Syphilis in the 21st Century: Sex, Sores, Science, and Surveillance

Syphilis in Men

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Conflict of Interest Disclosure

• None
42-year-old man in San Francisco

- Sex partners are men
- HIV-negative
- Taking PrEP
- Painless penile sore for one day
- Laboratory testing (standing orders) for HIV, syphilis, and pharyngeal, rectal, and urine tests for gonorrhea and chlamydia: all negative
- Sees primary care physician
In primary care...

- Empiric HSV treatment with valacyclovir
- HSV PCR: negative
- Existing sore persists
- Another sore develops
- PCP refers to dermatology
One week later...

- Two painless ulcers
- Exam: Indurated, non-tender
- Skin/mucous membranes otherwise WNL
What’s the best next step in evaluation and management?

1. Repeat HSV PCR
2. Repeat HSV PCR and continue empiric treatment for HSV
3. Repeat serologic test for syphilis
4. Repeat serologic test for syphilis and empiric treatment for syphilis
5. Skin biopsy with special stain for *T. pallidum*
Empiric treatment for primary syphilis
Repeat syphilis serology
  - *T. pallidum* enzyme immunoassay: reactive
  - RPR: reactive, 1:1 titer
Case reported to San Francisco Department of Public Health
Clinical follow up: ulcers healed one week later
Learning points from case

1. Sensitivity of serologic tests
2. Chancres
3. Epidemiology
4. Treatment
5. Public health
Learning points from case

1. Sensitivity of serologic tests
2. Chancre
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Sensitivity of serologic tests for syphilis: Window period

This case

Sensitivity of serologic tests for syphilis: Prozone reaction

- Excessive antibody interferes with nontreponemal test performance (RPR, VDRL)
- Dilute serum to overcome prozone reaction
- Does NOT apply to treponemal tests (EIA, TPPA, TPHA)
- Typically occurs in secondary syphilis with substantial disease

- VDRL initially nonreactive
- After dilution, 1:64 titer
- Treponemal test reactive
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Single chancre — penis

Common locations on penis
• Near frenulum
• Foreskin
Multiple chancres — penile
Differential diagnosis: Penile chancres

• Infectious
  – Viral (HSV, zoster)
  – Bacterial (*S. aureus*)
  – Chancroid (N=7 in USA in 2017)
  – Granuloma inguinale — rare
  – LGV — rare cause of genital ulcer disease; proctocolitis among MSM

• Inflammatory
  • Behçet disease, fixed drug eruption, psoriasis, lichen planus

• Trauma, including factitial

• Neoplastic

https://www.cdc.gov/std/stats17/tables/43.htm; https://www.cdc.gov/std/stats17/other.htm
Chancre — extragenital
Learning points from case

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Syphilis — Rates of Reported Cases by Stage of Infection, United States, 1941–2017

NOTE: Data collection for syphilis began in 1941; however, syphilis became nationally notifiable in 1944. Refer to the National Notifiable Disease Surveillance System (NNDSS) website for more information: https://wwwn.cdc.gov/nndss/conditions/syphilis/.
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Men
- 88% of cases overall
- 58% of cases overall
- 80% of cases among men

MSM
- 58% of cases overall
- 80% of cases among men

30,644
Syphilis in the United States: on the rise?

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Stonewall riot: June, 1969
First report of AIDS: June, 1981
HAART: July, 1996

Rate, per 100,000 population

Year

MSM
MSW
Women

Effective HIV treatment
PrEP
Internet and hook-up apps
Methamphetamine and other drug use

Ask about gender(s) of sex partner(s)!

• 4 cases in men who have sex with men
• All with visual symptoms
  – Vision loss, flashing lights, blurry vision → uveitis
  – No other symptoms or signs of syphilis
Clinical Advisory: Ocular Syphilis in the United States

Updated March 24, 2016

200 cases reported over the past 2 years from 20 states

What to do?

- All patients: neurologic, ocular, and otic review of systems
- No ocular symptoms: neuro exam including all cranial nerves
- Ocular symptoms: ophthalmology evaluation, consider LP
- Neuro or otic symptoms: neuro evaluation, consider LP
- Treat neuro, ocular and otic syphilis according to neurosyphilis guidelines
- Report cases to health department
Neurosyphilis

**Early Neurosyphilis: Review of Systems** *(pertinent positive symptoms)*

**GENERAL/CONSTITUTIONAL:** headache, fever, fatigue, weakness, dizziness

**HEAD, EYES, EARS, NOSE AND THROAT:**
- Eyes: pain, redness, loss of vision, double or blurred vision, photophobia, flashing lights or spots
- Ears: ringing in the ears, loss of hearing

**GASTROINTESTINAL:** nausea, vomiting

**MUSCULOSKELETAL:** neck pain/stiffness, muscle weakness

**NEUROLOGIC:** headache, dizziness, muscle weakness, confusion, loss of consciousness, seizures, difficulty speaking

**PSYCHIATRIC:** confusion

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**Early Neurosyphilis: Focused Neurologic Exam**

- **Cranial Nerve Exam:** assess for cranial nerve palsies (key maneuvers in bold)
  - II: visual acuity, visual fields
  - II, III: pupillary reactions to light and accommodation
  - III, IV, VI: extraocular movements, inspect for ptosis
  - V: corneal reflexes and jaw strength/movements, facial sensation
  - VII: facial movements (raise eyebrows, frown, tightly close eyes, show teeth smile, puff out both cheeks)
  - VIII: hearing (rub fingers together)
  - IX: swallowing, gag reflex, rise of palate
  - V, VII, X, XII: voice and speech
  - XI: trapezius muscle inspection & shoulder shrug
  - XII: inspection of tongue and lateral movement of tongue while protruded

- **Motor:** assess for weakness/hemiplegia
  - Muscle strength testing upper and lower extremities

- **Nuchal Rigidity Testing:** assess for meningeal inflammation
  - Chin to chest- stiffness/pain with flexion of neck, flexion of hips and knees in response to neck flexion (Brudzinski's sign)
  - Jolt accentuation maneuver- worsening of headache when patient rotates head rapidly from side to side

- **Deep Tendon Reflexes:** assess for hyperreflexia
  - Biceps
  - Supinator
  - Knee
  - Ankle

Indications for CSF Examination (CDC)

- Neurologic, otologic, or ophthalmic signs or symptoms
- Suspected treatment failure
- Evidence of active tertiary syphilis

- Does not depend on HIV infection status or on titer


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Percentage of men who have sex with women only reporting selected behaviors

https://www.cdc.gov/mmwr/volumes/68/wr/mm6806a4.htm?s_cid=mm6806a4_w
Percentage of men who have sex with women only reporting selected behaviors

- Rates even higher among women
- Rates highest in Western USA
- Not seen among MSM

https://www.cdc.gov/mmwr/volumes/68/wr/mm6806a4.htm?s_cid=mm6806a4_w
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Treatment of primary, secondary, and early non-primary non-secondary syphilis without neurosyphilis in adults

- Benzathine penicillin G 2.4 million units intramuscular, single dose

- Penicillin-allergic patients
  - Non-Pregnant: Doxycycline 100 mg orally twice per day for 14 days
  - Pregnant: Desensitize, treat with benzathine penicillin G 2.4 MU IM x 1 (or 2)


Jarisch-Herxheimer reaction

- Flu-like reaction within 24 hours of treatment
- Triggered by cytokine release as treponemes die
- Typically seen with higher titers
- Warn patients!

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Public health and syphilis prevention and control

• How public health can help physicians
  – Prior titers and treatment verification
  – Follow up and partner notification
  – Consultation in complicated clinical cases
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- How physicians can help public health
  - Physicians must report cases (even if lab reports)
  - Provides useful clinical information (staging) that helps prioritize follow up
  - Inform patient that health department might follow up
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