

# Sexually Transmitted Infections: Burning Issues

Jeffrey D. Klausner, MD, MPH  
Professor of Medicine and Public Health  
University of California Los Angeles  
David Geffen School of Medicine  
Los Angeles, California



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## Learning Objectives

After attending this presentation, learners will be able to:

- Diagnose and manage gonorrhea
- List treatment options for chlamydia
- Describe manifestations of syphilis

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Centers for Disease Control and Prevention  
**MMWR**  
Morbidity and Mortality Weekly Report  
Weekly / Vol. 66 / No. 13  
April 7, 2017

**State-Specific Rates of Primary and Secondary Syphilis Among Men Who Have Sex with Men — United States, 2015**  
Wu H, Zhou FN<sup>1,2</sup>, Backlund EL<sup>3</sup>, Lacey R, Gray RW<sup>4</sup>, Bi S, Beardsley RL<sup>5</sup>, Thomas L, Cole RK<sup>6</sup>.  
Morbidity and Mortality Weekly Report

**Dallas County saw nation's highest increase for chlamydia and gonorrhea rates last year, study shows**  
Morbidity and Mortality Weekly Report

**Single Dose Versus 3 Doses of Intramuscular Benzathine Penicillin for Early Syphilis in HIV: A Randomized Clinical Trial**  
Morbidity and Mortality Weekly Report

**MAJOR ARTICLE**

**IDA** **hivmo**

**America May Be Heading Into an STD Epidemic—and Gay and Bi Men Are Going to Be the Hardest Hit**  
Morbidity and Mortality Weekly Report

**FDA News Release**  
**FDA permits marketing of first test to aid in the diagnosis of a sexually-transmitted infection known as Mycoplasma genitalium**  
Morbidity and Mortality Weekly Report

**Adherence to CDC Recommendations for the Treatment of Uncomplicated Gonorrhea — STD Surveillance Network, United States, 2016**  
Smith T, Moore J<sup>1</sup>, Kinkaid M<sup>2</sup>, Klevens H<sup>3</sup>, Dworkin K<sup>4</sup>, Tennyson J<sup>5</sup>, Eitman J<sup>6</sup>, Wilson D<sup>7</sup>, Mark S, Hoopes S<sup>8</sup>.  
Morbidity and Mortality Weekly Report

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### Case

28 year old HIV-infected man with urethral discharge



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### Differential Diagnosis of Urethritis

**Infectious**

- Neisseria gonorrhoeae*
- Chlamydia trachomatis*
- Mycoplasma genitalium* \*new FDA-approved test, Jan 2019
- Trichomonas vaginalis*
- Herpes simplex virus 1 and 2*
- Oral flora---streptococci, anaerobes, haemophilus sp.

**Non-infectious**

- Trauma—physical, chemical, sex-play related
- Autoimmune—reactive arthritis

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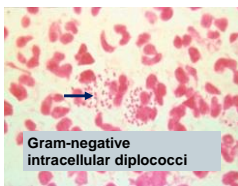
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### Uncomplicated gonococcal infection



Gram-negative intracellular diplococci

*Neisseria gonorrhoeae*

- Urethra
- Cervix
- Pharynx
- Rectum

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### Detection of *N. gonorrhoeae* infection

	Sensitivity	Specificity
Gram stain	92%	90%
Culture	95%	100%
DNA/RNA amplification*	95%	99%

\*May be used on clinician- or self-collected vaginal, cervical, rectal, pharyngeal and urine specimens

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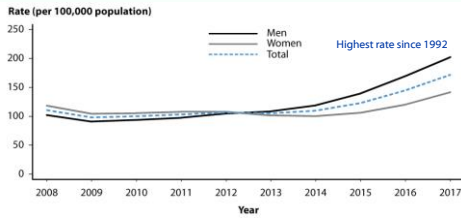
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### Gonorrhea is increasing in both sexes



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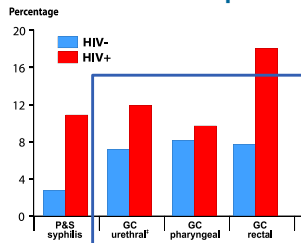
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### Gonorrhea is common in extra-genital sites and HIV-infected patients



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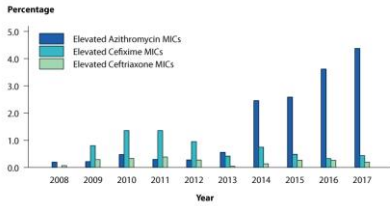
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### Resistance of *Neisseria gonorrhoeae* to azithromycin, cefixime and ceftriaxone



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### Multi-drug treatment for gonorrhea

**Ceftriaxone 250 mg IM once**  
**Azithromycin 1 gm PO once**



**Plus partner treatment**



**Retesting at 3 months**

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Clinical Infectious Diseases

#### BRIEF REPORT

### Implementation of a Rapid Genotypic Assay to Promote Targeted Ciprofloxacin Therapy of *Neisseria gonorrhoeae* in a Large Health System

Lao-Tay Alim-Bilat,<sup>1</sup> Ramsey M. Humphries,<sup>2</sup> Paera Hemarajata,<sup>3</sup> Ashima Bhatt,<sup>1</sup> Mark W. Paudyal,<sup>4</sup> Mark A. Sieders,<sup>5</sup> and Jeffrey D. Klausner<sup>1\*</sup>  
<sup>1</sup>David Geffen School of Medicine, University of California, Los Angeles (UCLA), <sup>2</sup>Department of Laboratory Medicine, David Geffen School of Medicine, UCLA, <sup>3</sup>Visiting School of Public Health, UCLA, <sup>4</sup>Alameda County Department of Public Health, Oakland, and <sup>5</sup>Department of Medicine, Harvard Medical School and Massachusetts General Hospital, Boston, Massachusetts, <sup>6</sup>Division of Infectious Diseases, Department of Medicine, David Geffen School of Medicine, University of California, Los Angeles, and <sup>7</sup>Department of Epidemiology, Fielding School of Public Health, University of California, Los Angeles

### Molecular GyrA assay detects S91 predicts Cipro susceptibility

**Gyrase A**

- Gyrase is target of Ciprofloxacin

Ser 91  
 -TCC-  
 I  
 -TTC-  
 Phe-91

Mutated Ser 91 is necessary and sufficient for resistance.  
 WT GyrA 98.2% sensitive and 98.6% specific.

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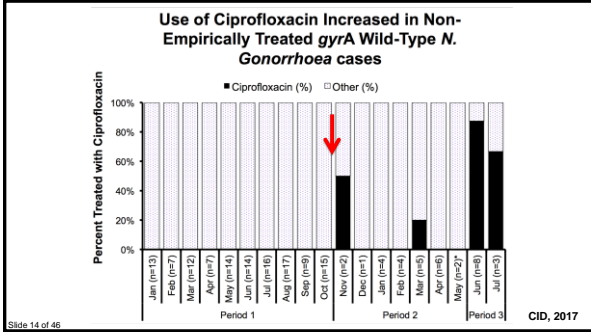
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### Case

28 year old HIV-infected male here for a check-up

He has one regular partner and occasional partners he meets at various venues, clubs and via social media

He has no symptoms

What STD screening tests are appropriate?

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### STI screening in Men who have Sex with Men

- *Chlamydia trachomatis*/ *Neisseria gonorrhoeae*
  - throat, rectum, urine
- Syphilis (Treponemal Ab, if reactive then RPR)
- Avoid
  - Anal PAP smear
  - Routine Herpes simplex virus-1/2 antibody testing

US CDC 2015, USPSTF, 2013

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**Test results**

Throat – CT/NG negative  
Urine – CT/NG negative  
Rectum – **CT positive**, NG negative  
Blood – TPPA positive, RPR negative

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**ARS 1: What is the best treatment for rectal chlamydia?**

- 1) Azithromycin 1 gm orally once
- 2) Doxycycline 100 mg orally twice daily for 7 days
- 3) Amoxicillin 500 mg po tid x 7 days
- 4) Levofloxacin 500 mg po qd x 7 days

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**What is the best treatment for rectal chlamydia?**

- 1) Azithromycin 1 gm orally once
- 2) **Doxycycline 100 mg orally twice daily for 7 days**
- 3) Amoxicillin 500 mg po tid x 7 days
- 4) Levofloxacin 500 mg po qd x 7 days

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*Treponema pallidum pallidum*, bacterial spirochete

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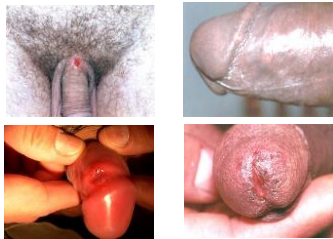
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### Primary syphilis – penile chancres



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### Secondary syphilis: trunk rash



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Secondary syphilis: palmar and plantar lesions



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



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Latent syphilis

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### Those syphilis tests

- **Non-treponemal tests (RPR, VDRL)**
  - 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)
- **Treponemal tests (FTA-Abs, TPPA, TP EIA/CIA, rapid TP)**
  - Antibody to Treponemal antigen
  - More sensitive and develop earlier
  - 85% stay positive for life
  - Indicate past or current infection

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Klausner, Current STD Diagnosis and Management 2007

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### Syphilis and HIV-infection

- Overlapping primary and secondary stage
- Slower titer decline
- No difference in therapy
- Two-fold increased risk for neurosyphilis

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### Injectable penicillin is treatment of choice for primary, secondary, early latent syphilis

- Single intramuscular injection  
2.4 MU benzathine penicillin
- Prophylactic treatment:
  - Syphilis case contacts
  - < 90 days



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## No difference in single vs. 3 doses B-PCN in HIV-infected

Clinical Infectious Diseases  
MAJOR ARTICLE



Single Dose Versus 3 Doses of Intramuscular Benzathine Penicillin for Early Syphilis in HIV: A Randomized Clinical Trial

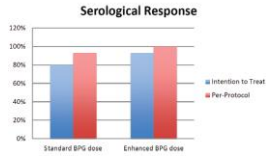


Figure 2. Intention-to-treat and per-protocol analyses of the comparison between a single dose vs 3 doses of 2.4 million units of intramuscular benzathine penicillin G (BPG) for early syphilis in human immunodeficiency virus-infected individuals. Abbreviation: BPG, benzathine penicillin G.

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## ARS 2: What are recommended indications for lumbar puncture?

- 1) RPR titer > 1:32
- 2) CD4 T cell count < 350 cells/ml
- 3) Visual changes
- 4) Headache

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## What are recommended indications for lumbar puncture?

- 1) RPR titer > 1:32
- 2) CD4 T cell count < 350 cells/ml
- 3) Visual changes
- 4) Headache

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**CDC recommended indications for lumbar puncture**

- 1) Neurologic symptoms or signs
- 2) Suspected ocular (or otic) syphilis
- 3) Treatment failure
- 4) Tertiary syphilis

HIV infection, immunosuppression or elevated RPR titer, while associated with increased risk for neurosyphilis, are not indications for CSF analysis

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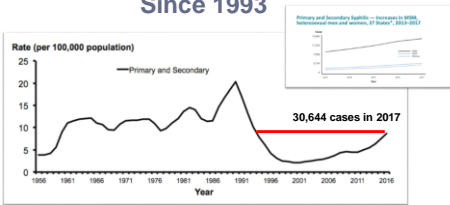
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**Highest Rate of New Cases of Syphilis Since 1993**



Kojima and Klausner, Curr Int Dis Reports, 2018

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THE REAL WORLD OF STD PREVENTION

**Doxycycline Prophylaxis to Reduce Incident Syphilis among HIV-Infected Men Who Have Sex With Men Who Continue to Engage in High-Risk Sex: A Randomized, Controlled Pilot Study**

Robert K. Bolan, MD,\* Matthew R. Barnes, MPH,\*\* Robert E. Weiss, PhD,† Brian P. Flynn,\* Arlene A. Lathowitz, PhD,§ and Jeffrey D. Klausner, MD, MPH\*

TABLE 3. Results of GLMMs for STDs (n = 30)\*

Outcome	No. Visits With Outcome		Follow-Up Analysis (Through 48 wk)		On-Drug Analysis (Through 36 wk)	
	Doxycy Arm	CM Arm	P	OR (95% CI)	P	OR (95% CI)
STI contraction						
Gonorrhea or chlamydia only	4	8	0.18	0.36 (0.08-1.56)	0.25	0.42 (0.09-1.89)
Syphilis only	2	7	0.10	0.24 (0.04-1.33)	0.16	0.27 (0.04-1.73)
Any STD (gonorrhea, chlamydia, syphilis, or any combination thereof)	6	15	0.02	0.27 (0.09-0.83)	0.07	0.30 (0.08-1.09)

\*ORs or rate ratios below 1 indicate the decrease in odds/rates in the doxycycline arm compared with CM arm; OR or rate ratios above 1 indicate increased odds/rates in the doxy arm compared with the CM arm.

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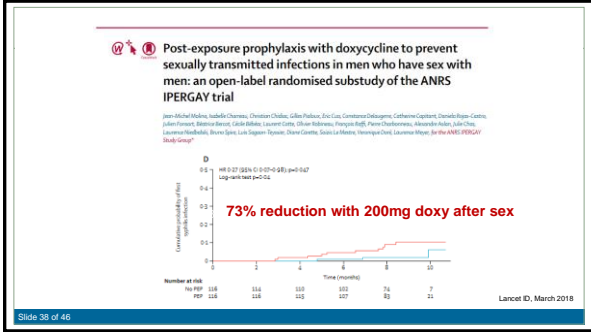
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### Sources for more STD information

- **CDC**  
- [www.cdc.gov/std](http://www.cdc.gov/std)
- **Current STD Textbook**

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### Questions and Answer

1950s      1960s      2000s      2010s

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