

## Chapter 10

# Perinatal Infections

Certain infections that occur in the antepartum or intrapartum period may have a significant effect on the fetus and newborn. Appropriate antepartum and intrapartum care of the mother and subsequent care of the newborn soon after birth can reduce the frequency of or ameliorate many serious problems and can minimize the risk of subsequent transmission in the nursery. In addition, some infections, such as influenza and varicella, may have more severe outcomes in pregnant women than in other adults. Communication and cooperation among all perinatal care personnel are essential to obtain the best results. The infections discussed in this chapter have been selected on the basis of new and evolving information that affects management.

## Viral Infections

### Cytomegalovirus

Cytomegalovirus (CMV), a member of the herpesvirus group, is the most common congenital viral infection. Approximately 1% of newborns are infected with CMV in utero and excrete CMV after birth. Approximately 10% of infants with congenital CMV infection have signs of infection at birth, with manifestations including intrauterine growth restriction, jaundice, purpura, hepatosplenomegaly, microcephaly, intracerebral calcifications, and retinitis; developmental delays in early childhood are common. Sensorineural hearing loss is the most common sequela of congenital CMV infection, which makes CMV the leading nongenetic cause of sensorineural hearing loss in children in the United States, accounting for one third of all cases.

#### *Transmission*

Transmission occurs via transplacental passage of the virus, contact of the infant with infectious secretions at the time of birth, ingestion of infected breast milk, or transfusion of blood from seropositive donors. Infection acquired intra-

partum from maternal cervical secretions or postpartum from human milk usually is not associated with clinical illness in term infants. In preterm infants, infection resulting from human milk or from transfusion from CMV-seropositive donors has been associated with systemic infections, including lower respiratory tract disease and disseminated disease. Both primary CMV infection and reactivation of a latent infection can occur during pregnancy and result in congenital CMV infection. CMV-associated illness in a congenitally infected infant is more likely to occur in an infant born to a mother with primary CMV infection, especially among pregnant women infected before the third trimester.

Breastfeeding is not contraindicated for term infants of mothers who are seropositive carriers of CMV and have a past history of CMV infection. Transmission of CMV to newborns who receive milk from human milk banks can be minimized by limiting donor milk to CMV-negative donors or by ensuring appropriate pasteurization. (For breastfeeding guidelines, see Chapter 8.) Transmission via transfusion has been virtually eliminated by the use of blood from CMV-negative donors, the use of frozen deglycerolized red blood cells, and filtration to remove white blood cells.

### *Screening*

Because there is neither a vaccine for prevention of infection nor an established, effective therapy for acute CMV infection, routine serologic screening of women or neonates is of no proven benefit. Testing generally is limited to pregnant women and neonates in whom CMV exposure is suspected. Routine serologic testing of personnel in newborn nurseries is not recommended.

### *Diagnosis*

Active infection with CMV in pregnant women can be diagnosed by polymerase chain reaction (PCR) or viral culture of CMV from urine, saliva, throat swab specimens, or other body tissues. Serologic tests that detect CMV antibodies (immunoglobulins M and G) are widely available and can be used to document susceptibility to CMV or primary infection. Congenital CMV infection can be diagnosed if an infant has the virus detected in his or her urine, saliva, blood or other tissues within 2–3 weeks after birth. Later in infancy, differentiation between intrauterine and perinatal infection is difficult to determine. Isolation of the virus or detection of CMV genome by PCR from amniotic fluid is the most sensitive test for detecting fetal infection. Fetal blood obtained by cordocentesis may be tested for CMV-specific immunoglobulin M (IgM), but this test is less sensitive than culture or PCR of amniotic fluid.

### *Treatment*

No treatment is currently indicated for CMV infection in healthy individuals. Antiviral treatment is used for immunocompromised patients who have either sight-related or life-threatening illnesses due to CMV infection. There are limited data suggesting the possible benefits of parenteral administration of the antiviral medication ganciclovir in neonates ill with congenital CMV involving the central nervous system to protect against hearing deterioration and to decrease the risk of neurodevelopmental impairment. However, intravenous treatment with ganciclovir requires prolonged (42-day) hospitalization, has significant adverse effects (eg, neutropenia) that may force discontinuation of treatment, and places the infant at increased risk of an adverse event associated with prolonged intravenous therapy. There are little data regarding the efficacy of ganciclovir therapy in preterm infants with perinatally acquired CMV infection.

There is limited evidence that administration of CMV hyperimmune globulin to pregnant women with a primary CMV infection can lower the risk of congenital CMV disease. However, there are insufficient efficacy data to recommend its use at this time.

### **Enteroviruses**

The enteroviruses comprise a group of viruses that includes the polioviruses, Coxsackie viruses, echoviruses, and other enteroviruses. Through the widespread use of vaccines, wild-type poliovirus infection has been eliminated from the Western Hemisphere as well as the Western Pacific and European regions. Nonpolio enteroviral infections are common and are spread by fecal–oral and respiratory routes. Enteroviruses are common and pregnant women are frequently exposed to them, especially during summer and fall months. Most enterovirus infections during pregnancy cause mild or no illness in the mother. However, infection in the third trimester can trigger labor.

Enteroviruses rarely cross the placenta and cause disease in the fetus. Vertical transmission of enteroviruses can occur at birth after exposure to virus-containing maternal blood or cervical secretions. Signs of an enterovirus infection in the neonate generally begin 3–7 days after birth. Neonates who acquire infection perinatally or within days of birth are at risk of severe disease. Manifestations can include pneumonia, exanthems, aseptic meningitis, encephalitis, paralysis, hepatitis, conjunctivitis, myocarditis, and pericarditis.

Diagnosis is confirmed by recovery of the virus from swabs of the throat or rectum and samples of stool, cerebrospinal fluid, or blood. Polymerase chain reaction testing of spinal fluid is more sensitive than a culture.

No specific therapy is available. Immune globulin given intravenously has been used in life-threatening neonatal infections, suspected viral myocarditis, and enterovirus 71 neurologic disease, but efficacy data are lacking. Hospitalized newborns should be managed with standard as well as contact precautions.

## Hepatitis A Virus

The hepatitis A virus (HAV) is a small RNA virus that can produce either asymptomatic infection or acute illness. Serious effects of HAV infection are uncommon. Hepatitis A virus has little effect on pregnancy and rarely is transmitted perinatally. The risk of transplacental transmission to the fetus is negligible, and there is no evidence that the virus is a teratogen. The most common mode of transmission is by the fecal–oral route. Diagnosis is confirmed by the demonstration of anti-HAV IgM antibodies in infant serum.

Vaccines for hepatitis A are highly effective and approved for use during pregnancy, if indicated. Although vaccine safety in pregnancy has not been established, the theoretical risk to the developing fetus is negligible because the vaccine contains inactivated, purified viral proteins. Pregnant women with the following risk factors are candidates for hepatitis A vaccination: history of or current intravenous drug use, travel to endemic regions, residence in communities with a high prevalence of hepatitis A, working or having close contact with HAV-infected primates, diagnosis of chronic liver disease or receipt of a liver transplant, or receiving clotting factor concentrate for treatment of a clotting disorder. Immunoglobulin is effective for both pre-exposure and postexposure prophylaxis, does not pose a risk to either a pregnant woman or her fetus, and should be administered during pregnancy if indicated.

Nosocomial outbreaks have been reported in neonatal intensive care units, but these are rare. Prevention of virus spread is based on contact precautions. With appropriate hygienic precautions, breastfeeding by a mother with HAV infection is permissible. Although immunoglobulin has been administered to newborns if the mother's symptoms began 2 weeks before delivery through 1 week after delivery, the efficacy of this practice has not been established.

## Hepatitis B Virus

Hepatitis B virus (HBV) is a small DNA virus that contains three principal antigens: 1) hepatitis B surface antigen (HBsAg), 2) hepatitis B core antigen, and 3) hepatitis B e antigen (HBeAg). People acutely infected with HBV may be asymptomatic or symptomatic. Among people with symptomatic HBV infection, the spectrum of signs and symptoms is varied and includes subacute

illness with nonspecific symptoms (eg, anorexia, nausea, or malaise), clinical hepatitis with jaundice, or fulminant hepatitis. Transmission of HBV occurs through contact with infected blood or bodily fluids (ie, semen, cervical secretions, and saliva).

Perinatal transmission of HBV infection is highly efficient and generally occurs from exposure to maternal blood during labor and delivery. If appropriate and timely treatment is not instituted, perinatal infection occurs in 70–90% of infants born to mothers who are both HBsAg positive and HBeAg positive. Transplacental passage of HBV is rare. More than 90% of infants who are infected perinatally will develop chronic HBV infection.

### *Antepartum Screening and Immunization*

Because historical information about risk factors identifies less than one half of chronic carriers, serologic testing for HBsAg is recommended for all pregnant women as part of routine prenatal care. A copy of the original laboratory report should be entered into the patient's medical record at the delivery hospital. Women who have not been screened prenatally, those who are at high risk of infection (eg, intravenous drug users and women with a recurrence of sexually transmitted infections [STIs]), and those with clinical hepatitis should be tested at admission for delivery. Pregnant women with chronic HBV should be informed about transmission risks and ways to prevent newborn infection. Although recent studies have demonstrated potential benefit from antiviral treatment in decreasing the risk of in utero HBV infection in women with high viral loads late in pregnancy, this approach is not yet recommended.

Women who are HBsAg negative but who have risk factors for HBV infection should be offered vaccination during pregnancy. The recommended adult dose of HBV vaccine is 10–20 micrograms (1 mL) injected into the deltoid muscle. A series of three doses is required; the second and third doses are given 1 month and 6 months after the first dose. A two-dose schedule, administered at time zero and again 4–6 months later, is available for adolescents aged 11–15 years using the adult dose of a hepatitis B recombinant vaccine.

Hepatitis B vaccine also is recommended for household contacts and sexual partners of chronic carriers of HBV (ie, those who are positive for HBsAg) unless immunity has previously been demonstrated. Nonimmunized sexual partners of individuals with acute HBV infection should receive a single dose of hepatitis B immune globulin (HBIG) and should begin an HBV vaccine series if their test results are serologically negative.

*Neonatal Immunization*

Universal HBV immunization is recommended for all neonates. Delivery hospitals should develop policies and procedures that ensure administration of the vaccine as part of the routine care of all medically stable infants weighing at least 2,000 g at birth, unless there is a physician's order to defer immunization and the serologic status of the mother is documented in the infant's medical record. Three intramuscular doses are required to provide effective protection (Table 10-1).

*Hepatitis B Surface Antigen-Negative Mother.* For neonates born to women who are known to be HBsAg negative, the first 0.5 mL dose of monovalent vaccine should be administered preferably before discharge from the hospital or by 2 months of age. The second dose is given 1–2 months later; and the

**Table 10-1. Hepatitis B Immunoprophylaxis Scheme by Infant Birth Weight\***

Maternal Status	Infant Birth Weight 2,000 g or More	Infant Birth Weight Less than 2,000 g
HBsAg positive	<p>Hepatitis B vaccine + HBIG (within 12 hours of birth)</p> <p>Continue vaccine series beginning at 1–2 months of age according to recommended schedule for infants born to HBsAg-positive mothers</p> <p>Check anti-HBs and HBsAg after completion of vaccine series<sup>†</sup></p> <p>HBsAg-negative infants with anti-HBs levels <math>\geq 10</math> mIU/mL are protected and need no further medical management</p> <p>HBsAg-negative infants with anti-HBs levels <math>&lt; 10</math> mIU/mL should be reimmunized with a second three-dose vaccine series and retested</p> <p>Infants who are HBsAg positive should receive appropriate follow-up, including medical evaluation for chronic liver disease</p>	<p>Hepatitis B vaccine + HBIG (within 12 hours of birth)</p> <p>Continue vaccine series beginning at 1–2 months of age according to recommended schedule for infants born to HBsAg-positive mothers</p> <p>Immunize with four vaccine doses; do not count birth dose as part of vaccine series</p> <p>Check anti-HBs and HBsAg after completion of vaccine series<sup>†</sup></p> <p>HBsAg-negative infants with anti-HBs levels <math>\geq 10</math> mIU/mL are protected and need no further medical management</p> <p>HBsAg-negative infants with anti-HBs levels <math>&lt; 10</math> mIU/mL should be reimmunized with a second three-dose series and retested</p> <p>Infants who are HBsAg positive should receive appropriate follow-up, including medical evaluation for chronic liver disease</p>

(continued)

**Table 10-1. Hepatitis B Immunoprophylaxis Scheme by Infant Birth Weight\***  
(continued)

Maternal Status	Infant Birth Weight 2,000 g or More	Infant Birth Weight Less than 2,000 g
HBsAg status unknown	<p>Test mother for HBsAg immediately after admission for delivery</p> <p>Hepatitis B vaccine (within 12 hours of birth)</p> <p>Administer HBIG (within 7 days) if mother tests HBsAg positive; if mother's HBsAg status remains unknown, some experts would administer HBIG (within 7 days)</p> <p>Continue the three-dose vaccine series beginning at 1–2 months of age according to recommended schedule based on mother's HBsAg result</p>	<p>Test mother for HBsAg immediately after admission for delivery</p> <p>Hepatitis B vaccine (within 12 hours of birth)</p> <p>Administer HBIG if mother tests HBsAg positive or if mother's HBsAg result is not available within 12 hours of birth</p> <p>Continue vaccine series beginning at 1–2 months of age according to recommended schedule based on mother's HBsAg result</p> <p>Immunize with four vaccine doses; do not count birth dose as part of the three-dose vaccine series</p>
HBsAg negative	<p>Hepatitis B vaccine at birth<sup>†</sup></p> <p>Continue vaccine series beginning at 1–2 months of age</p> <p>Follow-up anti-HBs and HBsAg testing not needed</p>	<p>Delay first dose of hepatitis B vaccine until 1 month of age or hospital discharge, whichever is first</p> <p>Continue the three-dose vaccine series beginning at 2 months of age</p> <p>Follow-up anti-HBs and HBsAg testing not needed</p>

Abbreviations: HBsAg, hepatitis B surface antigen; HBIG, hepatitis B immune globulin; anti-HBs, antibody to HBsAg.

\*Extremes of gestational age and birth weight no longer are a consideration for timing of hepatitis B vaccine doses.

<sup>†</sup>Test at 9–18 months of age, generally at the next well-child visit after completion of the primary series. Use testing method that allows determination of a protective concentration of anti-HBs (10 mIU/mL or greater).

<sup>‡</sup>The first dose may be delayed until after hospital discharge for an infant who weighs 2,000 g or greater and whose mother is HBsAg negative, but only if a physician's order to withhold the birth dose and a copy of the mother's original HBsAg-negative laboratory report are documented in the infant's medical record.

American Academy of Pediatrics. Red book: report of the Committee on Infectious Diseases, 29th. Elk Grove Village (IL): American Academy of Pediatrics; 2012.

third dose, by 6–18 months of age. Alternatively, vaccines can be administered at 2-month intervals, concurrent with other childhood vaccines, at 2, 4, and 6 months of age.

Because of suboptimal immune response in some preterm infants, the current American Academy of Pediatrics recommendation is to delay the start of hepatitis B immunization in low-risk preterm infants (whose mothers are HBsAg negative) who weigh less than 2,000 g at birth until they reach the chronologic age of 30 days, regardless of initial birth weight or gestational age. Preterm infants weighing 2,000 g or more and low birth weight infants who are medically stable and showing consistent weight gain when discharged from the hospital before 30 days of age can receive the first dose of vaccine at the time of discharge. The appropriate dose (Table 10-2) can be given into the anterolateral thigh muscle of neonates.

*Hepatitis B Surface Antigen-Positive Mother.* Newborns of HBsAg-positive women should receive timely postexposure prophylaxis and follow-up. Both term and preterm infants born to women known to be HBsAg positive should receive one 0.5 mL dose of HBIG within 12 hours of birth and monovalent hepatitis B vaccine. Prophylaxis for exposed newborns can prevent perinatal HBV infection in approximately 95% of neonates when HBIG is given within 12 hours after birth and the three-dose immunization series is completed. The initial dose of HBV vaccine can be administered concurrently with HBIG but should be given at a different site. No special care of the infant is indicated other than removal of maternal blood to avoid the virus contaminating the skin. The second dose of vaccine should be administered at 1–2 months of chronologic age, regardless of the infant's gestational age or birth weight. The third dose should be given at 6 months of age. For preterm infants who weigh less than 2,000 g at birth, the initial vaccine dose is given at birth but is not counted in the required three-dose schedule; therefore, these infants receive four doses: 1) at birth, 2) when their weight reaches 2,000 g or at 2 months of age, 3) 1–2 months later, and 4) at 6 months of age.

At 1–3 months after completion of the immunization schedule for newborns of HBsAg-positive women, testing is indicated to ensure immune response or to identify neonates who have become chronically infected. Breastfeeding of newborns by HBsAg-positive women poses no additional risk for the transmission of HBV.

*HBsAg Status Unknown.* Newborns of women whose HBsAg status is unknown should receive HBV vaccine within 12 hours of birth in a dose appropriate for neonates born to HBsAg-positive women. The woman's blood should be obtained for testing at hospital admission for delivery. If the woman subsequently is found to be HBsAg positive, the neonate should receive HBIG

**Table 10-2. Recommended Dosages of Hepatitis B Vaccines**

Patients	Vaccine *		Combination Vaccine
	Recombivax HB <sup>†</sup> Dose, µg (mL)	Engerix-B <sup>‡</sup> Dose, µg (mL)	Twinrix <sup>§</sup>
Infants of mothers who are HBsAg-negative and children and adolescents younger than 20 years	5 (0.5)	10 (0.5)	Not applicable
Infants of mothers who are HBsAg-positive (HBIG [0.5 mL] also is recommended)	5 (0.5)	10(0.5)	Not applicable
Adults 20 years or older	10 (1.0)	20 (1.0)	20 (1.0)
Adults undergoing dialysis and other immunosuppressed adults	40 (1.0) <sup>  </sup>	40 (2.0) <sup>  </sup>	Not applicable

Abbreviations: HBsAg, hepatitis B surface antigen; HBIG, hepatitis B immune globulin.

\*Both vaccines are administered in a three-dose schedule at 0, 1, and 6 months; four doses may be administered if a birth dose is given and a combination vaccine is used (at 2, 4, and 6 months) to complete the series. Only single-antigen hepatitis B vaccine can be used for the birth dose. Single-antigen or combination vaccine containing hepatitis B vaccine may be used to complete the series.

<sup>†</sup>Available from Merck & Co Inc.

- A two-dose schedule, administered at 0 months and then 4 to 6 months later, is licensed for adolescents 11–15 years of age using the adult formulation of Recombivax HB (10 micrograms).
- A combination of hepatitis B (Recombivax, 5 micrograms) and *Haemophilus influenzae* type b (PRP-OMP) vaccine is recommended for use at 2, 4, and 12–15 months of age (Comvax). This vaccine should not be administered at birth (before 6 weeks of age) or after 71 months of age.

<sup>‡</sup>Available from GlaxoSmithKline Biologicals. The U.S. Food and Drug Administration also has licensed this vaccine for use in an optional four-dose schedule at 0, 1, 2, and 12 months for all age groups. A 0-, 12-, and 24-month schedule is licensed for children 5–16 years of age, and a 0-, 1-, and 6-month schedule is licensed for adolescents 11–16 years of age.

- A combination of diphtheria and tetanus toxoids and acellular pertussis (DTaP), inactivated poliovirus (IPV), and hepatitis B (Engerix-B, 10 micrograms) is recommended for use at 2, 4, and 6 months of age (Pediarix). This vaccine should not be administered at birth (before 6 weeks of age) or at 7 years of age or older.

<sup>§</sup>A combination of hepatitis B (Engerix-B, 20 micrograms) and hepatitis A (Havrix, 720 enzyme-linked immunosorbent assay units [ELU]) vaccine (Twinrix) is licensed for use in people 18 years of age and older in a three-dose schedule administered at 0 months, 1 month, and 6 or more months later. Alternately, a four-dose schedule at days 0, 7, and 21–30 followed by a booster dose at 12 months may be used.

<sup>||</sup>Special formulation for adult dialysis patients given at 0, 1, and 6 months.

<sup>¶</sup>Two 1.0-mL doses given in one or two injections in a four-dose schedule at 0, 1, 2, and 6 months of age. American Academy of Pediatrics. Red book: report of the Committee on Infectious Diseases, 29th. Elk Grove Village (IL): American Academy of Pediatrics; 2012.

as soon as possible (within 7 days of birth) and should receive the second and third doses of vaccine as recommended for infants of HBsAg-positive women. Both maternal HBsAg test results and the infant's hepatitis vaccine administration should be documented in the infant's medical record.

## Hepatitis C Virus

Hepatitis C virus (HCV) is a small RNA virus that has at least six identified, distinct genotypes, with broad geographic variation and widely ranging prognoses for both disease progression and response to therapy. The prevalence of HCV infection in the general population of the United States is estimated to be approximately 1.8% but varies in different populations in proportion to risk factors. The primary known route of transmission is parenteral exposure to blood and blood products from individuals who are infected with HCV. Sexual transmission among monogamous couples is uncommon, as is transmission among family contacts. In most cases, no source can be identified. The risk of maternal–fetal (vertical) transmission of HCV ranges from 2% to 12%. The risk of transmission, which correlates with maternal HCV RNA levels, appears to be increased for women also infected with human immunodeficiency virus (HIV). Neonates infected with HCV usually appear healthy. Of infants perinatally infected, approximately 20% will clear their infection. Maternal HCV infection is not a contraindication to breastfeeding.

Infection with HCV is diagnosed serologically by the presence of HCV antibodies via a third-generation enzyme immunoassay, which has a sensitivity of 97% and specificity of 99%. Positive antibody test results should be confirmed with a more specific anti-HCV assay (ie, recombinant immunoblot assay) or HCV-specific RNA testing and genotyping. Liver enzyme and function tests should be performed in patients with positive test results for the antibodies, because as many as 70% of patients with HCV infection develop chronic liver disease, with cirrhosis ultimately developing in 20–25% of these patients. However, data suggest that liver function tests are not helpful in assessing the development of aggressive hepatitis and cirrhosis.

Children born to HCV-positive women should be tested for HCV infection. However, antibody testing should be deferred until at least 18 months of age, when passively transferred maternal HCV antibodies have decreased below detectable levels. If earlier diagnosis of HCV infection is desired, testing for HCV RNA could be performed at age 1–2 months. Hepatitis C virus RNA testing should then be repeated at a subsequent visit, independent of the initial HCV RNA test result.

Currently, no preventive measures are available to lower the risk of vertical HCV infection in infants. Routine serologic testing during pregnancy for HCV infection is not recommended. Testing should be reserved for women seeking evaluation or care for an STI, including HIV, or whose histories suggest an increased risk of infection, such as blood transfusions before 1990, intravenous drug use, occupational or recreational percutaneous exposure, or mucosal surface blood exposure. The natural history of perinatally acquired hepatitis C infection is the subject of ongoing studies. Immune globulin manufactured in the United States does not contain antibodies to HCV and has no role in postexposure prophylaxis. Immunoglobulin G and antiviral agents are not recommended for postexposure prophylaxis of infants born to women with HCV. Recently, benefits have been demonstrated in nonpregnant adults infected with HCV when treated with pegylated interferon. Benefits in pregnant women or to the fetus and newborn by potentially decreasing vertical transmission await further study.

## Herpes Simplex Virus

Herpes simplex virus (HSV) is a DNA virus with two distinct species: HSV type 1 (HSV-1) and HSV type 2 (HSV-2). Most genital infections with HSV are caused by HSV-2. However, genital HSV-1 infections are increasingly recognized as the cause of genital herpes infection. Genital herpes infection is classified as primary when it occurs in a woman with no evidence of prior HSV infection (ie, seronegative for both HSV-1 and HSV-2), as a nonprimary first episode when it occurs in a woman with a history of heterologous infection (eg, first HSV-2 infection in a woman with prior HSV-1 infection or vice versa), and as recurrent when it occurs in a woman with clinical or serologic evidence of prior genital herpes (of the same serotype). In most adults with unequivocal serologic evidence of HSV-2 infection, the infection has not been diagnosed clinically, indicating that most primary infections are asymptomatic.

### *Antepartum Management*

Women who have primary genital HSV infection in late pregnancy (whether symptomatic or asymptomatic) and who give birth vaginally have a high risk (30–50%) of transmitting the virus to their infants. Similarly, nonprimary first-episode HSV infection occurring late in pregnancy also has a high risk of vertical transmission. The risk of transmission during a vaginal delivery is much lower with recurrent infection (less than 2–5%). Currently, most newborns infected with HSV are delivered to women who have asymptomatic or unrecognized infections.

*Diagnosis.* Although routine antepartum genital cultures for HSV screening are not recommended, all suspected herpes virus infections should be evaluated and confirmed through viral detection techniques (viral culture or PCR viral antigen detection) or by type-specific serologic antibody testing. For patients who do not present with active lesions or whose lesions have negative culture or PCR test results, type-specific serologic assays that accurately distinguish between HSV-1 and HSV-2 antibodies can be useful in confirming a clinical diagnosis of genital herpes. Valid type-specific assays for HSV antibodies must be based upon HSV-specific glycoprotein G. The U.S. Food and Drug Administration has approved several such assays (refer to [www.fda.gov](http://www.fda.gov) for a current list). Routine antepartum genital HSV cultures in asymptomatic patients with a recurrence of disease are not recommended.

*Antiviral Therapy.* At the time of the outbreak of a primary herpes infection, antiviral treatment may be administered orally to pregnant women to reduce the duration and the severity of the symptoms as well as reduce the duration of viral shedding. The efficacy of suppressive therapy during pregnancy to prevent recurrences near term has been evaluated in numerous studies. In pregnant women near term, acyclovir use has been found to reduce the risk of clinical HSV recurrence at delivery and decrease both HSV shedding at delivery and the rate of cesarean delivery for a recurrence of genital herpes. Women with a history of a recurrence of genital herpes should be offered suppressive viral therapy at or beyond 36 weeks of gestation. Acyclovir can be administered orally to pregnant women with first-episode genital herpes or a severe recurrence of herpes, and intravenous administration is indicated for pregnant women with severe genital HSV infection or with disseminated herpetic infections.

*Patient Counseling on Prevention.* All pregnant women and their partners should be asked about a history of genital HSV infection. Couples should be educated about the natural history of genital HSV infection and should be advised that, if either partner is infected, they should abstain from sexual contact while lesions or prodromes are present. To minimize the risk of sexual transmission, use of condoms is recommended for HSV-infected individuals when asymptomatic. However, protection provided by condoms is incomplete (estimated to be approximately 50% effective). Susceptible pregnant women should avoid sexual contact during the last 6–8 weeks of gestation if their partners have active genital HSV infections. In addition, oral–genital sexual contact should be avoided in the latter weeks of pregnancy to avoid acquisition of HSV-1 in susceptible individuals.

### *Intrapartum Management*

Women with a history of genital HSV infection should be questioned about recent symptoms and should undergo careful examination of the perineum before delivery. If no lesions are observed, infants can be delivered vaginally. A detailed examination of the cervix is not required because recurrent infections rarely cause isolated cervical lesions.

Cesarean delivery is indicated for all women with active genital HSV lesions or with a typical herpetic prodrome at the time of delivery. In patients with active HSV infection and ruptured membranes at or near term, a cesarean delivery should be performed as soon as the necessary personnel and equipment can be readied. In active HSV infection and premature rupture of membranes remote from term, there is no consensus on the gestational age at which the risks of prematurity outweigh the risks of HSV. When expectant management is elected, treatment with an antiviral drug may be considered. Local neonatal infection can result from the use of fetal scalp electrode monitoring in patients with a history of herpes, even when maternal lesions are not present. However, if there are indications for fetal scalp monitoring, it may be appropriate in a woman who has a history of HSV recurrence and no active lesions.

Contact precautions, use of gown or gloves, and covering of all lesions (in addition to standard precautions), should be used for women with clinically evident or serologically confirmed primary genital HSV infection or nongenital HSV infection in the labor, delivery, recovery, and postpartum care areas. For a recurrence of mucocutaneous lesions, standard precautions are sufficient. Infected family members and others in contact with the infant also should use contact precautions. Health care personnel and the woman herself should use gloves for direct contact with the infected area or with contaminated dressings, and meticulous handwashing is essential. Labor, delivery, recovery rooms require only routine, careful cleaning and disinfection before using the rooms for other patients.

### *Neonatal Diagnosis*

Most neonatal infections are caused by HSV-2, although infection with HSV-1 also can occur. Most infants who develop HSV infection acquire the infection during passage through the infected maternal lower genital tract or by ascending infection to the fetus, sometimes even though membranes apparently are intact. Less common sources of neonatal infection include postnatal transmission from the parents, hospital personnel, or other close contact, most often from a nongenital infection (eg, mouth, hands, or around the breasts).

Uncommonly, intrauterine transmission occurs, and signs of infection appear within 48 hours of birth.

*Infants Born to Women With Active Lesions at Delivery.* Infants born vaginally to women with active lesions require close observation. Specimens for HSV cultures should be obtained at 24 hours after birth from skin lesions, conjunctiva, nasopharynx, mouth, and rectum in healthy appearing newborns exposed to HSV. If skin lesions are present, blood buffy coat and cerebrospinal fluid HSV cultures should be obtained. Cerebrospinal fluid also should be studied by PCR, which is a sensitive method for detecting HSV DNA. Acyclovir therapy should be initiated if the infant has clinical signs of infection, the cultures or PCR test results are positive, or if HSV infection is otherwise strongly suspected.

Some experts recommend empiric treatment with acyclovir for infants born vaginally to a mother with symptomatic primary herpes infection, pending results of cultures, although no data exist to support the efficacy of this approach. Other experts recommend awaiting positive culture results or clinical manifestations of infection before starting acyclovir therapy if the mother has a prior history of genital herpes infection. Parents and physicians should be educated about the signs and symptoms of neonatal HSV infection, which include vesicular lesions of the skin, respiratory distress, seizures, or signs of sepsis. A newborn with any of these manifestations should be evaluated immediately for possible HSV infection and treated pending results of the evaluation.

Infants born vaginally (or by cesarean delivery if membranes have ruptured) to women with active HSV lesions should be physically separated from other infants and managed with contact precautions if they remain in the nursery during the incubation period; an isolation room is not essential. Alternatively, the infant may stay with the mother in a private room after the mother has been instructed on proper preventive care to reduce postpartum transmission.

*Infants Born to Asymptomatic Women With History of Genital Herpes.* The risk of HSV infection is extremely low in infants born vaginally to asymptomatic women with a history of a recurrence of genital herpes and in those born to symptomatic women by cesarean delivery before rupture of membranes. Infants born by cesarean delivery to women with herpetic lesions with intact membranes should be cultured for HSV, as recommended previously for infants exposed by vaginal delivery, and should also be observed. The length of in-hospital observation is empirical and is based on risk factors, local resources,

and access to adequate follow-up. Special isolation precautions are not needed for these infants. Parents should be instructed to report early signs of infection. Antiviral therapy should be initiated if culture results from the infant are positive or if HSV infection is strongly suspected for other reasons.

### *Neonatal Treatment*

Cultures obtained from the eye, mouth, or rectum of infants born to women who are known or who are strongly suspected of being infected with HSV can assist in management decisions. A positive culture obtained 24 hours or more after delivery suggests HSV infection and is an indication for immediate institution of acyclovir therapy, even in the absence of symptoms. The dosage of acyclovir is 60 mg/kg per day in three divided doses, given intravenously for 14 days for disease of the skin, eyes, and mouth and for 21 days in central nervous system disease or disseminated disease. Of treated infants, 5–10% will develop recurrent disease requiring retreatment in the first month of life. Six months of oral acyclovir suppressive therapy for infants with clinical HSV infection (skin, eyes, mouth, or CNS) has been demonstrated to reduce the risk of a recurrence of HSV infection.

Infants with HSV disease should be managed in a facility that provides neonatal intensive care and consultation with an infectious diseases specialist. The infant should be physically segregated and managed with contact precautions for the duration of the illness; an isolation room is desirable.

Although HSV infection is more likely to occur at a site of skin trauma, no data indicate that the circumcision of male infants who may have been exposed to HSV at birth should be postponed. It may be prudent, however, to delay circumcision for approximately 1 month in infants at the highest risk of disease (eg, infants delivered vaginally to women with active genital lesions).

### *Contact of Infants With Infected Mothers*

A woman with active HSV infection should be taught about her infection and about hygienic measures to prevent postpartum transmission of herpes to her infant. Before touching her newborn, the woman should wash her hands carefully and use a clean barrier to ensure that the infant does not come into contact with lesions or potentially infectious material. If the woman has genital HSV infection, her infant can room with her after she has been instructed in protective measures. Breastfeeding is permissible if the woman has no vesicular herpetic lesions in the breast area and other active cutaneous lesions are covered.

A woman with herpes labialis (cold sore) or stomatitis should not kiss or nuzzle her infant until the lesions have cleared. Careful hand hygiene is important. She should wear a disposable surgical mask when she touches her infant until the lesions have crusted and dried. Herpetic lesions on other skin sites should be covered. Direct contact of an infant with other family members or friends who have active HSV infection should be avoided.

## **Human Immunodeficiency Virus**

Acquired immunodeficiency syndrome (AIDS) is caused by HIV type 1 (HIV-1) and, less commonly, HIV type 2 (HIV-2), a related virus. Human immunodeficiency virus type 2 is extremely uncommon in the United States but is more common in West Africa and South America.

### *Transmission*

Human immunodeficiency virus has been isolated from blood (including lymphocytes, macrophages, and plasma), cerebrospinal fluid, pleural fluid, human milk, semen, cervical secretions, saliva, urine, and tears. However, only blood, semen, cervical secretions, and human milk have been implicated epidemiologically in the transmission of infection. Well-documented modes of HIV transmission in the United States are sexual contact (both heterosexual and homosexual), skin penetration by contaminated needles or other sharp instruments, transfusion of contaminated blood products, and mother-to-infant transmission during pregnancy, around the time of labor and delivery, and postnatally through breastfeeding. Cases of probable HIV transmission from HIV-infected caregivers to their infants through feeding blood-tinged premasticated food have been reported in the United States.

Before effective perinatal HIV interventions, the risk of infection for a neonate born to an HIV seropositive mother was approximately 25% (range, 13–39%). All pregnant women who are infected with HIV should be offered antiretroviral drug regimens, which will likely decrease the HIV viral load to undetectable levels.

The exact timing of transmission from an infected mother to her infant is uncertain. Evidence suggests that in the absence of breastfeeding, 30% of transmission occurs before birth and 70% occurs around the time of delivery.

### *Antepartum Management*

Clear medical benefits are derived from pregnant women knowing their HIV serostatus. Demonstrated benefits include early diagnosis and treatment to

delay active disease in women and significant reduction in perinatal transmission through early treatment.

*Prenatal Screening.* All pregnant women should be told that HIV screening is recommended during pregnancy and that an HIV test is part of the routine panel of prenatal tests unless it is declined (opt-out screening). If a woman declines HIV testing, this should be documented in the medical record. Repeat testing in the third trimester (preferably before 36 weeks of gestation) is recommended for women in areas with a high HIV prevalence, women known to be at high risk of acquiring HIV infection, and women who declined testing earlier in pregnancy. In some states, it is necessary to obtain the woman's written authorization before disclosing her HIV status to health care providers who are not members of her health care team. Obstetrician–gynecologists should be aware of and comply with their states' legal requirements for perinatal HIV screening.

The conventional HIV testing algorithm, which may take up to 2 weeks to complete if a result is positive, begins with a screening test, the enzyme-linked immunosorbent assay (ELISA) that detects antibodies to HIV; if the test results are positive, a confirmatory test (either a Western blot or an immunofluorescence assay) is performed. If the ELISA test result is positive and the Western blot or immunofluorescence assay test result is negative, the woman is not infected and repeat testing is not indicated.

If the screening and confirmatory test results are both positive, the patient should be given her results in person. The implications of HIV infection and vertical transmission should be discussed with the patient. Additional laboratory evaluation, including CD4 count, HIV viral load, HIV antiretroviral resistance testing, hepatitis C virus antibody, HBsAg, complete blood count with platelet count, and baseline chemistries with liver function tests, will be useful before prescribing antiretroviral prophylaxis. Coordination of care of the mother and fetus should be done in consultation with an infectious disease or obstetric infectious disease specialist.

*Maternal Antiretroviral Therapy.* Combination antiretroviral drug regimens that maximally suppress viral replication are recommended for HIV-1 infected adults. Pregnancy does not preclude the use of these standard antiretroviral regimens. Offering antiretroviral therapy to infected women during pregnancy, either to treat HIV-1 infection or to reduce perinatal transmission or both, should be accompanied by discussion of the known and unknown short-term and long-term benefits and risks of such therapy for affected women and their infants. It is recommended that zidovudine chemoprophylaxis be included in the antiretro-

viral combination regimen, except in cases of known intolerance. No significant short-term adverse effects have been observed from zidovudine use other than mild, self-limited anemia in the infants. In addition, infants have been monitored for several years and no untoward effects of zidovudine have been observed.

Current recommendations for adults are that plasma viral load determinations be done at baseline and every 3 months or after changes in therapy. Additionally, CD4+ T-lymphocyte counts should be monitored during pregnancy. Because of the rapid advances in this area, refer to the Centers for Disease Control and Prevention (CDC) ([www.cdc.gov](http://www.cdc.gov)) and the U.S. Department of Health and Human Services AIDSinfo web sites (<http://www.aidsinfo.nih.gov/>) for treatment recommendations.

### *Intrapartum Management*

As noted, a substantial proportion of neonatal HIV cases occur as a result of exposure to the virus during labor and delivery. Intrapartum strategies to prevent mother-to-child transmission include rapid HIV antibody testing for women with unknown HIV status during labor and delivery; administration of antepartum, intrapartum, and neonatal antiretroviral prophylaxis; and cesarean delivery performed before the onset of labor and before rupture of membranes in women with viral loads of more than 1,000 copies per milliliter.

*Rapid HIV Testing.* Any woman whose HIV status is unknown during labor and delivery should be given a rapid HIV test, unless she declines (opt-out screening), in order to provide an opportunity to begin prophylaxis before delivery. A negative rapid HIV test result is definitive. A positive HIV test result is not definitive and must be confirmed with a supplemental test, such as a Western blot test or immunofluorescence assay.

If the rapid HIV test result at labor and delivery is positive, the obstetric provider should take the following seven steps:

1. Tell the woman she may have HIV infection and that her infant also may be exposed.
2. Explain that the rapid test result is preliminary and that false-positive test results are possible.
3. Assure the woman that a second test is being done right away to confirm the positive rapid test result.
4. Immediate initiation of antiretroviral prophylaxis should be recommended without waiting for the results of the confirmatory test to reduce the risk of transmission to the infant.

5. Once the woman gives birth, discontinue maternal antiretroviral therapy until the result of the confirmatory test is known.
6. Tell the woman that she should postpone breastfeeding until the confirmatory result is available because she should not breastfeed if she is infected with HIV.
7. Inform pediatric care providers (depending on state requirements) of positive maternal test results so that they may institute the appropriate neonatal prophylaxis.

*Route of Delivery.* A viral load obtained late in the third trimester is useful to guide the decision concerning mode of delivery. Consistent results indicating a significant relationship between route of delivery, viral load, and vertical transmission of HIV have been published. This body of evidence indicates that when care includes scheduled cesarean delivery (performed before the onset of labor and before the rupture of membranes) and zidovudine therapy, the likelihood of vertical transmission of HIV is reduced to approximately 2%. There are insufficient data to demonstrate a benefit of cesarean delivery performed after the onset of labor or rupture of membranes. Thus, a scheduled cesarean delivery at 38 weeks of gestation without an amniocentesis for lung maturity is recommended for all HIV-1 infected pregnant women with viral loads greater than 1,000 copies per milliliter near the time of delivery (or who have an unknown viral load), whether or not they are receiving antiretroviral prophylaxis. It is clear that the rate of maternal morbidity is higher with cesarean delivery than with vaginal delivery. However, the benefit to the infant outweighs the increased maternal morbidity associated with cesarean delivery (see also “Cesarean Delivery” in Chapter 6).

Women with plasma viral loads less than 1,000 copies per milliliter have a low risk of vertical transmission (less than 2%), even without routine use of scheduled cesarean delivery. There are not enough data to demonstrate a benefit of scheduled cesarean delivery for women with plasma viral loads of less than 1,000 copies per milliliter. The decision regarding route of delivery in these circumstances must be individualized. The patient’s autonomy in making the decision regarding route of delivery must be respected.

Because HIV may be present in blood, vaginal secretions, amniotic fluid, and other fluids, standard precautions should be followed strictly during all vaginal and cesarean deliveries. Gloves should be used when handling the infant until blood and amniotic fluid have been removed from the infant’s skin.

### *Postpartum Management*

After delivery, HIV infected women can receive care in the postpartum care unit, with the use of standard precautions. Human immunodeficiency virus RNA has been detected in both the cellular and cell-free fractions of human breast milk, and breastfeeding has been implicated in the transmission of HIV infection. Women in developed countries who are infected with HIV should be counseled not to breastfeed their babies, and they should not donate to milk banks. Obstetric providers may need to refer women who are infected with HIV to another health care provider with special expertise in HIV infection for continuing medical care after pregnancy. Few infants with HIV infection show clinical evidence of infection in the first weeks after delivery.

To minimize risk to health care personnel, routine standard precautions should be used when caring for the infant. Prompt and careful removal of blood from the infant's skin is important. There is no need for other special precautions or for isolation of the infant from an HIV-infected mother; rooming-in is acceptable. Gloves should be worn for contact with blood or blood-containing fluids, for procedures that entail exposure to blood and for diaper changes.

### *Evaluation and Management of Exposed Newborns*

**Screening and Antiretroviral Prophylaxis.** Newborn infants born to women who are HIV-infected or whose HIV status is unknown should have a rapid antibody test performed as soon as possible after birth and receive postpartum antiretroviral drugs within 12 hours of birth to reduce the risk of perinatal HIV-1 transmission. Because of possible contamination with maternal blood (and a high incidence of false-positive test results), umbilical cord blood should not be used for this determination. If the result is positive, a confirmatory test should be performed. If the confirmatory test result is negative, antiretroviral drugs should be stopped. For infants with a positive confirmatory test result, a 6-week course of zidovudine is recommended. Infants born to HIV-infected women who did not receive antiretroviral therapy before the onset of labor should receive a 2-drug prophylaxis regimen.

Maternal health information should be reviewed to determine if the infant may have been exposed to maternal coinfections (such as tuberculosis, syphilis, toxoplasmosis, hepatitis B or hepatitis C, cytomegalovirus, or HSV), and diagnostic testing and treatment of coinfections in the infant should be based on maternal findings and evaluation of the infant. Immunizations and tuberculosis

screening should be given in accordance with current published guidelines. Both mother and infant should have prescriptions for HIV drugs when they leave the hospital, and the infant should have an appointment for a postnatal visit at 2–4 weeks of age to monitor medication adherence and to screen the infant for anemia from zidovudine therapy. Pediatricians should provide counseling to parents and caregivers of HIV-1 exposed infants about HIV-1 infection, including anticipatory guidance on the course of illness, infection-control measures, care of the infant, diagnostic tests, and potential drug toxicities.

*Diagnostic Testing.* Because passively transferred maternal HIV-1 antibodies may be detectable in an exposed but uninfected infant's bloodstream until 18 months of age, assays that directly detect HIV-1 DNA or RNA (generically referred to as HIV-1 nucleic acid amplification tests [NAATs]) represent the preferred method of diagnostic testing of infants and young children younger than 18 months. Approximately 30–40% of HIV-infected infants will have a positive HIV DNA PCR assay result in samples obtained before 48 hours of age. A positive result by 48 hours of age suggests in utero transmission. Approximately 93% of infected infants have detectable HIV DNA by 2 weeks of age, and approximately 95% of HIV-infected infants have a positive HIV DNA PCR assay result by 1 month of age.

All HIV-1 exposed infants should undergo virologic testing with HIV-1 DNA or RNA assays at 14–21 days of life, and if results are negative, the tests should be repeated at 1–2 months of age and again at 4–6 months of age. An infant is considered infected if two separate samples test positive. For infants with negative virologic test results, many experts confirm the absence of HIV-1 infection with HIV-1 antibody assay testing at 12–18 months of age. If infection is confirmed, a pediatric HIV specialist should be consulted for advice regarding antiretroviral therapy and care.

*Pneumocystis jiroveci pneumonia prophylaxis.* *Pneumocystis jiroveci* pneumonia is the most common opportunistic infection in HIV-1 infected infants and children. All HIV-1 exposed infants should be considered for prophylaxis beginning at 4–6 weeks of age. Infants in whom HIV-1 is diagnosed should be given prophylaxis until 1 year of age, at which time reassessment is made on the basis of age-specific CD4+ T-lymphocyte count and percentage thresholds. Infants with indeterminate HIV-1 infection status should receive prophylaxis starting at 4–6 weeks of age until they are deemed to be presumptively or definitively uninfected.

## Human Papillomavirus

Infections caused by the human papillomavirus (HPV) are common. More than 100 types of HPV exist, more than 40 of which can infect the genital area. Infection with certain HPV types can cause genital warts and a recurrence of respiratory papillomatosis (eg, HPV-6 and HPV-11) as well as cervical and anogenital carcinomas (eg, HPV-16 and HPV-18). Most cervical HPV infections are transient. Persistent infection is more likely with oncogenic types. Cervical or vaginal HPV infections usually are asymptomatic. Pap tests are less useful for the diagnosis of subclinical cervical infection. Most genital HPV infections are sexually transmitted.

Genital HPV infections may be exacerbated during pregnancy. Papillary lesions (condylomata acuminata) may proliferate on the vulva and in the vagina, and lesions can become increasingly friable during pregnancy. Cryotherapy, laser therapy, and trichloroacetic acid can be used safely to treat genital HPV infection in pregnancy. Imiquimod, sinecatechins, podophyllin, and podofilox should not be used during pregnancy because they may be toxic to the fetus. Fetal death has been reported after treating the mother with large topical doses of podophyllin. Currently, there are two FDA-approved vaccines shown to be effective in preventing HPV infection in adolescents and young adults. HPV vaccines have not been shown to have a harmful effect on pregnancy when inadvertent administration occurs, but pregnant women should not be vaccinated. If a woman discovers she is pregnant during the vaccine schedule, she should delay completing the three-dose series until after she gives birth. Women who are breastfeeding can receive the vaccine.

The risk that an infant born to a mother who has a genital HPV infection will develop subsequent respiratory papillomatosis is very small. These lesions are thought to result from aspiration of infectious secretions during passage through the birth canal. Because the risk of respiratory papillomatosis is so low, cesarean delivery is not recommended for the sole purpose of protecting the infant from HPV infection. In women with extensive condylomata, however, cesarean delivery may be necessary because of poor vaginal or vulvar distensibility and the related increased likelihood of extensive vulvovaginal lacerations. Infants born to mothers with HPV infection should receive routine care in the nursery.

## Influenza Virus

Influenza A and influenza B viruses are the main types of human influenza virus that are responsible for seasonal influenza epidemics each year. During the course of influenza season, different types and subtypes of influenza viruses can

circulate and cause illness. Influenza viruses are spread from person to person primarily through hand-to-hand contact and large-particle respiratory droplet transmission. Contact with respiratory-droplet contaminated surfaces is another possible source of transmission. Uncomplicated influenza illness is characterized by the abrupt onset of constitutional and respiratory signs and symptoms (eg, fever, myalgia, headache, malaise, nonproductive cough, sore throat, and rhinitis) and typically resolves after 3–7 days, but malaise can persist for up to 14 days.

Pregnant women and young children are at greater risk of serious influenza complications, which can include influenza or secondary bacterial pneumonia, ear infections, sinus infections, dehydration, and worsening of chronic medical conditions, such as congestive heart failure, asthma, or diabetes. Pregnant women also have higher mortality and hospitalization rates than nonpregnant women. Preventing influenza during pregnancy is an essential element of prenatal care, and the most effective strategy for preventing influenza is annual immunization. Immunizing pregnant women against seasonal influenza can protect the mother and is associated with reduced febrile respiratory viral illness in her infant. Obstetrician–gynecologists are an important source of information and advice on immunization for pregnant women and play a crucial role in recommending influenza vaccine to every pregnant woman.

The seasonal trivalent inactivated influenza vaccine is safe for pregnant women and their unborn infants and can be given during any trimester. The CDC Advisory Committee on Immunization Practices recommends that all women who are pregnant during influenza season (October through May in the United States) receive the trivalent inactivated influenza vaccine at any point in gestation. Regardless of gestational age, vaccination early in the season is optimal. Live attenuated influenza vaccine is contraindicated for pregnant women.

No study to date has shown an adverse consequence of the inactivated influenza vaccine in pregnant women or their offspring. Thimerosal, a mercury-containing preservative used in multidose vials of influenza vaccine, has not been shown to cause any adverse effects except for occasional local skin reactions. There is no scientific evidence that thimerosal-containing vaccines cause adverse effects in children born to women who received vaccines with thimerosal. Hence, the Advisory Committee on Immunization Practices does not indicate a preference for thimerosal-containing or thimerosal-free vaccines for any group, including pregnant women. In addition to the benefits of immunization for pregnant women, a prospective, controlled, randomized trial demonstrated fewer cases of laboratory-confirmed influenza in infants whose

mothers had been immunized compared with women in the control group, as well as fewer cases of respiratory illness with fever. Maternal immunity is the only effective strategy in newborns because the vaccine is not approved for use in infants younger than 6 months.

Infants born to mothers with a suspected influenza infection should room in with their mothers. Those requiring hospitalization in the neonatal intensive care units should be placed in an isolation room and given routine supportive care. All health care professionals who care for high-risk newborns should receive seasonal influenza vaccine annually as soon as the vaccine becomes available. Antiviral chemoprophylaxis can be used in infected family members or health care providers who are unimmunized and who are likely to have ongoing close exposure to infants who are younger than 12 months. Because antiviral resistance patterns can change over time, antiviral drug recommendations are updated regularly. Physicians are advised to monitor local antiviral resistance surveillance data and visit the CDC's "Vaccines & Immunizations" web page (<http://www.cdc.gov/vaccines/>) for current immunization information and recommendations. Additional health care provider and patient immunization information and resources are available on the American College of Obstetrician and Gynecologists' "Immunization for Women" web site, which can be accessed at <http://www.immunizationforwomen.org>.

## Human Parvovirus

Parvovirus B19 is a DNA virus that causes childhood exanthem erythema infectiosum, also known as fifth disease. Transmission most commonly occurs through respiratory secretions and hand-to-mouth contact. In immunocompetent adults, the most common symptoms of parvovirus B19 infection are a reticular rash on the trunk and peripheral arthropathy, although approximately 33% of infections are asymptomatic. Most individuals experience mild infection and have a complete recovery.

### *Perinatal Transmission*

Parvovirus B19 infects fetal erythroid precursors and causes anemia, which can lead to nonimmune hydrops, isolated pleural and pericardial effusions, intrauterine growth restriction, and death. Parents should be reassured that although the rate of intrauterine transmission is high (approximately 50%), the risk of fetal death is between 2% and 6%, and most infected infants are healthy at birth. More than one half of pregnant women are immune to parvovirus B19. In most cases of B19 infection during pregnancy, the fetus is not affected. Most reported

maternal infections that have resulted in fetal death occur between the 10th week and 20th week of pregnancy, and fetal death and spontaneous abortion usually have occurred 4–6 weeks after infection. Congenital anomalies caused by parvovirus have been reported in small series and rare case reports. However, the determination that parvovirus is a teratogen remains unproven at this time.

### *Diagnosis and Management*

Because of widespread asymptomatic parvovirus infection in adults and children, all women are at some risk of exposure, particularly those exposed to school-aged children. Pregnant women who learn that they have been exposed to parvovirus B19 should be counseled about the potential risk to the fetus and have serologic testing (ELISA, and Western blot tests) to determine if they are immune. If they are nonimmune, the test should be repeated in 3–4 weeks and paired samples tested to document whether the woman becomes seropositive for parvovirus.

If seroconversion does occur, the fetus should be monitored for 10 weeks by serial ultrasound examination to evaluate for the presence of hydrops fetalis, placentomegaly, and growth disturbances. If hydrops fetalis develops, percutaneous umbilical blood sampling should be performed to determine the fetal hematocrit, leukocyte and platelet count, and viral DNA in preparation for supportive care.

### *Prevention*

In view of the high prevalence of parvovirus B19 seropositive women, the low risk of ill effects to the fetus, and the fact that avoidance of childcare or teaching can reduce but not eliminate the risk of infection, pregnant women should not be excluded from workplaces where B19 is present. Pregnant health care workers should be aware that otherwise healthy patients with erythema infectiosum are contagious the week before, but not after the onset of rash. In contrast, patients who are immunocompromised or who have a hemoglobinopathy remain contagious from before the onset of symptoms through the time of the rash. Routine infection control practices, such as standard precautions and droplet precautions, reduce transmission.

## **Respiratory Syncytial Virus**

Respiratory syncytial virus (RSV), an RNA virus of the family Paramyxoviridae, is a common cause of respiratory infection in infancy and the most common cause of hospitalization for lower respiratory illness in infants. Characteristics

that increase the risk of severe RSV lower respiratory tract illness are preterm birth; cyanotic or complicated congenital heart disease, especially conditions causing pulmonary hypertension; chronic lung disease; and immunodeficiency disease or therapy causing immunosuppression at any age.

### *Transmission*

Respiratory syncytial virus usually occurs in annual fall and winter epidemics and during early spring in temperate climates. Spread among household and child care contacts, including adults, is common. Transmission usually is by direct or close contact with contaminated secretions, which may occur from exposure to large-particle droplets at short distances (less than 3 feet) or fomites. Enforcement of infection-control policies is important to decrease the risk of health care-related transmission of RSV.

### *Diagnosis and Treatment*

Rapid diagnostic assays, including immunofluorescent and enzyme immunoassay techniques for detection of viral antigen in nasopharyngeal specimens, are available commercially and generally are reliable in infants and young children. Primary treatment is supportive and should include hydration, careful clinical assessment of respiratory status, including measurement of oxygen saturation, use of supplemental oxygen, suction of the upper airway, and if necessary, intubation and mechanical ventilation.

### *Prophylaxis*

Prophylaxis to prevent RSV in infants at increased risk of severe disease, particularly those with chronic lung disease receiving medical management on a long-term basis, is available using an intramuscular monoclonal antibody—palivizumab. Prophylaxis with palivizumab decreases the risk of severe RSV disease and hospitalization by approximately 50%. Palivizumab is administered as a maximum of three to five monthly intramuscular injections (15 mg/kg per dose) during RSV season, with the first dose typically administered in November in North America. The current American Academy of Pediatrics' recommendations for RSV prophylaxis are listed here and summarized in Table 10-3:

- Infants with chronic lung disease. In order to be considered a candidate for RSV prophylaxis, infants with chronic lung disease require ongoing medical management (eg, supplemental oxygen, diuretics, corticosteroids, bronchodilator therapy) within 6 months before the onset of RSV

season. Those with more severe chronic lung disease may benefit from prophylaxis for two RSV seasons.

- Infants without chronic lung disease who were less than 32 weeks of gestation at birth. Infants born at 29–32 weeks of gestation may benefit from prophylaxis up to 6 months of age, whereas those born at 28 weeks of gestation or younger may benefit from prophylaxis up to 12 months of age.
- Infants without chronic lung disease who were 32 0/7–34 6/7 weeks of gestation at birth. Respiratory syncytial virus prophylaxis should be limited to infants who are at greatest risk of hospitalization due to RSV, namely infants younger than 3 months of age at the onset of the RSV season or born during the RSV season and who are likely to have an increased risk of exposure to RSV. Epidemiologic data suggest that RSV infection is more likely to occur and more likely to lead to hospitalization for infants in this gestational age group when either of the following two risk factors is present: 1) infant attends child care or 2) has a sibling or child living in the home who is younger than 5 years of age. Infants in this gestational age category should receive prophylaxis until they reach the age of 3 months. Palivizumab should not be given beyond 90 days of age in these infants. Therefore, this group should receive a maximum of three monthly injections.
- Infants with congenital heart disease. Infants with hemodynamically significant congenital heart disease should receive palivizumab throughout RSV season and may benefit from prophylaxis for two RSV seasons.

Respiratory syncytial virus can be transmitted in the hospital setting and may cause serious disease in high-risk newborns. The major means to prevent RSV disease in the hospital is strict observance of infection control practices, including identifying and cohorting RSV-infected patients. Palivizumab is not indicated as a control measure for hospital outbreaks of RSV infection.

A critical aspect of RSV prevention is parent education about the importance of avoiding exposure to and transmission of the virus. Preventive measures include limiting, when feasible, exposure to contagious settings, such as child care centers. The importance of hand hygiene should be emphasized in all settings, including the home.

## Rubella

Rubella virus is an RNA virus that can manifest clinically as postnatal rubella or congenital rubella syndrome. Before widespread use of rubella vaccine, rubella

**Table 10-3. Maximum Number of Monthly Doses of Palivizumab for Respiratory Syncytial Virus Prophylaxis**

Infants Eligible for a Maximum of Five Doses	Infants Eligible for a Maximum of Three Doses
Infants younger than 24 months with chronic lung disease and requiring medical therapy	Preterm infants with gestational age of 32 weeks, 0 days to 34 weeks, 6 days with at least one risk factor, and born 3 months before or during RSV season
Infants younger than 24 months and requiring medical therapy for congenital heart disease	
Preterm infants born at 31 weeks, 6 days of gestation or less	
Certain infants with neuromuscular disease or congenital abnormalities of the airways	

Abbreviation: RSV, respiratory syncytial virus.

Policy statements—Modified recommendations for use of palivizumab for prevention of respiratory syncytial virus infections. American Academy of Pediatrics Committee on Infectious Diseases. *Pediatrics* 2009;124:1694–701.

was an epidemic disease. More recently, infection has occurred in foreign-born or underimmunized people, because endemic rubella has been eliminated from the United States. Clinical disease usually is mild and characterized by a generalized erythematous maculopapular rash, lymphadenopathy, and slight fever.

Maternal rubella during pregnancy can result in miscarriage, fetal death, or congenital rubella syndrome. The most common manifestations associated with congenital rubella syndrome are ophthalmologic (cataracts, pigmentary retinopathy, microphthalmos, and congenital glaucoma), cardiac (patent ductus arteriosus, peripheral pulmonary artery stenosis), auditory (sensorineural hearing impairment), and neurologic (behavioral disorders, meningoencephalitis, and mental retardation). Mild forms of congenital rubella syndrome can be associated with few or no obvious clinical manifestations at birth.

### *Antepartum Management*

Surveillance for susceptibility to rubella infection is essential in prenatal care. Each patient should have serologic screening for rubella immunity at the first prenatal visit unless she is known to be immune by previous serologic testing. Seropositive women do not need further testing, regardless of their subsequent history of exposure. If a seronegative pregnant woman is exposed to rubella or develops symptoms that suggest infection, she should be retested for rubella-specific antibody. Specimens should be obtained as soon as possible after exposure, again 2 weeks later, and, if necessary, 4 weeks after exposure. Acute

and chronic serum specimens should be tested on the same day in the same laboratory. Detection of rubella-specific IgM antibodies usually indicates recent infection, but false-positive test results occur. Isolation of the virus from throat swabs establishes a diagnosis of acute rubella.

If rubella is diagnosed in a pregnant woman, she should be advised of the risks of fetal infection; the choice of pregnancy termination should be discussed. Structural malformation may be caused by infection during embryogenesis, and although fetal infection may occur throughout pregnancy, defects are rare when infection occurs after the 20th week of gestation.

The rubella vaccine is a live-attenuated virus and is highly effective with few adverse effects. However, rubella vaccination is not recommended during pregnancy. Women found to be susceptible during pregnancy should be offered vaccination postpartum and before discharge from the hospital. Breastfeeding is not a contradiction to receiving the rubella vaccine. After immunization, women should be advised to avoid conception for 1 month. However, a woman who conceives within 1 month of rubella vaccination or who is inadvertently vaccinated in early pregnancy should be counseled that the teratogenic risk to the fetus is theoretic. Although asymptomatic fetal infection can occur, no case of congenital rubella syndrome has arisen from a woman given the current rubella vaccine (human diploid vaccine RA 27/3) during pregnancy. Therefore, receipt of the rubella vaccine during pregnancy is not an indication for termination of pregnancy. All suspected cases of congenital rubella syndrome, whether caused by wild-type virus or vaccine virus infection, should be reported to local and state health departments. A pregnant household member is not a contraindication to vaccination of a child.

### *Neonatal Management*

Infants who show signs of congenital rubella infection or who were born to women with a history of rubella during pregnancy should be managed with contact isolation. Care of the infant should be restricted to personnel who are immune to rubella. Efforts should be made to obtain viral cultures from the infant to document the infection. Affected infants should be considered contagious until 1 year of age unless nasopharyngeal and urine cultures (after 3 months of age) are repeatedly negative for the rubella virus.

### **Varicella Zoster Virus**

Varicella zoster virus (VZV) is a highly contagious DNA herpesvirus that is transmitted by respiratory droplets or close contact. The primary infection

causes chickenpox, which is characterized by fever, malaise, and a maculopapular pruritic rash that becomes vesicular. The disease usually is a benign and self-limited illness in children; severe complications, such as encephalitis and pneumonia, are more common in adults than in children. After the primary infection, VZV remains dormant in sensory ganglia and can be reactivated to cause a vesicular erythematous skin rash known as herpes zoster. The antibody to VZV develops within a few days after the onset of infection, and prior infection with VZV confers lifelong immunity.

Varicella in pregnant women can result in VZV transmission to the fetus or newborn. Intrauterine VZV infection can cause congenital varicella syndrome or neonatal varicella. Congenital varicella syndrome is manifested by low birth weight, cutaneous scarring, limb hypoplasia, microcephaly, chorioretinitis, and cataracts. It occurs in 1.5% of infants born to women who contract VZV in the first 28 weeks of gestation. Fetuses infected by VZV during the second half of gestation can develop zoster early in life without having had extruterine chickenpox. The onset of varicella in pregnant women 5 days before to 2 days after delivery may result in severe varicella in newborns, which, if untreated, has a high mortality rate.

### *Antepartum Management*

Diagnosis of maternal VZV infection usually is based on clinical findings, and laboratory testing is not needed, especially if a rash occurs after known exposure. The VZV antigen can be demonstrated within skin lesions or vesicular fluid by immunofluorescence. Varicella infection also can be documented by the detection of the fluorescence antibody to the membrane antigen or of the VZV antibody by ELISA. Pregnant women who are seronegative for VZV (per expeditious determination of the VZV membrane antigen or equivalent anti-VZV antibody status) can receive varicella immune globulin up until 10 days postexposure, but it is not known whether this will prevent or ameliorate fetal infection.

Varicella during pregnancy can be treated with oral acyclovir to minimize maternal symptoms. Maternal treatment with acyclovir has not been shown to ameliorate or prevent the fetal effects of congenital varicella syndrome. Pregnant women with VZV infection should be advised of pulmonary complications and to seek medical care immediately if any pulmonary symptoms develop. Although women with VZV infection during pregnancy are no more likely to develop varicella pneumonia than are other adults, varicella pneumonia is more

severe during pregnancy. Maternal varicella complicated by pneumonia should be treated with intravenous acyclovir, because intravenous acyclovir may reduce maternal morbidity and mortality associated with varicella pneumonia.

### *Neonatal Management*

Neonatal VZV infection is associated with a high neonatal death rate when maternal disease develops from 5 days before delivery up to 48 hours postpartum as a result of the relative immaturity of the neonatal immune system and the lack of protective maternal antibody. Varicella zoster immune globulin should be given to infants born to women who develop varicella during this interval, although this does not universally prevent neonatal varicella. Infants who develop varicella within the first 2 weeks of life should be treated with intravenous acyclovir.

Infants born at less than 28 weeks of gestation or less than 1,000 g who are exposed to VZV postnatally are at increased risk of severe varicella, regardless of maternal history. These infants should receive varicella zoster immune globulin regardless of the maternal history of varicella or varicella zoster serostatus. Hospitalized, preterm infants born at 28 weeks of gestation or later who are exposed postnatally to chickenpox and whose mothers have no history of chickenpox also should receive varicella zoster immune globulin.

### *Infection Control*

Hospitalized women with VZV infection must be kept under airborne and contact precautions. Similar precautions are recommended for infants born to mothers with varicella and, if still hospitalized, should continue during the incubation period (21 days or 28 days). Infants with VZV infection should be isolated in a private room for the duration of the illness. Infants with congenital VZV infection acquired earlier in gestation do not require special precautions or isolation unless vesicular lesions are present. Hospitalized infants who are exposed postnatally should be isolated from 8 days to 21 days after onset of the rash in the index case.

### *Immunization*

Pregnant women should not be vaccinated, and vaccinated women should be advised to avoid pregnancy for 1 month after each dose because of concern about possible fetal effects. Surveillance data to date on fetal outcomes after inadvertent vaccine exposures, however, have not found any cases of fetal varicella syndrome. Women who do not have varicella immunity should receive

the first dose of VZV vaccine in the postpartum period before discharge from the birthing facility. A pregnant household member is not a contraindication to vaccination of a child. (For the most current immunization schedules and recommendations, please visit the CDC's "Vaccines & Immunizations" web page at <http://www.cdc.gov/vaccines>.)

## West Nile Virus

West Nile virus is associated with fever, rash, arthritis, myalgias, weakness, lymphadenopathy, and meningoencephalitis. This virus is carried by mosquitoes and birds and can be transmitted through blood transfusion or organ transplant. To date, outcomes of 72 pregnancies have been published, and there has been only one fetus with proven intrauterine infection and subsequent bilateral chorioretinitis. It is unclear whether pregnant women are more susceptible to West Nile virus and whether the disease is more severe. Transmission through breast milk also is possible, but most infants infected by this route are asymptomatic or have mild symptoms. Women with symptoms should not be discouraged from breastfeeding. Pregnant and breastfeeding mothers should be encouraged to wear protective clothing, minimize their outdoor exposure at dawn and dusk when mosquitoes are most active, and use insect repellent containing N,N-diethyl-3-methylbenzamide (known as DEET) as a preventive measure.

## Bacterial Infections

### Anthrax Exposure

Anthrax infections are diagnosed by isolating *Bacillus anthracis* from body fluids or by measuring specific antibodies in the blood of persons suspected to have the disease. It is recommended that asymptomatic pregnant and lactating women who have been exposed to a confirmed environmental contamination or a high-risk source as determined by the local Department of Health (not the women's health care provider) receive prophylactic treatment. A variety of antimicrobial regimens are available. Although some of these drugs may present risks to the developing fetus, these risks are clearly outweighed by the potential morbidity and mortality from anthrax. Guidelines for prophylactic treatment of anthrax and treatment of suspected active cases of anthrax are changing continually, and the CDC's web site (<http://emergency.cdc.gov/agent/anthrax/>) should be consulted for the latest recommendations.

## Chlamydial Infection

*Chlamydia trachomatis* is the most common reportable STI in the United States, with high rates among sexually active adolescents and young adults. Important risk factors for chlamydial infection include unmarried status, recent change in sexual partner, multiple concurrent partners, age 25 years or younger, inner-city residence, history or presence of other STIs, and little or no prenatal care. Most infected women have few symptoms, but *C trachomatis* may cause urethritis and mucopurulent (nongonococcal) cervicitis. Chlamydial infection also is associated with postpartum endometritis and infertility. Infection may be transmitted from the genital tract of infected women to their neonates during birth.

### *Antepartum Management*

All pregnant women should be screened for chlamydial infection during the first prenatal care visit, and women at increased risk should be tested again in the third trimester (see also “Routine Laboratory Testing in Pregnancy” in Chapter 5). The diagnosis of *C trachomatis* infection is based on a cell culture, direct fluorescent antibody staining, enzyme immunoassay, DNA probe, or NAATs (eg, PCR). Nucleic acid amplification tests are the most sensitive diagnostic measure.

Treatment should be administered to women who have known *C trachomatis* infection (ie, with mucopurulent cervicitis) or whose neonates are infected. Women whose sexual partners have nongonococcal urethritis or epididymitis are presumed to be infected and also should be treated. Simultaneous treatment of partners is an important component of the therapeutic regimen. Doxycycline and ofloxacin are contraindicated in pregnancy. Recommended regimens for treating *C trachomatis* infection in pregnant women include 1 g azithromycin orally in a single dose or amoxicillin 500 mg orally three times daily for 7 days. Alternative regimens in pregnant women include erythromycin base (500 mg orally four times a day for 7 days or 250 mg orally four times daily for 14 days) or erythromycin ethylsuccinate (800 mg orally four times daily for 7 days or 400 mg orally four times daily for 14 days). Erythromycin estolate is contraindicated during pregnancy because of drug-related hepatotoxicity. A test of cure is recommended in pregnancy 3–4 weeks after completion of treatment regimens to confirm successful treatment.

### *Neonatal Management*

Approximately 50% of infants born to women who have untreated chlamydial infection become colonized with *C trachomatis*. Of these, 25–50% will mani-

fest a purulent conjunctivitis a few days to several weeks after delivery, and 5–20% will develop pneumonia 2–19 weeks after delivery. Infections generally are mild and responsive to antimicrobial therapy. Infants with chlamydial conjunctivitis or pneumonia should be treated with oral azithromycin for 5 days or erythromycin base or ethylsuccinate for 14 days. Topical treatment of conjunctivitis is ineffective. If hospitalized, infants should be managed with standard precautions.

## Gonorrhea

Gonorrhea, caused by the gram-negative bacterium *Neisseria gonorrhoeae* is one of the most commonly reported bacterial STIs. Women younger than 25 years are at highest risk of gonorrhea infection, as are those of black, Hispanic, American Indian, or Alaska Native ethnicity. Other risk factors for gonorrhea include a previous gonococcal infection, other STIs, new or multiple sexual partners, inconsistent condom use, commercial sex work, and illicit drug use. Gonococcal infection of the genital tract in females often is asymptomatic, and common clinical syndromes are vaginitis, urethritis, endocervicitis, and salpingitis. Asymptomatic infection in females can progress to pelvic inflammatory disease, with tubal scarring that can result in ectopic pregnancy or infertility. Perinatal transmission also can occur, which results in neonatal gonococcal infection.

### *Antepartum Management*

All pregnant women with risk factors for gonorrhea or living in an area in which the prevalence of *N gonorrhoeae* is high should be screened for *N gonorrhoeae* at the first prenatal visit (see also “Routine Laboratory Testing in Pregnancy” in Chapter 5). A repeat test should be obtained in the third trimester for women at increased risk of gonorrhea and other STIs. Nucleic acid amplification tests (eg, PCR) are highly sensitive and specific for detecting *N gonorrhoeae* when used on endocervical or vaginal swab and urine specimens. Cultures are the most widely used tests for identifying *N gonorrhoeae* from nongenital sites.

Because of the prevalence of penicillin-resistant, tetracycline-resistant and fluoroquinolone-resistant *N gonorrhoeae*, the recommended treatment is combination therapy with a single intramuscular dose of ceftriaxone plus oral azithromycin. A test-of-cure is not recommended routinely in individuals with uncomplicated gonorrhea who are treated with this first-line therapy. If ceftriaxone is unavailable, second-line therapy would be a single oral dose of cefixime plus oral azithromycin; however, a test-of-cure 1 week after treatment

is required. If penicillin allergy prohibits the use of a cephalosporin, a single oral dose of azithromycin may be used but a test of cure is required 1 week after treatment. Because concurrent infection with *C trachomatis* is common, patients with gonococcal infections should be treated for chlamydial infection (unless it has been excluded) and should be evaluated for co-infection with syphilis, HIV, and other STIs. All cases of gonorrhea must be reported to public health officials.

### *Neonatal Management*

Gonococcal infection in the newborn usually involves the eyes. Antimicrobial prophylaxis soon after delivery is recommended for all neonates (see also “Conjunctival (Eye) Care” in Chapter 8). Infants born to women with active gonorrhea should receive a single dose of cefotaxime (100 mg/kg given intravenously or intramuscularly). Single-dose systemic antibiotic therapy is effective treatment for gonococcal ophthalmia and prophylaxis for disseminated disease.

In addition to ophthalmia, neonatal disease may include scalp abscess, vaginitis, and systemic disease with bacteremia, arthritis, meningitis, or endocarditis. Infants with clinical gonococcal disease should be hospitalized, and cultures of blood, cerebrospinal fluid, eye discharge, or other sites of infection should be obtained. For infants with positive cultures (ie, disseminated infection), the recommended antimicrobial therapy is cefotaxime (50–100 mg/kg per day, divided into two doses given every 12 hours). The duration of antibiotic treatment depends on the site of infection; 7 days is recommended for disseminated infection; 10–14 days is recommended for meningitis and 14 days is recommended for arthritis. Infected infants should be managed with standard precautions. Tests for concomitant infection with *C trachomatis*, congenital syphilis, and HIV infection should be performed.

### **Group B Streptococci**

Group B streptococci (GBS), also known as *Streptococcus agalactiae*, emerged as an important cause of perinatal morbidity and mortality in the 1970s. Between 10% and 40% of pregnant women are colonized with GBS in the vagina or rectum. Group B streptococci can cause maternal urinary tract infection, amnionitis, endometritis, sepsis, or, rarely, meningitis. Vertical transmission of GBS during labor or delivery can result in invasive infection in the newborn during the first 6 days after birth (early-onset group B streptococcal infection) characterized primarily by sepsis or pneumonia, or, less frequently, meningitis. Implementation of national guidelines for intrapartum antibiotic

prophylaxis since the 1990s has resulted in an approximate 80% reduction in the incidence of early-onset neonatal sepsis due to GBS. Yet, GBS remains the leading cause of infectious mortality and morbidity in neonates.

The primary risk factor for early-onset group B streptococcal neonatal infection is maternal intrapartum colonization with GBS. Other clinical risk factors include gestational age of less than 37 weeks, rupture of membranes for 18 or more hours, intra-amniotic infection, young maternal age, and black race. Infants born to women who have previously given birth to a GBS-infected neonate or who have heavy GBS colonization, such as that seen with group B streptococcal bacteriuria, are at substantial risk of early-onset infection.

In 2010, the CDC revised its guidelines for the prevention of early-onset group B streptococcal disease in newborns. The updated recommendations continue to focus on universal antenatal GBS screening at 35–37 weeks of gestation and intrapartum antibiotic prophylaxis for GBS-positive women and for women with threatened preterm labor but include important changes for clinical practice, which are summarized here. For more information on screening, see “Routine Laboratory Testing in Pregnancy” in Chapter 5. The complete CDC guidelines are available at <http://www.cdc.gov/groupbstrep/guidelines/guidelines.html>.

### *Intrapartum Management*

Indications for intrapartum antibiotic prophylaxis are summarized in Table 10-4. Intrapartum prophylaxis for GBS is not recommended for women undergoing a planned cesarean delivery in the absence of labor and rupture of membranes, regardless of the gestational age, even in GBS-positive women. All patients undergoing cesarean delivery should have prophylactic antibiotics administered before the incision to reduce the risk of postoperative infections (see also “Cesarean Delivery” in Chapter 6). When culture results are not available, intrapartum antibiotic prophylaxis should be offered only on the basis of the presence of intrapartum risk factors for early-onset GBS disease (see Table 10-4). The administration of intrapartum antibiotic prophylaxis to a woman with rupture of membranes for 18 hours or more with a culture negative for GBS at 35–37 weeks of gestation is strongly discouraged; in these clinical scenarios, antibiotics should be administered only if there is chorioamnionitis or other indications, such as pyelonephritis.

Intrapartum antibiotic prophylaxis is most effective if administered at least 4 hours before delivery at recommended doses. However, no medically necessary obstetric procedure should be delayed in order to achieve 4 or more

**Table 10–4. Indications and Nonindications for Intrapartum Antibiotic Prophylaxis to Prevent Early-Onset Group B Streptococcal Disease**

Intrapartum GBS Prophylaxis Indicated	Intrapartum GBS Prophylaxis Not Indicated
Previous infant with invasive GBS disease GBS bacteriuria during any trimester of the current pregnancy	Colonization with GBS during a previous pregnancy (unless an indication for GBS prophylaxis is present for current pregnancy)
Positive GBS screening culture during current pregnancy* (unless a cesarean delivery, is performed before onset of labor on a woman with intact amniotic membranes)	GBS bacteriuria during previous pregnancy (unless another indication for GBS prophylaxis is present for current pregnancy)
Unknown GBS status at the onset of labor (culture not done, incomplete, or results unknown) and any of the following:	Cesarean delivery performed before onset of labor on a woman with intact amniotic membranes, regardless of GBS colonization status or gestational age
<ul style="list-style-type: none"> <li>• Delivery at less than 37 weeks of gestation†</li> <li>• Amniotic membrane rupture greater than or equal to 18 hours</li> <li>• Intrapartum temperature greater than or equal to 100.4°F (greater than or equal to 38.0°C)‡</li> <li>• Intrapartum NAAT§ positive for GBS</li> </ul>	Negative vaginal and rectal GBS screening culture result in late gestation* during the current pregnancy, regardless of intrapartum risk factors

Abbreviations: GBS, group B streptococci; NAAT, nucleic acid amplification test.

\*Optimal timing for prenatal GBS screening is at 35–37 weeks of gestation.

†Recommendations for the use of intrapartum antibiotics for prevention of early-onset GBS disease in the setting of preterm delivery are included in the complete guidelines, which are available at <http://www.cdc.gov/groupbstrep/guidelines/guidelines.html>.

‡If amnionitis is suspected, broad-spectrum antibiotic therapy that includes an agent known to be active against GBS should replace GBS prophylaxis.

§NAAT testing for GBS is optional and may not be available in all settings. If intrapartum NAAT result is negative for GBS but any other intrapartum risk factor (delivery at less than 37 weeks of gestation, amniotic membrane rupture at 18 hours or more, or temperature greater than or equal to 100.4°F [greater than or equal to 38.0°C]) is present, then intrapartum antibiotic prophylaxis is indicated.

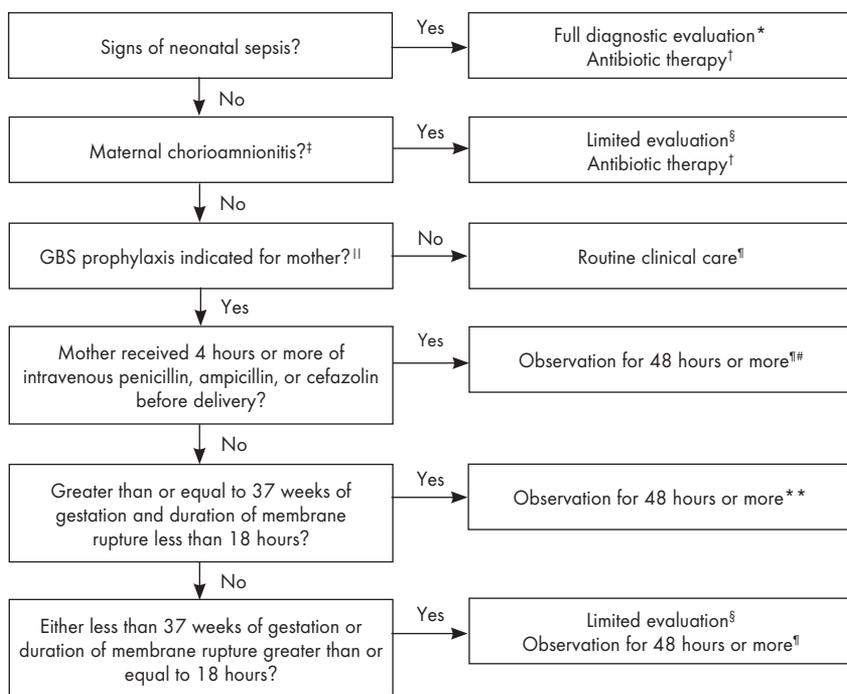
Verani JR, McGee L, Schrag SJ. Prevention of perinatal group B streptococcal disease—revised guidelines from CDC, 2010. Division of Bacterial Diseases, National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention (CDC). *MMWR Recomm Rep* 2010;59(RR–10):1–36.

hours of GBS prophylaxis before delivery. Penicillin is the agent of choice, with ampicillin as an acceptable alternative. Cefazolin is the drug of choice for penicillin allergy without anaphylaxis, angioedema, respiratory distress, or urticaria. Erythromycin is no longer recommended under any circumstances because nearly 50% of GBS strains are resistant to this drug. Group B streptococcal isolates from women at high risk of anaphylaxis should be tested for

susceptibility to clindamycin and erythromycin, and clindamycin can be used for prophylaxis if susceptibility to both drugs is documented. Vancomycin use is recommended only if the isolate is resistant to clindamycin and erythromycin. However, neither clindamycin nor vancomycin has been evaluated in the prevention of early-onset GBS disease.

### Neonatal Management

The 2010 CDC guidelines for the prevention of early-onset GBS disease among newborns are summarized in Figure 10-1. Recommended management continues to be based on clinical signs, the presence of maternal risk factors, and the likely efficacy of intrapartum antibiotic prophylaxis (or maternal antimicrobial treatment in the case of clinical chorioamnionitis) in preventing early-onset



**Fig. 10-1.** Algorithm for secondary prevention of early-onset group B streptococcal disease among newborns. Abbreviation: GBS, group B streptococci.

\*Full diagnostic evaluation includes a blood culture, a complete blood count, including white blood cell differential, platelet counts, chest radiograph (if respiratory abnormalities are present), and lumbar puncture (if patient is stable enough to tolerate procedure and sepsis is suspected).

<sup>†</sup>Antibiotic therapy should be directed toward the most common causes of neonatal sepsis, including intravenous ampicillin for GBS and coverage for other organisms (including *Escherichia coli* and other gram-negative pathogens) and should take into account local antibiotic resistance patterns.

<sup>‡</sup>Consultation with obstetric providers is important to determine the level of clinical suspicion for chorioamnionitis. Chorioamnionitis is diagnosed clinically and some of the signs are nonspecific.

<sup>§</sup>Limited evaluation includes blood culture (at birth), and complete blood count with differential and platelets (at birth, 6–12 hours of life, or both).

<sup>||</sup>GBS prophylaxis is indicated if one or more of the following is present: 1) mother is GBS positive within preceding 5 weeks; 2) GBS status unknown, with one or more intrapartum risk factors, including less than 37 weeks of gestation, duration of rupture of membranes for 18 hours or more, or temperature greater than or equal to 100.4°F (greater than or equal to 38.0°C); 3) group B streptococcal bacteriuria during current pregnancy; 4) history of a previous infant with group B streptococcal disease.

<sup>¶</sup>If signs of sepsis develop, a full diagnostic evaluation should be conducted and antibiotic therapy initiated.

<sup>#</sup>If greater than or equal to 37 weeks of gestation, observation may occur at home after 24 hours if other discharge criteria have been met, access to medical care is readily available, and a person who is able to comply fully with instructions for home observation will be present. If any of these conditions is not met, the infant should be observed in the hospital for at least 48 hours and until discharge criteria are achieved.

\*\*Some experts recommend a complete blood count with differential and platelets at 6–12 hours of age.

Verani JR, McGee L, Schrag SJ. Prevention of perinatal group B streptococcal disease—revised guidelines from CDC, 2010. Division of Bacterial Diseases, National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention (CDC). *MMWR Recomm Rep* 2010;59(RR-10):1–36.

disease. (Please refer to the CDC web site, <http://www.cdc.gov/groupbstrep/index.html>, for the latest recommendations to help prevent early onset GBS infection in neonates.) There is no known method for the prevention of late-onset neonatal GBS infection.

## Listeriosis

The major cause of epidemic and sporadic listeriosis infection is food-borne transmission of the bacterium *Listeria monocytogenes*. Incriminated foods include unpasteurized milk, cheese, and other dairy products; undercooked poultry; and prepared meats, such as hot dogs, deli meats, and pâté, and some contami-

nated fresh fruits and vegetables. Asymptomatic fecal and vaginal carriage can result in sporadic neonatal disease, which can cause early-onset neonatal infections from transplacental or ascending intrauterine infection or from exposure during delivery. Maternal infection has been associated with preterm delivery and other obstetric complications. Late-onset neonatal infection results from acquisition of the organism during passage through the birth canal or possibly from environmental sources. To prevent pregnancy-related listeria infections, pregnant women are advised not to eat unpasteurized dairy products, undercooked foods, or unwashed fresh fruits and vegetables.

*Listeria monocytogenes* can be recovered on blood agar media from cultures of usually sterile body sites (eg, blood or cerebrospinal fluid). Special techniques may be needed to recover *L monocytogenes* from sites with mixed flora (eg, vagina, rectum). Because of morphologic similarity to diphtheroids and streptococci, a culture isolate of *L monocytogenes* mistakenly can be considered a contaminant or saprophyte.

Prompt diagnosis and antibiotic treatment of maternal listeriosis may prevent fetal or perinatal infection. *Listeria monocytogenes* is uniformly sensitive to ampicillin, but there may be a synergistic benefit from adding gentamicin. Signs of listeriosis in the newborn vary widely and often are nonspecific. The clinical picture is similar to that of GBS infection with early-onset and late-onset syndromes. Therapy with intravenous ampicillin and an aminoglycoside is recommended for neonatal infections. (For additional information and resources, please visit the CDC online at [http://www.cdc.gov/ncbddd/pregnancy\\_gateway/infections-listeria.html](http://www.cdc.gov/ncbddd/pregnancy_gateway/infections-listeria.html).)

## **Pertussis**

Pertussis, commonly known as whooping cough, is a respiratory infection that initially is manifested as coryza before the onset of paroxysms of cough that last for weeks. Complications in adults include pneumonia, sleep disturbance, rib fracture, and incontinence. In the first 6 months of life, illness is more severe, and infant complications include pneumonia, seizures, encephalopathy, and death. Newborns are thought to be protected from infection if high concentrations of passively transferred pertussis-specific antibodies are present.

### ***Immunization During Pregnancy***

Universal immunization is recommended to prevent transmission of pertussis. Women should ideally receive the tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccine (Tdap) before conception. However, there is no

evidence that antenatal vaccination with Tdap causes any adverse effects specific to pregnancy. Moreover, immunization with Tdap during pregnancy has been associated with an increase in diphtheria and pertussis antibody levels in newborns of vaccinated mothers. Women's health care providers should implement a Tdap vaccination program for pregnant women who previously have not received Tdap. Health care providers should administer Tdap during pregnancy, preferably during the third trimester or late second trimester (ie, after 20 weeks of gestation). Alternatively, if not administered during pregnancy, Tdap should be administered immediately postpartum to ensure pertussis immunity and reduce the risk of transmission to the newborn. Regardless of the trimester, health care providers are encouraged to report Tdap administration to the appropriate manufacturer's pregnancy registry.

Additional guidelines for the administration of Tdap during pregnancy are outlined in the following paragraphs. Extensive information for health care providers and consumers about Tdap and other vaccines can be obtained at [www.cdc.gov/vaccines](http://www.cdc.gov/vaccines) and on the American College of Obstetricians and Gynecologists' immunization web site at [www.immunizationforwomen.org/](http://www.immunizationforwomen.org/).

**Tetanus Booster.** If a tetanus and diphtheria (TD) booster vaccination is indicated during pregnancy (ie, more than 10 years since the previous TD vaccination) for a woman who has previously not received Tdap, then health care providers should administer the Tdap vaccine during pregnancy, preferably during the third or late second trimester (ie, after 20 weeks of gestation).

**Wound Management.** As part of standard wound management care to prevent tetanus, a tetanus toxoid-containing vaccine might be recommended for a pregnant woman if 5 years or more have elapsed since the previous TD booster vaccination. If a TD booster is indicated for a pregnant woman who previously has not received Tdap, health care providers should administer Tdap.

**Unknown or Incomplete Tetanus Vaccination.** To ensure protection against maternal and neonatal tetanus, pregnant women who never have been vaccinated against tetanus should receive three vaccinations containing tetanus and reduced diphtheria toxoids during pregnancy. The recommended schedule is 0, 4 weeks, and 6–12 months. One dose of the TD booster vaccine should be replaced by Tdap, preferably during the third trimester or late second trimester (ie, after 20 weeks of gestation).

### *Vaccination of Adolescents and Adults in Contact With Infants*

The CDC Advisory Committee on Immunization Practices recommends that adolescents and adults (eg, siblings, parents, grandparents, child care providers,

including individuals aged 65 years and older) who have or who anticipate having contact with an infant younger than 12 months and who have not received Tdap previously should receive a single dose of Tdap to protect against pertussis and reduce the likelihood of transmission. Ideally, these adolescents and adults should receive Tdap at least 2 weeks before they have contact with the infant.

### *Neonatal and Infant Management*

Infected infants younger than 6 months of age frequently require hospitalization for supportive care and to manage complications, but those less than 3 months of age account for most of the pertussis-related mortality. Antimicrobial agents given during the catarrhal stage may lessen the severity of the disease. Azithromycin is the drug of choice in all age groups.

## **Tuberculosis**

Tuberculosis is caused by infection with organisms of the *Mycobacterium tuberculosis* complex, which primarily affects the lungs. Clinical manifestations include feelings of sickness or weakness, weight loss, fever, and night sweats. The symptoms of tuberculosis also include coughing, chest pain, and the coughing up of blood. The risk of developing tuberculosis is highest during the 6 months after infection and remains high for 2 years; however, many years can elapse between initial tuberculosis infection and the onset of tuberculosis. Once considered rare in the United States, the incidence of tuberculosis has increased considerably in women of childbearing age. In endemic areas, the incidence of tuberculosis may approach 0.1% of pregnant women.

Tuberculosis is diagnosed in an individual with infection who also has signs, symptoms, positive cultures, or radiographic manifestations of *M tuberculosis*. Isolation of *M tuberculosis* by culture from early morning gastric aspirate, sputum, pleural fluid, or other body fluids establishes the diagnosis of active disease. *Mycobacterium tuberculosis* is slow growing, usually requiring 2–10 weeks for isolation from cultured materials. Smears to demonstrate acid-fast bacilli should be performed on sputum and body fluids.

Latent tuberculosis infection is defined by a positive Mantoux tuberculin skin test or interferon-gamma release assay in an individual with no physical findings of disease and either a normal chest X-ray or only granuloma or calcification in the lung parenchyma, or regional lymph nodes, or both. The purpose of treating latent tuberculosis infection is to prevent progression to disease.

### *Antepartum Management*

All pregnant women who are at high risk of tuberculosis should be screened with a Mantoux tuberculin skin test with purified protein derivative (PPD) or an interferon-gamma release assay when they begin receiving prenatal care (see also “Routine Laboratory Testing in Pregnancy” in Chapter 5). When the result of a tuberculin skin test or interferon-gamma release assay is positive, the time of conversion usually is not known. If a chest X-ray is normal, some experts prefer to delay treatment of latent tuberculosis infection until after delivery because pregnancy itself does not increase the risk of progression to disease and because of an increased risk of drug-induced hepatotoxicity during pregnancy and immediately postpartum. Other experts recommend treatment with monthly monitoring for hepatotoxicity. Although isoniazid is not known to be teratogenic, most experts recommend waiting to start therapy until the second trimester of pregnancy.

Treatment regimens for tuberculosis are based on the presence or absence of tuberculosis disease, primarily determined by chest X-ray findings and sputum culture and, in the absence of disease, the likelihood of progressing to disease. The risk of progression to disease is highest in the 2 years after conversion to positive PPD. For this reason, the recommended medication in women known to have converted within the previous 2 years (such as known contacts of other tuberculosis cases) but with no evidence of disease is isoniazid (300 mg per day) starting after the first trimester and continuing for 9 months. For women who are infected with HIV, some experts would recommend 12 months of isoniazid therapy. All pregnant women receiving isoniazid also should take pyridoxine (50 mg daily) to mitigate the risk of peripheral neuritis.

If tuberculosis is diagnosed in a pregnant woman (by positive cultures, compatible clinical findings, or X-ray findings), prompt, multidrug therapy is recommended to protect both the woman and the fetus. Isoniazid and rifampin, supplemented initially by ethambutol are recommended drugs. Pyrazinamide frequently is used for the first 2 months in a three-drug or four-drug regimen. Although safety data in pregnancy have not been published, many experts have used the drug in pregnant women with no apparent problems for the woman or the fetus. Therapy with isoniazid and rifampin is continued for at least 6 months for drug-susceptible disease.

### *Neonatal Management*

In utero infection can occur as a result of hematogenous dissemination, which seeds the placenta; or as a result of aspiration of infected amniotic fluid in utero. Neonatal infection may occur at the time of delivery as a result of aspiration of

tubercle bacilli in women with tuberculosis endometritis. On the rare occasions in which congenital tuberculosis is suspected, diagnostic evaluations and treatment of the infant and the mother should be initiated promptly.

Management of a newborn whose mother (or other household contact) is suspected of having tuberculosis is based on individual considerations. Whenever possible, separation of the mother and the infant should be minimized. Differing circumstances and resulting recommendations are listed as follows:

- The mother has a positive tuberculin skin test or interferon-gamma release assay result but a negative X-ray result. If the mother is asymptomatic, the infant needs no special evaluation or therapy and no separation of the mother and the infant is required. Because the tuberculin skin test or interferon-gamma release assay result could be a marker of an unrecognized case of contagious tuberculosis within the household, other household members should be tested and have further evaluation, as needed.
- The mother has an abnormal chest X-ray but no evidence of current tuberculosis. If the mother's chest X-ray is abnormal but the history, physical examination, sputum smear, and X-ray indicate no evidence of current tuberculosis, the infant can be assumed to be at low risk of *M tuberculosis* infection. The radiographic abnormality in this circumstance probably is because of another cause or because of a quiescent focus of tuberculosis. In the latter case, the mother may develop contagious, pulmonary tuberculosis, if untreated, and should receive appropriate therapy if not treated previously. She and her infant should receive follow-up care. Other household members should be tested and appropriately evaluated.
- The mother has clinical or radiographic evidence of contagious tuberculosis. The mother should be reported immediately to the public health department so that investigation of all household members can be performed within several days. All contacts should have a tuberculin skin test or interferon-gamma release assay, chest X-ray, and physical examination. The infant should be evaluated for congenital tuberculosis and should be tested for HIV infection. The mother and the infant should be separated until both are receiving appropriate therapy and the mother is deemed to be not contagious. Women with tuberculosis disease who have been treated appropriately for 2 or more weeks and who are not considered contagious can breastfeed. Other household members should be tested and appropriately evaluated.

If congenital tuberculosis is excluded, isoniazid is given until the infant is 3–4 months of age, at which time a tuberculin skin test should

be performed. If the tuberculin skin test result is positive, the infant should be reassessed for tuberculosis disease. If disease is not present, isoniazid should be continued for a total of 9 months; children infected with HIV should be treated for 12 months. If the skin test result is negative and the mother and other family members with tuberculosis have good adherence and response to treatment, and are no longer infectious, isoniazid may be discontinued.

- The mother has disease caused by multidrug-resistant (MDR) *M tuberculosis* or has poor adherence to treatment and directly observed therapy is not possible. The infant should be separated from the ill family member. Bacille Calmette–Guérin vaccination may be considered for the infant, especially if the family member has MDR tuberculosis (see the following paragraph on “Bacille Calmette–Guérin Vaccine”). Because the response to the vaccine in infants may be delayed, the infant should be separated from the ill family member for at least several weeks after vaccination. In general, in the United States directly observed therapy of the infant is preferred. The efficacy of any therapy for contacts of MDR tuberculosis is unknown. An expert in childhood tuberculosis should be consulted when this is a consideration.

**Isoniazid Therapy.** Breastfeeding is considered safe during maternal antituberculosis therapy. Breastfed infants of women taking isoniazid therapy should receive a multivitamin supplement, including pyridoxine.

**Bacille Calmette–Guérin Vaccine.** Bacille Calmette–Guérin vaccine is a live vaccine prepared from attenuated strains of *Mycobacterium bovis*. Bacille Calmette–Guérin immunization in the United States should be considered only for individuals with a negative tuberculin skin test result who are not infected with HIV and who are at high risk of intimate and prolonged exposure to patients with persistently infectious pulmonary tuberculosis or MDR tuberculosis, cannot be removed from the source of exposure, and cannot be placed on long-term preventive therapy.

## Spirochetal Infections

### Syphilis

Syphilis is a systemic disease caused by infection with the spirochete *Treponema pallidum*. Rates of infection are highest in urban areas and the rural South. In adults, syphilis is more common in individuals with HIV infection. Acquired

syphilis almost always is contracted through direct sexual contact with ulcerative lesions of the skin or mucous membranes of infected people. Congenital syphilis most often is acquired through hematogenous transplacental infection of the fetus, although direct contact of the infant with infectious lesions during or after delivery also can result in infection. Transplacental infection can occur throughout pregnancy and at any stage of maternal infection.

### *Antepartum Management*

All pregnant women should be serologically screened for syphilis as early as possible in pregnancy. False-negative serologic test results may occur in early primary infection, and infection after the first prenatal visit is possible. For communities and populations with a high prevalence, serologic testing also is recommended at 28–32 weeks of gestation and at delivery (as well as after exposure to an infected partner). Some states require all women to be screened for syphilis at delivery.

The specificity of serologic testing is high if both a nontreponemal screening test (Venereal Disease Research Laboratories [VDRL] or rapid plasma reagin [RPR] test result) and a subsequent treponemal serologic test result are reactive. Microscopic dark-field and histologic examinations for spirochetes are most reliable when lesions are present.

Pregnant women with syphilis should be treated with a penicillin regimen appropriate to the stage of infection. Women who are allergic to penicillin should be desensitized and then treated with the drug. Tetracycline and doxycycline are contraindicated during pregnancy. Erythromycin and azithromycin are suboptimal treatment options because neither reliably cures maternal infection nor treats an infected fetus. Women should be observed for signs of a Jarisch–Herxheimer reaction (an immune response to toxins released when spirochetes die), which may cause fever, nonreassuring fetal status, and preterm labor.

Women with syphilis should be queried about illicit substance use, especially cocaine. Results of the maternal serologic tests and treatment, if given, should be recorded in the neonate's medical record or be made available to the neonate's pediatrician.

### *Neonatal Management*

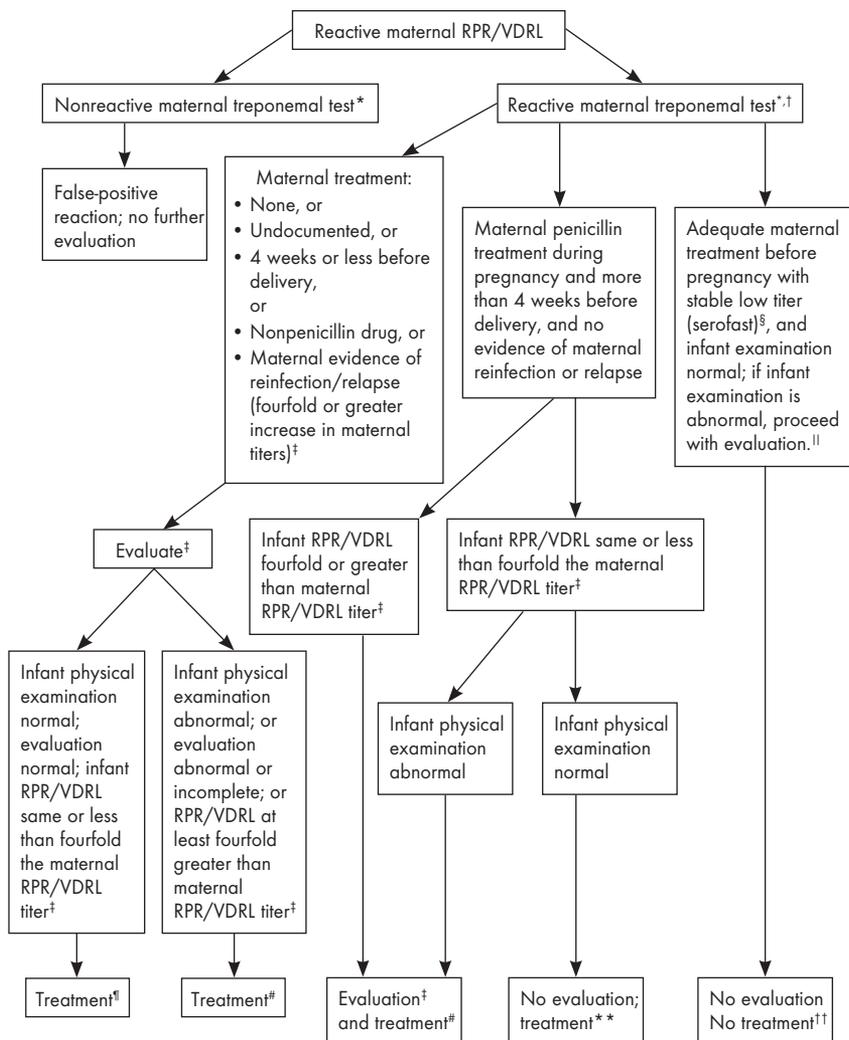
An infant should be evaluated for congenital syphilis if he or she is born to a mother with a positive treponemal test result who has one or more of the following conditions:

- Syphilis and HIV infection

- Untreated or inadequately treated syphilis
- Syphilis during pregnancy treated with a nonpenicillin regimen and inadequate regimen, such as erythromycin
- Syphilis during pregnancy treated with an appropriate penicillin regimen that failed to produce the expected fourfold decrease in nontreponemal antibody titer after therapy
- Syphilis treated less than 1 month before delivery (because treatment failures occur, and the efficacy of treatment cannot be assumed without sufficient time for an expected decrease in nontreponemal antibody titer)
- Syphilis treatment not documented
- Syphilis treated before pregnancy but with insufficient serologic follow-up during pregnancy to assess the response to treatment and current infection status

The diagnostic and therapeutic approach to infants delivered to mothers with syphilis is outlined in Figure 10-2. Management decisions are based on the three possible maternal situations: 1) maternal treatment before pregnancy, 2) adequate maternal treatment and response during pregnancy, or 3) inadequate maternal treatment or inadequate maternal response to treatment (or reinfection) during pregnancy.

For proven or probable congenital syphilis (based on the infant's physical examination and radiographic and laboratory testing), the preferred treatment is aqueous crystalline penicillin G, administered intravenously. The dosage should be based on chronologic age rather than gestational age and is 50,000 units/kg, intravenously, every 12 hours (for infants 1 week of age or younger) or every 8 hours (for infants older than 1 week). Alternatively, procaine penicillin G, 50,000 units/kg, intramuscularly, can be administered as a single daily dose for 10 days; no treatment failures have occurred with this formulation despite its low cerebrospinal fluid concentrations. When the infant is at risk of congenital syphilis because of inadequate maternal treatment or response to treatment (or reinfection) during pregnancy but the infant's physical examination, radiographic imaging, and laboratory analyses are normal (including infant RPR/VDRL either the same as or less than fourfold the maternal RPR/VDRL), some experts would treat the infant with a single dose of penicillin G benzathine (50,000 units/kg intramuscularly), but most still would prefer 10 days of treatment. If more than 1 day of therapy is missed, the entire course should be restarted. Data supporting use of other antimicrobial agents (eg, ampicillin) for



**Fig. 10-2.** Algorithm for evaluation and treatment of infants born to mothers with reactive serologic test results for syphilis. Abbreviations: FTA-ABS, fluorescent treponemal antibody absorption; MHA-TP, microhemagglutination test for antibodies to *Treponema pallidum*; RPR, rapid plasma regain; TP-EIA, *T pallidum* enzyme immunoassay; TP-PA, *T pallidum* particle agglutination; VDRL, Venereal Disease Research Laboratory.

\*FTA-ABS, MHA-TP, TP-EIA, or TP-PA.

<sup>†</sup>Test for human immunodeficiency virus (HIV) antibody. Infants of HIV-infected mothers do not require different evaluation or treatment.

<sup>‡</sup>A fourfold change in titer is the same as a change of 2 dilutions. For example, a titer of 1:64 is fourfold greater than a titer of 1:16, and a titer of 1:4 is fourfold lower than a titer of 1:16.

<sup>§</sup>Women who maintain a VDRL titer 1:2 or less or an RPR 1:4 or less beyond 1 year after successful treatment are considered serofast.

<sup>||</sup>Complete blood cell and platelet count; cerebrospinal fluid examination for cell count, protein, and qualitative VDRL; other tests as clinically indicated (eg, chest radiographs, long-bone radiographs, eye examination, liver function tests, neuroimaging, and auditory brainstem response).

<sup>#</sup>Treatment (option 1 or option 2, below), with many experts recommending treatment option 1. If a single dose of benzathine penicillin G is used, then the infant must be fully evaluated, full evaluation must be normal, and follow-up must be certain. If any part of the infant's evaluation is abnormal or not performed, or if the cerebrospinal fluid analysis is rendered uninterpretable, then a 10-day course of penicillin is required.

<sup>#</sup>Treatment option 1: Aqueous penicillin G, 50,000 units/kg, intravenously, every 12 hours (1 week of age or younger) or every 8 hours (older than 1 week); or procaine penicillin G, 50,000 units/kg, intramuscularly, as a single daily dose for 10 days. If 24 or more hours of therapy are missed, the entire course must be restarted.

<sup>\*\*</sup>Treatment option 2: Benzathine penicillin G, 50,000 units/kg, intramuscularly, single dose.

<sup>††</sup>Some experts would consider a single intramuscular injection of benzathine penicillin (treatment option 2), particularly if follow-up is not certain.

American Academy of Pediatrics. Red book: report of the Committee on Infectious Diseases, 29th. Elk Grove Village (IL): American Academy of Pediatrics; 2012.

treatment of congenital syphilis are not available. When possible, a full 10-day course of penicillin is preferred, even if ampicillin initially was provided for possible sepsis. Use of agents other than penicillin requires close serologic follow-up to assess adequacy of therapy.

Infants who have a normal physical examination and a serum quantitative nontreponemal serologic titer either the same as or less than fourfold (eg, 1:4 is fourfold lower than 1:16) the maternal titer are at minimal risk of syphilis if they are born to mothers who completed appropriate penicillin treatment for syphilis during pregnancy and more than 4 weeks before delivery, and if the mother had no evidence of reinfection or relapse. Although a full evaluation may be unnecessary, these infants should be treated with a single intramuscular injection of penicillin G benzathine because fetal treatment failure can occur despite adequate maternal treatment during pregnancy. Alternatively, these infants may be examined carefully, preferably monthly, until their nontreponemal serologic test results are negative.

Infants who have a normal physical examination and a serum quantitative nontreponemal serologic titer either the same as or less than fourfold the

maternal titer, whose mothers' treatment was adequate before pregnancy, and whose mothers' nontreponemal serologic titer remained low and stable before and during pregnancy and at delivery (VDRL less than 1:2; RPR less than 1:4) require no evaluation. Some experts, however, would treat with penicillin G benzathine as a single intramuscular injection if follow-up is uncertain.

## Lyme Disease

Lyme disease is caused by a spirochete (*Borrelia burgdorferi*) transmitted by the bite of a deer tick. The early localized stage of the disease is characterized by a distinctive "bull's-eye" skin lesion (erythema migrans) that occurs in 60–80% of patients and nonspecific, flu-like symptoms. Early disseminated disease can result in multiple erythema migrans several weeks after a tick bite, cranial nerve palsies (especially cranial nerve VII) or carditis within 4–6 weeks after the onset of early signs and symptoms. A late manifestation of Lyme disease is relapsing arthritis, usually pauciarticular and affecting large joints. Patients in the later stages of Lyme disease usually will be seropositive, but false-positive and false-negative test results are common.

Suspicion of early maternal infection is based on a history of exposure to tick bites, the presence of the distinctive erythema migrans rash, and nonspecific, flu-like symptoms. Adequately treated patients may never develop antibodies to spirochetes. Because congenital infection occurs with other spirochetal infections, there has been concern that an infected pregnant woman could transmit *B burgdorferi* to her fetus. No causal relationship between maternal Lyme disease and congenital abnormalities caused by *B burgdorferi* has been documented. No evidence shows that Lyme disease can be transmitted via breast milk. The neonate's health care provider should be informed when maternal disease is suspected.

Recommended treatment of suspected early disease in pregnant women is amoxicillin, 500 mg three times per day, for 2–3 weeks. For women who are allergic to penicillin, erythromycin is recommended for 2–3 weeks. For patients who are unable to tolerate erythromycin, cefuroxime axetil is an alternative for patients with immediate and anaphylactic hypersensitivity to penicillin who have undergone penicillin desensitization.

The best preventive measure is to avoid heavily wooded areas. If entrance into such areas is necessary, long-sleeved shirts and long pants tucked in at the ankle are helpful. Prophylactic antibiotic therapy for deer tick bites is not recommended routinely.

## Parasitic Infections

### Malaria

Although malaria mainly is confined to tropical areas of Africa, Asia, and Latin America, international travel and migration have made malaria a disease to consider in developed countries. The classic symptoms are high fever with chills, rigors, sweats, and headache.

Malaria infection may be more severe in pregnant women and also may increase the risk of adverse outcomes of pregnancy, including spontaneous abortion, stillbirth, preterm birth, and low birth weight. Because of the risk to both the woman and the fetus, and because no chemoprophylactic regimen is completely effective, pregnant women (or women likely to become pregnant) should avoid travel to malaria-endemic areas. If travel to a malaria-endemic area is necessary, appropriate consultation should be sought for chemoprophylaxis recommendations based on the malaria species and drug-resistance patterns prevalent in that area. (For current information and recommendations from the CDC, visit [www.cdc.gov/travel](http://www.cdc.gov/travel).)

Congenital malaria is rare. Signs and symptoms resemble those of neonatal sepsis. Definitive diagnosis (of the mother and the infant) relies on identification of the parasite on stained blood films. Both thick and thin films should be examined. Treatment of infection is based on the infecting species, possible drug resistance, and severity of disease. If malaria is a diagnostic consideration in a pregnant woman or newborn, consultation with appropriate specialists is recommended for optimal patient management.

### Toxoplasmosis

Toxoplasmosis is a protozoan infection caused by *Toxoplasma gondii*. Infection is acquired by foodborne transmission (consuming cysts in undercooked meat of infected animals or insect contamination of food), zoonotic transmission (by contact with oocysts from the feces of infected cats or by contact with contaminated soil or water), or through mother-to-child transmission during pregnancy. Infected women generally are asymptomatic. In the immunocompetent adult, the clinical course is benign and self-limited.

Congenital infection is more common after maternal infection in the third trimester; however, the sequelae from first-trimester fetal infection are more severe. Congenitally infected infants are healthy appearing at birth in 70–90%

of cases. Signs of congenital infection at birth may include maculopapular rash, generalized lymphadenopathy, hepatosplenomegaly, chorioretinitis, hydrocephaly, microcephaly, and intracranial calcifications. Neonates of women who are infected with both HIV and *T gondii* should be evaluated for congenital toxoplasmosis.

### *Antepartum Management*

Routine serologic screening of pregnant women is not indicated, except in the presence of HIV infection. Because the presence of antibodies before pregnancy indicates immunity, the appropriate time to test for immunity to toxoplasmosis in women at risk is before conception.

The diagnosis of maternal infection is based on serologic test results for the detection of *Toxoplasma*-specific antibodies. Both immunoglobulin G (IgG) and IgM testing should be used for the initial evaluation of patients suspected to have toxoplasmosis. A positive IgG titer indicates infection with the organism at some time in the past. A negative IgM test essentially excludes recent infection, but a positive IgM test is difficult to interpret because *Toxoplasma*-specific IgM antibodies may be detected for as long as 18 months after acute acquired infection. In addition, false-positive test results are common with commercially available kits. Before making treatment recommendations, confirmation of diagnosis should be made based on results obtained in a reference laboratory. (Additional information on laboratory diagnosis of toxoplasmosis is available from the CDC web site at <http://www.dpd.cdc.gov/dpdx/HTML/Toxoplasmosis.htm>.)

Treatment of the pregnant woman with acute toxoplasmosis reduces but does not eliminate the risk of congenital infection. Identification of acute maternal infection necessitates immediate institution of treatment until results of fetal testing are known. Spiramycin, which concentrates in the placenta, may reduce the risk of fetal transmission by 60%, but as a single agent, it does not treat established fetal infection. Spiramycin is available only through the U.S. Food and Drug Administration after serologic confirmation at a reference laboratory; it is recommended for pregnant women at risk unless fetal infection is documented. If fetal infection is established, pyrimethamine, sulfonamides, and folic acid are added to the regimen because they more effectively eradicate parasites in the placenta and in the fetus than spiramycin alone. With treatment, even early fetal infection with toxoplasmosis can result in successful pregnancy outcomes.

### *Neonatal Management*

A definitive diagnosis of congenital toxoplasmosis can be made prenatally by either detecting parasite DNA in amniotic fluid by PCR, or documenting anti-toxoplasma IgM and immunoglobulin A antibodies in fetal blood. Congenital toxoplasmosis can be diagnosed serologically by the detection of anti-toxoplasma-specific IgM or immunoglobulin A antibodies soon after birth or by the persistence of anti-toxoplasma IgG beyond 12 months of age. If the diagnosis is suspected (but unconfirmed) at the time of birth, ophthalmologic, auditory, and neurologic examinations should be performed.

For healthy appearing infants and those with clinical signs of congenital toxoplasmosis, pyrimethamine and sulfadiazine (supplemented with folinic acid) are recommended for approximately 1 year. Infants with congenital toxoplasmosis should be managed in consultation with infectious disease specialists. (Additional professional and patient information is available on the CDC web site at <http://www.cdc.gov/parasites/toxoplasmosis/>.)

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