"THE STATE OF SYPHILIS" Early Neurosyphilis in HIV-Infected Patients and an Update on Effective Partner Notification

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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, University of California AIDS Research Program and Gen-Probe, Inc., Focus Technologies, and Cerexa provided research funding to Dr. Klausner**

- **Communications Strategies, Inc. and King Pharmaceuticals, Inc. supported Dr. Klausner to conduct various educational programs**

Disclosure

- **Dr. Hook is a Faculty member of the of University of Alabama at Birmingham**

In the past 12 months:

- **Dr. Hook has held consulting agreements with Communications Strategies, Inc., King Pharmaceuticals, Inc and Abbott Laboratories**

- **Dr. Hook has received research support from the CDC, NIAID, Becton-Dickinson and Abbott Laboratories**

Bicillin® L-A (penicillin G benzathine injectable suspension) and Bicillin C-R (penicillin G benzathine and penicillin G procaine injectable suspension)

BICILLIN® L-A (penicillin G benzathine injectable suspension) is indicated in the treatment of infections due to penicillin G sensitive microorganisms that are susceptible to the low and very prolonged serum levels provided by this particular dosage form. These include mild-to-moderate upper respiratory tract infections due to susceptible streptococci (including streptococcal pharyngitis), syphilis, yaws, bejel, and pinta. It is also indicated as prophylactic treatment for rheumatic fever and glomerulonephritis.

BICILLIN® C-R (penicillin G benzathine and penicillin G procaine injectable suspension) is indicated in the treatment of moderately severe infections due to penicillin-G-susceptible microorganisms that are susceptible to serum levels common to this particular dosage form. These include upper respiratory tract infections, scarlet fever, erysipelas, skin and soft-tissue infections due to susceptible streptococci, and pneumonia and otitis media due to susceptible pneumococci.

NOTE: This formulation should not be used in the treatment of venereal disease, including syphilis.

Bicillin® L-A (penicillin G benzathine injectable suspension) and Bicillin C-R (penicillin G benzathine and penicillin G procaine injectable suspension)

Important Safety Information for BICILLIN® L-A and BICILLIN® C-R

Do not inject intravenously or admix with other intravenous solutions. There have been reports of inadvertent intravenous administration of penicillin G benzathine which has been associated with cardiorespiratory arrest and death.

Penicillin G is contraindicated in patients with a history of hypersensitivity reactions to any of the penicillins and BICILLIN C-R in patients with a history of hypersensitivity reaction to procaine. Before use, identify previous hypersensitivity reactions to penicillins, cephalosporins, or other allergens. If allergic reaction occurs, discontinue use and initiate appropriate therapy.

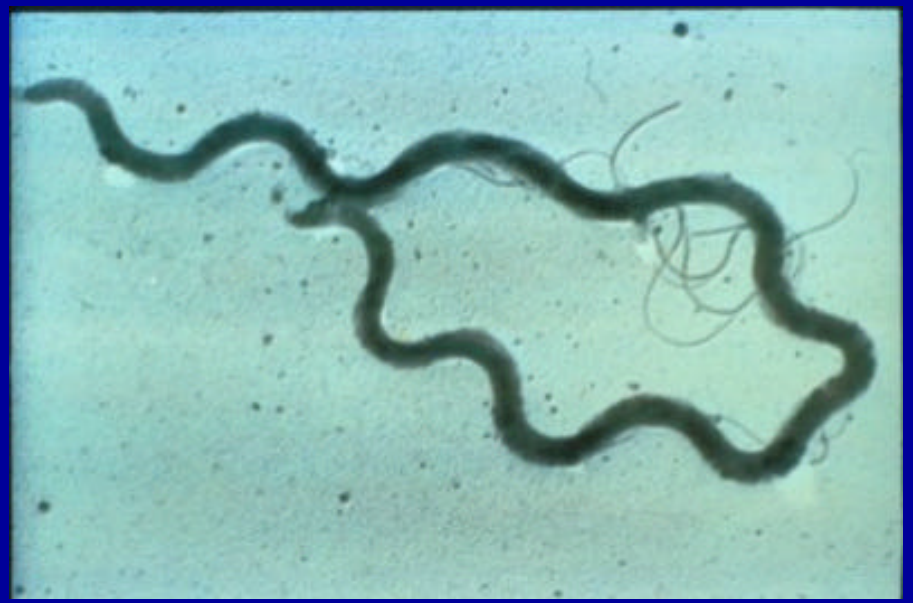
Pseudomembranous colitis has been reported with nearly all antibacterial agents, including penicillin, and may range in severity from mild to life-threatening.

Give only by deep intramuscular injection. Do not inject into or near nerves or arteries; severe neurovascular or other damage may occur. Adverse reactions include but are not limited to: gastrointestinal, hypersensitivity, central nervous system, dermatologic, hematologic, and injection site reactions.

Please see full Prescribing Information available at www.bicillin.com.

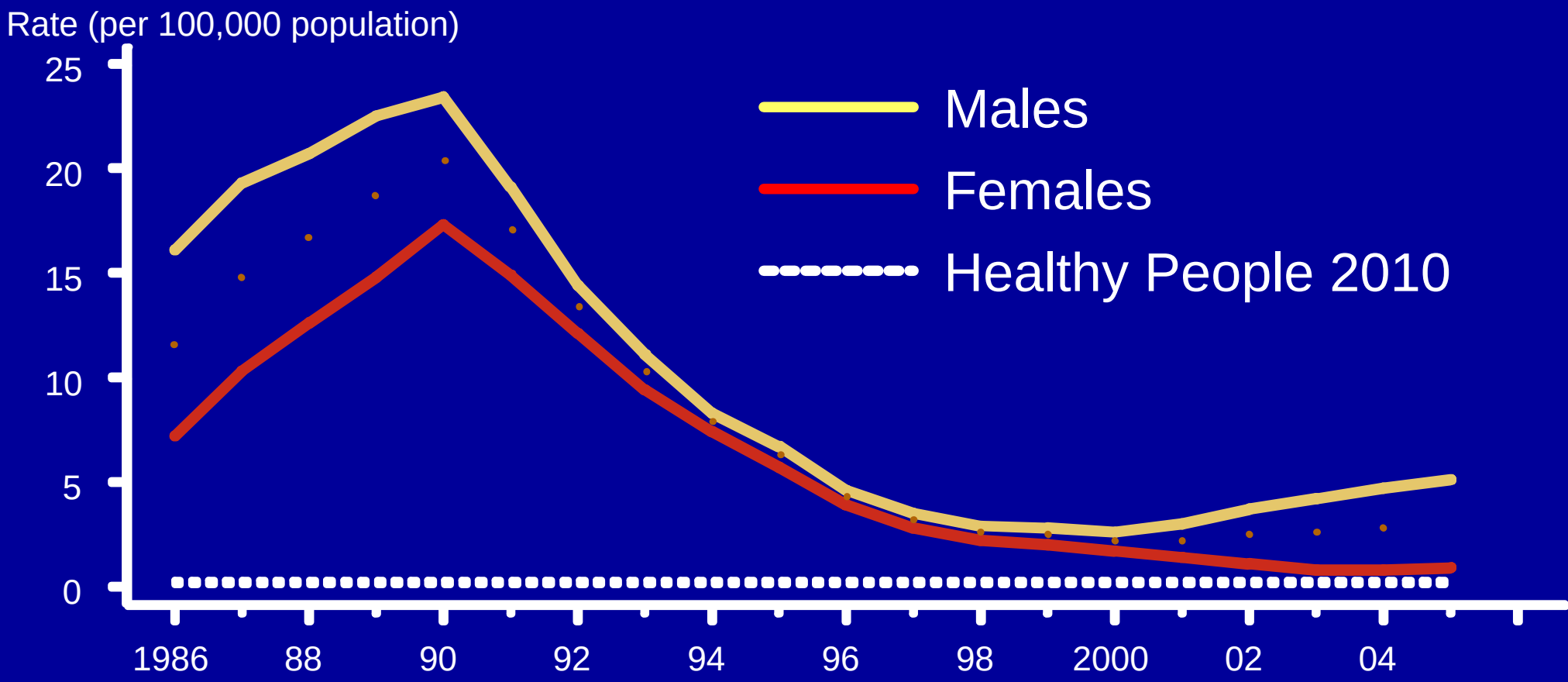
Syphilis Biology

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



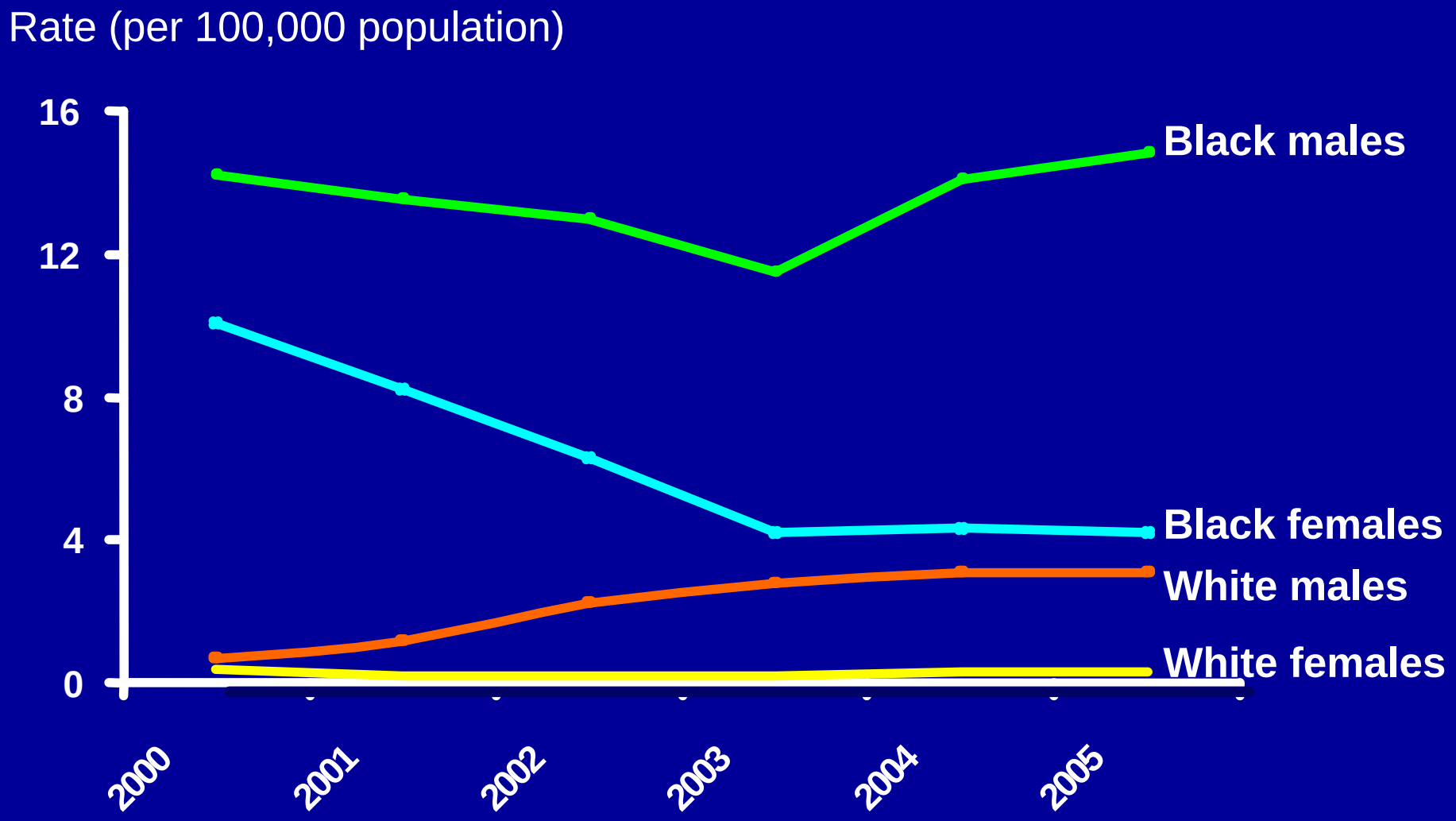
San Francisco City Clinic Web site www.dph.sf.ca.us/sfcityclinic/stdbasics/syphilis.asp
Path: STD Basics: Syphilis (accessed August 15, 2007)

Primary and secondary syphilis — Rates by sex: United States, 1986–2005 and the Healthy People year 2010 target



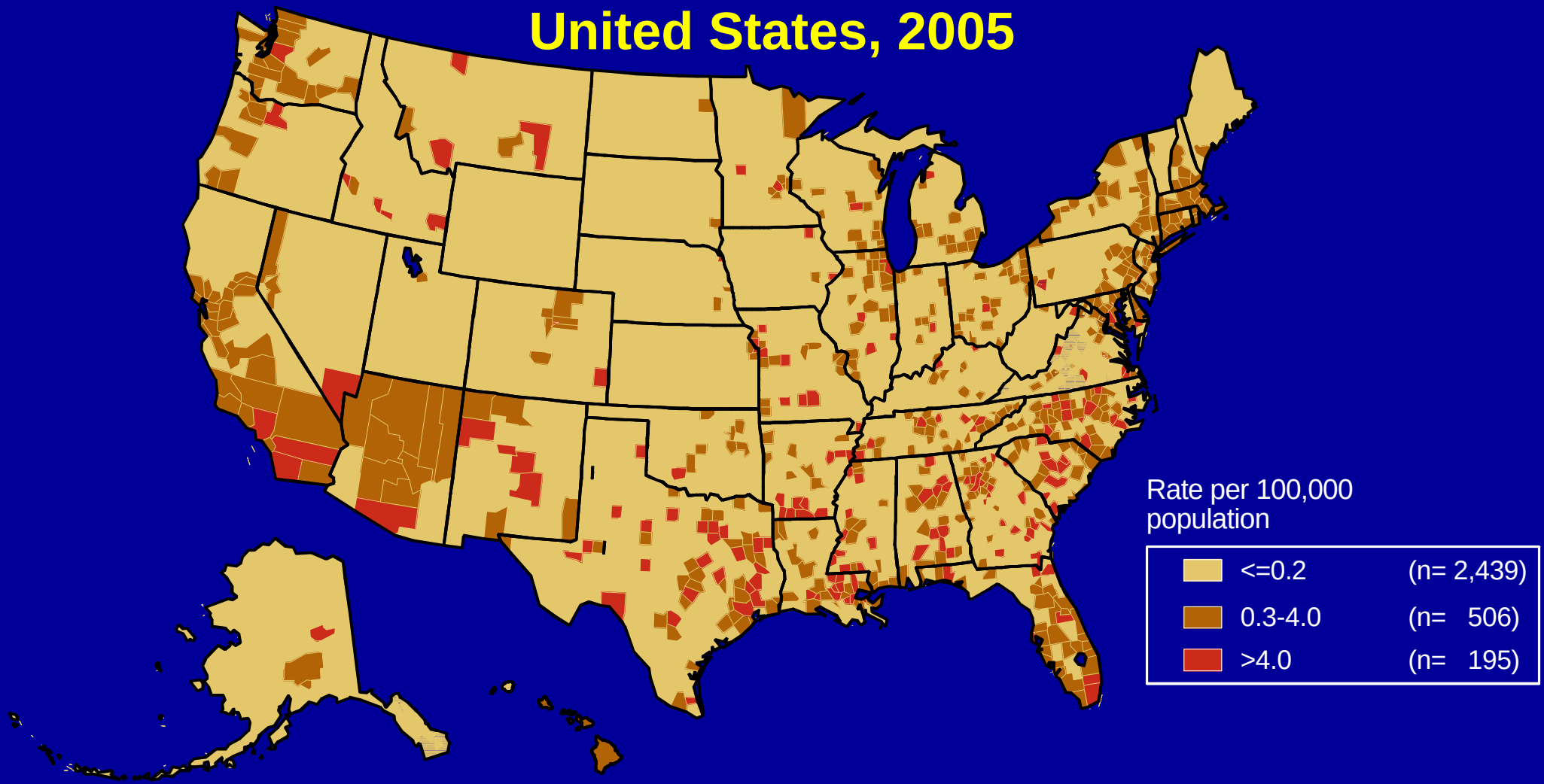
CDC Division of STD Prevention. Syphilis Surveillance Report, Sexually Transmitted Diseases Surveillance 2005 Supplement, Page 13: Figure 2.

Primary and secondary syphilis: Black and White rates by sex, 2000-2005



2005 data provisional, CDC

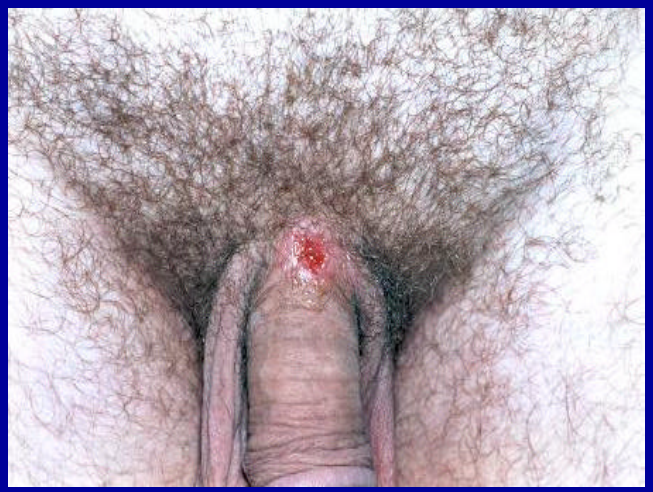
Primary and secondary syphilis — Rates by county: United States, 2005

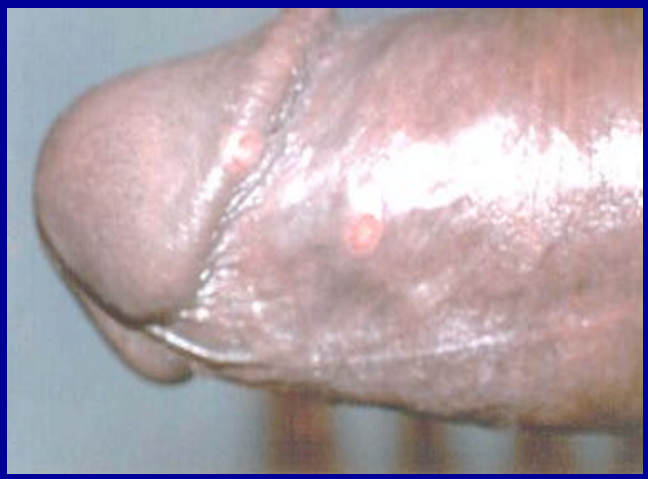


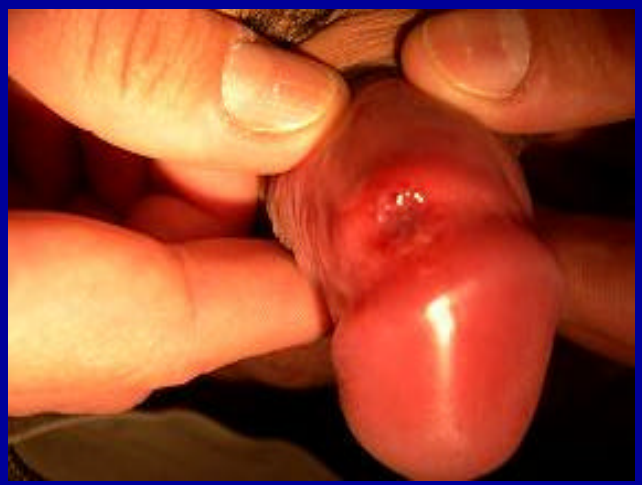
Note: The Healthy People 2010 target for P&S syphilis is 0.2 case per 100,000 population. In 2005, 2,434 (77.5%) of 3,140 counties in the U.S. reported no cases of P&S syphilis.

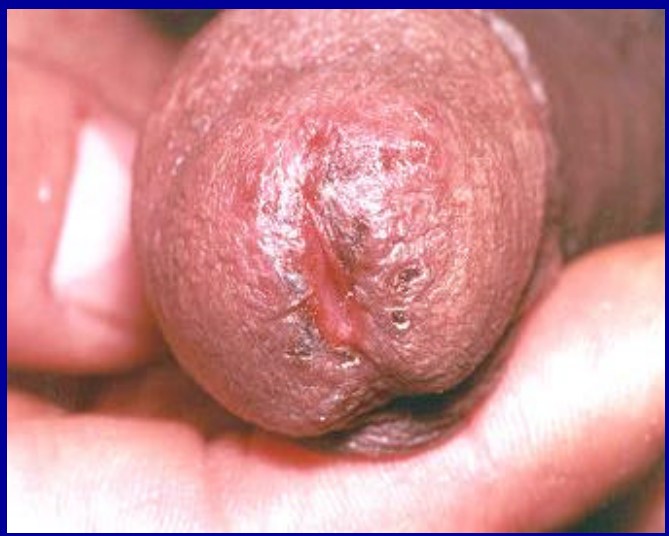
CDC Division of STD Prevention. Syphilis Surveillance Report, Sexually Transmitted Diseases Surveillance 2005 Supplement, Page 18: Figure 11.

Primary syphilis—chancres



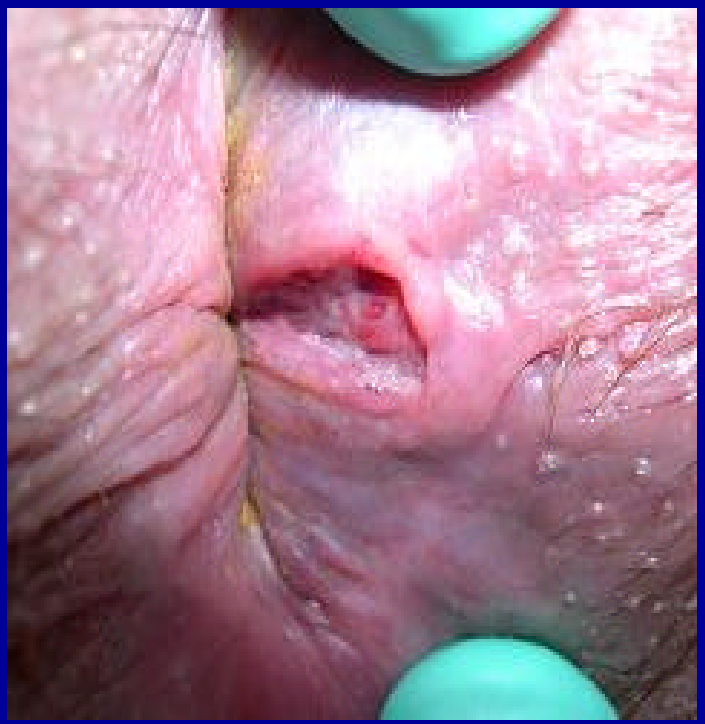




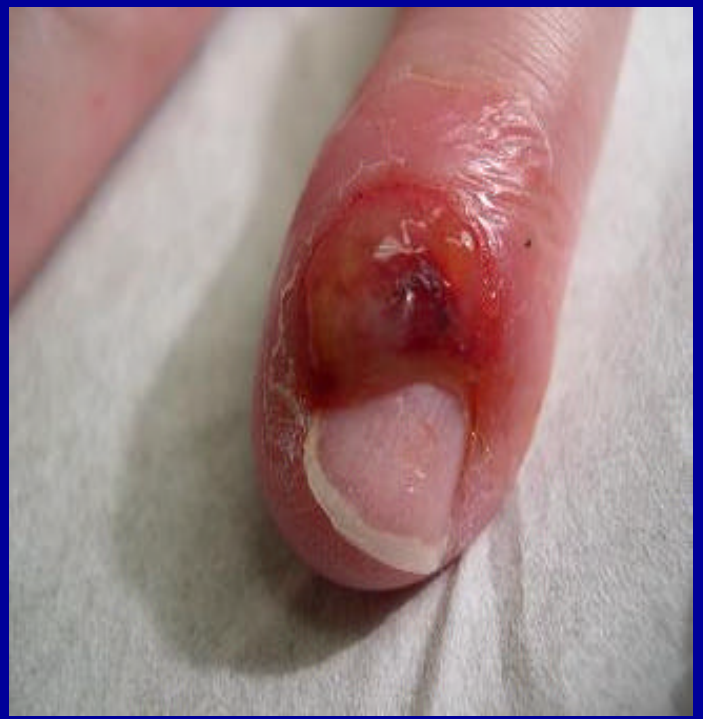


Photos courtesy of Jeffrey D. Klausner, MD

Primary syphilis—chancres



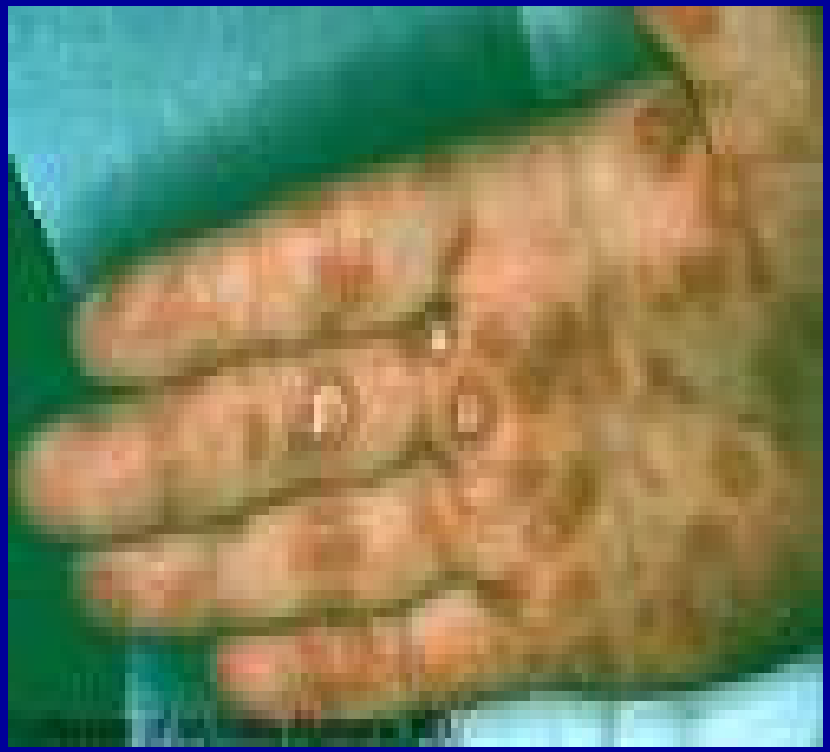
anorectal



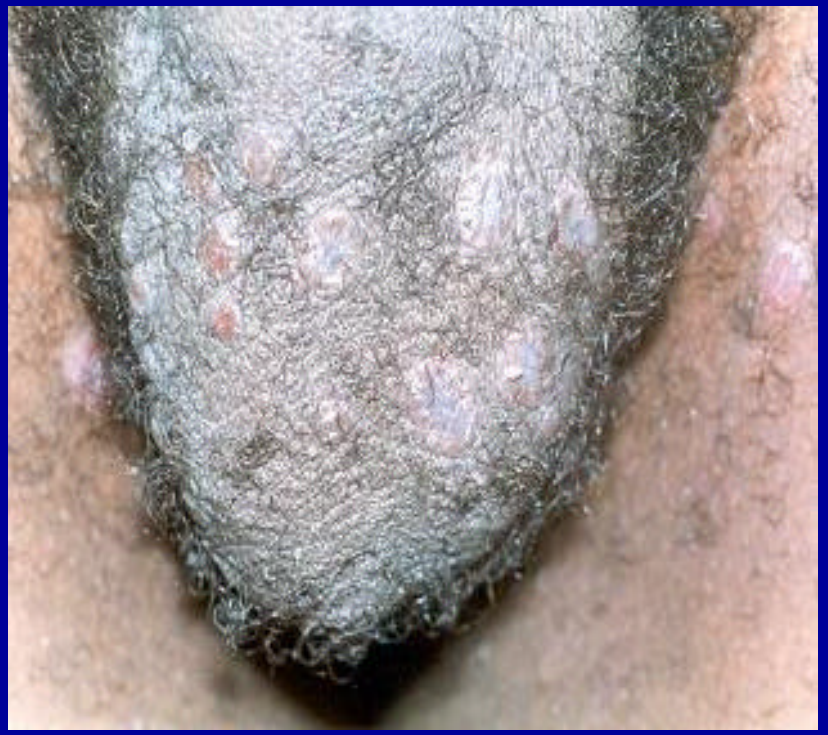
finger

Photos courtesy of Jeffrey D. Klausner, MD

Secondary syphilis—annular rashes



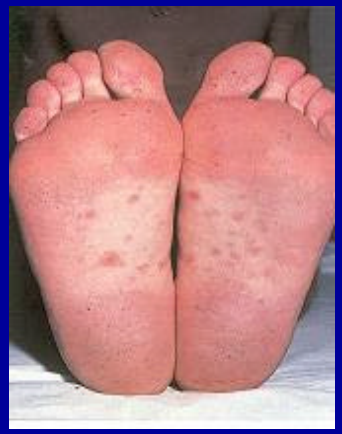
palms

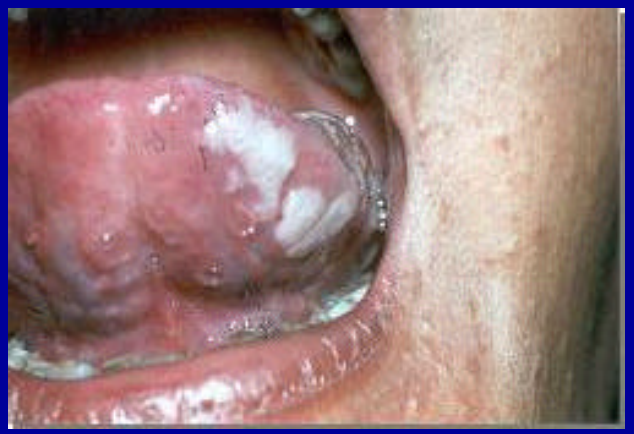


scrotum

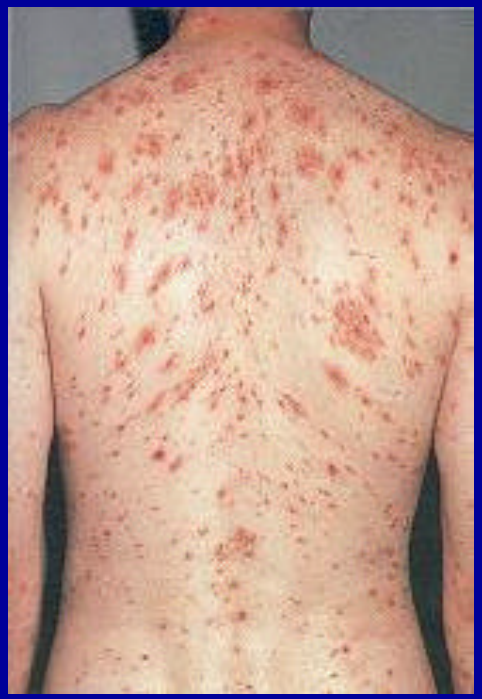
Photos courtesy of Jeffrey D. Klausner, MD

Secondary syphilis





Mucous patches



Rash

Condylomata lata

Photos courtesy of Jeffrey D. Klausner, MD

Physical Examination

- General
- Skin—rule out hair loss (alopecia); rule out rash
- Oropharynx—rule out chancres, mucous patches
- Penis/ scrotum—rule out chancres/ rash
- Anus—rule out *condylomata lata*

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

Case 1

- 38-year-old HIV-infected male
- CD4=395, viral load <50
- Noting declines in visual activity, difficulty reading newspaper – not trauma-related
- 6 sex partners in past 2 months (via Internet)

Clinical information on file with Edward W. Hook, III, MD

Case 1

Physical Examination

- **Suggestive of iritis**
- **Diffuse, macular non-puritic rash over back and trunk**

RPR titer= 1:64

Should an LP be performed?

Clinical information on file with Edward W. Hook, III, MD

Case 1

NOT FOR DIAGNOSIS… this patient has ocular neurosyphilis. In some settings lumbar puncture might be performed to provide information for follow-up or to rule out other infectious processes.

Clinical information on file with Edward W. Hook, III, MD

Case 2

- 40-year-old HIV-infected MSM patient
- On ART (anti-retroviral therapy) for past 4 years; good adherence
- Feels in good health
- Physical examination is normal
- CD4 count 380; viral load <50

RPR titer= 1:32

Clinical information on file with Edward W. Hook, III, MD

Case 2

- Urine and rectal swab tests negative for gonorrhea and chlamydial infections
- Neurologic evaluation is normal
- Patient acknowledges prior treatment for gonorrhea and rectal herpes infections; says he has never been diagnosed with/treated for syphilis in the past

Should an LP be performed?

Clinical information on file with Edward W. Hook, III, MD

Case 2

LP is performed

- **Opening pressure is 26 mm of CSF**
- **Cell count is 40 (100% lymphocytes)**
- **CSF protein is 48%**
- **CSF VDRL and cryptococcal antigen assays are negative**
- **Cultures pending**

What should be done now?

Clinical information on file with Edward W. Hook, III, MD

Additional evaluation

- Physical examination with particular attention to skin, palms/soles, oral cavity, genital and anus
- Neurologic examination

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, gumma, etc.
4) Late or unknown latent in HIV-infected patients

Centers for Disease Control and Prevention, 2006 STD Treatment Guidelines, *MMWR*, 2006. p. 8. Available at www.cdc.gov/std.

Further history

- Prior syphilis testing history
- Sexual history
  - Gender and number of sex partners 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
- Medical history including STD history, current medications, allergies and chronic illnesses
- Review of Systems with focus on neurologic complaints, particularly hearing, visual or balance

Neurosyphilis Treatment*

- **Primary Therapy**
  - Aqueous penicillin G IV 18-24 MU daily administered as 3-4 MU every 4 hours or continuous infusion for 10-14 days
  - Follow-up treatment with penicillin G benzathine (Bicillin®-LA) 2.4 MU IM weekly for three weeks
- **Alternative Therapy**
  - Procaine penicillin 2.4 MU IM daily **PLUS**
  - Probenecid 500 mg PO 4 x daily, both for 10-14 days or
  - Follow-up treatment with penicillin G benzathine (Bicillin®-LA) 2.4 MU IM weekly for three weeks
  - Consideration in penicillin allergic patients: Ceftriaxone 2 g IM or IV 1 x daily for 10-14 days
- **Follow-Up CSF Evaluation**
  - To document resolution of CSF abnormalities
  - Repeat every 6 months until cell count normalizes, protein and VDRL will take longer to normalize
  - CSF should be normal by 2 years; if not, consider retreatment

* Neurosyphilis treatment indicated for adult patients

Centers for Disease Control and Prevention, 2006 STD Treatment Guidelines, *MMWR*, 2006. p. 11. Available at: **www.cdc.gov/std**.

Neurosyphilis and HIV Infection

- Currently neurosyphilis is more common in early infection (< 1 year) than late infection
- Neurosyphilis is more common in HIV-infected than HIV-uninfected patients
- CSF abnormalities may be due to HIV-infection (elevated CSF white blood cell count or protein) versus syphilis

1. Simon, R., Neurosyphilis: Current Diagnosis & Treatment of Sexually Transmitted Diseases, Jeffrey D. Klausner; Edward W. Hook, III, 2007. p. 130.
2. Mills, L., Sexually Transmitted Diseases in HIV-Infected Persons: Current Diagnosis & Treatment of STDs. p. 143.

Partner management

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

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

Centers for Disease Control and Prevention, 2006 STD Treatment Guidelines, MMWR, 2006. p. 4. Available at www.cdc.gov/std.

Syphilis: Case 3

- 44-year-old HIV-infected male diagnosed with secondary syphilis
- Patient reports meeting partner online, in sex clubs and has two steady partners

Clinical information on file with Jeffrey D. Klausner, MD

Notification of Partners

- **Patient referral**
- **Provider or third party (health department) referral**
- **Contract referral**

Notification May Vary by Partner Type

- **Internet partners – thru Web sites, Inspot.org**
- **Steady Partners – patient or provider referral**
- **Sex Club Partners – likely none, if anonymous**

Based on Jeffrey D. Klausner, MD's clinical experience

Internet Partner Notification

Patient referral – contact via

- e-mail
- Inspot.org
- Telephone
- In person

Provider referral – contact via

- e-mail – many providers have online access
- Membership
- Immediate online partner notification

Based on Jeffrey D. Klausner, MD's clinical experience

Patient Referral

- Requires coaching and counseling
- Can be time consuming but often effective
- Requires follow-up, i.e. contract
- In person

Based on Jeffrey D. Klausner, MD's clinical experience

Provider Referral

- **Local health department often contacts reported primary, secondary or early cases**
- **Has trained staff with specific expertise**
- **Assures confidentiality**

Based on Jeffrey D. Klausner, MD's clinical experience

Evaluation of Disease Intervention Strategies

- **Landis, SE., et al. Results of a randomized trial of partner notification in cases of HIV infection in North Carolina. *NEJM* 1992, 326:101-106.**

- **Peterman, T., et al. Partner notification for syphilis: a randomized, controlled trial of three approaches. *Sex Transm Dis*. 1997 Oct;24(9):511-8**

Partner Management in Syphilis

Stage	Partner period	Management
Primary syphilis	< 90 days	Treat*
Primary/ 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® L-A) 2.4 MU IM once**

Centers for Disease Control and Prevention, 2006 STD Treatment Guidelines, *MMWR,* 2006. p. 4. Available at www.cdc.gov/std.

Early 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. 4, 6, 15. Available at www.cdc.gov/std.

Syphilis Prevention

- **Counsel patients on correlation between increased risk of syphilis infection and increased number of sex partners**
- **Advise patients on importance of consistent and correct use of condoms for all types of sexual activity**
- **Regular screening 3-6 months is recommended for persons who have more than one sex partner**

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

Summary

- **Syphilis is increasing in the U.S. mostly in gay men and other men who have sex with men**
- **Treatment of syphilis requires use of penicillin G benzathine (Bicillin® L-A)**
  - ***Bicillin® C-R is not indicated for syphilis***
- **Prevention efforts must focus on new target populations, new strategies and enhanced partner services**

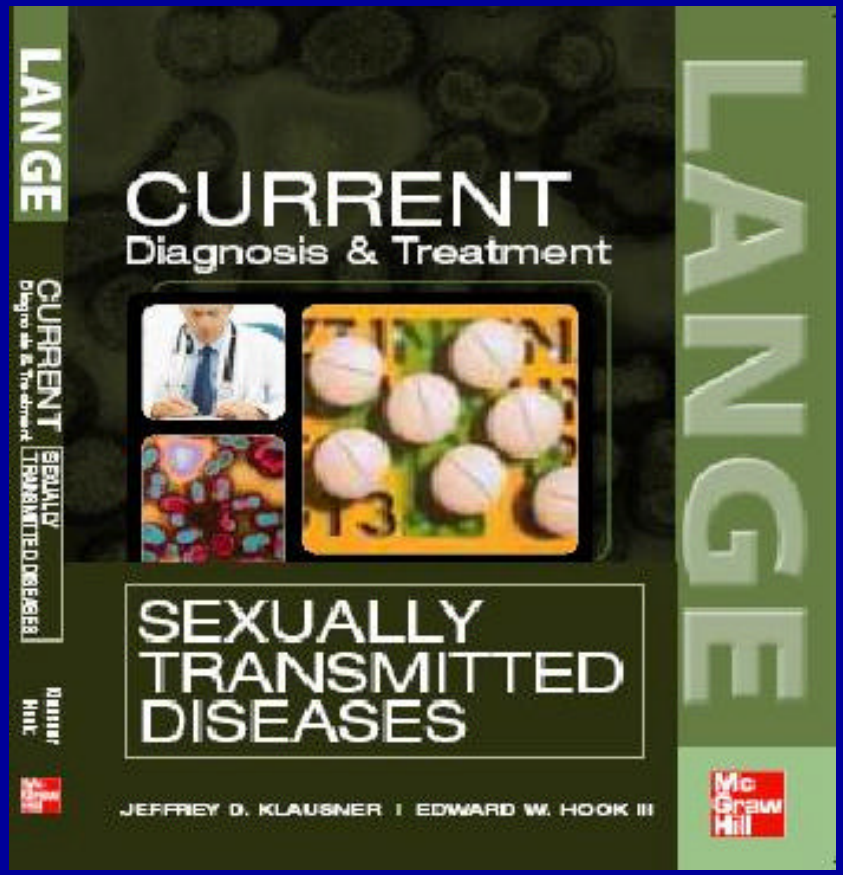
Based on Jeffrey D. Klausner, MD's clinical experience

Web Resources

- **www.cdc.gov/std**
- **www.ncsddc.org**
- **www.stdhivtraining.org**
- **www.stdtest.org (SF residents)**
- **www.Inspot.org**
- **www.sfcityclinic.org**

www.bicillin.com

Sources for more STD information



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Questions?

Ask Drs. Hook or Klausner (“Dr K”)

www.bicillin.com