

Syphilis Update 2018: Clinical and Laboratory Considerations

Bradley Stoner, MD, PhD
Washington University in St. Louis



**St. Louis STD/HIV
Prevention Training Center**

**Chicago Dept. of Public Health
Bi-Annual STI Conference
October 2, 2018**

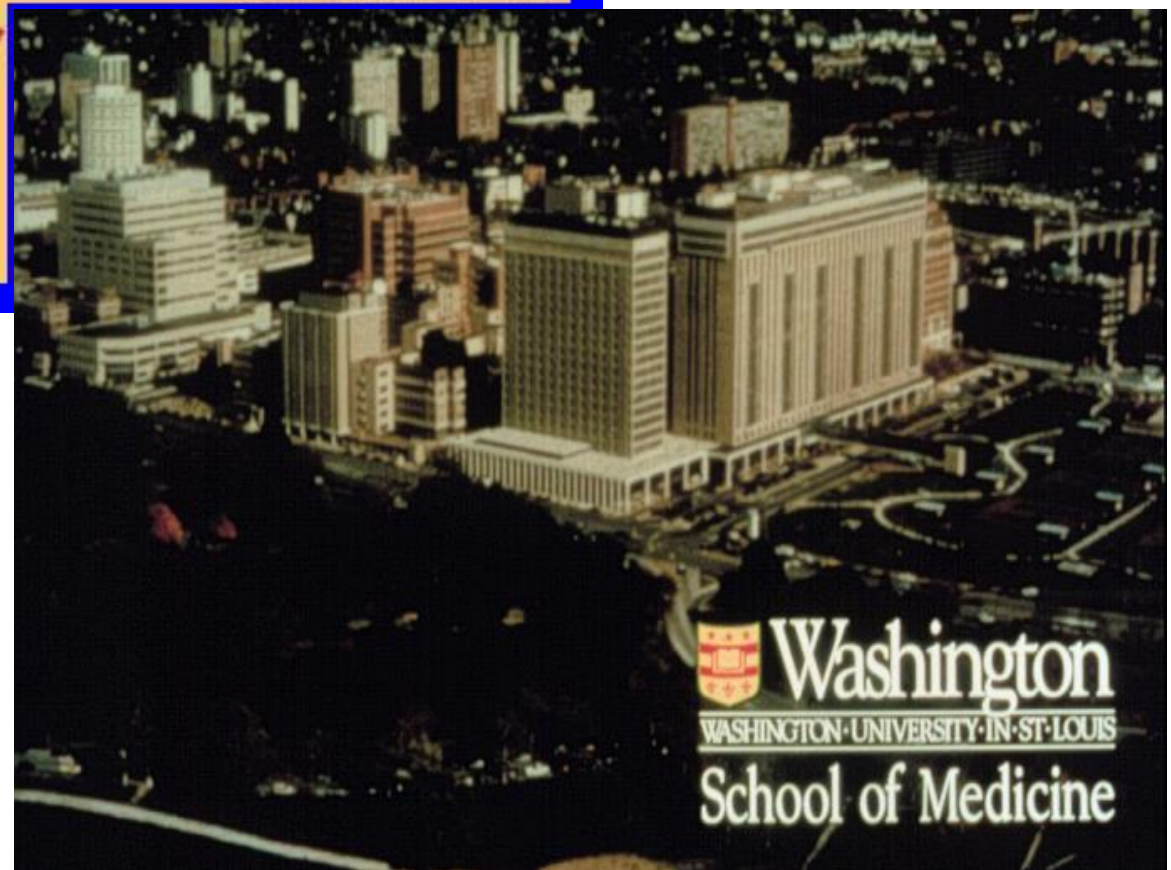
DEPARTMENT OF MEDICINE

DIVISION OF INFECTIOUS DISEASES

ST. LOUIS

STD/HIV Prevention Training Center

Accredited training in the diagnosis and management
of sexually transmitted diseases



Disclosure: Bradley Stoner, MD, PhD

- No relevant financial interests



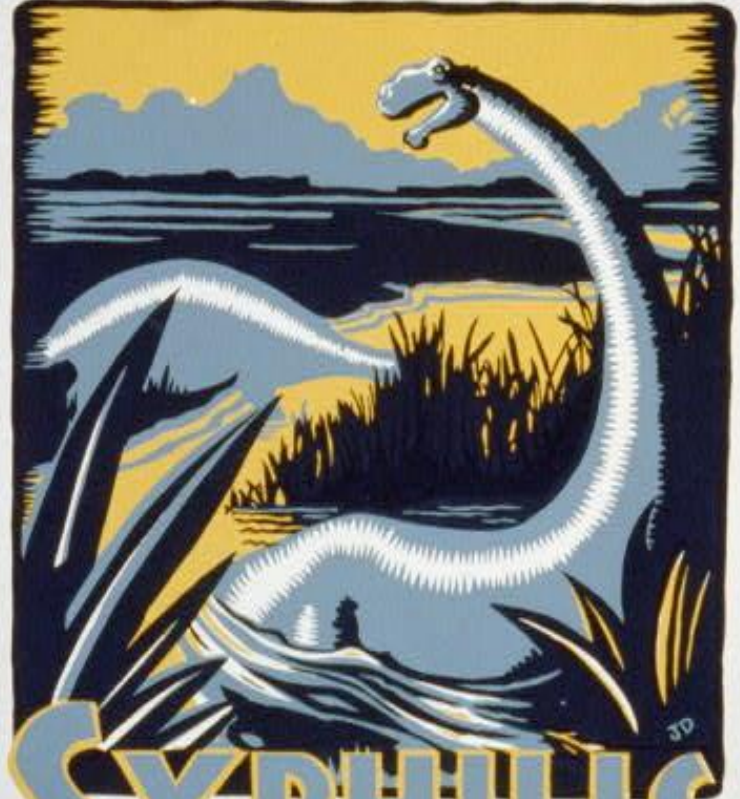
THE ENEMY IS SYPHILIS



Enlist employees in a campaign against it

MADE IN U.S.A. BY W.P.A. 1945

AS OLD AS CREATION



SYPHILIS

IS NOW CURABLE

CONSULT YOUR PHYSICIAN

TOWN OF KEMPSTEAD
W.H. RUNCIE, M.D., HEALTH OFFICER

FEDERAL PROJECT

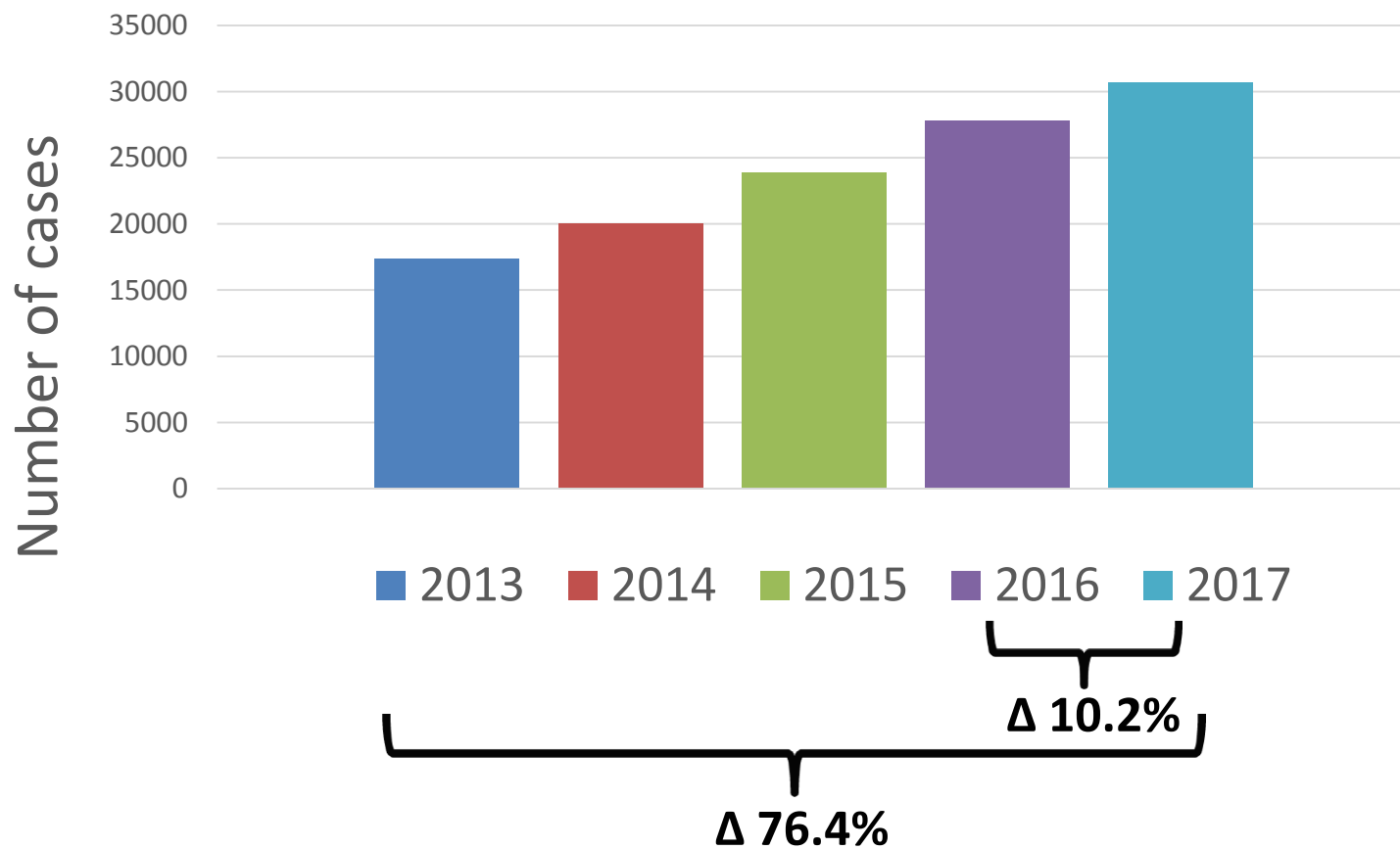
Syphilis - *Treponema pallidum*



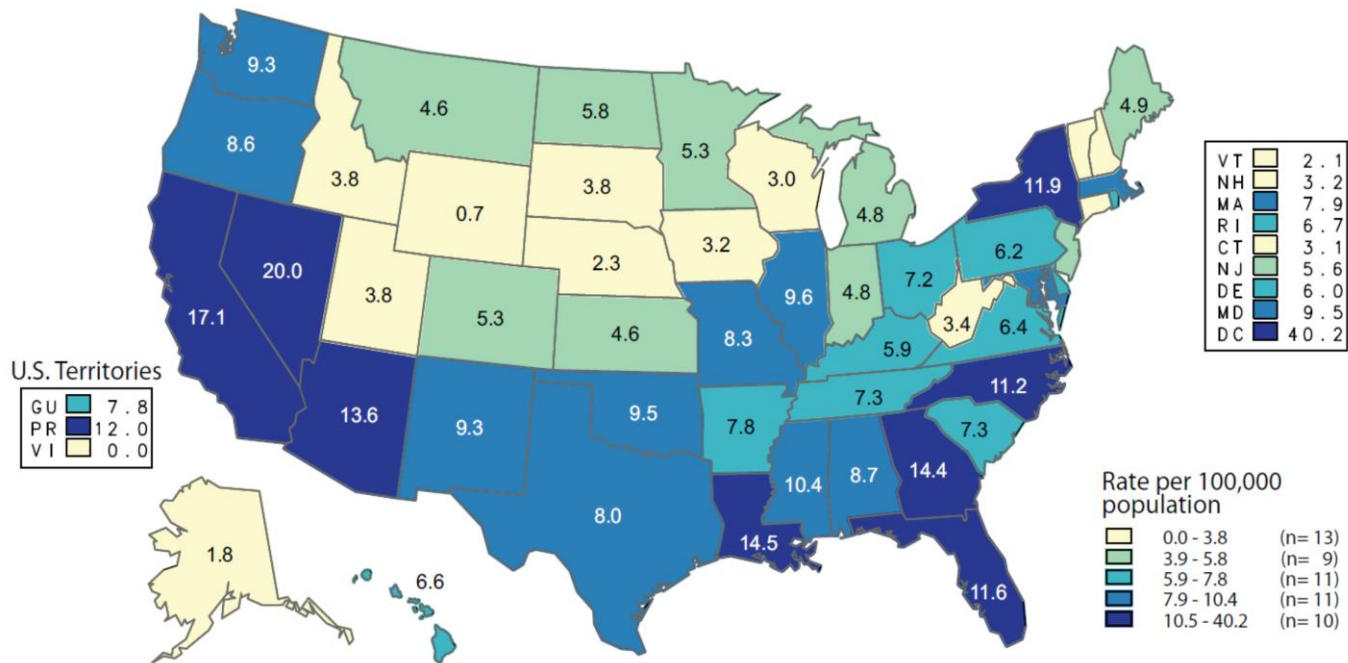
What's new with syphilis

- Rates continue to increase
 - MSM
 - Congenital
- Changes in staging and clinical classification
- Increasing reports of ocular infection

P&S Syphilis in the US 2013-2017

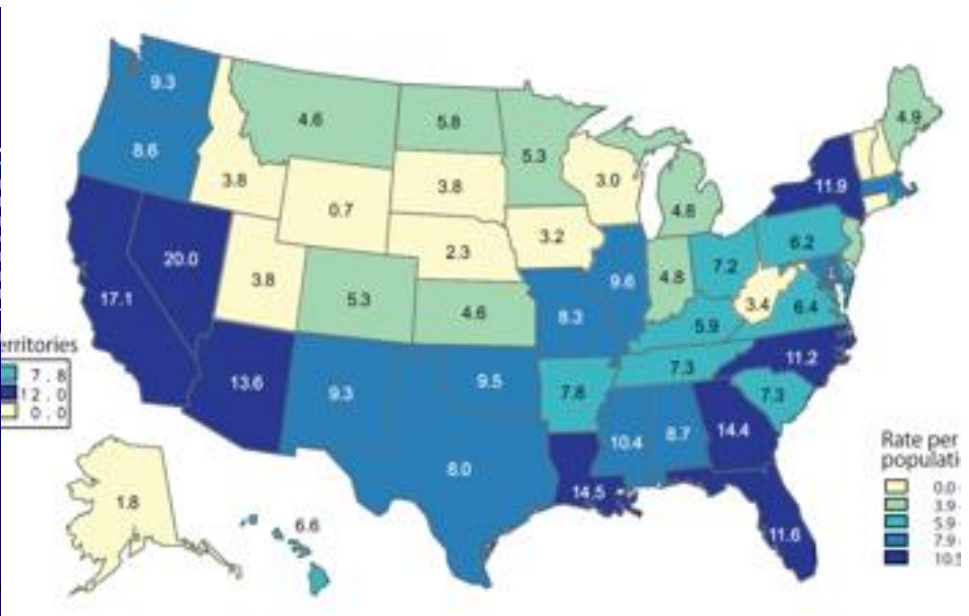
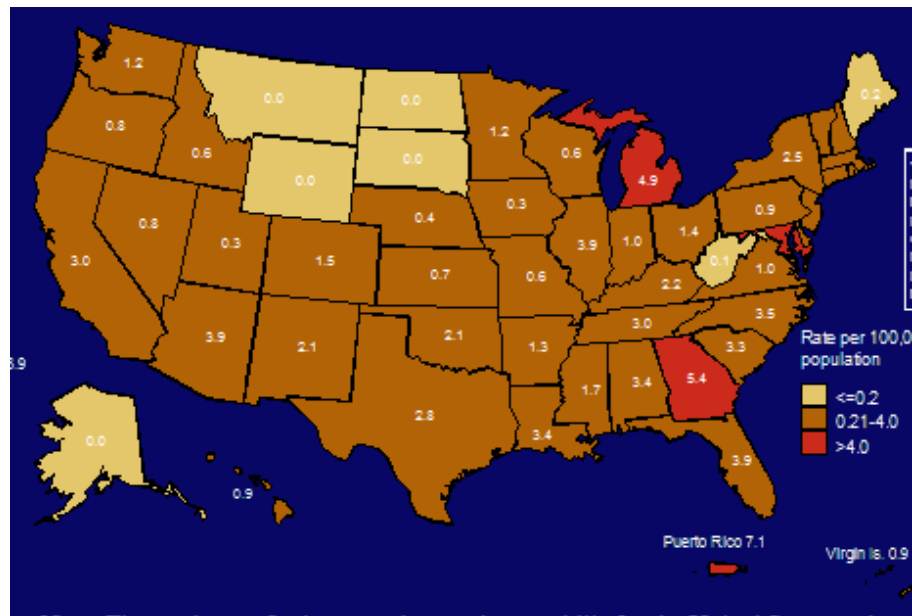


Primary and Secondary Syphilis — Rates of Reported Cases by State, United States and Outlying Areas, 2017



NOTE: The total rate of reported cases of primary and secondary syphilis for the United States and outlying areas (including Guam, Puerto Rico, and the Virgin Islands) was 9.5 per 100,000 population. See Section A1.11 in the Appendix for more information on interpreting reported rates in the outlying areas.

ACRONYMS: GU = Guam; PR = Puerto Rico; VI = Virgin Islands.

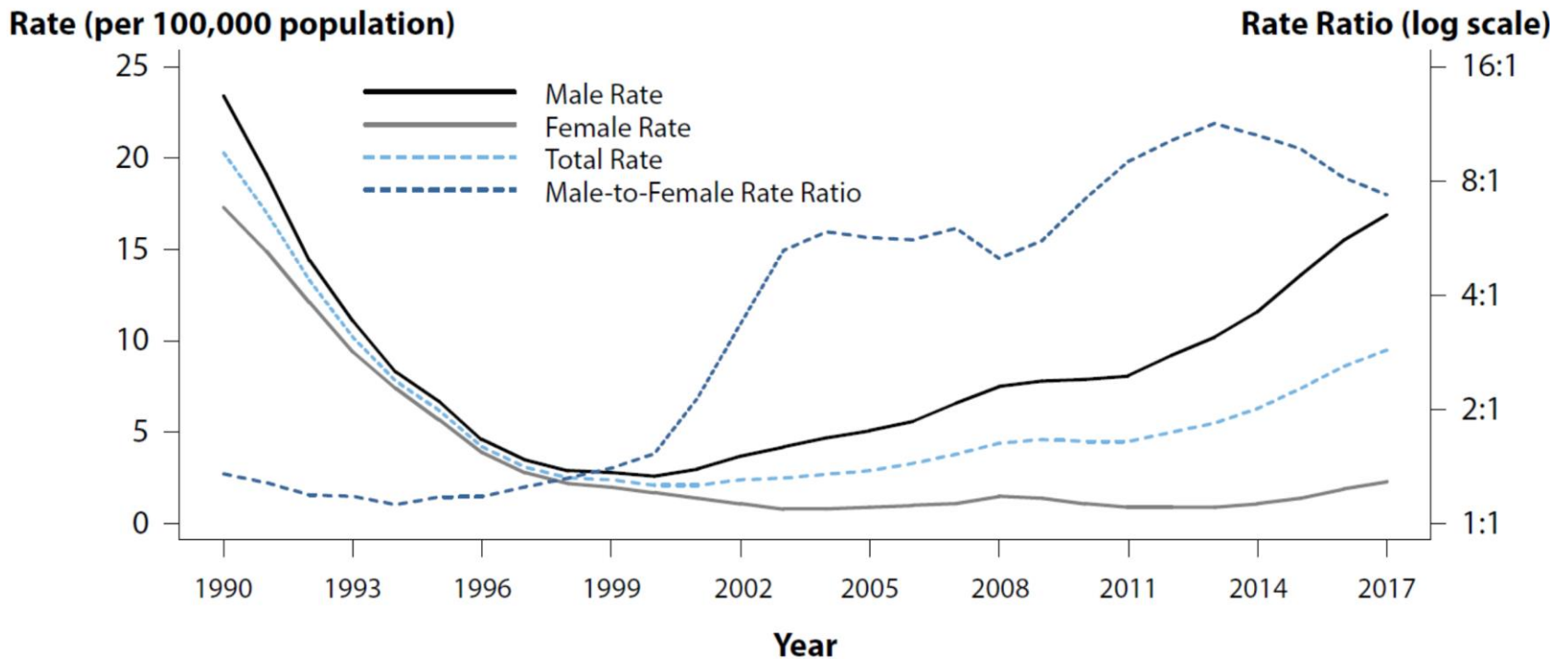


2002

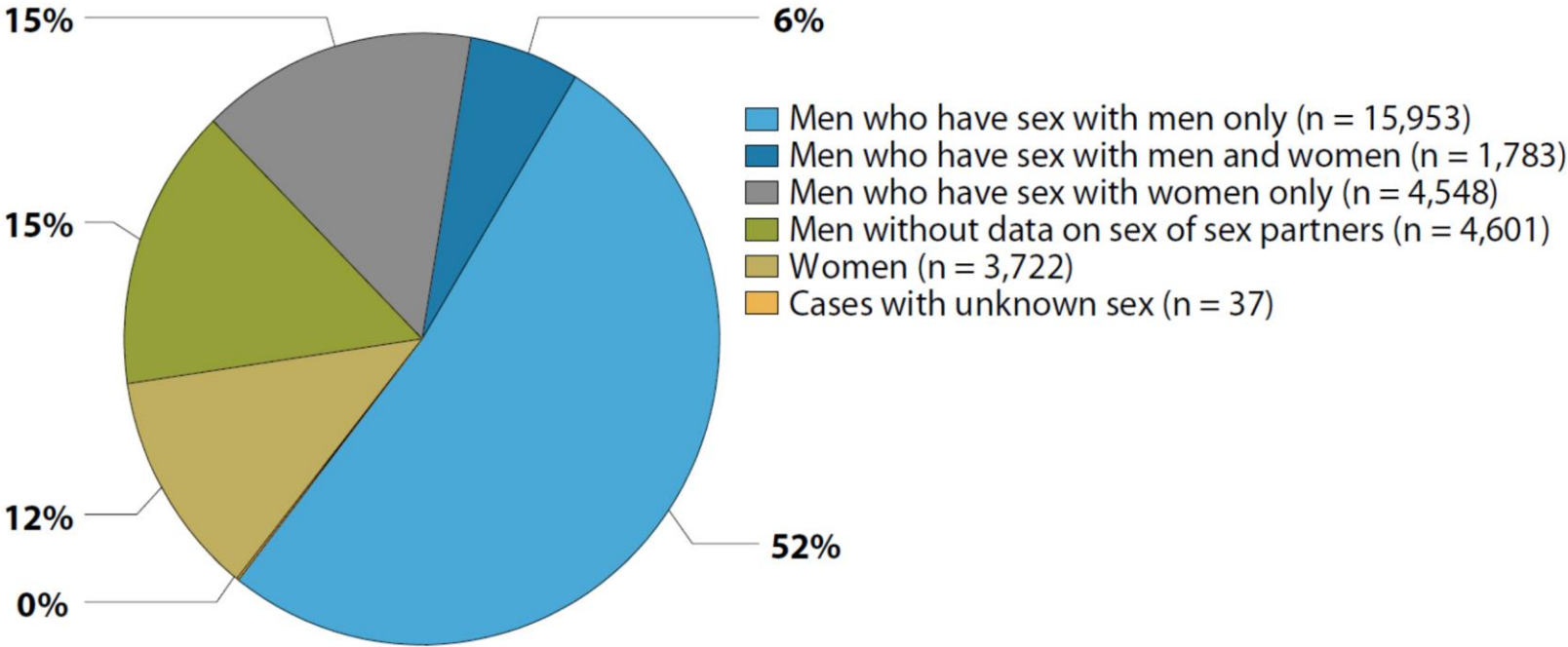


2017

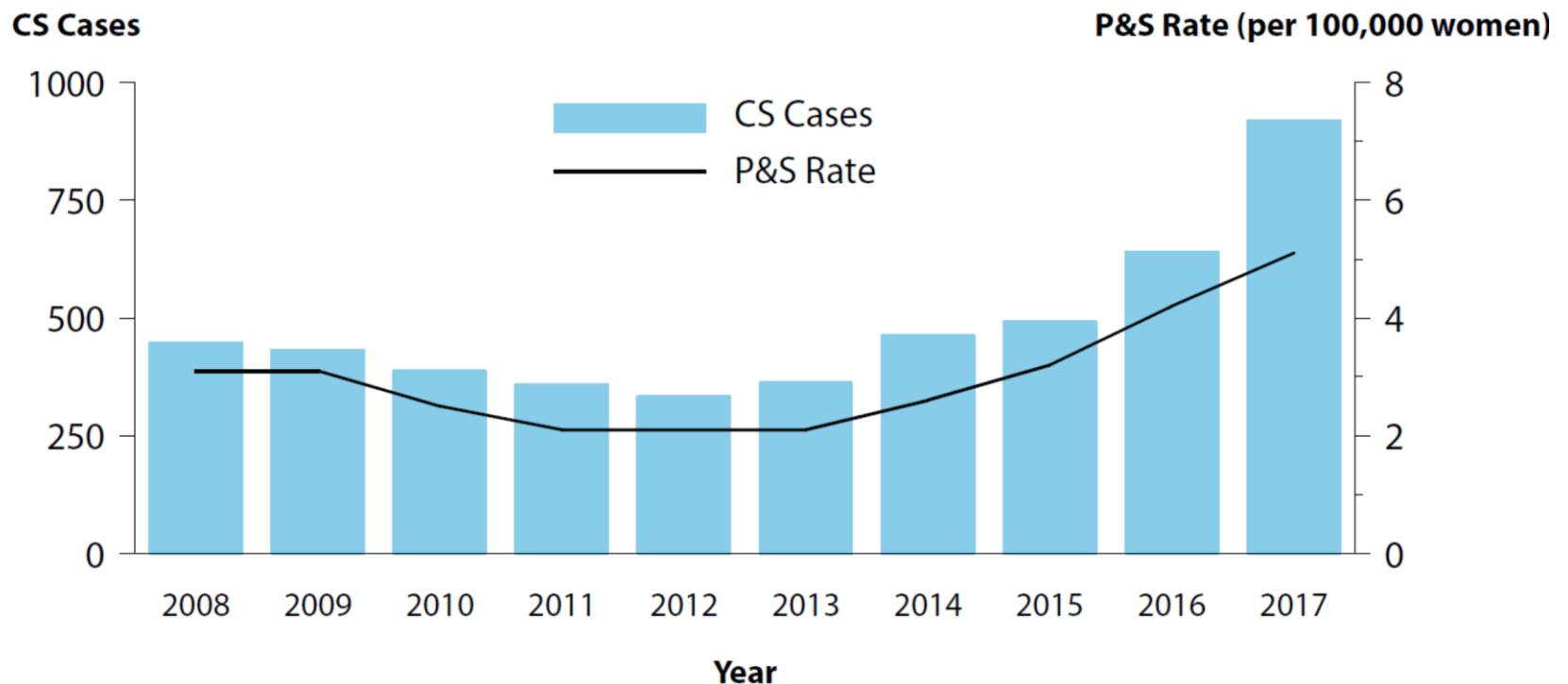
Primary and Secondary Syphilis — Rates of Reported Cases by Sex and Male-to-Female Rate Ratios, United States, 1990–2017



Primary and Secondary Syphilis — Distribution of Cases by Sex and Sexual Behavior, United States, 2017



Congenital Syphilis — Reported Cases by Year of Birth and Rates of Reported Cases of Primary and Secondary Syphilis Among Women Aged 15–44 Years, United States, 2008–2017

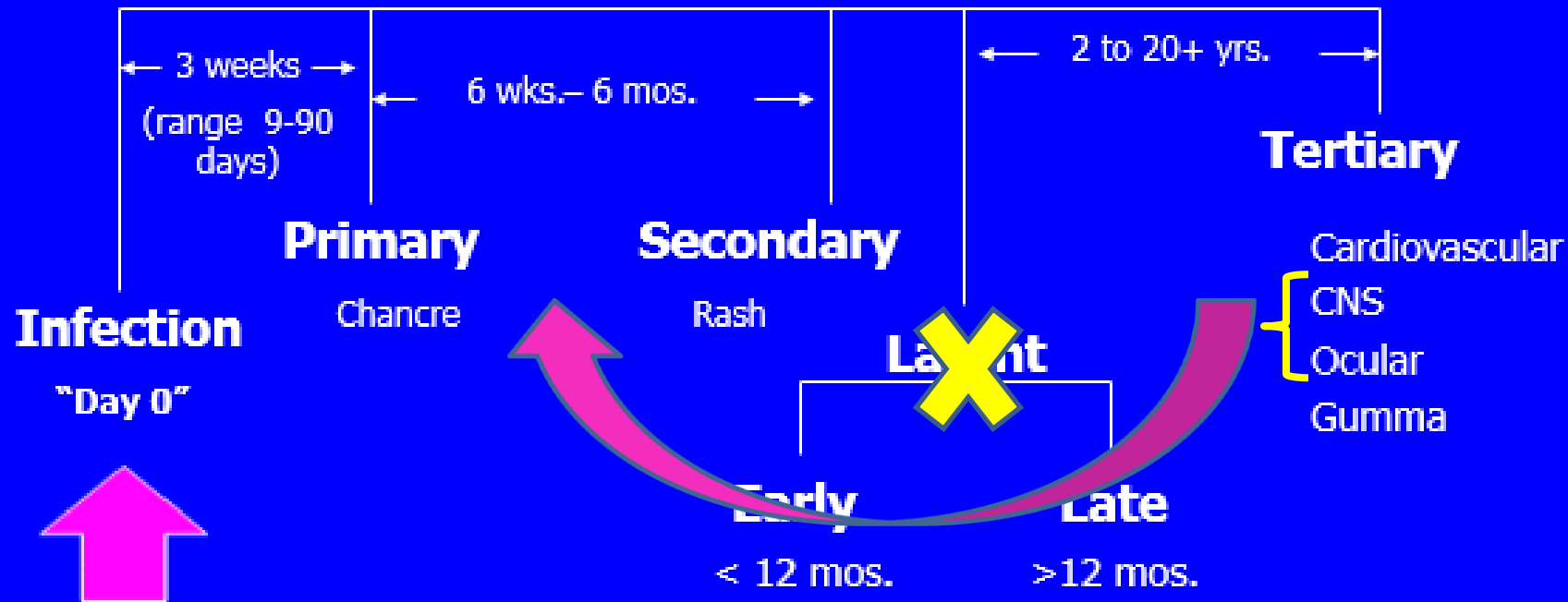


ACRONYMS: CS = Congenital syphilis; P&S = Primary and secondary syphilis.

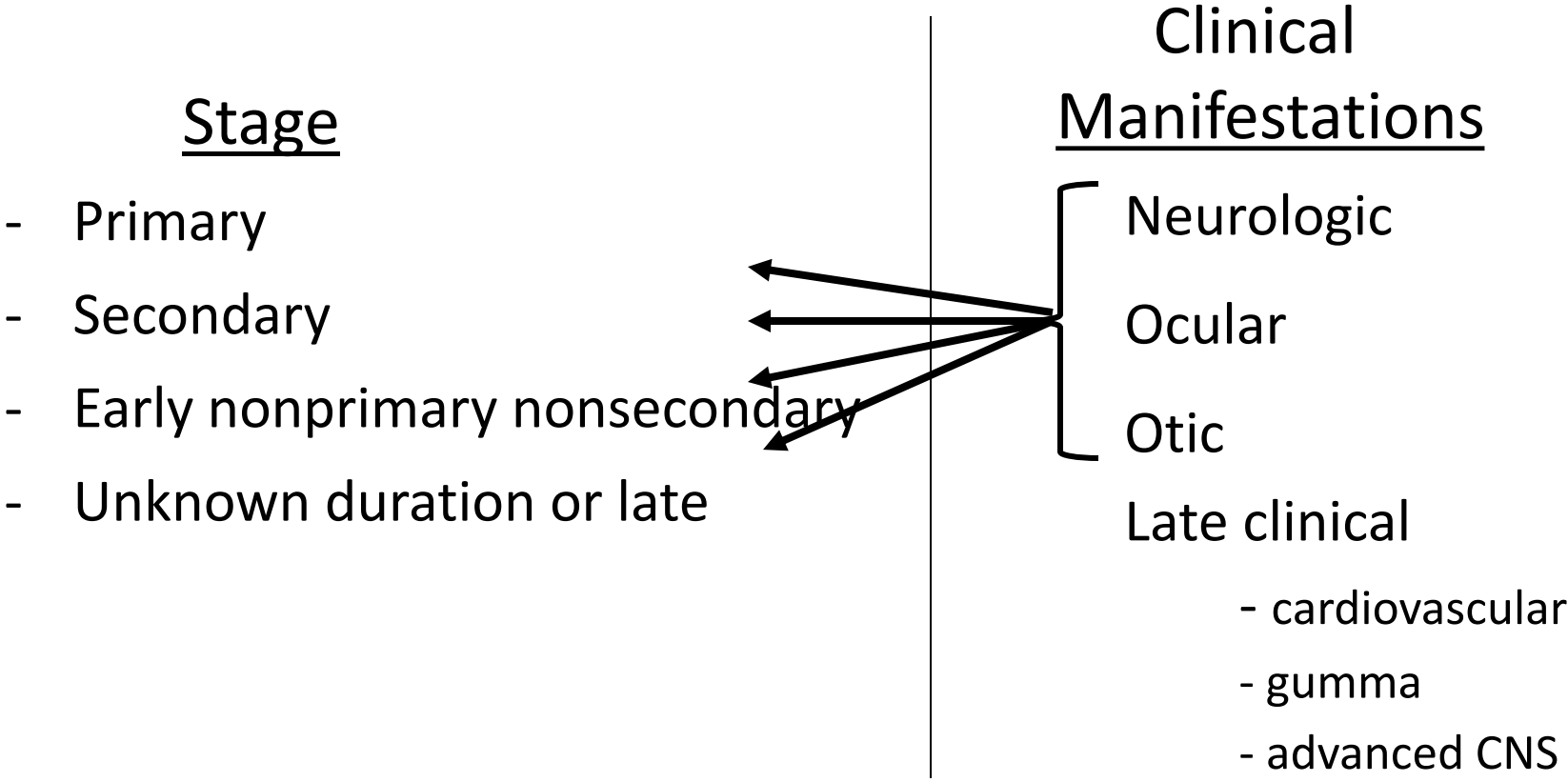
Traditional approach to staging

- Primary
- Secondary
- Latent
 - early latent: < 1 year
 - late latent: ≥ 1 year
- Late (tertiary)
 - neurosyphilis
 - cardiovascular syphilis
 - gummatous syphilis

Clinical presentation of syphilis



2018 revised syphilis classification



Primary syphilis

- The first manifestation of infection
- Characterized by development of chancre
- Incubation period
 - average 3 wks. from time of exposure
 - range 9 - 90 days
- Chancre occurs at site of bacterial invasion

Primary syphilis - chancre



Primary syphilis - chancre



Primary syphilis - chancre



Secondary syphilis

- Evidence of systemic spread of infection
- Characterized by palmar-plantar rash
 - other skin and mucous membrane lesions
- Typically develops 3 - 6 weeks following development of primary lesions (chancre)

Secondary syphilis



Secondary syphilis

30.
Rash of
secondary
syphilis
involving
palms
and feet



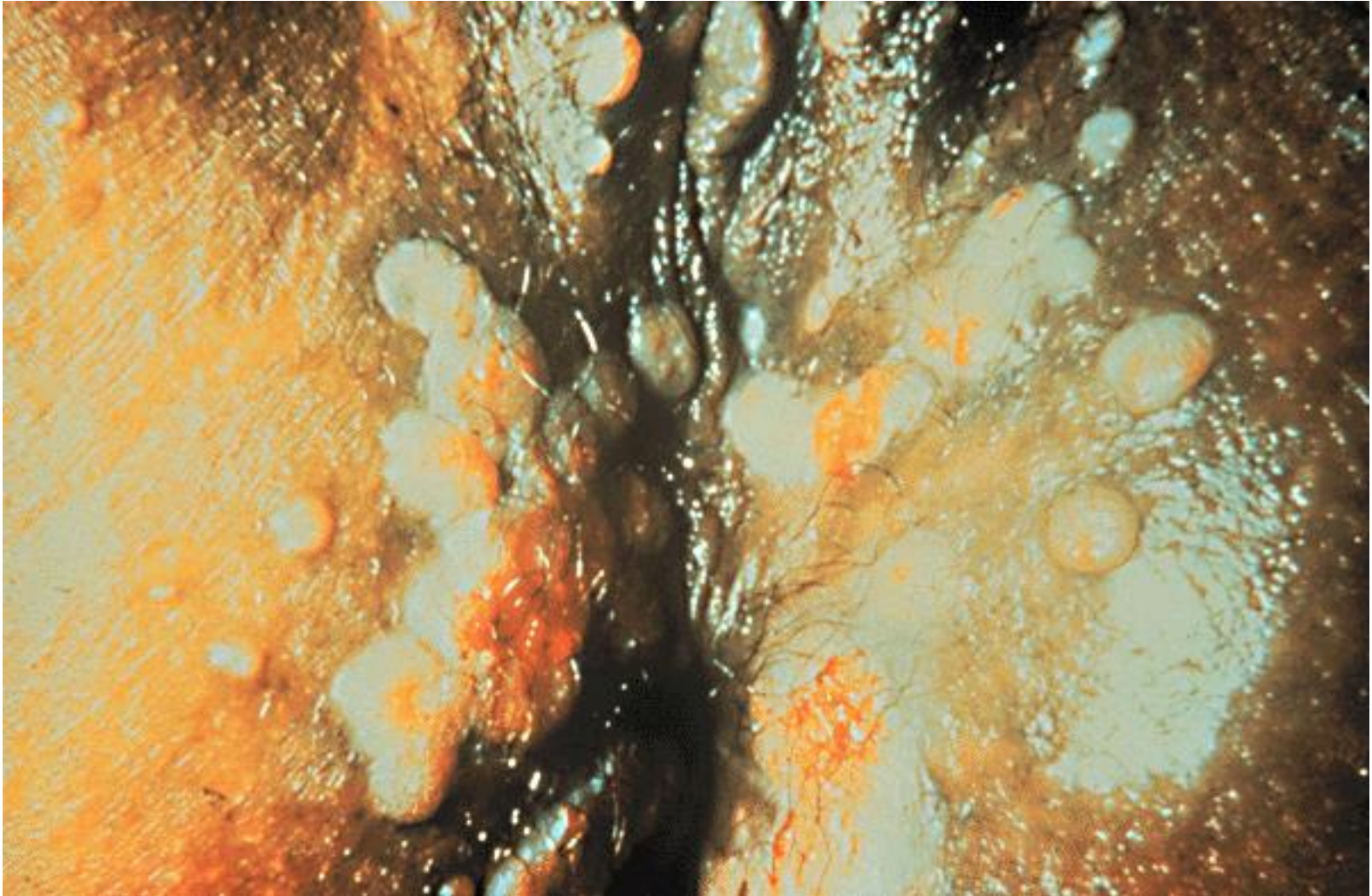
Secondary syphilis



Condylomata lata

- A form of secondary syphilis
 - papular lesions on moist body areas
 - uncommon, but increasingly reported

Condylomata lata



Early nonprimary nonsecondary syphilis

- Infection within the past 12 months
- No primary or secondary manifestations

(No longer called “early latent” because neurologic, ocular, or otic involvement may occur at any stage)

Unknown duration or late syphilis

- Infection > 12 months ago, or unclear how long the patient has been infected
- No primary or secondary manifestations

(May include neurologic, ocular, otic, or late clinical manifestations)

Other clinical manifestations

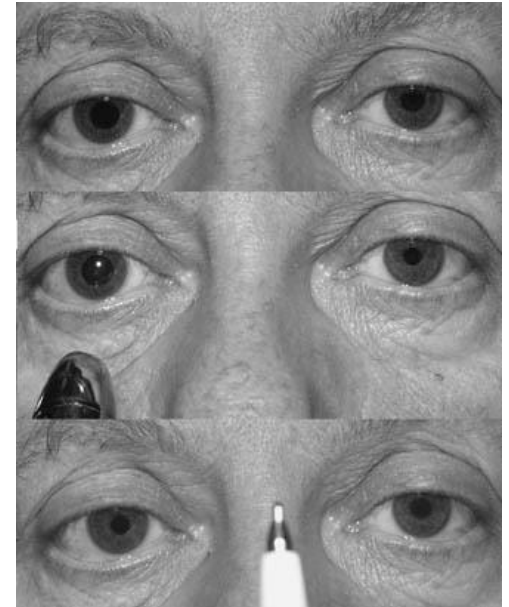
- Neurologic
 - asymptomatic
 - meningeal
 - meningovascular (stroke)
 - long-term complications
- Otic
 - uveitis, vasculitis, neuropathy
 - decreased vision → blindness
- Ocular
 - sensorineural hearing loss
 - tinnitus, vertigo
- Late clinical (tertiary)
 - cardiovascular
 - skin
 - bone
 - late CNS involvement

Late clinical (tertiary) syphilis

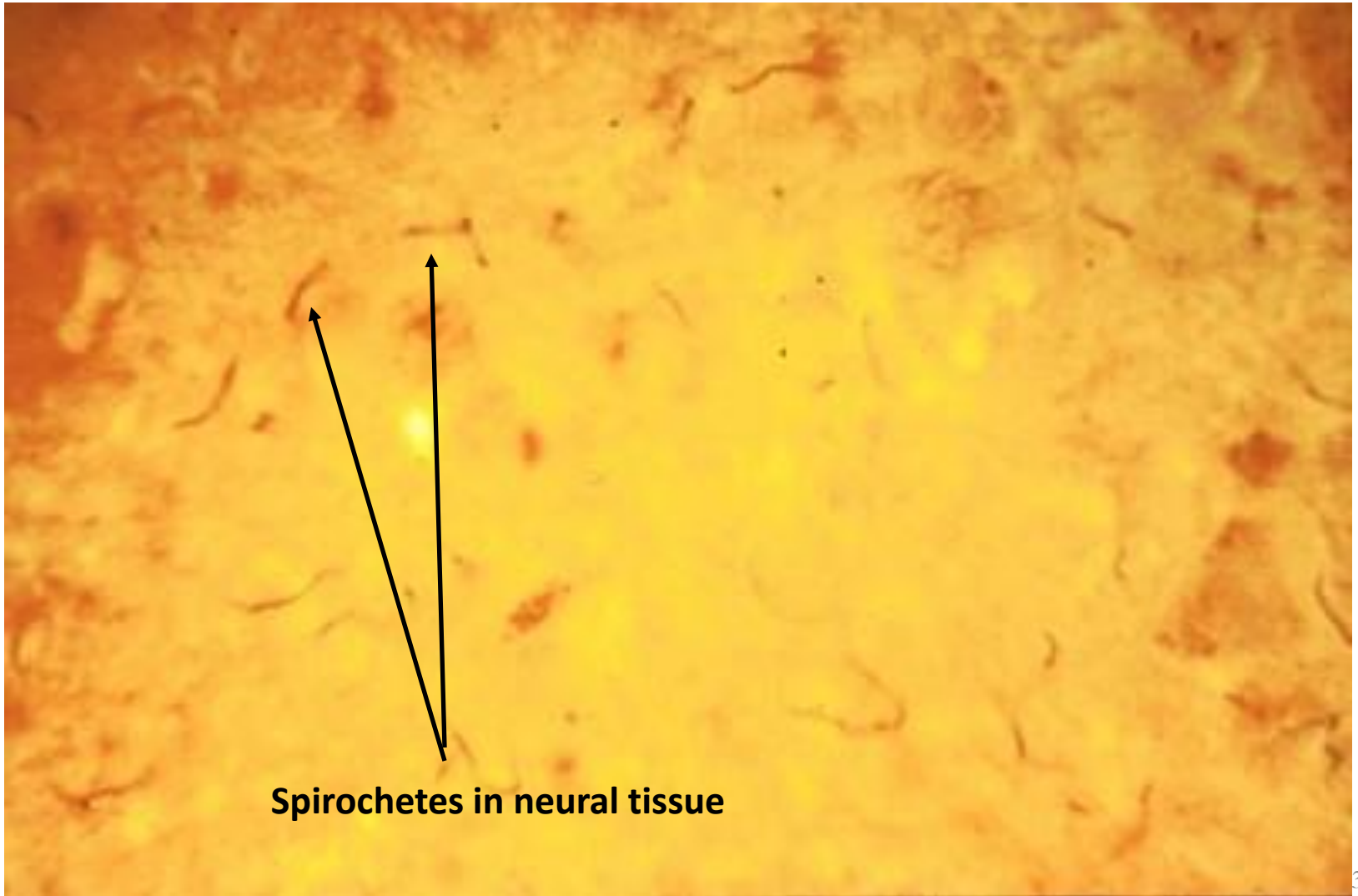
- Late neurologic manifestations
 - general paresis, dementia, tabes dorsalis
- Cardiovascular manifestations
 - aortitis, coronary vessel disease
- Skin and bone involvement
 - gummatous lesions, osteitis

Parenchymatous neurosyphilis

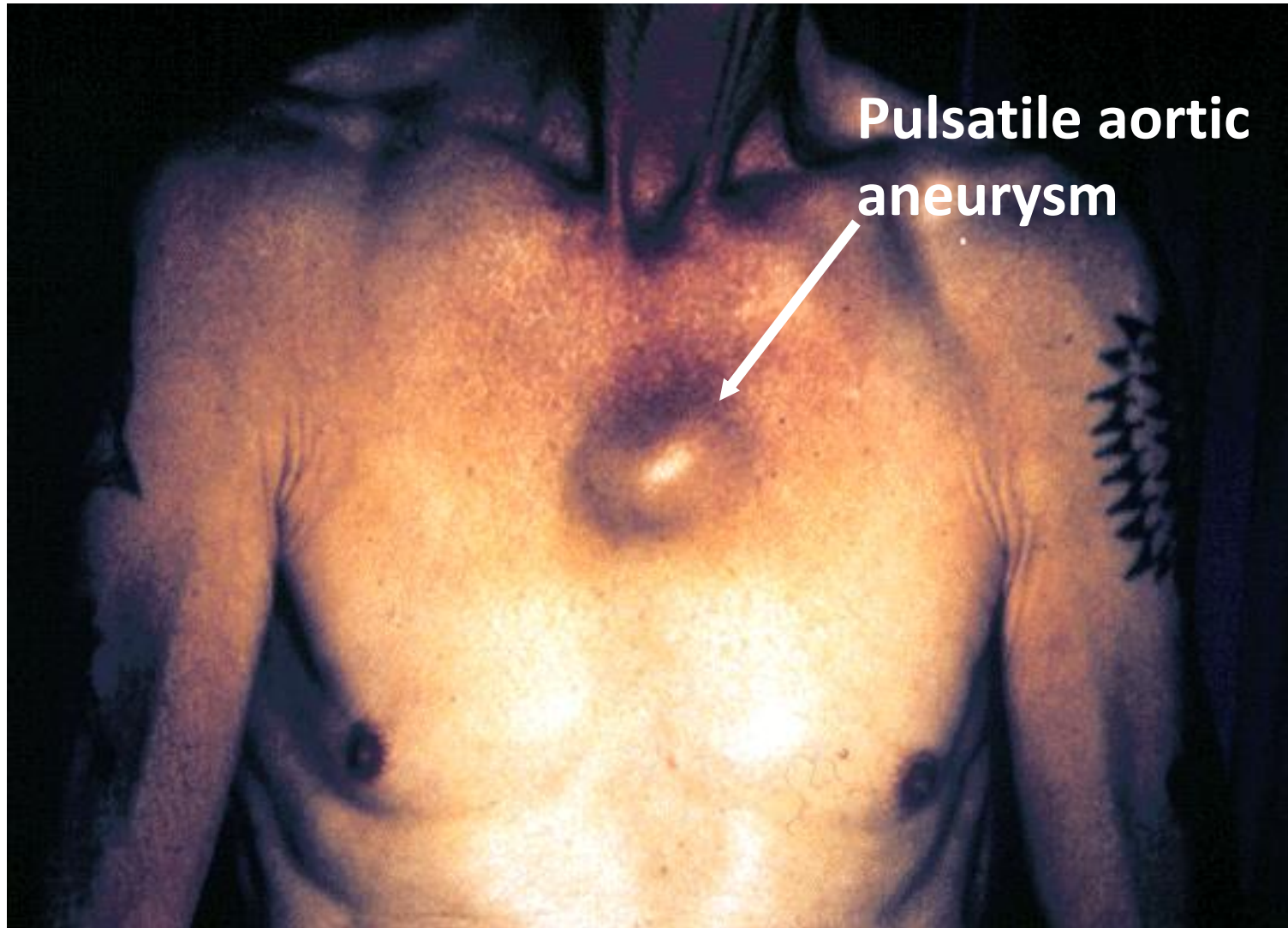
- General paresis
 - neurologic findings include:
 - Argyll Robertson pupils
 - Small, irregular
 - Do not constrict to light (don't react)
 - Do constrict when focusing (accommodate)
 - slurred speech, expressionless face
 - ultimately leads to *dementia paralytica* (confusion, psychosis, seizures)



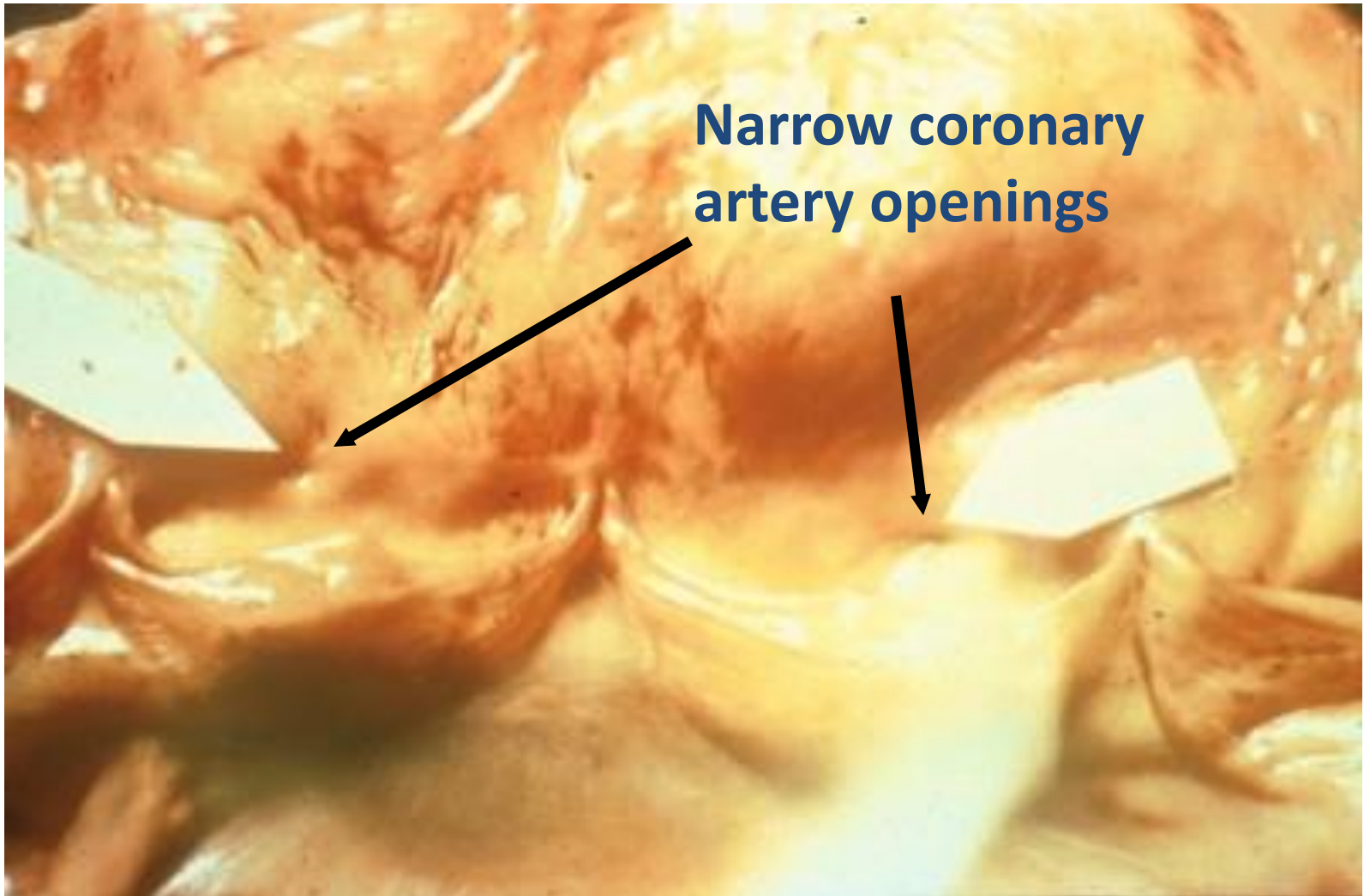
Parenchymatous neurosyphilis



Cardiovascular syphilis



Cardiovascular syphilis



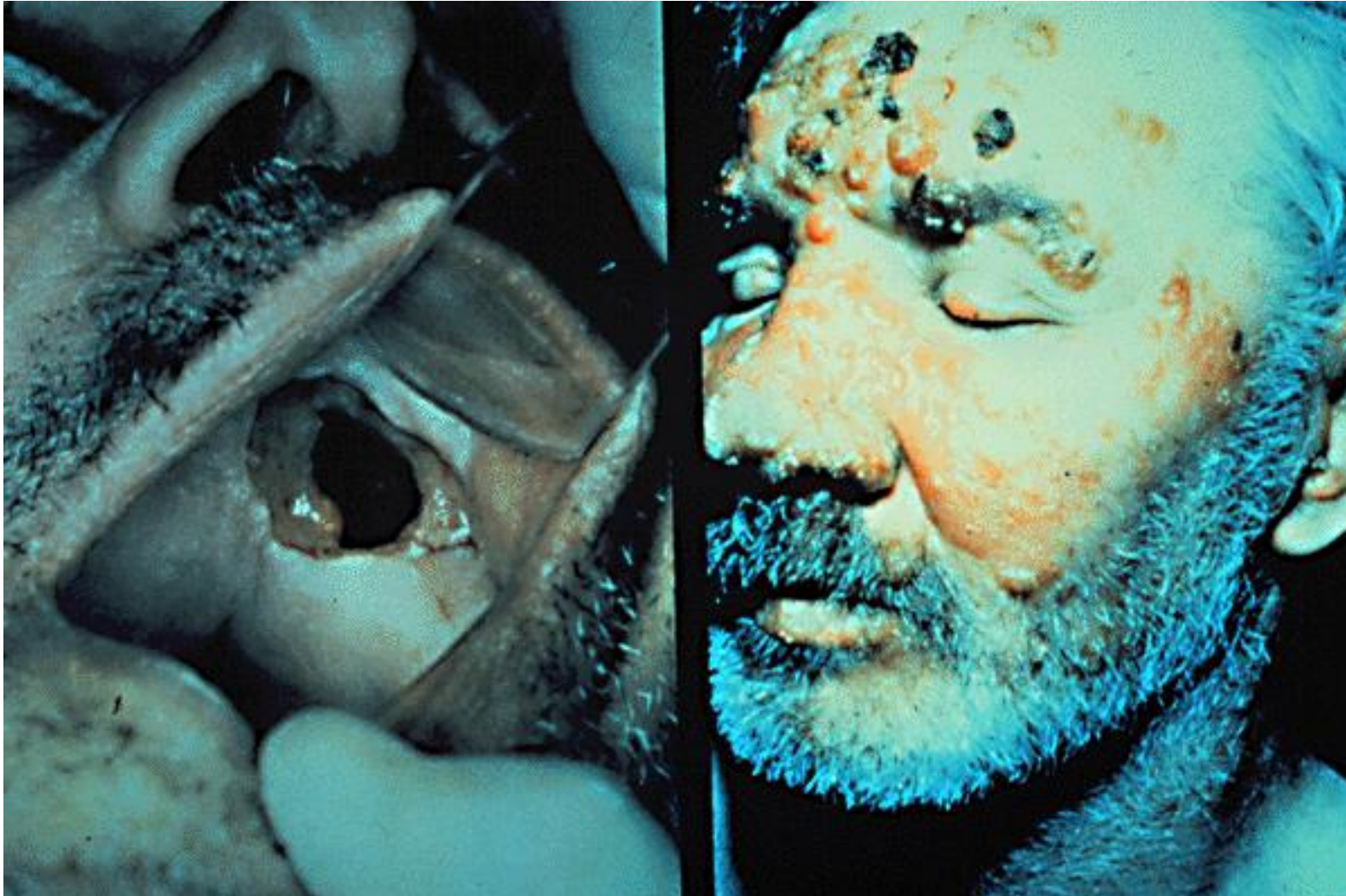
Gummatous syphilis



Gummatous syphilis



Gummatous syphilis



Diagnosing syphilis

- Darkfield microscopy
 - direct visualization of bacteria from lesions
 - not widely available in clinical sites

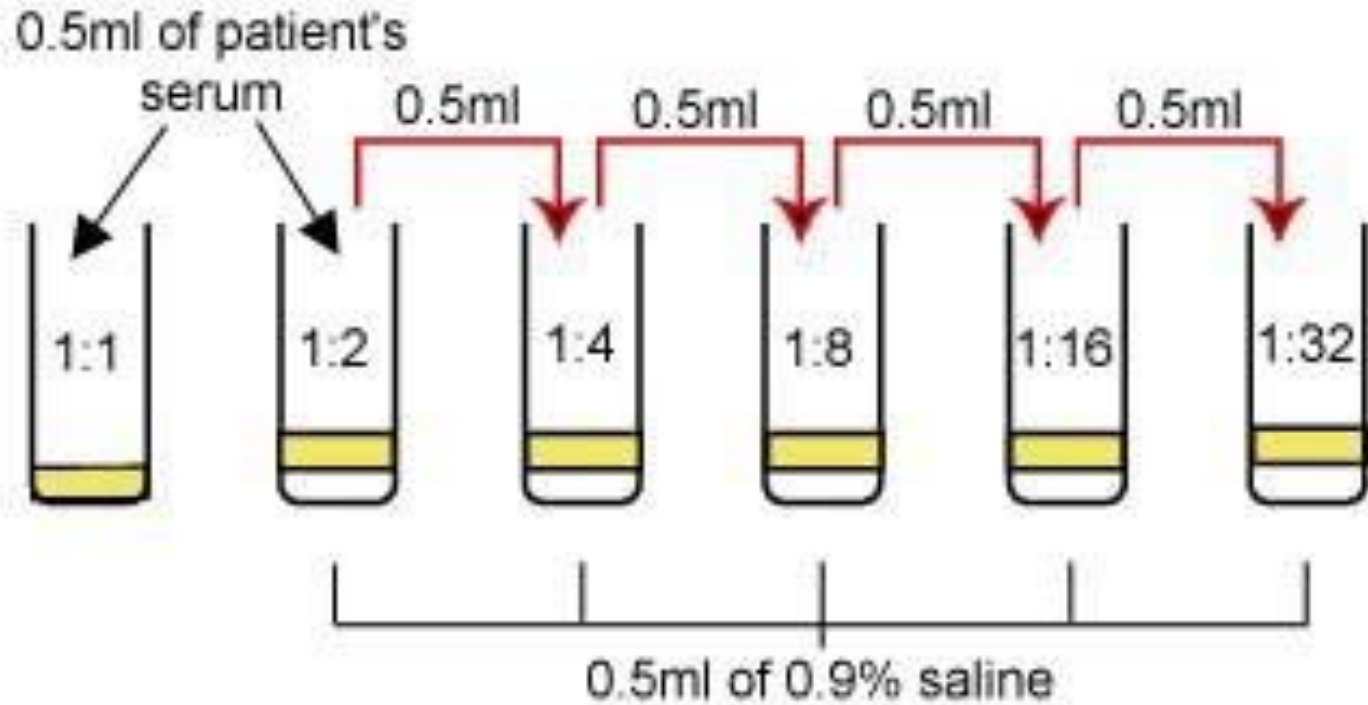
Darkfield microscopy



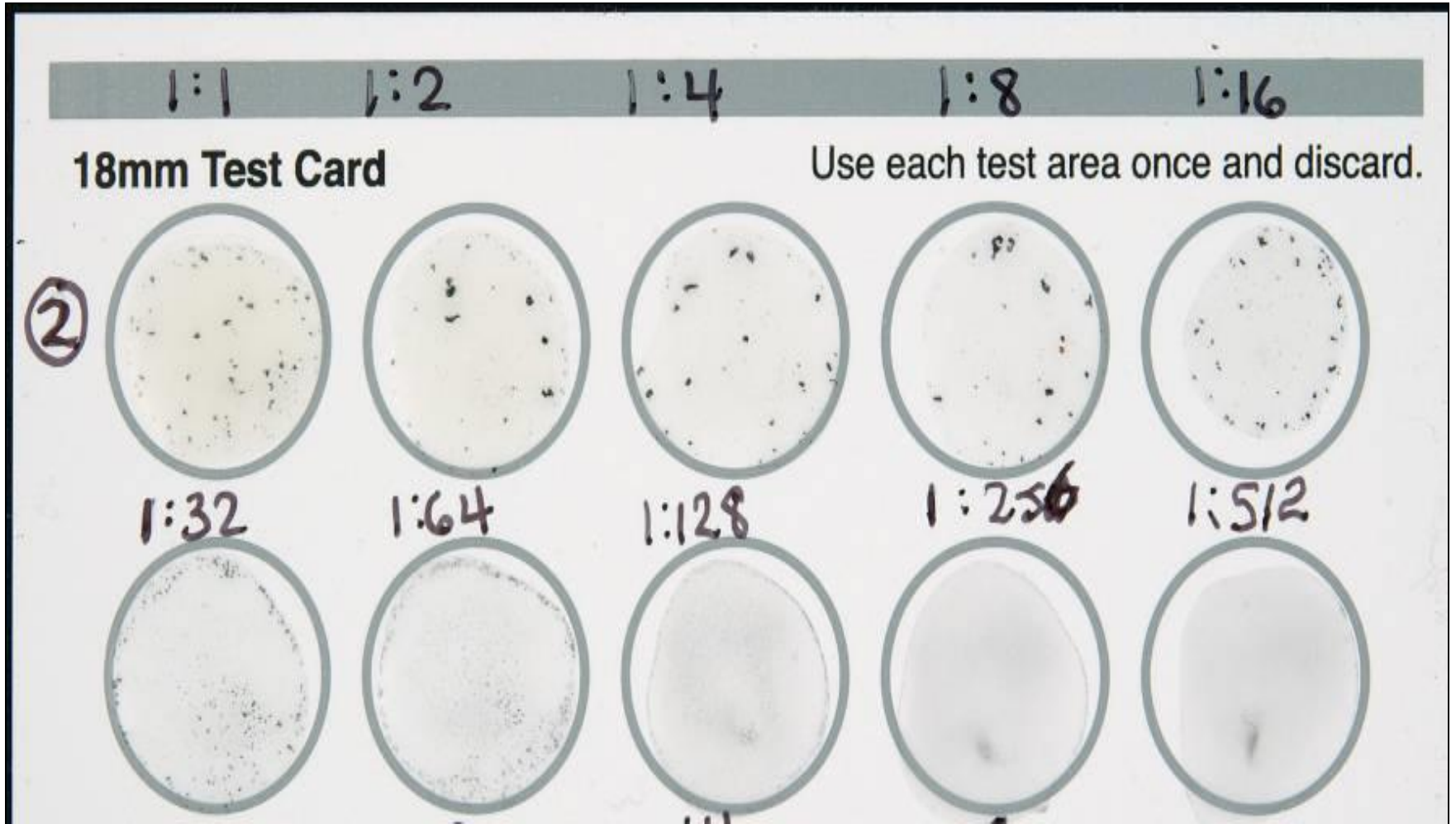
Diagnosing syphilis

- Serologic diagnosis
 - Traditional sequence testing
 - screen with non-treponemal test (RPR or VDRL)
 - confirm with treponemal test (FTA-ABS or TP-PA)
 - “Reverse sequence” testing
 - screen with treponemal test (EIA or CIA)
 - confirm with nontreponemal test (RPR or VDRL)

RPR: serial dilutions



Reading the RPR



Reverse sequence testing

- Many laboratories are switching to screening tests based on detection of *treponemal* antibody
- This can lead to confusion in diagnosis

Be careful...

- EIA tests cannot distinguish active disease from old (treated) disease
- Lots of confusion re: management of patients with discrepant serology

EIA+ RPR- may be

- no syphilis (false positive EIA) ?
- prior treated syphilis (with appropriate loss of RPR reactivity) ?
- old untreated syphilis (with loss of RPR reactivity) ?

Syphilis - treatment

- Early syphilis (primary, secondary, early nonprimary nonsecondary)
 - Benzathine PCN-G 2.4 mU IM x 1 dose
- Unknown duration or late syphilis
 - Benzathine PCN-G 2.4 mU IM q week x 3 doses

Syphilis – penicillin allergy

- Doxycycline 100mg po bid (or tetracycline 500mg po qid)
 - treat for 2 weeks for early syphilis
 - treat for 4 weeks for unknown or late syphilis

Neurosyphilis and cardiovascular syphilis

- Recommended
 - aqueous crystalline PCN-G 3-4 million units IV q4h x 10-14 d
- Alternate
 - daily procaine penicillin plus probenecid
 - daily ceftriaxone

Jarisch-Herxheimer Reaction

- Systemic reaction which occurs when large quantities of toxins are released into the body as syphilis organisms die
 - fever, chills, headache, muscle aches
 - resolves within 1-2 days
- Treat with acetaminophen, conservative care
 - emphasize this is NOT an allergic reaction

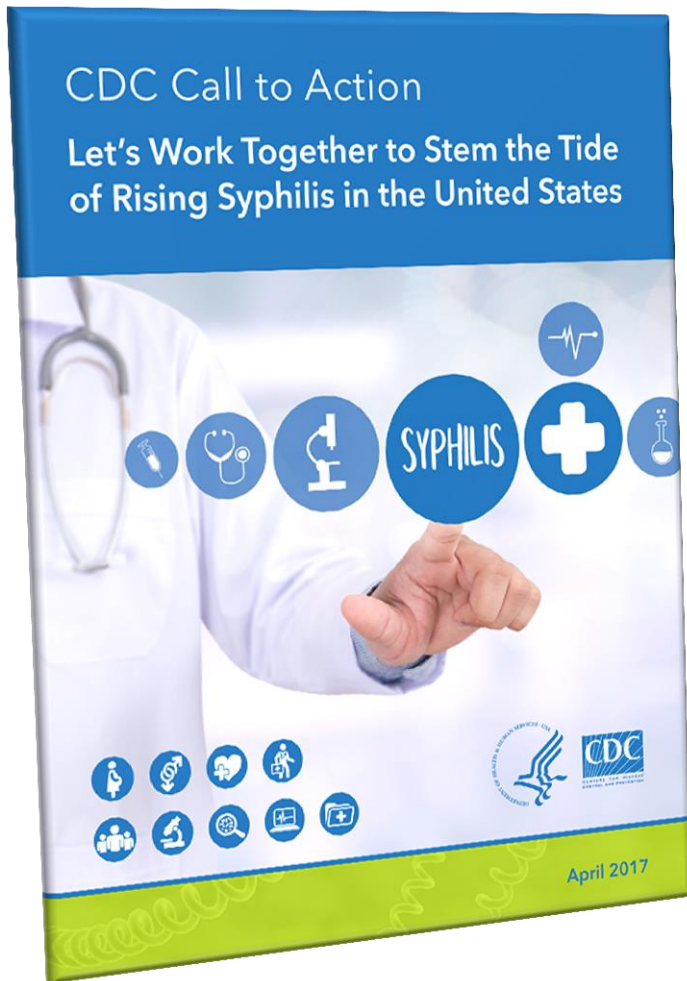
Question

- You are caring for a 23 yo female who is 8 weeks pregnant. She has syphilis. She is allergic to penicillin. Which of the following drugs will you use to treat her?
 1. Ceftriaxone
 2. Erythromycin
 3. Doxycycline
 4. Ciprofloxacin
 5. Penicillin

Answer

- Penicillin

The patient must be desensitized and treated with PCN, since no other medication effectively crosses the placenta



CDC Call to Action

- **Syphilis rates are increasing among women, their babies, and men throughout the United States.**
- **Untreated syphilis can cause severe medical issues.**
- **Efforts are needed:**
 - ✓ **to create new tools;**
 - ✓ **to detect and treat syphilis;**
 - ✓ **increase testing;**
 - ✓ **control the further spread of syphilis; and**
 - ✓ **improve electronic medical records in order to improve patient outcomes.**
- **URL: <https://www.cdc.gov/std/syphilis/resources.htm>**

Let's Work Together to Stem the Tide of Rising Syphilis in the United States

New Tools Are Needed for Syphilis Prevention and Control

There is an urgent need for new tools to prevent, diagnose, treat, and manage syphilis. This will allow people to protect themselves from getting syphilis or learn quickly and easily if they have it; and help health care professionals monitor, and assure effective treatments for years to come.

0

NUMBER OF VACCINES AVAILABLE TO PREVENT SYPHILIS

0

NUMBER OF BLOOD TESTS TO DIAGNOSE ACTIVE SYPHILIS INFECTION

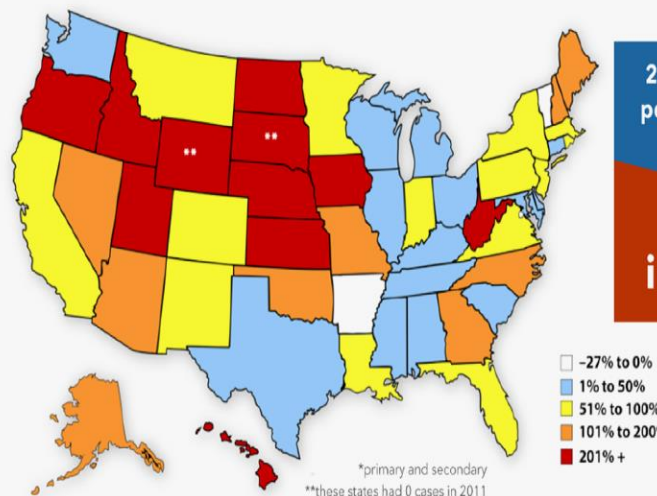
75

NUMBER OF YEARS CURRENT SYPHILIS TREATMENTS HAVE BEEN IN USE

74,702

NUMBER OF CASES OF SYPHILIS DIAGNOSED IN 2015

Percent change in syphilis* rate from 2011 to 2015



-27% - 0%: AK, VT 1% - 50%: WA, TX, MS, AL, TN, KY, SC, IL, OH, WI, MI, MD, DE, CT 51% - 100%: CA, MT, CO, NM, LA, FL, MN, IN, NY, PA, VA, MA, RI 101% - 200%: NV, AZ, AK, OK, MO, GA, NC, NH, ME 201%+: OR, ID, UT, WY, ND, SD, NE, KS, IA, WV, HI

Resources

- 1) STD Clinical Consultation Network – get your clinical questions answered by an expert in your region
 - stdccn.org
- 2) National STD Curriculum – self-study modules, Q&A, continuing education credits
 - std.uw.edu