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 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

Approximately 1% of all newborns are infected with cytomegalovirus (CMV) in utero and excrete CMV after birth. Although the majority of congenital CMV infections are asymptomatic, approximately 5% of infected neonates are symptomatic at birth.

Transmission occurs via transplacental passage of the virus, contact of the fetus with infectious secretions at the time of birth, ingestion of infected breast milk, or transfusion of blood from seropositive donors. 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. Newborns of women who are seronegative and who receive milk from human milk banks are at risk of developing CMV disease. This can be minimized by limiting donor milk to CMV-negative donors or by ensuring appropriate pasteurization. Both primary CMV infection and reactivation of a
latent infection can occur in the mother and result in congenital CMV infection. Symptomatic CMV infection in a congenitally infected infant is more likely to occur in an infant born to a mother with primary CMV infection. Although ganciclovir and CMV hyperimmune globulin have been used to treat some congenitally infected infants, these are not recommended routinely because of insufficient efficacy data.

Because there is neither a vaccine for prevention of infection nor effective therapy for acute maternal infection, routine serologic screening of women or neonates is of little benefit. Testing generally is limited to pregnant women in whom CMV exposure is suspected. Routine serologic testing of personnel in newborn nurseries is not recommended.

Although the presence of immunoglobulin M (IgM) CMV antibody is highly suggestive of primary maternal infection, false-positive and false-negative test results occur. Positive IgM test results should be confirmed by viral culture or viral DNA quantitation assays on maternal blood. Establishing that seroconversion has occurred is the most accurate method for documenting primary maternal infection. Isolation of the virus or detection of CMV genome by polymerase chain reaction (PCR) from amniotic fluid is the most sensitive test for detecting fetal infection. Fetal blood obtained by cordocentesis may be tested for CMV-specific IgM, but this test is less sensitive than culture or PCR of amniotic fluid. For an infected fetus, ultrasound abnormalities or cordocentesis to detect elevated hepatic enzymes, anemia, and thrombocytopenia may be prognostic of severe infection.

Unequivocal evidence of CMV infection in the neonate who has not been diagnosed in utero requires recovery of the virus within 3 weeks of birth. Later in infancy, differentiation between intrauterine and perinatal infection is difficult to determine. For breastfeeding guidelines, see Chapter 7.

**Enteroviruses**

Wild-type poliovirus infection has been eliminated from the Western Hemisphere. Other enteroviral infections (coxsackieviruses, echoviruses, and polioviruses) are common and are spread by fecal–oral and respiratory routes. Infection in the third trimester can trigger labor. Signs of maternal infection often are mild and nonspecific.

Maternal enterovirus infections rarely cross the placenta and cause disease in the fetus. Vertical transmission of enteroviruses may occur at birth following exposure to virus-containing maternal blood or cervical secretions. Symptoms
in an enterovirus-infected neonate generally begin between 3 days and 7 days after birth. Neonates who acquire infection without maternal antibody are at risk for 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 the anus and samples of stool, spinal fluid, or blood. Polymerase chain reaction testing of spinal fluid is more sensitive than a culture.

No specific therapy is commercially available. Hospitalized newborns should be managed with contact as well as standard precautions.

**Hepatitis A Virus**

Hepatitis A virus (HAV) 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.

Vaccines for hepatitis A are highly effective and approved for use. Although vaccine safety in pregnancy has not been established, the risk to the developing fetus is minimal because the vaccine contains inactivated, purified viral proteins. Pregnant women with the following risk factors are candidates for vaccination: intravenous drug users, travelers to endemic regions, those living in communities with a high prevalence of hepatitis A, women who work with HAV-infected primates, women with either chronic liver disease or a liver transplant, and women with clotting disorders who receive clotting factor concentrate. Immunoglobulin is effective for both preexposure and postexposure prophylaxis and can be used during pregnancy.

Nosocomial outbreaks have been reported in neonatal intensive care units, but these are infrequent. Prevention of the spread of the virus is based on contact precautions, with emphasis on careful handwashing. With appropriate hygienic precautions, breastfeeding by a mother with HAV infection is permissible. Although immunoglobulin has been administered to newborns in specific situations, the efficacy of this practice has not been established.

**Hepatitis B Virus**

Perinatal transmission of Hepatitis B virus (HBV) infection generally occurs from exposure to maternal blood during labor and delivery. Perinatal infection
occurs in 70–90% of infants born to mothers who are both hepatitis B surface antigen (HBsAg) and hepatitis B e antigen (HBeAg) positive if appropriate and timely treatment is not instituted. Transplacental passage of HBV is rare. More than 90% of infants who are infected perinatally will develop chronic HBV infection.

Maternal Infection
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 transferred to the patient’s medical record at the delivery hospital. Women who have not been screened during prenatal care, those who are at high risk for infection (eg, intravenous drug users and women with recurrent sexually transmitted diseases [STDs]), and those with clinical hepatitis should be tested at admission in labor or for complications of pregnancy.

Pregnant women with chronic HBV should be informed about transmission risks and ways to prevent newborn infection. Newborns of HBsAg positive women should receive timely postexposure prophylaxis and follow-up.

Women who are HBsAg negative but who have risk factors for HBV infection should be offered vaccination during pregnancy. The adult dose of HBV vaccine is 10–20 µg (1 mL) injected into the deltoid muscle; intramuscular injection in the buttocks may not be as effective and is not recommended. A series of three doses is required; the second and third doses are given 1 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 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 persons 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.

Newborn Immunization
Universal HBV immunization is recommended for all neonates. Delivery hospitals should develop policies and procedures that ensure administration of a birth dose 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 in the infant’s medical record. Three intramuscular doses are required to provide effective protection (Table 9–1). For neonates born to women who are known to be HBsAg

### Table 9–1. Hepatitis B Immunoprophylaxis Schedule by Infant Birth Weight*

<table>
<thead>
<tr>
<th>Maternal Status</th>
<th>Infant ≥2,000 g</th>
<th>Infant &lt;2,000 g</th>
</tr>
</thead>
<tbody>
<tr>
<td>HBsAg positive</td>
<td>Hepatitis B vaccine plus HBIG (within 12 h of birth)</td>
<td>Hepatitis B vaccine plus HBIG (within 12 h of birth)</td>
</tr>
<tr>
<td></td>
<td>Continue vaccine series beginning at 1–2 mo of age according to recommended schedule for infants born to HBsAg-positive mothers.</td>
<td>Continue vaccine series beginning at 1–2 mo of age according to recommended schedule for infants born to HBsAg-positive mothers.</td>
</tr>
<tr>
<td></td>
<td>Check anti-HBs and HBsAg after completion of vaccine series.†</td>
<td>Check anti-HBs and HBsAg after completion of vaccine series.†</td>
</tr>
<tr>
<td></td>
<td>HBsAg-negative infants with anti-HBs levels ≥10 mIU/mL are protected and need no further medical management.</td>
<td>HBsAg-negative infants with anti-HBs levels ≥10 mIU/mL are protected and need no further medical management.</td>
</tr>
<tr>
<td></td>
<td>HBsAg-negative infants with anti-HBs levels &lt;10 mIU/mL should be reimmunized with three doses at 2-mo intervals and retested.</td>
<td>HBsAg-negative infants with anti-HBs levels &lt;10 mIU/mL should be reimmunized with three doses at 2-mo intervals and retested.</td>
</tr>
<tr>
<td></td>
<td>Infants who are HBsAg positive should receive appropriate follow-up, including medical evaluation for chronic liver disease.</td>
<td>Infants who are HBsAg positive should receive appropriate follow-up, including medical evaluation for chronic liver disease.</td>
</tr>
<tr>
<td>HBsAg status unknown</td>
<td>Test mother for HBsAg immediately after admission for delivery.</td>
<td>Test mother for HBsAg immediately after admission for delivery.</td>
</tr>
<tr>
<td></td>
<td>Hepatitis B vaccine (by 12 h)</td>
<td>Hepatitis B vaccine (by 12 h)</td>
</tr>
<tr>
<td></td>
<td>Administer HBIG (within 7 days) if mother tests HBsAg positive.</td>
<td>Administer HBIG if mother tests HBsAg positive or if mother’s HBsAg result is not available within 12 h of birth.</td>
</tr>
<tr>
<td></td>
<td>Continue vaccine series beginning at 1–2 mo of age according to recommended schedule based on mother’s HBsAg result.</td>
<td>Continue vaccine series beginning at 1–2 mo of age according to recommended schedule based on mother’s HBsAg result.</td>
</tr>
<tr>
<td></td>
<td>Immune with 4 vaccine doses; do not count birth dose as part of vaccine series.</td>
<td></td>
</tr>
</tbody>
</table>
negative, the first dose of vaccine should be administered during the newborn period or by 2 months of age, although administration of the first dose before hospital discharge is preferred; the second dose 1–2 months later; and the third dose by 6–18 months of age. Alternatively, vaccines may 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 neonates, the current American Academy of Pediatrics (AAP) recommendation is to delay the start of hepatitis B immunization in low-risk preterm neonates who weigh less than 2,000 g at birth until they reach the chronologic age of 1 month, regardless of initial birth weight or gestational age. The appropriate dose (Table 9–2) can be given into the anterolateral thigh muscle of neonates. Both term and preterm neonates born to women known to be HBsAg positive should receive both hepatitis B vaccine and one dose of HBIG within 12 hours of birth. Prophylaxis for exposed newborns can prevent perinatal HBV infection in approximately 95% of neonates when the three-dose immunization series is completed and HBIG is given within 12 hours after birth. The initial
A dose of HBV vaccine can be administered concurrently with HBIG but should be given at a different site. No special care of the neonate 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 neonate’s gestational age or birth weight. The third dose should be given at 6 months of age. For preterm neonates who weigh less than 2,000 g at birth, the initial vaccine dose is given at birth but is not counted in the

Table 9–2. Recommended Dosages of Hepatitis B Vaccines

<table>
<thead>
<tr>
<th>Patients</th>
<th>Recombivax HB† Dose, μg (mL)</th>
<th>Engerix-B‡ Dose, μg (mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infants of HBsAg-negative mothers and children and adolescents younger than 20 years of age</td>
<td>5 (0.5)</td>
<td>10 (0.5)</td>
</tr>
<tr>
<td>Infants of HBsAg-positive mothers (HBIG [0.5 mL] also is recommended)</td>
<td>5 (0.5)</td>
<td>10 (0.5)</td>
</tr>
<tr>
<td>Adults 20 years of age or older</td>
<td>10 (1)</td>
<td>20 (1)</td>
</tr>
<tr>
<td>Adults undergoing dialysis and other immunosuppressed adults</td>
<td>40 (1)§</td>
<td>40 (2)‖</td>
</tr>
</tbody>
</table>

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

†Available from Merck & Co Inc. A two-dose schedule, administered at 0 months and then 4–6 months later, is available for adolescents 11–15 years of age using the adult formulation of Recombivax HB (10 μg). A combination of hepatitis B (Recombivax, 5 μg) and Haemophilus influenzae type b (PRP-OMP) vaccine is recommended for use at 2, 4, and 12–15 months of age (Comvax). This vaccine cannot be administered at birth, before 6 weeks of age, or after 71 months of age.

‡Available from GlaxoSmithKline Biologicals. The U.S. Food and Drug Administration has licensed this vaccine for use in an optional four-dose schedule at 0, 1, 2, and 12 months of age. A combination of hepatitis B (Engerix-B, 20 μg) and hepatitis A (Havrix, 720 ELU) vaccine (Twinrix) is licensed for use in people 18 years of age and older in a three-dose schedule administered at 0, 1, and 6 or more months later. A combination of diphtheria and tetanus toxoids and acellular pertussis (DTaP), inactivated poliovirus (IPV), and hepatitis B (Engerix-B 10 μg) is recommended for use at 2, 4, and 6 months of age (Pediarix). This vaccine cannot be administered at birth, before 6 weeks of age, or at ≥7 years of age or older.

§Special formulation for dialysis patients

‖Two 1-mL doses given in one site in a four-dose schedule at 0, 1, 2, and 6 months of age.

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 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.

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 on admission. If the woman subsequently is found to be HBsAg positive, the neonate should receive HBIG as soon as possible (within 7 days of birth) and should receive the second and third doses of vaccine as recommended for neonates of HBsAg positive women. Both maternal HBsAg test results and the infant's immunization should be documented in the infant's medical record.

**Hepatitis C Virus**

Hepatitis C virus (HCV) is the principal cause of non-A, non-B hepatitis. The prevalence of HCV infection in the general population of the United States is estimated to be 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.

Infection with HCV is diagnosed serologically by the presence of HCV antibodies or by detection of HCV RNA. Positive enzyme immunoassay antibody test results should be confirmed by additional testing with a more specific assay, such as recombinant immunoblot assay, particularly when individuals at low risk are being tested. As many as 70% of patients with HCV infection develop chronic liver disease, and cirrhosis ultimately develops in 20–25% of these patients. Therefore, liver enzyme and function tests should be performed in patients who test positive for the antibodies.

Routine serologic testing during pregnancy for HCV infection is not recommended. Testing should be reserved for those whose histories suggest an increased risk of infection, such as blood transfusions before 1990, intravenous drug use, or occupational or recreational percutaneous or mucosal surface blood exposure.
Women who are infected with HCV should be advised that transmission of HCV by breastfeeding is possible but has not been documented. According to current guidelines of the U.S. Public Health Service, maternal HCV infection is not a contraindication to breastfeeding. The decision to do so should be based on an informed discussion between the woman and her health care provider.

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 infected with human immunodeficiency virus (HIV). 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 neonates born to women with HCV. The natural history of perinatally acquired hepatitis C infection is the subject of ongoing studies. 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, the presence of two or more PCR-RNA measurements after 1 month of age will identify infants infected through vertical transmission.

**Herpes Simplex Virus**

**Treatment and Counseling During Pregnancy**

Genital herpes may be caused by herpes simplex virus (HSV) type 2 (HSV-2) (in approximately 80–85% of cases) or by HSV type 1 (HSV-1). The prevalence of infection with HSV-2 has increased 30% in the past few decades, so that overall seroprevalence for HSV-2 is approximately 30% in females in the United States. Most adults with unequivocal serologic evidence of HSV-2 infection have not been diagnosed clinically, indicating that most primary infections are asymptomatic. Nevertheless, all women and their partners should be asked about a history of genital HSV infection. A genital herpes infection is classified as primary when it occurs in a woman with no evidence of prior HSV infection (ie, seronegative to both HSV-1 and HSV-2), 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), and recurrent when it occurs in a woman with clinical or serologic evidence of prior genital herpes (of the same serotype).
Women who have primary genital HSV infection in late pregnancy (whether symptomatic or asymptomatic) and who give birth vaginally have a high risk (30–60%) of transmitting the infection to their neonates. Similarly, nonprimary first-episode HSV infection occurring late in pregnancy also has a high risk of vertical transmission to the neonate. The risk of transmission during a vaginal delivery is much lower with recurrent disease (less than 2–5%). Distinguishing between primary, nonprimary first episode, and recurrent HSV infection in women on the basis of clinical findings is not accurate. A combination of positive viral detection and negative serologic test results or evidence of seroconversion is necessary to diagnose HSV infection. To correctly classify the type of HSV infection, the HSV type and type-specific maternal antibodies are needed. 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 for a current list). Currently, most newborns infected with HSV are delivered to women who have asymptomatic or unrecognized infections.

In a meta-analysis of acyclovir use among pregnant women near term, it was concluded that acyclovir treatment orally reduces the risk of clinical HSV recurrence at delivery, cesarean delivery for recurrent genital herpes, and the risk of HSV shedding at delivery. Acyclovir is indicated intravenously to treat severe maternal genital HSV infection (eg, disseminated infection that includes encephalitis, pneumonitis, and hepatitis). Although long-term safety and efficacy of administering acyclovir systemically have not been established, no evidence has been found of any adverse effects to the fetus.

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.

**Obstetric 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, neonates may 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 the rare case of active HSV infection and premature rupture of membranes remote from term, the risks of potential intrauterine infection versus those of prematurity must be individualized. Local neonatal infection may 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 recurrent HSV 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, and postpartum care areas. For recurrent 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. The labor and delivery rooms require only routine, careful cleaning and disinfection before using the rooms for other patients.

**Management of Infection in Exposed Newborns**

Most neonatal infections are caused by HSV-2, although infection with HSV-1 also can occur. Most neonates 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); and postnatal transmission in the nursery from another infected neonate, probably from the hands of personnel attending the neonates.

Neonates born vaginally through infected birth canals with active lesions (or viral shedding) require close observation because, as noted, the transmission
rate of HSV is as high as 50% for neonates of women with active primary or nonprimary first episode genital herpes at or near term. Specimens for herpes cultures should be obtained at 24–48 hours after birth from urine, stool or rectum, mouth, eye, and nasopharynx. Some experts recommend empiric treatment with acyclovir (20 mg/kg intravenously every 8 hours) for infants born vaginally to a mother with symptomatic primary herpes infection, pending results of cultures and clinical course, 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. Parents and providers 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 neonate with any of these manifestations should be evaluated immediately for possible HSV infection. Specimens for HSV culture should be obtained from skin lesions, conjunctiva, nasopharynx, mouth, rectum, urine, blood buffy coat, and cerebrospinal fluid. Cerebrospinal fluid also should be studied by PCR. Acyclovir therapy should be initiated if the cultures or PCR test results are positive or if HSV infection is otherwise strongly suspected.

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

The risk of HSV infection is extremely low in neonates born vaginally to asymptomatic women with a history of recurrent genital herpes and in those born to symptomatic women by cesarean delivery before rupture of membranes. Special isolation precautions are not needed for these neonates. Neonates born by cesarean delivery to women with herpetic lesions with intact membranes should be cultured for HSV as recommended previously for neonates exposed by vaginal delivery, and they should be observed. The length of in-hospital observation is empirical and is based on risk factors, local resources, and access to adequate follow-up. Parents should be instructed to report early signs of infection. Antiviral therapy should be initiated if culture results from the neonate are positive or if HSV infection is strongly suspected for other reasons.
Early Diagnosis and Management of Disease in Neonates

Cultures obtained from the eye, mouth, or rectum of neonates 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 24–48 hours or more after delivery suggests HSV infection and is an indication for immediate institution of antiviral therapy, even in the absence of symptoms. Direct fluorescent antibody staining of scrapings of skin, eye, or mucus membrane lesions can provide a rapid diagnosis. Polymerase chain reaction is a sensitive method for detecting HSV DNA; it is useful for examining spinal fluid samples.

The neonate should be physically segregated and managed with contact precautions for the duration of the illness; an isolation room is desirable. Personnel having contact with skin lesions or potentially infectious secretions should use gowns and gloves. Antiviral therapy is effective in the treatment of neonatal HSV infection and should be initiated promptly if HSV is suspected. Neonates with HSV disease should be managed in a facility that provides level III subspecialty care and consultation. Of treated neonates, 5–10% will develop recurrences requiring retreatment in the first month of life. The value of long-term suppressive or intermittent acyclovir therapy for neonates with disease of the skin, eyes, or mouth is being evaluated.

Although HSV infection is more likely to occur at a site of skin trauma, no data indicate that the circumcision of male neonates 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 neonates at the highest risk of disease (eg, neonates delivered vaginally to women with active genital lesions).

Contact of Neonates With Infected Mothers

A woman with HSV infection should be taught about her infection and about hygienic measures to prevent postpartum transmission of the infection to her neonate. Before touching her newborn, the woman should wash her hands carefully and use a clean barrier to ensure that the neonate does not come into contact with lesions or potentially infectious material. If the woman has genital HSV infection, her newborn may 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 all active cutaneous lesions are covered.

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

**Prevention**

In a meta-analysis, significant benefits with use of acyclovir beginning at 36 weeks of gestation were shown in women with a history of HSV infection. Some authorities have recommended routine serological screening for HSV infection among all pregnant women. However, the cost-effectiveness of this approach has not been established and currently neither the American College of Obstetricians and Gynecologists (ACOG) or the Centers for Disease Control and Prevention (CDC) recommend this seroscreening.

**Human Immunodeficiency Virus**

**Etiology**

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.

**Epidemiology**

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-fetus transmission before or near the time of birth and from breastfeeding. Infection with HIV continues to spread among women of childbearing age and is occurring increasingly in rural, as well as urban, areas. The predominant risk behavior is unprotected sexual intercourse. Before effective perinatal HIV interventions, the incidence of perinatal HIV infection mirrored increases in STDs in women.

Before the introduction of antiretroviral therapy in pregnancy, 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, thereby decreasing the maternal-to-child transmission rate to less than 2%.

The exact timing of transmission from an infected mother to her neonate is uncertain. Evidence suggests that in the absence of breastfeeding, 30% of transmission occurs before birth and 70% occurs around the time of delivery. Most prenatal transmission probably occurs close to delivery. Breastfeeding has been documented to be a mechanism of maternal-to-child transmission.

**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.

Pregnant women universally should be tested for HIV infection with patient notification as part of the routine battery of prenatal blood tests unless they decline the test (ie, opt-out approach) as permitted by local and state regulations. Refusal of testing should be documented. 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. Women at high risk for HIV infection should be retested during the third trimester, ideally before 36 weeks of gestation. Repeat testing in areas with a high HIV prevalence also should be considered.

If a woman’s HIV status is unknown during labor and delivery, she should be given a rapid HIV test unless she declines. A rapid HIV test is an HIV screening test with results available within hours. 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; however, antiretroviral prophylaxis should be initiated (with consent) without waiting for the results of the confirmatory test to reduce further the risk of possible transmission to the infant. According to CDC guidelines, if a mother’s HIV status is still unknown after delivery, the newborn should be tested using the rapid HIV test as soon as possible so that appropriate antiretroviral prophylaxis can be given, if necessary. Neonatal antiretroviral prophylaxis is most beneficial when begun no more than 12 hours after birth.

The individual providing health care for the newborn should be informed of the mother’s HIV serostatus to ensure appropriate care and testing. In some
states, physicians are required to obtain the mother’s written authorization before disclosing her HIV status to other health care providers who are not members of the woman’s health care team, such as her neonate’s health care provider. Health care providers who are not experienced in the care of pregnant, HIV-infected women may want to refer to providers who are knowledgeable in this area for specialty care.

Prenatal and intrapartum administration of zidovudine (ZDV) to pregnant women who are infected with HIV has been shown to reduce the rate of HIV transmission to newborns by 68% (from 25.5% to 8.3%). No significant short-term side effects were observed from ZDV use other than mild, self-limited anemia in the neonates. Neonates have been monitored for several years and no untoward effects of ZDV have been observed. Thus, it is recommended that ZDV chemoprophylaxis be included in the antiretroviral combination regimen.

Substantial advances have been made in the understanding of the pathogenesis of HIV-1 infection and in the treatment and monitoring of HIV-1 disease. Accordingly, these have resulted in changes in standard antiretroviral therapy for HIV-1 infected adults. More aggressive combination drug regimens that maximally suppress viral replication are now recommended. Pregnancy should not preclude the use of optimal therapy. Offering antiretroviral therapy to HIV-1 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 infected women and their neonates. Standard antiretroviral therapy should be discussed with and offered to pregnant women infected with HIV-1. Additionally, to prevent perinatal transmission, ZDV chemoprophylaxis should be incorporated into the antiretroviral regimen.

As noted, a substantial proportion of HIV cases occur as a result of exposure to the virus during labor and delivery. Consistent results indicating a significant relationship between route of delivery and vertical transmission of HIV have been published. This body of evidence indicates that cesarean delivery performed before the onset of labor and before the rupture of membranes (scheduled cesarean delivery) reduces the likelihood of vertical transmission of HIV (to approximately 2%) compared with either unscheduled cesarean delivery or vaginal delivery. This is true whether or not the patient is receiving ZDV. There are not enough data to address the question of how long after the onset of labor or rupture of the membranes the benefit is lost. It is clear that the rate of maternal morbidity is higher with cesarean delivery than with vaginal delivery. There is a gradient of benefit for the neonate to be gained from cesarean delivery, with
the greatest benefit to be gained from scheduled procedures in women at highest risk for vertical transmission with relatively high plasma viral loads. Women infected with HIV whose viral loads are greater than 1,000 copies/mL should be offered scheduled cesarean delivery at 38 weeks of gestation without an amniocentesis for lung maturity to further reduce the risk of vertical transmission of HIV beyond that achievable with ZDV prophylaxis alone. There are insufficient data to demonstrate a benefit of cesarean delivery performed after the onset of labor or rupture of membranes.

Women with very low plasma viral loads (less than 1,000 copies/mL) were found to 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/mL. 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.

Current recommendations for adults are that plasma viral load determinations should be done at baseline and every 3 months or following changes in therapy. Additionally, CD4+ T-lymphocyte counts should be followed during pregnancy. Because of the rapid advances in this area, refer to the CDC (www.cdc.gov) and the HIV/AIDS Treatment Information Service (www.hivatis.org) for treatment recommendations.

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 infected with HIV should be counseled not to breastfeed their babies, and they should not donate to milk banks.

Serial testing for HIV should be performed on neonates born to seropositive mothers. Infants born to HIV infected women should be tested by HIV DNA PCR during the first 48 hours of life. Because of possible contamination with maternal blood, umbilical cord blood should not be used for this determination. A second test should be performed at 1–2 months of age. A third test is recommended at 2–4 months of age. Any time an infant has test results that are positive for HIV, testing should be repeated on a second blood sample as soon as possible to confirm the diagnosis. An infant is considered infected if two separate samples are positive.

Early identification of infected neonates is essential for adequate medical management. Antiretroviral therapy is indicated for most children who are infected with HIV. Whenever possible, enrollment into clinical trials should be
encouraged. Therapeutic strategies are changing rapidly, so primary care physicians are encouraged to participate in the care of children infected with HIV in consultation with specialists. Several web sites provide information regarding diagnosis and therapy (www.hivatis.org, www.atis.org).

If a neonate is found to be HIV seropositive when the maternal serostatus is unknown, the health care provider for the child should ensure that this information and its significance are relayed to the mother. With her consent, and possibly written authorization as required by state law, it also should be communicated to her health care provider.

Because HIV (as well as other viral agents, such as HBV) may be present in blood, vaginal secretions, amniotic fluid, and other fluids, standard precautions (previously known as universal precautions) should be followed strictly during all vaginal and cesarean deliveries. Gloves should be used when handling the placenta or the neonate until blood and amniotic fluid have been removed from the neonate’s skin.

After delivery, HIV infected women can receive care in the postpartum care unit, with the use of standard precautions. Obstetric providers may need to refer women who are infected with HIV to another health care provider for continuing medical care after pregnancy. Few neonates 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. Prompt and careful removal of blood from the neonate’s skin is important. There is no need for other special precautions or for isolation of the neonate from an HIV-infected mother; rooming-in is acceptable. Gloves should be worn for contact with blood or blood-containing fluids and for procedures that entail exposure to blood. Gloving for all infant diaper changes is now considered part of standard precautions for hospital personnel.

**Human Papillomavirus**

Infections by human papillomaviruses (HPV) are common. Infection with certain types of HPVs (such as HPV 16, 18, 31, 33, and 35) cause genital warts as well as cervical and anogenital carcinomas. Approximately 90% of cervical HPV infections are transient. Persistent infection is more likely with oncogenic types. Cervical or vaginal HPV infections usually are asymptomatic. Studies using DNA diagnostic techniques detect the virus in up to 40% of sexually active young women. Pap tests are less useful for the diagnosis of subclinical cervical infection. Most genital HPV infections are sexually transmitted.
Human Parvovirus

Parvovirus B19 is the cause of erythema infectiosum. Most public attention has focused on parvovirus B19 infection (fifth disease) because of its ability to cause fetal death. 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. Fetal death or miscarriage occurs in less than 10% of infected pregnancies. Parvovirus B19 can infect fetal erythroid precursors and cause anemia, which can lead to nonimmune hydrops and death. Most reported maternal infections that have resulted in fetal death occur between the 10th and 20th week of pregnancy, and fetal death and spontaneous abortion usually have occurred 4–6 weeks after infection. Third-trimester maternal infections causing hydrops fetalis and death have been described. Congenital anomalies caused by par-
vovirus have been reported in small series and rare case reports. However, the determination that parvovirus is a teratogen remains unproven at this time.

Because of widespread asymptomatic parvovirus infection in both adults and children, all women are at some risk of exposure, particularly those with school-aged children. Pregnant women who learn that they have been in contact with children who were either in the incubation period of erythema infectiosum or in an aplastic crisis should be counseled about the potential risk to the fetus and should be offered serologic testing for parvovirus IgG and IgM. Fetal ultrasound examination will detect hydrops, but the frequency with which serial measurements should be performed is not known. In some cases, maternal serum alpha-fetoprotein levels may be elevated by the presence of fetal hydrops. A hydropic fetus can be treated by intrauterine transfusion when severe anemia has been documented by cordocentesis, although spontaneous resolution may occur.

In view of the high prevalence of parvovirus B19, the low risk of ill effects to the fetus, and the fact that avoidance of child care or teaching can reduce but not eliminate the risk of infection, pregnant women should not be excluded routinely from workplaces where B19 is present. Pregnant health care workers should be aware that otherwise healthy patients with erythema infectiosum are contagious during the week before the onset of rash and are not contagious 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 handwashing, standard precautions, and droplet precautions reduce transmission.

Respiratory Syncytial Virus

Respiratory syncytial virus (RSV) is a common cause of respiratory infection in infancy and the most common cause of hospitalization for lower respiratory illness in newborns. Preterm newborns and those with chronic lung disease of prematurity or congenital heart disease are at increased risk for severe RSV disease. Prophylaxis to prevent RSV in newborns at increased risk for severe disease, particularly those with chronic lung disease receiving medical management on a long-term basis, is available using RSV intravenous immune globulin or an intramuscular monoclonal antibody, palivizumab. Prophylaxis with palivizumab will decrease the risk of severe RSV disease and hospitalization by approximately 50%. Palivizumab is administered as 5 monthly intramuscular injections (15 mg/kg per dose) during RRV season, with the first
dose typically administered in November. The current AAP recommendations are as follows:

1. Respiratory syncytial virus prophylaxis should be considered for newborns and children younger than 24 months of age with chronic lung disease of prematurity who require ongoing medical management within 6 months before the RSV season, including supplemental oxygen, diuretics, corticosteroids, or bronchodilator therapy. Those with more severe chronic lung disease may benefit from prophylaxis for two RSV seasons.

2. Newborns without chronic lung disease of prematurity born at less than 32 weeks of gestation also may benefit from RSV prophylaxis. Newborns born at 28 weeks of gestation or younger may benefit from prophylaxis up to 12 months of age, whereas those born at 29–32 weeks of gestation may benefit from prophylaxis up to 6 months of age.

3. Given the large number of patients born between 32 weeks and 35 weeks of gestation and the cost of the drug, palivizumab use in this population should be reserved for newborns with at least two additional risk factors (see “Passive Immunization” in Chapter 8 for a list of risk factors).

4. Children who are 24 months of age or younger with hemodynamically significant cyanotic or acyanotic congenital heart disease will benefit from 5 monthly intramuscular injections of palivizumab (15 mg/kg per dose).

5. Respiratory syncytial virus may be transmitted in the hospital setting and may cause serious disease in higher-risk newborns. The major means to prevent RSV disease is strict observance of infection control practices, including identifying and cohorting RSV-infected patients.

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 handwashing should be emphasized in all settings, including the home, particularly during periods when contact with high risk children who have a respiratory infection can occur.

Rubella

Prevention and Management During Pregnancy

Between 2001 and 2004, there were fewer than 25 cases of rubella each year and a total of 4 cases of congenital rubella syndrome reported in the United
States. At the present time, most cases of rubella and congenital rubella syndrome in this country occur in persons who were born outside the United States.

Surveillance for susceptibility to rubella infection is essential in prenatal care. Each patient should be screened serologically at the first prenatal visit unless she is known to be immune by a previous serologic test. 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 antibody titers to establish whether infection has occurred. Specimens should be obtained as soon as possible after exposure, again 2 weeks later, and, if necessary, 4 weeks after exposure. Serum specimens from both acute and convalescent periods should be tested on the same day in the same laboratory; a negative test result in all samples indicates infection has not occurred, whereas a positive test result in the second sample, but not the first (seroconversion), indicates recent infection. Detection of rubella-specific IgM antibodies usually indicates recent infection, but false-positive results occur. Isolation of the virus from throat swabs establishes a diagnosis of acute rubella.

If rubella is diagnosed in a pregnant woman, the patient 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 while fetal infection may occur throughout pregnancy, defects are rare when infection occurs after the 20th week of gestation. The overall risk of defects during the third trimester is probably no greater than that associated with uncomplicated pregnancies. If a woman chooses not to terminate her pregnancy, administration of immune globulin as soon as possible after exposure may be considered. However, no data demonstrate that immune globulin prevents fetal infection. The absence of clinical signs in a woman who has received immune globulin does not guarantee that infection has been prevented.

The rubella vaccine is a live attenuated virus and is highly effective with few side effects in women of reproductive age who are susceptible to rubella. 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.

Rubella vaccination is not recommended during pregnancy. Following 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 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. However, 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**

Neonates who show signs of congenital rubella infection or who were born to women known to have had rubella during pregnancy, including neonates with few or no obvious clinical manifestations at birth, should be managed with contact isolation, preferably in a private room. Care of the neonate should be provided only by personnel known to be immune to rubella. Efforts should be made to obtain viral cultures from the neonate and to document the infection. Neonates with congenital rubella 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**

Women with varicella–zoster virus (VZV) infection (chickenpox) during pregnancy are no more likely to develop varicella pneumonia than are other adults, but varicella pneumonia is more severe during pregnancy. Therefore, pregnant women with VZV infection should be observed closely for pulmonary symptoms. Although no evidence indicates that maternal administration of VZV immune globulin (VZIG) after exposure reduces the rare occurrence of congenital varicella syndrome, postexposure prophylaxis with VZIG may prevent or ameliorate the illness in nonimmune pregnant women, as it does in other adults. However, VZIG is no longer available, but VariZIG has become available under an investigational new drug application submitted to the U.S. Food and Drug Administration. It is a purified human immune globulin preparation made from plasma containing high levels of antivaricella antibodies and is administered intramuscularly. Most women (70–90%) with a negative or uncertain history of varicella are immune. A positive history of varicella is highly predictive of serologic immunity (greater than 95%), and it is unnecessary to perform serologic testing in such women. A pregnant woman who has been exposed to VZV (through intimate or household contact) and who has no history of prior infection should be tested for immunity. If she is not immune,
administration of VariZIG should be considered within 96 hours of exposure. If chickenpox is diagnosed during pregnancy, antiviral therapy with acyclovir is another consideration.

Fetal infection after maternal varicella during the first half of pregnancy occasionally results in varicella embryopathy, which may include limb atrophy and scarring of the skin of the extremities as well as central nervous system and ocular manifestations. The incidence of congenital varicella syndrome among infants born to mothers with varicella is approximately 2% when infection occurs before 20 weeks of gestation.

Varicella infection can be fatal for an infant if the mother develops varicella within 5 days before to 2 days after delivery. All infants with this type of exposure should receive VariZIG.

Extremely low birth weight neonates (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, because of the poor transfer of antibodies across the placenta early in pregnancy. Hospitalized, preterm neonates 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 VariZIG.

Hospitalized women with VZV infection must be kept under airborne and contact precautions. Hospitalized neonates born to women with active VZV infection should be isolated until 21 days of age (if IVIG is not given) or until 28 days of age (if IVIG is given). Hospitalized neonates who are exposed postnatally should be isolated from 8 days to 21 days after onset of the rash in the index case. Neonates with VZV infection should be isolated in a private room, and airborne and contact precautions should be maintained for the duration of the illness. Neonates with congenital VZV infection acquired earlier in gestation do not require special precautions or isolation unless vesicular lesions are present. Mothers with zoster should not be in the nursery, and both mother and baby should be isolated.

Live-attenuated VZV vaccine, licensed in 1995, routinely is recommended for susceptible children, beginning at 12 months of age, and adolescents. Susceptible adults, particularly those in high-risk categories, also should be offered immunization. For adolescents and adults, the primary vaccination series consists of two doses, administered subcutaneously, 4–8 weeks apart.

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. Women who do not have varicella immunity should
receive the first dose of VZV vaccine in the postpartum period before hospital or birth center discharge. Surveillance data to date on fetal outcomes after inadvertent vaccine exposures, however, have not found any cases of fetal varicella syndrome. A pregnant household member is not a contraindication to vaccination of a child.

**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 (DEET) as a preventative measure.

**Bacterial Infections**

**Group B Streptococci**

The proportion of pregnant women colonized with group B streptococci (GBS) ranges from approximately 10–30%, but colonization may be transient. Although antepartum rectal or genital colonization usually is asymptomatic, GBS may account for significant peripartum infection (eg, endometritis, amnionitis, and urinary tract infections).

Before adoption of national prevention guidelines, an estimated 7,600 episodes of GBS sepsis occurred annually in newborns (a rate of 1.8 per 1,000 live births) in the United States, with more than 300 deaths annually among neonates younger than 90 days. Invasive GBS disease in the newborn primarily is characterized by sepsis, pneumonia, and meningitis. Vertical transmission of GBS during labor or delivery may result in invasive infection in the newborn during the first week of life. Known as early-onset GBS infection, this now constitutes approximately 50% of GBS disease in newborns. Late-onset GBS disease in the newborn also may occur as a result of vertical transmission or of
nosocomial or community-acquired infection. In recent years, there have been reports of invasive GBS disease occurring beyond 3 months of age (late, late-onset disease), usually in very low birth weight preterm neonates.

The risk of early-onset disease is increased by preterm birth (birth at less than 37 weeks of gestation), a prolonged interval (18 hours or more) between rupture of amniotic membranes and delivery, and intraamniotic infection (maternal temperature at or above 38°C [100.4°F]). Other factors associated with a higher risk of early-onset disease include GBS bacteriuria during pregnancy and previous delivery of a neonate with GBS disease. However, up to 40% of cases of early-onset disease occur in neonates with no risk factors.

In 1996, the CDC, ACOG, and AAP recommended the first national GBS prevention guidelines. In 2002, these were revised to recommend the culture-based prevention strategy only (Fig. 9-1). The culture-based approach requires obtaining a single swab from the lower vagina (introitus) and perianal area, placing the swab in transport media, and culturing in selective broth media. Use of prenatal cultures remote from term to identify women who are colonized with GBS at delivery may not be accurate, and the CDC, ACOG, and AAP recommend obtaining rectovaginal cultures at 35–37 weeks of gestation. All women with positive culture of GBS should be treated with intrapartum antibiotic prophylaxis. If the culture status is unknown when a patient presents with labor or premature rupture of membranes (PROM), then prophylaxis should be given if any of the following conditions exist:

- Women with preterm labor (less than 37 weeks of gestation)
- Preterm PROM (less than 37 weeks of gestation)
- Rupture of membranes 18 hours or longer
- Maternal fever during labor (at or above 38°C [100.4°F]).

Women with GBS bacteriuria during their current pregnancy or women who previously gave birth to an infant with early-onset GBS disease are candidates for intrapartum antibiotic prophylaxis. When culture results are not available, intrapartum prophylaxis should be offered only on the basis of the presence of intrapartum risk factors for early-onset GBS disease.

Other key points provided in the 2002 guidelines include changes in recommended antibiotics for patients who cannot take penicillin. Recommended antibiotics for intrapartum prophylaxis are given in the table showing recommended regimens (Table 9–3). As described previously, emerging resistance to erythromycin and clindamycin have shaped these recommendations. A key change for obstetricians is the need to get a detailed history from colonized
women who report penicillin allergy to determine whether they are at high risk for anaphylaxis. Among penicillin-allergic patients, women at high risk for anaphylaxis are defined as those who have experienced immediate hypersensitivity to penicillin, including a history of penicillin-related anaphylaxis, and those with other conditions, such as asthma or treatment with β-adrenergic blocking agents, that would make anaphylaxis more dangerous or difficult to treat.

Women undergoing a planned cesarean delivery in the absence of labor or membrane rupture do not require GBS prophylaxis even if their rectovaginal culture is positive. This recommendation is based on evidence that the risk of neonatal early-onset disease was sufficiently low in this circumstance and that

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**Fig. 9–1.** Indications for intrapartum antibiotic prophylaxis to prevent perinatal group B streptococcal disease under a universal prenatal screening strategy based on combined vaginal and rectal cultures collected at 35–37 weeks of gestation from all pregnant women. Abbreviation: GBS, group B streptococci. *If onset of labor or rupture of amniotic membranes occurs earlier than 37 weeks of gestation and there is a significant risk for preterm delivery (as assessed by the clinician), follow the suggested algorithm for GBS prophylaxis as indicated by the Centers for Disease Control and Prevention. †If amnionitis is suspected, broad-spectrum antibiotic therapy that includes an agent known to be active against GBS should replace GBS prophylaxis. (Schrag S, Gorwitz R, Fultz-Butts K, Schuchat A. Prevention of perinatal group B streptococcal disease. Revised guidelines from CDC. MMWR Recomm Rep 2002;51(RR-11):1–22.

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Vaginal and rectal GBS screening cultures at 35–37 weeks of gestation for all pregnant women (unless patient had GBS bacteriuria during the current pregnancy or a previous infant with invasive GBS disease)
the potential risks associated with intrapartum antibiotics outweighed the benefits. The guidelines also propose an algorithm for GBS testing and prophylaxis for women with preterm labor or PROM. (Please refer to the CDC web

**Table 9–3. Recommended Regimens for Intrapartum Antimicrobial Prophylaxis for Perinatal Group B Streptococcal Disease Prevention**

<table>
<thead>
<tr>
<th>Regimens</th>
<th>Antimicrobial</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recommended</td>
<td>Penicillin G, 5 million units IV initial dose, then 2.5 million units IV every 4 hours until delivery</td>
</tr>
<tr>
<td>Alternative</td>
<td>Ampicillin, 2 g IV initial dose, then 1 g IV every 4 hours until delivery</td>
</tr>
<tr>
<td>If penicillin allergic</td>
<td></td>
</tr>
<tr>
<td>• Patients not at high risk</td>
<td>Cefazolin, 2 g IV initial dose, then 1 g IV every 8 hours until delivery</td>
</tr>
<tr>
<td>for anaphylaxis</td>
<td></td>
</tr>
<tr>
<td>• Patients at high risk for</td>
<td>Clindamycin, 900 mg IV every 8 hours until delivery</td>
</tr>
<tr>
<td>anaphylaxis†</td>
<td>or</td>
</tr>
<tr>
<td>—GBS susceptible to clindamycin and erythromycin§</td>
<td>Erythromycin, 500 mg IV every 6 hours until delivery</td>
</tr>
<tr>
<td>—GBS resistant to clindamycin or erythromycin or susceptibility unknown</td>
<td>Vancomycin, 1 g IV every 12 hours until delivery</td>
</tr>
</tbody>
</table>

Abbreviations: GBS, group B streptococci; IV, intravenously

* Broader-spectrum agents, including an agent active against GBS, may be necessary for treatment of chorioamnionitis.

† History of penicillin allergy should be assessed to determine whether a high risk for anaphylaxis is present. Penicillin-allergic patients at high risk for anaphylaxis are those who have experienced immediate hypersensitivity to penicillin including a history of penicillin-related anaphylaxis; other high-risk patients are those with asthma or other diseases that would make anaphylaxis more dangerous or difficult to treat, such as persons being treated with beta-adrenergic–blocking agents.

‡ If laboratory facilities are adequate, clindamycin and erythromycin susceptibility testing should be performed on prenatal GBS isolates from penicillin-allergic women at high risk for anaphylaxis.

§ Resistance to erythromycin often but not always is associated with clindamycin resistance. If a strain is resistant to erythromycin but appears susceptible to clindamycin, it may still have inducible resistance to clindamycin.

|| Cefazolin is preferred over vancomycin for women with a history of penicillin allergy other than immediate hypersensitivity reactions, and pharmacologic data suggest it achieves effective intraamniotic concentrations. Vancomycin should be reserved for penicillin-allergic women at high risk for anaphylaxis.

Listeriosis

The major cause of epidemic and sporadic listeriosis infection is food-borne transmission. Incriminated foods include unpasteurized milk, cheese, and other dairy products; undercooked poultry; and prepared meats, such as hot dogs, deli meats, and pâté. 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 hot dogs or luncheon meats unless they are steaming hot and to avoid unpasteurized soft cheeses.

*Listeria monocytogenes* can be recovered on blood agar media from cultures of usually sterile body sites (e.g., blood, cerebrospinal fluid). Special techniques may be needed to recover *L monocytogenes* from sites with mixed flora (e.g., 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 highly sensitive to ampicillin, but there may be a synergistic benefit from ampicillin plus gentamicin. Signs of listeriosis in the newborn vary widely and often are nonspecific. The clinical picture may be similar to that of GBS infection with early- and late-onset syndromes. Therapy with intravenous ampicillin and an aminoglycoside is recommended for neonatal infections. (Resources from the CDC include an information sheet at: www.fsis.usda.gov/fact_sheets/Listeriosis_and_pregnancy_what_is_your_risk/index.asp.)

Pertussis

Pertussis, commonly known as whooping cough, is a respiratory disease commonly causing paroxysms of cough. Complications in adults include pneumonia, sleep disturbance, rib fracture, and incontinence. In the first six months of life, symptoms are more severe, and infant complications include pneumonia, seizures, encephalopathy, and death.
Infants younger than 6 months of age frequently require hospitalization for supportive care and to manage complications. Antimicrobial agents given during the catarrhal stage may lessen the severity of the disease. Azithromycin is the drug of choice for treatment of pertussis in infants younger than 1 month of age. Although there is a risk of developing infantile hypertrophic pyloric stenosis associated with erythromycin use, that risk is outweighed by the risk of severe pertussis and life-threatening complications from the disease in infants younger than 1 month of age. All infants younger than 1 month of age should be monitored for infantile hypertrophic pyloric stenosis after treatment with any macrolide.

In addition to standard precautions, droplet precautions are recommended for 5 days after initiating effective therapy, or if appropriate antimicrobial therapy is not given in older individuals, until 3 weeks after the onset of paroxysms.

Universal immunization is recommended to prevent transmission of pertussis. The diphtheria and tetanus toxoids and acellular pertussis (DTaP) vaccine is given to children at 2, 4, 6, and 12–18 months of age and 4–6 years of age. The adolescent and adult tetanus and reduced diphtheria toxoids and acellular pertussis (Tdap) vaccines are approved as a booster dose for those who were vaccinated for pertussis in childhood. The Tdap vaccine is offered routinely to adolescents and adults between the ages of 11–64 years, including immediate postpartum women who have not previously received Tdap. The Tdap vaccine may be offered if a tetanus and diphtheria vaccine was given at age 5 years or older.

The Tdap vaccine is not contraindicated in pregnancy. It can be given to pregnant women in place of a tetanus and diphtheria vaccine and should be given if there is an outbreak of pertussis. Because there is little data on the safety of Tdap in pregnancy, health care providers are encouraged to report Tdap vaccination during pregnancy, regardless of trimester (sanofi pasteur [800] 822-2463).

**Gonorrhea**

*Management in Pregnant Women*

Gonorrhea occurs most commonly in individuals aged 15–29 years, and the highest reported incidence occurs in young men aged 20–24 years. In females, the highest rates are in adolescents aged 15–19 years. Risk factors include lower socioeconomic status, single status, early onset of sexual activity, multiple sexual partners, and substance use.

Pregnant women with risk factors for or symptoms of gonorrhea should be tested for *Neisseria gonorrhoeae* at an early prenatal visit. A repeat test should be obtained in the third trimester for women at increased risk for gonorrhea.
and other STDs. Polymerase chain reaction tests for detecting *N gonorrhoeae* have generally replaced cultures.

Because of the prevalence of penicillin-resistant *N gonorrhoeae*, an extended spectrum (third-generation) cephalosporin (ceftriaxone 125 mg intramuscularly or cefixime 400 mg orally) is recommended for treatment. Tetracyclines and fluoroquinolones are contraindicated in pregnancy. Women who cannot tolerate a cephalosporin should be administered a single 2-g dose of spectinomycin intramuscularly. Because concurrent infection with *Chlamydia trachomatis* is common, patients with gonococcal infections also should be treated for chlamydial infection (unless it has been ruled out) and should be evaluated for coinfection with syphilis, HIV, and other STDs. Either erythromycin or amoxicillin is recommended for the treatment of presumptive or diagnosed *C trachomatis* infection during pregnancy. Azithromycin in a single dose (1 g) is a recommended regimen for the treatment of *C trachomatis* infection in nonpregnant individuals, but because well-controlled, adequate studies in pregnant women have not been performed, it is an alternate regimen for pregnant women. A test-of-cure is not recommended routinely in persons with uncomplicated gonorrhea, provided that symptoms resolve. All cases of gonorrhea must be reported to public health officials.

**Neonatal Clinical Manifestations**

Infection in the newborn usually involves the eyes. Antimicrobial prophylaxis soon after delivery is recommended for all neonates. If a woman with ruptured membranes has known gonorrheal infection, the newborn must be treated immediately. Applications of a 1 cm ribbon of sterile ophthalmic ointment containing tetracycline (1%) or erythromycin (0.5%) in each lower conjunctival sac are considered equally effective in preventing gonococcal ophthalmia. An occasional case of gonococcal ophthalmia or disseminated gonococcal infection can occur in neonates born to women with gonococcal disease. Neonates born to women with active gonorrhea should receive a single dose of ceftriaxone, 125 mg, intravenously or intramuscularly; for low birth weight neonates, the dose is 25–50 mg/kg of body weight. Cefotaxime in a single dose (100 mg/kg given intravenously or intramuscularly) is an alternative. 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. Neonates with clinical gonococcal disease should be hospitalized, and
cultures of blood, cerebrospinal fluid, eye discharge, or other sites of infection should be obtained. For neonates with positive cultures (ie, disseminated infection), the recommended antimicrobial therapy is ceftriaxone (25–50 mg/kg per day, intravenously or intramuscularly, not to exceed 125 mg given in a single daily dose) or cefotaxime (50–100 mg/kg per day, divided into two doses given every 12 hours). Cefotaxime is preferred for neonates with hyperbilirubinemia. The duration of antibiotic treatment depends on the site of infection; a single dose is adequate for conjunctivitis, whereas 7 days is recommended for disseminated infection; 10–14 days is recommended for meningitis. Infected neonates should be managed with standard precautions.

**Chlamydia**

*Chlamydia trachomatis* has been detected in the cervix of 2–13% of pregnant women and generally is found in 5% or more of women in all populations. Prevalence is highest (about 37%) in sexually active adolescent females. Unrecognized infection is common. Important risk factors for chlamydial infection include unmarried status, recent change in sexual partner, multiple concurrent partners, age younger than 25 years, inner-city residence, history or presence of other STDs, and little or no prenatal care. Pregnant women should be screened for chlamydia infection during the first prenatal care visit, and women at increased risk (women aged 25 years or younger or women who have a new, or more than one, sexual partner) may be tested again in the third trimester.

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; approximately 50% of neonates born to infected women become colonized with *C trachomatis*. Purulent conjunctivitis develops a few days to several weeks after delivery in 25–50% of neonates who acquire *C trachomatis* infection, and neonatal pneumonia occurs in 5–20%. The diagnosis of *C trachomatis* infection is based on a cell culture, direct fluorescent antibody staining, enzyme immunoassay, DNA probe, or 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. Limited data on azithromycin in pregnant women suggests that it is safe and efficacious. Recommended regimens for treating *C trachomatis* infection in pregnant women include 1 g azithromycin in a single dose or amoxicillin 500 mg, orally, three times daily for 7 days. Alternative regimens in pregnant women include erythromycin base, 250 mg orally, four times daily for 14 days; erythromycin ethylsuccinate, 800 mg orally, four times daily for 7 days; erythromycin ethylsuccinate, 400 mg orally, four times daily for 14 days; or erythromycin base, 500 mg orally, 4 times daily for 14 days. Note that erythromycin estolate is contraindicated during pregnancy because of drug-related hepatotoxicity. Repeat testing, preferably by culture, should be done 3 weeks after completion of treatment regimens to confirm successful treatment.

Neonates born to women known to have untreated chlamydial infection should be evaluated and monitored for development of disease. Chlamydial infections in the neonate generally are mild and responsive to antimicrobial therapy. Prophylactic cesarean delivery is not warranted. Routine instillation of topical erythromycin or tetracycline into the conjunctival sac of the neonate shortly after birth has not been proved to prevent neonatal conjunctivitis or other infections caused by *C trachomatis*. Neonates with chlamydial conjunctivitis or chlamydial pneumonia should be treated with oral erythromycin for 14 days. If hospitalized, patients should be managed with standard precautions. Recent evidence shows an association between infantile hypertrophic pyloric stenosis and orally administered erythromycin in infants younger than 6 weeks of age.

**Tuberculosis**

**Screening**

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. All pregnant women who are at high risk for tuberculosis should be screened with a Mantoux test with purified protein derivative (PPD) when they begin receiving prenatal care. High-risk factors for tuberculosis include:

- Human immunodeficiency virus infection
- Close contact with individuals known or suspected to have tuberculosis
- Medical risk factors known to increase risk of disease (eg, lymphoma, diabetes mellitus, chronic renal failure, immunosuppression)
- Birth in a country with a high prevalence of tuberculosis
• Medically underserved status
• Low socioeconomic status
• Alcohol addiction
• Intravenous drug use
• Residence in a long-term care facility (e.g., correctional institutions, mental institutions, nursing homes and facilities)
• Health care professionals working in facilities where the risk of exposure to *Mycobacterium tuberculosis* is increased

**Definitions and Diagnosis**

Latent tuberculosis infection is defined by a positive tuberculin skin test 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. Tuberculosis disease 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.

**Management During Pregnancy**

Treatment regimens for tuberculosis are based on the presence or absence of active disease, primarily determined by chest X-ray findings and sputum culture and, in the absence of active disease, the likelihood of progressing to disease. The risk of progression to active 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 but with no evidence of active disease is isoniazid (300 mg per day) starting after the first trimester and continuing for 9 months. For women who are infected with HIV, the duration of isoniazid therapy is 12 months.

Pregnant women should be skin tested if they have a specific risk factor for latent tuberculosis infection or active tuberculosis. When the skin test is positive, the time of conversion usually is not known. If a chest X-ray is normal, some experts prefer to delay treatment until after delivery because pregnancy
itself does not increase the risk for 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. All pregnant women receiving isoniazid also should take pyridoxine.

If a pregnant woman is diagnosed with active disease (by positive cultures or by compatible clinical or X-ray findings), prompt, multidrug therapy is recommended to protect both the woman and the fetus. Isoniazid and rifampin, supplemented by ethambutol if isoniazid drug resistance is suspected, currently are recommended drugs. Pyrazinamide frequently is used in a three- or four-drug regimen, but safety data in pregnancy have not been published. Therapy is continued for at least 6 months for drug-susceptible disease.

**Neonatal Management**

Because tuberculosis usually is transmitted by inhalation of droplet nuclei produced by an adult or adolescent with infectious primary tuberculosis, acquisition of *M. tuberculosis* by newborns generally occurs only after delivery. Infection can occur before birth as a result of hematogenous dissemination, which seeds the placenta; as a result of infected amniotic fluid in utero; or at the time of delivery as a result of fetal 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 neonate 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 (or contact) and the neonate should be minimized. Differing circumstances and resulting recommendations are listed as follows:

- **The mother (or household contact) has a negative X-ray result**—If the mother is asymptomatic, no separation of the mother and the neonate is required. The mother usually is a candidate for treatment of latent tuberculosis infection. The newborn needs no special evaluation or therapy. Because the positive tuberculin test result could be a marker of an unrecognized case of contagious tuberculosis within the household, other household members should have Mantoux tests with PPD and further evaluation.

- **The mother (or household contact) has an abnormal chest X-ray result**—If the X-ray result is abnormal, the mother and the neonate
should be separated until the mother has been evaluated and, if active tuberculosis disease is found, until she is receiving antituberculosis therapy and sputum AFB smears are negative. Other household members should have Mantoux tests with PPD and further evaluation.

• The mother (or household contact) has an abnormal chest roentgenogram but no evidence of active disease—If the mother’s chest roentgenogram is abnormal but the history, physical examination, sputum smear, and roentgenogram indicate no evidence of active disease, the neonate 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, active tuberculosis, if untreated, and should receive appropriate therapy if not treated previously. She and her neonate should receive follow-up care. Other household members should have Mantoux tests with PPD and further evaluation.

• The mother (or household contact) has clinical or radiographic evidence of active, possibly contagious tuberculosis—The mother (or household contact) 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, chest roentgenogram, and physical examination. The neonate should be evaluated for congenital tuberculosis and should be tested for HIV infection. The mother and the neonate should be separated until both are receiving appropriate therapy and the mother is deemed to be noncontagious. If the infant is receiving isoniazid, separation is not necessary. Other household members should have skin testing and further evaluation.

If congenital tuberculosis is excluded, isoniazid is given until the neonate is 3–4 months of age, at which time the Mantoux test with PPD should be repeated. If the skin test result is positive, the child should be reassessed for tuberculosis. If disease is not present, isoniazid should be continued for a total of at least 9 months for skin conversion; 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 neonate should be evaluated at monthly intervals during treatment.

If the mother (or household contact) has disease caused by multiple-drug-resistant *M tuberculosis* or has poor adherence to treatment and directly observed therapy is not possible, the neonate should be separated from the ill family member and bacille Calmette–Guérin (BCG) vaccination may be con-
considered for the neonate. Because the response to the vaccine in neonates may be delayed and inadequate for prevention of tuberculosis, directly observed therapy of the affected household contact is preferred.

Untoward effects of isoniazid therapy in newborns are rare. The incidence of hepatitis during isoniazid therapy is so low in otherwise healthy neonates that routine determination of serum aminotransferase concentrations is not recommended. The maternal use of isoniazid is considered to be compatible with breastfeeding. Breastfeeding is considered safe during maternal antituberculosis therapy as long as the neonate is not concurrently taking oral antituberculosis therapy. (If both the mother and the neonate are taking antituberculosis therapy, excessive drug concentrations may occur in the neonate.) Breastfed neonates of women taking isoniazid therapy should receive a multivitamin supplement, including pyridoxine. Drugs in breast milk should not be considered effective treatment or prophylaxis of the neonate.

Bacille Calmette–Guérin vaccine is a live vaccine prepared from attenuated strains of *Mycobacterium bovis*. Although BCG vaccination is recommended by the Expanded Programme on Immunization of the World Health Organization and is widely used throughout the world, BCG vaccination use in the United States is limited to selected circumstances. Bacille Calmette–Guérin vaccine should be considered only for uninfected neonates and children who are at high risk of intimate and prolonged exposure to patients with persistently infectious pulmonary tuberculosis, who cannot be removed from the source of exposure, and who cannot be placed on long-term preventive therapy. The vaccine also should be considered for neonates who are continuously exposed to patients infected with *M tuberculosis* that is resistant to isoniazid and rifampin and who cannot be removed from the source of exposure.

**Spirochetal Infections**

**Syphilis**

Syphilis persists in the United States; rates of infection are highest in urban areas and the rural South. All pregnant women should be serologically screened for syphilis as early as possible in pregnancy and again at delivery (as well as after exposure to an infected partner). Because false-negative serologic tests results may occur in early primary infection and infection after the first prenatal visit is possible, patients who are considered to be at high risk for syphilis or who are from areas of high prevalence should be retested at the beginning of the third trimester.
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.

Congenital syphilis most often is acquired through hematogenous transplacental infection of the fetus, although direct contact of the neonate 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.

**Treatment for Pregnant Women**

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 is suboptimal because poor transplacental passage or poor patient compliance may result in failure to cure infection in the fetus.

Women with syphilis should be queried about 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.

**Evaluation of Newborns for Congenital Infection**

No newborn should leave any hospital without determination of the syphilis serologic status of his or her mother. A neonate 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 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)
• 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

Neonates born to women with any of the preceding conditions should be evaluated for syphilis. This evaluation should include the following components:

• Physical examination
• Quantitative nontreponemal and a treponemal serologic test for syphilis on the infant’s serum sample
• Cerebrospinal fluid evaluation, including a VDRL test, cell count, and protein evaluation
• Long-bone X-ray (unless the diagnosis has been otherwise established)
• Complete blood cell and platelet counts
• Other clinically indicated tests (eg, chest X-ray)
• Pathologic examination of the placenta or umbilical cord, if available, also is recommended

The VDRL or RPR test commonly is used to evaluate newborns for congenital infection with *Treponema pallidum*. For testing, serum from the neonate is preferred to umbilical cord blood because the latter can produce false-positive and false-negative results.

A diagnosis of congenital syphilis is frequently difficult to establish because clinical evidence of infection may not be apparent at birth and serologic test results may be equivocal or difficult to interpret. A reactive serologic test result for syphilis (eg, VDRL, RPR, or fluorescent treponemal antibody absorption test) on neonatal blood does not necessarily indicate that the neonate is infected. If the reaction is caused only by passively transferred maternal antibody, the neonate’s VDRL titer usually is lower than the mother’s and usually reverts to negative in 4–6 months. A positive fluorescent treponemal antibody absorption test result caused by passively transferred antibody may take up to 1 year to become negative. A persistently reactive serologic test result for syphilis suggests infection, and an increasing titer is almost diagnostic.

Clinical symptoms of early congenital syphilis frequently are absent or non-specific. Long-bone X-rays may be useful in establishing a diagnosis in neonates with suspected congenital syphilis.
Moist, open syphilitic lesions are infectious. Standard precautions are sufficient for neonates with suspected or proven congenital syphilis. Health care personnel and parents should wear gloves when handling the neonate until antibiotic therapy has been administered for at least 24 hours. Individuals in intimate contact with the neonate before isolation precautions and treatment were instituted should be examined for the presence of lesions 2–3 weeks later and tested serologically for infection.

Parenteral penicillin G remains the preferred therapy for syphilis at any stage. Treatment of neonates with congenital syphilis is summarized in Table 9–4. Cases of syphilis must be reported to the public health authorities.

**Table 9–4. Recommended Treatment of Neonates (<4 Weeks of Age) With Proven or Possible Congenital Syphilis**

<table>
<thead>
<tr>
<th>Clinical Status</th>
<th>Evaluation</th>
<th>Antimicrobial Therapy*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proven or highly probable disease†</td>
<td>CSF analysis for VDRL, cell count, and protein</td>
<td>Aqueous crystalline penicillin G, 100,000–150,000 units/kg per day, administered as 50,000 unit/kg per dose, IV, every 12 h during the first 7 days of life and every 8 h thereafter for a total of 10 days or Penicillin G procaine, ‡ 50,000 units/kg per day, IM, in a single dose for 10 days</td>
</tr>
<tr>
<td>Normal physical examination and serum quantitative nontreponemal titer the same or less than fourfold the maternal titer:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(a)(i) Mother was not treated or inadequately treated or has no documented treatment; (ii) mother was treated with erythromycin or other nonpenicillin regimen; (iii) mother received treatment ≤4 weeks before delivery</td>
<td>CSF analysis for VDRL, cell count, and protein CBC and platelet count Long-bone radiography</td>
<td>Aqueous crystalline penicillin G, IV, for 10 days§ or Penicillin G procaine, ‡ 50,000 units/kg, IM, in a single dose for 10 days§ or Penicillin G benzathine, ‡ 50,000 units/kg, IM, in a single dose§</td>
</tr>
</tbody>
</table>

(continued)
Lyme Disease

Lyme disease is caused by a spirochete (*Borrelia burgdorferi*) transmitted by the bite of a deer tick. Early stages of the disease are characterized by a distinctive “bull’s-eye” skin lesion (erythema migrans) that occurs in 60–80% of patients and nonspecific, flulike symptoms. Untreated disease can result in neurologic or cardiac manifestations within 4–6 weeks after the onset of early signs and symptoms. A late manifestation of Lyme disease is arthritis, usually intermittent inflammatory arthritis of a large joint. Untreated patients can develop joint involvement ranging from mild to moderate arthralgia to chronic destructive joint disease. No definitive early diagnostic tests, including serology, are com-

<table>
<thead>
<tr>
<th>Clinical Status</th>
<th>Evaluation</th>
<th>Antimicrobial Therapy*</th>
</tr>
</thead>
<tbody>
<tr>
<td>(b)(i) Adequate maternal therapy given ≥4 wk before delivery; (ii) mother has no evidence of reinfection or relapse</td>
<td>None</td>
<td>Clinical, serologic follow-up, and penicillin G benzathine, 50,000 units/kg, IM, in a single dose(^{11})</td>
</tr>
<tr>
<td>(c) Adequate therapy before pregnancy and mother’s nontreponemal serologic titer remained low and stable during pregnancy and at delivery</td>
<td>None</td>
<td>None(^{*})</td>
</tr>
</tbody>
</table>

Abbreviations: CBC, complete blood count; CSF, cerebrospinal fluid; IM, intramuscularly; IV, intravenously; VDRL, Venereal Disease Research Laboratories

*If more than 1 day of therapy is missed, the entire course should be restarted.

\(^1\)Abnormal physical examination, serum quantitative nontreponemal titer that is fourfold greater than the mother’s titer, or positive result of dark-field or fluorescent antibody test of body fluid(s)

\(^*\)Penicillin G benzathine and penicillin G procaine are approved for IM administration only.

\(^*\)A complete evaluation (CSF analysis, bone radiography, CBC) is not necessary if 10 days of parenteral therapy is administered but may be useful to support a diagnosis of congenital syphilis. If a single dose of penicillin G benzathine is used, then the infant must be evaluated fully, the 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 CSF analysis is uninterpretable, the 10-day course of penicillin is required.

\(^{11}\)Some experts would not treat the infant but would provide close serologic follow-up.

\(^*\)Some experts would treat with penicillin G benzathine, 50,000 units/kg, as a single IM injection if follow-up is uncertain.

commercially available. 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 skin lesion, and nonspecific, flulike 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.)

Congenital malaria is rare. Signs and symptoms resemble those of neonatal sepsis. Definitive diagnosis (of the mother and the neonate) 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*. Approximately 15% of women in the United States have antibodies to this organism. Infection is acquired from eating infected raw or poorly cooked meat and from exposure to oocysts in the stools of infected members of the cat family. Infected women generally are asymptomatic.

Although congenital infection is more common after maternal infection in the third trimester, the sequelae from first-trimester fetal infection are more severe. Signs of congenital infection at birth may include chorioretinitis, hydrocephaly, microcephaly, and intracranial calcifications; however, most affected neonates are asymptomatic. Neonates of women who are infected with both HIV and *T. gondii* should be evaluated for congenital toxoplasmosis.

The diagnosis of maternal infection is based on serologic test results. Routine 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. Demonstration of seroconversion is the best method of confirming the diagnosis of acute infection. A significant increase in IgG titer in paired samples taken 2–4 weeks apart (tested simultaneously) or the presence of *T. gondii*-specific IgM most often indicates recent or current infection.

Although the presence of antitoxoplasma IgM antibodies is suggestive of acute infection, such IgM antibodies may persist for several months. In addition, false-positive test results are common with commercially available kits. Before making treatment recommendations, confirmation of increased antitoxoplasma IgM antibodies should be obtained in a reference laboratory.
A definitive diagnosis of congenital toxoplasmosis can be made prenatally by: 1) detecting the parasite in amniotic fluid by PCR, or 2) documenting antitoxoplasma IgM and IgA antibodies in fetal blood. If the diagnosis is suspected (but unconfirmed) at the time of birth, ophthalmologic, auditory, and neurologic examinations should be performed. Congenital toxoplasmosis can be diagnosed serologically by the detection of antitoxoplasma-specific IgM or IgA antibodies soon after birth or by the persistence of antitoxoplasma IgG beyond 12 months of age.

Therapy of infected mothers with spiramycin (available through the U.S. Food and Drug Administration) may reduce the incidence of fetal infection but will not prevent sequelae in the fetus if congenital infection does occur. The combination of pyrimethamine and sulfadiazine should be considered if the mother acquires infection during the third trimester, although the efficacy of such therapy has not been proved. In one study, routine neonatal screening for toxoplasmosis with early treatment of infected neonates decreased the frequency of long-term sequelae. However, in the United States, routine screening during pregnancy currently is not recommended, except in women infected with HIV.

For neonates with both symptomatic and asymptomatic congenital toxoplasmosis, pyrimethamine and sulfadiazine (supplemented with folinic acid) are recommended. The duration of therapy is prolonged (1 year) and has been shown to improve outcome. Neonates with congenital toxoplasmosis should be managed in consultation with infectious disease specialists. (Please refer to the CDC web site for further professional and patient information: www.cdc.gov/ncidod/dpd/parasites/toxoplasmosis.)

**Resources**


Targeted tuberculin testing and treatment of latent tuberculosis infection. The official statement of the American Thoracic Society was adopted by the ATS Board of Directors, July 1999. This is a Joint Statement of the American Thoracic Society (ATS) and the Centers for Disease Control and Prevention (CDC). This statement was endorsed by the Council of the Infectious Diseases Society of America. (ISDA), September 1999, and the sections of this statement. Am J Respir Crit Care Med 2000;161:S221–47.

Guidelines for Perinatal Care was developed through the cooperative efforts of the American Academy of Pediatrics (AAP) Committee on Fetus and Newborn and the American College of Obstetricians and Gynecologists (ACOG) Committee on Obstetric Practice. The guidelines should not be viewed as a body of rigid rules. They are general and intended to be adapted to many different situations, taking into account the needs and resources particular to the locality, the institution, or the type of practice. Variations and innovations that improve the quality of patient care are to be encouraged rather than restricted. The purpose of these guidelines will be well served if they provide a firm basis on which local norms may be built.

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