Syphilis: A Case-based Review

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Percent Sensitivity by Stage of Untreated Syphilis

Adapted from Atlas of Sexually Transmitted Diseases and AIDS. S. Morse, A. Moreland, K. Holste, K. Taylor

Serologic Interpretation

RPR NonReactive / FTA-ABS NonReactive
No Syphilis Diagnosis
Incubating syphilis infection

RPR NonReactive / FTA-ABS Reactive
Very Early Primary Syphilis
Secondary Syphilis w Prozone
Late untreated syphilis w sero-reversal of RPR
History of Treated Syphilis
Syphilis Xrd inadvertently in past
False-negative Non-Treponemal test
False-positive Treponemal Test (rare)

RPR Reactive / FTA-ABS NonReactive
Biologic False Positive
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RPR Reactive / FTA-ABS Reactive
Positive Syphilis Diagnosis
Lyme disease
Endemic (non-sexual) treponemal ds

BIOLOGIC FALSE POSITIVE REACTIONS CAUSES

ACUTE (< 6 months)

Physiologic
Pregnancy
Vaccinations
Smallpox
Typhoid
Yellow fever
Acute Infections (e.g.)
Herpes variola-zoster
Herpes simplex
Infectious mononucleosis
Measles
Mumps
Viral hepatitis
HIV sero-conversion illness
Pneumonia (incl. Mycoplasma)
Lyme disease

CHRONIC > 6 months

Physiologic
Older age
Chronic Infection (e.g.)
Tuberculosis
Lymphogranuloma venereum
Malaria
HIV/AIDS
Autoimmune Disorders (e.g.)
Lupus
Rheumatoid arthritis
Autoimmune thyroiditis
Other Conditions (e.g.)
Malnutrition
Malignancy
Hepatic cirrhosis

Genital Ulcer Disease

The Usual Suspects

Genital Herpes - Herpes Simplex Virus type 1 & 2
Primary Syphilis - Treponema pallidum
Chancroid - Haemophilus ducreyi
Lymphogranuloma Venereum (LGV) - C. trachomatis
Donovanosis - Klebsiella granulomatis

Candidiasis/Balanitis
Aphthous major
Bectel's disease
Fixed Drug Eruption
Stevens Johnson Syndrome

Lichen Planus (Erosive)
Erythema Multiforme
Reiter's Syndrome
Trauma
Cancer - Squamous Cell
Diagnosis of Chancroid

• Clinical Diagnosis: Bubo c/ painful ulcers
• Important to rule out Syphilis and HSV

Chancroid (Haemophilus ducreyi)

• Gram negative coccobacillus with short incubation (3-10 days, average ~5)
• Endemic in regions of sub-Saharan Africa, SE Asia, India, South America, Caribbean
• Men typically present with genital ulceration
• Women usually present w/ non-ulcerative symptoms (Vaginal discharge or bleeding; pain with defecation/urination/sex; ulcers are usually sub-clinical)
• Painful Adenitis in 40-50% cases (80% of Syphilis)
• Systemic symptoms generally absent
LGV: Clinical Presentation

- **Primary lesion**
  - small non-painful genital papule at site of inoculation after an incubation period of 3 – 30 days, can ulcerate
  - May remain undetected in rectum, vagina

- **Secondary clinical manifestations**
  - 2-6 weeks after primary lesion
  - Tender inguinal, femoral adenopathy, Uni- or bilateral, may progress to fluctuance (buboes)
  - Proctitis or proctocolitis associated with receptive anal intercourse, often times hemorrhagic

- **Tertiary complications**
  - Lymphoedema, abscesses, granulomas, strictures

LGV: Treatment

- Consider Presumptive Treatment for LGV
  - Anal receptive sex and signs/symptoms of proctitis especially among MSM
  - Chlamydia + anorectal specimen: S/Sx proctitis or HIV+ status
  - Genital ulcer with extensive lymphadenopathy

- Doxycycline 100mg PO BID x 21 days (preferred)
- Azithromycin 1g PO q week x 3 weeks (lacking clinical data, but probably effective)

Characteristics of Ulcerating Genital Infections

<table>
<thead>
<tr>
<th></th>
<th>Syphilis</th>
<th>HSV</th>
<th>Chancroid</th>
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<tbody>
<tr>
<td>Number</td>
<td>Single (60%)</td>
<td>Multiple</td>
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</tr>
<tr>
<td>Edges</td>
<td>Well demarcated</td>
<td>Erythematous</td>
<td>Irregular</td>
</tr>
<tr>
<td>Round/Oval</td>
<td></td>
<td>Cratered</td>
<td>Undermined</td>
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<tr>
<td>Depth</td>
<td>Variable</td>
<td><strong>Superficial</strong></td>
<td>Deep/Excavated</td>
</tr>
<tr>
<td>Base</td>
<td>Clean</td>
<td>Min. Vascular</td>
<td>Serous</td>
</tr>
<tr>
<td>Induration</td>
<td>+</td>
<td>-</td>
<td><strong>PURULENT</strong></td>
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<td>Min. Vascular</td>
<td>Vascular/Friable</td>
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<tr>
<td>Painful</td>
<td>-</td>
<td>+/-</td>
<td>+++</td>
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<tr>
<td>Nodes</td>
<td>Firm</td>
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<td><strong>Fluctuant</strong></td>
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Syphilis Staging

**Primary**
- Muco-cutaneous Ulceration

**Secondary**
- Localized or Diffuse Cutaneous Eruption
- Mucous Patches
- Condyloma Lata
- Patchy Alopecia

**Latent**
- Asymptomatic at Treatment
MANY OF THESE CLINICAL PHOTOS HAVE BEEN MADE AVAILABLE FROM NYU DEPARTMENT OF DERMATOLOGY
Differential Diagnosis of Secondary Syphilis

- Pityriasis Rosea
- Drug eruption
- Viral exanthem
- Acute HIV
- Sarcoidosis (annular lesions)

- Any Rash of Unknown Origin, especially with systemic complaints
Syphilis Staging: Latent Infection

Any of the following during the 12 months prior to Dx = EARLY LATENT

Any of the following > 12 months prior to Dx = LATE LATENT

- Unequivocal Signs/Symptoms
- Serologic Conversion
- Exposure to an infectious case
- Four-fold (2 dilution) rise in titer in a previously treated patient
- Only possible exposure

Relevance of Accurate Staging of Syphilis Infection

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<td>Currently Infectious ?</td>
<td>YES</td>
<td>Possible</td>
<td>No</td>
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| Duration of Rx | Bicillin LA IM x1  
Doxy PO x 2 weeks | Bicillin LA IM x3  
Doxy PO x4 weeks |
| Management of Sexual Contacts | Previous 3 months | Previous 6 months | Previous 12 months |
| Serologic Response to Rx | RPR titer: 2 dilutions in 6 - 12 months | If RPR >= 1:32: 2 dilutions in 12 - 24 months |

If HIV+: ?LP

New in 2010 CDC Rx Guidelines
Treatment Regimens

Syphilis – Issues Underscored in 2010 CDC Treatment Guidelines

• Must ensure use of Bicillin LA (not C-R)
• Azithromycin (2g oral) not recommended
• Ceftriaxone possible alternative to PCN based on limited clinical studies
  – risk allergic cross-reactivity
  – optimal dose not defined
• Caution- Any non-PCN regimen in HIV+

Based on 2010 CDC Treatment Guidelines

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Response to Therapy by Syphilis Stage

* Primary, Secondary Syphilis
  Resolution of symptoms
  By 6-12 months- Fall in RPR titer by 2 titers

* Early Latent, Late Latent Syphilis
  If RPR titer < 1:32 -
  Fall in RPR titer by 2 titers within 12-24 months

??? HIV-infected Patients

Approach to Inadequate Serologic Response to Treatment

• Evaluate for possible re-infection
• Re-screen for HIV
• Consider suboptimal treatment
  –Incorrect staging of infection
  –Non-compliance with oral therapy
• Rule out Neurosyphilis (CSF exam)
• Re-treat with Bicillin 2.4 mU IM x 3
Latent Syphilis: Indications for CSF Exam

- Neurologic or Ophthalmic Signs/Symptoms
- Evidence of Active Tertiary (aortitis, gumma)
- Inadequate Serologic Response to Treatment
- HIV+ with Late Latent or Latent Unknown Dur.

HIV+ patients
- RPR $\geq 1:32$
- CD4 $\leq 350$

Although associated with clinical and CSF abnormalities consistent with neurosyphilis, no data that CSF exam improved outcomes

Treatment: 3 mo. 6 mo. 9 mo. 12 mo. 1.5 yrs

1:128 1:64 1:32 1:16 1:8 1:4 1:2 1:1

SEROFAST RPR

Initial EIA Treponemal Test

No syphilis diagnosis
(Recent infection cannot be ruled out)

Syphilis (old or new)
- No Hx: Rx
- Hx of Syphilis: reRx if ↑ titer

? Old Rxed Syphilis
If no known Hx Rx

2nd Treponemal Test
(FTA-ABS; TP-PA)

No Rx or use a 3rd treponemal test as a ‘tie-breaker’
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**RPR (Rapid Plasma Reagin) Test**

- Antibody (Patients Serum)
- Test Antigen
- Chromagen

**FTA-ABS (Fluorescent Treponemal Ab Absorption)**

- Antibody (Patients Serum)
- Treponema pallidum Test Antigen
- Fluorescein-conjugated Animal Antiserum to Human Antibody
- Chromagen