

# South Australian Perinatal Practice Guideline

# Tuberculosis in pregnancy

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## Note:

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

Information in this 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 purpose of this guideline is to provide clinicians with information on Tuberculosis disease in pregnancy. It includes details of risk factors to guide clinicians with targeted antenatal screening, maternal diagnosis and management, infection control measures and neonatal management.



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## Summary of Practice Recommendations

Women who have recently arrived from an area with a high prevalence of TB or have had close contact with someone with infectious TB should be referred to the Chest Clinic

Women who have symptoms and signs suspicious of active TB, are HIV positive or have had a recent positive TST should be referred to the Chest Clinic

Identification of risk factors, early diagnosis, prompt treatment and isolation of a woman with suspected pulmonary TB are important infection control measures

Transmission-based airborne precautions should be used for all suspected or confirmed cases of pulmonary TB

The risk of congenital TB should be assessed by a Paediatrician at birth if the mother has disseminated TB, pelvic TB, pulmonary or extra-pulmonary disease



## Abbreviations

AFB	Acid fast bacilli
AIDS	Acquired immunodeficiency syndrome
BCG	Bacille Calmette-Guérin
CDI	Communicable Diseases Intelligence
DoH	Department of Health
et al	And others
g	Gram(s)
≥	Greater than or equal to
HIV	Human immunodeficiency virus
INH	Isoniazid
kg	Kilogram(s)
LTBI	Latent Tuberculosis Infection
<	Less than
M,C&S	Microscopy, culture and sensitivity
mg	Milligram(s)
NHMRC	National Health and Medical Research Council
%	Percent
PPD	Purified Protein Derivative
TST	Tuberculin skin test
TB	Tuberculosis

## Tuberculosis

- > Tuberculosis (TB) is caused by *Mycobacterium tuberculosis* complex (MTBC), a slow growing, and aerobic, acid-fast bacillus (AFB). The MTBC consists of *Mycobacterium tuberculosis*, and rarely *Mycobacterium bovis* and *Mycobacterium africanum*
- > Tuberculosis is a notifiable disease. The South Australian Public Health Act 2011 requires that notification should be made within three days of suspicion or confirmation to the South Australian TB Services (Telephone: 8225483 or Fax 82225398)
  - > More detail on the notification process and access to the appropriate notification form are available from the SA Health website at: URL:  
<http://www.sahealth.sa.gov.au/NotifiableDiseaseReporting>

## Tuberculosis infection

- > Inhalation of tubercle bacilli results in a primary infection which usually resolves without clinical features. Small numbers of TB bacilli can remain in a latent form commonly known as Latent Tuberculosis Infection (LTBI) and in most persons never progresses to active TB. This episode is detected by immunological testing:
  - > Tuberculin Skin test (Mantoux technique)- preferred test<sup>1</sup>
  - > Interferon Gamma Release Assay (IGRA)
- > LTBI is not infectious, but is associated with a risk of reactivation and development of active disease
  - > 10-15 % lifetime risk in a healthy adult
  - > Up to 10 % annual risk in immunocompromised
- > There is no evidence that pregnancy increases the risk of TB reactivation



## Tuberculosis disease

### Clinical features

- > Most Tuberculosis in Australia is pulmonary (60 -70 %)
- > Common symptoms of TB disease / reactivation include:
  - > Cough
  - > Fever
  - > Night sweats
  - > Weight loss
  - > Haemoptysis
- > In pregnancy the presentation is usually similar to that of the non-pregnant woman but in some can be deceptive with non-specific pregnancy like symptoms
- > TB lymphadenitis is the most common extra-pulmonary manifestation; however the disease can occur in any part of the body, including the pleura, bone, kidneys and the meninges. The range of symptoms will depend on the site of disease

### Route of transmission

- > Air-borne
  - > Pulmonary and laryngeal cases that are smear positive for AFBs on sputum sampling are potentially the most infectious
  - > Extra-pulmonary cases are usually non-infectious but can be associated with pulmonary disease
  - > High risk procedures including sputum induction, nebuliser treatment and bronchoscopy, can result in transmission of infection
- > Congenital (very rare in Australia)
  - > Maternal haematogenous spread via the umbilical vein from disseminated disease
  - > Antenatal aspiration or ingestion of infected amniotic fluid
  - > Direct from genital disease

### Infection control

- > The most important measures are the early diagnosis, and prompt treatment and isolation of a woman with suspected pulmonary TB
- > Early diagnosis in a low TB prevalence population such as Australia depends on recognition of risk factors for TB
  - > Overseas born – 80 to 90 % of annual notifications are born overseas from high TB prevalence countries
  - > Recent arrival to Australia – the risk of TB reactivation is highest in the first 5 years after infection
  - > Recent contact with a pulmonary TB case
- > Transmission-based airborne precautions should be used for all suspected or confirmed cases of pulmonary TB. These include:
  - > Placement in a negative pressure single room with separate toilet facilities
  - > Use of N95 particulate filter masks for health care worker (fit testing required) and visitors and surgical masks for patients during movement within the hospital
- > Staff who are immune-compromised should be advised about their increased susceptibility to TB infection and preferably not be involved in the direct care of infectious TB cases



## Antenatal screening

- > TB disease risk factors screening should be part of the antenatal workup
- > Antenatal tuberculin skin test (TST) screening is not routinely done because it is not recommended to treat Latent Infection during pregnancy except in certain instances
- > TST should be undertaken in those with a history of recent TB contact e.g. household or are HIV positive

## Risk factors for LTBI

- > History of past TB contact
- > In Australia, most TB (about 80 to 90 %) occurs in migrants, particularly from:
  - > South East Asia / Subcontinent
  - > Africa
  - > Papua New Guinea
- > The risk of new migrants developing active TB is greatest in the first 2-5 years after arrival
- > Immune-compromised women are at high risk of developing active TB if they are infected with *M. Tuberculosis*. However the screening tests are less predictive and a careful history of TB exposure is required

## Maternal diagnosis

- > Women who have symptoms and signs suspicious of active TB should be immediately referred to the Chest Clinic, Royal Adelaide Hospital, for further investigation
- > To help confirm diagnosis:
  - > Obtain sputum x 3 for AFBs (early morning preferred)
  - > Chest X-ray with abdominal shielding
- > Women with the following risk factors should be referred to The Chest Clinic, Royal Adelaide Hospital for further assessment:
  - > Women with HIV infection
  - > Recent arrival from area with a high prevalence of TB
  - > Women who have had close contact with infectious TB
  - > Positive TST (if this has recently been performed on site or elsewhere)

## Maternal management

### TB infection

- > Providing there is no evidence of disease, prevention treatment of TB infection is offered (6-9 months of Isoniazid) but usually deferred until 2-3 months postpartum
- > Exceptions to this include:
  - > Immune-compromised persons especially those with HIV infection
  - > Persons with evidence of recent infection

### TB disease

- > Treatment is with the standard 4 drug regimen that includes **isoniazid, rifampicin, ethambutol and pyrazinamide** (see below)
- > All patients should be considered for directly observed therapy to ensure good adherence that minimises the risk of acquired drug resistance or relapse
- > Advice on management should be sought from the SA TB Services at the Royal Adelaide Hospital Chest Clinic





## Neonatal management

- > The risk of congenital TB should be assessed by a Paediatrician at birth if:
  - > Maternal disseminated TB or pelvic TB
  - > Mother has pulmonary or extra-pulmonary disease diagnosed perinatal or immediately postpartum

## Evidence of congenital TB

- > Congenital TB is difficult to distinguish from other congenital or neonatal infections and has a high mortality if not diagnosed and treated early. Symptoms and signs are non-specific and include:
  - > Preterm birth / low birth weight
  - > Respiratory distress, fever, hepatomegaly and / or splenomegaly, poor feeding, lethargy are most frequent presenting features
- > Other possible signs include:
  - > Lymphadenopathy, abdominal distention, ear discharge, typical maculopapular, umbilicated skin lesions

## Investigations

- > Tracheal aspirate, gastric washings, urine and CSF specimens for acid fast bacillus (AFB) culture
- > Placenta for AFB culture and histology
- > Chest X-ray
- > Complete blood picture (CBP), liver function tests (LFTs), inflammatory markers

## Management

- > A four drug TB regimen that includes rifampicin, isoniazid, pyrazinamide\* and an injectable agent such as streptomycin\* or amikacin is recommended by the American Paediatric Society (Consult South Australian TB Services for further advice, RAH Chest Clinic)
  - > \* Pyrazinamide and streptomycin are not registered in Australia but are available via the Special Access Scheme
- > Exclusively breastfed infants should receive pyridoxine 5 mg daily
  - > Crush and dissolve one 25mg tablet in 5 mL water for injection to make a 5 mg/mL solution. Administer 1 mL (5mg) and discard remainder<sup>5</sup>

## No evidence of TB

- > Babies of women with confirmed pulmonary TB and taking effective treatment are not separated from the mother
  - > Commence oral Isoniazid (INH) 10 mg / kg daily
  - > Also add oral pyridoxine 5 mg daily
  - > Follow up with TST at 6 weeks, 3 and 6 months
  - > If TST is abnormal ( $\geq 5$  mm), assess for disease, and use a low threshold for 4 drug treatment if active TB cannot be confidently excluded. Minimum will be 9 months of INH in the healthy baby
  - > If TST is negative at 6 months INH can be discontinued
  - > Bacille Calmette-Guérin (BCG) vaccine is no longer routinely recommended but should be considered in those with a significant likelihood of future exposure to TB



## Tuberculosis drugs and pregnancy

### First line drugs

#### Isoniazid

- > ADEC Category A. Widely used in pregnancy since the 1970s for the treatment of active TB disease (5 mg / kg once daily, maximum 300 mg)
  - > Increased risk of hepatotoxicity has been reported in pregnancy (approximately 2 %)<sup>2</sup>
  - > Other side effects include nausea, rash arthralgia's, memory loss, peripheral neuropathy

#### Rifampicin

- > ADEC Category C. Widely used in pregnancy since the 1970s for the treatment of active TB disease (10 mg / kg once daily, maximum 450 mg if < 50 kg or 600 mg if ≥ 50 kg)
  - > Side effects: hepatotoxicity, bone marrow suppression, nausea rash and polyarthralgia
- > Reported to cause haemorrhagic tendency in the newborn when given late in pregnancy.
  - > Give vitamin K supplementation to the mother if rifampicin is used in the last few weeks of pregnancy
  - > Administer vitamin K postpartum to the baby (as per NHMRC recommendations)
- > Rifampicin is a powerful cytochrome inducer and has numerous drug interactions

#### Pyrazinamide

- > Not registered in Australia, available via the Special Access Scheme
- > Limited pregnancy data available, but no reports of fetal malformations or significant adverse events (25 mg / kg once daily, maximum 2 g)
  - > Side effects – hepatotoxicity, rash, arthralgia's

#### Ethambutol

- > ADEC Category A. Safe to use in pregnancy (15 mg / kg once daily)
  - > Side effects: optic neuritis (common), headache, confusion, nausea, vomiting and malaise

#### Pyridoxine (B6)

- > Used as a supplement with isoniazid to prevent peripheral neuropathy (25 mg once daily)

### Breastfeeding

- > The above drug treatments (isoniazid, rifampicin, pyrazinamide, ethambutol and pyridoxine) are excreted in breast milk however breastfeeding should be encouraged.
- > The amount of medication in the breast milk does not provide sufficient TB treatment or prophylaxis for the breastfed infant
- > Breastfed babies that are not receiving TB drug therapy should be given 5mg of pyridoxine daily on the days that their mother receives her isoniazid therapy.
- > If a breastfeeding mother and baby are both on anti-TB therapy, there is a small risk of toxic levels in the baby
- > Where practical, advise the mother to take her medication immediately after a breastfeed to minimise this risk to the baby



## Tuberculin skin test (TST) (mantoux skin test)

### Background

- > Hypersensitivity to tuberculin Purified Protein Derivative (PPD) follows either natural infection with either Mycobacterium tuberculosis or with mycobacteria that induce cross-reactivity, or Bacille Calmette-Guerin (BCG) vaccination
- > The tuberculin (Mantoux) skin test is used:
  - > To detect latent infection in contacts of patients with tuberculosis (TB) and other potentially infected individuals
  - > As an aid to the diagnosis of TB
  - > As a prelude to vaccination with BCG<sup>3</sup>

### Tuberculin skin test (TST)

- > The TST is not affected by pregnancy
- > Intradermal injection (into the skin of the upper third of the flexor surface of the forearm, producing a peau d'orange bleb 4 to 10 mm in diameter) of 0.1 mL of 5 Tuberculin Units / 0.1mL solution of purified protein derivative (PPD), ("Tubersol" supplied by Sanofi-Pasteur) with induration measured at 48-72 hours. In certain circumstances, 2-step skin testing may be required. It is used to detect individuals previously infected who may test negative to tuberculin initially, but who show a strong reaction if the same procedure is repeated 1 to 2 weeks later

### Interpretation of tuberculin skin test positivity

- > Induration (not erythema)  $\geq$  5 mm diameter in pregnant women with human immunodeficiency virus (HIV) infection, close contact with someone with infectious TB, or a chest X-ray suggestive of previous TB
- > Induration (not erythema)  $\geq$  10 mm diameter in recent arrivals (< 5 years) from high prevalence areas, injecting drug users, residents / employees of prisons, homeless shelters, residential facilities for acquired immunodeficiency syndrome (AIDS)
- > The reaction to PPD may be suppressed by viral infection, live vaccines (not used in pregnancy), recent surgery, sarcoidosis, immunosuppressant drugs and illnesses such as Hodgkin's disease, lymphoma and HIV infection. The reaction also wanes with age, so that most adults vaccinated with BCG in childhood have negative tuberculin reactions





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## Useful web sites:

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## Acknowledgements

The South Australian Perinatal Practice Guidelines gratefully acknowledge the contribution of clinicians and other stakeholders who participated throughout the guideline development process particularly:

### Write Group Lead

Dr Rick Stapledon  
Dr Simon Cameron  
Prof Paul Goldwater

### Write Group Members

Catherine Leggett

### Other major contributors

SAPPG Work Group 2004-2014

### SAPPG Management Group Members

Sonia Angus  
Dr Kris Bascomb  
Lyn Bastian  
Elizabeth Bennett  
Dr Feisal Chenia  
John Coombas  
A/Prof Rosalie Grivell  
Dr Sue Kennedy-Andrews  
Jackie Kitschke  
Catherine Leggett  
Dr Anupam Parange  
Dr Andrew McPhee  
Rebecca Smith  
A/Prof John Svigos  
Dr Laura Willington



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## Document Ownership & History

**Developed by:** SA Maternal, Neonatal & Gynaecology Community of Practice  
**Contact:** [HealthCYWHSPerinatalProtocol@sa.gov.au](mailto:HealthCYWHSPerinatalProtocol@sa.gov.au)  
**Endorsed by:** SA Safety and Quality Strategic Governance Committee  
**Next review due:** 17 June 2019  
**ISBN number:** 978-1-74243-100-0  
**PDS reference:** CG144  
**Policy history:** Is this a new policy (V1)? **N**  
Does this policy amend or update an existing policy? **Y**  
If so, which version? **V3**  
Does this policy replace another policy with a different title? **N**  
If so, which policy (title)?

Approval Date	Version	Who approved New/Revised Version	Reason for Change
15 Jun 2018	V3.1	SA Safety and Quality Strategic Governance Committee	Review date extended to 5 years following risk assessment. New template.
17 Jun 2014	V3	SA Safety and Quality Strategic Governance Committee	Reviewed
21 Apr 2009	V2	Maternal and Neonatal Clinical Network	Reviewed
27 Apr 2004	V1	Maternal and Neonatal Clinical Network	Original approved version.

