





Syphilis

CDNA National Guidelines for Public Health Units

Version 2.0

Date: September 2024

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Title: Syphilis CDNA National Guidelines for Public Health Units

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Summary of revision history

Version	Date	Revised by	Changes
Version 2.0	September 2024	CDNA	Full review of the document was undertaken by the National BBV STI Surveillance Sub-committee (NBBVSTISSC), an expert sub-committee of CDNA, to reflect changes in epidemiology and public health response
Version 1.1	June 2018	CDNA	Document further updated for currency and revised formatting.
			 syphilis point of care testing (Page 15 of the SoNG and pp. 43-45 of Appendix D) frequency of testing during pregnancy within the context of an outbreak (page 18 and 25)
Version 1.0	June 2015	CDNA	Developed by syphilis SoNG Working Group

Disclaimer

These guidelines for public health units (PHUs) outline Australia's national minimum standard for the routine public health management of syphilis. They are intended to reflect the current evidence base, with pragmatic guidance provided where evidence is still evolving. Jurisdictions may implement policies that exceed the national minimum standard based on the local epidemiological context, available resources, and other factors. The Communicable Diseases Network Australia (CDNA) will review and update these recommendations as new information becomes available.

Readers should not rely solely on the information contained within these guidelines. Guideline information is not intended to be a substitute for advice from other relevant sources, including, but not limited to, advice from a public health specialist or other health professional. Clinical judgment and discretion may be required to interpret and apply these guidelines. PHUs should refer to and follow jurisdictional guidance regarding disease management where appropriate.

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Endorsed by CDNA: 25 September 2024 Endorsed by AHPC: 31 October 2024 Released by Health: 5 November 2024

Table of Contents

1.	Summary	6
	Public Health Priority	. 6
	Case management	. 7
	Management of contacts	. 7
2.	The disease	8
	Infectious agent	. 8
	Reservoir	. 8
	Mode of transmission	. 8
	Incubation period	. 8
	Infectious period	. 8
	Clinical presentation and outcome	. 9
	Disease occurrence and public health significance 1	10
	Population groups at risk1	10
3.	Routine prevention activities 1	12
	Testing recommendations1	12
4.	Surveillance objectives1	13
5.	Data management 1	14
	Notification requirements1	14
6.	Communications 1	15
7.	Case definition1	16
	Infectious Syphilis (less than two years duration)1	16
	Syphilis (more than 2 years or unknown duration)	16
	Syphilis - Congenital	16
8.	Testing1	17
	Syphilis serology1	17
	Treponemal specific tests	17
	Non-treponemal tests	18
	Reporting and interpretation of tests	19
	Nucleic Acid Amplification Tests (NAAT)	20
	Point of care tests for syphilis	20
9.	Case management	22

Response times	2
Case investigation22	2
Case treatment	3
Monitoring response to treatment24	4
Syphilis in pregnancy	5
Education and infection control measures	5
10. Contact management 27	7
Identification of contacts27	7
Contact definition	7
Lookback periods for contact tracing27	7
Contact management	3
Response times	9
Presumptive empirical treatment	9
Education and infection control measures	9
11. Special situations)
Outbreaks)
Communication with affected populations)
Public Health Review of Congenital Syphilis Cases	1
12. References	2
Appendix A: Jurisdiction specific guidelines	1
Appendix B: Syphilis fact sheet	5
Appendix C: Public health unit/Department of Health checklist	3
Appendix D: Syphilis case investigation form	7

1. Summary

The response to a notified case of syphilis is a shared responsibility between Public Health Units (PHUs) and individual diagnosing and/or treating clinicians. The balance of this responsibility may vary between Australian jurisdictions, and in different situations.

These Guidelines are primarily intended for PHUs and should be adapted to suit local practices and priorities.

Public Health Priority

Public health priority classification and response

High

- Congenital syphilis, confirmed, or probable
- Infectious syphilis, confirmed or probable, in a pregnant person
- Infectious syphilis in a woman of reproductive age (15-49 years*) with unknown pregnancy status
- Non-infectious syphilis in a pregnant person
- Any syphilis notification in a child <16 years of age

Routine

- Infectious syphilis, confirmed or probable case in a person confirmed as not pregnant
- Non-infectious syphilis in a person confirmed as not pregnant

*Note: Definition of reproductive age may vary across jurisdictions. The term women is used, but it acknowledged that this may also include people with a uterus who are non-female identifying.

Priority Classification	Public health response timeline	Data entry timeline
High	Respond to suspected, probable, and confirmed cases as soon as possible (generally within 1 working day)	Within 3 working days
Routine	Response should be carried out as a part of routine duties	Within 5 working days

Surveillance case definitions for <u>infectious syphilis</u> (less than 2 years duration), <u>non-infectious syphilis</u> (more than 2 years or unknown duration), and <u>congenital syphilis</u> are developed, approved and regularly reviewed by the Communicable Diseases Network of Australia.

Case management

Case management is the responsibility of the treating clinician, however PHUs should ensure that case investigations have been completed. See <u>Section 9</u>.

Determine pregnancy status in females in accordance with local clinical guidelines. All cases of syphilis in pregnancy should be discussed with a clinician with expertise in the area to ensure appropriate treatment and management. See <u>Section 9</u>, Syphilis in Pregnancy.

Root cause analysis must be done for congenital syphilis cases as per local processes. Cases of congenital syphilis should be treated in consultation with a specialist paediatrician as per local guidelines. See <u>Section 9</u>.

Management of contacts

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 PHUs 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. See <u>Section 10</u>.

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 pathogen.

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 (such as via transfusion or injection drug use), by non-sexual personal contact with infected lesions, or by accidental direct inoculation. Breast feeding does not result in the transmission of syphilis unless a syphilitic lesion or secondary syphilis rash is present on the breast.

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 to clinical presentation and outcome section below) when moist mucocutaneous lesions are present; at this point transmission risk is 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 early syphilis infection. The risk of infection in the unborn baby of a pregnant woman with untreated primary or secondary syphilis is extremely high, approaching 100%. If left untreated, late syphilis (syphilis infection more than one to two years prior to pregnancy) results in a 12% risk of a stillbirth, a 9% risk of neonatal death, a 2% risk of giving birth to an infected infant and a 77% chance of giving birth to an uninfected infant.¹ Infected infants with moist mucocutaneous lesions are a potential source of infection.

Clinical presentation and outcome

Cases are diagnosed using a combination of history, clinical assessment and serology.

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.

<u>Primary syphilis</u>: usually begins with a lesion, i.e., a chancre which begins as a papule 10-90 days after infection. It soon ulcerates 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 accompanied by regional lymphadenopathy, however atypical multiple and painful lesions can occur in some cases. The ulcer heals spontaneously over the course of a few weeks². Clinical suspicion of syphilis should be very high for all presentations of a painless, indurated genital ulcer. However, all genital ulcers should be considered potential primary syphilis signs and trigger testing.

<u>Secondary syphilis</u> usually occurs 4-10 weeks after onset of the primary lesion. Symptoms include headache, fatigue, lymphadenopathy, low grade fever, sore throat, rash, mucocutaneous lesions, condylomata lata (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.

<u>Early latent syphilis</u> refers to infection acquired within the previous two years that is no longer symptomatic.

<u>Late latent syphilis</u> refers to syphilis of more than two years duration, in the absence of clinical signs or history of treatment. People with late latent syphilis are asymptomatic for many years.

<u>Tertiary syphilis</u>: 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 symptoms were derived in the pre-antibiotic era and are a guide only:

- bone and skin lesions at any time after two years but usually between two and 15 years
- o cardiovascular disease at 20-30 years
- three types of central nervous system disease (meningovascular at 5-12 years, and general paresis and tabes dorsalis usually at 15-25 years).

<u>Congenital syphilis</u> occurs when *T. pallidum* crosses the placenta and infects the foetus at any time during pregnancy. If untreated, this can result in intrauterine foetal death, stillbirth, neonatal death, or a premature baby. In the early stages of congenital syphilis, the baby may be severely affected at birth (with hepatomegaly, ascites, hydrops, foetal anaemia); more frequently the baby may not present any observable sign. If the diagnosis is not made at this point, the baby may 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 manifestations of congenital syphilis correspond to tertiary disease in the adult and can be prevented by early diagnosis and treatment of the infant.

Disease occurrence and public health significance

Syphilis is increasingly common/endemic in the Australian population with higher rates in some communities, including gay, bisexual and other men who have sex with men (GBMSM) and Aboriginal and Torres Strait Islander peoples. Diagnosis rates are increasing among non-Indigenous people living in urban/metropolitan areas, HIV negative GBMSM and people who inject drugs.³⁻⁵

Rates in Aboriginal and Torres Strait Islander people have been increasing since 2011, especially among those living in remote areas of Australia, after sustained periods of decline³. Despite a substantial increase in rates in the non-Indigenous population in recent years, there has been ongoing higher and disproportionate burden of disease among Aboriginal and Torres Strait Islander peoples.⁶

One of the most significant public health implications of syphilis lies in its impact on the developing foetus in utero. Congenital syphilis is an entirely preventable disease and thus, it is an event that represents a failure of the health system, including affordable and accessible primary health care, delivery systems for antenatal care and for syphilis control programs. Persistent visual and auditory impairment after early neurosyphilis is also a public health issue.⁷ The interaction of *T. pallidum* with HIV is of public health significance due to shared transmission routes and syphilis biologically enhancing the transmission and acquisition of HIV.

Population groups at risk

Any person can acquire syphilis through unprotected vaginal, anal, or oral sex with an infectious person. In Australia, populations at higher risk of syphilis include Aboriginal and Torres Strait Islander peoples, people who inject drugs that lead to disinhibiting sexual behaviour, GBMSM, heterosexual people with multiple partners, female partners of GBMSM, sex workers, people from culturally and linguistically diverse (CALD) backgrounds, people experiencing socio-economic disadvantage, prisoners, women of reproductive age, people who experience homelessness, and people who have

unprotected sex in overseas countries where syphilis is prevalent.

In an analysis of enhanced syphilis surveillance data, it was found that infectious syphilis notification rates among Aboriginal and/or Torres Strait Islander women of reproductive age increased by >300% between 2012 and 2021⁸. Notification of infectious syphilis among non-Indigenous females of reproductive age has also substantially increased, particularly in major cities of Australia. Rates among the Aboriginal and/or Torres Strait Islander population in remote settings remain 15 times higher than the non-Indigenous population in major cities. Increasing rates in both populations pose a concurrent risk of congenital syphilis and adverse pregnancy outcomes.

3. Routine prevention activities

A combination of coordinated syphilis prevention activities is more effective than an isolated, single activity. Key pillars of prevention include education, screening, treatment and partner notification, with detail on these in relevant sections of the SoNG.

Sexual health promotion and education programs aim to increase awareness of syphilis and other sexually transmissible infections and empower people to adopt safer sex practices such as condom use and regular testing, thus reducing infection acquisition and transmission risk. These programs are targeted to priority groups including young people, pregnant people and their partners, GBMSM, Aboriginal and Torres Strait Islander peoples, sex workers, people who inject drugs, and prisoners.

Testing recommendations

<u>National STI testing guidelines</u> recommend that testing for syphilis and HIV is included in all standard asymptomatic STI check-ups, in addition to recommended testing for specific populations of concern such as those listed above. Please refer to the current guidelines (see <u>https://sti.guidelines.org.au/</u>) for syphilis testing guidance. Jurisdictional guidelines may differ, so it is important to consult local testing guidelines to ensure appropriate testing is undertaken.

4. Surveillance objectives

The objectives of surveillance are to:

- Monitor trends in syphilis by person, place and time, to enable timely response strategies and evaluate intervention and prevention strategies.
- Enable timely detection and identification of infectious and congenital syphilis cases to facilitate rapid response to the management of cases and their contacts.
- Enable timely detection and identification of syphilis cases in pregnant people and in women of reproductive age and monitor prevalence among pregnant people to inform the prevention of congenital syphilis
- Enable timely detection of clusters and outbreaks of syphilis to facilitate implementation of control measures.

5. Data management

Notification requirements

All confirmed and probable cases should be entered on to the National Notifiable Diseases Surveillance System (<u>NNDSS</u>) by state and territory PHUs.

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

Data for confirmed and probable cases of infectious syphilis (syphilis <2 years duration) and congenital syphilis should be entered into jurisdictional notifiable conditions databases within three working days of confirmation.

Data for confirmed cases of late syphilis infection (syphilis >2 years or unknown duration) should be entered into jurisdictional notifiable conditions databases within five working days of confirmation.

6. Communications

Details of confirmed and probable cases of infectious (i.e. primary, secondary, early latent) syphilis and congenital syphilis are notified to the state/territory in accordance with statutory requirements; usually including the patient's name, date of birth, sex, Indigenous status, country of birth, address or post code, date of onset or date of specimen collection, and whether laboratory testing has been requested. Additional information collected during follow-up should also be documented including: pregnancy status, possible sources of infection, exposure risk, sex worker status, other people thought to be at risk and follow up actions taken, such as documentation of appropriate treatment, evidence of dropping RPR titre and completed contact tracing.

State/territory Communicable Disease Branches (CDB) will notify the case to the National Notifiable Diseases Surveillance System (NNDSS) and should inform CDNA of infectious syphilis clusters or outbreaks of national relevance. Interjurisdictional outbreaks requiring national coordination may require support from the National Incident Centre (NIC).

7. Case definition

National case definitions are regularly reviewed. The current versions can be found via the following links:

Infectious Syphilis (less than two years duration)

Syphilis (more than 2 years or unknown duration)

Syphilis - Congenital

8. Testing

National laboratory case definitions are regularly reviewed, and the current version can be found via the following link:

Syphilis laboratory case definition

Culture is not available. Syphilis is principally diagnosed by serology (treponemal specific and non- treponemal tests). If lesions are present, diagnosis may involve nucleic acid amplification test (NAAT) or direct demonstration of the organism by dark-field microscopy or direct fluorescent antibody test (direct antigen detection). Placental specimens and cerebrospinal fluid are also suitable specimens for NAAT. Current NAATs cannot reliably detect *T. pallidum* in blood at any stage of infection.

Syphilis serology

There are two types of syphilis serology tests: treponemal specific tests and nontreponemal 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 people living with HIV or those treated very early in infection. These tests do not necessarily indicate active infection. Non-treponemal tests detect antibodies to 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

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

<u>*T. pallidum* immunoassays</u>: Immunoassays are suitable for automation and are 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 immunoassays (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.

<u>Fluorescent treponemal antibody absorption test (FTA-ABS)</u>: Sensitivity varies with disease stage: primary 78-100%, secondary 93-100%, early latent 94-100% and late latent 85-93%. Specificity is 87-100%⁹. 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.

<u>*T. pallidum* IgM EIA</u>: 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 used¹⁰. 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 \leq 1:8. Non-treponemal tests in use today are known as the VDRL (venereal diseases research laboratory) test 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%.¹¹ Specificity is 98% (if treponemal specific tests positive)¹². A false-negative response can occur in cases in which high antibody titers interfere with the antigen-antibody lattice network formation that is necessary for visualizing a positive flocculation test (the prozone phenomenon). The prozone phenomenon most commonly occurs when undiluted serum is used and can occur during any phase of syphilis.

See Therapeutic Goods Administration (TGA) for information on availability of tests.

Reporting and interpretation of tests

There is a period after infection when both treponemal specific and non-treponemal serology may be negative. In general, 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 treponemal specific test are 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 (i.e., 2, 4, 6, 8 etc). Figure 1, developed by Gavin Hart, indicates the typical RPR response following syphilis infection¹³.



Figure 1: Variation in RPR titre after infection¹³

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, for example, from 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 most 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 based on 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 due to inter-laboratory variation in RPR results.

Treponemal specific and non-treponemal tests do not distinguish between subspecies 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 Papua New Guinea, Indonesia, the Solomon Islands, Vanuatu and parts of central and west Africa.¹⁴ It is possible that people from these regions who acquired these conditions as children will still have the antibodies this would result in reactive treponemal serology without ever having had infectious syphilis. Treponemal serology needs to be interpreted in light of clinical findings and whether the patient is from as yaws endemic country. See <u>Yaws (Endemic treponematoses) (who.int)</u> for further information on yaws.

Nucleic Acid Amplification Tests (NAAT)

If an individual presents with clinically observable lesions (such as ano-genital and ulcers or lesions associated with secondary syphilis), it is recommended to collect swabs, scrapings, or biopsies for a NAAT such as a PCR test for *T. pallidum*. This test can also be done on placental specimens (including paraffin embedded tissueⁱ), ocular and cerebrospinal fluid. These tests are highly sensitive and specific and are now available in most states, but are not recommended for testing blood.¹⁵

Point of care tests for syphilis

There is currently only one syphilis point of care test registered by the Therapeutic Goods Administration in Australia, the Determine Syphilis TP[™]. The Determine Syphilis TP[™] is a treponemal specific immunochromatographic test that can be used 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.¹⁶⁻¹⁹ Interpretation requires access to the individual's previous syphilis serology and treatment history. Over-treatment can result if treatment is triggered based on point of care test result alone. In an outbreak

ⁱ Please note this is not a preferred specimen and some laboratories may not proceed with testing.

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:

- 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 (QC) 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:

- prevalence of past syphilis infection (generally they should only be used in populations with low rates of past syphilis infection);
- syphilis point of care testing can still be useful in high prevalence contexts, if guidance is provided to not use in people with a history of syphilis (rather use syphilis serology)
- development of clinical protocols, training and an appropriate clinical governance system;
- always perform laboratory-based testing in parallel for all reactive results and for negative results wherever feasible; and
- ensuring there is a process to notify reactive results to public health authorities and, where applicable, notify all test results to the relevant syphilis register.

For application in local contexts refer to testing guidelines in the relevant jurisdiction.

9. Case management

Response times

HIGH public health priority is advised for:

- Congenital syphilis, confirmed, or probable
- Infectious syphilis, confirmed or probable, in a pregnant person
- Infectious syphilis in a woman of reproductive age (15-49 years*) with unknown pregnancy status
- Non-infectious syphilis in a pregnant person
- Any syphilis notification in a child <16 years of age

The public health response for HIGH priority cases should be as soon as possible, generally within one working day.

For all other syphilis cases, the public health response is **ROUTINE**. Follow up should be prioritised according to jurisdictional guidelines.

* Definition of reproductive age range may differ across jurisdictions. The term woman is used, but it acknowledged that this may also include people with a uterus who are non-female identifying.

Case investigation

On notification of a case of confirmed or probable infectious syphilis, begin follow up investigation and notify the state/territory Communicable Diseases Branch (CDB).

The response to a notification will normally be carried out in collaboration with the diagnosing and/or treating clinician/service. Contact tracing is important and will depend on jurisdictional arrangements and may include PHU staff conducting a case interview and assisting with contact management.

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
- ensure the case or relevant caregiver are aware of their diagnosis
- 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
- determine pregnancy status of a female of reproductive age, 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.

- review that stage-appropriate case treatment has been completed and documented in relevant jurisdictional databases, including notification databases and/or syphilis registers
- seek the diagnosing clinician's permission to contact the case or relevant caregiver (where possible) before engaging in direct contact; although this may not always be practicable it is included as a courtesy to the treating doctor
- ensure that relevant local contact tracing processes have occurred
- review the case history and test results to ensure that the correct case classification has been recorded in notification data.

Identification of the person or service best placed to conduct contact tracing is a local decision best made on a case-by-case basis. The culture and gender of the contact tracer and whether they are known to and trusted by the case are relevant factors to consider.

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. Follow up of contacts who are pregnant, and contacts of pregnant people should be prioritised. See the <u>Australasian Contact Tracing Guidelines</u> for further information.

Case treatment

Patients who present with symptoms consistent with infectious syphilis (classically a relatively painless, indurated genital ulcer or symptoms / signs of secondary syphilis) should be treated at the time of first presentation and syphilis serology collected. PCR swabs should be taken from relevant lesions, including anogenital and oropharyngeal ulcers and other lesions, and blood taken for syphilis testing on the same day. Cases who present with potentially syphilitic lesions including mucocutaneous ulcers and other lesions should have a swab taken for *Treponema pallidum (T. pallidum)* species *pallidum* PCR and blood taken for syphilis testing at the time of first presentation; empirical treatment is highly recommended unless there is a medical contraindication. Refer to the <u>Therapeutic Guidelines</u> for assessment of management of a patient with a reported penicillin allergy. Please refer to <u>STI guidelines</u> for details if recommended testing for syphilis and any other STI testing to consider²⁰.

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

Pregnant cases of infectious syphilis require urgent prompt follow up and treatment with a penicillin-based regimen 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 benzylpenicillin, available via the Pharmaceutical Benefits Scheme prescriber bag to facilitate timely treatment.

For cases of infectious syphilis of less than two years duration, one dose of benzathine benzylpenicillin 2.4 million units (1.8g) IMI given as two injections containing 1.2 MU (0.9g) is required. For cases of non-infectious syphilis or syphilis infection of more than two years or unknown duration, a course of three doses benzathine benzylpenicillin 2.4 million units (1.8g) IMI, weekly for three weeks is required.

Cases of congenital syphilis should be treated in consultation with a specialist paediatrician. Refer to local guidelines for details.

For detailed information on therapeutic agents for tertiary syphilis see the <u>Australian</u> <u>STI guidelines²⁰</u>.

If penicillin is contraindicated, seek specialist advice from an infectious diseases physician, or sexual health physician.

Effective treatment of syphilis does not confer immunity against *T. pallidum*, and people can get re-infected. Certain groups are at higher risk of re-infection. Clinical presentation of re-infection 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 infection.

Monitoring response to treatment

At the time of the first treatment dose, repeat blood should be collected for RPR or VDRL test to provide an accurate baseline used to monitor response to treatment and check for re-infection.

Treatment of infectious syphilis is adequate if there is a four-fold (two dilution) drop in RPR titre, e.g., 1 in 64 to 1 in 16, by 6 (up to 12) months. All patients should be reviewed clinically and have repeat RPR testing at 3 months, then at 6 months and (if necessary) at 12 months after completing treatment. Refer to jurisdictional and/or Australasian Society of Infectious Diseases (ASID) guidelines²¹ for further details on monitoring response after treatment in pregnancy. Comparison of results on serial samples should always be done with parallel testing. Results from different laboratories for an

individual patient should not be compared.

Please note: Patients with low starting RPR titres, late diagnoses, and individuals who have been re-infected may be left with fixed reactive (serofast) RPR titres (e.g., 1 in 16) despite adequate treatment, in up to a quarter of patients.

Serological testing up to 8 weeks after treatment (unless symptoms appear²²) should be avoided as it may show an increase in RPR; this does not indicate treatment failure.

Cases of infectious syphilis are no longer considered infectious 7 days after one dose of benzathine benzylpenicillin or until all symptoms have resolved (whichever is later). Completion of adequate treatment for syphilis does not confer immunity and re-infection can occur.

Please refer to local testing guidelines for further steps, if available. <u>Guidelines</u> suggest a bare minimum frequency of testing – respective physicians can choose more testing depending on the case.

Syphilis in pregnancy

National guidelines recommend a minimum of 3 (three) syphilis tests for every pregnant person during each pregnancy: at the first antenatal visit, at 26-28 weeks, and at 36 weeks or birth (whichever is earlier). Neonates should not be discharged without confirming that the mother's syphilis status has been documented at least once during pregnancy. If in doubt, maternal syphilis serology should be ordered at birth. Additional risk-based screening: additional testing, including opportunistic and at birth, should be considered based on clinical indication as per the local guidelines.

Due to the extreme risk of vertical transmission of syphilis, particular care is required to ensure adequate treatment in pregnancy, and 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 while it is often the same as in the non-pregnant state, local guidelines should be consulted. IM benthazine benzylpenicillin is the recommended treatment. Seek specialist support where this is not possible as desensitisation may be required. Contact tracing and treatment for the pregnant person'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 pregnant person's RPR during and following pregnancy is essential and should start at 3 months after the first dose of benzathine benzylpenicillin (refer to ASID²¹ or jurisdictional guidelines for further detail); this is important for monitoring the response to treatment and prompt detection and treatment of re-infection. For adequate treatment of syphilis in pregnancy, treatment must be completed at a minimum of 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. If the pregnant person required treatment for syphilis during the pregnancy, or the infant is considered to be high risk according to the respective jurisdictional guidelines, the neonate should be examined for clinical signs of congenital syphilis and comprehensive laboratory investigations should be undertaken (i.e. venous blood for syphilis serology read in parallel with maternal serology, IgM, placental PCR). If any initial assessments are abnormal and/or adequate treatment did not occur in pregnancy, treatment for congenital syphilis and additional investigations should be considered.

All cases of congenital syphilis must be consistently identified, and a root cause analysis undertaken for each case to identify individual risk factors (e.g., pregnant people not able to access antenatal care, or with co-occurring needs) and health system contributing factors to inform improvement activities at both clinical and system levels, with mechanisms made available to implement recommended changes to practice.

It is critical to focus on pregnant people diagnosed during pregnancy who are then lost to follow-up. All attempts should be made to contact the individual e.g. home visits (multiple if necessary), flags on electronic medical records that this is a high-risk pregnancy requiring syphilis treatment and/or further testing. Check with other relevant services regarding contact, including mental health, alcohol and other drugs, homelessness services, Justice Health and Department of Communities and Justice. Contact with other services should be considered on a case-by-case basis and in context of local relevant legislation.

Contact tracing and treatment for the pregnant person's partner/s are critical to minimise the potential for re-infection as this represents a particular threat to the unborn baby.

Education and infection control measures

Cases of infectious syphilis need to be informed of the infectious nature of their disease, the possibility they might be infectious even in the absence of symptoms, and to abstain from sexual activity for 7 days post-treatment or until symptoms have completely resolved (whichever is longer). Physical isolation of cases or their sexual contacts is not required. The importance of contact tracing and follow up and repeat syphilis serology testing to monitor the response to treatment should be emphasised. Also, advise no sexual contact with current or previous sexual partners until all sexual partners have been tested, treated if necessary and are no longer infectious. The case should be informed that they are likely to continue to have positive treponemal specific tests for life, even after successful treatment, and that previous infection does not protect them from getting reinfected again.

10. 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 units 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 <u>Australasian Contact Tracing Guidelines</u>.

Identification of contacts

The aim of identifying contacts of infectious syphilis is to prevent disease transmission by providing empirical presumptive treatment and testing to identify infection. Comprehensive assessment of contacts at the initial consultation is crucial.

Contact definition

Anyone who has had sex (including oral sex) with a person who has infectious syphilis requires follow-up as a contact. Correct staging of the index case's infection is essential as it determines the lookback period for contact tracing (3 to 12 months depending on stage). All contacts should be offered syphilis testing. In addition, presumptive treatment on the day of testing should be offered to contacts of primary and secondary syphilis and contacts of early latent syphilis where sexual contact occurred in the previous three months. For late latent or tertiary syphilis, testing is recommended for current partners only. For further information regarding contact tracing refer to the <u>Australasian Contact Tracing Guidelines</u>.

Unborn and newborn babies of pregnant people diagnosed with syphilis or suspected to have syphilis during the pregnancy should also be treated as contacts, regardless of maternal treatment, and relevant pathology tests and clinical assessments for congenital syphilis should be undertaken. Refer to local clinical practice guidelines for presumptive treatment of neonates who are being investigated for congenital syphilis.

Testing of older children may also be indicated where there is a strong suspicion of untreated syphilis infection during a past pregnancy.

Lookback periods for contact tracing

The infectious period depends on the stage of infection in the case and determines the time frame for contact tracing.

- For cases with symptoms of 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 symptoms of secondary syphilis, contacts should be traced for the duration of the case's symptoms plus six months; or to last negative test; if uncertain, contacts to 12 months prior to presentation are to be traced
- For asymptomatic cases of probable infectious syphilis and early latent syphilis of less than two years duration, contacts to 12 months prior to presentation or to the most recent negative test are to be traced (whichever is shorter).
- For cases of non-infectious syphilis, only long-term partner/s only and children of women with uncertain duration of infection). If any doubt as to whether the patient has early latent or late latent syphilis, contact trace as for early latent syphilis.
- If the stage of syphilis is unclear, contact your local sexual health specialist service for advice.

Contact management

In addition to presumptive empirical treatment, for all sexual contacts of patients with primary or secondary syphilis regardless of serology, 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 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 responsible primary health, sexual health, and public health staff 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 online contact tracing tools have been developed. These include <u>'Let them know'</u>, '<u>The Drama Down Under</u>' (for GBMSM), and <u>Better to Know</u> (for Aboriginal and/or Torres Strait Islander people). Some jurisdictions may offer jurisdiction-specific services.

The highly transmissible nature of syphilis, and specifically its capacity to spread rapidly through a population and to cause both foetal death and severe congenital complications if transmitted to a pregnant person, demands an urgent and prompt response from primary care and public health/sexual health clinic staff. Contacts tracing of an early syphilis case should be a high priority, higher than contact tracing for other STIs (chlamydia, gonorrhoea) where serious complications do not occur as acutely. Rigorous and immediate attempts are required to avoid further sexual transmission and potential 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.

Where a person discloses they are a contact of a syphilis case, to optimise case assessment and management during the initial consultation, the following should be undertaken:

- Presumptive empirical treatment
- Complete pregnancy test for females aged 15-49
- Assess for signs and symptoms
- Obtain sexual history/if any sexual contact in last 3 months
- Determine any previous infections and/or 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 tested and treated on the same day as the case's treatment (e.g. if regular partner) or as soon as possible. If the contacts are elsewhere and referral has been necessary, the responsible primary health, sexual health, and public health staff should aim to ensure that all contacts are seen and treated within two weeks of the case's diagnosis.

Presumptive empirical treatment

Persons who were sexually exposed to a patient with primary, secondary, or early latent syphilis in the last 3 months should be treated presumptively with one dose of benzathine benzylpenicillin 2.4 million units (1.8g) prior to the receipt of their syphilis serology results.

Education and infection control measures

Contacts of infectious syphilis need to be informed about the infectious nature of the disease, the possibility they might be infected and infectious even in the absence of symptoms, and to abstain from sexual activity for 7 days after they have received empirical presumptive treatment, or their syphilis serology shows that they have not been infected (whichever is earlier). The importance of follow up and repeat syphilis serology testing to monitor the response to treatment should be emphasised.

11. Special situations

Outbreaks

Syphilis outbreaks are more likely to occur in particular populations. The term 'outbreak' is taken to mean the occurrence of more cases than expected for the population or group under consideration. The objective of public health management of outbreaks of syphilis is to interrupt transmission and prevent further cases and congenital syphilis cases. Once an outbreak is either suspected or recognised there is an immediate need to initiate a coordinated response. A significant syphilis outbreak is a complex public health challenge. The ideal response will be multi-strategic, informed by local knowledge, and attentive to detail in its execution. It will be enhanced where positive relationships already exist between the stakeholders.

In Australia, an increase in syphilis cases was first reported in remote Queensland in 2011, with a multijurisdictional outbreak declared in central and northern Australia in 2015. This outbreak was predominantly among Aboriginal and Torres Strait Islander communities in remote settings, reflecting failures of the health system including inadequate access to timely testing and treatment, and the impact of social determinants of health. Further outbreaks have occurred in urban areas, among GBMSM. Increasingly, Australia is experiencing more widespread syphilis infections, however a disproportionate burden of disease remains for Aboriginal and Torres Strait Islander Islander peoples.

Syphilis clusters may also occur in association with certain sexual networks. It is important to pay attention to confidentiality and the sensitivities associated with STIs when managing syphilis clusters and outbreaks. GBMSM who are highly sexually active are at increased risk of acquiring syphilis.

Communication with affected populations

Responding to syphilis outbreaks requires community and health service engagement, consultation and dialogue with affected populations that have had a recent history of discrimination, racism and stigma. These meetings have the following objectives: to inform and educate community (and health staff); to establish a trusting basis for on-going dialogue; and to seek advice and codesign where possible proposed control strategies. Relationships between nominated community representatives and the outbreak response team are crucial to effectiveness of outbreak control. Communication with Aboriginal and Torres Strait Islander people about STIs in their communities is always sensitive and should be undertaken in a culturally safe manner, with input and support from relevant First Nations employees.

Community leaders are necessary partners in addressing a syphilis outbreak. Their

co-operation, input and support are critical to effective intervention. This situation calls for frank explanation and discussion in language appropriate to the level of health literacy of the community members and should commence from the early stages of any initiative so that there is an opportunity for community members to contribute to the design, implementation, and evaluation of the proposed programs.

Engaging early with the state-based peak Aboriginal and Torres Strait Islander community-controlled health organisations is important. This may be particularly useful in opening up communication with communities without a community-controlled health service.

Public Health Review of Congenital Syphilis Cases

The occurrence of a case of congenital syphilis is a sentinel event reflecting potential missed opportunities for prevention in the public health, antenatal and primary health care systems, and reflects a failure of the health system. Therefore, it is important to formally review each case of congenital syphilis as a reportable incident for the purpose of health system improvement and preventing future avoidable cases. Refer to jurisdictional guidelines for details of public health review processes. For example, the <u>Guidelines for public health review of congenital syphilis case</u>.

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Appendix A: Jurisdiction specific guidelines

National Communicable Disease Surveillance – Australian Government Department of Health and Aged Care

<u>Silver Book (STI/ BBV management guidelines) – Government of WA – Department of Health</u>

Syphilis in Pregnancy: Queensland clinical guidelines - Queensland Health

Communicable Disease Control Guidance - Syphilis - Queensland Health

Congenital syphilis guidelines for the Northern Territory

Remote Primary health care manuals

NT Guidelines for the Management of Sexually Transmitted Infections in the Primary Health Care setting

NSW Health Policy Directive: Syphilis in Pregnancy and Newborns (PD2023_029)

NSW Health syphilis control guidelines

South Australian Perinatal Practice Guideline Syphilis in Pregnancy

Australasian Society for HIV, Viral Hepatitis and Sexual Health Medicine – Syphilis decision making tool

Melbourne Sexual Health Centre - Syphilis treatment guidelines

Australasian Society for Infectious Diseases – Management of Perinatal Infections

Appendix B: Syphilis fact sheet

See Health Direct Syphilis (https://www.healthdirect.gov.au/syphilis).

Appendix C: Public health unit/Department of Health checklist

Contact the patient and/or the patient's doctor to:

- Obtain patient's risk exposure history
- Obtain patient's previous syphilis testing and treatment history (this information might be available from a state or regional syphilis register/database)
- Identify likely source of infection
- Confirm onset of symptoms (if any)
- Confirm results of relevant pathology tests
- Ensure that the patient is aware of diagnosis
- Ensure that adequate treatment has been given, and document details in relevant jurisdictional databases
- Ensure that contact tracing has commenced.
- Contact the laboratory to:
- Check samples received and obtain any outstanding results.

Confirm case:

- Assess information against case definition
- Stage syphilis in consultation with specialist advice
- Enter data into jurisdictional infectious disease notification database

Appendix D: Syphilis case investigation form

Public Health Unit/Sexual Health Clinic undertaking case investigation: Notification ID [.]				
Case details				
Family name:				
Given names:				
Date of birth: $d d / m m / y y y y$ Sex registered at birth: $\Box M \Box F \Box$ Non-binary sex Gender at diagnosis: $\Box M \Box F \Box$ Non-binary gender				
Female patients: Pregnant Not pregnant Unknown				
If currently pregnant, what was the gestation (in weeks) at the time of initial diagnosis:				
Experienced recent delivery or loss of pregnancy \Box Yes \Box No				
Date of recent delivery or loss of pregnancy:				
Note: Infectious syphilis occurring in a pregnant person requires HIGH public health response due to the risk of congenital infection				
Indigenous Status:				
Aboriginal but not Torres Strait Islander origin				
Torres Strait Islander but not Aboriginal origin				
Both Aboriginal and Torres Strait Islander origin				
Neither Aboriginal nor Torres Strait Islander origin				

□ Not stated/inadequately described

Address

Postcode		
Country of birth:	□ Australia	□ Other, specify

Language mostly spoken at home: □ English □ Other, specify □ Unknown

Past history

This relates to the most recent syphilis results prior to the current result

Previous syphilis testing: 🗆 Yes	□ No	
Unknown If yes, provide details		

	Date	Result
Last treponemal specific test	d d / m m / y y y y	
Last RPR	d d / m m / y y y y	

Previous syphilis diagnosis:

□ Yes

□ No

🗆 Unknown

Date of last syphilis notification: d d / m m / y y

Previous syphilis treatment:

□Yes

□No

□Unknown If yes, provide details

Date given	Drug	Dose	Route	Comments

Other relevant information

Disease details

Symptoms at time of diagnosis:

- PrimarySecondary
- □ Tertiary

□ No symptoms

Specific symptoms:

□ Chancre

 \Box Skin rashes

□ Condyloma lata

□ Ocular symptoms

□ Neurological symptoms

□ Other

If symptoms present, date of onset: d	d / m	m /	У	У	У	У
If primary syphilis, site of infection:					Ur	ogenital

- □ Anorectal
- □ Oropharyngeal
- □ Other
- 🗆 Unknown

Laboratory results:

□ Positive PCR/dark ground microscopy of lesion

□ Reactive RPR/VDRL

- □ Reactive /TPHA
- □ Reactive EIA
- \Box Other, specify

Stage of infection: \Box Primary (for example chancre)

□ Secondary (for example rashes)

 \Box Early neurosyphilis (clinical/lab evidence of infection in previous 2

years)

 \Box Early latent (asymptomatic; lab evidence of infection in previous 2

years)

□ Late latent (asymptomatic; infection >2 years or at an unknown time)

- □ Tertiary (late symptomatic)
- □ Old treated syphilis infection
- Congenital syphilis

Health service where patient was diagnosed:

- □ Public hospital
- □ Private hospital
- □ Sexual health clinic
- □ Family planning
- \Box GP
- □ Aboriginal health service
- □ Prison/detention centre
- □ Public/community health clinic
- □ Other, specify

Reason for presentation to health service:

- □ Symptoms
- □ Contact of syphilis
- □ Contact of other STI
- □ STI Screening
- □ Antenatal care, gestation/40
- □ Other, specify

Risk information

Where was the infection most probably acquired?

- \Box This state
- □ Interstate, specify.....
- □ Overseas, specify
- □ Unknown

Sex of partner from whom the infection was most probably acquired

- \Box Opposite sex
- \Box Same sex
- □ Either sex
- □ Unknown
- □ Not sexually acquired

Type of sex partner from whom the infection was most probably acquired

□ Regular	🗆 Casual	Sex worker	□ Client (of a sex	k worker)
□ Other, spec	ify		Unknown	□ Not sexually
acquired				

Where did patient meet the sex partner from whom the infection was most probably acquired?

Brothel	□ Beat	Internet	Sex on premises venue
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□ Other, specify	🗆 Unknown
------------------	-----------

□ N/A, regular partner or already known to patient

Most likely mode of transmission:
 Vaginal intercourse, insertive

\Box Anal sex, insertive \Box Anal sex, receptive	Unknown	Not sexually
acquired		

Management

Treatment details

Date given	Drug	Dose	Route	Comments

Other relevant information

Contact tracing:

□ Patient agreed to notify partners

□ Health service will notify partners, name of health service.....

□ Other, specify