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Infectious Disease

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Infectious diseases remain a leading cause of maternal and neonatal mortality during pregnancy, labor, and the puerperium.[1] In the United States alone, despite a fivefold reduction in the last 50 years, the pregnancy-related maternal morality rate remains at approximately 9 per 100,000 live births,[2,3] with infections still accounting for 3% to 10%.[4]

Although profound changes are observed in the immune system during pregnancy, it remains unclear whether pregnant women are more susceptible to infection. Pregnancy does, however, complicate the management of infectious diseases due to concerns regarding fetal well-being and the effect of pregnancy on antimicrobial agents. Although a detailed discussion of drug therapy in pregnancy is beyond the scope of this chapter and can be found elsewhere,[5,6] a few points should be reinforced. Pregnancy dramatically alters drug pharmacokinetics, which refers to how a drug moves through the body. Changes in drug absorption, via reductions in gastric emptying and acid secretion, increased intestinal motility, and increased pulmonary tidal volume (which may affect inhaled drugs), are observed. Furthermore, the volume of distribution for drugs is significantly enlarged during pregnancy with increases in plasma volume of 50%, total body water of 7 to 8 L, and body fat of 20% to 40%. Although these volume alterations would be expected to decrease drug levels, albumin concentrations decline, and free fatty acid and lipoprotein values rise, leading to increases in circulating free (biologically active) drug levels.[7] Metabolism and elimination of drugs are also altered in pregnancy, with hormonally mediated reductions in hepatic metabolism and increases in renal clearance. The net effect of pregnancy-induced alterations on drug pharmacokinetics and efficacy is often unpredictable.

Despite an expressed interest in conducting research in women, even during pregnancy, by governmental agencies and the pharmaceutical industry, concerns over current or future fetal well-being make drug trials difficult to conduct. Many drugs have not been validated for efficacy or safety in human pregnancy, and recommendations often rely on animal model data. Although thalidomide-associated embryopathy cast doubt on the ability of animal studies to predict human teratogenicity, every drug later found to be teratogenic in humans caused similar effects in animals (with the possible exception of misoprostol). With the exception of highly polarized large molecules such as heparin, all maternally administered drugs cross the placenta to some degree. The effect of fetal exposure depends on an interaction of gestational timing, dose, and duration of exposure, as well as poorly defined genetic and environmental factors. As a general rule, a fetus is at highest risk for injury during the period of embryogenesis (days 17–54 postconception). Certain infections, as certain drugs, have been shown to be teratogenic (Table 26.1).

The most common pregnancy and puerperium infections result from ascending contamination of the uterine cavity from the lower genital tract flora and include such conditions as intraamniotic infection (also referred to as chorioamnionitis), urinary tract infection and pyelonephritis, postpartum endometritis, and (rarely) pelvic inflammatory disease. Such infections are often polymicrobial in nature, involving both aerobic and anaerobic organisms.[5] Offending organisms may include the following:

Anaerobes: *Peptostreptococcus* spp., *Prevotella* spp., *Bacteroides fragilis* group, *Fusibacterium* spp., *Porphyromonas asacchrolyticus*, *Clostridium* spp., *Mobiluncus* spp.

Aerobes: Groups A, B, and D streptococci, enterococci, *Escherichia coli*, *Klebsiella* spp., *Proteus* spp., *Staphylococcus aureus*, *Gardnerella vaginalis*

Other: Genital mycoplasmas, *Chlamydia trachomatis*, *Neisseria gonorrhoeae*

In addition to polymicrobial infectious conditions, specific infections occur in pregnant women as they do in their nonpregnant counterparts. Due to the overwhelming diversity of these infections, a discussion of the obstetric and anesthetic implications of every infection is not possible. Thus, a series of tables summarizing the prevention (Table 26.2) and management of infections in pregnancy (Tables 26.3, 26.4) are included. Several infections have been singled out for further discussion, including a review of the causative organisms, modes of transmission, maternal and fetal effects, recommendations for counseling and management, and anesthetic implications.

TABLE 26.1. Infections with known teratogenic effects.

Infection	Effects	Comments
Cytomegalovirus	Hydrocephaly, microcephaly, chorioretinitis, microphthalmos, cerebral calcifications, intrauterine growth restriction, mental retardation, deafness.	Most common congenital infection. Congenital infection occurs in 40% of cases after primary infection during pregnancy and in 14% of cases after recurrent infection. Of infected infants, physical effects are present in 20% after primary infection and 8% after secondary infection. No effective therapy exists.
Rubella	Microcephaly, mental retardation, cataracts, deafness, congenital heart disease. All organ systems may be affected.	The rate of permanent organ damage is 50% if the infection is acquired during the first trimester; 6% if infection occurs in mid-pregnancy. Immunization of nonpregnant adults and children is necessary for prevention. Although the live attenuated virus vaccine has not been shown to cause the malformations of congenital rubella syndrome, immunization is not recommended during pregnancy.
Syphilis	Effects range from hydrops fetalis, fetal demise (if infection is severe) to detectable abnormalities of skin, teeth, and bones (if infection is mild).	Penicillin treatment is effective to prevent progression of damage. Severity of fetal damage depends on duration of fetal infection (damage is worse if infection is diagnosed at >20 weeks). Prevalence is increasing.
Toxoplasmosis	All organ systems must be affected. Most common manifestations include chorioretinitis and other central nervous system effects (microcephaly, hydrocephaly, cerebral calcifications). Severity of manifestations depends on duration of disease.	Low prevalence during pregnancy (0.1%–0.5%). Initial maternal infection must occur during pregnancy to place fetus at risk. *Toxoplasma gondii* is transmitted to humans by raw meat or exposure to infected cat feces. The incidence of fetal infection increases as gestational age increases (9%–10% in first trimester; 60% in the third trimester). However, the severity of congenital infection is greater in the first trimester than at the end of gestation.
Varicella	May affect all organ systems. Common manifestations include skin scarring, chorioretinitis, cataracts, microcephaly, hypoplasia of the hands and feet, muscle atrophy.	Overall risk of congenital varicella is low (about 2%–3%), and it occurs most commonly between 7 and 21 weeks gestation. Varicella zoster immunoglobulin should be administered to newborns exposed in utero during the last 4–7 days of gestation. No adverse effect from herpes zoster.

Source: Adapted from Teratology. ACOG Educational Bulletin No. 236, April 1997.

General Anesthetic Management

Although no clear consensus exists in the literature or from clinical practice regarding the use of regional anesthesia in parturients with suspected or documented infections, an analysis based on risk versus benefit appears to favor its use in most cases. Because most viral infections seed the central neuraxis early in their course, regional techniques offer little additional risk for viral spread. With bacterial infections, the risk of meningitis or spinal-epidural abscess formation following central neuraxial techniques appears exceedingly low. Despite the prevalence of bacteremia (up to 60% in healthy parturients with the insertion of a urinary catheter[8]) and the frequent absence of clinical signs in septic[9] or infected parturients,[10] only a few such cases of neuraxial infections have been reported following central neuraxial techniques.[11] Neuraxial techniques in high-grade infections, however, are not completely without risk. Carp et al.[12] noted that when cisternal punctures were performed in bacteremic rats, bacterial cultures could be isolated from the cerebrospinal fluid. By contrast, when the rats were pretreated with antibiotics, no bacterial cultures were obtained. Although the applicability of an animal model using cisternal punctures with bacteria of known antibiotic sensitivities has been questioned, it seems reasonable that the risk of bacterial infections can be reduced through the use of antibiotics before regional techniques in infected parturients. As such, the use of antibiotic therapies before regional anesthesia may be prudent in patients with established infections. Should a high-grade infection exist, attention to intravascular volume replacement, additional monitoring, and potentially abstaining from regional techniques, especially in parturients with overt signs of sepsis, should be considered.

Although general anesthesia is often utilized for operative deliveries in patients with suspected or documented systemic infections,[13] a 16-fold-greater incidence of mortality in all parturients has been associated with its use, primarily due to an inability to secure the airway and commence ventilation.[14] While the urgency of the situation or comorbidities may have accounted for the higher mortality observed, the use of regional techniques are often excluded without consideration of their potential benefit. However, should general anesthesia be ultimately selected, induction and maintenance agents with limited cardiovascular and hemodynamic consequences, particularly in critically ill parturients with sepsis, should be chosen with care. Ketamine and etomidate have been utilized successfully in such cases. In addition, although hyperkalemia from succinylcholine has never been reported in a patient with chorioamnionitis, should infections be severe or prolonged, the use of a rapid-acting nondepolarizing agent, such as rocuronium, should be considered.

Group B Streptococcus

Group B β-hemolytic streptococcus (GBS), or *Streptococcus agalactiae*, is the most common bacterium associated with neonatal infection and the leading cause of life-threatening

TABLE 26.2. Chemoprophylaxis in pregnancy.

Infection (causative organism)	Primary therapy	Alternative therapy	Comments
Postpartum endometritis	Cefazolin 1 g IV × 1 dose or Ampicillin 1–2 g IV × 1 dose or Clindamycin 600–900 mg IV and gentamicin 1.5 mg/kg IV × 1 dose		Prophylaxis should be administered preoperatively to women at high risk. Once-daily dose of gentamicin has not been validated for efficacy or safety during pregnancy and in the puerperium. Other aminoglycosides may be substituted for gentamicin (Aztreonam is effective but is expensive and is therefore reserved for women with renal insufficiency).
Bacterial endocarditis (primary against enterococci)	Ampicillin 2 g IM/IV and gentamicin 1.5 mg/kg IM/IV within 30 min of delivery plus Ampicillin 1 g IM/IV or amoxicillin 1 g po × 1 dose within 6 h of delivery	Vancomycin 1 g IV over 1–2 h and gentamicin 1.5 mg/kg IM/IV within 30 min of delivery (no postdelivery dose)	The American Heart Association does not recommend antibiotic prophylaxis for cesarean delivery or normal vaginal delivery, with the possible exception of high-risk women for whom it is optional.
Pyelonephritis (mainly *Escherichia coli*)	Nitrofurantoin 50–100 mg po each night before bedtime or Sulfisoxazole 500 mg po each night before bedtime		Consider antibiotic suppression after acute pyelonephritis or recurrent urinary tract infection (UTI) in pregnancy, and in women at high risk for UTI/pyelonephritis.
Group B streptococcus (GBS)	Penicillin G 5 million units IV loading dose, followed by 2.5 million units IV q4h	Ampicillin 2 g IV loading dose, followed by 1–2 g q4–6h or Clindamycin 600 mg IV q6h or 900 mg IV q8h or Erythromycin 500 mg IV q6h	Intrapartum, but not antepartum, chemoprophylaxis against GBS has been shown to decrease early-onset neonatal GBS sepsis.
Genital herpes simples virus (usually HSV-2)	Acyclovir 200 mg po qid from 35–36 weeks gestation to delivery (not postpartum) or Acyclovir 400 mg po bid from 35–36 weeks gestation to delivery (not postpartum)	Famciclovir 250 mg po bid or Valacyclovir 250 mg po bid or Valacyclovir 500 mg po daily or Valacyclovir 1 g po daily	Suppression therapy reduces the frequency of recurrences by ~75% in patients with ≥6 recurrences/year. Goal of suppression is to decrease the incidence of HSV prodrome and/or genital lesion in labor that would necessitate cesarean delivery. Suppression may be offered to women with first-episode genital HSV infection during the index pregnancy or frequent recurrence.
Sexual assault (*Chlamydia trachomatis*, *Neisseria gonorrhoeae*, *Trichomonas vaginalis*)	Ceftriaxone 125 mg IM × 1 dose PLUS Metronidazole 2 g po × 1 dose PLUS Azithromycin 1 g po × 1 dose or doxycycline 100 mg po bid × 7 days	For alternative treatments, refer to sections in this table that specifically address alternative therapeutic options for each of the potential infectious agents under consideration.	Hepatitis B vaccine should be administered with follow-up at 1–2 and 4–6 months after first dose. Testing for HIV and possible antiretroviral prophylaxis should be considered.

Source: Adapted from 1998 Recommendations by the Centers for Disease Control and Prevention. (Rayburn WF. Treatment of sexually transmitted disease. J Reprod Med 1998;43:471–476.)

perinatal infections in the United States.[15] A gram-positive encapsulated coccus that produces β-hemolysis on blood agar, GBS is responsible for an overall rate of neonatal infection of 1 to 3 per 1000 live births, 10 per 1000 deliveries in women colonized with GBS, and 40 to 50 per 1000 live births complicated by preterm delivery.[16]

Early-onset neonatal GBS infection, which accounts for 80% to 85% of all cases, is characterized by neonatal respiratory distress, apnea, pneumonia, and septic shock within 1 week of delivery. Confirmed by a positive blood culture, the infection has an overall mortality rate of 5% (but the rate may be as high as 25% among preterm infants), with surviving

TABLE 26.3. Treatment of sexually transmitted diseases in pregnancy.

Infection (causative organism)	Primary therapy	Alternative therapy	Comments
Bacterial vaginosis (BV) (*Proteus* species, *Mobiluncus* species, *Mycoplasma hominis*, *Gardnerella vaginalis*)	Metronidazole 250 mg po tid × 7 days	Metronidazole 2 g po × 1 dose or Clindamycin 300 mg po bid × 7 days or Metronidazole gel (0.75%) one applicator full (5 g) intravaginally bid × 5 days [recommended for low-risk pregnant women only]	BV is associated with adverse perinatal outcome, including low birth weight and preterm birth. Pregnant women with symptomatic BV should be treated. It remains unclear whether screening/treatment of asymptomatic women improves perinatal outcome. Lower dose of metronidazole is recommended to reduce risk to fetus. Clindamycin vaginal gel is not recommended (may be associated with an increase in preterm delivery)
Chancroid (*Haemophilus ducreyi*)	Azithromycin 1 g po × 1 dose or Ceftriaxone 250 mg IM × 1 dose or Erythromycin base 500 mg po qid × 7 days		Exclude HSV, *T. pallidum.* Consider HIV screening (erythromycin is recommended for HIV+ women). Ciprofloxacin is an alternative treatment, but is contraindicated in pregnancy.
Chlamydial infections (*Chlamydia trachomatis*)	Erythromycin base 500 mg po qid × 7 days or Amoxicillin 500 mg po tid × 7 days	Erythromycin base 250 mg po qid × 14 days or Erythromycin ethylsuccinate 800 mg po qid × 7 days or Erythromycin ethylsuccinate 400 mg po qid × 14 days or Azithromycin 1 g po × 1 dose	Erythromycin estolate, doxycycline, and ofloxacin are contraindicated in pregnancy. There are insufficient data to recommend the routine use of azithromycin in pregnancy. Repeat cultures 3 weeks after therapy has been completed because of the high rate of noncompliance and the lower efficacy of erythromycin treatment regimens.
Gonococcal infections (*Neisseria gonorrhoeae*)	Cefixime 400 mg po × 1 dose or Ceftriaxone 125 mg IM × 1 dose plus a regimen effective against possible concomitant infection with *C. trachomatis:* Erythromycin base 500 mg po qid × 7 days or Amoxicillin 500 mg po tid × 7 days or Azithromycin 1 g po × 1 dose or Doxycycline 100 mg po × 7 days	Spectinomycin 2 g IM × 1 dose or Ceftizoxime 500 mg IM × 1 dose or Cefotaxime 500 mg IM × 1 dose or Cefotetan 1 g IM × 1 dose or Cefoxitin 2 g IM × 1 dose with probenecid 1 g po × 1 dose	Azithromycin 2 g po single dose is effective, but expensive and causes GI upset (1 g dose is ineffective). In pregnancy, quinolones (ofloxacin, ciprofloxacin, lomefloxacin, enoxacin, norfloxacin) and tetracycline are contraindicated. If cephalosporins cannot be tolerated, treat with spectinomycin 2 g IM × 1 dose. For disseminated gonococcal infection, treat in hospital setting with ceftriaxone 25–50 mg/kg/day IM/IV daily × 7 days or cefotaxime25 mg/kg IM/IV bid × 7 days (up to 10–14 days if meningitis is documented).
Genital herpes simplex virus (usually HSV-2)	First clinical episode of genital herpes: Acyclovir 400 mg po tid × 7–10 days or until clinically resolved or Acyclovir 200 mg po 5×/day × 7–10 days or until clinically resolved or Famciclovir 250 mg po tid × 7–10 days or until clinically resolved or Valacyclovir 1 g po bid × 7–10 days or until clinically resolved		Topical acyclovir is less effective than oral treatment, and is discouraged. First clinical episode during pregnancy may be treated with acyclovir. Safety of valacyclovir and famciclovir in pregnancy is not well established, but benefits may outweigh risks. Treatment must be initiated during prodrome or within 1 day of onset of lesions for patient to experience benefit from therapy.

TABLE 26.3. *Continued.*

Infection (causative organism)	Primary therapy	Alternative therapy	Comments
	Recurrent clinical episodes of genital herpes: Acyclovir 400 mg po tid × 5 days or Acyclovir 200 mg po 5×/day × 5 days or Acyclovir 800 mg po bid × 5 days or Famciclovir 125 mg po bid × 5 days or Valacyclovir 500 mg po bid × 5 days Disseminated herpes: Acyclovir 5–10 mg/kg IV q8h × 5–7 days		
Genital warts (human papillomavirus, HPV)	Cryotherapy with cryoprobe or liquid nitrogen or Trichloroacetic acid (TCA) 80%–90%, apply only to warts. Use powder with talc or baking soda to remove unreacted acid. Repeat weekly if necessary, or Surgical removal.	Intralesional interferon or Laser surgery	Imiquimod, podofilox, and podophyllin are contraindicated in pregnancy. Thus, therapy during pregnancy is severely limited. No therapy has been shown to eradicate or affect the natural history of HPV. If lesions persist after one type of treatment, other therapies should be considered. Genital warts are not a contraindication to vaginal birth, but may bleed excessively at delivery.
Pubic lice (pediculosis pubis)	Permethrin 1% cream rinse, applied to affected areas and washed off after 10 min or Pyrethrins with piperonyl butoxide, applied to affected areas and washed off after 10 min.		Lindane 1% shampoo is not recommended for use in pregnant or lactating women. Toxicity related to prolonged lindane exposure includes seizures and aplastic anemia. Decontaminate clothing and bedding, or remove from body contact for at least 72 h. Fumigation is not necessary. Evaluate and retreat in 1 week if symptoms persist or lice observed. Treat sexual partners.
Scabies (*Sarcoptes scabiei*)	Permethrin cream (5%), applied to all areas of the body from the neck down and washed off after 8–14 h.	Sulfur (6%) precipitated in ointment, applied thinly to all areas nightly for 3 consecutive nights; wash off previous application before applying new one. Wash off thoroughly 24 h after the last application.	Lindane is not recommended in pregnant or lactating women. Decontaminate clothing and bedding. Pruritis may persist for several weeks. Consider treatment after 1 week if still symptomatic. Both sexual and close personal and household contacts within the preceding month should be examined and treated. Scabies among children is generally not sexually transmitted. Treatment of entire populations may be required to control scabies epidemics.
Trichomonas (*Trichomonas vaginalis*)	Metronidazole 2 g po × 1 dose	Metronidazole 500 mg po bid × 7 days	Metronidazole is not recommended in the first trimester. If treatment fails, consider 375–500 mg bid × 7 day regimen. If repeated failure, consider 2 daily × 3–5 days.
Syphilis[a] (*Treponema pallidum*)	Primary/secondary/early latent syphilis: Benzathine penicillin G, 2.4 million units IM × 1 dose (usually administered as 1.2 million units into each buttock). Some experts recommend a second dose of penicillin for such women 1 week after initial dose.		Routine screening for syphilis at first prenatal visit. High-risk women should be screened again at 28 weeks and at delivery. All women with syphilis should be offered HIV testing. Penicillin is effective in preventing transmission to fetuses and for treating established infection in fetuses. Women treated in the second half of pregnancy are at risk for preterm labor, possibly due to Jarisch–Herxheimer reaction.

(*Continued*)

TABLE 26.3. *Continued.*

Infection (causative organism)	Primary therapy	Alternative therapy	Comments
	Late latent/tertiary/unknown duration: Benzathine penicillin G, 2.4 million units IM/week × 3 weeks (7.2 million units total). Neurosyphilis: Aqueous crystalline penicillin G, 12–24 million units IV daily (administered as 2–4 million units IV q4h) × 10–14 days or Aqueous procaine penicillin G, 2.4 million units IM daily plus probenecid 500 mg PO qid × 10–14 days.		If pregnant patient with syphilis is penicillin allergic, desensitize and treat with penicillin. Doxycycline and tetracycline are contraindicated in pregnancy. Erythromycin cannot be relied upon to treat the infected fetus. Insufficient data on azithromycin or ceftriaxone.

[a]Adapted from Centers for Disease Control: 1998 guidelines for treatment of sexually transmitted diseases. MMWR 1998;47:28–49.
Source: Adapted from 1998 Recommendations by the Centers for Disease Control and Prevention. (Rayburn WF. Treatment of sexually transmitted diseases. J Reprod Med 1998;43:471–476.)

neonates often exhibiting significant long-term neurologic sequelae. By contrast, late-onset GBS infection usually results from community- or hospital-acquired (nosocomial) infections in preterm infants and presents as meningitis or sepsis more than 1 week after birth.

Transmission of early-onset neonatal GBS infection results almost exclusively during labor and delivery in parturients from lower genital or gastrointestinal tract colonization rather than transplacental passage. Not sexually transmitted, GBS is a commensal organism that intermittently colonizes the lower genital tract of 20% (range, 15%–40%) of women at any one time.[17] An estimated 8% to 10% crossover of GBS carrier status exists during each trimester, and thus determination of GBS carrier status is not recommended at the first prenatal visit. Half of all infants born to women colonized with GBS will become colonized with GBS; however, most are asymptomatic.[15]

A number of strategies have been proposed to prevent early-onset GBS infection, including intrapartum maternal and postpartum neonatal antibiotic regimens. However, such antibiotic use has been associated with the emergence of antibiotic resistance,[18] an increased incidence of early-onset neonatal sepsis due to non-GBS organisms,[19] and maternal anaphylaxis (estimated as 1:60,000 for penicillin).[20] Because of these limitations, routine administration of GBS chemoprophylaxis is not recommended for all women in labor. Instead, two independent prophylaxis protocols have been proposed and deemed acceptable for select parturients by the American College of Obstetricians and Gynecologists (ACOG).[15,16]

A *risk factor-based protocol* involves intrapartum treatment of pregnancies with one or more risk factors, including preterm labor, preterm premature rupture of the membranes, prolonged rupture of membranes (≥18 h regardless of gestational age), a prior GBS-infected infant, maternal fever in labor (≥100.4°F), and GBS bacteriuria or urinary tract infection at any time during the index pregnancy. No attempt is made to identify women colonized with GBS. This protocol results in intrapartum treatment of 20% to 25% of pregnant women with prevention of 65% to 70% of GBS disease.[15,16]

A *culture-based protocol* involves intrapartum prophylaxis of women who are known GBS carriers or whose GBS carrier status is unknown. To predict carrier status in labor, GBS cultures should be sent as late as possible during pregnancy, but before the onset of labor (ideally, 35–37 weeks gestation), to accurately reflect GBS carrier status at delivery.[21] Because GBS colonization increases from the cervix to the introitus, the culture should be taken by generously swabbing the lower vagina, perineum, and perianal area using a single cotton swab, and the swab should be placed briefly into the anal canal. A speculum should not be used. The "perineal" (not cervical) swab should be inoculated into Todd–Hewitt broth or selective blood agar, stored at room temperature, and transported to the laboratory within 8 h of collection. Processing in the laboratory will usually take 48 h. Antimicrobial susceptibility is not routinely done, as most GBS organisms are pansensitive. Rapid screening tests for GBS carrier status in labor have been developed, but are more difficult to perform, not available in all hospitals at all times, and have poor sensitivity in identifying women with low levels of GBS colonization. The culture-based protocol results in treatment of 15% to 20% of pregnant women with prevention of 70% to 80% of GBS disease.[15,16]

Should the decision be made to proceed with intrapartum GBS chemoprophylaxis, a number of general guidelines should be followed. Intravenous penicillin G, instead of ampicillin, is the antibiotic of choice due to a narrower spectrum and reduced likelihood of leading to antibiotic resistance. A minimum of 4 h of antibiotic prophylaxis is recommended, with discontinuance at delivery.

Anesthetic Management

Although group B β-hemolytic streptococcus has been implicated as the cause of meningitis in two parturients who had

TABLE 26.4. Treatment of other infections in pregnancy.

Infection (causative organism)	Primary therapy	Alternative therapy	Comments
Asymptomatic bacteriuria (primarily *E. coli*; also *Klebsiella/Enterobacter* sp, *Proteus* sp, Group B streptococci, enterococci)	Nitrofurantoin macrocrystals 50–100 mg po qid × 3 days or Nitrofurantoin monohydrate 100 mg po bid × 3 days or Cephalexin 250–500 mg po qid × 3 days	Ampicillin 250–50 mg po qid × 3 days or Amoxicillin 250–500 mg po tid × 3 days or Trimethaprim/sulfamethoxazole 160 mg/180 mg po bid × 3 days or Trimethoprim 200 mg po bid × 3 days or Sulfisoxazole 2 g loading dose po followed by 1 g po qid × 3 days	Complicates 2%–9% of pregnancies. Consider treatment when 25,000–100,000 colony-forming units/mL of a single pathogenic organism are found in a clean-catch midstream urine specimen. Single-dose treatment is effective but has a higher failure rate; a 3-day course is usually recommended. Obtain a follow-up culture 7–10 days after completion of treatment.
Pyelonephritis (mainly *E. coli*)	Ampicillin 1–2 g IV q6h and gentamicin 1.5 mg/kg q8h or Ceftriaxone 1–2 g IM/IV q24h	Trimethaprim/sulfamethoxazole 160 mg/800 mg IV q12h or Gentamicin 1.5 mg/kg q8h	Treat IV until asymptomatic and afebrile for 24–48 h, followed by oral antibiotics to complete 10 days of therapy. After acute treatment, obtain a follow-up culture in 7–10 days, place on prophylactic therapy, and perform periodic screening.
Intraamniotic infection (mainly Group B streptococci, *E. coli*)	Ampicillin 2 g IV q4–6h and gentamicin 1.5 mg/kg IV q8h intrapartum or Penicillin 2.5–5 million units q4–6h and gentamicin 1.5 mg/kg IV q8h intrapartum plus Clindamycin 900 IV q8h or Metronidazole 500 mg IV q8h added after delivery only if delivery is by cesarean	Ampicillin/sulbactam 3 g IV q6h or Cefotetan 2 g IV q12h or Cefoxitin 2 g IV q6h or Cefotaxime 25 mg/kg IM/IV q12h plus Clindamycin 900 IV q8h or Metronidazole 500 mg IV q8h added after delivery only if delivery is by cesarean	Intraamniotic infection remains a clinical diagnosis (fetal tachycardia, uterine tenderness and contractions, maternal tachycardia and fever). Amniotic fluid culture remains the gold standard for diagnosis; Gram stain is only 50% sensitive. Delivery should be expedited, irrespective of gestational age. Following delivery, antibiotic coverage should probably be continued. If delivery is by cesarean, antibiotic coverage should also be broadened (clindamycin is preferred over metronidazole for lactating women).
Postpartum endometritis (polymicrobial infection with both anaerobes aerobes)	Clindamycin 900 mg IV q8h and gentamicin 1.5 mg/kg IV q8h with or without Ampicillin 1–2 g IV q4–6h or penicillin 2.5–5 million units IV q4–6h	Cefotetan 2 g IV q12h or Cefoxitin 2 g IV q6h or Cefotaxime 1–2 g IM/IV q6–8h or Piperacillin 3–4 g IM/IV q4–6h or Ampicillin/sulbactam 3 g IV q6h	Treatment should be continued until the patient has been asymptomatic and afebrile for 24–48 h. Around 10% of patients will not be cured with initial therapy. Approximately 20% of treatment failures are due to resistant organisms. Women who do not respond within 48–72 h often have another source of fever (drug fever, wound infection, septic pelvic thrombophlebitis, infected hematoma, abscess, retained products of conception).
Vulvovaginal candidiasis (*Candida albicans* and other *Candida* species, *Torulopsis* species, or other yeasts)	Butoconazole 2% cream 5 g intravaginally × 3 days or Clotrimazole 1% cream 5 g intravaginally × 7–14 days or Clotrimazole 100 mg vaginal tablet × 7 days or		In pregnancy, topical azole products should be used rather than nystatin. Most effective are butoconazole, clotrimazole, and terconazole; 7-day regimens are preferred.

(*Continued*)

TABLE 26.4. *Continued.*

Infection (causative organism)	Primary therapy	Alternative therapy	Comments
	Clotrimazole 100 mg vaginal tablet, two tablets × 3 days or Clotrimazole 500 mg vaginal tablet × 1 dose or Miconazole 2% cream 5 g intravaginally × 7 days or		Oral agents such as ketoconazole (100 mg po single dose) and fluconazole (150 mg po single dose) may be as effective as topical agents, but potential toxicity and drug interactions must be considered.
	Miconazole 200 mg vaginal suppository, 1 dose × 3 days or Miconazole 100 mg vaginal suppository, 1 dose × 7 days or Tioconazole 6.5% ointment 5 g intravaginally × 1 dose or Terconazole 0.4% cream 5 g intravaginally × 7 days or Terconazole 0.8% cream 5 g intravaginally × 3 days or Terconazole 80 mg suppository, 1 dose × 3 days		Treatment of sexual partners has not been shown to decrease frequency of recurrences.
Malaria (*Plasmodium falciparum*, *P. vivax, P. malariae, P. ovale*)	Chloroquine 1 g po × 1 dose; then 500 mg at 6, 24, 48 h; then weekly until delivery plus Proguanil 200 mg po qd	Quinine 650 mg po tid × 3–7 days plus Sulfadoxine/pyrimethamine 3 tablets × 1 dose on day 3 of treatment	Malaria is the major cause of fetal growth restriction worldwide. Primaquine should not be used in pregnancy because the drug crosses the placenta and can cause hemolytic anemia in a parturient with glucose-6-phosphate dehydrogenase (G6PD) deficiency. Cerebral malaria should be treated with IV quinine gluconate.
Listeriosis (*Listeria monocytogenes*)	Ampicillin 1–2 g IV q6h and gentamicin 1.5 mg/kg IV q8h	Trimethaprim/sulfamethoxazole 160 mg/800 mg IV q12h or Erythromycin 500–2000 mg IV q6h	The best length of therapy is not known. Treat IV until asymptomatic and afebrile for 24–48 h. Consider prompt delivery if listeria amnionitis is confirmed.
Pelvic inflammatory disease (PID) (*N. gonorrhoeae*, *C. trachomatis*, *Gardnerella vaginalis*, etc.)	Regimen A Cefoxitin 2 g IV q6h or Cefotetan 2 g IV q12h plus Doxycycline 100 mg IV/po q12h plus Doxycycline 100 mg po bid × 14 days total Regimen B Clindamycin 900 mg IV q8h plus Gentamicin 2 mg/kg IV/IM loading dose then 1.5 mg/kg maintainence dose q8h plus Doxycycline 100 mg po bid × 14 days total or clindamycin 450 mg po qid × 14 days total	Ampicillin/sulbactam 3 g IV q6h and doxycycline 100 mg IV/po q12h or Azithromycin 500 mg IV × 2 days followed by 500 mg po × 10 days	PID in pregnancy is very rare. All pregnant women with PID should be hospitalized and treated with IV therapy. Quinolones (ciprofloxacin, ofloxacin) are contraindicated in pregnancy. Treatment may be discontinued 24 h after clinical improvement. When tubo-ovarian abscess is present, surgery may be required, and clindamycin may be preferred for continued therapy. Other 2nd- and 3rd-generation cephalosporins may be effective, but clinical data are limited.

TABLE 26.4. *Continued.*

Infection (causative organism)	Primary therapy	Alternative therapy	Comments
Tuberculosis (*Mycobacterium tuberculosis*)	Positive PPD/no active disease: Isoniazid 300 mg po daily after delivery for 6–9 months or Isoniazid 300 mg po daily after first trimester for 6–9 months (for high-risk women, including recent seroconversion, recent immigrant, known recent TB contact, immunocompromised women, skin test >15 mm and not previously treated) Active disease: Isoniazid 300 mg po daily × 9–12 months plus Rifampin 600 mg po daily × 9–12 months plus/or Ethambutol 2.5 g (15 mg/kg) po daily × 9–12 months or until sensitivity of the AFB culture returns plus Pyridoxine 50 mg po daily × 9–12 months		Isoniazid prophylaxis should be avoided in the puerperium because of the high incidence of hepatic toxicity. In pregnancy, drugs such as kanamycin, streptomycin, capreomycin (congenital deafness), ethionamide (teratogenic), and cycloserine (CNS side effects) are contraindicated Pyrazinamide may be used in place of ethambutol, but this approach is not generally recommended as there are limited data on pyrazinamide use in pregnancy.

Source: Adapted from 1998 Recommendations by the Centers for Disease Control and Prevention. (Rayburn WF. Treatment of sexually transmitted disease. J Reprod Med 1998;43:471–476.)

epidural labor analgesia,[22,23] nosocomial skin organisms are the most likely culprits for these rare cases of meningitis.[24] In addition, in three retrospective analyses of parturients with documented chorioamnionitis,[25–27] representing a total of 923 patients, no cases of epidural abscess or meningitis were noted, despite the absence of antibiotic coverage before receiving the regional techniques and the presence of fever, bacteremia, and leukocytosis in a number of parturients. Overall, these data suggest that the infectious risk following regional techniques in parturients with group B β-hemolytic streptococcus is very rare. However, as the possibility cannot be excluded, it would be prudent, as with other systemic infections, to request and initiate appropriate antibiotic therapy before the administration of regional techniques and to avoid such techniques in women with overt signs of sepsis.

Cytomegalovirus

Cytomegalovirus (CMV) is a double-stranded DNA herpesvirus transmitted by contact with infected blood, saliva, urine, breast milk, or through sexual contact. The mean incubation period is 40 days (range, 28–60 days). Although a brief, self-limited, flu-like illness with fever, chills, malaise, myalgia with leukocytosis, and elevated liver function tests may be experienced, the majority of infected adults are asymptomatic. After the initial infection, CMV, similarly to other herpesviruses, remains latent in host cells and may reactivate. In rare cases, recurrent disease may be caused by infection with a different strain of the virus.

Diagnosis requires a high index of clinical suspicion. Although the CMV virus can be detected 2 to 3 weeks following a primary infection by culture or polymerase chain reaction (PCR), the diagnosis is usually confirmed by serologic testing, either with positive seroconversion or a minimum fourfold increase in anti-CMV IgG titers over 3 to 4 weeks. The presence of anti-CMV IgM is a useful, but not completely reliable, method of establishing a primary infectious process; IgM titers may be nondetectable during an acute infection and may persist for months.[28] The reported sensitivity of CMV IgM serologic assays ranges from 50% to 90%.[28]

The prevalence of CMV infection in pregnant women varies from 0.7% to 4% for primary infections and up to 13.5% for recurrent infections.[29] Vertical transmission may occur via a transplacental route with primary or recurrent CMV infections, exposure to contaminated genital tract secretions with vaginal birth, or through breast-feeding. Occurring at any stage of pregnancy, fetal infections are most common during the third trimester; however, more serious sequelae follow first trimester transmission. The risk of vertical transmission during primary and recurrent maternal CMV infections is 30% to 40%[30] and 0.15% to 2%, respectively,[31]

with more severe fetal neurologic morbidity following primary infections.[32]

Cytomegalovirus is the most common congenital infection, occurring in 0.2% to 2.2% of all neonates,[32] and is the leading cause of congenital hearing loss. Prenatally, CMV infection can be suspected following a documented maternal primary infection or suggestive ultrasound findings; these include abdominal, liver, and lateral cerebrospinal fluid (CSF) ventricle calcifications, ventriculomegaly, hydrops fetalis, echogenic bowel, ascites, and hepatosplenomegaly.[33] Structural anomalies, especially within the central nervous system, dictate a much poorer fetal prognosis. Diagnostic confirmation can usually be made through detection of CMV in amniotic fluid by culture or PCR. Fetal blood sampling for antibody response is less sensitive due to the immaturity of the fetal immune system,[34] and alterations of platelet count and liver function tests are nonspecific. Although most infants with congenital CMV are asymptomatic at birth, evidence of the aforementioned ultrasound findings, as well as growth restriction, jaundice, petechiae, and thrombocytopenia, may be observed.[35]

No therapies are currently available for maternal or fetal CMV infection, and thus routine serologic screening for CMV during pregnancy is not recommended.[36] Although the antiretroviral therapies ganciclovir or foscarnet have been used for CMV retinitis in AIDS patients, the use of ganciclovir in combination with CMV hyperimmune gamma globulin in CMV-infected neonates has not been shown to prevent long-term neurologic sequelae.[37] A vaccine is under development but remains currently unavailable. Patient education efforts thus should focus on preventative measures, including careful handling of potentially infected articles (such as diapers) and thorough handwashing when around young children or immunocompromised individuals. In addition, avoidance of high-risk behaviors such as intravenous drug use and sharing of needles should be emphasized when appropriate. Barrier contraception should be encouraged as a method of contraception.

Anesthetic Management

To date, there are no data regarding the implications of CMV on anesthesia.

Hepatitis

One of the most serious infections that can occur during pregnancy, viral hepatitis can be caused by a diverse collection of viruses, including CMV, Epstein–Barr, varicella zoster, coxsackie B, herpes simplex, and rubella. However, a family of seven hepatitis viruses, designated by the letters A through E, G, and TT, are the predominant sources of the disease process; although the viruses are distinct, similarities in clinical manifestations, diagnosis, management, and obstetric and anesthetic implications can be observed. The following information concerns this family of hepatitis viruses.

Malaise, fatigue, anorexia, nausea, and right upper quadrant or epigastric pain are the most common symptoms of acute viral hepatitis, and these symptoms are often accompanied by signs of jaundice, upper abdominal tenderness, and hepatomegaly. Hepatitis A and E are usually self-limited, but hepatitis B, C, and D frequently progress to a chronic carrier state.[38] Hepatitis G and TT may also result in a carrier state; however, their ability to exist independent of other hepatitis forms as acute or chronic hepatitis has yet to be established.[39,40] Although the majority of chronic carriers are asymptomatic, up to one third eventually develop chronic active or persistent hepatitis. Should cirrhosis follow, the signs of end-stage liver disease, including jaundice, muscle wasting, ascites, spider angiomas, palmar erythema, and ultimately hepatic encephalopathy often ensue. Hepatitis D, the defective virus that requires hepatitis B for replication and expression, progresses to severe disease more often than any other form of viral hepatitis. Of patients with chronic hepatitis D, 70% to 80% ultimately develop cirrhosis and portal hypertension, with 15% undergoing rapid progression to death.[41] By contrast, only 15% to 30% of patients with chronic hepatitis B develop cirrhosis, and the progression is much slower.

Diagnosis of viral hepatitis usually begins with a battery of general liver tests that demonstrate a marked increase in serum concentrations of alanine aminotransferase (ALT; previously SGPT), aspartate aminotransferase (AST; previously SGOT), and bilirubin. Initial evaluation should include hepatitis A IgM (anti-HA IgM), hepatitis B surface antigen (HBsAg), and hepatitis C polymerase chain reaction (HC PCR).[42] Additional testing can include testing for hepatitis B core antibody (anti-HBc IgM), which appears between the time when surface antigen and antibodies appear, hepatitis D (HD PCR), hepatitis E (anti-HE), and hepatitis G (anti-HG). Liver biopsies are rarely required during pregnancy. With severe cases, coagulation abnormalities (especially prothrombin time) and hyperammonemia can be observed; however, neutropenia and lymphopenia are often replaced by a relative lymphocytosis.

Management of parturients infected with hepatitis should begin with avoidance of activities that can result in upper abdominal trauma, maintenance of good nutrition, and avoidance of intimate contact until the involved parties receive appropriate prophylaxis as outlined next. Should more severe signs be present, hospitalization and correction of nutritional, fluid, electrolyte, and coagulation disorders is recommended. Although not a specific therapy for the various hepatitis viruses, interferon-alpha has been demonstrated to alter the natural course of acute hepatitis B, C, and D. Multiple side effects, however, including myelosuppression, autoantibody formation, thyroid disturbances, and possible cardiotoxicity, limit its use. In addition, interferon is not recommended during pregnancy because of the possible abortifacient effect.[38]

As these treatments are not completely curative, the emphasis has been placed on the prevention of viral hepatitis through education and immunization. Passive immunization with antibody immunoglobulin (IG) preparations purified

TABLE 26.5. Incidence and transmission of hepatitis viruses.

Type	Virus	Incidence[a]	Transmission	Vertical transmission	Perinatal transmission
A	RNA	1/1000	Fecal-oral	No	No
B	DNA	Acute: 1–2/1000 Chronic: 5–15/1000	Parenteral-sexual	Yes	Yes
C	RNA	6/1000	Parenteral-sexual?	Rare	Yes
D	RNA	Unknown	Parenteral-sexual	Yes	Yes
E	RNA	Unknown	Fecal-oral	Yes	Not reported
G	RNA	Unknown	Parenteral-sexual	Yes	Not reported
TT	DNA	Unknown	Parenteral-sexual?	Yes	Not reported

[a]Incidence in the United States during pregnancy.

from the plasma of normal donors is active against hepatitis A, B, and D (through immunization against B). A specific immunoglobulin against hepatitis B (HBIG) is also available and has been demonstrated to be more efficacious than standard IG preparations. Of note, plasma-derived IG preparations are considered to be of no infectious risk because of an ethanol fractionation process that inactivates viral (including the human immunodeficiency virus, HIV) and other bloodborne infectious diseases. IG can be given during pregnancy and does not pose a risk to the woman or her fetus.[38] Two active immunizations, Recombivax HB and Engerix B, have been developed against hepatitis B and, because they are produced via yeast cultures with recombinant DNA technologies, pose no infectious risk. Should exposure to hepatitis A or B (before immunization) occur, passive immunoglobulins should be administered as soon as possible. With hepatitis B, the more specific HBIG should be given, and an immunization series of three vaccinations should be commenced. These regimens are approximately 75% effective in preventing hepatitis A and B (and thus D).[42] Currently no immunoprophylaxis is available for hepatitis C or E, and there is insufficient evidence regarding the effects of IGs on hepatitis G or TT.

The Centers for Disease Control and Prevention and the American College of Obstetricians and Gynecologists recommend hepatitis B virus screening (HbsAg) for all pregnant women.[38] Seropositive women should have serum transaminases measured and be encouraged to inform their sexual partners and children of the need for testing and vaccination. Universal active hepatitis immunization is recommended for all infants born in the United States. When the mother is seronegative, infant immunization should commence preferably before discharge and no later than 2 months of age. When the mother is seropositive (HBsAg positive) or those of unknown status, infants should receive both passive and active immunization treatments, starting within 12 h after birth (Table 26.5).

Anesthetic Management

As a principal organ responsible for glucose hemostasis, fat metabolism, drug and hormone metabolism, bilirubin formation and excretion, and protein synthesis, the liver is involved in a number of physiologic activities of great concern to anesthesiologists. Although progression to fulminant liver failure is not typical of the disease during pregnancy, rapid deterioration[43] and liver transplantation have been reported.[44] Of special relevance to the administration of regional anesthesia is the production of clotting factors; however, as only 20% to 30% of normal coagulation factors is necessary to prevent bleeding, severe liver dysfunction must be present before the onset of significant coagulopathies. Nonetheless, clotting abnormalities should be suspected and evaluated, and a low threshold for replacement of clotting factors should be considered.

In terms of general anesthesia, the accentuated effects and prolonged elimination time of drugs, due to decreased protein binding and metabolism respectively, should be considered. Infrequent reports of independent hepatic injury following administration of halothane, sevoflurane, desflurane, and even isoflurane have drawn no definitive causal relationships[45]; however, avoidance of hypoxia and reduced hepatic blood flow when using these agents, especially in patients with preexisting hepatic disease undergoing prolonged procedures with operative interventions in close proximity to the liver, has been recommended.[46]

Human Immunodeficiency Virus

An RNA virus that possesses a unique reverse transcriptase enzyme which encodes proviral DNA into the nucleus of the host cells, human immunodeficiency virus (HIV) currently affects an estimated 13.8 million women infected worldwide.[47] Delays in diagnosis and treatment of the female gender and the ease of fetal transfer[48] represent significant parturient concerns. A multisystem disease, HIV primarily attacks cells positive for the CD4 surface antigen, especially helper T lymphocytes, which play an integral role in cell-mediated immunity, B cell activation, and antibody production. Associated alterations in macrophage activation and neutrophil function lead to an overall increased vulnerability to bacterial, viral, fungal, parasitic, and mycobacterial infections, as well as certain malignancies. Although the combined effect of HIV and pregnancy on the immunologic system remains unclear,[49,50] an increase in acquired immunodeficiency syndrome (AIDS) or AIDS-related complex has been observed in the postpartum period.[51]

At any time during the course of the disease, but particularly within a month of the primary infection, patients may present with a mononucleosis-like illness with symptoms of headache, meningismus, fever, altered mental status, and isolated cranial nerve palsies. In part these alterations are the result of very early involvement of the brain and cerebral spinal fluid; before the onset of AIDS, the virus titer in the brain is higher than in any other organ.[52] With disease progression, HIV infects the microglial and monocytic cells, resulting in an often fulminate disturbance in mental function followed by motor and gait abnormalities. This process, referred to as AIDS–dementia complex (ADC), is the most frequent neurologic diagnosis in AIDS patients. Disorders of the spinal cord (vacuolar myelopathy), nerve roots (CMV polyradiculitis), and peripheral nerves [distal sensory polyneuropathy (DSP)] may also occur. A relationship between HIV and hematologic disorders including thrombocytopenia and thrombotic microangiopathies (TMA) occurs with a 5% to 15% incidence.[53] The etiology of these effects, which is independent of the clinical status of the patient,[53] has several hypothesized mechanisms, including antiplatelet antibodies, circulating immune complexes, megakaryocyte infection, and bone marrow suppression.[54]

On a population basis, pregnancy rates among women with HIV infection are comparable with uninfected women until the onset of AIDS opportunistic infections, when the rates fall considerably.[55] During pregnancy, with advanced disease (CD4 counts below 30% or progression to AIDS), an increase in adverse outcomes including miscarriage, premature rupture of membranes, preterm delivery, and low birth weight has been observed.[49,50] The transfer of HIV from mother to infant accounts for nearly all the cases of HIV infection in children and depends on a number of maternal, fetal, and viral factors. HIV transmission may occur at any time. With early gestational infection, fetal loss occurs frequently.[56] Recent randomized and observational trials in both the developing and developed nations have indicated that shorter antenatal regimens,[57] and even postpartum neonatal treatment,[58] are successful in dramatically reducing the transmission rate.

Two particular interventions deserve attention: reducing antepartum maternal plasma HIV RNA levels and limiting intra- and postpartum neonate exposure to maternal blood, genital, and breast secretions. The first intervention, using antiviral medications in therapy-naïve parturients to reduce their viral load, was validated by the AIDS Clinical Trials Group (ACTG) Protocol 076, in which zidovudine (ZDV) therapy reduced the rate of vertical transmission of HIV infection from 25.5% to 8.3%.[59] In this trial, ZDV was administered orally and intravenously to parturients before and during delivery, respectively, and orally to their infants for 6 weeks after birth. Further study is needed to identify the optimal medications, time period, and long-term impact for this and other therapies; one potential concern is the creation of multidrug-resistant strains of HIV and other comorbid infections later in the course of the parturient's disease process.

The second intervention, elective cesarean delivery before the onset of labor or membrane rupture, was evaluated by the International Perinatal HIV Group via a meta-analysis of 15 prospective cohort studies (5 European and 10 North American) conducted between 1982 and 1996.[60] The HIV transmission rate associated with elective cesarean delivery before onset of labor and membrane rupture was compared to either vaginal or cesarean delivery performed after these events. With the restriction of the primary analysis to 8533 mother–infant pairs for whom the route, circumstances of delivery, and neonatal HIV status were known, a strongly protective effect of elective cesarean delivery was discovered (odds ratio, 0.43; 95% confidence interval, 0.33–0.56). These results suggest that either labor or membrane rupture could potentially increase the risk of vertical HIV transmission. However, the indiscriminate use of cesarean delivery may not necessarily be beneficial, as an increase in maternal morbidity and mortality from an operative delivery, particularly in Third World countries, has been observed in this population.[61]

Additional fetal concerns may lead to a cesarean delivery. Because IgG antiplatelet antibodies have been detected in HIV-infected patients,[62] transplacental passage with resultant fetal thrombocytopenia and systemic or intracranial hemorrhage may occur. Thus, in addition to the inoculation risk, procedures involving the puncture of fetal skin or epithelium, including funipuncture and scalp sampling, are avoided to decrease the risk of fetal bleeding. This concern may offer another indication, in the scenario of nonreassuring external fetal monitoring with the inability to do fetal scalp pH samples or intrauterine monitoring, to perform an operative delivery.

Collectively, these concerns have shaped the components of an "optimal approach"[63] for limiting maternal fetal transmission, which includes promoting earlier HIV detection, using antiretroviral therapy during pregnancy, selecting obstetric interventions, including elective cesarean delivery, and using neonatal antiretroviral therapy.

Anesthetic Management

Patients known to be HIV positive should undergo a comprehensive evaluation, because even mild or nonspecific symptoms are compatible with advanced disease. Prior or current clinical manifestations including anemia or thrombocytopenia and other opportunistic or sexually transmitted infections, as well as current or prior use of HIV-related therapies, adverse drug events, and illicit drug use, should be documented.

When the use of a regional anesthetic is contemplated, the initial assessment should closely evaluate the status of the hematologic and neurologic systems. Although the theoretical risk of exacerbating a preexisting neurologic disorder exists, in the absence of overt disease or mass effects the limited available data confirm the safety of regional anesthesia in HIV-positive women.[64] Should a headache occur after a regional technique, a full differential diagnosis, including diseases witnessed in HIV patients, should be considered. If the

headache is deemed to result from a dural puncture, initial therapies should be conservative: bedrest, analgesics, oral hydration, and caffeinated products. Should this management fail, an epidural blood patch can be considered. Although theoretical infectious implications of a blood patch have been raised,[65,66] and alternatives such as the use of extradural saline or heterologous HIV-negative blood have been suggested,[67] it should be remembered that detection of HIV within the central nervous system occurs early within the disease course. Three reports have noted the absence of adverse events following blood patch in HIV-positive patients. Although the studies collectively represent only 13 patients,[67,68] in one study 6 patients underwent serial neuropsychologic testing for as long as 2 years,[68] and no adverse neurologic or infectious sequelae were observed.

Few data exist on the effects of general anesthesia in the HIV-infected parturient. Of concern, however, is the potential for increased sensitivity to medications and the possibility of increased morbidity. In terms of increased sensitivity, a significantly prolonged response to a single dose of vecuronium has been reported in five HIV-positive patients; although the reasons for this prolonged effect were unclear, speculation was placed on existing peripheral neuropathies due to HIV and its treatment.[69] Whether this is true for all classes and types of neuromuscular relaxant medications is not known. Also unknown are the effects of gammaaminobutyric acid (GABA) receptor drugs (i.e., barbiturates, benzodazepines, and propofol). While HIV patients are speculated to be more sensitive due to the relationship between the receptor and interleukin 1,[70] a cytokine released in response to viral and bacterial infections, the actual clinical effects have not been studied.

In terms of increased morbidity, although general anesthesia can cause a small transient depression in immune function in normal patients,[71] the effects in the parturient with HIV are unknown. Other theoretical concerns include difficulties in intubation because of the pharyngeal lymphatic hypertrophy observed in some HIV-infected patients[72] and the potential for the endotracheal tube to serve as a conduit for oral pathogens to the pulmonary tree.

Herpes Simplex Virus

A member of the DNA Herpesviridae family, herpes simplex virus (HSV) has two major types, designated HSV-1 and HSV-2, which are primarily responsible for nongenital (gingivostomatitis, keratoconjunctivitis) and genital lesions, respectively. An estimated 500,000 new cases of genital herpes, one of the most common viral pathogens, are diagnosed each year, with more than 45 million Americans infected. HSV-2 infections are more common in women, perhaps reflecting a more effective transmission rate, and approximately 30% of the female American population has antibodies to HSV-2.[73]

Three stages of HSV infection have been identified, based on clinical presentation and serology. First-episode primary genital HSV occurs when herpes antibodies are absent at the time of infection. First-episode nonprimary genital HSV occurs when the acquisition of one type of HSV occurs when antibodies to the other type exist. Recurrent infection occurs when reactivation of genital HSV occurs when antibodies of the same type are present.

Initial HSV genital infections and recurrences may be with or without symptoms. When symptomatic, primary infections appear 2 to 14 days following exposure as ruptured vesicles on the vulva, vagina, and or cervix. Lesions usually resolve within 3 weeks without treatment but may persist up to 6 weeks with secondary bacterial or mycotic infections. Commonly accompanied by localized pain, HSV infections may also present with systemic symptoms (malaise, myalgia, and fever) in up to two thirds of cases. Recurrent disease is generally accompanied with less severe symptoms. Viral shedding presents an infectious risk and may occur in the absence of symptoms (i.e., subclinical shedding). Although significant variation in the frequency, severity, and duration of shedding exists, shedding occurs less frequently with recurrent herpes. When primary genital herpes occurs during pregnancy, an increased frequency of viral shedding occurs.

Approximately 1500 to 2000 newborns contract herpes each year, mostly from contact with infected maternal secretions during the perinatal period. Although believed to be an infrequent occurrence, in utero transmission can occur, resulting in a variety of anomalies or the onset of preterm labor and delivery. Neonatal disease occurs in 30% to 60% of the cases when a neonate comes in contact with the virus and may result in localized [skin, eye, mouth, and central nervous system (CNS)] or disseminated disease. Neonatal mortality increases dramatically with the disseminated disease, that is, from 15% to 57%.[74]

Diagnosis of HSV is dependent on virus isolation; however, specimen sampling and transporting difficulties limit test sensitivity, even with overt infections, to 60% to 70%.[75] A positive test is strongly suggestive of a nonprimary first or recurrent episode. More sensitive techniques are under investigation, and serologic tests should soon be able to reliably identify and even distinguish the two HSV forms. Due to the low yield of viral cultures and the presence of asymptomatic viral shedding, virologic monitoring or screening is not recommended.

Primary HSV infection presents the highest vertical transmission risk, and antiviral therapy with acyclovir has been demonstrated to reduce viral shedding, pain, and duration. Recurrent HSV infections may benefit from acyclovir therapy as well, although smaller reductions in viral shedding are believed to occur. Acyclovir, which can cross the placenta, concentrate in the amniotic fluid and breast milk, and reach therapeutic levels in the fetus, has been safely used during pregnancy,[76] although the improved bioavailability of valacyclovir and famciclovir may provide greater benefit.[77] Be-

cause of their beneficial effects, antiviral agent prophylaxis has been recommended for those parturients closer to term (>35 weeks gestation), those experiencing first-episode primary or nonprimary genital infections, or those having frequent (>12/year) recurrences.[78] Cesarean delivery should be performed on women with first-episode or recurrent HSV who have active genital lesions or prodromal symptoms at time of delivery.

Anesthetic Management

The management of women with primary HSV remains controversial because of the viremia and CNS involvement, including headaches, meningitis, and, rarely encephalitis, that occur. Potential for inoculation of the central neuraxial tissues exists with regional anesthetic techniques, and this must be weighed against the benefit derived. By contrast, as recurrent HSV is not associated with a viremia,[79] no contradiction to regional techniques exists, provided the needle is not placed through a lesion, and no overt CNS involvement is present.

The use of central neuraxial morphine in HSV parturients also remains controversial because of the suggestion that oral HSV is reactivated by the facial itching that can follow epidural and intrathecal morphine.[80] As this facial itching has also been suggested to serve only as a marker and not a trigger of oral HSV lesions,[81] further investigation is needed to evaluate this potential association. A final concern is HSV lesions of the skin, termed herpetic whitlows, which present an occupational, infectious hazard when contact with the lesions occur. Should contact occur, handwashing and oral antiviral medications may prevent an infection from occurring.[82]

Listeria

Listeria monocytogenes is a facultative anaerobic, gram-positive rod that produces β-hemolysis on blood agar. Rarely occurring in the population at large, *L. monocytogenes* infections have been estimated to occur at a 20-fold-higher rate during pregnancy.[83] Pregnancy-related decreases in T-cell-mediated immunity, a major defense against listeriosis, have been speculated to play a role. Although the exact pathogenesis of listeriosis is poorly understood, epidemics have demonstrated an association with the ingestion of contaminated food, especially nonpasteurized dairy products.[84]

Approximately two thirds of pregnant women with listeriosis present with fever, headache, myalgias, and other nonspecific flu-like symptoms, and one third will experience gastrointestinal symptoms, particularly diarrhea. Severe complications, including meningitis, encephalitis, adult respiratory distress syndrome, and death, are usually associated with an underlying debilitating disease or immunosuppression. Maternal fever followed by preterm labor (especially in the setting of an abnormal fetal heart rate tracing and "fetal distress" in labor) or in utero fetal demise has been associated with *Listeria*. Diagnostic confirmation requires isolation of *L. monocytogenes* from maternal or neonatal blood, fetal membranes, gastric aspirates, amniotic fluid, and placental tissue. Placental histology with evidence of microabscesses and a distinct multifocal villitis can also suggest the diagnosis following delivery.[85]

Intrauterine infections during pregnancy are believed to occur through hematogenous dissemination at the time of maternal septicemia; however, ascending organisms from the lower genital tract or perirectal area may also be responsible. Adverse pregnancy outcomes from listeriosis infections may occur at any gestational age, and perinatal mortality has been estimated to range from 20% to 50%. In Europe, *Listeria* has been reported to account for 0.5% to 3% of all cases of spontaneous abortion and preterm labor.[86]

When *Listeria* infection is suspected, prompt initiation of antibiotic therapy may improve perinatal survival.[83] Although the best antibiotic regimen has not been identified by clinical trials, parenteral ampicillin with gentamicin is usually given (see Table 26.4). Trimethaprim/sulfamethoxazole and erythromycin are also effective. Neonates should treated aggressively with broad-spectrum antibiotics, although the length of therapy is unknown. Perinatal outcome is determined primarily by the gestational age at delivery and complications related to prematurity.

Anesthetic Management

To date, there are no data regarding the implications of *Listeria* on anesthesia.

Lyme Disease

A disease caused by the spirochete *Borrelia burgdorferi sensu lato*, Lyme disease is the most common vector-borne disease in the United States. Also common in Europe, the spirochete is of a different genospecies, with the two most dominant being *B. garinii* and *B. afzelii*. Transmitted by the bite of deer ticks (*Ixodes scapularis*) and western black-legged ticks (*I. pacificus*), Lyme disease in the United States has increased about 25 fold since national surveillance began in 1982, with a mean of approximately 12,500 cases annually.[87] Lyme disease is most likely transmitted to humans during the tick nymph stage, when the ticks are most likely to feed and their small size prevents them from being noticed. The transmission of the infection most likely takes place after approximately 2 or more days of feeding. Lyme disease spirochetes can spread from the site of the tick bite by cutaneous, lymphatic, and bloodborne routes and have been identified in spinal, synovial, and amniotic fluids.

The most common presentation of Lyme disease is a characteristic "bull's eye" rash called erythema migrans, accompanied by nonspecific symptoms such as fever, malaise, fatigue, headache, myalgias, and arthalgias. Most individuals present with symptoms after an incubation period of 7 to 14

days, but some infected individuals are asymptomatic or only experience nonspecific symptoms. Rarely, cardiac and neurologic manifestations may occur. During pregnancy, *B. burgdorferi* can infect both the placenta and fetus; however, the risk for and timing of infection are unknown. Although maternal infection has been associated with preterm delivery, stillbirths, fetal neurologic abnormalities, and delayed neonatal effects [respiratory distress and sudden infant death syndrome (SIDS)], the overall risk of adverse outcomes appears low. Recent prospective and case-control studies have demonstrated no association between maternal Lyme disease and fetal cardiac defects.[88,89]

Diagnosis of Lyme disease is based primarily on clinical findings, and treatment is often commenced on the basis of symptoms or known exposure. Serologic testing may provide valuable diagnostic information; however, the tests are of variable sensitivity and specificity. A number of serologic tests are available, and the CDC recommends testing initially with an enzyme-linked immunosorbent assay (ELISA) or an indirect fluorescent antibody (IFA) test, with the more specific Western immunoblot (WB) test reserved for when equivocal results are obtained.

Treatment with doxycycline or amoxicillin (cefuroxime or erythromycin in persons allergic to the first two regimens) for 3 to 4 weeks is generally effective in early disease. With more advanced disease, particularly with neurologic manifestations, administration of intravenous ceftriaxone or penicillin for at least 4 weeks, noting that treatment failures may occur and that some symptoms may persist even with successful treatment. Aggressive treatment of Lyme disease during pregnancy may be warranted with the belief that a reduction in fetal or neonatal infection may occur, although the efficacy of this therapy is unknown.[90]

Antibiotic treatment in early disease may blunt an antibody response; however, patients with disseminated or late-stage disease usually have strong serologic reactivity and demonstrate expanded WB immunoglobulin G (IgG) banding. Antibodies, which often persist for months or years even after successful treatment, do not confer immunity from reinfection. A recombinant outer-surface protein A vaccine (LYMErix) for the prevention of Lyme disease has been developed, although it is not recommended during pregnancy.[87] Unfortunately, the vaccine does not protect all recipients against infection with *B. burgdorferi* and offers no protection against other tickborne diseases.

Anesthetic Management

Although the generalized malaise, skin lesions, and arthralgias are the most prominent symptoms of Lyme disease, CNS and cardiac system involvement may occur, and these have important implications for anesthesiologists. Meningitis, encephalitis, and motor and sensory peripheral neuropathies may occur,[91] and the avoidance of central neuraxial blockade may be prudent in these patients. In terms of cardiac anomalies, conduction blockade, pericarditis, valvular disorders, and cardiomyopathy have all been noted with Lyme disease[92,93]; as a consequence, an ECG, a directed cardiac examination, and possibly other tests should be considered before anesthesia.

Parvovirus B19

Composed of a single-stranded DNA virus, parvovirus B19 is responsible for childhood exanthem erythema infectiosum (fifth disease) and transient aplastic crisis in patients with underlying hemoglobinopathy. Even in immunocompromised individuals, parvovirus B19 infections are usually mild, requiring only supportive care.[94]

The disease is transmitted most commonly through respiratory secretions and hand-to-mouth contact. Infected persons remain infectious for 5 to 10 days following exposure.[95] Household members of infected persons have an approximately 50% risk of infection.[96] With the onset of a reticular rash on the trunk or other symptoms such as peripheral arthropathy, a loss of infectious risk occurs. Maternal diagnosis can be made through ELISA or WB tests of parvovirus B19 antibodies or through direct visualization of viral particles in infected tissues. IgM and IgG antibodies are produced in response to an infection and last a few months and indefinitely, respectively. When only IgG is detected, this represents both a prior infection and immunity. Seropositivity to parvovirus B19 increases with age, and more than 60% of adolescents and adults have antibodies.

Transplacental transmission of parvovirus B19 has been reported to be as high as 33%,[97] although the risk of serious fetal morbidity, such as hydrops fetalis, and spontaneous abortion and stillbirth is low.[98] Serious sequelae occur with infections before 20 weeks gestational age; however, should the fetus survive, long-term development tends to be normal.[99] Fetal parvovirus B19 can be diagnosed through the detection of viral particles or DNA in fetal specimens, including serum, amniotic fluid, placenta, or autopsy tissues.[100] Ultrasonography to detect the presence of hydrops for up to 10 weeks following maternal infection has also been advocated.[94]

Treatment for parvovirus B19 is primarily supportive. Should hydrops fetalis occur, treatment is unfortunately limited to performing percutaneous umbilical blood sampling for transfusion preparation if anemia is present.[101]

Anesthetic Management

To date, there are no data regarding the implications of parvovirus on anesthesia.

Rubella

Rubella is caused by a single-stranded RNA virus belonging to the togavirus family for which humans are the only natural host. Extremely contagious, with an attack rate within closed popu-

lations close to 100%, rubella is infectious from 7 days before to 14 days following the associated rash. Since rubella has a peak incidence among children 5 to 9 years of age and confers immunity for life once infected, only 6% to 8% of women of reproductive age remain susceptible to infection with rubella virus.[102]

Rubella is a respiratory disease transmitted by airborne or direct contact. The incubation period varies from 14 to 21 days. Due to the usually mild presentation of the disease, clinical diagnosis may be difficult. When present, symptoms can include a maculopapular 3-day rash of the face that can spread to the trunk and extremities, postauricular or occipital adenopathy, fever, transient arthralgias, and arthritis. Pregnancy does not affect the clinical manifestations.[103] Diagnosis can occur through viral isolation from nasopharyngeal secretions; however, few laboratories provide this service, and isolation takes 4 to 6 weeks. Testing for the more sensitive rubella-specific IgM antibody, which appears rapidly and remains detectable for up to 1 month or longer, is recommended. A fourfold increase in rubella-specific IgG may also be used for diagnostic confirmation.

Although transplacental infection may occur with primary maternal rubella infection, transmission rarely occurs with reinfection. Fetal infection can be confirmed through the detection of rubella-specific IgM or viral cultures from fetal blood or by rubella DNA isolation from chorionic villi.[104] Such testing, however, is rarely utilized, as the infection severity does not correlate accurately with viral presence. Congenital rubella syndrome results in a number of manifestations, including fetal growth restriction, ophthalmologic abnormalities (cataracts, microphthalmia, glaucoma, chorioretinitis), cardiac malformations, and neurologic manifestations (mental retardation, microcephaly, encephalitis). Sensorineural deafness is the most common consequence; however, thrombotic thrombocytopenic purpura, hepatosplenomegaly, myocarditis, pneumonitis, anemia, and jaundice may also be observed.

Although fetal infection may occur at any stage of pregnancy, the gestational age affects the manifestations,[105] with first trimester maternal infection producing a high incidence (70%–90%) of developmental malformations. By contrast, although structural defects do not occur as a consequence of infection during the third trimester of pregnancy, deafness and mental retardation may result. Moreover, the absence of clinical signs at birth does not exclude the possibility of subclinical damage or subsequent impairment; manifestations of congenital rubella infection (including endocrinopathies, hearing or visual impairment, and progressive panencephalitis) may develop up to 10 to 20 years later in 70% of individuals. Consequently, offspring of women who have sustained rubella infections during pregnancy should undergo long-term follow-up.

There is no effective treatment for rubella. Rubella vaccines produce seroconversion and long-term immunity from infection in 95% of cases. Complications of rubella vaccination include mild and self-limiting flu-like symptoms, fever, lymphadenopathy, and rash. Rubella vaccination is not recommended during pregnancy because of theoretical concerns of fetal damage. Despite this recommendation, the risk of congenital rubella syndrome from vaccination within 3 months of conception is considered negligible.[106] Clinicians should routinely offer the rubella vaccine to all potentially susceptible women lacking contraindications for vaccination.

Anesthetic Management

To date, there are no data regarding the implications of rubella on anesthesia.

Syphilis

An indolent systemic infection caused by the spirochete *Treponema pallidum*, syphilis has undergone a dramatic resurgence due to an increase in intravenous drug abuse and HIV.[107] Currently, the incidence of syphilis is 5 to 7 per 100,000 in the United States. Although men and women are currently infected in equal proportions, 80% of women with syphilis are of reproductive age, potentially risking fetal transmission.[107]

Transmitted most commonly through sexual contact, syphilis infection results in 30% to 50% of the cases where contact with a person with primary or secondary syphilis occurs.[108] This high transmission rate is due to the ability of *T. pallidum* to pass across abraded skin as well as intact mucous membranes. During pregnancy, no alterations occur in the characteristic clinical stages of the disease.

Because *T. pallidum* cannot be cultured, the diagnosis of syphilis requires either direct visualization of the organism (by dark-field microscopy or fluorescent antibody staining) or, more commonly, serologic testing. Newer diagnostic techniques (i.e., PCR) are currently being developed. Lumbar puncture is often performed, even during pregnancy, to assist in the evaluation of CNS symptoms, syphilis of unknown or advanced stages, and when concurrent immunosuppression exists. CSF abnormalities suggestive of syphilis infection include elevated counts of white cells ($\geq$5 cells/mm^3) and total proteins ($\geq$45 mg/dL), normal glucose concentrations, and a positive syphilis serologic test.

Antenatal syphilis poses a significant threat to the pregnancy and fetus and, if untreated, is associated with intrauterine growth restriction, stillbirth (30%), preterm birth, neonatal death (10%), and congenital infection ($>$60%).[107,109] Only 20% of children born to mothers with untreated syphilis will be normal.[110] *T. pallidum* readily crosses the placenta, and transmission can occur at any time during pregnancy and at any stage of the disease.[110] However, both the disease stage and fetal gestational age influence the rate of perinatal transmission. Vertical transmission is more common with primary (50%) and secondary syphilis (50%) as compared with early latent (40%), late latent (10%), and even tertiary syphilis (10%).[111] Universal antepartum screening and treatment with appropriate antibiotics could virtually eliminate syphilis dur-

ing pregnancy. Serologic screening should occur at the first prenatal visit and, in high-risk populations, again during the third trimester and at delivery. Mothers properly treated have a 1% to 2% risk of fetal transmission versus 70% to 100% for untreated mothers.[112]

Penicillin is the treatment of choice for syphilis in both pregnant and nonpregnant individuals due to its efficacy and the lack of resistant strains. Treatment is directed according to the stage of disease. Following treatment, treponemal antibody serologic titers should be checked at 1, 3, 6, 12, and 24 months. Titers should decrease fourfold by 6 months and become nonreactive by 12 to 24 months.[108] Titers that do not decrease appropriately suggest either treatment failure or reinfection, and treatment should be repeated. Treatment failure should be further evaluated by a lumbar puncture to evaluate CNS involvement and HIV testing.

In nonpregnant individuals with a history of penicillin allergy, recommended alternatives for the syphilis treatment include doxycycline, tetracycline, or erythromycin. In parturients, however, erythromycin fails to cross the placenta predictably, and doxycycline and tetracycline have adverse effects on developing bone and tooth enamel. As such, penicillin desensitization and treatment is the only satisfactory treatment, and treatment can be achieved either orally (which is simpler and safer) or intravenously.[113,114] Desensitization involves exposing the patient to a small amount of penicillin and gradually increasing the dose until an effective level is reached. The procedure requires approximately 4 h to accomplish and requires close patient monitoring.

Anesthetic Management

Significant concerns of late-stage syphilis include infection of the aorta and posterior neuraxial columns and roots. Aortic manifestations include regurgitation and aneurysms primarily of the ascending thoracic aorta; these entities create anesthetic implications in terms of the need for precise hemodynamic control and stability. Posterior column and root degeneration results in deterioration in sensation to position, deep pain, and temperature and disturbances in bladder control. Although little information exists on the effects of anesthesia in patients with syphilis, when significant posterior column involvement exists, consideration should be given to avoiding central neuraxial blockade, as the recovery from these forms of anesthesia may be difficult to assess.

Toxoplasmosis

Caused by the intracellular parasite *Toxoplasma gondii*, toxoplasmosis infects more than 60 million people in the United States alone.[115] Contact with infected materials such as animal feces or soil and ingestion of infected undercooked meats are common routes of infection. Rarely, infected blood transfusions or organ transplants may result in the disease.[115]

Infection usually presents as asymptomatic cervical lymphadenopathy, but after an incubation period of 5 to 18 days, nonspecific symptoms such as night sweats, fever, malaise, myalgias, and hepatosplenomegaly may occur. An intact immune system usually allows for a benign and self-limited course. By contrast, infection in immunosuppressed individuals and fetuses in utero can result in chorioretinitis, hearing loss, mental retardation, seizures, and hepatosplenomegaly. Vertical transmission risk is dependent on the timing of maternal infection, increasing from 10% to 60% from the first to third trimesters.[116] Earlier fetal transmission results in more severe disease, which is revealed in 55% to 85% of infected neonates not at birth but at later stages of life.

Although isolation of *T. gondii* from bodily fluids establishes an acute infection, serologic testing for antibodies is the primary method of diagnosis. IgM antibodies appear first, reach maximum levels in 1 month, and are followed by the immunity-conferring IgG antibodies. As high titers of both IgM and IgG may persist for years, both tests should be used for the initial evaluation. Although the Sabin–Feldman IgG test is the gold standard, it is performed in only a few laboratories; consequently, IFA, indirect hemagglutination, and ELISA testing are often used. Unfortunately, serologic assays for toxoplasmosis are not well standardized and have high false-positive rates. Therefore, serial testing 3 weeks apart, with specimen saving for repeat testing in recognized reference laboratories, has been recommended. In the United States, routine screening during pregnancy is currently not recommended, except for women with HIV or other exceptional circumstances.[117] In countries with a high prevalence of seropositivity, such as France and Austria, however, serologic screening has had a favorable impact and is routinely performed.[118]

Prior infection and treatment of toxoplasmosis before pregnancy does not confer a congenital transmission risk.[94] However, should the disease be diagnosed and treatment initiated during pregnancy, a risk of congenital infection exists.[119] Spiramycin, a drug available only through the U.S. Food and Drug Administration, may reduce fetal transmission by 60%[120] and should be started immediately. Fetal ultrasonography [for ventriculomegaly, intracranial calcifications, microcephaly, ascites, hepatosplenomegaly, and intrauterine growth restriction (IUGR)] and fetal blood sampling for IgM after 20 weeks gestation has been recommended.[94] Should fetal infection be established, pyrimethanmine, sulfonamides, and folinic acid are added to increase the efficacy against placental and fetal parasites.[121] Infants with congenital toxoplasmosis should continue treatment of pyrimethamine and sulfadiazine, alternating monthly with spiramycin, for 1 year. Treatment may diminish intracranial calcifications and improve neurologic function.[122]

Anesthetic Management

To date, there are no data regarding the implications of toxoplasmosis on anesthesia. However, as alterations in the pro-

duction or destruction of clotting proteins may occur during periods of hepatosplenomegaly, clotting parameters should be evaluated before surgical and anesthetic interventions. Should moderate or severe symptoms exist, careful evaluation for other potentially coexisting morbidities is prudent.

Tuberculosis

Tuberculosis (TB) refers to infection with *Mycobacterium tuberculosis*. After declining steadily for three decades, the number of cases of maternal and fetal TB reported annually in the United States began to rise again in the 1980s due to increases in both HIV infections and multidrug-resistant strains.[123] Although there is no apparent increase in TB progression during or immediately after pregnancy, most infected parturients are symptomatic and convert to a positive response to purified protein derivative (PPD) skin testing. Less common presentations include peritonitis, meningitis, mastitis, and paraplegia secondary to spinal osteomyelitis (Pott's disease).

Diagnosing TB can be difficult. Pregnant women considered to be at high risk for TB (including women with symptoms suggestive of TB, known recent exposure, seroconversion within the past 1 to 2 years, immunocompromised patients, and recent immigrant status) should be skin tested. Skin testing involves intradermal injection of 5 tuberculin units of PPD and measurement of the induration (not erythema) in 48 to 72 h. Interpretation of the PPD test depends on the risk status of the patient and is not affected by pregnancy. A positive reaction requires further investigation to exclude active disease, which includes a chest X-ray (usually a single anteroposterior view with abdominal shielding in pregnancy), submission of early-morning sputum specimens for smear and culture, and appropriate biopsy specimens if there is evidence of extrapulmonary disease. Although the demonstration of acid-fast bacilli (AFB) raises the possibility of TB, subsequent culture confirmation is mandatory because sputum may contain strains of nontuberculous mycobacterium.

Fetal TB transmission is believed to occur via ingestion or aspiration of infected amniotic fluid or direct seeding via the umbilical vein. During pregnancy, therapy does not differ, and a two-drug regimen, usually isoniazid (with pyridoxine) and rifampin, should be used for a minimum of 9 months. Extensive experience with isoniazid during pregnancy has noted its ability to cross the placenta with no apparent teratogenic effects.[124] Although rifampin crosses the placenta and may theoretically cause fetal injury through inhibition of DNA-dependent RNA polymerases, no such damage has been reported. Ethambutol can be added to the two-drug regimen should resistance exist, although an association with retrobulbar neuritis in adults has been noted; fetal exposure to ethambutol, however, appears safe. Streptomycin is contraindicated in pregnancy due to an association with VIIIth nerve injury and hearing impairment in up to 17% of infants. Ethionamide and cycloserine have been known to cause fetal neurologic injuries and should be avoided.

Postpartum, close physical contact with infected individuals may allow for neonatal transmission as well. Infants with congenital TB usually do not manifest signs of disease for several days to weeks after delivery, resulting in delayed treatment and a mortality rate approaching 50%.[125] In the majority of cases, nonspecific signs including respiratory distress, fever, lethargy, failure to thrive, lymphadenopathy, and hepatosplenomegaly are the only clues. With early diagnosis and treatment, however, neonatal treatment is usually successful.[126] Daily isoniazid and rifampin are the usual neonatal therapy, but a four-drug regimen (including isoniazid, rifampin, streptomycin, and pyrazinamide) is utilized for drug-resistant strains.

Mothers taking antituberculous medications can breastfeed; however, approximately 20% and 11% of the mother's isoniazid and other antituberculous drugs, respectively, appear in breast milk.[124] Thus, if an infected infant is also being independently treated, a dose reduction should be considered. With noninfected infants, although controversy surrounds leaving the child with the mother in the immediate postpartum period, in about 2 weeks on treatment, the mother should become noninfectious. Interestingly, bacille Clamette–Guérin (BCG) vaccine has limited efficacy in preventing disseminated tuberculosis in children[127] and may allow for the reactivation of an infection acquired previously. A history of BCG vaccination, which does not alter the interpretation of the PPD skin test, should not influence the subsequent management.

Anesthetic Management

Sometimes associated with severe restrictive lung disease, the pulmonary effects of TB represent the main concern for anesthesiologists. Although general anesthesia may be a consideration, should an emergent surgical delivery be necessary, the risk of massive hemoptysis with positive pressure ventilation in these patients has been described.[128] The extrapulmonary TB involvement of the CNS, pericardium, liver, and bone marrow are concerning as well. Vertebral column involvement, although usually of the thoracic spine, can affect other segments, and instability of the cervical spine has been reported.[129] This vertebral column involvement may present difficulties in placement and function of regional techniques or with induction and intubation during general anesthesia.

The treatment for TB may create important implications as well, significant toxicity of the peripheral nervous system, liver, and kidneys being reported with isoniazid. Peripheral neuropathy is preventable and reversible with pyridoxine. Should significant peripheral neuropathy and impairment of hepatic function be observed, a baseline neurologic status examination and laboratory analysis for coagulopathies, respectively, should be considered.

Varicella Zoster

Varicella zoster virus (VZV) is a DNA herpesvirus transmitted by respiratory droplets or close contact, with a very high transmission rate among susceptible contacts of 60% to 90%.[94] Known as chickenpox, the primary infection is characterized by fever, malaise, and a maculopapular, pruritic rash that is infectious 48 h before the rash until vesiculation and crusting are complete. In children, the primary infection is usually benign and self-limited. By stark contrast, in adults, severe complications such as encephalitis and pneumonitis can result; although less than 5% of varicella cases occur among individuals over 20 years of age, 55% of varicella-related deaths occur in this group.[130] Although antibodies against VZV develop within a few days of the onset of the infection and confer lifelong immunity, the virus remains latent in the sensory ganglia. With reactivation, a vesicular erythematous rash localized to one or more cutaneous dermatomes occurs, and this is known as herpes zoster.

The diagnosis of the primary infection is based on clinical findings. Although not required, tests identifying within skin lesions and vesicular fluid antigens or antibodies, by immunofluorescence or ELISA, respectively,[131] can be performed. Due to the highly contagious nature of VZV, only 5% of adults do not have protective immunity,[132] and consequently varicella infection is uncommon in pregnancy, occurring in 0.4 to 0.7 per 1000 live births.[131] Should infection occur, however, significant maternal, fetal, and neonatal effects result. Varicella pneumonitis is particularly serious in pregnancy, with a maternal mortality rate of 50%.[133] Fetal infection is difficult to diagnose. Ultrasound findings (including hydrops fetalis, echogenic foci in the liver and bowel, cardiac malformations, limb deformities, microcephaly, or IUGR) are nonspecific. Moreover, virus identification by antibodies, cultures, or DNA identification in chorionic villi, amniotic fluid, or fetal blood is difficult and does not accurately predict the severity of fetal infection.[134,135] Ultimately, fetal skin scarring, limb hypoplasia, chorioretinitis, and microcephaly may occur.[136,137] Neonatal VZV infection is associated with a high mortality rate, especially when maternal disease develops from 5 days before to 2 days after delivery. This is a result of the relative immaturity of the neonatal immune system and the lack of protective maternal antibodies.[138]

Oral acyclovir, if instituted within 24 h of the rash, has been shown to reduce the number and duration of new lesions and improve the constitutional symptoms in healthy adults.[139] Although appearing safe for use in pregnancy, oral acyclovir has not been shown to prevent or ameliorate the fetal effects of congenital varicella syndrome.[140] Maternal varicella complicated by pneumonitis should be treated with intravenous acyclovir. Varicella immunoglobulin (VZIG) should be given to infants born to women who develop varicella between 5 days before and 2 days after delivery, although this does not universally prevent neonatal varicella.[141]

Because treatment options are limited, efforts should be made to identify and vaccinate nonpregnant women of childbearing age who are nonimmune.[132] As the vaccine is a live attenuated strain, it is not approved for use during pregnancy, and conception should be delayed until 1 month after the second vaccination dose is given. Nonimmune women should also be counseled to avoid contact with individuals who have chickenpox; however, if exposure occurs, administration of VZIG should occur as soon as possible, up to 72 h afterward, to prevent or attenuate the maternal disease.[142] Unfortunately, should VZIG fail to prevent the disease, no alterations of fetal infection occur as the result of its administration.

Anesthetic Management

As mentioned, varicella pneumonia can be critical, and infected patients are often admitted to the intensive care unit, where adult respiratory distress syndrome (ARDS) therapy with intubation and ventilator support may ensue. Should anesthesia be necessary in an unintubated patient with respiratory distress, such as for cesarean delivery to improve the health of the mother as well as the fetus, the use of general anesthesia is most likely the best option. Should regional anesthesia be attempted, the degree of pulmonary compromise may become unacceptable, especially with a high anesthetic level and the patient in the supine with left uterine displacement position.

The most frequent contact anesthesiologists have with patients with VZV is when reactivation of the latent virus occurs and patients seek help for pain management. The debilitating pain is difficult to control, and a number of topical agents and invasive blockades of sympathetic, peripheral nerve, and even central neuraxial pathways have been evaluated with only limited success.[143]

Summary

A number of infections are associated with significant maternal and fetal consequences. In general, perinatal infections have more serious fetal consequences when they occur early in gestation, because they may disrupt organogenesis. By contrast, second and third trimester infections are more likely to cause neurologic impairment or growth disturbances. With few exceptions, treatment of infectious diseases is not altered substantially by pregnancy; however, as infectious diseases often dramatically affect the outcome of the pregnancy, obstetric and anesthetic management decisions should be directed with awareness of these pathogens to optimize the outcome for mother and infant.

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