

Name	Causative agent: Treponema pallidum
Reservoir &	Humans
Transmission	Direct contact (mainly sexual) with infected individual
Incubation Period	10 days to 3 months. Usually, 3 weeks
Common	Symptoms based on stages of infection:
Symptoms	<ul> <li>Primary syphilis classically presents as a single painless ulcer or chancre at the site of infection but can also present with multiple, atypical, or painful lesions.</li> <li>Secondary syphilis manifestations can include skin rash, mucocutaneous lesions, and lymphadenopathy.</li> <li>Latent infections may be lacking clinical manifestations. Latent syphilis acquired within the preceding year is referred to as early latent syphilis; all other cases of latent syphilis are classified as late latent syphilis or latent syphilis of unknown duration.</li> <li>Tertiary syphilis can present with cardiac involvement, syphilitic growths on organs and skin, gait disturbances (tabes dorsalis) and general paresis.</li> <li>Neurosyphilis, ocular syphilis, and otosyphilis - Neuro, ocular, and otic manifestations can occur at any stage of disease. Neurosyphilis can include severe headache, trouble with muscle movements, muscle weakness or paralysis, numbness, and changes in mental status. Ocular syphilis can include eye pain or redness, floaters, sensitivity to light, and changes in vision. Otosyphilis may include hearing loss, ringing, buzzing, roaring, or tinnitus, dizziness, or vertigo.</li> <li>Congenital - Having syphilis can lead to a low-birth-weight infant, early delivery, or stillborn. An infected infant may be born without signs or symptoms of disease. Untreated infants can have health</li> </ul>
Gold Standard	problems such as cataracts, deafness, seizures, or death  Treponemal serological test, darkfield microscopy, enzyme
Diagnostic Test	immunoassay (EIA), PCR. Darkfield examinations and molecular tests
	for detecting <i>T. pallidum</i> directly from lesion exudate or tissue are the definitive methods for diagnosing early syphilis and congenital syphilis.
Risk Groups	Any sexually active person that has unprotected vaginal, anal, or oral sex; higher in men who have sex with men (MSM)
Geographic Significance	Worldwide

## What is syphilis?

Syphilis is a sexually transmitted infection (STI) caused by the bacterium *Treponema pallidum*. Syphilis can cause serious health effects without adequate treatment. Syphilis is divided into stages (primary, secondary, latent, and tertiary). There are different signs and symptoms associated with each stage. The disease course is complex and variable.

### What is the occurrence of syphilis?

According to CDC (2023), syphilis case reports continue to increase since reaching a historic low in 2000 and 2001. During 2021, there were 176,713 new cases of syphilis (all stages). Gay, bisexual, and other men who have sex with men (MSM) are experiencing extreme effects of



syphilis. They account for 36% of all primary and secondary (P&S) syphilis cases in the 2021 STD Surveillance Report <a href="https://www.cdc.gov/std/statistics/2021/overview.htm#Syphilis">https://www.cdc.gov/std/statistics/2021/overview.htm#Syphilis</a>. They also account for 47% of all male P&S cases. However, case rates are increasing among heterosexual men and women in recent years. Congenital syphilis continues to be a concern in the United States. Congenital syphilis occurs when a pregnant person passes syphilis to their baby. Final 2021 data show more than 2,800 cases of congenital syphilis.

### How is syphilis transmitted?

Syphilis spreads from person-to-person by direct contact with a syphilitic sore, known as a chancre. Chancres can occur in, on, or around the penis; vagina; anus; rectum; and lips or mouth. Syphilis can spread during vaginal, anal, or oral sex. Syphilis can also be spread from an infected mother to her fetus.

# Who is at risk for syphilis?

Any sexually active person can get syphilis, as well as other STIs, through unprotected vaginal, anal, or oral sex. Men account for the most cases of syphilis, with most of those cases occurring among gay, bisexual, and other MSM.

## What are the signs and symptoms of syphilis?

Syphilis has been divided into the following stages based on clinical findings, which guide treatment and follow-up:

- Primary One or more painless ulcerative lesions (chancres). Lesions are typically on the genitals, in the rectal area or in the mouth; because they are painless, an infected person may not be aware of them.
- Secondary A rash, often including the palms and soles of the feet, with swollen lymph nodes. Other symptoms can include fever, sore throat, headache, weight loss, myalgia, fatigue, mucous patches, wart-like genital lesions, and hair loss.
- Latent The latent (hidden) stage of syphilis is a period when there are no visible signs or symptoms of syphilis. Without treatment, syphilis will remain in the body, even though there are no signs or symptoms. Early latent syphilis occurs with infection within past 12 months. Late latent syphilis occurs with infection more than 12 months. Latent syphilis of unknown duration is when there is not enough evidence to confirm initial infection was within the previous 12 months.
- Concurrent, uncontrolled HIV infection may alter the clinical presentation of primary and secondary stages of syphilis, which may delay the diagnosis and treatment of syphilis; thus, increasing the risk of progression to tertiary syphilis, including neurosyphilis.
- Tertiary Neurological findings usually predominate such as dementia, tabes dorsalis, and may include many other systemic findings to include gummas lesions and variable involvement of other organ systems.
- Infection of the central nervous system (neurosyphilis), visual system (ocular syphilis), or auditory system (otosyphilis) can occur at any stage of syphilis, but it is commonly identified during the early stages and can present with or without additional CNS involvement. Neurosyphilis presents as cranial nerve dysfunction, meningitis, meningovascular syphilis, or acute altered mental status. Ocular syphilis often presents as panuveitis but can involve structures in both the anterior and posterior segment of the eye, including conjunctivitis, anterior uveitis, posterior interstitial keratitis, optic neuropathy, and retinal vasculitis. Otosyphilis typically presents with cochleo-vestibular symptoms, including tinnitus, vertigo, and sensorineural hearing loss. Hearing loss can be unilateral or bilateral, have a sudden onset, and progress rapidly.

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Congenital - If a pregnant woman has syphilis, the infection can be spread to their unborn
fetus. Having syphilis can lead to a low-birth-weight infant. It can also make it more likely
that the fetus will be delivered too early or stillborn. An infected infant may be born without
signs or symptoms of disease. However, if not treated immediately, the infant may develop
serious problems within a few weeks.

# What are the potential complications of syphilis?

Potential complications include cranial nerve dysfunction, meningitis, stroke, acute altered mental status, tabes dorsalis, permanent vision or hearing loss. Syphilis in pregnant women can lead to low-birth-weight infants, prematurity, or stillborn. Untreated infants infected with syphilis can have health problems such as cataracts, deafness, seizures, or death.

### How is syphilis diagnosed?

- Darkfield examinations and molecular tests for detecting *T. pallidum* directly from lesion exudate or tissue are the definitive methods for diagnosing early syphilis and congenital syphilis.
- A presumptive diagnosis of syphilis requires use of two laboratory serologic tests: a
  nontreponemal test (i.e., Venereal Disease Research Laboratory [VDRL] or rapid plasma
  reagin [RPR] test) and a treponemal test (i.e., the *T. pallidum* passive particle agglutination
  [TP-PA] assay, various EIAs, chemiluminescence immunoassays [CIAs] and immunoblots,
  or rapid treponemal assays).
- Use of only one type of serologic test (nontreponemal or treponemal) is insufficient for diagnosis and can result in false-negative results among persons tested during primary syphilis and false-positive results among persons without syphilis or previously treated syphilis.
- For further guidance on nontreponemal tests and traditional algorithm, treponemal tests and reverse sequence algorithm, cerebrospinal fluid evaluation, and evaluation of infants for congenital syphilis, please refer to the 2021 STI Treatment Guidelines at https://www.cdc.gov/std/treatment-guidelines/syphilis.htm.

## How is syphilis treated?

- Penicillin G, administered parenterally, is the preferred drug for treating patients in all stages
  of syphilis. The preparation used, the dosage, and the length of treatment depend on the
  stage and clinical manifestations of the disease.
- Selection of the appropriate penicillin preparation is important because *T. pallidum* can reside in sequestered sites (e.g., the CNS and aqueous humor) that are poorly accessed by certain forms of penicillin. Combinations of benzathine penicillin, procaine penicillin, and oral penicillin preparations are not considered appropriate for syphilis treatment. Reports have indicated that practitioners have inadvertently prescribed combination long- and short-acting benzathine-procaine penicillin (Bicillin C-R) instead of the standard benzathine penicillin product (Bicillin L-A) recommended in the United States for treating primary, secondary, and latent syphilis. Practitioners, pharmacists, and purchasing agents should be aware of the similar names of these two products to avoid using the incorrect combination therapy agent for treating syphilis.
- Parenteral penicillin G is the only therapy with documented efficacy for syphilis during pregnancy. Pregnant women with syphilis at any stage who report penicillin allergy should be desensitized and treated with penicillin.
- The Jarisch-Herxheimer reaction is an acute febrile reaction frequently accompanied by headache, myalgia, and fever that can occur within the first 24 hours after the initiation of any syphilis therapy; it is a reaction to treatment and not an allergic reaction to penicillin.

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Patients should be informed about this possible adverse reaction and how to manage it if it occurs. The Jarisch-Herxheimer reaction occurs most frequently among persons who have early syphilis, presumably because bacterial loads are higher during these stages. Antipyretics can be used to manage symptoms; however, they have not been proven to prevent this reaction. The Jarisch-Herxheimer reaction might induce early labor or cause fetal distress in pregnant women; however, this should not prevent or delay therapy.

 For further guidance, please refer to the 2021 STI Treatment Guidelines at https://www.cdc.gov/std/treatment-guidelines/syphilis.htm.

## How can syphilis be prevented?

The only way to avoid being infected with syphilis is to not have vaginal, anal, or oral sex. If a person is sexually active, the following safer sex practices can lower the chances of getting and spreading syphilis:

- Being in a long-term, mutually monogamous relationship with a partner who has been tested and has negative STI test results.
- Proper use of latex condoms with every sexual encounter. Condoms prevent transmission of syphilis by preventing contact with chancre or other syphilitic lesions. Sometimes these lesions occur in areas not covered by a condom. Contact with these lesions can still transmit syphilis, thus teach infected people to avoid sexual activity while lesions are present.
- Regular testing and early treatment to prevent spread.
- Partner notification and treatment to prevent reinfection.
  - The following sex partners of persons with syphilis are considered at risk for infection and should be confidentially notified of the exposure and need evaluation:
    - Partners who have had sexual contact within 3 months, plus the duration of symptoms for persons who receive a diagnosis of primary syphilis;
    - Within 6 months, plus duration of symptoms for those with secondary syphilis; and
    - Within 1 year for persons with early latent syphilis.

### What are some Public Health considerations?

- When reporting syphilis in the Disease Reporting System Internet (DRSI)
  - o Specify the stage of the disease and any diagnosed clinical manifestation.
  - Refer to the Armed Forces Reportable Medical Events (AFRME) 2022 guidelines to determine the case classification and for criteria on what is acceptable as evidence of having acquired syphilis within the preceding 12 months.

#### References:

Defense Health Agency. 2022. Armed Forces Reportable Medical Events: Guidelines and Case Definitions.

https://www.health.mil/Reference-Center/Publications/2022/11/01/Armed-Forces-Reportable-Medical-Events Guidelines

Heymann, David L. ed. 2022. *Control of Communicable Diseases Manual*. 21st Edition. Washington, DC: APHA Press.

"Syphilis," Centers for Disease Control and Prevention (CDC), last reviewed April 11, 2023. https://www.cdc.gov/std/syphilis/default.htm