

## **CMV – A disease with many faces**

### **Sabine Leitner**

The cytomegalie infection is the most common congenital virus infection, even more common than rubella and toxoplasmosis, causing irreversible damages to the child. Through some simple information about possible causes of infection or ways of transmission, pregnant women can be protected from a primary infection.

The human cytomegalovirus (CMV) belongs to the family of herpesviruses and bears the name HHV-5 (HCMV). It is a virus that, after infection, will remain in the person's body (e.g. in lung cells and salivary glands) for life. As with all other herpesviruses, this is possible due to their latency mechanism: They manage to circumvent the immune defence and remain in the latently infected cell. Transmission occurs by droplet infection through urine, blood, saliva, tear fluid, genital secretions, organ transplants and, after birth, also through breast milk.

So far, there is no vaccination available. One new option for primarily infected pregnant women is a therapy with hyperimmunoglobulins.

### **No problem for immunocompetent people**

The virus is widespread all around the world. In Germany, it is assumed that the infection rate is at 40 to 80 percent of the general population, the same as for other herpesviruses. In developing countries, the rate is at up to 100%. Usually, the CMV infection of immunocompetent children and adults occurs without noticing and without any health impairment. In rare cases only, there are temporary flu-like symptoms. For a short time, some may also suffer from fatigue and lack of strength. More seldom are additional symptoms like fever and pain in the limbs. After the first infection, the body reacts by a formation of antibodies, only after that the person is CMV-antibody positive.

### **A high risk for others**

A lack of knowledge of one's own CMV immune status bears a risk for the unborn child whose mother got primarily infected during pregnancy. The immune system of foetuses is not yet mature enough to control the virus so that severe disease symptoms may appear that will later become manifest in a chronic course and irreversible long-term consequences.

The same applies to persons with a weak immune system, including persons with an HIV infection and those having received organ or stem cell transplants.

### **The transmission from mother to child**

#### **Primary infection of pregnant women**

An estimated 40 percent of pregnant women have not yet been infected with CMV and are CMV-negative.

The CMV-negative pregnant woman herself does not have any immunocompetence against the virus and will start to produce antibodies only after the onset of a primary infection. After the primary infection, the virus may be transmitted through the placenta. 10 to 25 percent of these unborn babies where the virus was transmitted through the placenta already show damages due to the infection right after birth. Many of these children suffer from hearing or speech disorders.

Another consequence is a mental impairment with a permanent IQ below 70 in spite of intensive early learning initiatives.

The mother's infection will mostly pass unnoticed as described above.

A large number of newborns with a CMV infection that began during pregnancy do not show any symptoms in the beginning. This is called asymptomatic progression. However, approximately 8 percent of these children will also develop deficits at a later date.

Possible consequences of the mother's primary infection during pregnancy for the child include:

- hearing impairments as severe as complete hearing loss (consequence: speech impairments)
- retinitis (eye inflammation)
- feeding problems, eating disorders
- circular haemorrhages (blueberry muffin lesions)
- hepatosplenomegaly (enlargement of liver and spleen)
- pneumonia
- colitis (inflammation of the intestines)
- hepatitis (inflammation of the liver)
- anaemia
- thrombocytopenia
- microcephaly (smaller brain)
- brain calcifications
- convulsive seizures
- epilepsy
- neuro-muscular defects
- mental retardation
- premature birth

#### Reinfection of CMV-seropositive pregnant women

This type of CMV transmission is very rare. It is the reactivation of already existent viruses. One possible cause can be an immunodeficiency of the mother. Only up to 1 percent of the newborns of such CMV-positive mothers are congenitally infected. Due to the mother's existing antibody structure, the foetuses are better protected. Secondarily infected newborns can also incur hearing damages or other damages of the central nervous system.

#### Breast milk of CMV-positive pregnant women

Almost all women who are already CMV-positive reactivate the cytomegalovirus when breastfeeding. CMV transmission through breast milk after birth is no problem for mature and healthy newborns. Thanks to the child's immune system, this acquired CMV infection passes without any symptoms and usually without any long-term consequences.

For premature infants, however, the CMV transmission through breast milk may cause problems.

Particularly premature infants with a birth weight of less than 1,500 grams are at risk. In such cases, the transmission may cause a symptomatic infection as neither the infant's immune system has been fully developed nor the antibodies acquired from the mother are sufficient. Premature infants are in danger of developing all kinds of the above-mentioned consequences of the infection.

In such cases it is recommended to sterilise the breast milk. Newborns whose immune system is weakened by another disease should be treated in a similar way as premature infants.

#### Prenatal diagnostics of a primary CMV infection

Presently, the systematic cytomegaly serology is unfortunately not part of mandatory testing. Pregnant women can, however, have their serology status tested by their gynaecologists for a price of approximately 30 euros.

Virus serology:

- Anti – CMV – IgG / IgM
- Avidity
- Immunoblot

Several parameters need to be taken into account in order to differentiate between primary and secondary infection. The estimated time of infection can be determined by this procedure on the basis of the virus-antibody ratio found.

In case of a primary infection, there are various continuative diagnostic procedures in order to find out whether the unborn child is infected.

Virus culture:

- urine
- amniotic liquor
- polymerase chain reaction; PCR\*\*
- blood
- urine
- amniotic liquor

If the time of the amniocentesis is too close to the beginning of the primary infection it is possible that the number of virus antigens accumulated is so small that evidence is not yet possible.

A cell culture and a urine test in addition to the amniocentesis after 21 weeks of pregnancy provide maximum certainty for the diagnosis of a fetal CMV infection. Should the pregnant woman be seronegative, it is recommended to repeat the test every 4 to 6 weeks (in case of suspicion of exposure also earlier or more often) and to inform her about possible sources of infection. In few cases only, CMV infections are diagnosed during ultrasound checks on the basis of fetus mutations.

#### Therapy of the prenatal CMV infection

In case of a primary infection during pregnancy, a CMV therapy with hyperimmunoglobulins is an option. It involves a high concentration of CMV antibodies which, due to the passive immunisation of the mother, are transferred to the child through the placenta and can decrease the rate of infection as well as possible damages to the child.

Education alone can already prevent an infection. Moreover, pregnant women should be encouraged to have their serology status tested. Additionally, any cold, any flu-like infection during pregnancy might be a sign. Should a pregnant woman show such symptoms, should she feel weak and lack energy, a test is to be performed and repeated four weeks after recovery. A large part of primary infections can be prevented by hygiene measures.

Protective measures for seronegative women during pregnancy:

- Good hand hygiene with water and soap
- No joint use of knives, forks, spoons, etc. with
- Any persons in one's own environment
- No mutual exchange of food covered with saliva
- Strictly avoid kisses on the mouth
- Avoid contact with persons who are presently infectious
- Up to 20 percent of all infants below 3 years of age excrete the CMV virus via urine and saliva. Pay attention during diaper changes, with toys, etc.
- Always wear gloves!
- Have your partner tested

Depending on the respective German federal state, there are different rules and regulations for educators and health professionals:

- employment ban for these occupational groups if dealing with children under the age of 3
- Examination of safety at work with regard to the immune status initiated by the employer
- Assignment of a different task during pregnancy by the employer. More information about this situation is available from the local office of industrial safety.

### **The newborn**

After an infection of the child in the womb it cannot be predicted whether there will be damages and, if so, how severe these might be. Even in case of twins, one child might be affected and the other may not. Right after birth, many children seem to be healthy but start to show symptoms during the first days. Others, on the other hand, are already born with severe damages – possibly even with multiple physical handicaps.

Feeding problems as well as a high susceptibility to infections with fever attacks, an enlarged liver or spleen, hardness of hearing, retinitis, pneumonia, atypical tonicities or blueberry muffin lesions in newborns may be signs of a CMV infection. If required, those children are presently treated with an antiviral therapy.

### **Support for affected parents and children**

When a pregnant woman or a mother after the birth of her child is confronted with CMV diagnosis she is in need of intensive counselling and support. Often the child's health threat is causing lots of stress for the parents. A decline into trauma needs to be avoided through professional counselling and support. The parents feel absolutely helpless and at the same time worry about their child.

CMV manifests itself through a large range of clinical pictures. The worst for parents is the uncertainty with regard to the progression and outcome of their child's disease. In such cases, empathetic and competent support by gynaecologists and midwives is required. In many cases, it is recommended to ask for additional help.

Further information can be found at:

[www.cmv-selbsthilfegruppe.de](http://www.cmv-selbsthilfegruppe.de)

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