The Ongoing Syphilis Epidemic
Among Men Who Have Sex With Men (MSM)

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Conflict of Interest Disclosure

• Prevention Health Labs, Inc.: Co-Founder
• Arrowhead Pharmaceuticals Corp.: Shareholder
• Synta Pharmaceuticals, Inc.: Shareholder
• Madrigal Pharmaceuticals, Inc.: Shareholder
Ongoing Syphilis Epidemic Among MSM

- Defining epidemiologic terms
- Epidemiology of syphilis among MSM in the United States
- Is the epidemic real?
- Public health approaches to syphilis prevention and control
Defining epidemiologic terms
Looking at syphilis

Laboratory  Clinic  Population

Syphilis — Rates of Reported Cases by Stage of Infection, United States, 1941–2015

RATES (per 100,000 population)

Total Syphilis

Early Latent

Primary and Secondary

Year
Syphilis from a population health perspective

[Image: Syphilis — Rates of Reported Cases by Stage of Infection, United States, 1941–2015]

- **Total Syphilis**
- **Early Latent**
- **Primary and Secondary**

**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://www.cdc.gov/ndss/conditions/syphilis/](https://www.cdc.gov/ndss/conditions/syphilis/)

[https://www.cdc.gov/std/stats15/slides.htm](https://www.cdc.gov/std/stats15/slides.htm)
## Epidemiologic terms

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Surveillance for Cancer Incidence and Mortality — United States, 2013

Incidence rates by ethnicity, all cancer sites combined, female — United States, 1999–2013

*Endemic*
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HIV Surveillance – Men Who Have Sex with Men (MSM) through 2015

Diagnoses of HIV Infection among Male Adults and Adolescents, by Transmission Category, 2010–2014—United States and 6 Dependent Areas

Note: Data include persons with a diagnosis of HIV infection regardless of stage of disease at diagnosis. Data have been statistically adjusted to account for missing transmission category. “Other” transmission category not displayed as it comprises less than 1% of cases.

Heterosexual contact
Injection drug use (IDU)
Male-to-male sexual contact and IDU

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Estimates of New HIV Infections in the United States

Figure 1. Estimated New HIV Infections, Extended Back-Calculation Model, 1977–2006, Overall


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Epidemic

Hyper-endemic (?)

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FIGURE. Number of confirmed and probable cases of mumps (N = 317) on the University of Illinois at Urbana-Champaign campus, by month of onset — Illinois, April 2015–May 2016

Abbreviation: MMR = measles, mumps, rubella.

https://www.cdc.gov/mmwr/volumes/65/wr/pdfs/mm6529a2.pdf
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Ebola Virus Disease — Sierra Leone and Guinea, August 2015

Figure 1. Reported number of confirmed Ebola virus disease cases, by World Health Organization reporting week — Guinea and Sierra Leone, February 2014–August 2015

https://www.cdc.gov/mmwr/pdf/wk/mm6435.pdf
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<td>Cluster</td>
<td>Aggregation of cases grouped in place and time suspected to be greater than the number expected, even though the expected number may not be known</td>
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FIGURE. Number of persons (N = 242) infected with human immunodeficiency virus, by date of diagnosis — Roka Commune, Cambodia, November 9, 2014–February 28, 2015

Abbreviations: HIV = human immunodeficiency virus; NCHADS = National Center for HIV/AIDS, Dermatology and Sexually Transmitted Diseases; TB = tuberculosis.

https://www.cdc.gov/mmwr/volumes/65/wr/pdfs/mm6506a2.pdf
In December 2014, health authorities reported 30 HIV cases in a commune where only four had been reported during the preceding year....
Epidemiology of syphilis among MSM in the USA
Primary and secondary cases

- 1999: 6,617
- 1999: National Plan to Eliminate Syphilis
- 2000: 5,979
- 2015: 23,872

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://www.cdc.gov/nndss/conditions/syphilis/.
Primary and Secondary Syphilis — United States, 2005–2013

- MSM
  - Percent of all cases: 76%
  - Percent of male cases: 84%

http://www.cdc.gov/mmwr/pdf/wk/mm6318.pdf
Syphilis in the United States: on the rise?

Thomas A Peterman*, John Su, Kyle T Bernstein and Hillard Weinstock
Division of STD Prevention, National Centre for HIV, Hepatitis, STD, and TB Prevention, Centers for Disease Control and Prevention, Atlanta GA, USA
Author for correspondence: tap1@cdc.gov

B

Syphilis elimination plan: October 1999

Year

Cases


MSM
Women
MSW

• Methamphetamine use: 19%
• Use of Internet to meet sex partner(s): 36%
• Meth and Internet users had more sex partners than non-users
High rates of co-infection among MSM

- MSM with P&S syphilis at STD clinics
- HIV co-infection in 21%–59%

Pre-exposure prophylaxis for HIV (PrEP)

- 2010: NEJM publishes iPrEx trial
- 2012: FDA approves PrEP
- 2015: High rates of STDs among MSM on PrEP in California (but no new HIV infections!)

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

http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm312210.htm;
Repeat syphilis among MSM — California

Risk Factors for Repeat Syphilis in Men Who Have Sex With Men, San Francisco

- 7% within 1 year
- ↑ among MSM with HIV

Repeat Syphilis Among Men Who Have Sex With Men—San Diego County, 2004–2009

- 12% within 2 years
- ↑ among MSM with HIV


- 6% within 2 years
- ↑ among MSM with HIV, Black MSM, MSM with multiple sex partners

Sophie Woolston, MD; Stephanie E. Cohen, MD; Robyn N. Fanfair, MD; Sarah C. Lewis, MD; Christina M. Marra, MD; Matthew R. Golden, MD

- Seattle: 4 cases; all among MSM
- San Francisco: 8 cases; six among MSM

https://www.cdc.gov/mmwr/pdf/wk/mm6440.pdf
388 cases (0.6% of total syphilis cases)
69% MSM
51% living with HIV
28% with primary or secondary syphilis
22% had other neurosyphilis symptoms
Symptoms: blurry vision (64%), vision loss (33%), eye pain or red eye (14%)

https://www.cdc.gov/mmwr/volumes/65/wr/pdfs/mm6543a2.pdf
Clinical Advisory: Ocular Syphilis in the United States

• Screen syphilis patients for visual complaints
• Test all syphilis patients for HIV if not known to be HIV-positive
• Perform neuro exam including cranial nerves in all syphilis patients
• Refer syphilis patients with ocular complaints for ophtho exam and LP
• Treat ocular syphilis according to neurosyphilis recommendations
• Report ocular syphilis cases to health department within 24 hours

https://www.cdc.gov/std/syphilis/clinicaladvisoryos2015.htm
Is the epidemic real?
Is the epidemic real?

- Have case definitions changed?
- Has type of surveillance changed (active vs. passive)?
- Has effectiveness of surveillance changed?
- Have reporting requirements changed?
- Have screening guidelines changed?
- Have testing technologies changed?
Is the epidemic real?

• Have case definitions changed?

Syphilis, secondary

Clinical description

A stage of infection caused by T. pallidum characterized by localized or diffuse mucocutaneous lesions (e.g., rash — such as non-pruritic macular, maculopapular, papular, or pustular lesions), often with generalized lymphadenopathy. Other symptoms can include mucous patches, condyloma lata, and alopecia. The primary ulcerative lesion may still be present. Because of the wide array of symptoms possibly indicating secondary syphilis, serologic tests for syphilis and a thorough sexual history and physical examination are crucial to determining if a case should be classified as secondary syphilis.

Laboratory criteria for diagnosis

• Demonstration of T. pallidum in clinical specimens by darkfield microscopy, or by polymerase chain reaction (PCR) or equivalent direct molecular methods

Case classification

Probable: a case that meets the clinical description of secondary syphilis with a nontreponemal (VDRL, RPR, or equivalent serologic methods) titer ≥4 AND a reactive treponemal test (FTA-ABS, TP-PA, EIA, CIA, or equivalent serologic methods).

Confirmed: a case that meets the clinical description of secondary syphilis (with at least one sign or symptom) that is laboratory confirmed

Is the epidemic real?

- Have case definitions changed?

Syphilis surveillance case definitions revised in 2013

Examples:
- Physician diagnosis no longer establishes a case — must meet the surveillance case definitions
- "Secondary syphilis" now requires BOTH a reactive treponemal test AND a nontreponemal titer ≥4

Is an epidemic real?

• Have case definitions changed?
• Has type of surveillance changed?
  – Active surveillance: health agency solicits reports
  – Passive surveillance: data are sent to the health agency without prompting

https://www.cdc.gov/OPHSS/CSELS/DSEPD/SS1978/Glossary.html#surveillanceActive
Is an epidemic real?

- Have case definitions changed?
- Has type of surveillance changed?
- Has effectiveness of surveillance changed?
Is an epidemic real?

- Have case definitions changed?
- Has type of surveillance changed?
- Has effectiveness of surveillance changed?
- Have reporting requirements changed?
**Title 17, California Code of Regulations (CCR) §§2500, §§2593, §§2641-2643 and §§2800-2812.**

Every health care provider, knowing of or in attendance on a case or suspected case of any of the diseases or conditions listed below, must report to the local health officer for the jurisdiction where the patient resides.

1. **Syphilis to STD Reporting**
2. **Report within one working day of identification**

**SEXUALLY TRANSMITTED DISEASES (STD)**

- Syphilis
  - Primary (lesion present)
  - Secondary
  - Early latent < 1 year
  - Late latent > 1 year
  - Congenital
- Neurosyphilis
- Chlamydia
- Gonorrhea
- Chancroid
- Pharyngeal
- Urethral/Cervical
- Rectal
- Urine
- Other

**Syphilis Test Results**

- **RPR**
- **VDRL**
- **FTA/MHA**
- **CSF-VDRL**
- **Other**

**Gender of Sex Partners last 12 months:**

- Male
- Transgender (M to F)
- Transgender (F to M)
- Female
- Unknown
- Refused

**STD TREATMENT INFORMATION**

- **Treated (Drugs, Dosage, Route):**
- **Date Treatment Initiated:**
  - Month
  - Day
  - Year
- **Untreated:**
  - Will treat
  - Unable to contact patient
  - Refused treatment
  - Referred to:
Is an epidemic real?

- Have case definitions changed?
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- Has effectiveness of surveillance changed?
- Have reporting requirements changed?
- Have screening guidelines changed?
Public health recommendations: Syphilis screening for MSM

- Screen at least annually
- Screen every 3–6 months if risk behaviors persist or if they or their sexual partners have multiple partners

Public health recommendations: Syphilis screening for MSM

- Screen at least annually
- Screen every 3–6 months if risk behaviors persist or if they or their sexual partners have multiple partners


- Screen MSM
- Optimal frequency not clear
- Every three months may be better than annually
- Grade A recommendation (high certainty that the net benefit is substantial)
Is an epidemic real?

- Have case definitions changed?
- Has type of surveillance changed?
- Has effectiveness of surveillance changed?
- Have reporting requirements changed?
- Have screening guidelines changed?
- Has screening effectiveness changed?
Increased Sexually Transmitted Disease Testing Among Sexually Active Persons Receiving Medical Care for Human Immunodeficiency Virus Infection in the United States, 2009–2013


1Division of HIV/AIDS Prevention, and 2Division of STD Prevention, National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention, Centers for Disease Control and Prevention, Atlanta, Georgia

Testing increased significantly among HIV-infected MSM during 2009–2013 (58% to 69%)

Is an epidemic real?

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- Have screening guidelines changed?
- Has screening effectiveness changed?
- Have testing technologies changed?
Discordant Results from Reverse Sequence Syphilis Screening — Five Laboratories, United States, 2006–2010

- New EIA/CLIA treponemal tests
- Reverse sequence screening: treponemal test before nontreponemal test
- Possible false-positive results from EIA/CLIA

FIGURE. CDC-recommended algorithm for reverse sequence syphilis screening (treponemal test screening followed by nontreponemal test confirmation)*
Public health approaches to syphilis prevention and control
Reproductive rate equation

\[ R_0 = \beta \times c \times d \]

\( R_0 \): Reproductive rate
- \( > 1 \): epidemic sustained
- \( < 1 \): epidemic NOT sustained

\( \beta \): Probability of transmission (30–50%)

\( c \): Number of sexual contacts

\( d \): Duration of infectiousness
Reproductive rate equation

\[ R_0 = \beta \times c \times d \]

- **\( R_0 \): Reproductive rate**
  - \( > 1 \): epidemic sustained
  - \( < 1 \): epidemic NOT sustained

- **\( \beta \): Probability of transmission (30–50%)**
  - Use condoms

- **\( c \): Number of sexual contacts**
  - Have fewer partners

- **\( d \): Duration of infectiousness**
  - Screen, test, promptly treat
Screen, test, and promptly treat

- Screening guidelines (CDC, USPSTF)
- Outreach to gay men/other MSM
- Reporting requirements for physicians and laboratories
- Public health follow up with syphilis patients to identify, test, and treat sex partners
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