

“SYPHILIS EDUCATION TODAY”

Treponemal EIA Testing... Clearing Up the Confusion

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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., 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



Primary Syphilis - Chancres



Secondary Syphilis



Mucous Patches



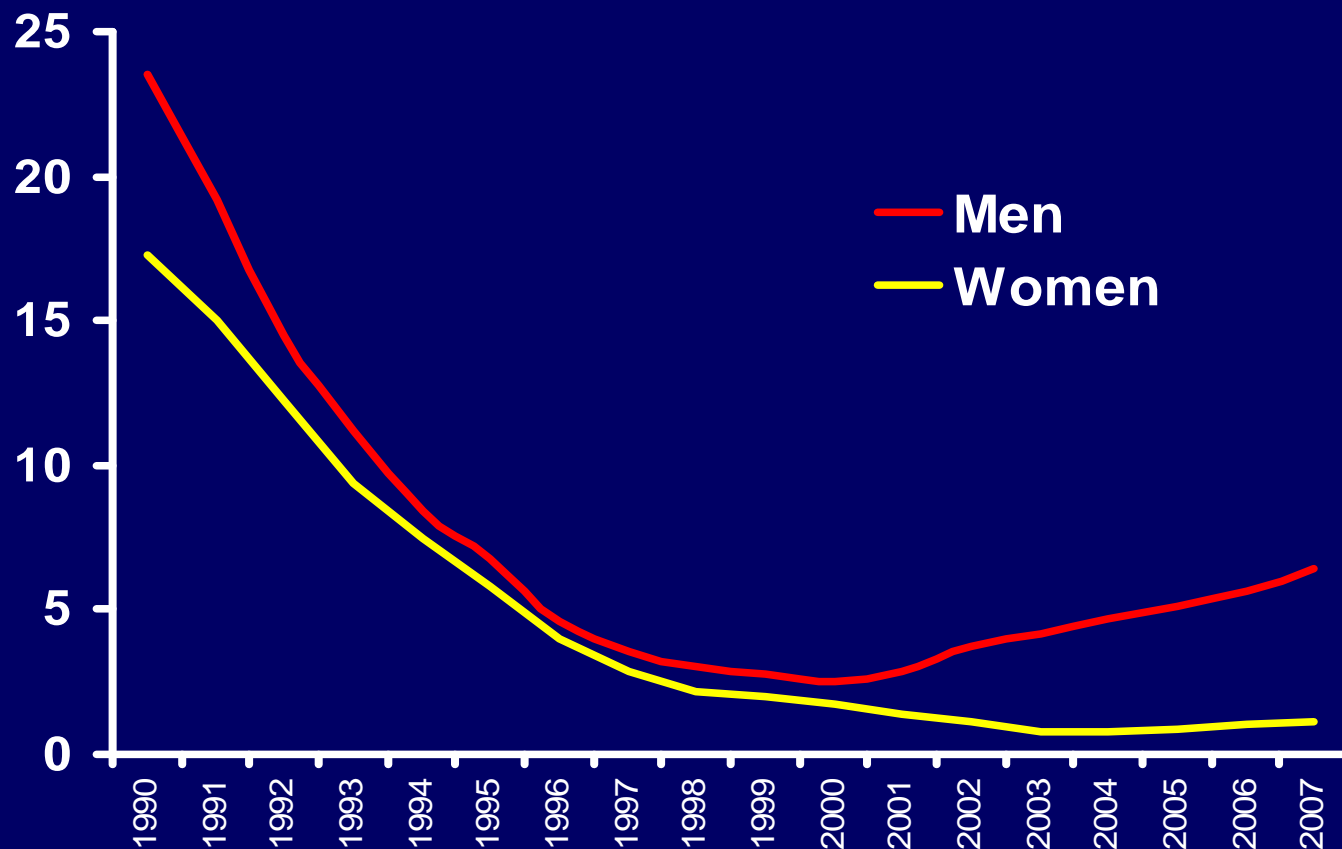
Rash



Condylomata
Lata

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

Rate (per 100,000 men/women)

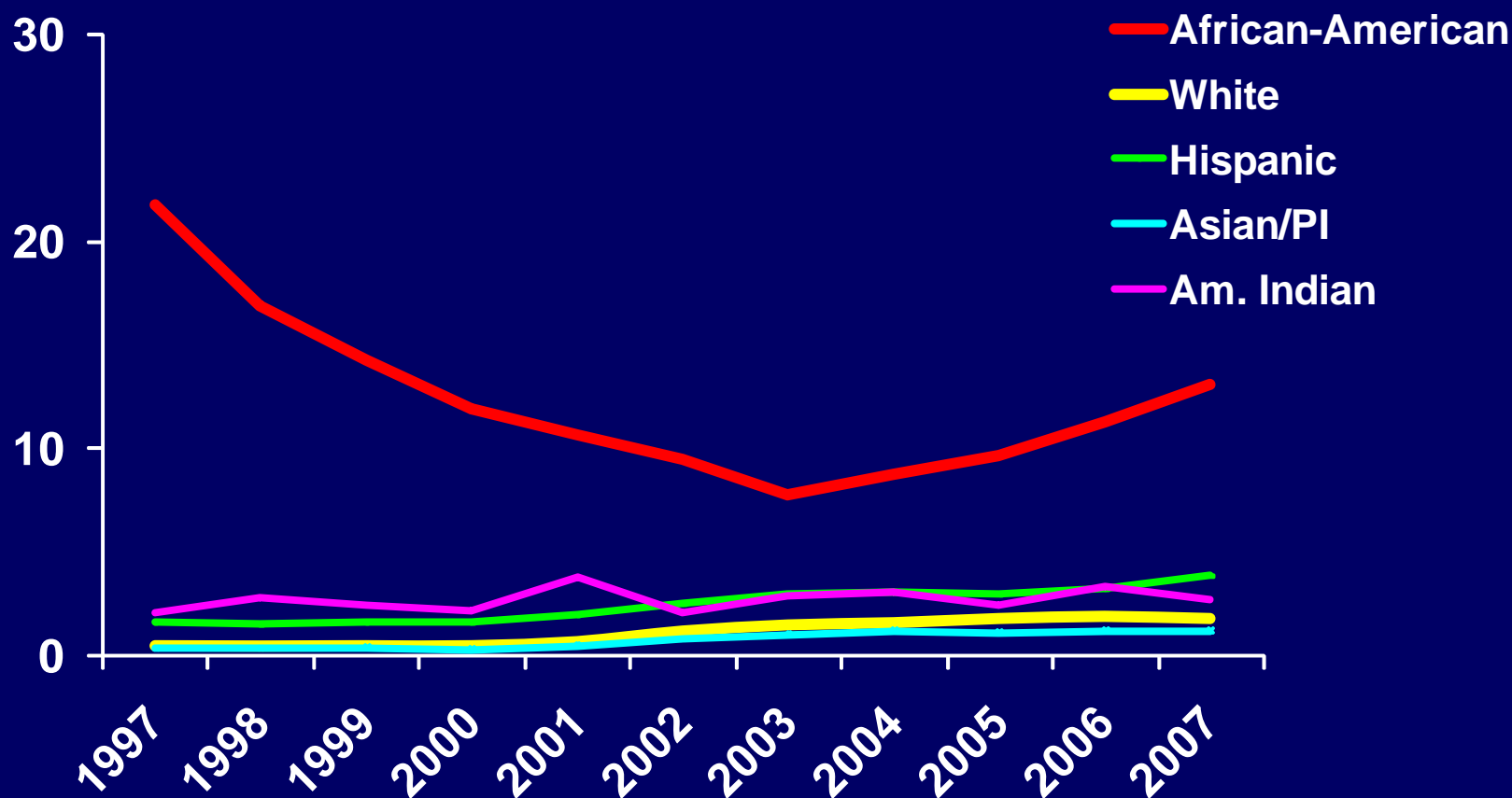


* 2007 data are preliminary

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

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

Rate (per 100,000 population)

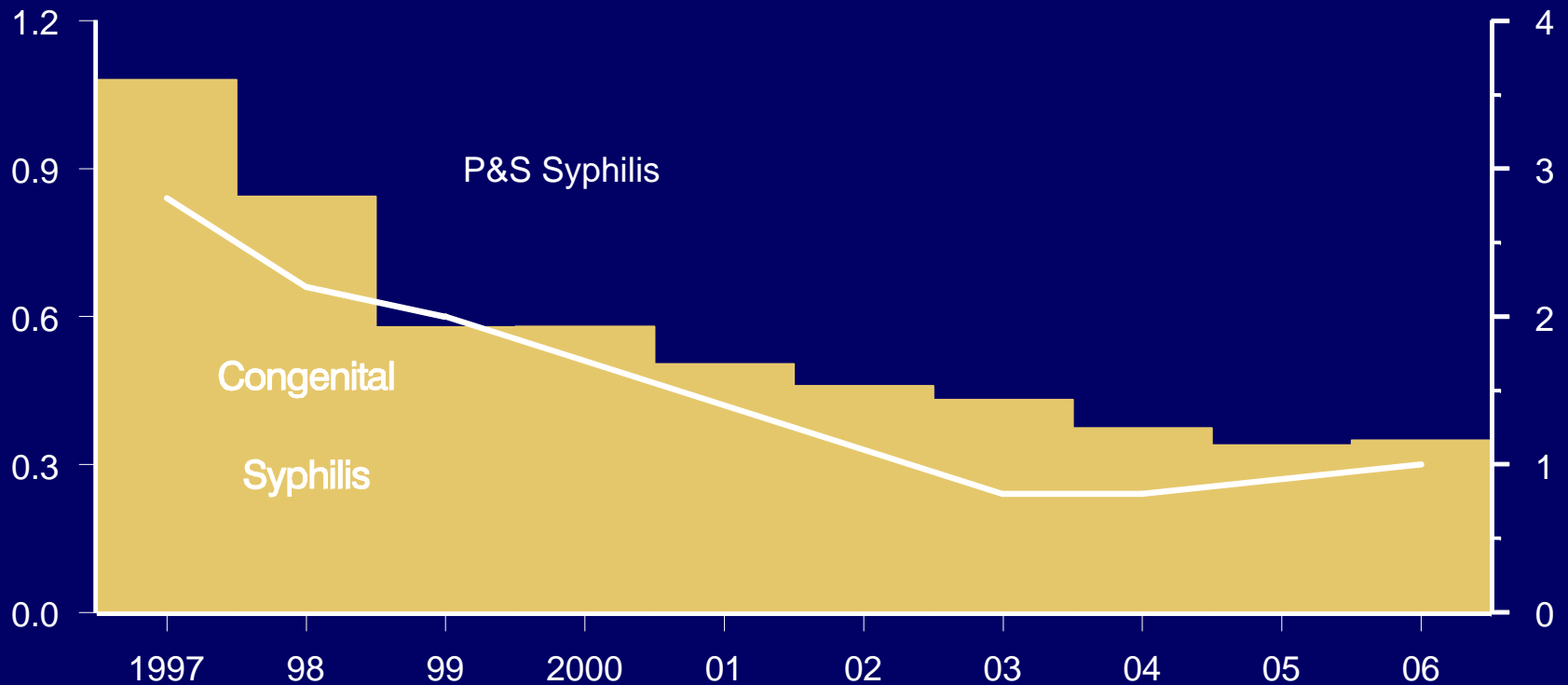


* 2007 data are preliminary

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

CS cases (in thousands)

P&S rate (per 100,000 women)



Summary

- Syphilis is increasing with highest rates among men, in particular gay men and other men who have sex with men
- Blacks disproportionately impacted
- Small increases in congenital syphilis are concerning

Case 1

- 36 year old man c/o fatigue and sweats
- Went to his doctor, found to be mildly jaundice and diagnosed with hepatitis
 - ALT = 66 U/L
 - AST = 84 U/L
 - Alk phos = 480 U/L
 - T bilirubin = 4.2 mg/dL

Case 1

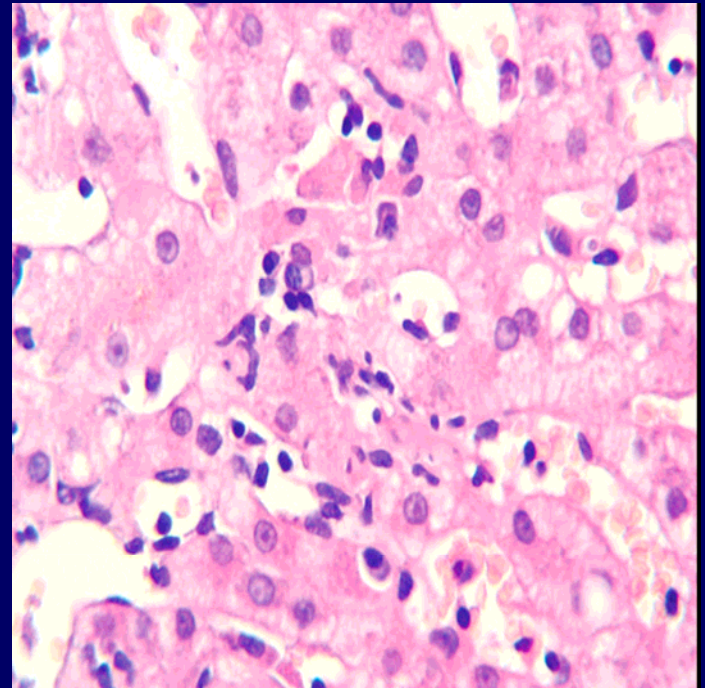
- Further history revealed he was a sexually active gay man, had 4 recent partners he had met online. He denied recent meth use.
- Physical examination was unremarkable
- Further work-up for hepatitis was unrevealing
 - Hepatitis A Ab+, hepatitis B sAb+, Ag-, hepatitis C Ab-
- But his TP EIA was +, index value 4.5

Case 1

- Does the patient have syphilis?
 - Need RPR or VDRL result
 - RPR was 1:64
- Does the patient have syphilis?
 - Sexual risk, reactive confirmed titers, compatible clinical illness (syphilis-associated hepatitis)

Syphilis and hepatitis

- Hepatitis not common in early syphilis
- Often alk. phos/bili >> ALT/AST
- Resolved with syphilis treatment
- One reported cases of fulminant liver failure requiring transplant¹



Hepatic sinusoids are infiltrated by inflammatory cells (lymphocytes and plasma cells). Hepatocytes display lytic necrosis and apoptosis (haematoxylineosin, 40X)
From: Noto P et al. Int J STD AIDS. 2008 Jan;19(1):65-6.

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.



Serologic Treatment Follow-up

- In HIV-uninfected patients: 6 and 12 months
 - 4-fold decline by 6 months consistent with cure
 - Failure of 4-fold at 12 months may necessitate CSF analysis to rule out neurosyphilis
- In HIV-infected patients: 3, 6, 9, 12 and 24 months
 - 4-fold decline by 12 months consistent with cure
 - Failure of 4-fold at 12-24 months may necessitate CSF analysis to rule out neurosyphilis

Partner Treatment

- All sex partners in the prior 6 months (secondary) should be notified
- Those with recent sexual contact (< 90 days) should receive epidemiologic 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

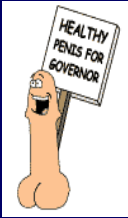


Do not substitute Bicillin® C-R for Bicillin® L-A in the treatment of syphilis. Bicillin® C-R is NOT indicated for the treatment of syphilis.

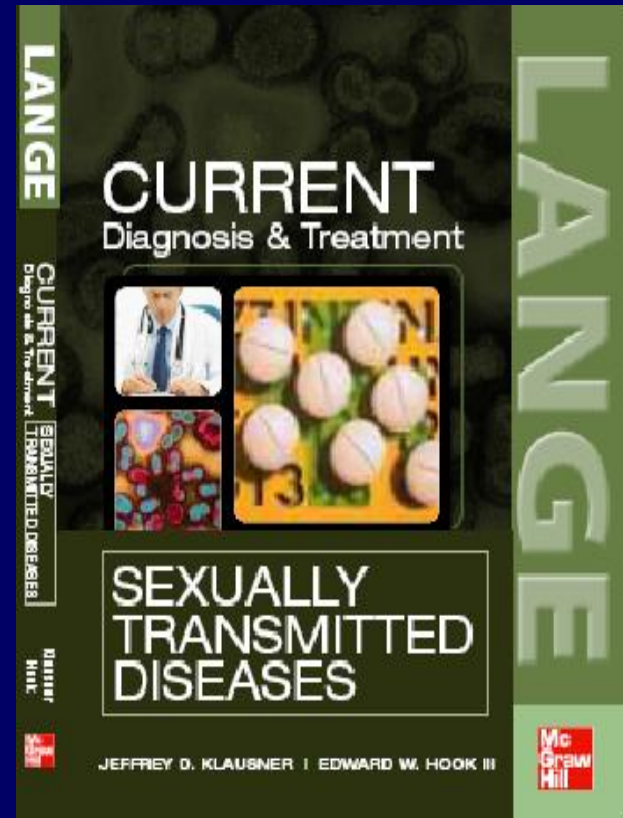
Summary

- 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

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”)

Syphilis Testing using an EIA Rationale and Interpretation

Thomas A. Peterman, MD, MSc
Division of STD Prevention
Centers for Disease Control and Prevention

Dr. Peterman is a Captain in the U.S. Public Health Service, and Chief of the Field Epidemiology Unit, Division of STD Prevention, CDC, Atlanta GA.

He claims that he has no conflict of interest

Syphilis tests

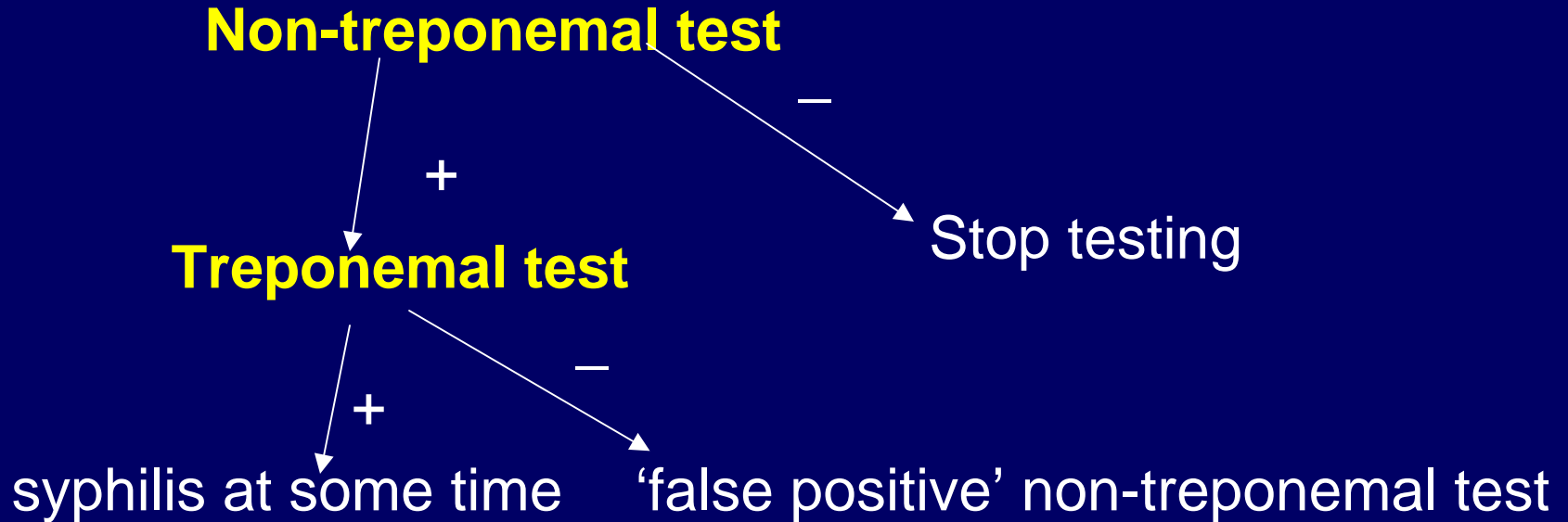
Non-treponemal tests—RPR, VDRL

- Antibodies to cardiolipin—not specific to syphilis
- 1-2% of U.S. positive (?false positive)
(pregnancy, HIV, IDU, TB, rickettsial infections, etc.)
- Decreases when early syphilis is treated (follow titers)

Treponemal tests—TPPA, FTA-ABS, TP-EIA

- Treponemal antigen
(also detects subspecies that cause yaws, pinta)
- Remains positive after treatment
- Reagents cost more

Traditional syphilis screening approach



Traditional syphilis screening approach

Non-treponemal test

+

Treponemal test

— Stop testing

+

syphilis at some time

—

'false positive' non-treponemal test

Previously treated for syphilis?

No

treat for syphilis

Yes

Non-treponemal test titer increased ≥ 4 fold from last?

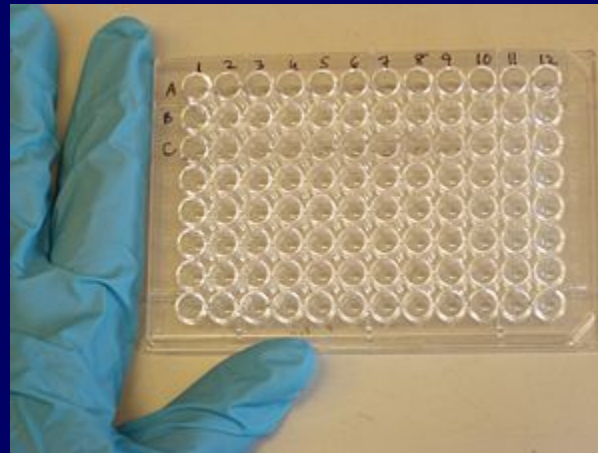
No

Serofast,
previously treated syphilis.
No need to re-treat

Yes

Re-infection
or treatment failure.
Re-treat

Some high-volume labs are using automated treponemal Enzyme Immunoassays (EIAs) to save money...



Automated syphilis screening approach MMWR 2008;57:872

Treponemal Test

6% + - 94%

Non-Treponemal Test

No syphilis diagnosis. Recent infection cannot be ruled out.

44% + - 56%

Syphilis, old or new. Treatment usually indicated unless previously treated. Retreat if titer has increased \geq 4-fold.

Probably old treated syphilis. Treatment may be indicated if not previously treated. If false-positive screening treponemal test suspected, or if not previously treated, retest with a different treponemal test.

Second Treponemal Test

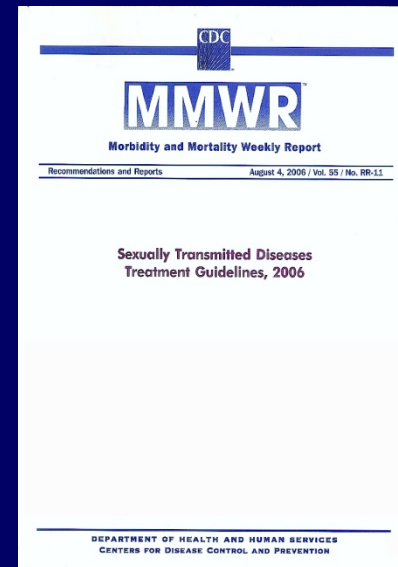
83% + - 17%

Treat--unless there is a history of treatment.

No treatment, or a third treponemal test could be used to resolve the discrepancy between the two treponemal tests.

CDC STD Treatment Guidelines

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



Questions?

Ask Dr. Peterman