Financial Relationships With Commercial Entities

Dr Augenbraun has no relevant financial affiliations to disclose. (Updated 08/05/20)

Learning Objectives

After attending this presentation, learners will be able to:

- Describe the natural history of syphilis
- Initiate diagnostic work up for syphilis
- Manage syphilis
• spirochete *Treponema pallidum* spp. *pallidum*

• Other treponemal pathogens:
  - *T. pallidum* spp. pertenue (yaws)
  - *T. pallidum* spp. endemicum (bejel)
  - *T. carateum* (pinta)

  Cannot be cultivated in vitro

---

**Syphilis — Rates of Reported Cases by Stage of Infection, United States, 1941–2018**

<table>
<thead>
<tr>
<th>Year</th>
<th>Early Non-Primary</th>
<th>Primary and Secondary</th>
</tr>
</thead>
<tbody>
<tr>
<td>1941</td>
<td>800</td>
<td>500</td>
</tr>
<tr>
<td>1952</td>
<td>400</td>
<td>300</td>
</tr>
<tr>
<td>1963</td>
<td>200</td>
<td>100</td>
</tr>
<tr>
<td>1974</td>
<td>100</td>
<td>50</td>
</tr>
<tr>
<td>1985</td>
<td>50</td>
<td>25</td>
</tr>
<tr>
<td>1996</td>
<td>25</td>
<td>10</td>
</tr>
<tr>
<td>2007</td>
<td>10</td>
<td>5</td>
</tr>
<tr>
<td>2018</td>
<td>5</td>
<td>2.5</td>
</tr>
</tbody>
</table>

* Per 100,000.

NOTE: See section A1.3 in the Appendix for more information on syphilis case reporting.

---

**Primary and secondary syphilis case rates (per 100,000), New York City, 1940-2017**

<table>
<thead>
<tr>
<th>Year</th>
<th>Rate (per 100,000)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1940</td>
<td>80</td>
</tr>
<tr>
<td>1950</td>
<td>60</td>
</tr>
<tr>
<td>1960</td>
<td>40</td>
</tr>
<tr>
<td>1970</td>
<td>20</td>
</tr>
<tr>
<td>1980</td>
<td>10</td>
</tr>
<tr>
<td>1990</td>
<td>5</td>
</tr>
<tr>
<td>2000</td>
<td>2.5</td>
</tr>
<tr>
<td>2010</td>
<td>1.5</td>
</tr>
<tr>
<td>2017</td>
<td>1</td>
</tr>
</tbody>
</table>

*All data non-sensitive*
Primary and Secondary Syphilis — Reported Cases by Sex and Sex of Sex Partners and HIV Status, United States, 2018

ACRONYMS: MSM = Gay, bisexual, and other men who have sex with men; MSW = Men who have sex with women only.

Congenital Syphilis — Reported Cases by Year of Birth and Rates of Reported Cases of Primary and Secondary Syphilis Among Females Aged 15–44 Years, United States, 2009–2018

ACRONYMS: CS = Congenital syphilis; P&S = Primary and secondary syphilis.
Natural History of Syphilis

- Early CNS invasion - clinical implications?
- Acute Symptomatic Meningitis
- Asymptomatic Meningitis
- Meningovascular events
- General Paresis
- Tabes dorsalis
- Gumma
- Ocular and otic

Neurosyphilis should be considered for anyone with serologic evidence of syphilis and neuropsychiatric and/or ocular or otic disease.

Chancre of Primary Syphilis
Ocular Syphilis

- Eye involvement occurs most frequently in secondary syphilis and late syphilis.
- Almost every part of the eye can be involved.
- The vast majority of eye problems associated with syphilis are also associated with many other infectious and non-infectious diseases.
- Therefore, there are almost no eye findings that are absolutely specific for syphilis.
Following April 2015 report, eight jurisdictions (CA, FL, IN, MD, NYC, NC, TX, WA) reviewed syphilis surveillance and case data.

- 388 suspected ocular syphilis were identified: 157 in 2014 and 231 in 2015 (0.53% and 0.65%)
- 93% men (high proportion MSM), 51% HIV co-infected
- 64% had symptoms; 54% blurry vision; 28% vision loss
- 15% had a specific dx: Uveitis (n=72); retinitis (n=20), optic neuritis (n=18) and retinal detachment

- Of 136 patients with available data, 64 (47%) had one eye involved and 72 (53%) had both eyes involved.
- 174 had CSF results, 122 (70%) had +CSF VDRL.

**Diagnostics:**

**Traditional Serologic Testing**

**Two-step testing:**

- **NTST:** Non-Treponemal Serologic Test (e.g. RPR, VDRL)
  - can be quantified
  - rises with active disease or failed therapy
  - declines with successful therapy or latency

- **TST:** Treponemal Serologic Test (e.g. FTA, TPPA, Treponemal IgG)
  - not quantifiable
  - life long reactivity
Treponemal Serologic Tests (TSTs) as Screening Tests- 'Reverse Algorithm'

- EIA (T. pallidum sonicate or recombinant antigen)
- Low cost, automation, standardization etc.
- More sensitive and more specific than traditional NTSTs
- Doesn't distinguish new, old, treated or untreated
- Recent CAP survey: 63% used traditional algorithm (Rhoads et al Arch Pathol Lab Med 2017)

Testing and Treatment Approach

EIA Reactive

RPR Reactive

TPTA R

TPPA R

BFP

Unless previously treated
Stage and Rx by CDC recs

CDC Syphilis Screening Recommendations

- All pregnant women at 1st prenatal (early)
- Retest at 28 weeks and at delivery if high risk
- MSM at least annually
- MSM every 3-6 months if high risk
- HIV if sexually active at first visit and annually
- HIV more frequently if high risk
From: Increased Syphilis Testing of Men Who Have Sex With Men: Greater Detection of Asymptomatic Early Syphilis and Relative Reduction in Secondary Syphilis


To Treat is First to Stage

- **Primary, Secondary and Early Latent**
  Benzathine penicillin 2.4million units IM once (Jarisch-Herxheimer Rxn)

- **Late Latent and Latent of Unknown Duration**
  Benzathine penicillin 2.4million units IM once weekly for three weeks

- **Late Tertiary Syphilis Except Neurosyphilis**
  R/O Neurosyphilis then same as latent syphilis
  *Intervals between weekly doses optimally no more than 7-9 days.
  In pregnancy definitely no missed doses!*

  *Pregnant women and HIV+ pts get standard therapies.

Alternatives to Penicillin

- **Tetracyclines (Doxycycline)**
  Two weeks for early or four weeks for latent

- **Ceftriaxone**
  - Dose and duration unclear

  *There are no alternatives to penicillin in pregnancy*
**Who needs an LP to Rule Out Neurosyphilis?**

- "If you think about doing an LP then do an LP"
- Diagnosis requires CSF evaluation
- CDC STD Rx Guideline:
  - neurologic or ophthalmic signs or symptoms,
  - evidence of active tertiary syphilis (e.g., aortitis and gumma),
  - treatment failure-definition?
  - HIV: RPR>1:32 and/or CD4 <350???

---

**CSF Abnormalities**

- CSF VDRL-highly specific, variably sensitive
- CSF WBC-lymphocytic pleocytosis/ not specific in HIV+
- CSF protein elevations
- CSF FTA-ABS-sensitive, not approved for this use
- PCR?
- Cytokines?

---

**Neurosyphilis Treatment**

- Aqueous PCN G 18-24mu qd in divided doses for 10-14 days (follow with Rx for latent)
- Alternative: Procaine PCN G 2.4mu IM daily + probenecid 500mg po qid 10-14days
- Ceftriaxone- dose? Duration?
- Doxycycline?
- Ocular Syphilis- treat as NS with or without +CSF findings but LP should be done to follow if abnormal
- Partner notification
- HIV testing
- Two fold declines in non treponemal serologic test like the RPR over 3-6m early and 12-24m in latent
- Some titers never go away
- Some titers don't decline properly
- CSF WBC should resolve 3-6 months, VDRL over a much longer period
- CSF usually normal if the RPR becomes non reactive.