

Syphilis

NSW Control Guideline for Public Health Units

Revision history

Version	Date	Revised by	Changes	Approval
1.0	01/06/2015	CDWG	Revision	CDNA/AHPPC
1.1	01/08/2016	CDB	Case definition	CHO
2.0	09/2016	CDB	Update to align with the Syphilis Series of National Guidelines (SoNG) v1.0 (endorsed 15 Jan 2015, released 21 Aug 2016), localised for NSW as indicated by [hard brackets].	CHO
3.0	20/03/2019	CDB	Update to align with the Syphilis Series of National Guidelines (SoNG) v1.1 (endorsed 17 July 2018, released 03 Aug 2018), localised for NSW as indicated by [hard brackets].	CHO
4.0	4/10/2019	CDB	Update to implement timely follow-up of all women of reproductive age in line with changing epidemiological trends in NSW as indicated by [hard brackets]	CHO

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1. Summary

Public health priority

[Confirmed, probable, or possible case of Infectious syphilis; Syphilis - more than 2 years or unknown duration, or Syphilis-unspecified, unless known to represent previously treated syphilis] in a pregnant female: URGENT

[Confirmed, probable, or possible case of Infectious syphilis; Syphilis - more than 2 years or unknown duration, or Syphilis-unspecified, unless known to represent previously treated syphilis in a female of reproductive age (<46 years): HIGH]

Infectious syphilis, confirmed or probable case in a male or non-pregnant female: HIGH

Congenital syphilis: [URGENT]

Non-infectious syphilis [in a male or non-pregnant female]: ROUTINE

*[*Note that the 'possible' and 'Syphilis-unspecified' classifications refer to recording options in the NSW Notifiable Conditions Information Management System (NCIMS) pending classification according to the national case definitions.]*

Priority Classification	Public health response timeline	Data entry timeline
Urgent	Act as soon as possible, respond within 24 hours	Within 1 working day
High	Act as soon as possible, generally within one working day	Within 3 working days
Routine	Action should be carried out as part of routine duties	Within 5 working days

Case management

Immediately on notification of a case of confirmed or probable infectious syphilis, begin follow up investigation and notify the state/territory public health authority [NSW Communicable Diseases Branch (CDB)] or syphilis register in accordance with jurisdictional statutory requirements.

Cases who present with symptoms consistent with infectious syphilis (a painless, indurated genital ulcer or symptoms / signs of secondary syphilis) must be treated at the time of first presentation.

Cases of infectious syphilis diagnosed on serology should be treated as soon as possible (and ideally within two days) of diagnosis.

For cases of syphilis of less than two years duration, one dose of benzathine penicillin 1.8g (2.4 million units) by intra-muscular injection (IMI) is required. For syphilis of more than two years or unknown duration, a course of three doses benzathine penicillin 1.8g (2.4 million units) IMI, 7 days apart, is required.

At the time of the first treatment dose, blood should be collected for (rapid plasma regain test) RPR to provide the baseline used to assess response to treatment and check for re-infection.

RPR testing, by the same laboratory that undertook the baseline assessment, at 3-6 and 12 months following treatment, is important to determine the response of treatment.

Infectious cases are rendered non-infectious 5 days after one dose of benzathine penicillin and all symptoms are resolved (whichever is longer). Completion of adequate treatment for syphilis does not confer immunity and re-infection can occur, frequently in some risk groups, especially HIV infected men who have sex with men (MSM).

Particular care is required to ensure adequate treatment in pregnancy, because of the extreme risk of in-utero infection of the foetus. Serological follow-up of the maternal RPR during and following the pregnancy is essential. Syphilis infection may occur after screening in early pregnancy or following reinfection after treatment. Specialist paediatric review is recommended for the children of all women treated for syphilis in pregnancy^{1,2,3}

Contact management

The aim of identifying contacts of infectious syphilis is to prevent disease transmission by offering testing to identify infection before the onset of clinical symptoms and providing empirical treatment. Timely contact tracing lies at the heart of an effective public health response to syphilis and needs to be prioritised.

Anyone who has had sex (including oral sex) with a person who has confirmed or probable infectious syphilis is a contact. Unborn babies and infants of women with infectious syphilis are also contacts.

Stage of index case	Look-back period for sexual contacts	Management
Primary	Duration of symptoms plus 3 months	Perform syphilis testing Serology
Secondary	Duration of symptoms plus 6 months	PCR swab collection if a lesion is present
Early latent and probable infectious	12 months	Give 1.8g (2.4 million unit) benzathine penicillin without waiting for serology results

2. The disease

Infectious agent

The causative agent is the spirochaete bacterium, *Treponema pallidum subspecies pallidum*. There are a number of other *Treponema pallidum* subspecies that cause non-venereal infections including: *pertenue* (yaws), *endemicum* (bejel or endemic non-venereal syphilis) and *carateum* (pinta).

Reservoir

Treponema pallidum subspecies pallidum is an obligate human parasite.

Mode of transmission

In the vast majority of cases, syphilis is spread by direct contact with skin lesions or mucous membranes of an individual with infectious syphilis during anal, oral or vaginal intercourse. Vertical transmission can occur at any time during pregnancy and at any stage of syphilis.

Less commonly, syphilis is transmitted by infected blood (transfusion, drug users), by non-sexual personal contact with infected lesions or by accidental direct inoculation.

Incubation period

The incubation period is 10 to 90 days with a median of 3 weeks to the onset of primary syphilis.

Infectious period

Syphilis is most infectious during the primary and secondary stages of the disease (refer section below) when moist mucocutaneous lesions are present, with transmission risk being up to 50% per sexual contact. The infectious period is defined as the first two years of infection, if untreated, however the period of high infectivity lasts for 12 months from the onset of infection. Sexual transmission is uncommon after two years of infection.

The risk of maternal trans-placental transmission to the unborn baby is also highest in infectious syphilis. The risk of infection in the unborn baby of a pregnant woman with primary or secondary syphilis is extremely high, approaching 100%. If left untreated, the risk of vertical transmission diminishes over years but may never disappear.

Infected infants with moist mucocutaneous lesions are a potential source of infection.

Clinical presentation and outcome

Clinical presentation may be highly variable and many cases do not follow the classical stages listed below. Neurosyphilis can occur in any stage of syphilis.

Primary syphilis: The primary lesion, a chancre, begins as a papule 10-90 days after infection, soon ulcerating to form an indurated ulcer at the site of inoculation; this may be on external or internal genitalia or a non-genital site, e.g. lip, tongue, pharynx, anus, rectum. This is usually a single indurated and relatively painless lesion and accompanied by regional lymphadenopathy, however atypical multiple and painful lesions can occur. The ulcer heals spontaneously over the course of a few weeks⁴. Clinical suspicion of syphilis should be high for all presentations of a painless, indurated genital ulcer. However in an outbreak setting all genital ulcers should be considered to be potential primary syphilis cases.

Secondary syphilis usually occurs 4 to 10 weeks after onset of the primary lesion. Symptoms include headache, fatigue, lymphadenopathy, low grade fever, sore throat, rash, mucocutaneous lesions, condylomata lata (large, raised, whitish or grey, flat-topped lesions found in warm moist areas) and alopecia. Ocular and neurological symptoms may also occur. Secondary syphilis may commence prior to the resolution of the primary lesion. Untreated secondary syphilis symptoms persist for 3-12 weeks after which the patient enters the early latent phase. Symptomatic relapses of secondary syphilis occur in 25% of untreated cases, mainly in the first 12 months after infection.

Early latent syphilis refers to syphilis of less than two years duration (infectious syphilis) in a person who has no symptoms or signs of infection at the time of diagnosis.

Syphilis of more than two years duration, in the absence of clinical signs, is called late latent syphilis. People with late latent syphilis are asymptomatic for many years. Historically, between one quarter and one third of infected and untreated individuals will ultimately develop tertiary syphilis. The following timelines for development of tertiary syphilis were derived in the pre-antibiotic era and are a guide only. Bone and skin lesions at any time after 2 years but usually between 2 and 15 years, cardiovascular disease at 20-30 years and three types of central nervous system disease (meningo-vascular at 5-12 years, and general paresis and tabes dorsalis usually at 15-25 years).

Treponema pallidum crosses the placenta and infects the foetus at any time in the pregnancy. If untreated, this can result in intrauterine foetal death, stillbirth or a premature baby with congenital syphilis. In early congenital syphilis, the infected baby may be severely affected at birth (with hepatomegaly, ascites, hydrops, foetal anaemia) or more frequently, may not present any observable sign. If the diagnosis is not made then, the baby will present later with non-specific complaints (rhinitis, failure to thrive, pneumonia), nearly always within three months of birth.

Neonates with severe disease have a worse prognosis. Late congenital syphilis corresponds to tertiary disease in the adult and can be prevented by early diagnosis and treatment of the infant.

Persons at increased risk of disease

Populations at highest risk of syphilis include Aboriginal and/or Torres Strait Islander people in remote Australia, men who have sex with men (MSM), female partners of MSM and people who have unprotected sex in overseas countries where syphilis is prevalent. Effective treatment of syphilis does not confer immunity against *Treponema pallidum*, and these high risk groups are at risk of reinfection.

Clinical presentation of reinfection may be similar to primary or secondary symptomatic infection, but often presents as asymptomatic (or pre-symptomatic) rises in serology parameters and is indistinguishable from early latent infection¹.

Particular issues of special relevance to MSM and Aboriginal and/or Torres Strait Islander people are discussed in [section 12](#) and [Appendix 4](#), respectively, of this document.

Disease occurrence and public health significance

Syphilis is no longer rare in Australia with high rates in some communities, including MSM and Aboriginal and Torres Strait Islander people. The rate in the non-Indigenous female population is increasing, albeit from a low baseline. Syphilis rates declined among MSM with the onset of the HIV epidemic but have climbed consistently since the late 1990's. Rates in Aboriginal and Torres Strait Islander people have increased in recent years, especially those living in remote areas, after sustained periods of decline. Overall notification rates in Aboriginal and Torres Strait Islander people remain well above the general population and outbreaks continue to occur.

The public health significance of syphilis lies in its impact on the developing foetus in utero and the interaction of *Treponema pallidum* with the human immunodeficiency virus (HIV). Congenital syphilis is an entirely preventable disease and represents a failure of the health system. Its occurrence reflects a failure of delivery systems for antenatal care and for syphilis control programs. In addition to shared transmission routes syphilis biologically enhances both the transmission and acquisition of HIV; hence syphilis control and HIV prevention are closely aligned.

3. Routine prevention activities

A combination of coordinated prevention activities is more effective than an isolated, single activity.

Sexual health promotion and education programs aim to increase awareness of increase awareness of syphilis and other sexually transmitted infections and empower people to adopt safe sex practices thus reducing their risk of both acquiring and transmitting infection. These programs are targeted to priority groups including young people, MSM, Aboriginal and Torres Strait Islander populations, sex workers and prisoners.

4. Surveillance objectives

- Provide baseline data to enable detection of changes in disease trends including evaluation of intervention strategies
- Enable timely detection and identification of cases of infectious syphilis to facilitate rapid response to the management of cases and their contacts

¹ This is a problematic area – many reinfections in MSM & HIV MSM would not be detected⁵ without regular screening as per STIGMA¹⁶ guidelines.

- Enable timely detection of clusters and outbreaks to facilitate early intervention to control transmission
- Inform the prevention of congenital syphilis

5. Data management

[Check NCIMS ELR workflows daily for syphilis unspecified cases. Manual entry for new notifications should occur within five working days of notification, unless the notification is for a female of reproductive age (<46 years) in which case manual entry should occur within one working day of notification.

All new notifications should be checked for duplicates on NCIMS. Possible duplicate syphilis notifications received through ELR are managed by CDB in consultation with Public Health Units.

- Where there is sufficient evidence to meet the case definition for confirmed or probable infectious syphilis (e.g. positive PCR from an ulcer, laboratory definitive evidence, or laboratory suggestive evidence and positive IgM) classify/enter the new notification appropriately.
- Where there is insufficient evidence to meet the case definition for confirmed or probable syphilis, classify/enter these new notifications into NCIMS as syphilis unspecified pending collection of enhanced surveillance information.

To assist in identifying subsequent re-infections for previously notified syphilis cases in NCIMS (where subsequent notifications are not notified by ELR), enter the non-specific treponemal antibody tests (e.g. VDRL, RPR) in the laboratory results question package in NCIMS. Note: A 4-fold rise in RPR suggests that the notification represents a re-infection and should be managed in the same way as a new infection.

All syphilis cases should be classified or excluded on NCIMS within 90 days of initial notification with the information available to the PHU Any additional information received after this time should be added to the NCIMS event and the event should be reclassified if necessary. At least two attempts should be made to obtain enhanced surveillance information to assist correct classification. The valid options for case classification are:

- Syphilis – infectious (probable or confirmed)
- Syphilis >2yrs or unknown duration (confirmed only)
- Congenital syphilis (probable or confirmed)]

Data for confirmed and probable cases of infectious (i.e. primary, secondary, early latent) syphilis and congenital syphilis should be entered into jurisdictional notifiable conditions databases [NCIMS] within one day of confirmation

Data for confirmed cases of non-infectious (i.e. late latent, tertiary) syphilis should be entered into jurisdictional notifiable conditions databases [NCIMS] as soon as possible following confirmation.

Syphilis is a notifiable disease under the public health acts of all states and territories, and nationally. Cases of reactive serology are reported by pathology laboratories to public health authorities. In some jurisdictions the medical and/or nurse practitioner who diagnoses a case of syphilis is also required to notify the jurisdictional public health authority.

6. Communications

Notify confirmed and probable cases of infectious (i.e. primary, secondary, early latent) syphilis and congenital syphilis in accordance with jurisdictional statutory requirements [Enter/classify confirmed and probable cases of infectious syphilis in NCIMS; notify CDB of any possible, probable or confirmed congenital syphilis cases] ; include the patient's date of birth, sex, indigenous status, address, date of onset, laboratory status, possible sources of infection, other people thought to be at risk and follow up action taken.

State/territory Communicable Disease Branches (CDB) should inform CDNA of outbreaks of infectious syphilis. Interjurisdictional outbreaks requiring national coordination may require support from the National Incident Room (NIR). See [Appendix 4](#) for information about outbreaks in remote populations.

7. Case definition

Infectious Syphilis – less than two years duration (includes primary, secondary and early latent)

Reporting

Confirmed and probable cases should be notified.

Confirmed case

A confirmed case requires either:

- Laboratory definitive evidence

or

- Laboratory suggestive evidence **and** clinical evidence.

Laboratory definitive evidence

- Seroconversion in past two years: treponemal specific test² reactive when previous treponemal specific test non-reactive within past two years **and** the latest result is confirmed by **either** a reactive non-treponemal test³ **or** a different reactive treponemal specific test

or

- A fourfold or greater rise in non-treponemal antibody titre compared with the most recently recorded titre within past two years, **and** a reactive treponemal specific test

Laboratory suggestive evidence

- Demonstration of *Treponema pallidum* by darkfield microscopy (not oral lesions), direct fluorescent antibody microscopy (direct antigen test), equivalent microscopic methods (e.g. silver stains), or DNA methods (e.g. nucleic acid testing)

or

- A reactive treponemal specific test confirmed by either a reactive non-treponemal test or a different reactive treponemal specific test

or

² Treponemal specific tests are: IgG or total Ab immunoassay (EIA or CLIA), *Treponema pallidum* haemagglutination assay (TPHA), *Treponema pallidum* particle agglutination assay (TPPA), Fluorescent Treponemal Antibody Absorption (FTA-Abs), 19S-IgM antibody test, or IgM immunoassay, Treponemal Ab specific immunochromatography (ICT) assay. See [section 8](#) for further details

³ Non-treponemal tests are: Rapid Plasma Reagin (RPR), Venereal Disease Research Laboratory (VDRL). See [section 8](#) for further details.

- A reactive non-treponemal test confirmed by a treponemal specific test

Clinical evidence

- Presence of a primary chancre (or ulcer)

or

- Clinical signs of secondary syphilis.

Probable case

A probable case requires that case does not meet the criteria for a confirmed case **and**

either:

a) In a person with no known previous reactive serology: no history of adequate treatment of syphilis, or endemic treponemal disease, **and**

- Contact with an infectious case **and** laboratory suggestive evidence.

or

- Laboratory suggestive evidence **and** RPR ≥ 16 .

or

- Positive syphilis IgM **and** laboratory suggestive evidence.

or

b) In a person with previous reactive serology: a fourfold or greater rise in non- treponemal antibody titre when the previous serology was done more than two years ago.

and

- Contact with an infectious case

or

- Positive syphilis IgM

Syphilis - more than 2 years or unknown duration:

Reporting

Only **confirmed cases** should be notified.

Confirmed case

A confirmed case requires that the case does not meet the criteria for a case of infectious syphilis less than 2 years duration **and either:**

Laboratory definitive evidence

or

Laboratory suggestive evidence **and** clinical evidence.

Laboratory definitive evidence

A reactive treponemal specific test² which is confirmed **either** by a reactive non-treponemal test³ or a different treponemal specific test

and

- In a person with no known previous reactive serology: no history of adequate treatment of syphilis, or endemic treponemal disease (e.g. Yaws)

or

- In a person with previously reactive serology: a fourfold or greater rise in non-treponemal antibody titre when the previous serology was done more than two years ago.

Note: In a high prevalence area, only one reactive treponemal specific test result is necessary.

Laboratory suggestive evidence

Demonstration of *Treponema pallidum* by darkfield microscopy (not oral lesions), direct fluorescent antibody microscopy (direct antigen detection), equivalent microscopic methods (e.g. silver stains), or DNA methods (e.g. nucleic acid testing).

Clinical evidence

Clinical, radiological or echocardiographic signs of tertiary syphilis.

Syphilis - Congenital

Reporting

Both **confirmed cases** and **probable cases** should be notified, including syphilis-related stillbirth.⁶

Confirmed case

A confirmed case requires **laboratory definitive evidence**.

Laboratory definitive evidence

Mother and child both seropositive by a treponemal specific test²

and

One or more of the following:

- Direct demonstration of *Treponema pallidum* by any of the following: nucleic acid amplification (NAA) test, dark field microscopy, fluorescent antibody or silver stain - in specimens from lesions, nasal discharge, placenta, umbilical cord, cerebrospinal fluid (CSF), amniotic fluid or autopsy material

or

- Detection of *Treponema pallidum* specific IgM in the child

or

- The child's serum non-treponemal³ serology titre at birth is at least fourfold greater than the mother's titre.

Probable case

A probable case requires **laboratory suggestive evidence AND clinical evidence.**

Laboratory suggestive evidence

- Direct demonstration of *Treponema pallidum* as described under laboratory definitive evidence (above), but without serological confirmation in the child.

or

- Child seropositive on non-treponemal testing in the absence of IgM testing

or

- A reactive CSF non-treponemal test (VDRL or RPR) in a child.

or

- A child who remains seropositive by a treponemal specific test at 15 months of age, which is confirmed either by another, different reactive treponemal specific test or a reactive non-treponemal test, in the absence of post-natal exposure to *Treponema pallidum*, including the non-venereal subspecies *Treponema pallidum* subsp. *pertenue* (Yaws) or subsp. *endemicum* (Bejel, endemic syphilis).

Clinical evidence

- Any evidence of congenital syphilis on physical examination

or

- Any evidence of congenital syphilis on radiographs of long bones

or

- An elevated CSF cell count or protein (without other cause)

or

- The mother is seropositive in the perinatal period AND has no documented evidence of adequate treatment⁴.

Notes:

1. A stillbirth where the foetal death has occurred after a 20 week gestation or in a foetus which weighs greater than 500g should be counted as clinical evidence towards a case where laboratory suggestive or definitive evidence exists.

2. Treponemal-specific tests: see footnote 2 and [section 8](#)

IgM assays should not be used for screening purposes.

Treponema pallidum-specific rapid immunochromatography (ICT) assays for use as point-of-care tests are now becoming available, but their performance has not yet been fully established. Positive ICT results should be confirmed with a second treponemal specific assay.

3. Non-treponemal tests: see footnote 3 and [section 8](#). Any positive sera should be tested by serial dilution to provide an end-titre. Non-treponemal tests may be used to monitor efficacy of treatment. Mother and child sera should be collected contemporaneously and tested in parallel and cord blood should not be used for the investigation of congenital syphilis.
4. Treatment is considered adequate if
 - a. a stage-appropriate penicillin-containing regimen was used 30 days or more prior to delivery **and**
 - b. all antenatal and delivery pathology investigations were performed and results verified **and**
 - c. there is no evidence of reinfection.
5. Treatment with macrolides alone during pregnancy in penicillin-allergic women is no longer regarded as adequate therapy as resistance to macrolides in *T pallidum* is increasingly common (now >50% in Australia) and may arise during therapy. Expert advice should be sought in such cases.
6. Although the risk of congenital syphilis is much higher in early-stage disease, in the presence of untreated syphilis the birth of an unaffected child does not guarantee that subsequent children will not be affected.

8. Laboratory testing

Laboratory case definitions for syphilis are available on the [Department of Health web site](http://www.health.gov.au/internet/main/publishing.nsf/Content/cda-phln-syphilis.htm) (<http://www.health.gov.au/internet/main/publishing.nsf/Content/cda-phln-syphilis.htm>).

Culture is not available. Syphilis is principally diagnosed by serology (treponemal specific and non-treponemal tests), and sometimes (if lesions are present) by nucleic acid amplification techniques or direct demonstration of the organism by dark-field microscopy or direct fluorescent antibody techniques (direct antigen detection).

Syphilis serology

There are two types of syphilis serology tests: treponemal specific tests and non-treponemal tests. Treponemal specific tests detect antibodies to antigens specific to pathogenic *T. pallidum*. They become reactive after infection with *T. pallidum* and usually remain reactive indefinitely regardless of adequate treatment, however partial or complete loss of treponemal specific antibodies over time occurs in a minority of patients, especially HIV-infected or those treated very early in infection. They do not necessarily indicate active infection. Non-treponemal tests detect reagin (a combination of lecithin, cholesterol and cardiolipin), a substance similar to that generated in response to spirochaete-induced damage to cellular membranes. Tests based on detection of antibodies to reagin are a useful indicator of disease activity.

Treponemal and non-treponemal serology tests are less than 100% sensitive in primary syphilis so syphilis serology may be negative in the presence of a chancre.

Treponemal specific tests

- Agglutination assay tests: *T. pallidum* particle agglutination (TPPA), *T. pallidum* haemagglutination (TPHA), microhaemagglutination assay for antibodies to *T. pallidum* (MHA-TPTPPA). These assays detect IgM well and show sensitivity in early syphilis roughly equivalent to IgM immunoassays.

- *T. pallidum* immunoassays: Immunoassays are suitable for automation and is favoured by many laboratories as a suitable screening test for infectious syphilis. The recombinant (IgG or total antibody) immunoassay antibody test is probably the most sensitive treponemal specific test post primary syphilis, and it is highly specific. There are a variety of different immunoassays in use; the most common tests in Australia are enzyme immunoassays (EIA), chemo-luminescent immunoassays (CLIA) and chemiluminescent microparticle immunoassay (CMIA). Immunoblot assays are also used by a few laboratories. Sensitivity and specificity of different immunoassays at various stages of syphilis will vary with antigen type and concentration used.
- Fluorescent treponemal antibody absorption test (FTA-ABS). Sensitivity varies with disease stage: primary 86%, secondary 100%, early latent 98% and late latent 73%. Specificity is 97%.⁷ This test is less commonly used as a confirmatory test since the introduction of EIAs and other immunoassays as it is technically difficult, labour intensive and subjective, but is still used with CSF
- *T. pallidum* IgM EIA: this test is sometimes used in the investigation of congenital syphilis and early acquired syphilis. In primary syphilis sensitivity is 86.5% and specificity oscillates between 91 and 99.8% depending on the assay used.⁸ Sensitivity is lower in later disease stages and in re-infections, but its presence indicates active disease. This test should not be used for screening purposes as occasional low-level false positive results occur.

Non-treponemal tests

- Non-treponemal tests do not detect antibody to *T. pallidum* but to reagin and are a useful indicator of disease activity. Other conditions (infections and autoimmune conditions) can also induce antibodies to reagin, leading to false positive results but with titres generally ≤ 8 . Non-treponemal tests in use today are known as VDRL (venereal diseases research laboratory) and RPR (rapid plasma reagin).
- The VDRL test requires microscopy and is usually used only on cerebrospinal fluid, although it may also be used on serum (but not plasma)
- The RPR is performed on serum or plasma. Sensitivity varies according to disease stage: primary 86%; secondary 100%; early latent 98%, late latent 73%.⁷ Specificity is 98% (if treponemal specific tests positive).⁸

Reporting and interpretation of tests

There is a period after infection when both treponemal specific and non-treponemal serology may be negative. Generally speaking the treponemal specific test (e.g. EIA) becomes reactive within 2-4 weeks and the RPR becomes reactive within 3-4 weeks post infection.

Most laboratories in Australia now use a treponemal specific test as the first (screening) test following a request for syphilis serology. If reactive, a non-treponemal test (e.g. RPR) and another specific treponemal specific test is performed.

Most laboratories report treponemal specific tests as reactive or non-reactive.

The RPR, if reactive, is reported as a titre – the endpoint of a serial dilution: 1 in 2, 1 in 4, 1 in 8, 1 in 16, 1 in 32 etc. which represents the highest dilution giving a reaction. A higher dilution suggests more active disease. The results are reported as the reciprocal of the highest dilution (ie. 2, 4, 8, 16 etc). Figure 1, developed by Gavin Hart, indicates the typical RPR response following syphilis infection.¹⁰

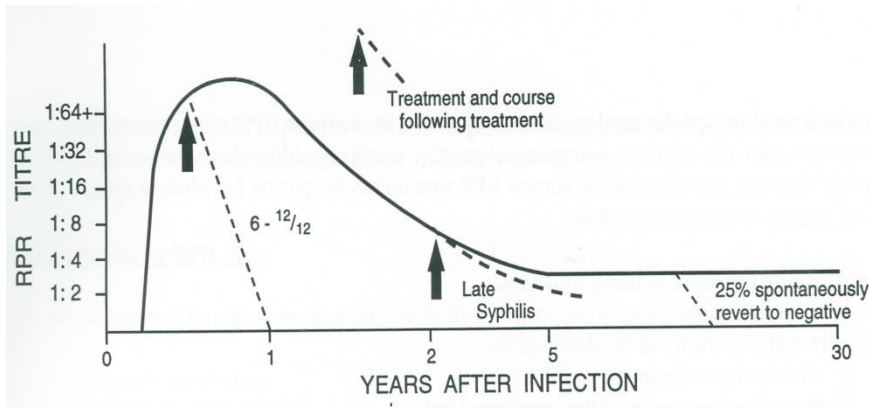


Figure 1: Variation in RPR titre after infection

The RPR test is also used to monitor response to treatment. An adequate response to treatment in infectious syphilis is defined as a four-fold (or two-dilution) drop in RPR e.g. 1 in 128 to 1 in 32 on parallel testing by 6 months, though the rapidity of this decline varies according to disease stage at treatment. This test becomes non-reactive in the majority of patients if infection is diagnosed and adequately treated early in its course. Patients with high RPR titres, late diagnoses and individuals who have been re-infected will be left with fixed reactive (serofast) RPR titres (e.g. 1 in 16) despite adequate treatment, in up to a quarter of patients.

Re-infection is generally diagnosed on the basis of changes in RPR titre. A four-fold or two-titre rise in RPR, e.g. 1 in 2 to 1 in 8, following previous adequate treatment is considered a re-infection. PCR may be useful if ulcerated or moist lesions are present.

The non-treponemal test results rely on subjective judgements by the operator reading the test. The reproducibility of the result will vary according to the skill of the operator and the antigen preparation used. Comparison of results on serial samples should always be done in parallel. Results from different laboratories for an individual patient should not be compared.

Treponemal specific and non-treponemal tests do not distinguish between sub-species of *Treponemes*. In some parts of remote Australia yaws and non-venereal endemic syphilis were common up until the late 1960s and yaws remains common in PNG, Indonesia, the Solomon Islands, Vanuatu and parts of central and west Africa.¹¹ It is possible that people from these regions who acquired these conditions as children will still have the antibodies giving them reactive treponemal serology without ever having had infectious syphilis.

Nucleic acid amplification techniques

If an individual has clinically observable lesions (e.g. genital ulcer, lesions of secondary syphilis), a dry swab, scrapings or biopsies for a nucleic acid amplification (NAA) test such as a polymerase chain reaction (PCR) test for *Treponema pallidum* should be collected. This test can also be done on placental specimens (including paraffin embedded tissue), ocular fluids and CSF. These tests are highly sensitive and specific and are now available in most states, but are not recommended for testing blood.¹²

Point of care rapid tests for syphilis⁴

There is currently only one syphilis point of care test registered by the Therapeutic Goods Administration in Australia, the Determine Syphilis TP™ manufactured by Alere, now Abbott. The Determine Syphilis TP™ is a treponemal specific immunochromatographic test that can be used

⁴ See: [Appendix 4](#). Guidelines for the Public Health Management of Syphilis Outbreaks in Remote Populations in Australia for further discussion on the use of point of care testing in the current context

with whole-blood samples from either finger-prick or venepuncture. Point of care syphilis tests, used in combination with conventional syphilis serology and treatment history data, can facilitate case identification and reduce time to treatment for infectious syphilis.^{13,14,15} Interpretation requires access to the individual's previous syphilis serology and treatment history. If treatment is triggered on the basis of the rapid test alone, then over-treatment can result. In an outbreak situation, this may be considered an acceptable risk, especially for people who have no known history of past syphilis and where follow-up is uncertain.

There are a number of limitations with current syphilis point of care tests:

- currently tests cannot distinguish current from previous syphilis infection, due to either the absence of, or non-quantified nature, of a non-treponemal component;
- even in ideal use sensitivity and specificity are slightly lower than laboratory based assays;
- the tests are moderately complicated and require staff to be specifically trained in their use;
- there are quality control issues with the storage, tracking and QC validation of test batches and
- the results may not be captured by current notification and testing registries.

The following issues should be considered when implementing syphilis point of care tests:

- the prevalence of past syphilis infection (generally they should only be used in populations with low rate of past syphilis infection);
- development of clinical protocols, training and an appropriate clinical governance system;
- perform laboratory based testing in parallel for all reactive results and for negative results wherever feasible; and
- ensure there is a process to notify reactive results to public health authorities and, where applicable, notify all test results to the syphilis register.

Please refer to [Appendix 4](#) for further consideration on the use of syphilis point of care tests in outbreak contexts.

9. Case management

Response times

Prioritisation of the public health response to a case of confirmed or probable infectious syphilis is HIGH. Infectious syphilis occurring in a pregnant woman requires URGENT public health response due to the risk of congenital infection.

[Respond to possible, probable, and confirmed cases of congenital syphilis, or any otherwise classified syphilis notification in an infant aged ≤12 months within one working day of notification. Ascertain and document in the relevant NCIMS data fields the pregnancy status and Indigenous status of all women of reproductive age (aged <46 years) within one working day of notification. Where the diagnosing facility is a local sexual health service, the relevant PHU may follow established regular communication arrangements to ascertain pregnancy status and Indigenous status. For all notifications, send a follow up letter and questionnaire to diagnosing doctors within 3 working days of notification.]

Investigation

Immediately on notification of a case of confirmed or probable infectious syphilis, begin follow up investigation [In NSW, for any syphilis notification where the patient is managed by a doctor not known to have experience in the management of syphilis, refer the notification to local sexual health services on the day of notification to enable sexual health clinic staff to offer timely assistance to the doctor and complete the notification form. For syphilis notifications where the diagnosing doctor is known to have experience in managing syphilis, send a follow up letter and questionnaire within one working day of notification] and notify the state/territory CDB [Enter/classify case in NCIMS (refer to [section 5](#))].

[PHU's may make special arrangements with their sexual health service to facilitate timely and efficient assistance to inexperienced clinicians.

For cases diagnosed by a Sexual Health Service, or clinicians known to the PHU to have expertise in sexual health, the PHU may make special arrangements to facilitate efficient notification and collection of enhanced surveillance information, for example, arranging for distribution or collection of completed forms on a regular basis (at least monthly).]

Response procedure

Case investigation

[Congenital cases]

[The response to a notification will normally be carried out in collaboration with the case's managing doctor(s). Regardless of who does the follow-up, for possible, probable or confirmed cases of congenital syphilis or any otherwise classified syphilis notification in an infant aged ≤ 12 months, PHU staff should ensure that action has been taken to:

- Complete the CDONCALL Report and send to CD on-call as soon as practicable.
- Confirm results of relevant pathology tests, presence of clinical signs for the child, and maternal serological test results to determine whether the child meets the case definition and record these information in the relevant NCIMS data fields.
- Classify case in NCIMS
- Collect outstanding information using the congenital syphilis form and record these information in the relevant NCIMS data fields where applicable.
- Refer to appropriate specialist for management]

Non congenital cases

The response to a notification will normally be carried out in collaboration with the case's managing doctor(s). Regardless of who does the follow-up, for confirmed and probable cases of infectious syphilis, PHU staff should ensure that action has been taken to:

- confirm results of relevant pathology tests
- confirm the onset date and symptoms of the illness
- obtain a full sexual history, including contact history; conduct a physical examination and testing for other STIs, including HIV, in accordance with local clinical guidelines
- find out if the case has had syphilis previously and if so, obtain details of previous syphilis tests and treatments and where these were carried out
- find out if the case or relevant care-giver has been informed of their diagnosis and seek the doctor's permission to contact the case or relevant care-giver (where possible) before

beginning the interview; although this may not always be practicable it is included as a courtesy to the treating doctor

- review case and contact management to ensure they have been completed
- review the case history and test results to ensure that the correct syphilis stage has been recorded in notification data.

[Pregnant cases

[The response to a notification will normally be carried out in collaboration with the case's managing doctor(s). Regardless of who does the follow-up, for all cases of syphilis in a pregnant women who cannot be clearly identified as previously adequately treated syphilis, PHU staff should ensure that action has been taken by the managing doctor(s) to:

- ascertain treatment status,
- ensure that all sexual contacts have been treated and tested,
- consider referral to appropriate specialist service for management to ensure comprehensive follow-up of the case and contacts.

All cases without documentation of stage-appropriate treatment at least 30 days prior to the estimated delivery date (see section Syphilis in pregnancy) should be notified to CDB. The responsibility to follow-up with the managing clinician(s) remains with PHUs, with advice from CDB if required.

[Cases under 16 years]

[As Mandatory Reporters, any health worker who has reasonable grounds to suspect that a child or young person may be at risk of significant harm must make an immediate report to the Community Services Child Protection Helpline on 132 111.

Where a case of syphilis is reported in a child <16 years old, the PHU must send a letter to the doctor who requested the test to undertake an assessment of the risk of harm according to the mandatory reporting guidelines and obligations under the Children and Young Persons (Care and Protection) Act 1998.

Where a case of syphilis is reported in a child aged 12 years or under, the PHU must also directly contact the doctor (eg by telephone) to ensure that mandatory reporting obligations have been addressed. If no contact can be made, the PHU should contact the Child Well Being Unit (1300 480 420) or make a direct report to the Community Services Child Protection Helpline (132111).

The PHU should make reasonable attempts to record in NCIMS the Indigenous status of all cases under 16 years, for example by checking the LHD patient management system and/or calling the diagnosing doctor.

All actions should be documented in the NCIMS record.]

Who is the best person to conduct the contact tracing interview? This is a local decision best made on a case-by-case basis. The culture and gender of the interviewer and whether or not they are known to and trusted by the case are relevant factors to consider.

When to interview cases about their contacts? Symptomatic patients should be interviewed in relation to their contacts when they first present, while early latent cases diagnosed on serology findings should be interviewed when seen for treatment.

Interviewing cases about their sexual contacts must be undertaken on a voluntary basis. The cooperation of the case is critical. The interview must be conducted in a private space and without hurrying. It needs to be approached with care and sensitivity and accompanied by clear information in language the individual understands. The way syphilis is spread and the importance

of tracing all sexual contacts who may have been exposed should be explained. The case should be assured of the confidential nature of these disclosures and that the contact/s will not be told the identity of the person who named them, only the type of infection to which they have been exposed.

A clinical review at one-week post-treatment is recommended and gives the health care provider the opportunity to ask again about contacts. Even if contact names were provided at the first interview, further careful inquiry would be appropriate, e.g. “..... Is there anyone else you think should be seen?”

When a case has named a contact, they should be asked whether this is their regular partner. If it is, then they should be asked “who else?” If the named contact is not a regular partner, then they should be asked about their regular partner/s. If the interviewer believes there are other contacts that remain un-named, the question may be asked differently. For example, the case may find it easier to remember their contacts if the inquiry is related to significant events: “where were you on your birthday? Did you have a party? Who were you with then?” or “what was happening at the rodeo? Who were you with then?”

The interviewer should always expect more than one contact, and never assume the gender of any contact. The interviewer should also consider asking the case about their friendship group: “who, in your group, do you think should also have a test?” (social contact tracing).

If a case has not named any contacts, or the named contacts do not have syphilis, or a case and contact name only each other, both case and contact must be re-interviewed. Consultation with a local health worker as to the appropriate approach may be helpful, but must not compromise confidentiality.

Case treatment

Cases who present with symptoms consistent with infectious syphilis (a painless, indurated genital ulcer or symptoms / signs of secondary syphilis) must be treated at the time of first presentation.

Cases of infectious syphilis diagnosed on serology should be treated as soon as possible (and ideally within two days) of diagnosis. Rapid referral and confirmation of treatment is required if a case moves away from the location where they were diagnosed before undergoing treatment.

Cases of infectious syphilis who are known to be pregnant require urgent follow up and treatment to minimise the possibility of vertical transmission. Breast feeding does not result in the transmission of syphilis, unless an infectious lesion is present on the breast.

The treatment for syphilis generally recommended is long-acting benzathine penicillin.

For cases of confirmed infectious syphilis of less than two years duration, one dose of benzathine penicillin 1.8g (2.4 million units) IMI , OR procaine penicillin 1.5 g IM, daily for 10 days is required. For probable cases of infectious syphilis or syphilis of more than two years or unknown duration, a course of three doses benzathine penicillin 1.8g (2.4 million units) IMI, 7 days apart, OR procaine penicillin 1.5 g IM, daily for 15 days is required.

Cases of congenital syphilis should be treated in consultation with a specialist paediatrician. The recommended treatment is benzylpenicillin 50mg/kg IMI or IVI, 12 hourly for 10 days or procaine penicillin 50mg/kg IMI daily for 10 days.

For detailed information on therapeutic agents for tertiary syphilis see the current edition of *Therapeutic Guidelines: Antibiotics* www.tg.org.au

If penicillin is contraindicated, seek specialist advice from an infectious diseases, or sexual health, physician. Individuals who are allergic to penicillin should be considered for desensitization in the first instance (especially if pregnant). For non-pregnant patients who are hypersensitive to penicillins if desensitisation is not possible, doxycycline 100 mg orally, 12-hourly for 14 days can

be used. Ceftriaxone may also be an option, but efficacy has not been formally proven. Do NOT attempt to treat syphilis with macrolides.

Monitoring response to treatment

At the time of the first treatment dose, blood should be collected for RPR to provide the baseline used to assess response to treatment and check for re-infection.

Treatment of infectious syphilis is considered to be adequate if there is a four-fold (two titre) drop in RPR, e.g. 1 in 64 to 1 in 16, by 6 (up to 12) months. RPR testing, by the same laboratory that undertook the baseline assessment, at 3-6 and 12 months following treatment, is important to determine the response of treatment. Comparison of results on serial samples should always be done in parallel. Results from different laboratories for an individual patient should not be compared

Testing too soon after treatment should be avoided as it may show an increase in RPR; this does not indicate treatment failure.

Infectious cases are rendered non-infectious 5 days after one dose of benzathine penicillin. Completion of adequate treatment for syphilis does not confer immunity and re-infection can occur.

Syphilis in pregnancy

Due to the extreme risk of vertical transmission of syphilis particular care is required to ensure adequate treatment in pregnancy, all cases of syphilis in pregnancy should be discussed with a clinician with expertise in the area. Treatment of syphilis in pregnancy is according to disease stage and is usually the same as in the non-pregnant state. Contact tracing and treatment for the woman's partner/s are critical to minimise the potential for re-infection as this represents a particular threat to the unborn baby.

[Serological follow-up of the maternal RPR during and following the pregnancy is essential; this is important for monitoring the response to treatment and prompt detection and treatment of re-infection. In NSW, consult with a specialist service to determine appropriate follow-up testing during pregnancy and after birth. For treatment of syphilis in pregnancy to be considered adequate, stage-appropriate penicillin treatment needs to be completed at least] one month (30 days) prior to delivery. Ideally there should be a demonstrated four-fold (two-titre) drop in maternal RPR, e.g. 1 in 64 to 1 in 16, prior to birth.¹⁸ The neonate should be examined and investigated based on a risk assessment taking into account adequacy of maternal treatment. Based on the risk assessment and the findings of the initial clinical examination and any available test results, treatment of the baby for congenital syphilis should be considered. Specialist infectious disease paediatric advice is recommended.]

All cases of congenital syphilis must be consistently identified, reported and then investigated to identify factors for improvement at both clinical and system levels, with mechanisms made available to implement recommended changes to practice.

Education

Cases of infectious syphilis need to be informed of the infectious nature of their disease, even in the absence of visible lesions or symptoms, and to abstain from sexual activity for 5 days post-treatment or until symptoms have completely resolved (whichever is the longer). The importance of follow up and repeat syphilis serology testing to monitor the response to treatment should be emphasised. The case should be informed that they may continue to have positive treponemal specific tests for life even after successful treatment.

Isolation and restriction

Cases of infectious syphilis should abstain from sexual activity for five days after receiving treatment or until symptoms have completely resolved (whichever is longer).

Active case finding

Testing for syphilis is recommended when:

- There is a clinical presentation of a suggestive genital ulcer (chancre of primary syphilis) or symptoms/signs of secondary syphilis
- A person is diagnosed with another STI – at the time of diagnosis and 3 months later
- A sexual contact of a person diagnosed with an STI is being evaluated
- A person requests an STI check, and
- In pregnancy, according to national and local clinical guidelines. The Royal Australian and New Zealand College of Obstetricians and Gynaecologists recommends syphilis testing of all pregnant women at the first antenatal visit and again at 28 weeks in those at high-risk. Women at high-risk includes all Aboriginal and Torres Strait Islander women. [In NSW, all Aboriginal and Torres Strait Islander women and women whose babies will identify as Aboriginal or Torres Strait Islander should have a second syphilis screen at 24-28 weeks gestation] In the jurisdictions affected by an ongoing syphilis outbreak, most antenatal care guidelines for at-risk populations within the outbreak areas recommend syphilis serology screening 5 times around the pregnancy: at the booking visit, again at 28 weeks, at 36 weeks, at delivery, and 6 weeks post-partum. Local guidelines exist within those areas that might recommend different or additional times for testing; cross-reference with direction from local authorities is advised. In those areas where point of care tests are used, serology confirmation of current infection or stages is recommended. Syphilis testing in pregnancy is essential for early detection and treatment of new infections and re-infections.

Periodic syphilis testing is currently recommended for asymptomatic people in high risk groups, including:

- Young, asymptomatic Aboriginal and Torres Strait Islander populations in specific regions. Recommendations vary between regions and are based on local evidence and expert opinion. Health staff should be aware that the requirement of a blood sample for syphilis testing might deter some young people from participating. Outside of outbreak situations, opportunistic syphilis testing of asymptomatic older Aboriginal and Torres Strait Islander people (>40 years) in pursuit of diagnoses of infectious syphilis should be actively discouraged because this group is not at increased risk of infectious syphilis and testing without a clinical indication is likely to result in unnecessary treatment of people with positive treponemal specific tests who were treated many years ago for venereal and/or non-venereal syphilis and/or yaws.
- MSM. The STIGMA (Sexually Transmissible Infections in Gay Men Action Group) guidelines¹⁶ recommend annual STI testing, including syphilis testing, for all MSM who have had sex with a man in the past one year; 3-6 monthly testing for MSM who have had unprotected anal intercourse, more than 10 partners in the past 6 months, group sex or used recreational drugs during sex; and 3 monthly testing for MSM with HIV.
- Women whose sexual partner/s are MSM.
- Sex workers. STI prevalence in Australian sex workers is low. However, periodic 6-12 monthly testing is recommended.

10. Environmental evaluation

Not applicable

11. Contact management

It is recommended that jurisdictions ensure that primary health, sexual health and public health staff are made aware of their roles and responsibilities in relation to contact tracing for infectious syphilis. Roles may vary between jurisdictions and between different regions within a jurisdiction. It is also recommended that public health services maintain active oversight of contact tracing processes for infectious syphilis cases even where they do not provide staff to actively support the contact tracing effort. Contact tracing staff should be guided by the Australasian Contact Tracing Manual <http://ctm.ashm.org.au/>

Identification of contacts

The aim of identifying contacts of infectious syphilis is to prevent disease transmission by offering testing to identify infection before the onset of clinical symptoms and providing empirical treatment.

Contact definition

Anyone who has had sex (including oral sex) with a person who has confirmed or probable infectious syphilis is a contact. Unborn and newborn babies of women with infectious syphilis are also contacts.

How far back to trace? The infectious period depends on the stage of infection.

- For cases with primary syphilis, contacts should be traced for the duration of the case's symptoms plus three months; if uncertain, contacts to six months prior to presentation are to be traced
- For cases with secondary syphilis, contacts should be traced for the duration of the case's symptoms plus six months; if uncertain, contacts to 12 months prior to presentation are to be traced
- For cases of probable infectious syphilis and early latent syphilis, contacts to 12 months prior to presentation are to be traced.

Contact management

In addition to empirical treatment, contact management should include:

- Obtaining a sexual history including inquiry for symptoms or a recent history of symptoms and a clinical examination for signs of syphilis and other STIs
- Investigations for other STIs, according to local clinical guidelines.
- Informing contacts of their test results at the earliest opportunity after the results of investigations become available.
- If it was difficult to locate the contact or if their follow-up is likely to be difficult or delayed, consider obtaining a full sexual history including a sexual contact history at the initial consultation.

Patient and provider referral are the two main methods of alerting contacts. In the former, the case notifies their contacts while in the latter, the health care provider organises the notification and treatment of contacts. In remote populations, provider referral is the principal method of contact tracing used. When patient referral is used, contact management as outlined above should occur within two weeks of case treatment and the health staff responsible should confirm with the patient that this has occurred. If delays in patient referral occur, the patient should be offered additional support to undertake patient referral and the option to change to provider referral.

Innovative contact tracing tools have been used in MSM settings. These include on-line patient referral tools such as [The Drama Downunder's 'Let him know' website](#)

(<http://www.thedramadownunder.info/notify/>) and the WA AIDS Council M Clinic's peer-led service delivery. On-line partner notification services have been developed by the [Australian Council of AIDS Organisations for Aboriginal people](http://www.bettertoknow.org.au/) (<http://www.bettertoknow.org.au/>) and by the [Melbourne Sexual Health Clinic](http://www.letthemknow.org.au/) (<http://www.letthemknow.org.au/>).

How much effort should be put into finding contacts of infectious syphilis? The highly transmissible nature of infectious syphilis, and specifically its capacity to spread rapidly through a population and to cause both foetal death and severe congenital complications if transferred to a pregnant woman, demands an urgent response from primary care and public health/sexual health clinic staff. Tracing the contacts of early syphilis should be a high priority, higher than contact tracing for other STI (chlamydia, gonorrhoea) which can cause serious complications but not so acutely. Rigorous and immediate efforts are called for. Half-hearted attempts will result in further sexual transmission and potentially result in serious avoidable outcomes such as congenital syphilis. If contact tracing is not effective, the patient is at high risk of being re-infected after treatment.

Response times

Timely contact tracing lies at the heart of an effective public health response to syphilis and needs to be prioritised. Contacts of infectious syphilis who live locally should be seen and treated within two working days of the case's treatment. If the contacts are elsewhere and referral has been necessary, health staff should aim to ensure that all contacts are seen and treated within two weeks of the case's treatment.

Empirical treatment

Persons who were sexually exposed to a patient with primary, secondary, or early latent syphilis should be treated presumptively with one dose of benzathine penicillin 1.8g (2.4 million units) regardless of their syphilis serology results.

Education

Contacts of infectious syphilis need to be informed about the infectious nature of the disease, the possibility that they might be infected and infectious even in the absence of symptoms, and to abstain from sexual activity for 5 days after they have received empirical treatment or their syphilis serology shows that they have not been infected. The importance of follow up and repeat syphilis serology testing to monitor the response to treatment should be emphasised.

Isolation and restriction

Sexual contacts of infectious syphilis should abstain from sexual activity for five days after receiving treatment.

12. Special situations

Syphilis outbreaks are more likely to occur in particular populations. In Australia, recent outbreaks have occurred in MSM and Aboriginal and Torres Strait Islander populations (See [Appendix 4](#) which comprises Guidelines for the Public Health Management of Syphilis Outbreaks in Remote Populations in Australia). Syphilis clusters may also occur in association with certain sexual networks. It is important to pay attention to confidentiality and the sensitivities associated with sexually transmitted infections when managing syphilis clusters and outbreaks.

MSM who participate in highly sexually active subcultures are at increased risk of acquiring syphilis. Due to the diversity of the MSM population in relation to syphilis infection, any initiative developed must take into account the varying subpopulations, e.g. HIV positive and negative MSM; younger and older MSM (MSM <30 years contribute the highest number of syphilis notifications among HIV negative MSM whereas MSM aged 40-49 years contribute the highest number of syphilis notifications among HIV positive MSM); and those with differing stages of syphilis including symptomatic and asymptomatic infections. The *National Gay Men's Syphilis Action Plan* outlines priority actions to achieve a sustained reduction in the incidence of infectious syphilis in MSM.¹⁶

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14. Appendices

Appendix 1. Syphilis fact sheet

Appendix 2. PHU Checklist

Appendix 3. Syphilis notification forms

Appendix 4. Guidelines for the Public Health Management of Syphilis Outbreaks in Remote Populations in Australia

15. NSW Jurisdiction specific issues

[Management of syphilis cases- referral to sexual health for inexperienced clinicians]

[For all syphilis laboratory notifications where the patient is managed by doctors not known to have experience in the management of syphilis, refer the notification to local sexual health clinic on the day of notification to enable sexual health clinic staff to offer timely assistance to the doctor and complete the notification form.]