

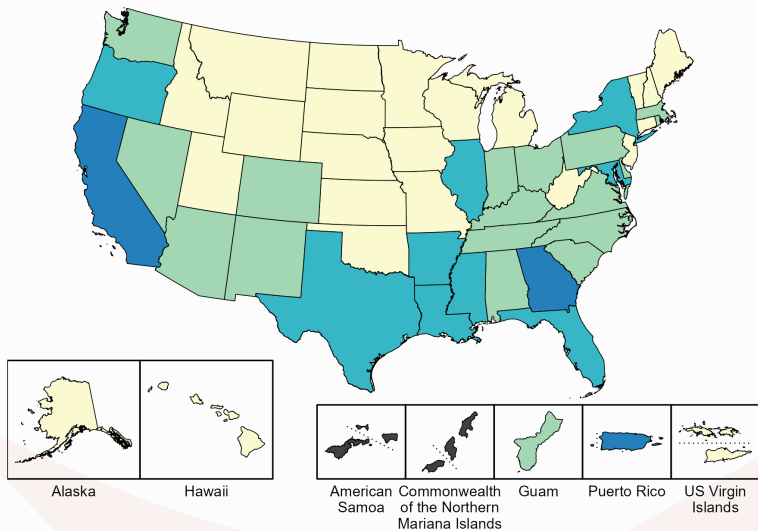
# Ending the Syndemic Series

## Syphilis Epidemiology, Diagnosis, Staging and Treatment

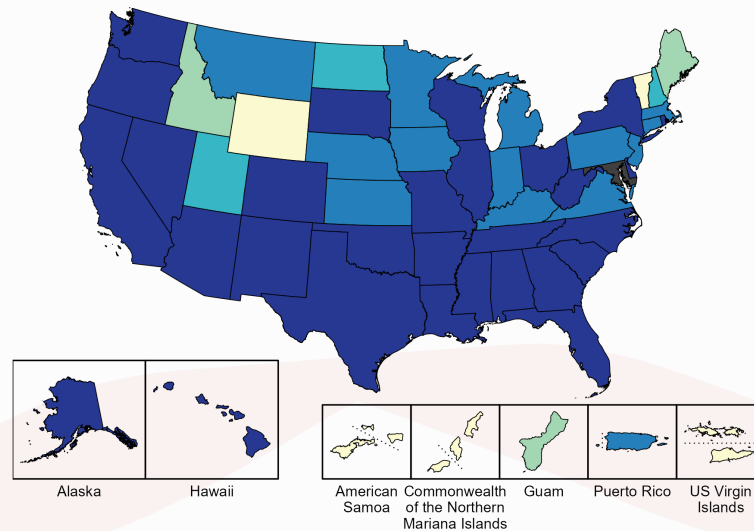
Jorge Mera, MD

# Primary and Secondary Syphilis – Rates\* of Reported Cases by State, United States, 2021

2012



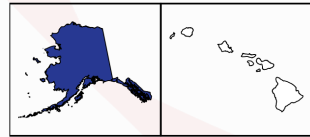
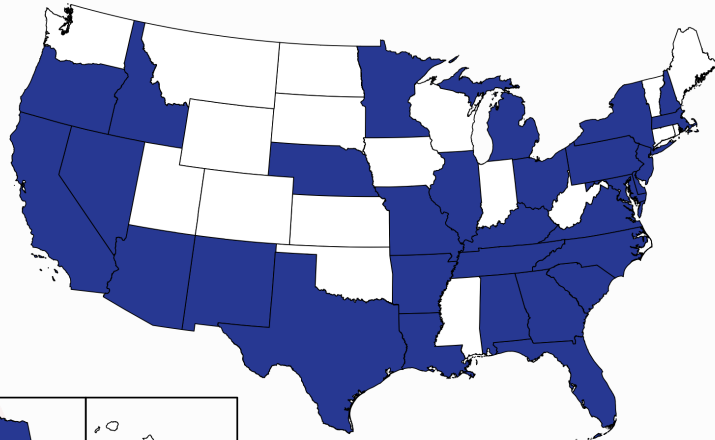
2021



Rate\*  0.0–3.0  3.1–4.8  4.9–7.5  7.6–11.4  11.5–48.7  Unavailable

# Congenital Syphilis — Reported Cases by Year of Birth and State, United States and Territories, 2012 and 2021

2012



Alaska

Hawaii



American Samoa

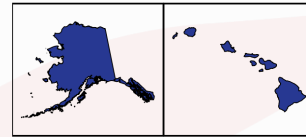
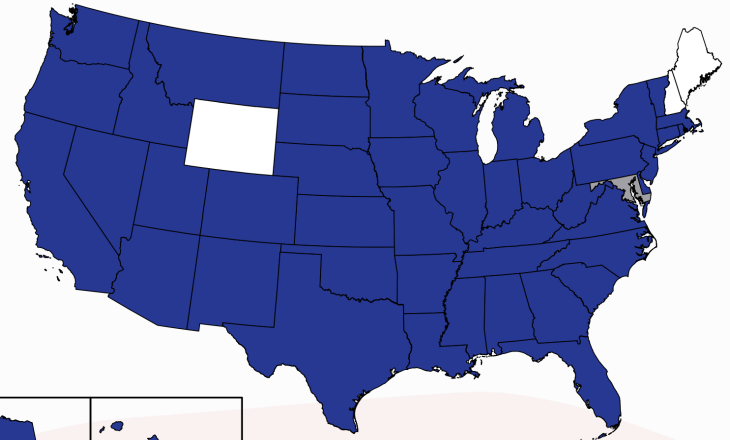
Commonwealth of the Northern Mariana Islands

Guam

Puerto Rico

US Virgin Islands

2021



Alaska

Hawaii



American Samoa

Commonwealth of the Northern Mariana Islands

Guam

Puerto Rico

US Virgin Islands

Reported Cases ■ ≥1 case  No cases  Unavailable

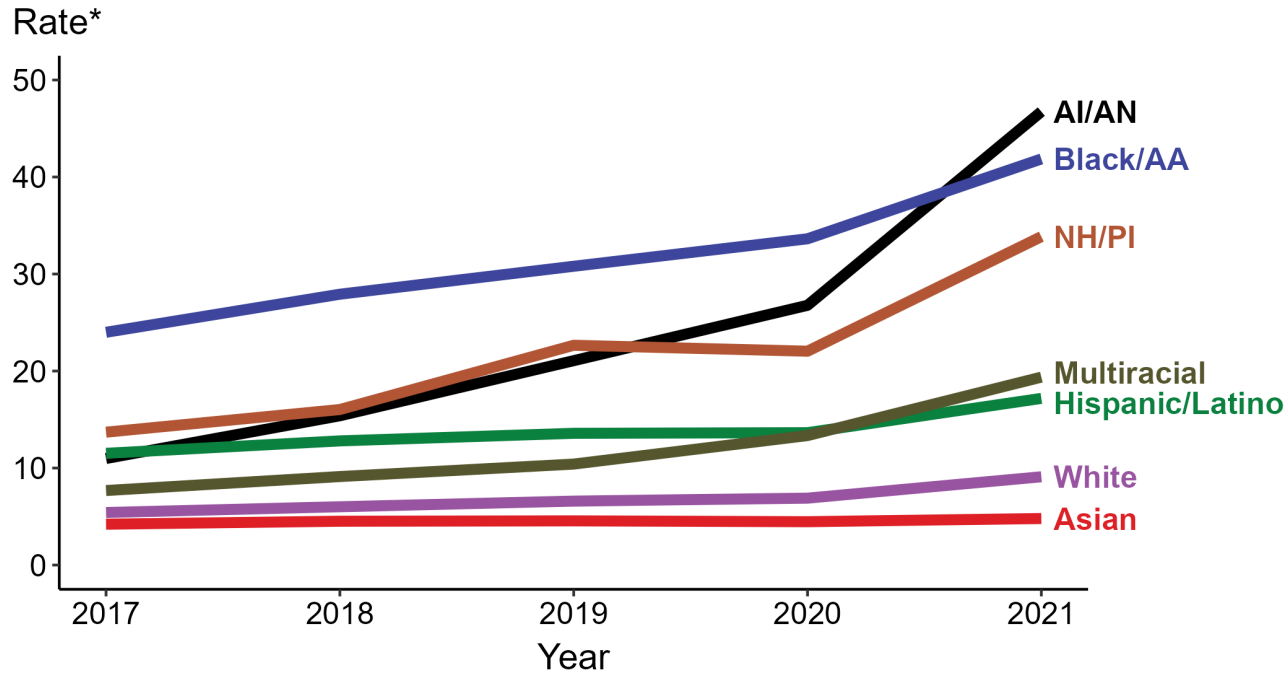
## Primary and Secondary Syphilis — Reported Cases and Rates of Reported Cases by State, Ranked by Rates, United States, 2021

Rank	State	Cases	Rate per 100,000 Population
1	South Dakota	436	48.7
2	New Mexico	724	34.2
3	Arkansas	990	32.7
4	Oklahoma	1,225	30.7
5	Nevada	939	29.9
	<b>US TOTAL</b>	<b>53,767</b>	<b>16.2</b>

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

Rank	State	Cases	Rate per 100,000 Population
1	Arizona	181	232.3
<b>2</b>	<b>New Mexico</b>	<b>44</b>	<b>205.7</b>
3	Louisiana	110	191.5
4	Mississippi	64	182.0
5	Texas	680	182.0
	<b>US TOTAL</b>	<b>2,855</b>	<b>77.9</b>

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

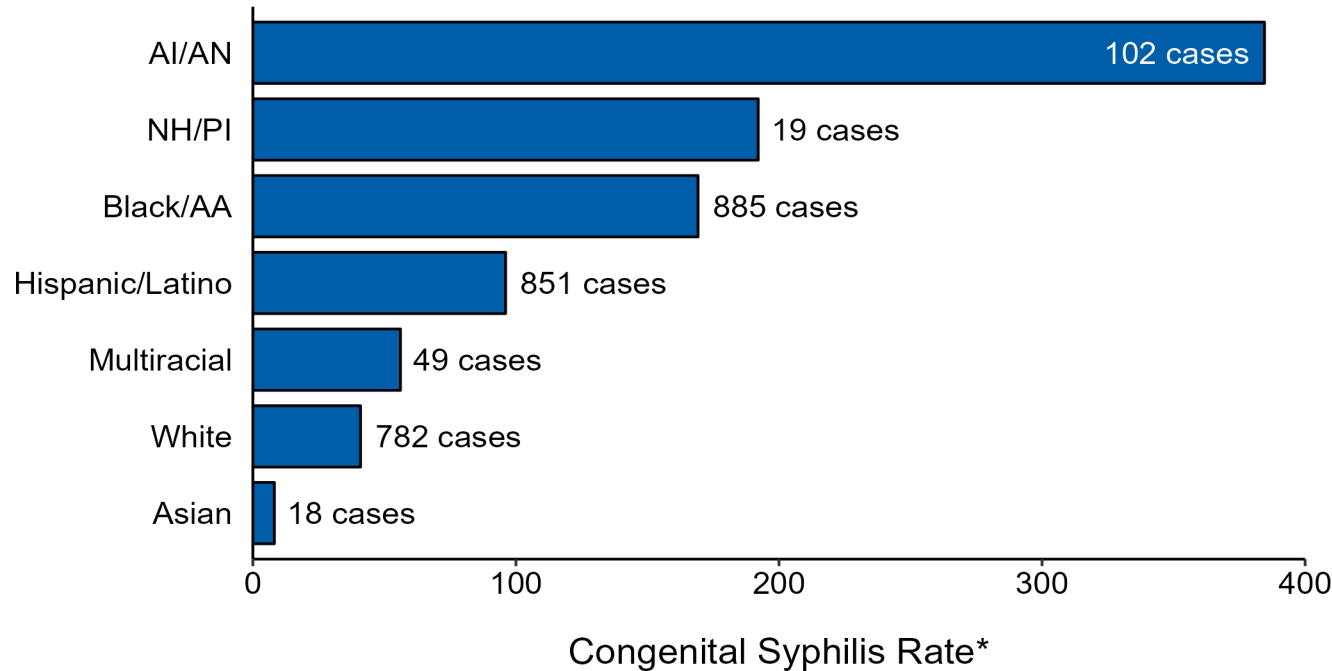


\* Per 100,000

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/2021/figures.htm>

# Congenital Syphilis – Case Counts and Rates of Reported Cases by Race/Hispanic Ethnicity of Mother, United States, 2021



In 2021, a total of 149 congenital syphilis cases (5.2%) had missing, unknown, or other race and were not reported to be of Hispanic ethnicity.

# Syphilis

- Sexually transmitted infection caused by the bacterium *Treponema pallidum*
- **Sexual** (horizontal) and vertical transmission
- Average incubation period is **21 days** (can range from 10-90 days)
- **Four stages**
  - Primary
  - Secondary
  - Early (non-primary, non-secondary)
  - Unknown duration or late





# Case Definitions: Primary Syphilis

- **A single chancre** marks the onset of primary syphilis (can be multiple)
- **Usually firm, round, and painless**  
Located where syphilis enters the body
- Can appear in **difficult to notice** locations (anus, vagina)
- **Lasts 3 to 6 weeks** and heals regardless of whether a person receives treatment
- If untreated, **will progress** to the secondary stage

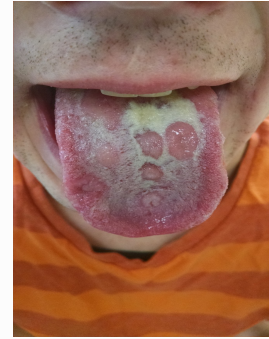


# Case Definitions: Secondary Syphilis

- **Skin rashes**
  - Usually does not itch, may appear as rough, red, brown spots
- **Mucous membrane lesions**
  - Sores in the mouth, vagina or anus mark the second stage of symptoms
- **Other symptoms:**
  - Fever, swollen lymphs, sore throat, hair loss, aches and pains
- **Resolves** regardless of whether a person receives treatment
- If untreated, **will progress** to the latent and possible tertiary stages



Torso rash



Mucous patches



Alopecia



Palmar rash



Plantar rash

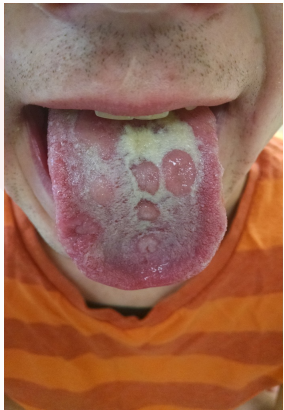


Condyloma lata

# 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 rash



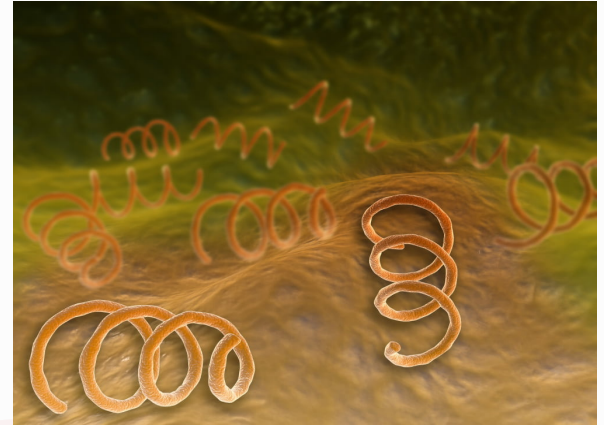
Condyloma lata



Alopecia

# Case Definitions: Latent Syphilis

- Latent (hidden) stage of syphilis is when there are no visible signs or symptoms of syphilis
- Early latent syphilis is where infection occurs **within the past 12 months**
- Late latent syphilis is where infection occurs **more than 12 months ago**
- Latent syphilis of unknown duration is when there is **not enough evidence** to confirm initial infection was within the previous 12 months

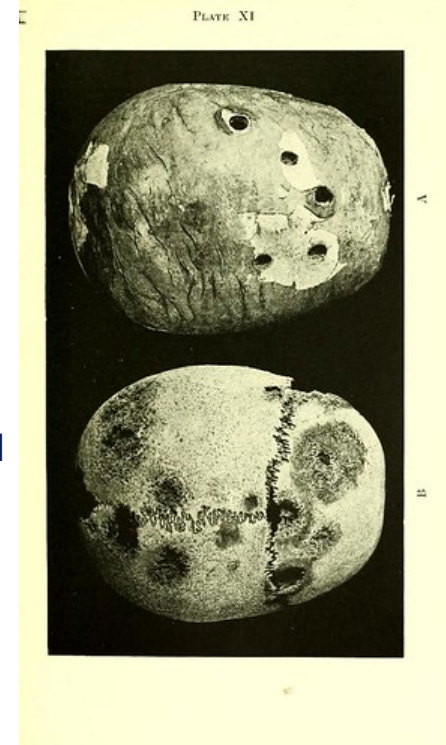


# Late Clinical Manifestations/Tertiary Syphilis

## Clinical Description

Late clinical manifestations of syphilis (tertiary syphilis) may include inflammatory lesions of:

1. Cardiovascular system (e.g., aortitis, coronary vessel disease),
2. Skin (e.g., gummatous lesions),
3. Bone (e.g., osteitis),
4. Other structures including the upper and lower respiratory tracts, mouth, eye, abdominal organs, reproductive organs, lymph nodes, and skeletal muscle)
5. Neurologic manifestations (e.g., general paresis and tabes dorsalis)

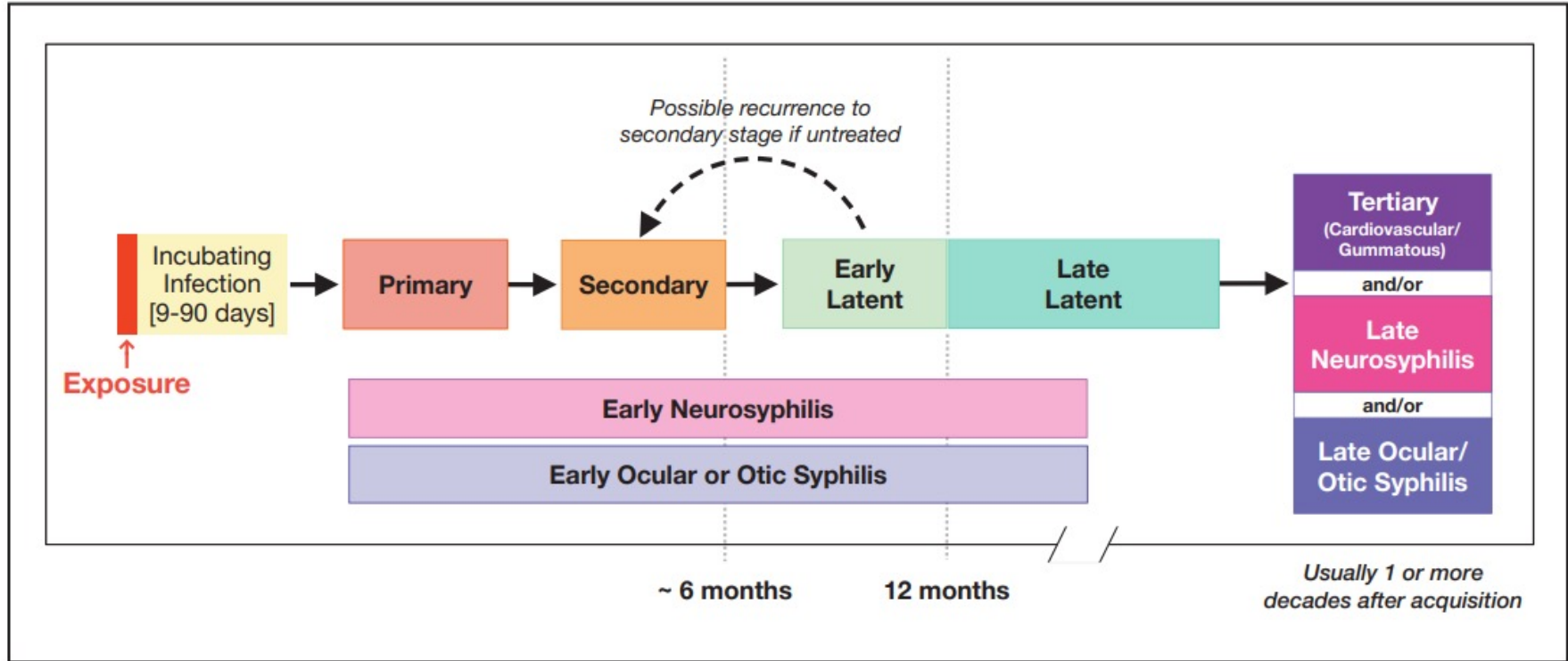




# Neurologic Manifestations can occur at any stage

Neurosyphilis	Ocular syphilis	Otosyphilis
<p>Infection of the central nervous system with <i>T. pallidum</i>, as evidenced by manifestations including:</p> <ol style="list-style-type: none"> <li>1. Syphilitic meningitis,</li> <li>2. Meningovascular syphilis,</li> <li>3. General paresis,</li> <li>4. Dementia,</li> <li>5. Tabes dorsalis</li> </ol> <p><b>Clinical Presentation:</b></p> <ul style="list-style-type: none"> <li><i>Severe headache</i></li> <li><i>Focal weakness</i></li> <li><i>Numbness</i></li> <li><i>Altered mental status</i></li> </ul>	<p>Infection of any eye structure with <i>T. pallidum</i>. Can involve any structure in the anterior and posterior eye segment including:</p> <ol style="list-style-type: none"> <li>1. Conjunctivitis</li> <li>2. Anterior, posterior or pan uveitis</li> <li>3. Posterior interstitial keratitis</li> <li>4. Optic neuropathy</li> <li>5. Retinal vasculitis</li> </ol> <p><b>Clinical Presentation:</b></p> <ul style="list-style-type: none"> <li><i>Eye pain or redness</i></li> <li><i>Floating spots in field of vision</i></li> <li><i>Sensitivity to light</i></li> <li><i>Can lead to permanent blindness</i></li> </ul>	<p><i>Infection of the cochleovestibular system with T. pallidum,</i></p> <p>Typically presents with cochleo-vestibular symptoms including</p> <ol style="list-style-type: none"> <li>1. Tinnitus</li> <li>2. Vertigo</li> <li>3. Sensorineural hearing loss</li> <li>4. Unilateral/Bilateral</li> <li>5. Have a sudden onset</li> <li>6. Progress Rapidly</li> </ol>

# The Natural History of Untreated Syphilis



# Case Definitions: Early Latent (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

(1) Report of symptoms consistent with syphilis within prior 12 months

OR

(1) Sexual contact with a known case (or sexual debut) within prior 12 months



# 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 infections 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

(1) Sexual contact with a known case > 12 months ago

OR

(1) Neurologic, ocular, otic signs without evidence of acquiring infection in prior 12 months.

# Serologic Tests for Syphilis

## Nontreponemal

- Antibodies to cardiolipin-cholesterol-lecithin antigen
- Qualitative or quantitative
- Tend to disappear with treatment
- Titer used to follow response to therapy
  - 4-fold change (two dilutions) is clinically significant
- VDRL, RPR

## Treponemal

- Antibodies to Treponemal antigens
- Qualitative
- Remain reactive for life
- Appear earlier and more specific
  - *T. pallidum* enzyme immunoassay (TP-EIA)
  - Chemiluminescence immunoassays (CLIA)
  - *T. pallidum* particle agglutination assay (TP-PA)
  - Fluorescent treponemal antibody absorption (FTA-ABS) test

# Rapid/Point-of-Care Testing

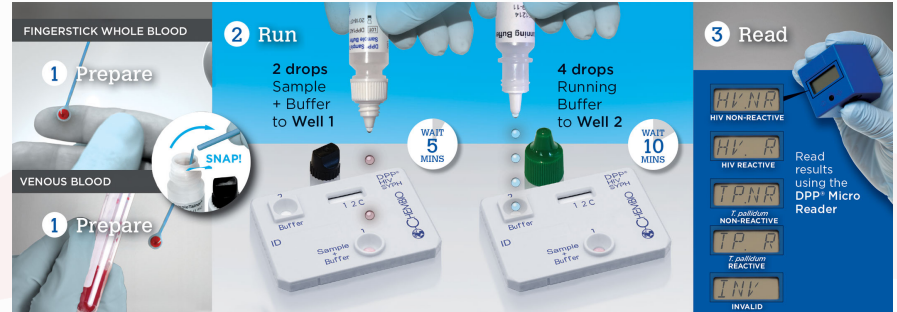
## Health Check:

Rapid syphilis test (10 minute results)  
Treponemal antibody test

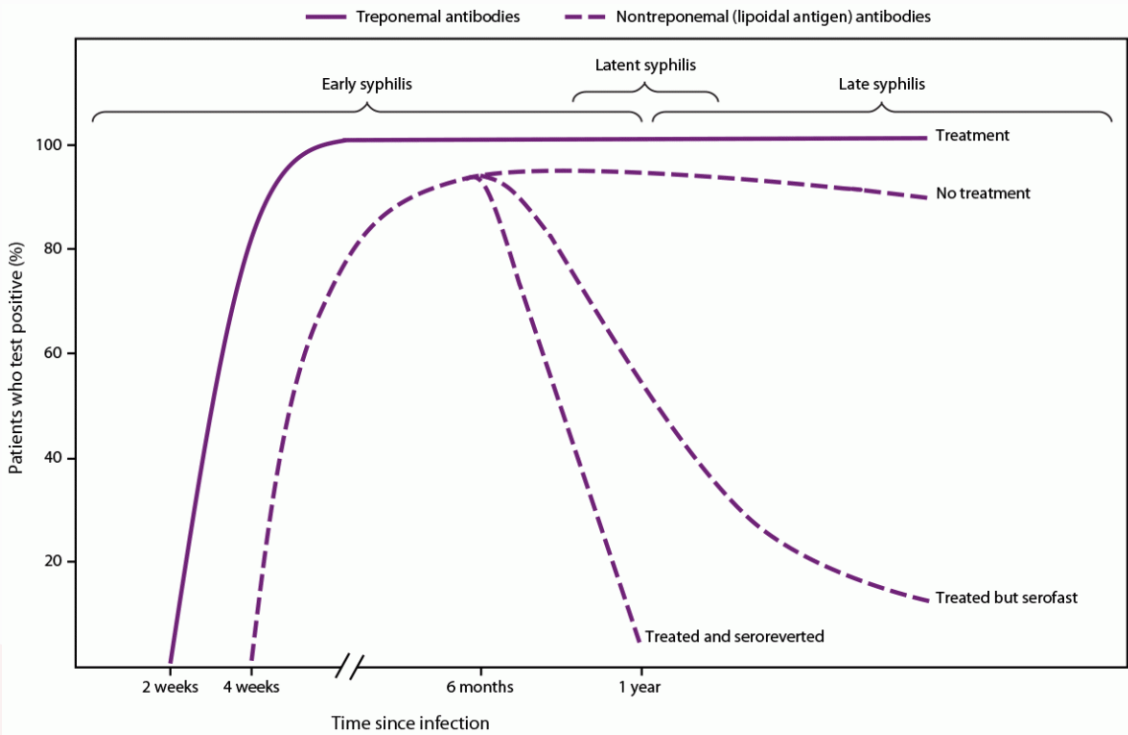


## Chembio:

Dual rapid HIV-Syphilis test (15 minute results)  
HIV-1/2 antibody test / Treponemal antibody test

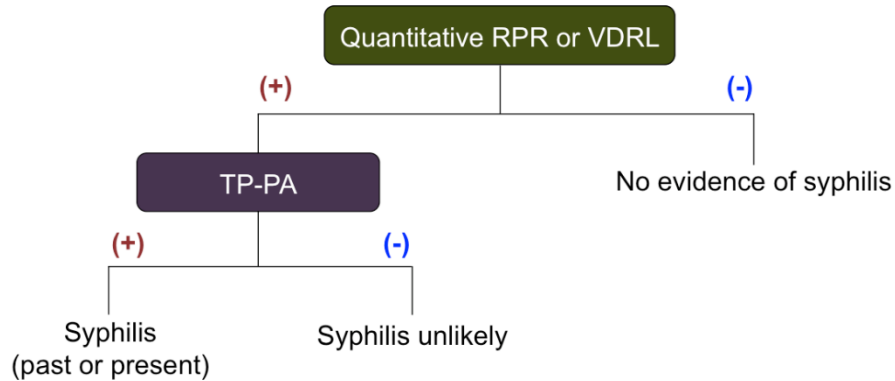


# Serologic response to infection with *Treponema pallidum*, the causative agent of syphilis

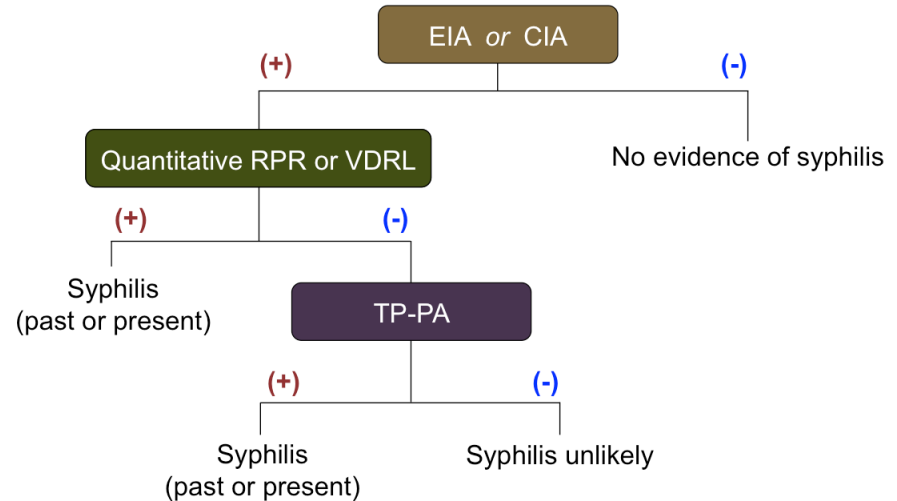


# Syphilis testing algorithms

## Traditional Sequence



## Reverse Sequence



# Syphilis Screening Guidelines

## CDC

- Asymptomatic persons at increased risk\*
- MSM - at least annually
  - Every 3 to 6 months if at increased risk
- All pregnant women at the first prenatal visit, and at 28 weeks of gestation and at delivery if at high risk\*\*

## IHS

- **Annual syphilis testing for persons ages 13 and older**
  - For at least 2 consecutive years
- Turn on the annual Electronic Health Record reminder at all sites
- Provide three-point syphilis testing for all pregnant people

\* History of incarceration or transactional sex work, residence in region with high rates, race/ethnicity with high rates, male < 29 yo

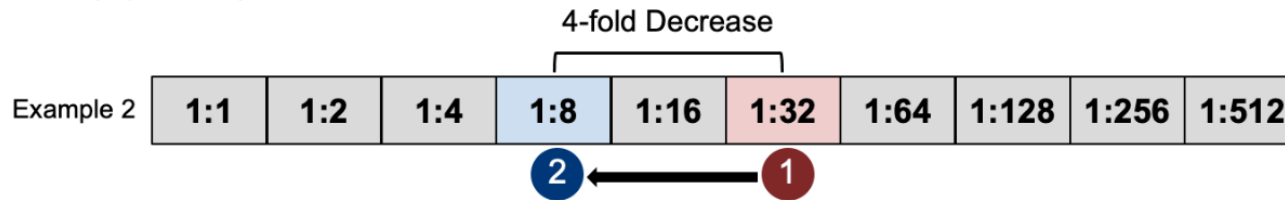
\*\*Patient lives in a community with high syphilis morbidity or is at risk for syphilis acquisition during pregnancy (SUD, STIs during pregnancy, multiple partners, a new partner, partner with STIs)

# Syphilis Treatment

STAGE		
<p><b>Primary &amp; Secondary, Early non-primary, non secondary</b></p>	<p><b>Late Latent/or Unknown Duration</b></p>	<p><b>Neurosyphilis, ocular syphilis and otosyphilis</b></p>
<p>Benzathine penicillin 2.4 million units IM in <b>a single dose</b></p> <p>Doxycycline 100mg BID for <b>14 days</b></p>	<p>Benzathine penicillin 2.4 million units total administered as <b>3 doses</b> of 2.4 million units IM each at <b>1-week intervals</b></p> <p>Doxycycline 100mg BID for <b>28 days</b></p>	<p>Aqueous crystalline penicillin G 18-24 million units per day, administered as 3-4 million units by IV <b>every 4 hours or continuous infusion for 10-14 days</b></p> <p>Alternative: procaine penicillin G 2.4 million units IM 1x/day PLUS probenecid 500 mg orally 4x/day, <b>both for 10-14 days</b></p>

# Follow-up testing

- Adequate serologic response to treatment:  $\geq 4$ -fold decline in nontreponemal titer
  - Early Syphilis Primary/secondary/early latent: within 12 months
  - Late Syphilis: Late Latent, tertiary: within 24 months
  - Persons with HIV: within 24 months
- Serofast (lack of seroreversion): persistent nontreponemal titer after treatment





# Syphilis

- **Three things every patient with syphilis needs:**
  - Neurologic system review for indications for further assessment
  - Assessment of pregnancy status
  - Baseline RPR on day of treatment
- **Neurosyphilis**
  - No longer need to repeat the lumbar puncture (LP) at 6 months after treatment
    - If patient is recovered and has no symptoms
  - In case of ocular and otic syphilis:
    - No LP needed if patient does not have neurological symptoms or findings

# Management of sex partners

- Partner A is diagnosed with primary, secondary, or early latent syphilis. If partner B had sexual contact with partner A:
  - < 90 days before the diagnosis of syphilis, then partner B **should be treated presumptively for early syphilis, even if serologic tests are negative.**
  - > 90 days before the diagnosis of syphilis, then partner B should be treated for early syphilis only if serologic tests are not available or follow-up is uncertain. If serologic tests are negative, no treatment is needed.

# DoxyPEP: Post Exposure Prophylaxis

Take **1 dose of Doxycycline 200mg** 24-72 hours after condomless sex

- Found a **65% reduction in chlamydia, gonorrhea, and syphilis** among men who have sex with men (**MSM**) and transgender women
- Further analyses are needed to determine the effects of intermittent doxycycline use on antimicrobial resistance and long-term effects on the gut
- Not for use in pregnant people.

# References

- See prior didactic on STI screening recommendations
- National STD curriculum: <https://www.std.uw.edu/>
- CDC STI Treatment Guidelines, 2021  
<https://www.cdc.gov/std/treatment-guidelines/default.htm>
- CDC guide to taking a sexual history  
<https://www.cdc.gov/std/treatment/sexualhistory.pdf>
- DHHS *Guidelines for the Use of Antiretroviral Agents in HIV-1 Infected Adults & Adolescents.*  
<https://clinicalinfo.hiv.gov/en/guidelines>

# References

- ❖ CDC STD 2021 Treatment Guideline:  
<https://www.cdc.gov/std/treatment-guidelines/default.htm>
- ❖ STD Prevention Training Centers:  
<https://www.cdc.gov/std/projects/nnptc.htm>
- ❖ STD online self-study: <https://www.std.uw.edu/>
- ❖ CDC self-study: <http://www.cdc.gov/std/training/std101/home.htm>
- ❖ USPS Task Force:  
<https://www.uspreventiveservicestaskforce.org/uspstf/>

# Resources

- National Clinician Consultation Center  
<http://nccc.ucsf.edu/>
  - HIV Management
  - Perinatal HIV
  - HIV PrEP
  - HIV PEP line
  - HCV Management
  - Substance Use Management
- Present on ECHO
  - <https://hsc.unm.edu/scaetc/programs-services/echo.html>
- AETC National HIV Curriculum  
<https://aidsetc.org/nhc>
- AETC National Coordinating Resource Center  
<https://targethiv.org/library/aetc-national-coordinating-resource-center-0>
- HIVMA Resource Directory  
<https://www.hivma.org/globalassets/ektron-import/hivma/hivma-resource-directory.pdf>
- Additional trainings  
[scaetcecho@salud.unm.edu](mailto:scaetcecho@salud.unm.edu)
- [www.scaetc.org](http://www.scaetc.org)

# Resources

- National Clinician Consultation Center <http://nccc.ucsf.edu/>
  - HIV Management
  - Perinatal HIV
  - HIV PrEP
  - HIV PEP line
  - HCV Management
  - Substance Use Management
- Present case on ECHO <https://echo.unm.edu/locations-2/echo-hubs-superhubs-united-states/>
- AETC National HIV Curriculum <https://aidsetc.org/nhc>
- AETC National Coordinating Resource Center <https://targethiv.org/library/aetc-national-coordinating-resource-center-0>
- Additional trainings [scaetcecho@salud.unm.edu](mailto:scaetcecho@salud.unm.edu)
- [www.scaetc.org](http://www.scaetc.org)

# IHS/Tribal Resources

- Sexually Transmitted Infections (STI) Initiative: STI Toolkit. [https://www.ihs.gov/sites/nptc/themes/responsive2017/display\\_objects/documents/sti/Express-STI-Guide.pdf](https://www.ihs.gov/sites/nptc/themes/responsive2017/display_objects/documents/sti/Express-STI-Guide.pdf)
- <https://www.indiancountryecho.org/resource-hubs/syphilis-resources/> The STOP SYPHILIS campaign offers free materials, including print materials, social media posts, and short educational videos.
- Go to [www.stopsyphilis.org](http://www.stopsyphilis.org) For questions about field testing and treatment policies and procedures, contact Tina Tah, Public Health Nursing Consultant, by e-mail at [tina.tah@ihs.gov](mailto:tina.tah@ihs.gov)