Maternal Laboratory Assessment and Fetal Risk of Cytomegalovirus Infection

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(See the Major Article by Leruez-Ville et al, on pages 1428–35.)

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Congenital cytomegalovirus (CMV) infection is a leading cause of hearing, cognitive, and motor disability in children for which medical science has yet to provide prevention or cure. Although vaccines aimed at prevention of congenital infection are being developed, there are significant challenges to be overcome and it could easily be a decade or longer before a CMV vaccine is licensed for prevention of maternal or congenital infection. The source of CMV infection for a young mother is often within her own family (eg, a child who acquired CMV in day care or an intimate partner), making prevention by limiting exposure particularly difficult. When primary CMV infection is identified during pregnancy, management options are limited. Passive immunization with CMV immune globulin has been studied as a means to prevent fetal infection in pregnant women with primary CMV infection [1]. This expensive intervention is now being offered to pregnant women, although convincing evidence of efficacy is lacking. Accurate diagnosis and timing of maternal infection is a prerequisite for counseling pregnant women with gestational CMV infection on the risks and possible consequences of fetal infection.

Leruez-Ville et al examined data from nearly 5000 women who were screened for CMV infection at the first prenatal visit to determine whether markers for recent CMV infection could be used to predict occurrence of fetal infection [2]. Women were tested for antibody to CMV prior to the 14th week of gestation. Sera that were positive for both immunoglobulin G (IgG) and immunoglobulin M (IgM) antibody were then tested for CMV IgG antibody avidity using 2 commercially available assays. Seventy-two women had low or intermediate results on the avidity tests, further evidence of first-trimester primary infection. Maternal serum from this group was tested for CMV using real-time polymerase chain reaction (PCR), and amniotic fluid or newborn urine was tested for CMV by PCR. In the group of women with first-trimester CMV infection (CMV IgM positive, low or intermediate avidity), fetal infection was found in 26% of those with low CMV IgG avidity and 6% of those with intermediate avidity. Maternal serum PCR was positive in 80% (8/10) of cases with fetal infection compared with 23% (7/30) with no fetal CMV infection. The combination of avidity and maternal serum PCR results appeared to improve the ability to predict fetal infection among women with serological evidence of first-trimester primary CMV infection.

This study provides further evidence that among pregnant women who are tested for CMV infection, widely available laboratory tests can identify those who are most likely to have primary CMV infection, and more important, those who have greater risk of transmitting CMV to the fetus. This information could be of clinical value for physicians who have the difficult task of counseling or guiding the prenatal care of a pregnant woman who was found to be CMV IgM antibody positive. Although the approach studied by Leruez-Ville et al should be reproducible anywhere similar laboratory capability is available, the probability for fetal infection based on specific laboratory results will likely vary where different laboratory methods or commercial assays are used. The 2 commercial assays used to measure CMV IgG avidity in Leruez-Ville et al’s study gave quite different results for intermediate avidity level. With the VIDAS assay, 67% of samples from CMV IgM-positive sera had intermediate avidity compared to only 19% with the LIAISON...
assay. A more useful comparison of the 2 assays would have included positive and negative predictive values for fetal infection based on low avidity or intermediate avidity. As the authors point out, inconsistency in results obtained with various commercially available avidity assays has been described [3]. Use of different avidity assays will likely affect the accuracy of prediction of fetal infection. It is also important for readers to note that this study only reported fetal infection rates for pregnancies in which there was strong serological evidence of primary CMV infection in the first trimester. The congenital infection rates for babies born to mothers who were CMV IgM antibody positive with high IgG avidity or for those who were CMV IgM antibody negative or who had primary CMV infection after the first trimester were not reported. Therefore it is uncertain what overall proportion of congenital infections was identified or affected by the algorithm used in this study. It is well known that congenital CMV infection can occur in infants born to mothers with past rather than primary CMV infection.

Should all women be screened for primary CMV infection at the first prenatal visit? Although this is a controversial issue, the current consensus of opinion seems to be “No.” The American College of Obstetricians and Gynecologists, its Canadian counterpart, and an international perinatal association have addressed the issue and none has endorsed universal prenatal screening for maternal CMV infection [4–6]. Until we have interventions that can decrease the risk of fetal infection in pregnancies complicated by maternal CMV infection or interventions other than termination of pregnancy when fetal CMV infection has occurred, enthusiasm for prenatal CMV screening will remain limited. However, some obstetric clinics may choose to screen women for CMV infection, and some pregnant women will be tested because they are suspected of having a CMV infection or are at high risk for infection based on exposure history. The Leruez-Ville study provides data that could guide laboratory evaluation and counseling when first-trimester maternal CMV infection is suspected.

**Note**

Potential conflicts of interest. The author has served as a consultant to Merck, Astellas, Vical, and the State of Montana regarding prevention of CMV infection and has received research support from Sanofi Pasteur. In addition, the author has partial interest in a patent relevant to CMV vaccine.

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**References**