Syphilis

Manitoba Health
Public Health
Communicable Disease Control Unit

Case Definition

Primary Syphilis
Identification of *Treponema pallidum* by darkfield microscopy or fluorescent antibody examination or nucleic acid amplification techniques in material from a chancre, or in aspirated material from a regional lymph node

or

Presence of one or more typical (usually painless) lesions (chancres) and one of the following:

- reactive treponemal serology (regardless of non-treponemal test results), in individuals with no previous history of syphilis;
- a four-fold or greater increase in titre over the last known non-treponemal test in individuals with a past history of syphilis treatment.

Clinical case: History of sexual exposure, within the past 10 to 90 days, to a partner with a confirmed diagnosis of infectious syphilis

Secondary Syphilis
Identification of *T. pallidum* from mucocutaneous lesions or condylomata lata, and reactive serology (both non-treponemal and treponemal)

or

Presence of other signs of secondary syphilis (see below) and one of the following:

- reactive syphilis serology (non-treponemal and treponemal);
- a four-fold or greater increase in titre over the last known non-treponemal test.

Early Latent Syphilis
An asymptomatic person with reactive non-treponemal and treponemal serology who, within the past year, has had any one of the following:

- non-reactive syphilis serology;
- symptoms suggestive of primary or secondary syphilis;
- exposure to a sex partner with primary, secondary or early latent syphilis.

Late Latent Syphilis
An asymptomatic person with reactive treponemal serology (regardless of non-treponemal serology reactivity) who does not meet the criteria for early latent syphilis, has not been previously treated for syphilis, and in whom central nervous system involvement has been ruled out. Examination of cerebrospinal fluid is recommended for persons with neurologic symptoms or signs, or with RPR titre more than 1:16. See Health Canada's *Canadian STD Guidelines, 1998 Edition* (see **Additional Resources**) for additional information on indications for CSF examination. If in doubt, consult an infectious disease specialist.

Tertiary Syphilis other than Neurosyphilis
A broad range of characteristic signs and symptoms involving the cardiovascular system, bone, skin or other structures, in the absence of other known causes of these abnormalities, plus reactive treponemal serology (regardless of non-treponemal serology reactivity), and no clinical or laboratory evidence of neurosyphilis.

Neurosyphilis
Reactive treponemal serology (regardless of non-treponemal serology reactivity) and at least one of the following:

- clinical evidence of neurosyphilis and CSF pleocytosis (particularly lymphocytes) in the absence of other known causes;
- clinical evidence of neurosyphilis and elevated CSF protein in the absence of other known causes;
- reactive non-treponemal test in non-bloody cerebrospinal fluid.

Congenital Syphilis
Identification of *T. pallidum* by dark-field microscopy, fluorescent antibody examination, nucleic acid amplification techniques, or other specific stains in specimens of material from nasal discharge, placental umbilical cord, autopsy material or skin lesions of a neonate.

or

Reactive syphilis serology (nontreponemal and treponemal) from venous blood (not cord blood) in an infant/child with clinical, laboratory or radiographic evidence of congenital syphilis, whose mother is without documented evidence of recommended treatment for syphilis in pregnancy.

Surveillance reports include only laboratory-confirmed cases.

Reporting Requirements

- All positive syphilis tests are reportable by laboratory.
- All cases are reportable by attending health care professional.

Clinical Presentation/Natural History

Primary Syphilis
Characterized by one or more painless indurated ulcers (chancres). A chancre marks the point of entry of *T. pallidum*. Regional lymphadenopathy is often present, and clinical findings usually occur about three weeks after infection with *T. pallidum.*

Secondary Syphilis
Represents a bacteremic stage of infection. Clinical findings include a skin rash, which is often generalized and bilateral. Symmetrical macular, papular, follicular, papulosquamous or pustular skin lesions are often present, and there is often involvement of the palms and soles. Condylomata lata (syphilis warts) are often present in the genital tract. Other signs include mucous patches, generalized lymphadenopathy, fever and malaise, splenomegaly, alopecia areata and iritis. Signs of secondary syphilis usually occur approximately six weeks after an untreated primary stage.

Early Latent Syphilis
In early latent syphilis, the clinical presentation is by definition asymptomatic.

Late Latent Syphilis
In late latent syphilis, the clinical presentation is by definition asymptomatic.

Late Syphilis
Classical manifestations of late syphilis include gumma formation, cardiovascular lesions, neurological lesions, tabes dorsalis and general paresis of the insane. These manifestations are rarely seen now, even in endemic areas. For details, consult a textbook such as Holmes *et al.* (see **Additional Resources**).

Congenital Syphilis
There are a variety of early and late signs of congenital syphilis. For details, consult a textbook such as Holmes *et al.* (see **Additional Resources**).

The likelihood of perinatal transmission of syphilis depends both upon duration of infection in the mother (the longer the duration of an untreated infection, the more likely that the fetus will be infected) and the stage of pregnancy at which maternal infection is acquired (fetal infection is less common during the first trimester of pregnancy).

Infection of the fetus may result in:

- intrauterine death and stillbirth;
- a liveborn infant with active (secondary) lesions;
- a liveborn infant who develops secondary lesions during infancy;
- a liveborn child who develops late manifestations, particularly around puberty.

A presumptive diagnosis of congenital syphilis applies to any infant in whom a four-fold increase in titre over the infant's previous titre is demonstrated. A presumptive diagnosis is made in symptomatic neonates with reactive non-treponemal tests if the mother was not treated adequately for syphilis during pregnancy.

If the neonate is asymptomatic, has positive serology, and the mother was not treated adequately for her infection with penicillin, the infant should be treated without awaiting criteria for a presumptive diagnosis.

A **peripheral** blood sample from the infant and not **cord blood**, should be sent for testing along with a sample of the mother's blood.

Etiology

Syphilis is caused by the spirochete *Treponema pallidum.*

Epidemiology

Reservoir: Humans

Transmission: Transmission is by direct contact with infectious exudates from moist early lesions of skin and mucous membranes of infected persons during sexual contact. Fetal infection occurs through placental transfer or at delivery, through contact with lesions or secretions.

Occurrence:

General: Worldwide. In some developing countries, the prevalence of syphilis seropositivity among antenatal women is as high as 10-15%.

Manitoba: Endogenous transmission has virtually ceased. The last known cases of local transmission occurred in 1996. Since then, few cases of infectious syphilis have been reported, all imported. Approximately 17 cases of syphilis have been reported to Manitoba Health annually over the past few years, the majority of which are in the late latent phase, and most of which probably represent old treated syphilis (intentionally or "accidentally" treated).

Incubation Period: Ten to 90 days, usually about three weeks.

Susceptibility and Resistance: Susceptibility is universal, and the transmission probability after a single sexual exposure is estimated to be about 30%. It remains to be established whether protective immunity develops after infection.

Period of Communicability: Variable. Syphilis is infectious during primary, secondary and early latent stages and also in mucocutaneous recurrences. Congenital transmission is most probable during primary and secondary maternal syphilis, but can occur in the latent period.

Diagnosis

Based on history, physical examination and laboratory investigation. In establishing a diagnosis, it is essential that the stage of syphilis be accurately assessed and documented, in order to ensure appropriate management of cases and contacts. A positive darkfield microscopy test on material from a chancre or aspirated material from a regional lymph node is diagnostic. Positive tests on these materials for fluorescent antibody or for DNA by nucleic acid amplification assays are also diagnostic.

Serologic tests for syphilis are indispensable for diagnosis of individuals, for following the effect of therapy and for screening purposes. They detect antibodies formed during the course of syphilitic infection and are of two basic types:

Non-treponemal or Reagin Tests
Reaginic antibodies are immunoglobulins directed against a lipoidal antigen that results from the interaction of host tissues with *T. pallidum* and/or from *T. pallidum* itself.

The classic reagin test is the Venereal Disease Research Laboratory (VDRL) slide test in which heated serum is tested for its ability to floculate a suspension of cardiolipin-lecithin antigen. The rapid plasma reagin card test (RPR) is used by Cadham Provincial Laboratory (CPL) and is more sensitive than the VDRL.

Serial reagin tests are useful to determine the stage of the disease; a four-fold rise in titre may indicate a recent infection, re-infection in an adequately treated person, or relapse in an inadequately treated person. Adequate treatment of infectious syphilis is indicated by a four-fold or greater decline in titre within one year.

Titres should generally become non-reactive or weakly reactive within 12 months following treatment of primary syphilis and within 24 months after treatment for secondary syphilis. Treatment of late latent or late syphilis usually has little or no effect on the titre and should not be used to gauge the adequacy of the treatment. Titres tend to become lower with time, but serum frequently remains reactive, usually in low titre.

Specific Treponemal Tests

Confirmatory test

The *T. pallidum* particle agglutination assay (TP-PA) measures specific treponemal antibody, is easier to perform than the FTA-abs, and is as specific as the FTA-abs, though slightly less sensitive during primary disease. Reports from CPL refer to the TP-PA as a confirmatory test. It usually remains positive for life.

Reference test

The fluorescent treponemal antibody absorption (FTA-abs) test is an indirect immunofluorescent antibody test using *T. pallidum* from rabbit testis as the antigen. Its interpretation is subjective and requires great attention to detail. Its principal use is to verify the diagnosis of syphilis. It usually remains positive for life. Reports from CPL refer to this as the reference test.

The comparative reactivities of these tests are shown in the following table:

Test	Sensitivity*	
	Primary	Secondary
Non-treponemal (reaginic) tests		
VDRL	80%	99%
RPR	86%	99%
Specific treponemal tests		
TP-PA	82%	100%
FTA-abs	98%	100%

* Percentage of cases detected by the test.

Key Investigations

- Interview case for history of exposure, risk behaviours, contacts, adequacy of treatment and promotion of safer sex practices.
- Interview contacts and provide epidemiological treatment if indicated (see below under **Management of Contacts**), with risk assessment and promotion of safer sex practices.

Control

Management of Cases:

- Cases should be interviewed for history of exposure, risk assessment, contacts, and promotion of safer sex practices. Test for HIV infection and other STDs if indicated.
- Benzathine penicillin is the cornerstone of syphilis treatment, with crystalline penicillin G used for the treatment of neurological and congenital syphilis. Tetracyclines and erythromycin may be satisfactory alternatives for persons with penicillin allergy. See the attached provincial "*Sexually Transmitted Diseases Treatment Guidelines*" and Health Canada's "*Canadian STD Guidelines*", 1998 edition for details (see **Additional Resources**).
- Manitoba Health provides free drugs for STD treatment to non-hospital based practitioners in the provincial jurisdiction.
- The following principles of case management apply:
  - Immediate antimicrobial therapy for all cases of infectious syphilis.
  - Interview within one working day whenever possible.
  - Evaluation one week after onset of therapy to document clinical response.
  - All persons with syphilis should be counselled concerning the risks of HIV infection and HIV testing should be offered.
- Seroreactive persons should be expeditiously evaluated. This evaluation should include a history and physical examination, as well as a

quantitative non-treponemal test and a confirmatory treponemal test.

- If the FTA-abs test is non-reactive and there is no clinical evidence of syphilis, treatment may be withheld. Both the quantitative non-treponemal test and the confirmatory test should be repeated within four weeks. If there is clinical or serologic evidence of syphilis or if the diagnosis of syphilis cannot be excluded with reasonable certainty, the person should be treated.
- Persons for whom there is documentation of recommended treatment for syphilis in the past need not be treated again unless there is clinical or serologic evidence of re-infection such as darkfield-positive lesions or a four-fold rise in titre when a reagin test is used.
- Repeat serologic tests as follows:
  - For infectious syphilis and congenital syphilis at three, six and 12 months after treatment.
    - For syphilis of more than one year's duration at six and 12 months after treatment.
    - Neurosyphilis should be managed in consultation with an infectious disease specialist.
- Re-treatment should be considered when:
  - clinical signs or symptoms of syphilis persist or recur;
  - there is a four-fold increase in titre with a reagin test;
  - a reagin test showing a high titre initially fails to show a four-fold decrease within a year.
- Persons who require re-treatment should be re-treated according to the schedules recommended for syphilis of more than one year's duration. In general, a person should be re-treated only once, since they may maintain stable, low titres when non-treponemal tests are used. All cases of infectious syphilis should abstain from sexual activity until they and their sex partners are appropriately treated and clinical signs are no longer present.
- Cases in hospital should be managed with routine infection control precautions.
- **Syphilis in pregnancy**
  - If the pregnant woman has received recommended penicillin treatment during pregnancy, the risk to the infant is low. However, all infants should be examined carefully at birth, and at frequent intervals thereafter, until non-treponemal serologic tests are negative.
  - Infected infants are frequently asymptomatic at birth and may be seronegative if the maternal infection occurred late in gestation. Infants should be treated at birth if maternal treatment was inadequate, unknown, or with drugs other than penicillin, or if adequate follow-up of the infant cannot be ensured. Infants with congenital syphilis should have a CSF examination before treatment. If the mother is known to have positive syphilis serology and was inadequately treated, RPR and TP-PA tests should be obtained on the infant venous blood.
  - Children discovered to have syphilis after the newborn period should have a CSF examination. Any child who is thought to have congenital syphilis or who has neurologic involvement should be treated with crystalline penicillin G. Older children with definite acquired syphilis and a normal neurologic examination may be treated with benzathine penicillin. Children with a history of penicillin allergy should be managed in consultation with an infectious disease specialist.
  - Women, who have been treated for infectious syphilis during their pregnancy, should have monthly quantitative non-treponemal serologic tests for the remainder of the pregnancy. Women who show a four-fold rise in titre should be treated again. After delivery, follow-up is as outlined for non-pregnant persons.

- **Syphilis In HIV-infected Persons:**
  - All sexually active persons with syphilis should be counselled regarding HIV testing.
  - No change in therapy for early syphilis for HIV co-infected patients is recommended. However, some authorities advise CSF examination and/or treatment with a regimen appropriate for neurosyphilis for all patients co-infected with syphilis and HIV, regardless of the clinical stage of syphilis. In all cases, careful follow-up is necessary to ensure adequacy of treatment.
  - Persons with early syphilis, whose titres increase or fail to decrease four-fold within six months, should undergo CSF examination and be retreated. In such persons, CSF abnormalities could be due to HIV-related infection, neurosyphilis or both.

Management of Contacts:

- It is extremely important that sexual contacts of cases of infectious syphilis be identified and evaluated promptly.
- All sex partners should be clinically evaluated (see below) and have a serologic (reagin) test for syphilis.
- Persons who have been exposed to infectious syphilis within the preceding three months should be epidemiologically treated as for early syphilis.

Patient's Stage	Examine All Sex Contacts Exposed
Primary syphilis	- during the three months prior to onset of chancre and - up to and including the interview date
Secondary syphilis	- during the six months prior to onset of clinical symptoms and - up to and including the interview date
Early latent	- during the 12 months prior to making the diagnosis

- If, however, the interviewer can elicit the following history, the interview period can be established more accurately.
  - If the patient has had a negative RPR in the last year, he/she is interviewed back three months from the date of the negative RPR.
  - If the patient gives a reliable description of a primary chancre, he/she can be interviewed three months back from the first day of the appearance of the chancre.
  - If the patient gives a reliable description of secondary symptoms, he/she can be interviewed six months back from the first day of the appearance of the secondary symptoms.

Patient's Stage	Examine All Sex Contacts Exposed
Non-infectious syphilis	- only those contacts who have been regular long-term sexual partners need to be investigated.

- **Children of Persons with Non-Infectious Syphilis**
  - Young children of persons with non-infectious syphilis should be assessed to ensure that they are free of the sequelae of congenital syphilis.
  - If any child shows evidence of congenital syphilis, serologic tests for syphilis (both reaginic and specific treponemal tests) should be done on all children of the family. If the results are positive, further investigation is indicated, as described above.

Preventive Measures:

- High risk persons should have screening tests annually:
  - persons with multiple sex partners;
  - persons with other sexually transmitted diseases;
  - partners of the above;
  - persons with HIV infection.
- All pregnant women should have a non-treponemal serologic test for syphilis, such as the VDRL or RPR test, at the time of the first prenatal visit. Treponemal tests such as the FTA-abs test should not be used for routine screening. For women suspected of being at high risk for syphilis (see above), a second non-treponemal test should be performed during the third trimester.

Additional Resources

For Health Care Professionals:

- *Sexually Transmitted Diseases Treatment Guidelines*, revised March 1998. Available from Audiovisual and Publications Department, Manitoba Health, telephone (204) 786-7112, fax (204) 772-7213.
- *Canadian STD Guidelines, 1998 Edition*. Available from Audiovisual and Publications Department, Manitoba Health, telephone (204) 786-7112, fax (204) 772-7213.
- Holmes KK, Sparling PF, Mårdh P-A, Lemon SM, Stamm WE, Piot P, Wasserheit JN, eds. *Sexually Transmitted Diseases, Third Edition*. New York: McGraw-Hill, 1999.
- STD/HIV Information Line (Winnipeg RHA), 940-2200
- AIDS/STD Information (Village Clinic/Nine Circles Community Health Centre)
  Winnipeg, 945-2437
  Outside Winnipeg, 1-800-782-2437
- Facts of LIFE Line (Sexuality Education Resource Centre)
  Winnipeg, 947-9222
  Outside Winnipeg, 1-800-452-1957