South Australian Perinatal Practice Guidelines

Syphilis in pregnancy

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 latent syphilis, vertical transmission occurs in around 10 % (Hollier & Cox 1998)
- 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 (Mein 1996)

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
- However, if not treated, the infection progresses to the secondary stage

Secondary stage

- 2 to 8 weeks after appearance of the chancre

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- 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 will resolve with or without treatment
- Without treatment, the infection will progress to the latent and possibly late stages of disease. This stage also lasts about 2 to 6 weeks

Latent stage

- Early latent syphilis begins when primary and secondary symptoms disappear and only serology will reveal the presence of infection. This is usually defined as less than 2 years duration
- Relapse may occur and the patient is 'infectious'
- Late latent syphilis follows with infectivity being reduced only to vertical transmission or via transfused contaminated blood. This is defined as latent syphilis of more than 2 years of duration
- May be no symptoms or obvious signs of disease - usually lasts for the remainder of the individual's life

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 s useful in determining disease activity and response to treatment while the TPPA confirms exposure to Treponima pallidum
- 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

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

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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

Jarisch-Herxheimer reaction

- This reaction is a common occurrence in the treatment of early syphilis in adults (including pregnant women in up to 45 %) and consists of fever, chills, malaise, hypotension and tachycardia. It begins within 2 hours of treatment, peaks at 8 hours and disappears in 24 - 36 hours. Management is supportive care. It may precipitate uterine contractions, preterm labour, and / or signs of fetal compromise on external fetal monitoring in pregnant women treated in the second half of pregnancy. Women should be counselled to report symptoms of labour or decreased fetal activity; evaluation and treatment as indicated

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 one year
- 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

Administration of benzathine penicillin

- To minimise pain with intramuscular injection of benzathine penicillin:
  - Mix each vial of benzathine penicillin (0.9 grams) (1.2 million units) with 2 mL water for injection and 2 mL lignocaine 1 %.
  - Draw up using a 5 mL syringe and 19 g needle. Swirl to dissolve – DON'T SHAKE - continue to swirl until ready to administer using 19 g needle
  - Administer 2 injections of 4 mL into the upper outer quadrant of each buttock (total of 2.4 million units)

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

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- 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 after which tetracyclines cause discolouration of the baby's teeth). Dose: 100 mg orally twice daily for 14 days
- 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: http://www.stdservices.on.net/notification/notification.htm
- 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, myalgias, and exacerbation of cutaneous lesions (Myles et al. 1998)
- There is a risk of preterm labour and fetal compromise with J-H reaction in the second half of pregnancy (Myles et al. 1998)

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

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- If maternal treatment was inadequate, or was treated with a non penicillin regimen < 4 weeks before birth, 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 50 mg / kg IM as one dose
- For other infants:
  - Procaine penicillin (50 mg / kg) daily IM for 10 days

  OR
  - Benzylpenicillin (50 mg / kg) 12 hourly IV for 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 ongoing 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)

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- 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) 12 hourly 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)

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Useful web sites

SA Department of Health – You've got what - syphilis
http://www.health.sa.gov.au/PEHS/Youve-got-what/ygw-syphilis.pdf

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

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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)
RPR	Rapid Plasma Reagin
TPPA	Treponema Pallidum Particle Agglutination
VDRL	Venereal Disease Research Laboratory test

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