“SYPHILIS EDUCATION TODAY”
Preventing Syphilis Exposure in HIV+ Individuals – A Review of New Guidelines for Prevention and Treatment of Syphilis in the HIV-Infected Population

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September 4-5, 2008
Disclosure

• Dr. Klausner is an employee of the City & County of San Francisco and a Faculty member of the University of California, San Francisco

In the past 12 months:

• The NIH, CDC, California HIV Research Program and Gen-Probe, Inc., Focus Technologies, and Cerexa provided research funding to Dr. Klausner

• Communications Strategies, Inc., CSI Medical Education and King Pharmaceuticals, Inc. supported Dr. Klausner to conduct various educational programs
Syphilis Biology

• Treponema pallidum a spirochete bacterium spread through sexual contact—oral, anal or vaginal sex
• Humans only host
• Facilitates HIV transmission

San Francisco City Clinic Web site http://www.sfcityclinic.org/stdbasics/syphilis.asp
Primary Syphilis - Chancres

Photos courtesy of Jeffrey D. Klausner, MD
Primary Syphilis - Chancres

Photos courtesy of Jeffrey D. Klausner, MD
Secondary Syphilis

Rash

Mucous Patches

Condylomata Lata

Photos courtesy of Jeffrey D. Klausner, MD
Secondary Syphilis – Annular Rashes

Photos courtesy of Jeffrey D. Klausner, MD
Prophylactic Syphilis Treatment for Adults

- Penicillin G benzathine (Bicillin® L-A)* 2.4 million units (MU) intramuscular (IM) once

- **Penicillin-allergic:**
  - Non-Pregnant:
    - Doxycycline 100 mg PO BID x 14 days
  - Pregnant:
    - Test for hypersensitivity, desensitize, treat with penicillin G benzathine 2.4 MU IM once

* **Do not substitute** Bicillin® C-R for Bicillin® L-A in the treatment of syphilis. Bicillin® C-R is NOT indicated for the treatment of syphilis.

Primary and Secondary Syphilis Rates in the United States, 1981–2007*

Rate (per 100,000 population)

* 2007 data are preliminary

Hillard Weinstock, Division of STD Prevention, CDC, Presentation at STD National Conference, March 11, 2008
Primary and Secondary Syphilis Rates by Sex, United States, 1990–2007*

Rate (per 100,000 men/women)

* 2007 data are preliminary

Hillard Weinstock, Division of STD Prevention, CDC, Presentation at STD National Conference, March 11, 2008
Primary and Secondary Syphilis: Rates by Race and Ethnicity, 1997–2007*

Rate (per 100,000 population)

- African-American
- White
- Hispanic
- Asian/PI
- Am. Indian

* 2007 data are preliminary

<table>
<thead>
<tr>
<th></th>
<th>2004</th>
<th>2007*</th>
<th>% Change</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>6,722</td>
<td>9,502</td>
<td>+41.3</td>
</tr>
<tr>
<td>Women</td>
<td>1,255</td>
<td>1,671</td>
<td>+33.1</td>
</tr>
<tr>
<td><strong>Race/Ethnicity</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>African-American</td>
<td>3,071</td>
<td>4,944</td>
<td>+60.9</td>
</tr>
<tr>
<td>White</td>
<td>2,982</td>
<td>3,664</td>
<td>+22.8</td>
</tr>
<tr>
<td>Hispanic</td>
<td>1,196</td>
<td>1,728</td>
<td>+44.5</td>
</tr>
<tr>
<td>Asian/PI</td>
<td>143</td>
<td>166</td>
<td>+16.1</td>
</tr>
<tr>
<td>American Indian/NA</td>
<td>73</td>
<td>67</td>
<td>-11.0</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>7,980</td>
<td>11,181</td>
<td>+40.1</td>
</tr>
</tbody>
</table>

* 2007 data are preliminary
Primary and Secondary Syphilis — Rates by County: United States, 2006

Note: The Healthy People 2010 target for P&S syphilis is 0.2 case per 100,000 population. In 2006, 2,360 (75.2%) of 3,140 counties in the U.S. reported no cases of P&S syphilis.
Primary and Secondary Syphilis by Sex and Sexual Orientation in 23 States, 2005-2007*

Number of Cases

- MSM
- Heterosexual men
- Women

* 2007 data are preliminary
Primary and Secondary Syphilis Among MSM by Race/Ethnicity in 23 States, 2005-2007*

Number of Cases

- White
- African-American
- Hispanic

* 2007 data are preliminary
## Congenital Syphilis — Reported Cases for Infants <1 Year of Age and Rates of Primary and Secondary Syphilis Among Women, 1997–2006

<table>
<thead>
<tr>
<th>Year</th>
<th>CS cases (in thousands)</th>
<th>P&amp;S rate (per 100,000 women)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1997</td>
<td>1.2</td>
<td>0.0</td>
</tr>
<tr>
<td>1998</td>
<td>0.9</td>
<td>0.3</td>
</tr>
<tr>
<td>1999</td>
<td>0.6</td>
<td>0.6</td>
</tr>
<tr>
<td>2000</td>
<td>0.3</td>
<td>0.9</td>
</tr>
<tr>
<td>2001</td>
<td>0.2</td>
<td>1.2</td>
</tr>
<tr>
<td>2002</td>
<td>0.1</td>
<td>1.5</td>
</tr>
<tr>
<td>2003</td>
<td>0.1</td>
<td>1.8</td>
</tr>
<tr>
<td>2004</td>
<td>0.1</td>
<td>2.1</td>
</tr>
<tr>
<td>2005</td>
<td>0.1</td>
<td>2.4</td>
</tr>
<tr>
<td>2006</td>
<td>0.1</td>
<td>2.7</td>
</tr>
</tbody>
</table>
Summary

• Syphilis is increasing
• Highest rates among African-American men
• Rates of syphilis among MSM continue to increase; MSM account for >60% of all P&S syphilis cases
• Small increases over past 3 years in women, especially in the South, are concerning
Case 1

- 42-year-old man presents complaining of new skin rash
Medical History

- Medical history including STD history, current medications, allergies and chronic illnesses
- Sexual history
  - Gender and number of sex partners in past 12 months, type of sex, last sexual exposure, partners with syphilis
  - Other risk behaviors like methamphetamine or Viagra use, Internet, sex club/bath house
- Prior HIV and syphilis testing history
- Review of Systems with focus on neurologic complaints, particularly hearing, visual or balance
Serologic Test Results

- Syphilis EIA positive, RPR 1:128
- Is further syphilis testing required?
  - Use of TP EIA in clinical practice
  - TP identified old and new infection
  - Requires RPR to measure titer of infection
- HIV-1 antibody positive
Physical and Neurological Examination

- Physical examination with particular attention to skin, palms/soles, oral cavity, genitals and anus
- Neurologic examination
  - General
  - Cranial nerve evaluation—rule out oculomotor (III), facial (VII), auditory (VIII) dysfunction
    - Pupillary reaction vs. accommodation
    - Smile, hearing assessment
  - Dorsal columns
    - Vibration and position sense
  - Gait and balance
Indications for CSF analysis*

1) Neurologic findings in patients with syphilis including visual or hearing abnormalities
2) Syphilis treatment failure
3) Tertiary syphilis—cardiovascular, skeletal, etc.
4) Late or unknown latent in HIV-infected patients

*Centers for Disease Control and Prevention, 2006 STD Treatment Guidelines, MMWR, 2006. Available at www.cdc.gov/std
Syphilis Treatment

- **Penicillin G benzathine (Bicillin® L-A)**
  - 2.4 million units (MU) intramuscular (IM) once

- **Penicillin-allergic:**
  - **Non-Pregnant:**
    - Doxycycline 100 mg PO BID x 14 days
  - **Pregnant:**
    - Test for hypersensitivity, desensitize, treat with penicillin G benzathine 2.4 MU IM once

* Do not substitute Bicillin® C-R for Bicillin® L-A in the treatment of syphilis. Bicillin® C-R is NOT indicated for the treatment of syphilis.

Partner Management

- Notify, evaluate and provide epidemiologic treatment* for recent partners
- Inform partners of potential syphilis/HIV exposure and offer HIV testing

* Penicillin G benzathine (Bicillin ®-LA) 2.4 MU IM once
## Partner Management in Syphilis

<table>
<thead>
<tr>
<th>Stage</th>
<th>Partner period</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary syphilis</td>
<td>&lt; 90 days</td>
<td>Treat* and test</td>
</tr>
<tr>
<td>Secondary syphilis</td>
<td>&lt; 6 months</td>
<td>Test and treat, if infected</td>
</tr>
<tr>
<td>Early latent syphilis</td>
<td>&lt; 1 year</td>
<td>Test and treat, if infected</td>
</tr>
</tbody>
</table>

* Treat with penicillin G benzathine (Bicillin \(^\text{®}\)-LA) 2.4 MU IM once
Treatment Follow-up

• Repeat serologic tests at 3, 6, 9, 12 and 24 months
  – 4-fold decline by 12 months consistent with cure
  – Failure of 4-fold at 12 months may necessitate CSF analysis to rule out neurosyphilis
Summary

• Syphilis is increasing in the United States
  – Highest rates in African-American men
  – Most cases occurring in gay men and other men who have sex with men

• Treatment of syphilis requires use of penicillin G benzathine (Bicillin® L-A)
  – Avoid Bicillin® C-R, not indicated for syphilis
  – Follow patients closely after treatment
More Information and Questions!

- SFDPH City Clinic  
  www.sfcityclinic.org  
  Jeff.Klausner@sfdph.org

- State of CA STD Branch  
  www.std.ca.gov

- CDC STD Treatment Guidelines 2006  
  www.cdc.gov/std

- www.Bicillin.net
Questions?

Ask Dr. Klausner ("Dr. K")
HIV Opportunistic Infection Guidelines: Syphilis

Kimberly Workowski, MD
Syphilis Workgroup Leader, HIV OI Guidelines
Team Lead, STD Treatment Guidelines Unit
Epidemiology/Surveillance Branch, DSTDP/CDC

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Disclosure

- Emory University Infectious Disease faculty
- Clinical Research funding (HIV, Hepatitis C, vaginal microbicides)- NIH, CDC, Abbott, Gilead, BMS, Tibotec
- Contractor- Division of STD Prevention, Guidelines Unit, CDC
HIV Opportunistic Infection Guidelines: Syphilis

• The guidelines are available at http://AIDSinfo.nih.gov
General Principles

• Syphilic genital ulceration increases risk of HIV sexual acquisition and transmission
• Management principles similar
  – Frequent clinical/serologic monitoring
• Subtle variations in clinical presentation
  – Multiple/deep ulcers, concomitant primary/secondary
• Neurosyphilis can occur at any stage
  – Uveitis, meningitis may be more common
Diagnosis

- Dx based on direct direction or serologic evaluation
- No formal evaluation of serologic test performance in HIV+ patients
- Responses to nontreponemal tests may be atypical
  - False positive tests more common in HIV+
  - False negative test – repeat serology, exclude prozone, biopsy, DFA
- Treponemal EIA (screening)- identifies previous treatment, untreated late syphilis
- Transient decrease in CD4 or increase in VL (early syphilis)
Evaluation of CNS Involvement

• CNS or ocular clinical findings
• Frequent treponemal CNS invasion in early syphilis regardless of HIV status (protein, pleocytosis)
• CSF exam- neuro/ocular sx, tertiary, tx failure, latent syphilis/HIV+ (CDC STD Treatment Guidelines 2006)
  – RPR >1:32 regardless of stage (Marra 2004, Libois 2007)
  – CD4 <350 (3.1x); RPR >1:32 (6x) (Marra)
• No data to suggest CSF abnormalities in early syphilis reliably predict the need for aggressive NS tx
Rating Scheme for Treatment Recommendations

**Strength of the Recommendation**

- **A** – Strong Evidence for efficacy and clinical benefit
- **B** – Moderate evidence for efficacy but only limited clinical benefit
- **C** – Evidence is insufficient to support a recommendation (optional)
- **D** – Moderate evidence for lack of efficacy or for adverse outcomes

**Quality of the Evidence**

- **I** – At least one properly conducted randomized trial
- **II** – At least one well designed clinical trial (cohort, case controlled analytic studies)
- **III** – expert opinion
Treatment Recommendations
Primary, Secondary, EL

- Penicillin treatment of choice regardless of HIV status
  - Benzathine Pcn G x 1
  - Benefit of additional injections unproven
    - Enhanced tx (IM+oral) no benefit
  - PCN alternatives
    - Not well evaluated
    - Close serologic and clinical monitoring
    - Azithromycin 2 gm (resistance/tx failure)
Treatment Recommendations
Latent Syphilis & Neurosyphilis

• Benz PCN 3 wkly injections AIII
• Non Pcn alternatives
  – Doxycycline X 28 d- insufficient evaluation BIII
  – Close clinical and serologic monitoring
• Neurosyphilis -IV PCN AII Procaine/Proben BII
  – Additional 1-3 wkly x Benz Pcn CIII
• Sulfa allergy- no probenecid DIII
• PCN allergy- densensitization BIII or ceftriaxone CIII
Response to Therapy

• Frequent clinical and serologic monitoring
  – Early stage- 3, 6, 9, 12, 24 months
  – Latent syphilis- 6, 12, 18, 24 months

• Serologic responses similar to HIV- patients
  – Subtle variation in temporal pattern of response

• 15-20% of persons may remain serofast
  – Probably don’t represent tx failure
  – Serologic detection of reinfection based on 4x titer increase above baseline
Management of Treatment Failure

- CSF evaluation and retreatment
- Retreatment of early stage syphilis
  - Sustained four increase in RPR after initial reduction
  - Persistent of recurring signs or sx
  - Strongly consider for failure of RPR decline 4x 6-12 months after tx  **BIII**
  - Benzathine Pcn wkly X 3  **BIII** or IV PCN  **CIII**
Management of Treatment Failure

- Retreatment of late latent syphilis
  - Repeat CSF evaluation, tx NS if consistent with CNS involvement
  - Clinical signs or sx
  - 4x increase in RPR or less than 4X decline 12-24 month after tx  
    **BIII**
  - Benz Pcn wkly x 3  
    **BIII** or NS regimen  
    **CIII**
Prevention Recommendations

• Routine discussion of sexual behavior
  – client-centered risk reduction messages
• Routine serologic screening at least annually
  – More frequent screening dependent on risk behaviors
    (every 3-6 months)
• Intensified counseling
• Evaluation for other STDs
Pregnancy

- All pregnant women screened in first trimester
  - Additional testing among women at high risk
- Rates of fetal transmission highest in early syphilis
- Insufficient data about serologic response in HIV+ women
- Some treatment failures after single Benz Pcn (HIV-)
  - Consider second injection **BIII**
- Pcn allergy – desensitization **AIII**
  - No pcn alternatives proven safe and effective for maternal infection or prevention of fetal infection
  - Insufficient data on azi or ceftriaxone **DIII**
  - Tetracyclines- teeth staining, hepatotoxicity **DIII**
CDC STD Treatment Guidelines

- Authoritative source of STD treatment and management
- Screening, prevention and vaccination strategies, treatment regimens
- Order hard copies http://www.cdc.gov/std/treatment
- Pocket guides, wall charts
Questions?

Ask Dr. Workowski
Thank you

Special thanks to CSI Medical Education