



Congenital Syphilis on the Rise: Preventable and Treatable in Indian Country

Maternal Child Health ECHO May 26, 2022

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Disclosures

- NONE

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.



Overview

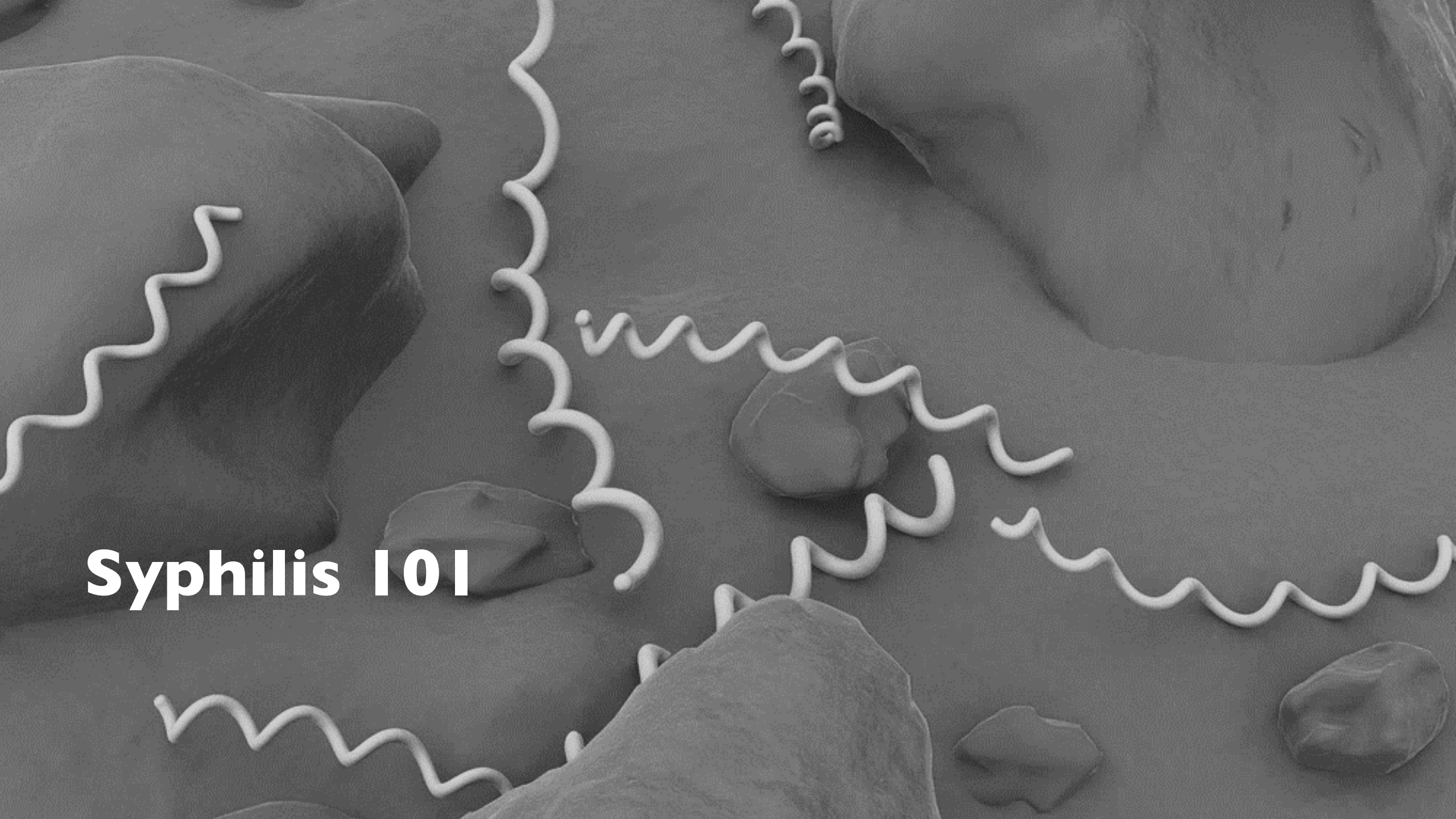
- Syphilis 101
 - Pathophysiology
 - Clinical features
- Epidemiology
- Syphilis in Pregnancy
 - Diagnosis
 - Treatment
- Congenital Syphilis Prevention
- Case Presentation



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Syphilis 101



Syphilis

- Caused by spirochete bacterium *Treponema pallidum*
- Transmission
 - Direct contact with a syphilitic lesion during vaginal, anal, or oral sex
 - Transplacentally during pregnancy



Clinical Stages

1. Syphilis goes through several stages.
2. Stages start with primary, then may not progress linearly.
3. Characterized by episodes of active disease interrupted by periods of latency.
4. Signs/symptoms and transmission risks vary by stage.



Clinical Stages

Primary

Painless ulcer
(chancre)

- Appears 10 to 90 days after infection
- **Sore goes away even if person is not treated**
- Patient may never be aware of a chancre

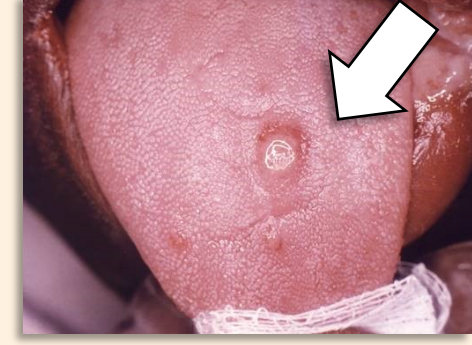
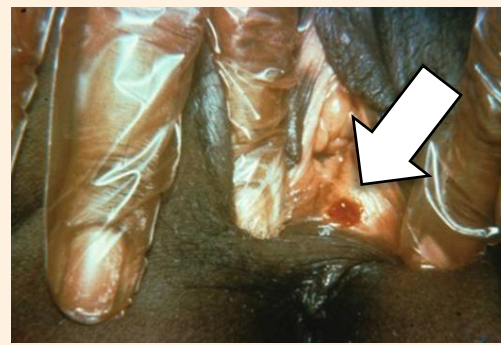
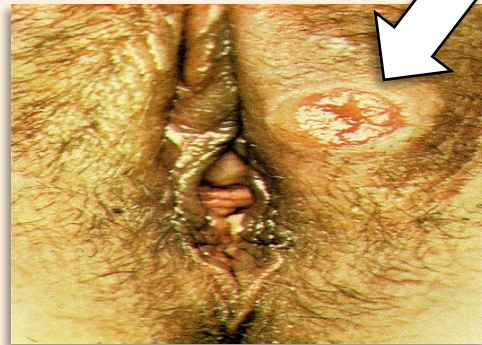
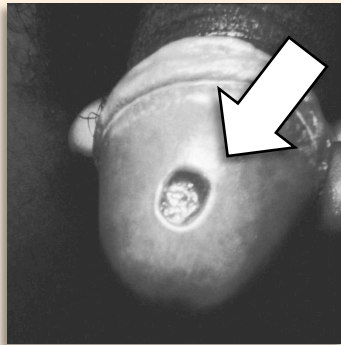


Clinical Stages

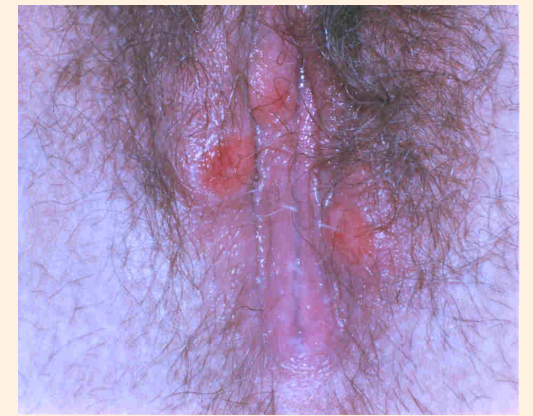
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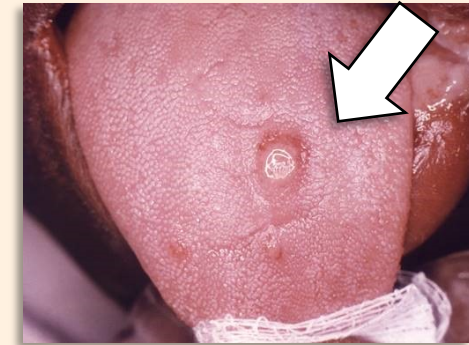
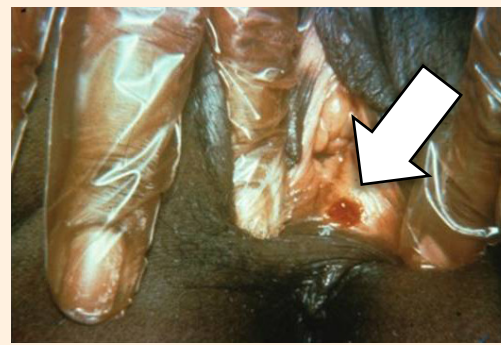
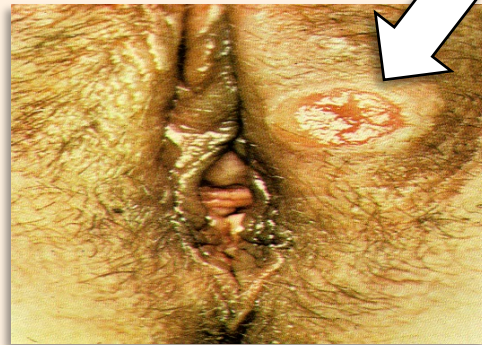
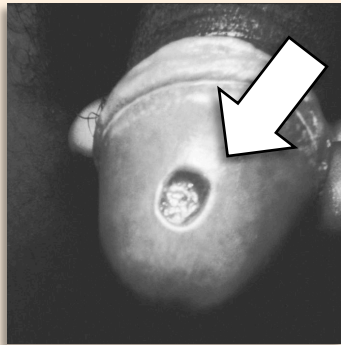
Clinical Stages



Primary

Painless ulcer
(chancre)

- Appears 10 to 90 days after infection “Kissing” Lesion
- **Sore goes away even if person is not treated**
- Patient may never be aware of a chancre



Clinical Stages

Primary	Secondary
Painless ulcer (chancre)	Rash Mucocutaneous lesions Lymphadenopathy

- *Usually* occurs 3 to 6 weeks after primary syphilis
- Patients may only have one subtle skin change
- **Symptoms also go away even if not treated!**

Clinical Stages



Secondary

Rash

Mucocutaneous
lesions
Lymphadenopathy



- *Usually* occurs 3 to 6 weeks after primary syphilis
- Patients may only have one subtle skin change
- **Symptoms also go away even if not treated!**



Clinical Stages



Secondary

Rash

Mucocutaneous lesions
Lymphadenopathy

- Usually occurs 3 to 6 weeks after primary syphilis
- Patients may only have one subtle skin change
- **Symptoms also go away even if not treated!**



Palmar Lesions



Plantar Lesions



Condyloma Lata



Clinical Stages



Secondary

Rash

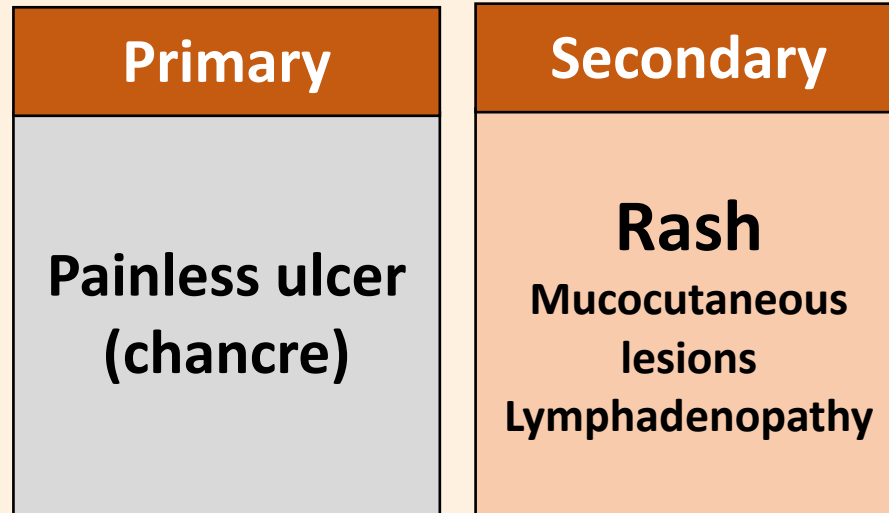
Mucocutaneous lesions

Lymphadenopathy

- Usually occurs 3 to 6 weeks after primary syphilis
- Patients may only have one subtle skin change
- **Symptoms also go away even if not treated!**



Clinical Stages



P&S Syphilis

- Most infectious stages
- Indicate recent acquisition

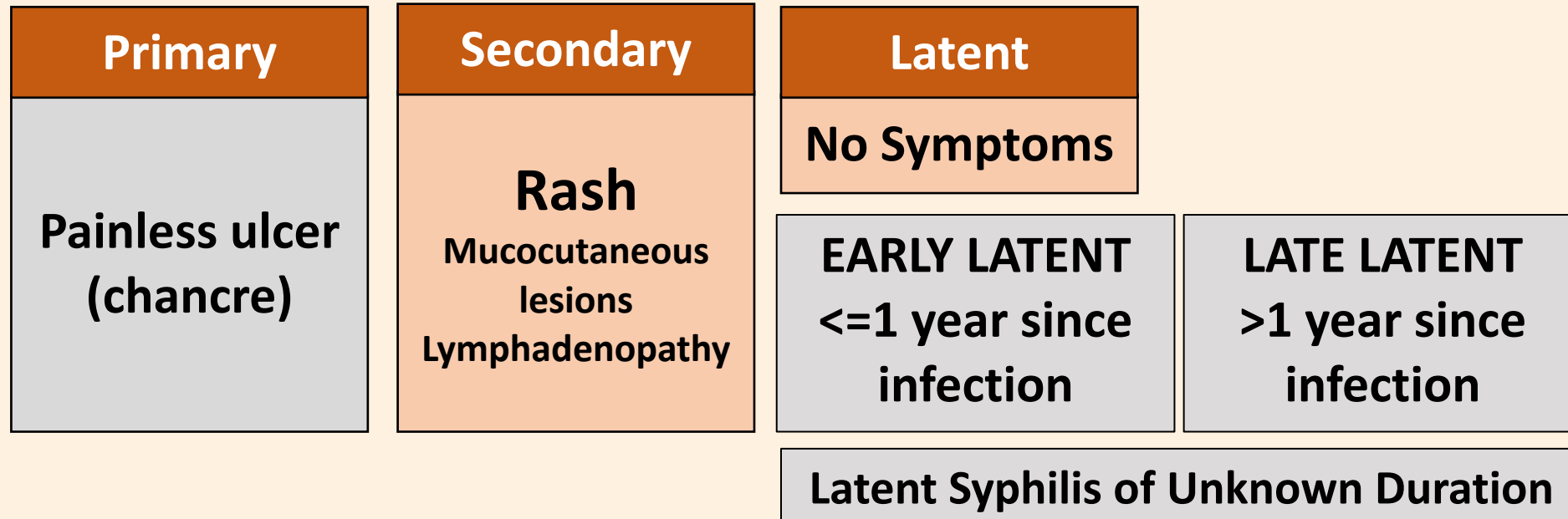


Clinical Stages

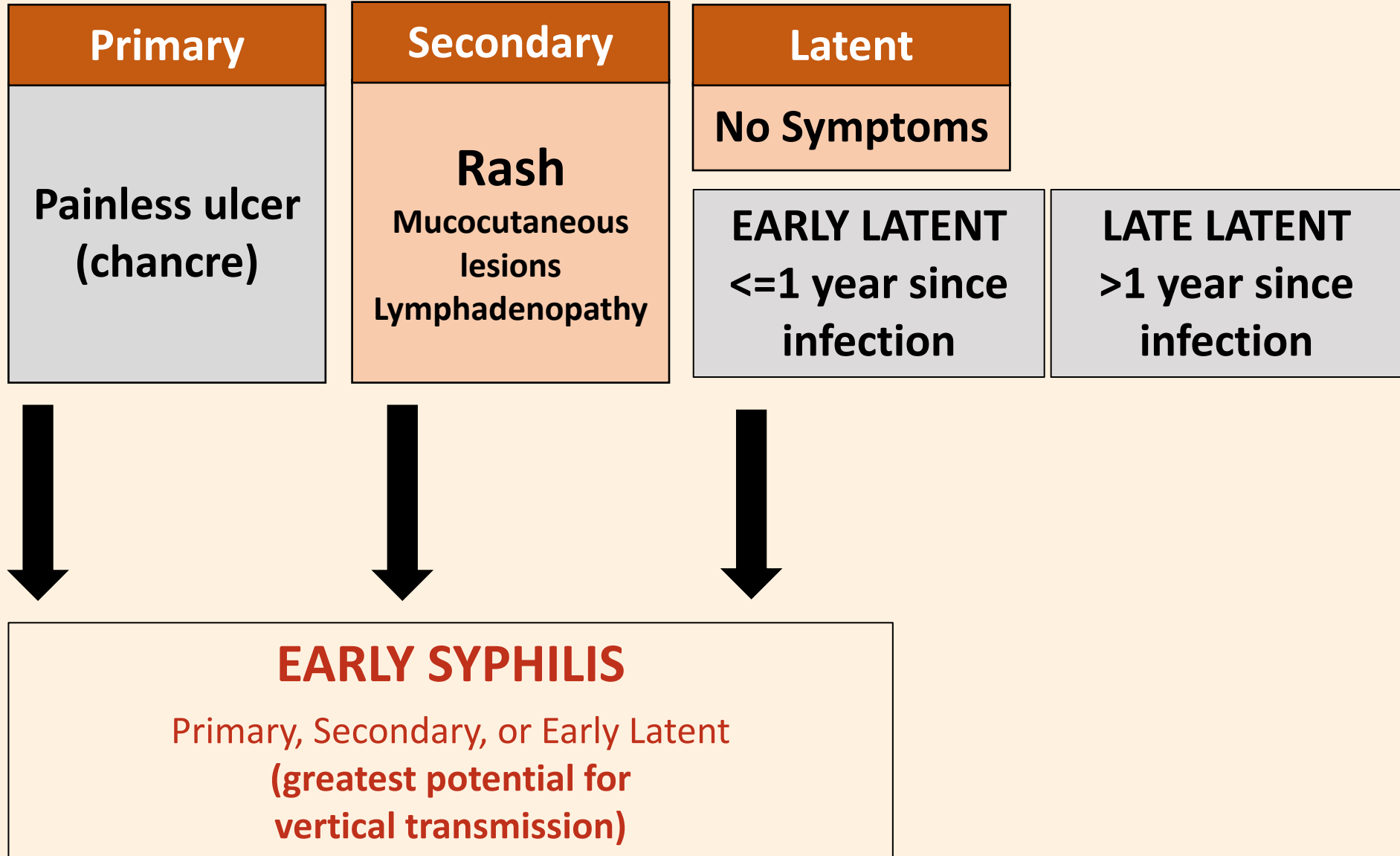
Primary	Secondary	Latent
Painless ulcer (chancre)	Rash Mucocutaneous lesions Lymphadenopathy	No Symptoms



Clinical Stages

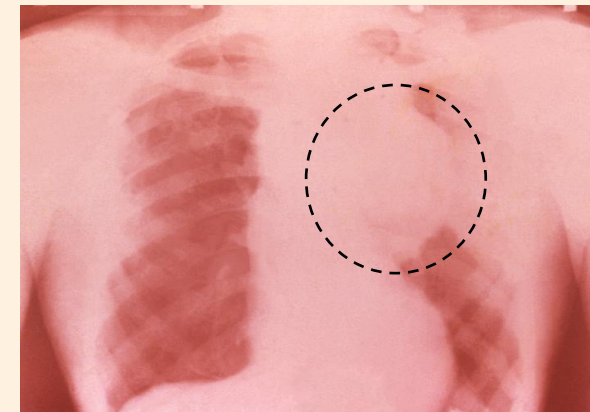


Clinical Stages



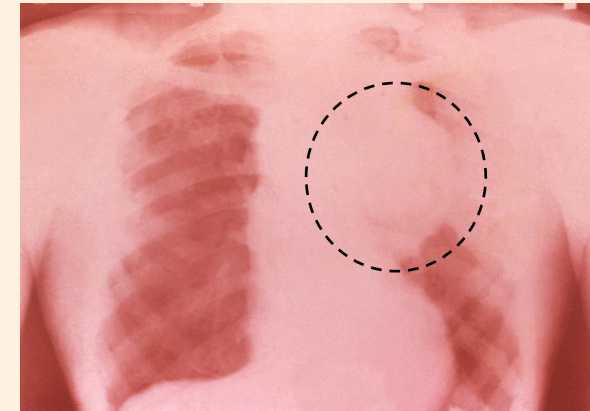
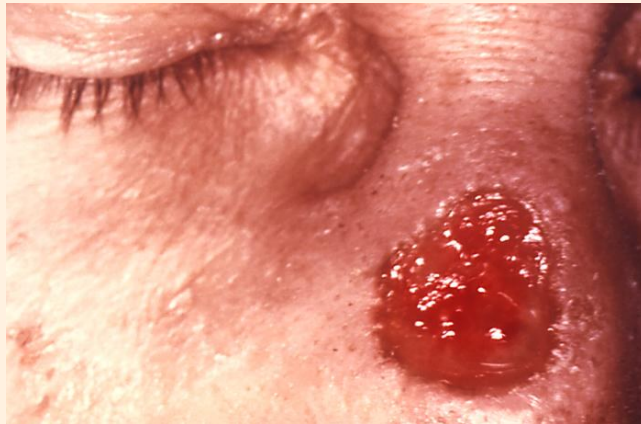
Clinical Stages

Primary	Secondary	Latent	Tertiary
Painless ulcer (chancre)	Rash Mucocutaneous lesions Lymphadenopathy	No Symptoms	Cardiovascular Gummatous lesions (skeletal, mucosal, ophthalmic)



Clinical Stages

Primary	Secondary	Latent	Tertiary
Painless ulcer (chancre)	Rash Mucocutaneous lesions Lymphadenopathy	No Symptoms	Cardiovascular Gummatous lesions (skeletal, mucosal, ophthalmic)



Clinical Stages

Primary	Secondary	Latent	Tertiary
Painless ulcer (chancre)	Rash Mucocutaneous lesions Lymphadenopathy	No Symptoms	Cardiovascular Gummatous lesions (skeletal, mucosal, ophthalmic)

Neurosyphilis can occur at any stage.



Congenital syphilis is an infection with *Treponema pallidum* in an infant or fetus, **acquired** when a pregnant person has **untreated or inadequately treated** syphilis.

Placentas often have signs of infection and inflammation.

Vertical transmission is highest with early stages of maternal syphilis, specifically **secondary syphilis**.



Syphilis during pregnancy is associated with:

- Miscarriage
- Stillbirth
- Preterm delivery
- Perinatal death
- Congenital infection



Congenital Syphilis (CS)

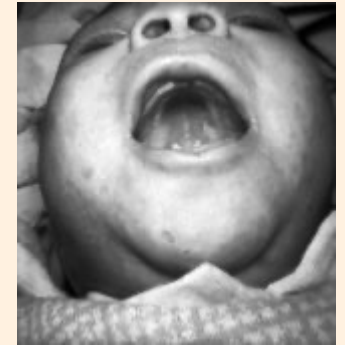
- **Early CS (first 2 years of life)**
 - Hepatosplenomegaly
 - Rash
 - Snuffles
 - CNS invasion
 - Bone abnormalities



Snuffles



Umbilical
Lesion



Mucous
Patches



Periostitis



Rash



Congenital Syphilis (CS)

- **Early CS (first 2 years of life)**
 - Hepatosplenomegaly
 - Rash
 - Snuffles
 - CNS invasion
 - Bone abnormalities
- **Late CS (over 2 years old)**
 - Preventable with treatment before 3 months old
 - Hutchinson's triad



Interstitial
keratitis



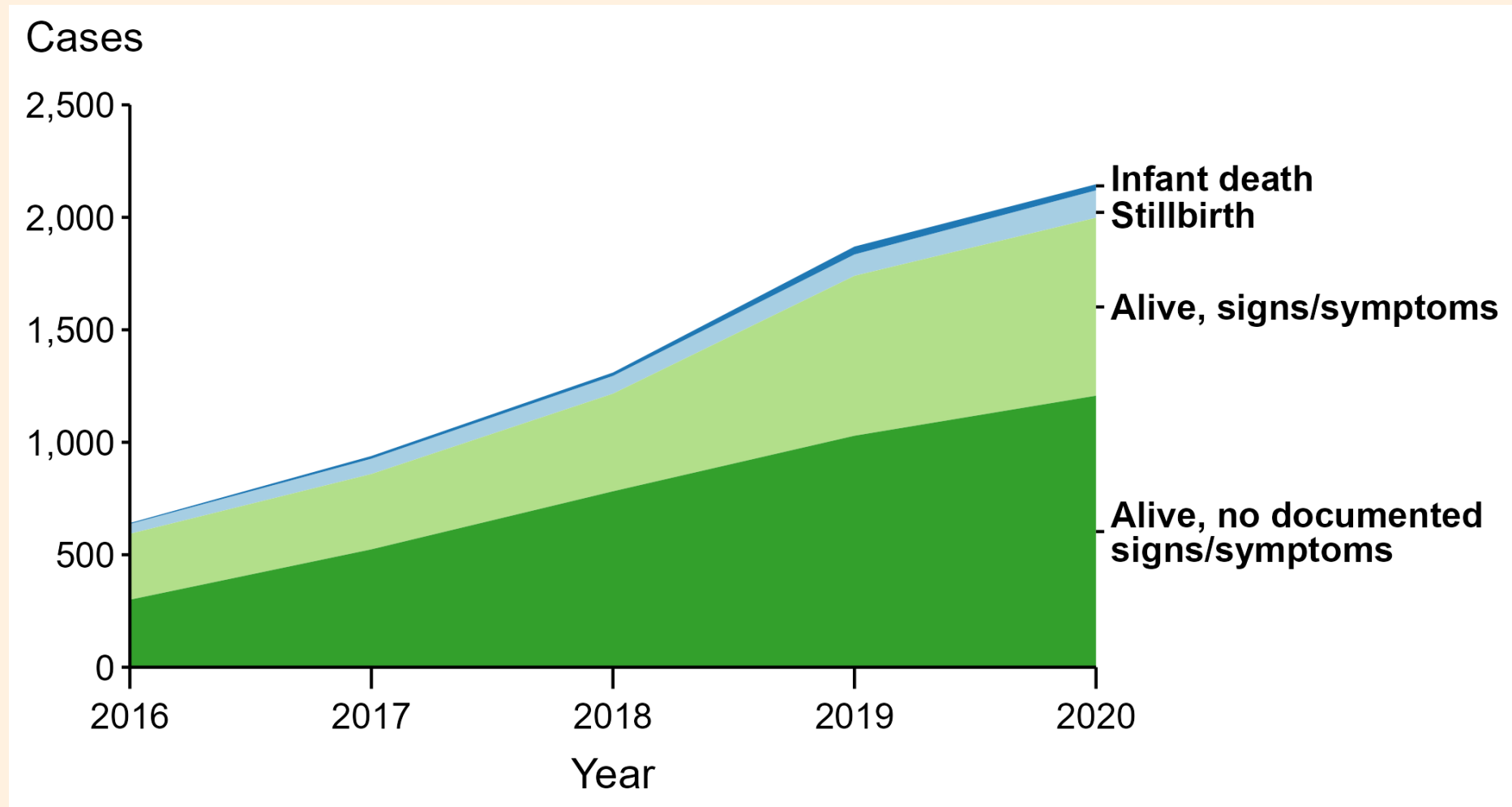
Hutchinson's
teeth



Frontal
bossing



Most neonates with CS have no signs or symptoms





Timely diagnosis and treatment of maternal syphilis can **prevent** congenital syphilis.

**Timely = initiated at least 30 days before delivery*

The background is a dark gray, textured surface. A prominent white, wavy line, resembling a stylized path or a series of connected loops, winds across the scene. Several dark, rounded, rock-like shapes are scattered throughout, some appearing to be partially covered or surrounded by the white line. The overall aesthetic is abstract and minimalist.

Epidemiology



THE
STATE OF STDs
IN THE
UNITED STATES,
2019

**STDs increased for the
6th year, reaching a
new all-time high**



1.8 million
CASES OF CHLAMYDIA
19% increase since 2015



616,392
CASES OF GONORRHEA
56% increase since 2015



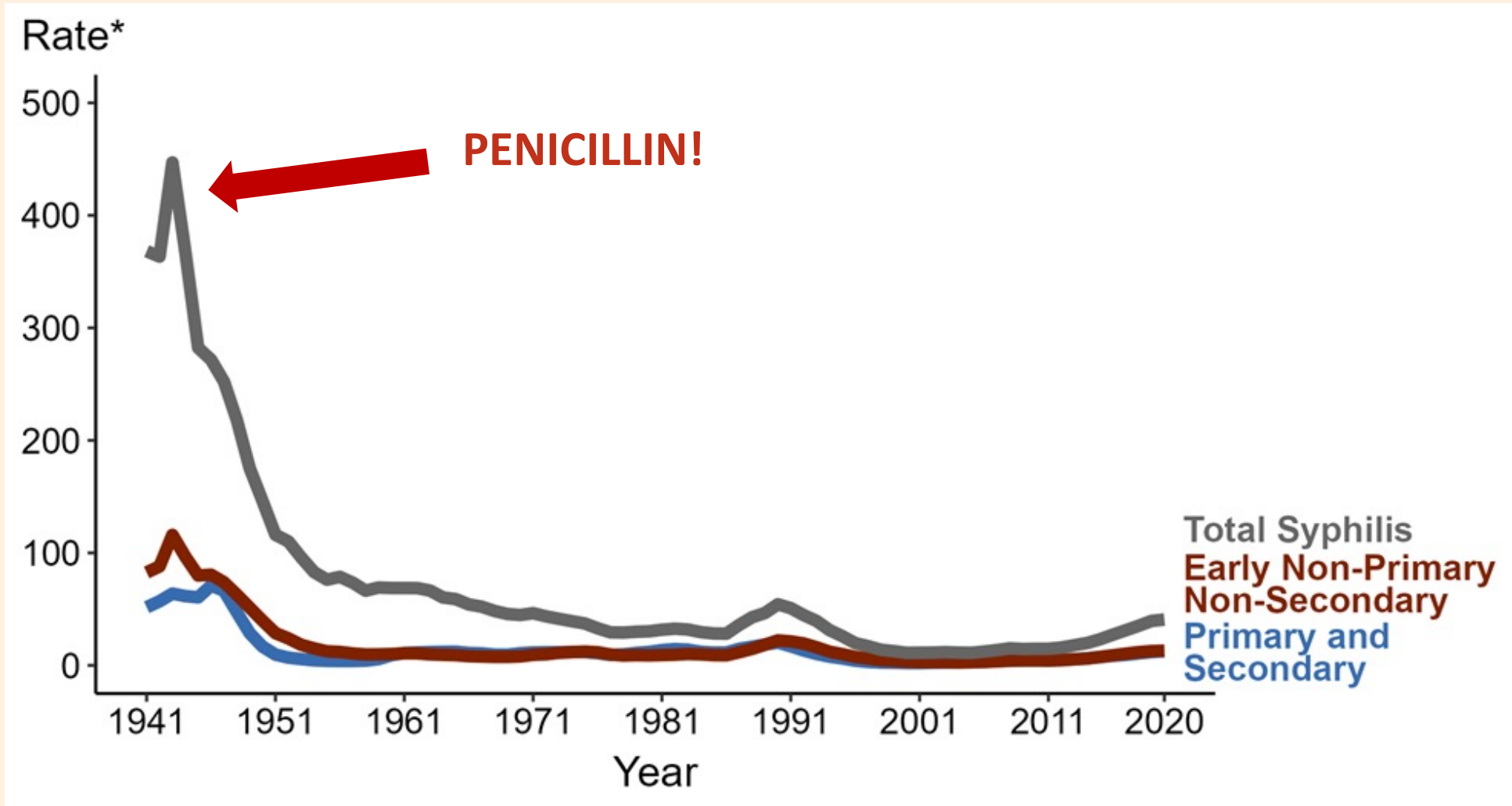
129,813
CASES OF SYPHILIS
74% increase since 2015



1,870
CASES OF SYPHILIS
AMONG NEWBORNS
279% increase since 2015

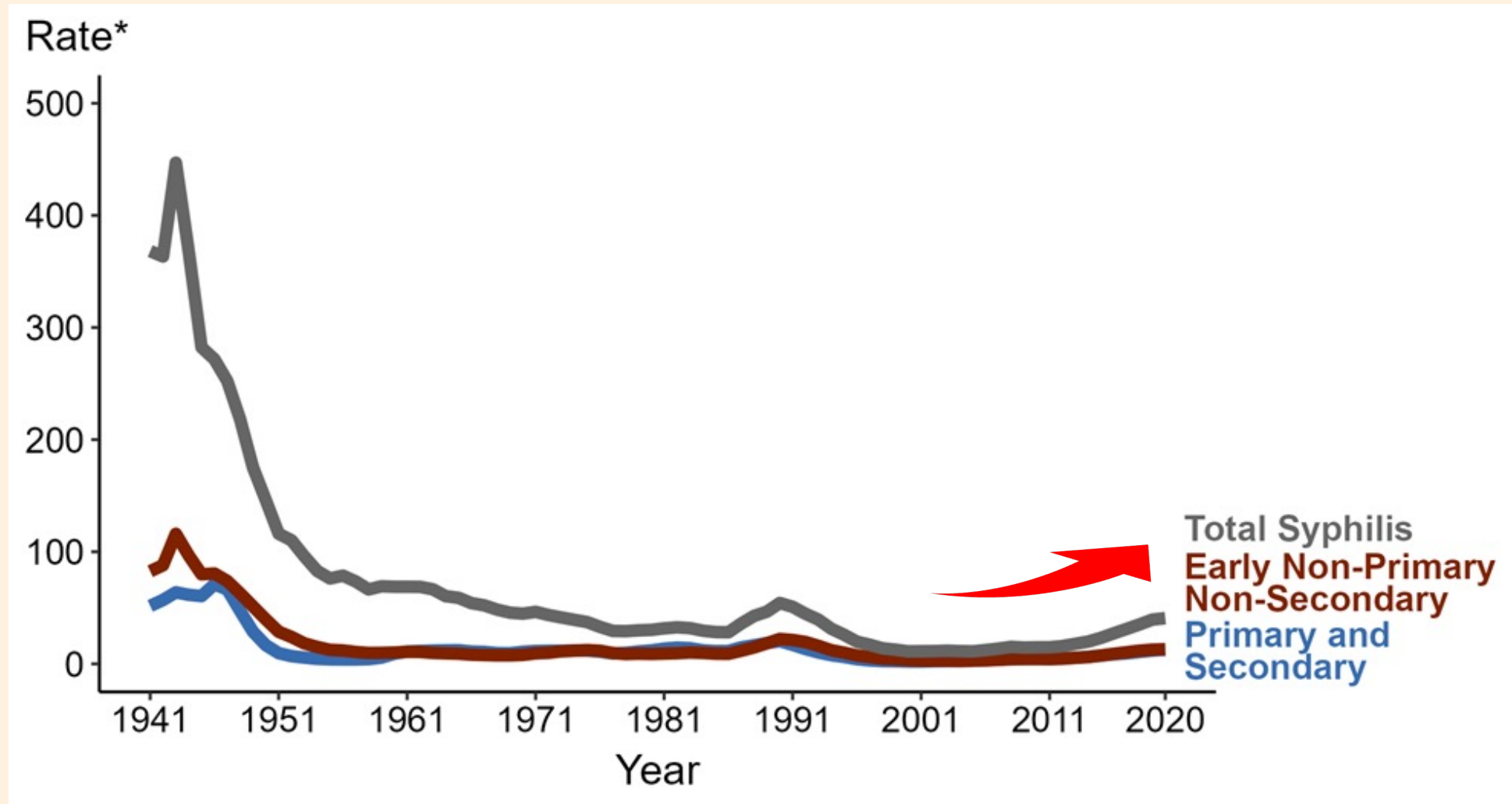
LEARN MORE AT: www.cdc.gov/std/

Syphilis rates declined after introduction of penicillin

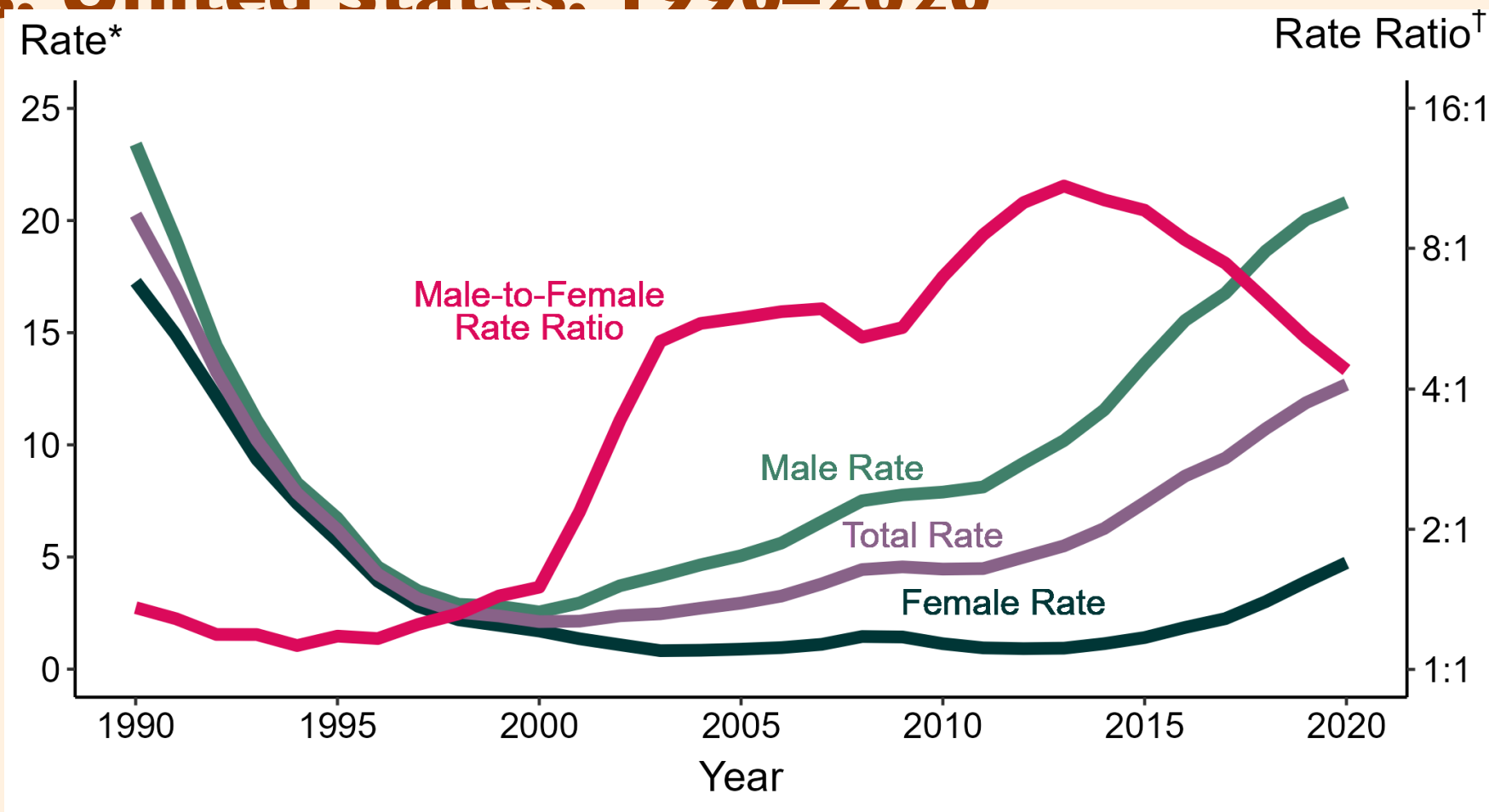


* Per 100,000

Syphilis rates rising again



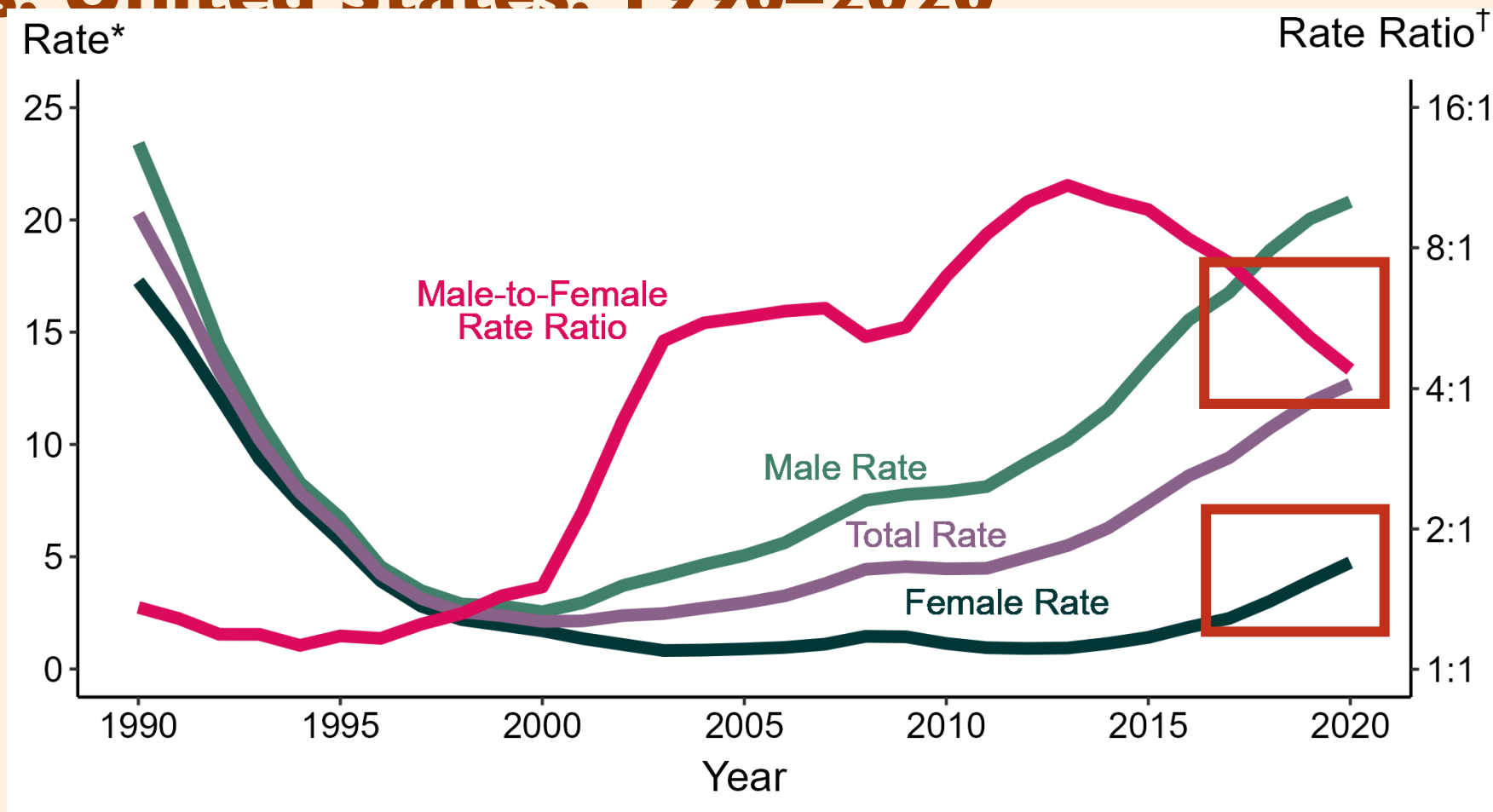
Primary and Secondary Syphilis — Rates of Reported Cases by Sex and Male-to-Female Rate Ratios, United States, 1990–2020



* Per 100,000

† Log scale

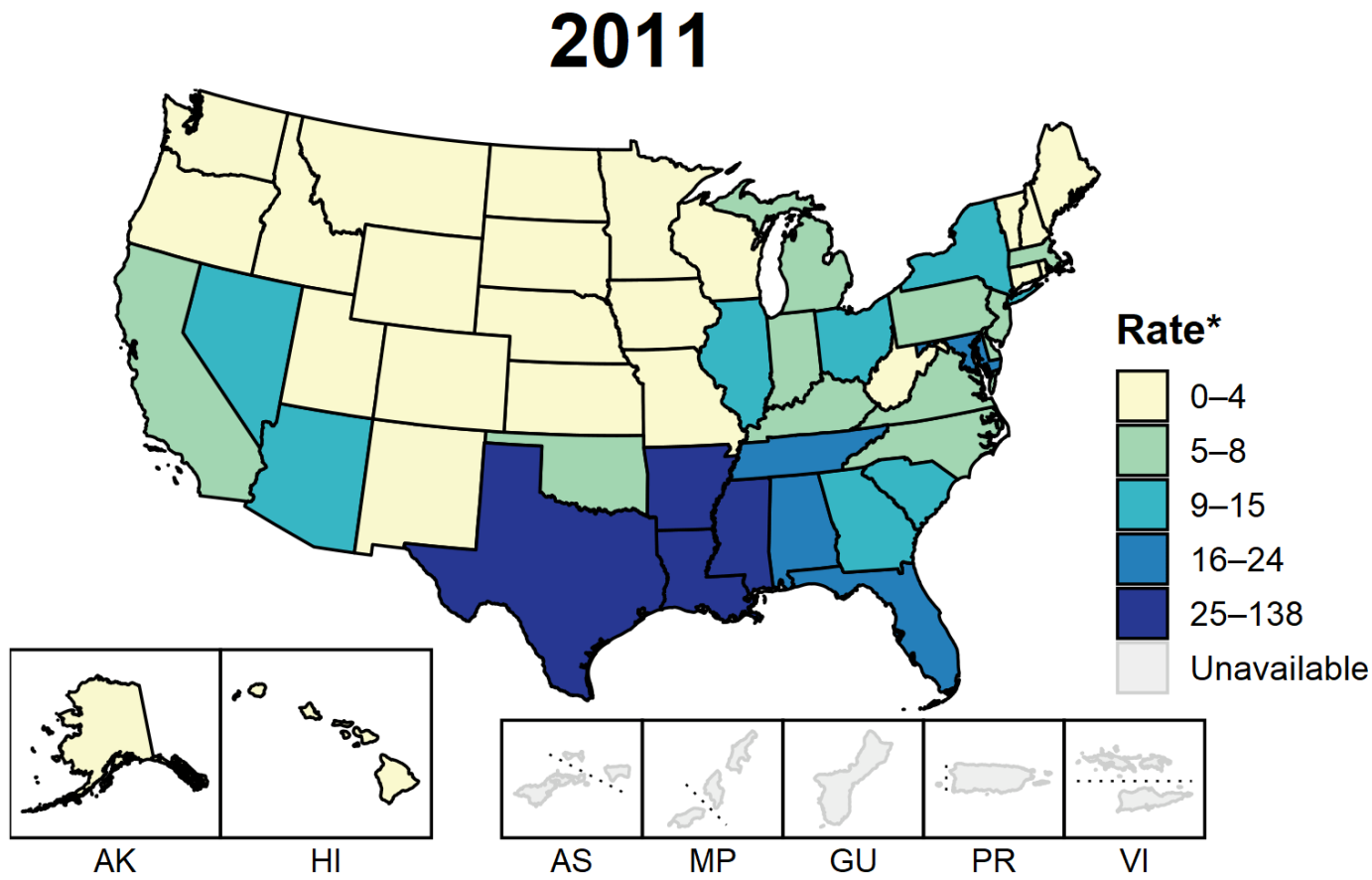
Primary and Secondary Syphilis — Rates of Reported Cases by Sex and Male-to-Female Rate Ratios, United States, 1990–2020



* Per 100,000

† Log scale

Syphilis (All Stages) — Rates of Reported Cases Among Women Aged 15-44 Years by State, United States and Territories, 2011–2020

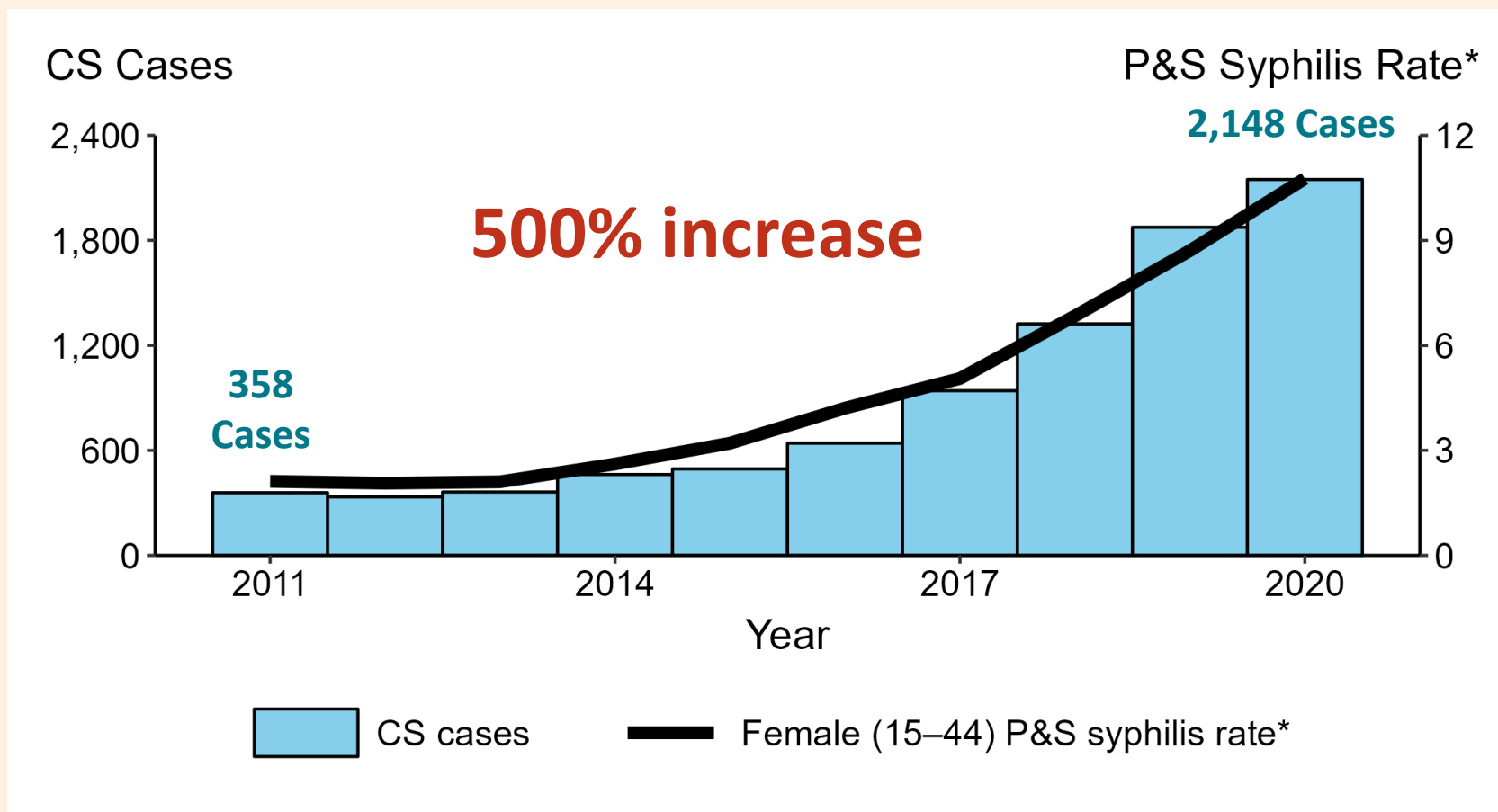


* Per 100,000



**Congenital
syphilis is
increasing.**

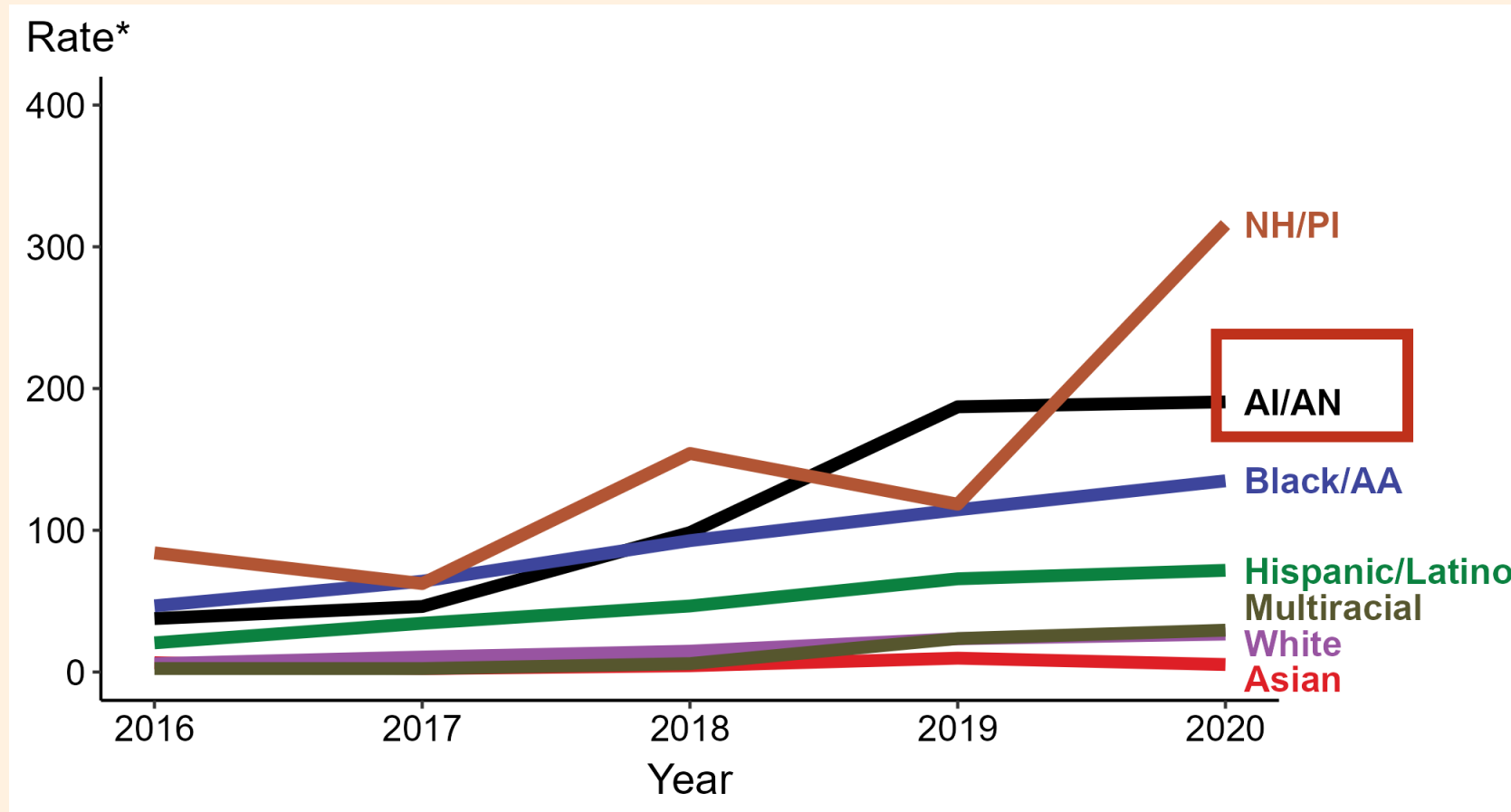
Congenital Syphilis — Reported Cases by Year of Birth and Rates of Reported Cases of Primary and Secondary Syphilis Among Women Aged 15–44 Years, United States, 2011–2020



* Per 100,000

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

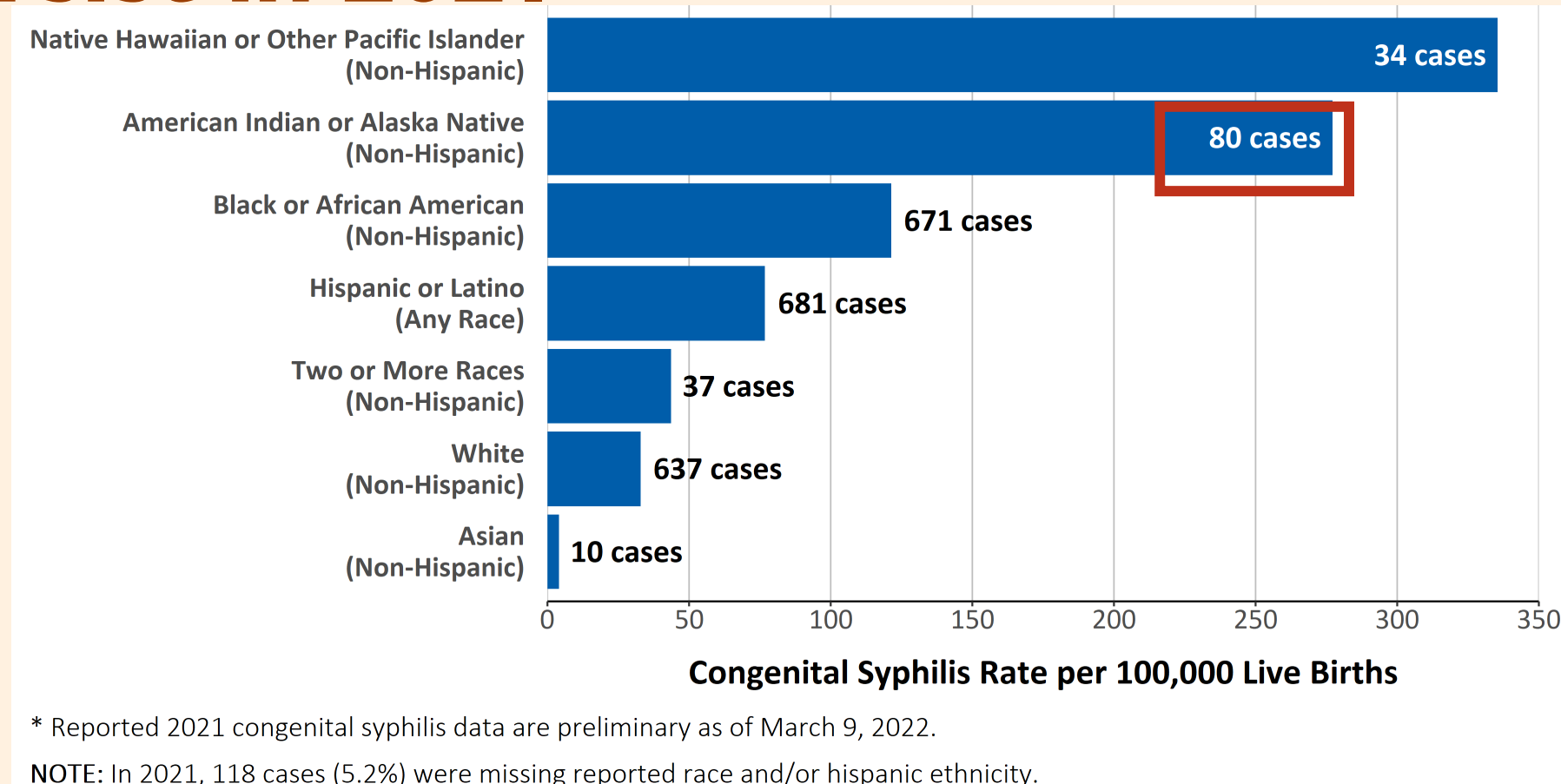
Congenital Syphilis — Rates of Reported Cases by Year of Birth, Race/Hispanic Ethnicity of Mother, United States, 2016–2020



* Per 100,000 live births

ACRONYMS: AI/AN = American Indian/Alaska Native; Black/AA = Black or African American; NH/PI = Native Hawaiian/Pacific Islander

Racial and ethnic disparities in rates of reported congenital syphilis continued to persist in 2021*



Congenital Syphilis — Case Counts and Rates of Reported Cases by Race and Hispanic Ethnicity, United States, 2021*

A grayscale micrograph showing numerous white, corkscrew-shaped bacteria (Treponema pallidum) against a dark, textured background. The bacteria are distributed across the frame, with some appearing in clusters and others individually. The background has a mottled, almost crystalline appearance with various shades of gray and black, suggesting a complex biological or material surface.

Syphilis in Pregnancy

Syphilis Diagnosis


- Direct detection tests for syphilis are not widely available.
 - Darkfield microscopy
 - Polymerase chain reaction (PCR)
 - Direct fluorescent antibody test for *T. pallidum* (DFA-TP)
- **Syphilis is usually diagnosed with serologic tests.**



T. pallidum on Darkfield

There are two types of serologic tests for syphilis.

Tests	Non-Treponemal	Treponemal
Examples	RPR, VDRL	FTA-ABS, TPPA, EIA, CIA
Method	Detects <u>NON-specific</u> antibodies caused by inflammation	Detects <u>specific antibodies</u> against <i>T. pallidum</i>
Results	Quantitative	Qualitative
Positivity	Positive in active disease	Remains positive forever (85%)



BOTH a treponemal test and a nontreponemal test are needed to confirm the diagnosis of syphilis.

Testing Early in Pregnancy

- All pregnant people should be tested for syphilis early in pregnancy.
- Most states mandate testing at the first prenatal visit.
- **Consider testing at the time pregnancy confirmation if follow up may be an issue.**



Repeat Testing at 28-Weeks and Delivery

- For pregnant people in **high prevalence areas or who are at high individual risk**, retesting at 28 weeks and delivery is recommended.
- Individual risk factors include:
 - **Multiple prior STIs**
 - Recent incarceration
 - Substance misuse
 - Homelessness
 - Transactional sex



CDC STD Treatment Guidelines



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Repeat Testing at 28-Weeks and Delivery

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*** Consider sexual networks!**



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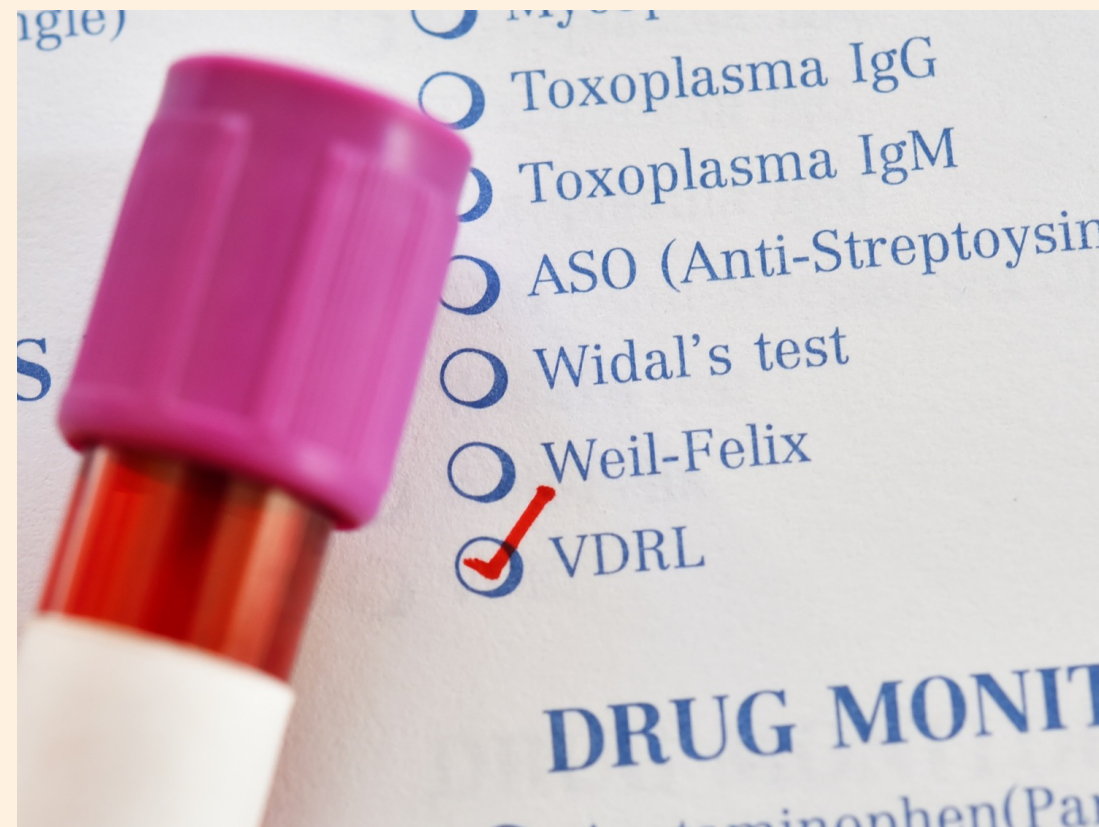
CDC STD Treatment Guidelines

Screening at Delivery

- **All high-risk people should be screened at delivery.**
- High prevalence or individual risk factors including:
 - Multiple prior STIs
 - Recent incarceration
 - Substance misuse
 - Homelessness
 - Transactional sex



No mother or baby should be discharged from the hospital without **documentation of maternal syphilis testing during pregnancy**, and again at **delivery if high risk.**



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Stillbirth

- All people who have a fetal death at **≥20 weeks** should be **tested for syphilis**.






Penicillin G is the only known effective antimicrobial for **preventing maternal transmission** to the fetus and for treating fetal infection.

Recommended Regimens for Penicillin G in Pregnancy


- Early Syphilis (primary, secondary, and early latent)
 - 2.4 million units **x 1 dose**
- Late or Unknown Duration Syphilis
 - 2.4 million units **x 3 at 1-week intervals**
 - Optimal treatment interval: 7 days
 - Acceptable treatment interval: up to 9 days

**Treatment must be initiated 30 days before delivery to prevent congenital syphilis.*





Pregnant people who have a history of penicillin allergy should be desensitized and treated with penicillin.



Adequate maternal treatment during pregnancy is efficacious in preventing CS.



Congenital Syphilis Prevention

Recommendations to Address CS Challenges

No timely prenatal care No timely syphilis testing	<ul style="list-style-type: none">- Identify pregnant people with syphilis outside of prenatal care- Reduce barriers to prenatal care and family planning
No timely syphilis testing despite timely prenatal care	<ul style="list-style-type: none">- Screen all pregnant people at the first prenatal visit
No adequate treatment despite timely syphilis diagnosis	<ul style="list-style-type: none">- Immediate follow-up of positive syphilis test results- Reduce barriers to adequate syphilis treatment
Late seroconversion	<ul style="list-style-type: none">- Repeat screening at 28 weeks and delivery in high prevalence areas or for people with high risk- Educate patients and encourage condoms

Implications for Public Health

- Collaboration between public health and health care
- Understand local missed prevention opportunities
- Implement tailored prevention efforts



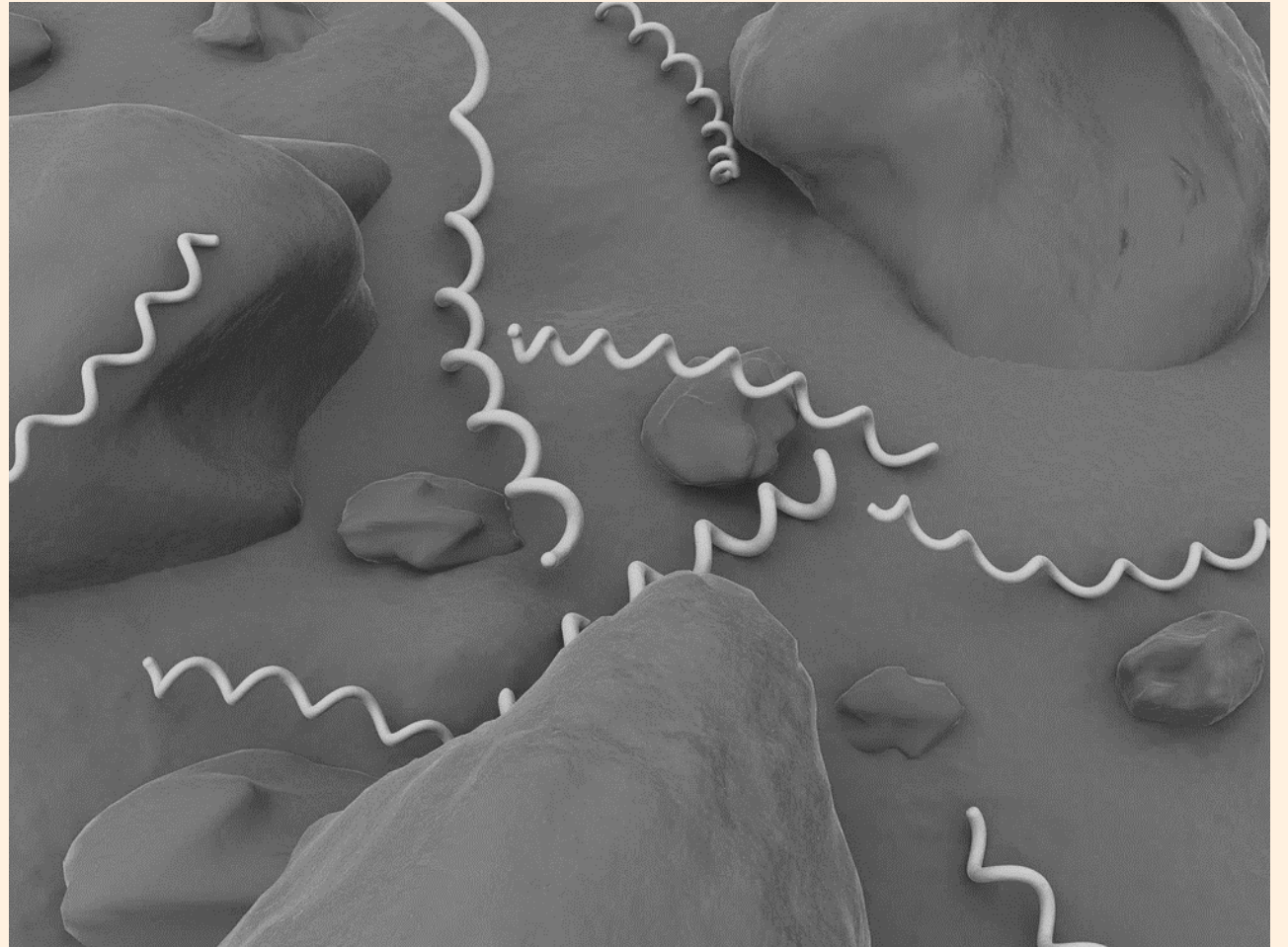
Takeaways

- **Test everyone** at first prenatal care visit
- **Treat people immediately**
- Encourage **partner treatment**
- Repeat testing at 28 weeks and delivery
- **Condoms!**
- Test people outside of prenatal care
- **Improve clinical documentation**
- Report immediately to health department
- **Understand missed opportunities**
- Partner with public health



Acknowledgements

- Dr. Aliza Machefsky
- Dr. Melanie Taylor
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- Dr. Alison Ridpath
- Dr. Andria Apostolou
- Dr. Geniel Harrison
- Tam Lutz
- Karuna Tirumala



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Case Example

- 25 yo female patient G4P3 w/ h/o chlamydia, trichomonas and primary syphilis, RPR 1:32 during this pregnancy. EDC 7/30/22
- After labs resulted was contacted multiple times prior to receiving dose of IM Benzathine PCN 2.4 million units on 4/27/22
- OB history: last delivery by c-section 1/14/21 by c-section at 6 months, positive at that time for GC/Chlamydia, no prenatal care at that time.
- Social history: Alcohol, THC and methamphetamine use disorder, incarcerated after arrest for intoxication, remains in jail, previously living with family. Primary sexual partner had recent sexual encounter with patient's sister
- The patient has not received pre-natal care.



Resources



National STD
Curriculum

- CDC Division of STD Prevention:
[cdc.gov/std/default.html](https://www.cdc.gov/std/default.html)
- CDC STD Surveillance Report:
<https://www.cdc.gov/std/statistics/2020/default.htm>
- 2021 STI Treatment Guidelines:
<https://www.cdc.gov/std/treatment-guidelines/default.htm>
- National Network of STD Prevention Training Centers:
www.nnptc.org www.STDCCN.org
- National Coalition for Sexual Health:
www.ncshguide.org/providers
- National STD Curriculum:
www.std.uw.edu



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National Network of STD Clinical Prevention Training Centers

University of Washington STD
Prevention Training Center

St. Louis STD/HIV
Prevention Training Center

Sylvie Rattelle
STD/HIV Prevention
Training Center

New York City STD/HIV
Prevention Training
Center

California
Prevention Trainin
Center

STD/HIV Prevention
Training Center at
Johns Hopkins

Denver Prevention
Training Center

Alabama–North Carolina
STD /HIV Prevention
Training Center

STD Treatment Resources:

www.nnptc.org

Clinical Consultations:

www.STDCCN.org



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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^s (or greater) higher than the mother's titer at delivery (e.g., maternal titer = 1:2, neonatal titer \geq 1:8 or maternal titer = 1:8, neonatal titer \geq 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)

Scenario 1: Confirmed Proven or Highly Probable Congenital Syphilis

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



Scenario 2: Possible Congenital Syphilis

- Any neonate who has a normal physical examination and a serum quantitative nontreponemal serologic titer equal to or less than fourfold of the maternal titer at delivery (e.g., maternal titer = 1:8, neonatal titer \leq 1:16) and one of the following:
 - The mother was not treated, was inadequately treated, or has no documentation of having received treatment.
 - The mother was treated with erythromycin or a regimen other than those recommended in these guidelines (i.e., a nonpenicillin G regimen).^{††}
 - The mother received the recommended regimen but treatment was initiated <30 days before delivery.
- **Recommended Evaluation**
 - CSF analysis for VDRL, cell count, and protein**
 - CBC, differential, and platelet count
 - Long-bone radiographs



Scenario 2: Possible Congenital Syphilis

Recommended Regimens, Possible 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

OR

Benzathine penicillin G 50,000 units/kg body weight/dose IM in a single dose

Scenario 3: Congenital Syphilis Less Likely

- Any neonate who has a normal physical examination and a serum quantitative nontreponemal serologic titer equal or less than fourfold of the maternal titer at delivery (e.g., maternal titer = 1:8, neonatal titer \leq 1:16) and both of the following are true:
 - The mother was treated during pregnancy, treatment was appropriate for the infection stage, and the treatment regimen was initiated \geq 30 days before delivery.
 - The mother has no evidence of reinfection or relapse.
- **Recommended Evaluation**
 - No evaluation is recommended.



Scenario 3: Congenital Syphilis Less Likely

Recommended Regimen, Congenital Syphilis Less Likely

Benzathine penicillin G 50,000 units/kg body weight/dose IM in a single dose*

* Another approach involves not treating the newborn if follow-up is certain but providing close serologic follow-up every 2–3 months for 6 months for infants whose mothers' nontreponemal titers decreased at least fourfold after therapy for early syphilis or remained stable for low-titer, latent syphilis (e.g., VDRL <1:2 or RPR <1:4).

Scenario 4: Congenital Syphilis Unlikely

- Any neonate who has a normal physical examination and a serum quantitative nontreponemal serologic titer equal to or less than fourfold of the maternal titer at delivery[§] and both of the following are true:
 - The mother's treatment was adequate before pregnancy.
 - The mother's nontreponemal serologic titer remained low and stable (i.e., serofast) before and during pregnancy and at delivery (e.g., VDRL \leq 1:2 or RPR \leq 1:4).
- **Recommended Evaluation**
 - No evaluation is recommended.



Scenario 4: Congenital Syphilis Unlikely

Recommended Regimen, Congenital Syphilis Unlikely

No treatment is required. However, any neonate with reactive nontreponemal tests should be followed serologically to ensure the nontreponemal test returns to negative (see Follow-Up). Benzathine penicillin G 50,000 units/kg body weight as a single IM injection might be considered, particularly if follow-up is uncertain and the neonate has a reactive nontreponemal test.



Adequate Maternal Treatment of Syphilis

1. Completion of a penicillin-based regimen
2. Appropriate for the mother's stage of syphilis
3. Initiated **≥ 30 days before delivery**

Identification of maternal syphilis must occur ≥ 30 days before delivery to prevent congenital syphilis.



Evaluating Infants for Congenital Syphilis Algorithm

