STDs in the HIV-infected Population

Laura H. Bachmann, MD, MPH
Associate Professor of Medicine
WG (Bill) Hefner Medical Center
Salisbury, NC
Wake Forest University Health Sciences
Winston-Salem, NC
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
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

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.
Sexual Transmission of HIV

HIV RNA in Semen (Log_{10} copies/ml)

1/100 - 1/1000
1/500 - 1/2000
1/1000 - 1/10,000
1/30 - 1/200

Risk of Transmission Reflects **Genital** Viral Burden

Acute HIV and STD Episodes

HIV RNA in Semen (\(\log_{10} \text{copies/ml}\))

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)**

<table>
<thead>
<tr>
<th>Site of Exposure</th>
<th>Count (Percentage)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rectal, throat and genital</td>
<td>56 (33.1%)</td>
</tr>
<tr>
<td>Rectal and throat</td>
<td>19 (11.2%)</td>
</tr>
<tr>
<td>Rectal and genital</td>
<td>5 (3.0%)</td>
</tr>
<tr>
<td>Throat and genital</td>
<td>59 (34.9%)</td>
</tr>
<tr>
<td>Rectum only</td>
<td>3 (1.8%)</td>
</tr>
<tr>
<td>Throat only</td>
<td>11 (6.5%)</td>
</tr>
<tr>
<td>Genital only</td>
<td>16 (9.5%)</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Site(s) positive</th>
<th>No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genital(^a) and oral(^b) sites positive</td>
<td>23 (28.0)</td>
</tr>
<tr>
<td>Genital site only positive</td>
<td>28 (34.1)</td>
</tr>
<tr>
<td>Oral site only positive</td>
<td>31 (37.8)</td>
</tr>
<tr>
<td>Total genital or oral sites positive</td>
<td>82 (100.0)</td>
</tr>
</tbody>
</table>

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

Kent et al. CID 2005
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.

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); 2006 CDC STD Treatment Guidelines.
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. influenzae*
  - Other enteric organisms

- Genital ulcer disease
  - *Herpes simplex virus*
  - *T. pallidum*
  - *H. ducreyi*
  - *K. granulomatis*
## Differential Features of Sexually Transmitted Genital Ulcers

<table>
<thead>
<tr>
<th></th>
<th>Lesions</th>
<th>Tenderness</th>
<th>Edge</th>
<th>Base</th>
<th>Adenopathy</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Syphilis</strong></td>
<td>Usually single</td>
<td>None or mild</td>
<td>Indurated</td>
<td>Clean</td>
<td>Indolent</td>
</tr>
<tr>
<td><strong>Chancroid</strong></td>
<td>Usually multiple</td>
<td>Marked</td>
<td>Soft</td>
<td>Dirty</td>
<td>Tender, fluctuant</td>
</tr>
<tr>
<td><strong>Herpes</strong></td>
<td>Multiple</td>
<td>Marked</td>
<td>Soft</td>
<td>Clean</td>
<td>Tender</td>
</tr>
<tr>
<td><strong>Donovanosis</strong></td>
<td>Multiple</td>
<td>None</td>
<td>Serpiginous, may be white</td>
<td>Beefy red, granulation tissue</td>
<td>Erosive lesions overlying nodes</td>
</tr>
<tr>
<td><strong>LGV</strong></td>
<td>Single</td>
<td>None</td>
<td>Soft</td>
<td>Eroded papule</td>
<td>Prominent, tender</td>
</tr>
</tbody>
</table>
Empirically covered with...

- Bicillin 2.4 million units IM
- Ceftriaxone 1gm IV q12
- Doxycycline 100mg po BID
- Metronidazole 500mg IV q8h
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
NATURAL HISTORY OF
SYPHILIS

20-50%

Exposure … 1° 2° Latent 3°
33% 25% 33%

Slide courtesy of Edward Hook, III, MD
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)
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

<table>
<thead>
<tr>
<th>Treatment Group</th>
<th>3 Mo.</th>
<th>6 Mo.</th>
<th>12 Mo.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Usual</td>
<td>25% (175)</td>
<td>24% (157)</td>
<td>18% (137)</td>
</tr>
<tr>
<td>Enhanced</td>
<td>29% (189)</td>
<td>19% (172)</td>
<td>17% (144)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>HIV-Status</th>
<th>3 Mo.</th>
<th>6 Mo.</th>
<th>12 Mo.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>38% (76)*</td>
<td>28% (69)</td>
<td>21% (61)</td>
</tr>
<tr>
<td>Negative</td>
<td>24% (287)</td>
<td>19% (259)</td>
<td>16% (219)</td>
</tr>
</tbody>
</table>

*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

Ref: 2006 CDC STD Treatment Guidelines
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
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?