

# Queensland Clinical Guidelines

*Translating evidence into best clinical practice*

## Maternity and Neonatal Clinical Guideline

### Syphilis in pregnancy

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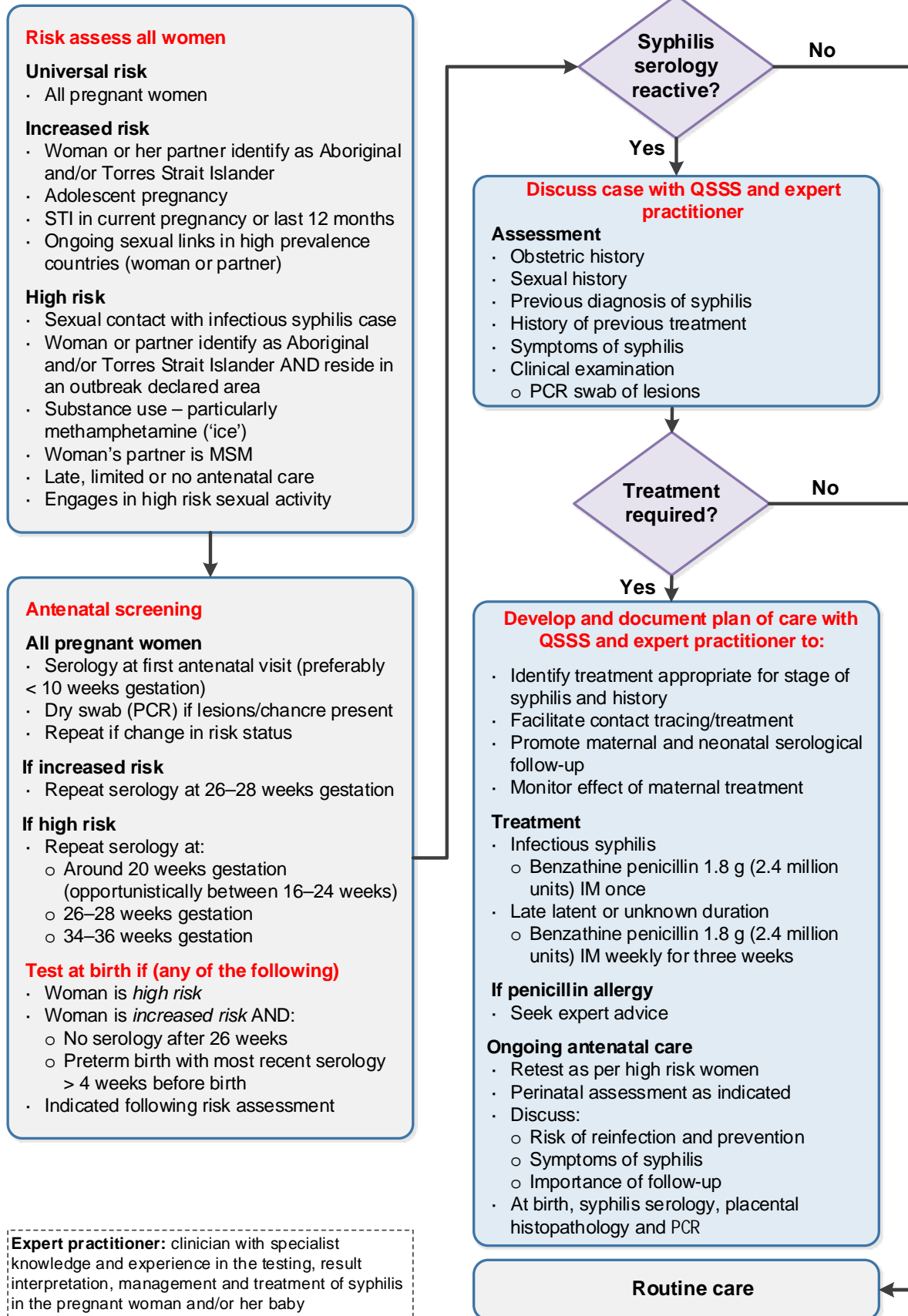
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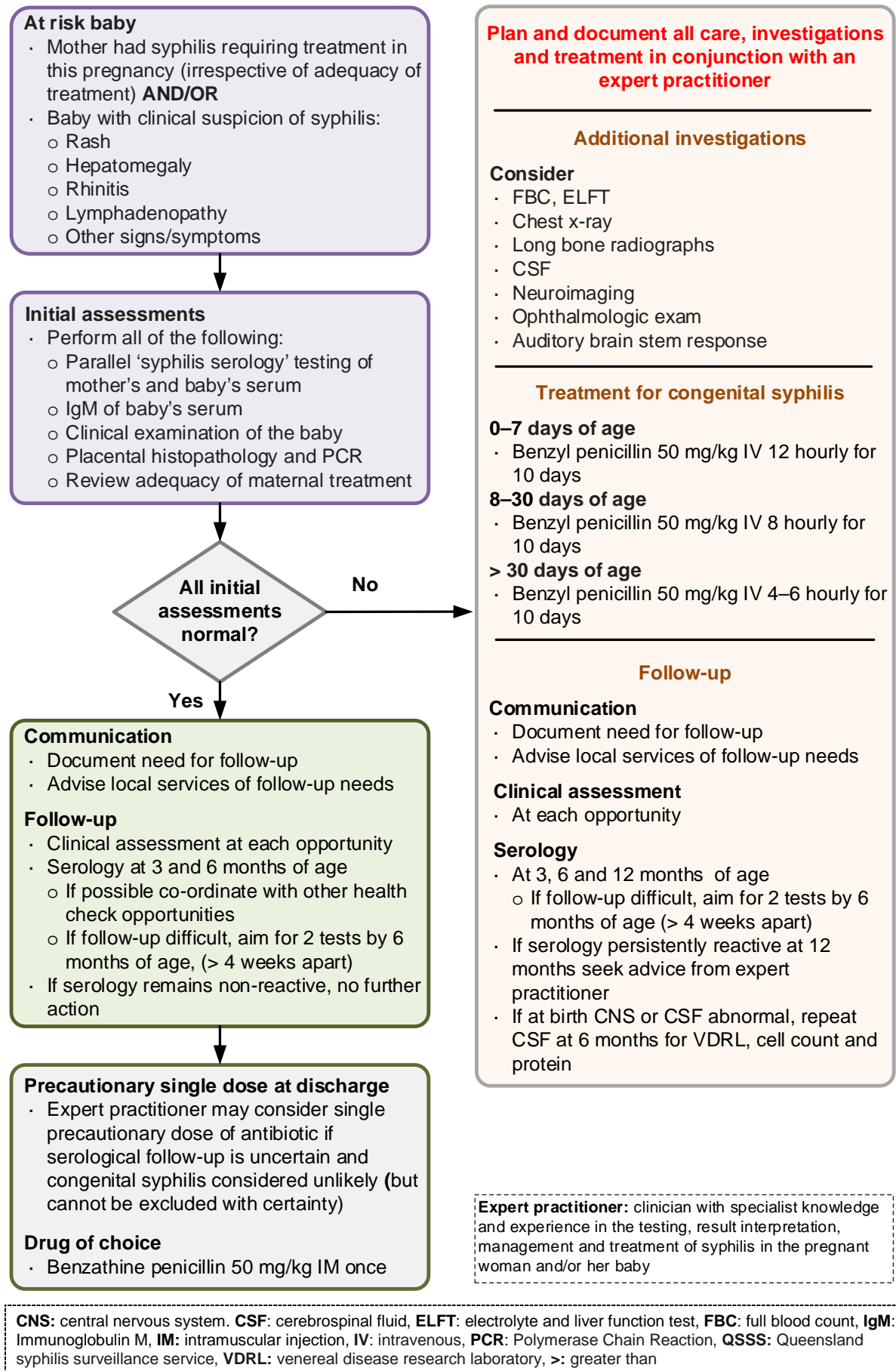
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**Flow Chart: Antenatal care**



**IM:** intramuscular injection, **MSM:** Men who have sex with men, **PCR:** Polymerase Chain Reaction **QSSS:** Queensland Syphilis Surveillance Service, **STI:** sexually transmitted infection, **<:** less than ≤ less than or equal to

**Flow Chart: Baby care**



**Abbreviations**

CSF	Cerebrospinal fluid
FHR	Fetal heart rate
GP	General Practitioner
HIV	Human immunodeficiency virus
IgM	Immunoglobulin M
IV	Intravenous
JHR	Jarisch Herxheimer Reaction
PCR	Polymerase Chain Reaction
POC	Point of care
QSSS	Queensland Syphilis Surveillance Service
SOP	Standard operating procedure
STI	Sexually transmitted infection
USS	Ultrasound
VDRL	Venereal Diseases Research Laboratory

**Definition of terms**

Adequate treatment	In a pregnant woman, 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. <sup>1</sup>
Expert practitioner	In this guideline an 'expert practitioner' is a clinician with specialist knowledge and experience in the testing, result interpretation, management and treatment of syphilis in the pregnant woman and/or her baby. May include (but is not limited to) an infectious disease physician, sexual health physician, obstetrician or neonatologist with expertise in the management of syphilis.
High risk sexual activity	Oral, anal or vaginal intercourse with people from high risk groups, which include men who have sex with men (MSM), people with multiple partners, transgender people, sex with anonymous partners, commercial sex worker, sexual partner linked with an area where the prevalence of syphilis is known to be high.
Infectious syphilis	Syphilis of less than two years duration (includes primary, secondary and early latent stages). Consider the possibility of infectious syphilis if duration is unknown and there are no symptoms and/or no evidence of adequate treatment.
Syphilis requiring treatment in pregnancy	In this guideline, <i>syphilis requiring treatment in pregnancy</i> is used to mean infectious syphilis that is treated during the current pregnancy OR syphilis of unknown duration or late latent syphilis that is untreated, has been inadequately treated, or where there is no history of adequate treatment and therefore requires treatment during this pregnancy.
Late or limited antenatal care	First presentation for antenatal care occurs in the third trimester, or the recommended antenatal testing and assessment is incomplete.
Health care providers	May include (but not limited to) neonatologist, paediatrician, social worker, Aboriginal and Torres Strait Islander health worker, infectious disease specialist, sexual health clinicians, public health unit personnel, general practitioner, QSSS, midwife, nurse, nurse practitioner, obstetrician, personnel managing follow-up and/or contact tracing.
Pinta/yaws/bejel	Infections caused by bacteria that are closely related to <i>Treponema pallidum</i> . Pinta affects only the skin while yaws and bejel can also affect the joints and bones. Not endemic in Australia.
QSSS	Queensland Syphilis Surveillance Service (QSSS) is an important source of information, support and advice for health care providers engaged in the detection and management of women and/or their babies with syphilis. QSSS holds records on testing and treatment histories for Queensland.
Screening	The systematic application of tests, examinations or other procedures with the intention of identifying previously unrecognised health conditions. <sup>2</sup>
Serology	In this guideline, <i>serology</i> is used to mean blood tests demonstrating the presence or absence of <i>treponemal palladium</i> . May include a variety of laboratory techniques or test types. <i>Reactive serology</i> is used to indicate a positive finding of <i>treponemal palladium</i> derived from any laboratory technique.

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## 1 Introduction

Globally, maternal syphilis is the most common infection associated with stillbirth in low-resource settings.<sup>3</sup> The public health significance of syphilis lies in its impact on the developing fetus and its ability to enhance both the acquisition and transmission of the human immunodeficiency virus (HIV).<sup>1,4</sup> Rates are higher in Aboriginal and/or Torres Strait Islander people, especially in northern and central Australia, and among men who have sex with men (MSM).<sup>5</sup> In 2016 notifications for infectious syphilis in Aboriginal and/or Torres Strait Islander people occurred at 5.4 times the rate of non-Indigenous people in Australia nationwide.

### 1.1 Outbreak areas

In 2015, a multijurisdictional syphilis outbreak group (MJSO) of the Communicable Diseases Network Australia (CDNA) was formed in response to an ongoing outbreak of infectious syphilis among young Aboriginal and/or Torres Strait Islander people living in regional, rural and remote areas of northern Australia.<sup>6,7</sup> A number of Hospital and Health Services (HHS) have been declared syphilis outbreak affected areas and these are listed on the Queensland Government website for Communicable disease control guidance—syphilis.

### 1.2 Prevalence in Australia

Table 1. Prevalence in Australia

Aspect	Consideration
<b>Prevalence</b>	<ul style="list-style-type: none"> <li>• In Australia, highest rates of infectious syphilis notifications between January 2011 to November 2017 reported in Aboriginal and/or Torres Strait people in the following groups<sup>1,6,8</sup>:               <ul style="list-style-type: none"> <li>○ Young people under 35 years old (particularly amongst 15–29 years of age)</li> <li>○ Living in remote and regional areas of Australia</li> </ul> </li> </ul>
<b>Congenital syphilis</b>	<ul style="list-style-type: none"> <li>• 43 cases notified in Australia between 2007 and 2017<sup>9,10</sup> <ul style="list-style-type: none"> <li>○ 55% (24) of cases identified as Aboriginal and/or Torres Strait Islander<sup>9</sup></li> </ul> </li> <li>• In 2016, the notification rate of congenital syphilis in the Aboriginal and/or Torres Strait Islander population was 18 times higher than the non-indigenous rate (5.4 per 100,000 live births versus 0.3 per 100,000 live births)<sup>11</sup></li> <li>• In Queensland, seven outbreak associated deaths reported from January 2011 to September 2018</li> </ul>

### 1.3 Clinical impact

Table 2. Clinical impact

Aspect	Consideration
<b>Maternal impact</b>	<ul style="list-style-type: none"> <li>• Maternal syphilis is thought to increase the risk of vertical transmission of HIV and other sexually transmitted infections (STI)<sup>12</sup></li> <li>• Although estimates vary, approximately 50% of women with syphilis requiring treatment in pregnancy suffer adverse pregnancy outcomes<sup>13,14</sup></li> <li>• In the absence of effective treatment<sup>15,16</sup> maternal/fetal impacts include:               <ul style="list-style-type: none"> <li>○ 25% of pregnancies result in a second trimester miscarriage or stillbirth</li> <li>○ 11% of pregnancies result in a neonatal death at term</li> <li>○ 13% of pregnancies result in a preterm or low birth weight infant</li> </ul> </li> </ul>
<b>Fetus/baby</b>	<ul style="list-style-type: none"> <li>• Placental infiltration reduces blood flow to the fetus and may lead to growth restriction<sup>16,17</sup> <ul style="list-style-type: none"> <li>○ Refer to Table 12. Prenatal diagnosis</li> </ul> </li> <li>• Rates of transmission to babies born to women with untreated syphilis are estimated to be<sup>15,18</sup>:               <ul style="list-style-type: none"> <li>○ 70% for primary and secondary syphilis</li> <li>○ 40% for early latent syphilis</li> <li>○ 10% for late latent syphilis</li> </ul> </li> </ul>
<b>Longer term implications</b>	<ul style="list-style-type: none"> <li>• 27% of untreated babies who survive to 30 days are likely to develop symptoms of congenital syphilis,<sup>17-19</sup> including:               <ul style="list-style-type: none"> <li>○ Neurological and developmental delays</li> <li>○ Musculoskeletal problems</li> </ul> </li> </ul>
<b>Risk reduction</b>	<ul style="list-style-type: none"> <li>• Early screening of all pregnant women, and identification of high risk pregnancies and babies can prevent adverse perinatal outcomes<sup>15,16</sup></li> </ul>



## 1.4 Notifiable disease

Table 3. Disease notification

Aspect	Consideration
<b>Context</b>	<ul style="list-style-type: none"> <li>• Syphilis is a controlled notifiable disease in Queensland as per the Public Health Act (2005)<sup>19</sup></li> <li>• Routine reporting is the cornerstone of syphilis surveillance and aids<sup>20</sup>:               <ul style="list-style-type: none"> <li>○ Identification of new cases and their contacts</li> <li>○ Timely and appropriate management of cases</li> <li>○ Prevalence monitoring among pregnant women</li> <li>○ Analysis of trends among different populations and geographical areas</li> <li>○ Evaluation of the effectiveness of prevention strategies</li> </ul> </li> </ul>
<b>Queensland Syphilis Surveillance Service (QSSS)</b>	<ul style="list-style-type: none"> <li>• QSSS is automatically notified of all positive syphilis serology results</li> <li>• QSSS may not initially know if the result:               <ul style="list-style-type: none"> <li>○ Indicates a new, old, treated or untreated infection</li> <li>○ Relates to a woman who is pregnant</li> </ul> </li> <li>• QSSS will contact the diagnosing clinician directly to discuss results</li> <li>• Syphilis case reporting forms are sent for completion</li> <li>• Refer to Definition of terms re role of QSSS</li> <li>• Contact:               <ul style="list-style-type: none"> <li>○ Telephone: 1800 032 238</li> <li>○ North Queensland email: <a href="mailto:North-Qld-Syphilis-Surveillance-Centre@health.qld.gov.au">North-Qld-Syphilis-Surveillance-Centre@health.qld.gov.au</a></li> <li>○ Southern Queensland email: <a href="mailto:QLD-Syphilis-Surveillance-Service@health.qld.gov.au">QLD-Syphilis-Surveillance-Service@health.qld.gov.au</a></li> </ul> </li> </ul>

## 1.5 Clinical standards

Table 4. Clinical standards

Aspect	Consideration
<b>Confidentiality</b>	<ul style="list-style-type: none"> <li>• A perceived or actual lack of confidentiality, particularly in smaller and remote communities, may impede presentation for diagnosis, treatment and contact tracing<sup>21</sup></li> <li>• Maintaining confidentiality is a key factor to ensuring adequate follow-up, educational opportunities and contact tracing</li> </ul>
<b>Information for women</b>	<ul style="list-style-type: none"> <li>• Offer information and discuss syphilis and syphilis testing during pregnancy               <ul style="list-style-type: none"> <li>○ Informed consent is required prior to specimen collection</li> </ul> </li> <li>• Support the woman to improve her knowledge of syphilis in pregnancy               <ul style="list-style-type: none"> <li>○ Refer to Queensland Clinical Guideline Parent information</li> </ul> </li> <li>• If treatment is declined discuss with the woman implications for herself, her partner(s) and her baby               <ul style="list-style-type: none"> <li>○ Contact an expert practitioner about the ongoing plan of care</li> </ul> </li> </ul>
<b>Culturally appropriate care</b>	<ul style="list-style-type: none"> <li>• Support education and training to develop and maintain cultural competence among health care providers<sup>21-23</sup></li> <li>• Involve Aboriginal and/or Torres Strait Islander health workers, health practitioners, hospital liaison officers, spiritual leaders, Elders and language interpreters, according to the preferences of the individual woman</li> <li>• Recognise the importance of family and community in the health care decision-making of Aboriginal and/or Torres Strait Islander people, for both prevention strategies and care delivery</li> </ul>
<b>Practitioner education and training</b>	<ul style="list-style-type: none"> <li>• Support health care providers, including those who may come into contact with pregnant women (e.g. in emergency departments) to access education and training about<sup>21</sup>:               <ul style="list-style-type: none"> <li>○ Syphilis in pregnancy</li> <li>○ Local referral pathways for ongoing care and follow-up</li> <li>○ Opportunistic screening and/or presumptive treatment</li> </ul> </li> <li>• Engage local Aboriginal and/or Torres Strait Islander Cultural Practice Programs to support the HHS in providing culturally appropriate care</li> </ul>
<b>Infection control</b>	<ul style="list-style-type: none"> <li>• Follow standard infection control procedures</li> </ul>

## 1.6 Service level responsibilities

Table 5. Service level responsibilities

Aspect	Consideration
<b>Local protocols</b>	<ul style="list-style-type: none"> <li>• Develop local protocols that:               <ul style="list-style-type: none"> <li>○ Are appropriate in the context of the service—including culturally appropriate</li> <li>○ Identify strategies to maximise diagnosis and treatment opportunities (e.g. follow-up after failure to attend, opportunistic screening, combined appointments, extending outreach services, increasing understanding of the importance of syphilis testing in high risk groups)</li> <li>○ Consider supply, storage and access to appropriate medication</li> <li>○ Identify how ultrasound scans (USS) will be accessed and results reviewed (e.g. review by higher level service) within the service</li> <li>○ Identify strategies to provide safe care during and after treatment</li> </ul> </li> <li>• Identify the most appropriately skilled health care providers to:               <ul style="list-style-type: none"> <li>○ Conduct clinical examinations of the woman</li> <li>○ Perform neonatal examination and assessment</li> </ul> </li> </ul>
<b>Testing at birth</b>	<ul style="list-style-type: none"> <li>• HHS may decide that testing all women in a defined demographic at birth is preferable to applying conditional decisions to testing</li> <li>• When there is optional (rather than recommended) testing at birth, there is a greater chance that women who are 'at risk' are not identified as such and are not appropriately tested</li> </ul>
<b>Referral pathways</b>	<ul style="list-style-type: none"> <li>• Establish local referral pathways, that are culturally appropriate, to support access to care for women with syphilis in pregnancy</li> <li>• At the time of presentation, individualise the most appropriate pathway to the woman's circumstances (e.g. from emergency department)—consider:               <ul style="list-style-type: none"> <li>○ Likelihood of attendance if referred elsewhere</li> <li>○ Issues that may impact on attendance for follow-up (e.g. cost of presenting elsewhere for treatment)</li> <li>○ Opportunity for routine antenatal screening for syphilis</li> <li>○ Referral to maternity services for ongoing antenatal care</li> </ul> </li> <li>• If presumptive treatment is the best option [refer to section 4.3 Treatment of syphilis in pregnancy]</li> </ul>
<b>Follow-up of babies at risk of congenital syphilis</b>	<ul style="list-style-type: none"> <li>• Formalise responsibility for follow-up of babies born to women at risk of congenital syphilis               <ul style="list-style-type: none"> <li>○ Identify the most appropriate service as relevant to the local context (e.g. paediatric outpatient clinic or outreach service)</li> <li>○ Establish a local process for initiating and ensuring follow-up occurs, including if baby discharged prior to pathology result availability</li> </ul> </li> <li>• Use audit processes to monitor and review follow-up care and clinical outcomes</li> </ul>
<b>Communication</b>	<ul style="list-style-type: none"> <li>• Communicate with the multidisciplinary team—the identified referral pathways and responsibility for follow-up</li> <li>• Inform health care providers who may encounter women with syphilis in pregnancy (e.g. in emergency departments, general practitioners) about the referral pathways</li> <li>• Collaborate and coordinate with local clinical and community services (e.g. Aboriginal and/or Torres Strait Islander medical services, community organisations and programs, mental health services, drug and alcohol programs, young parent programs, women's groups, criminal justice systems<sup>5,21</sup>)</li> </ul>
<b>Model of care</b>	<ul style="list-style-type: none"> <li>• Involve the multidisciplinary health care team as appropriate to the circumstances</li> <li>• If syphilis requiring treatment in pregnancy, involve the woman, QSSS and an expert practitioner early in the development of a plan of care</li> </ul>

## 2 Aetiology of syphilis

Table 6. Aetiology

Aspect	Consideration
<b>Cause</b>	<ul style="list-style-type: none"> <li>• Bacterial infection caused by the spirochaete bacterium <i>Treponema pallidum</i><sup>4,12,24-28</sup></li> <li>• <i>Treponema pallidum</i> is an obligate human parasite</li> </ul>
<b>Transmission</b>	<ul style="list-style-type: none"> <li>• Direct contact with infectious lesions of the mucous membranes or abraded skin<sup>29,30</sup>:               <ul style="list-style-type: none"> <li>○ Almost always as sexually transmitted infection</li> <li>○ Contact with moist mucocutaneous lesions of an infected baby</li> </ul> </li> <li>• Vertical transmission (transplacental passage) during pregnancy:               <ul style="list-style-type: none"> <li>○ <i>Treponema pallidum</i> readily crosses the placenta</li> <li>○ Can occur as early as 9–10 weeks gestation</li> <li>○ Can occur at any stage of disease, including during incubation, although risk is greatest in infectious syphilis</li> <li>○ Can occur several years after initial infection in the untreated woman</li> <li>○ More commonly occurs in the last two trimesters<sup>30</sup></li> </ul> </li> <li>• Less commonly:               <ul style="list-style-type: none"> <li>○ Infected blood (e.g. shared needles during injecting drug use)</li> <li>○ Non-sexual cutaneous contact with infected lesions</li> </ul> </li> </ul>
<b>Incubation</b>	<ul style="list-style-type: none"> <li>• Mean incubation 21 days (range 9–90 days) from contact to the development of a chancre<sup>16,26</sup> <ul style="list-style-type: none"> <li>○ Larger infectious dose results in earlier ulcers</li> </ul> </li> </ul>
<b>Infectious period</b>	<ul style="list-style-type: none"> <li>• First two years of infection<sup>1</sup> <ul style="list-style-type: none"> <li>○ If untreated, period of high infectivity is 12 months</li> <li>○ Sexual transmission uncommon after two years of infection</li> </ul> </li> <li>• Infectious cases become non-infectious seven days after one dose of benzathine penicillin, or when all symptoms have resolved, whichever is longer<sup>31</sup></li> <li>• Immunity is not conferred by treatment or previous infection—re-infection can occur</li> </ul>
<b>Reactive serology</b>	<ul style="list-style-type: none"> <li>• Isolated reactive tests (a non-treponemal or a treponemal test) are not adequate for diagnosis of syphilis<sup>27</sup></li> <li>• Serology results remain reactive after adequate treatment of syphilis, therefore reactive results do not necessarily indicate the need for treatment</li> <li>• Refer to Appendix B: Laboratory tests</li> <li>• Refer to Appendix C: Interpretation of results</li> </ul>

## 2.1 Clinical stages of syphilis

Approximately 50% of women will have no symptoms and will only be diagnosed by serological testing.<sup>32</sup>

Table 7. Stages of syphilis

Stage	Presentation
<b>Primary</b>	<ul style="list-style-type: none"> <li>• Lesions begin as a raised papule that ulcerates (chancre) and may<sup>16,26,4:</sup> <ul style="list-style-type: none"> <li>○ Be painless or painful (approximately half reported as painful)<sup>33</sup></li> <li>○ Be solitary or multiple (approximately one third reported as multiple)<sup>33</sup></li> <li>○ Typically occur at the site of inoculation (e.g. vagina, penis, anus, rectum, lips, in or on the mouth)</li> <li>○ Discharge clear serum—may also be purulent, destructive</li> <li>○ Spontaneously heals within three to six weeks without treatment</li> </ul> </li> </ul>
<b>Secondary</b>	<ul style="list-style-type: none"> <li>• Follows untreated primary stage four to eight weeks after appearance of the primary lesion (can occur while primary lesion still present)</li> <li>• Diffuse inflammatory response characterised by generalised mucocutaneous lesions affecting skin, mucous membranes and lymphnodes<sup>4</sup></li> <li>• Rash may be generalised but characteristically affects palms and soles<sup>26</sup> <ul style="list-style-type: none"> <li>○ Can vary widely and mimic other infectious and non-infectious conditions (e.g. drug eruptions, pityriasis rosea)</li> <li>○ Often symmetrical and non-itchy</li> <li>○ May be maculo-papular (50–70%), papular (12%) or macular (10%)</li> </ul> </li> <li>• In warm and moist areas of the body (e.g. anus, labia) flat, wart-like plaques develop as a result of the spread of the treponemes from the primary lesion<sup>16</sup> (condylomata lata)</li> <li>• May be associated with non-specific constitutional symptoms lasting two to six weeks (e.g. malaise, fever, lymphadenopathy, headaches, weight loss, muscle aches, patchy alopecia, sore throat)</li> <li>• Resolves spontaneously without treatment in 3–12 weeks</li> <li>• May reoccur in the first year and rarely in the second year</li> </ul>
<b>Latent</b>	<ul style="list-style-type: none"> <li>• May be divided into<sup>25,27:</sup> <ul style="list-style-type: none"> <li>○ Early latent (infection for less than two years)</li> <li>○ Late latent (infection for two years or more)</li> <li>○ Syphilis of unknown duration</li> </ul> </li> <li>• Characterised by reactive serology with no clinical manifestations</li> <li>• If untreated 15–40% develop tertiary infection</li> </ul>
<b>Tertiary</b>	<ul style="list-style-type: none"> <li>• Can affect any organ system<sup>4,16</sup></li> <li>• Occurs in approximately one-third of untreated patients</li> <li>• Main manifestations are: <ul style="list-style-type: none"> <li>○ Neurological disease (neurosyphilis)—can occur at any stage of syphilis <ul style="list-style-type: none"> <li>§ Signs can include: cranial nerve dysfunction, hearing loss, tinnitus, diminished vision, meningitis, stroke (acute), mental status changes/alteration and loss of vibration sense</li> </ul> </li> <li>○ Cardiovascular disease (cardiosyphilis) <ul style="list-style-type: none"> <li>§ Signs can include: aortic root dilatation, aortic regurgitation and/or coronary ostial lesions<sup>34,35</sup></li> </ul> </li> <li>○ Gummatous lesions (gumma)</li> </ul> </li> </ul>

### 3 Antenatal screening

Women and their partners who are tested and receive appropriate treatment during the first two trimesters of pregnancy are 2.24 times more likely to have a healthy baby than those receiving syphilis treatment during the third trimester.<sup>27,36</sup>

#### 3.1 Risk groups

Identifying women at increased risk of syphilis can be challenging. Membership of one or more groups defined by common characteristics does not necessarily equate to an increased or decreased individual risk. Groups known to have a higher incidence of syphilis are identified in Table 10. Recommended screening by risk group. Use clinical judgement and sensitivity when assessing for risk of syphilis and the need for additional screening.

#### 3.2 Recommended screening

There is no definitive evidence to support recommendations for screening frequency or interval in declared outbreak or non-outbreak affected areas. The screening recommendations in Table 10. Recommended screening by risk group are based on the consensus view of the working party and clinical experts.

#### 3.3 Ongoing risk of infection and re-infection

Table 8. Ongoing risk Infection and re-infection

Aspect	Consideration
<b>Assessing ongoing risk</b>	<ul style="list-style-type: none"> <li>• Maintain awareness of the ongoing risk of infection/re-infection after initial screening and/or treatment for syphilis</li> <li>• As part of routine antenatal care, assess for changes in risk behaviours/status, for example:               <ul style="list-style-type: none"> <li>○ Change or addition of sexual partner(s)</li> <li>○ Change in risk behaviours (e.g. methamphetamine use)</li> <li>○ High risk sexual activity</li> </ul> </li> <li>• Actively consider if repeat screening is indicated</li> </ul>
<b>Preventative strategies</b>	<ul style="list-style-type: none"> <li>• Advise condom use (male or female condoms, dental dams) to help prevent syphilis infection and re-infection during pregnancy (as well as other STIs)               <ul style="list-style-type: none"> <li>○ Condoms reduce the risk of syphilis only when the infected area or site is protected from direct contact</li> </ul> </li> <li>• Encourage communication about change in sexual partners</li> <li>• Offer information about safe sex practices including:               <ul style="list-style-type: none"> <li>○ Increased risk if sexual partner(s) engage in male to male sex</li> <li>○ Avoiding drug use during pregnancy</li> <li>○ Signs and symptoms of STIs</li> </ul> </li> <li>• If woman or partner treated for syphilis requiring treatment in pregnancy, advise to abstain from sexual activity for seven days (or until symptoms have resolved whichever is longer) after both have received adequate treatment</li> </ul>

#### 3.4 Point of care testing

Table 9. Point of care testing

Aspect	Consideration
<b>Context</b>	<ul style="list-style-type: none"> <li>• Laboratory based syphilis serology is the standard for routine antenatal testing</li> <li>• Point of care (POC) testing is preferable to not testing at all</li> <li>• POC devices are<sup>1</sup>:               <ul style="list-style-type: none"> <li>○ Unable to differentiate new infection from previously treated infections</li> <li>○ Marginally inferior (sensitivity and specificity) compared with serology</li> </ul> </li> </ul>
<b>Implementation</b>	<ul style="list-style-type: none"> <li>• May be useful in selected settings<sup>12,37</sup> to facilitate greater access to testing, reduce time to treatment initiation and/or where follow-up is uncertain</li> <li>• Use requires standard processes for<sup>1</sup>:               <ul style="list-style-type: none"> <li>○ Training and competency certification of staff</li> <li>○ Quality assurance</li> <li>○ Confirmation of preliminary reactive POC testing by laboratory serology</li> </ul> </li> </ul>

### 3.5 Risk groups and recommended screening for syphilis

Table 10. Recommended screening by risk group

Risk group	Relevant to the following groups of pregnant women	Recommended screening
<b>Universal risk</b>	<ul style="list-style-type: none"> <li>All pregnant women</li> </ul>	<ul style="list-style-type: none"> <li>Routinely at the first antenatal appointment and preferably before 10 weeks gestation<sup>22</sup></li> <li>Request ‘<i>syphilis serology</i>’ on antenatal pathology forms                             <ul style="list-style-type: none"> <li>Pathology laboratories will determine the individual test as per their standard operating procedure (SOP)</li> </ul> </li> <li>Review serology results at antenatal visits and at the time of birth</li> <li>If risk of exposure or change in risk status during pregnancy (e.g. change of sexual partners), repeat screening<sup>27</sup></li> <li>If suspicious lesions, dry swab for polymerase chain reaction (PCR), full STI check and collect serology</li> </ul>
<b>Increased risk</b>	<ul style="list-style-type: none"> <li>Woman or her partner(s) identify as Aboriginal and/or Torres Strait Islander<sup>1</sup></li> <li>Adolescent pregnancy</li> <li>STI in the current pregnancy or preceding 12 months</li> <li>The woman and/or her partner(s) have ongoing sexual links in high prevalence countries (e.g. migrants or refugees)</li> </ul>	<ul style="list-style-type: none"> <li>As for <b>universal risk</b> (all pregnant women) <b>AND</b></li> <li>Routinely repeat screening at 26–28 weeks gestation<sup>38</sup></li> <li>Test at birth if (either of the following):                             <ul style="list-style-type: none"> <li>Serology NOT collected at or after 26 weeks gestation</li> <li>Preterm birth with most recent serology more than four weeks before birth</li> </ul> </li> </ul>
<b>High risk</b>	<ul style="list-style-type: none"> <li>Sexual contact with an infectious syphilis case</li> <li>Woman or her partner(s) identify as Aboriginal and/or Torres Strait Islander AND the woman or her partner(s) reside in a declared outbreak area</li> <li>Substance use during pregnancy—particularly methamphetamine (‘ice’)</li> <li>Woman’s partner is a man who has sex with men (MSM)</li> <li>Late, limited or no antenatal care [refer to Definition of terms]</li> <li>Engages in high risk sexual activity [refer to Definition of terms]</li> </ul>	<ul style="list-style-type: none"> <li>As for <b>universal risk</b> (all pregnant women) <b>AND</b></li> <li>Routinely repeat screening at<sup>31</sup>:                             <ul style="list-style-type: none"> <li>Around 20 weeks (perform opportunistically between 16–24 weeks gestation)</li> <li>26–28 weeks gestation</li> <li>34–36 weeks gestation</li> </ul> </li> <li>Test at birth if (any of the following):                             <ul style="list-style-type: none"> <li>Syphilis requiring treatment in pregnancy</li> <li>Woman is <i>high risk</i></li> <li>Indicated following risk assessment</li> </ul> </li> </ul>

## 4 Management of syphilis requiring treatment in pregnancy

If syphilis requiring treatment in pregnancy or the woman has signs and symptoms of syphilis, conduct a clinical assessment and develop a plan of care (including any treatment) in consultation with the woman, QSSS and an expert practitioner to:

- Ensure appropriate staging of the disease
- Confirm treatment recommendations are appropriate for the stage of infection and case history
- Facilitate treatment, contact tracing, and maternal and neonatal follow-up

### 4.1 Maternal assessment

Table 11. Clinical assessment

Aspect	Consideration
<b>History</b>	<ul style="list-style-type: none"> <li>• Obstetric and sexual history<sup>26</sup></li> <li>• Direct question for symptoms of syphilis (e.g. genital rashes, lumps and sores, including if current partner is symptomatic)</li> <li>• Previous syphilis testing               <ul style="list-style-type: none"> <li>○ Antenatal screening</li> <li>○ Blood donation</li> <li>○ Sexual health screening</li> </ul> </li> <li>• Potential for previous infection with non-venereal <i>Treponema pallidum</i> infection               <ul style="list-style-type: none"> <li>○ Childhood skin infections (e.g. yaws, bejel or pinta)</li> <li>○ Previously resident in endemic country</li> </ul> </li> </ul>
<b>Obstetric history</b>	<ul style="list-style-type: none"> <li>• Previous adverse pregnancy outcomes</li> <li>• Identify live births and consider if children may now have late congenital disease               <ul style="list-style-type: none"> <li>○ Initiate follow-up as indicated</li> </ul> </li> </ul>
<b>Clinical examination</b>	<ul style="list-style-type: none"> <li>• Syphilis requiring treatment in pregnancy               <ul style="list-style-type: none"> <li>○ Genital examination</li> <li>○ Skin examination including torso, eyes, mouth, scalp, palms and soles</li> <li>○ If neurological symptoms, conduct a neurological examination</li> </ul> </li> <li>• Symptomatic late disease               <ul style="list-style-type: none"> <li>○ Skin</li> <li>○ Musculoskeletal (congenital)</li> <li>○ Cardiovascular system (for signs of aortic regurgitation)</li> <li>○ Nervous system</li> </ul> </li> </ul>
<b>Investigations</b>	<ul style="list-style-type: none"> <li>• Dry swab suspicious genital lesions for PCR</li> <li>• Collect serum and request 'syphilis serology' on pathology forms</li> <li>• Recommend screening for other STIs</li> <li>• In consultation with an expert practitioner, consider other investigations as relevant to circumstances</li> </ul>
<b>Previous syphilis diagnosis</b>	<ul style="list-style-type: none"> <li>• If previous syphilis diagnosis, identify:               <ul style="list-style-type: none"> <li>○ Year and place of diagnosis</li> <li>○ Treatment received (drug, route, duration)</li> <li>○ Serological results</li> </ul> </li> <li>• Consider pregnant women with reactive serology as having syphilis requiring treatment in pregnancy unless an adequate treatment history is available<sup>31</sup></li> <li>• Collaborate with QSSS and/or expert practitioner about recommended management</li> </ul>
<b>Serological follow-up during pregnancy</b>	<ul style="list-style-type: none"> <li>• As for high risk groups (or as agreed with an expert practitioner) for the remainder of the pregnancy               <ul style="list-style-type: none"> <li>○ Refer to 3.5 Risk groups and recommended screening for syphilis</li> </ul> </li> <li>• Refer to Appendix C: Interpretation of results</li> </ul>

## 4.2 Prenatal assessment

Table 12. Prenatal diagnosis

Aspect	Consideration
<b>Context</b>	<ul style="list-style-type: none"> <li>Before 18–20 weeks fetal abnormalities are not usually seen because of fetal immunologic immaturity<sup>16</sup></li> <li>An abnormal USS is not diagnostic of fetal infection and a normal USS does not exclude fetal infection<sup>28</sup></li> </ul>
<b>USS examination</b>	<ul style="list-style-type: none"> <li>If syphilis requiring treatment in pregnancy is diagnosed after 20 weeks gestation, request an USS to evaluate for congenital syphilis<sup>31</sup> <ul style="list-style-type: none"> <li>Do not delay treatment to achieve USS</li> </ul> </li> <li>Include on request form:           <ul style="list-style-type: none"> <li>Relevant history (e.g. serology, gestation, treatment)</li> </ul> </li> <li>Request assessment of:           <ul style="list-style-type: none"> <li>Placental size</li> <li>Amniotic fluid volume (single deepest pocket)</li> <li>Middle cerebral artery (MCA) Doppler velocity</li> <li>Liver size and echodensity</li> </ul> </li> </ul>
<b>Ongoing monitoring</b>	<ul style="list-style-type: none"> <li>Suspect fetal infection if there are characteristic findings on USS after 20 weeks in a woman with syphilis requiring treatment in pregnancy<sup>24,28</sup></li> <li>Formulate a plan about ongoing monitoring in collaboration with a maternal fetal medicine specialist</li> <li>If presumptive diagnosis of congenital syphilis, consider sequential monitoring to assess fetal well-being and response to treatment</li> </ul>
<b>Successful treatment</b>	<ul style="list-style-type: none"> <li>With successful treatment<sup>24</sup>:           <ul style="list-style-type: none"> <li>MCA abnormalities, ascites and polyhydramnios usually resolve within one month</li> <li>Followed by resolution of placentomegaly</li> <li>Hepatomegaly can take months to resolve after maternal treatment<sup>28</sup></li> </ul> </li> <li>Rarely required intrauterine transfusion for fetal anaemia</li> </ul>

### 4.2.1 Ultrasound findings

Table 13. Ultrasound findings

Timing	Finding	Description
<b>Early findings</b>	Hepatomegaly (70–80%)	<ul style="list-style-type: none"> <li>Liver length greater than 95<sup>th</sup> percentile for estimated gestational age</li> </ul>
	Placentomegaly (27%) <sup>24,39</sup>	<ul style="list-style-type: none"> <li>Placental thickness greater than two standard deviations for estimated gestational age<sup>24</sup></li> </ul>
<b>Later findings<sup>24</sup></b>	Anaemia (33%) based on MCA Doppler	<ul style="list-style-type: none"> <li>Middle cerebral artery greater than 1.5 multiple of median (MoM)</li> </ul>
	Polyhydramnios (12%)	<ul style="list-style-type: none"> <li>Single deepest pocket equal to or greater than 8 cm</li> </ul>
	Ascites/hydrops (10%)	<ul style="list-style-type: none"> <li>Hydrops: two or more cavities with abnormal fluid collections</li> </ul>



### 4.3 Treatment of syphilis in pregnancy

Table 14. Treatment of syphilis in pregnancy

Aspect	Consideration
<b>Presumptive treatment</b>	<ul style="list-style-type: none"> <li>If syphilis requiring treatment in pregnancy is suspected and there is concern about not re-presenting for care, treat the woman <i>and</i> her partner(s) without waiting for serology results<sup>1</sup></li> </ul>
<b>Therapy</b>	<ul style="list-style-type: none"> <li>Only penicillin has been shown to be effective in pregnant women<sup>16,24</sup></li> <li>Long acting, IM penicillin formulations are required as short acting formulations (e.g. benzyl penicillin) are ineffective</li> <li>Recommend antibiotic therapy immediately at the time of diagnosis</li> <li>Collect a serological specimen on the day treatment is started to provide an accurate baseline for assessment of future response to treatment</li> <li>Refer to Appendix C: Interpretation of results</li> </ul>
<b>Drug of choice</b>	<ul style="list-style-type: none"> <li>For women not hypersensitive to penicillin who have syphilis of less than two years duration (primary, secondary and early latent stages) recommend<sup>24,27,40,41,38</sup>: <ul style="list-style-type: none"> <li>Benzathine penicillin 1.8 g (2.4 million units) IM once</li> <li>Administer as a divided dose of two injections of 900 mg each (one in each of the ventrogluteal regions or in the upper outer quadrant of each buttock<sup>42</sup>)</li> </ul> </li> </ul>
<b>Second dose</b>	<ul style="list-style-type: none"> <li>Insufficient evidence to recommend a second dose for treatment of syphilis requiring treatment in pregnancy</li> </ul>
<b>Penicillin hypersensitivity</b>	<ul style="list-style-type: none"> <li>Seek expert advice<sup>27,31,40</sup> about allergy delabelling and desensitisation (preferred option)</li> <li>Refer to Electronic Therapeutic Guidelines (eTG)<sup>43</sup></li> </ul>
<b>Not recommended</b>	<ul style="list-style-type: none"> <li>Macrolides,<sup>27</sup> ceftriaxone, azithromycin</li> <li>Tetracycline and doxycycline are contraindicated in the second and third trimester of pregnancy<sup>31</sup></li> </ul>

### 4.4 Treatment of late latent or syphilis of unknown duration

Includes women where adequate previous treatment cannot be verified. Discuss individual cases and circumstances with the QSSS and an expert practitioner.

Table 15. Treatment of late latent or syphilis of unknown duration

Aspect	Consideration
<b>Drug of choice</b>	<ul style="list-style-type: none"> <li>For women not hypersensitive to penicillin who have syphilis of more than two years duration (late latent), or unknown duration, recommend<sup>1,31,32</sup>: <ul style="list-style-type: none"> <li>Benzathine penicillin 1.8 g (2.4 million units) IM weekly for three weeks</li> <li>Administer as a divided dose of two injections of 900 mg each (one in each of the ventrogluteal regions or in the upper outer quadrant of each buttock<sup>42</sup>)</li> </ul> </li> </ul>

### 4.5 Monitoring serological response to treatment

Table 16. Monitoring serological response to treatment

Aspect	Consideration
<b>Follow-up after treatment</b>	<ul style="list-style-type: none"> <li>Collect serial syphilis serology after treatment for syphilis as may: <ul style="list-style-type: none"> <li>Aid assessment of maternal response to/adequacy of treatment [refer to Appendix C: Interpretation of results]</li> <li>Aid investigation and diagnosis of congenital syphilis [refer to Table 21. Laboratory assessment]</li> </ul> </li> <li>Follow testing schedule as for high risk women [refer to Table 10. Recommended screening by risk group]</li> </ul>
<b>Communication</b>	<ul style="list-style-type: none"> <li>Discuss the importance of serological follow-up with the woman at the time of treatment, including implications for neonatal management</li> <li>Document the woman's serological response to treatment in the health record</li> </ul>

## 4.6 Jarisch Herxheimer Reaction (JHR)

JHR is an acute non-allergic reaction to penicillin that may occur in pregnant women after administration. Symptoms can be acute, or absent, and last up to 24 hours.<sup>24</sup> Do not delay treatment to avoid potential symptoms of JHR as the risk of adverse outcomes are likely to be higher without treatment [refer to Table 2. Clinical impact].

Table 17. Jarisch Herxheimer Reaction

Aspect	Consideration
<b>Context</b>	<ul style="list-style-type: none"> <li>• Thought to result from the rapid killing of spirochetes causing copious release of endotoxins, lipopolysaccharides, prostaglandins, and cytokines, leading to an acute inflammatory response<sup>24</sup></li> <li>• More common during treatment for infectious syphilis<sup>24</sup> due to high bacterial burden<sup>31</sup></li> <li>• Case studies report JHR occurs in up to 44% of pregnant women treated for syphilis<sup>44,45</sup></li> <li>• Concerns about JHR relevant only to the first dose of treatment</li> </ul>
<b>Symptoms</b>	<ul style="list-style-type: none"> <li>• Onset within 2–12 hours post treatment and lasts several hours<sup>44</sup></li> <li>• Usually self-limiting<sup>44,46</sup> resolving by 24 hours after treatment<sup>24</sup></li> <li>• Fever, headaches, rigors, joint pain chills, malaise, transient accentuation of cutaneous lesions<sup>47</sup>, hypotension and tachycardia<sup>38,40</sup></li> <li>• May precipitate uterine contractions (56–67%), decreased fetal movements (67%) and abnormal fetal heart rate (FHR) tracings (50%)<sup>24</sup></li> <li>• In severely affected pregnancies preterm birth and stillbirth have been reported<sup>24</sup></li> </ul>
<b>Management</b>	<ul style="list-style-type: none"> <li>• <b>Do not delay treatment</b> due to concerns about adequacy of monitoring</li> <li>• Offer information to women about JHR <ul style="list-style-type: none"> <li>○ Refer to Queensland Clinical Guideline Parent information</li> </ul> </li> <li>• Advise women to: <ul style="list-style-type: none"> <li>○ Stay well hydrated, rest and take paracetamol for pain or fever</li> <li>○ Contact their health care provider, or nearest birth unit, if they experience regular cramping or contractions, a change in fetal movements or fever within 24 hours post administration</li> </ul> </li> <li>• Recommended increased maternal and fetal surveillance for: <ul style="list-style-type: none"> <li>○ Women with a known co-infection of HIV</li> <li>○ Fetal USS abnormalities</li> </ul> </li> <li>• Consider increased maternal and fetal surveillance if<sup>48,49</sup>: <ul style="list-style-type: none"> <li>○ Viable gestation</li> <li>○ Known high syphilis titres</li> </ul> </li> <li>• Consider inpatient management for higher risk groups (as above) <ul style="list-style-type: none"> <li>○ Supportive management relevant to symptoms (e.g. antipyretics, intravenous fluids, tocolysis)</li> </ul> </li> <li>• If inpatient management not practical (e.g. in a remote setting) consider: <ul style="list-style-type: none"> <li>○ Outreach follow-up contact in the community (e.g. by phone, text or personal contact)</li> <li>○ Fetal heart rate (FHR) auscultation or cardiotocography pre and post administration<sup>31,50</sup></li> </ul> </li> </ul>

## 4.7 Contact management

The aim of contact management (or partner notification) is to interrupt the chain of disease transmission. For the infected person, contact management aims to eradicate infection and prevent re-infection. For sexual partners of infected people, contact management aims to identify and treat undiagnosed syphilis.<sup>51</sup>

Table 18. Contact management

Aspect	Consideration
<b>Context</b>	<ul style="list-style-type: none"> <li>Of contactable sexual partners of pregnant women with infectious syphilis, 40–60% will also have an infection<sup>26</sup></li> </ul>
<b>Definition of a contact</b>	<ul style="list-style-type: none"> <li>Anyone who has had sex (including oral and/or anal sex) with a person who has infectious syphilis</li> <li>Unborn and newborn babies of women with syphilis requiring treatment in pregnancy</li> <li>Discuss contact management at the time of diagnosis and emphasise the importance of providing a complete history of all sexual contacts</li> </ul>
<b>Contact tracing</b>	<ul style="list-style-type: none"> <li>Diagnosing and treating clinician is responsible for the contact management plan               <ul style="list-style-type: none"> <li>Involve contact tracing support officers, the QSSS and an expert practitioner in contact management as required</li> <li>Women may prefer to follow-up contacts themselves or request assistance to do so</li> </ul> </li> <li>Offer information about online sites to advise partner(s) (e.g. Better to Know<sup>52</sup>, Let them know<sup>53</sup>, The Drama Downunder<sup>54</sup> (MSM specific site))</li> </ul>
<b>Look back period for contact tracing</b>	<ul style="list-style-type: none"> <li>If primary syphilis<sup>1</sup>:               <ul style="list-style-type: none"> <li>Duration of symptoms plus three months</li> <li>If duration uncertain, six months prior to presentation</li> </ul> </li> <li>If secondary syphilis:               <ul style="list-style-type: none"> <li>Duration of symptoms plus six months</li> <li>If duration uncertain 12 months prior to presentation</li> </ul> </li> <li>If early latent or unknown duration:               <ul style="list-style-type: none"> <li>12 months prior to presentation</li> </ul> </li> </ul>
<b>Pregnant contacts</b>	<ul style="list-style-type: none"> <li>If the woman is identified as a contact during pregnancy, treat presumptively without waiting for serology results</li> </ul>
<b>Treatment of contacts</b>	<ul style="list-style-type: none"> <li>If exposed to infectious syphilis, recommend empirical treatment regardless of syphilis serology results               <ul style="list-style-type: none"> <li>Benzathine penicillin 1.8 g (2.4 million units) IM once<sup>24,27,40,41,38</sup></li> <li>Administer as a divided dose of two injections of 900 mg each (one in each of the ventrogluteal regions or in the upper outer quadrant of each buttock<sup>42</sup>)</li> </ul> </li> <li>Obtain sexual history (including symptoms)</li> <li>Clinical examination for signs of syphilis and other STIs               <ul style="list-style-type: none"> <li>Collect serology for syphilis and other STI tests as indicated</li> </ul> </li> <li>Inform contacts of their test results at the earliest opportunity</li> <li>Do not:               <ul style="list-style-type: none"> <li>Record the name of the index case in the contacts' health record</li> <li>Disclose the name of the index case to a contact</li> </ul> </li> <li>Discuss with contacts:               <ul style="list-style-type: none"> <li>Infectious nature of the disease</li> <li>Possibility of infection even in the absence of symptoms or reactive serology</li> <li>Importance of follow-up and repeat serology testing</li> <li>Need to abstain from sexual activity for seven days after treatment or until symptoms (if present) have resolved—whichever is longer</li> </ul> </li> </ul>
<b>Re-infection</b>	<ul style="list-style-type: none"> <li>Provide advice about preventing re-infection               <ul style="list-style-type: none"> <li>Refer to Section 3.3 Ongoing risk of infection and re-infection</li> </ul> </li> </ul>

## 4.8 Birth considerations

Table 19. Birth considerations

Aspect	Consideration
<b>Timing and place of birth</b>	<ul style="list-style-type: none"> <li>• Planned preterm birth for neonatal concerns may be indicated when there is a high risk of fetal treatment failure (e.g. progressive worsening signs of congenital syphilis or hydrops on USS<sup>24</sup>)               <ul style="list-style-type: none"> <li>◦ Refer to Table 12. Prenatal diagnosis</li> </ul> </li> <li>• Plan place of birth in conjunction with an expert practitioner (e.g. consider clinical service capability framework in relation to expected condition of baby at birth)</li> </ul>
<b>Intrapartum care</b>	<ul style="list-style-type: none"> <li>• All routine intrapartum care is indicated</li> <li>• Notify medical officer/paediatrician/neonatologist about maternal syphilis stage, treatment and fetal USS findings<sup>24</sup></li> </ul>
<b>Syphilis serology at birth</b>	<ul style="list-style-type: none"> <li>• Recommend syphilis serology at birth if <sup>1,55,51</sup> (any of the following):               <ul style="list-style-type: none"> <li>◦ Syphilis requiring treatment in pregnancy</li> <li>◦ Woman is <i>high risk</i></li> <li>◦ Woman is <i>increased risk</i> AND                   <ul style="list-style-type: none"> <li>§ Serology NOT collected after 26 weeks</li> <li>§ Preterm birth with most recent serology more than four weeks before birth</li> </ul> </li> <li>◦ Indicated following risk assessment</li> </ul> </li> <li>• Refer to 3.5 Section Risk groups and recommended screening for syphilis</li> <li>• Refer to Appendix C: Interpretation of results</li> </ul>
<b>Placental histopathology</b>	<ul style="list-style-type: none"> <li>• If syphilis requiring treatment in pregnancy, request placental histopathologic examination of the placenta and/or umbilical cord for PCR               <ul style="list-style-type: none"> <li>◦ Not diagnostic but improves detection in both liveborn and stillborn babies<sup>24</sup></li> </ul> </li> <li>• Follow local protocol for collection of dry swab between the chorion and amnion for PCR<sup>56</sup> (may be collected by maternity clinicians or by pathology staff upon receipt of placenta at laboratory)</li> <li>• Store and transport entire placenta fresh (not frozen) or in sodium chloride 0.9% (not formalin)</li> <li>• Placenta often large, thick, and pale—characteristic findings<sup>57,58</sup>:               <ul style="list-style-type: none"> <li>◦ Hydrops placentalis, chronic villitis (plasma cells, mixed acute and chronic infiltrate), perivillous fibrous proliferation (onion skin vessels), normoblastemia, necrotizing funisitis, acute chorioamnionitis, plasma cell deciduitis</li> </ul> </li> <li>• Umbilical cord<sup>59</sup> <ul style="list-style-type: none"> <li>◦ Oedematous and may resemble a "barber's pole" with spiral stripes of red and light blue discoloration alternating with streaks of chalky white</li> <li>◦ May be significantly inflamed with an abscess-like foci of necrosis within Wharton's jelly, centred around the umbilical vessels<sup>24</sup> (necrotizing funisitis<sup>57</sup>)</li> </ul> </li> </ul>
<b>Breastfeeding</b>	<ul style="list-style-type: none"> <li>• <i>Treponema pallidum</i> is not transferred in breast milk</li> <li>• Recommend breastfeeding unless an infectious lesion (e.g. chancre) is present on the woman's breast and/or axillae<sup>28</sup></li> </ul>
<b>Discharge</b>	<ul style="list-style-type: none"> <li>• Provide written advice to community health practitioners, especially those responsible for follow-up (e.g. general practitioners (GP), rural and remote health care providers)</li> <li>• Advise the woman, and family, of the importance of follow-up appointments and testing</li> <li>• Offer information about safe sexual health practices and STI testing</li> <li>• Notify QSSS of discharge</li> </ul>
<b>Follow-up after birth</b>	<ul style="list-style-type: none"> <li>• If syphilis requiring treatment in pregnancy recommend clinical and serological follow-up at three, six and 12 months</li> <li>• Discuss with the QSSS and an expert practitioner if titres:               <ul style="list-style-type: none"> <li>◦ Do not decrease four-fold within 12 months</li> <li>◦ Increase four-fold</li> </ul> </li> <li>• If syphilis (any stage) diagnosed within three months postpartum, assess the baby for congenital syphilis</li> </ul>

## 5 Congenital syphilis

Congenital syphilis is passed from an infectious mother via the placenta and can have multiple presentations. Assessment, diagnosis and treatment is multifaceted and requires a multidisciplinary approach. More than 70% of babies born to untreated women with infectious syphilis may be infected<sup>18</sup>.

Suspect congenital syphilis in babies born to women who:

- Had syphilis requiring treatment in pregnancy irrespective of adequacy of treatment
- Limited or no antenatal care
- Are diagnosed as having syphilis (any stage) within three months postpartum

### 5.1 Initial assessment

If congenital syphilis is a possibility, do all of the following:

- Conduct a full clinical examination
- Collect syphilis serology
- Review placental histopathology and PCR
- Review maternal serology and adequacy of treatment during pregnancy
- Collaborate with QSSS and an expert practitioner about the ongoing plan of care

#### 5.1.1 Clinical examination

Table 20. Clinical assessment

Aspect	Consideration
<b>Clinical examination</b>	<ul style="list-style-type: none"> <li>• Physical examination performed ideally by a neonatologist or paediatrician<sup>39,60,61</sup> <ul style="list-style-type: none"> <li>○ Other health care providers may perform the clinical examination as appropriate to the local health care context</li> </ul> </li> <li>• 60–90% asymptomatic at birth</li> <li>• Signs and symptoms often subtle, non-specific and variable</li> <li>• Usually appear by three months of age, most often by five weeks</li> </ul>
<b>Hepatomegaly</b>	<ul style="list-style-type: none"> <li>• Hepatomegaly almost always present with congenital syphilis—may be associated with splenomegaly<sup>57,60,61</sup> (but not splenomegaly in isolation)</li> <li>• May have abnormal liver function tests (LFT)</li> <li>• Associated with jaundice and cholestasis</li> </ul>
<b>Rhinitis</b>	<ul style="list-style-type: none"> <li>• Usually during the first week of life and seldom after the third month</li> <li>• White nasal discharge, may be bloody (secondary to mucosal erosion) or purulent if secondary bacterial infection</li> <li>• Nasal discharge contains spirochaetes, is contagious, and can transmit infection by direct contact</li> <li>• Use direct detection testing (e.g. PCR) to confirm diagnosis<sup>39,60,61</sup></li> </ul>
<b>Rash</b>	<ul style="list-style-type: none"> <li>• Usually appears one to two weeks after the rhinitis</li> <li>• Commonly presents with peeling of the hands and feet</li> <li>• Maculopapular consisting of small, initially red or pink spots</li> <li>• Progresses over one to three weeks, followed by desquamation and crusting becoming dusky red or copper-coloured <ul style="list-style-type: none"> <li>○ Pigmentation may persist</li> </ul> </li> <li>• Use direct testing (e.g. PCR) to confirm diagnosis<sup>39,60,61</sup></li> </ul>
<b>Generalised lymphadenopathy</b>	<ul style="list-style-type: none"> <li>• Common manifestation</li> <li>• Palpable epitrochlear lymphadenopathy is highly suggestive<sup>60,61</sup></li> </ul>
<b>Other signs</b>	<ul style="list-style-type: none"> <li>• Nonimmune fetal hydrops</li> <li>• Soft tissue swelling of the fingers and/or hands<sup>62</sup> (dactylitis)</li> <li>• Failure to move extremity secondary to pain (pseudoparalysis of Parrot)</li> <li>• Ophthalmologic manifestations (e.g. loss of eyebrows, chorioretinitis, uveitis, cataract, glaucoma, and chancre of the eyelid)</li> <li>• Nephrotic syndrome<sup>39,60,61,63,64,65</sup> (immune complex mediated; responsive to penicillin)</li> <li>• Gastrointestinal manifestations (e.g. rectal bleeding (from ileitis), necrotising enterocolitis, malabsorption)</li> </ul>

## 5.1.2 Serology/histopathology

Table 21. Laboratory assessment

Aspect	Consideration
<b>Mother and baby serology</b>	<ul style="list-style-type: none"> <li>· Relationship between maternal and baby's titre can indicate likelihood of congenital syphilis               <ul style="list-style-type: none"> <li>○ A baby's non-treponemal titre that is four-fold or more the maternal titre<sup>31</sup> is diagnostic of congenital syphilis</li> <li>○ A baby's non-treponemal titre that is less than four-fold the maternal titre <i>may</i> indicate congenital syphilis and requires additional confirmatory tests                   <ul style="list-style-type: none"> <li>§ IgM may assist clarification and interpretation</li> </ul> </li> <li>○ Refer to Appendix C: Interpretation of results</li> </ul> </li> </ul>
<b>Serology</b>	<ul style="list-style-type: none"> <li>· Collect serology from baby               <ul style="list-style-type: none"> <li>○ Do not use umbilical cord blood due to risk of false positive<sup>59</sup></li> <li>○ Venepuncture preferable to heel prick collection</li> </ul> </li> <li>· Test mother and baby syphilis serology in parallel to aid diagnosis of congenital syphilis</li> <li>· Request <i>syphilis serology</i><sup>66</sup> including IgM<sup>38</sup> <ul style="list-style-type: none"> <li>○ IgM antibodies do not normally cross the placenta therefore, a positive IgM is strongly indicative of infection in the symptomatic baby (but is not diagnostic in isolation<sup>26,67</sup>)</li> <li>○ Negative IgM does not exclude congenital syphilis—liaise with an expert practitioner</li> </ul> </li> </ul>
<b>Dry swab and PCR</b>	<ul style="list-style-type: none"> <li>· Dry swab and request PCR of suspicious mucocutaneous lesions or body fluids identified on clinical examination<sup>25</sup></li> </ul>
<b>Placental histopathology</b>	<ul style="list-style-type: none"> <li>· Review placental histopathology and PCR (if available)               <ul style="list-style-type: none"> <li>○ Refer to Table 19. Birth considerations</li> </ul> </li> </ul>

## 5.2 Further investigations

In consultation with an expert practitioner, consider the need for further investigations if any of the following<sup>38</sup>:

- Clinical examination is abnormal
- Serology or dry swab PCR is abnormal
- Placental investigations are positive
- Inadequate maternal treatment

Table 22. Further investigations

Aspect	Consideration
<b>Haematology</b>	<ul style="list-style-type: none"> <li>• Collect full blood count (FBC), electrolytes and liver function tests (ELFT)</li> <li>• Haematological abnormalities               <ul style="list-style-type: none"> <li>○ Anaemia<sup>39,63</sup> <ul style="list-style-type: none"> <li>§ Direct antiglobulin titre (DAT) negative hemolytic anaemia</li> <li>§ Non-hemolytic anaemia after the neonatal period</li> </ul> </li> <li>○ Thrombocytopenia</li> <li>○ Leukopenia or leukocytosis</li> <li>○ Haemolysis often accompanied by cryoglobulinemia, immune complex formation, and macroglobulinemia                   <ul style="list-style-type: none"> <li>§ Does not respond to therapy and may last for weeks</li> </ul> </li> </ul> </li> </ul>
<b>Cerebral spinal fluid (CSF)</b>	<ul style="list-style-type: none"> <li>• Collect CSF</li> <li>• CSF abnormalities               <ul style="list-style-type: none"> <li>○ Reactive CSF venereal diseases research laboratory (VDRL)<sup>39,63</sup></li> <li>○ CSF pleocytosis (greater than 20–25 white blood cell/microL) for babies less than one month</li> <li>○ Elevated CSF protein at less than one month of age:                   <ul style="list-style-type: none"> <li>§ Term baby greater than 150 mg/L</li> <li>§ Preterm baby greater than 170 mg/L</li> </ul> </li> </ul> </li> <li>• All CSF tests above reported to have low specificity and sensitivity</li> <li>• If abnormal CSF values, consider the possibility of meningitis (e.g. Group B streptococcus, herpes simplex virus)</li> <li>• Discuss findings with an expert practitioner</li> </ul>
<b>Radiography</b>	<ul style="list-style-type: none"> <li>• Abnormal long bone radiographs<sup>68,39,63</sup> <ul style="list-style-type: none"> <li>○ Common manifestation (60–80%)</li> <li>○ May be the sole manifestation in a baby born to a woman with untreated syphilis</li> <li>○ Usually present at birth but may appear in first few weeks of life</li> <li>○ Characteristically abnormalities are:                   <ul style="list-style-type: none"> <li>§ Bilateral, symmetric and periosteal</li> <li>§ Can affect multiple bones but most frequently femur, humerus, and tibia</li> </ul> </li> </ul> </li> <li>• Abnormal chest X-ray—generalised infiltrate involving all lung areas</li> </ul>

## 5.3 Diagnosis and treatment of congenital syphilis

Diagnosis of congenital syphilis can be difficult as maternal reactive antibodies can be transferred through the placenta, complicating the interpretation of serologic tests for syphilis.

**Consult with QSSS and an expert practitioner about maternal and neonatal serology, results of additional investigations and to plan treatment and follow-up**

Table 23. Treatment for congenital syphilis according to age

Age	Consideration
<b>0–7 days</b>	<ul style="list-style-type: none"> <li>• Benzyl penicillin <b>50 mg/kg IV 12 hourly for 10 days</b> <sup>1,31,38</sup></li> <li>• Alternative: procaine penicillin 50 mg/kg IM daily for 10 days</li> </ul>
<b>8–30 days</b>	<ul style="list-style-type: none"> <li>• Benzyl penicillin <b>50mg/kg IV 8 hourly for 10 days</b></li> <li>• Alternative: procaine penicillin 50 mg/kg IM daily for 10 days</li> </ul>
<b>More than 30 days</b>	<ul style="list-style-type: none"> <li>• Benzyl penicillin <b>50mg/kg IV 4–6 hourly for 10 days</b></li> <li>• Alternative: procaine penicillin 50 mg/kg IM daily for 10 days</li> </ul>
<i>If peripheral intravenous access difficult, consider percutaneous intravenous catheter</i>	

## 5.4 Discharge

Follow local processes and pathways to maximise follow-up opportunities for the baby. Refer to Section 1.5 Clinical standards.

Table 24. Discharge

Aspect	Consideration
<b>Discharge advice</b>	<ul style="list-style-type: none"> <li>· Inform parents of the results of tests and implications for future health care</li> <li>· Advise parents of the importance of attending for all follow-up appointments and tests (including routine appointments as identified in the personal health record ('red book'))</li> <li>· Provide parents with written documentation about syphilis test results, diagnosis (if known) and treatment (e.g. in the personal health record or as separate documentation if parents prefer)</li> <li>· Review woman's serology during previous pregnancies and consider whether older siblings require testing</li> </ul>
<b>Establish community connections</b>	<ul style="list-style-type: none"> <li>· Notify health care providers involved in follow-up, that the baby is to be discharged</li> <li>· If baby discharged prior to serology results available, liaise with QSSS and an expert practitioner about ongoing follow-up and management</li> <li>· Provide written advice of test results and treatment to relevant community health care providers (e.g. GP, child health nurse, indigenous health worker)</li> <li>· If appropriate make direct telephone contact with other health care providers</li> </ul>

### 5.4.1 Uncertainty about baby's follow-up

Table 25. Uncertainty about follow-up

Aspect	Consideration
<b>Precautionary single dose</b>	<ul style="list-style-type: none"> <li>· A precautionary single dose of antibiotic may be considered<sup>31</sup> if at the time of discharge, there is concern about serological follow-up for a baby in whom congenital syphilis is considered very unlikely (but in whom it cannot be excluded with certainty)—for example: <ul style="list-style-type: none"> <li>○ Adequate maternal treatment in the current pregnancy <b>AND</b></li> <li>○ Normal clinical assessment <b>AND</b></li> <li>○ 10-day treatment course is not indicated <b>AND</b></li> <li>○ Reactive serology (similar or increased titre compared with maternal serology)<sup>1</sup> but a diagnosis of congenital syphilis is not confirmed</li> </ul> </li> </ul>
<b>Recommendation</b>	<ul style="list-style-type: none"> <li>· A single dose antibiotic is NOT adequate for treatment of congenital syphilis</li> <li>· A single dose antibiotic may be prescribed by an expert practitioner and paediatric infectious diseases specialist if indicated</li> <li>· Drug of choice: <ul style="list-style-type: none"> <li>○ Benzathine penicillin 50 mg/kg IM once<sup>31</sup></li> </ul> </li> </ul>



## 5.5 Follow-up of baby

Table 26. Serological follow-up

Aspect	Consideration
<b>Context</b>	<ul style="list-style-type: none"> <li>· In most cases, reactive serology represents passive transfer of maternal antibody, but a positive IgM assay indicates neonatal infection<sup>69</sup></li> <li>· Passively acquired antibodies decline over time, and become undetectable at 12 to 18 months<sup>69</sup></li> <li>· Decline in antibody titres is usually seen by three months in uninfected babies</li> </ul>
<b>Clinical assessment</b>	<ul style="list-style-type: none"> <li>· Conduct a clinical assessment of the baby at each opportunity as clinical signs and symptoms may not present at birth</li> </ul>
<b>Serum collection</b>	<ul style="list-style-type: none"> <li>· If possible, collect by venepuncture</li> <li>· If venepuncture not possible, collection via heel prick is acceptable               <ul style="list-style-type: none"> <li>○ At least 0.5 mL of blood</li> <li>○ Into a serum separator tube (SST)—(microtainer 600 microlitre)</li> </ul> </li> </ul>
<b>If congenital syphilis</b>	<ul style="list-style-type: none"> <li>· Follow-up serology<sup>69,70</sup>:               <ul style="list-style-type: none"> <li>○ At three, six and 12 months of age</li> <li>○ If non-reactive at 12 months, no further testing required</li> </ul> </li> <li>· If follow-up testing is potentially difficult:               <ul style="list-style-type: none"> <li>○ Aim to repeat testing at least twice in the first six months of life (with at least four weeks between tests)<sup>31,39,71</sup></li> <li>○ Consider feasibility of testing at routine follow-up appointments (e.g. immunisation, infant health checks)</li> </ul> </li> </ul>
<b>If initial serology negative</b>	<ul style="list-style-type: none"> <li>· If initial baby's serology is negative and the mother was adequately treated, follow-up at three and six months<sup>72</sup></li> <li>· If serology remains negative at six months, no further testing is required<sup>69</sup></li> </ul>
<b>Persistently reactive serology</b>	<ul style="list-style-type: none"> <li>· If non-treponemal tests remain reactive at 12 months, re-evaluate (e.g. CSF analysis, long bone radiography and other tests as indicated<sup>69</sup>)</li> <li>· Seek advice from QSSS and an expert practitioner about re-treatment<sup>38</sup></li> </ul>
<b>CSF</b>	<ul style="list-style-type: none"> <li>· If at birth there was central nervous system disease or abnormal CSF               <ul style="list-style-type: none"> <li>○ Repeat CSF for VDRL, cell count and protein at 6 months of age</li> </ul> </li> <li>· If repeat CSF at 6 months is abnormal, retreatment is indicated</li> </ul>

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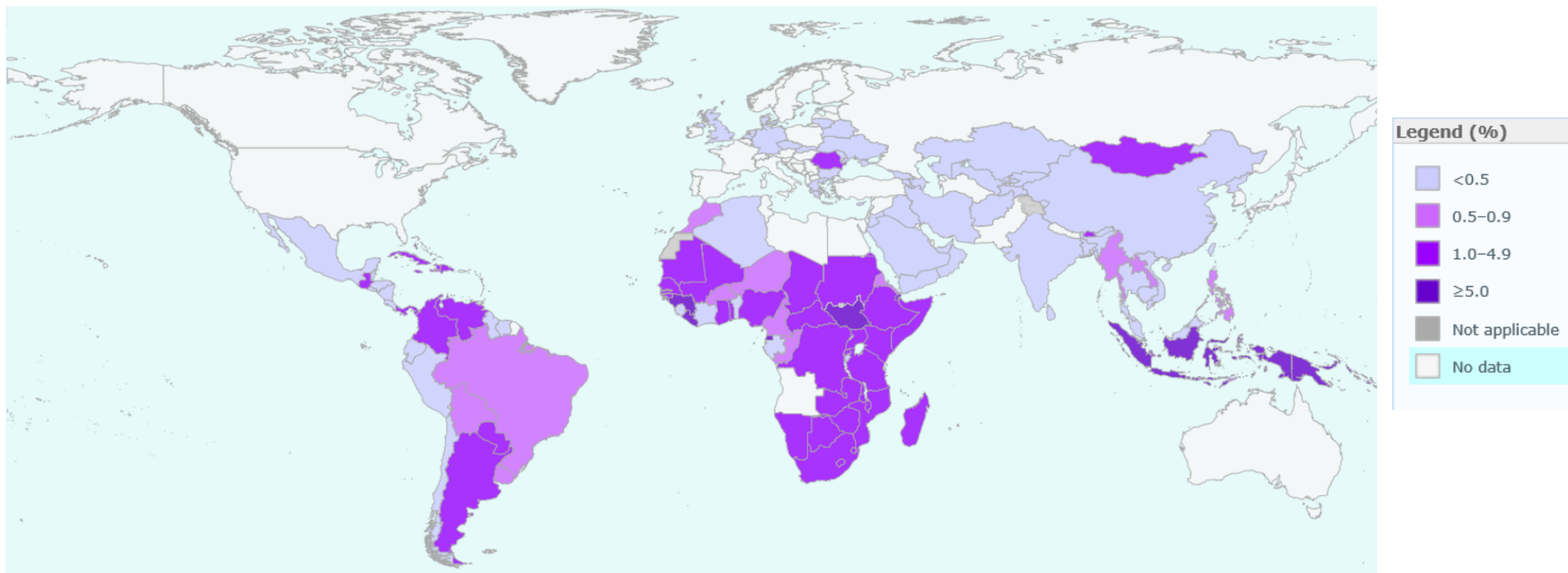
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## Appendix A: Percent of positive antenatal care attendees

### Antenatal attendees positive for syphilis by country

% of population



Source: World Health Organisation 2018. Percentage of antenatal care attendees positive for syphilis: Latest reported since 2008 [cited 2018, June 20]  
[http://gamapserver.who.int/gho/interactive\\_charts/sti/anc\\_syphilis\\_positive/atlas.html](http://gamapserver.who.int/gho/interactive_charts/sti/anc_syphilis_positive/atlas.html)

Countries with no data: do not submit antenatal data separate from other syphilis data

## Appendix B: Laboratory tests

Laboratory tests are determined by individual pathology laboratories based on availability and local protocols. Requesting 'syphilis serology' on the pathology form will initiate tests, as per local availability and preferences.

Test type	Consideration
<b>Availability</b>	<ul style="list-style-type: none"> <li>In Queensland, private and public pathology laboratories may perform only some (or all) of the non-treponemal and treponemal tests for syphilis listed below</li> </ul>
<b>Non-treponemal tests</b>	<ul style="list-style-type: none"> <li>Reported as a titre (e.g.1:2; 1:8, 1:64) which corresponds to the highest dilution factor that still yields a positive result</li> <li>Detect anti-lipid immunoglobulin M or G (IgM or IgG) antibodies which can also be produced in other conditions, therefore not highly specific for syphilis</li> <li>Usually becomes reactive within three to four weeks post infection</li> <li>In Queensland includes:               <ul style="list-style-type: none"> <li>Macroscopic rapid plasma reagin (RPR) on serum</li> <li>Microscopic VDRL                   <ul style="list-style-type: none"> <li>§ Pathology Queensland performs VDRL only on CSF although other private laboratories may perform on serum</li> </ul> </li> </ul> </li> </ul>
<b>Treponemal specific tests</b>	<ul style="list-style-type: none"> <li>Reported as reactive or non-reactive</li> <li>Detect antibodies against treponemal specific antigens, therefore highly specific for syphilis               <ul style="list-style-type: none"> <li>Do not differentiate venereal syphilis from non-venereal syphilis (e.g. yaws, bejel and pinta)</li> <li>Do not distinguish between current syphilis infection and previous treated or non-treated infection</li> </ul> </li> <li>Usually become reactive within two to four weeks post infection</li> <li>Usually remain reactive (85%) for life regardless of treatment</li> <li>In Queensland includes:               <ul style="list-style-type: none"> <li>Treponema pallidum antibodies (TPGE)</li> <li><i>Treponema pallidum</i> haemagglutination assay (TPHA)</li> <li><i>Treponema pallidum</i> particle agglutination (TPPA)</li> <li>Fluorescent treponemal antibody absorption test (FTA-ABS)</li> <li><i>Treponema pallidum</i> enzyme immunoassays for IgG or IgM (EIA)</li> <li>Chemiluminescent immunoassay (CMIA)</li> </ul> </li> </ul>
<b>Direct detection test</b>	<ul style="list-style-type: none"> <li>Detects the presence or absence of treponemes in the exudate from lesions of primary, secondary or early congenital syphilis</li> <li>In Queensland includes:               <ul style="list-style-type: none"> <li>Nucleic acid amplification tests (NAAT) using polymerase chain reaction (PCR) on dry swab of lesion</li> </ul> </li> <li>No longer performed:               <ul style="list-style-type: none"> <li>Darkfield microscopy tests</li> <li>Direct fluorescent antibody (DFA)</li> </ul> </li> </ul>

## Treponemal and non-treponemal test combinations

Treponemal test*	Non-treponemal test*	Likely interpretation
Reactive	Reactive	<ul style="list-style-type: none"> <li>Syphilis, yaws, bejel or pinta</li> </ul>
Negative	Reactive	<ul style="list-style-type: none"> <li>May be false positive</li> <li>Retest after two to three weeks</li> <li>Seek advice from QSSS/expert practitioner</li> </ul>
Reactive	Negative	<ul style="list-style-type: none"> <li>Primary or latent syphilis</li> <li>Previously treated syphilis</li> <li>Yaws, bejel or pinta</li> <li>May be a false positive if only one reactive treponemal test</li> </ul>
Negative	Negative	<ul style="list-style-type: none"> <li>No syphilis</li> <li>Incubating syphilis</li> </ul>

\*May be reported as 'reactive' or 'positive' and 'non-reactive' or 'negative'

## Appendix C: Interpretation of results

Note: Interpret results in consultation with an expert practitioner and QSSS.

Aspect	Consideration
<b>Expert advice</b>	<ul style="list-style-type: none"> <li>• Seek advice from QSSS and the expert practitioner, especially:               <ul style="list-style-type: none"> <li>○ When interpreting reactive results</li> <li>○ Planning treatment</li> <li>○ If negative result in the presence of clinical suspicion</li> </ul> </li> </ul>
<b>Routine antenatal screening</b>	<ul style="list-style-type: none"> <li>• Testing performed as per local laboratory SOP</li> <li>• Testing sequence is commonly:               <ul style="list-style-type: none"> <li>○ Initial treponemal test</li> <li>○ If reactive, confirmed with a second treponemal test</li> <li>○ If both treponemal tests are reactive the laboratory performs a non-treponemal test to assist with staging and monitoring</li> </ul> </li> </ul>
<b>Diagnosis</b>	<ul style="list-style-type: none"> <li>• Interpret laboratory results in the light of the treatment history and clinical findings</li> <li>• Isolated reactive tests (a non-treponemal or a treponemal test) are not adequate for diagnosis<sup>27</sup></li> </ul>
<b>Serological activity of syphilis</b>	<ul style="list-style-type: none"> <li>• Non-treponemal titre at diagnosis helps<sup>31</sup>:               <ul style="list-style-type: none"> <li>○ Stage infection</li> <li>○ Provides a baseline to assess response to treatment</li> </ul> </li> <li>• An initial non-treponemal titre of<sup>31</sup>:               <ul style="list-style-type: none"> <li>○ Greater than 1:8 usually indicates active disease and the need for treatment</li> <li>○ Less than or equal to 1:8 does not exclude infectious syphilis, particularly if clinical signs suggestive of syphilis or adequate treatment of syphilis not documented</li> </ul> </li> </ul>
<b>Monitoring effect of treatment</b>	<ul style="list-style-type: none"> <li>• Non-treponemal test<sup>1</sup> <ul style="list-style-type: none"> <li>○ Expected to decrease following effective treatment and may increase in untreated active infection</li> <li>○ A sustained four-fold or greater increase using the same testing method (preferably tested in parallel with the original specimen)—suggests re-infection or treatment failure (e.g. from 1:4 to 1:16)</li> <li>○ A four-fold fall in titre after treatment within six to 12 months after treatment suggests an adequate response to treatment</li> <li>○ Serofast reactive titres may occur despite adequate treatment particularly if titre high or late diagnosis</li> </ul> </li> <li>• Treponemal tests may be negative before a chancre develops and may be negative for up to two weeks afterwards<sup>1</sup></li> </ul>
<b>False negative</b>	<ul style="list-style-type: none"> <li>• Non-treponemal test:               <ul style="list-style-type: none"> <li>○ Occurs in up to 1–2% of serum tested<sup>67</sup></li> <li>○ May occur in secondary or early latent syphilis, particularly if HIV positive</li> </ul> </li> </ul>
<b>False positive</b>	<ul style="list-style-type: none"> <li>• May occur occasionally with any serological test<sup>1</sup></li> <li>• Non-treponemal false positive can have multiple causes as anti-phospholipid antibodies detected by non-treponemal tests are produced by a variety of conditions<sup>67</sup> <ul style="list-style-type: none"> <li>○ 90% have a titre of less than 1:8<sup>67</sup></li> <li>○ More likely if pregnant, autoimmune diseases, injecting drug use<sup>67</sup>, older individuals</li> </ul> </li> <li>• Consider if persistent reactivity in a single antigen test with absence of:               <ul style="list-style-type: none"> <li>○ Symptoms of syphilis</li> <li>○ History of syphilis</li> <li>○ Concomitant positive anti-treponemal IgM</li> </ul> </li> </ul>

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