

SYPHILIS

✓ DISEASE AND EPIDEMIOLOGY

Clinical Description:

An acute or chronic disease characterized clinically by a primary lesion, a secondary eruption involving skin and mucous membranes, long periods of latency, and late lesions of the skin, bone viscera, the CNS and cardiovascular system.

Primary Syphilis: In the primary stage of syphilis, a painless chancre appears within 14 to 21 days at the site of inoculation. Chancres most frequently occur in the genital, perineal or anal area; however, any part of the body may be infected.

Secondary Syphilis: In the secondary stage, disseminated skin rash and lesions of the mucous membranes are most common. Other manifestations include malaise, lymphadenopathy, mucous patches (elevated patches in the mouth or anus), condylomata lata (syphilitic wart-like lesions generally in the perineal and perirectal areas) and alopecia (patchy hair loss).

Latent Syphilis: In this stage of infection, the patient is entirely free of symptoms. Latent syphilis is subdivided into early, late and unknown categories based on the duration of the infection.

Early Latent Syphilis: Early latent syphilis is an asymptomatic period occurring in the first year after infection.

Late Latent Syphilis: Late latent syphilis is an asymptomatic period occurring greater than 1 year after infection.

Latent Syphilis, unknown duration: Latent syphilis of unknown duration is an asymptomatic period when the date of initial infection is unknown.

Neurosyphilis: In this stage of syphilis, there is evidence of central nervous system infection.

Late Syphilis: In this stage of syphilis, clinical manifestations may include inflammatory lesions of the cardiovascular system, skin and bone.

Congenital Syphilis: Infants may or may not have signs of disease or they present up to 2 years of age with hepatosplenomegaly (enlarged liver), snuffles, lymphadenopathy, mucocutaneous lesions, osteochondritis (fragments of cartilage become loose within a joint) and pseudoparalysis, edema, rash, hemolytic anemia, and thrombocytopenia (reduced number of platelets).

Causative Agent:

Syphilis is caused *Treponema pallidum*, a corkscrew shaped bacteria (spirochete).

Differential Diagnosis:

The differential diagnosis for primary syphilis includes chancroid, granuloma inguinale, trauma to the penis, lymphogranuloma venereum, malignancy or a fixed drug eruption may cause lesions resembling a chancre. The differential diagnosis for secondary syphilis includes pityriasis rosea, erythema multiforme or a drug eruption.

Laboratory identification:

There are various tests for syphilis:

- Darkfield examination – a darkfield examination (by microscopy) of exudate from a chancre is diagnostic for syphilis
- Some tests can cheaply and rapidly identify syphilis, but are not specific, and are known as non-treponemal tests:
 - Rapid plasma reagin (RPR) is a test that is not specific for syphilis. The RPR is a useful screening test.
 - Venereal disease research laboratory test (VDRL) is typically used only on CSF to diagnose neurosyphilis.
- Various serological tests, known as treponemal tests, are used to confirm a diagnosis of syphilis in patients who have a reactive non-treponemal test, these include:
 - Fluorescent treponemal antibody (FTA)
 - EIA/ELISA
 - Microhemagglutinin (MHA-TP)
 - Fluorescent Treponemal Antibody Absorption (FTA-ABS)
 - Treponema pallidum hemagglutination assay (TPHA)
 - Treponemal pallidum antibody (TP-PA)

The advantage to screening with non-treponemal tests is that, once a patient is treated, their non-treponemal test will return to negative, whereas treponemal tests continue to appear positive.

Treatment:

Penicillin G., administered parenterally, is the preferred drug for all stages of syphilis.

Primary Secondary or Early Latent Syphilis

Benzathine penicillin G 2.4 million units IM in a single dose

Late Latent Syphilis or Latent Syphilis of Unknown Duration or Late Syphilis

Benzathine penicillin G 7.2 million units total, administered as 3 doses of 2.4 million units IM each at 1 week intervals

Neurosyphilis

Aqueous crystalline penicillin G 18-24 million units per day, administered as 3-4 million units IV every 4 hours or continuous infusion, for 10-14 days.

Congenital Syphilis

Aqueous crystalline penicillin G 100,000-150,000 units/kg/day, administered as 500,000 units/kg/dose IV every 12 hours during the first 7 days of life and every 8 hours thereafter for a total of 10 days

OR

Procaine penicillin G 50,000 units/kg/dose IM in a single daily dose for 10 days

For additional treatment options and alternatives, please go to www.cdc.gov/std/treatment for the Sexually Transmitted Disease Treatment Guidelines, 2006

Case fatality:

Up to 20% of untreated cases die from this disease. Untreated early syphilis in pregnant women results in perinatal death in up to 40% of cases.

Reservoir:

Humans are the only known natural hosts.

Transmission:

Syphilis is transmitted through oral, vaginal, or rectal sex. Transmission may also occur across the placenta prior to birth. Transmission rarely occurs by blood transfusion.

Susceptibility:

Susceptibility is universal, though only approximately 30% of exposures result in infection.

Incubation period:

The incubation period of primary syphilis is 9-90 days – median 21 days. The incubation period is 3-12 months for secondary syphilis.

Period of communicability:

Patients are most infectious during the primary and secondary stages of syphilis when lesions or rash are present.

Epidemiology:

Syphilis, which is rare in much of the industrialized world, persists in the United States and developing countries. In 2005, primary and secondary cases reported increased for the fifth consecutive year. Although the rate of syphilis infection increased mostly among men, the rate also increased among women. The incidence of acquired and congenital syphilis increased dramatically in the United States during the late 180s and early 1990s but subsequently declined in all areas, but the rates remain disproportionately high in urban areas and the rural areas of the South. Overall increases in rates during 2000-2004 were observed only among men.

 **PUBLIC HEALTH CONTROL MEASURES**

Public health responsibility:

- Investigate all suspect cases of disease and fill out and submit appropriate disease investigation forms.
- Provide education to the general public and clinicians, regarding disease transmission and prevention.
- Identify clusters or outbreaks of this disease.

- Identify sources of exposure and stop further transmission.

Prevention:

Emphasis should be placed on early detection and effective treatment of patients with transmissible syphilis and their contacts.

- Educate the community in general health promotion measures;
 - Provide health and sex instruction that teaches the value of delaying sexual activity until the onset of sexual maturity as well as the importance of establishing mutually monogamous relationships and reducing the numbers of sexual partners;
- Protect the community and controlling STDs in sex workers and their clients;
 - Discourage multiple sexual partners and anonymous or casual sexual activity;
 - Teach methods of personal prophylaxis applicable before, during and after exposure, especially the correct and consistent use of condoms.
- Provide health care facilities for early diagnosis and treatment;
 - Encourage their use through education of the public about symptoms of sexually transmitted infections and modes of spread;
 - Make these services culturally appropriate and readily accessible, and acceptable, regardless of economic status;
 - Establish intensive case-finding programs that include interviewing patients and partner notification;
 - Repeated serological screening within special populations with known high incidence of STDs.
 - Follow cases serologically to exclude other STD infections such as HIV.

Chemoprophylaxis:

All sexual partners should receive prophylaxis.

Vaccine:

None

Isolation and quarantine requirements:

Isolation: Avoid sexual contact until treatment is completed

Hospital: Standard body substance precautions

Quarantine: Not applicable

CASE INVESTIGATION

Reporting:

All cases of syphilis are reportable, even asymptomatic (latent) syphilis..

Case definition:

Syphilis (1996):

Syphilis, primary

Clinical description

A stage of infection with *Treponema pallidum* characterized by one or more chancres (ulcers); chancres might differ considerably in clinical appearance.

Laboratory criteria for diagnosis

Demonstration of *T. pallidum* in clinical specimens by darkfield microscopy, direct fluorescent antibody (DFA-TP), or equivalent methods.

Case classification

Probable: a clinically compatible case with one or more ulcers (chancres) consistent with primary syphilis and a reactive serologic test (nontreponemal: Venereal Disease Research Laboratory [VDRL] or rapid plasma reagin [RPR]; treponemal: fluorescent treponemal antibody absorbed [FTA-ABS] or microhemagglutination assay for antibody to *T. pallidum* [MHA-TP])

Confirmed: a clinically compatible case that is laboratory confirmed

Syphilis, secondary

Clinical description

A stage of infection caused by *T. pallidum* and characterized by localized or diffuse mucocutaneous lesions, often with generalized lymphadenopathy. The primary chancre may still be present.

Laboratory criteria for diagnosis

Demonstration of *T. pallidum* in clinical specimens by darkfield microscopy, DFA-TP, or equivalent methods

Case classification

Probable: a clinically compatible case with a nontreponemal (VDRL or RPR) titer greater than or equal to 4

Confirmed: a clinically compatible case that is laboratory confirmed

Syphilis, latent

Clinical description

A stage of infection caused by *T. pallidum* in which organisms persist in the body of the infected person without causing symptoms or signs. Latent syphilis is subdivided into early, late, and unknown categories based on the duration of infection.

Case classification

Probable: no clinical signs or symptoms of syphilis and the presence of one of the following:

- No past diagnosis of syphilis, a reactive nontreponemal test (i.e., VDRL or RPR), and a reactive treponemal test (i.e., FTA-ABS or MHA-TP)
- A past history of syphilis therapy and a current nontreponemal test titer demonstrating fourfold or greater increase from the last nontreponemal test titer

Syphilis, early latent

Clinical description

A subcategory of latent syphilis. When initial infection has occurred within the previous 12 months, latent syphilis is classified as early latent.

Case classification

Probable: latent syphilis (see [Syphilis, latent](#)) in a person who has evidence of having acquired the infection within the previous 12 months based on one or more of the following criteria:

- Documented seroconversion or fourfold or greater increase in titer of a nontreponemal test during the previous 12 months
- A history of symptoms consistent with primary or secondary syphilis during the previous 12 months
- A history of sexual exposure to a partner who had confirmed or probable primary or secondary syphilis or probable early latent syphilis (documented independently as duration less than 1 year)
- Reactive nontreponemal and treponemal tests from a person whose only possible exposure occurred within the preceding 12 months.

Syphilis, late latent

Clinical description

A subcategory of latent syphilis. When initial infection has occurred greater than 1 year previously, latent syphilis is classified as late latent.

Case classification

Probable: latent syphilis (see Syphilis, latent) in a patient who has no evidence of having acquired the disease within the preceding 12 months (see Syphilis, early latent) and whose age and titer do not meet the criteria specified for latent syphilis of unknown duration.

Syphilis, latent, of unknown duration

Clinical description

A subcategory of latent syphilis. When the date of initial infection cannot be established as having occurred within the previous year and the patient's age and titer meet criteria described below, latent syphilis is classified as latent syphilis of unknown duration.

Case classification

Probable: latent syphilis (see Syphilis, latent) that does not meet the criteria for early latent syphilis, and the patient is aged 13-35 years and has a nontreponemal titer greater than or equal to 32

Neurosyphilis

Clinical description

Evidence of central nervous system infection with *T. pallidum*

Laboratory criteria for diagnosis

A reactive serologic test for syphilis and reactive VDRL in cerebrospinal fluid (CSF)

Case classification

Probable: syphilis of any stage, a negative VDRL in CSF, and both the following:

- Elevated CSF protein or leukocyte count in the absence of other known causes of these abnormalities
- Clinical symptoms or signs consistent with neurosyphilis without other known causes for these clinical abnormalities

Confirmed: syphilis of any stage that meets the laboratory criteria for neurosyphilis

Syphilis, late, with clinical manifestations other than neurosyphilis (late benign syphilis and cardiovascular syphilis)

Clinical description

Clinical manifestations of late syphilis other than neurosyphilis may include inflammatory lesions of the cardiovascular system, skin, and bone. Rarely, other structures (e.g., the upper and lower respiratory tracts, mouth, eye, abdominal organs, reproductive organs, lymph nodes, and skeletal muscle) may be involved. Late syphilis usually becomes clinically manifest only after a period of 15-30 years of untreated infection.

Laboratory criteria for diagnosis

Demonstration of *T. pallidum* in late lesions by fluorescent antibody or special stains (although organisms are rarely visualized in late lesions)

Case classification

Probable: characteristic abnormalities or lesions of the cardiovascular system, skin, bone, or other structures with a reactive treponemal test, in the absence of other known causes of these abnormalities, and without CSF abnormalities and clinical symptoms or signs consistent with neurosyphilis

Confirmed: a clinically compatible case that is laboratory confirmed

Comment

Analysis of CSF for evidence of neurosyphilis is necessary in the evaluation of late syphilis with clinical manifestations.

Syphilitic Stillbirth

Clinical case definition

A fetal death that occurs after a 20-week gestation or in which the fetus weighs greater than 500 g and the mother had untreated or inadequately treated* syphilis at delivery

Comment

For reporting purposes, syphilitic stillbirths should be reported as cases of congenital syphilis.

*Inadequate treatment consists of any non-penicillin therapy or penicillin given less than 30 days before delivery.

Case Investigation Process:

- Fill out a morbidity form
- Conduct a Client Interview
- Fill out a client interview record on original patient and field records for contacts and suspects identified
- Conduct field investigations on contacts and suspects
- Treatment and follow-up for contacts
- Re-interview client for additional contacts and suspects
- Complete interview record

Outbreaks:

A syphilis outbreak occurs when the observed rate of disease in a geographical area exceeds the normal (endemic) rate.

Identification of case contacts:

The stage of disease determines the criteria for partner notification:

- For primary syphilis, all sexual contacts during the 3 months preceding onset of symptoms.
- For secondary syphilis, all sexual contacts during the 6 months preceding onset of symptoms.
- For early latent syphilis, all sexual contacts of the preceding year, if time of primary and secondary cannot be established.
- For late and late latent syphilis, long-term partners, and children of infected mothers.
- For congenital syphilis, all members of the immediate family.
 - If adequate and appropriate treatment of the mother prior to the last month of pregnancy cannot be established, all infants born to seroactive mothers should be treated.

Case contact management:

A fundamental feature of programs for syphilis control is the interviewing of patients to identify sexual contacts from whom infection was acquired in addition to those whom the patient infected. All sexual partners of confirmed cases of primary syphilis during the 3 months preceding onset of symptoms should be examined, tested, and treated. All sexual partners of confirmed cases of secondary syphilis during the 6 months preceding onset of symptoms should be examined, tested, and treated. For early latent syphilis, all sexual contacts of the preceding year, if time of primary and secondary cannot be established should be examined and tested. All cases of confirmed cases of early syphilis exposed within 90 days of examination should receive treatment. For late and late latent syphilis, long-term partners, and children of infected mothers should be examined and tested. For congenital syphilis, all members of the immediate family should be examined and tested. If adequate and appropriate treatment of the mother prior to the last month of pregnancy cannot be established, all infants born to seroactive mothers should be treated. All patients who have syphilis should be tested for HIV.

REFERENCES

Active Bacterial Core Surveillance Report, Emerging Infections Program Network, Centers for Disease Control, 2005.

Centers for Disease Control, Case Definitions for Infectious Conditions Under Public Health Surveillance. MMWR 46 (RR-10), 1997.1

Control of Communicable Diseases Manual (18th Edition), Heymann, D.L., Ed; 2004.

Red Book: 2003 Report of the Committee on Infectious Diseases (26th Edition), Larry K. Pickering MD, Ed; 2003.

Principles and Practice of Infectious Disease (6th Edition), Gerald L. Mandell, John E. Bennett, and Raphael Dolin Eds; 2005.

Massachusetts Department of Public Health, Guide to Surveillance, Reporting and Control, 2006.

ARUP Labs; Physician's Guide to Laboratory Test Selection and Interpretation

Johns Hopkins Point of Care Information Technology

Sexually Transmitted Diseases (3rd Edition), King K. Holmes, P Frederick Sparling, Der-Anders Mardh, Stanley M. Lemon, Walter E. Stamm, Peter Piot, Judith N. Wasserheit, 1999

CDC Sexually Transmitted Diseases Treatment Guidelines, 2006

CDC Summary of Notifiable Disease – United States, 2005