

Indian Health Service

Syphilis Response: Best Practices

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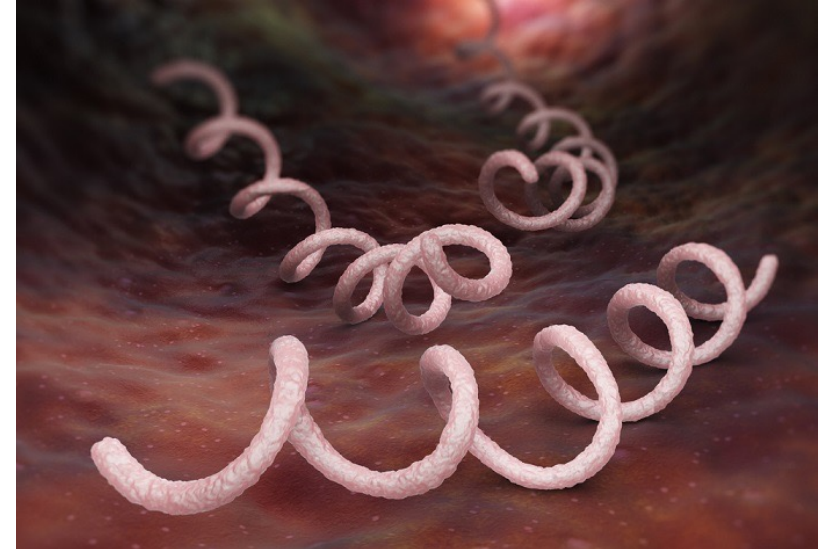
NATIONAL HIV/HCV/STI PROGRAM, IHS HQ

SEPTEMBER 24, 2024

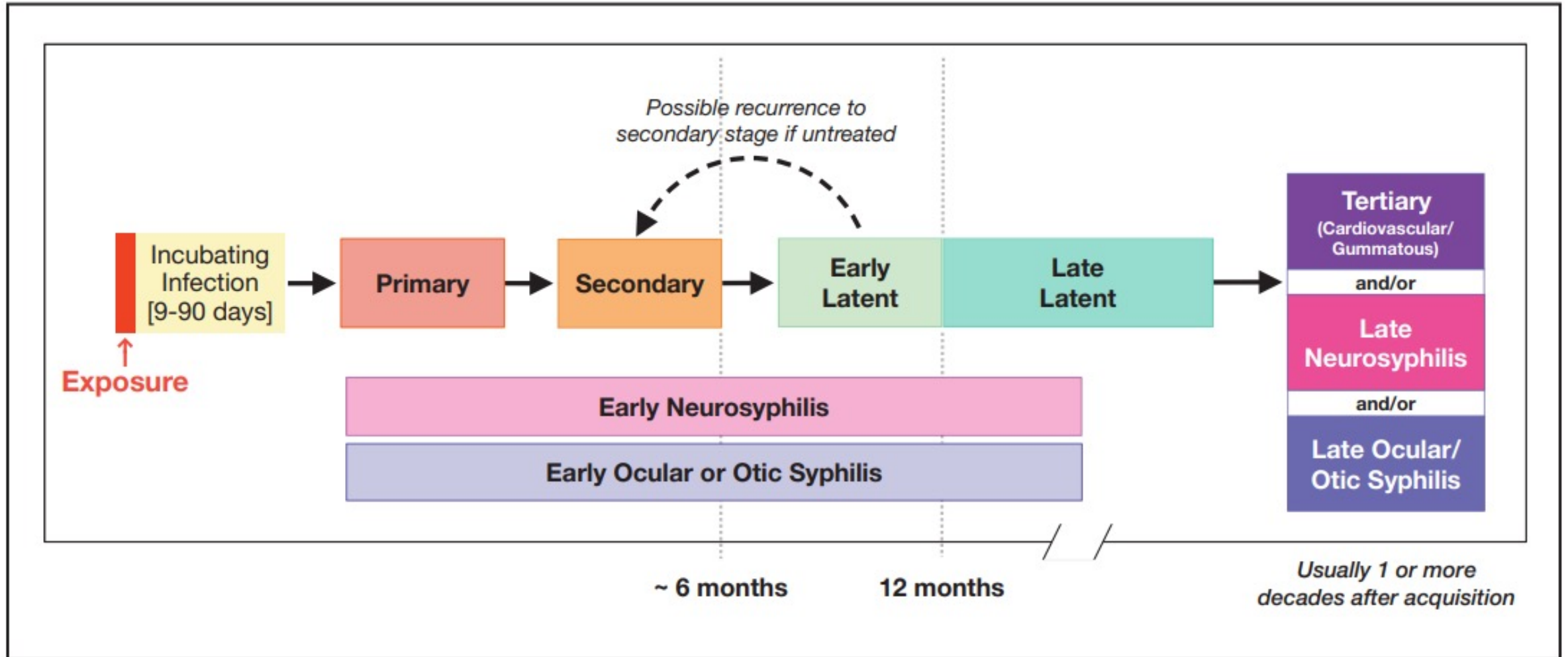


Syphilis

- Sexually transmitted infection (STI) caused by the bacterium *Treponema pallidum*
- Sexual, vertical and horizontal transmission
- Average time between syphilis acquisition and start of symptoms is 21 days (can range from 10-90 days)



The Natural History of Untreated Syphilis



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 locations that are difficult to notice (anus, vagina)
- Lasts 3 to 6 weeks and heals regardless of whether a person receives treatment
- If untreated, will progress to the secondary stage



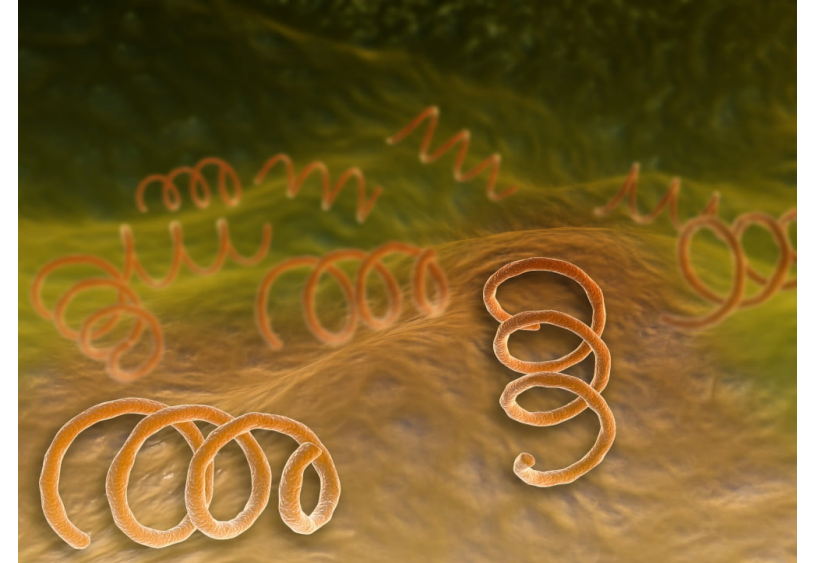
Secondary Syphilis

- Skin rashes and/or mucous membrane lesions (sores in the mouth, vagina or anus) mark the second stage of symptoms
- Usually does not itch, may appear as rough, red, brown spots
- May be accompanied by 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 stage



Latent Syphilis

- Latent (hidden) stage of syphilis is when there are no visible signs or symptoms of syphilis
- Early latent syphilis is latent syphilis where infection occurs **within the past 12 months**
- Late latent syphilis is latent syphilis 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



Neurologic Manifestations of Syphilis

Can occur at any stage

Neurosyphilis (Nervous System)	Ocular Syphilis (Visual System)	Otosyphilis (Auditory/Vestibular System)
<ul style="list-style-type: none">- Severe headache- Trouble with muscle movements- Paralysis- Numbness- Altered mental status	<ul style="list-style-type: none">- Eye pain or redness- Floating spots in field of vision- Sensitivity to light- Can lead to permanent blindness	<ul style="list-style-type: none">- Ringing in ears (tinnitus)- Balance difficulties- Vertigo- Can lead to permanent hearing loss

Congenital Syphilis

- Occurs when a pregnant person with syphilis passes the infection on to their baby during pregnancy
- Testing for pregnant people is recommended at the **first prenatal visit, during the third trimester (28 weeks), and at the time of delivery**
- Any person who delivers a **stillborn infant after 20 weeks gestation** should receive testing for syphilis
- Untreated syphilis in pregnant people results in infant death in **up to 40 percent** of cases



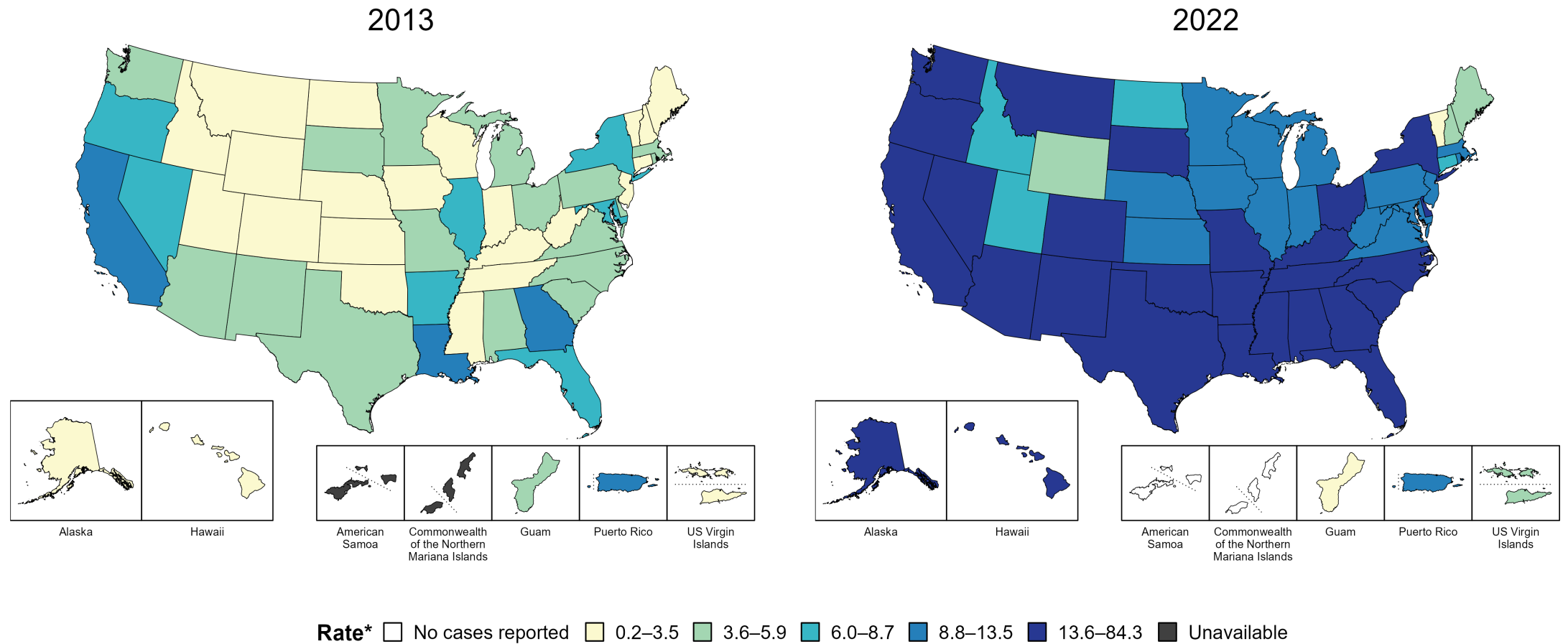
Congenital Syphilis

- Syphilitic Stillbirth is defined as a fetal death that occurs **after 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 the completion of a penicillin-based regimen, in accordance with CDC treatment guidelines, appropriate for the stage of infection, **initiated 30 or more days before delivery**

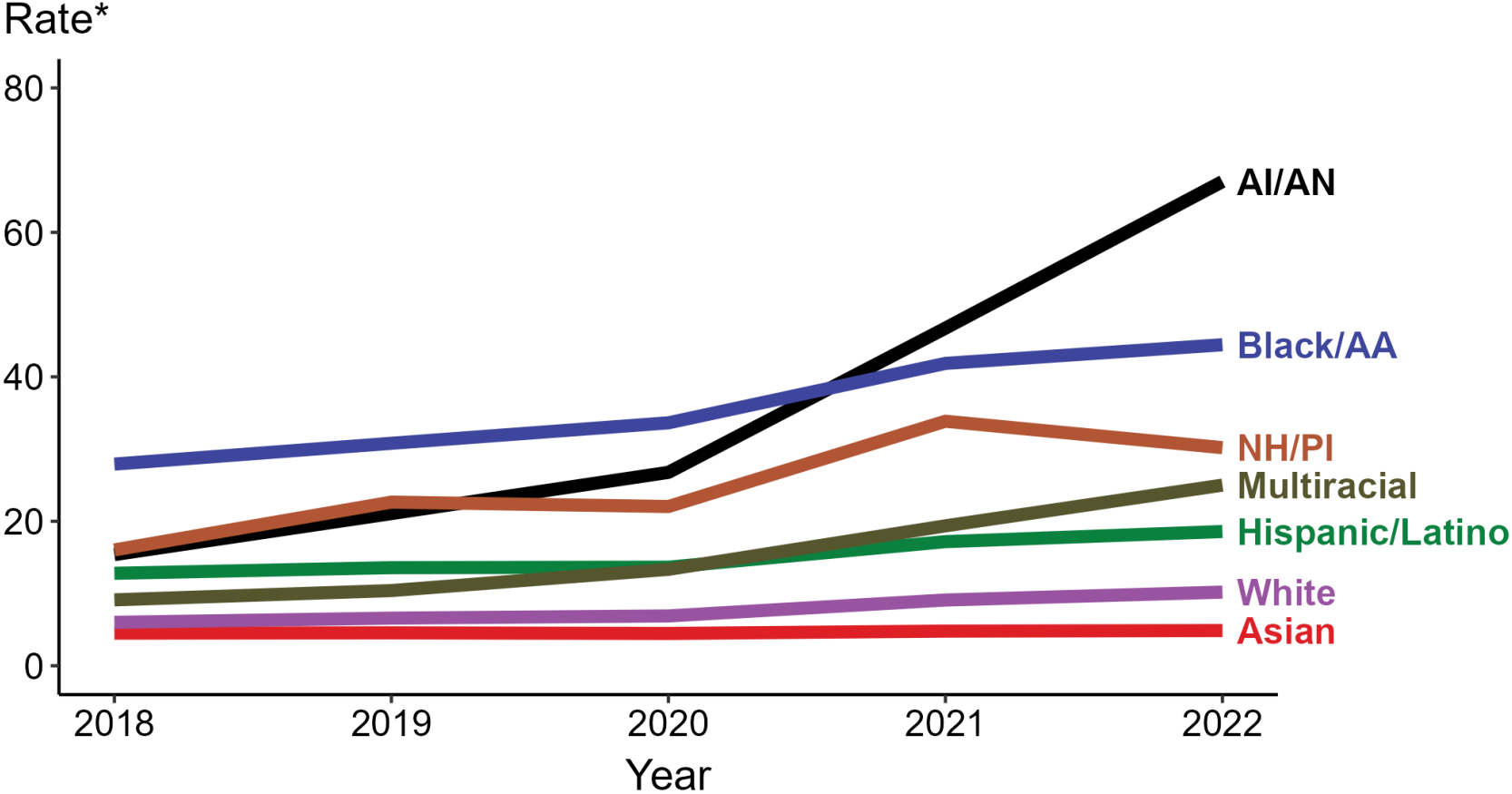
Treatment (Congenital Syphilis)

Scenario 1: Confirmed, proven or highly probable congenital syphilis	Scenario 2: Possible congenital syphilis	Scenario 3: Congenital syphilis less likely	Scenario 4: Congenital syphilis unlikely
<p>Neonate with a physical exam consistent with CS, nontreponemal serology 4-fold greater than mother's</p>	<p>Normal physical exam and a serum nontreponemal titer equal to or < 4-fold of the maternal titer at delivery and one of the following:</p> <ol style="list-style-type: none"> 1) The mother was not treated, was inadequately treated, or has no documentation of treatment 2) The mother was treated with erythromycin or a regimen not recommended in these guidelines 3) The mother received recommended regimen but treatment was initiated <30 days before delivery 	<p>Neonate with a normal physical examination and a serum nontreponemal titer equal to or <4-fold of the maternal titer at delivery and both of the following are true:</p> <p>The mother was treated during pregnancy and the mother has no evidence of reinfection or relapse</p>	<p>Neonate with: a normal physical exam, serum nontreponemal serology equal to or less than 4-fold mother's at delivery and, mother's treatment was adequate before pregnancy, mother's nontreponemal titer remained low and stable before and during pregnancy and at delivery</p>
<p>Evaluation: CSF with VDRL, cell count, protein, CBC/diff, long bone radiographs, neuro eval (eye, auditory)</p>	<p>CSF with VDRL, cell count, CBC/ diff, long-bone radiographs</p>	<p>No evaluation is recommended</p>	<p>No evaluation is recommended</p>
<p>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 Procaine penicillin G 50,000 units/kg body weight/dose IM in a single daily dose for 10 days</p>	<p>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 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</p>	<p>Treatment: Benzathine penicillin G 50,000 units/kg body weight/dose IM in a single dose</p>	<p>No treatment recommended</p>

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

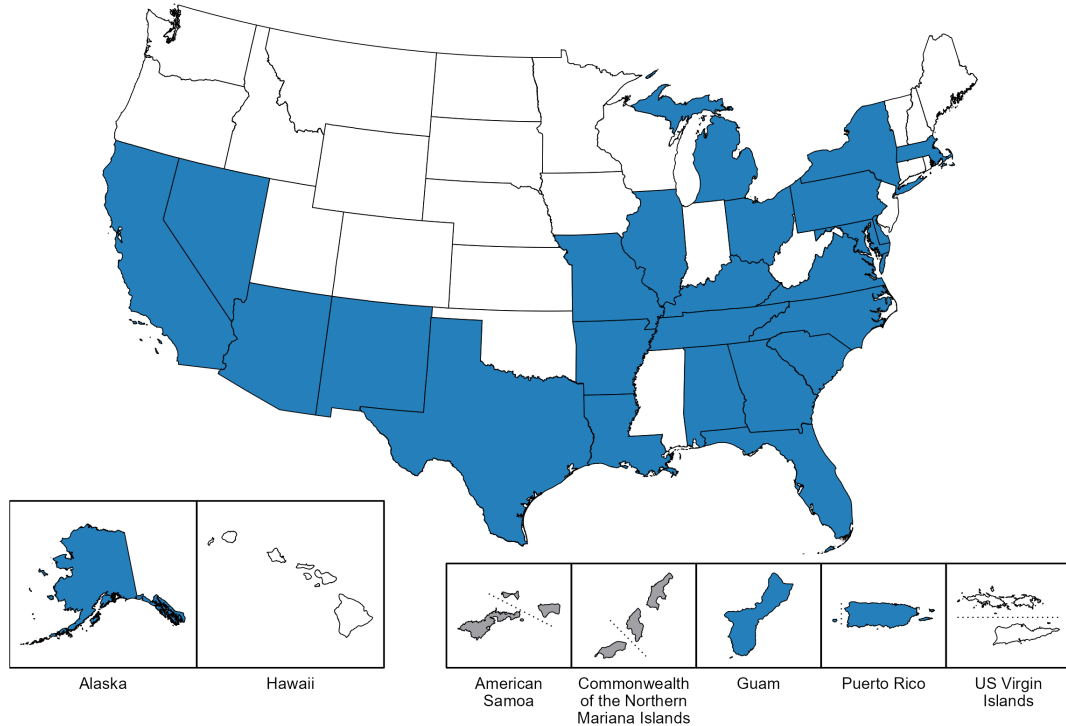


Primary and Secondary Syphilis — Rates of Reported Cases by Race/Hispanic Ethnicity, United States, 2018–2022

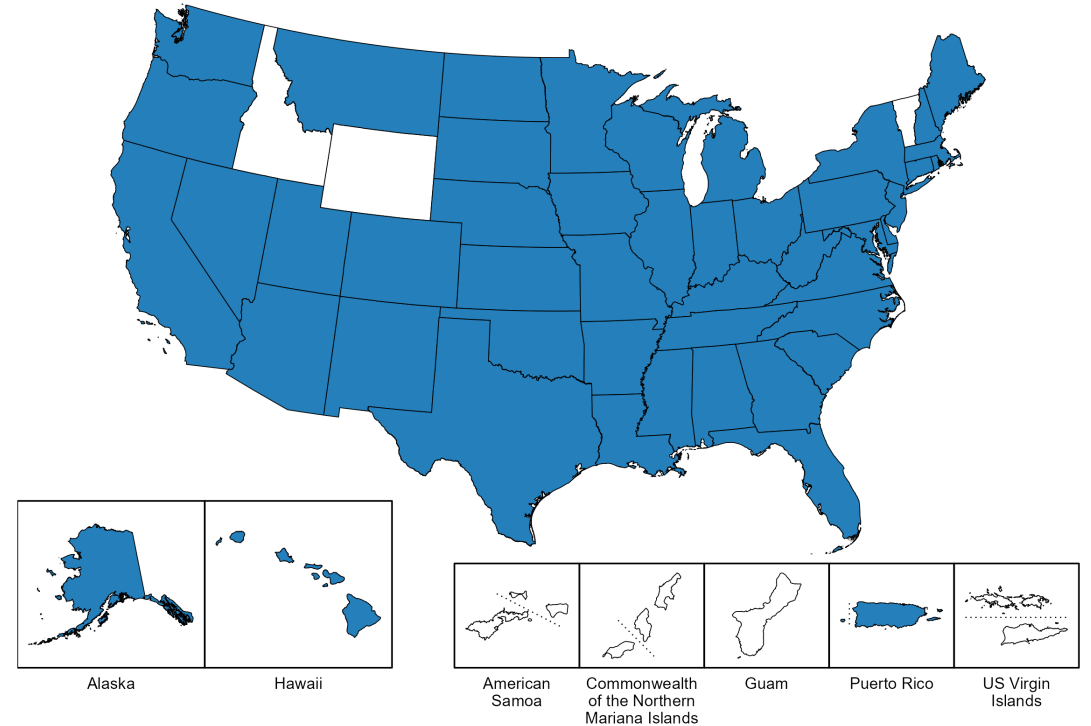


Congenital Syphilis — Reported Cases by Year of Birth and Jurisdiction, United States and Territories, 2013 and 2022

2013

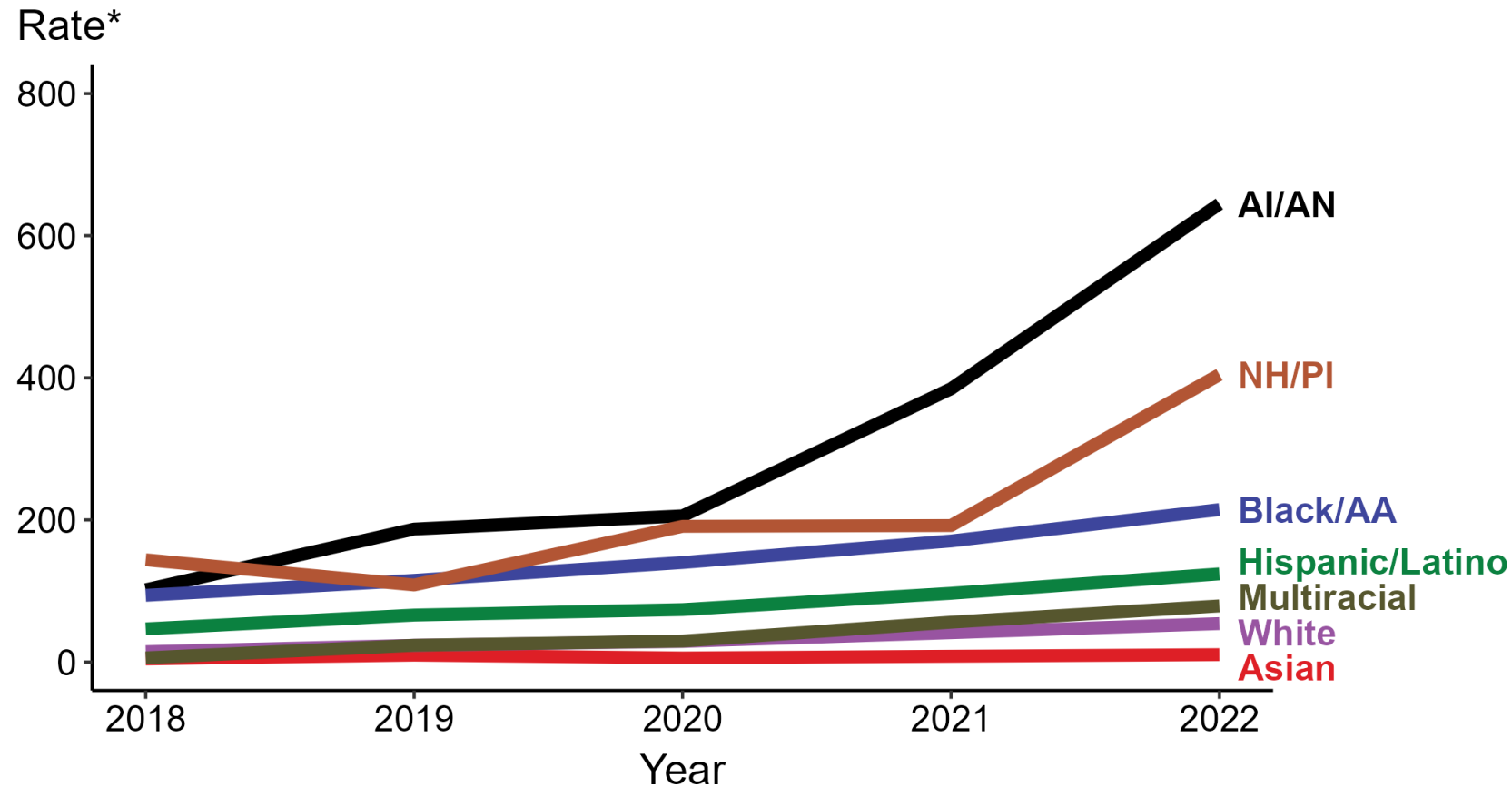


2022



Reported Cases ■ ≥1 case □ No cases ■ Unavailable

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



CMO letter

- **Offer annual syphilis testing** for persons aged 13 and older to eliminate syphilis transmission by early case recognition
- Prescribe and administer **Penicillin G Benzathine for every age and every stage** of syphilis infection in the absence of contraindications to therapy
 - The IHS National Supply Service Center (NSSC) and IHS Pharmaceutical Prime Vendor report that all orders for Bicillin are currently being fulfilled
 - For questions about how to order this medication, please get in touch with Weston.Thompson@ihs.gov at NSSC
- **Turn on the annual Electronic Health Record reminder** at all sites to facilitate testing for two years or until incidence rates decrease locally to baseline

CMO letter

- **Provide three-point syphilis testing for all pregnant people** at the first prenatal visit, the beginning of the third trimester, and delivery
- Adoption of an **HIV/Viral Hepatitis/STI testing bundle** (plus pregnancy test when appropriate) at all sites to screen broadly:
 - Syphilis screening test with reflex rapid plasma regain and treponema pallidum particle agglutination
 - HIV serology (with documentation of consent if required in the local state jurisdiction)
 - Screening for gonorrhea and chlamydia at three sites: Urine, Pharynx, Rectum
 - Screening for hepatitis B and C
 - Pregnancy test

CMO Letter

- Adopt and **provide Express STI Testing** services at all sites
 - Provide universal screening and treatment for syphilis in **Urgent Care and Emergency Department settings**, as many individuals utilize Urgent Care and Emergency Departments as their primary access to care
- Provide field testing outside hospitals and clinics to increase screening rates
 - Utilize **point-of-care, rapid syphilis, or dual HIV/syphilis antibody tests** in order to provide **immediate treatment**
- Provide **field treatment for syphilis** whenever necessary for adults diagnosed with syphilis and their partners
 - Note: When field testing, **provide immediate treatment** following a reactive syphilis antibody result if there is uncertainty that the individual may not follow up appropriately

Rapid/Point-of-Care Testing

Healthcheck: Rapid syphilis test (10 minute results)

Treponemal antibody test

[Diagnosics Direct VSC-11-01 - McKesson Medical-Surgical](#)



Rapid/Point-of-Care Testing

Chembio: Dual rapid HIV-Syphilis test (15 minute results)

HIV-1/2 antibody test / Treponemal antibody test

[Chembio Diagnostic 65-9502-0 - McKesson Medical-Surgical](#)

1 Prepare
FINGERSTICK WHOLE BLOOD
VENOUS BLOOD

2 Run
2 drops Sample + Buffer to Well 1
4 drops Running Buffer to Well 2
WAIT 5 MINS
WAIT 10 MINS

3 Read
Read results using the DPP Micro Reader

HIV NON-REACTIVE
HIV REACTIVE
T. pallidum NON-REACTIVE
T. pallidum REACTIVE
INVALID



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



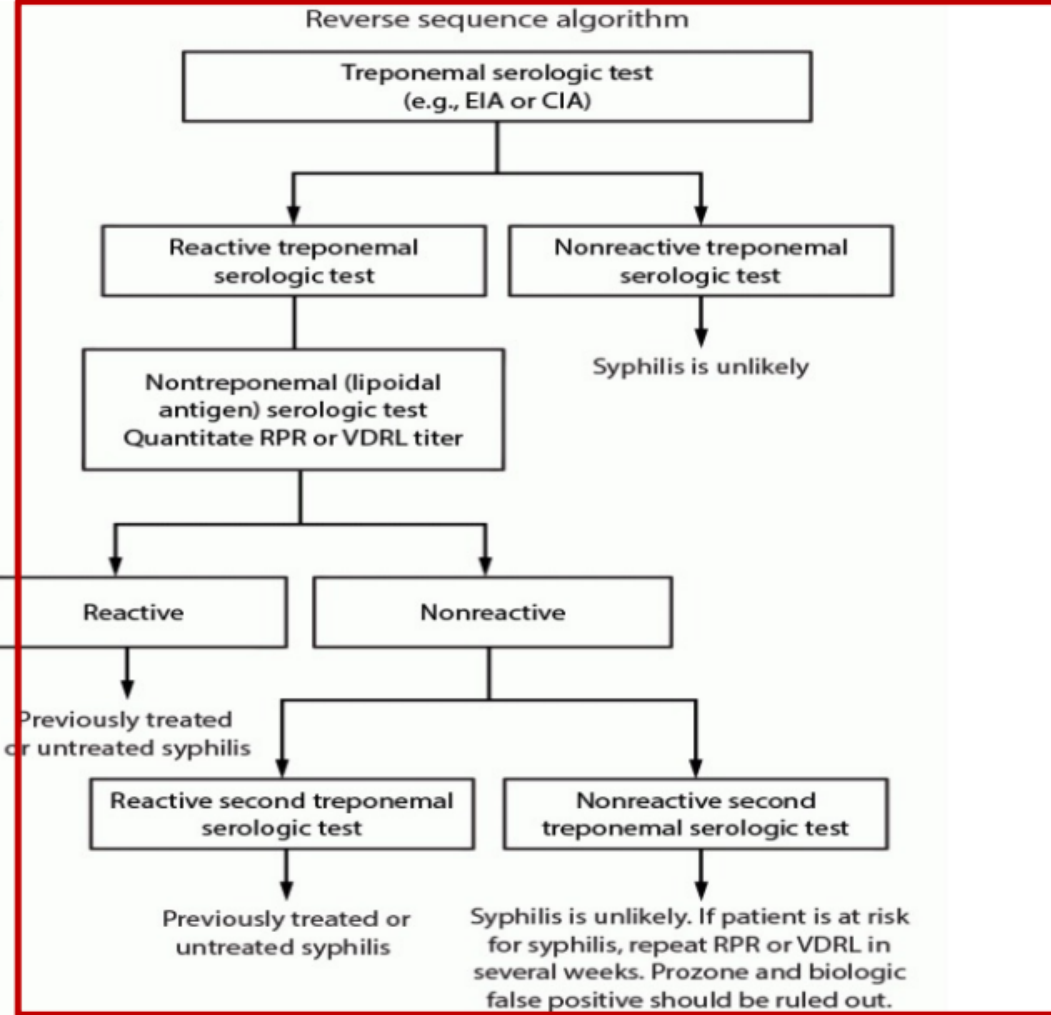
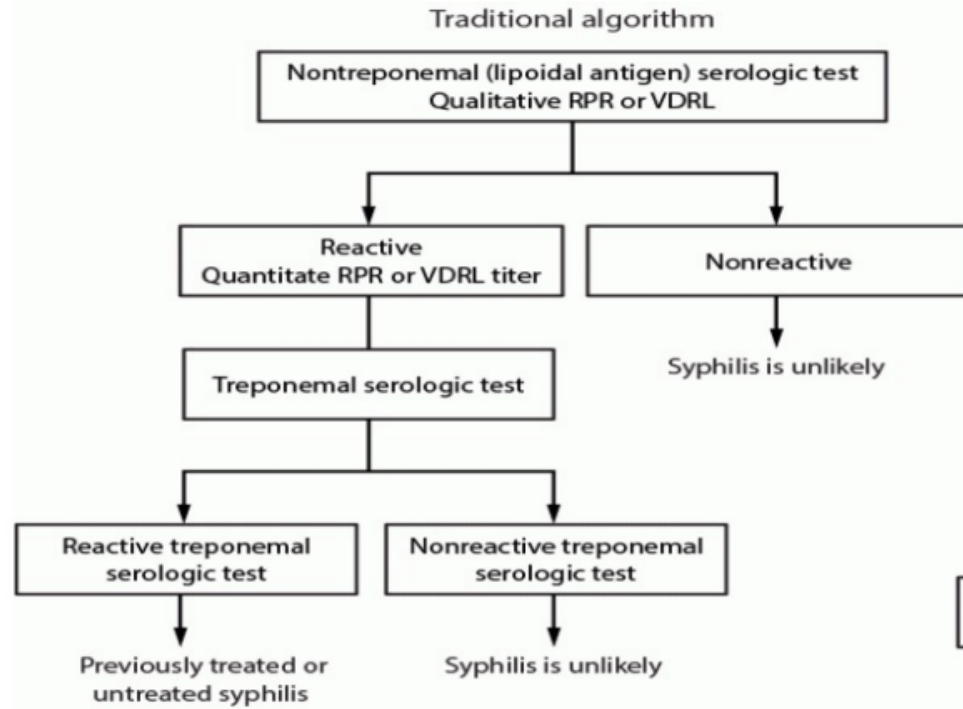
Visit iwantthekit.org and <https://spthb.org/programs/our-grants/native-test/>

- **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](#)

Serologic Diagnosis of Syphilis



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

Prozone Effect

- Rare false-negative phenomenon (most common with primary and secondary syphilis, people living with HIV, pregnancy), even when symptomatic
- The detection of antigen-antibody interactions is dependent on the formation of antigen-antibody complexes that clump cells together
- Excess antibodies in serum or antigens in the assay can interfere with the development of a lattice if each antibody molecule binds to a single antigen epitope
- Only occurs with nontreponemal tests (RPR, VDRL)
- Higher dilutions needed to remove the prozone, clinicians have to request (labs do not know stage of syphilis)

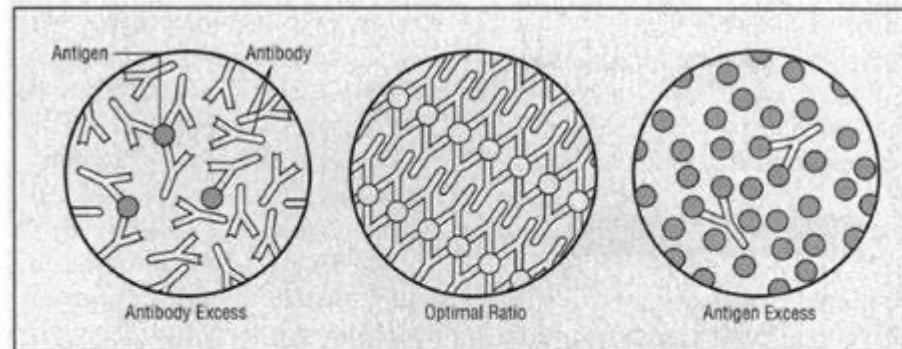


Figure 2. The optimal ratio of antigen to antibody (middle) yields an insoluble precipitate in the classic precipitation test. The prozone phenomenon occurs in the situation depicted to the left (antibody excess). By diluting the specimen with antibody excess, the optimal antigen-antibody ratio will be obtained and the test will become positive.¹⁹

CMO Letter

- **Presumptive treatment of syphilis** for anyone having signs or symptoms of syphilis or with known exposure to syphilis
 - Provide testing and treatment with Penicillin G Benzathine for all contacts and partners, including non-beneficiaries
- **Offer and provide DoxyPEP** to appropriate populations indicated in the IHS guidelines to prevent bacterial STIs, including syphilis, chlamydia and gonorrhea



Treatment

STAGE		
Primary & Secondary, Early non-primary, non secondary	Late Latent/or Unknown Duration	Neurosyphilis, ocular syphilis and otosyphilis
Benzathine penicillin 2.4 million units IM in a single dose Doxycycline 100mg BID for 14 days	Benzathine penicillin 2.4 million units total administered as 3 doses of 2.4 million units IM each at 1- week intervals Doxycycline 100mg BID for 28 days	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 Alternative: procaine penicillin G 2.4 million units IM 1x/day PLUS probenecid 500 mg orally 4x/day, both for 10-14 days

Field Treatment

- Necessary components to initiate treatment of syphilis in the field:
 - Standing Orders
 - Availability of public health nursing staff
 - Coordination with pharmacy
- Temperature controlled coolers for maintaining PCN at 2-8°C
- Emergency kit with epi-pen and standing orders that cover use
- Flexibility/availability to meet patients



Eligibility

Field treatment is offered for patients with syphilis or other STIs who cannot access care at a facility:

- Transportation difficulties
- Child care
- Privacy concerns
- Substance use
- Pregnancy with limited/lack of prenatal care



Concerns

- Misconceptions re: penicillin allergy
 - Majority of patients listed as having a penicillin allergy were not allergic



Considerations

- Personnel: avoid providing care alone – team with PHN, pharmacist, tribal STI worker, or any other approved staff
- Confirm that there is adequate cell phone service and emergency services (911 and EMS) are available
 - Medical questions
 - Security
 - Roadside assistance
- Screen for exclusionary criteria: history of true penicillin allergy and/or serious complications
- Ensure all supplies and equipment are available for transport

DoxyPrEP (Pre-Exposure Prophylaxis)

Take **Doxycycline 100mg daily** prior to having condomless sex

In a pilot study, 30 MSM living with HIV with previous syphilis (two or more episodes since HIV diagnosis) were randomly assigned to doxycycline 100 mg for 48 weeks versus a financial incentive-based behavioral intervention

Results: **73% reduction in any bacterial STI** at any site for the intervention group, without substantial differences in sexual behavior



DoxyPEP: Post Exposure Prophylaxis

Take **1 dose of Doxycycline 200mg** within 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
- CDC and IHS have released guidelines:
 - A reminder that current studies have shown effectiveness among MSM and transgender women, but not yet among cis-gender women or other populations
 - Only Doxycycline has been studied, no other antibiotics

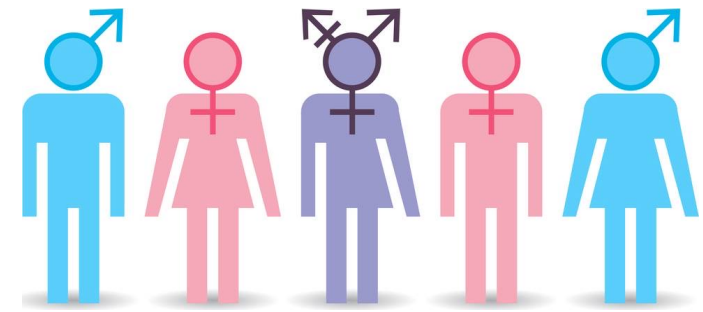


Considerations

- Further analyses needed to determine effects of intermittent doxycycline use on antimicrobial resistance and long-term effects on the gut
- Not enough evidence to broadly include populations outside of MSM/TGW in guidelines at this time
 - One study conducted in Kenya did not show a significant decrease in STIs, but medication adherence was a factor
 - DoxyPEP study currently recruiting women in US
- Doxycycline is contraindicated for pregnant people. Doxycycline may cause fetal tooth staining and decay

Doxycycline Analysis

- **Mucosal Pharmacology of Doxycycline for Bacterial STI Prevention in Men and Women (first pharmacologic data on mucosal doxycycline at the STI exposure site)**
 - Eleven cis-gender males and nine females supplied blood and mucosal swabs up to seven days after receiving a single dose of Doxycycline 200mg
 - Rectal, vaginal, cervical biopsies, urethral swabs were collected 24 hours after taking medication
- **Findings: Doxycycline exposure was found up to 96 hours in rectal and vaginal secretions and was twice that of the plasma concentration**
 - Doxy levels remained above the minimum inhibitory concentrations for at least:
 - Four days for *chlamydia trachomatis*
 - Three days for *Treponema pallidum*
 - Two days for *Neisseria gonorrhoeae*
 - Doxycycline effectively spreads to mucosal sites and the data calculates high vaginal efficacy



Implementation

- Who should receive DoxyPEP?
 - MSM/TGW on HIV PrEP or living with HIV
 - If not on HIV PrEP, MSM/TGW with history of STIs within the past 12 months, engages in sex work, has sex under the influence of drugs (chemsex)
- 3-month schedule: Provide enough meds and replenish after HIV/STI screening
- If patient is having signs and symptoms of an STI:
 - Should get immediate testing and treatment; abstain until 1 week post-treatment
- ICD-10 diagnosis code: Z20.2
(Contact with and [suspected] exposure to infections with a predominantly sexual mode of transmission)

Marketing

- Dating/Hook-up Apps
 - Grindr has agreed to provide four free advertisements a year for any I/T/U program
 - Ads are turned on for 24 hours at a time
- NPTC medication update
- IHS STI webpage
- Indian Country ECHO
- New IHS HIV PrEP Guidelines



STI PREVENTION
DoxyPEP

What is DoxyPEP?
A post-exposure preventative treatment for syphilis, chlamydia, and gonorrhea.

Why take DoxyPEP?

- To reduce the risk of getting a sexually transmitted infection (STI).
- To prevent the spread of STIs.

How to take DoxyPEP?

- Take 2 tablets of Doxycycline within 72 hours of a condomless sex.
- One dose of Doxycycline per day.

Who can take DoxyPEP?
DoxyPEP is recommended for gay, bisexual, and other cis-gender men who have sex with other men and transgender women with a history of at least one bacterial STI (gonorrhea, chlamydia or syphilis) in the last 12 months.

Important to know:

- DoxyPEP is not a replacement for HIV PEP or PrEP.
- Take DoxyPEP as prescribed.
- Talk to your provider about DoxyPEP.

For more information, please contact your local healthcare facility or your primary care provider. To learn more visit <https://www.drown.org/services/doxypep/>



Incentives

- Used to enhance screening and adherence to treatment
- \$30 limit per person/per visit
- Can not come in the form of cash or anything that can easily be converted into cash
- [IHS pharmacist-led STI screening program resulted in 10 fold increase using incentives](#)



Resources

- Sexually Transmitted Infections (STI) Initiative: STI Toolkit
- Reference the Syphilis Resources Hub online at <https://www.indiancountryecho.org/syphilis-resources>
- The **Native Health Resources** offer free materials, including print materials, social media posts, and short educational videos. Go to [Home | Native Health Resources](#)
- 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 or Melissa Wyaco, Navajo Area Nursing Consultant, by e-mail at melissa.wyaco@ihs.gov

Contact Information

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