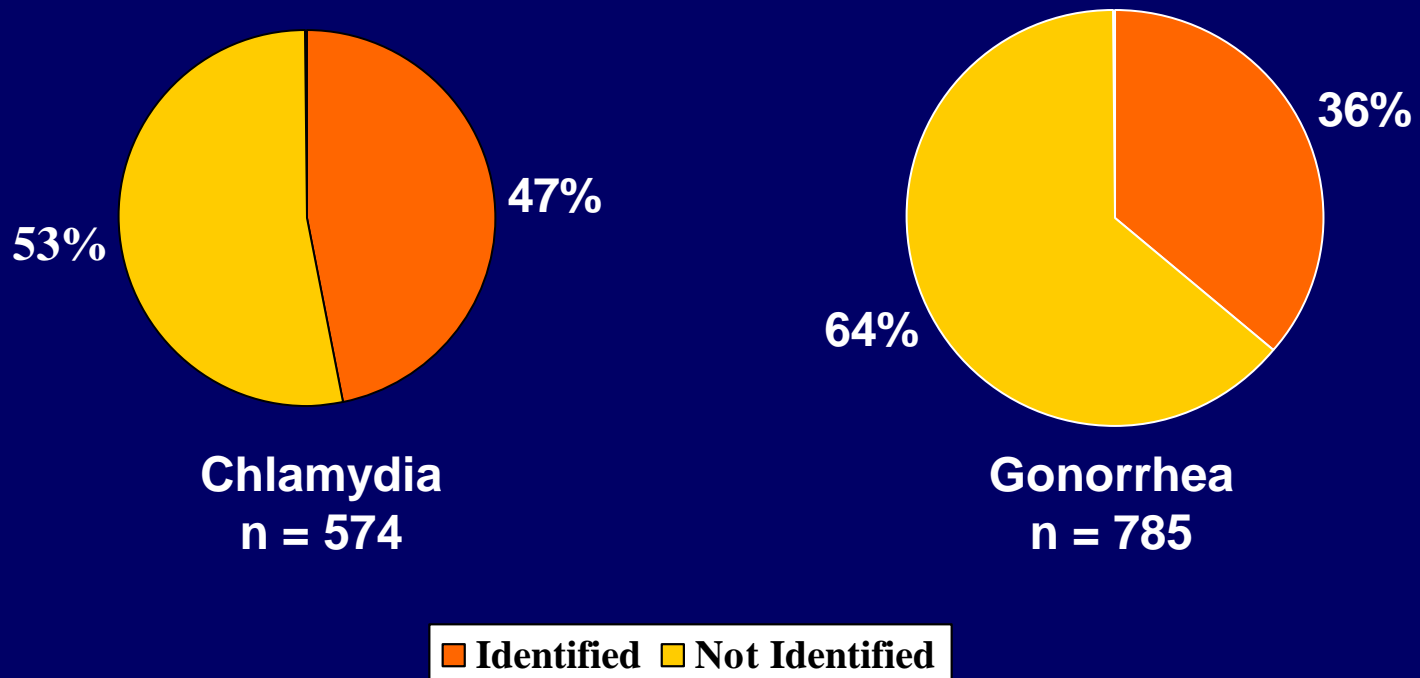
Site(s) positive	No. (%)
Genital^aand oral^b sites positive	23 (28.0)
Genital site only positive	28 (34.1)
Oral site only positive	31 (37.8)
Total genital or oral sites positive	82 (100.0)

Bachmann LH, Johnson RE, Cheng H, Markowitz LE, Papp JR, Hook III EW. J Clin Microbiol 2009. 47 (4): 902-907.

NAATS for Detection of Rectal GC and CT

- **GC**
 - Culture se 66.7-71.9% and sp 99.7-100%
 - PCR se 91.4-95.8% and sp 96-98.5%
 - SDA se 97.1-100% and sp 96-98.8%
 - TMA se 100% and sp 95.5-98.3%
- **CT**
 - Culture se 36.1-45.7% and sp 99.4-99.7%
 - PCR se 80.1-95.5% and sp 91.8-98.5%
 - SDA se 92.2-100% and sp 89.6-96.4%
 - TMA se 100% and sp 88.8-95.6%

Proportion of Chlamydial and Gonococcal Infections That Would Not Be Identified if Only Urine/Urethral Screening Performed Among Gay/Bisexual Men: San Francisco – 2003



Subsequent Routine Visits

- **Screening should be repeated at least annually for all patients who are sexually active.**
- **More frequent screening (i.e. 3-month to 6-month intervals) may be indicated for asymptomatic persons at higher risk.**
- **Patients with positive GC or CT should be rescreened in 3mo**

Back to the patient...

- She should be tested for:
 - Oral GC
 - Vaginal/cervical GC/CT
 - Rectal GC/CT
 - *Trichomonas vaginalis*
 - Syphilis
 - Pap test

Case #2

- **36yo BM, MSM, with HIV dx 2002 through routine screening**
- **Off HAART since 2005**
- **Presents as new patient 1/2010 and reports lower abdominal pain, scrotal and penile swelling x 3d**
- **Sex with 1 male partner 30d before, +IA (protected) and oral sex.**
- **Applying neosporin to penis for relief**

Case #2 cont.

- **Exam: marked edema involving the right scrotum and extending into the right inguinal canal. Marked tenderness and warmth. Left testicle normal. Glans penis with superficial ulcers. Indurated cleaned-based ulcers located circumferentially on the prepuce, around the glans. +penile d/c. Oral and rectal exam normal. Skin with multiple hyperpigmented papules involving both UE and upper back**



STI Syndromes

- **Acute epididymitis/orchitis**
 - *C. trachomatis*
 - *N. gonorrhoeae*
 - *E. coli*
 - *H. influenza*
 - Other enteric organisms
- **Genital ulcer disease**
 - *Herpes simplex virus*
 - *T. pallidum*
 - *H. ducreyi*
 - *K. granulomatis*

Differential Features of Sexually Transmitted Genital Ulcers

	Lesions	Tenderness	Edge	Base	Adenopathy
Syphilis	Usually single	None or mild	Indurated	Clean	Indolent
Chancroid	Usually multiple	Marked	Soft	Dirty	Tender, fluctuant
Herpes	Multiple	Marked	Soft	Clean	Tender
Donovanosis	Multiple	None	Serpiginous, may be white	Beefy red, granulation tissue	Erosive lesions overlying nodes
LGV	Single	None	Soft	Eroded papule	Prominent, tender

Empirically covered with...

- **Bicillin 2.4 million units IM**
- **Ceftriaxone 1gm IV q12**
- **Doxycycline 100mg po BID**
- **Metronidazole 500mg IV q8h**

Expert Opinion

Results

- WBC 22.7K with 63% polys
- HIV VL 89,150 and CD4 743 (13%)
- Urine culture: >100K pansensitive E. coli
- Urine NAATS - +GC and +CT
- Oral NAATS – negative GC
- RPR 1:32; +TPPA
- HSV 1 & 2 Ab neg
- Underwent urgent scrotal exploration, right orchiectomy for dead testicle (?torsion)

Case #3

- **32 yr BM with HIV diagnosed 1.5yr ago presents with rash of 1mo duration**
- **Abstinent following diagnosis up until approx. 6mo ago**
- **Sex with 1 male HIV+ partner**
- **Condoms with RA and IA but not oral**







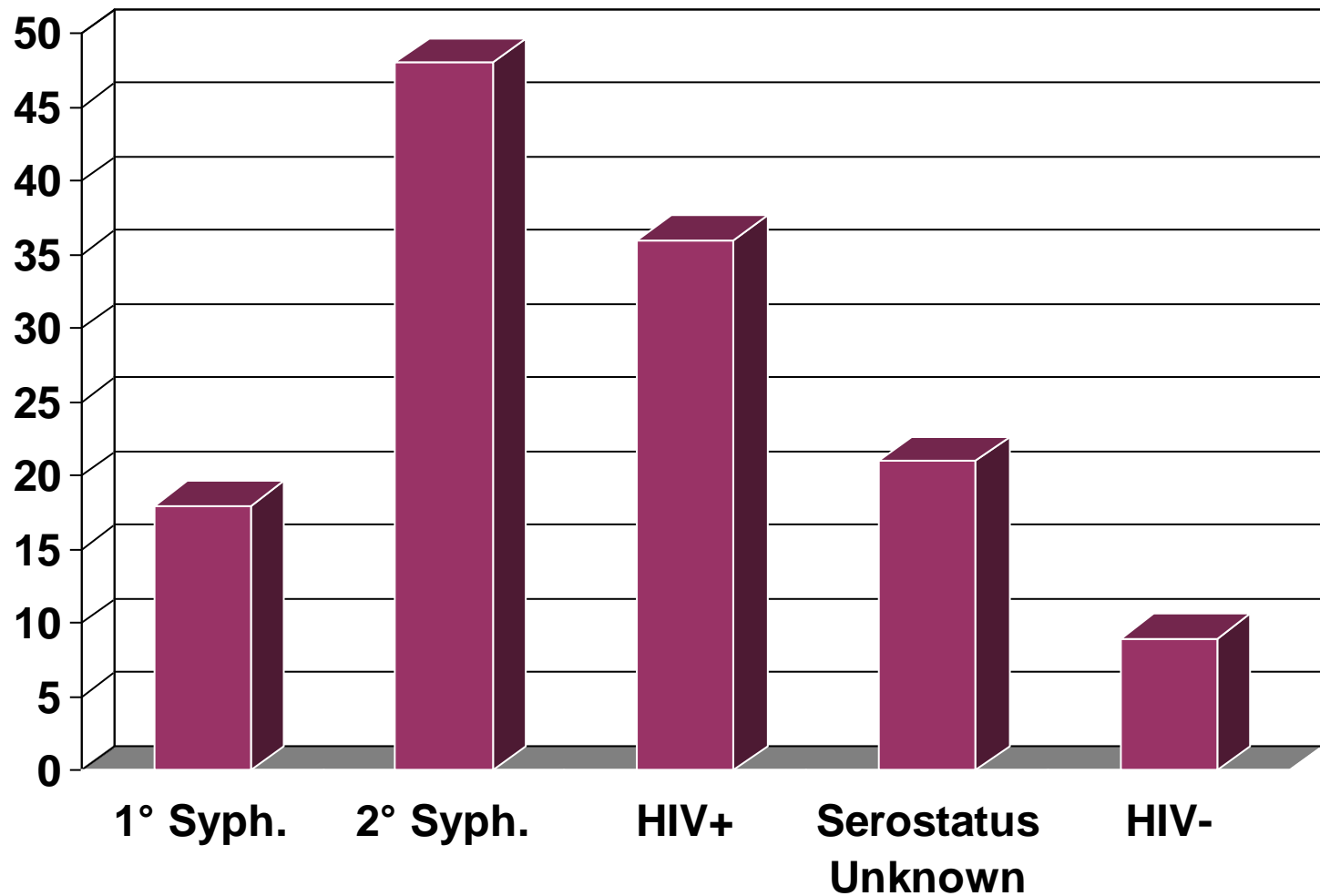




RPR 1:128
TPHA neg

Rash resolves with 2.4MU
Bicillin

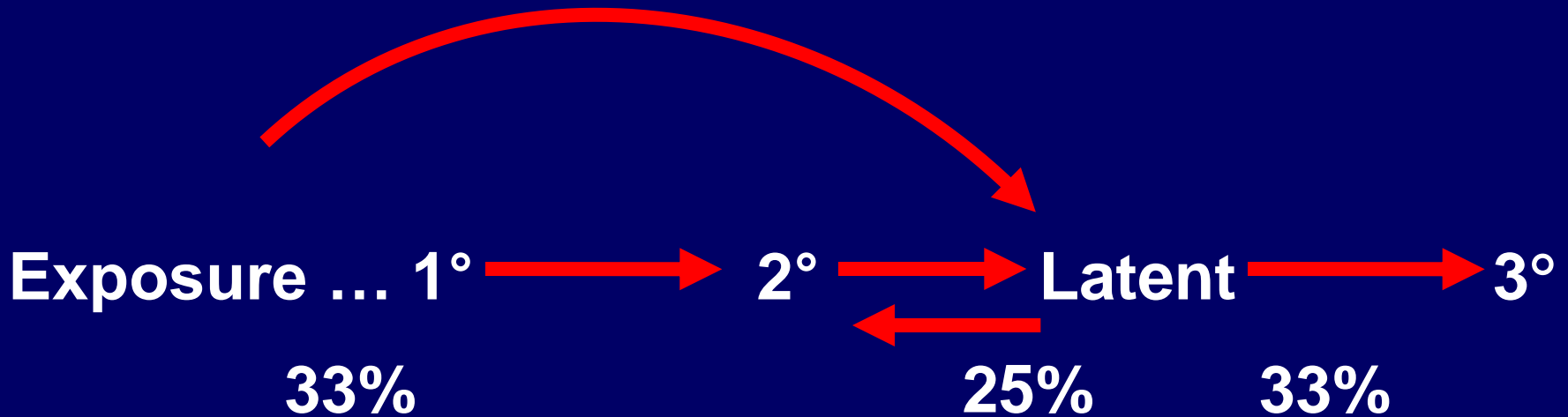
MSM - Oral Sex Only - Chicago, IL 2000-2002



Transmission of primary and secondary syphilis by oral sex --- Chicago, Illinois, 1998—2002. MMWR. October 22, 2004 / 53(41);966-968.

NATURAL HISTORY OF SYPHILIS

20-50%



2006 STD TREATMENT GUIDELINES

Syphilis in HIV Infected Patients

**Treat as Recommended for Patients
Without HIV Infection**

**Closer Follow-up
(3, 6, 9, 12, and 24 mos)**

2006 CDC STD TREATMENT GUIDELINES

Early Syphilis

Recommended

Benzathine Penicillin G, 2.4 Mu IM

Penicillin Allergy

Doxycycline 100 mg PO, BID x 14d

Limited Data

Ceftriaxone 1.0 g IM or IV x 8-10d

Azithromycin 2.0g PO

2006 STD TREATMENT GUIDELINES

Early vs. Late Latent Syphilis

Early Latent Syphilis

Documented Seroconversion Past Year

Unequivocal history of 1 , 2 syphilis symptoms,
past year

Sex partner with 1 , 2 , or EL syphilis, past year

Late Latent Syphilis

All others

(STS Titers Do Not Differentiate Early vs. Late
Latent Syphilis)

2006 CDC STD TREATMENT GUIDELINES

Late Latent and Tertiary Syphilis

**Benzathine Penicillin G 2.4 Mu IM
weekly x 3**

Penicillin Allergy

Doxycycline 100 mg PO, BID x 28

SYPHILIS THERAPY: RESPONSE TO THERAPY*

- **Primary or Secondary Syphilis – Fourfold (2 dilution) or greater decline in RPR or VDRL titers by time of 6 month follow-up**
- **Early Latent Syphilis – Fourfold (2 dilution) or greater decline in RPR or VDRL titers by time of 12-24 month follow-up**
- **Late syphilis – Takes longer for significant drop and if titer very low (i.e. 1:2), may never drop**

* Use same nontreponemal test for f/u

Ref: 2006 CDC STD Treatment Guidelines

TREATMENT OF EARLY SYPHILIS IN HIV-INFECTED AND UNINFECTED PERSONS

	3 Mo.	6 Mo.	12 Mo.
Treatment Group			
Usual	25% (175)	24% (157)	18% (137)
Enhanced	29% (189)	19% (172)	17% (144)
HIV-Status			
Positive	38% (76)*	28% (69)	21% (61)
Negative	24% (287)	19% (259)	16% (219)

*P < 0.05

Rolfs et al, NEJM

Indications for LP

- Neurologic signs at any stage (including eye disease and hearing loss)
- HIV+ and syphilis of unknown duration
- Use of non-PCN regimen (latent syphilis)
- Tertiary syphilis
- Clinical failure
- Failure of titers to decrease 4-fold (2 dilution) without evidence of clinical failure within 6-12mo time frame

LP in HIV-infected patients with syphilis and no neurologic symptoms

Ghanem et al. CID 2009;48(6): 816-821

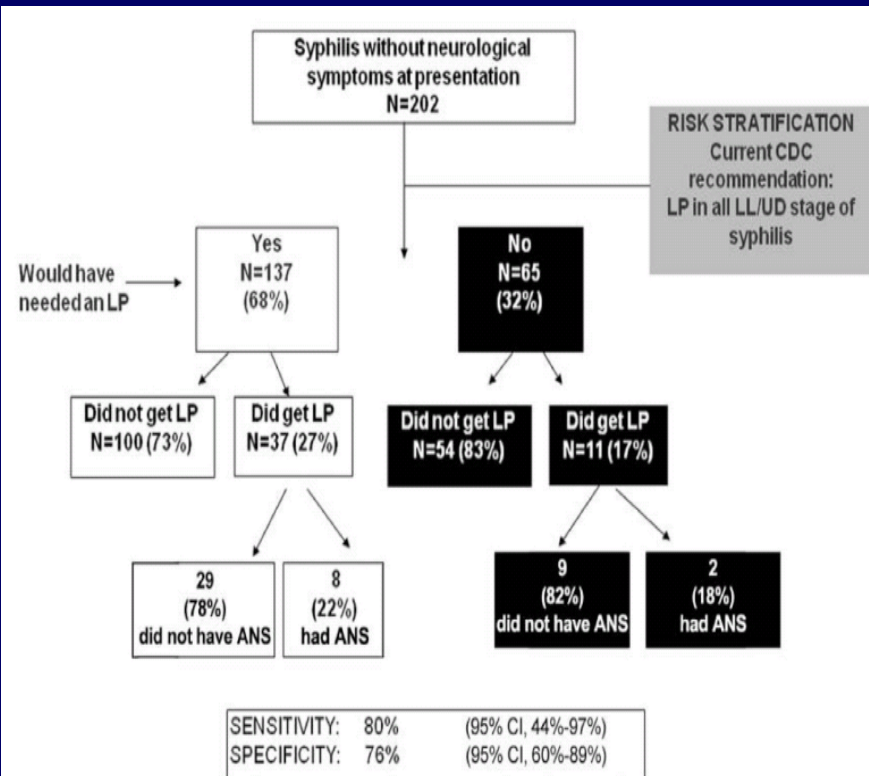


Figure 1.

Retrospective application of the first risk stratification criterion, which was based on current Centers for Disease Control and Prevention (CDC) recommendations for performance of lumbar puncture (LP) at the time of syphilis diagnosis in all late latent and unknown duration stages of syphilis. ANS, asymptomatic neurosyphilis; LL, late-latent stage of syphilis; UD, unknown duration of syphilis.

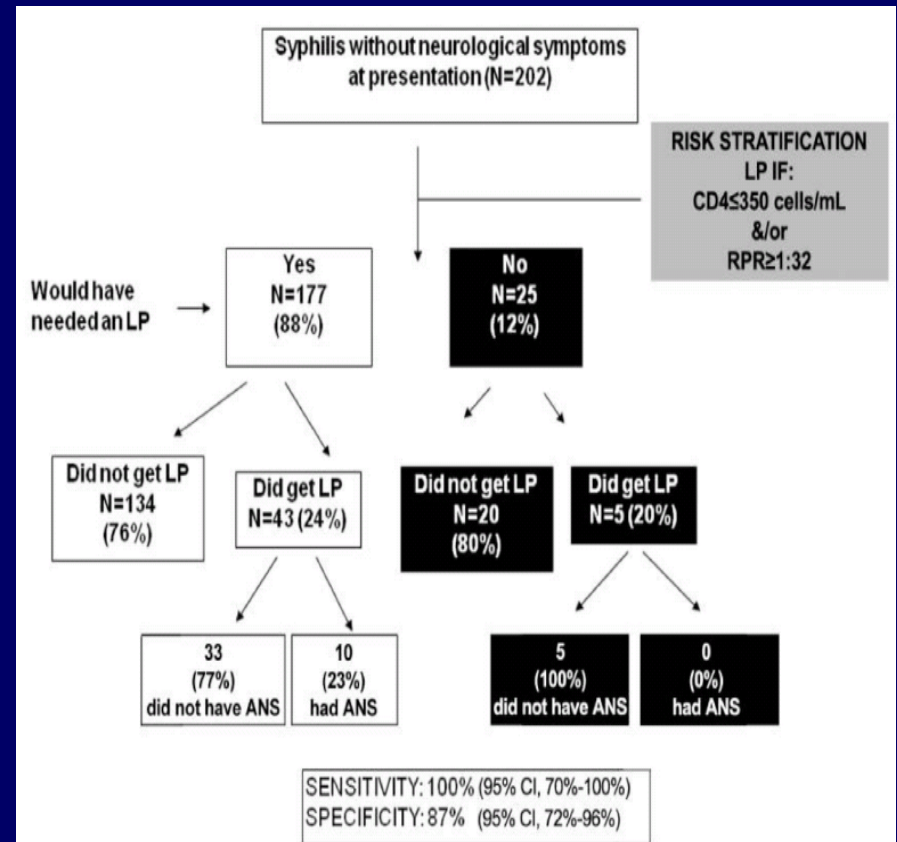
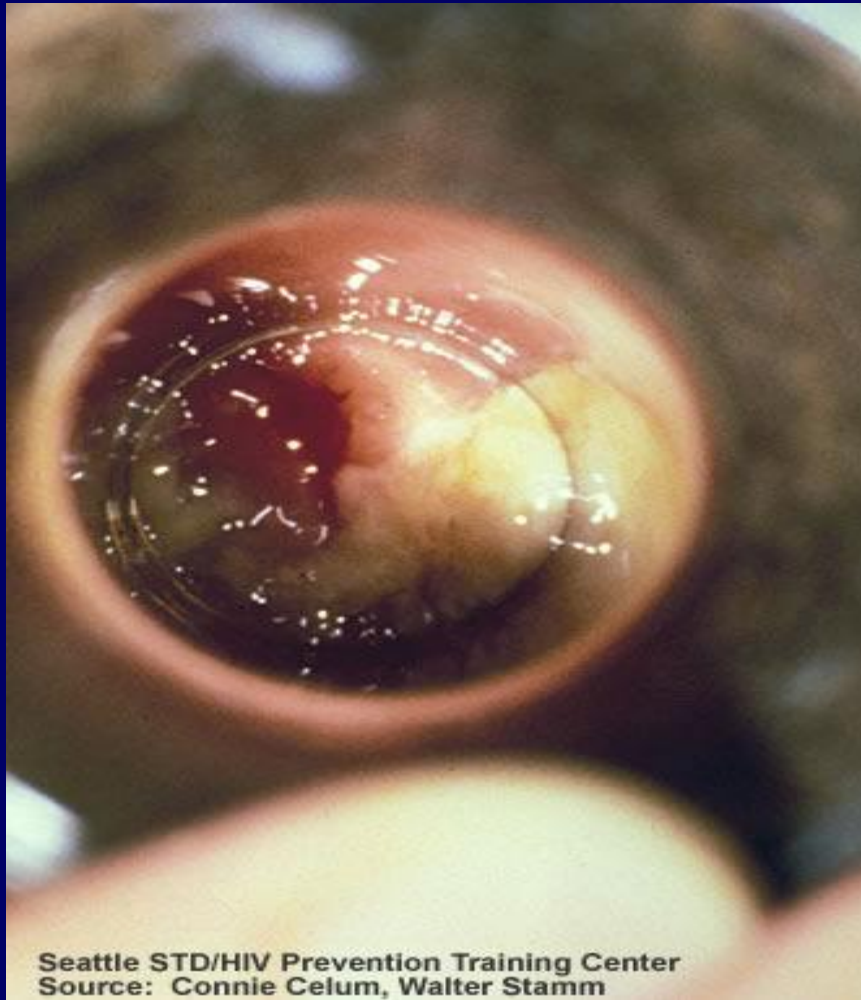


Figure 2.

Retrospective application of the second risk stratification criterion, which was based on performance of a lumbar puncture (LP) in patients with a CD4 cell count ≤ 350 cells/mL and/or a rapid plasma reagin (RPR) titer ≥ 1:32. ANS, asymptomatic neurosyphilis.

Case #4

- 26yo WM presents for HIV f/u
- Dx with HIV in 2007, off therapy for several mo
- Nadir CD4 70
- Multiple male partners, filming home-grown gay porn movies
- Unprotected RA, IA, oral
- Several days of tenesmus, pus on stools, rectal bleeding, rectal pain
- Contact to chlamydia



Seattle STD/HIV Prevention Training Center
Source: Connie Celum, Walter Stamm

Proctitis

Evaluation and Treatment

- Evaluate for *C. trachomatis*, *N. gonorrhoeae*, *T. pallidum* and HSV
- Treat empirically with:
 - Ceftriaxone 250mg IM x 1
 - Doxycycline 100mg po BID x 7 (?21)d
 - HSV or syphilis treatment if clinically compatible

Test Results

- Oral GC+
- Rectal GC+
- Rectal CT-
- Rectal HSV-
- RPR-

Trichomonas vaginalis

- **Most common curable STD in HIV+ women**
 - 6.1% to 33% for studies using wet prep +/- culture; up to 52.6% with nucleic acid amplification testing
- **Multiple studies support the epidemiological association between TV and HIV**
- **TV treatment reduced vaginal HIV shedding over a 1-3 month period and that HIV-infected women with TV had higher prevalence of HIV RNA in vaginal secretions than those without TV.**

Trichomonas vaginalis

Diagnostics and Treatment 2010

Diagnostics

- Wet Prep
- Culture
- APTIMA Combo 2
TMA
- PCR

Treatment

- Recommendation to change treatment regimen in HIV+ women to metro 500mg po BID x 7d?
- Rescreen +TV in 3mo

Expert opinion

HCV transmission amongst MSM

- **Cross-sectional and cohort studies demonstrate increased prevalence of HCV in MSM**
 - Unprotected anal sex
 - Multiple partners
 - Rough sexual techniques
 - Co-infection with HIV/STD
- **Recent evidence that HCV emerging as STI (Europe, US, Canada)**

**What else can we do to help
our patients stay healthy?**

Perceived Barriers to Provider-Delivered Behavioral Intervention

- **Time**
 - To obtain accurate information
 - To work it in
 - To develop a tailored plan
- **Knowledge**
- **Comfort**
- **Our “religion”**
- **Provider fatalism**

Provider-Delivered Interventions in the HIV Primary Care Setting

- **Partnership for Health**
Richardson JL et al, AIDS 2004
- **Options/Opciones Project**
Fisher JD et al, JAIDS 2005
- **Positive STEPS**
Gardner LI et al, AIDS Patient Care and STDs 2008
- **Ask, Screen, Intervene**
NNPTC, AETC collaboration

Questions?