STD Screening & Management: Syphilis

Christian B. Ramers, MD, MPH
Assistant Medical Director
Family Health Centers of San Diego – Ciaccio Memorial Clinic
1/10/13

ACCREDITATION STATEMENT: University of California, San Diego School of Medicine is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians. The University of California, San Diego School of Medicine designates this educational activity for a maximum of one credit per hour AMA PRA Category 1 Credits™. Physicians should only claim credit commensurate with the extent of their participation in the activity.
1) Describe changing epidemiology of Syphilis in MSM and HIV+ populations
2) List recent/upcoming changes in Syphilis screening tests
3) Review clinical stages and corresponding treatment of syphilis
<table>
<thead>
<tr>
<th>Recommendations and Reports</th>
<th>December 17, 2010 / Vol. 59 / No. RR-12</th>
</tr>
</thead>
</table>

**Sexually Transmitted Diseases**

**Treatment Guidelines, 2010**
Guidelines for Prevention and Treatment of Opportunistic Infections in HIV-Infected Adults and Adolescents

Recommendations from CDC, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America
Poll 1: Which of the following is TRUE regarding Syphilis in the United States?

1. Rates are declining overall due to prevention efforts
2. Antibiotic resistance is becoming a problem for treatment algorithms
3. Some populations are seeing the highest rates in 20 years
4. Incidence is basically steady, but prevalence is rising
Syphilis – Epidemiology

Early syphilis in King County, WA, by year and sexual orientation, 1994-2010

Source: PHSKC Sentinel Providers Newsletter 4/2011
Primary & Secondary Syphilis Cases by Gender – California (1996-2010)

Source: CA Dept of Public Health – STD Control Branch
Case #1 - JT

• **HPI:** 24 yo male presents to urgent care with 1-2 weeks malaise, headache, fevers, rash

• **PMedHx:** Previously healthy

• **SocHx:**
  - Social EtOH and occasional Tobacco
  - Has experimented with methamphetamine
  - MSM, 7 lifetime partners, new partner x 3 months

• **PEX:** T 38.2, 94, 128/78, 97%, 165 lbs
Case #1: Rash
Poll 2: Which of the following is the best approach?

1. CSF VDRL
2. Serum RPR
3. Syphilis IgG
4. Syphilis IgG and HIV Antibody
5. Syphilis IgG and HIV Viral load
6. 2.4 million units Benzathine PCN

NOW, think about testing later
Poll 3: What is the Diagnosis?

1. Primary Syphilis (w/ chancre)
2. Secondary Syphilis
3. Early Latent Syphilis
4. Late Latent Syphilis
5. Tertiary Syphilis
Syphilis – Background (stages)

1º: Chancre
2º: Rash, fever, HA, malaise
Latent: No Sx
3º: Gumma, bone, cardiac, nerve disease

"Early" syphilis if <1 year

75% 25% 30%

5-50 years

Primary Syphilis - Chancre

Photo Courtesy of J. Marrazzo, MD
‘Dory Flop Sign’ of Syphilis

Katz KA. Arch Dermatol. 2010. 146(5); 572
Secondary Syphilis - Rash
Secondary Stage - Mucous Patches

Photos courtesy of King County STD clinic
Syphilis – Diagnosis

• *T. pallidum*, can’t be cultured
• Darkfield Microscopy
• Non-Treponemal Tests
  • RPR – Rapid Plasma Reagin
  • VDRL – Venereal Disease Research Laboratory
• Treponemal Tests
  • FTA-ABS – fluorescent treponemal Ab - absorption
  • TPPA – T. pallidum particle agglutination
  • (*NEW*) TP-EIA – T. pallidum enzyme immunoassay
Syphilis – Diagnosis (algorithms)

• Typical diagnostic algorithm:
  
  • **SCREEN**: Non-treponemal test: RPR or VDRL
  
  • **CONFIRM**: Treponemal test: FTA-ABS or TP-PA
  
  • **FOLLOW**: non-treponemal titer: RPR or VDRL

• Many labs now incorporating **TP-EIA** testing due to increased sensitivity, high throughput
Low tech vs high tech

180 tests per hour, no manual pipetting
Syphilis – Reverse Screening Algorithm

- EIA (Syphilis IgG) used for screening
- Positive EIA confirmed with RPR & TP-PA
- RPR titer still used to follow treatment

MMWR – July 8, 2011 – 60 (26); 873-877
## Syphilis - Treatment

<table>
<thead>
<tr>
<th>Clinical Stage</th>
<th>Treatment</th>
<th>Alternative</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary</strong></td>
<td>Benzathine PCN G 2.4 million U IM x 1</td>
<td>Doxycycline 100 mg PO BID x 14d</td>
</tr>
<tr>
<td><strong>Secondary</strong></td>
<td>(same as above)</td>
<td>(same as above)</td>
</tr>
<tr>
<td><strong>Early Latent (&lt;1 yr)</strong></td>
<td>(same as above)</td>
<td>(same as above)</td>
</tr>
<tr>
<td><strong>Late Latent (&gt; 1 yr)</strong></td>
<td>Benzathine PCN G 2.4 million U IM QWeek x 3</td>
<td>Doxycycline 100 mg PO TID x 21d</td>
</tr>
<tr>
<td><strong>Latent (Unk Duration)</strong></td>
<td>(same as above)</td>
<td>(same as above)</td>
</tr>
<tr>
<td><strong>Late</strong></td>
<td>(same as above)</td>
<td>(same as above)</td>
</tr>
<tr>
<td><strong>Neurosyphilis</strong></td>
<td>PCN G 4 million U IV Q4 hrs x 14 days</td>
<td>Procaine PCN G 2.4 million U IM + Probenecid 500 mg PO QID x 14 d</td>
</tr>
<tr>
<td><strong>Congenital</strong></td>
<td>PCN G 50,000 U/kg Q8-12 hrs x 14 days</td>
<td>Procaine PCN G 50,000 U/kg IM QD x 14 days</td>
</tr>
</tbody>
</table>

Source: 2010 CDC STD Treatment Guidelines
Syphilis – Management Issues

- **Use standard treatment according to STAGE**
- **Jarisch-Herxheimer Reaction**
  - Systemic reaction to Syphilis THERAPY
  - Can occur at all stages of syphilis (90% of 1°, 2°, 50% others)
  - Self limited; Usually resolves in ≤ 24 hours
  - TX: Supportive care, reassurance
- **Serologic follow-up**
  - Non-treponemal test (RPR/VDRL) day of treatment as baseline
  - Repeat at 3, 6, 9, 12, 18, 24 months
  - Adequate response is 4-fold decline at 12-24 months
Syphilis – Management Issues

• **Partner Screening & Treatment** (in prior 90 days)
  - Screen with Syphilis IgG → RPR if negative
  - Benzathine PCN 2.4 million IU x 1 for ALL
  - Further treatment/evaluation based on individual situation

• **Neurosyphilis**
  - Poorer neurosyphilis treatment response with low CD4, no ARV
  - CNS invasion occurs in early syphilis regardless of HIV or neurologic symptoms (protein, pleocytosis)
  - Clinical significance unknown (HIV+/-)
Evaluation of CNS in Syphilis, HIV+, 2010

• Clinical and CSF consistent with neurosyphilis associated with RPR ≥ 1:32 and/or CD4 ≤ 350
  - Criteria likely sensitive, but non-specific (many negative LPs)
  - Unless neurologic symptoms present, CSF exam has *not been associated with improved clinical outcomes*
  - Guidelines non-directive, LP decision at providers discretion

• Three approaches:
  - LP for all HIV+ patients with syphilis, regardless of stage
  - LP using algorithm based on CD4 and syphilis titer
    • Treat for neurosyphilis if CSF WBC elevated or CSF-VDRL reactive
  - LP only if symptoms/signs indicate CNS involvement

Neurologic/Ophthalmologic Symptoms?

- No

  - HIV?
    - No
      - RPR ≥ 1:32
        - No
          - No LP
        - Yes
          - Consider LP
    - Yes
      - CD4 < 350 or RPR ≥ 1:32
        - No
          - No LP
        - Yes
          - LP

- Yes

25
Syphilis – Summary

• Screening Algorithms may change... check your local listings
• Syphilis Epidemiology has surged in recent years, perhaps fueled by ‘treatment as prevention’
• Treat **ALL** contacts w/Benzathine PCN IM x 1
• Tell your MSM patients about Syphilis epidemic & screen for Syphilis!
• Consider LP in HIV populations with syphilis

Source: PHSKC Sentinel Providers Newsletter 4/2011
**Bonus Case #2**

- **HPI:** 18 year old man presents for routine pre-college physical and to get paperwork signed.
- He has no symptoms, a normal exam, but states he did was treated for Gonorrhea 6 months ago.

- **Current Labs (today):**
  - POSITIVE TP-EIA, POSITIVE TPPA, RPR titer of 1:8

- **Prior Labs (6 months ago):**
  - RPR at STD clinic NEGATIVE

- **Diagnosis:**
  Early latent Syphilis

- **Treatment:**
  Benzathine PCN G 2.4 Million U IM x 1
Bonus Case #3

- **HPI:** 18 year old man presents for routine pre-college physical and to get paperwork signed
- He has no symptoms, a normal exam, and has not been seen at any clinic since becoming sexually active at age 15.
- **Current Labs (today):**
  - POSITIVE TP-EIA, POSITIVE TPPA, RPR titer of 1:8
- **Prior Labs:**
  - None
- **Diagnosis?**
  - Syphilis of Unknown Duration
- **Treatment?**
  - Benzathine PCN G 2.4 Million U IM Qweek x 3