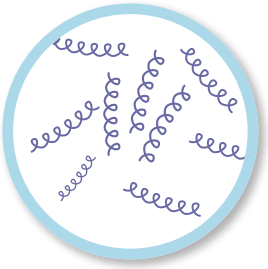
Together against syphilis

Protecting American Indian and Alaska Native communities

Syphilis cases are on the rise



Treponema pallidum, the bacteria that causes syphilis, is spread through contact with infectious lesions during oral, anal, and vaginal sex. Typically, it is most transmissible early after infection.

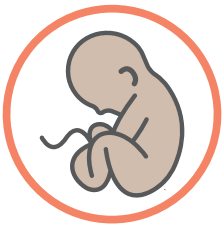
It can also cross the placenta during pregnancy and cause adverse birth outcomes including stillbirth and neonatal death.

American Indian and Alaska Native people had the highest rates of syphilis in 2022.[1]

Cases of syphilis have nearly doubled from 2018 to 2022.

2x

Congenital syphilis rates rose more than 5-fold during the same period.



5x

Almost 9 in 10 cases could have been prevented with testing and treatment.[2]

If left undiagnosed and untreated, syphilis can progress with devastating consequences.

FIGURE 1. Risks of untreated syphilis

Adults

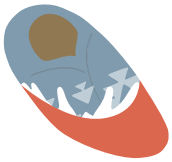
- Psychiatric manifestations (e.g., memory loss, personality changes)
- Brain infection
- Eye infection, blindness
- Ear infection, deafness
- Cardiovascular syphilis

Pregnant patients

Transmission to the fetus or unborn baby resulting in:

- Pregnancy loss
- Early delivery
- Stillbirth
- Death of infant shortly after birth
- Low birth weight

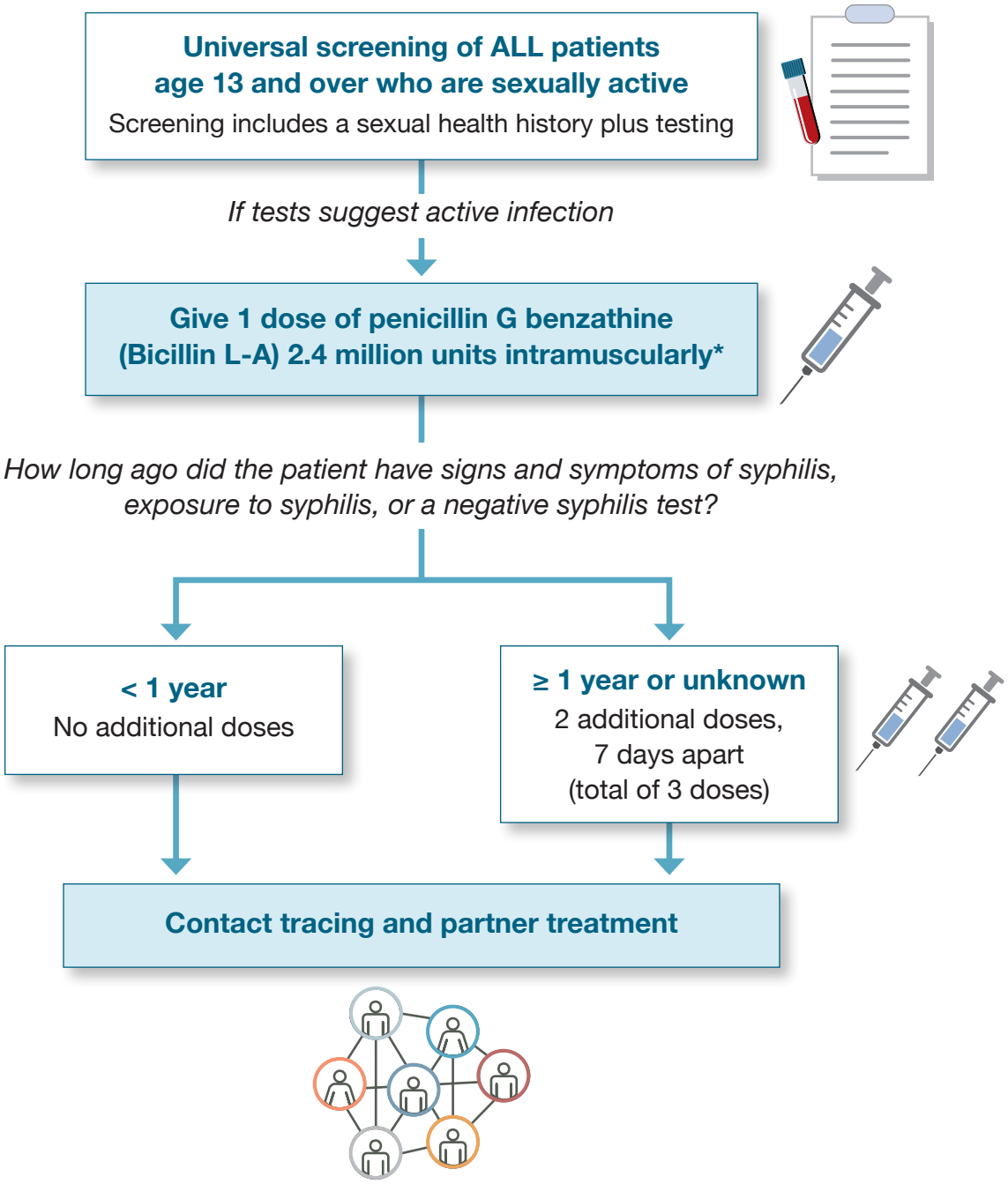
Babies



- Deformed bones
- Enlarged liver and spleen, jaundice
- Meningitis
- Brain and nerve problems, like blindness or deafness

Steps to stop syphilis

FIGURE 2. An approach to identifying and treating syphilis



Everyone has a role in preventing the further spread of syphilis. Best practices include the engagement of multiple team members to diagnose patients with syphilis, treat with appropriate duration of benzathine penicillin, and identify partners who require testing and treatment.

*Screen patients for otic, ocular, or neurosyphilis which requires treatment with intravenous penicillin.

Universal screening for syphilis

ALL patients age 13 and older who are sexually active should be screened for syphilis.[3]

Pregnant patients require testing to prevent devastating effects of syphilis in babies. Test at the first prenatal visit, at the beginning of the third trimester, and at the time of delivery.

FIGURE 3. Two blood tests detect syphilis infection and gauge treatment response.[4]

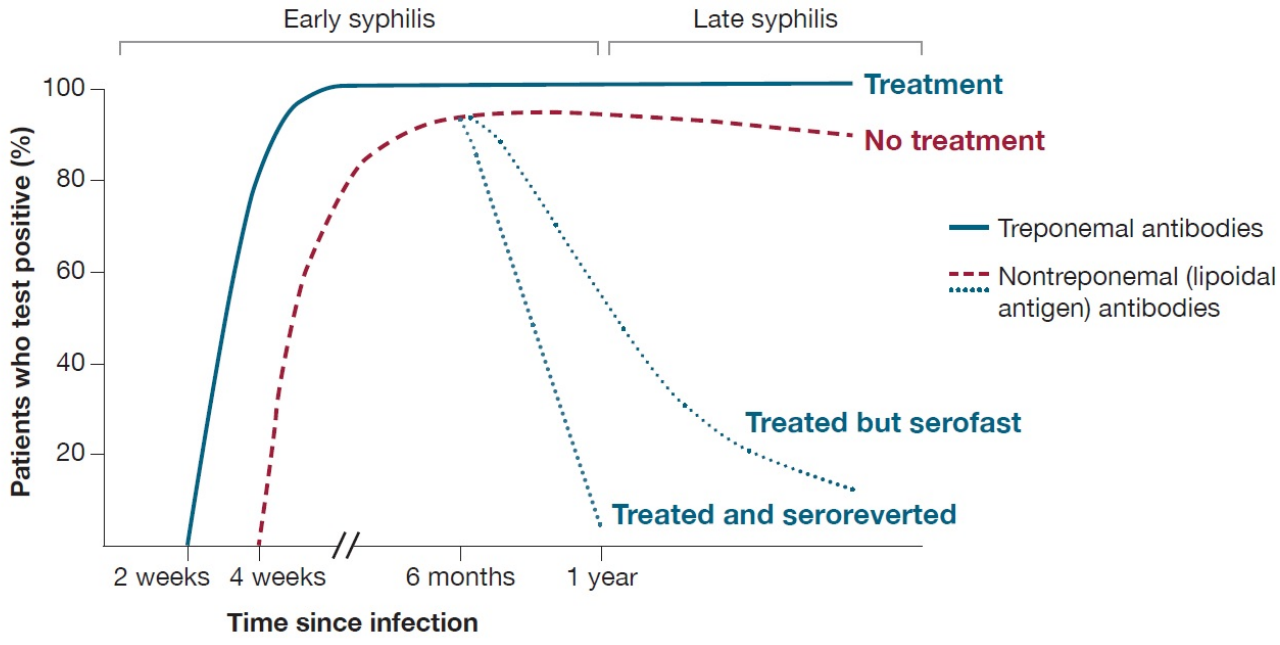
Nontreponemal test (RPR)

- Antibody response to lipoidal antigens found in *T. pallidum* infection
- 11% of patients with reactive tests do not have syphilis

Treponemal test

- Detects antibody response antigens specific to *T. pallidum* infection
- Remains positive for a lifetime, unless treated early (75-85% stay positive)

FIGURE 4. Serologic response to syphilis infection over time[4]



Serofast: Antibodies maintained after treatment; titers will not be nonreactive.
Seroreverted: Patients have nondetectable nontreponemal antibodies, after prior infection.

Continue screening patients annually for at least 2 years until rates return to baseline locally.[3] Think of shared risk factors for other STIs: For patients with a reactive syphilis test, identify and treat patients with other STIs using a "syndemic" approach. See page 9.

Serologic results drive treatment decisions

Treponemal test

- Often reactive even after successful treatment
- Cannot be used alone to diagnose active infection
- Requires a reactive nontreponemal test to diagnose active infection

Nontreponemal (RPR or VDRL) titers

These titers change based on syphilis status, detecting new syphilis cases and reinfection.

Look for 4-fold or greater change in titers in patients with prior syphilis infections.

4x **INCREASE in titers:** active infection or reinfection, if previously treated

4x **DECREASE in titers:** treated infection

TABLE 1. Example case scenarios for using nontreponemal (RPR) titers in patients with a positive treponemal test result

Scenario	Prior titer	Current titer	Interpretation
Patient with new infection	Non-reactive	1:4	New infection
Patient with prior infection	1:32	1:8	Adequately treated infection (with confirmed documentation of treatment completion)
	1:8	1:32	Reinfection

Patients with conditions like HIV may require infectious disease specialist consultation.

Do NOT diagnose and treat based on new titers alone. Seek to find prior syphilis test results to determine prior history of diagnosis and treatment to ensure the correct current diagnosis and appropriate treatment needed.

A recent syphilis exposure (within 4 weeks) may not result in a reactive nontreponemal test.

Follow up with patients who have a reactive test to determine the proper treatment duration. Trace all sexual contacts to contain the spread of syphilis.

Treat syphilis with penicillin

TABLE 2. Determine the number of doses needed based on patient factors.

Treatment		Factors
 x1	Penicillin G benzathine 2.4 million units IM	• Exposure in prior 12 months • Signs of syphilis in prior 12 months • Prior negative syphilis test in prior 12 months
 x3	Penicillin G benzathine 2.4 million units IM given weekly (total dose 7.2 million units)	• Exposure ≥12 months ago • Signs of syphilis ≥12 months ago and untreated • Prior negative test >12 months ago • Unknown duration

Ocular, otic, and neurosyphilis can occur at any stage or duration of infection and require IV aqueous penicillin treatment.

Jarisch-Herxheimer reaction is an acute, febrile reaction. Patients may also have a headache and myalgia. This reaction occurs most frequently in early syphilis. Pregnant patients may also have early labor or fetal distress. **This is not a reason to delay or avoid treatment.**

Penicillin allergy

Benzathine penicillin G is the most effective, simplest treatment option for all patients.

- **Fewer than 10% of patients** who report a penicillin allergy actually have an allergy (e.g., hives, anaphylaxis).[5]
- Nausea, vomiting, and a family history of penicillin allergy are not true penicillin allergies.[5]
- **Benzathine penicillin G is the only recommended treatment for pregnant patients.** A penicillin desensitization or allergy consultation may be required.

PEN-FAST

Think about using an allergy tool like **PEN-FAST**[6] to clarify the penicillin allergy in non-pregnant adults.

Determine treatment duration and identify sexual contacts

Because signs of syphilis can resolve on their own regardless of treatment and are often not in a visible place on the body, many patients may not know when they were exposed.

Take a sexual history.

- If not completed during screening, **ask patients about their sexual health** and take a sexual history (Table 3) to identify exposures and associated symptoms.
- **Obtain prior (historical) RPR results** from clinical or public health record searches. Perform a new nontreponemal test to identify potential reinfection in an asymptomatic patient.
- **Solicit prior treatment for syphilis;** patients may be able to recall treatment if they received an injection.

Connect with relevant public health departments.

- **Link to** IHS, state, county, local and tribal **public health departments** for records.
  - Determine prior treatment
  - Assist with partner services (contact tracing)
- Reach out to state health departments to **trace out of state treatment.**

Trace sexual contacts.

- **Identify sexual partners** who should be screened and possibly treated for syphilis to help reduce the local spread of infection.
- Share options to **self-refer sexual partners** for testing and treatment for patients unable to provide contact information for sexual partners.
- **Treat sexual contacts with penicillin and test for other STIs.** This includes non-beneficiaries to “prevent the spread of disease or public health hazard.”

Programs like **Native Test** allow patients to self-collect clinical specimens for testing at home. If results are positive, patients are given information on where to get treatment in their area. Learn more at **nativetest.org.**

To get started

Let's talk about sex

Sexual health is a critical part of a holistic approach to caring for patients. **Start the conversation** by making it clear that you talk about sexual health with all patients.

> *"I ask all my patients questions about their sexual health. Would it be OK if I ask you some questions?"*

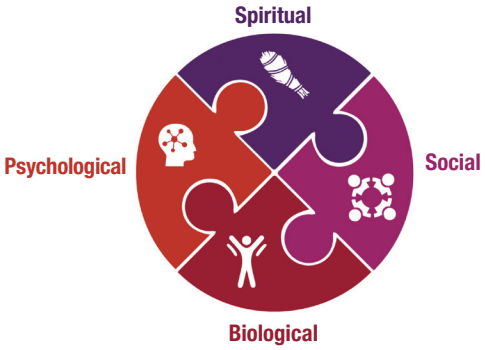


TABLE 3. A framework for asking about sexual health

Domain	Sample questions
Partners	• *Are you currently having sex of any kind—oral, vaginal, or anal—with anyone?* • *What is/are the sex(es) of your sex partner(s)?* • *In recent months, how many sex partners have you had?* • *Do you or your partner(s) currently have other sex partners?*
Practices	• *What kinds of sexual contact do you or have you had? What parts of the body were involved?* • *Have you or any of your partners used drugs?* • *Have you exchanged sex for your needs (e.g., money, housing, drugs)?*
Protection from STIs	• *Do you and your partner(s) discuss STI prevention?* • *What prevention tools do you use, if any?* • *How often do you use this/these methods?*
Past history of STIs	• *Have you ever been tested for STIs and HIV?* • *Have you ever been diagnosed with an STI? When? Were you treated?* • *Have you had recent symptoms, or symptoms that keep coming back?* • *Has your current partner(s) or any former partners ever been diagnosed or treated for an STI?* • *Do you know your partner's HIV status?*
Pregnancy intention	• *How important is it to you to prevent pregnancy?* • *If trying to prevent pregnancy, what methods are you using?*

Develop a plan to prevent STIs such as barrier methods, DoxyPEP, and PrEP for HIV.

The "syndemic" approach

Identify and treat other STIs.

Adopt an **HIV/Viral Hepatitis/STI testing bundle**, which includes:

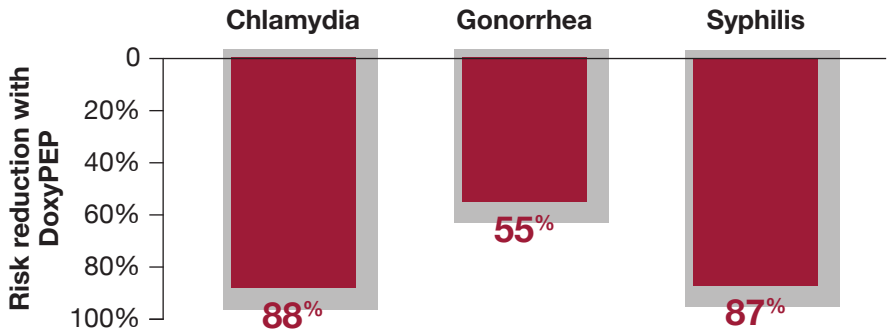
- Syphilis testing
- HIV serology (with consent documentation if required)
- Gonorrhea and chlamydia testing (from all relevant sites of exposure—urine, vagina, pharynx, rectum)
- Hepatitis B and C
- Pregnancy test

STI Express Sample Toolkit

Sexually active persons can be exposed and infected with multiple STIs.

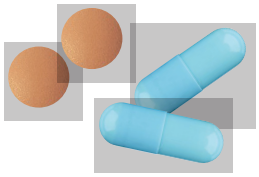
Offer DoxyPEP.

CDC currently recommends the use of doxycycline for postexposure prophylaxis (DoxyPEP) for the prevention of bacterial STIs—chlamydia, gonorrhea, and syphilis—in men who have sex with men and transgender women.[8]



Prescribing DoxyPEP:

- **Directions:** Take at least 24 hours but no more than 72 hours after condomless sex.
- **Dose:** Two 100 mg pills of doxycycline, monohydrate or hyclate may be taken as frequently as once daily.
- **Prescribe 30 days of therapy with refills** and adjust based on patient feedback.



- **Follow up with the patient every 3-6 months** to assess for bacterial STIs and HIV.

All patients should be screened and/or treated for STIs prior to using DoxyPEP.
If a patient taking DoxyPEP has signs or symptoms of an STI, test and treat immediately.

Build a team to combat syphilis

Standing orders

Protocols to guide field testing and treatment can reduce the spread of syphilis by providing criteria to identify infection and administer treatment quickly.

Case investigation

Following up on prior treatment and infection with local public health departments can be completed by trained members of the healthcare team.

Community outreach and education

Point of care (POC) testing[10]

- **This is a treponemal assay;** it remains positive even if patients have been successfully treated.
- Encouraged testing settings include:[11]
  - **Community outreach events** by outreach providers, including public health nurses (e.g., tribal fairs, soup kitchens, shelters, jails, etc.)
  - **Street outreach** to persons experiencing homelessness
  - **Home visits** for contact investigation or STI treatment
- **Not recommended for patients with a previous syphilis infection.**

Talk to patients about protecting themselves and others

Think presumptive treatment, especially in patients with high risk for loss of follow-up

Next steps for a reactive POC test:[10]

- **Obtain a blood draw** to analyze in a lab; serologic testing is the diagnostic standard.
- **Ask about signs and symptoms** of syphilis.
- **Look for symptoms of ocular, otic, and neurosyphilis.**
- **Link to follow-up.** Explain that the results from POC testing aren't definitive and further testing is needed.
- **Recommend immediate treatment** with penicillin G benzathine, especially for patients at high risk (e.g., syphilis symptoms, known exposure, or positive rapid treponemal test).

Key points

- Syphilis is on the rise.
- Use a script to discuss sexual health with all patients, including STI prevention.
- Implement universal STI testing.
- Learn about syphilis staging.
- Treat syphilis—every age, every stage.

Protect the babies. Test for syphilis in pregnant patients.

RESOURCES

ihs.gov/sti

nativehealthresources.com

courses.nnptc.org/eLearning.html

References:

(1) Centers for Disease Control and Prevention. Sexually Transmitted Infections (STIs): Tables. 2024; https://www.cdc.gov/std/statistics/2022/tables.htm. Accessed Sept 5, 2024. **(2)** McDonald R, et al. Vital Signs: Missed Opportunities for Preventing Congenital Syphilis–United States, 2022. *MMWR Morb Mortal Wkly Rep.* 2023 Nov 17;72(46):1269-1274. **(3)** Christensen L. Syphilis Epidemic Letter. Feb 15, 2024; https://www.ihs.gov/sites/newsroom/themes/responsive2017/display_objects/documents/2024_Letters/DTLL_DUIOLL_021524.pdf. Accessed Aug 16, 2024. **(4)** Papp JR, et al. CDC Laboratory Recommendations for Syphilis Testing, United States, 2024. *MMWR Recomm Rep.* 2024;73(1):1-32. **(5)** Centers for Disease Control and Prevention. Sexually Transmitted Infections Treatment Guidelines, 2021: Managing Persons Who Have a History of Penicillin Allergy. https://www.cdc.gov/std/treatment-guidelines/penicillin-allergy.htm. Accessed Aug 29, 2024. **(6)** Copaescu AM, et al. Efficacy of a Clinical Decision Rule to Enable Direct Oral Challenge in Patients With Low-Risk Penicillin Allergy: The PALACE Randomized Clinical Trial. *JAMA Intern Med.* 2023;183(9):944-952. **(7)** Centers for Disease Control and Prevention. Expedited Partner Therapy. July 16, 2024; https://www.cdc.gov/sti/hcp/clinical-guidance/expedited-partner-therapy.html. Accessed Sept 5, 2024. **(8)** Bachmann LH, et al. CDC Clinical Guidelines on the Use of Doxycycline Postexposure Prophylaxis for Bacterial Sexually Transmitted Infection Prevention, United States, 2024. *MMWR Recomm Rep.* 2024;73(2):1-8. **(9)** Luetkemeyer AF, et al. Postexposure Doxycycline to Prevent Bacterial Sexually Transmitted Infections. *N Engl J Med.* 2023;388(14):1296-1306. **(10)** National Syphilis and Congenital Syphilis Syndemic Federal Task Force. Considerations for the Implementation of Point of Care (POC) Tests for Syphilis. June 2024; https://www.hhs.gov/sites/default/files/nscss-considerations-for-the-implementation-of-syphilis-poc-tests.pdf. Accessed Aug 16, 2024. **(11)** Indian Health Service. Fall 2023 IHS STI Treatment Guideline. https://www.ihs.gov/sites/nptc/themes/responsive2017/display_objects/documents/sti/IHS-STI-Guidance.pdf. Accessed Aug 27, 2024.

These are general recommendations only; specific clinical decisions should be made by the treating clinician based on an individual patient's clinical condition.

These materials were created by Alosa Health, a nonprofit educational organization which accepts no funding from any pharmaceutical company. They were printed and distributed through a program with the Indian Health Service.

Oct 2024