South Australian Perinatal Practice Guideline

# Syphilis in Pregnancy and the Neonate

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#### Note:

This guideline provides advice of a general nature. This statewide guideline has been prepared to promote and facilitate standardisation and consistency of practice, using a multidisciplinary approach. The guideline is based on a review of published evidence and expert opinion.

Information in this state-wide guideline is current at the time of publication.

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Health practitioners in the South Australian public health sector are expected to review specific details of each patient and professionally assess the applicability of the relevant guideline to that clinical situation.

If for good clinical reasons, a decision is made to depart from the guideline, the responsible clinician must document in the patient's medical record, the decision made, by whom, and detailed reasons for the departure from the guideline.

This statewide guideline does not address all the elements of clinical practice and assumes that the individual clinicians are responsible for discussing care with consumers in an environment that is culturally appropriate, and which enables respectful confidential discussion. This includes:

- The use of interpreter services where necessary,
- Advising consumers of their choice and ensuring informed consent is obtained,
- Providing care within scope of practice, meeting all legislative requirements, and maintaining standards of professional conduct, and
- · Documenting all care in accordance with mandatory and local requirements

Note: The words woman/women/mother/she/her have been used throughout this guideline as most pregnant and birthing people identify with their sex assigned at birth. However, for the purpose of this guideline, these terms include people who do not identify as women or mothers, including those with a non-binary identity. All clinicians should ask the pregnant person what their preferred term is and ensure this is communicated to the healthcare team.

#### Explanation of the Aboriginal artwork.

The Aboriginal artwork used symbolises the connection to country and the circle shape shows the strong relationships amongst families and the Aboriginal culture. The horseshoe shape design shown in front of the generic statement symbolises a woman and those enclosing a smaller horseshoe shape depicts a pregnant woman. The smaller horseshoe shape in this instance represents the unborn child. The artwork shown before the specific statements within the document symbolises a footprint and demonstrates the need to move forward together in unison.

Australian Aboriginal Culture is the oldest living culture in the world, yet Aboriginal people continue to experience the poorest health outcomes when compared to non-Aboriginal Australians. In South Australia, Aboriginal women are 2–5 times more likely to die in childbirth and their babies are 2–3 times more likely to be of low birth weight. The accumulative effects of stress, low socio-economic status, exposure to violence, historical trauma, culturally unsafe and discriminatory health services, and health systems are all major contributors to the disparities in Aboriginal maternal and birthing outcomes. Despite these unacceptable statistics, the birth of an Aboriginal baby is a celebration of life and an important cultural event bringing family together in celebration, obligation, and responsibility. The diversity between Aboriginal cultures, language and practices differ greatly and so it is imperative that perinatal services prepare to respectfully manage Aboriginal protocol and provide a culturally positive health care experience for Aboriginal people to ensure the best maternal, neonatal and child health outcomes.

## Purpose and Scope of PPG

This guideline provides clinicians with information on screening and management of syphilis during pregnancy, birth and postpartum. It includes recommendations for universal and additional screening in at-risk groups and the management of syphilis in pregnancy and in case of neonatal congenital syphilis. This guideline also includes health promotion information.



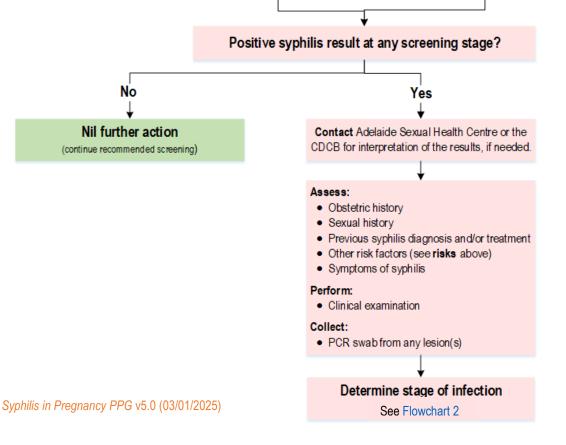
# Flowchart 1| Syphilis Screening, Risk Assessment, and Initial Management

#### Is the woman at increased risk for syphilis in pregnancy?

#### Risks:

- · Identify as an Aboriginal and/or Torres Strait Islander person (due to the current statewide outbreak)
- History of any STI diagnosis, or is a sexual contact of a person diagnosed with an STI (in current pregnancy or previous 12 months)
- · Has had no antenatal care, or presents for their first antenatal visit at/or after 28 weeks gestation
- · Has had new sexual partner(s) since they became pregnant
- · Has had sex with men who have sex with men
- Uses (or partner uses) illicit substances

	No ★	Yes ♦
Timing of Screen	<u>No</u> Identified Risk(s)	Identified Risk(s)
First antenatal visit	Screen all	Screen all
26-28 weeks gestation	Screen all	Screen all
36 weeks gestation (or at time of preterm birth)	Screen all	Screen all
Birth	<ul> <li>Screen only if 36 week screen has not been collected</li> <li>Store placenta until result available</li> </ul>	<ul> <li>Screen all</li> <li>Store placenta until result available</li> </ul>
6 week postnatal check	No screening required	Screen all







# Flowchart 2| Stages of Syphilis Infection and Management in Pregnancy

1. Determine stage of infection and commence appropriate treatment (see below)

2. Discuss with ID/Sexual health physician, if required

3. Notify CDCB who will refer for contact tracing

Symptom(s)	Stage	Risk of Vertical Transmission	Management/Treatment	Advise Client	Practice Points
Chancre (ulcer) –	— Primary -	High (approx. 100% – transmission)	<ul> <li>(Infectious Syphilis)</li> <li><u>Before 28 weeks gestation:</u></li> <li>Benzathine penicillin 2.4 million units IM (as two injections at once, one in each buttock).</li> </ul>		<ul> <li>Advice woman to stay well hydrated, rest and take paracetamol for pain or fever.</li> <li>Discuss Jarisch-Herxheimer Reaction (JHR) which can occur in &gt; 40% of syphilis cases (symptoms may include)</li> </ul>
Systemic illness: e.g., rash, hepatitis, – lymphadenopathy.	– Secondary -	High (approx. 100% transmission)	<ul> <li>After 28 weeks gestation:</li> <li>Benzathine penicillin 2.4 million units IM (as two injections at once, one in each buttock).</li> <li>Repeat dose in 7 days (Total 2 doses).</li> </ul>	Avoid sex for 7 days after the first treatment dose and 7 days after sexual partner(s) first treatment dose.	<ul> <li>fever, chills, headache, myalgia and uterine contractions if the pregnancy is &gt; 20 weeks).</li> <li>If pregnancy is &gt; 20 weeks, consider inpatient management for 24-hours after the first benzathine</li> </ul>
Asymptomatic < 2 years	— Early Latent	Moderate (approx. 100% – transmission)	<ul> <li>And</li> <li>Repeat syphilis serology on the same day as first treatment dose for RPR monitoring. Do <u>not</u> wait for results to start treatment.</li> <li>Seek expert advice if penicillin allergy and/or signs of neurosyphilis.</li> </ul>		<ul> <li>penicillin dose.</li> <li>If first dose was given in an outpatient setting, advise woman to contact their healthcare provider/nearest birth unit, if they experience regular cramping or contractions, a change in fetal movements, or fever</li> </ul>
Asymptomatic > 2 years	— Late Latent	Low (approx. 10% – transmission)	<ul> <li>(Including unknown duration)</li> <li>Benzathine penicillin 2.4 million units IM (as two injections at once, one in each buttock), every 7 days for 3 weeks (Total 3 doses)</li> <li>If a dose is missed or there is an interval of &gt; 7 days between doses, consider restarting course in consultation with expert practitioner.</li> </ul>	Avoid sex for 7 days after first treatment dose and partner(s) has/have been tested and excluded for syphilis, or 7 days after sexual partner(s) first treatment dose if positive	<ul> <li>within 24 hours.</li> <li>Educate about symptoms of syphilis, risk of reinfection and prevention, and importance of follow-up.</li> <li>At birth: collect syphilis serology blood from both mother and baby, placental histopathology and PCR and syphilis PCR from nasal secretion lesions on the baby.</li> </ul>
			See expert advice if penicillin allergy and/or signs of neurosyphilis.	for syphilis.	Follow up all syphilis results.
Multisystem (approx.20-30 years <del>–</del> after infection)	– Tertiary -	- Negligible -	Contact Infectious Diseases/Sexual Health Physician.		

Note: Treatment of maternal syphilis must be completed 30 days or more before birth, to prevent vertical transmission.

Syphilis in Pregnancy PPG v5.0 (03/01/2025)



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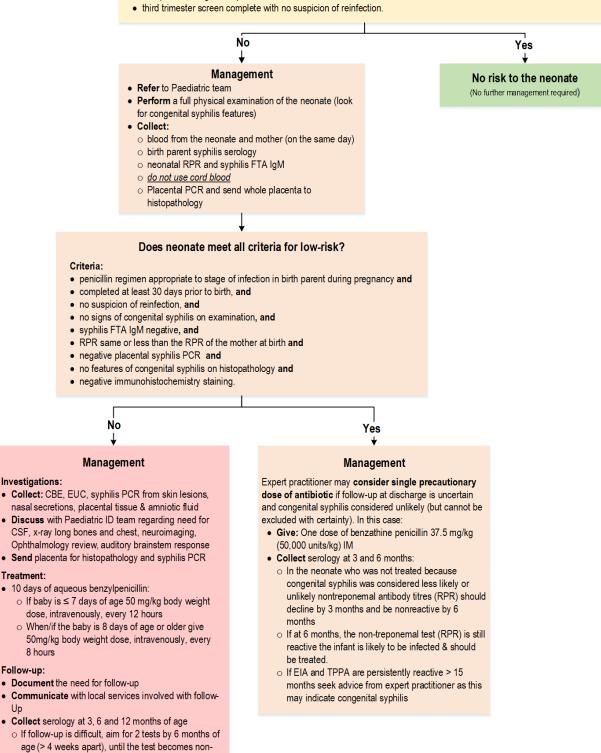
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## Flowchart 3 Management of the Neonate with Positive Syphilis Serology Mother

#### Does maternal history meet all criteria for low-risk neonate?

#### Criteria:

- · completed syphilis treatment with appropriate penicillin dose(s) prior to pregnancy, and
- adequate serological response, and



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# Summary of Practice Recommendations

Syphilis is a notifiable condition.

Universal screening for syphilis is recommended in **all** pregnancies and has increased from one to three universal screens as per Communicable Disease Control Branch (CDCB) and approved by Health Chief Executives Council (HCEC) (see <u>flowchart 1</u>).

Two additional postnatal screens should be offered to all people with an identified increased risk of acquiring syphilis in pregnancy (see <u>flowchart 1</u>).

Untreated syphilis can lead to miscarriage, stillbirth, or congenital infection.

Almost all cases of congenital syphilis can be prevented through adequate treatment.

Treatment may be considered adequate if a stage-appropriate penicillin regimen was completed 30 days or more prior to birth and all antenatal and birth pathology investigations were performed and results verified and there is no evidence of re-infection. Timely diagnosis and treatment are therefore critical.

Repeat screening for other STIs, including HIV, should be performed in pregnant people with positive syphilis serology.

Once a positive syphilis serology has been confirmed, the stage of syphilis needs to be established (see <u>flowchart 2</u>).

Treatment of a pregnant woman **and** their sexual partner(s)/contact(s) should be carried out urgently and in consultation with an expert practitioner.

Follow up of a woman who have been treated for syphilis in pregnancy is important to detect reinfection and ensure optimal assessment and follow up of the baby.



# Abbreviations

AMIC	Aboriginal maternal and infant care		
CBE			
	· · ·		
CSF	cerebrospinal fluid		
CDCB	Communicable Disease Control Branch		
EIA	enzyme immunoassay		
EUC	electrolytes, urea and creatine		
FTA	fluorescent treponemal antibody		
g	gram(s)		
HBV	hepatitis B virus		
HCV	hepatitis C virus		
HIV	human immunodeficiency virus		
JHR	Jarisch-Herxheimer reaction		
ID	infectious diseases		
IM	intramuscular		
IUGR intrauterine growth retardation			
IV intravenous			
kg	kilogram(s)		
L	litre(s)		
LFT	liver function tests		
mg	milligram(s)		
mL millilitre(s)			
MU	million units		
MSM	men who have sex with men		
PCR	polymerase chain reaction		
POCT	point of care testing		
PPG	perinatal practice guideline		
RFDS	Royal Flying Doctor Service		
RPR	rapid plasma reagin		
STI	sexually transmissible infection		
T. Pallidum	Treponema pallidum		
ТРРА	Treponema pallidum particle agglutination		



# Definitions

Expert practitioner	A clinician with specialist knowledge and experience in the testing, result interpretation, management, and treatment of syphilis in antenatal care settings. May include (but is not limited to) an infectious diseases physician, sexual health physician, obstetrician, or neonatologist with expertise in the management of syphilis. For Aboriginal women, the inclusion of culturally safe and appropriate support from an Aboriginal health care clinician is needed.
Increased risk of syphilis in pregnancy	Pregnant women and those with partners who fit any of the criteria specified in table 2.
Infectious syphilis	Syphilis of less than two years' duration (includes primary, secondary, and early latent stages).
Partner notification	Or contact tracing, is the process of identifying sexual contacts and providing access to advice, testing and treatment. Treatment of infected partners will reduce individual complications from STIs, as well as reducing further sexual transmission. Perinatal service providers need cultural sensitivity, within a non- judgemental environment when planning and providing care for the Aboriginal woman. Aboriginal women may experience 'shame' in this context, given women's business. Sensitivities need to be culturally safe and appropriate and include an Aboriginal healthcare practitioner.
SA Syphilis Register	A secure, confidential, single state-wide database which aims to include all laboratory-positive syphilis cases diagnosed in Aboriginal and Torres Strait Islander South Australians which meet the syphilis national case definition. The register can also assist with partner notification.
Shared decision making	Shared decision making involves discussion and collaboration between a consumer and their healthcare providers. It is about bringing together the consumer's values, goals, and preferences with the best available evidence about benefits, risks and uncertainties of screening, investigations, and treatment, to reach the most appropriate healthcare decisions for that person.

# Introduction

Syphilis is a bacterial infection caused by the spirochete bacterium *Treponema pallidum*. If left untreated, syphilis during pregnancy can lead to spontaneous miscarriage (most commonly mid-trimester), preterm labour, stillbirth, neonatal death, or congenital syphilis with multi-system manifestations such as deafness, neurological impairment, organ damage and bone deformities which can lead to severe, lifelong disability. The most common outcome of syphilis in pregnancy is mid-trimester spontaneous miscarriage.

The risk of trans-placental transmission to the fetus is highest during infectious syphilis, with the risk of transmission almost 100% in both <u>primary</u> and <u>secondary</u> syphilis.<sup>1</sup> In established <u>late latent</u> syphilis, vertical transmission occurs in approximately 10% of cases.<sup>2</sup>

Australia is facing an escalating and diversifying syphilis epidemic, affecting multiple population groups. Nationally the number of syphilis cases more than tripled between 2013 to 2022, with a sixfold increase in reported cases among females.<sup>3</sup> This surge, especially among heterosexual females of reproductive age, has increased the risk of congenital syphilis nationally.



Since 2017, South Australia reported 47 cases of syphilis in pregnancy, with 13 cases occurring in 2023 alone. While Aboriginal and Torres Strait Islander women remain disproportionately represented among cases of syphilis in pregnancy, a high and increasing proportion of cases in pregnancy are reported among non-Indigenous females. These trends highlight diversification of the syphilis epidemic and escalating risk of congenital syphilis across multiple populations.

To prevent vertical transmission of syphilis and ensure the best outcomes for both mother and infant, cases of syphilis in pregnancy require robust support from the Communicable Disease Control Branch (CDCB) through the South Australian Syphilis Register.

# Congenital Syphilis

Nationally, 109 cases of congenital syphilis were notified between 2011 and 2023, with the majority (61%) recorded since the start of the COVID-19 pandemic. In 2023 alone, 20 cases of congenital syphilis were reported, the highest number on record.<sup>4</sup> Between 2016 and 2023, 89 congenital syphilis-associated deaths were reported in Australia.<sup>5</sup> Approximately two-thirds (62%) of these infants were from Aboriginal and Torres Strait Islander communities.<sup>5</sup> This equates to rates per 100,000 live births being on average 16 times that of non-Indigenous infants.<sup>5</sup>

In South Australia (SA), five neonatal congenital syphilis notifications were recorded between January 2017 and July 2024 (four were Aboriginal babies). Prior to 2017, congenital syphilis had not been reported in SA since the 1990s. This rise has disproportionately affected Aboriginal and Torres Strait Islander communities. Recent data indicates that for Aboriginal and Torres Strait Islander babies, Australia is no longer meeting World Health Organization triple elimination targets.<sup>5</sup>

Delayed detection of syphilis in pregnancy and delayed commencement of treatment at or post birth, are the common reasons for congenital cases nationally. Treatment for syphilis in pregnancy with benzathine penicillin should be stage appropriate and ideally begin at least 30 days before birth to reduce the risk of transmission in utero and prevent congenital syphilis.<sup>6–8</sup>

# Pregnancy Outcomes of Syphilis Infection

- Miscarriage
- > Stillbirth
- Prematurity and low birth weight
- Perinatal death
- > Born with signs of congenital syphilis
- Born as a healthy-looking baby but developing clinical signs of congenital syphilis later
- > Healthy non-infected baby if mother adequately treated at least 30 days before birth
- Consider syphilis serology for all women who have had an intrauterine death after 20 weeks gestation.<sup>9,10</sup>

# Populations at Increased Risk

Populations at increased risk of syphilis in pregnancy include people who:

- Identify as an Aboriginal and/or Torres Strait Islander person (due to the current (2024) statewide outbreak)
- Have a history of any sexually transmitted infection (STI) diagnosis or is a sexual contact of a person diagnosed with an STI (in current pregnancy or previous 12 months)
- Have had no antenatal care or presented for their first antenatal visit at or after 28 weeks gestation
- Have had new sexual partner(s) since they became pregnant
- > Have had sex with men who have sex with men
- > Uses illicit (or partner uses) substances.





For pregnant women and women with partners who are at increased risk consider screening at birth and at the 6-week postnatal check (see <u>flowchart 1</u>).

# **Clinical Features**

Untreated syphilis passes through distinct symptomatic stages (primary, secondary, and tertiary) as well as asymptomatic (latent) stages. While the infection is latent a diagnosis of syphilis can only be made by serology.<sup>11</sup>

There are characteristic clinical features for each stage of syphilis, however, syphilis can present with a wide variety of symptoms which can be mild or severe, characteristic or variable, or the infection can be asymptomatic.<sup>11,12</sup> Syphilis has been called "the great imitator" because the symptoms of syphilis can present like many other diseases.<sup>13</sup>

#### **Primary Stage**

Characterised by an ulcer(s) otherwise known as a chancre. Chancres are usually single but may be multiple in 30% of cases.<sup>11–13</sup> The chancre is typically firm, round, small and maybe painless or painful and appears at the site where direct contact has occurred.<sup>11,12</sup> Furthermore, there may be associated non-tender local lymphadenopathy.

The initial chancre may go unnoticed, particularly if located in the vagina, mouth, or anal region. Any anogenital ulcer should be considered syphilitic unless proven otherwise. Chancres are frequently difficult to find in females and men who have sex with men (MSM).<sup>11</sup> The chancre lasts 3 to 6 weeks (range 1-12 weeks) and heals without treatment.<sup>11,12,14</sup>

#### Secondary Stage

Occurs 2 to 8 weeks after resolution of the chancre but may occur any time in the following year if untreated.<sup>11,12</sup> Usually characterised by rash and systemic symptoms.<sup>14</sup> The non-itchy rash is often present in people with secondary syphilis.<sup>11,12</sup> The rash may be subtle or appear as rough red or reddish-brown spots, often on the trunk and palms of the hands and soles of feet.<sup>14</sup> Greyish-white, moist plaques or warty lesions may occur in the groin, inner thighs, armpits, umbilicus or under the breasts (condylomata lata).<sup>11,12</sup>

Mucosal surfaces such as inside the mouth, throat, genital area, vagina and anus can become red and raw (mucous patches).<sup>14</sup> There may be associated fever, swollen lymph glands, sore throat, patchy alopecia (hair loss), headaches, weight loss, muscle aches and fatigue.<sup>11,12</sup> Signs and symptoms last about 2 to 6 weeks and will resolve without treatment.<sup>14</sup> Recurrences may be observed in the first year, and in rare cases the second year.<sup>14</sup> Without treatment, the infection will become latent and may progress to late stages of disease.<sup>14</sup>

#### Latent Stage

Defined as zero-positivity without evidence of disease (asymptomatic):

- Early latent stage: Positive serology with no symptoms and infection acquired within the last 2 years.<sup>(14)</sup>
- Late latent stage: Asymptomatic infection beyond 2 years' duration. Infectivity is reduced only to vertical transmission or via transfused contaminated blood.<sup>14</sup>

#### **Tertiary Stage**

Can develop in up to 40% of untreated individuals.<sup>11,12</sup> May occur up to 20-40 years after initial infection and involve the brain and spinal cord (neurosyphilis), heart and blood vessels (cardiovascular syphilis), liver, bones and joints.<sup>14</sup>



#### Neurosyphilis

Can occur at any stage of syphilis infection.<sup>11,12</sup> Symptoms may include meningitis, cranial nerve palsies, change in vision, change in hearing, difficulty coordinating muscle movements, paralysis, numbness, dementia, psychosis and death.<sup>11,12,14</sup>

#### **Congenital Syphilis**

Intrauterine ultrasound findings suggestive of congenital syphilis include:

- hepatomegaly
- placentomegaly
- polyhydramnios
- ascites
- > abnormal middle cerebral arterial doppler assessment
- fetal hydrops
- bent, thickened or shortened fetal long bones.<sup>10</sup>

# Transmission

Almost all cases of syphilis are acquired through sexual contact with an infected partner(s). Transmission of the disease is categorised as acquired or vertical.

#### Acquired

In the majority of cases, syphilis is transmitted during sexual activity, by direct contact with lesions (e.g., chancres and *condylomata lata*) on a person with infective syphilis.<sup>14</sup> These lesions occur mainly on the external genitals; vagina; anus; or in the rectum.<sup>14</sup> Lesions can also occur on lips and in the mouth.<sup>14</sup>

Sexual transmission can occur during primary and secondary stages and any time in the first 2 years after infection.<sup>14</sup> Rarely, syphilis is transmitted by infected blood (transfusion, sharing injecting equipment), by nonsexual personal contact with infected lesions or by accidental direct inoculation.

#### Vertical

Vertical transmission can occur at any time during pregnancy, labour, and birth. Transmission is possible if pregnancy occurs at any stage of syphilis, up to 8 years after acquisition of infection. Congenital syphilis can occur when the spirochete is transmitted from a woman with untreated syphilis to the fetus.

Note: Syphilis can be transmitted vertically at any stage of pregnancy, labour and birth.

#### **Incubation Period**

- > 9 to 90 days, with an average of 3 weeks from contact to the development of a chancre.<sup>11</sup>
- The individual is no longer infectious 7 days after starting appropriate antibiotic treatment.<sup>14</sup>

## Diagnosis

- Syphilis serology blood sample should be collected and sent any time syphilis infection is suspected.<sup>15</sup>
- Where syphilitic lesions (primary or secondary) are suspected, syphilis PCR should also be sent using a swab suitable for molecular testing.<sup>15,16</sup>
- When there are no symptoms and signs, (i.e., latent syphilis), diagnosis occurs from serology. Noting that serology can take up to 3 months to become positive after infection.
- If syphilis serology returns positive it is highly recommended that further STI screening (including HIV) are undertaken.<sup>14,15</sup>

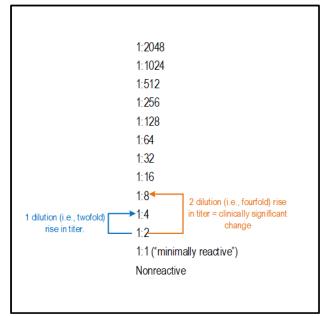




#### Syphilis Serology

- Collect a blood sample and send to pathology with a request for "syphilis serology".
- > Pathology laboratory will screen for syphilis using a Treponemal specific EIA screening test.<sup>15</sup>
  - If the EIA is reactive, the lab will automatically confirm with a *Treponemal Pallidum* (TPPA), and rarely FTA-abs.
- > TPPA positive result confirms exposure to *Treponema Pallidum*, but does not indicate whether the disease is active, inactive, or treated.
  - EIA and TPPA remain reactive for many years even after successful treatment.<sup>11</sup>
  - Pathology will not repeat the TPPA once it is positive.
- > The RPR will also be performed when screening and confirmatory tests are positive.
  - False positive results may occur (syphilis Elisa, RPR).<sup>11,15,17</sup>
- The RPR is reported as a titre and is useful in determining disease activity, response to treatment and reinfection.<sup>11,15</sup> For example:
  - EIA reactive, TPPA positive and RPR negative may represent very early infection, latent infection, or treated syphilis.
  - EIA reactive, TPPA positive and RPR 1:125 represents active syphilis.
    - After treatment of infectious syphilis an adequate response to treatment would be at least a four-fold drop in titre by 6-12 months. Conversely if the person were to be re infected in the future their RPR will increase by four-fold (see <u>table 1</u>).

Table 1: Example of syphilis RPR titres that indicate a clinically significant change in disease activity.



#### Interpretation of Syphilis Serology

Previous syphilis screening results, history of previous treatment and examination findings are important when interpreting the test results.

For assistance interpreting serology and advice please contact any of the following:

- > Adelaide Sexual Health Centre on 08 7117 2800 during business hours.
- > CDCB on 08 7425 7101 during business hours.
- > Contact an **infectious diseases** specialist out of hours.



#### **Point of Care Testing**

Some Aboriginal Community Controlled Health Services, drug and alcohol treatment services and prison health services in SA can undertake point of care testing (POCT) for syphilis using the Determine<sup>™</sup> Syphilis TP test. POCT is a treponemal antibody test. It requires a small drop of blood and a chase buffer and provides a result in 15 minutes. If possible, all people having POCT should also have blood taken for syphilis serology. If POCT is positive, serology will help to determine if the infection is active, inactive or treated.<sup>1,18</sup>

**Note:** Blood for serology should be taken before any treatment is commenced, so the RPR titre can be monitored.

Individual services should/refer to their clinical framework and procedure for syphilis POCT within their own clinics.

# Antenatal Syphilis Screening Recommendations

- Universal screening is recommended for all pregnancies (see <u>flowchart 1</u>).
- All pregnant women must be offered routine screening for syphilis (treponemal specific enzyme immunoassay) at:
  - first antenatal appointment,
  - o 26-28 weeks gestation, and
  - 36 weeks gestation or at time of any preterm birth, as part of routine antenatal screening blood tests (for a comprehensive list of tests see the *Antenatal Care* PPG in the A-to-Z listing found at <u>www.sahealth.sa.gov.au/perinatal).</u>
  - If there is no evidence that the third screen at 36 weeks gestation occurred:
    - then syphilis testing must also be offered at birth or before the neonate is discharged from the birthing hospital.
    - the placenta should be kept until a negative screen is confirmed.<sup>11,17</sup>
- At the time of testing, it is important to explain to the mother what syphilis is, the symptoms, the risks during pregnancy and the reasons increased testing may be recommended.<sup>14</sup>



Aboriginal Health Workers or AMIC Practitioners staff should be included in consultations to provide support to Aboriginal people. Where this service is unavailable, please contact WCHN **Aboriginal Health Division (08) 8303 1622** 

#### Additional Screening for at-Risk Groups

- Groups at increased risk of STIs in pregnancy (see <u>flowchart 1</u>) and pregnant women and those with partners with identified risk should be offered additional screening, at birth and at 6 weeks postpartum (at a minimum).
- > For testing offered at birth, the placenta should be kept until a negative screen is confirmed.<sup>11,17</sup>
- Pregnant women should be informed of this recommendation with corresponding documentation in their SA Pregnancy Record.
- Offer syphilis screening to all pregnant women who present in labour with no antenatal care, or if syphilis results unavailable.<sup>19</sup>



Aboriginal women should be offered or referred to an Aboriginal health professional as soon as practicable to ensure culturally sensitive and appropriate support.

#### Care of Aboriginal Women

Aboriginal women should be offered a female clinician/practitioner where available to acknowledge the importance of women's business remaining women's business. Where a female clinician is unavailable, the woman should be offered an Aboriginal Healthcare Worker (female) or appropriate female support.



Perinatal service providers need cultural sensitivity within a non-judgemental environment when planning care for the Aboriginal woman. Aboriginal women should be referred to an Aboriginal Health Professional, AMIC Practitioner or Aboriginal Healthcare Worker to support decisions and interpretation of care.

Health literacy will need to be considered in ensuring that care is culturally appropriate for Aboriginal women/consumers – visual/pictorial resources may be used to ensure Aboriginal women, particularly for APY Lands or NT understand in the absence of an interpreter.

The <u>Minymaku Kutju Tjukurpa: Women's Business Manual</u> outlines culturally appropriate care for rural and remote Aboriginal women found at <u>www.remotephcmanuals.com.au</u>.

# Notification of Syphilis Diagnosis to SA Health

Syphilis (including congenital syphilis) is a nationally notifiable disease. Notification must be made to the Communicable Disease Control Branch (CDCB) in South Australia **within 3 days** of suspecting or confirming a diagnosis of syphilis, using the <u>maroon syphilis notification form</u> found on the SA Health website under the <u>Notifiable Disease Reporting</u> page at <u>https://www.sahealth.sa.gov.au</u>.

Notifications of syphilis in pregnancy or a suspected congenital case contact: **1300 232 272** (24 hours, 7 days a week).



Ensure Aboriginal women have access to cultural support when discussing notifiable condition reporting. Aboriginal consumers may not accurately understand what this involves and may feel a sense of judgement, shame and fear of losing their baby if the process is unclear. Aboriginal women should be referred to an Aboriginal Health Professional to ensure care and management is culturally appropriate, safe and sensitive.

# Management Syphilis Infection

Successful management of syphilis in pregnancy depends on early detection and stage appropriate treatment of maternal infection, ideally before 28 weeks of gestation and at least 30 days before birth (<u>flowchart 1</u>).<sup>6–8</sup>

- Once a positive syphilis serology has been confirmed in pregnancy, establish the stage of syphilis (i.e., when the infection occurred) and whether effective treatment has already been given.<sup>15</sup>
- If effective treatment has been given it is important to monitor treatment response and exclude re-infection.<sup>15</sup>
- For assistance establishing the stage of syphilis contact the Adelaide Sexual Health Centre on 08 7117 2800 or CDCB on 08 7425 7101.
- For assistance with accessing past results or treatments for Aboriginal people, seek consent from the woman to contact their GP or Aboriginal Community Controlled Health Service or the SA Syphilis Register on <u>health.sasyphilisregister@sa.gov.au</u> or **1300 232 272.**
- Women with syphilis of less than 2 years duration and treated with penicillin may develop a <u>Jarisch-Herxheimer Reaction</u> (JHR).<sup>20,21</sup>
  - Women in the second half of pregnancy have increase the risk of preterm labour and fetal compromise.<sup>17,20,21</sup>
- It is recommended all women with viable pregnancies receive the first dose of benzathine penicillin G in an inpatient setting where fetal monitoring can occur for at least 24 hours.<sup>21</sup> Thereafter, the remaining benzathine penicillin G doses can be given in an outpatient setting.<sup>21,22</sup>
- > If inpatient management not practical (e.g., in a remote setting) consider:
  - 1. outreach follow-up contact in the community (e.g. by phone, text or personal contact)
  - 2. fetal heart rate (FHR) auscultation or cardiotocography pre and post administration<sup>23</sup>
  - 3. education on signs and symptoms of JHR and when to seek medical help.





For remote Aboriginal Communities, contact with Aboriginal Community Controlled Health services may be more appropriate due to location – and will consider the most appropriate method of follow up in this setting.

#### Multidisciplinary Management of Syphilis During Pregnancy

Involvement of infectious disease/sexual health physicians, woman's general practitioner or Aboriginal Community Controlled Health Service, midwife and obstetric team is crucial in treating and managing syphilis during pregnancy. Timely communication and referral between different teams helps to achieve best outcomes.



For Aboriginal women, Aboriginal Healthcare Worker and AMIC practitioners, where available, should be offered and/or included in consultations to provide cultural advice and support for Aboriginal women and their families.

# Pharmacological Treatment of Syphilis Infection

#### Primary, Secondary and Early Latent Syphilis

#### Benzathine Penicillin 2.4 million units, Intramuscular injection<sup>24</sup>

- Pregnant women diagnosed with infectious syphilis (primary, secondary, and early latent stages) prior to 28 weeks gestation require a single dose of intramuscular (IM) benzathine penicillin 2.4 million units (MU).
  - given as two IM injections of 1.2 MU, one in each buttock or ventrogluteal region, at the same visit.<sup>8,11,12,24,25</sup>
- If syphilis is diagnosed in the third trimester, a second dose of benzathine penicillin 2.4 MU is required 7 days after the first dose.<sup>8,11,12</sup>
  - A second dose of benzathine penicillin may be considered for pregnant women after 20 weeks gestation if the antenatal ultrasound shows evidence congenital syphilis.<sup>17</sup>

**Note:** If allergy to penicillin, seek expert advice about allergy de-labelling and desensitisation (see <u>allergy to penicillin</u> section in this guide). <sup>(1,12)</sup>

- Repeat blood test for syphilis serology on the day that syphilis treatment is commenced.
   Do not wait for results to commence treatment.
- Repeat RPR monthly (and at birth) to confirm falling, negative, low, or stationary titre.
   If titre is not falling, seek advice from an infectious disease or sexual health physician.<sup>1,12</sup>
- Neurosyphilis, including ocular syphilis, can present in the person in the early stages of syphilis, particularly in secondary syphilis. Seek expert input if any new neurological symptoms, including auricular or ocular symptoms occur.
- See <u>Partner notification/Contact management</u> section in this guide for management of sexual contacts.

Always repeat the RPR test on the day the treatment begins to ensure a peak RPR reading is obtain and therefore accurate record of post-treatment response.

#### Late Latent Syphilis

#### Weekly Benzathine Penicillin 2.4 million units, Intramuscular injection, for 3 weeks<sup>24</sup>

- Late latent syphilis (> 2 years), or of indeterminate duration in the absence of evidence of tertiary syphilis require weekly IM benzathine penicillin 2.4 MU for 3 weeks.
  - given as two IM injections of 1.2 MU, one in each buttock or ventrogluteal region, each time<sup>8,11,12,24,25</sup>
  - $\circ~$  administered for three weeks on days 0, 7, and 14.
  - If more than 24 hours late for a dose, consider restarting all 3 doses particularly after 28 weeks gestation.
    - if needed consult with a sexual health physician.





- Repeat blood test for syphilis serology/RPR on the day first dose of benzathine penicillin is given.
  - Do not wait for results to commence treatment.

**Tertiary Syphilis** 

- Intravenous (IV) Benzathine Penicillin 1.8 grams, 4 hourly for 10-14 days.
- Seek input from infectious diseases or sexual health physician.

#### **Penicillin Allergy**

- Penicillin allergy may be assessed against the 'suggested management of patients reporting hypersensitivity to penicillins in whom a beta-lactam antibiotic is the preferred drug' algorithm, see Antibiotics in the Peripartum Period PPG found in the A-Z listing at www.sahealth.sa.gov.au/perinatal.
- If a true allergy is ascertained discuss or refer urgently to immunology/allergy services for further assessment including allergy testing and desensitisation. The evidence for nonpenicillin regimens preventing congenital syphilis is weak.<sup>11</sup>
- > If desensitisation is not feasible, doxycycline could be used if hypersensitive to penicillin.
- If necessary, doxycycline may be used during the first 18 weeks of pregnancy (16 weeks post conception).
  - Doxycycline should be avoided after this time due to an association with irreversible teeth discolouration, enamel hypoplasia and inhibition of bone growth in the newborn following maternal use.<sup>26</sup>
  - Dose:
    - For primary, secondary, and early latent stages give 100 mg orally twice a day for 14 days
    - For late latent stage give 100 mg orally twice a day for 28 days.
- If penicillin desensitisation is not feasible and gestation greater than 18 weeks consult with infectious disease physician regarding treatment.
- > Repeat RPR monthly (and at birth) to confirm falling, negative, low or serofast titre.
  - If titre rising repeat treatment as may be due to re-infection.
- Macrolides are not recommended treatments for syphilis.<sup>1,12</sup>

# Jarisch-Herxheimer Reaction (JHR)

Up to 40% of people may develop a transient inflammatory reaction known as Jarisch-Herxheimer reaction (JHR) in the first 24 hours after administration of large doses of penicillin, this is especially noted in early syphilis.

JHR onset is approximately 6 hours after the first penicillin dose but can range between 2 and 24 hours after treatment and symptoms lasts several hours. It is thought that JHR is an immune system's response to the rapid killing of spirochetes. Symptoms include fever, chills, headache, myalgias, and exacerbation of cutaneous lesions.

**Note:** In the second half of the pregnancy (after 20 weeks) a JHR may precipitate uterine contractions, decrease fetal movements and cause abnormal fetal heart rate (FHR) tracings. In severely affected pregnancies preterm birth and stillbirth have been reported.<sup>27</sup>

#### **Management of JHR**

- > Do not delay treatment for syphilis over concerns regarding JHR.
- Symptomatic management of JHR includes paracetamol 1 gram every 4 to 6 hours (maximum 4 grams in 24 hours) and maintaining hydration, and tocolytics and intravenous (IV) fluids if required.



# Follow-up After Treatment

- Conduct a clinical assessment 4 weeks after treatment.
  - ensure sexual partner(s) has been treated and no sexual activity has occurred for pregnant woman and partner(s) while infectious.
- Repeat syphilis serology/ RPR monthly (and at birth) to confirm a falling, negative, low, or serofast titre.
  - If the titre is rising or not dropping, repeat treatment may be required. Consult with infectious diseases/sexual health physician.
- > Take a detailed sexual history and the treatment history of sexual partner(s) at every appointment and offer repeat STI screening as required.



All Aboriginal women should be offered cultural support with an Aboriginal Healthcare Worker, or AMIC Practitioner where available in the provision of care, treatment and development of management plans. Follow up in primary care requires good communication with the pregnant woman GP or Aboriginal Community Controlled Health Service.

#### Counselling

- Explain to the woman and her partner(s) (if applicable) that Syphilis is a notifiable condition.
   See <u>www.sahealth.sa.gov.au/NotifiableDiseaseReporting</u>
- Successful management of syphilis in pregnancy depends on early detection and treatment of maternal infection, ideally before 28 weeks of gestation and at least 30 days before birth.
- > The treatment regimen may vary, depending on the treatment history, treatment during pregnancy, risk of re-infection during pregnancy or presence of persisting high titres despite treatment.
- Explain the risks of congenital syphilis for the unborn baby and the infant.
- Stress the importance of testing any sexual contacts immediately and advise to avoid sex (including oral or anal sex) until:
  - 7 days after first treatment dose and
  - o 7 days after sexual partner(s)' first treatment dose
- Information about sexual contact notification can be found in <u>sexual partner/contact notification</u> and <u>management</u> section of this guide, or under the *notifiable STIs and partner notification* page in the SA Health website at <u>www.sahealth.sa.gov.au</u>.
- > Stress the importance of attending follow up tests and treatment.

#### Education

- > Encourage safer sex practices:
  - $\circ~$  use of condoms to reduce the risk of acquiring syphilis and other STIs
  - $\circ$   $\,$  condoms only work if they prevent direct contact with ulcers and other mucosal lesions
  - $\circ \;\;$  offer condoms to take away and show how to use if necessary
  - $\circ~$  encourage communication between sexual partners.
- Educate on:
  - $\circ~$  increased risk if sexual partner(s) engage in male-to-male sex or illicit substance use
  - $\circ~$  risk of reinfection in pregnancy
  - $\circ~$  avoid illicit substance and alcohol use during pregnancy.

# Sexual Partner(s)/Contact(s) Notification and Management

- Treatment of pregnant woman and their sexual contacts should be carried out urgently (as soon as practical, within 24 hours of results becoming available) and in consultation with an infectious disease/sexual health physician.
- Once a pregnant woman is diagnosed with syphilis or any STI, it is vital that testing and treatment of their sexual partners is properly considered, discussed, and supported.
- Partner(s) should be referred to appropriate available services, which may include Adelaide Sexual Health Centre, SHINE SA, or primary care services.







For some Aboriginal people with transient accommodation and movement, contact tracing can be challenging. Additionally, some areas will have limited ways of contact tracing due to the remoteness and transience. Cultural sensitivity is required in this context and cultural advice and support should be sought, in how to best manage tracing and contacts.

#### Definition

A sexual contact is defined as anyone who has had sex (including oral and/or anal) with a person whilst they had infectious syphilis as per trace back periods (see <u>table 2</u>)

#### Table 2: Syphilis Trace Back Periods14,15

Stage of Infection	Trace Back Period	
Primary	Duration of symptoms plus 3 months	
Secondary	Duration of symptoms plus 6 months If duration uncertain then count from 12 months prior to presentation	
Early latent or unknown duration	12 months prior to presentation	
Late latent and Tertiary	These stages are not infections to sexual partners, but as date of acquisition may not be known, it is recommended that the regular partner is tested for syphilis.	

#### **Vertical Transmission Contacts**

Vertical transmission contacts include all unborn and newborn babies of a woman that required treatment for syphilis in pregnancy.

**Note:** previous babies may need to be tested if vertical transmission in previous pregnancies cannot be excluded due to unknown syphilis duration.

#### Sexual Partner(s)/Contact(s) Notification

- At the time of diagnosis, determine all sexual contacts (see <u>table 2</u>) and emphasise the importance of providing a complete sexual history.
- Fear of the clinician not maintaining confidentiality can be a barrier to identifying sexual contacts. Explain that any information the pregnant woman provides will be confidential, but that their partners will need to be notified, although this can be done anonymously.<sup>9</sup>
- Options to notify sexual partner(s)/contacts include:
  - notification by health practitioner
  - notification by the pregnant woman (the pregnant woman independently informs their sexual contact(s)).
  - requesting support from CDCB
    - CDCB will refer all cases to partner notification.
  - anonymous notification services, such as:
    - Let them know: <u>http://www.letthemknow.org.au</u>
    - Better to know website at <u>www.bettertoknow.org.au</u> (for Aboriginal and Torres Strait Islander people).

#### Treatment for Sexual Partner(s)/Contact(s)

- Sexual partner(s)/contact(s) exposed to syphilis infection require treatment regardless of the syphilis serology results.
  - serology may take 3 months to become positive after acquisition of syphilis.
- > **Obtain** sexual history (including symptoms).
- > **Perform** a clinical examination for signs of syphilis and other STIs
- > Collect serology for syphilis on the day of treatment and other STI tests as indicated.
- Inform contacts of their test results at the earliest opportunity.
- > Give:
  - Benzathine Penicillin 2.4 million units, Intramuscular injection

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- (as two IM injections of 1.2 MU, one in each buttock or ventrogluteal region).
- > Do not:
  - $\circ~$  record the name of the index case in the contacts' health record
  - $\circ\;$  disclose the name of the index case to a contact.

#### Discuss:

- $\circ\;$  infectious nature of the disease.
- possibility of infection even in the absence of symptoms or reactive serology
- o importance of follow-up and repeat serology testing
- need to abstain from sexual activity for 7 days after treatment or until symptoms (if present) have resolved – whichever is longer
- explain Late Latent Syphilis
- $\circ$  Weekly Benzathine Penicillin 2.4 million units, Intramuscular injection, for 3 weeks^{24}
- Late latent syphilis (> 2 years), or of indeterminate duration in the absence of evidence of tertiary syphilis require weekly IM benzathine penicillin 2.4 MU for 3 weeks.
  - given as two IM injections of 1.2 MU, one in each buttock or ventrogluteal region, each time<sup>8,11,12,24,25</sup>
  - $\circ~$  administered for three weeks on days 0, 7, and 14.
- If more than 24 hours late for a dose, consider restarting all 3 doses particularly after 28 weeks gestation.
  - if needed consult with a sexual health physician.
- Repeat blood test for syphilis serology/RPR on the day first dose of benzathine penicillin is given.
  - Do not wait for results to commence treatment.

#### **Tertiary Syphilis**

#### Intravenous (IV) Benzathine Penicillin 1.8 grams, 4 hourly for 10-14 days.

Seek input from infectious diseases or sexual health physician.

#### **Penicillin Allergy**

- Penicillin allergy may be assessed against the 'suggested management of patients reporting hypersensitivity to penicillins in whom a beta-lactam antibiotic is the preferred drug' algorithm, see Antibiotics in the Peripartum Period PPG found in the A-Z listing at www.sahealth.sa.gov.au/perinatal.
- If a true allergy is ascertained discuss or refer urgently to immunology/allergy services for further assessment including allergy testing and desensitisation. The evidence for nonpenicillin regimens preventing congenital syphilis is weak.<sup>11</sup>
- > If desensitisation is not feasible, doxycycline could be used if hypersensitive to penicillin.
- If necessary, doxycycline may be used during the first 18 weeks of pregnancy (16 weeks post conception).
  - Doxycycline should be avoided after this time due to an association with irreversible teeth discolouration, enamel hypoplasia and inhibition of bone growth in the newborn following maternal use.<sup>26</sup>
  - Dose:
    - For primary, secondary, and early latent stages give 100 mg orally twice a day for 14 days
    - For late latent stage give 100 mg orally twice a day for 28 days.
- If penicillin desensitisation is not feasible and gestation greater than 18 weeks consult with infectious disease physician regarding treatment.
- Repeat RPR monthly (and at birth) to confirm falling, negative, low or serofast titre.
  - If titre rising repeat treatment as may be due to re-infection.
- Macrolides are not recommended treatments for syphilis.<sup>1,12</sup>
   Jarisch-Herxheimer Reaction (JHR).





# Postpartum Follow-Up

- Conduct a clinical assessment and repeat syphilis serology (RPR) at 3, 6, 12 months.
  - Successful treatment is a fourfold drop in the RPR titre within 12 months for infectious syphilis and within 18–24 months for late latent syphilis.
  - Titres that show a four-fold rise or do not decrease appropriately suggest either treatment failure, re-infection or undiagnosed neurosyphilis. Further treatment in these situations should be planned after seeking advice from an infectious diseases or sexual health physician.

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Aboriginal women and their family should be consulted in relation to any follow up plans, including appropriate referrals to ongoing care and service providers. Offering cultural support is imperative to ensure follow up arrangements are timely and accurate, for rural and remote communities.

#### Breastfeeding

- Breastfeeding is recommended as *T. pallidum* is not transmitted in breast milk.
- If there is a chancre present on the breast or axilla, the breastmilk should be discarded until 7 days after treatment and the lesion has healed.

# Congenital Syphilis Risk Assessment and Management

- Every baby born to a woman who has been treated for syphilis in their current pregnancy should be reviewed by a specialist (paediatrician or infectious diseases specialist) to determine their congenital syphilis risk (see <u>flowchart 3</u>).
- Most newborns with congenital disease have no clinical signs at the time of birth, signs may not occur for more than 2 years. There are two categories:
  - $\circ~$  early (occurring within the first 2 years of life).
  - late (recognised after 2 or more years after birth).



Aboriginal woman should be consulted on the care of the newborn baby in the first instance. Consult with and Aboriginal Healthcare Worker or AMIC Practitioner or the preferred aboriginal health professional. Aboriginal women, family or carer must be consulted about any decisions regarding maternal or neonatal care in the first instance. Culturally appropriate consultation improves outcomes for Aboriginal women, babies, and families.

# Newborn Risk Assessment

#### See flowchart 3

Does Maternal History Meet Criteria for Low-Risk Neonate?

1. Determine if the neonate meets the low-risk criteria for 'maternal history assessment' (table 3).

#### Table 3: Maternal History Assessment Criteria

- ✓ completed syphilis treatment with appropriate penicillin dose(s) before this pregnancy, and
- ✓ adequate serological response, and
- $\checkmark$  third trimester screen complete with no suspicion of reinfection.

If all the above 'maternal history assessment criteria' <u>are met</u>, then there is no risk to the neonate and no further management is required.

#### Does Neonate Meet all Criteria for Low-Risk?

2. For all neonates **that did not meet the low-risk** criteria for 'maternal history assessment criteria' above, determine their risk under the 'neonate assessment criteria' (<u>table 4</u>).



#### Table 4: Neonate Assessment Criteria

- Penicillin regimen appropriate to stage of infection in birth parent during this pregnancy, and
- ✓ Completed at least 30 days prior to birth, and
- ✓ No suspicion of reinfection, and
- ✓ No signs of congenital syphilis on examination, and
- ✓ Syphilis FTA IgM negative, and
- ✓ RPR same or less than the RPR of the birth parent at Negative placental syphilis PCR,
- ✓ No features of congenital syphilis on placental histopathology and negative immunohistochemistry staining.

# If all aspects of the above 'Neonate assessment criteria' are met, the neonate meets the criteria for low risk.

- An expert practitioner may consider single precautionary dose of antibiotic if follow-up at discharge is uncertain and congenital syphilis considered unlikely (but cannot be excluded with certainty). In this case management is:
  - Give stat dose of Benzathine penicillin 37.5 mg/kg (50,000 units/kg) IM.
  - Collect serology at 3 and 6 months:
    - In the neonate who was not treated because congenital syphilis was considered less likely, or unlikely nontreponemal antibody titres (RPR) should decline by 3 months and be nonreactive by 6 months.
    - If at 6 months, the non-treponemal test (RPR) is still reactive the infant is likely to be infected & should be treated.
    - If EIA and TPPA are persistently reactive > 15 months seek advice from expert practitioner as this may indicate congenital syphilis.

#### If all aspects of the above 'Neonate assessment criteria' <u>are not met</u>, the neonate <u>does not</u> meet the criteria for low risk.

- Collect:
  - CBE and EUC
  - Syphilis PCR from skin lesions, nasal secretions, placental tissue & amniotic fluid
- Discuss with paediatric ID team regarding need for CSF, x-ray long bones and chest, neuroimaging, ophthalmology review, auditory brainstem response.
- Send placenta for histopathology and syphilis PCR.
- Begin <u>treatment of congenital syphilis</u> (see below).

# Treatment of Congenital Syphilis

#### **First Line Treatment**

- 10 days of aqueous benzylpenicillin
  - If baby is  $\leq$  7 days of age, give 50 mg/kg body weight dose, intravenously, every 12 hours.
  - When/if the baby is 8 days of age or older, give 50mg/kg body weight dose, intravenously, every 8 hours.



#### Other Management

- > Ophthalmologic assessment.
- Brain stem evoked response audiometry to assess hearing.

# Examination of the Neonate for Features of Congenital Syphilis

#### Early Signs and Symptoms

- Usually occur within 3–7 weeks after birth and result from active disseminated fetal infection and the subsequent inflammatory response.
- > Hepatomegaly is common and may be associated with splenomegaly.
  - There may be abnormal LFTs/hepatitis, jaundice, and cholestasis or, ascites.
- > Rhinitis usually presents during first week of life and seldom occurs after the third month.
  - $\circ~$  White nasal discharge which may be bloody secondary to nasal ulcerations.
  - The discharge contains high concentrations of spirochetes and is therefore contagious.
  - Nasal discharge is the earliest sign of congenital syphilis and occurs 1–2 weeks before the rash.
- > Rash lesions on the skin and/or in the mouth.
  - o Intra-epidermal oedema leads to bullae most prominent on the hands and feet.
  - Even in the absence of bulla, desquamation is common and may be generalised.
  - A maculopapular rash consisting of small, initially red, or pink spots may progress to large pink macules that fade to a coppery hue, which may be covered by a silvery scale.
  - Condylomata lata affect the mucocutaneous and intertriginous areas.
- Lymphadenopathy which may be generalised.
  - Palpable epitrochlear lymphadenopathy is highly suggestive.
- Haematologic disturbances:
  - thrombocytopenia, anaemia (Coomb's negative normochromic, normo or macrocytic with striking reticulocytosis and erythrobalstosis), and leucocytosis or leukopenia.
- IUGR. Low birth weight, failure to thrive not explained by alternative diagnosis.
- Necrotising funisitis:
  - an inflammation of the umbilical cord characterised by spiral stripes of red and blue discolouration resembling a "barber's pole"
  - $\circ~$  at birth the placenta should be sent for histopathology and PCR.
- > Non-immune fetal hydrops.
- > Tissue swelling of fingers and/or hands (dactylitis).
- Inflammation of long bones (osteochondritis, perichondritis).
  - A skeletal survey is required to evaluate infants for congenital syphilis.
- Failure to move limbs secondary to pain caused by bony lesions/fractures (pseudo paralysis of Parrot).
- Ophthalmologic manifestations (e.g., loss of eyebrows, chorioretinitis, uveitis, cataracts, glaucoma, and chancre of the eyelid).
- > Eight (8<sup>th</sup>) cranial nerve (auditory) damage leading to hearing impairment.
- > Syphilitic nephrotic syndrome.
- Neurological involvement ranges from asymptomatic invasion by *T. pallidum* to acute syphilitic leptomeningitis.<sup>9,10,22,28</sup>

#### Late Signs and Symptoms

- Lesions often represent scars from undetected, early congenital lesions or a delayed reaction to on-going inflammation.
- Vasculitis at the time of birth damages tooth buds and results in abnormalities of the permanent teeth (peg-shaped upper incisors, short and notched, poorly developed first lower molars with multiple cusps).
- Interstitial keratitis may appear as photophobia, pain, or blurred vision first in one eye and then bilaterally, any time between 5 and 20 years of age.





- Eighth (8<sup>th</sup>) cranial nerve deafness is less common (usually in the first decade of life and may be unilateral or bilateral).
  - Facial abnormalities:
  - saddle nose

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- protuberant mandible.
- > Central nervous system involvement:
  - o intellectual disability
  - optic nerve atrophy
  - $\circ$  seizure disorders.
- Bone or joint involvement:
  - frontal bossing of the skull
  - o saber shins
  - hypertrophy of the sternoclavicular joints.9,10,22,28

## Laboratory Assessment for Congenital Syphilis

#### Table 5: Testing type and diagnosis of congenital syphilis.

Test	ting	Diagnosis of Congenital Syphilis
moth	nparison of her and y's serology	<ul> <li>In the presence of mother's positive syphilis serology relationship between mother and baby's non-treponemal titre can indicate the likelihood of congenital syphilis<sup>1,17</sup></li> <li>Collect serology from woman and baby on same day and ask for testing in parallel</li> <li>Do not use umbilical cord blood</li> <li>Venous sample is preferable to a heel prick collection</li> <li>If baby's RPR titre is ≥ four-fold higher than the mother's titre - diagnostic of congenital syphilis</li> <li>If baby's titre is &lt; four-fold the maternal RPR titre may still indicate congenital syphilis</li> <li>Baby's syphilis IgM, positive IgM is diagnostic of congenital syphilis<sup>1</sup> (IgM does not cross the placenta therefore IgM is strongly predictive of infection. A negative IgM does not exclude congenital syphilis, discuss with an expert)</li> <li>With follow up blood testing, an <u>uninfected</u> baby should have a negative RPR within the first 6 months and negative EIA/TPPA within 15 months<sup>1,17,21</sup></li> </ul>
Sypł	hilis PCR	<ul> <li>Collect a dry swab / or send fluid from any mucocutaneous lesions (ulcers, mucosal lesions and any nasal discharge from the baby), placenta, umbilical cord, amniotic fluid, CSF and request a syphilis PCR</li> <li>A positive PCR in any specimen site is diagnostic of congenital syphilis<sup>1</sup></li> </ul>
Histo	opathology	<ul> <li>Send whole placenta and umbilical cord for histopathology</li> <li>Positive placental or umbilical cord histopathology is diagnostic of congenital syphilis<sup>1</sup></li> </ul>



Table 6: Extra investigations of probable or confirmed congenital syphilis cases.			
Further investigati	Further investigations of probable/confirmed cases of congenital syphilis		
Blood       • CBE, EUC LFT <sup>9,22</sup> • In syphilis typically direct antiglobulin titre (DAT) negative haemolytic anaemia         • Non-haemolytic anaemia after the neonatal period         • Thrombocytopenia, leukopenia/ and or leucocytosis         • Haemolysis often accompanied by cryoglobulinaemia, immune complex for macroglobulaemia (does not respond to therapy and may persist for weeks)         • The CSF should be examined before treatment – Collect CSF         • Reactive FTA/RPR         • CSF pleocytosis (>20-25 WC/microL) for babies < 1 month <sup>9,22</sup> • Elevated CSF protein (term>150 mg/L, preterm> 170 mg/L)         • If CSF abnormal repeat CSF syphilis PCR evaluation every 3 months until norm			
		Skeletal survey/radiology	Metaphyseal lucent bands or metaphyseal servation

# Discharge and Follow-Up Care

- > Document the need for follow up.
- Communicate with local services involved with follow up Liaise with ongoing health care providers as appropriate, including GP, Aboriginal Community Controlled Health Service, RFDS, paediatrician, to coordinate discharge planning and follow up care of mother, baby, and sexual partner(s).
- > Take serology at 3, 6 and 12 months of age.
  - If follow-up is difficult, aim for two tests by 6 months of age (> 4 weeks apart), until the test becomes non-reactive.
- > If initial LP showed abnormalities, a follow up LP may be required.
- Ensure parents are aware of the results of investigations and implications for future health care.
- > Advise parents of the importance of attending follow up appointments with the paediatric team.
- Review previous serology in previous pregnancies and if necessary, test older siblings for syphilis.
- > See Postnatal follow-up of mother and breastfeeding advice.



# Useful Links

- Australian STI Management Guidelines for Use in Primary Care: www.sti.guidelines.org.au
- SA Health You've got what Syphilis: <u>CDCB\_YGW-Syphilis\_June2023.pdf</u> (sahealth.sa.gov.au)
- Dermnet NZ: <u>https://dermnetnz.org/topics/syphilis/</u>
- ASHM (Australasian Society for HIV, Viral Hepatitis and Sexual Health Medicine): Syphilis decision making tool: <u>https://www.ashm.org.au/resources/sexual-health-resources-list/decision-making-in-syphilis/</u>
- Australasian Contact Tracing Guideline Syphilis: <u>SYPHILIS | Contact Tracing</u> (ashm.org.au)
- The Minymaku Kutju Tjukurpa: Women's Business Manual outlines culturally appropriate care for rural and remote Aboriginal women: <u>https://remotephcmanuals.com.au/document/30938.html?publicationid=#8</u>

## Resources

Australian Charter of Healthcare Rights: (www.safetyandquality.gov.au) Australian Charter of Healthcare Rights | Australian Commission on Safety and Quality in Health Care

Australian Government Pregnancy, Birth and Baby: (<u>www.pregnancybirthbaby.org.au</u>) Pregnancy, Birth and Baby | Pregnancy Birth and Baby (pregnancybirthbaby.org.au)

Medicines Information: (sahealthlibrary.sa.gov.au) https://sahealthlibrary.sa.gov.au/friendly.php?s=SAPharmacy

SA Health Pregnancy: Pregnancy | SA Health

SAPPGs Web-based App: Practice Guidelines (sahealth.sa.gov.au)

Pathology Tests Explained: (https://pathologytestsexplained.org.au/) Pathology Tests Explained





# References

- Communicable Diseases Network Australia (CDNA). Syphilis CDNA National Guidelines for Public Health Units [Internet]. 2023 [cited 2024 Aug 30]. Available from: https://www.health.gov.au/resources/publications/syphilis-cdna-national-guidelinesfor-public-health-units?language=en
- 2. Hollier LM, Cox SM. Syphilis. Semin Perinatol. 1998 Aug 1;22(4):323-31.
- King J, McManus H, Kwon J, Gray R, McGregor S. HIV, viral hepatitis and sexually transmissible infections in Australia: Annual surveillance report 2023 [Internet]. UNSW Sydney; 2023 [cited 2024 Sep 3]. Available from: http://hdl.handle.net/1959.4/unsworks 84260
- 4. Australian Government Department of Health and Aged Care. National Notifiable Diseases Surveillance System (NNDSS) data visualisation tool [Internet]. Australian Government Department of Health and Aged Care; 2024 [cited 2024 Sep 3]. Available from: https://www.health.gov.au/resources/apps-and-tools/national-notifiable-diseases-surveillance-system-nndss-data-visualisation-tool
- 5. ASHM Health. Towards the Elimination of Congenital Syphilis in Australia: Building Consensus for Priority Actions Roundtable Report [Internet]. 2024 [cited 2024 Sep 3]. Available from: https://ashm.org.au/resources/towards-the-elimination-of-congenital-syphilis-in-australia-roundtable-report/
- 6. Queensland Health. Syphilis in pregnancy: Baby care [Internet]. 2020. Available from: https://www.health.qld.gov.au/\_\_data/assets/pdf\_file/0040/736888/f-sip-baby.pdf
- 7. Leslie SW, Vaidya R. Congenital and Maternal Syphilis. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 [cited 2024 Sep 4]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK537087/
- 8. World Health Organization. WHO guideline on syphilis screening and treatment for pregnant women [Internet]. Geneva: World Health Organization; 2017 [cited 2024 Sep 4]. Available from: https://iris.who.int/handle/10665/259003
- 9. De Santis M, De Luca C, Mappa I, Spagnuolo T, Licameli A, Straface G, et al. Syphilis Infection during pregnancy: fetal risks and clinical management. Infect Dis Obstet Gynecol. 2012;2012:430585.
- 10. Rac MWF, Revell PA, Eppes CS. Syphilis during pregnancy: a preventable threat to maternal-fetal health. Am J Obstet Gynecol. 2017 Apr;216(4):352–63.
- 11. Janier M, Unemo M, Dupin N, Tiplica GS, Potočnik M, Patel R. 2020 European guideline on the management of syphilis. J Eur Acad Dermatol Venereol JEADV. 2021 Mar;35(3):574–88.
- 12. British Association for Sexual Health and HIV (BASHH). Syphilis 2015 [Internet]. 2019 Jul [cited 2024 Aug 30]. Available from: https://www.bashh.org/resources/25/syphilis\_2015/
- Eijmael MJP, Bruin R de, Hira V, Koster T. A peculiar case of syphilis infection: The great imitator is on the rise. IDCases [Internet]. 2022 [cited 2024 Sep 4];28. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9136118/
- 14. Ong JJ, Bourne C, Dean JA, Ryder N, Cornelisse VJ, Murray S, et al. Australian sexually transmitted infection (STI) management guidelines for use in primary care 2022 update. Sex Health. 2023 Feb;20(1):1–8.
- ASHM Health. Decision Making In Syphilis [Internet]. 2021 [cited 2024 Sep 4]. Available from:
- https://ashm.org.au/resources/syphilis-decision-making-tool/
- SA Health. Health Alert Remain Alert for Syphilis [Internet]. scheme=AGLSTERMS.AglsAgent; corporateName=Department for Health and Wellbeing; address=11 Hindmarsh Square, Adelaide, SA, 5000; contact=+61 8 8226 6000; 2024 [cited 2024 Sep 4]. Available from:
  - https://www.sahealth.sa.gov.au/wps/wcm/connect/Public+Content/SA+Health+Internet/Public+health/Alerts/Health+alerts/Rem ain+Alert+for+Syphilis
- 17. CDC. Centers for Disease Control and Prevention. 2024 [cited 2024 Aug 30]. STI Treatment Guidelines. Available from: https://www.cdc.gov/std/treatment-guidelines/default.htm
- Liew ZQ, Ly V, Olson-Chen C. An old disease on the rise: new approaches to syphilis in pregnancy. Curr Opin Obstet Gynecol. 2021 Apr 1;33(2):78–85.
- 19. Gilmour LS, Best EJ, Duncanson MJ, Wheeler BJ, Sherwood J, Thirkell CE, et al. High Incidence of Congenital Syphilis in New Zealand: A New Zealand Pediatric Surveillance Unit Study. Pediatr Infect Dis J. 2022 Jan 1;41(1):66–71.
- 20. Dhakal A, Sbar E. Jarisch-Herxheimer Reaction. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 [cited 2024 Sep 4]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK557820/
- 21. Australasian Society for Infectious Diseases (ASID). Management of Perinatal Infections [Internet]. 2022 [cited 2024 Aug 30]. Report No.: 3rd Edition. Available from: https://anzasid.sharepoint.com/sites/E-Knowledge/Shared%20Documents/Forms/AllItems.aspx?id=%2Fsites%2FE%2DKnowledge%2FShared%20Documents%2FA SID%20Management%20of%20Perinatal%20Infections%203rd%20Edition%2Epdf&parent=%2Fsites%2FE%2DKnowledge% 2FShared%20Documents&p=true&ga=1
- 22. Lago EG, Vaccari A, Fiori RM. Clinical features and follow-up of congenital syphilis. Sex Transm Dis. 2013 Feb;40(2):85–94.
- 23. Kauffmann T, Silberman M. Fetal Monitoring. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 [cited 2024 Sep 4]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK589699/
- 24. Nathan L, Bawdon RE, Sidawi JE, Stettler RW, McIntire DM, Wendel GD. Penicillin levels following the administration of benzathine penicillin G in pregnancy. Obstet Gynecol. 1993 Sep;82(3):338–42.
- 25. Therapeutic Guidelines Limited. Antibiotic Syphilis [Internet]. 2019 [cited 2024 Aug 30]. Available from: https://tgldcdp.tg.org.au/viewTopic?etgAccess=true&guidelinePage=Antibiotic&topicfile=syphilis&guidelinename=Antibiotic&se ctionId=toc\_d1e340#toc\_d1e315
- 26. Royal Women's Hospital. Pregnancy and Breastfeeding Medicines Guide [Internet]. Victoria, Australia; 2024 [cited 2024 Aug 30]. Available from: https://thewomenspbmg.org.au/
- 27. Butler T. The Jarisch–Herxheimer Reaction After Antibiotic Treatment of Spirochetal Infections: A Review of Recent Cases and Our Understanding of Pathogenesis. Am J Trop Med Hyg. 2017 Jan 11;96(1):46–52.
- Wendel GD, Sheffield JS, Hollier LM, Hill JB, Ramsey PS, Sánchez PJ. Treatment of syphilis in pregnancy and prevention of congenital syphilis. Clin Infect Dis Off Publ Infect Dis Soc Am. 2002 Oct 15;35(Suppl 2):S200-209.





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