Tidsskriftet Tidsskrift for Den norske legeforening

# Congenital cytomegalovirus infection can be prevented

PERSPECTIVES

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## Around 250 children are born with cytomegalovirus infection in Norway every year, and up to 20 % develop permanent sequelae. Preventive measures can help avoid many of these cases.

Illustration photo: Ritter75/iStock

Congenital cytomegalovirus (CMV) infection can have potentially severe consequences for a child. Knowledge of this type of infection during pregnancy is perceived as low, both among healthcare personnel and the general population. Few seem to be aware that CMV infections during pregnancy can now be treated and prevented. There are effective and well-documented measures to prevent maternal infection and fetal transmission, and to reduce harm to the newborn.

## Half are at risk of primary infection

CMV is the most common cause of congenital infections, with a prevalence of 0.48 % in high-income countries (1, 2). The virus can be transmitted from mother to fetus either through a primary infection or a non-primary infection (reactivation of latent virus or reinfection with another CMV strain). The transplacental transmission rate is significantly higher with primary infection (32 %) than with non-primary infection (1 %) (1). Recent studies show that the risk of severe long-term complications is greatest with a primary infection around the time of conception and in the first trimester of pregnancy (3). A study from Norway showed that 54 % of pregnant women had previously experienced a CMV infection. This means that nearly half of all pregnant women in Norway will be at risk of acquiring a primary infection during pregnancy (4).

CMV is transmitted through bodily fluids. Children are often infected in kindergarten, and children under the age of three years excrete the virus in urine and saliva for an average of 18 months after a primary infection (5). This means that seronegative parents with children in kindergarten are at relatively high risk of acquiring a primary CMV infection (6–8). Children and adults typically have few symptoms, and any symptoms that do appear are indistinguishable from other viral infections that cause a flu-like illness.

> ***«In total, around 17–20 % of all children with congenital CMV infection will experience permanent sequelae»***

Among newborns with congenital CMV infection, approximately 10–15 % will exhibit symptoms at birth. These can range from mild and moderate to severe and life-threatening symptoms, including severe liver disease and involvement of the central nervous system, with late-onset neurological and sensory impairment (9). However, most newborns with congenital CMV infection show no obvious symptoms immediately after birth, but among these, 10–15 % will develop sequelae, usually in the form of hearing loss. In total, around 17–20 % of all children with congenital CMV infection will experience permanent sequelae (9).

## Effect of preventive measures

Preventive measures that reduce the risk of congenital CMV infection, as well as their effectiveness, are now well-documented (10). Primary prevention entails preventing maternal infection around the time of conception and in the early stages of pregnancy. Basic hygiene advice significantly reduces transmission and has long been recommended internationally (11–13). Seronegative pregnant women with children under the age of three years are at the highest risk for primary CMV infection. It is therefore recommended that

parents of young children who are planning a new pregnancy be diligent about handwashing after changing nappies and feeding. They should avoid sharing food, cutlery and crockery with the child, and kiss them on the forehead or cheek instead of the mouth.

Secondary prevention focuses on reducing transplacental transmission of CMV to the fetus in cases of confirmed maternal primary infection around the time of conception or in the first trimester. Early antiviral treatment with valacyclovir can reduce the risk of fetal infection and the incidence of severe sequelae when transmission has already occurred. Studies in this context show a 70 % reduction in the transmission of CMV from mother to fetus (14, 15). Treatment with oral valacyclovir is safe for both the pregnant woman and the fetus and is associated with few side effects (14). Early antiviral treatment of newborns with symptomatic CMV infection has also been shown to reduce the risk of hearing loss and neurological impairments (10, 16).

## Information about prevention

Preventive measures should be prioritised as they prevent disease. The COVID-19 pandemic has shown us that the population is capable of implementing basic infection control measures. The national clinical guidelines for obstetrics were recently updated with recommendations that healthcare personnel should provide pregnant women with information about hygiene measures in order to prevent infections during pregnancy. In addition to CMV, we know that influenza, SARS-CoV-2, parvovirus B19 and several other infections can have an adverse effect on pregnancy.

> ***«Healthcare personnel should provide pregnant women with information about hygiene measures in order to prevent infections during pregnancy»***

The national clinical guidelines for antenatal care recommend providing information on various lifestyle factors during pregnancy (16). Information on infection prevention should also be included. The information on CMV should focus on preventing primary infection around the time of conception and in the first trimester of pregnancy, as this is when the risk of fetal damage is greatest. The information should, therefore, also be available to women planning a pregnancy, for example, at child health centres, kindergartens, medical practices, fertility clinics and relevant websites, so that women can prevent primary CMV infection when planning for children. This is not feasible without improving the understanding of CMV among the target groups: couples planning a pregnancy, pregnant women and healthcare personnel.

## Screening of pregnant women?

Most cases of primary CMV infection in pregnant women go undiagnosed because it is often asymptomatic. In Norway, the current recommendation is to test for CMV during pregnancy if a primary infection is suspected in the mother or if findings in the fetus suggest the presence of the virus. Testing is in the form of measuring antibodies in a venous blood sample. If further CMV antibody testing is carried out, this should be done as early as possible, either when planning a pregnancy or in the early stages of pregnancy. In the case of a confirmed primary CMV infection around the time of conception or in the first trimester, the risk of transplacental transmission and severe fetal damage can be reduced by initiating antiviral treatment as soon as possible after primary infection. A primary CMV infection in the second or third trimester is very rarely associated with a serious illness in children (3). It is therefore not recommended to test pregnant women after the first trimester, nor is it recommended to test women who have already had a CMV infection, as it is not currently possible to diagnose a non-primary infection.

Should we offer testing to women who are planning a pregnancy to ascertain whether they have had a CMV infection? This could apply to, for example, women who are thinking about having a child or mothers attending child health centres for follow-up of a child. Should we encourage all women to get tested early in the first trimester in order to identify a primary CMV infection?

A European consensus report from a multidisciplinary group of experts on congenital CMV infection recommends testing pregnant women in the early stages of pregnancy, along with follow-up and retesting of seronegative women up to week 14 (10). Italy has implemented screening for this, and France has recently decided to introduce serological screening (17). Other countries do not currently recommend this (2). Before considering screening for pregnant women, health authorities in Norway should prioritise gathering nationwide data, implementing primary prevention measures and improving the understanding of congenital CMV infection.

## What do pregnant women want, and what do healthcare personnel know?

Should we worry pregnant women with information about CMV? Even with infection in the first trimester, the likelihood of fetal damage is less than 10 % (3). However, the risk is significant enough that we should try to prevent transmission. Studies have shown that pregnant women want to know about the virus and the options for infection control measures to reduce the risk of fetal transmission (12, 18). Studies from several countries show a consistent lack of knowledge about congenital CMV infection, despite the significant disease burden. Conditions with a far lower disease burden are much better known, both among the general public and healthcare personnel. Studies

indicate that knowledge of CMV infection is not only limited in the general population but also among medical students, midwives, general practitioners, paediatricians and gynaecologists (19, 20).

> ***«We cannot withhold information simply to avoid alarming the pregnant woman or because communication is challenging»***

Communication is difficult, and communicating with pregnant women about issues that may affect their unborn child is particularly challenging. A thoughtful and considered approach must be adopted here. However, we cannot withhold information simply to avoid alarming the pregnant woman or because communication is challenging. There are ethical issues to consider and address. Widespread testing for CMV infection in pregnant women after the first trimester must be avoided. If test results are positive at that point, it could cause significant concern for the pregnant woman, even though the risk of fetal harm at this stage of pregnancy is low. A high level of expertise is required in the field, both in primary care and the specialist health service, to ensure that pregnant women receive accurate and appropriate information. Clear guidelines are needed, along with a transparent, evidence-based and supportive health service that provides proper follow-up for pregnant women.

## The road ahead

With effective and straightforward infection control advice and the opportunity to treat pregnant women in the early stages of pregnancy to prevent fetal transmission of the virus around the time of conception and in the first trimester, the time has come for Norwegian health authorities to address the issues related to CMV and pregnancy.

We have a long road ahead, and we should start now by improving the understanding among healthcare personnel, advising women of childbearing age and pregnant women on infection control measures, and offering treatment to women diagnosed with a primary infection in the first trimester in order to prevent fetal transmission of the virus.

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Publisert: 9 April 2025. Tidsskr Nor Legeforen. DOI: 10.4045/tidsskr.25.0092
Received 7.2.2025, accepted 24.2.2025.