RESPONDING TO SYPHILIS: AN UPDATE IN EPIDEMIOLOGY AND CLINICAL CASE MANAGEMENT

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March 19, 2007
Disclosure

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

In the past 12 months:
• The NIH, CDC, University of California AIDS Research Program and Gen-Probe, Inc., has provided research funding to the City & County of San Francisco
• Communication Strategies, Inc. and King Pharmaceuticals, Inc. has supported Dr. Klausner and the City and County of San Francisco to conduct educational programs
Syphilis Biology

• *Treponema pallidum* a spirochete bacterium spread through sexual contact—oral, anal or vaginal sex

• Humans only host

• Facilitates HIV transmission

Rate (per 100,000 population)

- Males
- Females
- Healthy People 2010
Primary and secondary syphilis: Black and White rates by sex, 2000-2005

Rate (per 100,000 population)

- Black males
- Black females
- White males
- White females

2005 data provisional, CDC
Primary and secondary syphilis — Rates by county: United States, 2005

Note: The Healthy People 2010 target for P&S syphilis is 0.2 case per 100,000 population. In 2005, 2,434 (77.5%) of 3,140 counties in the U.S. reported no cases of P&S syphilis.
Case 1—Abnormal Blood Test

- 45 year old man underwent screening for syphilis
- RPR* 1:32, TPPA** reactive (FTA-Abs***)

*RPR = rapid plasma reagin
**TPPA = Treponema pallidum particle agglutination
***FTA-ABS = fluorescent treponema antibody absorption
Sexual History

- “Are you sexually active with men, women or both?”
- “In the past year, how many male, female sex partners have you had?”
  - Past 3 months, past 6 months?
- “What type of sex do you have—oral, anal, vaginal?”
  - Penis in your mouth, anus?
  - Your penis in partner’s mouth, anus, vagina?
Syphilis History

- Check city, country or state syphilis registry
- Has a doctor or nurse ever told you that you had syphilis?
- Have you ever been treated for syphilis?
  - Usual treatment is 1 or 2 injections of penicillin in the buttocks, sometimes weekly for 3 weeks
Physical Examination

- General including lymph nodes
- Skin—rule out hair loss (alopecia); rule out rash
- Oropharynx—rule out chancres, mucous patches
- Penis/ scrotum—rule out chancres/ rash
- Anus—rule out *condylomata lata*
Primary syphilis—chancre
Primary syphilis—chancre

anorectal
Secondary syphilis—annular rashes

palms

scrotum
Secondary syphilis

Mucous patches

Condylomata lata
Neurologic examination

• General—including reported visual and auditory function
• Cranial nerve evaluation—rule out oculomotor (III), facial (VII), auditory (VIII) dysfunction
  – Pupillary reaction vs. accommodation
    • Argyll-Robertson pupil
  – Smile
  – Hearing assessment
• Dorsal columns
  – Vibration and position sense
• Gait and balance
Case 1--Findings

• 1 steady female partner, 1 casual male partner 6 months ago, oral sex only
• Prior syphilis test 11 months ago negative
• Asymptomatic
• Normal physical examination
Stage and management

• Early latent syphilis
  – Syphilis acquired in the past year
• Treat for early syphilis
• Test for HIV infection
Early 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.
Treatment follow-up

• Repeat serologic tests at 6 and 12 months (more frequently in HIV-infected patients)
  – 4-fold titer decline consistent with cure
  – HIV-infected patients may take longer to observe 4-fold titer decline

• Repeat HIV test at 3 months
Partner management

• Notify, evaluate and provide epidemiologic treatment for recent partners
  – Male partner last sex > 6 months, test then treat
  – Female partner last sex < 3 months, treat and test
Syphilis Management

Syphilis RPR or VDRL Test

Negative
Re-screen in 3-12 months

Positive
Note titer, e.g., 1:2, 1:16, etc.

Confirm with TPPA

TPPA reactive

TPPA non-reactive
False positive

Stage patient*
Sexual history
Syphilis treatment history
Physical including neurological examination

Primary stage
Oral or genital chancre

Secondary stage
Rash
Condylomata lata
Mucous patches

Early latent
Asymptomatic
Prior negative test in past year

Unknown latent
Asymptomatic
No prior test

Late latent
Asymptomatic
Duration > 1 year

Treat as early syphilis
Penicillin G benzathine 2.4 mu intramuscular once

Treat as late syphilis
Penicillin G benzathine 2.4 mu intramuscular once weekly x 3
Case 2—New rash

- 36-year old HIV-infected male restaurant worker complains of rash for 3 weeks
- He noticed red lesions on his wrist and ankles
- Denies itchiness or worsening of rash at night or with warm shower
Evaluation

• Sexual history including medical history
  • History of allergies, new medications, exposures to pets, recent travel, or outdoor activity
• Syphilis history
• Physical and neurologic examination
• Serologic testing
  • Ideally stat RPR
  • Routine RPR (or VDRL) and TPPA (or FTA-ABS)
Macular rash on abdomen
Serology in Secondary Syphilis

- Rare reports of seronegative syphilis
- > 99% of patients will be seroreactive
- If seronegative, consider prozone reaction
  - Excess antibody prevents formation of antigen-antibody complex for test reactivity
  - Order repeat test with 1:10 dilution
- If seronegative, consider skin biopsy
Case 2—SeroLogic Test Results

RPR* 1:512, TPPA** reactive (FTA-Abs***)

*RPR = rapid plasma reagin
**TPPA = Treponema pallidum particle agglutination
***FTA-Abs = fluorescent treponema antibody absorbed
Case 2—Findings

- 15 casual male partners over the past 6 months, anal and oral sex
  - Frequent methamphetamine use with sex
- Prior syphilis test 6 months ago negative
- Macular body rash, including ankles and wrists; axillary adenopathy
- Normal neurologic examination
Stage and Management

• Secondary syphilis
  – Physical findings c/w syphilis
  – Syphilis likely acquired in the past 6 months
• Manage and treat for secondary syphilis
• Counsel and refer for substance use treatment
Secondary Syphilis Treatment

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

- **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
Treatment Follow-up

- Repeat serologic tests for syphilis at 3, 6, 9, and 12 months
- 4-fold decline at 12-months consistent with cure
Partner Management
Secondary Syphilis

• Notify, evaluate and provide treatment for all sex partners in past 6 months
  – Partners > 3 months, test then treat
  – Partners < 3 months, treat and test
• Treat with penicillin G benzathine (Bicillin® L-A) 2.4 MU IM once

• **PCN-allergic:**
  
  **Non-Pregnant:**
  Doxycycline 100 mg PO BID x 14 days

  **Pregnant:**
  Test for hypersensitivity, desensitize, treat penicillin benzathine G 2.4 MU IM once
Syphilis increases HIV viral load and decreases CD4 cell counts in HIV-infected patients with new syphilis infections

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![Diagram showing changes in HIV viral load associated with syphilis infection and syphilis treatment, according to the stage of syphilis. B–D, ‘Before-to-during’; D–A, ‘during-to-after’; S1, primary syphilis; S2, secondary syphilis. Boxplots show medians and upper and lower quartiles, whiskers encompass the extent of the data. Means are represented by filled circles.](image_url)
Case 3—Recent Onset of Hearing Loss

- 24 year old transgender (male to female) complains of 1 week of decreased hearing in left ear
- Denies recent exposure to loud noise, music, trauma
- No headache, ear pain, discharge, or fever
Case 3—Work-up

- Medical and sexual history
- Syphilis history
- Physical and neurologic examination
Case 3—Findings

• Denies recent illness, no new or current medications
• Sexually active with one steady male partner
• Last HIV and syphilis test 3 months ago both negative
• Physical and neurologic examination normal except for decreased hearing left ear
Case 3—Rule Out Neurosyphilis

- Serologic tests for syphilis
- CSF analysis
- No current indication for CT scan or MRI
Case 3—Laboratory Findings

- RPR 1:16, TPPA reactive
- CSF analysis
  - 15 white blood cells/high power field (elevated)
  - Protein = 75 mg/dL (elevated)
  - Glucose = 90 mg/dL (normal range)
  - CSF VDRL = 1:2 (abnormal)
Case 3—Neurosyphilis

• Stage patient as early syphilis—asymptomatic and infection < 1 year
  • Manage patient and partner for early syphilis

• Treat for neurosyphilis
Neurosyphilis Treatment

- Penicillin G IV 18-24 MU qD (3-4 MU q 4°) x 10-14 days; followed by penicillin G benzathine (Bicillin® L-A) 2.4 MU IM weekly x 1-3*

- *Penicillin-allergic:*
  Test for hypersensitivity, desensitize, and treat with penicillin G

*Most experts recommend > 1 additional dose*
Neurosyphilis Follow-up

• Repeat serologic tests 6 and 12 months
• Repeat CSF analysis at 6 months
  • Recent evidence suggests that 4-fold decline in serologic titer predicts decline in CSF titer
    (Marra et al., CROI, 2007)
Neurosyphilis and HIV Infection

• Currently neurosyphilis is more common in early infection (< 1 year) than late infection
• Neurosyphilis is more common in HIV-infected than HIV-uninfected patients
  – 2% versus < 1%
• CSF abnormalities may be due to HIV-infection (elevated CSF white blood cell count of protein) versus syphilis
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 Prevention

• Ask all patients about sexual activity, specific sexual behaviors, gender of sex partners and substance use

• Screen all sexually active male patients with male partners for syphilis; all pregnant women; and women with male partners at risk for syphilis
  – Local screening recommendations may vary

• Continue screening every 3-6 months in those with new partners or non-monogamous

• Provide risk-reduction counseling and substance use treatment services as indicated
## Partner Management in Syphilis

<table>
<thead>
<tr>
<th>Stage</th>
<th>Partner period</th>
<th>Management</th>
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</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>
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*Treat with penicillin G benzathine 2.4 MU IM once*
Partner Notification

www.inSPOT.org
An anonymous or confidential STD partner notification system
Summary

• Syphilis is increasing in the U.S. mostly 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

• Prevention efforts must focus on new target populations, addressing meth use and enhanced partner services
Web Resources

• www.cdc.gov/std
• www.ncsddc.org
• http://depts.washington.edu/nnptc/
• www.stdhivtraining.org
• www.sfcityclinic.org

• www.PROPSF.org
• www.stdtest.org (SF residents)
• www.inspot.org
• www.bicillin.net
Buck Syphilis

Buck Syphilis.org
Questions?

Ask Dr. Pamplin or Klausner (“Dr. K”)

www.bicillin.net