
# Syphilis Response Best Practices

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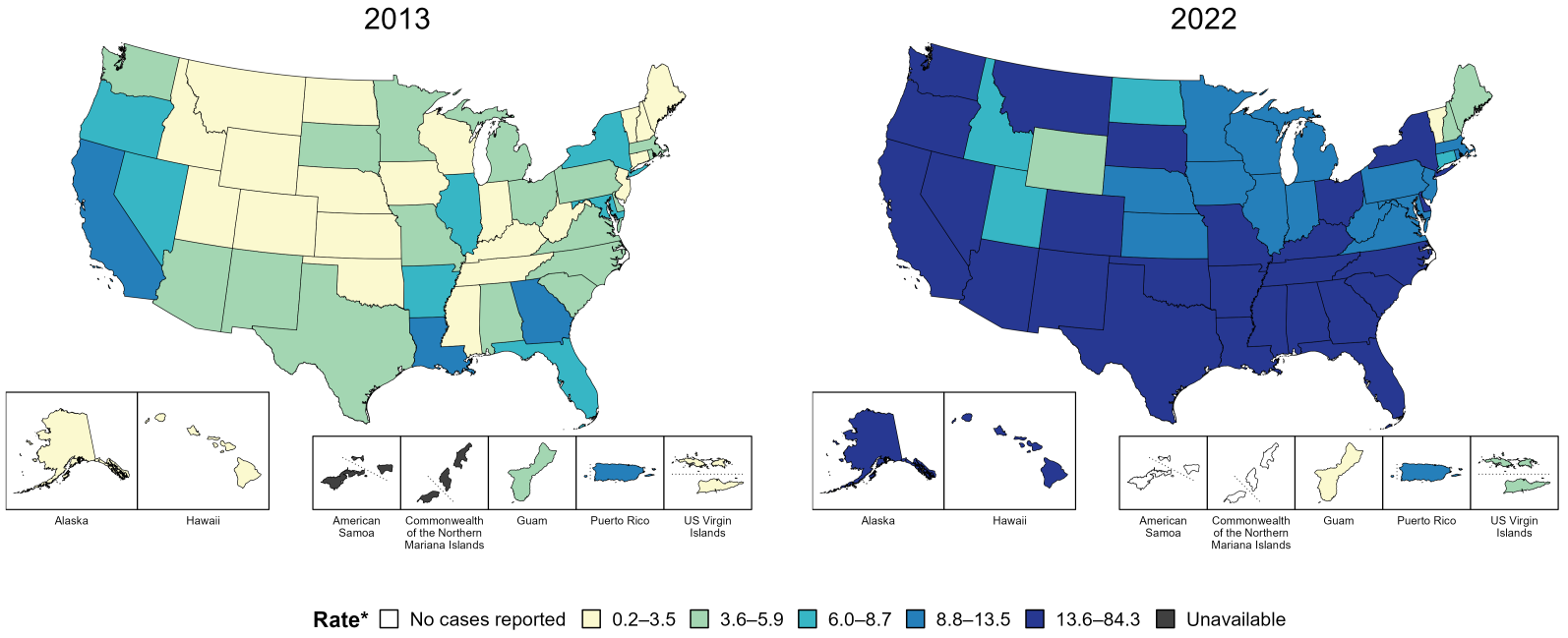
# Think Syphilis



# Primary and Secondary Syphilis — Rates of Reported Cases by Jurisdiction, United States and Territories, 2013 and 2022




* Per 100,000

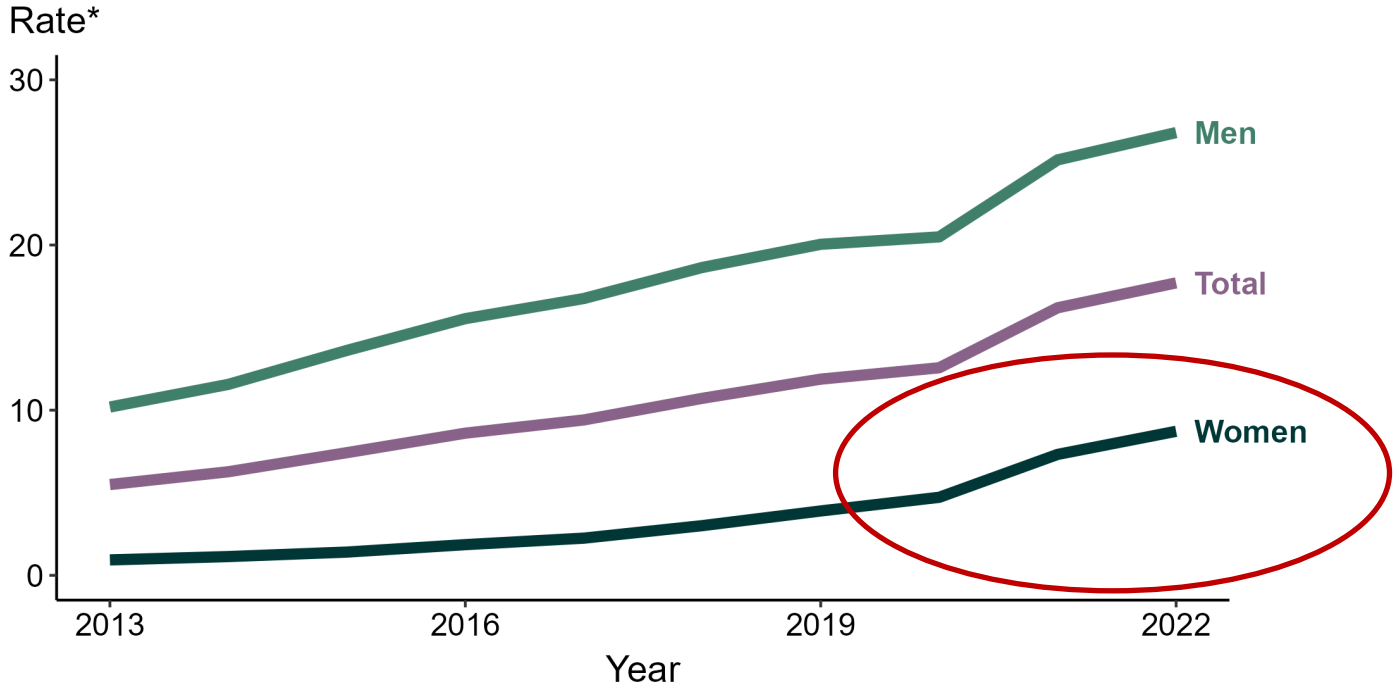
https://www.cdc.gov/std/statistics/2022/figures.htm

# CDC’s Atlas Plus: 20 years of CDC's surveillance data on HIV, viral hepatitis, STD, and TB

- AtlasPlus is an interactive tool that gives users the ability to **create customized tables, maps,** and charts using nearly 20 years of CDC's surveillance data on HIV, viral hepatitis, STD, and TB.
- AtlasPlus also provides access to indicators on *social determinants of health (SDOH)* allowing users to view social and economic data in conjunction with surveillance data for each disease.

About AtlasPlus | CDC NCHHSTP

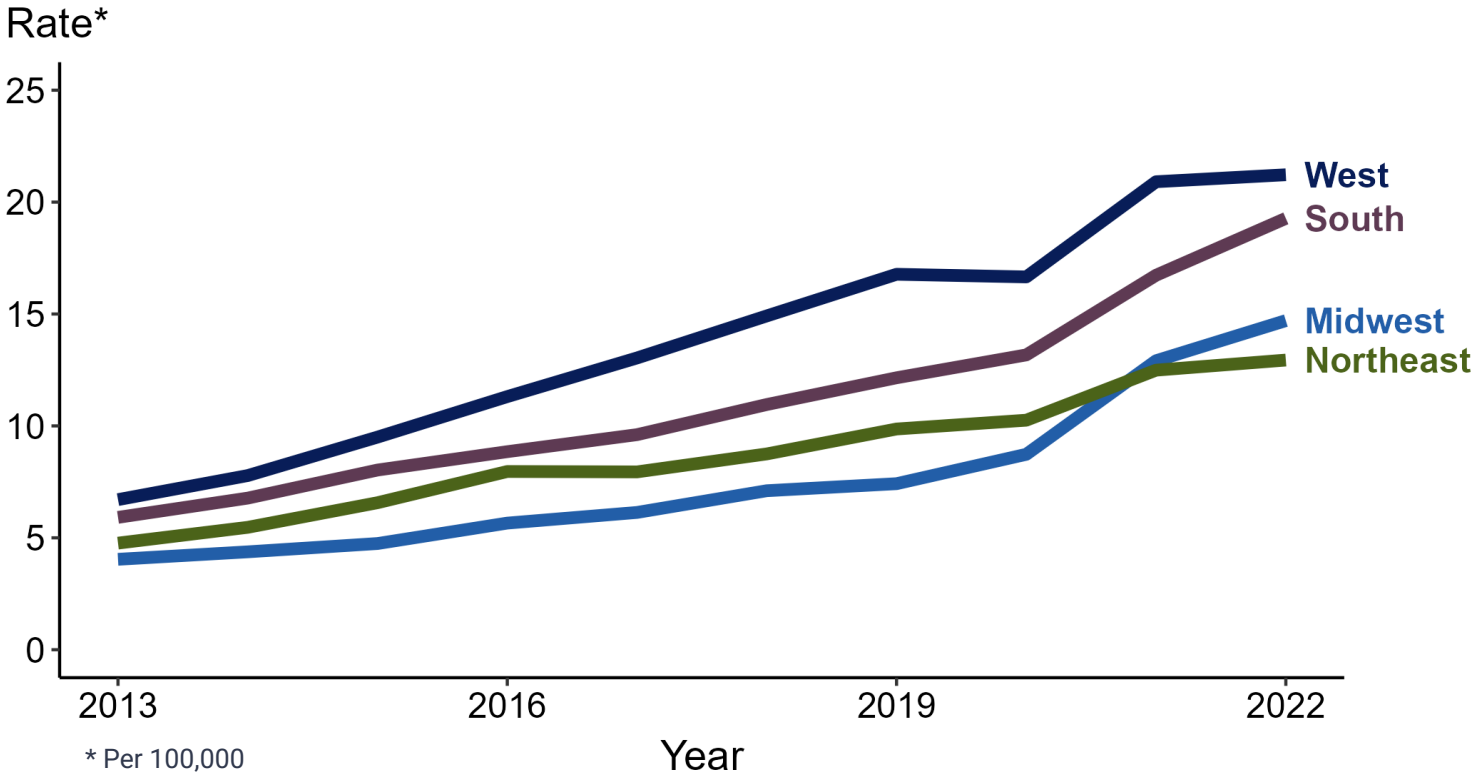
# Primary and Secondary Syphilis — Rates of Reported Cases by Sex, United States, 2013–2022




* Per 100,000

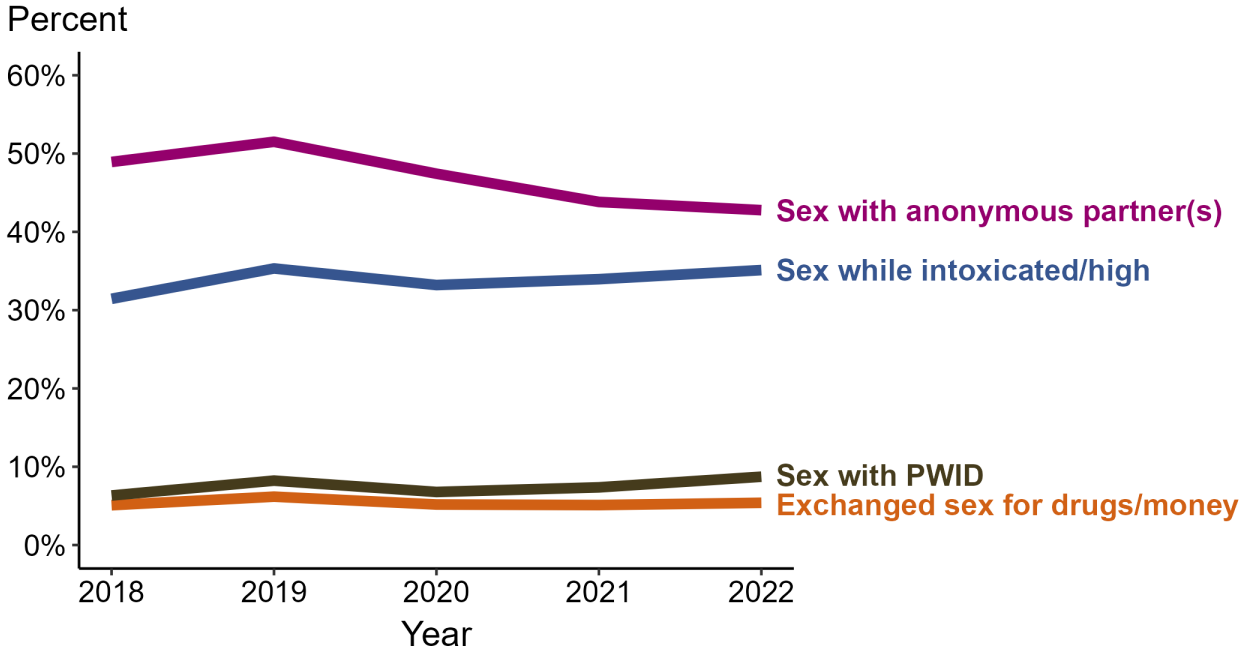
https://www.cdc.gov/std/statistics/2022/figures.htm

# Primary and Secondary Syphilis — Rates of Reported Cases by Region, United States, 2013–2022



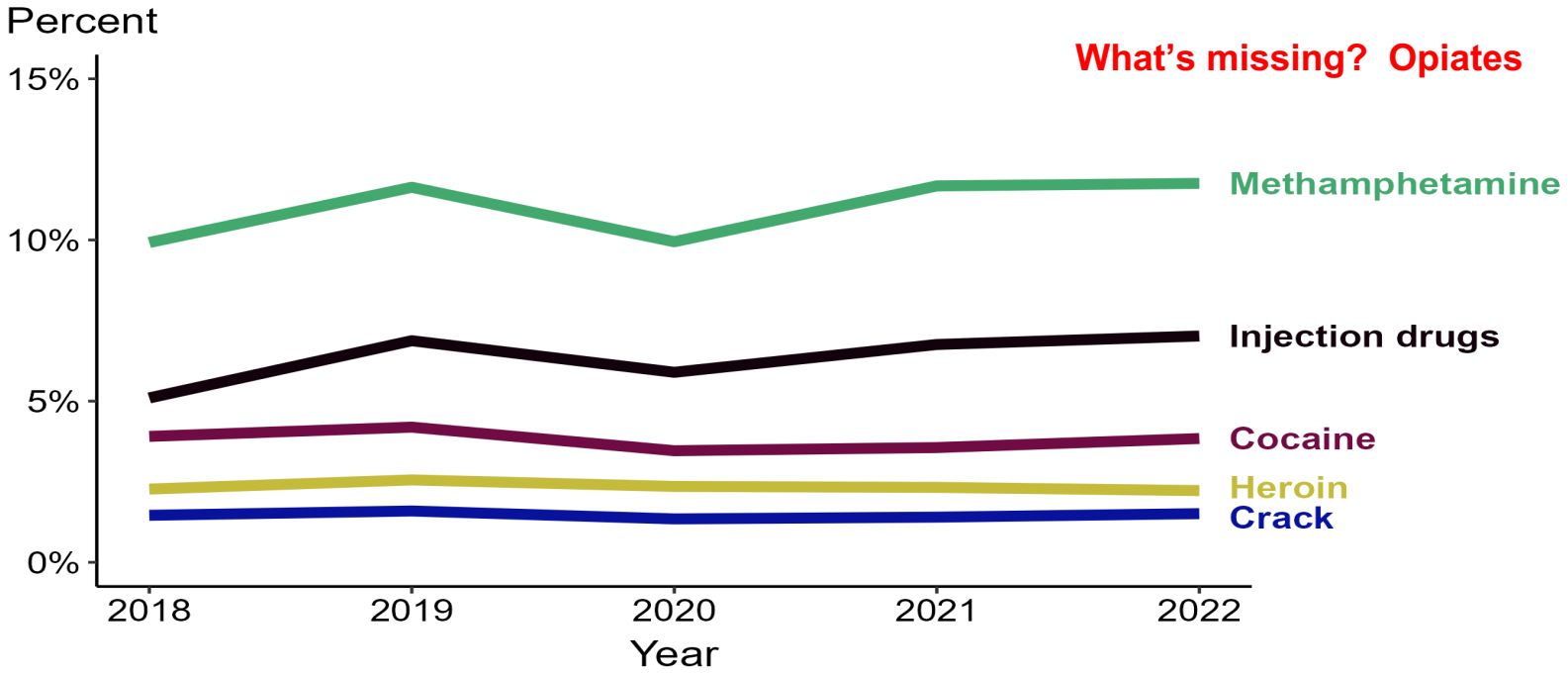

https://www.cdc.gov/std/statistics/2022/figures.htm

# Primary and Secondary Syphilis — Percentage of Cases Reporting Selected Sexual Behaviors*, United States, 2018–2022



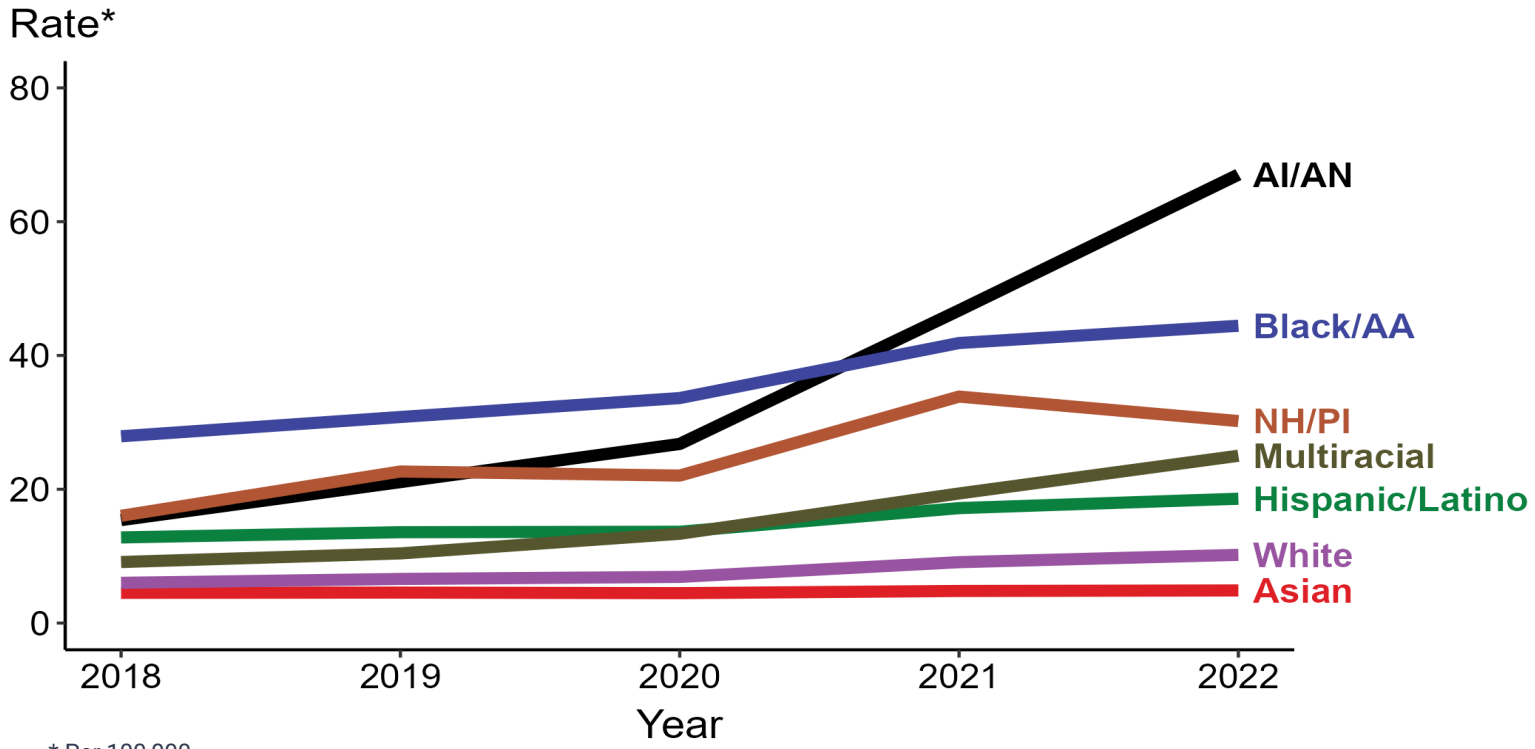

* Proportion reporting sex with PWID, sex with anonymous partners, sex while intoxicated/high on drugs, or exchanging drugs or money for sex within the last 12 months calculated among cases with known data (cases with missing or unknown responses were excluded from the denominator).
**ACRONYMS:** PWID = Person who injects drugs

# Primary and Secondary Syphilis — Percentage of Cases Reporting Selected Substance Use Behaviors*, United States, 2018–2022




* Proportion reporting injection drug use, methamphetamine use, heroin use, crack use, or cocaine use within the last 12 months calculated among cases with known data (cases with missing or unknown responses were excluded from the denominator).

# Primary and Secondary Syphilis — Rates of Reported Cases by Race/Hispanic Ethnicity, United States, 2018–2022

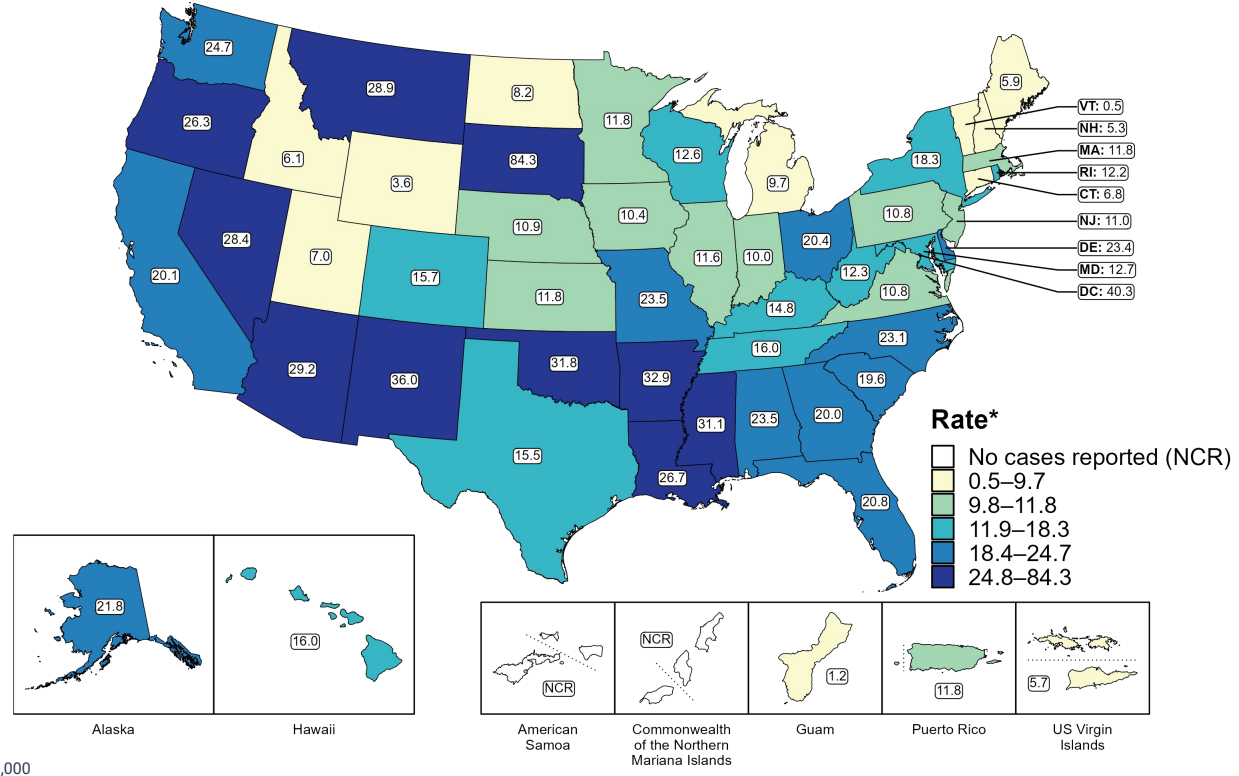



* Per 100,000

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

https://www.cdc.gov/std/statistics/2022/figures.htm

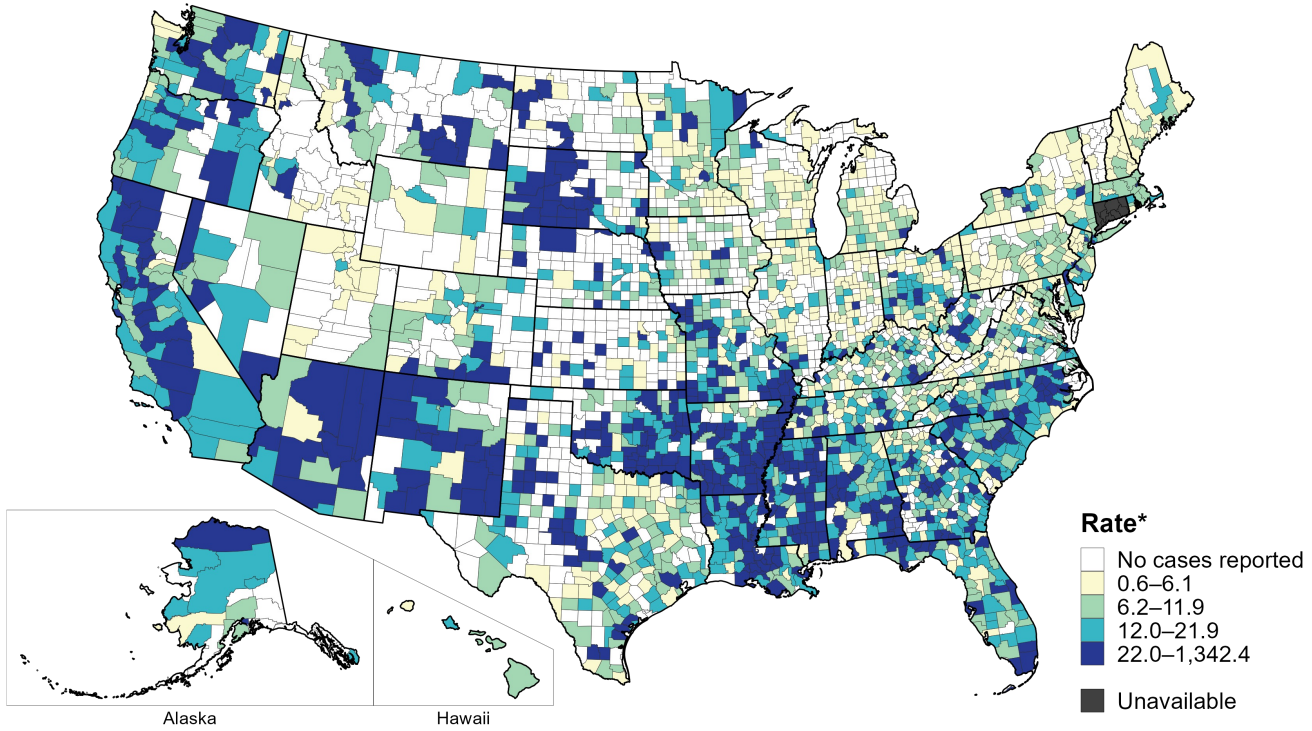
# Primary and Secondary Syphilis — Rates of Reported Cases by Jurisdiction, United States and Territories, 2022




* Per 100,000

https://www.cdc.gov/std/statistics/2022/figures.htm

# Primary and Secondary Syphilis — Rates of Reported Cases by County, United States, 2022




* Per 100,000

# Primary and Secondary Syphilis — Reported Cases and Rates by State, United States, 2022

| Rank* | State | Cases | Rate per 100,000 Population |
|---|---|---|---|
| 1 | South Dakota | 767 | 84.3 |
| 2 | New Mexico | 761 | 36.0 |
| 3 | Arkansas | 1,001 | 32.9 |
| 4 | Oklahoma | 1,278 | 31.8 |
| 5 | Mississippi | 913 | 31.1 |
| 6 | Arizona | 2,151 | 29.2 |
| 7 | Montana | 325 | 28.9 |
| 8 | Nevada | 902 | 28.4 |
| 9 | Louisiana | 1,225 | 26.7 |
| 10 | Oregon | 1,117 | 26.3 |
| 11 | Washington | 1,920 | 24.7 |
| 12 | Missouri | 1,454 | 23.5 |
| 13 | Alabama | 1,190 | 23.5 |
| 14 | Delaware | 238 | 23.4 |
| 15 | North Carolina | 2,473 | 23.1 |
| 16 | Alaska | 160 | 21.8 |
| 17 | Florida | 4,618 | 20.8 |
| 18 | Ohio | 2,402 | 20.4 |
| 19 | California | 7,849 | 20.1 |
| 20 | Georgia | 2,182 | 20.0 |
| 21 | South Carolina | 1,033 | 19.6 |
| 22 | New York | 3,603 | 18.3 |
| | **US TOTAL†** | **59,016** | **17.7** |

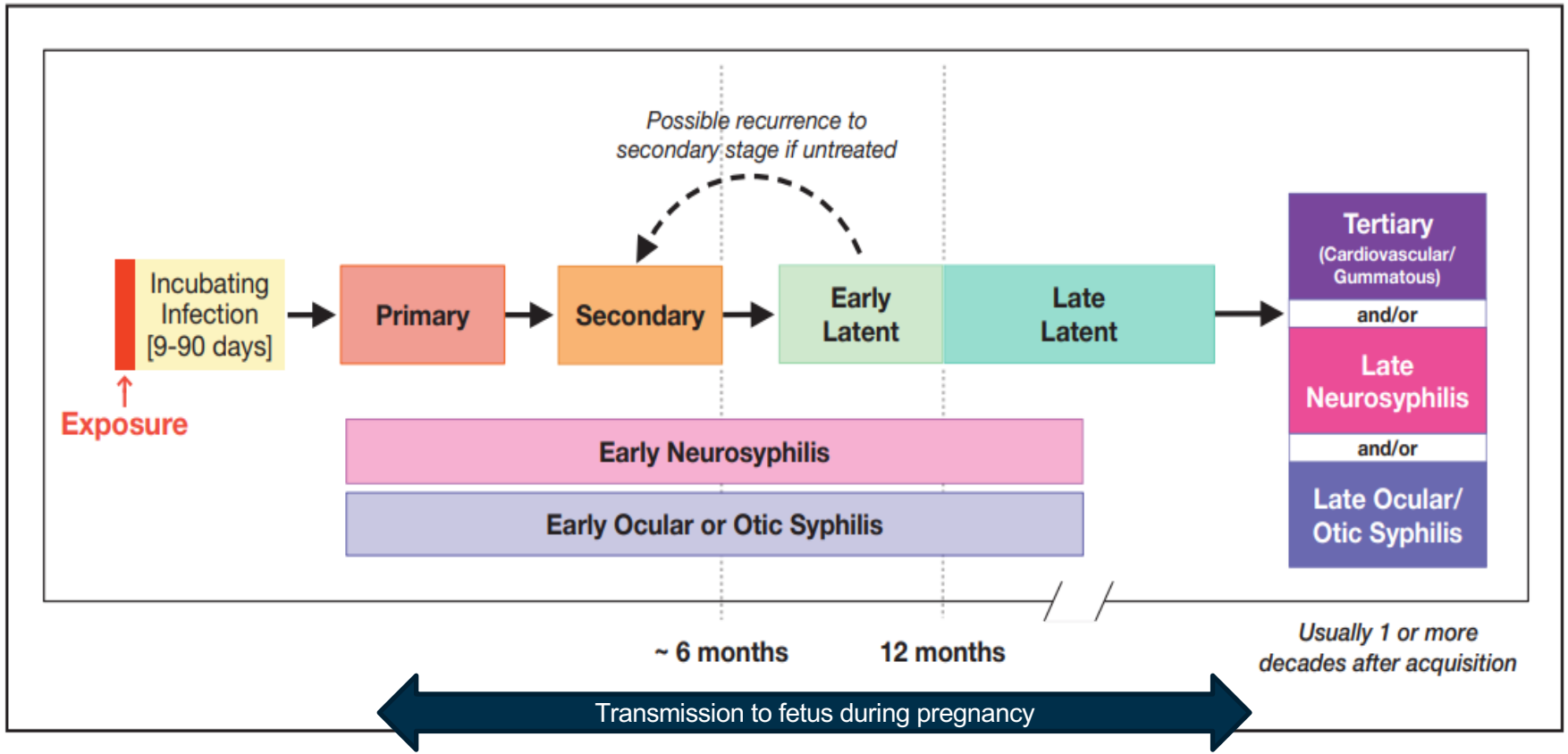
https://www.cdc.gov/std/statistics/2022/tables/21.htm

# Syphilis

- ***Treponema pallidum***
- Sexual, vertical, and horizontal transmission
- **Curable with penicillin**
- 4 stages

1. Primary
2. Secondary
3. Early (non-primary, non-secondary)
4. Unknown duration or late

# Natural History of Untreated Syphilis Infection




The Diagnosis, Management and Prevention of Syphilis An Update and Review. New York City Department of Health and Mental Hygiene Bureau of Sexually Transmitted Infections and the New York City STD Prevention Training Center . May 2019. https://www.nycptc.org/x/Syphilis_Monograph_2019_NYC_PTC_NYC_DOHMH.pdf

# Case Definitions:  Primary Syphilis

## Clinical Description

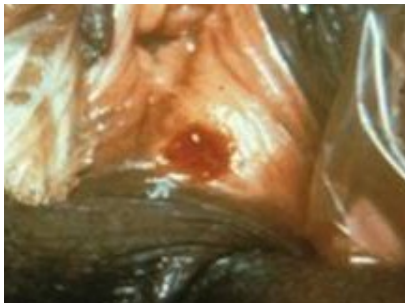
Characterized by one or more ulcerative lesions (e.g. chancre), which might differ in clinical appearance.

Classic Presentation

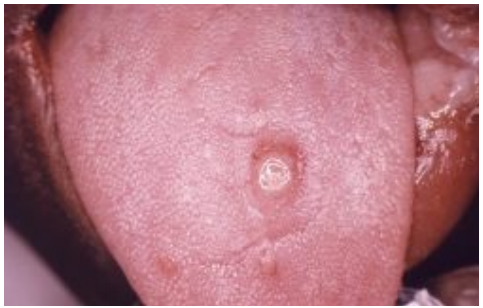
Single painless ulcer or chancre at the site of infection

Atypical Presentation

Multiple, atypical, or painful lesions at the site of infection



Vaginal



Tongue

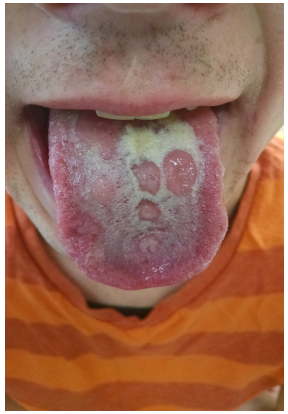
Penile

https://www.cdc.gov/std/syphilis/images.htm and https://www.cdc.gov/std/statistics/2019/case-definitions.htm

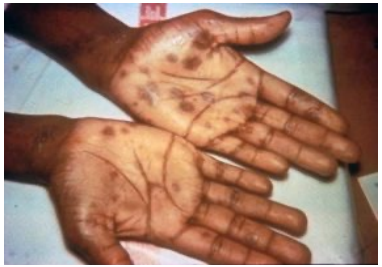
# Case Definitions:  Secondary Syphilis

## Clinical Description

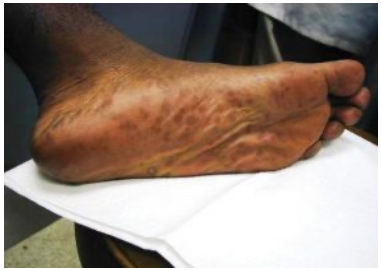
Characterized by localized or diffuse mucocutaneous lesions (e.g., rash – such as non-pruritic macular, maculopapular, papular, or pustular lesions), often with generalized lymphadenopathy. Other signs can include mucous patches, condyloma lata, and alopecia. The primary ulcerative lesion may still be present.

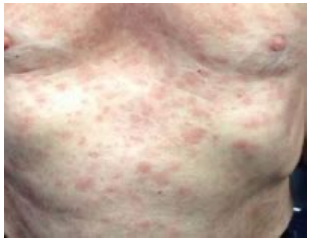


Mucous patches

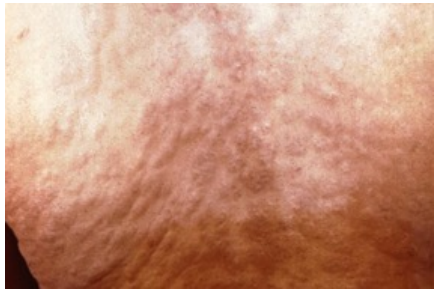


Palmar/plantar rash

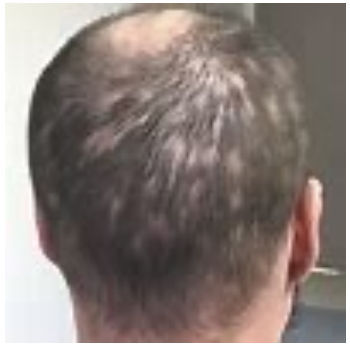




Torso/back rash



Condyloma lata



Alopecia

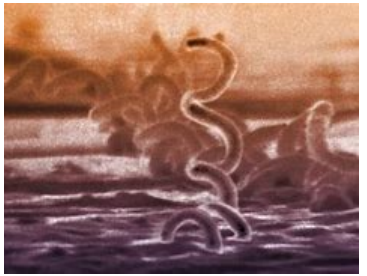

1. https://www.cdc.gov/std/syphilis/images.htm
2. https://www.cdc.gov/std/statistics/2019/case-definitions.htm

# Case Definitions:  Early (non-primary non-secondary)

## Clinical Description

Stage of infection caused by *T. pallidum* in which initial infection has **occurred within the previous 12 months**, but there are no current signs or symptoms of primary or secondary syphilis.

**Less than 12 months duration** by (1) interval from prior negative syphilis test (or 4-fold titer increase) OR (2) report of symptoms consistent with syphilis within  prior 12 months OR (3) sexual contact with a known case (or sexual debut) within prior 12 months



https://www.cdc.gov/std/statistics/2019/case-definitions.htm)

# Case Definitions:  Unknown duration or late

## Clinical Description

Stage of infection caused by *T. pallidum* in which initial infection has **occurred >12 months** previously or in which there is **insufficient evidence** to conclude that infection was acquired during the previous 12 months.

**Unknown or greater than 12 months** duration by: (1) interval from prior negative syphilis test (or 4-fold titer increase) OR (2) report of symptoms consistent with syphilis occurring > 12 months ago OR (3) sexual contact with a known case > 12 months ago (4) Neurologic, ocular, otic signs without evidence of acquiring infection in prior 12 months.

https://www.cdc.gov/std/statistics/2019/case-definitions.htm)

# Best Practice: Indian Health Service (I H S) Syphilis Screening Recommendations

***The Indian Health Service recommends universal 3 time-point syphilis screening during pregnancy/delivery***

1. At the first prenatal visit
2. In the beginning of the third trimester
3. At delivery

**Pregnant people using drugs often avoid pre-natal care due to fear of punitive measures. Emergency Departments/Urgent Care settings are critical partners in providing testing and treatment.*

***The Indian Health Service recommends universal screening for syphilis among persons ages 13 and older***

1. "Annual syphilis testing for persons aged 13 and older to eliminate syphilis transmission by early case recognition".
2. "Turn on the annual EHR reminder at all sites to facilitate testing for two years or until incidence rates decrease locally to baseline"
3. Expand screening in emergency/urgent care settings

Stop-Syphilis-Letter-2-15-24.pdf (indiancountryecho.org)

# Best Practice:  Provide “Express” STI Testing

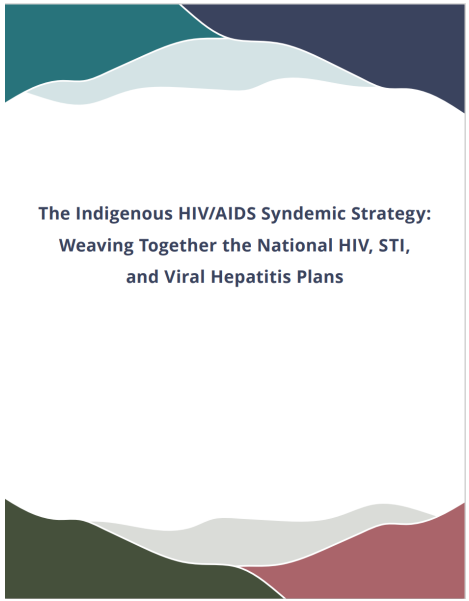
Express STI services refer to triage-based STI testing without need for a provider appointment or full clinical exam.

**Express STI services:**

1. increase clinic capacity and
2. reduce the time to treatment

https://www.indiancountryecho.org/resources/sample-toolkit-for-express-sti-resources/

# Overlapping Epidemics: "Syndemic" Bundle for Screening



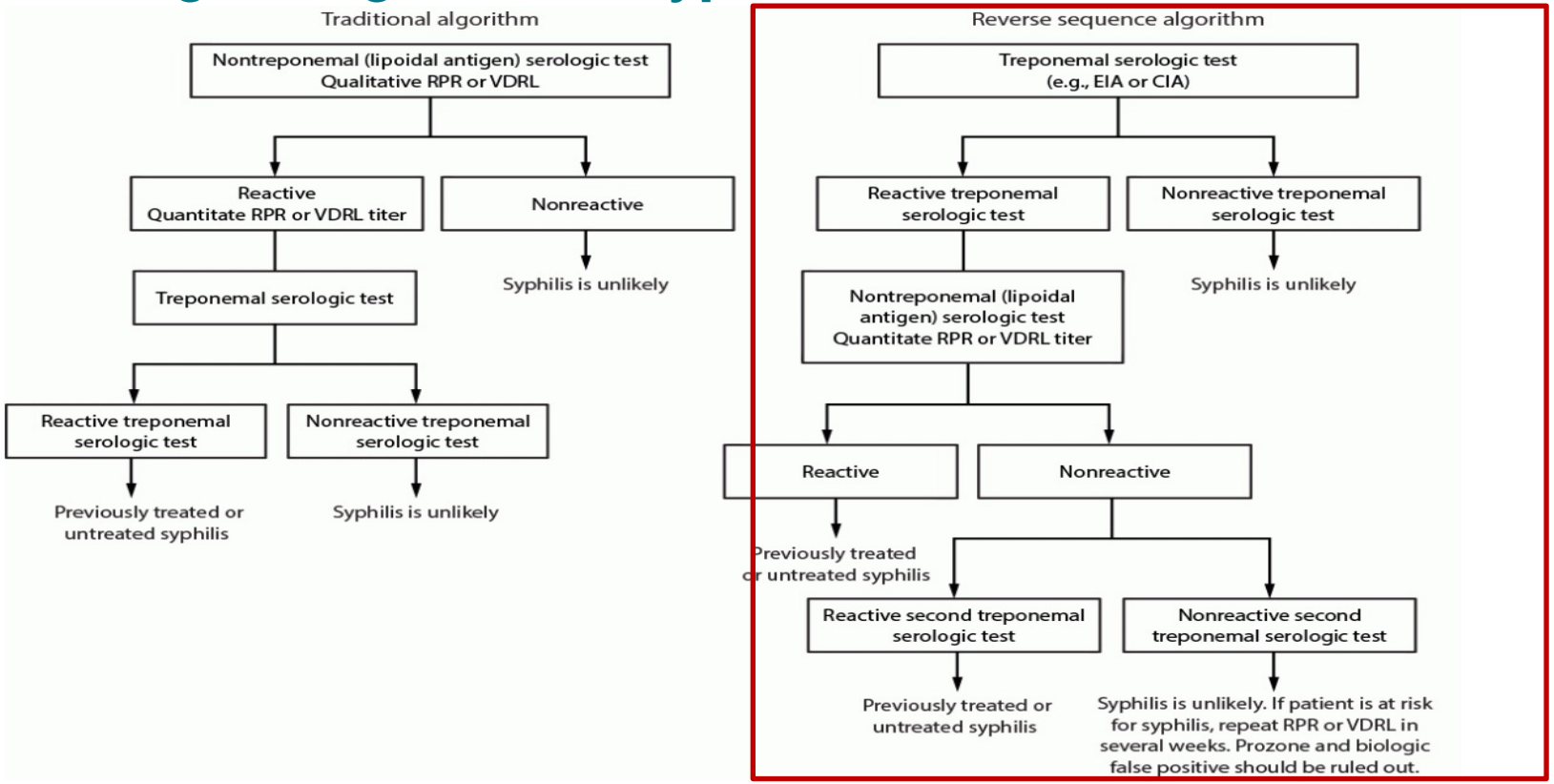

**Indian Health Service "Syndemic Bundle"**

1. Syphilis screening test with reflex RPR and TPPA
2. HIV serology (with documentation of consent if required in the local state jurisdiction)
3. Screening for gonorrhea and chlamydia at three sites: Urine, Pharynx, Rectum
4. Screening for hepatitis B and C
5. **Pregnancy test**

Stop-Syphilis-Letter-2-15-24.pdf (indiancountryecho.org)

https://www.indiancountryecho.org/indigenous-hiv-aids-syndemic-strategy/

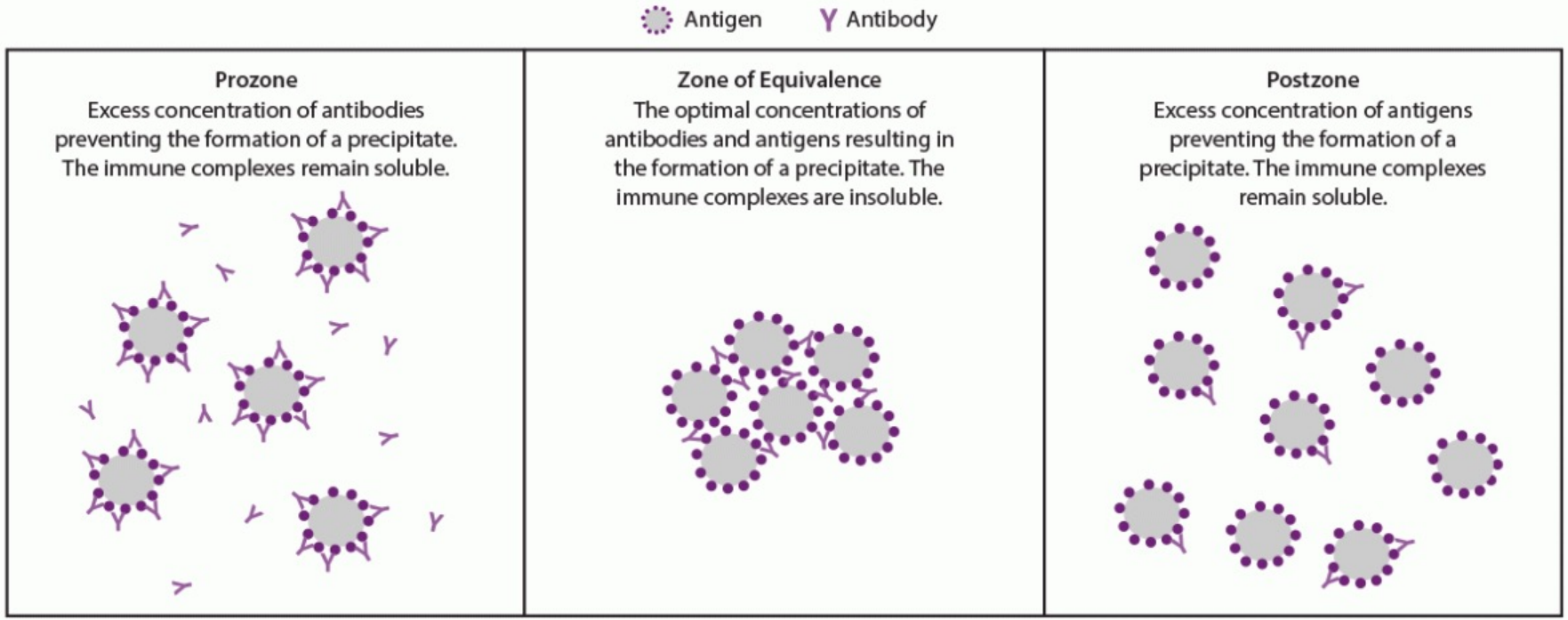
# Serologic Diagnosis of Syphilis




**Abbreviations:** CIA = chemiluminescence immunoassay; EIA = enzyme immunoassay; RPR = rapid plasma regain; TPPA = *Treponoma pallidum* particle agglutination; VDRL = Venereal Disease Research Laboratory.

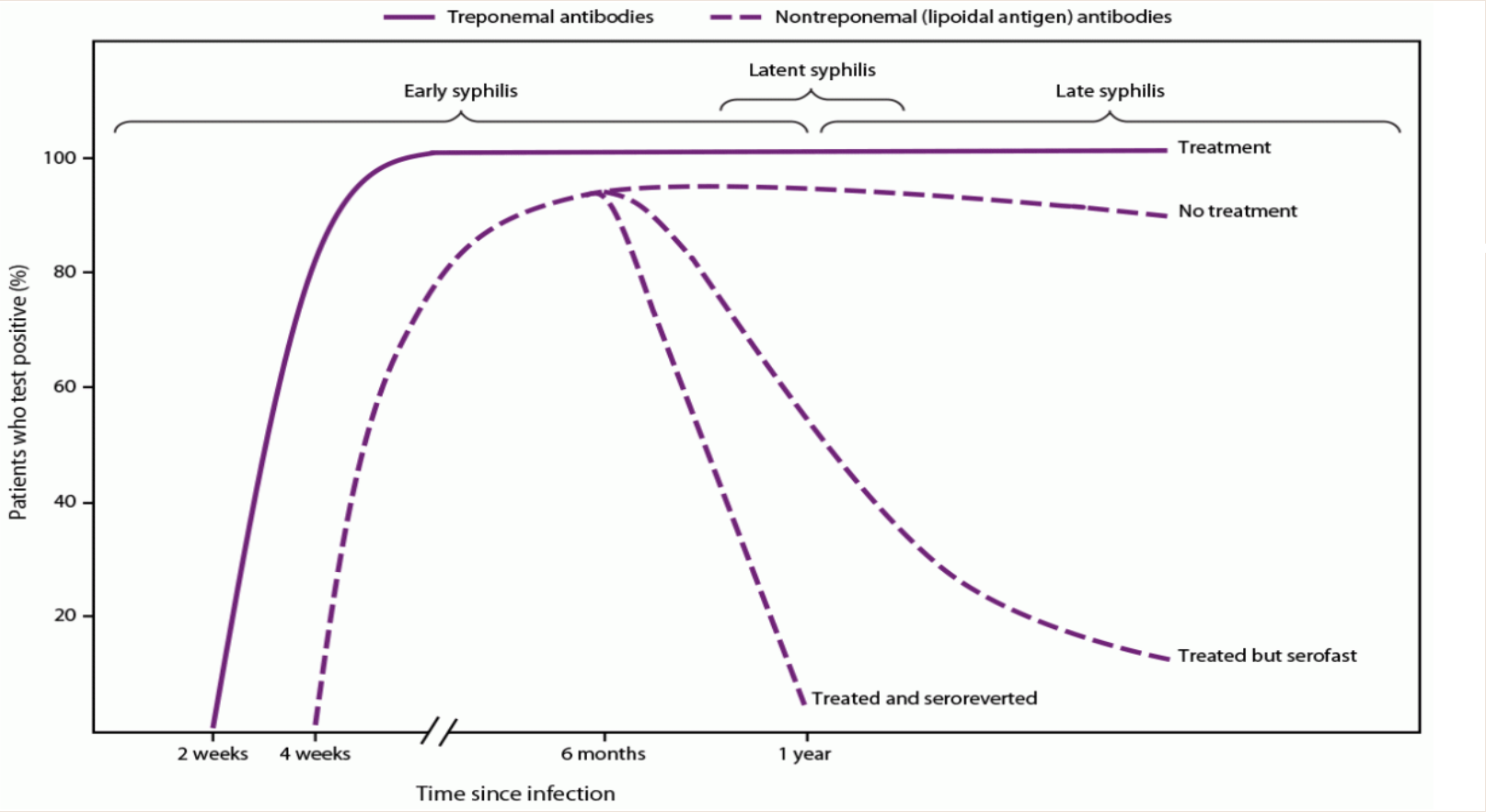
CDC Laboratory Recommendations for Syphilis Testing, United States, 2024 | MMWR

# Prozone phenomena




CDC Laboratory Recommendations for Syphilis Testing, United States, 2024 | MMWR

# Expected serologic response after treatment



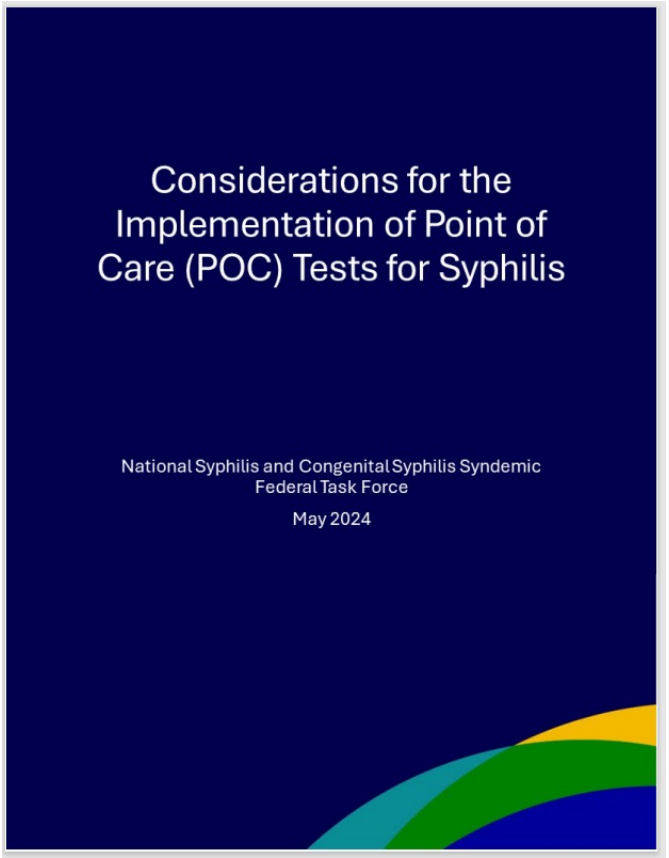

CDC Laboratory Recommendations for Syphilis Testing, United States, 2024 | MMWR

Adapted from Peeling RW, Mabey D, Kamb ML, Chen X-S, Radolf JD, Benzaken AS. Syphilis. Nat Rev Dis Primers 2017;3:17073.

# National Syphilis and Congenital Syphilis Syndemic (NSCSS) Federal Task Force

The group's mission is to leverage broad federal resources to reduce rates, promote health equity, and share resources with impacted communities. The HHS Task Force utilizes a syndemic approach because of the complex nature of this public health challenge, in which social and economic environments can exacerbate negative health outcomes.

Syphilis Is a Public Health Priority | HHS.gov, ADM Rachel Levine, Assistant Secretary of Health




**Where?** In general, point of care (POC) tests should be used where syphilis rates are high

**Who?** individuals who access health care infrequently and have difficulty with follow-up visits

**How?** POC tests generally can be conducted by trained non-clinical staff or clinicians within And outside clinical settings. Clinical staff can evaluate patients with positive POC test results and provide **treatment at the same visit.**

**Why?** In some settings and for some populations, the rapid results from a positive POC test create an opportunity to **treat syphilis during the same visit**

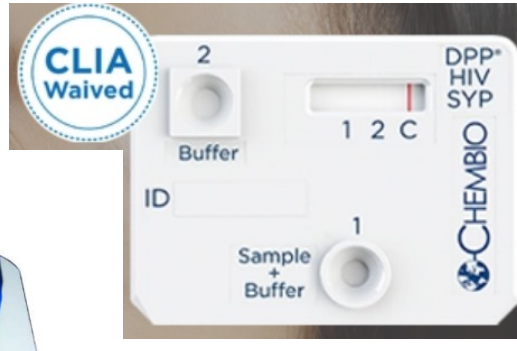
**What else?** POC tests should not be used in those previously diagnosed with syphilis.

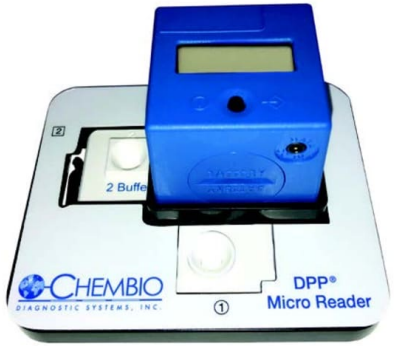
https://www.hhs.gov/sites/default/files/nscss-considerations-for-the-implementation-of-syphilis-poc-tests.pdf

# Rapid syphilis testing

**Chembio**

- FDA-approved and CLIA-waived rapid dual HIV/syphilis test
- Treponemal test component for syphilis
- Sensitivity:  >99% for HIV and >94% for T. pallidum
- Sample volume: 10 µl
- 15-minute results for dual rapid test
- Objective results using handheld digital reader  (DPP® Micro Reader)




DPP® HIV Syphilis USA – Chembio Diagnostics, Inc.

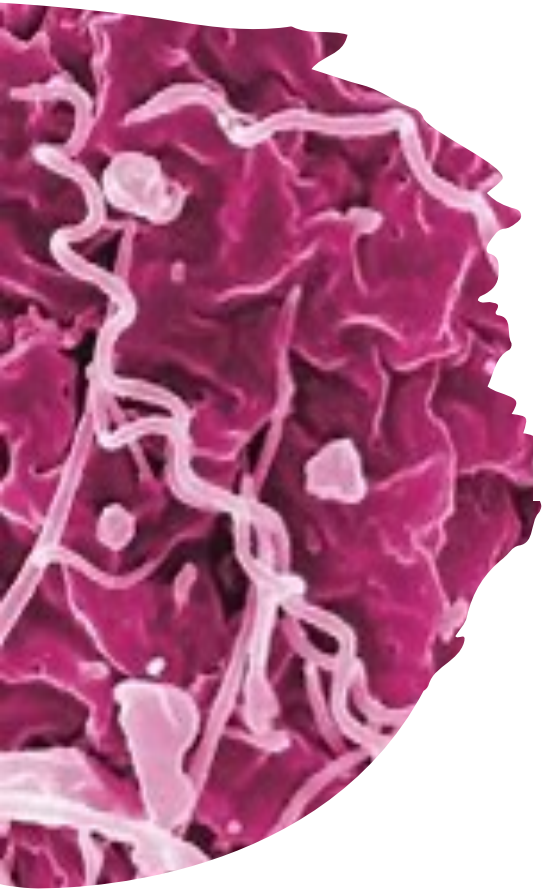
# Innovative patient-driven options for syphilis testing

- **Indigi-"I Want the Kit"**
- confidential at-home specimen collection
- self-sample, mail-based program
- HIV, chlamydia, gonorrhea, **syphilis** trichomoniasis, hepatitis B and C.
- Patient returns specimens for lab-based processing, results via IWTK website

Visit [iwantthekit.org](iwantthekit.org) and [https://spthb.org/programs/our-grants/native-test/](https://spthb.org/programs/our-grants/native-test/)

- **First syphilis at-home test**
- **First To Know Syphilis Test** is the first at-home, over the counter test to detect *Treponema pallidum* (syphilis) antibodies in human blood.
- **FDA** granted marketing authorization for at home use (Aug 16, 2024).


FDA Marketing Authorization Enables Increased Access to First Step of Syphilis Diagnosis | FDA






# Secure the Supply of Benzathine Penicillin

https://www.cdc.gov/std/treatment-guidelines/default.htm

# Treatment of syphilis in pregnant women

| Stage | | | | |
|---|---|---|---|---|
| **Primary** | **Secondary** | **Early non-primary, non secondary** | **Late Latent/ or Unknown Duration** | **Neurosyphilis, ocular syphilis and otic syphilis** |
| Benzathine penicillin 2.4 million units IM in a single dose | Benzathine penicillin 2.4 million units IM in a single dose | Benzathine penicillin 2.4 million units IM in a single dose | Benzathine penicillin 2.4 million units total administered as 3 doses of 2.4 million units IM each at 1-week intervals | Aqueous crystalline penicillin G 18-24 million units per day, administered as 3-4 million units by IV every 4 hours or continuous infusion for 10-14 days<br><br>Alternative: procaine penicillin G 2.4 million units IM 1x/day PLUS probenecid 500 mg orally 4x/day, both for 10-14 days |


* Doxycycline is an alternative oral treatment for syphilis in **Non-pregnant patients**
https://www.cdc.gov/std/treatment-guidelines/default.htm

# Penicillin Allergy

- Patients often are incorrectly labeled as allergic to penicillin
  - Evaluate what symptoms were experienced by patients with reported penicillin allergy

- Penicillin allergy causing anaphylaxis is rare
  - In studies that have incorporated penicillin skin testing and graded oral challenge among persons with reported penicillin allergy, the true rates of allergy are low, ranging from 1.5% to 6.1%.

- Allergies wane over time:
  - Approximately 80% of patients with a true IgE-mediated allergic reaction to penicillin have lost the sensitivity after 10 years
- ***Desensitization is recommended for pregnant women diagnosed with syphilis followed by treatment with penicillin.***

https://www.cdc.gov/std/treatment-guidelines/STI-Guidelines-2021.pdf .

# Field treatment with benzathine penicillin

Field treatment (non-clinical facility based) can be offered under standing orders and administered by nursing staff for patients with or exposed to syphilis who cannot access care at a facility due to:

1. **Pregnancy**
2. **Substance use**
3. Transportation difficulties
4. Childcare
5. Privacy concerns
6. Mental health issues
7. Risk for loss to follow-up


PHN Syphilis Field-Based Treatment Policy - Indian Country ECHO

# Presumptive treatment with benzathine penicillin

**Presumptive treatment** prior to receiving syphilis test results is recommended:

1. For patients with symptoms consistent with syphilis
2. For sexual contacts to syphilis cases
3. For patients testing positive using rapid testing prior to confirmatory results*


1. https://www.indiancountryecho.org/wp-content/uploads/2023/07/Stop-Syphilis-Letter-6-29-23.pdf
2. *Vital Signs: Missed Opportunities for Preventing Congenital Syphilis — United States, 2022 | MMWR (cdc.gov)
3. https://www.hhs.gov/sites/default/files/nscss-considerations-for-the-implementation-of-syphilis-poc-tests.pdf

# Doxycycline Post Exposure Prophylaxis (DoxyPEP)

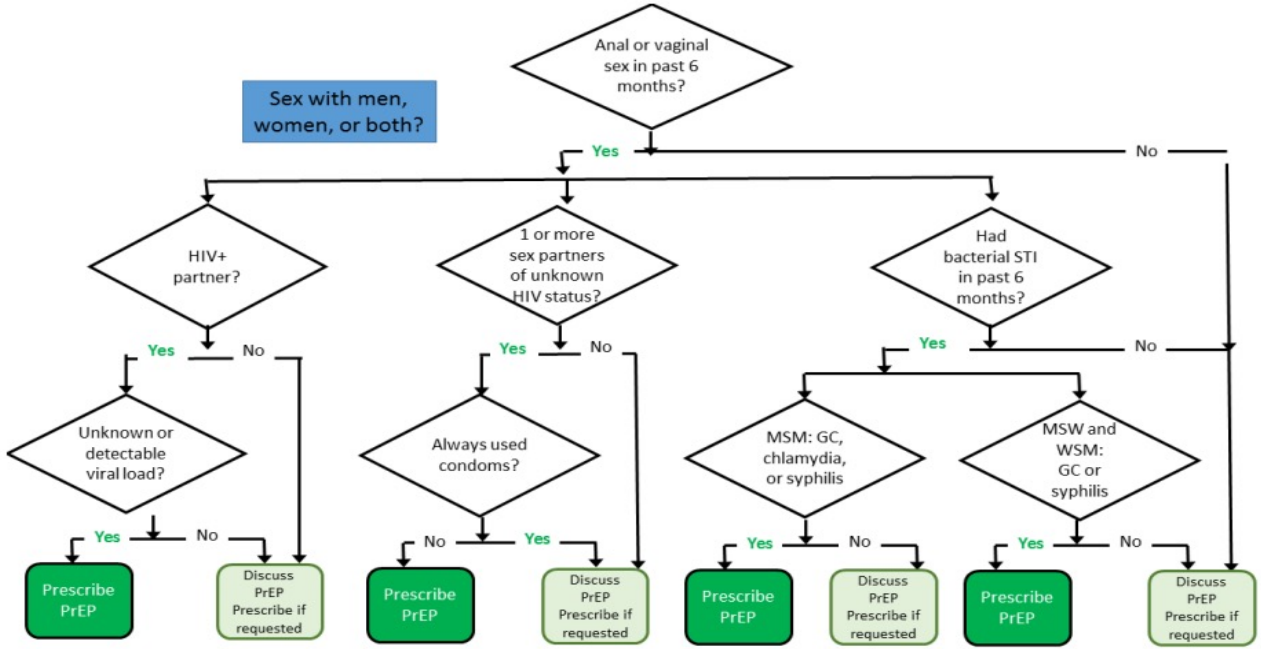
- One dose of Doxycycline 200mg
  < 72 hours after condomless sex


- Prevention of chlamydia, gonorrhea, and syphilis

- Who should receive DoxyPEP?
  - Men who have sex with men (MSM)/Trans Women (TGW) on HIV PrEP or living with HIV
  - If not on HIV PrEP, MSM/TGW with history of STIs within the past 12 months, sex work, chemsex (sex under the influence of drugs)

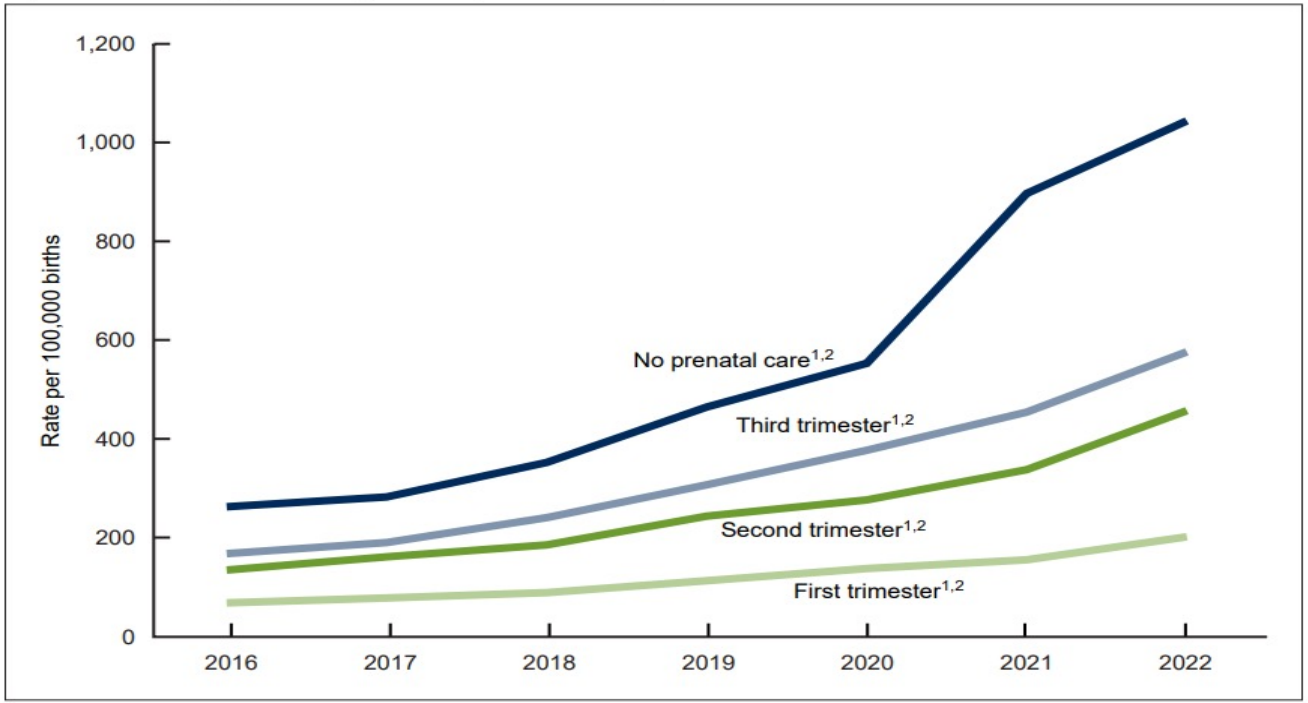
Guidelines for the Use of Doxycycline Post-Exposure Prophylaxis for Bacterial STI Prevention (cdc.gov)

# HIV Pre-exposure Prophylaxis (PrEP)



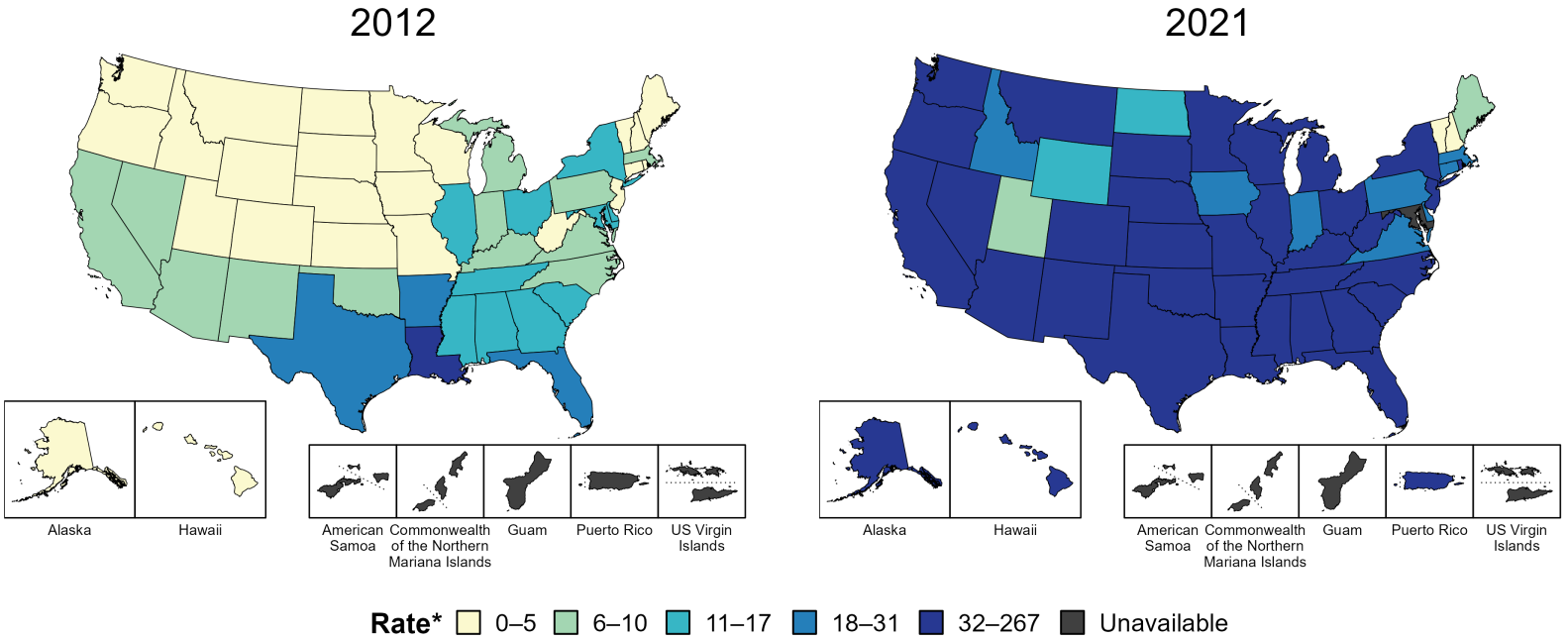

US Public Health Service: PREEXPOSURE PROPHYLAXIS FOR THE PREVENTION OF HIV INFECTION IN THE UNITED STATES – 2021 UPDATE, A CLINICAL PRACTICE GUIDELINE

# Maternal syphilis rate, by trimester prenatal care began: United States, 2016–2022




[1]Significant increasing trend from 2016–2022 ($p < 0.05$).
[2]Significant decreasing trend by timing of prenatal care for each year 2016–2022 ($p < 0.05$).
NOTES: In 2022, 2.2% (77,228) of mothers did not receive prenatal care. Access data table for Figure 4 at: https://www.cdc.gov/nchs/data/databriefs/db496-tables.pdf#4.
SOURCE: National Center for Health Statistics, National Vital Statistics System, natality data file.

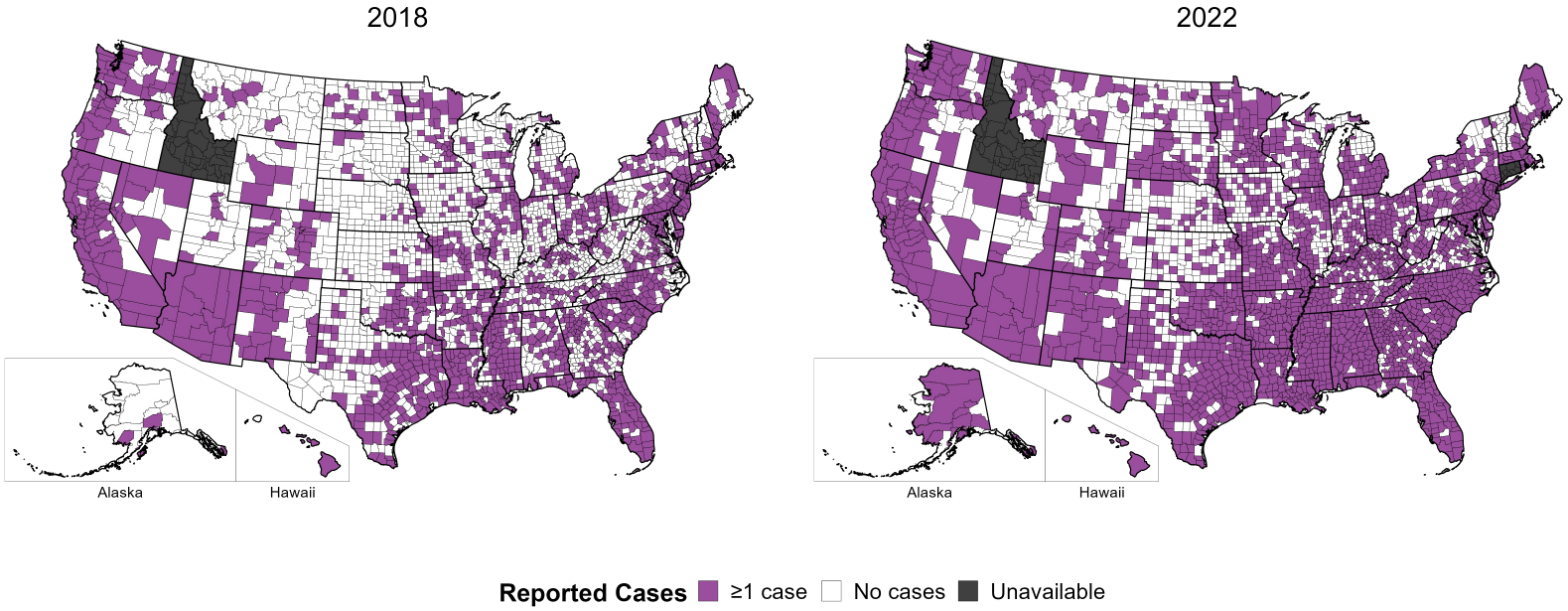
# Syphilis (All Stages) — Rates of Reported Cases Among Women Aged 15–44 Years by State, United States and Territories, 2012 and 2021




* Per 100,000

https://www.cdc.gov/std/statistics/2021/figures.htm

# Syphilis (All Stages) — Reported Cases Among Women Aged 15–44 Years by County, United States, 2018 and 2022



# Substance Use Among Persons with Syphilis During Pregnancy— Arizona and Georgia, 2018–2021

| Substance used | No. (%) | | Prevalence ratio[¶] (95% CI) |
|---|---|---|---|
| | Congenital syphilis (n = 360) | Noncongenital syphilis (n = 410) | |
| Any substance* | 173 (48.1) | 101 (24.6) | 1.95 (1.60–2.38) |
| Tobacco | 99 (27.5) | 46 (11.2)** | 2.45 (1.78–3.37) |
| Alcohol | 29 (8.1) | 20 (4.9)** | 1.65 (0.95–2.86) |
| Cannabis | 69 (19.2) | 56 (13.7)[††] | 1.40 (1.01–1.93) |
| Illicit use of opioids[§§] | 75 (20.8) | 14 (3.4)** | 6.09 (3.50–10.58) |
| Illicit, nonprescription substance[¶¶] | 101 (28.1) | 26 (6.4)** | 4.41 (2.94–6.63) |

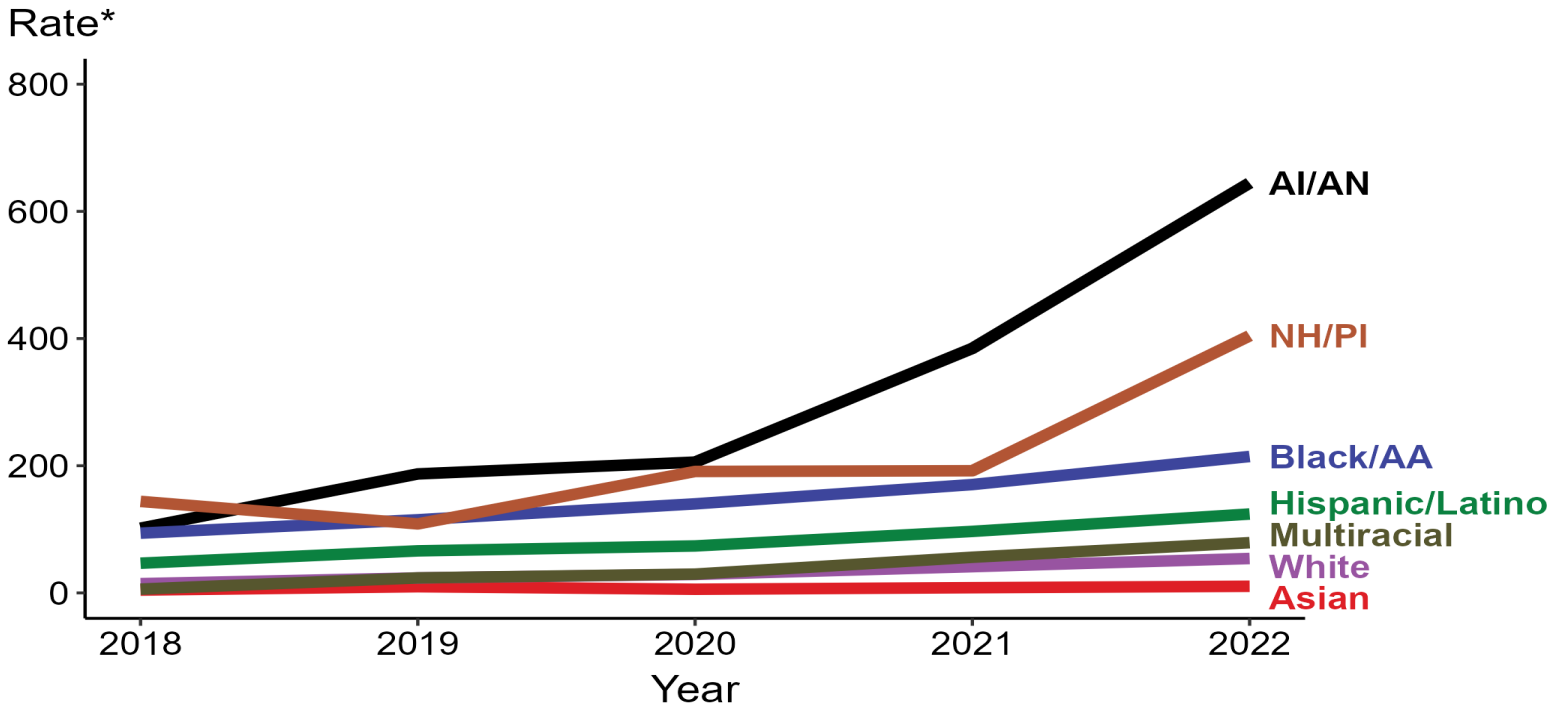
Substance Use Among Persons with Syphilis During Pregnancy — Arizona and Georgia, 2018–2021 | MMWR (cdc.gov)

# Congenital Syphilis — Reported Cases and Rates of Reported Cases by State, Ranked by Rates, United States, 2022

| Rank* | State† | Cases | Rate per 100,000 Live Births |
|---|---|---|---|
| 1 | New Mexico | 76 | 355.3 |
| 2 | South Dakota | 40 | 351.8 |
| 3 | Arizona | 219 | 281.1 |
| 4 | Texas | 922 | 246.8 |
| 5 | Oklahoma | 110 | 227.2 |
| 6 | Mississippi | 73 | 207.6 |
| 7 | Louisiana | 115 | 200.2 |
| 8 | Nevada | 65 | 193.0 |
| 9 | Arkansas | 69 | 191.9 |
| 10 | Hawaii | 27 | 172.9 |
| 11 | California | 616 | 146.5 |
| 12 | Montana | 15 | 133.6 |
| 13 | Alaska | 12 | 128.1 |
| 14 | Florida | 276 | 127.6 |
| 15 | Missouri | 82 | 118.1 |
| | **US TOTAL‡** | **3,755** | **102.5** |
| 16 | Oregon | 37 | 90.4 |
| 17 | Georgia | 101 | 81.4 |
| 18 | West Virginia | 13 | 75.6 |
| 19 | Tennessee | 61 | 74.6 |
| 20 | Alabama | 43 | 74.1 |

https://www.cdc.gov/std/statistics/2022/tables/31.htm

# Congenital Syphilis — Rates of Reported Cases by Year of Birth, Race/Hispanic Ethnicity of Mother, United States, 2018–2022

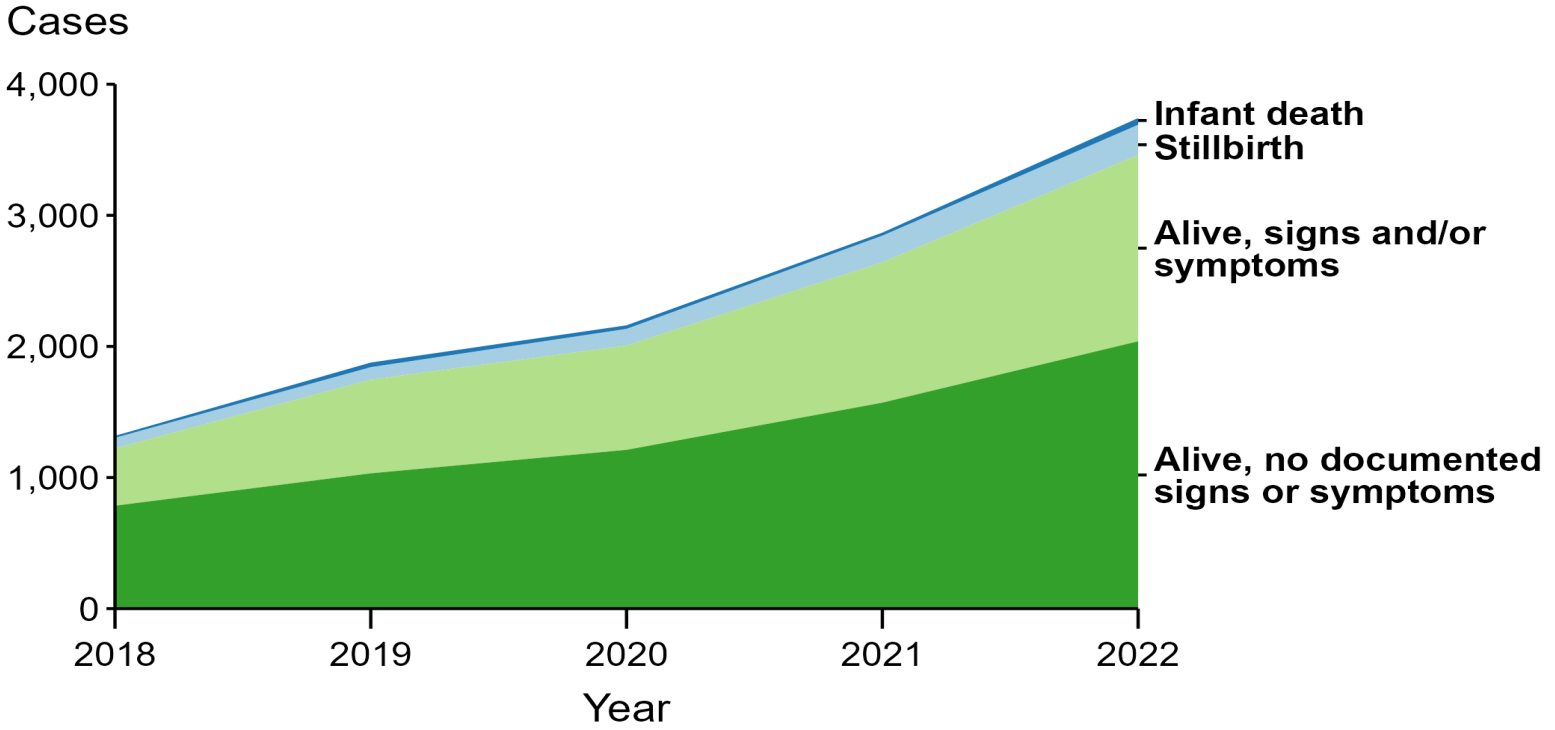



* Per 100,000 live births

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

https://www.cdc.gov/std/statistics/2022/figures.htm

# Congenital Syphilis — Reported Cases by Vital Status and Clinical Signs and Symptoms* of Infection, United States, 2018–2022




* Infants with signs and/or symptoms of congenital syphilis have documentation of at least one of the following: long bone changes consistent with congenital syphilis, snuffles, condylomata lata, syphilitic skin rash, pseudoparalysis, hepatosplenomegaly, edema, jaundice due to syphilitic hepatitis, reactive CSF-VDRL, elevated CSF WBC or protein values, or evidence of direct detection of *T. pallidum*.

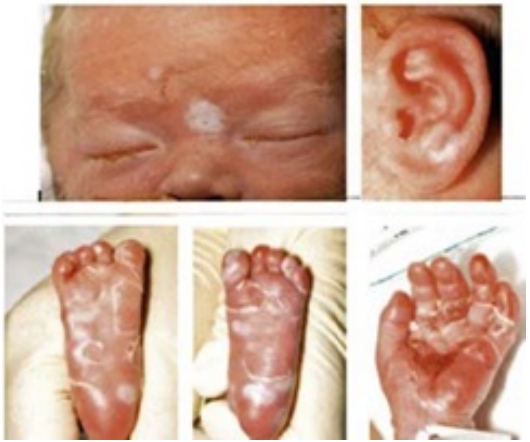
**NOTE:** Of the 11,999 congenital syphilis cases reported during 2018 to 2022, 33 (0.3%) did not have sufficient information to be categorized.

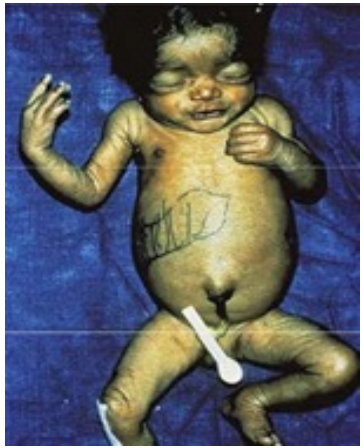
https://www.cdc.gov/std/statistics/2022/figures.htm

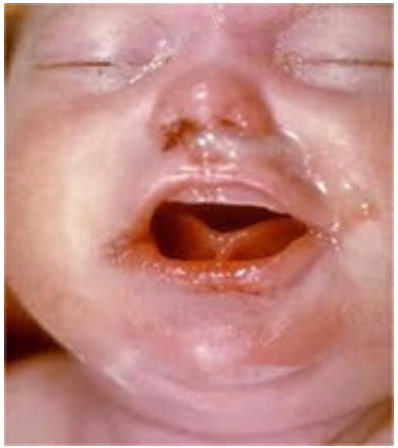
| **Scenario 1:**<br>**Confirmed, proven or highly probable congenital syphilis** | **Scenario 2:**<br>**Possible congenital syphilis** | **Scenario 3:**<br>**Congenital syphilis less likely** | **Scenario 4:**<br>**Congenital syphilis unlikely** |
|---|---|---|---|
| **Neonate with:**<br>• a physical exam consistent with CS<br>• serum quantitative nontreponemal serology 4-fold greater than mother's or<br>• a positive darkfield or PCR test of placenta, body fluids or positive silver stain of placenta or cord | **Neonate with** a normal physical exam and a serum quantitative nontreponemal serologic titer equal to or < 4-fold of the maternal titer at delivery and **one** of the following:<br>• The mother was not treated, was inadequately treated, or has no documentation of treatment.<br>• The mother was treated with erythromycin, or a regimen not recommended in these guidelines<br>• The mother received recommended regimen, but treatment was initiated <30 days before delivery. | **Neonate with** a normal physical examination and a serum quantitative nontreponemal serologic titer equal or <4-fold of the maternal titer at delivery and **both** of the following are true:<br>• The mother was treated during pregnancy, treatment was appropriate for the infection stage, and the treatment regimen was initiated ≥30 days before delivery.<br>• The mother has no evidence of reinfection or relapse | **Neonate with:**<br>• a normal physical exam<br>• serum quantitative nontreponemal serology equal to or less than 4-fold mother's at delivery and<br>• Mother's treatment was adequate before pregnancy<br>• Mother's nontreponemal titer remained low and stable before and during pregnancy and at delivery |
| **Evaluation:**<br>CSF with VDRL, cell ct, protein, CBC/diff, long bone radiographs, neurologic eval (eye, auditory, imaging) | CSF analysis for VDRL, cell count, and protein**<br>CBC, differential, long-bone radiographs | No evaluation is recommended | No evaluation is recommended |
| **Treatment:**<br>**Aqueous crystalline penicillin G** 100,000–150,000 units/kg/body wt./day, administered as 50,000 units/kg body wt./dose IV q 12 hours during the first 7 days of life and q 8 hours thereafter for a total of 10 days OR<br>**Procaine penicillin G** 50,000 units/kg body weight/dose IM in a single daily dose for 10 days | **Treatment:**<br>**Aqueous crystalline penicillin G** 100,000–150,000 units/kg/body wt./day, administered as 50,000 units/kg body wt./dose IV q 12 hours during the first 7 days of life and q 8 hours thereafter for a total of 10 days OR<br>**Procaine penicillin G** 50,000 units/kg body weight/dose IM in a single daily dose for 10 days OR | **Treatment:**<br>**Benzathine penicillin G 50,000** units/kg body weight/dose IM in a single dose<br>* 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 | **No treatment recommended**<br>• Benzathine penicillin 50,000 units/kg body weight as a single IM injection might be considered, if follow-up is uncertain and the neonate has a reactive nontreponemal test.<br>• Neonates should be followed serologically to ensure the nontreponemal test returns to negative |

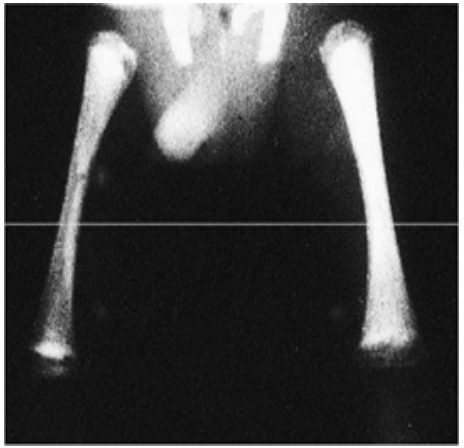
# Clinical Manifestations of Congenital Syphilis (CS)

**Approximately 40%–60% of infected infants have >1 of the following: hepatosplenomegaly, rash, generalized lymphadenopathy, skeletal abnormality, or nasal discharge**










1. Centers for Disease Control and Prevention. Congenital syphilis case definition. https://www.cdc.gov/std/statistics/2022/case-definitions.htm
2. World Health Organization. Birth defects surveillance: A manual for programme managers, 2nd Edition. December 2020. https://www.who.int/publications/i/item/9789240015395
3. Principles and practices of Pediatric Infectious Diseases. 6th Edition. 2018. Edited by: Sarah S. Long. ISBN. 978-0-323-75608-2
4. Red Book: 2024–2027 Report of the Committee on Infectious Diseases (33rd Edition)

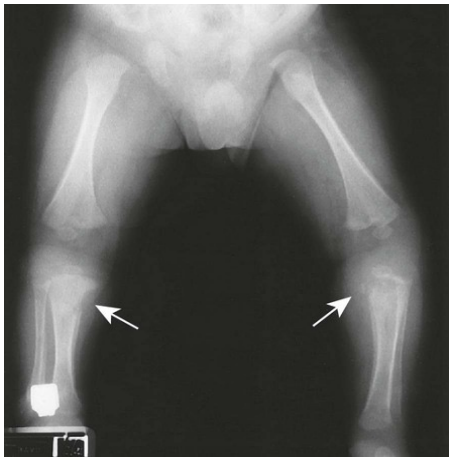
# Clinical Manifestations of Early Congenital Syphilis

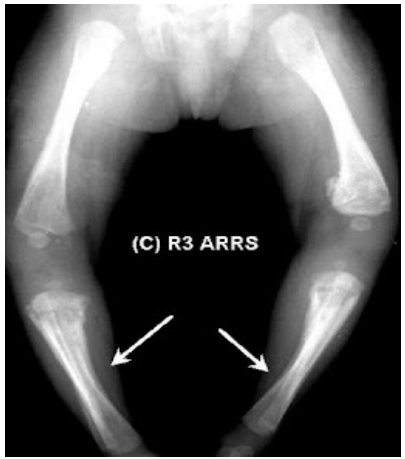
1. **Enlarged liver and spleen** with abnormal alkaline phosphatase
2. **Bone abnormalities,** Lesions include metaphysitis, periostitis, and osteitis.
3. **Pneumonia** (*pneumonia alba*)
4. **Anemia** (up to 75%), Hydrops fetalis is typically fatal.
5. **Elevated WBC** (50%) with significant monocytosis.
6. **Skin manifestations:** maculopapular desquamating rash (palms and soles) , petechial lesions (from thrombocytopenia) , vesiculobullous lesions that rupture (*Pemphigus syphiliticus)*
7. Generalized **lymphadenopathy**
8. **Abnormal CSF** in ~50% of symptomatic congenitally infected infants and in up to 10% of asymptomatic infants. Diagnosed by positive CSF VDRL test result or with abnormal elevation of CSF white blood cell (WBC) count or protein levels. Neurologic symptoms are rare
9. Clear nasal discharge. **Rhinitis**, or “snuffles,” (containing many spirochetes), mucosal erosion can cause bleeding.
10. **Nephrotic** syndrome (rare) is caused by immune complex disease, not treponemal invasion.

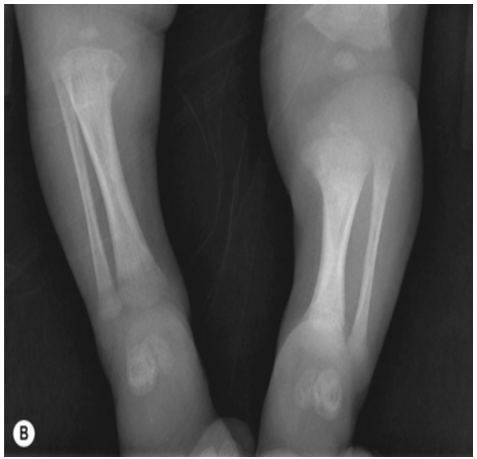
Principles and practices of Pediatric Infectious Diseases. 6th Edition. 2018. ISBN. 978-0-323-75608-2

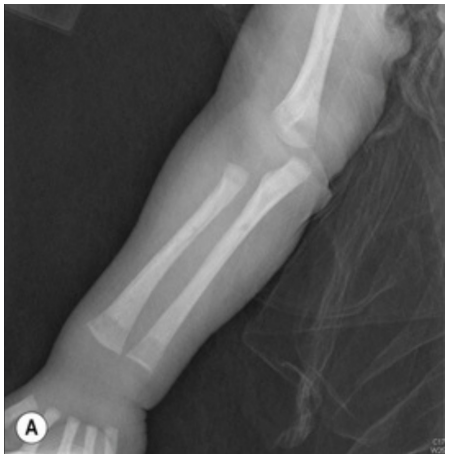
# Radiographic abnormalities in 95% of symptomatic and up to 20% of asymptomatic infants

- Lesions include metaphysitis, periostitis, and osteitis.
- Findings are symmetric and involve multiple long bones; the lower extremities are almost always affected.
- Metaphyseal lesions (osteochondritis) vary from punctate lucencies to more destructive changes, are seen earlier than periostitis.
- *Wimberger sign* (“cat bite”) describes osteitis and destruction of the proximal medial tibial metaphysis
- Lesions can be painful, resulting in pseudoparalysis of the affected limb (*pseudoparalysis of Parrot*).
- Periostitis appears radiographically as multiple layers of periosteal new bone formation.





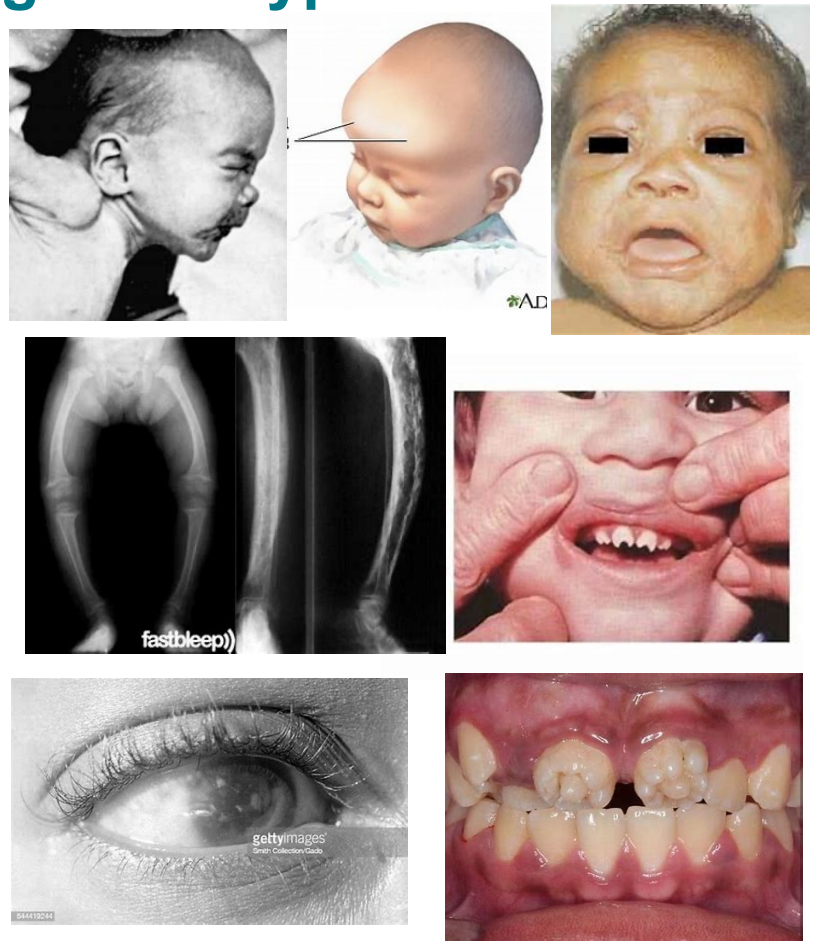




Principles and practices of Pediatric Infectious Diseases. 6th Edition. 2018. Edited by: Sarah S. Long. ISBN. 978-0-323-75608-2

# Clinical Manifestations of Late Congenital Syphilis in patients ≥2 years of age

- Bone malformations (frontal bossing, saddle nose and saber shins),
- Teeth (*Hutchinson* peg-shaped, notched *central incisors* and *mulberry* multi-cusped *first molars*),
- skin (*rhagades*, or linear scars, fanning out from the corner of the mouth)
- Interstitial keratitis
- Eighth nerve deafness result from longstanding chronic inflammation.
- Symmetric, chronic painless swelling of the knees (*Clutton joints*)
- Asymptomatic neurosyphilis is more common in than is symptomatic disease.
- Pathologic nervous system deficits including mental, motor, and sensory deficits, similar to those seen in acquired tertiary disease.



# Syphilitic Stillbirth

***Clinical case definition***

A fetal death that occurs **after a 20-week gestation** OR in which the fetus weighs **>500g** AND the **mother had *untreated or inadequately* treated* syphilis at delivery**.

* Adequate treatment is defined as completion of a penicillin-based regimen, in accordance with CDC treatment guidelines, appropriate for stage of infection, initiated 30 or more days before delivery.

***Comments:*** For **reporting** purposes, congenital syphilis includes:

1. cases of congenitally acquired syphilis among infants and children
2. syphilitic stillbirths

https://www.cdc.gov/std/statistics/2019/case-definitions.htm)

# Adult and Infant Case Management

**Addressing Congenital Syphilis includes:**

1) **Prioritize data sharing** across public health partners.
2) **Close communication** with state, county and tribal health departments.
3) **Support** for additional community-level healthcare staff performing **contact tracing** for syphilis, employed through tribal, state, or county health departments.
4) **Dedicated facility-level case managers** that track adult, pregnant, and infant patients with syphilis to ensure linkage to treatment and partner services

# Train Public Health Staff for Disease Intervention/Partner Services

## National Disease Intervention Training Program

### National Network of Disease Intervention Training Centers (NNDITC)

**Training plans available in CDC TRAIN**

- Disease Intervention Training Plan with Outbreak Response
- Introduction to Public Health Practice

**Skills-building Programs**

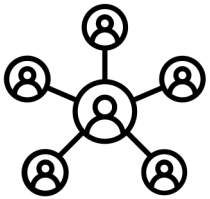
- Coaching for Enhanced Disease Intervention Skills (CEDIS)
- Facilitated Interview Practice Sessions
- Learning Collaboratives

https://www.cdc.gov/std/training/courses.htm

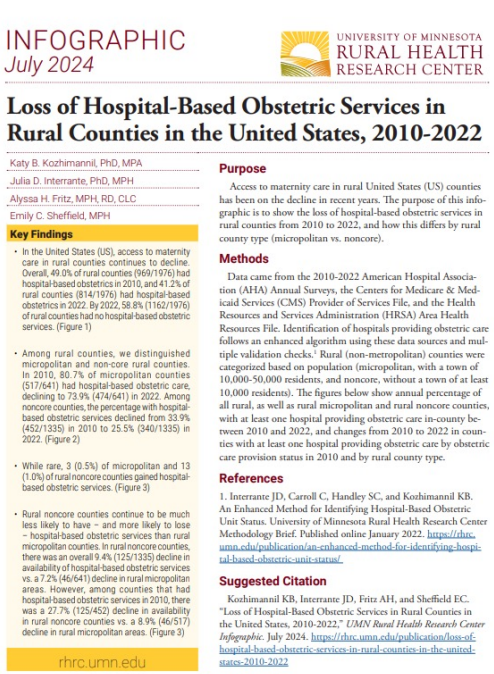
# Case Investigation and Contact Tracing

**Importance of identifying and referring sexual contacts/partners to syphilis cases for presumptive treatment to stop community-level transmission**

- **Partner services is an effective method to identify undiagnosed cases of syphilis and other STIs.  It has a higher yield than screening**.



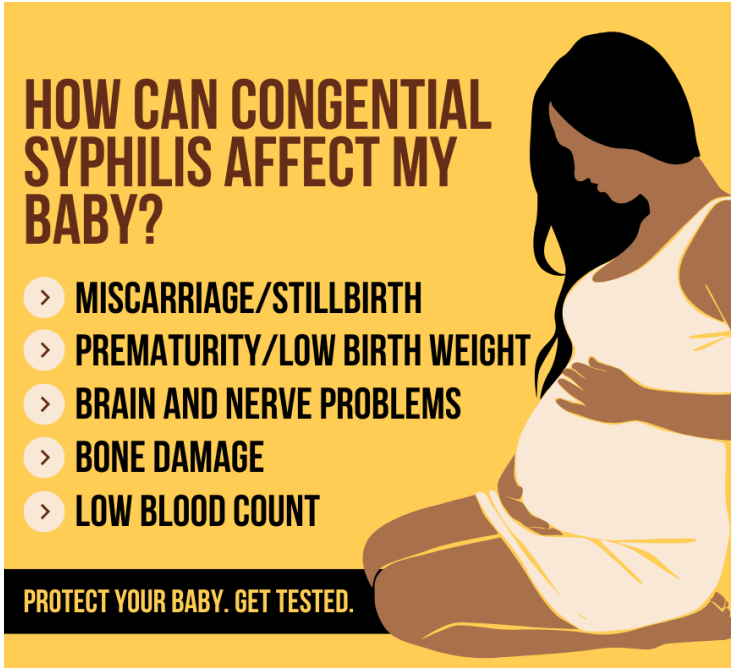
# Remove Barriers


# Patient Incentives

- Evidence based intervention in TB, medication-assisted treatment (MAT), diabetes adherence to care.  Being piloted for syphilis testing events and treatment
    - **Priority populations** (pregnancy, substance use)
    - Partners/Contacts treated
- Of programs using incentives in IHS, an internal survey found:
    - 90% would recommend their use
    - 100% said they would continue to use incentives

# Educate the Community

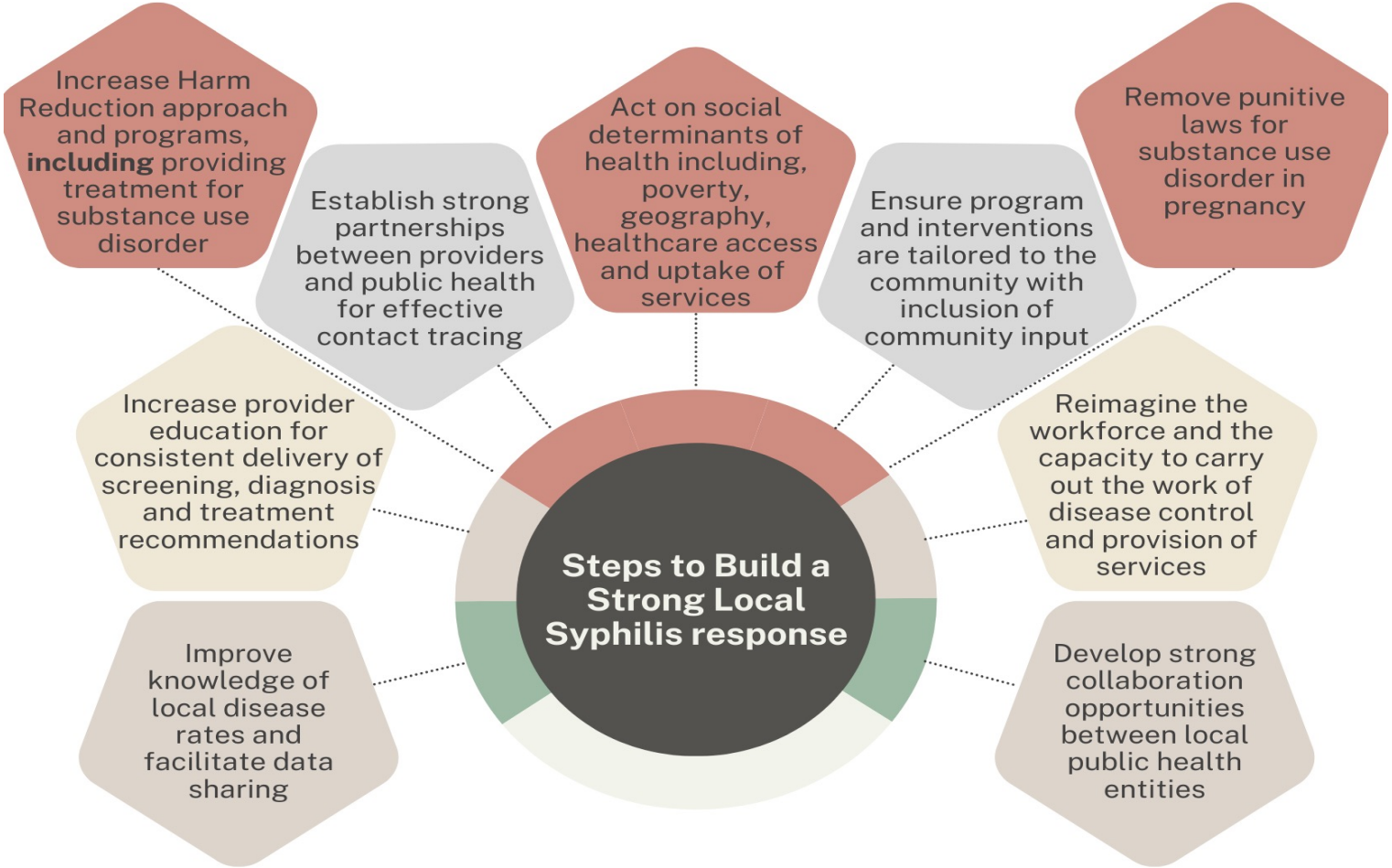
# About Syphilis: CDC Factsheet

About Syphilis | Syphilis | CDC

# Educate Providers

- Indian Country Infectious Disease ECHO: www.IndianCountryECHO.org
- CDC STD Treatment Guidelines: https://www.cdc.gov/std/treatment-guidelines/default.htm
- CDC STD Surveillance: https://www.cdc.gov/std/statistics/2022/default.htm
- CDC STD Prevention Training Centers: https://www.cdc.gov/std/training/default.htm
- University of Washington STD CME sessions: https://www.std.uw.edu/
- California Prevention Training Center Online: https://www.stdhivtraining.org/online_courses.html
- Johns Hopkins STD Prevention Training: https://www.stdpreventiontraining.com/
- New York City STD/HIV Prevention Training Center: https://www.nycptc.org/

# Build an Effective Syphilis Response



# Think Syphilis




MDT7@cdc.gov

# EXTRA SLIDES

# Scenario 1: Confirmed, Proven or Highly Probable Congenital Syphilis

**Definition:** (1) Infant with an abnormal **physical examination** that is consistent with congenital syphilis; **OR** (2) serum quantitative nontreponemal serologic titer that is fourfold (or greater) higher than the mother's titer at delivery **OR** (3)a **positive darkfield** test **OR PCR** of placenta, cord, lesions, or body fluids OR (4) a **positive silver stain** of the placenta/cord. (regardless of maternal treatment history)

**Evaluation:**

**CSF with VDRL, cell count, protein, CBC/diff, long bone radiographs, neurologic eval** (eye, auditory, imaging) **Other tests as clinically indicated** (e.g., chest radiograph, liver function tests, neuroimaging, ophthalmologic examination, and auditory brain stem response)

**Treatment:**

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

https://www.cdc.gov/std/treatment-guidelines/STI-Guidelines-2021.pdf

# Scenario 2: Possible Congenital Syphilis

**Definition:** 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 ≤1:16) **AND** one of the following:

(1) The mother was not treated, was inadequately treated, or has no documentation of having received treatment.

(2) The mother was treated with erythromycin or a non penicillin G regimen other than those recommended in these guidelines.

(3) The mother received the recommended regimen but treatment **was initiated <30 days before delivery**.

**Evaluation:**

CSF with VDRL, cell count, protein, CBC/diff, long bone radiographs, neurologic eval (eye, auditory, imaging)

**Treatment:**

**Aqueous crystalline penicillin** G 100,000–150,000 units/kg/body wt./day, administered as 50,000 units/kg body wt./dose IV q 12 hours during the first 7 days of life and q 8 hours thereafter for a total of 10 days **OR** Benzathine penicillin G 50,000 units/kg body weight/dose IM in a single dose

https://www.cdc.gov/std/treatment-guidelines/STI-Guidelines-2021.pdf

# Scenario 3: Congenital Syphilis Less Likely

**Definition:** Any neonate who has a normal physical examination and a serum quantitative nontreponemal serologic titer equal or less than fourfold higher than the maternal titer at delivery and both of the following are true:

(1)The mother was treated during pregnancy, treatment was appropriate for the infection stage, and the treatment regimen was initiated ≥30 days before delivery. **AND**
(2) The mother has **no evidence of reinfection or relapse**.

**Evaluation:**

No evaluation is recommended.

**Treatment:**

**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 lowtiter, latent syphilis (e.g., VDRL <1:2 or RPR <1:4).

https://www.cdc.gov/std/treatment-guidelines/STI-Guidelines-2021.pdf

# Scenario 3: Congenital Syphilis Less Likely

**Definition:** Any neonate who has a normal physical examination and a serum quantitative nontreponemal serologic titer equal or less than fourfold higher than the maternal titer at delivery and both of the following are true:

(1)The mother was treated during pregnancy, treatment was appropriate for the infection stage, and the treatment regimen was initiated ≥30 days before delivery. **AND**
(2) The mother has **no evidence of reinfection or relapse**.

**Evaluation:**

No evaluation is recommended.

**Treatment:**

**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 lowtiter, latent syphilis (e.g., VDRL <1:2 or RPR <1:4).

https://www.cdc.gov/std/treatment-guidelines/STI-Guidelines-2021.pdf

# Scenario 4: Congenital Syphilis *Unlikely*

**Definition:** 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:

(1)The mother's treatment was adequate before pregnancy.

(2) The mother's nontreponemal serologic titer remained low and stable (i.e., serofast) before and during pregnancy and at delivery (e.g., VDRL ≤1:2 or RPR ≤1:4).

**Evaluation:**

No evaluation is recommended.

**Treatment:**

**No treatment is required.** However, any neonate with reactive nontreponemal tests should be followed serologically to ensure the nontreponemal test returns to negative

**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.

https://www.cdc.gov/std/treatment-guidelines/STI-Guidelines-2021.pdf

# Infant Followup

**(1) All neonates with reactive nontreponemal tests should receive thorough follow-up examinations and serologic testing (i.e., RPR or VDRL) every 2–3 months until the test becomes nonreactive.**

**(2) For a neonate who was not treated because congenital syphilis was considered less likely or unlikely,** nontreponemal antibody titers should decrease by age 3 months and be nonreactive by age 6 months, indicating that the reactive test result was caused by passive transfer of maternal IgG antibody**.**

- **At age 6 months, if the nontreponemal test is nonreactive, no further evaluation or treatment is needed;**
- ***If the nontreponemal test is still reactive, the infant is likely infected and should be treated.***

**(4) Treated neonates who exhibit persistent nontreponemal test titers by age 6–12 months** should be reevaluated through CSF examination and managed in consultation with an expert. Retreatment with a 10-day course of a penicillin G regimen might be indicated.

**(5) Neonates with a negative nontreponemal test at birth and whose mothers were seroreactive at delivery** should be retested at age 3 months to rule out serologically negative incubating congenital syphilis at the time of birth.

https://www.cdc.gov/std/treatment-guidelines/STI-Guidelines-2021.pdf

# Congenital Syphilis Case Classification for Disease Reporting

1. **Confirmed:** Demonstration of ***Treponema pallidum*** in any infant body fluid or discharge, umbilical cord, autopsy, or placenta by darkfield, immunohistochemistry, staining, or other molecular testing (PCR) **OR**
2. **Probable:** An infant whose **mother had untreated or inadequately treated* syphilis at delivery,** regardless of signs in the infant **OR**
3. An infant or child who has a **reactive non-treponemal test for syphilis (Venereal Disease Research Laboratory [VDRL], rapid plasma reagin [RPR], or equivalent serologic methods) *AND* any one of the following**:
    1. Any evidence of congenital syphilis on physical examination
    2. Any evidence of congenital syphilis on radiographs of long bones
    3. A reactive cerebrospinal fluid (CSF) venereal disease research laboratory test (VDRL) test
    4. In a non-traumatic lumbar puncture, an elevated CSF leukocyte (white blood cell, WBC) count or protein (without other cause):

        Suggested parameters for abnormal CSF WBC and protein values:

        1. During the first 30 days of life, a **CSF WBC count of >15 WBC/mm3** or a **CSF protein >120 mg/dl** is abnormal.
        2. After the first 30 days of life, a **CSF WBC count of >5 WBC/mm3** or a **CSF protein >40 mg/dl,** regardless of CSF serology. The treating clinician should be consulted to interpret the CSF values for the specific patient.

*Adequate treatment is defined as completion of a penicillin-based regimen, in accordance with CDC treatment guidelines, appropriate for stage of infection, initiated 30 or more days before delivery.

STI Case Definitions in Effect During 2022 (cdc.gov)/
https://www.cdc.gov/std/statistics/2022/case-definitions.htm