UNC SCHOOL OF MEDICINE

UNC Center for Maternal & Infant Health

CMV in Pregnancy Selected References

1) Enders G, Bader U, Lindemann L, Schalasta G, Daiminger A. Prenatal diagnosis of congenital cytomegalovirus infections in 189 pregnancies with known outcome. Prenat Diagn 2001;21: 362-77.

2) Lipitz S, Achiron R, Zalel Y, Mendelson E, Tepperberg M, Gamzu R. Outcome of pregnancies with vertical transmission of primary cytomegalovirus infection. Obstet Gynecol 2002; 100:428-33.

3) Azam AZ, Vial Y, Fawer CL, Zufferey J, Hohlfeld P. Prenatal diagnosis of congenital CMV infection. Obstet Gynecol 2001; 97:443-7.

4) Bodéus M, Goubau P. Predictive value of maternal IgG avidity for congenital human cytomegalovirus infection. J Clin Virol 1999;12:3 - 8.

5) Nigro G, Adler S, La Torre R, Best A. Passive Immunization during Pregnancy for Congential Cytomegalovirus Infection. N Engl J Med 2005;353:1350-62.

6) Yinon Y, Farine D, Yudin M. Cytomegalovirus Infection in Pregnancy. SOGC Clinical Practice Guideline. J Obstet Gynaecol Can 2010; 32(4): 348-354.

Summary:

- Diagnosis of primary maternal CMV infection in pregnancy should be based on de-novo appearance of CMV specific IgG or on detection of specific IgM antibody associated with low IgG avidity
- In case of primary maternal infection, risk of uterine transmission and fetal infection is 30-40% and there is a risk of 20-25% for development of sequelae if the fetus is infected
- The prenatal diagnosis of fetal CMV infection should be based on amniocentesis, which should be done > 7 weeks after maternal infection and after 21 weeks of gestation. This interval is important as it takes 5-7 weeks following fetal infection and subsequent replication of the virus in the kidney for a detectable quantity of virus to be secreted in the amniotic fluid
- A secondary infection can be suggested by a rise in IgG titer without use of IgM or avidity. Detection and prediction of amniocentesis is not determined with secojndary infection due to low rate of fetal infection and sequelae
- Following diagnosis of fetal CMV infection, recommend US follow up every 2-4 weeks. Absence of sonographic findings does not guarantee a normal outcome.
- Quantitative determination of CMV DNA in AF may assist in predicting outcome
- Routine screening of pregnant women for CMV by serology testing is currently not recommended.
- Serologic testing for CMV may be considered for women with influenza-like illness during pregnancy or following detection of sonogpraphic findings consistent with CMV infection.
- Seronegative health care and child care workers may be offered serologic monitoring during pregnancy. Monitoring may also be considered for seronegative pregnant women who have a young child in day care.

7) Revello MG, Gerna G. Diagnosis and management of human cytomegalovirus infection in the mother, fetus, and newborn infant. Clin Microbiol Rev 2002;15:680–715.
8) Lazzarotto, T, et al. New advances in the diagnosis of congenital cytomegalovirus infection. Journal of Clinical Virology 41 (2008) 192-197.

Sens/spec of IgG avidity for detect primary maternal infection

Table adapted from Lazzarotto, 2008

Reference	Before weeks' EGA	Sensitivity	Specificity
Lazzarotto, 1997	16-18	92.8%	85.7%
Eggers, 2000	20	------	100%

Grangeot-Keros and Cointe, 2001	17	------	100%
Bodeus, 2001	12	100%	82.5%
Revello, 2004	12	92.8%	84.7%

* Sensitivity is 62.5% after 20 weeks EGA for IgG avidity

Prediction of congenital infection (positive urine CMV at birth)

Table adapted from Lazzarotto, 2008

Maternal Infection	Total	IgM positive	Avidity (low/moderate)	Avidity (high)	Congenital infection (%)
Not active	1367	0	0	1367	1 (0.1)
Primary true IgM + low/mod avidity	514	514	514	0	121 (25.0)
Primary serocoversion	183	183	183	0	53 (30.3)
Non-primary	336	336	0	336	6 (2)
Undefined	77	77	65 (all mod)	12	3 (4.7)

Prediction of congenital infection based on amniotic fluid viral detection:

* of 111 positive AF PCR, 22 fetus with <500 copies, all asymptomatic at birth and 9 normal at 6 years, 10 normal at 1-5 years, 3 normal at 6 months

* Prediction of congenital CMV infection based on q PCR copies/ml >500

Sensitivity 80.2%; Specificity 100%; PPV 100%; NPV 94.2%

* AF viral load < 10^3 low risk of symptomatic infection

9) Guerra. Ultrasound prediction of symptomatic congenital cytomegalovirus infection. Am J Obstet Gynecol 2008.

650 fetuses with mothers with serological evidence of primary infection, with congenital infection defined as positive urine at birth, US findings found in 23 of 154 congenitally infected fetuses (14.9%)

When fetal infection status is unknown, ultrasound abnormalities predict symptomatic infection in only a third of cases

- Abnormal US prediction of congenital infection:
  - Sensitivity: 14.93%; specificity 93.72%; PPV 45.1%; NPV 76.1%

- Abnormal US prediction of symptomatic congenital infection
  - Sensitivity: 20.9%; specificity 93.57%; PPV 35.3%; NPV 87.6%

Abnormal US finding in all fetuses from mothers with primary CMV infection demonstrated PPV of 35% for symptomatic infection

48% probability that a normal US excluded development of symptomatic fetal infection

10) Carlson,A , et al. Cytomegalovirus infection in pregnancy: should all women be screened? Reviews in Obstetrics and Gynecology 3 (2010)

Prevention of CMV infection in women who are or will become pregnant

- Educate women with young children/work with young children that they are at increased risk
- Attention to hygiene will help prevent CMV transmission
- Careful handling of potentially infected articles (diapers)
- Hand washing around young children
- Avoid sharing utensils

Avoid kissing children < 6 years on the mouth or cheek

Links to other CMV documents:

CMV Screening
CMV Diagnosis
HIG Protocol

Revised July 27, 2011.

Notification to Users

These algorithms are designed to assist the primary care provider in the clinical management of a variety of problems that occur during pregnancy. They should not be interpreted as a standard of care, but instead represent guidelines for management. Variation in practices should take into account such factors as characteristics of the individual patient, health resources, and regional experience with diagnostic and therapeutic modalities.