

## Syphilis (*Treponema pallidum*)

[See online here](#)

*Treponema pallidum* is a member of the *Spirochaetaceae* family. *T. pallidum* are gram-negative bacteria that are regarded by some as being too thin to be Gram stained. They are delicate, tightly spiraled, motile spirochete with tapered ends. These are microaerophilic bacteria that cannot be grown on standard culture media. These microbes are poorly stained, so cannot be detected by conventional light microscopy.



### *Treponema Pallidum*

*T. pallidum* can be detected in clinical samples through dark-field or phase-contrast microscopy or direct immunofluorescent staining. The bacteria cannot be cultured in standard culture media.

At least 4 subspecies are known:

1. *T. pallidum pallidum*, which causes syphilis
2. *T. pallidum endemicum*, which causes endemic syphilis

Syphilis is a **chronic systemic disease** that is transmitted **sexually**. The infection can be treated if detected early but manifests late and has significant morbidity if left untreated.

# Epidemiology of Syphilis

Syphilis can be **acquired** or **congenital**. It can also occur in **children** and **adolescents**. It is prevalent all over the world but is most common in underdeveloped countries. Sexually active groups are the most affected by the disease.

The highest incidence in the United States occurs among men who have sex with men and live in poor, minority communities in southern states. Rates in Western Europe are 4.4–10.4 per 100,000 population. Rates are increasing in eastern Europe and Russia.

## Transmission

**Acquired syphilis** is transmitted exclusively by sexual contact (i.e. vaginal, anal, and oral). Other modes of transmission are through blood transfusion or direct contact with infected tissues.

**Primary and secondary syphilis** rates peaked in 1989 in the United States; later, the annual rate declined by 90% until 2000. Since 2000, however, the total number of cases of primary and secondary syphilis has increased significantly.

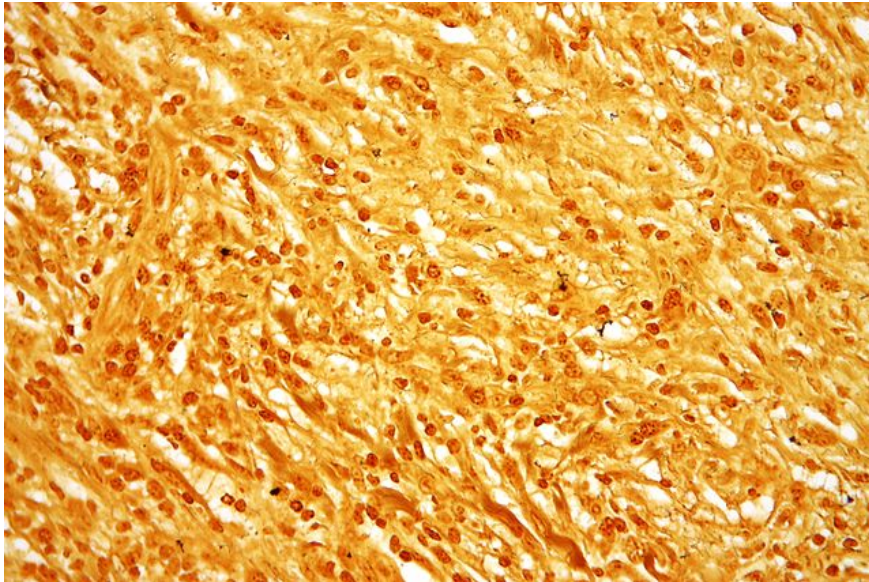
Rates of **congenital syphilis** also became more common after 2004 but have fallen since 2008. Congenital syphilis is transmitted through the placenta during pregnancy, or during childbirth through the child's direct contact with infectious lesions.

Women with active disease are more likely to transmit the disease to their fetus, compared to ones with latent infection. Early transmission can lead to fetal loss, preterm or low birth-weight infants, stillbirths, neonatal deaths, or infants born with a congenital disease.

The risk of transmission is highest during the **first 4 years of life**. Risk factors for congenital syphilis include limited access to healthcare, late or no prenatal care, maternal drug use, multiple sex partners, unprotected sexual contact, sex trade work, and inadequate treatment of syphilis during pregnancy.

## Clinical Manifestations and Laboratory Findings

Infected individuals often do not exhibit symptoms for years. The Centers for Disease Control and Prevention recommend screening of even young adults if they have lesions or positive risk factors.



**Image:** Micrograph showing *Treponema pallidum*, the spirochete that causes syphilis. Dieterle stain. By Nephron. License: [CC BY-SA 3.0](https://creativecommons.org/licenses/by-sa/3.0/)

## Primary syphilis

Primary disease occurs in the absence of any other disease and is characterized by a chancre and regional enlarged lymph nodes (lymphadenitis).

Initially, a small, painless papule is formed at the site of infection, usually the genitals, roughly 2-6 weeks after contact or transmission. Later, the papule becomes a clean, painless, and highly contagious ulcer with raised borders called a chancre.

**Chancres** are filled with *T. pallidum*, the organism causing the disease. Chancres can be found on extra-genital areas as well, making the disease difficult to diagnose. Lesions in the oral cavity can be misdiagnosed for aphthous ulcers or herpes. Lesions on the nipple can be mistaken for cellulitis or eczema.

**Painless lymphadenopathy** is a typical feature of this disease. The chancre heals after 4-6 weeks, becoming thin scar tissue. Patients who are not treated develop the symptoms of secondary syphilis after 2-10 weeks of healing.

## Secondary syphilis

Untreated primary syphilis becomes secondary syphilis. Patients present with generalized non-pruritic maculo-papular rash, generally on the palms and soles, along with pustular lesions. Various skin lesions include condylomata lata and white plaques.

Condylomata lata are grayish white or, sometimes, reddish erythematous wart-like lesions usually found around the anus and vagina. White plaques (mucous patches) may be found in mucous membranes.

Other clinical features include flu-like symptoms including low-grade fever, headache, malaise, [anorexia](#), weight loss, sore throat, arthralgias, and generalized lymphadenopathy.

### Systemic involvement

Renal, hepatic, and ophthalmologic involvement can also occur. Approximately 30% of

patients can have meningitis on cerebrospinal fluid examination, which shows pleocytosis and raised protein level. Without treatment, if the patient survives, secondary infection subsides after 1 month and then relapses after 1 year, sometimes becoming tertiary syphilis.

## Tertiary syphilis

Tertiary disease occurs in one-third of untreated cases. Patients usually present with neurologic, cardiovascular, and gummatous skin lesions.

## Diagnosis of Syphilis

It is difficult to diagnose this disease through the usual investigations, but specific labs along with correlation with history and examination results can lead to a diagnosis. Syphilis should be treated if suspected clinically and on the basis of epidemiology.

### For primary disease

The presence of *T. pallidum* can be confirmed by dark-field microscopy or direct fluorescent antibody testing on samples from skin lesions, placenta, or umbilical cord. Polymerase chain reaction is rarely performed. Serologic testing for antibodies is the principal diagnostic test. Patients with suspected *T. pallidum* infection should be screened using a non-treponemal test followed by a confirmatory treponemal test. These tests include:

- Venereal disease research laboratory tests
- Rapid plasma reagin tests

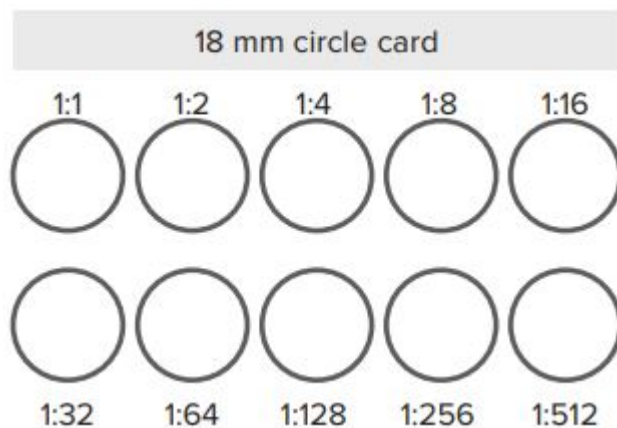


Image: Rapid plasma reagin, by Lecturio

Antibodies against phospholipid antigens on the surface of the organism that cross-react with **cardiolipin-lecithin-cholesterol antigens** of damaged host cells are detected in these tests. Both qualitative and quantitative tests can be done for screening and monitoring the therapy. **Antibody titers** increase with active disease, treatment failure, or in re-infection. Titers decrease with proper treatment.

### Biologic false:

Transient	Chronic
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<ul style="list-style-type: none"> <li>• Malaria</li> <li>• Brucellosis</li> <li>• Mononucleosis</li> </ul>	<ul style="list-style-type: none"> <li>• Autoimmune diseases (esp. SLE)</li> <li>• HIV infection</li> <li>• IV drug use</li> <li>• Leprosy</li> <li>• Hepatitis C</li> </ul>
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### Treponemal tests

Treponemal tests are done to confirm the diagnosis of syphilis and measure specific *T. pallidum* antibodies (immunoglobulin IgG, IgM, and IgA). These antibodies appear even before non-treponemal antibodies appear in the body. The tests include:

1. *T. pallidum* particle agglutination
2. *T. pallidum* hemagglutination assay
3. Fluorescent treponemal antibody absorption

**Treponemal antibody titers** are positive even after initial infection, and remain positive for life.

## Therapy of Syphilis

### Early syphilis (primary, secondary, or early latent syphilis):

- Benzathine penicillin G, 2.4 MU IM (single dose)
- Alternative regimens: doxycycline, 100 mg PO bid x 14 days and ceftriaxone 1 g IM or IV daily x 10–14 days and tetracycline 500 mg orally 4 times daily x 14 days and amoxicillin 3 g plus probenecid 500 mg, both given orally twice daily x 14 days

### Neurosyphilis (including otic and ocular):

- Penicillin G 18–24 MU IV daily (3–4 MU IV q 4 h) x 10–14 days
- Procaine penicillin G 2.4 MU IM daily, plus probenecid 0.5 g PO qid x 10–14 days
- Alternative: ceftriaxone 2 g IM or IV daily x 14 days

### Late latent syphilis, tertiary syphilis, or syphilis of unknown duration:

- Benzathine penicillin G 2.4 MU IM weekly x 3
- Alternative regimen: doxycycline 100 mg PO bid x 28 days

### During pregnancy:

- As for non-pregnant patients
- Penicillin-allergic patients should be desensitized and treated with penicillin

## References

[Syphilis](#) via medscape.com

[Syphilis: Causes, Symptoms, and Treatments](#) via medicalnewstoday.com

[VDRL Test and its Interpretation](#) via nih.gov

[Syphilis – CDC Fact Sheet](#) via cdc.gov

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