95 Viral Infections in the Fetus and Neonate

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Neonates, like older children and adults, are subject to viral infections acquired by horizontal routes, such as those due to influenza, rotavirus, and enteroviruses. They also are at risk for acquisition of viruses through routes that are unique to the perinatal setting where mother-to-child transmission (MTCT) occurs transplacentally, during birth, or from breast milk. The ability of certain viruses to establish chronic infection in the mother with persistence of infectious virus in blood, mucosa, or milk (herpesviruses, human immunodeficiency virus (HIV), human T-lymphotropic virus 1 (HTLV-1), hepatitis B and C) accounts for the key role vertical transmission plays in their epidemiology and clinical significance. Whether viruses that produce acute, self-limited infections in the mother, such as rubella, varicella-zoster virus (VZV), enteroviruses, and parvovirus B19, are transmitted to the fetus or newborn and produce disease depends on the timing of maternal infection in relation to gestation and parturition. Thus the clinical settings in which fetal and neonatal viral infections must be considered include pregnancy, the newborn nursery, and the evaluation of an ill newborn. This chapter provides an overview of the viral infections that occur in these settings. Detailed discussions of epidemiology, diagnosis, treatment, and prevention are presented in the chapters focused on specific viruses.

PATHOGENESIS

Many viral infections produce disease that is more severe in the fetus or neonate than in adults, children, or infants. Viral infection of the fetus probably follows maternal viremia or viral replication in the placenta. Developmental immaturity of fetal and neonatal cellular and humoral immune function is important in pathogenesis (see review by Lewis and Wilson[1]). Interferon-γ production by T lymphocytes is decreased; CD4+ T lymphocyte antigen-specific responses are delayed compared with adults; and T-cell help for B-cell differentiation is decreased. In addition, neonatal natural killer (NK) cells have an immature phenotype and decreased cytotoxicity against virus-infected cells. Viruses that infect the fetus early in gestation usually result in more damage than those that infect the fetus late in gestation.[2–4] Fetal infection before the third trimester occurs in the absence of substantial concentrations of maternally derived antibodies. Infections early in gestation encounter an immature immune system and developing fetal organs. Tissue damage, organ dysfunction, teratogenicity, and fetal demise are possible consequences of these infections.

Maternal antibody acquired transplacentally and antibody and immunocompetent cells present in colostrum and mother's milk

are important components of the neonate's defense against viral infection. A neonate infected by a virus to which the mother lacks immunity is prone to severe infection; neonatal infections caused by herpesviruses are illustrative. Transfusion-acquired CMV infections are rarely evident clinically in term infants of seropositive mothers, but can cause severe illness in small, antibody-negative premature infants. Herpes simplex virus (HSV) and VZV are more likely to cause severe disease in the neonate with absent or low concentrations of maternal antibodies.

EPIDEMIOLOGY

Virus Transmission from Mother to Child

Viruses for which MTCT has well-characterized clinical consequences are listed in Table 95-1 along with the main routes of transmission that result in clinical disease. The likelihood that maternal viral infection spreads to the fetus or neonate is determined by the occurrence of viremia, genital tract viral shedding, or virolactia. Exposure to maternal virus often is a result of chronic infection caused by cytomegalovirus (CMV), HIV, HSV, HTLV-1, hepatitis B, or hepatitis C. For these viruses the prevalence of infection in women of childbearing age and the incidence of new infections during pregnancy contribute to the overall prevalence of fetal or neonatal infection. In contrast, fetal or neonatal infection with VZV, rubella, parvovirus B19, hepatitis E virus, and a number of agents not listed in Table 95-1 is based on the incidence and timing of maternal infection in relation to pregnancy and delivery. MTCT of a number of viruses not listed in Table 95-1 is known to occur. Studies of GB virus C also known as hepatitis G virus, a hepatotropic flavivirus that produces chronic infection, show that 60% to 80% of infants born to mothers with viral RNA

in their blood are infected. Transiently elevated serum alanine aminotransferase concentrations have been noted, but there has been no associated illness in infants with perinatal infection.[5,6] Sporadic reports of congenital disease due to enteroviruses or adenovirus and frequent detection of viral nucleic acid by PCR testing of amniotic fluid suggest that transplacental transmission of these viruses may be more common than is appreciated.[7–10] The proportion of maternal infections that lead to fetal demise, stillbirth, neonatal disease, or asymptomatic infection is not well defined.

Infection of the newborn during birth occurs through exposure to maternal blood or secretions; it is the major route of MTCT for HSV, HIV, hepatitis B, and hepatitis C. Labor and delivery prolong the contact between the neonate's mucosal surfaces and maternal secretions and blood, facilitating transfer of viruses. The newborn who acquires virus during birth typically becomes viremic or sheds virus in other body fluids between 1 and 4 months of age. Intrapartum infection has well-known clinical consequences for the newborn in the case of HSV and HIV. Hepatitis B and hepatic C produce chronic infection that can progress to chronic hepatitis, cirrhosis, and hepatocellular carcinoma. Cytomegalovirus also is commonly spread from mother to infant during birth, but these infections do not appear to be clinically significant except perhaps in very low birthweight premature infants.

Vertical transmission of viruses through ingestion of human milk is important in the epidemiology of CMV, HTLV-1, and HIV. Although the quantity of virus present in human milk usually is low, the nursing infant is exposed to this potential source of infection multiple times per day for months. Breastfeeding is the major route for vertical transmission of CMV. In populations in which mothers nurse their infants routinely and rates of maternal seropositivity are high, most infants acquire CMV during the first year of life.[11] Transmission of CMV through mother's milk rarely causes acute illness or the types of sequelae that follow congenital infection; breast milk-acquired CMV infection in very low birthweight premature newborns is a possible exception (see Chapter 206, Cytomegalovirus). Both HIV and HTLV-1 can be transmitted through human milk, although the onset of infection usually is after the neonatal period.[12–14] Breast milk can also be a significant route of MTCT of GB virus C and TT virus, but neither of these has been proven to cause disease.[5,6,15] Transmission of rubella virus, HSV, and echovirus 18 has been reported when acute maternal infection was present while breastfeeding. It is believed that virolactia occurs during acute infections with these agents.[16–18] Viruses that are transmitted through blood could be transmitted during breastfeeding in the presence of bleeding or cracked nipples even in the absence of virolactia. Because of the consistent association of higher infant mortality with formula feeding, the potential transmission of maternal viral infection rarely should be a reason to interdict breastfeeding in developing countries, with the possible exception of HIV infection. In 2010, the World Health Organization updated recommendations on infant feeding in the context of maternal HIV infection, recommending that national authorities in each country decide which infant feeding practice will be supported.[19] Although the previous recommendation that "… replacement feeding should not be used unless it is acceptable, feasible, affordable, sustainable and safe" remains, the impact of antiretroviral treatment of mother and infant on reducing transmission of HIV through breast milk is acknowledged. The American Academy of Pediatrics Committee on Infectious Diseases has made specific recommendations regarding breastfeeding by mothers known to have certain viral infections (Table 95-2).[20]

Sources of Maternal Infection

The likelihood of maternal viral infections with the attendant risk of MTCT is affected by specific types of exposures. For example, because CMV infection is common in young children who shed CMV chronically, exposure to young children is one of the most important risk factors for maternal CMV infection. Sexual activity is a risk factor for the acquisition of HSV, CMV, HIV, and hepatitis

TABLE 95-1. Routes of Transmission for Selected Viruses for Which Mother-to-Child Transmission Has Well-Characterized Clinical Consequences

Virus	Clinical	Route[a]
Chikungunya virus	Fever, "sepsis," encephalopathy	Transplacental/intrapartum
CMV	Congenital infection syndrome	Transplacental
Dengue virus	Fever, rash, hepatosplenomegaly, thrombocytopenia, pleural effusion	Transplacental/intrapartum
Hepatitis B virus	Chronic liver disease	Intrapartum
Hepatitis C virus	Chronic liver disease	Intrapartum
Hepatitis E virus	Jaundice, hepatitis, liver failure	Transplacental/intrapartum?
HSV	Neonatal herpes	Intrapartum
HIV	Perinatal HIV/AIDS	Intrapartum, breast milk
Human papillomavirus	Laryngeal papillomatosis	Intrapartum
HTLV-1	Adult T cell leukemia	Breast milk
LCMV	Encephalopathy, chorioretinitis	Transplacental
Parvovirus B19	Anemia, hydrops	Transplacental
Rubella virus	Congenital rubella syndrome	Transplacental

CMV, cytomegalovirus; HSV, herpes simplex virus; HIV, human immunodeficiency virus; HTLV-1, human T-lymphotropic virus; LCMV, lymphocytic choriomeningitis virus.

[a]*Principal route responsible for clinical consequences.*

PART II Clinical Syndromes and Cardinal Features of Infectious Diseases: Approach to Diagnosis and Initial Management

SECTION N Infections of the Fetus and Newborn

TABLE 95-2. Summary of American Academy of Pediatrics Committee on Infectious Diseases Recommendations for the U.S. on Breastfeeding (or Provision of Mother's Milk) in the Presence of Maternal Viral Infection

Virus	Recommendation
Cytomegalovirus	Risk for very low birthweight preterm; no clear recommendation
Hepatitis B virus	No restriction
Hepatitis C virus	Discuss theoretical risk with mother
Human immunodeficiency virus	Do not breastfeed
Human T-lymphotropic virus 1	Do not breastfeed
Human T-lymphotropic virus 2	Do not breastfeed
Rubella	No restriction
Varicella	Follow recommendations for VariZig; no recommendations on breastfeeding
West Nile virus	Breastfeeding is recommended in endemic area; no recommendation for breastfeeding during infection

Modified from reference 20.

B virus infections and injecting drug use is a risk factor for HIV, hepatitis B, and hepatitis C. For viruses that cause acute, self-limited infections with seasonal or periodic epidemics such as parvovirus B19, rubella, and VZV, risk of maternal and congenital infection is related to epidemic activity in the community. Success in preventing congenital rubella infection is directly related to wide use of rubella vaccine to prevent outbreaks and thus prevent maternal exposure. In 2005, the Centers for Disease Control and Prevention announced the elimination of domestic rubella and congenital rubella syndrome in the United States.[21] In 2008, there were 11 known cases of rubella in the U.S., all of which were imported or related to imported cases; there was no congenital rubella.[22] Similar success is being achieved in other countries due to incorporation of rubella vaccine into routine childhood vaccine programs, along with national programs that include active surveillance and special efforts to achieve high immunization rates.[22]

Insect vectors and animals can be the source of maternal infections that are spread to the fetus or newborn. Mice excrete lymphocytic choriomeningitis virus (LCMV) and are the source of human infection. Congenital infection due to LCMV is likely underdiagnosed in the U.S. Maternal infection, especially in the first trimester, can lead to fetal infection with subsequent chorioretinitis, micro- or macrocephaly, and intracranial calcifications. Maternal exposure to rodents may be the key epidemiologic clue.[23,24] West Nile virus is a zoonotic pathogen with transplacental and breast-milk transmission reported in the U.S;[25,26] however, MTCT appears to be rare. Chikungunya virus, an emerging cause of febrile illness with arthralgia, myalgia, and rash in Africa, India, and Southeast Asia is transmitted to humans by *Aedes* mosquitoes. Maternal infection has been associated with transmission to the fetus and neonate; a transmission rate of approximately 50% was reported with maternal viremia at term.[27] Although it is unclear whether maternal infection affects the outcome of pregnancy, newborn infection is manifest by a sepsis-like illness, encephalopathy, and high fever and may be associated with central nervous system (CNS) sequelae.[27,28] Dengue virus also is transmitted by *Aedes* mosquitoes and infection is common in tropical areas. Rates of MTCT range from 12% to 60% when maternal infection occurs during pregnancy, and similar to Chikungunya virus, maternal viremia at term is strongly associated with neonatal infection.[29] Infected newborns can have a sepsis-like illness with fever, thrombocytopenia, hepatosplenomegaly, rash, and pleural effusion.

Postnatal Infection: Community Acquired and Nosocomial

Horizontal transmission of viruses to neonates from caregivers or family members occurs primarily through infected droplets or contaminated hands. Neonates are more vulnerable than older hosts because they are immunologically naive and their care requires repeated handling and close contact. In addition, hospitalized neonates are exposed to a continual influx of hospital personnel and new patients, creating multiple opportunities for the introduction and spread of viruses prevalent in the community.

Outbreaks of many different viruses in newborn nurseries have been described; enteroviruses, adenovirus, rotavirus, and respiratory syncytial virus are notable because they are common, difficult to control, and have significant clinical consequences.[9,30] Neonates are infected by the mother, other family members, or hospital personnel. Enterovirus and respiratory virus outbreaks in hospital nurseries usually are associated with community outbreaks. Blood products are a potential source of nosocomial CMV infection that could be clinically significant for premature newborns or babies born to CMV-seronegative mothers. These infections are prevented either by only administering CMV-negative blood to neonates or by using filters to remove leukocytes from blood.

Viruses are the leading cause of illness in patients who present to the hospital with fever prior to 3 months of age.[31] Enteroviruses are particularly common in this age group. Data from the National Enterovirus Surveillance System in the U.S. for the period 1983–2003 showed that 11.4% of all reported enterovirus infections occurred in neonates.[32] During summer and fall, enteroviruses account for the majority of hospitalizations in young infants with suspected sepsis.[9,31] A study of hospitalized, febrile infants reported PCR detection of enterovirus in 28.5% of cerebrospinal fluid samples collected during the enterovirus season (June through October) compared with 11.1% during other months.[33] Parechoviruses (previously echovirus 22 and 23) can cause a sepsis-like illness with rash in newborns.[34] Other viral infections are sporadic or seasonal causes of fever, systemic illness, gastrointestinal disease, and respiratory disease in infants including adenovirus, rotavirus, norovirus, astrovirus, influenza, HSV, respiratory syncytial virus (RSV), and others.[35–38]

CLINICAL MANIFESTATIONS

Prematurity and Low Birthweight

Maternal viral infection can involve the placenta and affect outcome for the infant even if fetal infection does not occur. The proportion of morbidities such as preterm birth or poor fetal growth that can be attributed to viral infection of the mother of fetus is not well defined. A virologic and serologic study of small-for-gestational-age neonates in Sweden did not find evidence that viral infection was causally associated with low birthweight.[39] Maternal herpangina has been associated with premature birth, low birthweight, and poor intrauterine growth.[40] Placental adenovirus infection has been associated with chorioamnionitis and preterm birth.[41] A study of newborn dried blood spots, using PCR to detect enterovirus RNA and herpesvirus DNA, reported an association between detection of CMV DNA and pregnancy-induced hypertension and preterm birth.[42] Adeno-associated virus-2, a member of the parvovirus family, has been reported in association with pre-eclampsia, stillbirth, and preterm birth.[43] Increased risk of prematurity, low birthweight, and other unfavorable pregnancy outcomes have been ascribed to maternal dengue infection; however, a review of 30 published studies concluded that evidence linking maternal infection to adverse pregnancy outcomes was inconclusive.[29]

Spontaneous Abortion and Stillbirth

It is possible that many unexplained spontaneous abortions, intrauterine fetal deaths, and stillbirths are due to unrecognized viral

infection, considering that most studies focus on one or a small number of viruses and few studies have employed modern molecular techniques for virus detection. A number of viruses, including poliovirus, measles, rubella, mumps, influenza, parvovirus B19, HSV, CMV, and nonpolio enteroviral infection, have been associated with spontaneous abortion or stillbirth.[44] Studies that have included controls and molecular techniques for virus detection suggest that viral infections probably account for many cases of unexplained fetal death and stillbirth. A histopathologic and molecular study of spontaneous abortions and fetal deaths found evidence of viral infection in 16 of 21 cases and in none of 26 controls; enterovirus/coxsackievirus accounted for 10 of the cases.[45] A study of placental tissue from 62 fetal deaths and 35 control pregnancies found evidence of CMV, parvovirus B19, and HSV in 16%, 13%, and 5% of cases, respectively; only 6% of placentas from control pregnancies were positive for any of these viruses.[46] A Swedish study reported PCR evidence of parvovirus B19 infection in placental or fetal tissue in 7 of 47 (15%) intrauterine fetal deaths, 2 of 37 (5%) miscarriages, and in none of 29 induced abortions and term, normal pregnancies.[47] A German study of 1018 pregnancies complicated by maternal parvovirus B19 infection reported a fetal death rate of 11% when maternal infection occurred prior to 20 weeks' gestation and no fetal demise following infections later in gestation.[48] The extent to which maternal HIV-1 infection in the absence of immune deficiency increases the risk of fetal death or stillbirth is not clear.[44] Declining CD4+ lymphocyte count and comorbidities are associated with increased risk of stillbirth, and in countries with high maternal seroprevalence, HIV-1 could be an important cause of stillbirth.

Syndrome of Congenital Infection

The presence of hepatomegaly, splenomegaly, microcephaly, petechiae, jaundice, dermal manifestations of erythropoiesis, poor intrauterine growth, chorioretinitis, intracranial calcifications, deafness, thrombocytopenia, direct hyperbilirubinemia, or hepatitis in the neonate suggests prenatal infection. Other findings occasionally associated with congenital infection are cardiac defects, hydrocephalus, prematurity, and anemia. Clinical findings suggestive of infection by a specific viral agent are listed in Table 95-3. However, clinical findings alone are not diagnostic; laboratory evaluation is essential in patients with suspected congenital viral infection.

Central Nervous System Infection

Viral encephalitis or meningitis in the neonate can result from prenatal or postnatal infection. Abnormalities suggestive of viral central nervous system disease often are subtle or nonspecific; they include lethargy, hypotonia, irritability, poor feeding, apnea, fever, and seizures. Prenatal viral infections can affect brain growth, leading to microcephaly. Although encephalopathy or encephalitis in the neonate has been noted with a number of viral infections, CMV, enteroviruses, and HSV are the agents most commonly implicated.

TABLE 95-3. Clinical Findings in the Newborn Suggesting a Specific Congenital Viral Infection

Agent	Features
Cytomegalovirus	Microcephaly, hearing loss, petechiae, cholestatic jaundice
Rubella	Cataracts, heart disease, deafness
Varicella-zoster virus	Scarring of skin, limb hypoplasia, ocular abnormalities
Herpes simplex virus	Hydranencephaly, ocular disease, skin scars
Lymphocytic choriomeningitis virus	Micro- or macro-cephaly, chorioretinitis

Sepsis Syndrome

Clinical manifestations suggestive of septicemia sometimes are associated with neonatal enterovirus, coxsackievirus, parechovirus, adenovirus, HSV, RSV, or influenza infections. Neonates with echovirus, parechovirus or coxsackievirus infection can manifest pallor, lethargy, hypotension, apnea, acidosis, and respiratory impairment.[9] Rapid progression of disseminated HSV infection can produce shock, coagulopathy, fulminant hepatitis, and diffuse lung disease.[49] Neonatal RSV and adenovirus infections also can cause nonspecific signs that mimic septicemia, such as apnea, lethargy, irritability, and poor feeding.[50] It is likely that other respiratory viruses have similar effects in the newborn.

Cardiac Insufficiency

Viral infections produce congestive heart failure in the fetus or neonate by causing anemia or by damaging the myocardium directly. Fetal infection with human parvovirus B19 characteristically leads to profound anemia. Although many fetuses appear to recover in utero, hydrops fetalis and fetal death can result.[51] Rare cases of nonimmune hydrops fetalis have been attributed to intrauterine CMV or adenovirus infection.[52,53] Viral myocarditis usually is due to coxsackie B viruses or echoviruses in the neonate and patients often present with cardiac failure or shock.[9]

Pulmonary Disease

Lower respiratory tract disease is an unusual manifestation of congenital or perinatal viral infection; respiratory tract symptoms occur usually as part of multisystem disease in disseminated neonatal HSV or VZV infection. Postnatal lower respiratory infection or pneumonia in the neonate can be due to any of the viruses that cause respiratory tract disease in older children, including RSV, parainfluenza virus, influenza viruses, adenovirus, enteroviruses, rotavirus, rhinovirus, metapneumovirus, and bocavirus. Respiratory virus infection in newborns is likely to produce more severe lung disease than occurs in older children and can manifest more nonspecifically as fever, lethargy, and poor feeding. Outbreaks of respiratory virus disease can cause substantial morbidity in neonatal nurseries.

Ocular Abnormalities

Table 95-4 lists ocular abnormalities that can be found in infants with congenital and neonatal viral infections.[54–57] Careful examination of a neonate's eyes, with the use of indirect

TABLE 95-4. Newborn Ocular Abnormalities Associated with Congenital and Neonatal Viral Infection

Abnormality	Agents
Cataracts	Rubella, CMV, HSV, LCMV, VZV
Chorioretinitis	CMV, HSV, LCMV, VZV, rubella
Optic atrophy	HSV, VZV, rubella, CMV, LCMV
Microphthalmia	CMV, rubella, LCMV
Coloboma	CMV, rubella
Keratoconjunctivitis	HSV
Pigment retinopathy	Rubella
Glaucoma	Rubella
Iritis	HSV, rubella
Anophthalmia	CMV
Peter anomaly[a]	CMV
Horner syndrome[b]	VZV

CMV, cytomegalovirus; HSV, herpes simplex virus; LCMV, lymphocytic choriomeningitis virus, VZV, varicella-zoster virus.

[a]*Central corneal/anterior-chamber synechiae, cataract.*

[b]*Ptosis, meiosis, and ipsilateral absence of facial sweating.*

ophthalmoscopy and slit lamp, is an important part of the evaluation of those with suspected congenital or neonatal infection. Abnormalities of the cornea and iris, chorioretinitis, vitritis, optic atrophy, and pigment retinopathy are the abnormalities most often detected in neonates with congenital infection. Chorioretinitis can be evident as scarring or as active lesions, sometimes accompanied by vitritis. Ocular abnormalities usually are associated with evidence of infection of other organs. In addition to association with visual impairment, ocular signs are important in congenital or neonatal viral infection because they may be predictive of central nervous system involvement.

Deafness

Deafness is commonly associated with congenital infection caused by rubella virus and CMV. Newborns with diminished hearing of unknown etiology should be evaluated for congenital infection. Congenital CMV infection accounts for approximately 15–20% of all cases of bilateral moderate to profound sensorineural hearing loss in children in the U.S.[58] Because congenital CMV infection can cause progressive hearing loss, serial hearing evaluations throughout infancy and early childhood are recommended.

APPROACH TO THE NEONATE WITH SUSPECTED VIRAL INFECTION

Differential Diagnosis

The presence, singly but especially in combination, of hepatomegaly, splenomegaly, petechiae, purpura, jaundice, microcephaly, encephalopathy, ocular abnormalities, anemia, thrombocytopenia, conjugated hyperbilirubinemia, or elevated serum hepatic transaminases should prompt the consideration of congenital viral infection. Nonspecific signs, such as fever, lethargy, anorexia, respiratory symptoms, and a sepsis-like syndrome, also suggest the possibility of perinatal viral infection as well as bacterial or fungal infection. Prenatal viral and nonviral infections, especially syphilis and toxoplasmosis, can be indistinguishable clinically from congenital viral infection. Miliary tuberculosis is rare and should be differentiated easily from viral infection, although central nervous system manifestations, hepatomegaly, and splenomegaly might initially suggest congenital infection.

Inborn errors of metabolism can cause encephalopathy, elevation of serum hepatic enzymes, thrombocytopenia, anemia, enlarged liver and spleen, jaundice, retinal pigment defects, and cataracts. Hypoglycemia, acidosis or alkalosis, hyperammonemia, crystalluria, urinary reducing substances, and a positive urine ferric chloride test result are clues to the presence of metabolic disease. Genetic abnormalities can produce CNS and other abnormalities so similar to those seen with congenital infection that the term "pseudo-TORCH" syndrome has been applied.[59–61] Liver disease associated with neonatal giant-cell hepatitis, biliary atresia, choledochal cyst, or intestinal obstruction can lead to hepatomegaly, splenomegaly, elevation of serum transaminases, and cholestatic jaundice. Anemia, hyperbilirubinemia, or hepatosplenomegaly due to rhesus or ABO isoimmunization, red blood cell biochemical defects, red blood cell structural defects, or immunologically mediated thrombocytopenia can be confused with congenital infection.

Fetal exposure to alcohol, anticonvulsants, or cocaine can impair brain growth, leading to microcephaly and neonatal encephalopathy similar to that observed in congenital infection. The prolonged use of intravenous vitamin E in premature infants has been associated with thrombocytopenia, encephalopathy, and cholestatic jaundice that could be confused with signs of congenital or neonatal viral infection. Congenital leukemia and neuroblastoma can present with anemia, thrombocytopenia, and organomegaly.

Laboratory Diagnosis

Laboratory testing should focus on identification of virus by culture or detection of viral nucleic acid or proteins in the appropriate specimens. The most likely etiologies should be selected on the basis of signs, laboratory abnormalities, and clinical context. The specimens required and the approach used for laboratory diagnosis depend on the specific viral infection being considered (see pathogen-specific chapters).

Measurement of maternal or neonatal antibody responses is of limited value but can contribute useful information in certain circumstances. Negative immunoglobulin (Ig) G antibody results for specific agents indicate that maternal infection is not present or is very recent, substantially reducing the likelihood of prenatal MTCT. The accuracy of IgM antibody testing of neonatal serum for viral diagnosis is highly variable, depending on the agent, assay used, and laboratory. Virus culture or PCR testing should be used to confirm specific positive or negative IgM antibody test results. Results of test panels for IgG or IgM antibody to multiple possible causes of infection ("TORCH titers") usually fail to establish an etiologic diagnosis or are not relevant; they should not be used as the sole laboratory diagnostic assay.[62,63]

Prevention and Treatment

Antiviral agents for treatment of congenital and neonatal infections are limited to acyclovir and ganciclovir (or valganciclovir) and antiretroviral agents. Acyclovir treatment of neonates with HSV infection can be life-saving and improves the quality of life for survivors.[49] Acyclovir also is indicated for perinatal VZV infection.[64] Antiviral treatment for severe symptomatic, congenital CMV infection also improves outcome.[65,66] Methods to protect neonates from perinatally transmitted HIV and hepatitis B are critically important. Management of infants with congenital or neonatal viral infection involves provision of supportive care and anticipation of complications, such as hearing loss, mental retardation, cerebral palsy, and chronic liver disease.

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