

# ***“THE STATE OF SYPHILIS” ADDRESSING THE CO-MORBIDITIES: HIV INFECTION AND SYPHILIS***

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# *Disclosure*

- Dr. Klausner is an employee of the City & County of San Francisco and 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., provided research funding to Dr. Klausner
- Communication Strategies, Inc. and King Pharmaceuticals, Inc. supported Dr. Klausner to conduct various educational programs

# Disclosure

- Dr. Erbelding is on the full-time faculty of Johns Hopkins University School of Medicine and receives salary support for her faculty role from Baltimore City Health Department

## *In the past 12 months:*

- The NIH and HRSA have provided research funding to Dr. Erbelding
- Dr. Erbelding has held consulting agreements with Communication Strategies, Inc., and King Pharmaceuticals, Inc; The Academic Alliance for Care and Prevention of AIDS in Africa; and MedCases Inc.

# **Bicillin® L-A**

## **penicillin G benzathine injectable suspension**

**WARNING: NOT FOR INTRAVENOUS USE. DO NOT INJECT INTRA-VENOUSLY 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. Prior to administration of this drug, carefully read the WARNINGS, ADVERSE REACTIONS, and DOSAGE AND ADMINISTRATION sections of the labeling.**

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 including: syphilis, yaws, bejel and pinta.

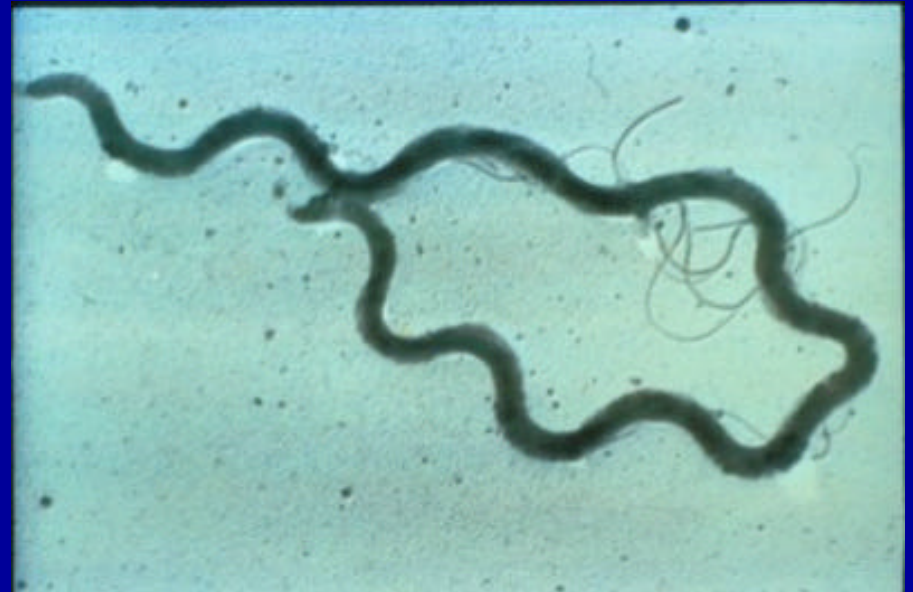
### **Important Safety Information**

Penicillin G benzathine is contraindicated in individuals with hypersensitivity to any penicillin-type antibiotic. Use with caution in individuals with histories of significant allergies and/or asthma. Give only by deep intramuscular injection. Do not inject by any other route, such as intra-arterial or intravenous. Do not inject into or near nerves or blood vessels, since such injection might produce neurovascular or other damage.

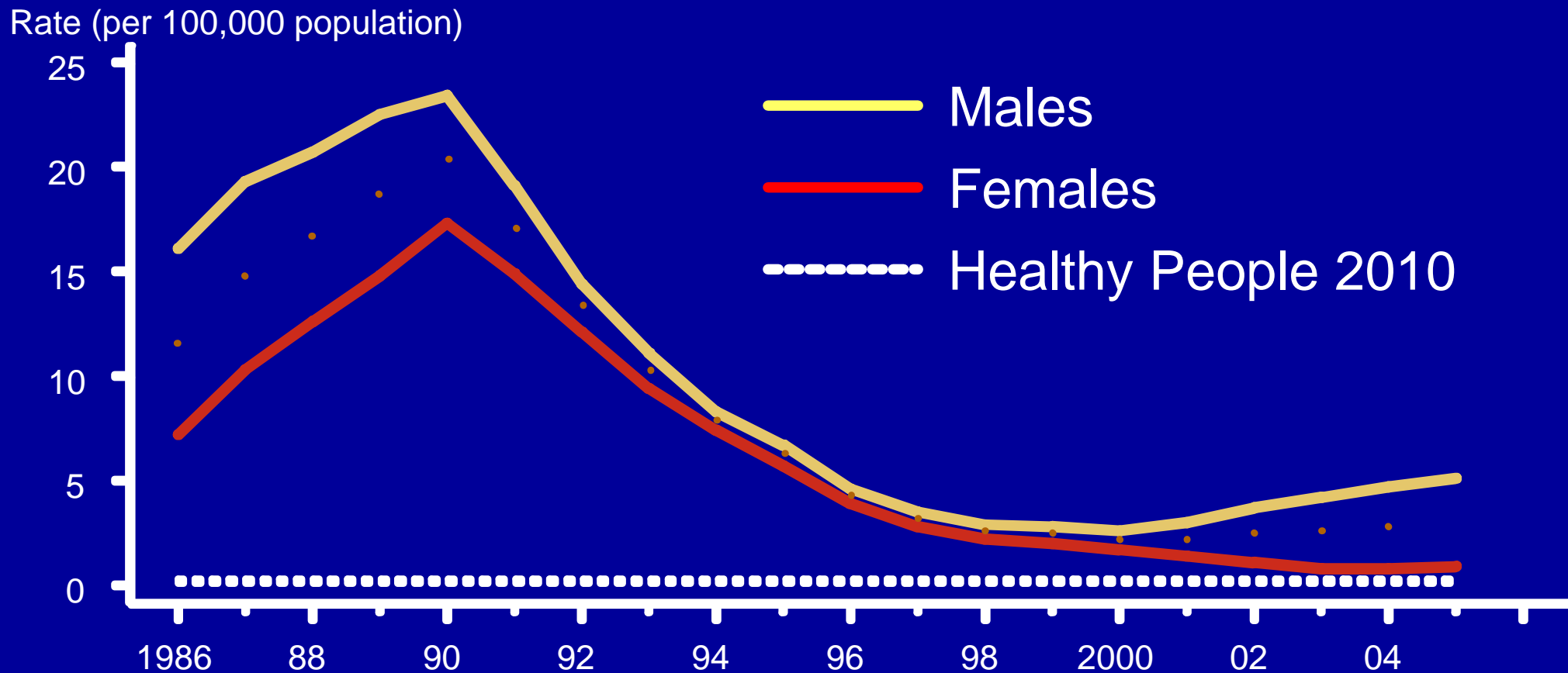
Please see accompanying full Prescribing information which may also be obtained at [www.bicillin.net](http://www.bicillin.net).

# Syphilis Biology

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

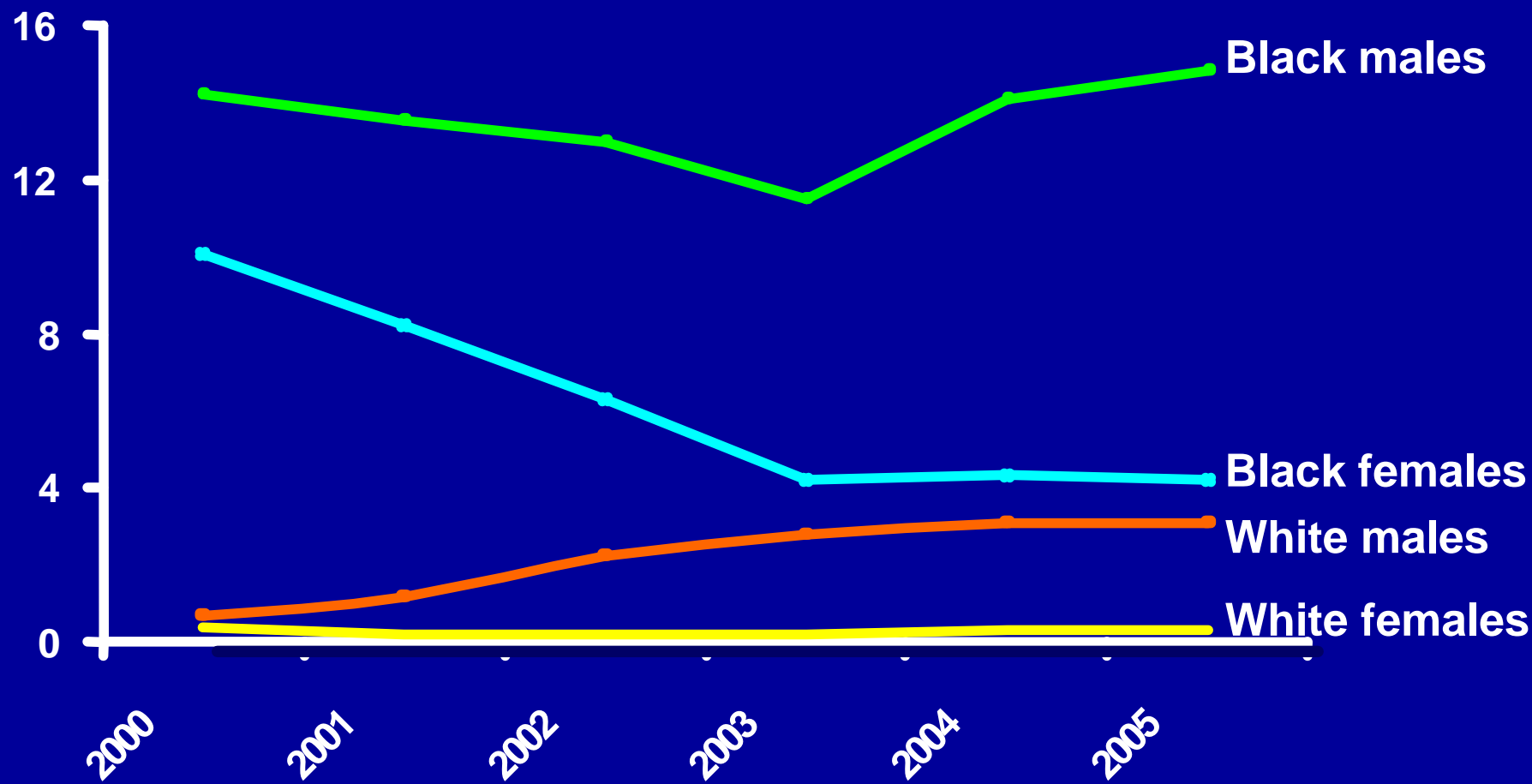


# Primary and secondary syphilis — Rates by sex: United States, 1986–2005 and the Healthy People 2010 target



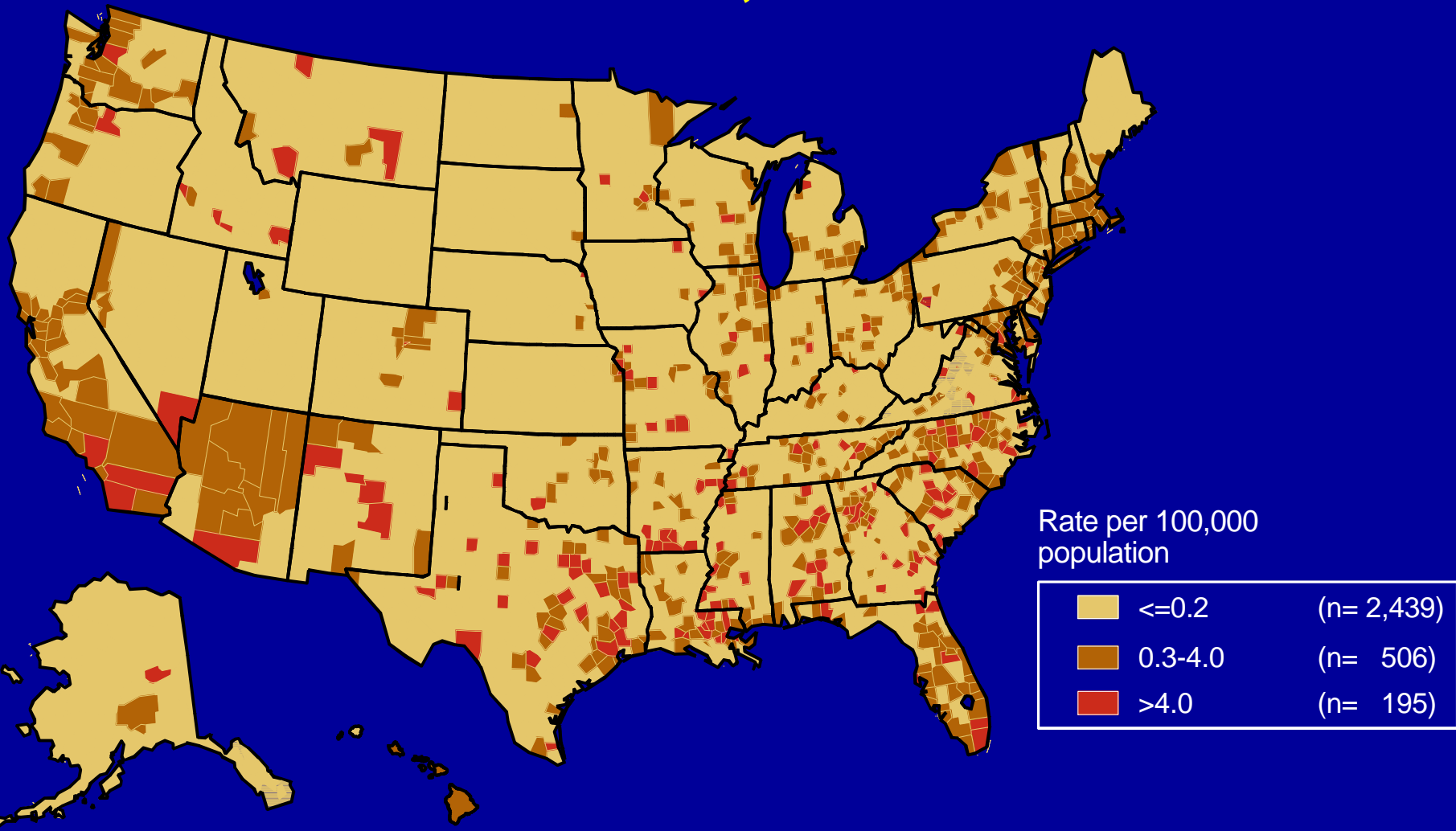
# Primary and secondary syphilis: Black and White rates by sex, 2000-2005

Rate (per 100,000 population)



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.



# Case 1

- 42 year old HIV-infected man has a reactive RPR confirmed with reactive TPPA\*
- RPR titer = 1:64

RPR = rapid plasma reagin

TPPA = Treponema pallidum particle agglutination

\*Alternative confirmatory test = fluorescent treponema antibody absorbed (FTA-ABS)

# Case 1

- What further history is required?
- Additional tests or evaluation?
- Treatment and follow-up?

# 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**

# Additional evaluation

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

# 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**

# Early 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.



# 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

# 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<sup>®</sup>-LA) 2.4 MU IM once



# Syphilis: Case 2

Emily J. Erbelding, MD, MPH

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# Case 2

A 22 yr old M presents for first visit for HIV care.

- Test HIV+ 18 months ago; MSM risk factor
- CD4 cell count unknown, never on therapy
- One HIV+ sex partner in past 6 months
- No STI history
- ROS: reports peeling rash on palms/soles x 2 weeks, also white plaques in mouth and on sides of tongue (told he had “thrush” by HIV+ friends and took their medicine to treat it). Also reported blurry vision over past week.

# Evaluation

- **Has had multiple episodes of oral sex with one HIV+ SP in past 6 months; prior to that 10 lifetime sexual partners. No drug or alcohol use.**
  - **No allergies or meds.**
  - **No pets. Recently moved to Baltimore from Miami.**
- **PE:**
  - **Vital signs normal.**
  - **Wore eyeglasses but fundoscopic exam grossly normal.**
  - **Oropharynx: white raised areas “with serpiginous borders” on buccal mucosa, lower lip (did not scrape off with tongue depressor)**
  - **Skin: Scaly peeling plaque-like lesions on palms and soles.**
  - **Genital: uncircumcised, painless “wartlike” lesion on dorsum of penis**

# Rash on palms



# Differential Diagnosis

- Oral lesions: thrush, oral hairy leukoplakia, aphthous ulcers
- Rash: psoriasis, Reiter's syndrome (keratoderma blennorrhagicum)
- Genital lesions: anogenital warts, herpes, syphilis, Behcet's disease

# Evaluation, continued

- RPR reactive, 1:2048 titer
- FTA-Abs reactive
- Ophthalmology evaluation: anterior uveitis
- CSF: protein 54 mg/dl, WBC 48/mm<sup>3</sup> (80% mononuclear cells), VDRL reactive (1:32 titer)

# Treatment and follow-up

- Hospitalized, IV penicillin G started
- Partner was RPR nonreactive but presumptively treated Bicillin®-LA (penicillin G benzathine) 2.4 million units
- Did not name additional partners
- Was eventually switched to ceftriaxone 2gms IV daily to complete 2 week course (convenience of outpatient therapy)
- Mucocutaneous lesions resolved by day 4 of therapy, visual symptoms within 1 week
- Serologic follow-up planned for 3,6,9,12,24 months

# Other management points

- Use of ceftriaxone for syphilis treatment
  - Experience with penicillin much more established
  - MIC data, animal models, and result of small randomized comparative trial support ceftriaxone use as alternative to penicillin<sup>1</sup>
- Need for additional Bicillin<sup>®</sup>-LA?
  - Shorter duration of sustained penicillin levels in neurosyphilis regimens
  - Some specialists recommend Bicillin<sup>®</sup>-LA (penicillin G benzathine) 2.4 mu IM per week for up to 3 weeks following the neurosyphilis treatment regimen
- Follow-up CSF evaluation
  - To document resolution of CSF abnormalities
  - Repeat every 6 months until cell count normalizes, protein and VDRL will take longer
  - CSF should be normal by 2 years

<sup>1</sup>Marra C: CID 30:540-544, 2000.



# Serology in Secondary Syphilis

- Rare reports of seronegative syphilis
- > 99% of patients will be seroreactive
- If seronegative, consider prozone reaction
  - Excess antibody prevents formation of antigen-antibody complex for test reactivity
  - Order repeat test with 1:10 dilution
- If seronegative, consider skin biopsy

# Treatment Follow-up

- Repeat serologic tests for syphilis at 3, 6, 9, and 12 months
- 4-fold decline at 12-months consistent with cure

# Partner Management

## Secondary Syphilis

- Notify, evaluate and provide treatment for all sex partners in past 6 months
  - Partners > 3 months, test then treat
  - Partners < 3 months, treat and test
- Treat with Bicillin<sup>®</sup> L-A (penicillin G benzathine) 2.4 million units IM once
- **PCN-allergic:**
  - Non-Pregnant:  
Doxycycline 100 mg PO BID x 14 days
  - Pregnant:  
Test for hypersensitivity, desensitize, treat  
Bicillin<sup>®</sup> L-A (penicillin G benzathine) 2.4 MU IM

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

Kate Buchacz<sup>a,b</sup>, Pragna Patel<sup>a,b</sup>, Melanie Taylor<sup>c,d</sup>, Peter R. Kerndt<sup>d</sup>, Robert H. Byers<sup>b</sup>, Scott D. Holmberg<sup>b</sup>, Jeffrey D. Klausner<sup>e,f</sup>

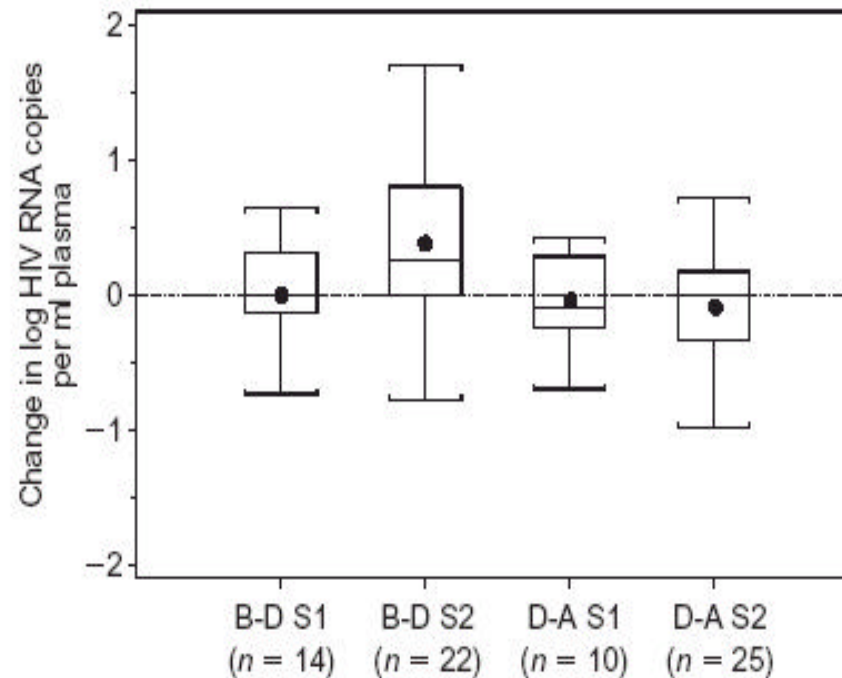


Fig. 1. Changes in HIV viral load associated with syphilis infection and syphilis treatment, according to the stage of syphilis. B-D, 'Before-to-during'; D-A, 'during-to-after'; S1, primary syphilis; S2, secondary syphilis. Boxplots show medians and upper and lower quartiles, whiskers encompass the extent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

# Neurosypphilis and HIV Infection

- Currently neurosypphilis is more common in early infection (< 1 year) than late infection
- Neurosypphilis is more common in HIV-infected than HIV-uninfected patients
  - 2% versus < 1%
- CSF abnormalities may be due to HIV-infection (elevated CSF white blood cell count or protein) versus sypphilis

# 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](http://www.cdc.gov/std)

# Syphilis Prevention

- Ask all patients about sexual activity, specific sexual behaviors, gender of sex partners and substance use
- Screen all sexually active male patients with male partners for syphilis; all pregnant women; and women with male partners at risk for syphilis
- Continue screening every 3-6 months in those with new partners or non-monogamous
- Provide risk-reduction counseling and substance use treatment services as indicated

# 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 2.4 MU IM once



# 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<sup>®</sup> L-A)
  - ***Avoid Bicillin<sup>®</sup> C-R, not indicated for syphilis***
- Prevention efforts must focus on new target populations, addressing meth use and enhanced partner services

# Web Resources

- [www.cdc.gov/std](http://www.cdc.gov/std)
- [www.ncsddc.org](http://www.ncsddc.org)
- <http://depts.washington.edu/nnptc/>
- [www.stdhivtraining.org](http://www.stdhivtraining.org)
- [www.sfcityclinic.org](http://www.sfcityclinic.org)
- [www.PROPSF.org](http://www.PROPSF.org)
- [www.stdtest.org](http://www.stdtest.org) (SF residents)
- [www.inspot.org](http://www.inspot.org)
- [www.bicillin.net](http://www.bicillin.net)

# Questions?

Ask Dr. Erbelding or Klausner (“Dr. K”)

[www.bicillin.net](http://www.bicillin.net)