The Resurgence of Syphilis: What Do We Do Now?

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Disclosures

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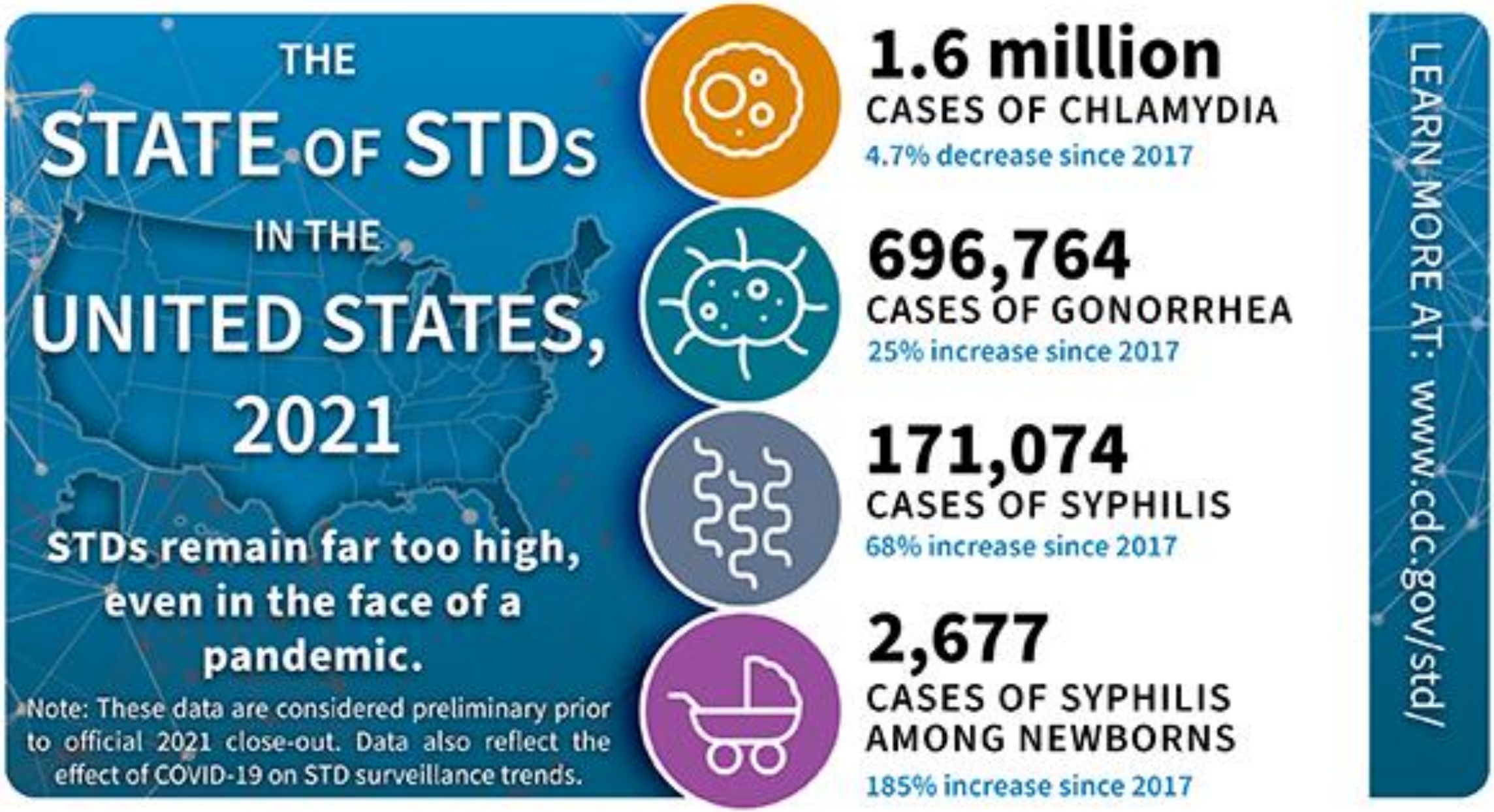
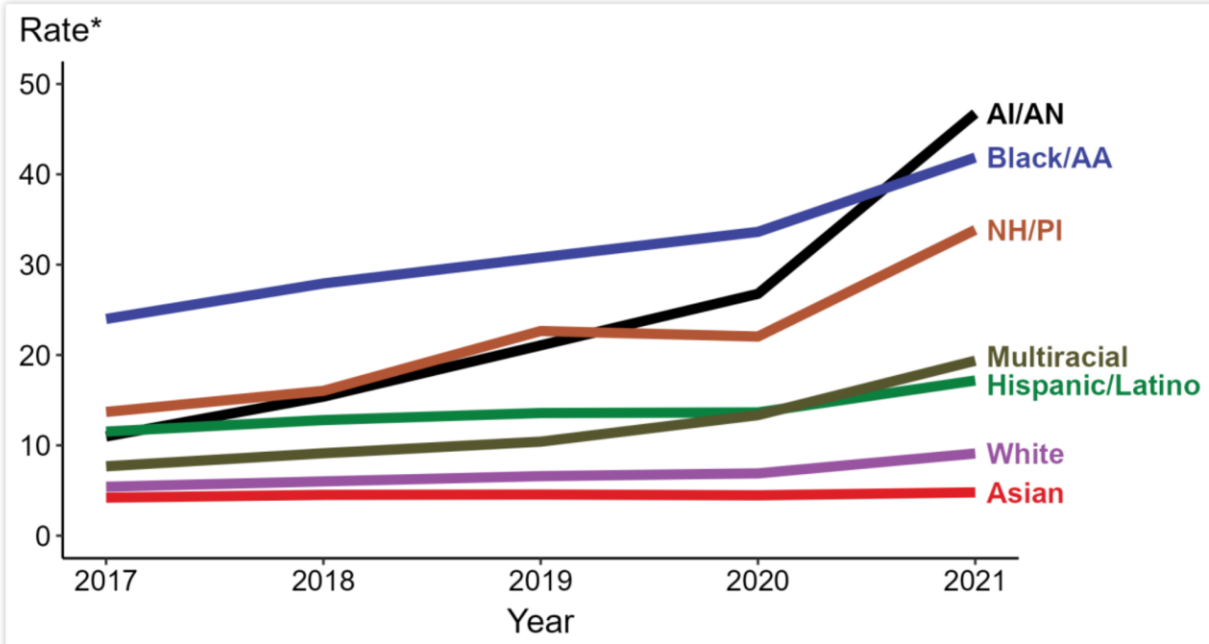

THE
STATE OF STDs
IN THE
UNITED STATES,
2021
STDs remain far too high, even in the face of a pandemic.
Note: These data are considered preliminary prior to official 2021 close-out. Data also reflect the effect of COVID-19 on STD surveillance trends.
1.6 million
CASES OF CHLAMYDIA
4.7% decrease since 2017
696,764
CASES OF GONORRHEA
25% increase since 2017
171,074
CASES OF SYPHILIS
68% increase since 2017
2,677
CASES OF SYPHILIS AMONG NEWBORNS
185% increase since 2017
LEARN MORE AT: www.cdc.gov/std/

Syphilis in 2021

Primary and Secondary Syphilis — Rates of Reported Cases by Race/Hispanic Ethnicity, United States, 2017–2021

Print



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, 2012–2021

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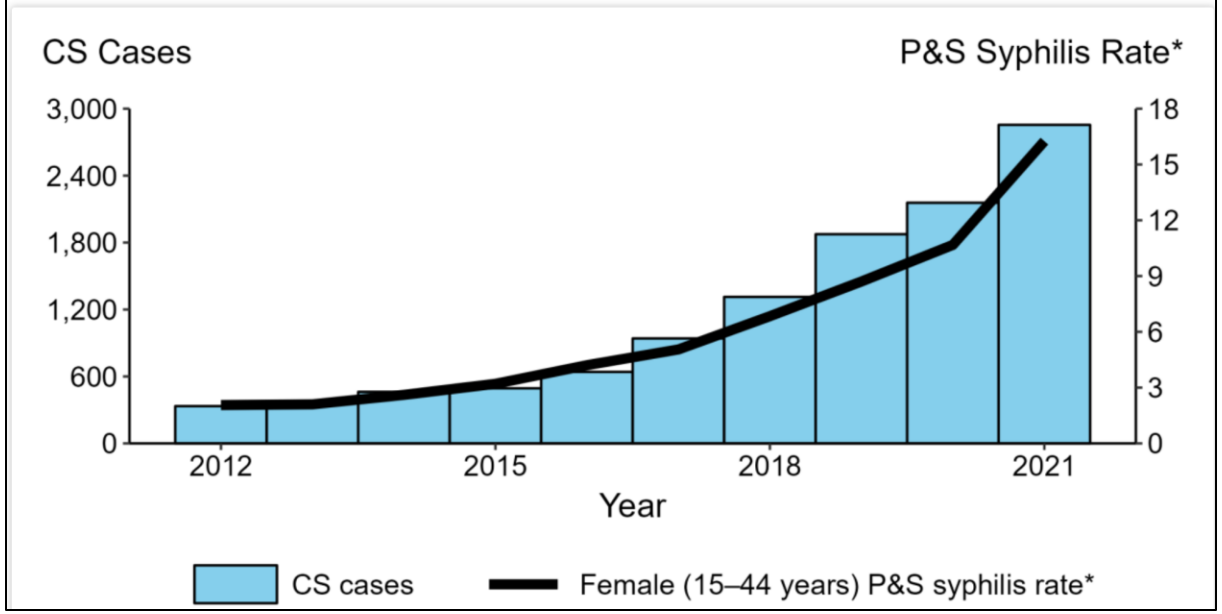


Ensure quality care

Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Recommendations and Reports / Vol. 70 / No. 4
July 23, 2021

Sexually Transmitted Infections Treatment Guidelines, 2021

Updates to CDC STI Screening Guidelines

Syphilis

Women	• Screen asymptomatic women at increased risk (history of incarceration or transactional sex work, geography, race/ethnicity) for syphilis infection[2,7]
Pregnant Women	• All pregnant women at the first prenatal visit[8] • Retest at 28 weeks gestation and at delivery if at high risk (lives in a community with high syphilis morbidity or is at risk for syphilis acquisition during pregnancy [drug misuse, STIs during pregnancy, multiple partners, a new partner, partner with STIs])[2]
Men Who Have Sex With Women	• Screen asymptomatic adults at increased risk (history of incarceration or transactional sex work, geography, race/ethnicity, and being a male younger than 29 years) for syphilis infection[2,7]
Men Who Have Sex With Men	• At least annually for sexually active MSM[2] • Every 3 to 6 months if at increased risk[2] • Screen asymptomatic adults at increased risk (history of incarceration or transactional sex work, geography, race/ethnicity, and being a male younger than 29 years) for syphilis infection[2,7]
Transgender and Gender Diverse People	• Consider screening at least annually based on reported sexual behaviors and exposure[2]
Persons with HIV	• For sexually active individuals, screen at first HIV evaluation, and at least annually thereafter[2,6] • More frequent screening might be appropriate depending on individual risk behaviors and the local epidemiology[2]

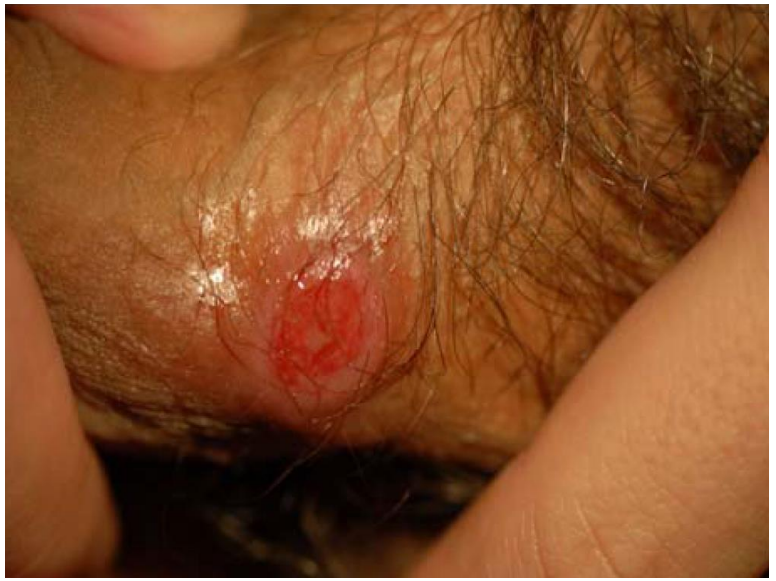
MUST KNOWS to understand syphilis

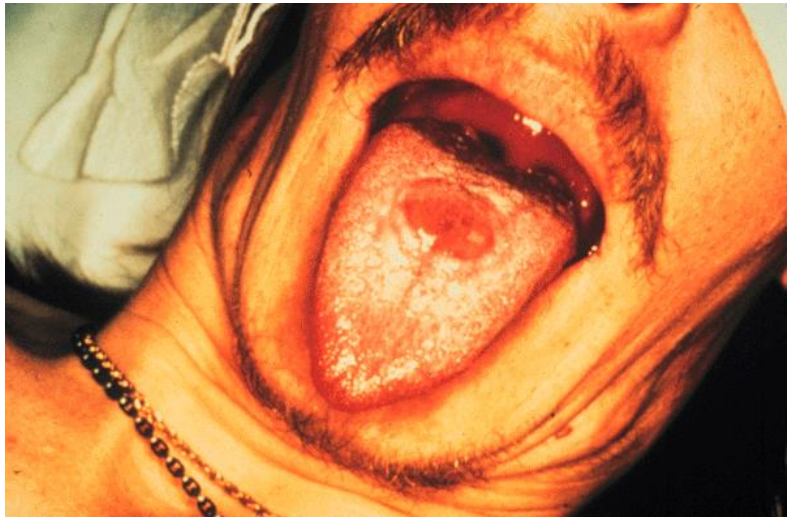
- Syphilis must be on the differential to be diagnosed
- Disseminates at every stage
- The more syphilis we see, the more unusual presentations we see.
- Recent rise in cases is somewhat due to an increase in association with drug use.
- Two things every patient with syphilis needs:
    - Neuro ROS→ if positive, continue with further assessment
    - Assessment of pregnancy status

Clinical presentation

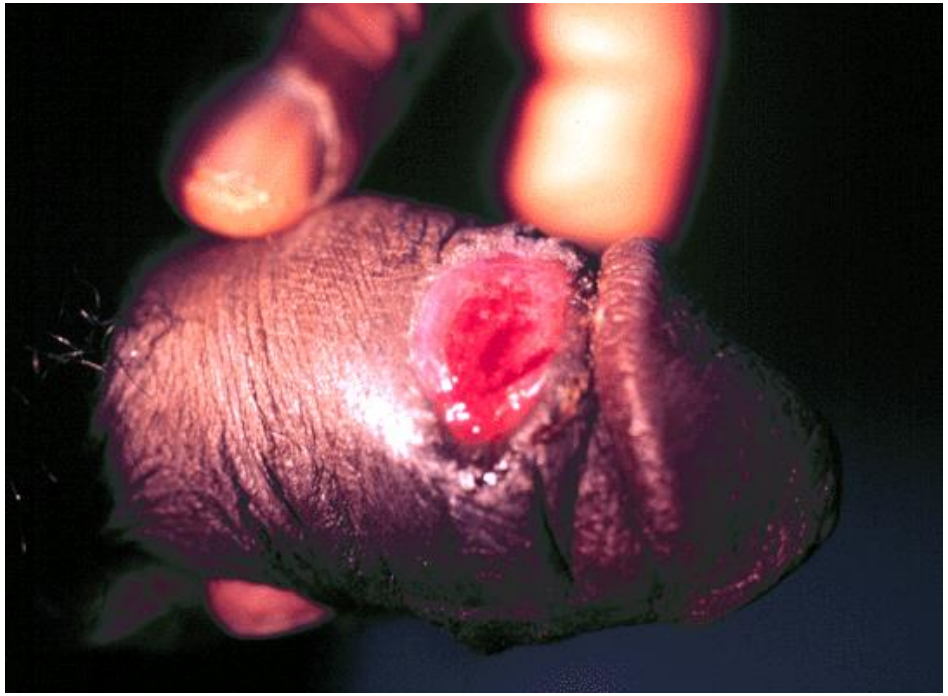
- Chancre is hallmark of primary infection: 10-90d after exposure
  - Painless (but not always*)
  - Can have more than one chancre.
  - Macrophages and activated T cells at chancre site—and highly associated with HIV acquisition
  - median time to HIV diagnosis is 1.6 years.**
  - New in 2021: Atypical presentations are more common (painful chancres, condyloma lata etc.)

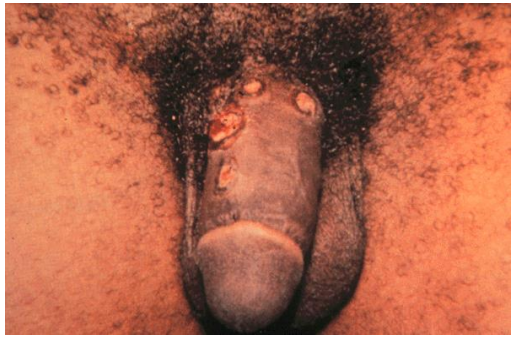
**Pathela et al CID 2015

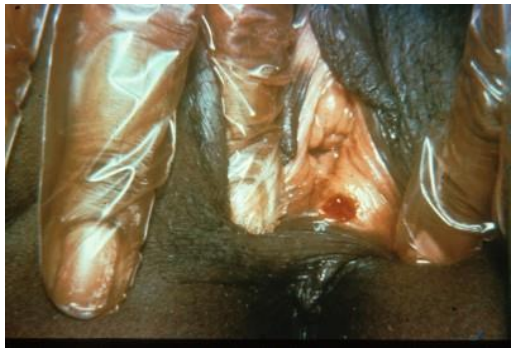


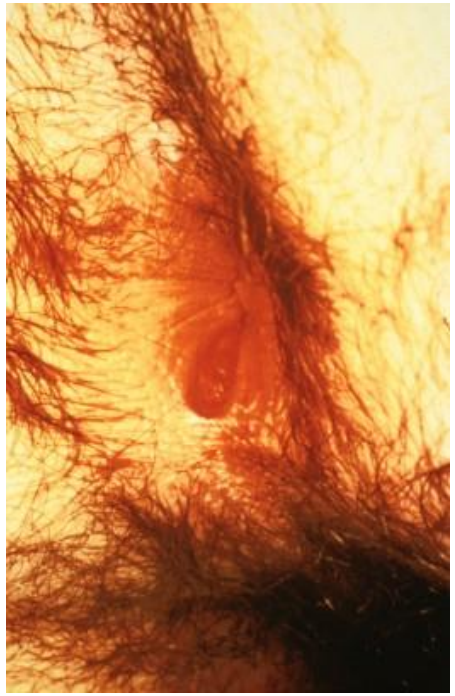


Primary syphilis - chancre





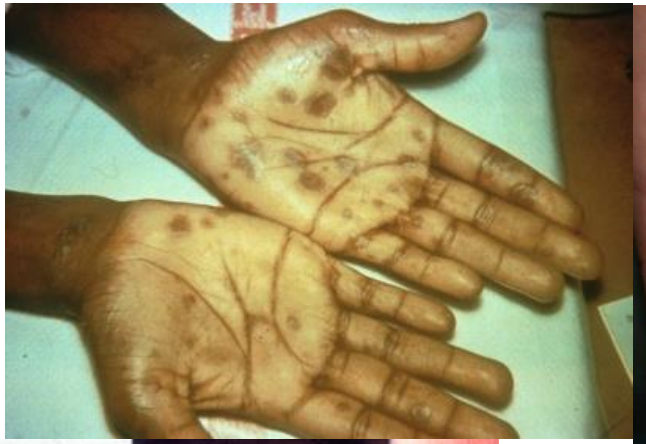


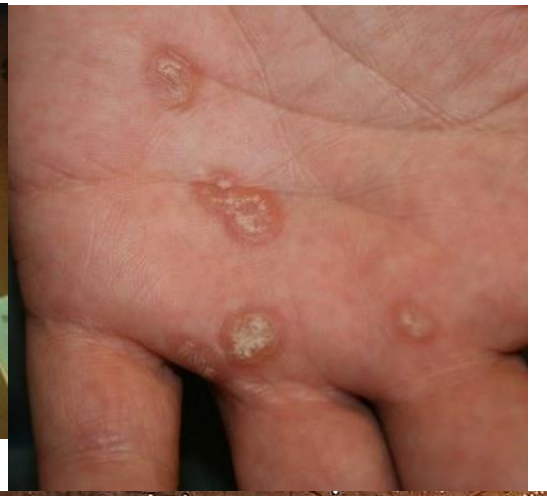


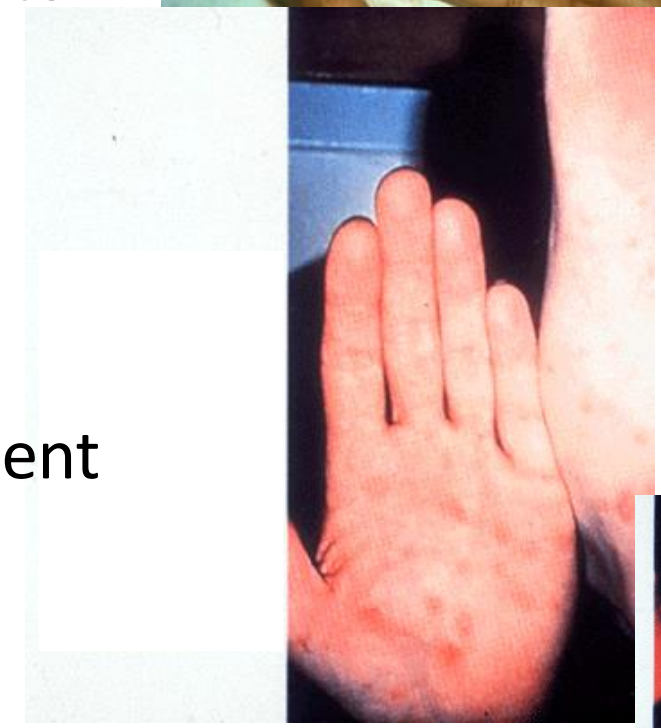
If HSV is on the differential, syphilis should be too.

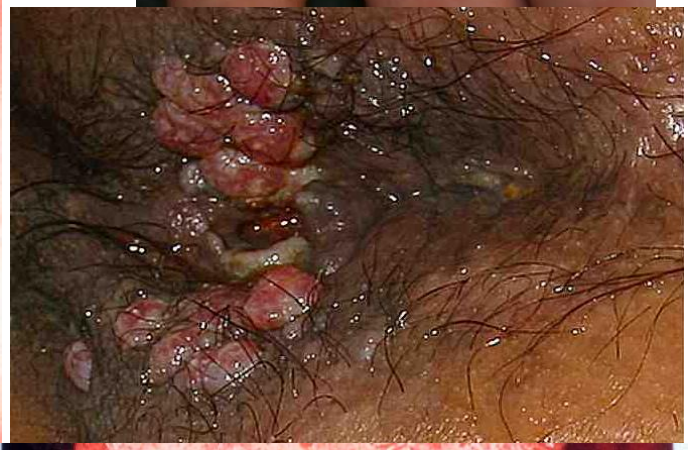
Secondary syphilis: It is not psoriasis

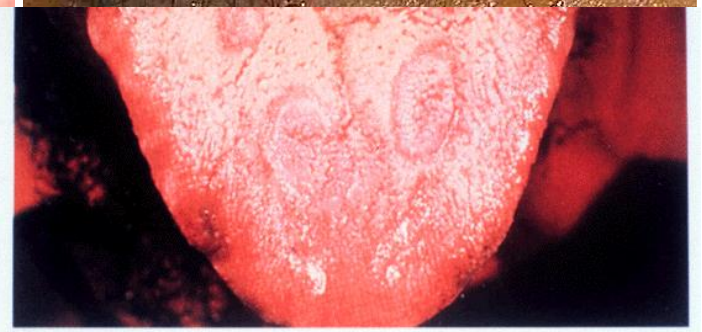
- Chancre heals spontaneously in 1 to 6 weeks
- Systematic symptoms (F, malaise, HA, LAN, etc) can occur
- Rash ultimately resolves, but infection is lifelong without treatment (latency)
- Condyloma lata!











31. Mucous patches on tongue in secondary syphilis

Late Clinical Manifestations/ Tertiary syphilis

Late Clinical Manifestations:

Late clinical manifestations of syphilis usually develop only after a period of 15–30 years of untreated infection. Therefore, if the patient has late clinical manifestations of syphilis, the case should be reported with the appropriate stage of infection (for most cases, unknown duration or late syphilis) and late clinical manifestations should be noted in the case report data.

Clinical description

Late clinical manifestations of syphilis (tertiary syphilis) may include inflammatory lesions of the cardiovascular system (e.g., aortitis, coronary vessel disease), skin (e.g., gummatous lesions), bone (e.g., osteitis), or other tissue. Rarely, other structures (e.g., the upper and lower respiratory tracts, mouth, eye, abdominal organs, reproductive organs, lymph nodes, and skeletal muscle) may be involved. In addition, certain neurologic manifestations (e.g., general paresis and tabes dorsalis) are also late clinical manifestations of syphilis.

Case

25 year old cisgender woman who presents for STI workup with no complaints. She reports 2 cisgender male sexual partners in the last 3 months, uses condoms occasionally. Her RPR is reactive at 1:256, with reactive TP-PA, nonreactive HIV test, negative G/C NAAT.

You call the health department, and she has no previous RPRs on file.

She returns to clinic, and she states that she has been having some vision changes which she describes as floaters and double vision at times, and that she has had a headache more frequently within the last week which she attributed to stress. The rest of her neuro ROS is benign. What should you do?

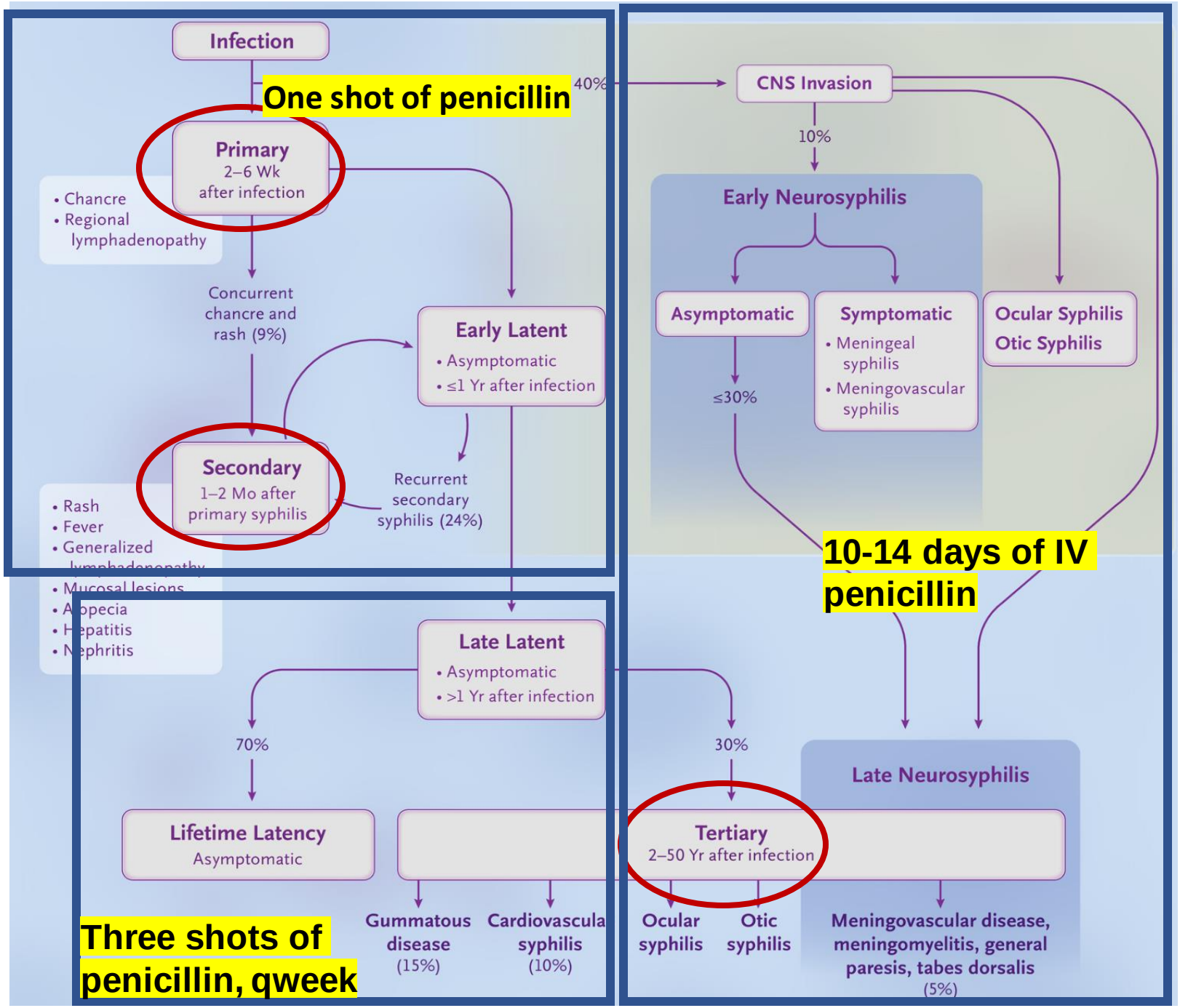
A) 1 shot 2.4 million units Bicillin as outpatient
B) 3x weekly 2.4 million units Bicillin as outpatient
C) Admit for LP and IV Penicillin G for 2 weeks
D) Admit for IV Penicillin G for 2 weeks without LP

Different Scenarios

1. Her CSF has 20 WBC, 0 RBC, Protein 60, Glucose 52, and CSF VDRL is nonreactive, what do you do now?

2. Plan to stay for 2 weeks of treatment. The primary team asks if she also needs treatment for latent syphilis of unknown duration and if she needs an extra Bicillin shot at the end of her 2 week course?

3. She has plans for 2 weeks of treatment but leaves at day 9. She then follows up as outpatient 3 months later and your team asks if she needs any further treatment. Her RPR is now 1:64. Thoughts?



Stages of Syphilis

Key Points:

- Without treatment, secondary syphilis can be recurrent.
- Ocular and otic syphilis can present at any stage of syphilis.
- Work with DIS/ health department to review patient's history

Ghanem KG, Ram S, Rice PA. The Modern Epidemic of Syphilis. *N Engl J Med*. 2020;382(9):845-854. doi:10.1056/NEJMra1901593

Treatment of Syphilis

- IM Penicillin G benzathine
- Doxycycline is not an alternative treatment but only for TRUE pen allergies
- IV penicillin for neuro/ ophtho/ otic syphilis
- No new data to warrant a change in treatment recommendations.
- Reaffirmation to reassure that a lack of serological response should be followed out to:
    - 12 months after syphilis of < 1 year duration
    - 24 month in case of syphilis of unknown duration or late syphilis
    - And that it may not be seen if RPR titer is <1:4

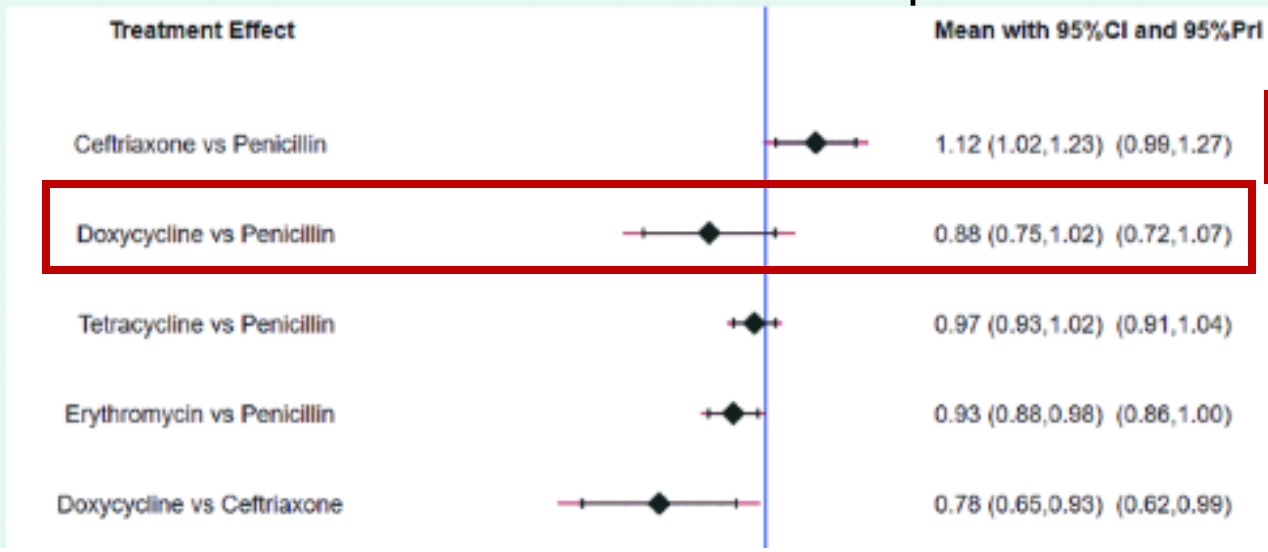
AMERICAN SOCIETY FOR MICROBIOLOGY | Microbiology Spectrum

RESEARCH ARTICLE
November/December 2022 Volume 10 Issue 6 e02977-22
https://doi-org.beckerproxy.wustl.edu/10.1128/spectrum.02977-22

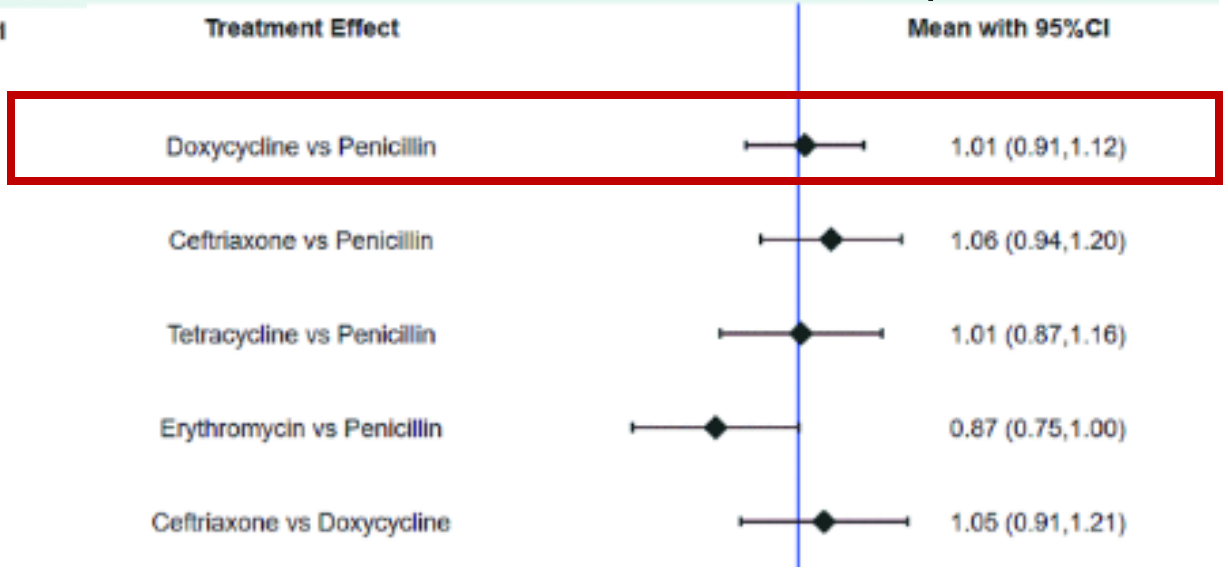
Efficacy and Safety of Treatments for Different Stages of Syphilis: a Systematic Review and Network Meta-Analysis of Randomized Controlled Trials and Observational Studies

Meixiao Liu[a], Yuxin Fan[a], Jingjing Chen[a], Jiaru Yang[a], Li Gao[a], Xinya Wu[a], Xin Xu[a], Yu Zhang[a], Peng Yue[a], Wenjing Cao[a], Zhenhua Ji[a], Xuan Su[a], Shiyuan Wen[a], Jing Kong[a], Guozhong Zhou[a], Bingxue Li[a], Yan Dong[a], Aihua Liu[a,b], Fukai Bao [a,b]

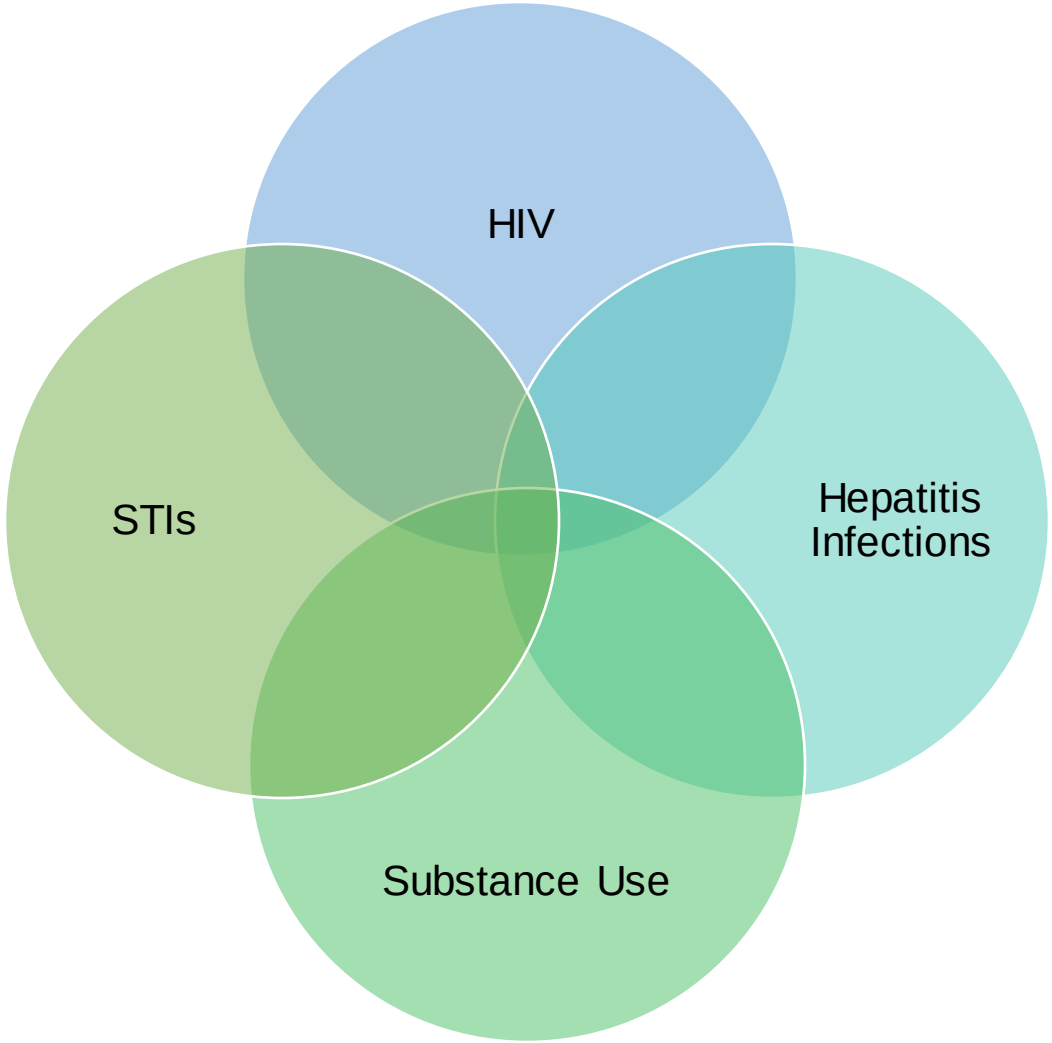
6 month follow up



12 month follow up

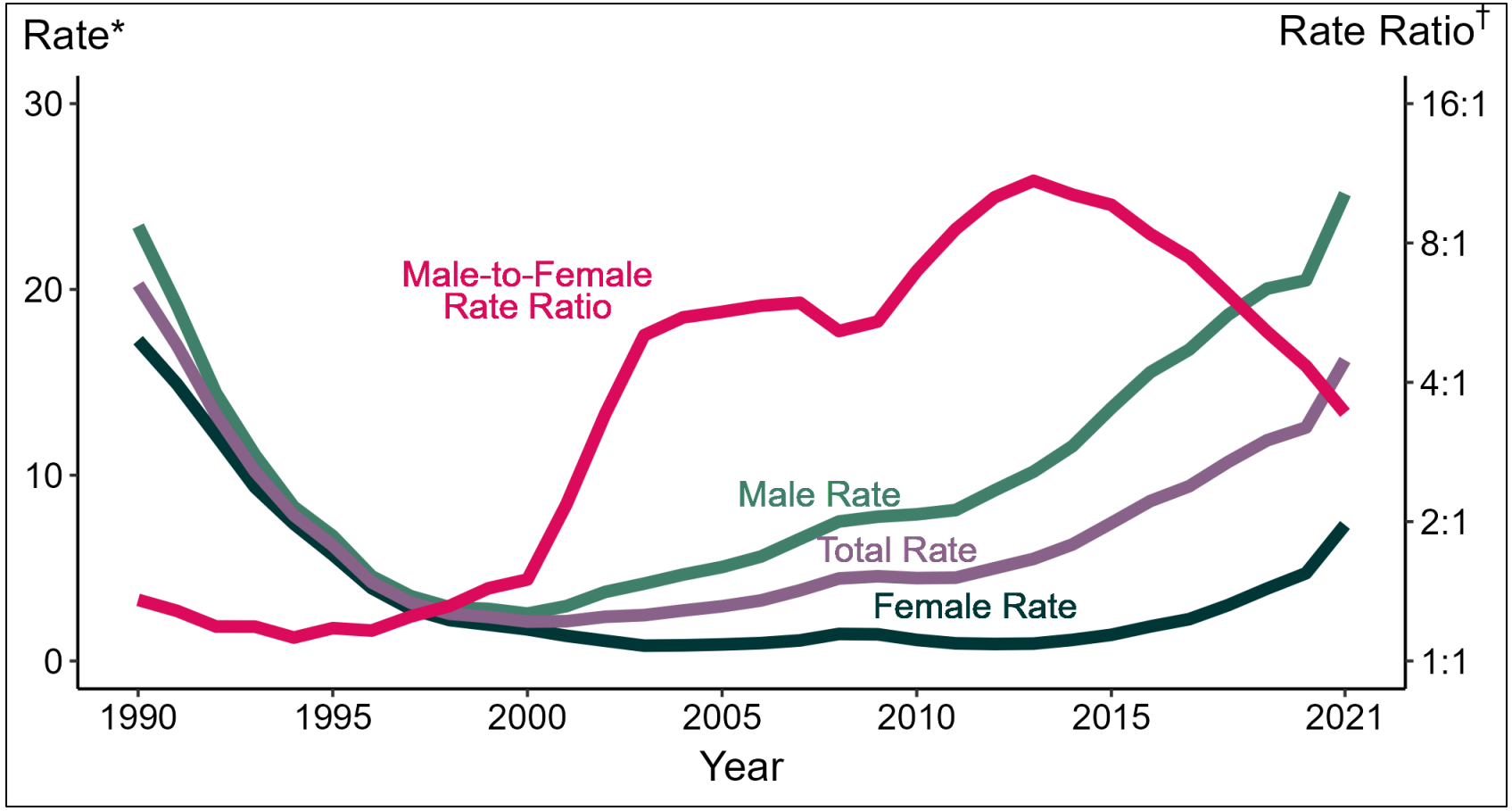


Have a syndemic approach



Congenital Syphilis

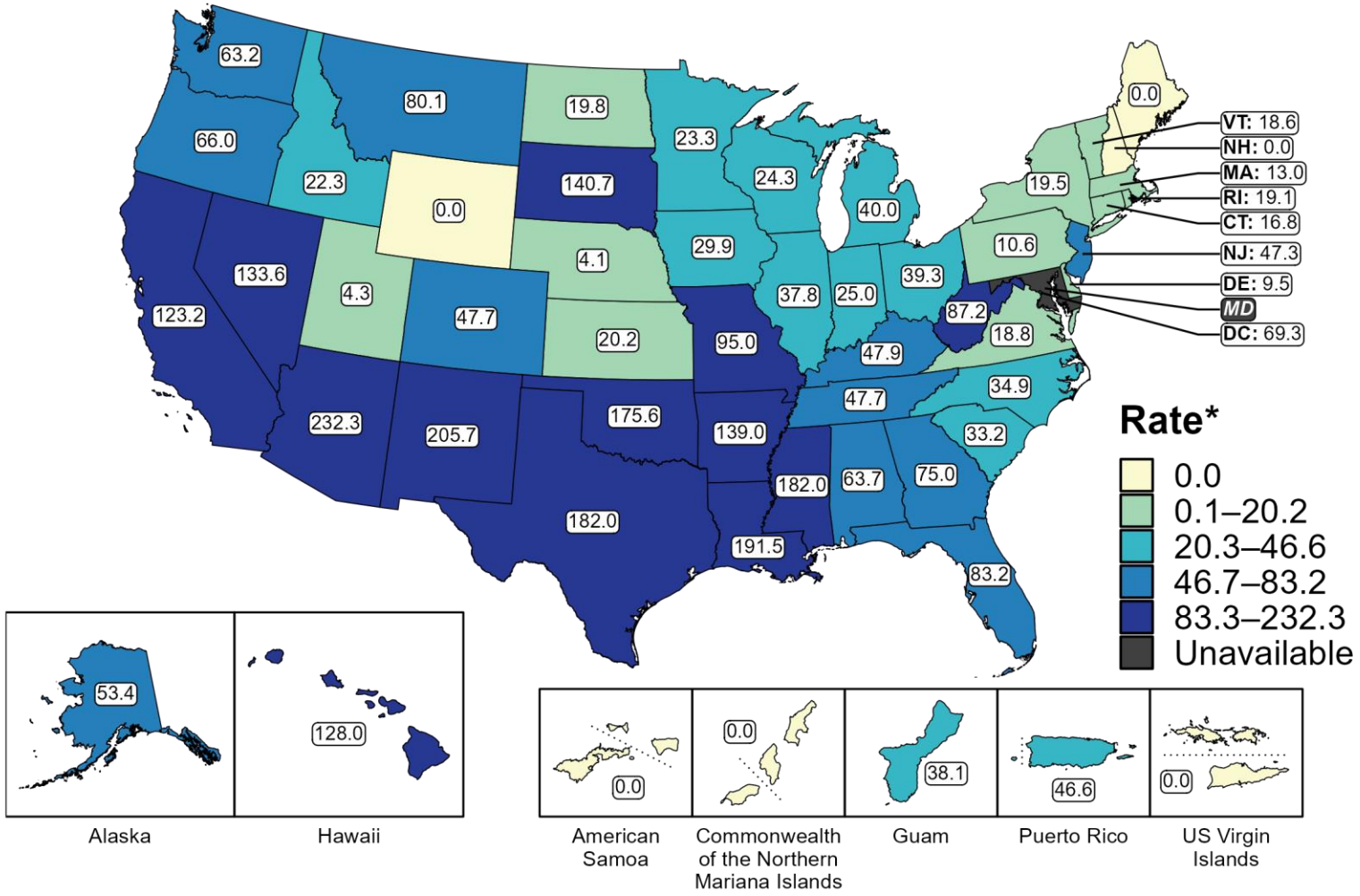
Primary and Secondary Syphilis — Rates of Reported Cases by Sex and Male-to-Female Rate Ratios, United States, 1990–2021



* Per 100,000

† Log scale

Congenital Syphilis — Rates of Reported Cases by State, United States and Territories, 2021



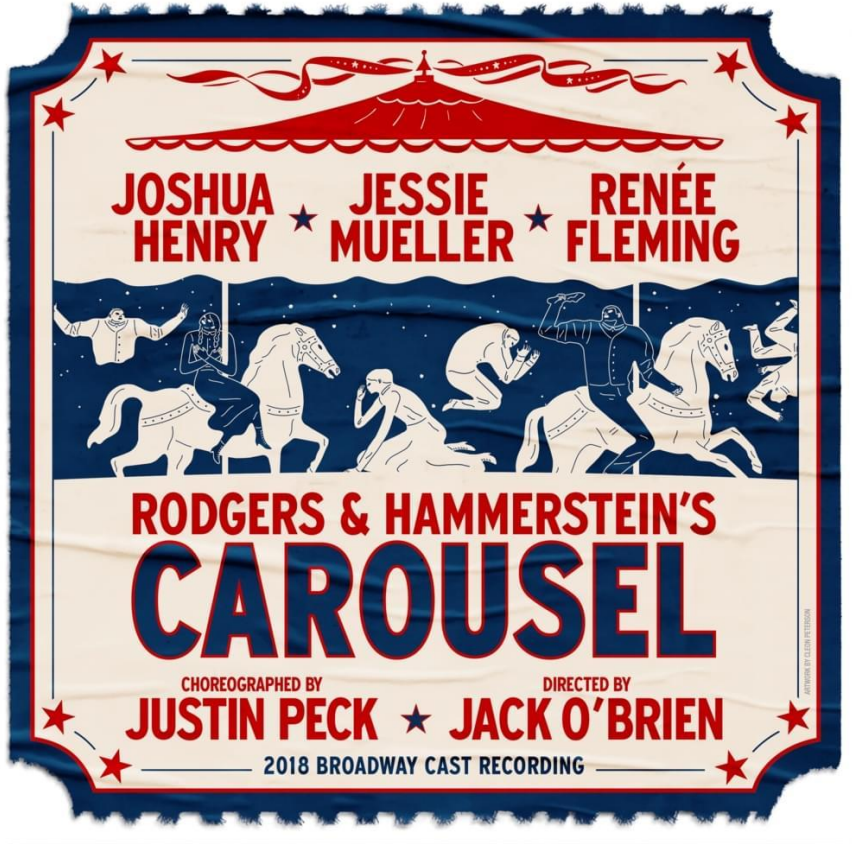
Congenital syphilis prevention: screening

- Screen all women in early pregnancy
- Screen again twice in third trimester “for communities and populations in which the prevalence of syphilis is high, and for women at high risk of infection”
    - Screen at 28 weeks
    - Screen again at delivery

Sexually Transmitted Diseases Treatment Guidelines 2021

Congenital syphilis prevention: Quality Care

- Access to packaged STI testing for people of childbearing potential.
- Counseling pregnant people on STI prevention
  - Especially in the later half of pregnancy: Consider HSV and syphilis
- Do not forget syphilis can occur in pregnancy
- Go to the CDC STI guidelines for diagnosis and classifying CS



Scenario 1: Confirmed Proven or Highly Probable Congenital Syphilis

Any neonate with

- an abnormal physical examination that is consistent with congenital syphilis;
- a serum quantitative nontreponemal serologic titer that is fourfold[§] (or greater) higher than the mother's titer at delivery (e.g., maternal titer = 1:2, neonatal titer ≥1:8 or maternal titer = 1:8, neonatal titer ≥1:32)[¶]; or
- a positive darkfield test or PCR of placenta, cord, lesions, or body fluids or a positive silver stain of the placenta or cord.

Recommended Evaluation

- CSF analysis for VDRL, cell count, and protein**
- Complete blood count (CBC) and differential and platelet count
- Long-bone radiographs
- Other tests as clinically indicated (e.g., chest radiograph, liver function tests, neuroimaging, ophthalmologic examination, and auditory brain stem response)

Recommended Regimens, Confirmed or Highly Probable Congenital Syphilis

Aqueous crystalline penicillin G 100,000–150,000 units/kg body weight/day, administered as 50,000 units/kg body weight/dose by IV every 12 hours during the first 7 days of life and every 8 hours thereafter for a total of 10 days

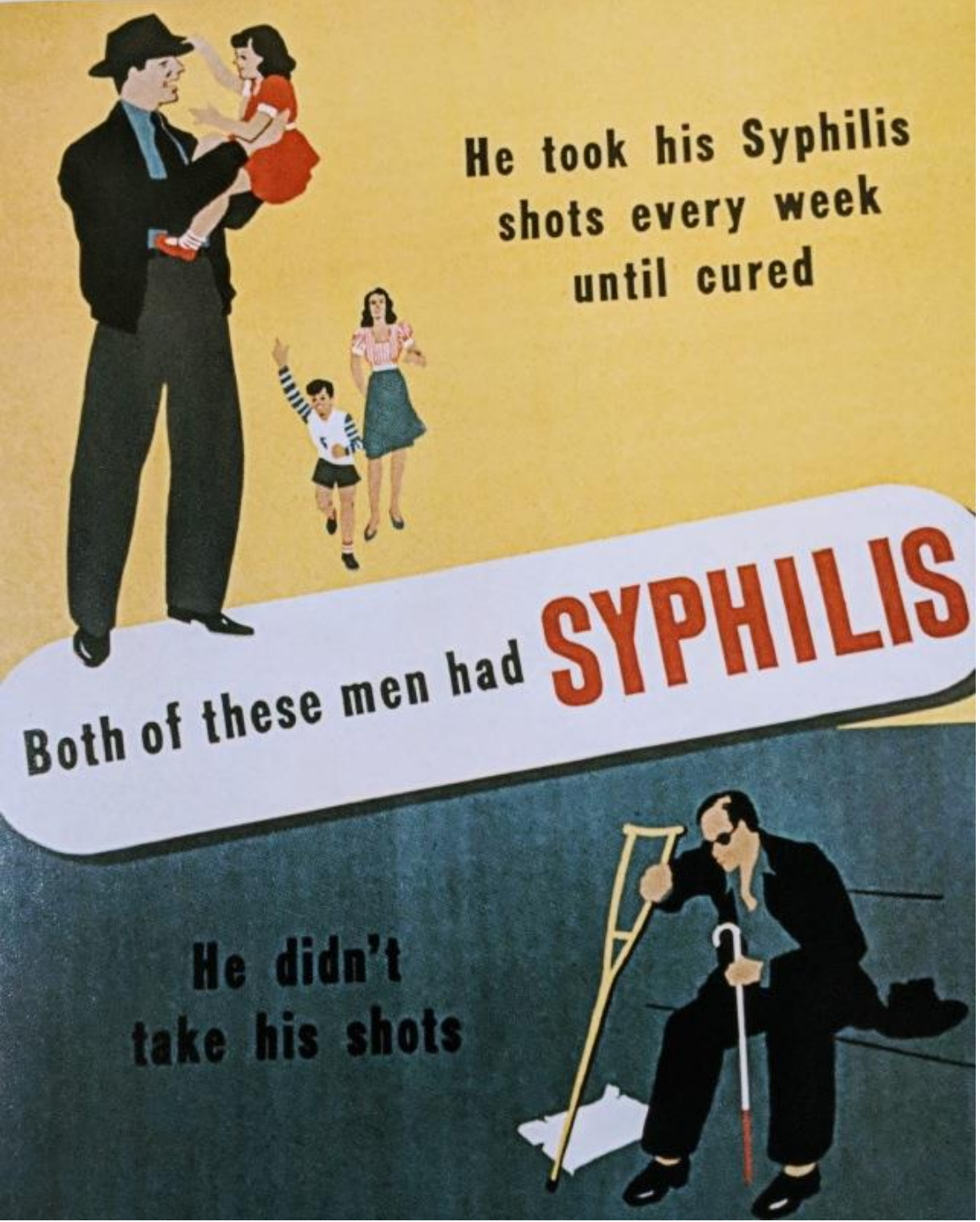
OR

Procaine penicillin G 50,000 units/kg body weight/dose IM in a single daily dose for 10 days

If >1 day of therapy is missed, the entire course should be restarted. Data are insufficient regarding use of other antimicrobial agents (e.g., ampicillin). When possible, a full 10-day course of penicillin is preferred, even if ampicillin was initially provided for possible sepsis (*648–650*). Using agents other than penicillin requires close serologic follow-up for assessing therapy adequacy.

Management of syphilis in pregnancy

- Obtain previous treatment history to help management.
- Management is the same as non-pregnant people.
- For P+S, ES, some give an additional IM dose 1 week after treatment.
- Goal is 7 days between doses of IM bicillin but if a person misses a dose, effort should be focused on getting the dose within 2 days.
  - Doses more than 9 days apart means restarting treatment.
- Ultrasound is used to monitor in second half of pregnancy but should not delay treatment.
- For patients with early syphilis or high titers, Jarisch-Herxheimer reaction counseling is advised.
- Recheck RPR 8 weeks after treatment.



The bad news: Treating maternal syphilis is hard

- Provider confusion over appropriate treatment for different syphilis stages
- Difficulty facilitating three weekly doses for late latent syphilis
- Difficulty managing penicillin allergies

Left: Unknown, 1941-1945

Slide: E. Daniels

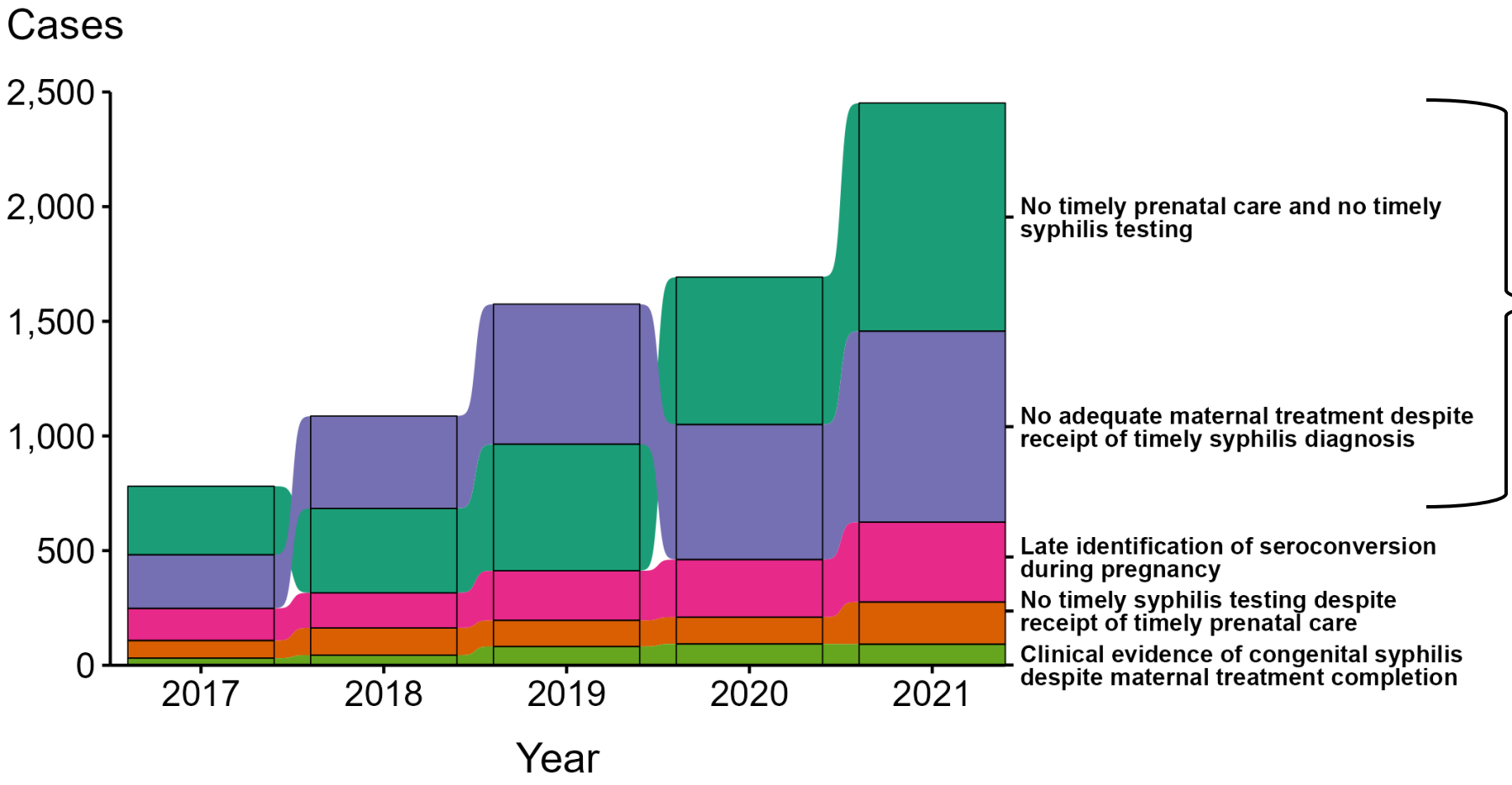
CDC: Providing a framework for missed prevention opportunities

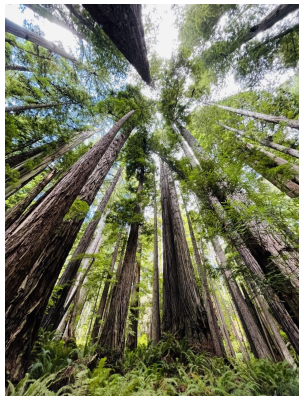
- Found that the most common missed prevention opportunities in the U.S. were:
  - A lack of adequate maternal treatment despite the timely diagnosis of syphilis (30.7%)
  - A lack of timely prenatal care (28.2%)
- Prevention opportunities change with time and vary by geographic region

Kimball et al. MMWR June 2020.

Kimball et al Peds 2021.

Congenital Syphilis — Missed Prevention Opportunities among Mothers Delivering Infants with Congenital Syphilis, United States, 2017–2021





NOTE: Of the 9,141 congenital syphilis cases reported during 2017 to 2021, 1,553 (17.0%) were not able to have the primary missed prevention opportunity identified due to insufficient information provided to CDC related to maternal prenatal care, testing, or treatment.

Congenital Syphilis is <u>preventable</u> but…

- Timely prenatal care
- Timely syphilis testing
- Timely, stage-appropriate maternal treatment
- Timely identification of treatment failure, relapse, and seroconversion during pregnancy

Deadline to start treatment:
30 days prior to delivery!

Case

26-year-old pregnant, cisgender female presents for a walk-in STI clinic visit. She is unhoused and does not have insurance.

She is 8 weeks gestation by dates, found to have RPR of 1:64, has never had syphilis testing in the past and currently has no symptoms and a normal physical exam. She states she is allergic to penicillin with history of rash and shortness of breath with amoxicillin, how would you proceed?

A syndemic approach

Free Inquiry - Special Issue: Gangs, Drugs & Violence *Volume 28, No. 1 May 2000 Page 13*

A DOSE OF DRUGS, A TOUCH OF VIOLENCE, A CASE OF AIDS: CONCEPTUALIZING THE SAVA SYNDEMIC

Merrill Singer, Hispanic Health Council

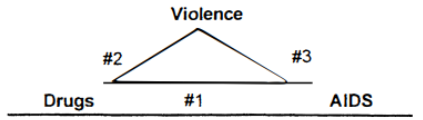
ABSTRACT

Gang violence, substance abuse and AIDS have been described as parallel epidemics in the U.S. inner city. This paper draws upon findings from a set of ethnographic and survey research projects in the Puerto Rican community of Hartford, CT to develop a conceptualization of the close interconnections between these three health and social problems. Rather than separate conditions, substance abuse, violence, and AIDS, referred to here as SAVA to stress the relationships among these three phenomena, are best thought of forming a single syndemic (a closely interrelated complex of health and social crises) that continues to take a significant toll on the lives and well-being of the urban poor.

INTRODUCTION

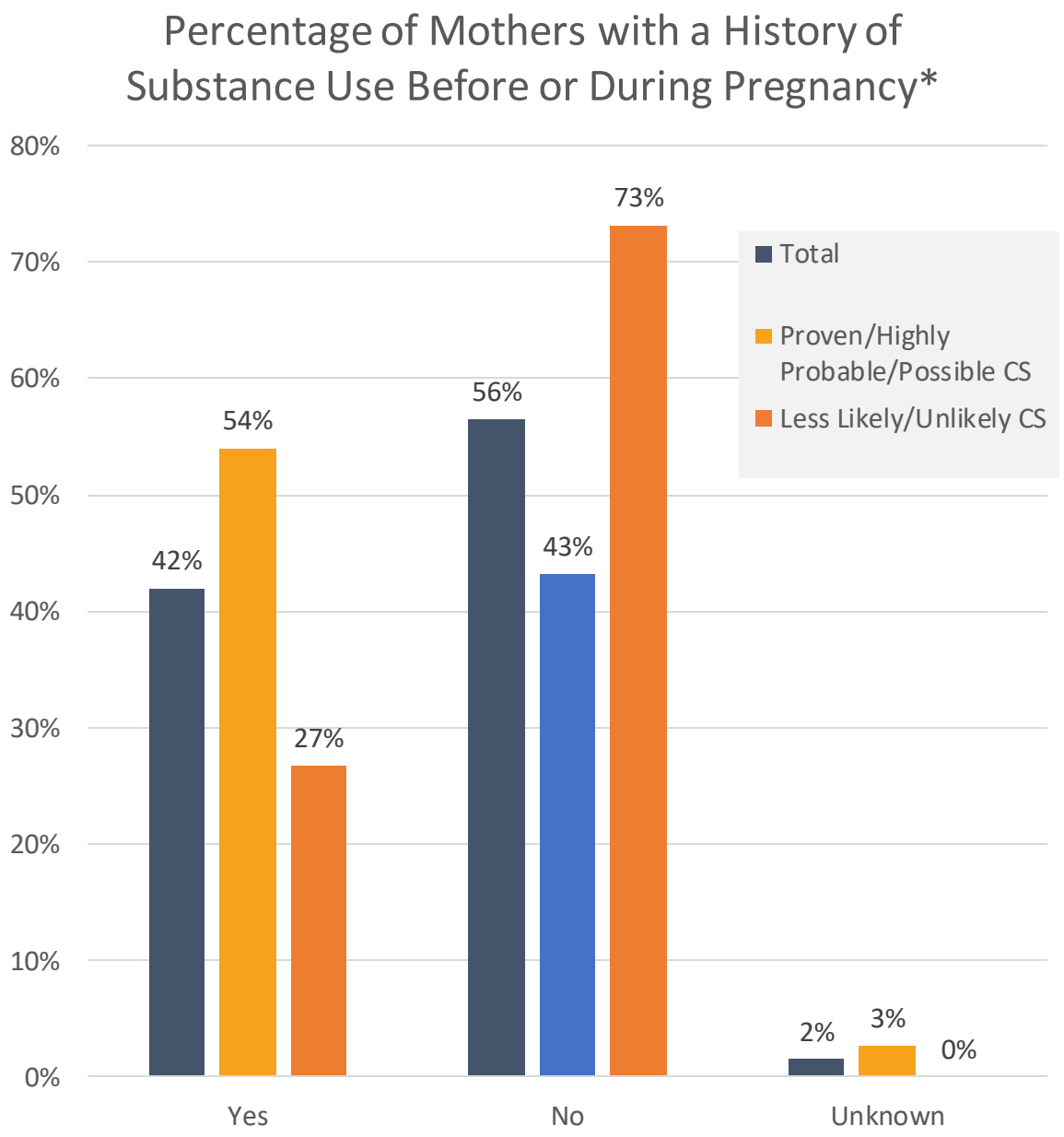
Gang-related and other violence, substance abuse, and AIDS have been described as concurrent epidemics among U.S. inner-city populations. The term epidemic, however, does not adequately describe the contemporary inner city health crisis, which is characterized by a set of closely interrelated, epidemic

FIGURE 1: SAVA Interconnections



Syndemics are stitched together by three rules:

1. two or more diseases **cluster** together in time or space;
2. these diseases **interact** in meaningful ways, whether social, psychological, or biological;
3. and harmful **social conditions** drive these interactions.



42% have a history of substance use

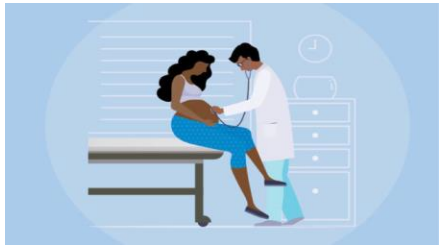
History of Substance Use*	% Total Cases of Potential CS (n=131)	% Proven/ Highly Probable/ Possible CS (n=74)	% Less Likely/ Unlikely CS (n=56)	χ^2	P Value[b]
Yes	42.0 (55)	54.1 (40)	26.8 (15)	12.22	0.002
No	56.5 (74)	43.2 (32)	73.2 (41)		
Unknown	1.5 (2)	2.7 (2)	0.0 (0)		

* Excluding alcohol, tobacco, and marijuana

[b] Comparison of Proven/Highly Probable and Possible CS vs. Less Likely and Unlikely CS. *P*-values were determined using the Chi-square test.

E. Daniels et al.

Beyond demographics, some themes emerge:



Limited Prenatal Care

Interactions with the Prison System

Housing instability

Intimate Partner Violence

Unemployment

Substance Use

Sex Work/Trafficking

DCFS Involvement

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A Syndemic approach to Congenital Syphilis

- **Ensure quality care**
- **Team management: DIS, clinician, community health worker, etc**
- **Assess for social vulnerabilities**
- **Learn from programs that are doing work in adjacent areas**
- **Collaborate**
- **Involve Community**
- **Always address prevention and stigma**

Condoms are Great, but….

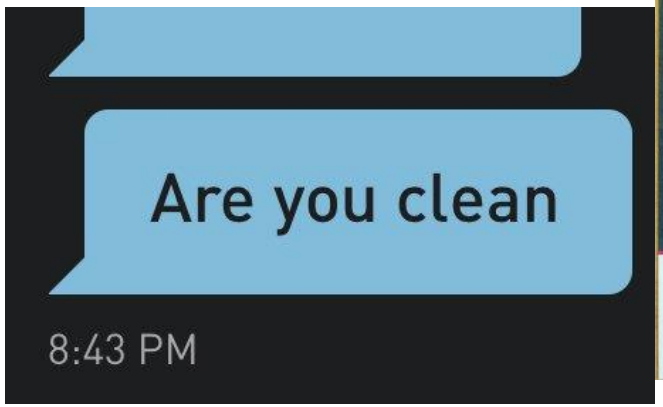
- STI prevention goes far beyond a piece of rubber (or latex)

- We need to address three main areas
  - Harm Reduction
  - Screening/Treatment
  - Destigmatization

Dismantling STI Stigma

Sex is part of the human experience… therefore so are STIs

- Normalize screening
- Normalize treatment
- Language Matters
  - STD vs STI
  - “Clean” vs “Dirty”
  - “Good” vs “Bad” behavior
  - “Who gave it to you?”



An example case

- Mom has adequate prenatal care with RPR NR at 8 wks gestation
- She presents with vaginal lesions at 35 weeks gestation
- HSV testing is negative.
- No other STI testing.
- Treated with valacyclovir.
- Presents in labor at 37 weeks.
- No RPR at delivery.
- Baby has work up at 5 months for slow weight gain and developmental delay.
- Hip xrays indicate periosteal abnormalities and CS is diagnosed.

Potential Access Challenges to Bicillin L-A®

CDC has received reports that some STD programs are currently unable to procure enough penicillin G benzathine (Bicillin L-A®) – the first-line recommended treatment for syphilis – to treat syphilis cases in their jurisdictions. The manufacturer anticipates the issue will be resolved in the next two months. In the meantime, they are working closely with CDC and FDA to address urgent requests.

During this time, programs should:

- Continue to follow CDC's Treatment recommendations. Penicillin G benzathine (Bicillin L-A®) is the only recommended treatment for pregnant people infected or exposed to syphilis.
  - Doxycycline 100mg PO BID for two weeks (for early syphilis) or for 4 weeks (for late latent or syphilis of unknown duration) is an alternative for the treatment of non-pregnant people with a penicillin allergy.
- Prioritize the use of Bicillin L-A® to treat pregnant people and babies with congenital syphilis.
- Notify DSTDP (stdshortages@cdc.gov) of any shortage or low inventories of Bicillin L-A® in your jurisdiction so CDC can continue to monitor this situation.
- Report any shortages to the Pfizer Supply Continuity Team at 844-646-4398 (select 1 and then select 3).

No-cost online clinical consultation on the prevention, diagnosis, and treatment of STDs by your Regional PTC Clinical Faculty

www.STDCCN.org

St. Louis
STI/HIV Prevention
Training Center

Action Priority Matrix