South Australian Perinatal Practice Guidelines

Mycobacterium Tuberculosis in pregnancy

Mycobacterium tuberculosis

- Tuberculosis (TB) is caused by *Mycobacterium tuberculosis* complex, a slow growing, and aerobic, acid-fast bacillus. Mycobacterium TB complex consists of Mycobacterium tuberculosis, and rarely *Mycobacterium bovis* and *Mycobacterium africanum*
- In Australia *Mycobacterium tuberculosis* is the cause of TB (NHMRC 2008)
- Tuberculosis is a notifiable disease. Notification should be made to the Communicable Disease Control Branch of the South Australian Department of Human Services as soon as possible and at least within three days of suspicion of diagnosis (DHS 2003)
- The appropriate notification form for reporting a notifiable disease or related death in South Australia may be downloaded and is available from:
- URL: http://www.dh.sa.gov.au/pehs/PDF-files/notifiable-disease-form.pdf

Clinical features

- Most people infected with Mycobacterium tuberculosis remain asymptomatic
- Common symptoms of TB disease / reactivation include:
  - Cough
  - Fever
  - Sweats
  - Weight loss
  - Haemoptysis
- TB lymphadenitis is the most common extrapulmonary manifestation; however the disease can occur in any part of the body, including the meninges, bone and kidneys
  - Concomitant nonspecific symptoms include fever, weight loss and night sweats (Knight et al. 2009)

Route of transmission

- Air-borne
- Lung disease is the most common form of TB, accounting for 60 to 70 % of notified TB cases in Australia. “Open” TB describes a case of pulmonary TB in whom tubercle bacilli gain access to the airways and are coughed and expectorated into the environment

Infection control

- Transmission-based airborne precautions (‘negative pressure’ single room with own toilet facilities, N95 mask, dedicated equipment) should be used when caring for a woman and or baby suspected of having “open” tuberculosis infection
- Preferably ‘immune’ health care workers (i.e. those that have been vaccinated with BCG) should be rostered to care for women / babies with tuberculosis. However, N95 mask is regarded as the most important infection control approach

Literature Review

ISBN number: UNKNOWN
Endorsed by: SA Maternal & Neonatal Clinical Network
Contact: South Australian Perinatal Practice Guidelines workgroup at: cywhs.perinatalprotocol@health.sa.gov.au

Government of South Australia
SA Health

Mycobacterium Tuberculosis in pregnancy

- In Australia, about 1000 cases of TB are notified to Australian health authorities each year (NHMRC 2008)
- The development, clinical presentation and progression of tuberculosis are not altered by pregnancy
- There is no evidence that pregnancy increases the risk of inactive TB becoming active
- There is a high risk of resistance to Isoniazid (INH), particularly for women with HIV, recent arrivals from an area of high incidence (defined as countries with an annual incidence >100 per 100,000 population (see http://www.who.int/tb/en/) and those who have had previous anti-TB treatment (Palasanthiran et al. 2002)
- Most cases of neonatal TB occur as a result of airborne spread after delivery (Palasanthiran et al. 2002)
- The tuberculin (mantoux) skin test is likely to be negative for the first few weeks of life, even if the neonate has TB. Conversion may take up to six months (Palasanthiran et al. 2002)

Antenatal screening

- Screening is recommended for women from high risk groups for TB infection (see below), including their contacts
- In Australia, most TB (about 70 to 80 %) occurs in migrants, particularly from:
    - South East Asia
    - Pacific Islands
    - Africa
    - Southern and Eastern Europe
    - Latin America
- High TB rates seen in people from Ethiopia, Somalia and the Sudan reflect recent changes in the composition of Australia's migrant and refugee intake (NHMRC 2008)
- Rates of TB are also high amongst indigenous groups (Aborigines and Torres Strait Islanders) and in Papuan New Guineans living in high incidence areas of Australia (NHMRC 2008)
- Immunocompromised women are at high risk of developing active TB if they are infected with Mycobacterium TB

Maternal diagnosis

- Refer to The Chest Clinic, Royal Adelaide Hospital, 275 North Terrace for Tuberculin skin test (TST) and further management for the following at risk pregnant women:
    - Women with HIV infection
    - Recent arrival from area with a high prevalence of TB
    - Women who have had close contact with infectious TB
    - Women who are **symptomatic** (have symptoms and signs compatible with TB) should be immediately referred to the Chest Clinic, Royal Adelaide Hospital, 275 North Terrace

Positive TST (if this has recently been performed on site or elsewhere)

- Refer to The Chest Clinic, Royal Adelaide Hospital, 275 North Terrace where she will

ISBN number: UNKNOWN
Endorsed by: SA Maternal & Neonatal Clinical Network
Contact: South Australian Perinatal Practice Guidelines workgroup at: cywhs.perinatalprotocol@health.sa.gov.au

Mycobacterium Tuberculosis in pregnancy

- be examined for signs of TB
- undergo a Chest X-ray with appropriate abdominal shielding

Maternal management

No evidence of TB

- All at risk women should be referred to the Chest Clinic, Royal Adelaide Hospital, 275 North Terrace
- The Clinic will reassess need of oral Isoniazid (INH) prophylaxis 300 mg daily post partum

Evidence of old pulmonary TB

- Refer to Chest Clinic, Royal Adelaide Hospital, 275 North Terrace for assessment
- i.e. High risk (e.g. HIV infection, diabetes, chronic renal failure, malignancy) or Mantoux conversion within the last 2 years
- If indicated, The Chest Clinic will provide INH prophylaxis 300 mg daily from the second trimester (give with oral Pyridoxine 50 mg daily)

Evidence of active TB

- Refer to Chest Clinic, Royal Adelaide Hospital, 275 North Terrace for treatment
- Immediate drug treatment will be provided by the Chest Clinic
- To help confirm diagnosis:
  - Obtain sputum x 3 MC&S, ZN
  - Obtain gastric washings x 3 MC&S, ZN
  - Obtain urine MC&S, ZN

Low risk of resistance to INH

- Refer to Chest Clinic, Royal Adelaide Hospital, 275 North Terrace
  - The Clinic will commence oral INH 300 mg daily (give with oral Pyridoxine 50 mg daily) and continue for nine months
  - plus oral Rifampicin 450 mg daily if weight is < 50 kg; 600 mg daily if weight is ≥ 50 kg and continue for nine months
  - plus oral Ethambutol 15 mg / kg daily and continue for two months
  - Use of Pyrazinamide is optional

High risk of resistance to INH

Under the auspices of the Chest Clinic

- Commence oral INH
  - 300 mg daily (give with oral Pyridoxine 50 mg daily) and continue for six months
- Commence oral Rifampicin
  - 450 mg daily if weight is < 50 kg
  - 600 mg daily if weight is ≥ 50 kg and continue for six months

ISBN number: UNKNOWN
Endorsed by: SA Maternal & Neonatal Clinical Network
Contact: South Australian Perinatal Practice Guidelines workgroup at: cywhs.perinatalprotocol@health.sa.gov.au

Government of South Australia
SA Health

Mycobacterium Tuberculosis in pregnancy

- Commence oral Ethambutol
  - 15 mg / kg daily and continue for two months
- Commence oral Pyrazinamide
  - 1.5 g daily if weight < 50 kg
  - 2 g daily if weight ≥ 50 kg and continue for two months
- Maternal TB is likely to be associated with haematogenous spread. The placenta or maternal genital tract may become infected, and result in congenital infection (very rare)

Neonatal management

- Paediatrician at birth to assess neonate for clinical evidence of congenital TB if:
  - Maternal active pulmonary TB
  - Mother is on anti-TB treatment (not infectious)
  - Mother has completed anti-TB treatment (not infectious)
  - Obtain opinion from The Chest Clinic, Royal Adelaide Hospital, 275 North Terrace

Evidence of congenital TB:

- 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

- These should be conducted by the Chest Clinic
  - Chest X-ray
  - Gastric aspirates x 3
  - Lumbar puncture (if clinical evidence present)

No evidence of TB

Follow the advice of the Chest Clinic

- If the mother has completed anti-TB treatment and the baby has no clinical evidence of congenital TB, follow up with a TST at three months
- Babies of women with active TB or non infectious but on anti-TB treatment should:
- Under the advice of the Chest Clinic:
  - commence oral Isoniazid (INH)
  - 5 – 15 mg / kg daily for six months
  - Add oral Pyridoxine 10 mg daily for breastfed infants
  - Follow up with TST at 3 and 6 months
  - If TST is negative at 6 months Bacille Calmette-Guérin (BCG) vaccine should be given if there is any possibility of future exposure to TB

Evidence of TB

Under the auspices of the Chest Clinic

- Commence oral INH
  - 5 – 15 mg / kg daily for six months
  - Add oral Pyridoxine 10 mg daily for breastfed infants
- Commence oral Rifampicin
  - 10 – 20 mg / kg daily for 6 months
- Commence oral Pyrazinamide
  - 15 – 30 mg / kg daily until drug susceptibility results are available
- Commence intravenous Amikacin

ISBN number: UNKNOWN
Endorsed by: SA Maternal & Neonatal Clinical Network
Contact: South Australian Perinatal Practice Guidelines workgroup at: cywhs.perinatalprotocol@health.sa.gov.au

Government of South Australia
SA Health

Mycobacterium Tuberculosis in pregnancy

- 15 mg / kg daily until drug susceptibility results are available
- Ethionamide or Prothionamide
  - 15 – 20 mg / kg daily until drug susceptibility results are available

Breastfeeding

- The above drug treatments are excreted in breast milk
- If a breastfeeding mother and baby are both on anti-TB therapy, there is a small risk of toxic levels in the baby
- Advise the mother to take her medication immediately after a breastfeed to minimize 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 (NHMRC 2008)

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) ≥ 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) ≥ 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 a 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

ISBN number: UNKNOWN
Endorsed by: SA Maternal & Neonatal Clinical Network
Contact: South Australian Perinatal Practice Guidelines workgroup at: cywhs.perinatalprotocol@health.sa.gov.au

Government of South Australia
SA Health

Mycobacterium Tuberculosis in pregnancy

References

1. National Health and Medical Research Council (NHMRC). The Australian Immunisation Handbook, 9th ed. Canberra: Australian Government Publishing Service; 2008. Available from URL: http://www.health.gov.au/internet/immunise/publishing.nsf/Content/Handbook-tuberculosis
2. Department of Health (DoH). Government of South Australia. Diseases Notifiable Under Section 30 of the Public and Environmental Health Act 1987. Department of Health [online] Nov 2008 [cited 2008 November 25]; [1 screen]. Available from URL: http://www.dh.sa.gov.au/pehs/PDF-files/0811-notifiable-disease-list.pdf
3. Palasanthiran P, Starr M, Jones C, editors. Management of perinatal infections. Sydney: Australasian Society for Infectious Diseases (ASID); 2002, emendations 2006.
4. Knight M, Kurinczuk J, Nelson-Piercy C, Spark, P, Brocklehurst P on behalf of UKOSS. Tuberculosis in pregnancy in the UK. BJOG 2009; 116: 584-588.

Useful web site:

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

Queensland guidelines for the treatment of tuberculosis in pregnancy. Available from URL: http://www.health.qld.gov.au/ph/documents/qtbcc/31044.pdf

Version control and change history

PDS reference: OCE use only

Version	Date from	Date to	Amendment
1.0	27 Apr 04	21 Apr 09	Original version
2.0	21 Apr 09	Current	reviewed

ISBN number: UNKNOWN
Endorsed by: SA Maternal & Neonatal Clinical Network
Contact: South Australian Perinatal Practice Guidelines workgroup at: cywhs.perinatalprotocol@health.sa.gov.au

Government of South Australia
SA Health