Aotearoa New Zealand STI Management Guidelines for Use in Primary Care

Syphilis

Cause

- *Treponema pallidum*, subspecies *pallidum*

Overview

- Increasing incidence in Aotearoa New Zealand in recent years particularly in Auckland and other North Island District Health Boards
- Most syphilis diagnosed in Aotearoa New Zealand is contracted within this country, however syphilis is also commonly diagnosed in migrants from countries with a high prevalence of syphilis, e.g. Eastern Europe, Southeast Asia, China, South America, Africa, Pacific Islands (especially Fiji)
- **Transmission** is through
    - Intimate contact with mucocutaneous skin, including vaginal, penile, anal and oral sex. Condoms are not fully protective
    - From mother to baby (mainly transplacental)
- **Syphilis is most commonly diagnosed in**
    - Men who have sex with men (MSM), however one third of notified cases are currently occurring in heterosexual people
    - Sexual contacts of people with syphilis
- Infectious syphilis is a notifiable condition
- Since 2016, there has been a trend to more cases of congenital syphilis, reflecting the increased incidence in women of reproductive age. Māori and Pacific Peoples are disproportionately affected
- Syphilis in pregnancy carries a very high risk of adverse pregnancy outcomes, and requires urgent specialist management. A New Zealand Sexual Health Society (NZSHS) Syphilis in Pregnancy guideline is available

- **Syphilis serology can be difficult to interpret, with potentially significant adverse consequences for the patient if incorrectly managed. Seek specialist advice for assistance in interpreting serology results if unsure**

Clinical presentation

Clinically, the disease has 3 stages; however approximately 50% of people will have no symptoms and will only be diagnosed by serological testing (see latent syphilis below). Neurosyphilis can occur at any stage of syphilis.

Early (infectious) syphilis
Primary syphilis • Patients may present with a genital ulcer or chancre that is often (not always) painless • The ulcer tends to be non-tender and usually has a well-defined margin with an indurated base • May be unnoticed especially if on anal skin, the cervix or in the mouth • Incubation period 10-90 days (average 3 weeks) • In about 30% of cases there may be multiple chancres • Inguinal lymph nodes are usually enlarged, rubbery and non-tender • Even if untreated, the chancre usually spontaneously heals within a few weeks

Secondary syphilis • The patient may present with constitutional symptoms such as fever, malaise, headache and lymphadenopathy • The skin is involved in over 90% of cases • The rash is usually generalised involving the trunk but may just affect the palms and soles • The rash can be easily confused with drug eruptions, pityriasis rosea or guttate psoriasis • There may be alopecia and condylomata lata (warty growths in the anogenital area) • There may be neurological signs of cranial nerve palsies, ophthalmic signs, sensorineural deafness and meningitis • Incubation period 2-24 weeks (average 6 weeks) • If untreated symptoms slowly resolve over a period of weeks, but may recur
Early latent (< 2 years) syphilis • Early latent implies recent infection within the last 2 years and therefore is treated as infectious syphilis • The person has positive syphilis serology with no associated clinical symptoms or signs • Some people never develop symptoms and will only be diagnosed by serological tests • If patients have not had any previous serology then staging may be difficult and management should be discussed with a specialist. If any doubt about duration of infection, treat as late latent disease
Late syphilis
Late latent (> 2 years) syphilis • Defined as asymptomatic infection that has been present for more than 2 years • After 24 months people are considered no longer infectious to sexual partners but transplacental transmission in pregnancy may still occur • Without treatment, patients are at risk of developing late symptoms or complications

Tertiary syphilis
• Late symptoms or complications may develop months or years later in approximately one third of cases if not treated • Complications include skin lesions (gummas), cardiovascular or neurological disease • People with tertiary syphilis are not infectious to sexual partners

See STI Atlas for images.

Indications for testing

- Patient with possible signs or symptoms of syphilis:
  - Genital or anal ulcers
  - Persisting oral lesions in people at risk for sexually transmitted infections (STIs)
  - Sexually active people with any genital symptoms or generalised rash
  - Any rash affecting the palms of the hands or soles of the feet, or that is persistent or unexplained
  - Pyrexia of unknown origin, unexplained persistent lymphadenopathy, unexplained liver function disturbance, alopecia
  - Neurological signs and symptoms including aseptic meningitis, cranial nerve palsies, sudden onset unilateral sensorineural deafness and dementia
  - Ocular symptoms, e.g. uveitis, optic neuritis
- Sexual contacts of people with syphilis
- MSM (at least annually, but ideally with every sexual health check)
- In pregnancy as part of routine antenatal screening. Consider rescreening in later pregnancy. For more detailed guidance, see NZSHS Syphilis in Pregnancy guideline and NZSHS position statement on re-testing pregnant women for syphilis infection or re-infection
- Routine immigration testing
- When doing a routine sexual health check

Note: If patient is a contact of a person with syphilis they will usually need empiric treatment at time of testing. Discuss with sexual health specialist. If patient is asymptomatic and not a syphilis contact, but is concerned about a specific recent sexual event, it is recommended to do a baseline test at

time of presentation and do a repeat test 3 months from the time of last sexual intercourse

Recommended tests
Symptomatic people and contacts of syphilis should be examined

Testing for syphilis should occur as part of a complete sexual health check

- Diagnosis is by a combination of serology, history and clinical assessment
- Note seroconversion may take up to 3 months after exposure to infection
- If clinical suspicion of syphilis, discuss with a sexual health specialist

Tests	Consideration
Syphilis serology	Blood specimens are usually screened with an EIA test. If the screening test is reactive, confirmatory RPR and TPPA/TPHA tests are performed
Swab of ulcer for *Treponema pallidum* PCR (specialist access only)	Diagnosis may be confirmed by direct identification of *T. pallidum* from an ulcer This test is only available through some specialist clinics in Aotearoa New Zealand, or following discussion with a specialist PCR testing may be positive before seroconversion in very early cases

EIA – Enzyme immunoassay

TPPA - *Treponema pallidum* Particle Agglutination Assay

TPHA - *Treponema pallidum* Hemagglutination Assay

RPR – Rapid plasma reagin

PCR - Polymerase chain reaction

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assistance in interpreting serology results if unsure

- In patients with prior treated syphilis, the EIA and TPPA/TPHA tests usually remain reactive for life, although seroreversion can rarely occur
- In approximately 25% of cases, the RPR will become non-reactive (seroreversal) after a number of years even without treatment. Therefore all people without a documented history of treatment should be treated even if they have a non-reactive RPR test
- RPR titres usually drop after treatment but may not change significantly in low-titre infections or in cases of late latent syphilis (serofast)
- A 4-fold (2 dilution) increase in RPR titre after treatment is indicative of re-infection

Management

- **Treatment should be given by, or following discussion with, a sexual health specialist**
- Patients should have syphilis serology repeated on the day treatment is commenced to provide an accurate baseline for monitoring
- **The penicillin formulation used for treatment must be long-acting, i.e. Bicillin L-A (benzathine benzylpenicillin tetrahydrate)**

Principle treatment option

Situation	Recommended
Early syphilis (primary, secondary, early latent)	Benzathine benzylpenicillin tetrahydrate 2.4 million units (1.2 million units/2.3 mL in each buttock), intramuscular injection, as a single dose
Late syphilis (late latent)	Benzathine benzylpenicillin tetrahydrate 2.4 million units (1.2 million units/2.3 mL in each buttock), intramuscular injection, once weekly for 3 weeks (day 1, 8 and 15)
Syphilis of unknown duration	Benzathine benzylpenicillin tetrahydrate 2.4 million units (1.2 million units/2.3 mL in each buttock), intramuscular injection, once weekly for 3 weeks (day 1, 8 and 15)

- Intramuscular benzathine penicillin may be painful due to volume and viscosity. The Bicillin-L-A prefilled syringe should be warmed to room temperature before use. 0.25 mL of lidocaine 2% may be added to each prefilled Bicillin L-A syringe to reduce injection pain
- **Jarisch-Herxheimer reaction** is a common reaction to treatment in patients with primary and secondary syphilis. It occurs 6-12 hours after commencing treatment, and is an unpleasant reaction of varying severity with fever, headache, malaise, rigors and joint pains, lasting for several hours. Symptoms are controlled with analgesics and rest. Patients should be alerted to the possibility of this reaction and reassured accordingly

Special Situations

Situation	Recommendation
Complicated e.g. neurosyphilis	May require cerebrospinal fluid (CSF) analysis and intravenous penicillin Refer or discuss those with neurological, ophthalmic, auditory or suspected tertiary disease with local sexual health or infectious diseases specialist
Pregnancy	Urgent specialist referral essential See also NZSHS Syphilis in Pregnancy Antenatal Management Guidelines
Allergy or contraindications to penicillin	Seek specialist advice If pregnant and history of penicillin allergy, refer urgently for sensitivity testing and desensitisation
HIV co-infection	Manage syphilis as per HIV seronegative cases

- **Advise to abstain from sex for 1 week from the start of treatment and until 1 week after sexual contact/s have been treated**
- Initiate contact tracing – see below for details
- Children of women newly diagnosed with syphilis should be tested, if it is possible that the index case acquired syphilis before or during pregnancy
- **Infectious syphilis is a notifiable condition**
- Consider HIV pre-exposure prophylaxis (PrEP) if infectious syphilis is

diagnosed in a male or transgender person who has anal sex with men

Partner notification and management of sexual contacts

- Over 20% risk of transmission per act of unprotected intercourse (for early syphilis)
- Contact tracing is important to prevent re-infection and reduce transmission
- Trace according to sexual history and clinical stage of infection:
    - Primary syphilis: **3 months** plus duration of symptoms
    - Secondary syphilis: **6 months** plus duration of symptoms
    - Early latent syphilis: **12 months**
    - Syphilis of unknown duration where RPR ≥ 1:32: **12 months**
    - Late latent syphilis: serological evaluation of current or last sexual contact and serological evaluation of children if index case is female
- Most patients choose to tell contacts themselves; giving written information can be helpful
- Notifying all contacts may not be possible e.g. if there is insufficient information or a threat of violence

Management of sexual contacts

- Contacts should have a full sexual health check, including general examination for signs of syphilis, and should be discussed with a sexual health specialist
- It can take up to 90 days for syphilis serology to become positive after infection, therefore contacts of infectious syphilis from within this time period should be treated empirically regardless of test results. Repeat serology is recommended in 3 months for those who decline empiric treatment
- Advise contacts to abstain from sex or use condoms until results are available, and for one week from the start of treatment
- If contacts test positive for an STI refer to specific guideline

Follow up

Review in **1 week** (in person or by phone): • Discuss test results • Check symptoms (if any) have resolved • Ask if any condomless sex in the week post-treatment • Check medication was completed and tolerated • Ensure notifiable contacts have been informed • Check if any risk of re-infection. Retreatment is necessary if re-exposed to an untreated contact
Test of cure **Infectious syphilis (primary, secondary, early latent syphilis)** • Repeat serology at 3, 6 and 12 months • Serological cure is defined by consistent 4-fold (2 dilutions) drop in RPR titre, e.g. from 1:32 to 1:8 • Failure of RPR titre to decrease 4-fold (2 dilutions) within 6 months is suggestive of treatment failure – re-evaluation with a sexual health specialist is strongly recommended • A subsequent 4-fold (2 dilution) rise in RPR titre is an indication of re-infection – re-evaluation is necessary **Late latent syphilis and tertiary syphilis (excluding neurosyphilis)** • Repeat serology at 6 and 12 months to ensure remains serofast. RPR titres often do not decrease following treatment for late latent syphilis • 4-fold (2 dilutions) increase in titre indicates either treatment failure or re-infection – re-evaluation with a sexual health specialist is strongly recommended
Retesting • Consider testing for other STIs, including HIV, if not undertaken at first presentation, or retesting after the window period

Indications for specialist referral

Referral to or discussion with a sexual health specialist is recommended for:

- All patients with newly reactive syphilis serology
- Concern for possible re-infection or relapse
- Assistance in interpreting serology results if unsure
- Contacts of people with infectious syphilis
- Syphilis in pregnancy

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Auditable outcomes

- 100% have had follow up serology tests by **6 months**

Useful patient resources
Just the facts

Healthy Sex

Endorsement: These guidelines have been endorsed by the Blood Borne Viruses and Sexually Transmitted Infections Standing Committee (BBVSS).

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