Syphilis — Types, Diagnosis and Treatment

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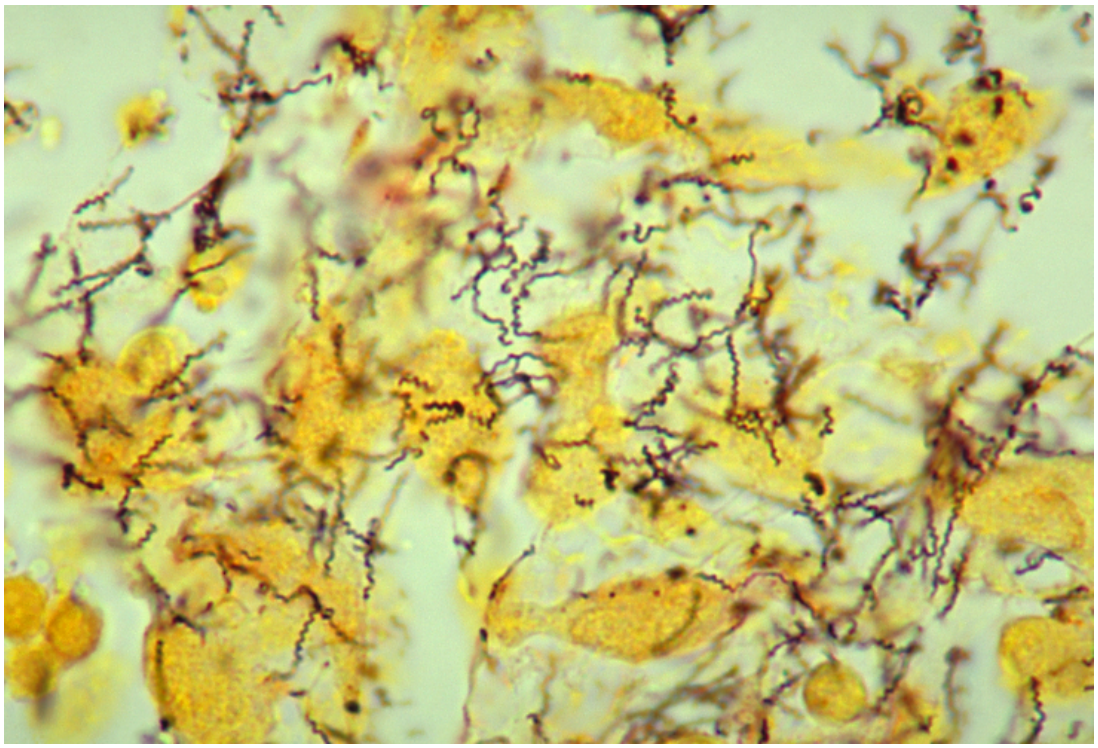
Syphilis is caused by *Treponema pallidum* (TP), a motile Spirochaetaceae that is common all over the world. TP can be transmitted via close sexual contact or transplacentally (vertically). Syphilis can be either acquired or congenital; both routes of transmission have early and late stages. TP invades the host body through breaches in the squamous or columnar epithelium affecting lymphatic nodes. It then disseminates through the bloodstream to all parts of the body.



Definition and Background of Syphilis

Syphilis is a **chronic systemic disease** that is easily treated in its early stages; however, untreated cases can lead to grave consequences and death. ***Treponema palladium*** is the causative factor of syphilis. It was described in 1905 by Schaudinn and Hoffman; Wasserman described the blood test for long-term forms of the infection.

The first outbreak of the illness was noted in 1495, when French soldiers invaded Naples and came down with a deadly disease, which they called ‘great pox’; much of Europe was devastated by the disease, with thousands of deaths.

During the First World War, syphilis was one of the key causes of disability and absence from duty in the United States Army; over 10,000 men were discharged and 7 million person-days were lost to the disease.

The illness has changed names over time; its monikers have included ‘French disease’, ‘Spanish fever’, and others. After syphilis was first discovered, no effective treatment existed. Because of this, sporadic epidemic outbreaks regularly occurred in different parts of the world.

Mercury was administered by the Esculaps of early medicine as a remedy against this infection; however, this chemical element was extremely toxic and had severe side effects, including death.

Etiology of Syphilis

Pathogenic treponemes are associated with the following 4 diseases:

- Venereal syphilis, caused by *T. pallidum pallidum*
- Yaws, caused by *T. pallidum pertenue*
- Endemic syphilis (bejel), caused by *T. pallidum endemicum*
- Pinta, caused by *T. carateum*

Ways of transmission

- Sexual contact
- Transplacental/congenital syphilis (vertical transmission route; 50–80% of neonates are exposed to the infection when it is present in the mother)
- Contact with contaminated blood (during transfusions) and tissues
- Personal contact (rare)

Types of syphilis

- Acquired
- Congenital

Epidemiology of Syphilis

United States

The Centers for Disease Control and Prevention analyzed data obtained from the National Notifiable Diseases Surveillance System for cases of primary and secondary syphilis diagnosed during 2005–2013 among homosexual, bisexual, and other men having sex with men (MSM). The figure obtained accounted for 5.3 cases per 100,000 population, a number that is twice as high as it was in the period between 2005 and 2013, when it was 2.9 per 100,000.

The highest prevalence was in the western regions of the country. Hispanics were the most affected, at 53.4%, from 1,291 cases in 2009 to 1,980 in 2012; followed by whites at 38.1%, from 2,449 cases in 2009 to 3,381 in 2012; and African Americans at 21.2%, from 2,267 cases in 2009 to 2,747 in 2012. By age group, the greatest percentage increases occurred among MSM aged 25–29 (53.2%, 1,073 cases in 2009 to 1,644 in 2012). Nonwhite women tend to contract syphilis more often than white women (13.3 times to 4 times, respectively).

International

In the developing world, including sub-Saharan Africa, as well as in Venezuela, syphilis has become a major public health problem. Although the disease has no racial predilection, **socioeconomic factors** play a pivotal role in its spread. The highest incidence of syphilis is seen in South and Southeast Asia, followed by Sub-Saharan Africa and then Latin America and the Caribbean.

Sex: Men contract syphilis more frequently than women. Also, syphilis has a strong affiliation with **HIV infection** in both drug users and those with a greater number of sexual partners.

Age: Adolescents and young adults who are drug users and have multiple sexual partners are also at risk of infection with TP.

Clinical Presentation of Syphilis

History

It is vital to take a full history of an affected patient in order to determine the stage of the disease. The history should include a **thorough sexual and social history**, including the number of sexual partners, condom use, history of sexually transmitted diseases in the patient and their partners, intravenous drug use, and exposure to blood products.

Image: Primary stage syphilis sore (chancre) on the surface of a tongue. By Centers for Disease Control and Prevention (CDC). License: Public Domain

Physical examination

Primary (10–90 days after exposure to the pathogen)

- Hard chancre on genitals
- Painless regional lymphadenopathy

Secondary (4–10 weeks after the first manifestation)

- General: fever, fatigue, pain in joints, sore throat, headache, anorexia, neck stiffness and poly-lymphadenopathy
- Skin: red or brown maculopapular, non-itchy rash
- Mucosa: patches, ‘snail track’ ulcers at the site of TP penetration

Late stages (tertiary; occur if there is inappropriate treatment or late administration of medication and thus the progression of the disease):

Image: Rash on the palms of both hands due to secondary syphilis. by Centers for Disease Control and Prevention (CDC). License: Public Domain

- Late benign: gummas (bone and viscera)
- Heart and vessels: affected aorta (inflammation of the wall and regurgitation)
- Neurosyphilis: meningovascular lesion, paralysis of the insane and tabes dorsalis

Without treatment, symptoms and signs may abate over 3–12 weeks; in 20% of cases, however, symptoms may recur in the early latency period (2 years).

Congenital syphilis

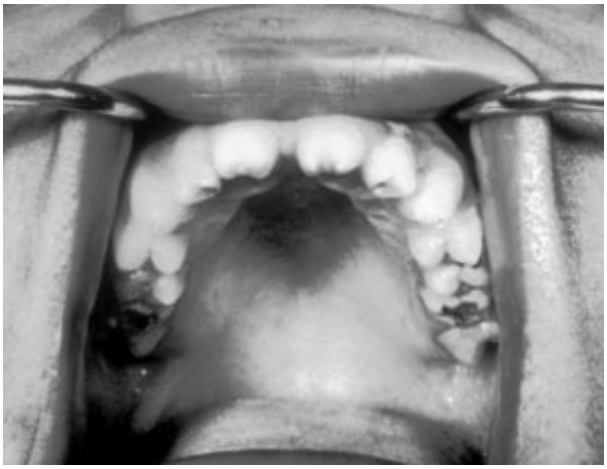


Image: A photograph of Hutchinson's teeth resulting from congenital syphilis. Hutchinson's teeth is a congenital anomaly in which the permanent incisor teeth are narrow and notched. Note the notched edges and 'screwdriver' shape of the central incisors. by CDC/Susan Lindsley. License: Public Domain

Early stages become apparent between 2–6 weeks after birth.

- Stillbirth or retardation of physical and mental development
- 'Snuffles': nasal infection
- Appearance of skin as in secondary syphilis

Late stages become apparent after 2 years age.

- Stigmata: abnormalities of long bones, sabre tibia
- Hutchinson’s teeth
- Eye problems: keratitis, uveitis, facial gummas
- Central nervous system diseases

Differential Diagnosis of Syphilis

- Chancroid
- Condyloma acuminata
- Cystitis in women
- Dermatologic manifestations of herpes simplex
- Drug eruptions
- Genital warts
- Granuloma inguinale (donovanosis)
- Herpes zoster
- HIV disease
- Lymphogranuloma venereum
- Urethritis
- Urinary tract infection in men
- Urinary tract infections during pregnancy in women
- Varicella-zoster virus
- Yaws

Diagnosis of Syphilis

Laboratory studies

Stages	Length of exposure to bacterium	Primary syphilis	Secondary syphilis (skin symptoms)	Tertiary syphilis (neurological problems)
Time after contact with infected person	Day 1	10 to 90 days	6 weeks to 6 months	10 to 30 years
Antibodytests				
Nontreponemal antibody tests: VDRL and RPR. Provide guidance for treatment		Highly informative (sensitive); nontreponemal antibodies are not found after 3 years adequate treatment.	Same as primary stage	VDRL is performed on CSF and administered in the diagnostics of neurosyphilis.
Treponemal antibody tests: FTA-ABS, TP-PA, immunoassays (IA). Proves the nontreponemal antibody test.		Specific; followed by nontreponemal antibody test in order to determine active and past infection.	Same as primary stage	The CSF FTA-ABS is used for diagnostics of neurosyphilis.
Direct detection tests (much less common):				

Microscopic exam, darkfield exam: a sample taken from the chancre is studied in a special microscopic examination		Detection of the bacteria in the biomaterial	N/a	N/a
Polymerase chain reaction (PCR)		Detection of the bacteria in the biomaterial	Genetic material in blood	Detects genetic material in blood and/or CSF sample

Imaging studies

- Computed tomography, as well as magnetic resonance imaging, can detect numerous infarcts in the brain tissue in neurosyphilis.
- X-ray examination is informative when there is a severe lesion of the bones suspected.

Staging of Syphilis

Acquired

- Primary syphilis
- Secondary syphilis
- Late (tertiary) stage
- Quaternary syphilis (nowadays extremely rare case owing to appropriate medication and diagnostics)

Congenital

- Early stages
- Late stages

Management of Syphilis

Pharmacotherapy

Stages	First-line treatment	Alternative treatment	Treatment options for pregnant patients	Monitoring
Primary, secondary, or early syphilis	Intramuscular benzathine penicillin G 2.4×106 U as a single dose	Single 2 g dose of azithromycin (second choice treatment), Azithromycin contraindicated for homosexual male partners and in pregnancy. Ceftriaxone 1 g daily for 10 days.	According to the CDC, pregnant women with a history of allergy should be desensitized and still get penicillin because erythromycin can’t pass the placenta and is not effective.	3, 6, 9, 12 and 24 months

Neurosyphilis	Intravenous aqueous penicillin G 4×106 U q4 hours or continuous infusion for 10-14 days	Procaine penicillin G 2.4×106 U daily with oral probenecid 500 mg q.i.d. for 10-14 days. Another option is ceftriaxone 2 g IM or IV daily for 10-14 days.		
Congenital syphilis	Neonates with normal CSF: intramuscular benzathine penicillin G 50,000 U/kg in a single dose. Neonates with abnormal CSF and babies with CNS involvement: intramuscular aqueous procaine penicillin G 50,000 U/kg/day for 10 days.			3, 6, 9, 12 and 24 months

Surgical intervention

Neither are required for direct treatment unless there are severe complications that lead to **secondary infection** of the skin and bone lesions and tertiary syphilis.

References

Primary and Secondary Syphilis via cdc.gov

Treponema pallidum via treponemapallidum.org

Pediatric Syphilis via medscape.com

Syphilis (Lues) via derm101.com

Syphilis Tests via labtestsonline.org

Notes