

Healthy Connections

STAY CONNECTED TO YOUR PATIENTS AT HOME

A Healthy Connections Homecare Services publication



Viral infections during pregnancy carry a risk of intrauterine transmission which may result in fetal pathology. The consequences of fetal infection depend on the type of the virus. In general, primary infections in pregnancy are more damaging than secondary infections or reactivations.

Cytomegalovirus:

Cytomegalovirus (CMV) is the most common cause of perinatal infection in the developed world and is a major cause of childhood deafness and neurological handicap. It is present in bodily fluids and person-to-person transmission usually occurs through sexual or close contact. Recurrent infections are usually caused by reactivation of an endogenous latent virus rather than reinfection by a new strain. The virus is usually highly concentrated in urine, seminal fluid, saliva, and breast milk. Viral culture is used to diagnose CMV infection, with most cultures becoming positive within 72-96 hours. PCR can identify the viral antigen within 24 hours.

Serologic testing is also of value in establishing the diagnosis of CMV infection. IgM titers usually decline rapidly over 1-2 months, but they can remain elevated for many months, limiting its utility for serological diagnosis. There is no single IgG titer that clearly differentiates an acute infection from a recurrent one. However, a change of fourfold or greater in the IgG titer over a period of two weeks is usually indicative of a recent acute infection. Another useful test for evaluating a CMV infection is IgG antibody avidity test. Presence of IgG antibody with low

Viral Infections During Pregnancy



Presented by:
Mark Peters, MD, FACOG
Perinatology

to moderate avidity in conjunction with present IgM antibody is consistent with an acute infection, while presence of high avidity IgG antibody indicates a recurrent infection.

Approximately 50-80% of adult women in the United States have serologic evidence of past CMV infection. However, presence of antibodies is not completely protective against reactivation, reinfection, or vertical transmission. Not all maternal infections result in fetal transmission. In fact, less than 50% of maternal primary infections and less than 2% of secondary infections lead to fetal infection. Furthermore, 5-15% of infants who develop congenital CMV as a result of primary mater-

nal infection are symptomatic at birth. This fraction is as low as 1% in secondary maternal infections. Approximately one third of the severely affected newborns die and majority of the survivors have major morbidity. Common clinical manifestations of severe neonatal infection include:

- Hepatosplenomegaly
- Intracranial calcifications
- Jaundice
- Growth restriction
- Microcephaly
- Chorioretinitis
- Hearing loss

Women with recent primary CMV infection should be offered prenatal diagnosis. Detection of quantitative viral DNA in the amniotic fluid and accurate ultrasound examinations are useful in management of pregnant women with suspected primary infection. Viral detection by culture or PCR is the most sensitive and specific test available for diagnosis. However, it is important to keep in mind that a negative amniotic fluid culture or PCR does not always exclude fetal infection. Also, detection of the virus in the amniotic fluid does not depict severity of fetal disease. Findings of ventriculomegaly, intracranial calcifications, hydrops, and growth restriction suggest serious fetal injury.

Treatment of congenital CMV
(Continued on inside)

TO:

Presented by:
Mark Peters, MD, FACOG
Perinatology



Viral Infections During Pregnancy

15701 W. Hardy Rd., Suite 3
Houston, Texas 77060
888.304.1800
www.hchcs.com

Healthy CONNECTIONS
"Stay Connected to Your Patient at Home"

A few words from Healthy Connections

To all of you who support our business, it is our great pleasure to serve you, your staff and your patients. Our success is due to our physicians, and we are so pleased to build upon that success. We truly appreciate you and your support of our company. Please feel free to contact us, personally, for any questions you may have regarding your patients or our services.

Our best for continued success throughout the year, Gaylynn, Tim & John

- Pre-Term Labor Program
- HUAM & Terbutaline Pumps
- Hyperemesis Program Reglan®/Zofran® Pumps
- In-home IV Hydration with pumps
- Total Parenteral Nutrition (TPN)
- Infusion/Antibiotic Therapy
- In-home Non-Stress Tests
- Pregnancy-induced Hypertension program
- Gestational Diabetes Teaching Program
- 17-OH Progesterone Injection Program

Healthy CONNECTIONS
"Stay Connected to Your Patient at Home"

Referrals call: 888.304.1800

For online referrals visit us at www.hchcs.com

Healthy Connections
STAY CONNECTED TO YOUR PATIENTS AT HOME

A quarterly publication produced by
Healthy Connections Homecare Services, Inc.

EXECUTIVE STAFF

Gaylynn Thomas, RN, BSN, COO
Publisher

Timothy B. Waterhouse, MD, MBA, FACOG
Medical Director

John Gee, RPh, President,
Pharmacy Director

Contributing writers of *Healthy Connections* have no business interest in Healthy Connection Homecare Services, Inc. The viewpoints and opinions expressed in this article do not necessarily represent the views or opinions of Healthy Connections Homecare Services, Inc. Questions concerning any of the articles may be addressed to Healthy Connections, 15701 W. Hardy Rd, Suite 3, Houston, Texas 77060 or by calling 888.304-1800.



infection is not as widely accepted. Antiviral treatment of maternal CMV infections with the aim of preventing fetal infection has not been evaluated. Treating newborns with asymptomatic congenital CMV infection is not recommended because of their low risk of sequelae.

Currently, there is neither an available CMV vaccine nor an effective method of passive prophylaxis. There are, however, certain steps pregnant women can take to reduce their risk of acquiring CMV. Good hygiene and handwashing especially after handling infants' diapers or toys, are measures that may reduce risk of CMV infection during pregnancy. Moreover, a recently published Phase II trial on a CMV glycoprotein B vaccine showed that this vaccine may have the potential to decrease the incident of maternal and congenital CMV infections. This trial involved women who were randomized to receive the CMV vaccine versus the placebo injections and they were followed for three years. Eight percent of those who received the vaccine became infected with CMV, compared to 14% in the placebo group, indicating approximately 50% reduction in maternal CMV infections. However, the trial was too small to determine whether the vaccine conferred immunity against congenital infections. Further studies are needed to evaluate efficacy, safety, and duration of protection offered by the vaccine.

Toxoplasma:

Toxoplasma gondii is an obligate intracellular protozoan with a complex life cycle. Maternal infection is transmitted by eating raw or undercooked meat infected with tissue cysts or through contact with oocytes in infected cat feces in contaminated litter or water. Infection rates are highest in areas of poor sanitation and crowded living. There are considerable geographical differences in incident rates, 0.8 per 10,000 live births

in the United States to 10 per 10,000 in France.

Approximately half the adults in the United States have immunity to this organism. Clinically significant infection occurs in 1 in 8,000 pregnancies. The vast majority of pregnant women infected with *T gondii* do not experience any symptoms. In an immunocompromised patient, however, the infection can be deleterious. Complications of toxoplasmosis in an immunocompromised individual include the following:

- Meningitis
- Encephalitis
- Intracranial abscess
- Pneumonitis
- Myocarditis
- Generalized lymphadenopathy

There is no consensus on screening or treatment strategy. In some European countries with high prevalence of toxoplasmosis, prenatal screening is routinely done. ACOG, however, recommends only screening women infected with HIV. The diagnosis of toxoplasmosis in the mother is primarily made by serologic testing. Because IgG may persist in high titers and IgM may be detectable for many years after the acute infection, a panel of tests performed in a reference laboratory is the recommended approach for making the diagnosis. Prior to initiation of management for acute toxoplasmosis, all IgG and IgM positive results should be submitted to a reference lab for IgG avidity testing. A high avidity result in the first 12 to 16 weeks of pregnancy essentially rules out an infection acquired during gestation. A low or equivocal IgG titer should be followed up with a repeat titer two to three weeks later.

Transmission to the fetus is very rare early in gestation, but gradually increases in frequency towards the end of gestation. The risk of fetal infection during the first trimester is <5% and it increases to approximately 70% close to term. Fur-

thermore, there is an inverse relationship between the frequency of transmission and the severity of the disease. When acute maternal infection is diagnosed, prenatal diagnosis of fetal toxoplasmosis should be attempted by amniotic fluid sampling for PCR. It is important to remember that the sensitivity and specificity of the test is significantly influenced by gestational age. For this reason, amniocentesis should be performed at 18 week or more to achieve higher sensitivity. Fetal ultrasound is recommended for women suspected or diagnosed as having acquired acute infection during pregnancy. Ultrasonographic findings suggestive of congenital toxoplasmosis include:

- Ventriculomegaly
- Intracranial and intrahepatic calcifications
- Hepatomegaly
- Splenomegaly
- Ascites

Treatment of pregnant women is believed to reduce the risk of congenital fetal toxoplasmosis. Controlled, randomized studies evaluating specific medications for treatment of toxoplasmosis are lacking. However, most authorities recommend combination therapy with pyrimethamine, sulfadiazine, and folinic acid in pregnant women who acquire the infection after 18 weeks of gestation. Pyrimethamine is not recommended for use in the first trimester because of concerns for teratogenicity. Some European countries have use spiramycin for treatment of acute maternal toxoplasmosis with excellent success. This medication is available in the United States through special permission from Center for Disease Control.

Primary prevention can be achieved through education targeted at women who have never been exposed to *T gondii*. Secondary prevention, aimed at preventing fetal infection during pregnancy, is appropriate for countries with a high

prevalence of toxoplasmosis such as France and Austria. This population may benefit from universal serologic screening and treatment with spiramycin when appropriate. There is no vaccine for *T gondii*.

Parvovirus:

Human parvovirus B19 is a potent inhibitor of the erythroid cell differentiation and is cytotoxic for erythroid precursor cells. The clinical disease is called erythema infectiosum or fifth disease. Also, in children or adults with an underlying hemoglobinopathy, parvovirus may cause an aplastic crisis. The virus is transmitted primarily by respiratory droplets and infected blood products. The maternal infection rate is highest in women with school-aged children and daycare workers. Approximately 50% of women of reproductive age have evidence of prior infection with long-lasting immunity. The incubation period is 4-20 days from exposure. The clinical manifestations of the disease include low-grade fever, headache, flu-like symptoms, and a "slapped cheek" facial rash. A lacelike rash may spread to trunk and extremities. Asymptomatic seroconversion following viremia with parvovirus B19, however, is common in both children and adults.

Parvovirus B19 infection during pregnancy can cause severe anemia, non-immune hydrops fetalis, and fetal death. These manifestations, however, seem to be rare. The risk of fetal complications depends on gestational age at the time of

maternal infection. In case of maternal infection during the first trimester, risk of fetal infection is 5-10%. If the infection develops during weeks 13-20, the risk of fetal infection decreases to 5% and if maternal infection occurs beyond 20 weeks, the risk of fetal hydrops is less than 1%.

The best way to confirm diagnosis of maternal parvovirus B19 infection is through serologic testing. Viral DNA may be detectable in maternal blood during the prodrome, but not after development of the rash. Fetal infection can be identified by detecting viral DNA in amniotic fluid or detection of fetal parvovirus B19 IgM through cordocentesis.

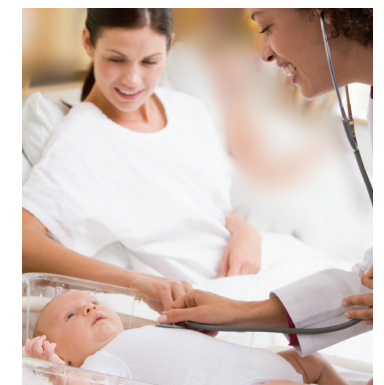
Once maternal infection is confirmed, the fetus should be assessed for anemia by use of middle cerebral artery (MCA) Doppler velocimetry, since increases in peak systolic velocity in this vessel correlate well with fetal hematocrit. Serial ultrasound exams should be performed for at least 8 weeks after documentation of maternal infection, as incubation period for fetuses may be longer than in adults. Fetal management is dependent on gestational age. Although cases of spontaneous resolution of fetal hydrops have been reported, review of literature supports a recommendation for intrauterine fetal transfusion in the setting of severe fetal anemia.

There is no evidence that antiviral treatment prevents maternal or fetal parvovirus infection. Pregnant women should be counseled that the risks of infection are approximately 5% for casual, infrequent contact, 20% for intense,

prolonged contact, and 50% for close, frequent interaction. There is no vaccine for human parvovirus B19 currently available, but immunogenic vaccines are currently under trial.

References

1. Creasy R, Resnik R, Iams J, et al: *Creasy and Resnik's Maternal-Fetal Medicine: Principles and Practice*. 6th Ed. Saunders Elsevier, 2009.
2. Cunningham G, Leveno K, Bloom S, et al: *Williams Obstetrics*. 23rd Ed. McGraw-Hill, 2010.
3. Ergaz Z, Ornoy A: *Parvovirus B19 in pregnancy*. *Reproductive Toxicology* 21:421, 2006.
4. Mendelson E, Aboudy Y, Smetana Z, et al: *Laboratory assessment and diagnosis of congenital viral infections: Rubella, cytomegalovirus (CMV), varicella-zoster virus (VZV), herpes simplex virus (HSV), parvovirus B19 and human immunodeficiency virus (HIV)*. *Reproductive Toxicology* 21:350, 2006.
5. Montoya JG, Rosso F: *Diagnosis and management of Toxoplasmosis*. *Clinics in Perinatology* 32:705, 2005.
6. Pass RF, Zhang C, Evans A, et al: *Vaccine prevention of maternal cytomegalovirus infection*. *New England Journal of Medicine* 360:1191, 2009.



Healthy CONNECTIONS
"Stay Connected to Your Patient at Home"

Referrals call: **888.304.1800**

For online referrals visit us at www.hchcs.com