

Cytomegalovirus

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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

The purpose of this guideline is to provide clinicians with information for management of cytomegalovirus infection in pregnancy. It includes details on indications for testing, referral, diagnosis and counselling. Newborn assessment and follow-up is also described.

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Summary of Practice Recommendations

Standard precautions should be used when caring for a woman or baby suspected of infection with CMV

Women should be tested for CMV infection if they have a history suggestive of CMV illness, exposure to known CMV infected individual or blood product, are immunocompromised or have abnormalities on routine antenatal ultrasound.

CMV screening should include IgG and IgM antibodies. Further CMV avidity testing may be required.

Women require specialist counselling as there are no measures available for the prevention or treatment of congenital CMV. Timely referral is paramount.

Fetal diagnosis is best achieved by a combination of fetal ultrasound, amniocentesis and + / - fetal serology.

Specific clinical, laboratory and radiological assessment of the newborn is required.

Asymptomatic babies also require paediatric follow-up for 2 years.

Women should be informed that risk of congenital CMV infection after primary maternal CMV infection remains elevated for up to four years post sero-conversion.

Abbreviations

AF	Amniotic fluid
ASID	Australasian Society for Infectious Diseases
CDNA	Communicable diseases network of Australia
CMV	Cytomegalovirus
et al.	And others
IgG	Immunoglobulin G
IgM	Immunoglobulin M
IUGR	Intrauterine growth restriction
MRI	Magnetic resonance imaging
mL	Millilitre/s
NHMRC	National Health and Medical Research Council
%	Percent
PCR	Polymerase chain reaction



Introduction

- > The incidence of primary cytomegalovirus (CMV) infection in pregnancy in Australia is estimated to be 6 per 1,000 pregnancies¹
- > 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^{2,4}:
 - > Deafness
 - > Mental disability
 - > Hepatitis
 - > Pneumonitis
 - > Blindness

Cytomegalovirus

- > Cytomegalovirus (CMV) is a beta herpes virus with a worldwide distribution⁵
- > 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 women⁴
- > Infection with CMV can also occur via:
 - > Sexual contact
 - > Blood transfusions
 - > Vertical transmission from mother to fetus

Infection precautions

- > Standard precautions (including the use of gloves and regular hand washing) 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. hand washing after contact with soiled nappies or respiratory secretions

Diagnosis

- > Obtain maternal serology for CMV
- > 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 –see ASID guideline for more detail: <https://www.asid.net.au/documents/item/368>)
- > 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)

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 (sensitivity around 30 – 50 %)

Amniocentesis

- > Consider amniocentesis for polymerase chain reaction (PCR) and culture
- > 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 >10³ 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 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 $\leq 1\%$ risk of transmission of CMV to the newborn
- > Most newborns will have asymptomatic congenital CMV ($\geq 99\%$)
- > 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)
- > PCR and/or Viral culture of urine and nasopharyngeal aspirate (N.B. viral culture no longer performed by IMVS)

Follow up

- > Consider Infectious Diseases input in regard to possible treatment with Ganciclovir / valganciclovir⁶
- > 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

For further information, refer to *Cytomegalovirus - Algorithm 4: Neonatal Diagnosis and Management* available from URL: <https://www.asid.net.au/documents/item/368>



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Other useful sites

Otis pregnancy website: Available from URL:

http://www.otispregnancy.org/otis_fact_sheets.asp

SA Health You've got what website see in A to Z index: Available from URL:

www.sahealth.sa.gov.au/YouveGotWhat

Centers for Disease Control and Prevention (CDC): Available from URL

<http://www.cdc.gov/cmvrisk/preg-women.html>



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