"SYPHILIS EDUCATION TODAY"

Preventing Syphilis Exposure in HIV+ Individuals – A Review of New Guidelines for Prevention and Treatment of Syphilis in the HIV-Infected Population

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Disclosure

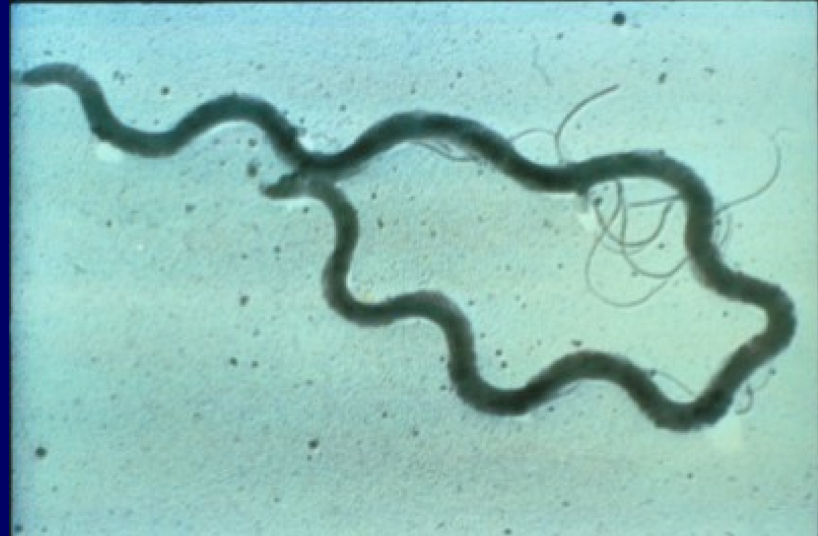
- Dr. Klausner is an employee of the City & County of San Francisco and a Faculty member of the University of California, San Francisco

In the past 12 months:

- The NIH, CDC, California HIV Research Program and Gen-Probe, Inc., Focus Technologies, and Cerexa provided research funding to Dr. Klausner
- Communications Strategies, Inc., CSI Medical Education and King Pharmaceuticals, Inc. supported Dr. Klausner to conduct various educational programs

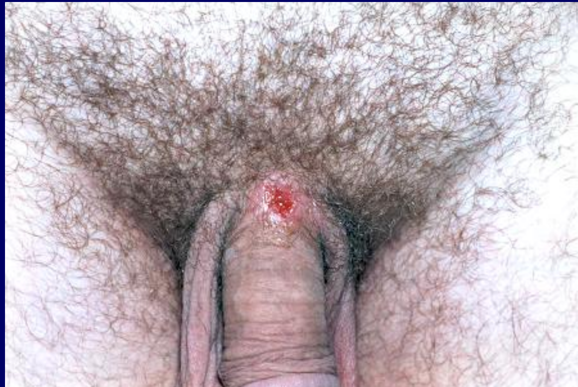
Syphilis Biology

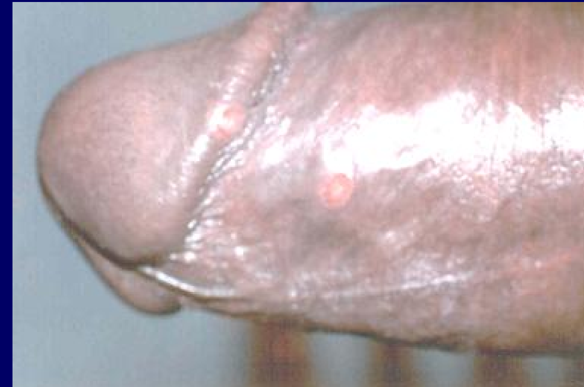
- Treponema pallidum a spirochete bacterium spread through sexual contact—oral, anal or vaginal sex
- Humans only host
- Facilitates HIV transmission

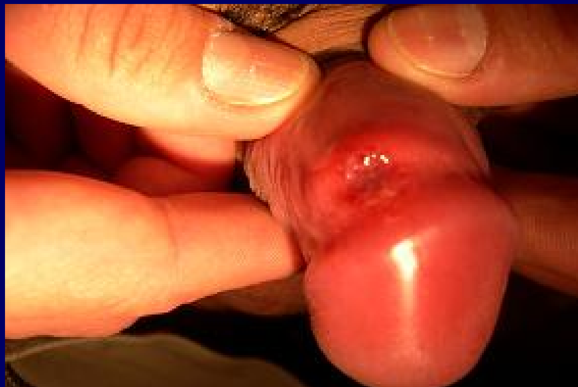


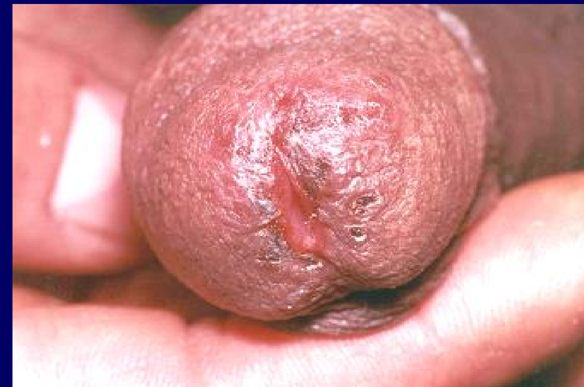
San Francisco City Clinic Web site http://www.sfcityclinic.org/stdbasics/syphilis.asp
Path: STD Basics: Syphilis (accessed August 15, 2007)

Primary Syphilis - Chancres



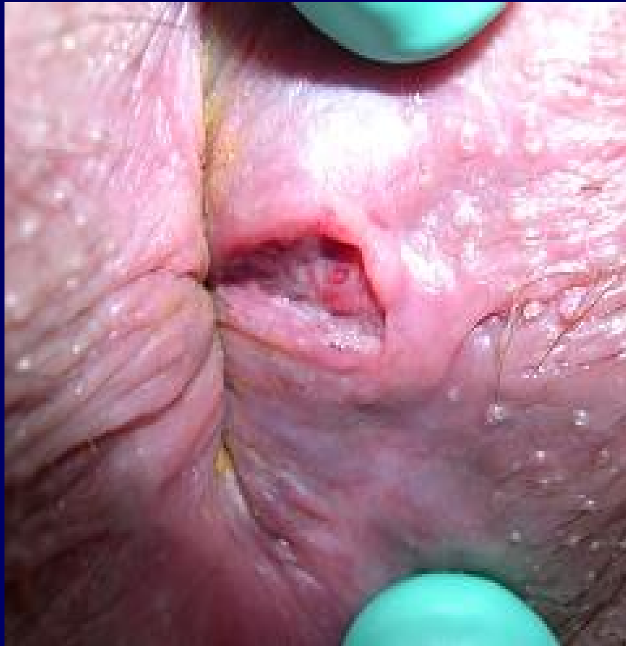




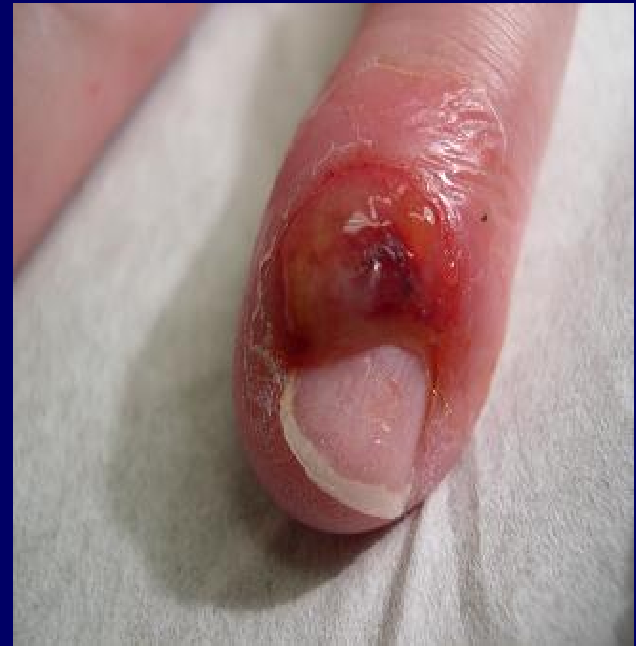


Photos courtesy of Jeffrey D. Klausner, MD

Primary Syphilis - Chancres



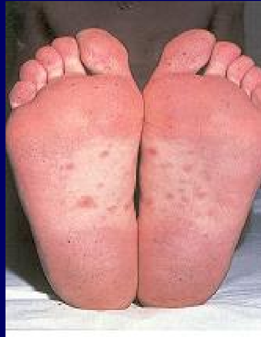
Anorectal

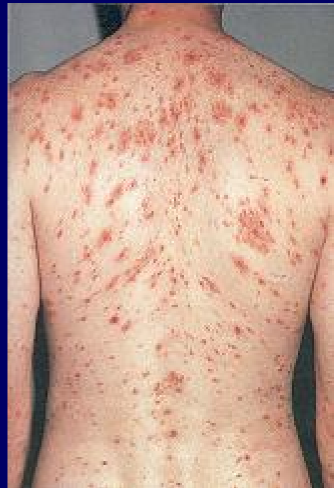


Finger

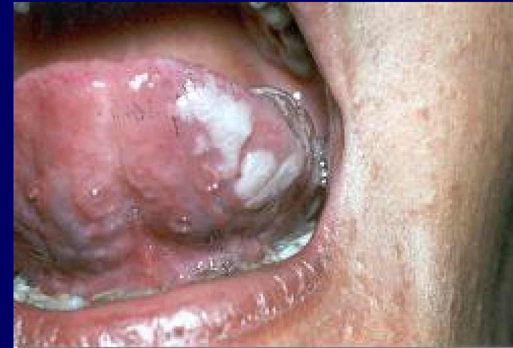
Photos courtesy of Jeffrey D. Klausner, MD

Secondary Syphilis





Rash

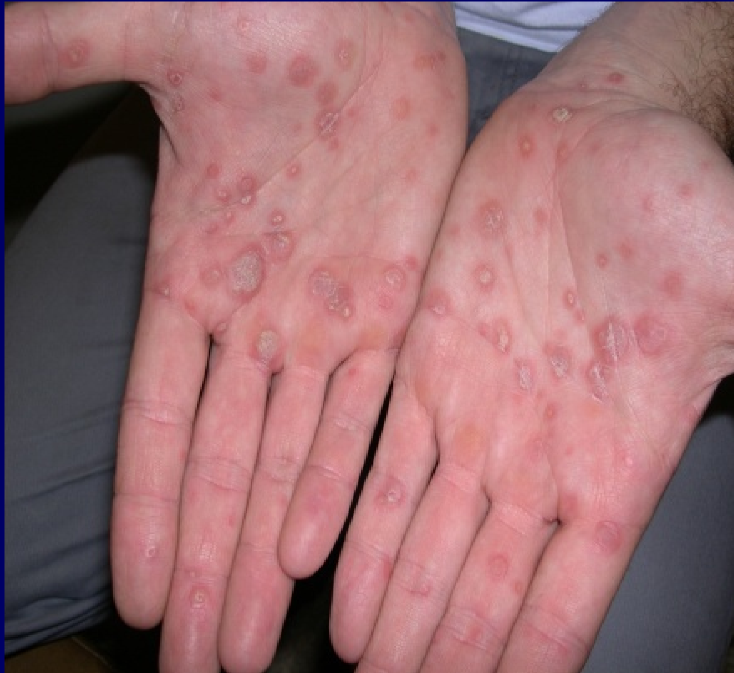


Mucous Patches

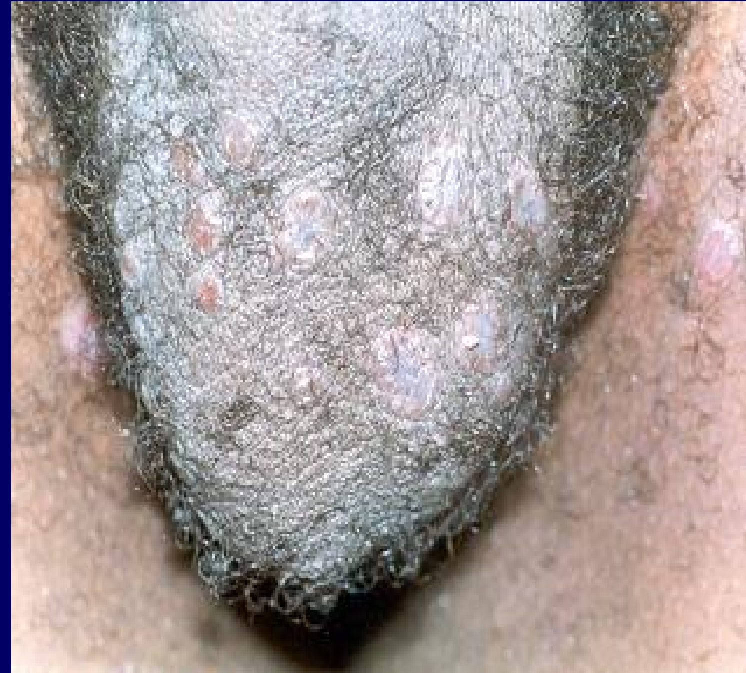
Condylomata Lata

Photos courtesy of Jeffrey D. Klausner, MD

Secondary Syphilis – Annular Rashes



Palms



Scrotum

Photos courtesy of Jeffrey D. Klausner, MD

Prophylactic Syphilis Treatment for Adults

- Penicillin G benzathine (Bicillin® L-A)* 2.4 million units (MU) intramuscular (IM) once

- ***Penicillin-allergic:***

  Non-Pregnant:

  Doxycycline 100 mg PO BID x 14 days

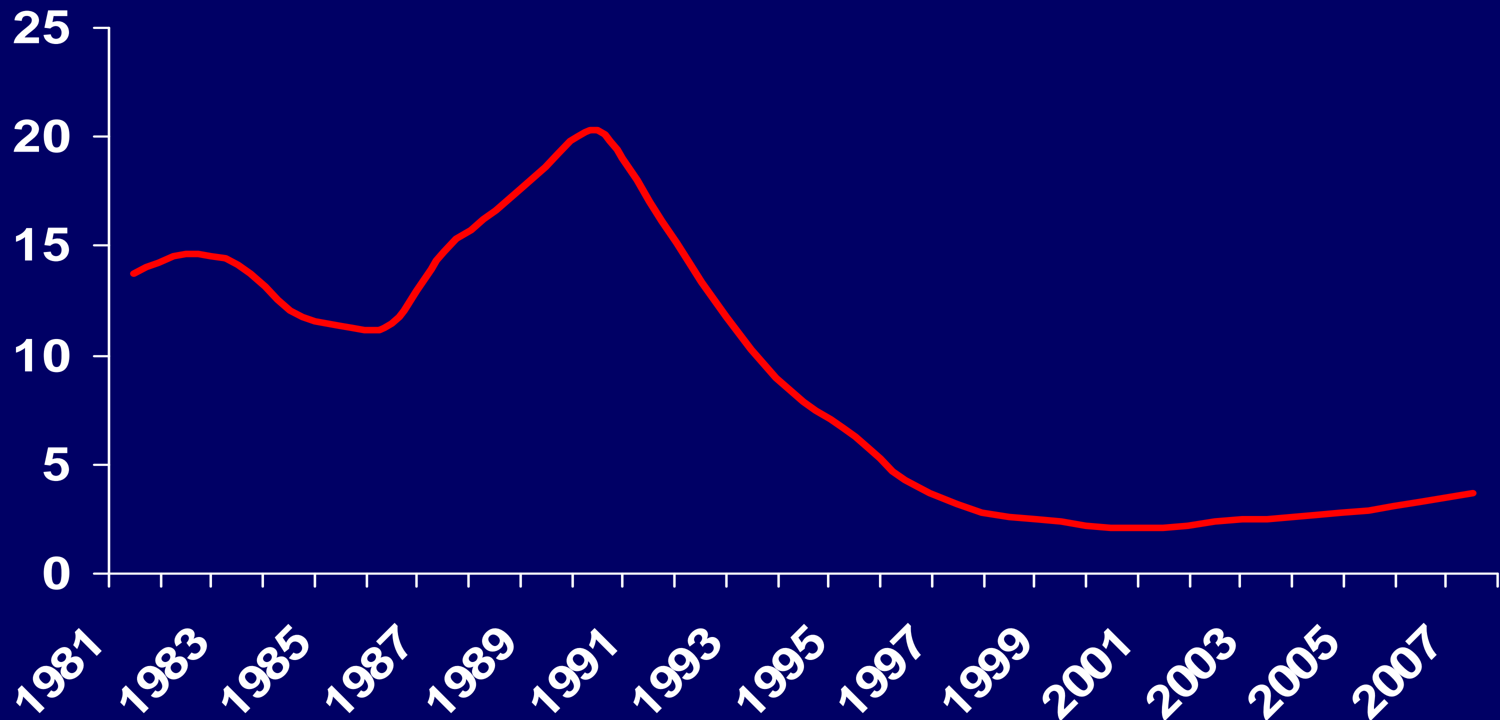
  Pregnant:

  Test for hypersensitivity, desensitize, treat with penicillin G benzathine 2.4 MU IM once

* **Do not substitute** Bicillin® C-R for Bicillin® L-A in the treatment of syphilis. Bicillin® C-R is NOT indicated for the treatment of syphilis.

Centers for Disease Control and Prevention, 2006 STD Treatment Guidelines, *MMWR,* 2006. p. 3. Available at www.cdc.gov/std.

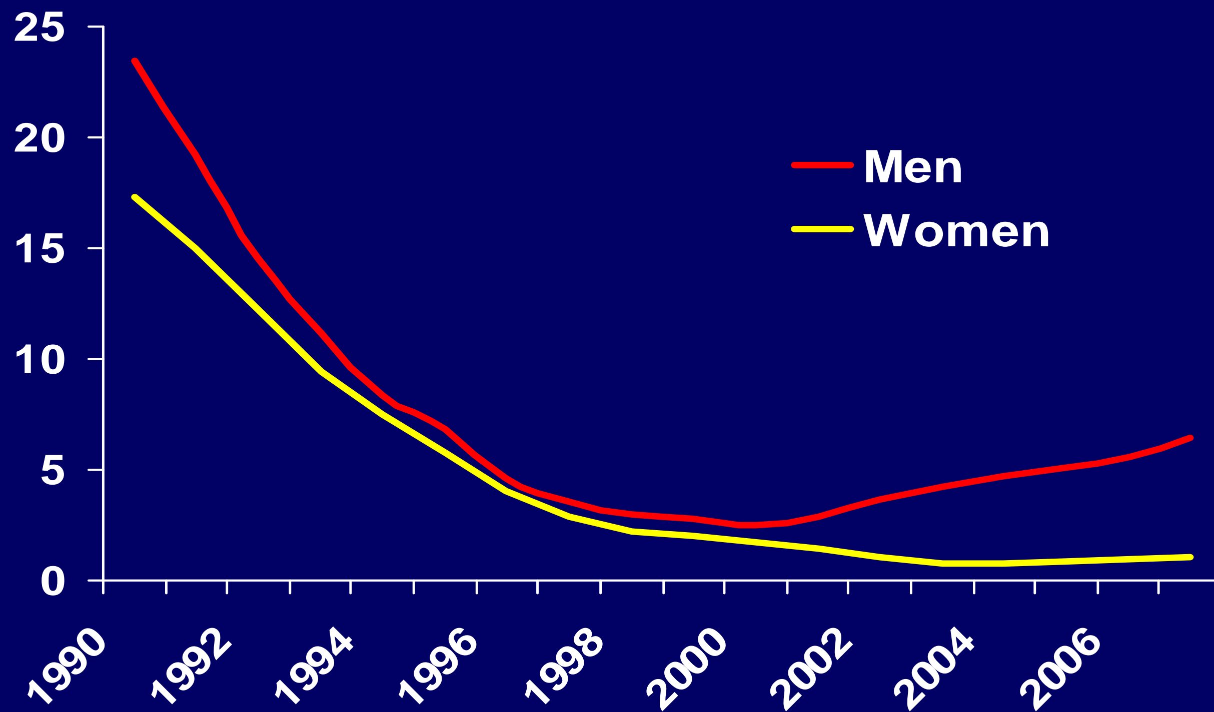
Primary and Secondary Syphilis Rates in the United States, 1981–2007*



* 2007 data are preliminary

Hillard Weinstock, Division of STD Prevention, CDC, Presentation at STD National Conference, March 11, 2008

Primary and Secondary Syphilis Rates by Sex, United States, 1990–2007*



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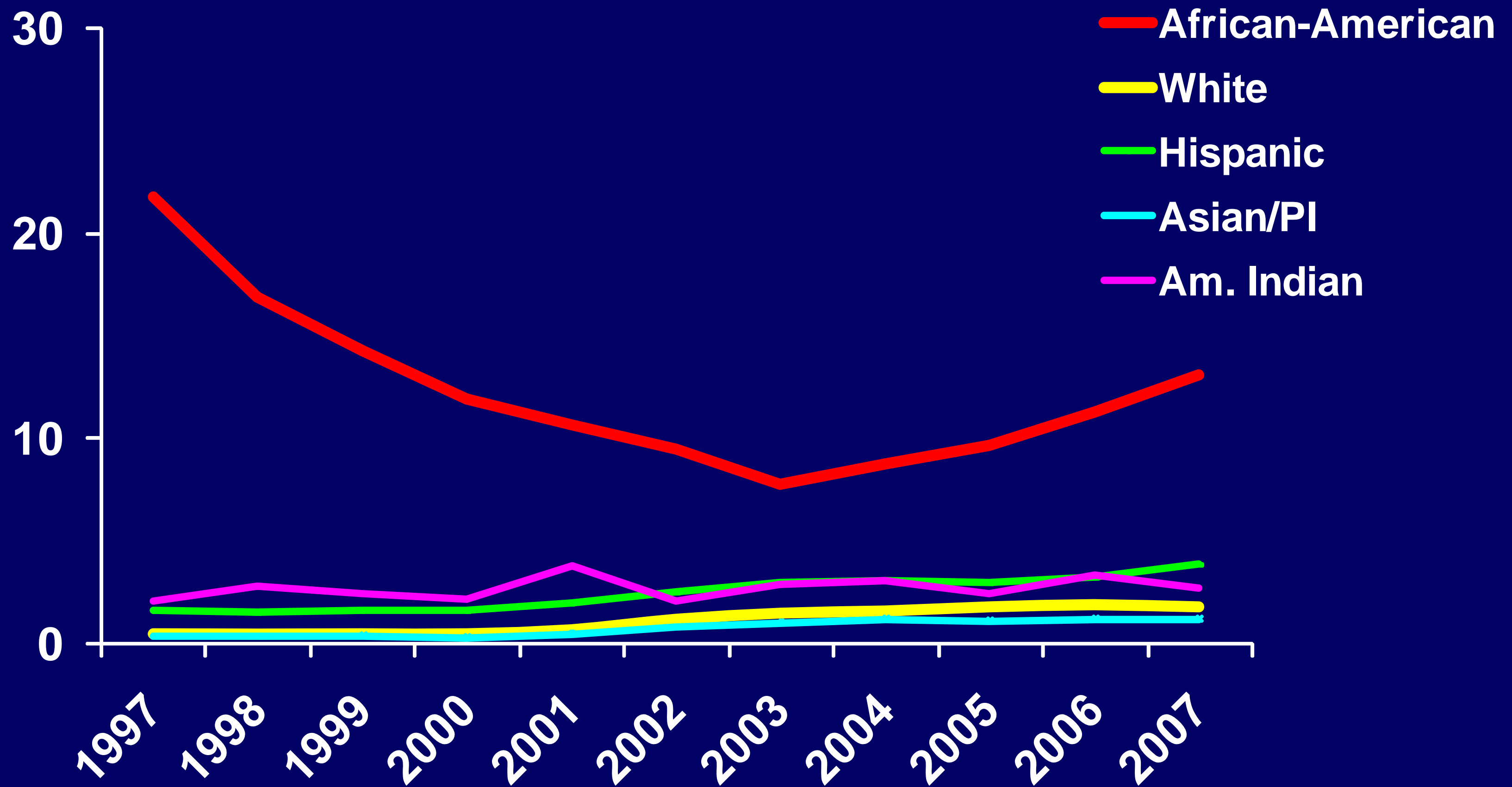
Hillard Weinstock, Division of STD Prevention, CDC, Presentation at STD National Conference, March 11, 2008

Primary and Secondary Syphilis: Rates by Race and Ethnicity, 1997–2007*



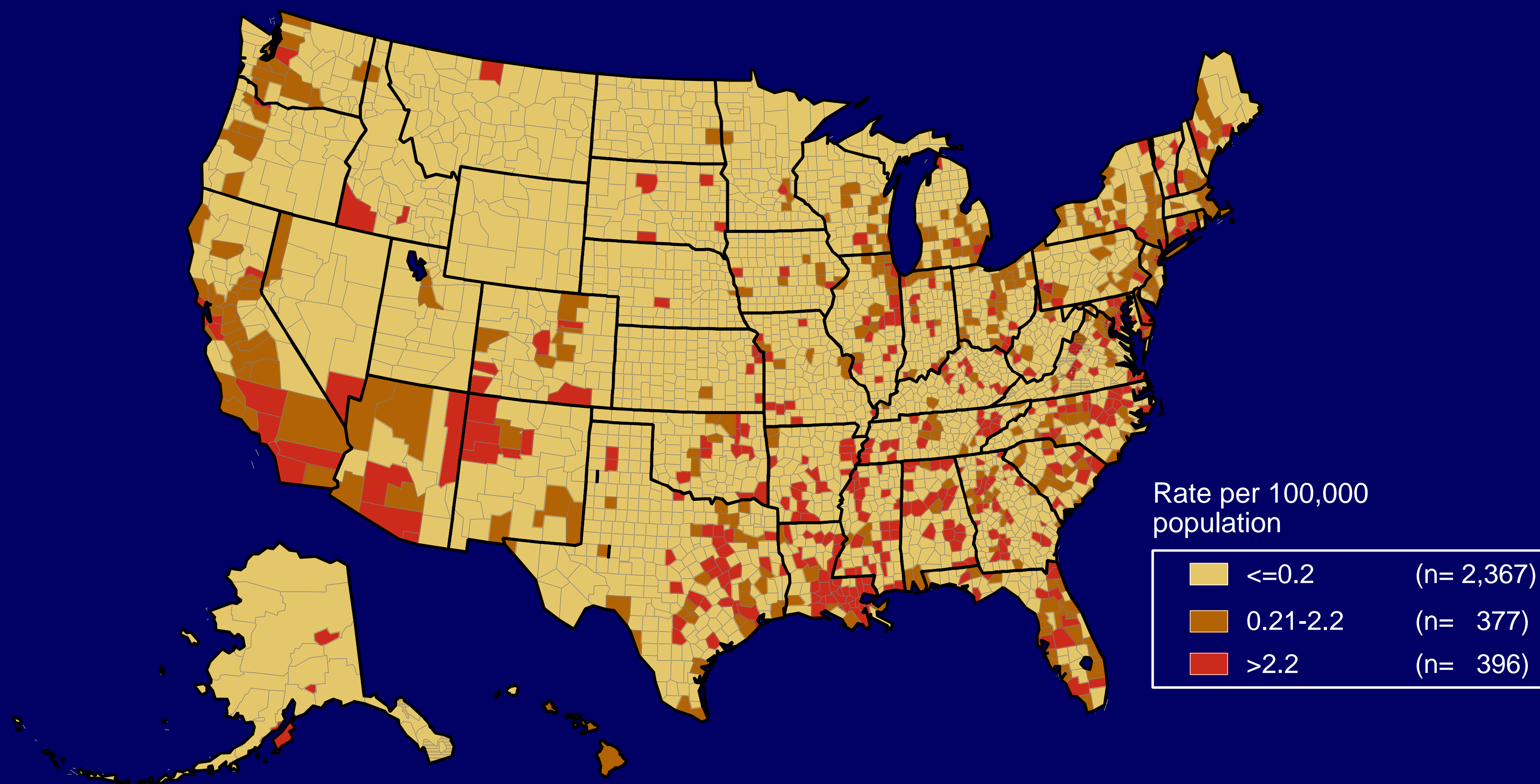
* 2007 data are preliminary

Primary and Secondary Syphilis Cases: United States, 2004-2007

	2004	2007*	% Change
Sex			
Men	6,722	9,502	+41.3
Women	1,255	1,671	+33.1
Race/Ethnicity			
African-American	3,071	4,944	+60.9
White	2,982	3,664	+22.8
Hispanic	1,196	1,728	+44.5
Asian/PI	143	166	+16.1
American Indian/NA	73	67	-11.0
Total	**7,980**	**11,181**	**+40.1**

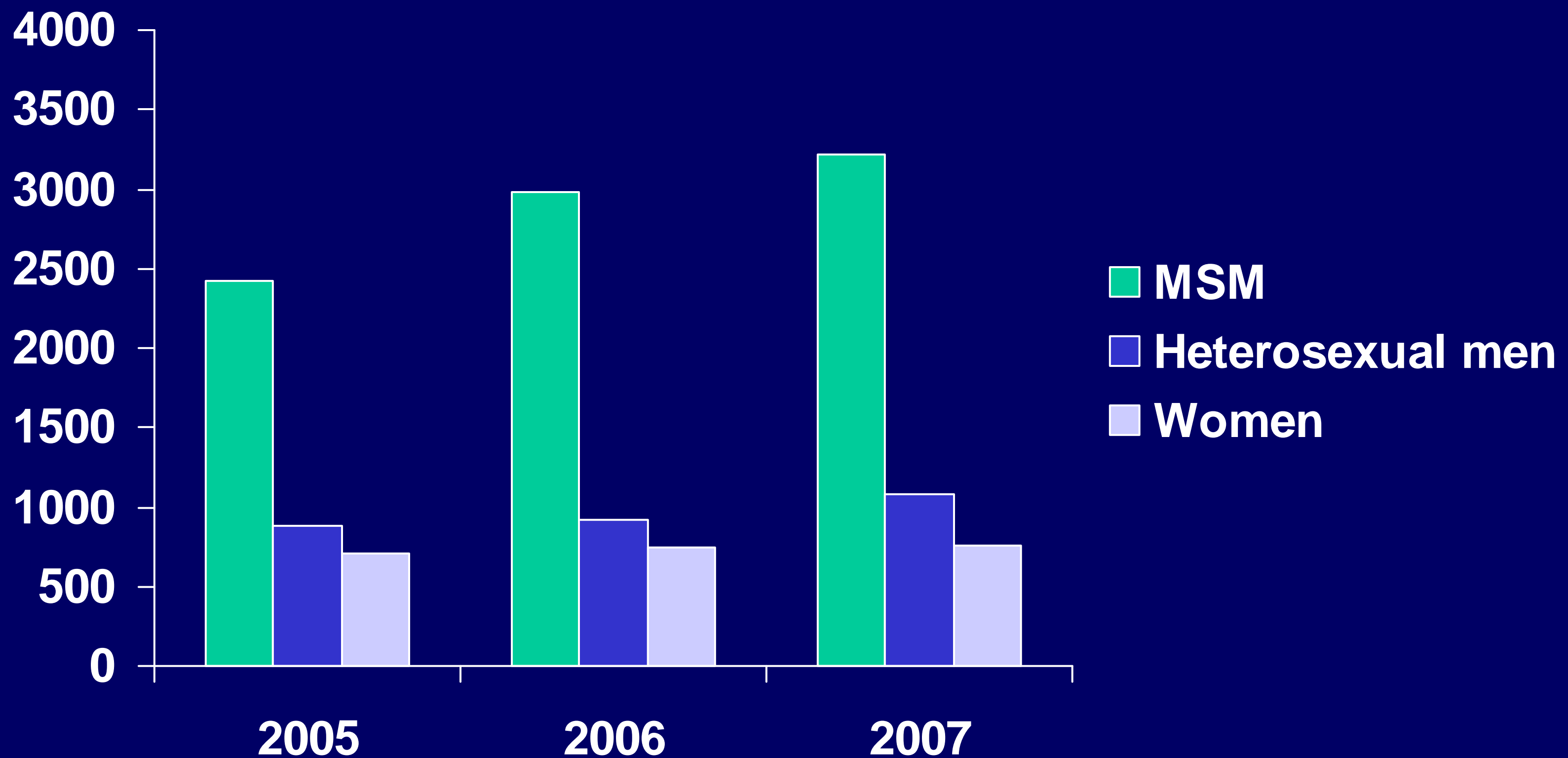
* 2007 data are preliminary

Primary and Secondary Syphilis — Rates by County: United States, 2006



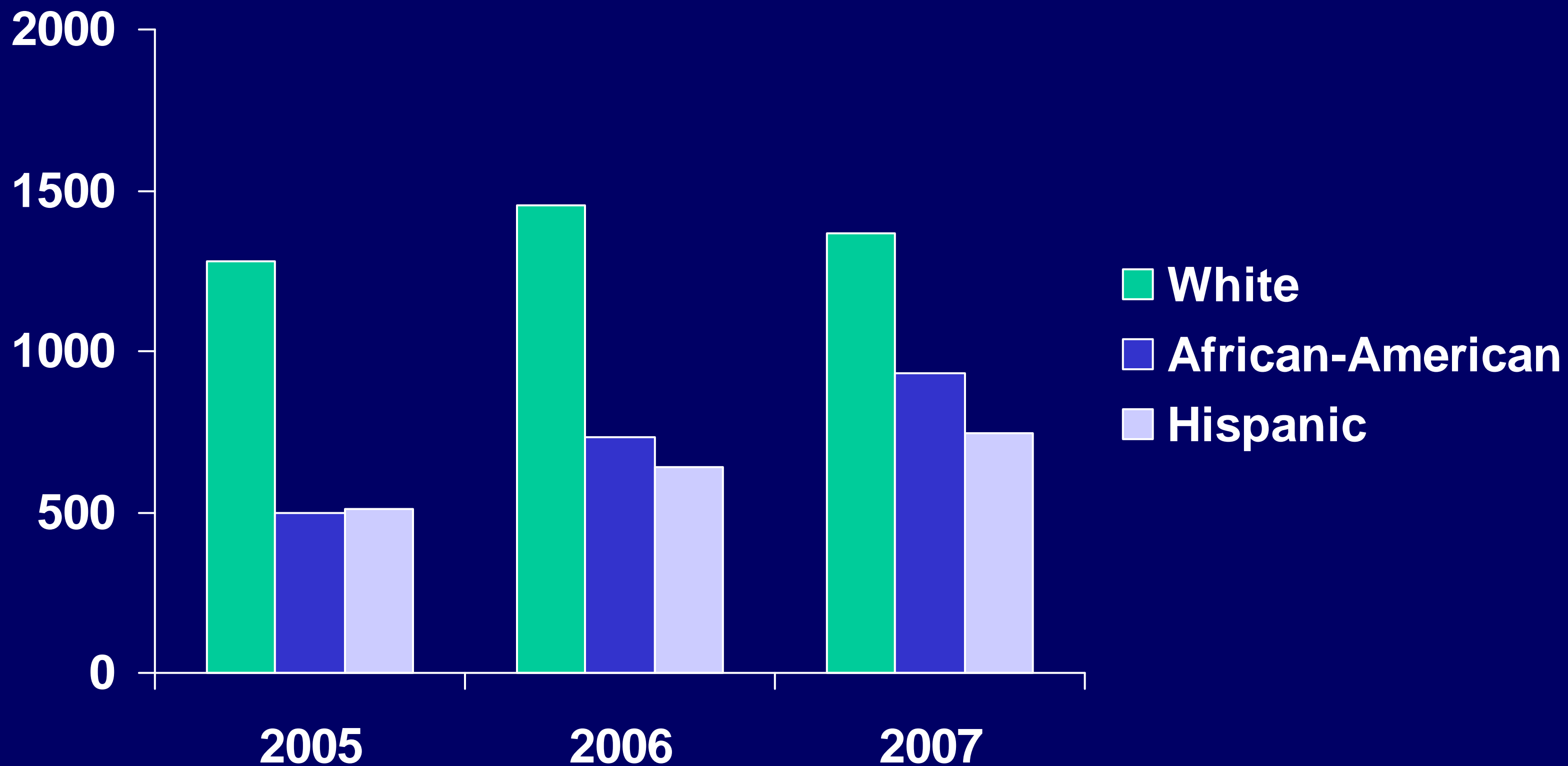
Note: The Healthy People 2010 target for P&S syphilis is 0.2 case per 100,000 population. In 2006, 2,360 (75.2%) of 3,140 counties in the U.S. reported no cases of P&S syphilis.

Primary and Secondary Syphilis by Sex and Sexual Orientation in 23 States, 2005-2007*



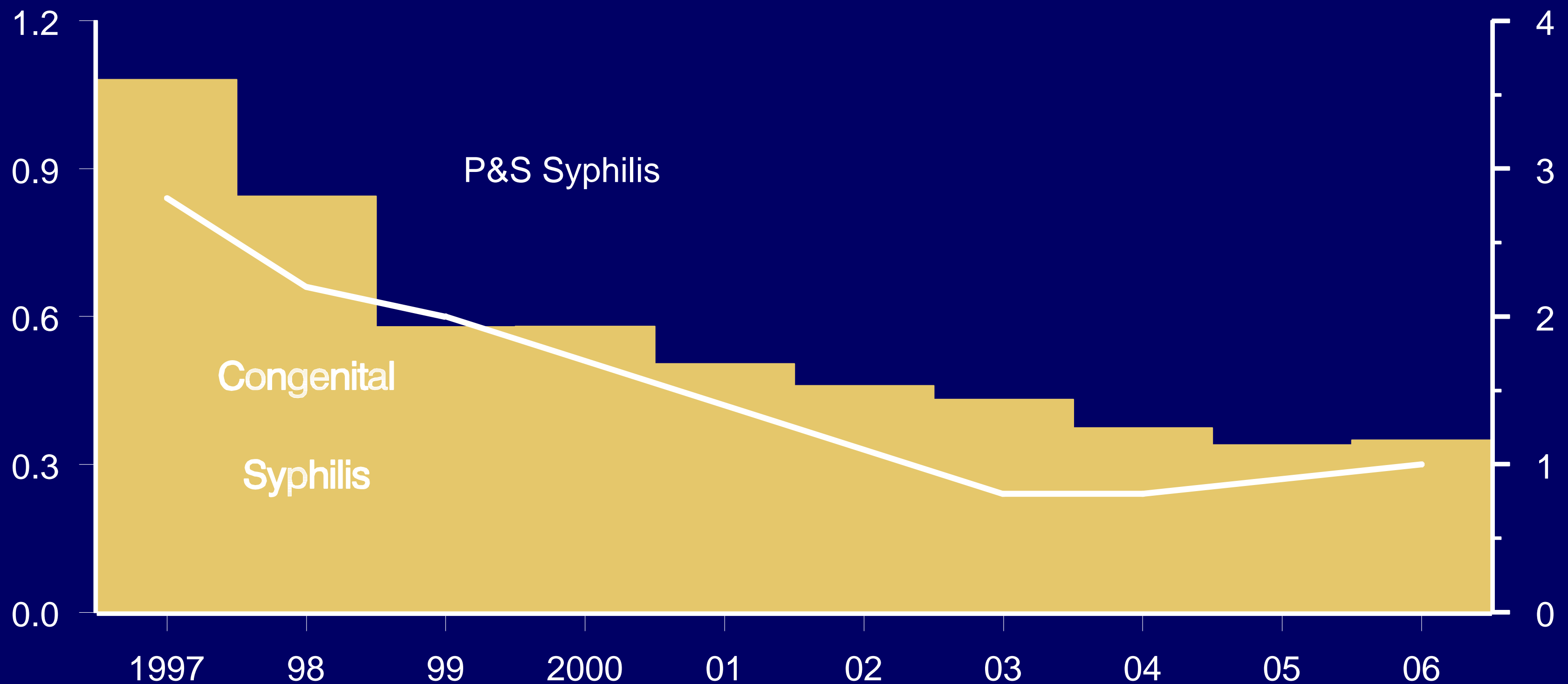
* 2007 data are preliminary

Primary and Secondary Syphilis Among MSM by Race/Ethnicity in 23 States, 2005-2007*



* 2007 data are preliminary

Congenital Syphilis — Reported Cases for Infants <1 Year of Age and Rates of Primary and Secondary Syphilis Among Women, 1997–2006

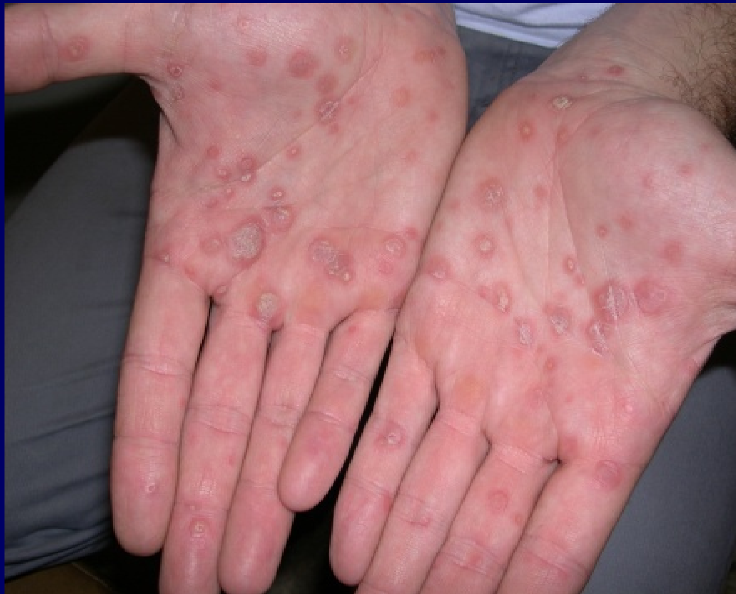


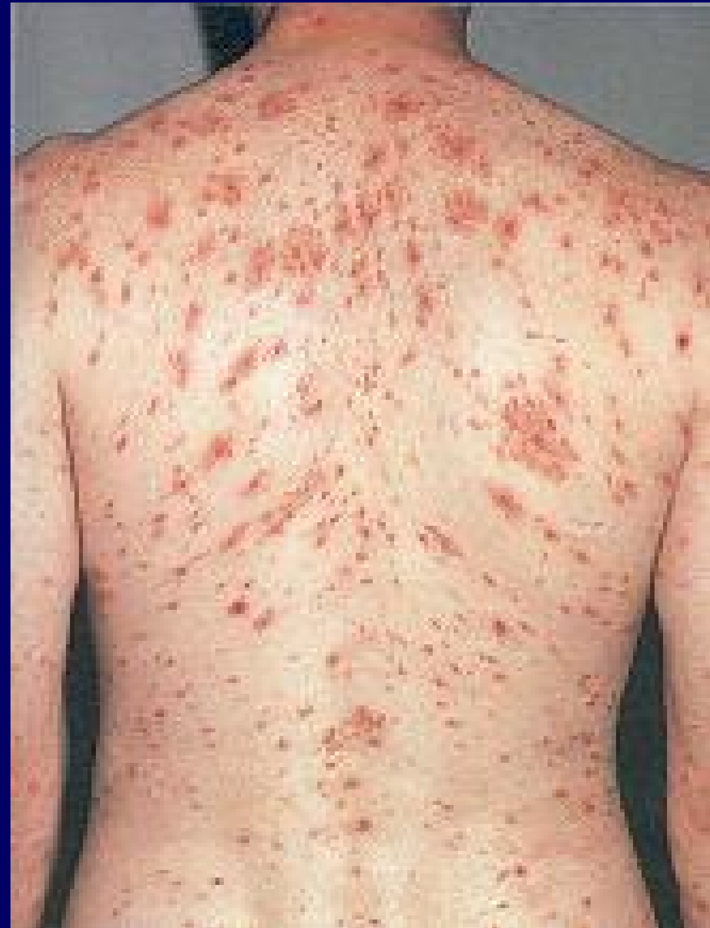
Summary

- Syphilis is increasing
- Highest rates among African-American men
- Rates of syphilis among MSM continue to increase; MSM account for >60% of all P&S syphilis cases
- Small increases over past 3 years in women, especially in the South, are concerning

Case 1

- 42-year-old man presents complaining of new skin rash





Medical History

- Medical history including STD history, current medications, allergies and chronic illnesses
- Sexual history
  - Gender and number of sex partners in past 12 months, type of sex, last sexual exposure, partners with syphilis
  - Other risk behaviors like methamphetamine or Viagra use, Internet, sex club/bath house
- Prior HIV and syphilis testing history
- Review of Systems with focus on neurologic complaints, particularly hearing, visual or balance

Serologic Test Results

- Syphilis EIA positive, RPR 1:128
- Is further syphilis testing required?
  - Use of TP EIA in clinical practice
  - TP identified old and new infection
  - Requires RPR to measure titer of infection
- HIV-1 antibody positive

CDC, MMWR, August 15, 2008. Syphilis Testing Algorithm Using Treponemal Tests for Initial Screening—Four Laboratories, New York City, 2005-2006. Vol 57 (32): 872-875.

Physical and Neurological Examination

- Physical examination with particular attention to skin, palms/soles, oral cavity, genitals and anus
- Neurologic examination
    - General
    - Cranial nerve evaluation—rule out oculomotor (III), facial (VII), auditory (VIII) dysfunction
        - Pupillary reaction vs. accommodation
        - Smile, hearing assessment
    - Dorsal columns
        - Vibration and position sense
    - Gait and balance

Indications for CSF analysis*

1) Neurologic findings in patients with syphilis including visual or hearing abnormalities
2) Syphilis treatment failure
3) Tertiary syphilis—cardiovascular, skeletal, etc.
4) Late or unknown latent in HIV-infected patients

•Centers for Disease Control and Prevention, 2006 STD Treatment Guidelines, MMWR, 2006.
Available at **www.cdc.gov/std**

Syphilis Treatment

- Penicillin G benzathine (Bicillin® L-A)* 2.4 million units (MU) intramuscular (IM) once

- ***Penicillin-allergic:***

  Non-Pregnant:

  Doxycycline 100 mg PO BID x 14 days

  Pregnant:

  Test for hypersensitivity, desensitize, treat with penicillin G benzathine 2.4 MU IM once

* **Do not substitute** Bicillin ® C-R for Bicillin ® L-A in the treatment of syphilis. Bicillin ® C-R is NOT indicated for the treatment of syphilis.

Centers for Disease Control and Prevention, 2006 STD Treatment Guidelines, *MMWR,* 2006. p. 3. Available at www.cdc.gov/std.

Partner Management

- Notify, evaluate and provide epidemiologic treatment* for recent partners
- Inform partners of potential syphilis/HIV exposure and offer HIV testing

* Penicillin G benzathine (Bicillin ® -LA) 2.4 MU IM once

Partner Management in Syphilis

Stage	Partner period	Management
Primary syphilis	< 90 days	Treat* and test
Secondary syphilis	< 6 months	Test and treat, if infected
Early latent syphilis	< 1 year	Test and treat, if infected

* Treat with penicillin G benzathine (Bicillin ® -LA) 2.4 MU IM once

Treatment Follow-up

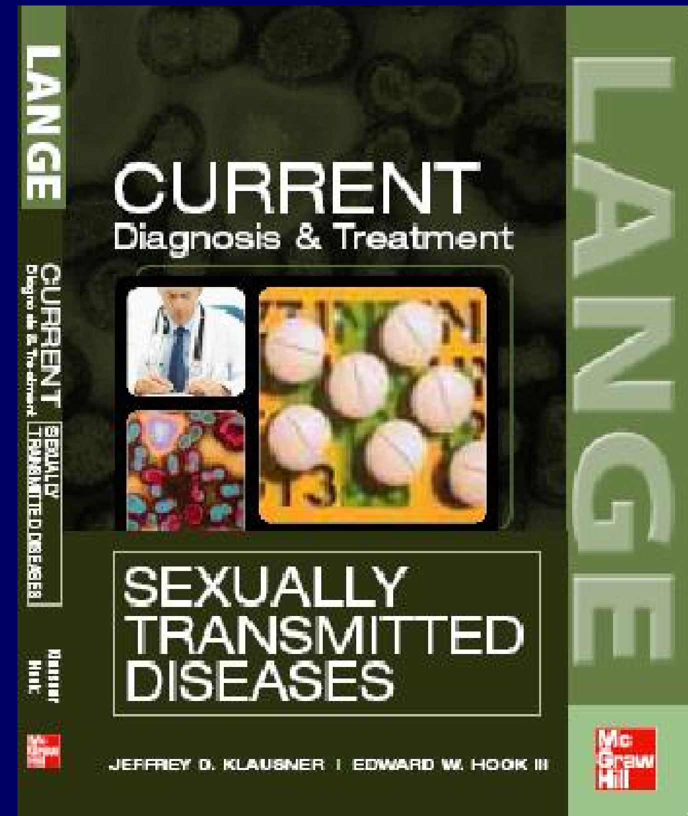
- Repeat serologic tests at 3, 6, 9, 12 and 24 months
  - 4-fold decline by 12 months consistent with cure
  - Failure of 4-fold at 12 months may necessitate CSF analysis to rule out neurosyphilis

Summary

- Syphilis is increasing in the United States
  - Highest rates in African-American men
  - Most cases occurring in gay men and other men who have sex with men
- Treatment of syphilis requires use of penicillin G benzathine (Bicillin® L-A)
  - Avoid Bicillin® C-R, not indicated for syphilis
  - Follow patients closely after treatment

More Information and Questions!

- SFDPH City Clinic
  www.sfcityclinic.org
  Jeff.Klausner@sfdph.org
- State of CA STD Branch
  www.std.ca.gov
- CDC STD Treatment Guidelines 2006
  www.cdc.gov/std
- www.Bicillin.net



Questions?

Ask Dr. Klausner ("Dr. K")

HIV Opportunistic Infection Guidelines: Syphilis

Kimberly Workowski, MD
Syphilis Workgroup Leader, HIV OI Guidelines
Team Lead, STD Treatment Guidelines Unit
Epidemiology/Surveillance Branch, DSTDP/CDC

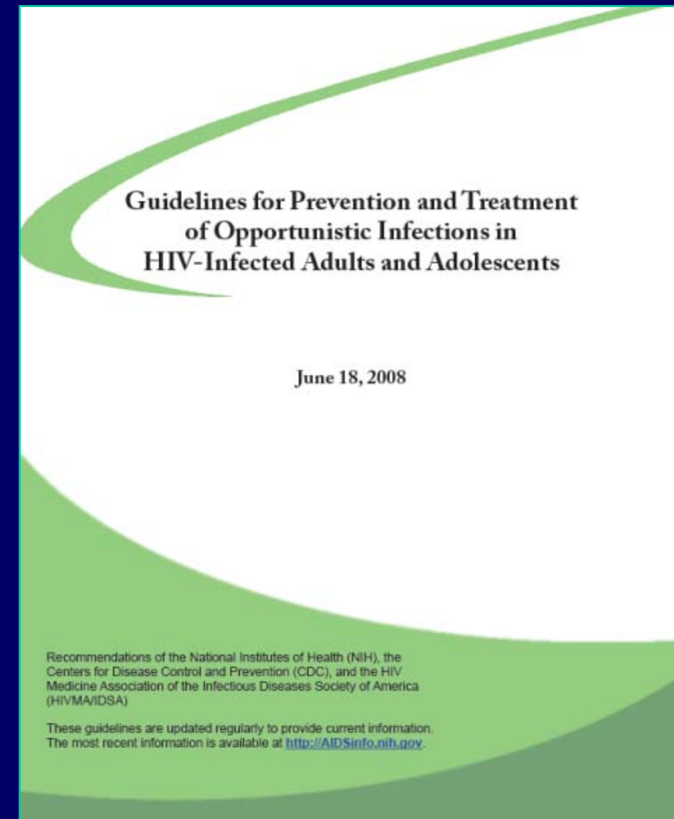
Professor of Medicine
Division of Infectious Diseases
Emory University

Disclosure

- Emory University Infectious Disease faculty
- Clinical Research funding (HIV, Hepatitis C, vaginal microbicides)- NIH, CDC, Abbott, Gilead, BMS, Tibotec
- Contractor- Division of STD Prevention, Guidelines Unit, CDC

HIV Opportunistic Infection Guidelines: Syphilis

- The guidelines are available at http://AIDSinfo.nih.gov


Guidelines for Prevention and Treatment of Opportunistic Infections in HIV-Infected Adults and Adolescents

June 18, 2008

Recommendations of the National Institutes of Health (NIH), the Centers for Disease Control and Prevention (CDC), and the HIV Medicine Association of the Infectious Diseases Society of America (HIVMA/IDSA)

These guidelines are updated regularly to provide current information. The most recent information is available at http://AIDSinfo.nih.gov.

General Principles

- Syphilic genital ulceration increases risk of HIV sexual acquisition and transmission
- Management principles similar
  - Frequent clinical/serologic monitoring
- Subtle variations in clinical presentation
  - Multiple/deep ulcers, concomitant primary/secondary
- Neurosyphilis can occur at any stage
  - Uveitis, meningitis may be more common

Diagnosis

- Dx based on direct direction or serologic evaluation
- No formal evaluation of serologic test performance in HIV+ patients
- Responses to nontreponemal tests may be atypical
  - False positive tests more common in HIV+
  - False negative test – repeat serology, exclude prozone, biopsy, DFA
- Treponemal EIA (screening)- identifies previous treatment, untreated late syphilis
- Transient decrease in CD4 or increase in VL (early syphilis)

Evaluation of CNS Involvement

- CNS or ocular clinical findings
- Frequent treponemal CNS invasion in early syphilis regardless of HIV status (protein, pleocytosis)
- CSF exam- neuro/ocular sx, tertiary, tx failure, latent syphilis/HIV+ (CDC STD Treatment Guidelines 2006)
  - RPR >1:32 regardless of stage (Marra 2004, Libois 2007)
  - CD4 <350 (3.1x); RPR >1:32 (6x) (Marra)
- No data to suggest CSF abnormalities in early syphilis reliably predict the need for aggressive NS tx

Rating Scheme for Treatment Recommendations

Strength of the Recommendation

- A – Strong Evidence for efficacy and clinical benefit
- B – Moderate evidence for efficacy but only limited clinical benefit
- C – Evidence is insufficient to support a recommendation (optional)
- D – Moderate evidence for lack of efficacy or for adverse outcomes

Quality of the Evidence

- I – At least one properly conducted randomized trial
- II – At least one well designed clinical trial (cohort, case controlled analytic studies)
- III – expert opinion

Treatment Recommendations
Primary, Secondary, EL

- Penicillin treatment of choice regardless of HIV status
  - Benzathine Pcn G x 1 **AII**
- Benefit of additional injections unproven
  - Enhanced tx (IM+oral) no benefit **DII**
- PCN alternatives **BIII**
  - Not well evaluated
  - Close serologic and clinical monitoring
  - Azithromycin 2 gm (resistance/tx failure) **CII**

Treatment Recommendations Latent Syphilis & Neurosyphilis

- Benz PCN 3 wkly injections **AIII**
- Non Pcn alternatives
  - Doxycycline X 28 d- insufficent evaluation **BIII**
  - Close clinical and serologic monitoring
- Neurosyphilis -IV PCN **AII** Procaine/Proben **BII**
  - Additional 1-3 wkly x Benz Pcn **CIII**
- Sulfa allergy- no probenecid **DIII**
- PCN allergy- densensitization **BIII** or ceftriaxone **CIII**

Response to Therapy

- Frequent clinical and serologic monitoring
  - Early stage- 3, 6, 9, 12, 24 months
  - Latent syphilis- 6, 12, 18, 24 months
- Serologic responses similar to HIV- patients
  - Subtle variation in temporal pattern of response
- 15-20% of persons may remain serofast
  - Probably don’t represent tx failure
  - Serologic detection of reinfection based on 4x titer increase above baseline

Management of Treatment Failure

- CSF evaluation and retreatment
- Retreatment of early stage syphilis
  - Sustained four increase in RPR after initial reduction
  - Persistent of recurring signs or sx
  - Strongly consider for failure of RPR decline 4x 6-12 months after tx **BIII**
  - Benzathine Pcn wkly X 3 **BIII** or IV PCN **CIII**

Management of Treatment Failure

- Retreatment of late latent syphilis
  - Repeat CSF evaluation, tx NS if consistent with CNS involvement
  - Clinical signs or sx
  - 4x increase in RPR or less than 4X decline 12-24 month after tx **BIII**
  - Benz Pcn wkly x 3 **BIII** or NS regimen **CIII**

Prevention Recommendations

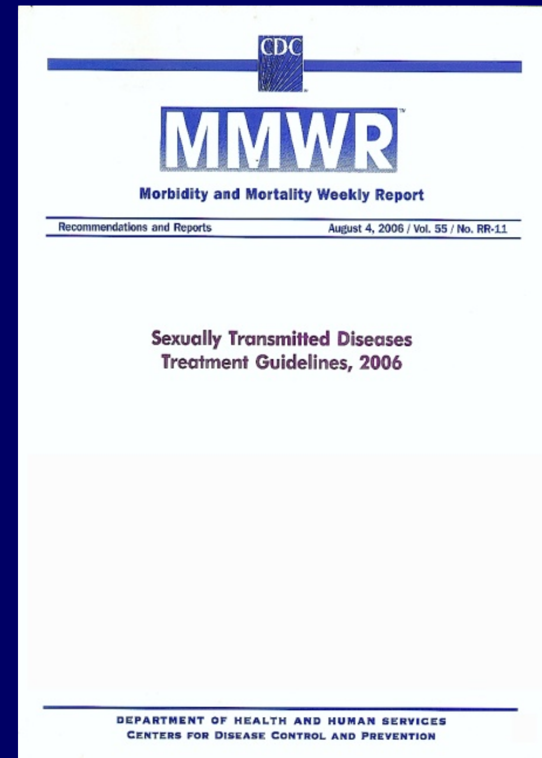
- Routine discussion of sexual behavior
  - client-centered risk reduction messages
- Routine serologic screening at least annually
  - More frequent screening dependent on risk behaviors (every 3-6 months)
- Intensified counseling
- Evaluation for other STDs

Pregnancy

- All pregnant women screened in first trimester
  - Additional testing among women at high risk
- Rates of fetal transmission highest in early syphilis
- Insufficient data about serologic response in HIV+ women
- Some treatment failures after single Benz Pcn (HIV-)
  - Consider second injection **BIII**
- Pcn allergy –desensitization **AIII**
  - No pcn alternatives proven safe and effective for maternal infection or prevention of fetal infection
  - Insufficient data on azi or ceftriaxone **DIII**
  - Tetracyclines- teeth staining, hepatoxicity **DIII**

CDC STD Treatment Guidelines

- Authoritative source of STD treatment and management
- Screening, prevention and vaccination strategies, treatment regimens
- Order hard copies http://www.cdc.gov/std/treatment
- Pocket guides, wall charts



Questions?

Ask Dr. Workowski

Thank you

Special thanks to CSI Medical Education