



# Prevention of congenital cytomegalovirus (CMV) infection

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This statement has been developed and reviewed by the Women's Health Committee and approved by the RANZCOG Board and Council.

A list of Women's Health Committee Members can be found in [Appendix A](#).

Disclosure statements have been received from all members of this committee.

The Committee acknowledges contributing authorship in [Appendix B](#).

**Disclaimer** This information is intended to provide general advice to practitioners. This information should not be relied on as a substitute for proper assessment with respect to the particular circumstances of each case and the needs of any patient. This document reflects emerging clinical and scientific advances as of the date issued and is subject to change. The document has been prepared having regard to general circumstances.

First endorsed by RANZCOG: March 2019  
Current: March 2019  
Review due: March 2022

**Objectives:** To provide guidance for maternity care providers and the community on the prevention of maternal cytomegalovirus (CMV) infection during pregnancy in order to reduce mother to child transmission (MTCT) of virus, fetal infection and clinical sequelae (symptomatic congenital CMV); and to provide a general overview of the diagnosis and management of congenital CMV.

**Outcomes:** Improved awareness about CMV prevention among maternity health care providers and improved routine provision of patient education on hygiene measures which have been shown to reduce CMV transmission during pregnancy.

**Target audience:** All health professionals responsible for providing maternity care, pregnant women and the general community.

**Values:** The evidence was reviewed by the Women's Health Committee (RANZCOG), and applied to local factors relating to Australia and New Zealand.

**Background:** This statement was first developed by Women's Health Committee in March 2019.

**Funding:** The development and review of this statement was funded by RANZCOG.

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## 1. Plain language summary

Cytomegalovirus (CMV) is a common virus that can be passed from person-to-person without their knowledge, usually via close contact. The most common sources of CMV infection are young children, as they are more likely to shed high levels of virus in their saliva, urine or nasal secretions for long periods. Women who catch CMV infection while pregnant may pass the virus to their unborn child. If infected, some of these children may have health problems such as hearing loss, developmental delay and learning problems. The most serious cases may end in stillbirth, infant death, or the severe condition of cytomegalic inclusion disease (CID).

Pregnant women can reduce their risk of being infected with CMV if given the following advice:

Do not share food drinks, or utensils used by children (under the age of 3 years)

Do not put a child's dummy / soother in your mouth

Avoid contact with saliva when kissing a child ("kiss on the forehead not on the lips")

Thoroughly wash your hands with soap and water for 15-20 seconds especially after changing nappies or feeding a young child or wiping a young child's nose or saliva

Clean toys, countertops and other surfaces that come into contact with children's urine or saliva

## 2. Summary of recommendations

Recommendation 1	Grade
All pregnant women and women trying to conceive, should be given information about CMV prevention as part of routine antenatal or prepregnancy care.	Consensus based recommendation <sup>1</sup>
Recommendation 2	Grade
Hygiene practices to reduce infection should be recommended to all pregnant women and women trying to conceive, regardless of their CMV serology status. While the greatest risk of mother to fetus transmission of infection (MTCT) occurs with maternal primary infection, congenital infection with long term complications occurs with similar levels of severity in primary and nonprimary (reactivation and/or reinfection) maternal infections.	Consensus based recommendation <sup>1</sup>
Recommendation 3	Grade
The specific recommended hygiene measures are <sup>1</sup> : <ul style="list-style-type: none"> <li>• Do not share food, drinks, or utensils used by young children (less than 3 years of age)</li> <li>• Do not put a child's dummy in your mouth</li> <li>• Avoid contact with saliva when kissing a child</li> <li>• Attention to hand hygiene, when changing nappies or when in contact with urine. Thoroughly wash hands with soap and water for 15–20</li> </ul>	Consensus based recommendation <sup>1</sup>

<p>seconds, especially after changing nappies/, feeding a young child, or wiping a young child's nose or saliva</p> <ul style="list-style-type: none"> <li>• Clean toys, countertops, and other surfaces that come into contact with children's urine or saliva, and not sharing a toothbrush with a young child.</li> </ul>	
<b>Recommendation 4</b>	<b>Grade</b>
Universal routine serological screening for CMV in pregnancy is not recommended.	Consensus based recommendation <sup>1,4</sup>
<b>Recommendation 5</b>	<b>Grade</b>
Pre-pregnancy or early pregnancy screening with CMV IgG may be considered for women who are high risk of infection. Early determination of CMV serostatus may aid in distinguishing between primary infection and reactivation/reinfection during <i>pregnancy if clinically indicated</i> , but does not remove the need to follow recommended hygiene measures.	Consensus based recommendation <sup>1-3</sup>
<b>Recommendation 6</b>	<b>Grade</b>
Women with suspected CMV infection in pregnancy should have CMV serology testing for IgG and IgM, and IgG avidity if CMV IgG and IgM are positive.	Consensus based recommendation <sup>2,5</sup>
<b>Recommendation 7</b>	<b>Grade</b>
Diagnosis of primary CMV is based upon: <ul style="list-style-type: none"> <li>• The new appearance of CMV-specific IgG in a woman who was previously seronegative or</li> <li>• The detection of CMV IgM antibody with low IgG avidity.</li> </ul>	Consensus based recommendation <sup>2,5</sup>
<b>Recommendation 8</b>	<b>Grade</b>
When congenital CMV infection is suspected on the basis of maternal serology or fetal ultrasound abnormalities, a referral to a maternal fetal medicine specialist, or specialist with expertise in perinatal infections is recommended.	Consensus based recommendation
<b>Recommendation 9</b>	<b>Grade</b>
All babies of mothers diagnosed with primary CMV infection during pregnancy, should have CMV testing performed with a CMV PCR of saliva or urine with the first 3 weeks of life.	Consensus based recommendation <sup>1</sup>
<b>Recommendation 10</b>	<b>Grade</b>
If an infant is diagnosed with congenital CMV, discussion with a paediatrician with experience in infectious diseases is recommended for further assessment and management.	Consensus based recommendation

### 3. Introduction

Cytomegalovirus (CMV) is the commonest cause of congenital infection<sup>6</sup> and affects 0.2-2.2% of births.<sup>7</sup> Most (90%) babies who are infected with CMV before birth are healthy at birth and have normal development. However 10-15% of all infected infants who are healthy at birth may still develop health problems in later childhood. Congenital CMV is the most important infective cause of sensorineural hearing loss and disability and is also associated with stillbirth<sup>8</sup>, cerebral palsy, learning problems and impaired school performance.<sup>9</sup> There is currently no effective vaccine to prevent maternal CMV infection, and no proven therapy to prevent or treat fetal infection.<sup>10,11</sup>

### 4. Discussion and recommendations

#### 4.1 Transmission

- 1) **Child to mother:** CMV is excreted in the saliva or urine of those with infection. Excretion of virus, particularly at high titre, occurs more frequently in children under two, particularly children in day care<sup>12</sup>. The virus can continue to be excreted for months to years.<sup>13</sup> CMV can be transmitted from urine and saliva to hands then to mucosal surfaces (e.g. mouth) or directly to the mucosal surfaces.<sup>14</sup> High risk groups include parents with a child in daycare (23% risk of seroconversion per year if they have children who are shedding CMV)<sup>13</sup>. Parental excretion of CMV occurs from the cervix, in semen, and in other bodily fluids.

- 2) **Mother to fetus:**

**The highest likelihood of MTCT is following maternal primary infection during the first trimester.** This is associated with a 30-40% risk of intrauterine transmission, and of the infected fetuses, around one third (~10% overall) will have some disease.<sup>15</sup> The consequences of CMV infection may be present in utero or at birth.<sup>1</sup> Fetal and newborn manifestations of congenital CMV include growth restriction, microcephaly, cerebral ventriculomegaly, intracerebral calcifications, ascites/hydrops, hepatosplenomegaly, chorioretinitis, thrombocytopenia, anaemia, stillbirth and neonatal death. Long term sequelae that may not be evident until later childhood include sensorineural hearing loss, delayed psychomotor development, cerebral palsy, and visual impairment.

In cases of maternal reinfection with CMV or reactivation of latent infection, the risk of fetal infection is lower (1-3%)<sup>16</sup> although, when fetal infection occurs, the potential for and severity of fetal morbidity is similar to cases of primary infection. On a population-basis, the majority of the health burden of congenital CMV is attributable to non-primary maternal infection, as the seropositivity (and hence latent infection) rate of the child bearing Australian population is 40-60%.<sup>17-19</sup> Therefore, any public health strategy should also address nonprimary infection as well as primary infection during pregnancy.

Simple hygiene measures have been shown to reduce the risk of maternal CMV infection in pregnancy.<sup>9-11</sup> International consensus guidelines<sup>1</sup> and Australian Federal and State health departments recommend pregnant women be given information on simple hygiene measures to prevent CMV prevention. However, the level of awareness about CMV infection in maternity care providers<sup>20</sup> and pregnant women in Australia and New Zealand is very low. (ref Lazzaro 2018 unpublished). A 2015 survey of RANZCOG members/fellows/diplomates and VIC and NSW midwives reported that less than 10% of maternity care providers routinely provided education on CMV prevention.<sup>20</sup>

Recommendation 1	Grade
All pregnant women and women trying to conceive, should be given information about CMV prevention as part of routine antenatal or prepregnancy care.	Consensus based recommendation <sup>1</sup>
Recommendation 2	Grade
Hygiene practices to reduce infection should be recommended to all pregnant women and women trying to conceive, regardless of their CMV serology status. While the greatest risk of mother to fetus transmission of infection (MTCT) occurs with maternal primary infection, congenital infection with long term complications occurs with similar levels of severity in primary or reactivation and/or reinfection maternal infections.	Consensus based recommendation <sup>1</sup>
Recommendation 3	Grade
<p>The specific recommended hygiene measures are<sup>1</sup>:</p> <ul style="list-style-type: none"> <li>• Do not share food, drinks, or utensils used by young children (less than 3 years of age)</li> <li>• Do not put a child's dummy in your mouth</li> <li>• Avoid contact with saliva when kissing a child</li> <li>• Attention to hand hygiene, when changing nappies or when in contact with urine. Thoroughly wash hands with soap and water for 15–20 seconds, especially after changing nappies/, feeding a young child, or wiping a young child's nose or saliva</li> <li>• Clean toys, countertops, and other surfaces that come into contact with children's urine or saliva, and not sharing a toothbrush with a young child</li> </ul>	Consensus based recommendation <sup>1</sup>

#### 4.2 Serological testing for CMV

Universal routine serological screening for CMV in pregnancy is not recommended, as past infection with CMV does not confer complete protection against reinfection or congenital CMV.<sup>1-4</sup> Pre-pregnancy or early pregnancy screening with CMV IgG may be considered for women who are high risk of infection. Some studies have shown women who are aware that they are susceptible to primary CMV infection on the basis of known seronegativity are more likely to practice hygiene measures.<sup>21,22</sup> Pre-pregnancy CMV serology may also aid in distinguishing between primary infection or nonprimary infections during pregnancy if clinically indicated, but does not remove the need to follow recommended hygiene measures.

The majority of women with acute CMV infection have no symptoms. However, serological and virological testing for CMV should be considered if a woman presents with flu-like illness, malaise, fever, and lymphadenopathy, or if fetal signs of CMV have been detected on ultrasound (i.e. case-finding, rather than screening).

Recommendation 4	Grade
Universal routine serological screening for CMV in pregnancy is not recommended.	Consensus based recommendation <sup>1-4</sup>
Recommendation 5	Grade
Pre-pregnancy or early pregnancy screening with CMV IgG may be considered for women who are high risk of infection. Early determination of CMV serostatus may aid in distinguishing between primary infection and reactivation/reinfection during <i>pregnancy if clinically indicated</i> , but does not remove the need to follow recommended hygiene measures.	Consensus based recommendation <sup>1-3</sup>
Recommendation 6	Grade
Women with suspected CMV infection in pregnancy should have CMV serology testing for IgG and IgM, and IgG avidity if CMV IgG and IgM are positive.	Consensus based recommendation <sup>2, 5</sup>

### 4.3 Diagnosis of primary CMV infection

Diagnosis of primary CMV should be based on appearance of CMV IgG during pregnancy in a woman who was previously seronegative; or detection of CMV IgM with low IgG avidity, if previous serology is unknown.<sup>2, 5</sup> (See Table 1). In general, the former is usually not available, as prior testing is often unavailable.

Interpretation of CMV serology can be difficult as the IgM response may last up for 16 weeks post infection, may reappear with reactivation or reinfection and false positives occur due to cross reaction with other viruses.<sup>24</sup> CMV IgG avidity is more useful for timing maternal infection if primary infection during pregnancy is suspected. A low CMV IgG avidity is suggestive of recent infection (<3 months); high avidity suggests infection >3 months ago; Intermediate avidity – is not informative for assessing timing of infection. The IgG avidity testing is now standard and comparable within a laboratory, although differences in the avidity index depend on the kit/ technique the laboratory used and serial results from different laboratories should be compared with caution.<sup>24</sup>

All laboratories in Australia are required to store serum from pregnant women following diagnostic testing for 12 months. Retrospective testing of stored sera from first trimester booking bloods can be useful to determine if a primary infection has occurred during pregnancy.

Recommendation 7	Grade
Diagnosis of primary CMV is based upon: <ul style="list-style-type: none"> <li>The new appearance of CMV-specific IgG in a woman who was previously seronegative or</li> <li>The detection of CMV IgM antibody with low IgG avidity.<sup>2, 5</sup></li> </ul>	Consensus based recommendation <sup>2, 5</sup>
Recommendation 8	Grade
When congenital CMV infection is suspected on the basis of maternal serology or fetal ultrasound abnormalities, a referral to a maternal fetal medicine specialist, or specialist with expertise in perinatal infections is recommended.	Consensus based recommendation

Table 1. Interpretation of CMV serology

Serology			Interpretation of serology	
IgM	IgG	IgG avidity	Interpretation	Action
-	-		Susceptible/ no evidence of recent infection	Educate about transmission. Consider repeat serology in 2-3 weeks if clinical suspicion of recent infection
+	-		Possible recent infection or false positive IgM	Repeat serology in 2 weeks and perform avidity if IgG then positive
+	+	Low	Recent primary infection	Refer – likely primary infection
+	+	Intermediate	Possible recent primary infection	Test stored sera, or manage as recent primary
+	+	High	Past infection	Refer- Non-primary (reinfection/ reactivation.

#### 4.4 Diagnosis of fetal infection

Fetal risk is dependent on the gestation at which maternal infection occurred, and whether it is primary infection or reactivation/ reinfection. The greatest risks are in first trimester with primary infection. However, timing of infection is often difficult to ascertain as the majority of infections are asymptomatic.

Prenatal diagnosis of fetal infection is performed with CMV nucleic acid tests (generally with PCR) on an amniocentesis sample. For optimal sensitivity and specificity, the amniocentesis needs to be performed >8 weeks after the suspected infection<sup>20</sup> and usually >21 weeks gestation.<sup>1, 2, 24</sup> Earlier amniotic fluid samples have a high falsely negative rate.<sup>25</sup>

#### 4.5 Management of suspected or proven congenital CMV infection

Guidelines for the investigation and management of infections in pregnancy including CMV are available from the Australian Society of Infectious Diseases (ASID)<sup>5</sup> and the International Consensus guidelines.<sup>1</sup> When congenital CMV infection is suspected on the basis of maternal serological findings or fetal ultrasound abnormalities, a referral to a maternal fetal medicine specialist, or specialist with expertise in perinatal infections is recommended.

There is no established or recommended treatment to prevent fetal infection after maternal primary infection.<sup>1, 26, 27</sup> Treatment options for fetuses with CMV confirmed on amniocentesis are currently evolving.<sup>1, 10, 11, 28</sup>



Serial ultrasound surveillance +/- MRI are recommended when cCMV is proven on amniocentesis to monitor for fetal growth restriction and structural abnormalities, in particular brain abnormalities.<sup>2, 24</sup> When both ultrasound and MRI are normal, the prognosis is generally good.<sup>29</sup>

#### 4.6 Neonatal investigation and management

All babies of mothers diagnosed with primary CMV infection during pregnancy, should have CMV testing performed at birth with a CMV PCR of saliva or urine within the first 3 weeks of life.<sup>1</sup> Testing must be performed within the first three weeks of life to distinguish congenital from postnatal CMV infection. If an infant is diagnosed with congenital CMV, discussion with a paediatrician with experience in infectious diseases is recommended for further assessment and management.<sup>1</sup> Long term follow up of hearing is recommended, regardless of the results of the infant hearing screen.

Testing for congenital CMV should be considered for infants that have an abnormal newborn hearing screen result.<sup>30</sup>

Breastfeeding should be encouraged. There is no evidence to suggest that postnatal CMV transmission during breastfeeding has any adverse effects on healthy infants.

<b>Recommendation 9</b>	<b>Grade</b>
All babies of mothers diagnosed with primary CMV infection during pregnancy, should have CMV testing performed with a CMV PCR of saliva or urine within the first 3 weeks of life.	Consensus based recommendation <sup>1</sup>
<b>Recommendation 10</b>	<b>Grade</b>
If an infant is diagnosed with congenital CMV, discussion with a paediatrician with experience in infectious diseases is recommended for further assessment and management.	Consensus based recommendation

## 5. References

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## 6. Useful links and resources

CMV Australia website

<http://www.cmv.org.au>

Palasanthiran P, Starr M, Jones C, Giles ML. Management of Perinatal Infections. Sydney: Australasian Society for Infectious Diseases (ASID) Inc; 2014. <https://www.asid.net.au/documents/item/368>

## 7. Links to other College statements

[Pre-pregnancy Counselling \(C-Obs 3a\)](#)

[Routine Antenatal Assessment in the Absence of Pregnancy Complications \(C-Obs 3b\)](#)

[Pre-pregnancy and Pregnancy Vaccinations \(C-Obs 44\)](#)

[Influenza Vaccination during Pregnancy \(C-Obs 45\)](#)

## 8. Patient information

A range of RANZCOG Patient Information Pamphlets can be ordered via:

<https://www.ranzcog.edu.au/Womens-Health/Patient-Information-Guides/Patient-Information-Pamphlets>

## Appendices

### Appendix A Women's Health Committee Membership

Name	Position on Committee
Professor Yee Leung	Chair and Board Member
Dr Gillian Gibson	Deputy Chair, Gynaecology
Dr Scott White	Deputy Chair, Obstetrics and Subspecialties Representative
Associate Professor Ian Pettigrew	Member and EAC Representative
Dr Kristy Milward	Member and Councillor
Dr Will Milford	Member and Councillor
Dr Frank O'Keeffe	Member and Councillor
Professor Sue Walker	Member
Dr Roy Watson	Member and Councillor
Dr Susan Fleming	Member and Councillor
Dr Marilyn Clarke	ATSI Representative
Associate Professor Kirsten Black	Member
Dr Thangeswaran Rudra	Member
Dr Nisha Khot	Member and SIMG Representative
Dr Judith Gardiner	Diplomate Representative
Dr Angela Brown	Midwifery Representative
Ms Ann Jorgensen	Community Representative
Dr Rebecca Proctor-Mackenzie	Trainee Representative
Prof Caroline De Costa	Co-opted member (ANZJOG member)
Dr Christine Sammartino	Observer

### Appendix B Contributing Authors

The Women's Health Committee acknowledges the contribution from Dr Antonia Shand, A/Prof Lisa Hui, Dr Zaynab El-Hamawi, dr Amanda Lazarro.

Reviewed by: Professor William Rawlinson (medical virologist), A/Prof Pamela Palasanthiran (paediatric infectious diseases specialist), Brendan McMullan (paediatric infectious diseases specialist and microbiologist, Sydney Children's Hospital Randwick NSW), Declarations of interest: None

### Appendix C Overview of the development and review process for this statement

#### *i. Steps in developing and updating this statement*

This statement was first published in March 2019. The Women's Health Committee carried out the following steps in reviewing this statement:

- Declarations of interest were sought from all members prior to reviewing this statement.
- Structured clinical questions were developed and agreed upon.
- An updated literature search to answer the clinical questions was undertaken.

- At the February 2019 teleconference, the existing consensus-based recommendations were reviewed and updated (where appropriate) based on the available body of evidence and clinical expertise. Recommendations were graded as set out below in Appendix B part iii)

*ii. Declaration of interest process and management*

Declaring interests is essential in order to prevent any potential conflict between the private interests of members, and their duties as part of the Women’s Health Committee.

A declaration of interest form specific to guidelines and statements was developed by RANZCOG and approved by the RANZCOG Board in September 2012. The Women’s Health Committee members were required to declare their relevant interests in writing on this form prior to participating in the review of this statement.

Members were required to update their information as soon as they become aware of any changes to their interests and there was also a standing agenda item at each meeting where declarations of interest were called for and recorded as part of the meeting minutes.

There were no significant real or perceived conflicts of interest that required management during the process of updating this statement.

*iii. Grading of recommendations*

Each recommendation in this College statement is given an overall grade as per the table below, based on the National Health and Medical Research Council (NHMRC) Levels of Evidence and Grades of Recommendations for Developers of Guidelines. Where no robust evidence was available but there was sufficient consensus within the Women’s Health Committee, consensus-based recommendations were developed or existing ones updated and are identifiable as such. Consensus-based recommendations were agreed to by the entire committee. Good Practice Notes are highlighted throughout and provide practical guidance to facilitate implementation. These were also developed through consensus of the entire committee.

Recommendation category		Description
Evidence-based	A	Body of evidence can be trusted to guide practice
	B	Body of evidence can be trusted to guide practice in most situations
	C	Body of evidence provides some support for recommendation(s) but care should be taken in its application
	D	The body of evidence is weak and the recommendation must be applied with caution
Consensus-based		Recommendation based on clinical opinion and expertise as insufficient evidence available
Good Practice Note		Practical advice and information based on clinical opinion and expertise

#### Appendix D Full Disclaimer

This information is intended to provide general advice to practitioners, and should not be relied on as a substitute for proper assessment with respect to the particular circumstances of each case and the needs of any patient.

This information has been prepared having regard to general circumstances. It is the responsibility of each practitioner to have regard to the particular circumstances of each case. Clinical management should be responsive to the needs of the individual patient and the particular circumstances of each case.

This information has been prepared having regard to the information available at the time of its preparation, and each practitioner should have regard to relevant information, research or material which may have been published or become available subsequently.

Whilst the College endeavours to ensure that information is accurate and current at the time of preparation, it takes no responsibility for matters arising from changed circumstances or information or material that may have become subsequently available.