# *Syphilis:*
## *A Re-emerging Disease*

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In the past several years, there has been a resurgence of syphilis in Canada, as well as internationally. After decreasing to rates of 0.4 to 0.6/100,000 from 1994 to 2000, the national rate of infectious syphilis rose to 1.5/100,000 in 2002 and preliminary data for 2004 show projected rates of 3.9/100,000.[1]

Many Canadian urban centres have had recent outbreaks of syphilis, mostly among gay and bisexual men and/or sex trade workers. Some outbreaks have been associated with the finding of anonymous sex partners through the Internet and at bathhouses. This indicates a possible increase in high-risk sexual behaviours and is especially troublesome due to the interactions between HIV and syphilis.

The resurgence of syphilis and the implications of misdiagnosis make it important for physicians to be familiar with the clinical features of syphilis. They need to maintain a high index of clinical suspicion, especially in patients with high-risk sexual practices.

### Randall's Concern

- Randall, 32, presents to the local sexually transmitted disease clinic with:
  - a five- to six-week history of penile ulcer,
  - a two-week history of skin rash and
  - a one-week history of arthralgia
- He admitted to recently having multiple male sexual partners and, while he usually uses condoms, he did not do so with his current partner.
- Physical examination reveals a single non-tender, indurated penile ulcer and a maculopapular skin rash. Serologic tests showed a rapid plasma reagin of 1:32 and a reactive *Treponema pallidum* partide aggulation.

## *What are the clinical features of syphilis?*

Syphilis is a sexually transmitted infection (STI) caused by *Treponema pallidum*. Transmission primarily occurs through direct sexual contact with infectious lesions (*e.g.*, a chancre). However, it may also be transmitted by blood transfusion or via the placenta. If untreated, the infection may

Table 1

## Stages of syphilis

| Stage | Major signs |
|---|---|
| Primary | • Painless ulcer or chancre that appears 10 to 90 days (usually three weeks) after exposure. It usually heals in three to six weeks, with or without treatment.<br>• Chancre may not be clinically evident (*i.e.,* in rectum or on cervix). |
| Secondary | • Develops four to six weeks after primary chancre.<br>• May develop a maculopapular or other skin rash involving the palms and soles.<br>• *Condyloma lata* (broad, flat, wart-like growths) may develop in moist areas, such as in the mouth, on the perineum and the perianal skin.<br>• Lymphadenopathy, patchy hair loss, muscle and joint aches, fever and malaise.<br>• Can cause neurologic, renal, ophthalmologic, gastrointestinal or hepatic disease.<br>• May overlap with primary stage; usually resolves within weeks to months, but can recur up to four years after initial infection. |
| Latent | • Asymptomatic: May relapse to secondary syphilis in the first four years.<br>• Early latent: Develops within the first year of the infection.<br>• Late latent: Develops more than one year after infection. |
| Tertiary | • May develop three to 10 years or more after primary stage.<br>• Includes cardiovascular syphilis, neurosyphilis and gummatous syphilis.<br>• Gummas are destructive granulomatous lesions that can occur in the skin, viscera, bone or mucosal tissue.<br>• Cardiovascular syphilis involves the aortic valve and root. |

progress through four stages that can overlap (Table 1). Individuals are infectious during the primary, secondary and early latent stages.

It is essential that clinical assessment includes a specific, non-judgmental and targeted sexual risk assessment. Clinical manifestations of syphilis may be non-specific and mimic other diseases. Syphilis should always be considered if a patient presents with atypical lesions or rashes within the context of high-risk sexual behaviour.

Genital ulcers, such as in primary syphilis, increase the risk of HIV infection three- to five-fold and HIV infection can cause an atypical presentation of syphilis.

Neurologic infection with syphilis may occur at any stage and is often asymptomatic. However, symptomatic neurosyphilis may present early (*i.e.*, a few weeks to years after primary infection) or late (*i.e.*, years to decades after primary infection). Symptoms of early neurosyphilis include meningitis, uveitis or stroke. Symptoms of late neurosyphilis include general paresis, dementia and tabes dorsalis.

Untreated or inadequately treated syphilis in pregnancy can result in congenital infection, prematurity or perinatal death. Infants with congenital syphilis may be asymptomatic for two or more years after birth (late congenital disease). However,

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some infants may be symptomatic within the first week to two years after birth (early congenital syphilis).

## How is syphilis diagnosed?

Fluid for dark field microscopy from genital ulcers or moist skin lesions confirms the diagnosis of syphilis. Serology in the early stages may be unreliable, as it can take several weeks after exposure for seroconversion to occur.

Initial serologic screening for syphilis with the non-specific non-treponemal antibody tests (*i.e.*, the venereal disease research laboratory slide test or the rapid plasma reagin test) is preferred because of the lower cost. These tests may also be useful in following response to therapy. Positive non-treponemal antibody tests can be confirmed with the specific treponemal antibody tests (fluorescent treponema antibody absorption test, treponema pallidum particle agglutination or microhemagglutination assay for *treponema pallidum*). The laboratory will do this automatically when there is a positive screening test. Testing of cerebrospinal fluid (CSF) is required to confirm the diagnosis of neurosyphilis.

*Serologic testing for syphilis should be included for all STI cases and as part of routine pre-natal care.*

## How is it treated?

Treatment is usually with long-acting benzathine penicillin G (2.4 million U, intramuscularly): single dose for infection of up to one year duration; three weekly doses for infections of more than one year duration.

An alternative treatment for non-pregnant patients allergic to penicillin is doxycycline, 100 mg, orally, twice daily, or tetracycline, 500 mg, orally, four times daily. Duration is 14 days for primary, secondary and early latent syphilis and 28 days for late latent or tertiary syphilis.

Neurosyphilis requires treatment with high-dose intravenous penicillin or intramuscular procaine penicillin with probenecid.

Follow-up serologic testing after treatment should be carried out to ensure the non-treponemal tests fall to low- or non-reactive levels within a specific time frame. Re-treatment may be necessary if this does not occur. Expert opinion may be required to determine adequate treatment. A follow-up examination of CSF is required to ensure adequate treatment of neurosyphilis.

## *What about prevention?*

Like other STIs, safer sex practices (consistent condom use, careful partner selection) are the keys to preventing syphilis. Serologic testing for syphilis should be included for all STI cases and as part of routine prenatal care. All patients who are positive for syphilis should have HIV testing.

All cases of syphilis should be referred to Public Health for investigation of the source and partner notification. With the growing use of the Internet for developing sexual partners, public health agencies are starting to use the Internet to provide education and prevention information, as well as partner notification.

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## Take-home message

- Syphilis is a re-emerging disease in Canada and internationally.
- It is important for physicians to be familiar with the clinical features of syphilis and to maintain a high index of clinical suspicion, especially in patients with high-risk sexual behaviour.
- Clinical assessment needs to include a specific, non-judgmental and targeted sexual risk assessment.
- All cases of syphilis should be referred to Public Health for investigation of the source and contact tracing.

Reference
1. Community Acquired Infections Division, Centre for Infectious Disease Prevention and Control, Public Health Agency of Canada, October 20, 2005.