

The Great Imitator Revealed: Syphilis

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Learning Objectives

After attending this presentation, learners will be able to:

- List the differential diagnosis of an anogenital ulcer
- Describe the preferred treatment for syphilis by stage
- Cite at least 3 means of syphilis prevention

Case

44 year old man with new
painless lesion near his
anus



Had a new sex partner 2
weeks ago

Anogenital Ulcer Differential Diagnosis

Sexually transmitted diseases

- Primary syphilis
- Genital herpes
- Chancroid

Other

- Fixed drug reactions
- Staph/ strep infections
- Autoimmune conditions
- Trauma
- Malignancy



1000x darkfield microscopy

Treponema pallidum pallidum, bacterial spirochete

Primary syphilis – penile chancres



ARS Question 1: What is best treatment?

1. Amoxicillin 500 mg PO TID x 10 days
2. Benzathine PCN-G 2.4 MU x 1
3. Benzathine PCN-G 2.4 MU x 3
4. Doxycycline 100 mg PO BID x 14 days
5. Ceftriaxone 250 mg IM once

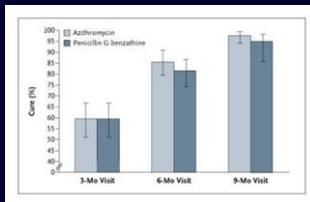
Injectable Penicillin G Benzathine Treatment of Choice for Primary Syphilis

- Single intramuscular injection penicillin G benzathine 2.4 MU
- Prophylactic treatment:
 - Syphilis case contacts < 90 days
- Notify partners up to 3 months



CDC STD Treatment Guidelines, 2015

Penicillin G benzathine cures syphilis



N=328, 52% HIV+, Tanzania

Riedner, G. et al. NEJM, 2005

Case

- 24 yo male with new onset of rash on chest and back, recently started on ART (ABC/3TC/DTG), has one regular partner





Differential Diagnosis: Generalized Rash

- Trunk rash
 - Secondary syphilis
 - Viral exanthem, *including acute HIV infection*
 - Pityriasis rosea
 - Drug eruption
 - Lichen planus
 - Psoriasis
 - Sarcoidosis
- Palmoplantar rash
 - Secondary syphilis
 - Erythema multiforme
 - Rocky Mountain spotted fever

Secondary syphilis: split papules, "moth-eaten" alopecia, mucous patches, and condyloma lata



Case

- RPR 1:16
- TPPA positive

ARS Question 2: What is best treatment?

1. Amoxicillin 500 mg PO TID x 10 days
2. Benzathine PCN-G 2.4 MU x 1
3. Benzathine PCN-G 2.4 MU x 3
4. Doxycycline 100 mg PO BID x 14 days
5. Doxycycline 100 mg PO BID x 28 days

Injectable Penicillin G Benzathine Treatment of Choice for Secondary Syphilis

- Single intramuscular penicillin G benzathine
- Prophylactic treatment:
 - Syphilis case contacts < 90 days
- Notify partners up to 6 months



CDC STD Treatment Guidelines, 2015

Epidemiology

CDC: STD rates skyrocketing in United States

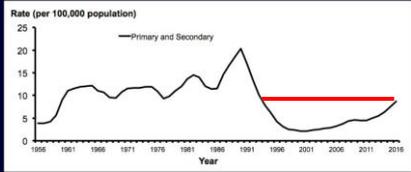
Syphilis rates are on the rise, and dating apps may be playing a role, experts say

Search: USA TODAY | Published 10:00 a.m. ET July 11, 2017 | Updated 10:40 a.m. ET July 11, 2017

Syphilis Rises Sharply Among Newborns

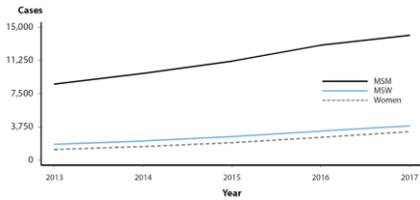
Along with an increase in adult infections, the rate of infants born with the disease has reached a 20-year high.

New Cases of Syphilis at Highest Rate Since 1994



Kojima and Klausner, Curr Inf Dis Reports, 2018

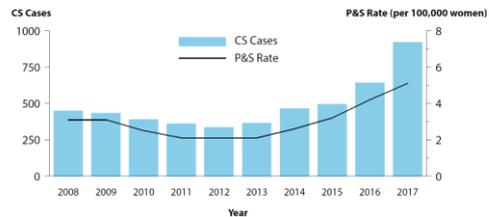
Primary and Secondary Syphilis — Reported Cases by Sex and Sexual Behavior, 37 States*, 2013–2017



* 37 states were able to classify >70% of reported cases of primary and secondary syphilis as either MSM, MSW, or women for each year during 2013–2017.
ACRONYMS: MSM = Gay, bisexual, and other men who have sex with men (collectively referred to as MSM); 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 Women Aged 15–44 Years, United States, 2008–2017



ACRONYMS: CS = Congenital syphilis; P&S = Primary and secondary syphilis.



Case

- 32 HIV-infected male, on HAART for 2 years, virologically suppressed
- New to your office with RPR reactive at 1:32, TPPA reactive
- Asymptomatic without any lesions or rash

ARS Question 3: What stage is this case?

1. Primary
2. Secondary
3. Latent, early
4. Latent, late
5. Latent, unknown duration

ARS Question 4: What is best treatment?

1. Amoxicillin 500 mg PO TID x 10 days
2. Benzathine PCN-G 2.4 MU x 1
3. Benzathine PCN-G 2.4 MU x 3
4. Doxycycline 100 mg PO BID x 14 days
5. Doxycycline 100 mg PO BID x 28 days

Injectable Penicillin G Benzathine Treatment of Choice for Latent Syphilis, Unknown Duration

- Intramuscular injection 2.4 MU benzathine penicillin weekly x 3
- Prophylactic treatment:
 - Syphilis case contacts < 90 days
- Notify partners up to 12 months



CDC STD Treatment Guidelines, 2015

Latent syphilis

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All Those Syphilis Tests

- **Non-treponemal tests (RPR, VDRL)**
 - Detects antibody to cardiolipin
 - Rise and fall with infection and treatment over time
 - 4-fold change in titer (1:2 to 1:8 or 1:64 to 1:16) is significant
 - Specificity = 98% (false-positives in IDU, auto-immune, etc)

Klausner, Current STD Diagnosis and Management 2007

All Those Syphilis Tests

- Treponemal tests (TPPA, FTA-Abs, TP EIA, rapid TP)
 - Detects antibody to Treponemal antigen
 - More sensitive and develop earlier but positive for “life” (85%)
 - Indicate past or current infection

Klausner, Current STD Diagnosis and Management 2007

Case

- 44 year old HIV-infected female, occasionally exchanges sex for money or drugs
- C/o 1 week headache, ringing in right ear with some hearing loss
- RPR 1:16, TPPA reactive

ARS Question 5: CSF analysis is necessary

1. Strongly agree
2. Moderately agree
3. Do not know
4. Disagree
5. Strongly disagree

Indications for CSF Analysis

- Neurological findings
- Ocular abnormalities
- Tertiary disease (dementia, aortic, gumma)
- Treatment failure
(lack of 4-fold decline at 6, 12 or 24 m)

CDC STD Treatment Guidelines, 2015

ARS Question 6: What is best treatment for neurosyphilis?

1. IV penicillin G 18-24 MU x 14 days
2. IV ceftriaxone 1 gm daily x 10 days
3. Doxycycline 100 mg PO BID x 14 days
4. IV penicillin G 18-24 MU 14 days PLUS penicillin G benzathine 2.4 MU IM on day 14

Syphilis and HIV infection

- Multiple chancres
- May present with overlapping primary and secondary manifestations
- Rarely abnormal serology but slower decline
- Increased risk early neurosyphilis

Zetola and Klausner, Clin Inf Dis 2007

Syphilis increases HIV viral load and decreases CD4 cell counts in HIV-infected patients with new syphilis infections

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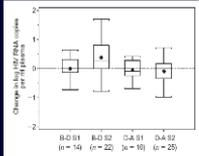


Fig. 1. Changes in HIV viral load associated with syphilis infection and syphilis treatment, according to the stage of syphilis. B-D, Before-to-during; D-A, during-to-after; S1, primary syphilis; S2, secondary syphilis. Boxplots show median and upper and lower quartiles, whiskers encompass the extent of the data. Means are represented by filled circles.

AIDS, 2004

Prevention

- Individual level
 - Reduce exposure
 - Reduce risk of infection after exposure
 - Reduce sequelae of infection
- Population level
 - ↓ R_0 (reproductive number)
 - Reduce duration of infection

Screening, Treatment and Partner Services



CDC Screening Recommendations for Syphilis

- **Pregnancy**
 - First visit
 - Repeat at 28-32 weeks in high-prevalence areas
- **Men who have sex with men**
 - Every year
 - More frequently (**every 3 months**) if
 - > 1 partner past 12 months
 - Meet partners online or in sex venues
 - Have sex in conjunction with illicit drug use (especially methamphetamine)
 - Have sex partners who participate in those activities

CDC STD Treatment Guidelines, 2015

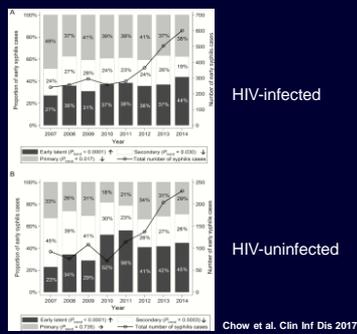


San Francisco, early 2000s



San Francisco, 2005

Increased Testing Associated with Decreased Secondary Syphilis, Australia, 2007-2014



Question-and-Answer

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