South Australian Perinatal Practice Guidelines

Cytomegalovirus in Pregnancy

Literature review

- The incidence of primary cytomegalovirus (CMV) infection in pregnancy in Australia is estimated to be 6 per 1,000 pregnancies
- Most primary CMV infections are asymptomatic and carry a 50 % risk of transmission to the fetus
- In Australia CMV causes abnormalities (200 – 600 babies each year), such as:
  - Deafness
  - Mental disability
  - Hepatitis
  - Pneumonitis
  - Blindness

  (Nigro et al. 1999; Rawlinson and Scott 2003)

Cytomegalovirus

- Cytomegalovirus (CMV) is a beta herpes virus with a worldwide distribution (NHMRC 2008)
- After primary infection, the virus remains present in the resting or latent phase (indicated by CMV specific IgG seropositive result)
- The virus can reactivate spontaneously or in conditions where immunity is suppressed including pregnancy
- Primary infection is limited to women who are CMV IgG negative. CMV infection leads to the production of CMV-specific IgM production which can persist for up to 2-3 years
- Reactivation occurs when CMV is isolated in a woman known to have CMV IgG

Route of transmission

- CMV is shed in saliva, urine and breast milk. Intermittent shedding is common, particularly in infected infants, children and pregnant women (Rawlinson and Scott 2003)
- Infection with CMV can also occur via:
  - Respiratory airborne droplet
  - Sexual contact
  - Blood transfusions
  - Vertical transmission from mother to fetus

Infection precautions

- Standard precautions (including the use of gloves and regular handwashing) should be used when caring for a woman or baby suspected of infection with CMV

Education

- Advise all pregnant women about simple infection control precautions e.g. wear gloves for nappy changes, hand washing after contact with soiled nappies or respiratory secretions

Diagnosis

- Obtain maternal serology for CMV

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Cytomegalovirus in Pregnancy

- IgG positive, IgM negative indicates past exposure
- IgG negative or positive with IgM positive requires further testing in 2-4 weeks. (Interpretation of CMV IgM results in pregnancy requires specialist virological interpretation)
- Seroconversion (IgG negative to positive) or a significant rise in IgG indicates a recent primary CMV infection

Serologic testing for cytomegalovirus is recommended for the following women in pregnancy:

- History suggestive of CMV illness
- Exposure to known CMV infected individual or blood product
- Immunocompromised
- Abnormalities on routine antenatal ultrasound (usually at 18 weeks)

High risk groups for primary CMV

- Day care workers (incidence of 11 % per annum)
- Parents with a child in day care (incidence of 20 – 30 % per annum)

Education

- Advise all pregnant women about simple infection control precautions e.g. wear gloves for nappy changes, hand washing after contact with soiled nappies or respiratory secretions

Management of primary maternal CMV infection

Clinical picture

- Women may present with a mononucleosis-like syndrome, flu-like symptoms, infection of the gastrointestinal tract, abnormal liver function or rashes

CMV infection management

- Supportive treatment

Fetal risk assessment

- Fetal diagnosis is best achieved by a combination of fetal ultrasound, amniocentesis and + / - fetal serology
- Positive results do not predict any degree of fetal damage

Ultrasound

- Consider serial fetal ultrasound to detect features associated with symptomatic congenital CMV infection (see below) (sensitivity around 30 – 50 %)

Amniocentesis

- Consider amniocentesis for polymerase chain reaction (PCR) and culture

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- Diagnosis by amniocentesis and testing amniotic fluid by PCR is about 45 % sensitive overall if performed < 20 weeks and 80 – 100 % sensitive if performed > 20 weeks gestation. Specificity approaches 100 %. Viral loads of $>10^3$ copies per mL are strongly correlated with symptomatic fetal infection. Virus isolation is less sensitive at 18 % and 56 % respectively

Fetal blood sampling

- Consult with a feto-maternal specialist for consideration of fetal blood sampling
- Consider fetal blood sampling for complete blood count, liver function tests, CMV-IgM and CMV PCR if > 21 weeks. Experience with fetal blood sampling is limited. CMV-IgM performed from 21 weeks is 50 – 80 % sensitive

Features associated with symptomatic congenital infection:

- Microcephaly
- Ascites
- Hydrops fetalis
- Oligo or polyhydramnios
- Hepatomegaly
- Pseudomeconium ileus
- Hydrocephalus (ventricular dilation)
- Intrauterine growth restriction (IUGR)
- Pleural or pericardial effusions
- Intracranial calcification
- Abdominal calcification

Maternal counselling

- Women with amniotic fluid (AF) positive samples by PCR or culture for CMV should be informed of their option to continue the pregnancy or consider termination (depending on gestational age)
- However, caution should be advised when interpreting findings as features associated with symptomatic congenital infection are not always predictive of the degree of fetal damage
- The risk of severe adverse neonatal neurological outcome is highest after primary infection in the first half of pregnancy

Features of fetal infection in early pregnancy include:

- Small for gestational age
- Microcephaly
- Intracranial calcifications

Features of fetal infection in late pregnancy include:

- Acute visceral disease (hepatitis, pneumonia, purpura and severe thrombocytopenia)

Future pregnancies

- Explain to the woman that the risk of congenital CMV infection after primary maternal CMV infection remains elevated for up to four years post sero-conversion (highest risk is in the first two years post seroconversion). The overall risk is 12.7 % post

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seroconversion and decreases to baseline 1 % risk by about 4 years post seroconversion. This information may be helpful in relation to the timing of a subsequent pregnancy

Congenital CMV management

- No measures are available for the prevention or treatment of congenital CMV

Maternal primary CMV infection

- There is a 50 % risk of transmission of CMV to the newborn
- The newborn will be symptomatic in 10 % of cases, and carry a 90 % risk of sequelae including:
  - Mortality rate 10 – 30 %
  - Neurological abnormalities (microcephaly, seizures, chorioretinitis, mental retardation)
  - Hearing loss (rate 18 %)

Maternal non-primary CMV infection (reactivation or reinfection)

- There is a ≤ 1 % risk of transmission of CMV to the newborn
- Most newborns will have asymptomatic congenital CMV (≥ 99 %)
- Of these, approximately 5 % will suffer sensory neural hearing loss and 2 % will suffer chorioretinitis
- If hearing is preserved at one year of age, intellectual development is unlikely to be affected

Management of the newborn

- Paediatrician at birth
- Detailed physical examination

Investigations

- Ophthalmology examination
- Cranial ultrasound (hydrocephaly)
- CT of brain (signs of intracranial calcification, ventriculomegaly, cerebral atrophy)
- Consider magnetic resonance imaging (MRI)

Laboratory investigations

- Should be done before 3 weeks of age
- Serology for CMV IgM, and viral detection by PCR (positive result indicates congenital CMV)
- Viral culture of urine and nasopharyngeal aspirate

Follow up

- Paediatric review of asymptomatic infants with congenital CMV every 3 – 6 months for the first 2 years (include neurodevelopmental assessment)
- The frequency of paediatric review of symptomatic infants with congenital CMV will depend on the extent of organ involvement

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For further information, follow link to Victorian Neonatal Handbook guideline on Cytomegalovirus infection
http://www.netsvic.org.au/nets/handbook/index.cfm?doc_id=4972#CMV

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3. Communicable Diseases Network of Australia (CDNA). Infection Control Guidelines for the prevention of transmission of infectious diseases in the health care setting. Part 4 – Managing infectious diseases in health care setting. Australian Government Department of Health and Ageing. Commonwealth of Australia 2004. Available from URL: http://www.health.gov.au/internet/main/publishing.nsf/Content/icg-guidelines-index.htm
4. Rawlinson W, Scott G. Cytomegalovirus. A common virus causing serious disease. Aust Family Physician 2003; 32: 789- 93.
5. National Health and Medical Research Council (NHMRC). The Australian Immunisation Handbook, 9th ed. Canberra: Australian Government Publishing Service; 2008.

Other useful sites

Otis pregnancy website: Available from URL:
http://www.otispregnancy.org/otis_fact_sheets.asp
http://otispregnancy.org/pdf/cytomegalovirus.pdf

SA Health You've got what website: Available from URL:
http://www.dh.sa.gov.au/pehs/Youve-got-what/ygw-cytomegalovirus-cmv.pdf

Centers for Disease Control and Prevention (CDC): Available from URL
http://www.cdc.gov/cmv/pregnancy.htm

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Version control and change history

PDS reference: OCE use only

Version	Date from	Date to	Amendment
1.0	08 April 04	05 May 09	Original version
2.0	05 May 09	current	

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