South Australian Perinatal Practice Guidelines

Toxoplasmosis in pregnancy

The 'Management of Perinatal Infections' guideline for Toxoplasmosis in pregnancy by the Australasian Society for Infectious Diseases 2002, emendations 2006 has been used to inform this practice guideline.

Toxoplasmosis

- Toxoplasmosis is caused by a parasite, *Toxoplasma gondii*. It is usually asymptomatic or may have mild non-specific symptoms (e.g. malaise, fever, and lymphadenopathy)
- Toxoplasma remains latent for life, with clinical reactivation confined to severely immunosuppressed individuals (Gilbert 2002)
- Infants of women who are seropositive before pregnancy are not at risk

Route of transmission

- Toxoplasmosis is acquired through
  - Eating raw or undercooked meat
  - Not washing hands thoroughly after handling raw meat or gardening, or contact with cats faeces (directly or indirectly through the soil, or possibly contaminated raw vegetables or fruits) (Di Mario *et al.* 2009)
- Direct contact with cats is rarely a source of transmission (Gilbert 2002)

Infection precautions

- Standard precautions

Literature review

- In Australia, primary infection with toxoplasmosis during pregnancy is rare (Gilbert 2002)
- The risk of maternal-fetal transmission and abnormalities related to congenital toxoplasmosis infection is related to the gestation at maternal seroconversion

≤ 13 week's gestation:

- 5 - 15 % risk of maternal-fetal transmission
- 60 - 80 % chance of abnormalities if infected

Second trimester:

- 25 - 40 % risk of maternal-fetal transmission
- 15 - 25 % chance of abnormalities if infected

Third trimester:

- 30 - 75 % risk of maternal-fetal transmission

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36 week's gestation:

- 72 % risk of maternal-fetal transmission
- 2 - 10 % chance of abnormalities if infected (Dunn et al. 1999; Palasanthiran et al. 2002)
- Abnormalities following severe congenital toxoplasmosis are more common amongst babies of women who seroconverted early in their pregnancy (Dunn et al. 1999; Langford 2002)
- Abnormalities related to congenital toxoplasmosis are:
  - Chorioretinitis
  - Hydrocephalus
  - Intracranial calcification
  - Mental retardation

Precautions to avoid maternal exposure to toxoplasmosis

Encourage all pregnant women to:

- Avoid raw / undercooked meat
- Avoid contamination of chopping boards, etc. with raw meat
- Wash hands after disposal of cat litter, gardening or handling raw meat
- Peel or wash raw fruit and vegetables thoroughly to remove contaminating soil (Gilbert 2002)

Maternal exposure

- Women who are pregnant in South Australia are not routinely screened for the presence of IgG antibodies or toxoplasma-specific IgM antibodies
- Consider serology (IgG and IgM antibodies to toxoplasma gondii) for women who are pregnant with symptoms of acute toxoplasmosis (e.g. malaise, fever, lymphadenopathy)

IgG and IgM negative

- Indicates no past infection
- Educate regarding precautions to avoid infection with toxoplasmosis
- Repeat if symptomatic

IgG positive IgM negative

- Indicates past infection

IgG and IgM positive

- Indicates possible recent infection
- IgM can remain positive for months or years; IgA, rising IgG level and / or low IgG avidity are more specific for recent infection
- Repeat serology for IgM, IgA, and / or IgG titre and avidity
- A repeat high positive IgM, positive IgA and low IgG avidity is consistent with recent toxoplasmosis

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Maternal management

Following confirmation of recent maternal toxoplasmosis

Investigations

- Ultrasound to detect abnormalities
- Amniocentesis for polymerase chain reaction (PCR) and / or culture at 18 – 20 weeks gestation or if ≥ 4 weeks after maternal infection
- PCR on amniotic fluid has a high sensitivity and specificity for the diagnosis of fetal infection (Karunajeewa et al. 2001)
- If the ultrasound and amniocentesis are negative, consider pharmacological treatment as below if maternal infection is fairly certain

Note: A Cochrane Review has shown there have been no randomised trials of treatment for toxoplasmosis in pregnancy (Peyron *et a.l* 2009). Treatment decisions should bear this in mind

Infection in first 12 weeks gestation

- Administer spiramycin [Rovamycine®] Not in stock in South Australia.
- May be able to obtain supply from Monash Medical Centre Pharmacy or otherwise within a week from overseas via LINK Pharmaceuticals Bridgepoint Mosman NSW 2088 (02) 9960 0150
- See Drug Interactions listed in Neonatal Management section.
    - Mild to moderate infections: 6,000,000 to 9,000,000 int. units (4 - 6 capsules of spiramycin [Rovamycine®] "500" per day) in 2 divided doses
    - Severe infections: 12,000,000 to 15,000,000 int. units (8 - 10 capsules of spiramycin [Rovamycine®] "500" per day) in 2 divided doses
- Counsel woman / partner regarding termination if amniocentesis PCR positive

Infection from 13 to 27 weeks

- Administer spiramycin [Rovamycine®] (sulfadoxine and pyrimethamine is no longer available)
- Mild to moderate infections: 6,000,000 to 9,000,000 int. units (4 - 6 capsules of spiramycin [Rovamycine®] "500" per day) in 2 divided doses
    - Severe infections: 12,000,000 to 15,000,000 int. units (8 - 10 capsules of spiramycin [Rovamycine®] "500" per day) in 2 divided doses
- If there is delay in obtaining spiramycin, administer **Atovaquone** 750 mg twice daily (or 1,500 mg once daily if necessary) with food for 21 days
- Alternatively, Azithromycin 500 mg daily for 3 days repeated weekly for 4 weeks may be tried. Its efficacy has not been proven but it has an IC_{50} of 1.2 mg / mL and concentrates in tissues, especially the placenta (Peyron and Wallon 2001)
- Counsel woman / partner regarding termination if ultrasound abnormal

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Infection from 28 to 42 weeks

- Administer spiramycin [Rovamycine®]
  - Mild to moderate infections: 6,000,000 to 9,000,000 int. units (4 - 6 capsules of spiramycin [Rovamycine®] "500" per day) in 2 divided doses
  - Severe infections: 12,000,000 to 15,000,000 int. units (8 - 10 capsules of spiramycin [Rovamycine®] "500" per day) in 2 divided doses

OR if unavailable…

- Administer **Atovaquone** 750 mg twice daily (or 1,500 mg once daily if necessary) with food for 21 days
- Alternatively, Azithromycin 500 mg daily for 3 days repeated weekly for 4 weeks may be tried

Intrapartum care

- Paediatrician at delivery
- Following delivery, newborn assessment should include physical examination for evidence of congenital toxoplasmosis (including ophthalmological examination and cerebral ultrasound)
- Placenta for histology / PCR
- May direct room-in with mother following initial assessment in nursery
- Use standard precautions (Parasites may be excreted in urine and other body fluids. A case of toxoplasmosis acquired during performance of an autopsy has been described) (Neu 1967)

Postnatal follow up

- Involvement of a specialist infectious diseases physician may be helpful

Neonatal management

Investigations

- Ophthalmological assessment and cerebral ultrasound
- Infant whole blood for PCR, and serology for toxoplasma-specific IgM and / or IgA, persistent IgG
- Cerebrospinal fluid for PCR

Asymptomatic congenital toxoplasmosis

- The majority of infected babies will be asymptomatic
- Includes babies with positive serology and / or IgG that persists for more than 6 months

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Symptomatic congenital toxoplasmosis

- A small minority of babies will have symptomatic congenital toxoplasmosis (IgM or PCR positive with an IgG titre significantly greater than mothers) e.g.:
  - Chorioretinitis / retinal scarring
  - Intracranial calcification
  - Hydrocephalus
  - Hepatosplenomegaly
  - Pneumonia
  - Thrombocytopenia
  - Lymphadenopathy
  - Myocarditis and IgM positive and / or abnormal placenta and / or cerebrospinal fluid abnormality (PCR positive)

Drug treatment

- Administer spiramycin oral syrup: available in 75 000 units / mL (25 mg / mL)
  - **Neonate:** Dosage by body weight; usual dosage 150,000 int. units / kg (50 mg / kg) twice daily

Drug Interactions:

- **Substrate** of CYP3A4 (major)
- CYP3A4 inducers: CYP3A4 inducers may decrease the levels/effects of spiramycin. Example inducers include aminoglutethimide, carbamazepine, nafcillin, nevirapine, phenobarbital, phenytoin, and rifamycins
- CYP3A4 inhibitors: May increase the levels/effects of spiramycin. Example inhibitors include azole antifungals, ciprofloxacin, clarithromycin, diclofenac, doxycycline, erythromycin, imatinib, isoniazid, nefazodone, nicardipine, propofol, protease inhibitors, quinidine, and verapamil
- Levodopa/carbidopa: Spiramycin has been reported to decrease carbidopa absorption and decrease levodopa concentrations

Follow up

- Continue above drug treatment for the first 12 months
- Repeat IgG at 6 months
- Regular paediatric / infectious diseases review is recommended

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10. British National Formulary for Children (BNFC). Drugs for toxoplasmosis – Spiramycin. London: The Royal Pharmaceutical Society of Great Britain; 2009.

Useful web sites:

Organisation of teratology information specialists – Toxoplasmosis and pregnancy. Available from URL:
http://www.otispregnancy.org/pdf/toxoplasmosis.pdf
South Australian Department of Health. You've got what – Toxoplasmosis
http://www.dh.sa.gov.au/pehs/Youve-got-what/ygw-toxoplasmosis.pdf

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Abbreviations

e.g.	For example
et al	And others
IgG	Immunoglobulin G
IgA	Immunoglobulin A
IgM	Immunoglobulin M
PCR	Polymerase chain reaction
WCH	Women's and Children's Hospital
mg	Milligram/s
mL	Millilitre/s

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