South Australian Perinatal Practice Guideline

Syphilis in Pregnancy

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 statewide 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

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 horse shoe shape design shown in front of the generic statement symbolises a woman and those enclosing a smaller horse shoe shape depicts a pregnant women. The smaller horse shoe 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 respectively 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 additional screening considerations for women at increased risk of acquiring syphilis, treatment, newborn care and health promotion information.

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Table of Contents

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Summary of Practice Recommendations

Congenital syphilis can be prevented through appropriate testing and treatment

All women should be screened for syphilis at their first antenatal appointment

Aboriginal women and women with Aboriginal partners are at higher risk of acquiring syphilis

During syphilis outbreaks, additional screening is required for 'at risk' women

All women identified at increased risk of acquiring syphilis require additional screening

Syphilis is a notifiable disease

Screening for other sexually transmitted diseases should be performed in women with positive syphilis serology

Once a positive syphilis serology has been confirmed the stage of syphilis needs to be established

Treatment of pregnant women AND their contacts should be carried out urgently and in consultation with an infection control consultant

Abbreviations

CSF	Cerebro-spinal fluid
g	Gram(s)
HBV	Hepatitis B virus
HCV	Hepatitis C virus
HIV	Human immunodeficiency virus
IM	Intramuscular
IMVS	Institute of Medical and Veterinary Science
IV	Intravenous
kg	Kilogram(s)
mg	Milligram(s)
mL	Millilitre(s)
PPG	Perinatal practice guideline
RPR	Rapid Plasma Reagin
TPPA	Treponema Pallidum Particle Agglutination
VDRL	Venereal Disease Research Laboratory test

Syphilis

- Syphilis is a bacterial infection caused by the spirochaete bacterium *Treponema pallidum*
- Untreated syphilis during pregnancy can lead to preterm labour, preterm birth, stillbirth, neonatal death, or congenital syphilis with multi-system manifestations such as deafness, neurologic impairment, and bone deformities
- Mid-trimester spontaneous miscarriage is the most common outcome of syphilis in pregnancy
- Infant transmission rates are between 25 and 64 % for primary, secondary or early latent syphilis. In established late latent syphilis, vertical transmission occurs in around 10 %[1]
- Congenital syphilis can be prevented through appropriate testing and treatment
- Aboriginal populations in remote communities of the Northern Territory are 25 times more likely to acquire syphilis than populations in other parts of Australia, possibly due to large reservoirs of infected people, lack of facilities or lack of access to facilities for diagnosis and treatment[2]

Notification

- Syphilis is a notifiable disease
- Notification must be made to the Communicable Disease Control Branch
- Notification is a confidential process and must occur within 3 days of suspecting or confirming a diagnosis of syphilis. Report of Notifiable Conditions Sexually Transmitted Infections or Related Death form is available from http://www.sahealth.sa.gov.au/NotifiableDiseaseReporting
- This form is not to be sent by email for reasons of confidentiality

Route of transmission

- Almost all cases occur as sexually transmitted infections
- Syphilis is passed from person to person through direct contact with a syphilis ulcer (chancre)
- Chancres occur mainly on the external genitals, vagina, anus, or in the rectum. They can also be on the mouth or lips and in the mouth
- Congenital syphilis can occur when the spirochete is transmitted from a pregnant woman with syphilis to her fetus

Incubation period

- 9 to 90 days, with an average of 3 weeks from contact to the development of a chancre
- The infectious period is during the primary and secondary stages and up to the first four years of the latent period
- The individual is no longer infectious 24 to 48 hours after starting appropriate antibiotic treatment

Clinical features

Primary stage

- Marked by the appearance of a single ulcer (chancre), but these may be multiple
- The chancre is firm, round, small and painless and appears at the site where syphilis is transmitted
- The chancre lasts 3 to 6 weeks (range 1-12 weeks) and heals without treatment

Secondary stage

- 2 to 8 weeks after resolution of the chancre but may occur any time in the following one -two years if untreated
- Skin rash - rough red or reddish brown spots on palms of the hands and soles of feet (not usually itchy). The rash may be generalised and florid or it may be faint
- Mucous membrane lesions or condylomata lata
- May also be fever, swollen lymph glands, sore throat, patchy alopecia, headaches, weight loss, muscle aches and fatigue. Signs and symptoms last about 2 to 6 weeks and will resolve without treatment and recurrences may occur usually in the first year and rarely in the second year
- Without treatment, the infection will become latent and may progress to late stages of disease

Latent stage

- Latent syphilis is defined as sero-positivity without evidence of disease
- Early latent syphilis defined as positive serology with no symptoms and infection acquired within the last 2 years
- Late latent syphilis is asymptomatic infection beyond 2 years duration with infectivity being reduced only to vertical transmission or via transfused contaminated blood

Tertiary stage

- The tertiary (third) stage of syphilis can develop in up to 40 % of untreated individuals
- May involve the brain and spinal cord (neurosyphilis), heart and blood vessels (cardiovascular syphilis), liver, bones and joints
- Acute Neurosyphilis can occur at any stage of syphilis infection
- Symptoms include: chronic meningitis, difficulty coordinating muscle movements, paralysis, numbness, gradual blindness, dementia and even death

Antenatal screening

- In South Australia, routine screening for syphilis (treponemal specific enzyme immunoassay) is offered to all pregnant women at their first antenatal appointment as part of the antenatal screen
- If the treponemal specific enzyme immunoassay is reactive it is confirmed with a Treponemal Pallidum Particle Agglutination (TPPA) assay and an RPR is performed. The RPR is reported as a titre. The RPR is useful in determining disease activity and response to treatment while the TPPA confirms exposure to Treponima pallidum

Women at increased risk

- Women at risk of acquiring syphilis should have repeat treponemal screening assay at 28 weeks of gestation and at the time of birth
- Screening for other sexually transmitted diseases (i.e. Chlamydia, gonorrhoea, HIV, HBV) should also be performed in women with positive syphilis serology

Screening during syphilis outbreaks for women in high risk communities

- The Communicable Disease Control Branch in SA issues public health alerts when a syphilis outbreak occurs, typically in Aboriginal people in northern and/or remote areas of the State
- Practitioners should be aware of the increased possibility of syphilis in Aboriginal people residing in or travelling from outbreak areas
- Additional syphilis screening should be undertaken for all Aboriginal women residing in high risk areas (or who have travelled through an outbreak area) as well as any woman (regardless of cultural background) with an Aboriginal partner residing in high risk areas (or who has travelled through an outbreak area)
- Additional screening required:
    - First antenatal visit (routine)
    - 28 weeks
    - 36 weeks
    - At birth
    - 6 week post-natal check
- Further information is available on the SA Health website www.sahealth.sa.gov.au (search "health alerts") or via the Communicable Disease Control Branch direct on telephone:

  1300 232 272 (24 hours/7 days)

Other causes of positive serology

- Women from parts of the world where endemic syphilis and / or Yaws, Bejel or Pinta are present may present with positive syphilis serology. Differentiation from subclinical forms of venereal syphilis can be difficult and such women (if previously untreated) should be given treatment as for latent syphilis.
- Treponemal tests for syphilis may remain positive for very many years even after successful treatment

Treatment

- Once a positive syphilis serology has been confirmed, establish the stage of syphilis in the mother (i.e. when the infection occurred) and whether effective treatment has already been given. If effective treatment has been given it is important to exclude re-infection
- Women with syphilis of less than 2 years duration and in the second half of pregnancy are at risk of preterm labour and fetal compromise if a Jarisch-Herxheimer reaction occurs with treatment. Consider concomitant prednisolone 20 mg bd for 3 doses to reduce Jarisch-Herxheimer reaction

Primary, secondary and early latent syphilis

- A single intramuscular injection of benzathine penicillin 1.8 g (2.4 million units) will cure a person who has had syphilis for less than two years
- Women diagnosed in the third trimester should be treated with a second dose of benzathine penicillin 1.8 g (2.4 million units) one week later
- If allergic to penicillin – consult with Infectious Diseases Consultant
- Sexual contacts in the last 3 months should also have the same treatment regardless of serology
- Repeat VDRL / RPR monthly (or at delivery) to confirm falling, negative, low or stationary titre. If titre is not falling, seek advice from an Infectious Diseases Consultant
- Sources vary as to whether one or two years represent the cut-off for early latent syphilis. Consult with Infectious Diseases Consultant regarding treatment

Late latent syphilis

- Late latent syphilis or syphilis of indeterminate duration in the absence of tertiary syphilis
- Intramuscular injection of benzathine penicillin 1.8 g (2.4 million units) once weekly for three doses

Allergy to penicillin

- Doxycycline could be used for pregnant women hypersensitive to penicillin in which desensitisation is not feasible, (safe for use during the first 18 weeks of pregnancy (16 weeks post conception) after which tetracyclines cause discolouration of the baby's teeth). Dose: 100 mg orally bd for 14 days
- If penicillin desensitisation is not feasible and gestation greater than 18 weeks consult with Infectious Disease Consultant regarding treatment
- Repeat VDRL / RPR monthly (or at delivery) to confirm falling, negative, low or stationary titre. If titre rising – repeat treatment as may be re-infection

Tertiary syphilis

- Intravenous benzylpenicillin 1.8 g every 4 hours for 15 days

Counselling

- Explain that Syphilis is a notifiable disease. Notification information is available at URL: www.sahealth.sa.gov.au/NotifiableDiseaseReporting
- Successful management of syphilis in pregnancy depends on early detection and treatment of maternal infection, ideally before 28 weeks of gestation
- Treatment of pregnant women AND their contacts should be carried out urgently and in consultation with an infection control consultant
- Stress the importance of examining any sexual contacts immediately and advise against further sexual contact until treatment is completed and contacts have been examined
    - Where possible sex partners from the last 3 months (if primary infection) and last 2 years (in the case of secondary and early latent syphilis) should be assessed and treated. Patients with late latent and tertiary syphilis are not infectious to sexual partners
- The treatment regimen may vary, depending on the maternal treatment history, maternal treatment during pregnancy, risk of re-infection during pregnancy or presence of persisting high maternal titres despite treatment
- Explain the risk of congenital syphilis in the newborn

- Explain that sexual contact during ulcerative syphilis increases the risk of HIV transmission
- Encourage safe sex practices e.g. use of condoms, limitation of alcohol, monogamous relationship
- Explain that up to 40 % of patients may develop a transient inflammatory reaction known as Jarisch-Herxheimer (J-H) in the first 24 hours after treatment with large doses of penicillin, especially in early syphilis. Symptoms include fever, chills, headache, myalgia's, and exacerbation of cutaneous lesions[3]
- There is a risk of preterm labour and fetal compromise with J-H reaction in the second half of pregnancy[3]

Newborn care

Low risk

- If the mother is treated with penicillin > 4 weeks before birth, the newborn risk is minimal. Follow-up involves clinical examination and serology on venous blood at birth and thereafter 3 monthly serology until the RPR is negative

High risk

- If maternal treatment was inadequate, or was given < 4 weeks before delivery or was a non-penicillin regimen, or if adequate follow-up of the baby cannot be assured, the baby should be treated at birth and have repeat serology for RPR at 3 and 6 months of age. The CSF should be examined before treatment if there is a substantial risk of congenital syphilis

Treatment

- Asymptomatic babies with normal CSF and for whom follow-up cannot be guaranteed
    - Benzathine penicillin G 37.5 mg / kg IM as one dose
- For other infants:
    - Procaine penicillin G 50 mg / kg IM daily for 10 days

    OR

    - Benzylpenicillin 50 mg / kg IV twice a day for the first 7 days and every 8 hours thereafter for a total of 10 days

Congenital syphilis

- 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:
    - Early (occurring within the first 2 years of life)
    - Late (recognised after 2 or more years after birth)

Early signs and symptoms

- Usually occur within 3-7 weeks after birth and result from active disseminated fetal infection and the subsequent inflammatory response
- Hepatosplenomegaly / hepatitis, jaundice, lesions on the skin and / or in the mouth, rhinitis, inflammation of long bones (osteochondritis, perichondritis), adenopathy, and haematologic disturbances (anaemia, thrombocytopenia)
- Low birth weight, failure to thrive

- Necrotising funisitis – an inflammation of the umbilical cord characterised by spiral stripes of red and blue discolouration resembling a “barber’s pole”

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 nerve deafness is less common (usually in the first decade of life and may be unilateral or bilateral)
- Facial abnormalities: saddle nose, protuberant mandible
- Central nervous system involvement: mental retardation, optic nerve atrophy, seizure disorders
- Bone or joint involvement: frontal bossing of the skull, saber shins, hypertrophy of the sternoclavicular joints

Treatment

- Benzylpenicillin 50 mg / kg twice a day IM or IV for 10 days

OR

- Procaine penicillin 50 mg / kg daily IM for 10 days

Postpartum follow-up

Maternal

- 4 weeks – clinical assessment and sexual partner review
- 3, 6, 12 months – clinical assessment and repeat serology (RPR)
- Successful treatment is a fourfold drop in the RPR / VDRL titre within 12 months
- Titres that show a four-fold rise or do not decrease appropriately suggest either treatment failure or re-infection. The treatment regimen should be repeated in these cases

Confirmed congenital syphilis

- VDRL / RPR at 1, 2, 4, 6, and 12 months of age or until non-reactive on 2 occasions (for neurosyphilis: repeat CSF examination at 6 months)

References

1. Hollier LM, Cox SM. Syphilis. Seminars in Perinatology 1998; 22:323-31
2. Mein J. Syphilis and Women's Health in the Northern Territory. Healthcare infection 1996; 1:13-15.
3. Myles TD, Elam G, Park-Hwang E, Nguyen T. The Jarisch-Herxheimer reaction and fetal monitoring changes in pregnant women treated for syphilis. ObstetGynecol1998;92:859-864

Useful web sites

> Australasian Society for Infectious Diseases, Management of Perinatal Infections, available at: https://www.asid.net.au/documents/item/368

> SA Health Communicable Disease Control Branch Useful internet short links available at: http://www.sahealth.sa.gov.au/wps/wcm/connect/0d455d80432ea08d83b9f78cd21c605e/SA-Health-CDCB-useful-links-for-GPs-v2.0-cdcb-20171027.pdf?MOD=AJPERES&CACHE=NONE&CONTENTCACHE=NONE

> SA Department of Health – You've got what – syphilis in the A to Z index at URL: www.sahealth.sa.gov.au/youvegotwhat

> Centers for Disease Control and Prevention http://www.cdc.gov/std/Syphilis/STDFact-Syphilis.htm

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