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Transmission of infectious diseases through breast milk and breastfeeding

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A large body of evidence clearly demonstrates the protective effects of breastfeeding and documents the transmission of specific infections to the infant through breast milk. The fear and anxiety that arise with the occurrence of any infectious disease are even greater in the situation of the breastfeeding mother-infant dyad. Uncertainty and lack of knowledge often lead to proscribing against breastfeeding out of fear, which then deprives the infant of the potential protective, nutritional, and emotional benefits of breastfeeding exactly at the time when they are most needed (see the dynamic nature of immunologic benefit, Chapter 5). Decisions concerning breastfeeding in the mother with an infectious illness should balance the potential benefits of breastfeeding versus the known or estimated risk of the infant acquiring a clinically significant infection via breastfeeding and the potential severity of the infection.

Documenting transmission of infection from mother to infant by breastfeeding requires not only the exclusion of other possible mechanisms of transmission but also the demonstration of the infectious agent in the breast milk and a subsequent clinically significant infection in the infant caused by a plausible infectious process. The first step is to establish the occurrence of a specific infection (clinically or immunologically evident) in the mother and demonstrate the persistence of the infectious agent in the mother such that it could still be transmitted to the infant. Isolation or identification of the infectious agent from the colostrum, breast milk, or an infectious lesion of the breast is important but not necessarily proof of transmission to the infant. Epidemiologic evidence of transmission must be considered, including identifying characteristics of the organism that relate an isolate from the infant to the maternal isolate. Infectious organisms can reach the breast milk either by secretion in the fluid or cellular components of breast milk or by contamination of the milk at the time of or after expression. A reasonable mechanism of infection via breast milk should be evident and proved through either

animal or human studies. Demonstration of a subclinical or clinically evident infection in the infant should follow these outlined steps.

Exclusion of other possible mechanisms of transmission (exposure to the mother or other persons/animals via airborne, droplet, arthropod, or vector modes of transmission or through direct contact with other infectious fluids) would complete the confirmation of transmission of infection via breastfeeding. It is essential to exclude prenatal or perinatal transmission of infection to the fetus/infant, but doing this can often be difficult.

Clinical case reports or studies confirming the isolation of an infectious agent from the milk are important. To determine a reasonable estimate of the risk of infection via breast milk, larger epidemiologic studies are needed, comparing infection rates in breastfed infants versus formula fed infants, addressing the issues just identified. Timing of breastfeeding is important relative to the timing of maternal infection and to the presence of a pathogen in colostrum or breast milk. The duration of breastfeeding is another important variable to consider in the estimate of risk, because shedding of a pathogen in breast milk may be intermittent.

These considerations are only some of the variables to be taken into account, in general, to assess the risk of transmission of an infectious agent from mother to infant via breast milk or breastfeeding. Efforts to prove transmission of infection in a particular maternal-infant dyad can be just as difficult and must consider many of the same factors.

This chapter focuses on a discussion of specific, clinically relevant, infectious agents and diseases, with reasonable estimates of the risk of infection to the infant from breastfeeding. The basic tenet concerning breastfeeding and infection is that *breastfeeding is rarely contraindicated in maternal infection*. The few exceptions relate to specific infectious agents with strong evidence of transmission and to the association of the infant's illness with significant morbidity and mortality.

The risk or benefit of breastfeeding relative to immunization of the mother or infant is discussed for certain microorganisms. Chapter 11 addresses use of antimicrobial agents in the breastfeeding mother, and Chapter 5 reviews how breastfeeding may protect against infection. Chapter 21 addresses specific concerns relating to banked breast milk and includes standards developed by the Human Milk Banking Association of North America to guide the appropriate handling of banked human milk relative to possible infectious agents.

INFECTION CONTROL CONSIDERATIONS

Isolation precautions have undergone some revisions in terminology and conceptualization.[99] Understanding that the transmission of microorganisms can occur with a known infection and with unrecognized sources of infection, recommendations have been made for standard precautions to be applied to all patients to protect health care workers from potentially infectious body fluids. Additionally, precautions based on the predominant modes of transmission have been recommended to protect against infection through the airborne route, direct contact, or contact with droplets. Although these precautions are intended to be used in clinical situations to protect health care workers, they may be applied in certain situations to the mother-infant dyad to prevent transmission of infectious agents from one to the other or to other hospitalized mothers and infants. These precautions are useful most often when the mother and infant are still hospitalized. The use of such precautions within the home is not meant to limit breastfeeding. They are intended to allow breastfeeding in the majority of cases and to facilitate the continuation of breastfeeding with some additional safeguards in certain situations, after short temporary periods of stopping breastfeeding and when to safely use expressed breast milk (see Appendix E).

Standard precautions

Standard precautions include preventing contact with blood, all body fluids, secretions and excretions, nonintact skin, and mucous membranes by

(1) careful handwashing before and after every patient contact; (2) use of gloves when touching body fluids, nonintact skin, or mucous membranes or any items contaminated with body fluids (linens, equipment, devices, etc.); (3) use of nonsterile gowns to prevent contact of clothing with body fluids; (4) use of masks, eye protection, or face shields when splashing with body fluids is possible; and (5) appropriate disposal of these materials. Standard precautions should be applied to all patients regardless of actual or perceived risks. *The CDC (Centers for Disease Control and Prevention) does not consider breast milk a body fluid with infectious risks for such policies*.

In considering the breastfeeding infant-mother dyad and standard precautions, body fluids other than breast milk should be avoided, and only in specified situations should breast milk also be avoided. In general, clothing or a gown for the mother and bandages, if necessary, should prevent direct contact with nonintact skin or secretions. Avoiding infant contact with maternal mucous membranes requires mothers to be aware of and understand the risks and to make a conscious effort to avoid this type of contact. The use of gloves, gowns, and masks by the infant for protection is neither practical nor appropriate. The recommendations concerning the appropriateness of breastfeeding and breast milk are addressed for specific infectious agents throughout this chapter. Human immunodeficiency virus (HIV) infection is an example of one infection that can be prevented by the use of standard precautions, including avoiding breast milk and breastfeeding. The recommendations concerning breastfeeding and HIV and the various variables and considerations involved are discussed later.

Airborne Precautions

Airborne precautions are intended to prevent transmission via droplet nuclei (dried respiratory particles smaller than 5 μm that contain microorganisms and can remain suspended in the air for long periods) or dust particles containing microorganisms. Airborne precautions include the use of a private room with negative-air-pressure ventilation and masks at all times. In the case of pulmonary tuberculosis (TB), respiratory protective devices (requiring personal fitting and seal testing before use) should be worn. Airborne precautions are recommended with measles, varicella or disseminated zoster, and TB. Breastfeeding in the situation of these maternal infections is prohibited for the infectious period. This is to protect against airborne contact with the mother and to allow the infant to be fed the mother's expressed breast milk by another individual. The exception to allowing breast milk would be local involvement of the breast by varicella-zoster lesions or *Mycobacterium tuberculosis*, such that the milk becomes contaminated by the infectious agent.

Transmission via droplets occurs when an individual produces droplets that travel only a short distance in the air and then contact a new host's eyes, nose, mouth, or skin. The common mechanisms for producing droplets include coughing, sneezing, talking (singing or yelling), suctioning, intubation, nasogastric tube placement, and bronchoscopy. Droplet precautions include the use of a private room (preferred) and a mask if within 3 feet (0.9 m) of the patient, in addition to standard precautions applied to all patients. Droplet precautions are recommended for adenovirus, diphtheria, respiratory infections, *Haemophilus influenzae, Neisseria meningitidis* or invasive infection, influenza, mumps, mycoplasma, parvovirus, pertussis, plague (pneumonic), rubella, and streptococcal pharyngitis, pneumonia, or scarlet fever. The institution of droplet precautions with a breastfeeding mother who has these infections should be specified for each particular infection. This may require some period of separation for the infant and mother (for duration of the illness, for short-term or complete treatment of the mother, for the infectious period) with use of expressed breast milk for nutrition in the interim. Prophylactic treatment of the infant, maternal use of a mask during breastfeeding or close contact combined with meticulous handwashing, and the mother's avoidance of touching

her mucous membranes may be adequate and reasonable with regard to certain infections.

Contact Precautions

Contact precautions are meant to prevent transmission of infection via direct contact (contact between the body surfaces of one individual with another) and indirect contact (contact of a susceptible host with an object contaminated with microorganisms from another individual). Contact precautions include cohorting or a private room, gloves and gowns at all times, and handwashing after removal of gown and gloves. Contact precautions are recommended for a long list of infections, such as diarrhea in diapered or incontinent patients with *Clostridium difficile* infection, *Escherichia coli* O157:H7, shigella, rotavirus, hepatitis A, respiratory illness with parainfluenza virus or respiratory syncytial virus, multidrug-resistant bacteria (e.g., enterococci, staphylococci, gram-negative organisms), enteroviral infections, cutaneous diphtheria, impetigo, herpes simplex virus infection, herpes zoster (disseminated or in immunocompromised individuals), pediculosis, scabies, *Staphylococcus aureus* skin infection, viral hemorrhagic fevers (e.g., Ebola, Lassa), conjunctivitis and abscesses, cellulitis, or decubiti that cannot be contained by dressings.[61] With regard to the breastfeeding infant-mother dyad, implementation of precautions for each of these infections in the mother requires meticulous attention to gowning and handwashing by the mother, as well as a specialized plan for each situation.

Each of these transmission-based precautions can be used together for organisms or illnesses that can be transmitted by more than one route. They should always be used in conjunction with standard precautions, which are recommended for all patients. The *Red Book: Report of the Committee on Infectious Diseases* by the American Academy of Pediatrics (AAP)[62] remains an excellent resource for infection control guidelines and recommendations to prevent transmission in specific situations and infections.

CLINICAL SYNDROMES AND CONDITIONS

Microorganisms produce a whole spectrum of clinical illnesses affecting the mother and infant. Many situations carry the risk of transmission of the involved organism from the mother to the infant, or vice versa; in general, however, the infant is at greater risk because of such factors as inoculum size and immature immune response. As always, the infection must be accurately diagnosed in a timely manner. Empiric therapy and initial infection control precautions should begin promptly, based on the clinical syndrome and the most likely etiologic agents. When dealing with a maternal infection, clarifying the possible modes of transmission and estimating the relative risk of transmission to the infant are essential first steps to decision making concerning the issues of isolating the mother from the infant and the appropriateness of continuing breastfeeding or providing expressed breast milk. Breastfeeding infrequently is contraindicated in specific maternal infections. Often the question of isolation and interruption of breastfeeding arises when symptoms of fever, pain, inflammation, or other manifestations of illness first develop in the mother and the diagnosis is still in doubt. A clinical judgment must be made as to the site of infection, probable organisms involved, possible or actual mechanisms of transmission of these organisms to the infant, estimated virulence of the organism, and likely susceptibility of the infant. Additionally, by the time the illness is clearly recognized or diagnosed in the mother, the infant has already been exposed. Given the dynamic nature of the immunologic benefits of breast milk, continuation of breastfeeding at the time of diagnosis or illness in the mother can provide the infant protection rather than continued exposure in most illnesses. Rarely is stopping breastfeeding necessary. Many situations associated with maternal fever do not require separation of the mother and infant, such as engorgement of the breasts, atelectasis, localized nonsuppurative phlebitis, or urinary tract infection (UTI).

Appendix E lists a number of clinical syndromes, conditions, and organisms that require infection control precautions in the hospital. This appendix also includes short lists of possible etiologic agents for these conditions and appropriate precautions and recommendations concerning breastfeeding for different scenarios or organisms. This chapter considers specific infectious agents that are very common, clinically significant, or of particular interest.

BACTERIAL INFECTIONS

Anthrax

Bacillus anthracis, a gram-positive, spore-forming rod, causes zoonotic disease world wide. Human infection typically occurs due to contact with animals or their products. Three forms of human disease occur: cutaneous anthrax (the most common), inhalation anthrax, and gastrointestinal disease (rare). Person-to-person transmission can occur as a result of discharge from cutaneous lesions, but there is no evidence of human-to-human transmission of inhalational anthrax. There is no evidence of transmission of anthrax via breast milk. Standard contact isolation is appropriate for hospitalized patients or patients with draining skin lesions.

The issue of anthrax as a biologic weapon has exaggerated its relative importance as a cause of human disease. The primary concerns regarding anthrax and breastfeeding are antimicrobial therapy or prophylaxis in breastfeeding mothers and the possibility that the infant and mother were exposed by intentional aerosolization of anthrax spores. The Centers for Disease Control and Prevention have published recommendations for treatment and prophylaxis in infants, children, and breastfeeding mothers.[47] Those recommendations include the use of ciprofloxacin, doxycycline, and amoxicillin as well as several other agents without discontinuing breastfeeding. There is little available information on ciprofloxacin and doxycycline in breast milk for the prolonged periods of therapy or prophylaxis (60 days) and their possible effect on infant's teeth and bone/cartilage growth over that time period. Depending on the clinical situation and sensitivity testing of the identified anthrax strain, other agents can be substituted to complete the 60-day course. The AAP has approved the use of ciprofloxacin and doxycycline for breastfeeding women for short courses of therapy (less than several weeks).

Simultaneous exposure of the infant and mother could occur from primary aerosolization or from spores "contaminating" the local environment. In either case decontamination of the mother-infant dyad's environment should be considered.

Breastfeeding can continue during the mother's therapy for anthrax, as long as she is physically well. Open cutaneous lesions should be carefully covered and depending on the situation, simultaneous prophylaxis for the infant may be appropriate.

Botulism

Considerable justifiable concern has been expressed because of the reports of sudden infant death from botulism. Infant botulism is distinguished from food-borne botulism from improperly preserved food containing the toxin and from wound botulism from spores entering the wound. Infant botulism occurs when the spores of *Clostridium botulinum* germinate and multiply in the gut and produce the botulinal toxin in the gastrointestinal tract.[14] The toxin binds presynaptically at the neuromuscular junction, preventing acetylcholine release. The clinical picture is a descending, symmetric flaccid paralysis. Not every individual who has *C. botulinum* identified in the stool experiences a clinical illness. The age of the infant seems to relate to their susceptibility to illness. The illness is mainly in children younger than 12 months of age; the youngest patient described in the literature was 6 days old. Most children become ill between 6 weeks and 6 months of age. The onset of illness seems to occur earlier in formula fed infants compared with breastfed infants. When a previously healthy infant under 6 months of age develops constipation, then weakness and difficulty sucking, swallowing, crying, or breathing, botulism is a likely diagnosis. The

organisms should be looked for in the stools, and electromyography (EMG) may or may not be helpful.

In a group reviewed by Arnon and associates,[16] 33 of 50 patients hospitalized in California were still being nursed at onset of the illness. A beneficial effect of human milk was observed in the difference in the mean age at onset, with breastfed infants being twice as old as formula fed infants with the disease. The breastfed infants' symptoms were milder. Breastfed infants receiving iron supplements developed the disease earlier than those who were breastfed but unsupplemented. Of the cases of sudden infant death from botulism, no infants were breastfed within 10 weeks of death. All were receiving iron-fortified formulas. In most cases, no specific food course of *C. botulinum* can be identified, but honey is the food most often implicated and corn syrup has been implicated in infants older than 2 months of age. Honey may contain botulism spores, which can germinate in the infant gut. However, botulin toxin has not been identified in honey. It has been recommended that honey not be given to infants under 12 months of age. This includes putting honey on a mother's nipples to initiate an infant's interest in suckling.

Arnon[15] reviewed the first 10 years of infant botulism monitoring worldwide. The disease has been reported from 41 of the 50 states and from eight countries on four continents. The relationship to breastfeeding and human milk is unclear. In general, the acid stools (pH 5.1 to 5.4) of human milk fed infants encourage *Bifidobacterium* species. Few facultative anaerobic bacteria, or clostridia, existing as spores, are present in breastfed infants. In contrast, formula fed infants have stool pHs ranging from 5.9 to 8.0, with few *bifidobacteria*, primarily gram-negative bacteria, especially coliforms and *Bacteroides* species. *C. botulinum* and toxin production declines with pH and usually stops below 4.6. Breast milk also contains the protective immunologic components.

The relationship between the introduction of solid foods or weaning in both formula fed and breastfed infants and the onset of botulism remains unclear. For the breastfed infant, the introduction of solid food may cause a major change in the gut with a rapid rise in the growth of enterobacteria and enterococci followed by progressive colonization by *Bacteroides* species, clostridia, and anaerobic streptococci. Feeding solids to formula fed infants minimally changes the gut flora as these organisms already predominate. Although more hospitalized infants have been breastfed, sudden-death victims are younger and have been formula fed, which supports the concept of immunologic protection in the gut of the breastfed infant.

Much work remains to understand this disease. Clinically, constipation, weakness, and hypotonicity in a previously healthy child constitute botulism until ruled out especially with recent dietary changes. At this time, no reason exists to suspect breastfeeding as a risk for infant botulism, and some evidence suggests a possible protective effect from breastfeeding. Breastfeeding should continue if botulism is suspected in the mother or infant.

Brucellosis

Brucella melitensis has been isolated in the milk of animals. Foods and animals represent the primary sources of infection in humans. Brucellosis demonstrates a broad spectrum of illness in humans, from subclinical to subacute to chronic illness with nonspecific signs of weakness, fever, malaise, body aches, fatigue, sweats, arthralgia, and lymphadenitis. In areas where the disease is enzootic, childhood illness has been described more frequently. The clinical manifestations in children are similar to those in adults.[167] Infection can occur during pregnancy, leading to abortion (infrequently), and can produce transplacental spread, causing neonatal infection (rarely). The transmission of *B. melitensis* through breast milk has been implicated in neonatal infection, although not proved.[167,168] Interruption of breastfeeding with breast pumping and discarding the milk to continue stimulation of milk production is appropriate; breastfeeding should then continue after an initial period of 48 to 72 hours of therapy in the mother. Acceptable medications for treating

the mother while continuing breastfeeding include streptomycin, tetracycline, trimethoprim-sulfamethoxazole (TMP-SMX), and rifampin (see Appendix E).

Chlamydial infections

Chlamydial infection is the most frequent sexually transmitted disease (STD) in the United States and is a frequent cause of conjunctivitis and pneumonitis in the infant from perinatal infection. The major determinant of whether chlamydial infection occurs in the newborn is the prevalence rate of chlamydial infection of the cervix.[228] Specific chlamydial immunoglobulin A (IgA) has been found in colostrum and breast milk in a small number of postpartum women who were seropositive for *Chlamydia*. No information is available on the role of milk antibodies in protection against infection in the infant.[243] It is not believed that *Chlamydia* is transmitted via breast milk. Use of erythromycin or tetracycline to treat the mother and oral erythromycin and ophthalmic preparations of tetracyclines, erythromycin, or sulfonamides to treat suspected infection in the infant are appropriate during continued breastfeeding. Separating the infant from a mother with chlamydial infection or stopping breastfeeding is not indicated.

Diphtheria

Corynebacterium diphtheriae causes several forms of clinical disease, including membranous nasopharyngitis, obstructive laryngotracheitis, and cutaneous infection. Complications can include airway obstruction from membrane formation and toxin-mediated central nervous system (CNS) disease or myocarditis. The overall incidence of diphtheria has declined even though immunization does not prevent infection but does prevent severe disease from toxin production. Fewer than five cases are reported annually in the United States.

Transmission occurs via droplets or direct contact with contaminated secretions from the nose, throat, eye, or skin. Infection occurs in individuals whether they have been immunized or not, but infection in those not immunized is more severe and prolonged. As long as the skin of the breast is not involved, no risk of transmission exists via breast milk. No toxin-mediated disease from toxin transmitted through breast milk has been reported in an infant.

Breastfeeding, along with chemoprophylaxis and immunization of the infant, is appropriate in the absence of cutaneous breast involvement (see Appendix E).

Haemophilus influenzae

Haemophilus influenzae type B can cause severe invasive disease such as meningitis, sinusitis, pneumonia, epiglottitis, septic arthritis, pericarditis, and bacteremia. Shock can also occur. Since the increased utilization of the *H. influenzae* type B conjugate vaccines, invasive disease caused by *Haemophilus* has decreased dramatically, more than 95%, in the United States. Most invasive disease occurs in children 3 months to 3 years of age. Older children and adults rarely experience severe disease but do serve as sources of infection for young children. Children younger than 3 months of age seem to be protected because of passively acquired antibodies from the mother, and some additional benefit may be received from breast milk.

Transmission occurs through contact with respiratory secretions, and droplet precautions are protective. No evidence suggests transmission through breast milk or breastfeeding. There is evidence that breast milk limits the colonization of *H. influenzae* in the throat.[126]

In the rare case of maternal infection, an inadequately immunized infant in the household is an indication to provide rifampin prophylaxis and close observation for all household contacts, including the breastfeeding infant. Expressed breast milk can be given to the infant during the 24-hour separation after the mother's initiation of antimicrobial therapy, or if the mother's illness prevents breastfeeding, it can be reinitiated when the mother is able (see Appendix E).

Leprosy

Although uncommon in the United States, leprosy occurs throughout the world. This chronic disease presents with a spectrum of symptoms depending on the tissues involved (typically the skin, peripheral nerves, and mucous membranes of the upper respiratory tract) and the cellular immune response to the causative organism, *Mycobacterium leprae*. Transmission occurs through long-term contact with individuals with untreated or multibacillary (large numbers of organisms in the tissues) disease.

Leprosy is not a contraindication to breastfeeding, according to Jeliffe and Jeliffe.[138] The importance of breastfeeding and urgency of treatment are recognized by experts who treat the infant and mother early and simultaneously. No mother-infant contact is permitted except to breastfeed. Dapsone, rifampin, and clofazimine are typically and safely used for the infant and mother regardless of the method of feeding (see Appendix D).

Listeriosis

Listeriosis is a relatively uncommon infection that can have a broad range of manifestations. In immunocompetent individuals, including pregnant women, the infection can vary from being asymptomatic to presenting as an influenza-like illness, occasionally with gastrointestinal (GI) symptoms or back pain. Severe disease occurs more frequently in immunodeficient individuals or infants infected in the perinatal period (pneumonia, sepsis, meningitis, granulomatosis infantisepticum).

Although listeriosis during pregnancy may manifest as mild disease in the mother and is often difficult to recognize and diagnose, it is typically associated with stillbirth, abortion, and premature delivery. It is believed that transmission occurs through the transplacental hematogenous route, infecting the amniotic fluid, although ascending infection from the genital tract may occur.[83] Early and effective treatment of the mother can prevent fetal infection and sequelae.[140,165] Neonatal infection occurs as either early- or late-onset infection from transplacental spread late in pregnancy, ascending infection during labor and delivery, infection during passage through the birth canal, or, rarely, during postnatal exposure.

No evidence in the literature suggests transmission of *Listeria* through breast milk. Treatment of the mother with ampicillin, penicillin, or TMP-SMX is not a contraindication to breastfeeding as long as the mother is well enough. Expressed colostrum or breast milk also can be given as long as the infant is able to feed orally. The management of lactation and feeding in neonatal listeriosis is conducted supportively, as it is in any situation in which the infant is extremely ill, beginning feeding with expressed milk or directly breastfeeding as soon as reasonable.

Meningococcal infections

Neisseria meningitidis most often causes severe invasive infections, including meningococcemia or meningitis often associated with fever and a rash and progressing to purpura, disseminated intravascular coagulation (DIC), shock, coma, and death.

Transmission occurs via respiratory droplets. Spread can occur from an infected, ill individual or from an asymptomatic carrier. Droplet precautions are recommended until 24 hours after initiation of effective therapy. Despite the frequent occurrence of bacteremia, no evidence indicates breast involvement or transmission through breast milk.

The risk of maternal infection to the infant after birth is from droplet exposure and exists whether the infant is breastfeeding or bottle feeding. In either case the exposed infant should receive chemoprophylaxis with rifampin, 10 mg/kg/dose every 12 hours for 2 days (5 mg/kg/dose for infants less than 1 month of age), or ceftriaxone, 125 mg intramuscularly (IM) once, for children less than 12 years of age. Close observation of the infant should continue for 7 days, and breastfeeding during and after prophylaxis is appropriate. The severity of maternal illness may prevent breastfeeding, but it can continue if the mother is able, once the mother and infant have begun receiving antibiotics for 24 hours. A period of separation from the index case for the first 24 hours of effective therapy is

recommended; expressed breast milk can be given during this period.

Pertussis

Respiratory illness caused by *Bordetella pertussis* evolves in three stages: *catarrhal* (nasal discharge, congestion, increasing cough), *paroxysmal* (severe paroxysms of cough sometimes ending in an inspiratory whoop, i.e., whooping cough), and *convalescent* (gradual improvement in symptoms).

Transmission is via respiratory droplets. The greatest risk of transmission occurs in the catarrhal phase, often before the diagnosis of pertussis. The nasopharyngeal culture usually becomes negative after 5 days of antibiotic therapy. Chemoprophylaxis for all household contacts is routinely recommended. No evidence indicates transmission through breast milk, with similar risk to breastfed and bottle fed infants.

In the case of maternal infection with pertussis, chemoprophylaxis for all household contacts, regardless of age or immunization status, is indicated. In addition to chemoprophylaxis of the infant, close observation and subsequent immunization (in infants older than 6 weeks of age) are appropriate. Despite chemoprophylaxis, droplet precautions and separation of the mother and infant during the first 5 days of effective maternal antibiotic therapy are recommended. Expressed breast milk can be provided to the infant during this period.

Tuberculosis

The face of TB is changing throughout the world. In the United States the incidence of TB rose during 1986 through 1993 and has been declining since then.[40] Increased rates of TB were noted in adults between 25 and 45 years of age, and because these are the primary childbearing years, the risk of transmission to children increased.

Tuberculosis during pregnancy has always been a significant concern for patient and physician alike.[213] It is now clear that the course and prognosis of TB in pregnancy are less affected by the pregnancy and more determined by the location and extent of disease, as defined primarily by the chest radiograph, and by the susceptibility of the individual patient. Untreated TB in pregnancy is associated with maternal and infant mortality rates of 30% to 40%.[229] Effective therapy is crucial to the clinical outcome in both pregnant and nonpregnant women. TB during pregnancy rarely results in congenital TB.

Any individual in a high-risk group for TB should be screened with a tuberculin skin test (TST). No contraindication or altered responsiveness to the TST exists during pregnancy or breastfeeding. Interpretation of the TST should follow the most recent guidelines, using different sizes of induration in different-risk populations as cutoffs for a positive test, as proposed by the CDC.[43] Figure 17-1 outlines the evaluation and treatment of a pregnant woman with a positive TST.[249]

Treatment of active TB should begin as soon as the diagnosis is made, regardless of the fetus' gestational age, because the risk of disease to the mother and fetus clearly outweighs the risks of treatment. Isoniazid, rifampin, and ethambutol have been used safely in all three trimesters. Isoniazid and pyridoxine therapy during breastfeeding is safe, although the risk of hepatotoxicity in the mother may be a concern during the first 2 months post partum.[245]

Congenital TB is extremely rare if one considers that 7 to 8 million cases of TB occur each year worldwide and that less than 300 cases of congenital TB have been reported in the literature. As with other infectious diseases presenting in the perinatal period, distinguishing congenital infection from perinatal or postnatal TB in the infant can be difficult.

Postnatal TB infection in infancy typically presents with severe disease and extrapulmonary extension (meningitis, lymphadenopathy, and bone, liver, spleen involvement). Airborne transmission of TB to infants is the major mode of postnatal infection because of close and prolonged exposure in enclosed spaces, especially in their own household, to any adult with infectious pulmonary TB. Potential infectious sources could be the mother or any adult caregiver, such as babysitters, daycare workers, relatives, friends, neighbors, and even health care workers.

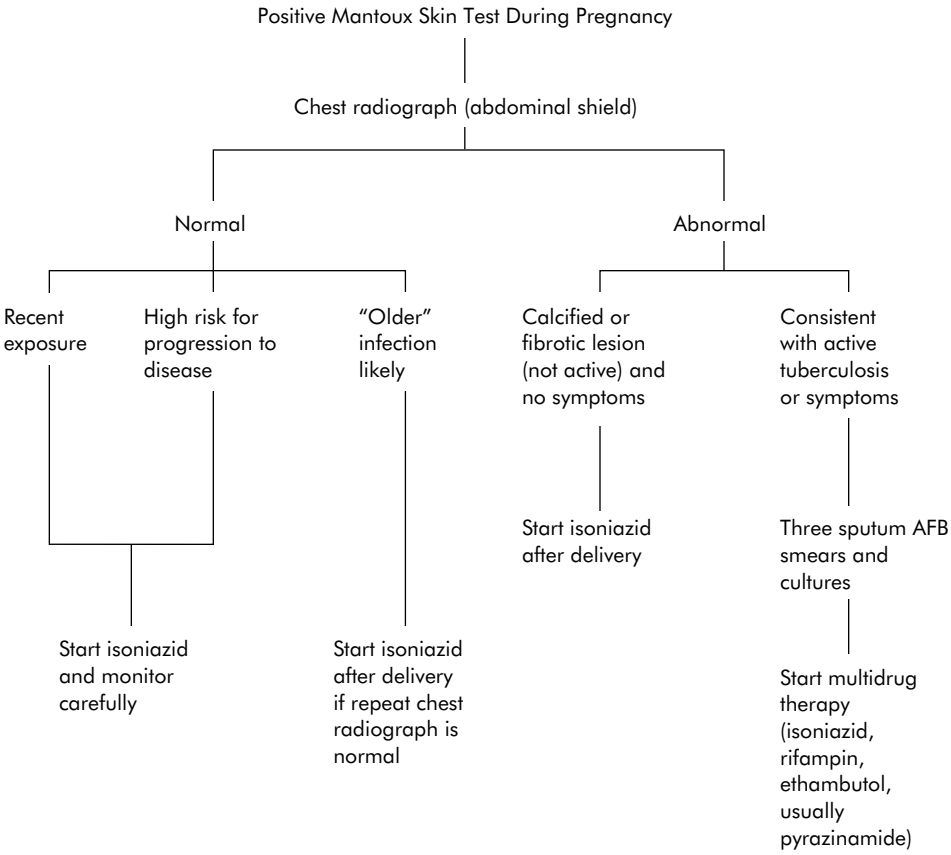


Figure 17-1. Evaluation and treatment of pregnant woman with positive tuberculin skin test. (From Starke JR: Tuberculosis, an old disease but a new threat to mother, fetus, and neonate. Clin Perinatol 24:107, 1997.)

The suspicion of TB infection or disease in a household with possible exposure of an infant is a highly anxiety-provoking situation (Fig. 17-2). Although protection of the infant from infection is foremost in everyone's mind, separation of the infant from the mother should be avoided when reasonable. Every situation is unique, and the best approach will vary according to the specifics of the case and accepted principles of TB management. The first step in caring for the potentially exposed infant is to determine accurately the true TB status of the suspected case (mother or household contact). This prompt evaluation should include a complete history (previous TB infection or disease, previous or ongoing TB treatment, TST status, symptoms suggestive of active TB, results of most recent chest radiograph, sputum smears, or cultures), physical examination, a TST if indicated, a new chest radiograph, and mycobacterial cultures and smears of any suspected sites of infection. All household contacts should be evaluated promptly, including history and TST with further evaluation as indicated.[43] Continued risk to the infant can occur from infectious household contacts who have not been effectively evaluated and treated.

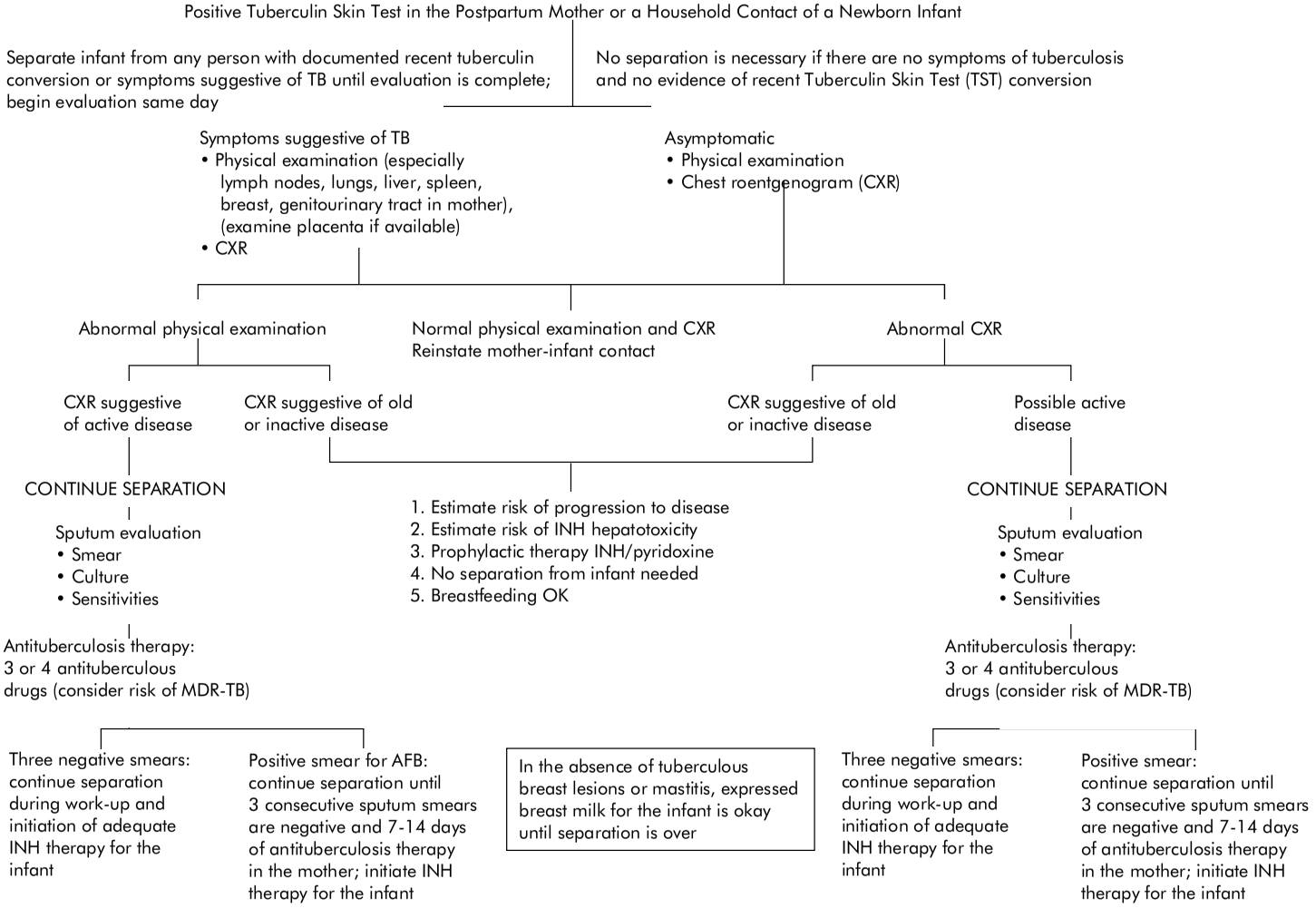


Figure 17-2. Management of newborn infant exposed to tuberculin-positive household contact.

The infant should be separated temporarily from the suspected source if symptoms suggest active disease or a recent TST documents conversion, and separation should continue until the results of the chest radiograph. Because of considerable variability in the course of illness and the concomitant infectious period, debate continues without adequate data about the appropriate period of separation.[178] This should be individualized given the specific situation. HIV testing and assessment of the risk of multidrug-resistant TB (MDR-TB) should be done in every case of active TB. Sensitivity testing should be done on every *Mycobacterium tuberculosis* isolate. Table 17-1 summarizes the management of the newborn infant whose mother (or other household contact) has TB.

Initiation of prophylactic isoniazid therapy in the infant has been demonstrated to be effective in preventing TB infection and disease in the infant. Therefore, continued separation of the infant and mother is unnecessary once therapy in both mother and child has begun.[75] The real risk to the infant requiring separation is from airborne transmission. Separation of the infant from a mother with active pulmonary TB is appropriate, regardless of the method of feeding. However, in many parts of the world, once therapy in the mother and prophylaxis with isoniazid in the infant has begun, the infant and mother are not separated. With or without separation, the mother and infant should continue to be closely observed throughout the course of maternal therapy to ensure good compliance with medication by both the mother and infant and to identify, early on, any symptoms in the infant suggestive of tuberculosis.

Tuberculous mastitis occurs very rarely in the United States but does occur occasionally in other parts of the world[110] and can lead to infection in the infant, frequently involving the tonsils. The mother usually has a single breast mass and associated axillary lymph node swelling and infrequently develops a draining sinus. TB of the breast can also present as a painless mass or edema. Involvement of the breast can occur with or without evidence of disease at other sites. Evaluation of extent of disease is appropriate, including lesion cultures by needle aspiration, biopsy, or wedge resection and milk cultures. Therapy should be with multiple antituberculosis medications, but surgery should supplement this, as needed, to remove extensive necrotic tissue or a persistently draining sinus.[13] Neither breastfeeding nor breast milk feeding should be done until the lesion is healed, usually 2 weeks or more. Continued antituberculosis therapy for 6 months in the mother and isoniazid for the infant for 3 to 6 months is indicated.

In the absence of tuberculous breast infection in the mother, transmission of TB through breast milk has not been documented. Thus, even though temporary separation of the infant and mother may occur pending complete evaluation and initiation of adequate therapy in the mother and prophylactic isoniazid therapy (10 mg/kg/day as a single dose) in the infant, breast milk can be expressed and given to the infant during the short separation. Breastfeeding can safely continue whether the mother, infant, or both are receiving antituberculosis therapy. Antituberculosis medications (isoniazid, rifampin, pyrazinamide, aminoglycosides, ethambutol, ethionamide, *p*-aminosalicylic acid) have been safely used in infancy, and therefore the presence of these medications in smaller amounts in breast milk is not a contraindication to breastfeeding.

Although conflicting, reports indicate that breastfeeding by TST-positive mothers does influence the infant's response to bacille Calmette-Guérin (BCG) vaccine, the TST, and perhaps the *M. tuberculosis* bacillus. Despite efforts to identify either a soluble substance or specific cell fractions (gamma/delta T cells) in colostrum and breast milk that affect the infant's immune responsiveness, no unified theory explains the various reported changes and no evidence has identified a consistent, clinically significant effect.[27,146,202,231]

Staphylococcal infections

Staphylococcal infection in the neonate can be caused by either *Staphylococcus aureus* or coagulase-negative staphylococci (most often *Staphylococcus epidermidis*) and can manifest in a wide

TABLE 17-1 Management of newborn whose mother (or other household contact) has tuberculosis (TB)

Mother/infant status	Additional workup recommended[1]	Therapy for mother/contact	Therapy for infant	Separation[2]	Breast milk[3]	Breast-feeding[3]
1. TB infection, no disease[4]	None for mother/contact	Prophylactic[5]	None	No	Yes	Yes
2. TB infection: abnormal CXR not suggestive of active disease		Decide active vs. inactive disease				
a. Symptoms or physical findings suggestive of active TB	Aerosolized sputums (culture, smears)[6]	Active disease: empiric[5]	Isoniazid[7]	Yes	Yes	No[8]
		Inactive disease: prophylactic[5]	None	No	Yes	Yes
b. No symptoms or physical findings suggestive of active TB	Aerosolized sputums in select cases	Prophylactic[5]	None	No	Yes	Yes
3. TB infection: abnormal CXR suggestive of active disease	Aerosolized sputums (culture, smears)[6]	Empiric therapy[5]	Isoniazid[7]	Yes	Yes	No[8]
4. Active pulmonary TB: suspected multi/drug-resistant (MDR) TB	Aerosolized sputums (culture, smears)[6]	Consult TB specialist for best regimen[9]	Consult pediatric TB specialist[9] Consider bacille Calmette-Guérin (BCG) vaccine	Yes	Yes	No
5. TB disease: suspected mastitis[10]	Aerosolized sputums (culture, smears)[6]	Empiric[5]	Isoniazid[7]	Yes	No[11]	No

(Continued)

TABLE 17-1 Management of newborn whose mother (or other household contact) has tuberculosis (TB)—cont'd

6. TB infection: status undetermined[12]	Perform/interpret CXR within 24 hours		Yes, until CXR interpreted (see a and b)	Yes	No
a. Abnormal CXR not suggestive of active disease	Proceed as in 2	As in 2	As in 2	As in 2	
b. Abnormal CXR suggestive of active disease	Proceed as in 3	As in 3	As in 3	As in 3	

Notes:

1. Further workup should always include evaluation of TB status of all other household (or close) contacts by tuberculin skin testing (TST), review of symptoms, physical examination, and chest x-ray film (CXR). Sputum smears and cultures should be done as indicated.
2. Separation should occur until interpretation of CXR confirms absence of active disease, or with active disease, separation should continue until individual is no longer considered infectious: three negative consecutive sputum smears, adequate ongoing empiric therapy, and decreased fever, cough, and sputum production. *Separation* means in a different house or location, not simply separate rooms in a household. Duration of separation should be individualized for each case in consultation with TB specialist.
3. This assumes no evidence of breast involvement, suspected TB mastitis, or lesion (except in status 5, when breast involvement is considered). Risk to infant is via aerosolized bacteria in sputum from the lung. Expressed breast milk can be given even if separation of mother and infant is advised.
4. TST positive, no symptoms or physical findings suggestive of TB, negative CXR.
5. *Prophylactic therapy:* isoniazid 10 mg/kg/day, maximum 300 mg for 6 months; pyridoxine 25 to 50 mg/day for 6 months. *Empiric therapy:* standard 3- or 4-drug regimens for 2 months, and treatment should continue for total of 6 months with isoniazid and rifampin when organism is shown to be sensitive. Suspected MDR-TB requires consultation with TB specialist to select optimum empiric regimen and for ongoing monitoring of therapy and clinical response.
6. Sensitivity testing should be done on any positive culture.
7. Isoniazid 10 mg/kg/day for 3 to 9 months depending on mother's or contact's status; repeat TST at 3 months and obtain normal CXR in infant before stopping isoniazid. Before beginning therapy, workup of infant for congenital or active TB may be appropriate. This workup should be determined by clinical status of infant and suspected, potential risk. TST after 4 weeks of age, with CXR, complete blood count, and erythrocyte sedimentation rate. Liver function tests, cerebrospinal fluid analysis, gastric aspirates, sonography/computed tomography of liver/spleen, and chest if congenital TB is suspected.
8. Breastfeeding is proscribed when separation of mother and infant is indicated because of risk of aerosolized transmission of bacteria. Expressed breast milk given to infant via bottle is acceptable in absence of mastitis or breast lesions.
9. Consult with TB specialist about MDR-TB. Empiric therapy will be chosen based on the most recent culture sensitivities of index patient or perhaps suspected source case, if known, as well as medication toxicities and other factors.
10. TB mastitis usually involves a single breast with associated axillary lymph node swelling and, infrequently, a draining sinus tract. It can also present as a painless mass or edema of breast.
11. With suspected mastitis or breast lesion caused by TB, even breast milk is contraindicated, until lesion or mastitis heals, usually 2 weeks or more.
12. Patient has a documented, recent TST conversion but has not been completely evaluated. Evaluation should begin and CXR done and evaluated in less than 24 hours to minimize separation of this person from infant. Further workup should proceed as indicated by symptoms, physical findings, and CXR results.

Data from Committee on Infectious Diseases, American Academy of Pediatrics: *Red Book: Report of the Committee on Infectious Diseases*, 26th ed. Elk Grove Village, IL. The Academy, 2003.

range of illnesses. Localized infection can be impetigo, cellulitis, or wound infection, and invasive or suppurative disease includes sepsis, pneumonia, osteomyelitis, arthritis, and endocarditis. *S. aureus* requires only a small inoculum (10 to 250 organisms) to produce colonization in the newborn, most often of the nasal mucosa and umbilicus.[132] By the fifth day of life, 40% to 90% of the infants in the nursery will be colonized with *S. aureus*.[87] The organism is easily transmitted to others from mother, infant, family, or health care personnel through direct contact. Outbreaks in the nursery were common in the past. Mothers, infants, health care workers, and even contaminated, unpasteurized, banked breast milk were sources of infection.[205] Careful use of antibiotics, changes in nursery layout and procedures, standard precautions, and cohorting as needed have decreased the spread of *S. aureus* in nurseries. Now the occurrence of methicillin-resistant *S. aureus* (MRSA) is a more common problem, requiring cohorting and occasionally epidemiologic investigation and careful infection control intervention. Breastfeeding can continue during diagnosis and treatment of closed, minor staphylococcal infection in the mother along with standard precautions.

S. aureus is the most common cause of mastitis in lactating women. One case of *staphylococcal scalded skin syndrome* (SSS) was reported by Katzman and Wald[142] in an infant breastfed by a mother with a lesion on her areola that did not respond to ampicillin therapy for 14 days. Subsequently the infant developed conjunctivitis with *S. aureus*, which produced an exfoliative toxin, and a confluent erythematous rash without mucous membrane involvement or Nikolsky's sign. No attempt to identify the exfoliative toxin in the breast milk was made, and the breast milk was not cultured for *S. aureus*. The child responded to intravenous (IV) therapy with naficillin. This emphasizes the importance of evaluating the mother and infant at the time of a suspected infection and the need for continued observation of the infant for evidence of a pyogenic infection or toxin-mediated disease, especially with breast lesions.

This case also raises the issue of when and how infants and mothers become colonized with *S. aureus* and what factors lead to illness and infection in each. Empiric therapy may be indicated depending on the infant's clinical status. For patients with major open lesions caused by *S. aureus* that cannot be fully contained, with MRSA, or with SSS, the CDC recommends contact precautions in addition to standard precautions for the duration of the illness. The concern is that staphylococci can be easily transmitted, colonization occurs, and potentially serious infection can occur later. With SSS the primary site of infection can be minimal (e.g., conjunctivitis, infection of a circumcision site), but a clinically significant amount of toxin can be produced and lead to severe disease in the infant. However, it seems reasonable that after initiating appropriate antistaphylococcal therapy for the mother for 24 hours, standard precautions and breastfeeding can be continued whether or not mastitis is present. Some individuals recommend bathing the mother and infant once with hexachlorophene to change the skin flora, but this does not address nasal carriage of *S. aureus*. With the current increasing prevalence of community-acquired MRSA various regimens for eradicating colonization with *Staphylococcus* have been proposed, although none have been proved highly efficacious in controlled trials. Usually these regimens include systemic therapy with one or two antimicrobial agents to which the organism is sensitive, topical antibiotics to both nares at least twice daily, and intermittent bathing with hexachlorophene or a similar agent. Often simultaneous treatment of all family members is recommended to eradicate colonization in the household. It is uncertain what role pets play in colonization of family members with *Staphylococcus aureus*. Evaluation of the infant's status at the time of decision making, continued close observation of the infant, and timely empiric therapy as needed in the infant are also appropriate. The mother and infant can room-in together, without contact with other mothers or infants until discharge.

Toxic shock syndrome (TSS) can result from *S. aureus* or *Streptococcus pyogenes* infection and

probably from a variety of antigens produced by other organisms. TSS-1 has been identified as a "superantigen" affecting the T lymphocytes and other components of the immune response, producing an unregulated and excessive immune response and resulting in an overwhelming systemic clinical response. TSS has been reported in association with vaginal delivery, cesarean birth, mastitis, and other local infections in the mother. Mortality rate in the mother may be as high as 5%.

The case definition of staphylococcal TSS includes meeting all four major criteria: fever greater than 38.9° C, rash (diffuse macular erythroderma), hypotension, and desquamation (associated with subepidermal separation seen on skin biopsy). The definition also includes involvement of three or more organ systems (gastrointestinal, muscular, mucous membrane, renal, hepatic, hematologic, or central nervous system); negative titers for Rocky Mountain spotted fever, leptospirosis, and rubeola; and lack of isolation of *S. pyogenes* from any source or *S. aureus* from the cerebrospinal fluid (CSF).[232] A similar case definition has been proposed for streptococcal TSS.[281] Aggressive empiric antibiotic therapy against staphylococci and streptococci and careful supportive therapy are essential to decreasing illness and death. Oxacillin, nafcillin, first-generation cephalosporins, clindamycin, erythromycin, and vancomycin are all acceptable antibiotics, even for the breastfeeding mother. The severity of illness in the mother may preclude breastfeeding, but it can be reinitiated when the mother is improving and wants to restart. Standard precautions, but allowing breastfeeding, are recommended.

Staphylococcal enterotoxin F (SEF) has been identified in breast milk specimens collected on days 5, 8, and 11 from a mother who developed TSS at 22 hours post partum.[269] *S. aureus* that produced SEF was isolated from the mother's vagina but not from breast milk. The infant and mother lacked significant antibody against SEF in their sera. The infant remained healthy beyond 60 days of follow-up. SEF is pepsin inactivated at pH 4.5 and therefore is probably destroyed in the stomach environment and presents little or no risk to the breastfeeding infant.[25] Breastfeeding can continue if the mother is able.

Coagulase-negative staphylococcal infection (*S. epidermidis* is the predominant isolate) produces minimal disease in healthy, full-term infants but is a significant problem in hospitalized or premature infants. Factors associated with increased risk of this infection include prematurity, high colonization rates in specific nurseries, invasive therapies (e.g., IV lines, chest tubes, intubation), and antibiotic use. Illness produced by coagulase-negative staphylococci can be invasive and severe in high-risk neonates, but rarely in mothers. At 2 weeks of age, for infants still in the nursery, *S. epidermidis* is a frequent colonizing organism at multiple sites, with colonization rates as high as 75% to 100%. Serious infections with coagulase-negative staphylococci (e.g., abscesses, IV line infection, bacteremia/sepsis, endocarditis, osteomyelitis) require IV therapy. Many strains are resistant to penicillin and the semisynthetic penicillins, so sensitivity testing is essential. Empiric or definitive therapy may require treatment with vancomycin, gentamicin, rifampin, teicoplanin, linezolid, or combinations of these for synergistic activity. Transmission of infection in association with breastfeeding appears to be no more common than with bottle feeding. Infection control includes contact and standard precautions, as with *S. aureus*. Occasionally, during presumed outbreaks, careful epidemiologic surveillance may be required, including cohorting, limiting overcrowding and understaffing, surveillance cultures of infants and nursery personnel, reemphasis of meticulous infection control techniques for all individuals entering the nursery, and rarely, removal of colonized personnel from direct infant contact.

Streptococcal infections

Group A

Streptococcus pyogenes (β-hemolytic group A *Streptococcus* [GAS]) is a common cause of skin and throat infections in children, producing pharyngitis, cellulitis, and impetigo. Illnesses produced by GAS can be classified in three categories: (1) impetigo, cellulitis, or pharyngitis without

invasion or complication; (2) severe invasive infection with bacteremia, necrotizing fasciitis, myositis, or systemic illness (e.g., streptococcal TSS); and (3) autoimmune-mediated phenomena, including acute rheumatic fever and acute glomerulonephritis. GAS can also cause puerperal sepsis, endometritis, and neonatal omphalitis. Significant morbidity and mortality rates are associated with invasive GAS infection; mortality rate is approximately 20% to 50%, with almost half the survivors requiring extensive tissue débridement or amputation.[218] Infants are not at risk for the autoimmune sequelae of GAS (rheumatic fever or poststreptococcal glomerulonephritis). Transmission is through direct contact (rarely indirect contact) and droplet spread. Outbreaks of GAS in the nursery are rare, unlike with staphylococcal infections. Either mother or infant can be initially colonized with GAS and transmit it to the other.

In the situation of maternal illness (extensive cellulitis, necrotizing fasciitis, myositis, pneumonia, TSS, mastitis), it is appropriate to separate the mother and infant until effective therapy (penicillin, ampicillin, cephalosporins, erythromycin) has been given for 24 hours. Breastfeeding should also be suspended and may resume after 24 hours of therapy.

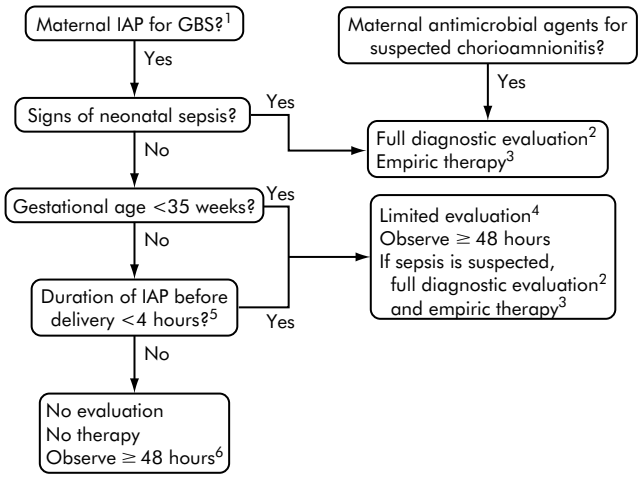
Group B

Group B Streptococcus (GBS, *S. agalactiae*) is a significant cause of perinatal bacterial infection. In parturient women, infection can lead to asymptomatic bacteriuria, UTI (often associated with premature birth), endometritis, or amnionitis. In infants, infection usually occurs between birth and 3 months of age (1 to 4 cases per 1000 live births). It is routinely classified by the time of onset of illness in the infant: early onset (0 to 7 days, majority less than 24 hours) and late onset (7 to 90 days, generally less than 4 weeks). Infants may develop sepsis, pneumonia, meningitis, osteomyelitis, arthritis, or cellulitis. Early-onset GBS disease is often fulminant, presenting as sepsis or pneumonia with respiratory failure. Almost three quarters of neonatal disease is early onset. Type III is the most common serotype causing disease.

Transmission is believed to occur in utero and during delivery. Colonization rates of mothers and infants have varied between 5% and 35%. Postpartum transmission is thought to be uncommon, although it has been documented. Risk factors for early-onset GBS disease include delivery before 37 weeks' gestation, rupture of membranes for longer than 18 hours before delivery, intrapartum fever, heavy maternal colonization with GBS, or low concentrations of anti-GBS capsular antibody in maternal sera.[62,63] The common occurrence of severe GBS disease before 24 hours of age in the neonate has lead to prevention strategies. Revised guidelines developed by the AAP Committees on Infectious Diseases and on the Fetus and Newborn[63] have tried to combine various variables for increased risk of GBS infection (prenatal colonization with GBS, obstetric and neonatal risk factors for early-onset disease) and provide intrapartum prophylaxis to those at high risk (Fig. 17-3).

Late-onset GBS disease is thought to be the result of transmission during delivery or in the postnatal period from maternal, hospital, or community sources. Dillon and associates[73] demonstrated that 10 of 21 infants with late-onset disease were colonized at birth, but the source of colonization was unidentified in the others. Gardner and associates[97] showed that only 4.3% of 46 children who were culture negative for GBS at discharge from the hospital had acquired GBS by 2 months of age. Anthony and associates[12] noted that many infants are colonized with GBS, but the actual attack rate for GBS disease is low and difficult to predict.

Acquisition of GBS through breast milk or breastfeeding is rare. Three cases of late-onset GBS disease associated with GBS in the maternal milk have been reported.[146,230] Two of the three mothers had bilateral mastitis, and the third was asymptomatic. It was not clear when colonization of the infants occurred or when infection or disease began. The authors discussed the possibility that the infants were originally colonized during delivery, subsequently colonized the mothers' breasts during breastfeeding, and then became reinfected at a later time. Butter and DeMoor[38] showed that infants initially colonized on their heads at birth



[1] If no maternal IAP for GBS was administered despite an indication being present, data are insufficient on which to recommend a single management strategy.

[2] Includes complete blood cell (CBC) count with differential, blood culture, and chest radiograph if respiratory abnormalities are present. When signs of sepsis are present, a lumbar puncture, if feasible, should be performed.

[3] Duration of therapy varies depending on results of blood culture, cerebrospinal fluid findings (if obtained), and the clinical course of the infant. If laboratory results and clinical course do not indicate bacterial infection, duration may be as short as 48 hours.

[4] CBC including WBC count with differential and blood culture.

[5] Applies only to penicillin, ampicillin, or cefazolin and assumes recommended dosing regimens.

[6] A healthy-appearing infant who was ≥38 weeks' gestation at delivery and whose mother received ≥4 hours of IAP before delivery may be discharged home after 24 hours *if* other discharge criteria have been met and a person able to comply fully with instructions for home observation will be present. If any one of these conditions is not met, the infant should be observed in the hospital for at least 48 hours and until criteria for discharge are achieved.

Figure 17-3. Empiric management of neonate born to mother who received intrapartum antimicrobial prophylaxis (IAP) for prevention of early-onset group B streptococcal (GBS) disease. CBC, complete blood count; CSF, cerebrospinal fluid. This algorithm is not an exclusive course of management. Variations that incorporate individual circumstances or institutional preferences may be appropriate. (From Committee on Infectious Diseases, American Academy of Pediatrics: Red Book Report of the Committee on Infectious Disease, 26th ed. Elk Grove, Ill, American Academy of Pediatrics, 2003, p 590.

had GBS cultured from their throat, nose, or umbilicus 8 days later. Whenever they cultured GBS from the nipples of mothers, the authors also found it in the nose or throat of the infants.

When a breastfed infant develops late-onset GBS disease, it is appropriate to culture the milk and treat the mother to prevent reinfection if the milk is culture positive for GBS, with or without clinical evidence of mastitis. There are rare reports of reinfection of the infant. Eradication of GBS colonization in the infant or the mother may be difficult with amoxicillin or rifampin. Breastfeeding can continue depending on the infant's ability to feed during GBS disease. Routine culturing of infants or breast milk to detect colonization is not recommended or useful. (See Chapter 16 for management of mastitis in the mother.) A mother or infant colonized or infected with GBS should be managed with standard precautions[62] while in the hospital. GBS endometritis in the mother necessitates separation of mother and infant for the first 24 hours of the mother's therapy, but expressed breast milk can be given to the infant during the separation. Timely evaluation of the infant for infection or illness and empiric therapy for GBS in the infant are appropriate until the child has remained well and cultures are subsequently negative at 72 hours. Occasionally, epidemiologic investigation in hospital will utilize culturing to detect a source of late-onset GBS disease in the nursery. This can be useful when more than one case of late-onset disease is detected with the same serotype. Cohorting in such a situation may be appropriate, but prophylactic therapy to eradicate colonization is impractical. Unlike GAS

infection, GBS infection in nurseries has not been reported to cause outbreaks.

Gonococcal infections

Maternal infection with *Neisseria gonorrhoeae* can produce a large spectrum of illness ranging from uncomplicated vulvovaginitis, proctitis, pharyngitis, conjunctivitis, or more severe and invasive disease, including pelvic inflammatory disease (PID), meningitis, endocarditis, or disseminated gonococcal infection. The risk of transmission from the mother to the infant occurs mainly during delivery in the passage through the infected birth canal and occasionally from postpartum contact with the mother (or her partner). There is negligible risk of transmission from breast milk, and *N. gonorrhoeae* does not seem to cause local infection of the breast. Infection in the neonate is most often ophthalmia neonatorum and less often a scalp abscess or disseminated infection. Mothers with presumed or documented gonorrhea should be reevaluated for other STDs, especially *Chlamydia trachomatis* and syphilis, because some therapies for gonorrhea are not adequate for either of these infections.

With the definitive identification of gonorrhea in the mother, empiric therapy should begin immediately, and the mother should be separated from the infant until completion of 24 hours of adequate therapy. Treatment of the mother with ceftriaxone, cefixime, penicillin, or erythromycin is without significant risk to the infant. Single-dose treatment with spectinomycin, ciprofloxacin, ofloxacin, or azithromycin has not been adequately studied but would presumably be safe for the infant given the 24-hour separation and a delay in breastfeeding without giving the infant the expressed breast milk (pump and discard). Doxycycline use in the nursing mother is not recommended.

Careful preventive therapy for ophthalmia neonatorum should be provided, and close observation of the infant should continue for 2 to 7 days, the usual incubation period. Empiric or definitive therapy against *N. gonorrhoeae* may be necessary depending on the infant's clinical status and should be chosen on the basis of the maternal isolate's sensitivity pattern. The mother should not handle other infants until 24 hours of adequate therapy, and the infant should be separated from the rest of the nursery population, with or without breastfeeding.

VIRAL INFECTIONS

Arboviruses

Arboviruses were originally a large collection of viruses grouped together because of the common mode of transmission through arthropods. They have now been reclassified into several different families: Bunyaviridae, Togaviridae, Flaviviridae, Reoviridae, and others. They include more than 30 human pathogens.

These organisms primarily produce either CNS infections (encephalitis, meningoencephalitis) or undifferentiated illnesses associated with fever and rash, severe hemorrhagic manifestations, and involvement of other organs (hepatitis, myalgia, polyarthritis). Infection with this array of viruses may also be asymptomatic and subclinical, although how often this occurs is uncertain. Some of the notable human pathogens include Bunyaviridae (California serogroup viruses), Hantavirus, Hantaan virus, Phlebovirus (Rift Valley fever), Nairovirus (Crimean-Congo hemorrhagic fever [CCHF]), Alphavirus (western, eastern, and Venezuelan equine encephalomyelitis viruses), Flavivirus (St. Louis encephalitis virus, Japanese encephalitis virus, dengue viruses, yellow fever virus, tick-borne encephalitis viruses), and Orbivirus (Colorado tick fever). Other than for CCHF and for reported cases of Colorado tick fever associated with transfusion, direct person-to-person spread does not seem to occur.

No evidence indicates that these organisms can be transmitted through breast milk. Standard precautions are sufficient. With any of these infections in a breastfeeding mother, the severity of the illness may determine the mother's ability to continue breastfeeding. Providing the infant with expressed breast milk is acceptable.

In general, treatment for these illnesses is supportive. However, ribavirin appears to decrease the severity of and mortality from Hantavirus pulmonary syndrome, hemorrhagic fever with renal failure, and CCHF. Ribavirin has been described as teratogenic in various animal species and is contraindicated in pregnant women. No information is available concerning ribavirin in breast milk, with little information available on the use of IV or oral ribavirin in infants.

Arenaviruses

Arenaviruses are single-stranded ribonucleic acid (RNA) viruses that infect rodents and are acquired by humans through the rodents. The six major human pathogens in this group are (1) lymphocytic choriomeningitis virus (LCMV), (2) Lassa fever virus, (3) Junin virus (Argentine hemorrhagic fever), (4) Machupo virus (Bolivian hemorrhagic fever), (5) Guanarito virus (Venezuelan hemorrhagic fever), and (6) Sabia virus. The geographic distribution of these viruses and the illness they cause are determined by the living range of the host rodent (reservoir). The exact mechanism of transmission to humans is unknown and hotly debated.[19,44,91] Direct contact and aerosolization of rodent excretions and secretions are probable mechanisms.

LCMV is well recognized in Europe, the Americas, and other areas. Perinatal maternal infection can lead to severe disease in the newborn, but no evidence suggests transmission through breast milk.[21,150] Standard precautions with breastfeeding are appropriate.

Lassa fever (West Africa) and Argentine hemorrhagic fever (Argentine pampas) are usually more severe illnesses with dramatic bleeding and involvement of other organs, including the brain. These fevers more frequently lead to shock and death than do the forms of hemorrhagic fever caused by the other viruses in this group. Person-to-person spread of Lassa fever is believed to be common, and transmission within households does occur.[144] This may relate to prolonged viremia and excretion of the virus in the urine of humans for up to 30 days.[207] The possibility of persistent virus in human urine, semen, and blood after infection exists for each of the arenaviruses. The possibility of airborne transmission is undecided. Current recommendations by the CDC[44] are to use contact precautions for the duration of the illness in situations of suspected viral hemorrhagic fever. No substantial information describes the infectivity of various body fluids, including breast milk, for these different viral hemorrhagic fevers. Considering the severity of the illness in the mother and the risk to the infant, it is reasonable to avoid breastfeeding in these situations if alternative forms of infant nutrition can be provided.

As more information becomes available, reassessment of these recommendations is advisable. There is a vaccine in clinical trials in endemic areas for Junin virus and Argentine hemorrhagic fever. Preliminary studies suggest it is very effective, but data are still being accumulated concerning the vaccine's use in children and pregnant or breastfeeding women.

Cytomegalovirus

Cytomegalovirus (CMV) is one of the human herpesviruses. Congenital infection of infants, postnatal infection of premature infants, and infection of immunodeficient individuals represent the most serious forms of this infection in children. The time at which the virus infects the fetus or infant and the presence or absence of antibodies against CMV from the mother are important determinants of the severity of infection and the likelihood of significant sequelae (congenital infection syndrome, deafness, chorioretinitis, abnormal neurodevelopment, learning disabilities).[151] About 1% of all infants are born excreting CMV at birth, and approximately 5% of these congenitally infected infants will demonstrate evidence of infection at birth (approximately 5 symptomatic cases per 10,000 live births). Approximately 15% of infants born after primary infection in the pregnant woman will manifest at least one sequela of prenatal infection.[62]

Various studies have detected that 3% to 28% of pregnant women have CMV in cervical cultures

and that 4% to 5% of pregnant women have CMV in their urine.[81,115] Perinatal infection certainly occurs through contact with virus in these fluids but usually is not associated with clinical illness in full-term infants. The lack of illness is believed to result from transplacental passive transfer of protective antibodies from the mother.

Postnatal infection later in infancy occurs via breastfeeding or contact with infected fluids (e.g., saliva, urine) but, again, rarely causes clinical illness in full-term infants. Seroepidemiologic studies have documented transmission of infection in infancy, with higher rates of transmission occurring in daycare centers, especially when the prevalence of CMV in the urine and saliva is high. CMV has been identified in the milk of CMV-seropositive women at varying rates (10% to 85%) using viral cultures or CMV deoxyribonucleic acid polymerase chain reaction (DNA-PCR).[115,192,248,271] CMV is more often identified in the breast milk of seropositive mothers than in vaginal fluids, urine, and saliva. The CMV isolation rate from colostrum is lower than that from mature milk.[115,247] The reason for the large degree of variability in identification of CMV in breast milk in these studies probably relates to the intermittent nature of reactivation and excretion of the virus, in addition to the variability, frequency, and duration of sampling of breast milk in the different studies. Some authors have hypothesized that the difference in isolation rates between breast milk and other fluids is caused by viral reactivation in cells (leukocytes or monocytes) in the breast leading to "selective" excretion in breast milk.[192] Vochem and associates[271] reported that the rate of virolactia was greatest at 3 to 4 weeks post partum, and Yeager and associates[285] reported significant virolactia between 2 and 12 weeks post partum. Antibodies (e.g., secretory IgA) to CMV are present in breast milk, along with various cytokines and other proteins (e.g., lactoferrin). These may influence virus binding to cells, but they do not prevent transmission of infection.[3,4,151,181,192,206,282]

Several studies have documented increased rates of postnatal CMV infection in breastfed infants (50% to 69%) compared with bottle fed infants (12% to 27%) observed through the first year of life.[81,181,248,271] In these same studies, full-term infants who acquired CMV infection postnatally were only rarely mildly symptomatic at the time of seroconversion or documented viral excretion. Also, no evidence of late sequelae from CMV was found in these infants.

Postnatal exposure of susceptible infants to CMV, including premature infants without passively acquired maternal antibodies against CMV, infants born to CMV-seronegative mothers, and immunodeficient infants, can cause significant clinical illness (pneumonitis, hepatitis, thrombocytopenia).[113,173] In one study of premature infants followed up to 12 months, Vochem and associates[271] found CMV transmission in 17 of 29 infants (59%) exposed to CMV virolactia and breastfed compared with no infants infected of 27 exposed to breast milk without CMV. No infant was given CMV-seropositive donor milk or blood. Five of the 12 infants who developed CMV infection after 2 months of age had mild signs of illness, including transient neutropenia, and only one infant had a short increase in episodes of apnea and a period of thrombocytopenia. Five other premature infants with CMV infection before 2 months of age had acute illness, including sepsis-like symptoms, apnea with bradycardia, hepatitis, leukopenia, and prolonged thrombocytopenia.[271]

Exposure of CMV-seronegative or premature infants to CMV-positive milk (donor or natural mother's) should be avoided.[239] Various methods of inactivating CMV in breast milk have been reported, including Holder pasteurization, freezing (−20° C for 3 days), and brief high temperature (72° C for 10 seconds).[81,92,107,246,285] One small, prospective study suggests that freezing breast milk at −20° C for 72 hours protects premature infants from CMV infection via breast milk. Sharland and associates reported on 18 premature infants (<32 weeks) who were uninfected at birth and exposed to breast milk from their CMV seropositive mothers.[239] Only one of 18 (5%) infants became positive for CMV at 62 days of life, and this infant was clinically asymptomatic. This transmission rate is considerably lower than others reported in the literature. CMV

seronegative and leukocyte–depleted blood products were used routinely. Banked breast milk was pasteurized and stored at –20° C for various time periods and maternal expressed breast milk was frozen at –20° before use whenever possible. The infants received breast milk for a median of 34 days (range, 11 to 74 days) and they were observed for a median of 67 days (range, 30 to 192 days). Breast milk samples pre- or postfreezing were not analyzed by PCR or culture for the presence of cytomegalovirus.[239] Yasuda and associates reported on 43 preterm infants (median gestational age 31 weeks) demonstrating a peak in CMV DNA copies, detected by a real-time PCR assay, in breast milk at 4 to 6 weeks post partum. Thirty of the 43 infants received CMV DNA-positive breast milk. Three of the 30 had CMV DNA detected in their sera, but none of the three had symptoms suggestive of CMV infection. Much of the breast milk had been stored at –20° C before feeding, which the authors propose is the probable reason for less transmission in this cohort.[284] The efficacy of such treatments to prevent CMV infection in premature infants has not been studied prospectively in a randomized control trial.

CMV-seropositive mothers can safely breastfeed their full-term infants because, despite a higher rate of CMV infection than in formula fed infants observed through the first year of life, infection in this situation is not associated with significant clinical illness or sequelae.

Dengue disease

Dengue viruses (serotypes dengue 1 to 4) are Flaviviruses associated primarily with febrile illnesses and rash; dengue fever (DF), dengue hemorrhagic fever (DHF,) and dengue shock syndrome (DSS). Although DHF and DSS occur frequently in children under 1 year of age, they are infrequently described in infants younger than 3 months of age.[112] Boussemart and associates[33] reported on two cases of perinatal/prenatal transmission of dengue and discussed eight additional cases in neonates from the literature. Prenatal or intrapartum transmission of the same type of dengue as the mother was confirmed by serology, culture, or PCR.

It has been postulated that more severe disease associated with dengue disease occurs when the individual has specific IgG against the same serotype as the infecting strain in a set concentration, leading to antibody-dependent enhancement (ADE) of infection. The presence of preexisting dengue serotype specific IgG in an infant implies either previous primary infection with the same serotype, passive acquisition of IgG from the mother (who had a previous primary infection with the same serotype), or perhaps acquisition of specific IgG from breast milk. There is no evidence in the literature for more severe disease in breastfed infants compared with formula fed infants.

There has been no interhuman transmission of dengue virus in the absence of the mosquito vector and no evidence of transmission via breast milk. Breastfeeding during maternal or infant dengue disease should continue as determined by the mother's or infant's severity of illness.

Epstein-Barr virus

Epstein-Barr virus (EBV) is a common infection in children, adolescents, and young adults. It is usually asymptomatic but most notably causes infectious mononucleosis and has been associated with chronic fatigue syndrome (CFS), Burkitt's lymphoma, and nasopharyngeal carcinoma. Because EBV is one of the human herpesviruses, concern has been raised about lifelong latent infection and the potential risk of infection to the fetus and neonate from the mother. Primary EBV infection during pregnancy is unusual because few pregnant women are susceptible.[102,130] Although abortion, premature birth, and congenital infection from EBV are suspected, no distinct group of anomalies is linked to EBV infection in the fetus or neonate. Also, no virologic evidence of EBV as the cause of abnormalities has been found in association with suspected EBV infection.

Culturing of EBV from various fluids or sites is difficult. The virus is detected by its capacity to transform B lymphocytes into persistent

lymphoblastoid cell lines. PCR and DNA hybridization studies have detected EBV in the cervix and in breast milk. One study, which identified EBV-DNA in breast milk cells in more than 40% of women donating milk to a breast milk bank, demonstrated that only 17% had antibody to EBV (only IgG, no IgM).[139]

The question of the timing of EBV infection and the subsequent immune response and clinical disease produced requires continued study. Differences exist among the clinical syndromes manifest at different ages. Infants and young children are asymptomatic, have illness not recognized as related to EBV, or have mild episodes of illness, including fever, lymphadenopathy, rhinitis and cough, hepatosplenomegaly, or rash. Adolescents or young adults who experience primary EBV infection more often demonstrate infectious mononucleosis syndrome or are asymptomatic. CFS is more common in adolescents and young adults. Burkitt's lymphoma, observed primarily in Africa, and nasopharyngeal carcinoma, seen in southeast Asia, where primary EBV infection usually occurs in young children, are tumors associated with early EBV infection.[256] These tumors are related to "chronic" EBV infection and tend to occur in individuals with persistently high antibody titers to EBV viral capsid antigen and early antigen. The questions of why these tumors occur with much greater frequency in these geographic areas and what cofactors (including altered immune response to infection) may contribute to their development remain unanswered.[17]

It also remains unknown to what degree breast milk could be a source of early EBV infection compared with other sources of EBV infection in the infant's environment. Similar to the situation of postnatal transmission of CMV in immunocompetent infants, clinically significant illness rarely is associated with primary EBV infection in infants. More data concerning the pathogenesis of EBV-associated tumors should be obtained before proscribing against breastfeeding is warranted, especially in areas where these tumors are common but the protective benefits of breastfeeding are high. In areas where Burkitt's lymphoma and nasopharyngeal carcinoma are uncommon, EBV infection in the mother or infant is not a contraindication to breastfeeding.

Filoviridae

Marburg and Ebola viruses cause severe and highly fatal hemorrhagic fevers. The illness often presents with nonspecific symptoms (conjunctivitis, frontal headache, malaise, myalgia, bradycardia) and progresses with worsening hemorrhage to shock and subsequent death in 50% to 90% of patients. Person-to-person transmission through direct contact, droplet spread, or airborne spread is the common mode of transmission. However, the animal reservoir or source of these viruses in nature for human infection has not been identified. Attack rates in families are 5% to 16%.[207] No postexposure interventions have proved useful in preventing spread, and no treatment other than supportive is currently available.

No information is available concerning these viruses in breast milk or additional risks or benefits from breastfeeding. Contact precautions are recommended for Marburg virus infections and contact and airborne precautions for Ebola virus infection. Given the high attack and mortality rates, these precautions should be carefully instituted and breastfeeding not allowed. If any other suitable source of nutrition can be found for the infant, expressed breast milk should also be proscribed for the infant of a mother with either of these infections.

Human herpesvirus 6

Human herpesvirus 6 (HHV-6) is a cause of exanthema subitum (roseola, roseola infantum) and is associated with febrile seizures. HHV-6 appears to be most similar to CMV based on genetic analysis. No obvious congenital syndrome of HHV-6 infection has been identified, although prenatal infection has been reported.[79] Seroepidemiologic studies show that most adults have already been infected by HHV-6. Therefore, primary infection during pregnancy is unlikely, but reactivation of latent HHV-6 infection may be more common. No

case of symptomatic HHV-6 prenatal infection has been reported. The significance of reactivation of HHV-6 in the pregnant woman and the production of infection and disease in the fetus and infant remains to be determined. Primary infection in children occurs most often between 6 and 12 months of age, when maternally acquired passive antibodies against HHV-6 are waning. Febrile illnesses in infants younger than 3 months of age have been described with HHV-6 infection, but infection before 3 months or after 3 years is uncommon.

Various studies involving serology and restriction enzyme analysis of HHV-6 isolates from mother/infant pairs support the idea that postnatal transmission and perhaps perinatal transmission from the mother are common sources of infection. At least one study was unable to detect HHV-6 in breast milk by PCR analysis in 120 samples, although positive control samples seeded with HHV-6-infected cells did test positive.[80]

Given the limited occurrence of clinically significant disease and the absence of sequelae of HHV-6 infection in infants and children, the almost universal acquisition of infection in early childhood (with or without breastfeeding) and the absence of evidence that breast milk is a source of HHV-6 infection, breastfeeding can continue in women known to be seropositive for HHV-6.

Herpes simplex virus

Herpes simplex virus types 1 and 2 (HSV-1, HSV-2) can cause prenatal, perinatal, and postnatal infection in the fetus and infant. Prenatal infection can lead to abortion, prematurity, or a recognized congenital syndrome. Perinatal infection is the most common (1 in 2000 to 5000 live births, 700 to 1500 cases per year in the United States) and is often fatal or severely debilitating. The factors that facilitate intrapartum infection and predict the severity of disease have been extensively investigated. Postnatal infection is uncommon but can occur from a variety of sources, including oral or genital lesions and secretions in mothers or fathers, hospital or home caregivers, and breast lesions in breastfeeding mothers. A number of case reports have documented severe HSV-1 or HSV-2 infections in infants in association with HSV-positive breast lesions in the mother.[77,212,255] Cases of infants inoculating the mother's breast have also been reported.

Breastfeeding, in the absence of breast lesions, in HSV-seropositive or culture-positive women is reasonable when accompanied by careful handwashing, covering other lesions, and avoiding fondling or kissing with oral lesions until all lesions are crusted. Breastfeeding during maternal therapy with oral or IV acyclovir can continue safely. Inadequate information exists concerning valacyclovir, famiciclovir, ganciclovir, and foscarnet in breast milk to make a recommendation at this time. Breastfeeding in women with active herpetic lesions on their breasts should be proscribed until the lesions are dried. Treatment of the mother's breast lesion with topical, oral, or even IV antiviral preparations may hasten recovery and decrease the length of viral shedding.

Rotaviruses

Rotavirus infections usually result in diarrhea accompanied by emesis and low-grade fever. In severe infections the clinical course can include dehydration, electrolyte abnormalities, and acidosis and can contribute to malnutrition in developing countries. In developed countries, rotavirus is often associated with diarrhea requiring hospitalization in children less than 2 years of age. Fecal-oral transmission is the most common route, but fomites and respiratory spread may also occur. Spread of infection occurs most often in homes with young children or in daycare centers and institutions. In hospitalized infants or mothers with rotavirus infection, contact precautions are indicated for the duration of the illness. No evidence indicates prenatal infection from rotavirus, but perinatal or postnatal infection from contact with the mother or others can occur.

There are no documented cases of transmission of rotavirus via breast milk. Breast milk does contain antibodies to rotavirus for up to 2 years. Although breastfeeding does not prevent infection

with rotavirus, it seems to decrease the severity of rotavirus-induced illness in children less than 2 years old.[60,84,125] At least one study suggested that this may represent simply the postponement of severe rotavirus infection until an older age.[60] This delay in rotavirus infection until the child is older may be beneficial in that the older child may be able to tolerate the infection or illness with a lower likelihood of becoming dehydrated or malnourished. Continuing breastfeeding during an episode of rotavirus illness with or without vomiting is appropriate and often helpful.

Several types of rotavirus vaccines are undergoing study in a variety of situations. Evidence indicates that maternal immunization with rotavirus vaccine can increase both transplacental acquisition of antibodies and secretory IgA (sIgA) in breast milk.[209] Additionally, oral rotavirus vaccines have been able to stimulate a good serologic response in both formula fed and breastfed infants, although the antigen titers may need to be modified to create an optimal response in all infants.[56] The actual protective effect of these vaccines in different situations and strategies will require measurement in prospective studies.

Rubella virus

Congenital rubella infection has been well described, and the contributing variables to infection and severe disease have been elucidated. The primary intervention to prevent congenital rubella has been to establish the existence of maternal immunity to rubella before conception, including immunization with rubella vaccine and reimmunization if indicated. Perinatal infection is not clinically significant. Postnatal infection occurs infrequently in children younger than 1 year of age because of passively acquired maternal antibodies. The predominant age of infection is 5 to 14 years old, and more than half of those with infections are asymptomatic. Postnatal rubella is a self-limited, mild viral infection associated with an evanescent rash, shotty adenopathy, and low-grade transient fever. It most often occurs in the late winter and spring. Infants with congenital infection shed the virus for prolonged periods from various sites and may serve as a source of infection throughout the year. Contact isolation is appropriate for suspected and proved congenital infection for at least 1 year, including exclusion from day care and avoidance of pregnant women, whereas postnatal rubella infection requires droplet precautions for 7 days after the onset of rash.

Rubella virus has been isolated from breast milk after natural infection (congenital or postnatal) and after immunization with live attenuated vaccine virus. Both IgA antibodies and immunoreactive cells against rubella have been identified in breast milk. Breastfed infants can acquire vaccine virus infection via milk but are asymptomatic. Because postpartum infection with this virus (natural or vaccine) is not associated with clinically significant illness, no reason exists to prevent breastfeeding after congenital infection, postpartum infection, or maternal immunization with this virus.

Varicella-zoster virus

Varicella-zoster virus (VZV) infection (varicella/chickenpox, zoster/shingles) is one of the most communicable diseases of humans, in a class with measles and smallpox. Transmission is believed to occur via respiratory droplets and virus from vesicles. Varicella in pregnancy is a rare event, although disease can be more severe with varicella pneumonia, and can be fatal.

Congenital VZV infection occurs infrequently, causing abortion, prematurity, and congenital malformations. A syndrome of malformations has been carefully described with congenital VZV infection, typically involving limb deformity, skin scarring, and nerve damage, including to the eye and brain.[101]

Perinatal infection can lead to severe infection in the infant if maternal rash develops 5 days or less before delivery and within 2 days after delivery. Illness in the infant usually develops before 10 days of age and is believed to be more severe because of the lack of adequate transfer of antibody from the mother during this period and transplacental spread

of virus to the fetus and infant during viremia in the mother. Varicella in the mother occurring prior to 5 days before delivery allows sufficient formation and transplacental transfer of antibodies to the infant to ameliorate disease even if the infant is infected with VZV. Mothers who develop varicella rash more than 2 days after delivery are less likely to transfer virus to the infant transplacentally; they pose a risk to the infant from postnatal exposure, which can be diminished by the administration of varicella-zoster immune globulin (VZIG) to the infant. Postnatal transmission is believed to occur through aerosolized virus from skin lesions or the respiratory tract entering the susceptible infant's respiratory tract. Airborne precautions are therefore appropriate in the hospital setting. Infants infected with VZV in utero or in the perinatal period (less than 1 month of age) are more likely to develop zoster (reactivation of latent VZV) during childhood or as young adults. Table 17-2 summarizes management of varicella in the hospitalized mother or infant.[101]

Postnatal varicella from nonmaternal exposure can occur but is generally mild when it develops after 3 weeks of age or when the mother has passed on antibodies against VZV via the placenta. Severe postnatal varicella does occur in premature infants or infants of varicella-susceptible mothers. When the mother's immune status relative to VZV is uncertain and measurement of antibodies to VZV in the mother or infant cannot be performed promptly (less than 72 hours), administration of VZIG to the infant exposed to varicella or zoster in the postnatal period is indicated. Ideally the mother's varicella status should be known before pregnancy, when varicella virus vaccine could be given if indicated.

VZV virus has not been cultured from milk, but VZV-DNA has been identified in breast milk.[288] Antibody against VZV has also been found in breast milk.[174] One case of suspected transfer of VZV to an infant via breastfeeding has been reported, but virus may have been transmitted by respiratory droplet or exposure to rash before the mother began antiviral therapy.[288] Isolation of the infant from the mother and interruption of breastfeeding should occur only while the mother remains clinically infectious, regardless of the method of feeding. Expressed breast milk can be given to the infant if no skin lesions involve the breasts, as soon as the infant has received VZIG. Persons with varicella rash are considered noninfectious when no new vesicles have appeared for 72 hours and all lesions have crusted, usually in 6 to 10 days. Immunocompetent mothers who develop zoster can continue to breastfeed if the lesions do not involve the breast and can be covered, because antibodies against VZV are provided to the infant via the placenta and breast milk and will diminish the severity of disease even if not preventing it. Conservative management in this scenario would include giving the infant VZIG as well (see Table 17-2).

Measles

Measles is another highly communicable childhood illness that can be more severe in neonates and adults. Measles is an exanthematous febrile illness following a prodrome of malaise, coryza, conjunctivitis, and cough and often Koplik's spots in the mouth. The rash usually appears 10 to 14 days after exposure. Complications can include pneumonitis, encephalitis, and bacterial superinfection. With the availability of vaccination, measles in pregnancy is rare (0.4 in 10,000 pregnancies),[101] although respiratory complications (primary viral pneumonitis, secondary bacterial pneumonia), hepatitis, or other secondary bacterial infections often lead to more severe disease in these situations.

Prenatal infection with measles may cause premature delivery without disrupting normal uterine development. No specific group of congenital malformations have been described in association with in utero measles infection, although teratogenic effects of measles infection in the pregnant woman may rarely manifest in the infant.

Perinatal measles includes transplacental infection when measles occurs in the infant in the first 10 days of life. Infection from extrauterine exposure usually develops after 14 days of life. The severity of illness after suspected transplacental

TABLE 17-2 Guidelines for preventive measures after exposure to chickenpox in the nursery or maternity ward

Type of exposure or disease	Chickenpox lesions present: Mother	Chickenpox lesions present: Neonate	Disposition
A. Siblings at home have active chickenpox when neonate and mother are ready for discharge from hospital.	No	No	1. Mother: if she has a history of chickenpox, she may return home. Without a history, she should be tested for varicella-zoster virus (VZV) antibody titer.* If test is positive, she may return home. If test is positive, she may return home. If test is negative, varicella-zoster immune globulin (VZIG)† is administered and she is discharged home. 2. Neonate: may be discharged home with mother if mother has history of varicella or is VZV antibody positive. If mother is susceptible, administer VZIG to infant and discharge home or place in protective isolation.
B. Mother has no history of chickenpox; exposed during period 6-20 days antepartum.‡	No	No	1. Exposed mother and infant: send home at earliest date unless siblings at home have communicable chickenpox.§ If so, may administer VZIG and discharge home, as above. 2. Other mothers and infants: no special management indicated. 3. Hospital personnel: no precautions indicated if there is a history of previous chickenpox or zoster. In absence of history, immediate serologic testing is indicated to determine immune status.* Nonimmune personnel should be excluded from patient contact until 21 days after an exposure. 4. If mother develops varicella 1 to 2 days post partum, infant should be given VZIG.

*Send serum to virus diagnostic laboratory for determination of antibodies to VZV by a sensitive technique (e.g., FAMA, LA, ELISA). Personnel may continue to work for 8 days after exposure pending serologic results because they are not potentially infectious during this period. Antibodies to VZV >1:4 probably are indicative of immunity.

†VZIG is available through the American Red Cross. The dose for a newborn is 1.25 mL (1 vial). The dose for a pregnant woman is conventionally 6.25 mL (5 vials).

‡If exposure occurred less than 6 days antepartum, mother would not be potentially infectious until at least 72 hours post partum.

§Considered noninfectious when no new vesicles have appeared for 72 hours and all lesions have crusted.

(Continued)

spread of virus to the infant varies from mild to severe and does not seem to vary with the antepartum or postpartum onset of rash in the mother. It is uncertain what role maternal antibodies play in the severity of the infant's disease. More severe disease seems to be associated with severe respiratory illness and bacterial infection. Postnatal exposure leading to measles after 14 days of life is generally mild, probably because of passively acquired antibodies from the mother. Severe measles in children younger than 1 year of age may occur because of declining passively acquired antibodies and complications of respiratory illness and rare cases of encephalitis.

TABLE 17-2 Guidelines for preventive measures after exposure to chickenpox in the nursery or maternity ward—cont'd

Type of exposure or disease	Chickenpox lesions present: Mother	Chickenpox lesions present: Neonate	Disposition
C. Onset of maternal chickenpox occurs antepartum[‡] or post partum.	Yes	No	1. Infected mother: isolate until no longer clinically infectious. If seriously ill, treat with acyclovir.[‖] 2. Infected mother's infant: administer VZIG[†] to neonates born to mothers with onset of chickenpox less than 5 days before delivery and isolate separately from mother. Send home with mother if no lesions develop by the time mother is noninfectious. 3. Other mothers and infants: send home at earliest date. VZIG may be given to exposed neonates. 4. Hospital personnel: same as B-3.
D. Onset of maternal chickenpox occurs antepartum.[§]			1. Mother: isolation unnecessary. 2. Infant: isolate from other infants but not from mother. 3. Other mothers and infants: same as C-3 (if exposed). 4. Hospital personnel: same as B-3 (if exposed).
E. Congenital chickenpox	No	Yes	1. Infected infant and mother: same as D-1 and D-2. 2. Other mothers and infants: same as C-3. 3. Hospital personnel: same as B-3.

[‖]Dosage of acyclovir for pregnant woman is 30 mg/kg/day; for seriously ill infant with varicella, 750 to 1500 mg/m^2/day.
From Gershon AA: Chickenpox, measles and mumps. In Remington JS, Klein JO (ed): Infectious Diseases of the Fetus and Newborn Infant. 4th ed. Philadelphia. WB Saunders, 1995.

Measles virus has not been identified in breast milk, whereas measles-specific antibodies have been documented.[1] Infants exposed to mothers with documented measles while breastfeeding should be given immune globulin and isolated from the mother until 72 hours after the onset of rash, which is often only a very short period after diagnosis of measles in the mother. The breast milk can be pumped and given to the infant because sIgA begins to be secreted in breast milk within 48 hours of onset of the exanthem in the mother. Table 17-3 summarizes management of the hospitalized mother and infant with measles exposure or infection.[101]

Mumps

Mumps is an acute transient benign illness with inflammation of the parotid gland and other salivary glands and often involving the pancreas, testicles, and meninges. Mumps occurs infrequently in pregnant women (1 to 10 cases in 10,000 pregnancies) and is generally benign. Mumps virus has been isolated from saliva, respiratory secretions, blood, testicular tissue, urine, CSF in cases of meningeal involvement, and breast milk. The period of infectivity is believed to be between 7 days before and 9 days after the onset of parotitis, with the usual incubation period being 14 to 18 days.

TABLE 17-3 Guidelines for preventive measures after exposure to measles in the nursery or maternity ward

Type of exposure or disease	Measles (prodrome or rash) present*		Disposition
	Mother	Neonate	
A. Siblings at home have measles* when neonate and mother are ready for discharge from hospital.	No	No	1. Neonate: protective isolation and immune globulin (IG) indicated unless mother has unequivocal history of previous measles or measles vaccination.† 2. Mother: with history of previous measles or measles vaccination, she may either remain with neonates or return to older children. Without previous history, she may remain with neonate until older siblings are no longer infectious, or she may receive IG prophylactically and return to older children.
B. Mother has no history of measles or measles vaccination exposure 6 to 15 days antepartum.‡	No	No	1. Exposed mother and infant: administer IG to each and send home at earliest date unless siblings at home have communicable measles. Test mothers for susceptibility if possible. If susceptible, administer live measles vaccine 8 weeks after IG. 2. Other mothers and infants: same unless clear history of previous measles or measles vaccination in the mother. 3. Hospital personnel: unless clear history of previous measles or measles vaccination, administer IG within 72 hours of exposure. Vaccinate 8 weeks or more later.
C. Onset of maternal measles occurs antepartum or post partum.§	Yes	Yes	1. Infected mother and infant: isolate together until clinically stable, then send home. 2. Other mothers and infants: same as B-3 except infants should be vaccinated at 15 months of age. 3. Hospital personnel: same as B-3.
D. Onset of maternal measles occurs antepartum or post partum.§	Yes	No	1. Infected mother: isolate until no longer infectious.§ 2. Infected mother's infant: isolate separately from mother. Administer IG immediately. Send home when mother is no longer infectious. Alternatively, observe in isolation for 18 days for modified measles,‖ especially if IG administration was delayed more than 4 days. 3. Other mothers and infants: same as C-2. 4. Hospital personnel: same as B-3.

*Catarrhal stage or less than 72 hours after onset of exanthem.

†Vaccination with live attenuated measles virus.

‡With exposure less than 6 days antepartum, mother would not be potentially infectious until at least 72 hours post partum.

§Considered infectious from onset of prodrome until 72 hours after onset of exanthem.

‖Incubation period for modified measles may be prolonged beyond the usual 10 to 14 days.

From Gershon AA: Chickenpox, measles and mumps. In Remington JS, Klein JO (ed): Infectious Diseases of the Fetus and Newborn Infant, 4th ed. Philadelphia, WB Saunders, 1995.

Prenatal infection with the mumps virus causes an increase in the number of abortions when infection occurs in the first trimester. A small increase in the number of premature births was noted in one prospective study of maternal mumps infection.[101] No conclusive evidence suggests congenital malformations associated with prenatal infection, not even with endocardial fibroelastosis, as originally reported in the 1960s.

Perinatal mumps (transplacentally or postnatally acquired) has rarely if ever been documented. Natural mumps virus has been demonstrated to infect the placenta and infect the fetus, and live attenuated vaccine virus has been isolated from the placenta but not from fetal tissue in women vaccinated 10 days before induced abortion. Antibodies to mumps do cross the placenta.

Postnatal mumps in the first year of life is typically very benign. No epidemiologic data suggest that mumps infection is more or less common or severe in breastfed infants compared with formula fed infants. Although mumps virus has been identified in breast milk and mastitis is a rare complication of mumps in the mature female, no evidence indicates that breast involvement occurs more frequently in lactating women. If mumps occurs in the mother, breastfeeding can continue because exposure has already occurred throughout the 7 days before the development of the parotitis, and sIgA in the milk may help to mitigate the symptoms in the infant.

Polioviruses

Poliovirus infections (types 1, 2, and 3) cause a range of illness, with 90% to 95% subclinical, 4% to 8% abortive, and 1% to 2% manifest as paralytic poliomyelitis. A review by Bates[22] from 1955 of 58 cases of poliomyelitis in infants younger than 1 month of age demonstrated paralysis or death in more than 70% and only one child without evidence of even transient paralysis. More than half the cases were ascribed to transmission from the mothers, although no mention was made of breastfeeding. Breastfeeding rates at the time were about 25%.

Prenatal infection with polioviruses does cause an increased incidence of abortion. Prematurity and stillbirth apparently occur more frequently in mothers who developed paralytic disease versus inapparent infection.[129] Although individual reports of congenital malformations in association with maternal poliomyelitis exist, no epidemiologic data suggest that polioviruses are teratogenic. Also, no evidence indicates that live attenuated vaccine poliovirus given during pregnancy is associated with congenital malformations.[58,114]

Perinatal infection has been noted in several case reports of infants infected in utero several days before birth who had severe disease manifesting with neurologic manifestations (paralysis) but without fever, irritability, or vomiting. Additional case reports of infection acquired postnatally demonstrate illness more consistent with poliomyelitis of childhood. These cases were more severe and involved paralysis, which may represent reporting bias.[58]

No data are available concerning the presence of poliovirus in breast milk, although antibodies to poliovirus types 1, 2, and 3 have been documented.[174] In this era of increasing worldwide poliovirus vaccination, the likelihood of prenatal or perinatal poliovirus infection is decreasing. Maternal susceptibility to poliovirus should be determined before conception and poliovirus vaccine offered to susceptible women. An analysis of the last great epidemic in Italy in 1958 was done using a population-based case-control study.[211] In 114,000 births, 942 infants were reported with paralytic poliomyelitis. A group of matched control subjects was selected from infants admitted to the hospital at the same time. Using the dichotomous variable of never breastfed and partially breastfed, 75 never-breastfed infants were among the cases and 88 among the control group. The authors determined an odds ratio of 4:2, with 95% confidence interval of 1.4 to 14, demonstrating that the risk of paralytic poliomyelitis was higher in infants never breastfed and lowest among those exclusively breastfed. Because by the time the diagnosis of poliomyelitis is made in a breastfeeding mother, the exposure of the infant to poliovirus from maternal secretions has already occurred, and because the breast milk already contains antibodies

that may be protective, no reason exists to interrupt breastfeeding. Breastfeeding also does not interfere with successful immunization against poliomyelitis with oral or inactivated poliovirus vaccine.[46]

Tumor virus in breast milk

No documented evidence indicates that women with breast cancer have RNA of tumor virus in their milk. No correlation between RNA-directed DNA polymerase activity has been found in women with a family history of breast cancer. RNA-directed DNA polymerase activity, a reserve transcriptase, is a normal feature of the lactating breast.[59,89,222]

Epidemiologic studies

Epidemiologic data conflict with the suggestion that the tumor agent is transmitted through the breast milk. The incidence of breast cancer is low among groups who had nursed their infants, including lower economic groups, foreign-born groups, and those in sparsely populated areas.[169] The frequency of breast cancer in mothers and sisters of a woman with breast cancer is two to three times that expected by chance. This could be genetic or environmental. Cancer actually is equally common on both sides of the family of an affected woman. If breast milk were the cause, it should be transmitted from mother to daughter. When mother-daughter incidence of cancer was studied, no relationship was found to breastfeeding.

Sarkar and associates[226] reported that human milk, when incubated with mouse mammary tumor virus, caused degradation of the particular morphology and decreased infectivity and reverse transcriptase activity of the virions. They suggest that the significance of this destructive effect of human milk on mouse mammary tumor virus may account for the difficulty in isolating the putative human mammary tumor agent. Sanner[225] showed that the inhibitory enzymes in milk can be removed by special sedimentation technique. He ascribes the discrepancies in isolating virus particles in human milk to these factors, which inhibit RNA-directed DNA polymerase.

Current position

The fear of cancer in the breastfed female offspring of a woman with breast cancer does not justify avoiding breastfeeding. Breastfed women have the same breast cancer experience as nonbreastfed women, and no increase is seen in benign tumors. Daughters of breast cancer patients have an increased risk of developing benign and malignant tumors because of their heredity, not because of their breastfeeding history.[180,184]

Unilateral breastfeeding (limited to the right breast) is a custom of Tanka women of the fishing villages of Hong Kong. Ing and associates[133] investigated the question, "Does the unsuckled breast have an altered risk of cancer?" They studied breast cancer data from 1958 to 1975. Breast cancer occurred equally in the left and the right breasts. Comparison of patients who had nursed unilaterally with nulliparous patients and with patients who had borne children but not breastfed indicated a highly significantly increased risk of cancer in the unsuckled breast. The authors conclude that in postmenopausal women who have breastfed unilaterally, the risk of cancer is significantly higher in the unsuckled breast. They believed that breastfeeding may help protect the suckled breast against cancer.[133]

Others[176] have suggested that Tanka women are ethnically a separate people and that left-sided breast cancer may be related to their genetic pool and not to their breastfeeding habits. No mention has been made of other possible influences, such as the impact of their role as "fishermen" or any inherent trauma to the left breast.[207]

In 1926, Lane-Claypon[204] stated that the breast that had never lactated was more liable to become cancerous. Nulliparity and absence of breastfeeding had been considered important risk factors for breast cancer. MacMahon and associates[169] reported in 1970 that age at first full-term pregnancy was the compelling factor, and the younger the mother, the less the risk.

In a collective review of the etiologic factors in cancer of the breast in humans, Papaioannou concludes, "Genetic factors, viruses, hormones, psychogenic stress, diet and other possible factors,

probably in that order of importance, contribute to some extent to the development of cancer of the breast."[204]

Wing[279] concluded in her 1977 review on human milk and health that "in view of the complete absence of any studies showing a relationship between breastfeeding and increased risk of breast cancer, the presence of virus-like particles in breast milk should not be a contraindication to breastfeeding." Henderson and associates[116] made a similar statement in 1974, whereas Vorherr[272] concluded in 1979 that the roles of pregnancy and lactation in the development and prognosis of breast cancer had not been determined.

Gradually, studies have appeared challenging the dogma. Brinton and associates,[35] McTiernan and Thomas,[177] and Layde and associates[158] showed the clearly protective effects of breastfeeding. Another example is a study conducted to clarify whether lactation has a protective role against breast cancer in an Asian people, regardless of confounding effects of age at first pregnancy, parity, and closely related factors.[287] In a hospital-based case-control study of 521 women without breast cancer, statistical adjustment for potential confounders and a likelihood ratio test for linear trend were done by unconditional logistic regression. Total months of lactation regardless of parity was the discriminator. Regardless of age of first pregnancy and parity, lactation had an independent protective effect against breast cancer in Japanese women.[287] Although breast cancer incidence is influenced by genetics, stress, hormones, and pregnancy, breastfeeding clearly has a protective effect. "There is a reduction in the risk of breast cancer among premenopausal women who have lactated. No reduction in the risk of breast cancer occurred among postmenopausal women with a history of lactation," according to Newcombe and associates,[191] reporting a multicenter study in 1993.

Hepatitis in the mother

The diagnosis of hepatitis in the pregnant woman or nursing mother causes significant anxiety. The first issue is determining the etiology of the hepatitis, which then allows an informed discussion of the risk to the fetus/infant. The differential diagnosis of acute hepatitis includes (1) common causes of hepatitis, such as hepatitis A, B, C, and D; (2) uncommon causes of hepatitis, such as hepatitis E and G, CMV, echoviruses, enteroviruses, EBV, HSV, rubella, VZV, yellow fever virus; (3) rare causes of hepatitis, such as Ebola virus, Junin virus and Machupo virus (cause hemorrhagic fever), Lassa virus, and Marburg virus; and (4) nonviral causes, such as hepatotoxic drugs, alcoholic hepatitis, toxoplasmosis, autoimmune hepatitis, bile duct obstruction, ischemic liver damage, Wilson's disease, α_1-antitrypsin deficiency, and metastatic liver disease. The following sections focus on hepatitis viruses A to G. Other infectious agents that can cause hepatitis are considered individually in other sections. Box 17-1 provides hepatitis terminology.

Martin and associates[172] outline a succinct diagnostic approach to the patient with acute viral hepatitis and chronic viral hepatitis (Figs. 17-4 and 17-5). The approach involves using the four serologic markers (IgM anti-HAV, HBsAg, IgM anti-HBcAg, anti-HCV) as the initial diagnostic tests. Simultaneous consideration of other etiologies of acute liver dysfunction is appropriate depending on the patient's history. If the initial diagnostic tests are all negative, subsequent additional testing for anti-HDV, HCV-RNA, HGV-RNA, anti-HEV, or HEV-RNA may be necessary. If initial testing reveals positive HBsAg, testing for anti-HDV, HBeAg, and HBV-DNA is appropriate. These additional tests are useful in defining the prognosis for the mother and the risk of infection to the infant. During the diagnostic evaluation, it is appropriate to discuss with the mother or parents the theoretic risk of transmitting infectious agents that cause hepatitis via breastfeeding. The discussion should include an evaluation of the positive and negative effects of suspending or continuing breastfeeding until the exact etiologic diagnosis is determined. The relative risk of transmission of infection to the infant can be estimated and specific preventive measures provided for the infant (Table 17-4).

BOX 17-1 Terminology for hepatitis

Hepatitis A Virus (HAV)	
IgM anti-HAV	Immunoglobulin M antibody against HAV
HAV-RNA	HAV ribonucleic acid
Hepatitis B Virus	
HBsAg	Hepatitis B surface antigen
HBeAg	Hepatitis Be antigen
HBcAg	Hepatitis B core antigen
Anti-HBe	Antibody against hepatitis Be antigen
IgM anti-HBcAg	IgM antibody against hepatitis B core antigen
HBV-DNA	HBV deoxyribonucleic acid
HBIG	Hepatitis B immune globulin
Hepatitis C Virus (HCV)	
Anti-HCV	Antibody against HCV
HCV-RNA	HCV ribonucleic acid
Hepatitis D Virus (HDV)	
Anti-HDV	Antibody against HDV
Hepatitis E Virus (HEV)	
HEV-RNA	HEV ribonucleic acid
Hepatitis G Virus (HGV)	
HGV-RNA	HGV ribonucleic acid
TT Virus (TTV)	
TTV-DNA	TT virus deoxyribonucleic acid
Other	
NANBH	Non-A, non-B hepatitis
ISG	Immune serum globulin

Hepatitis A

Hepatitis A virus (HAV) is usually an acute self-limited infection. The illness is typically mild, and generally subclinical in infants. Occasionally, HAV infection is prolonged or relapsing, extending over 3 to 6 months, rarely is fulminant, but does not lead to chronic infection. The incidence of prematurity after maternal HAV infection is increased, but no evidence to date indicates obvious birth defects or a congenital syndrome.[235,292] HAV infection in premature infants may lead to prolonged viral shedding.[219] Transmission is most often person to person (fecal-oral), and transmission in food-borne or water-borne epidemics has been described. Transmission via blood products and vertical transmission (mother to infant) are rare.[273] Transmission in daycare settings has been clearly described.

Infection with HAV in the newborn is uncommon and does not seem to be a significant problem. The usual period of viral shedding and presumed contagiousness lasts 1 to 3 weeks. Acute maternal HAV infection in the last trimester or in the postpartum period could lead to infection in the infant. Symptomatic infection can be prevented by immune globulin (IG) administration, and 80% to 90% of disease can be prevented by IG administration within 2 weeks of exposure. HAV vaccine can be administered simultaneously with IG without affecting the seroconversion rate to produce rapid and prolonged HAV serum antibody levels.

Transmission of HAV via breast milk has been implicated in one case report, but no data exist on the frequency of isolating HAV from breast milk.[273] Because HAV infection in infancy is rare and usually subclinical without chronic disease, and because exposure has already occurred by the time the etiologic diagnosis of hepatitis in the mother is made, no reason exists to interrupt breastfeeding with maternal HAV infection. The infant should receive IG and HAV vaccine, administered simultaneously.

Hepatitis B

Hepatitis B virus (HBV) infection leads to a broad spectrum of illness, including asymptomatic seroconversion, nonspecific symptoms (fever, malaise, fatigue), clinical hepatitis with or without jaundice, extrahepatic manifestations (arthritis, rash, renal involvement), fulminant hepatitis, and chronic HBV infection. Chronic HBV infection occurs in up to 90% of infants infected via perinatal and vertical transmission and in 30% of children infected between 1 to 5 years of age. Given the increased

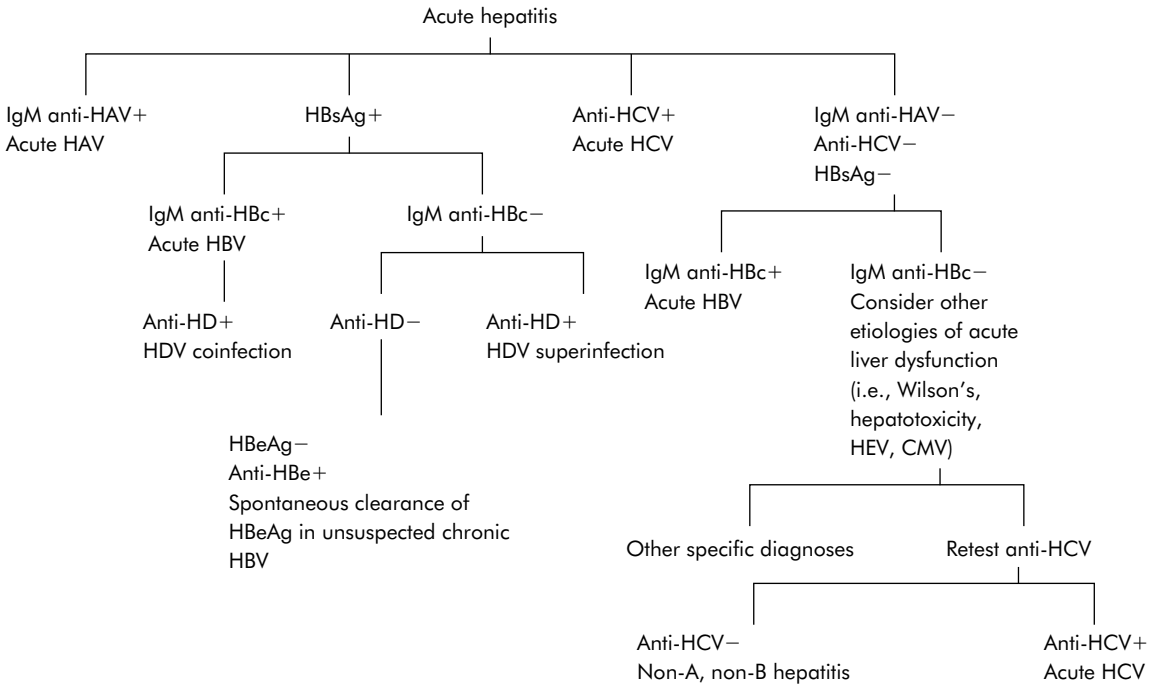


Figure 17-4. Diagnostic approach to patient with acute viral hepatitis. See Box 17-1 for definitions of abbreviations. (From Martin P, Friedman L, Dienstag J: Diagnostic approach. In Zuckerman A, Thomas H (eds): Viral Hepatitis: Scientific Basis and Clinical Management. Edinburgh, Churchill Livingstone, 1993.)

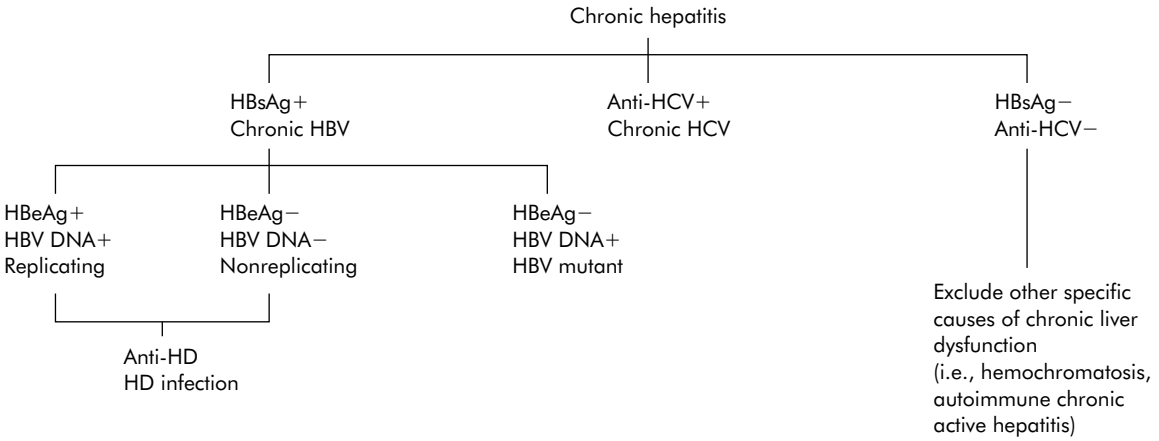


Figure 17-5. Diagnostic approach to patient with chronic viral hepatitis. See Box 17-1 for definitions of abbreviations. (From Martin P, Friedman L, Dienstag J: Diagnostic approach. In Zuckerman A, Thomas H (eds): Viral Hepatitis: Scientific Basis and Clinical Management. Edinburgh, Churchill Livingstone, 1993.)

TABLE 17-4 Viral hepatitis in association with breastfeeding*

Hepatitis	Virus	Identified in breast milk	Factors for peri/postnatal transmission	Prevention	Breastfeeding†
A	Picornaviridae (RNA)	?	Vertical transmission uncertain or rare HAV in pregnancy associated with premature birth	ISG HAV vaccine	Limited evidence of transmission via breastfeeding or of serious disease in infants Breastfeeding OK after ISG and vaccine
B	Hepadnaviridae (DNA)	HBsAg HBV-DNA	Increased risk of vertical transmission with HBeAg+, in countries where HBV is endemic or early in maternal infection, before Ab production	HBIG HBV vaccine	Low theoretic risk Virtually no risk after HBIG and HBV vaccine Breastfeeding OK after HBIG and vaccine
C	Flavivirus (RNA)	HCV-RNA detected	Increased risk when mother HIV+ and HCV+ or with increased HCV-RNA titers Vertical transmission uncommon	None	Positive theoretic risk Inadequate data on relative risk Breastfeeding OK after informed discussion with parents
D	Deltaviridae (RNA negative strand, circular)	?	Requires coinfection/superinfection with HBV Vertical transmission rare	None (except to prevent HBV infection, give HBIG/HBV vaccine)	Prevent HBV infection with HBIG and vaccine Breastfeeding OK after HBIG and vaccine
E	Caliciviridae (RNA)	+	Severe disease in pregnant women (20% mortality)	ISG and subunit vaccine being tested	Usually subclinical infection in children Breastfeeding OK
G	Related to calicivirus and flaviviruses (RNA)	?	Vertical transmission occurs	None	Inadequate data
TT	TT virus (DNA, circular, single stranded)	TIV-DNA detected	Vertical transmission occurs	None	Inadequate data

* See Box 17-1 for abbreviations. Ab, Antibody; HIV, human immunodeficiency virus.

†With any type of infectious hepatitis, discussion of what is known and not known concerning transmission should be related to the mother/parents, and together an informed decision can be made concerning breastfeeding.

Data from Committee on Infectious Diseases, American Academy of Pediatrics: Red Book: Report of the Committee on Infectious Diseases, 26th ed. Elk Grove, IL, The Academy, 2003.

risk of significant sequelae from chronic infection (chronic active hepatitis, chronic persistent hepatitis, cirrhosis, primary hepatocellular carcinoma), prevention of HBV infection in infancy is crucial. Transmission of HBV is usually through blood or body fluids (stool, semen, saliva, urine, cervical secretions).[62]

Vertical transmission either transplacentally or perinatally during delivery has been well described throughout the world. Vertical transmission rates in areas where HBV is endemic (Taiwan and Japan) are very high, whereas transmission to infants from HBV carrier mothers in other areas where HBV carrier rates are low is uncommon.[250] Transmission of HBV to infants occurs in up to 50% of infants when the mother is acutely infected immediately before, during, or soon after pregnancy.[291]

Hepatitis B surface antigen (HBsAg) is found in breast milk, but transmission by this route is not well documented. Beasley and associates[23,24] demonstrated that although breast milk transmission is possible, seroconversion rates are no different between breastfed and nonbreastfed infants in a long-term follow-up study of 147 HBsAg-positive mothers. Transmission, when it does happen, probably occurs during labor and delivery. The AAP Committee on Infectious Diseases stated in 2003 that "studies from Taiwan and England have indicated that breastfeeding by HBsAg-positive women does not increase significantly the risk of infection among their infants."[62]

Screening of all pregnant women for HBV infection is an essential first step to preventing vertical transmission. Universal HBV vaccination at birth and during infancy, along with administration of hepatitis B immune globulin (HBIG) immediately after birth to infants of HBsAg-positive mothers, prevents HBV transmission in more than 95% of cases. Breastfeeding by HBsAg-positive women is not contraindicated, but immediate administration of HBIG and HBV vaccine should occur. Two subsequent doses of vaccine should be given at the appropriate intervals and dosages for the specific HBV vaccine product. This decreases the small theoretic risk of HBV transmission from breastfeeding to almost zero.

When acute peripartum or postpartum hepatitis occurs in the mother and HBV infection is a possibility, with its associated increased risk of transmission to the infant, a discussion with the mother or parents should identify the potential risks and benefits of continuing breastfeeding until the etiology of the hepatitis can be determined. If an appropriate alternative source of nutrition is available for the infant, breast milk should be withheld until the etiology of the hepatitis is identified. HBIG and HBV vaccine can be administered to the infant who has not already been immunized or has no documented immunity against HBV.[251] If acute HBV infection is documented in the mother, breastfeeding can continue once immunization has begun.

Hepatitis C

Acute infection with hepatitis C virus (HCV) can be indistinguishable from hepatitis A or B infection; however, it is typically asymptomatic or mild. HCV infection is the major cause of bloodborne non-A, non-B hepatitis (NANBH). Chronic HCV infection is reported to occur 70% to 85% of the time regardless of age at time of infection. Sequelae of chronic HCV infection are similar to those associated with chronic HBV infection. Bortolotti and associates[32] described two groups of children with HCV infection whom they observed for 12 to 48 months. The first group of 14 children, who acquired HCV infection early in life, presumably from their mothers, all demonstrated biochemical evidence of liver disease in the first 12 months of life. Two of these children subsequently cleared the viremia and had normal liver function, an additional three children developed normal liver function despite persistent HCV viremia, and the remaining children had persistent viremia and abnormal liver function. The second group of 16 children, with chronic HCV infection, remained free of clinical symptoms of hepatitis, but 10 (62%) of them had mild alanine aminotransferase (ALT) elevations, and 7 (44%) of the 16 who had liver biopsies had histologic evidence of mild to moderate hepatitis.

The two commonly identified mechanisms of transmission of HCV are transfusions of blood or blood products and IV drug use. However, other routes of transmission exist, because HCV infection occurs even in the absence of obvious direct contact with significant amounts of blood. Other body fluids contaminated with blood probably serve as sources of infection. Transmission through sexual contact occurs infrequently and probably requires additional contributing factors, such as coinfection with other sexually transmitted agents or high viral loads in serum and other body fluids. Studies of transmission in households without other risk factors has demonstrated either very low rates of transmission or no transmission.

The reported rates of vertical transmission vary widely. In mothers with unknown HIV status or known HIV infection, the rates of vertical transmission were 4% to 100%, whereas the rates varied between 0% and 42% in known HIV-negative mothers.[74] These same studies suggest that maternal coinfection with HIV, HCV genotype, active maternal liver disease, and the serum titer of maternal HCV-RNA may be associated with increased rates of vertical transmission.[170,195,290] The correlation between HCV viremia, the HCV viral load in the mother and vertical transmission of HCV is well documented.[185,224,257,286] The clinical significance and risk of liver disease after vertical transmission of HCV are still unknown. The timing of HCV infection in vertical transmission is also unknown. In utero transmission has been suggested by some studies,[86] whereas intrapartum or postpartum transmission was proposed by Ohto and associates[196] when they documented the absence of HCV-RNA in the cord blood of neonates who later became HCV-RNA positive at 1 to 2 months of age. More recently, Gibb and associates reported two pieces of data supporting the likelihood of intrapartum transmission as the predominant time of vertical transmission: (a) low sensitivity of PCR for HCV RNA testing in the first month of life with a marked increase in sensitivity after that for diagnosing HCV infection in infants and (b) a lower transmission risk for elective cesarean section (without prolonged rupture of membranes) compared with vaginal or emergency cesarean section delivery.[103]

The risk of HCV transmission via breast milk is uncertain. Anti-HCV antibody and HCV-RNA has been demonstrated in colostrum and breast milk, although the levels of HCV-RNA in milk did not correlate with the titers of HCV-RNA in serum.[111,164] Nevertheless, transmission of HCV via breastfeeding (and not in utero, intrapartum, or from other postpartum sources) has not been proved in the small number infants studied. Transmission rates in breastfed and nonbreastfed infants appear to be similar, but various important factors have not been controlled, such as HCV-RNA titers in the mothers, examination of the milk for HCV-RNA, exclusive breastfeeding versus exclusive formula feeding versus partial breastfeeding, and duration of breastfeeding.[103,164,170,183,185,197,290] Zanetti and associates[290] documented the absence of HCV transmission in 94 mother-infant pairs when the mother had only HCV (no HIV) infection and no transmission in 71 mother-infant pairs who breastfed, including 23 infants whose mothers were seropositive for HCV-RNA. Eight infants in that study were infected with HCV, their mothers had both HIV and HCV, and three of these eight infants were infected with both HIV and HCV. The HCV-RNA levels were significantly higher in the mothers coinfected with HIV compared with those mothers with HCV alone.

Overall, (1) the risk of HCV infection via breastfeeding is very low, (2) the risk of HCV infection appears to be more frequent in association with HIV infection and higher levels of HCV-RNA in maternal serum, (3) no effective preventive therapies (IG or vaccine) exist, and (4) the risk of chronic HCV infection and subsequent sequelae with any infection is high. It is, therefore, appropriate to discuss the theoretic risk of breastfeeding in HCV-positive mothers with the mother or parents and to consider proscribing breast milk when appropriate alternative sources of nutrition are available for the infant. HIV infection is a separate contraindication to breastfeeding. Additional study is necessary to determine the exact role of breastfeeding in the transmission of HCV, including the quantitative

measurement of HCV-RNA in colostrum and breast milk, the relative risk of HCV transmission in exclusively or partially breastfed infants versus the risk in formula fed infants, and the effect of duration of breastfeeding on transmission.

The current position of the CDC is that no data indicate that HCV virus is transmitted through breast milk. Therefore, breastfeeding by a HIV-negative mother is not contraindicated.[20]

Infants born to HCV-RNA-positive mothers require follow-up through 18 to 24 months of age to determine the infant's HCV status, regardless of the mode of infant feeding. Infants should be tested for alanine aminotransferase and hepatitis C virus RNA at 3 months and 12 to 15 months of age. Alanine aminotransferase and anti-hepatitis C virus antibody should be tested at 18 to 24 months of age in order to confirm the infant's status: uninfected, ongoing hepatitis C infection, or past hepatitis C virus infection.

Hepatitis D

Hepatitis delta virus (HDV) is a defective RNA virus that causes hepatitis only in persons also infected with HBV. The infection occurs as either an acute coinfection of HBV and HDV or a superinfection of HBV carriers. This "double" infection results in more frequent fulminant hepatitis and chronic hepatitis, which can progress to cirrhosis. The virus uses its own HBV-RNA (circular, negative-strand RNA) with an antigen, HDAg, surrounded by the surface antigen of HBV, HBsAg. HDV is transmitted in the same way as HBV, especially through the exchange of blood and body fluids. HDV infection is uncommon where the prevalence of HBV is low. In areas where HBV is endemic, the prevalence of HDV is highly variable. HDV is very common in tropical Africa and South America as well as in Greece and Italy but is uncommon in the Far East and in Alaskan Eskimos, despite the endemic occurrence of HBV in these areas.[244]

Transmission of HDV has been reported to occur from household contacts and, rarely, through vertical transmission. No data are available on transmission of HDV by breastfeeding. HDV infection can be prevented by blocking infection with HBV; therefore, HBIG and HBV vaccine are the best protection. In addition to HBIG and HBV vaccine administration to the infant of a mother infected with both HBV and HDV, discussion with the mother or parents should include the theoretic risk of HBV and HDV transmission through breastfeeding. As with HBV, once HBIG and HBV vaccine have been given to the infant, the risk of HBV or HDV infection from breastfeeding is negligible. Therefore, breastfeeding after an informed discussion with the parents is acceptable.

Hepatitis E

Hepatitis E virus (HEV) is a cause of sporadic and epidemic, enterically transmitted NANBH, which is typically self-limited and without chronic sequelae. HEV is notable for causing high mortality rate in pregnant women. Transmission is primarily via the fecal-oral route, commonly contaminated water or food. High infection rates have been reported in adolescents and young adults (ages 15 to 40 years). Tomar reported that 70% of cases of HEV infections in the pediatric population in India manifest as acute hepatitis. Maternal-neonatal transmission was documented when the mother developed hepatitis E infection in the third trimester. Although HEV was demonstrated in breast milk, no transmission via breast milk was confirmed in the report. Five cases of transfusion associated hepatitis E were reported.[262] Epidemics are usually related to contamination of water. Person-to-person spread is minimal, even in households and daycare settings. Although IG may be protective, no controlled trials have been done. Animal studies suggest that a recombinant subunit vaccine may be feasible.[216]

HEV infection in infancy is rare, and no data exist on transmission of HEV by breastfeeding. There is no evidence of clinically significant postnatal HEV infection in infants or of chronic sequelae in association with HEV infection and no documented HEV transmission through breast milk. Currently no contraindication exists to breastfeeding with maternal HEV infection. IG has

not been shown to be effective in preventing infection, and no vaccine is available for HEV.

Hepatitis G

Hepatitis G virus (HGV) has recently been confirmed as a cause of NANBH distinct from hepatitis viruses A through E. Several closely related genomes of HGV, currently named GBV-A, -B, and -C, appear to be related to HCV, the Pestiviruses, and the Flaviviruses. Epidemiologically, HGV is most often associated with transfusion of blood, although studies have identified nontransfusion-related cases. HGV genomic RNA has been detected in some patients with acute and chronic hepatitis and a small number of patients with fulminant hepatits. GBV-C/HGV has also been found in some patients with inflammatory bile duct lesions, but the pathogenicity of this virus is unconfirmed. HGV-RNA has been detected in 1% to 3% of healthy blood donors in the United States.[6] Feucht and associates[88] described maternal-to-infant transmission of HGV in three of nine children. Two of the three mothers were coinfected with HIV and the third with HCV. None of these infants developed signs of liver disease. Neither the timing nor the mode of transmission was clarified. Lin and associates[163] reported no HGV transmission in three mother-infant pairs after cesarean delivery and discussed transplacental spread via blood as the most likely mode of HGV infection in vertical transmission. Wejstal and associates reported on perinatal transmission of HGV to 12 of 16 infants born to HGV viremic mothers, identified by PCR. HGV did not appear to cause hepatitis in the children.[274]

Fischler and associates[90] followed eight children born to HGV-positive mothers and found only one to be infected with HGV. That child remained clinically well, while his twin, also born by cesarean delivery and breastfed, remained HGV negative over 3 years of observation. Five of the other six children breastfed for variable periods without evidence of HGV infection. Ohto and associates examined HGV mother-to-infant transmission. Of 2979 pregnant Japanese women who were screened, 32 were identified as positive for GBV-C/HGV RNA by PCR; 26 of 34 infants born to the 32 HGV positive women were shown to be HGV RNA positive. Reportedly, none of the infants demonstrated a clinical picture of hepatitis, although two infants had persistent mild elevations (less than two times normal) of alanine aminotransferase. The viral load in mothers, who transmitted HGV to their infants, was significantly higher than in nontransmitting mothers. Infants delivered by elective cesarean section had a lower rate of infection (3 in 7) compared with infants born by emergency cesarean section (2 of 2) or born vaginally (21 of 25). In this study, HGV infection in breastfed infants was four times more common than in formula fed infants, but this difference was not statistically significant because only four infants were formula fed. The authors report there was no correlation between infection rate and duration of breastfeeding. Testing of the infants was not done frequently and early enough routinely through the first year of life to determine the timing of infection in these infants.[197] Schröter and associates reported transmission of HGV to 3 of 15 infants born to HGV RNA positive mothers at 1 week of age. None of 15 breast milk samples were positive for GBV-C/HGV RNA, and all of the children who were initially negative for HGV RNA in serum remained negative at follow-up between 1 to 28 months of age.[234]

The foregoing data suggest that transmission is more likely to be vertical, prior to, or at delivery rather than via breast feeding. The pathogenicity and the possibility of chronic disease due to HGV infection remain uncertain at this time. Insufficient data are available to make a recommendation concerning breastfeeding by the HGV-infected mother.

TT Virus

TT virus is a recently identified virus found in a patient (TT) with posttransfusion hepatitis not associated with the other hepatitis related viruses A through G. TTV has been described as an unenveloped, circular, single-stranded DNA virus.[199]

This virus is prevalent in healthy individuals, including healthy blood donors, as well as having been identified in patients with hepatitis. TTV DNA has been detected in infants of TTV-positive and TTV-negative mothers. Ohto and associates reported no TTV DNA was detected in cord blood from 38 infants, and it was detected in only 1 of 14 samples taken at 1 month of age. They noted an increasing prevalence, from 6 months (22%) to 2 years (33%), which they ascribed to acquisition via nonparenteral routes. In comparisons of the TTV DNA in TTV-positive mothers and their positive infants; 6 of 13 showed high level nucleotide sequence similarity, and 7 of 13 differed by greater than 10%.[198]

Schröter and associates reported on TTV DNA in breast milk examined retrospectively. Notably, TTV DNA was detected in 22 of 23 serum samples of infants at 1 week of age, who were born to 22 women viremic for TTV DNA. Twenty-four women who were negative for TTV DNA gave birth to 24 children who were initially negative for TTV DNA and remained negative throughout the observation period (mean 7.5 months, range 1 to 28 months). TTV DNA was detected in 77% of breast milk samples from TTV viremic women and in none of the breast milk samples from TTV-negative women. There was no clinical or laboratory evidence of hepatitis found in the 22 children who were observed to be TTV DNA positive during the period of this study.[234] Other authors have reported TTV in breast milk detected by PCR. They describe the absence of TTV DNA in infants at 5 days and 3 months of age, and 4 of 10 infants were positive for TTV DNA at 6 months of age, suggesting the late acquisition of infection via breastfeeding.[135]

TT virus is transmitted in utero and is found in breast milk. There is no evidence of clinical hepatitis in infants related to TTV infection, nor is there evidence for a late chronic hepatitis. Given the current available information there is no reason to proscribe breastfeeding by TTV-positive mothers. There is certainly more to be understood concerning the chronic nature of this infection and the possible pathogenesis of liver disease.

Human papillomavirus

Human papillomavirus (HPV) is a DNA virus with at least 70 different types. These viruses cause warts, genital dysplasia, cervical carcinoma (types 6 and 11), and laryngeal papillomatosis. Transmission occurs through direct contact and sexual contact. Laryngeal papillomas are believed to result from acquiring the virus in passage through the birth canal. Infection in pregnant women or during pregnancy does not lead to an increase in abortions or the risk of prematurity, and no evidence indicates intrauterine infection.

Diagnosis is usually by histologic examination or DNA detection. Spontaneous resolution does occur, but therapy for persistent lesions or growths in anatomically problematic locations is appropriate. Therapy can be with podophyllum preparations, trichloroacetic acid, cryotherapy, electrocautery, and laser surgery. Interferon is being tested in the treatment of laryngeal papillomas, with mixed results.[71] Prevention against transmission means limiting direct or sexual contact, but this may not be sufficient because lesions may not be evident, and transmission may still occur.

The breast is a rare site of involvement. Without breast lesions, there is no apparent risk from breast milk, and breastfeeding is acceptable.

Parvovirus

Human parvovirus B19 causes a broad range of clinical manifestations, including asymptomatic infection (most frequent manifestation in all ages), erythema infectiosum (fifth disease), arthralgia and arthritis, red blood cell (RBC) aplasia (less often decreased white blood cells or platelets), chronic infection in immunodeficient individuals, and rarely myocarditis, vasculitis, or hemophagocytic syndrome.

Vertical transmission can lead to severe anemia and immune-mediated hydrops fetalis, which can be treated, if accurately diagnosed, by intrauterine transfusion. Inflammation of the liver or CNS can be seen in the infant, along with vasculitis. If the child is clinically well at birth, hidden or persistent

abnormalities are rarely identified. No evidence indicates that parvovirus B19 causes an identified pattern of birth defects.

Postnatal transmission usually occurs person to person via contact with respiratory secretions, saliva, and rarely blood or urine. Seroprevalence in children at 5 years of age is less than 5%, with the peak age of infection occurring during the school-age years (5% to 40% of children infected). The majority of infections are asymptomatic or undiagnosed seroconversions.[263] Severe disease, such as prolonged aplastic anemia, occurs in individuals with hemoglobinopathies or abnormal RBC maturation. Attack rates have been estimated to be 17% to 30% in casual contacts but up to 50% among household contacts. In one study of 235 susceptible pregnant women, the annual seroconversion rate was 1.4%.[149]

There are no reports of transmission to an infant through breastfeeding. Excretion in breast milk has not been studied because of limitations in culturing techniques. Rat parvovirus has been demonstrated in rat milk. The very low seroconversion rate in young children and the absence of chronic or frequent severe disease suggest that the risk of parvovirus infection via breast milk is not significant. The possibility of antibodies against parvovirus or other protective constituents in breast milk has not been studied. Breastfeeding by a mother with parvovirus infection is acceptable.

RETROVIRUSES

Human T-cell leukemia virus type I

The occurrence of human T-cell leukemia virus type I (HTLV-I) is endemic in parts of southwestern Japan,[55,68,121,141,281] the Carribean, South America,[108] and sub-Saharan Africa. HTLV-I is associated with adult T cell leukemia/lymphoma (ATL) and a chronic condition with progressive neuropathy. The progressive neuropathy is called HTLV-I associated myelopathy or tropical spastic paraparesis (HAM/TSP).[93] Other illnesses have been reported in association with HTLV-I infection including dermatitis, uveitis, arthritis, Sjögren's syndrome in adults, and infective dermatitis and persistent lymphadenitis in children. Transmission of HTLV-I occurs most often through sexual contact, via blood or blood products, and via breast milk. Infrequent transmission does occur in utero or at delivery and with casual or household contact.[187]

Seroprevalence generally increases with age and varies widely in different regions and in populations of different backgrounds. In some areas of Japan, seropsitivity can be as high as 12% to 16%, but in South America, Africa, and some Caribbean countries the rates are 2% to 6%. In Latin America seropostive rates can be as high as 10% to 25% among female sex workers or attendees to STD clinics.[108] In blood donors in Europe, the seroprevalence of HTLV-I has been reported at 0.001% to 0.03%. The seroprevalence in pregnant women in endemic areas of Japan is as high as 4% to 5% and in nonendemic areas as low as 0.1% to 1.0%. HTLV-1 is not a major disease in the United States.[25] In studies from Europe the seroprevalence in pregnant women has been noted to be up to 0.6%. These pregnant women were primarily of African or Caribbean descent.[94]

HTLV-I antigen has been identified in breast milk of HTLV-I positive mothers.[147] Another report shows that basal mammary epithelial cells can be infected with HTLV-I and can transfer infection to peripheral blood monocytes.[162] Human milk from HTLV-I positive mothers caused infection in marmosets.[148,283] HTLV-I infection clearly occurs via breastfeeding and a number of reports document an increased rate of transmission of HTLV-I to breastfed infants compared with formula fed infants.[7,8,10,11,119,120,258] Ando and associates in two separate reports demonstrated a parallel decline in antibodies against HTLV-I in both formula fed and breastfed infants to a nadir at about 1 year of age and a subsequent increase in antibodies from 1 to 2 years of age. The percentage of children seropositive at 1 year of age was 3.0% and 0.6%, at 1.5 years of age it was15.2% and 3.9%, and at 2 years of age it was 41.9% and 4.6% in the breastfed and formula fed groups, respectively. A smaller group of children followed out through 11 to 12 years of age demonstrated no newly infected children after

2 years of age and no loss of antibody in any child who was seropositive at 2 years of age.[10,11]

Transmission of HTLV-I infection via breastfeeding is also clearly associated with the duration of breastfeeding.[258,259,276,277] It has been postulated that the persistence of passively acquired antibodies against HTLV-I offers some protection through 6 months of life (Table 17-5).

Other factors relating to HTLV-I transmission via breast milk have been proposed. Yoshinaga and associates presented data on the HTLV-I antigen producing capacity of peripheral blood and breast milk cells and showed an increased mother-to-child transmission rate when the mother's blood and breast milk produced large numbers of antigen-producing cells in culture.[289] Hisada and associates reported on 150 mothers and infants in Jamaica, demonstrating that a higher maternal provirus level and a higher HTLV-I antibody titer were independently associated with HTLV-I transmission to the infant.[124] Ureta-Vidal and associates reported an increased seropositivity rate in children of mothers with a high proviral load and elevated maternal HTLV-I antibody titers.[265]

Various interventions have been proposed to decrease HTLV-I transmission via breastfeeding. Complete avoidance of breastfeeding was shown to be an effective intervention by Hino and associates in large population of Japanese in Nagasaki.[122] There was an 80% decrease in transmission by avoiding breastfeeding. Breastfeeding for a shorter duration is another effective alternative. Ando and associates showed that freezing and thawing breast milk decreased the infectivity of HTLV-I.[9] Sawada and associates demonstrated in a rabbit model that HTLV-I immune globulin protected against HTLV-I transmission via milk.[227] It is reasonable to postulate that any measure that would decrease the maternal provirus load or increase the anti-HTLV-I antibodies available to the infant might decrease the risk of transmission. The overall prevalence of HTLV-I infection during childhood is unknown because the majority of individuals do not manifest illness until much later in life. The timing of HTLV-I infection in a breastfeeding population has been difficult to assess because of passively acquired antibodies from the mother and issues related to testing. Furnia and associates estimated the time of infection for a cohort of 16 breastfed infants in Jamaica.[95] The estimated median time of infection was 11.9 months as determined by PCR as compared with the estimated time of infection, based on whole virus Western blot, of 12.4 months.

In areas where the prevalence of HTLV-I infection (in the United States, Canada, or Europe) is rare, the likelihood that a single test for antibody against HTLV-I would be a false positive test is high compared with the number of true positive tests. Repeat testing is warranted in many situations.[55] Quantification of the antibody titer and the proviral load is appropriate in a situation when mother-to-child transmission is a concern. A greater risk of progression to disease in later life

TABLE 17-5 HTLV-I Transmission Related to the Duration of Breastfeeding

Author (reference)	Duration	Seroconversion Rate	Number of Children*
Takahashi[258]	≤6 months	4.4%	4/90
	≥7 months	14.4%	20/139
	(bottle-fed)	5.7%	9/158
Takezaki[259]	≤6 months	3.9%	2/51
	>6 months	20.3%	13/64
Wiktor[277]	< 12 months	9%	8/86
	≥ 12 months	32%	19/60

* Number of children positive for HTLV-I over the number of children examined.

has not been shown for HTLV-I infection through breast milk, but early-life infections are associated with the greatest risk of adult T-cell leukemia.[254]

The mother and family should be informed about all these issues. If the risk of lack of breast milk is not too great and formula is readily available and culturally acceptable, then the proscription of breastfeeding or at least a recommendation to limit the duration of breastfeeding to 6 months or less is appropriate to limit the risk of HTLV-I transmission to the infant. Freezing and thawing breast milk before giving it to the infant might be another reasonable intervention to decrease the risk of transmission. Neither immune globulin nor antiviral agents against HTLV-I are available at this time.

Human T-cell leukemia virus type II

Human T-cell leukemia virus type II (HTLV-II) is endemic in specific geographic locations, including Africa, the Americas, the Caribbean, and Japan. Transmission is primarily through IVDU, contaminated blood products, and breastfeeding. Sexual transmission occurs but its overall contribution to the prevalence of HTLV-II in different populations remains uncertain. Many studies have examined the presence of HTLV-I and II in blood products. PCR testing and selective antibody tests suggest that about one half of the HTLV seropositivity in blood donors is caused by HTLV-II.

HTLV-II has been associated with two chronic neurologic disorders similar to those caused by HTLV-I, tropical or spastic ataxia.[166] A connection between HTLV-II and glomerulonephritis, myelopathy, arthritis, T-hairy cell leukemia, and large granulocytic leukemia has been reported.

Mother-to-child transmission has been demonstrated in both breastfed and formula fed infants. It appears that the rate of transmission is greater in breastfed infants.[94,117,134,152,153,193,268,270] HTLV-II has been detected in breast milk.[117] Nyambi and associates reported that HTLV-II transmission did correlate with the duration of breastfeeding. The estimated rate of transmission was 20%. The time to serconversion (after the initial loss of passively acquired maternal antibodies) for infected infants seemed to range between 1 and 3 years of age.[193] Avoidance of breastfeeding and limiting the duration of breastfeeding are the only two possible interventions with evidence of effectiveness for preventing HTLV-II mother-to-child transmission.

With the current understanding of retroviruses, it is appropriate in cases of documented HTLV-II maternal infection to recommend avoiding or limiting the duration of breastfeeding and provide alternative nutrition when financially practical and culturally acceptable. The mother should have confirmatory testing for HTLV-II and measurement of the proviral load. The infant should be serially tested for antibodies to HTLV-II and have confirmatory testing if still seropositive after 12 to 18 months of age. Further investigation into the mechanisms of transmission via breast milk and possible interventions to prevent transmission should occur as it is for HIV-1 and HTLV-I.

Human immunodeficiency virus type 1

Human immunodeficiency virus type 1 (HIV-1) is transmitted through human milk. Refraining from breastfeeding is a crucial aspect of preventing perinatal HIV infection in the United States and many other countries. The dilemma is the use of replacement feeding in countries where breastfeeding provides infants with significant protection from illness and death due to other infections. The question of the contribution of breastfeeding in mother-to-child HIV-1 transmission is not a trivial one; when one considers the following:

1. The World Health Oganization (WHO) has estimated that there were 40 million people living with HIV-1 in 2003.
2. Over 90% of the children younger than 13 years old infected with HIV-1 have been infected by mother-to-child transmission.
3. WHO estimates that 5 million people were newly infected with HIV-1 in 2003, with children younger than 15 years old making up 700,000 of that 5 million.

4. Breastfeeding contributes an estimated 10% to 20% increase in the overall mother-to-child transmission rates, over and above intrauterine and intrapartum transmission.

The evidence of HIV transmission via breastfeeding is irrefutable. Two recent publications summarize the current evidence for HIV transmission via breastfeeding in the literature.[214,264] Since 1985, case reports have documented HIV transmission via breast milk to children around the world.[123,136,160,293] Primary HIV infection in breastfeeding mothers, with the concomitant high viral load, is associated with a particularly high rate of HIV transmission via breast milk. Palasanthiran and associates estimated that risk at 27%.[203] Large observational studies have demonstrated higher rates of HIV transmission in breastfed infants of mothers with chronic HIV infection compared with formula fed infants.[30,69,85] A systematic analysis of published reports estimated the additional risk of perinatal HIV transmission due to breastfeeding to be 14% (95% CI: 7% to 22%).[78] More recently published cohort studies similarly attributed additional risk of HIV transmission due to breastfeeding at 4% to 22% over and above the risk from prenatal and intrapartum transmission.[26,67,82] Laboratory reports demonstrate the presence of cell-free virus and cell-associated virus in breast milk as well as various immunologic factors that could block or limit infection.[37,109,188,190,200,233,261,266] A dose response has been observed, correlating the HIV viral load in human milk as well as the mother's plasma viral load with an increased transmission risk for the breastfed infant.[210,217,221,236]

Many of the potential risk factors associated with human milk transmission of HIV have been described. The cumulative risk of HIV transmission is higher the longer the duration of breastfeeding.[69,161,182,186,267] Maternal characteristics related to transmission of HIV via human milk include younger maternal age, higher parity, lower $CD4^+$ counts, higher plasma viral loads, and breast abnormalities (mastitis, abscess, or nipple lesions). Characteristics of human milk that relate to a higher risk of transmission include higher viral load in the milk, lower concentrations of antiviral substances (lactoferrin, lysozyme), and lower concentrations of virus-specific cytotoxic T-lymphocytes, secretory IgA, and IgM. Mixed breastfeeding is also associated with a higher risk of HIV transmission compared with exclusive breastfeeding.[64,65,260] The measurable benefits of breast milk versus the relative risk of HIV transmission to the infant due to exclusive breastfeeding (with optimization of other factors to decrease HIV transmission) has not yet been studied in a prospective fashion.[159]

There are a number of potential interventions to prevent breastfeeding transmission of HIV-1 that can be utilized (Box 17-2). The simplest and most effective is the compete avoidance of human milk. This is a practical solution in places like the United States and other countries where replacement feeding as well as other strictly medical interventions are feasible and reasonable, and the risk of not providing breast milk to the infant is negligible. In resource-poor situations, where the risk of other infections is high without the benefits of breast milk, then breastfeeding is appropriate along with any reasonable interventions to decrease HIV transmission via breast milk.

The complete avoidance of breastfeeding in certain situations may lead to increased risk of death due to other reasons besides HIV transmission. One study from Kenya showed improved HIV-1-free survival rates in a formula fed group of children born to HIV-positive mothers, but the breastfed and formula groups had similar mortality rates (24.4% versus 20.0%, respectively) as well as similar incidences of diarrhea and pneumonia over the first 2 years of life.[175] There was no difference in the two groups in terms of the prevalence of malnutrition, but the breastfed infants had better nutritional status in the first 6 months of life.

Potentially effective interventions include exclusive breastfeeding, early weaning, education, and support to decrease the likelihood of mastitis or nipple lesions. Other possible interventions include treating the mother with antiretroviral therapy to decrease the human milk viral load, treating the milk itself to decrease the viral load (by pasteurization or other methods),[200,201] treating acute conditions in the mother and the infant (e.g., mastitis,

BOX 17-2 Recommendations on breastfeeding and transmission of human immunodeficiency virus (HIV)

- Women and their health care providers need to be aware of the potential risk of transmission of HIV infection to infants during pregnancy and in the peripartum period, as well as through breast milk.
- Documented, routine HIV education and routine testing with consent of all women seeking prenatal care are strongly recommended so that each woman knows her HIV status and the methods available both to prevent the acquisition and transmission of HIV and to determine whether breastfeeding is appropriate.
- At delivery, education about HIV and testing with consent of all women whose HIV status during pregnancy is unknown are strongly recommended. Knowledge of the woman's HIV status assists in counseling on breastfeeding and helps each woman understand the benefits to herself and her infant of knowing her serostatus and the behaviors that would decrease the likelihood of acquisition and transmission of HIV.
- Women who are known to be HIV infected must be counseled not to breastfeed or provide their milk for the nutrition of their own or other infants.
- In general, women who are known to be HIV seronegative should be encouraged to breastfeed. However, women who are HIV seronegative but at particularly high risk of seroconversion (e.g., injection drug users and sexual partners of known HIV-positive persons or active drug users) should be educated about HIV with an individualized recommendation concerning the appropriateness of breastfeeding. In addition, during the perinatal period, information should be provided on the potential risk of transmitting HIV through breast milk and about methods to reduce the risk of acquiring HIV infection.
- Each woman whose HIV status is unknown should be informed of the potential for HIV-infected women to transmit HIV during the peripartum period and through breast milk and the potential benefits to her and her infant of knowing her HIV status and how HIV is acquired and transmitted. The health care provider needs to make an individualized recommendation to assist the woman in deciding whether to breastfeed.
- Neonatal intensive care units should develop policies that are consistent with these recommendations for the use of expressed breast milk for neonates. Current standards of the U.S. Occupational Safety and Health Administration (OSHA) do not require gloves for the routine handling of expressed human milk. However, health care workers should wear gloves in situations in which exposure to breast milk might be frequent or prolonged, such as in milk banking.
- Human milk banks should follow the guidelines developed by the U.S. Public Health Service, which include screening all donors for HIV infection and assessing risk factors that predispose to infection, as well as pasteurization of all milk specimens.

From Lawrence RA: A review of the medical benefits and contraindications to breastfeeding in the United States. In Maternal and Child Health Technical Information Bulletin, Washington, DC, US Health Resources and Services Administration, 1997.

breast lesions, infant candidiasis), and enhancing the infant's own defenses via immunization or antiretroviral therapy. There is limited information of the practicality and effectiveness of many of these interventions in clinical trials. Some of these may not be feasible in certain settings such as pasteurization or maternal antiretroviral therapy. Others may not be culturally acceptable such as treating expressed breast milk prior to giving it to the infant or even exclusive breastfeeding. Any method of treating the breast milk, to decrease viral load, will need to be clinically assessed as to its effect on the nutritional and protective benefits for the infant, including nutritional status, growth, development, and overall survival. It is unlikely that any single intervention or a combination of them will effectively decrease the risk of HIV-1 mother-to-child transmission to zero.[70]

The potential effect of breastfeeding on the HIV-positive mother needs to be assessed in relation to the mother's health status. Two studies have examined this and reported conflicting results. The first study from Kenya demonstrated a significantly higher mortality rate in breastfeeding mothers compared with a formula feeding group in the 2 years after delivery. The hypothesized explanation offered by the authors for this difference was increased metabolic demands, greater weight loss, and nutritional depletion.[189] A second study from South Africa showed an overall lower mortality rate in the two groups with no significant difference in mortality rate over 10 months of observation.[66]

In summary, breastfeeding of infants by HIV-positive mothers does lead to an increased risk of HIV infection in the infant. There is much still to be understood about the mechanisms of HIV transmission via breast milk and the action and efficacy of interventions to prevent such transmission. The complete avoidance of breastfeeding remains a crucial component for the prevention of perinatal HIV infection in the United States and many other countries. In resource-poor settings, where breastfeeding is the norm and where it provides vital nutritional and infection protective benefits, the WHO, UNICEF, and UNAIDS recommend education, counseling, and support for HIV-infected mothers so they can make an informed choice concerning infant feeding. Mothers choosing to breastfeed should receive additional education, support, and medical care to minimize the risk of HIV transmission and to optimize their own health status during and after breastfeeding. Mothers choosing to use replacement feedings should receive parallel education, support, and medical care for themselves and their infants to minimize the effect of the lack of breastfeeding. The decision about infant feeding for the HIV-positive mother remains a true dilemma—a choice between two equally unsatisfactory alternatives. It is only through continued research and education concerning the potential interventions to prevent HIV transmission via breast milk that we can minimize transmission and optimize infant nutrition and health.

Human immunodeficiency virus type 2

Human immunodeficiency virus type 2 (HIV-2) is an RNA virus in the nononcogenic, cytopathic lentivirus genus of retroviruses. It is genetically closer to *simian immunodeficiency virus* (SIV) than to HIV-1. The clinical disease associated with HIV-2 has similar symptoms to HIV-1 infection, but progresses at a slower rate to severe immunosuppression.

HIV-2 is endemic in west Africa and parts of the Caribbean and found infrequently in Europe and North and South America.[131,194] It is transmitted via sexual contact, blood, or blood products and from mother to child.

Routine testing for HIV-2 is recommended in blood banks. Antibody tests used for HIV-1 are only 50% to 90% sensitive for detecting HIV-2.[41] Specific testing for HIV-2 is appropriate whenever clinically or epidemiologically indicated.

Vertical transmission occurs infrequently. Ekpini and associates followed a large cohort of west African mothers and infants; 138 HIV-1 positive women, 132 HIV-2 positive women, 69 women seropositive for both HIV-1 and 2, and 274 HIV seronegative women. A few cases of perinatal HIV-2 transmission occurred, but no case of late postnatal transmission was observed.[82]

It is probable that HIV-2 transmission via breast milk is less common than with HIV-1, but there is insufficient data to say the risk of transmission is zero. Mothers who test positive for HIV-2 should be tested for HIV-1, and guidelines for breastfeeding should follow those for HIV-1 until additional information is available.

Rabies

Rabies virus produces a severe infection with progressive CNS symptoms (anxiety, seizures, altered mental status) that ultimately proceeds to death; few reports of survival exist. Rabies occurs worldwide except in Australia, Antarctica, and several island groups. In 1992 more than 36,000 cases of rabies were reported to WHO, a number that is

probably a marked underestimate of the actual cases.[42] Between 1990 and 2003, there were 37 cases of human rabies in the United States.[45,52] Postexposure prophylaxis is given to thousands of patients each year.

Rabies virus is endemic in various animal populations, including raccoons, skunks, foxes, and bats. Because of aggressive immunization programs, rabies in domesticated dogs and cats in the United States is uncommon. The virus is found in the saliva and nervous tissue of infected animals. Transmission occurs by bites, licking, or simply contact of oral secretions with mucous membranes or nonintact skin. Many cases of rabies in humans now lack a history of some obvious contact with a rabid animal. This may be a result of the long incubation period (generally 4 to 6 weeks, but can be up to 1 year, with reports of incubation periods of several years), a lack of symptoms early in an infectious animal, or airborne transmission from bats in enclosed environments (caves, laboratories, houses). Person-to-person transmission via bites has not been documented, although it has occurred in corneal transplants.[31] No evidence indicates transmission through breast milk.

In the case of maternal infection with rabies, many scenarios can occur before the onset of progressive, severe CNS symptoms. The progression and severity of maternal illness can preclude breastfeeding, but separation of the infant from the mother is appropriate regardless of the mother's status and method of infant feeding. Breastfeeding should not continue when the mother has symptoms of rabies, and the infant should receive postexposure immunization and close observation. Depending on the scenario, the nature of the mother's illness, the possible exposure of the infant to the same source as the mother, and the exposure of the child to the mother, postexposure immunization of the infant may be appropriate. A more common scenario is the mother's apparent exposure to rabies (without exposure for the infant), necessitating postexposure immunization of the mother with rabies vaccine. In the majority of cases, in the absence of maternal illness, breastfeeding can reasonably continue during the mother's five-dose immunization series over 28 days. In a rare situation in which apparent exposure of the mother and infant to rabies occurs together, postexposure treatment of both mother and infant should be instituted, and breastfeeding can continue.

Respiratory syncytial virus

Respiratory syncytial virus (RSV) is a common cause of respiratory illness in children and is relatively common in adults, usually producing milder upper respiratory tract infection in adults. No evidence indicates that RSV causes intrauterine infection, adversely affects the fetus, or causes abortion or prematurity. RSV does produce infection in neonates, causing asymptomatic infection, afebrile upper respiratory tract infection, bronchiolitis, pneumonia, and apnea. Mortality rate can be high in neonates, especially in premature infants and ill full-term infants, particularly those with preexisting respiratory disease (hyaline membrane disease, bronchopulmonary dysplasia) or cardiac disease associated with pulmonary hypertension.

RSV is believed to be transmitted via droplets or direct contact of the conjunctiva, nasal mucosa, or oropharynx with infected respiratory secretions. Documentation of RSV infection is rarely made in adults, and spread from the mother or other household contacts probably occurs before a diagnosis can be made. Therefore, risk of RSV transmission from breast milk is probably insignificant compared with transmission via direct or droplet contact in families. In nurseries, however, it is appropriate to make a timely diagnosis of RSV infection in the neonate to gain the benefit of treatment with ribavirin and to isolate the infant from the others to prevent spread in the nursery. RSV infection should be suspected in any infant with rhinorrhea, nasal congestion, or unexplained apnea, especially in October through March in temperate climates. Prophylaxis against RSV with specific intravenous immune globulin (RSV-IGIV) during this season for infants at highest risk of severe disease may be appropriate.

Considerable debate surrounds the effect of passively acquired antibodies against RSV on the

occurrence and severity of illness in the neonate and infant. It appears that a higher level of neutralizing antibody against RSV in the neonate decreases the risk of severe RSV disease.[105,154] However, some controversy remains concerning the measurable benefit of breastfeeding for preventing serious RSV disease.[2,36,76] Different studies have shown benefit and others no effect. Controlling for possible confounding factors (e.g., smoking, crowded living conditions) in these studies has been difficult. At this point, no reason exists to stop breastfeeding with maternal RSV infection, and infants with RSV infection should breastfeed unless their respiratory status precludes it.

Severe acute respiratory syndrome (SARS)

This term could be applied to any acute serious respiratory illness caused by or associated with a variety of infections agents; however, since 2003 it has been linked with SARS-associated coronavirus. In the global outbreak of 2002–2003 there were over 8400 probable cases of SARS and over 800 deaths. More than the actual number of affected individuals or its associated mortality rate (approximately 10% overall, but closer to 50% in persons over 65 years of age), it was what we did not know about this new unusual illness, and the tremendous publicity surrounding it, that made SARS such a sensation. We now know the cause of this illness, known as the SARS-associated coronavirus (SARS-CoV). SARS-CoV was shown to not be closely related to these previously characterized coronavirus groups.[171,220] Despite intense international collaboration to study the illness and the virus, there are still many things we do not know about it, such as the degree of infectiousness (Ro), the actual period of transmissibility, all the modes of transmission, how many people have an asymptomatic infection compared to those with symptoms or severe illness, how to make a rapid diagnosis of confirmed cases, and where it originated, just to name a few.

At least 21 cases of probable SARS in children have been described in the literature.[29,128,240,242] In general, the illness in children is a mild, nonspecific respiratory illness, but in adolescents it is more likely to progress to severe respiratory distress, as it does in adults. It has been reported that children are less likely to transmit SARS than adults.[128] The overall clinical course, the radiologic evolution, and the histologic findings of these illness are consistent with the host's immune response playing a significant role in disease production.

Five infants were born to mothers with confirmed SARS. The infants were born prematurely (26 to 37 weeks) presumably due to maternal illness. Although two of the five infants had serious abdominal illnesses (other coronaviruses have been associated with reported outbreaks of necrotizing enterocolitis), the presence of SARS-CoV could not be demonstrated in any of these infants.[240]

There was no mention of the mode of feeding for any of the reported cases of young children with SARS or the infants born to mothers with SARS. As with other respiratory viruses predominantly transmitted by droplets, transmission via breast milk is an insignificant mode of transmission, if it occurs at all. The benefits of breastfeeding being what they are, mothers with SARS should continue breastfeeding if they are able or expressed breast milk can be given to the infant, until the mother is able to breastfeed.

Smallpox

In this era of worry about biologic terrorism, smallpox is an important concern. The concern for the infant (breastfed or formula fed) is direct contact with the mother or a household member with smallpox. Smallpox is highly contagious in the household setting due to person-to-person spread via droplet nuclei or aerosolization from the oropharynx and direct contact with the rash. Additional potential exposures for the infant include the release of a smallpox aerosol into the environment by terrorists, contact with a smallpox-contaminated space or the clothes of household members exposed to an aerosol, and infection via contact with the mother's or a household member's smallpox vaccination site. These risks are the same

for breastfed and formula fed infants. There is no evidence for transmission of the smallpox virus via breast milk.

Relative to smallpox, a contact is defined as a person who has been in the same household or had face-to-face contact with the patient (with smallpox) after the onset of fever. Patients do not transmit infection until after progression from the fever stage to the development of the rash. An exposed contact does not need to be isolated from others during the postcontact observation period (usually 17 days) until the person develops fever. Temperature should be monitored daily in the exposed contact. Personal contact and breastfeeding between mother and infant can continue until the onset of fever, when immediate isolation (at home) should begin. Providing expressed breast milk for the infant of a mother with smallpox should be avoided because of the extensive nature of the smallpox rash and the possibility of contamination (from the rash) of the milk during the expression process. There is no literature documenting transmission of the smallpox virus via expressed breast milk.

The other issue for the breastfeeding infant is the question of maternal vaccination with smallpox in a pre-event vaccination program. Children over 1 year of age can be safely and reasonably vaccinated with smallpox in the face of a probable smallpox exposure. Smallpox vaccination of infants younger than 1 year of age is contraindicated. Breastfeeding is listed as a contraindication to vaccination in the pre-event vaccination program. It is unknown whether vaccine virus or antibodies are present in breast milk. The risk of infection due to contact or aerosolization of virus from a mother's smallpox vaccination site is the same for the breastfed and formula fed infant. The Advisory Committee on Immunization Practices also does not recommend pre-event smallpox vaccination of children younger than 18 years old.[275]

A report documents tertiary contact vaccinia in a breastfeeding infant.[96] A U.S. military person received a primary smallpox vaccination and developed a local reaction at the inoculation site. Despite reportedly observing appropriate precautions, the individual's wife developed vesicles on both areolae (secondary contact vaccinia). Subsequently, the breastfeeding infant developed lesions on her philtrum, cheek, and tongue. Both the mother and infant remained well and the infections resolved without therapy. Culture and PCR testing confirmed vaccinia in both the mother's and the infant's lesions. The breast milk was not tested.[96]

Sepkowitz reported on 27 cases of secondary vaccinia in households in a review from 1931 to 1981.[239] The CDC reported 30 suspected cases of secondary/tertiary vaccinia with 18 of those cases confirmed by culture or PCR. The 30 cases were related to 578,286 vaccinated military personnel. This is an incidence of 5.2 cases per 100,000 vaccinees and 7.4 cases per 100,000 primary vaccinees.[53] In a separate report on the civilian pre-event smallpox vaccination program, 37,802 individuals were vaccinated between January and June 2003 and there were no reported cases of contact vaccinia.[51]

The risk of contact vaccinia is low. The risk is from close or intimate contact. In the above-mentioned case, the risk for the infant was contact with the mother's breasts, the inadvertent site of her contact vaccinia. Breastfed and formula fed infants are equally at risk from close contact in the household of a smallpox vaccinee or a case of secondary vaccinia, and separation from the individual is appropriate in both situations. If the breast of the nursing mother is not involved, then expressed breast milk can be given to the infant.

West Nile virus

West Nile virus disease in the United States is one of the best examples of an emerging infectious disease taking on new importance in public awareness about health issues. In 2003, there were 9136 human cases of West Nile infection reported to the CDC (through 2/11/2004). Cases were reported from 45 states, including 6256 (68%) cases of West Nile fever (milder cases), 2718 (30%) cases of West Nile meningoencephalitis, and 228 deaths related to West Nile disease.[54] West Nile virus is endemic in Israel and parts of Africa. Outbreaks

have been reported from Romania (1996), Russia (1999), Israel (2000), and Canada (2002) as well as the United States (1999–2003).[208]

It is estimated that 150 to 300 asymptomatic cases of West Nile infection occur for every 20 febrile illnesses and for every one case of meningoencephalitis associated with West Nile virus. West Nile fever is usually a mild illness of 3 to 6 days' duration. The symptoms are relatively nonspecific, including malaise, nausea, vomiting, headache, myalgia, lymphadenopathy, and rash. West Nile disease is characterized by severe neurologic symptoms (e.g., meningitis, encephalitis, or acute flaccid paralysis, and occasionally optic neuritis, cranial nerve abnormalities, and seizures). Children are infrequently sick with West Nile virus infection and infants younger than 1 year of age have rarely been reported.[208] The case-fatality rate for 2003 in the United States was approximately 2.5%, but has been reported as high as 4% to 18% in hospitalized patients. The case-fatality rate for persons over 70 years of age is considered to be higher, 15% to 29% among hospitalized patients in outbreaks in Romania and Israel.[208]

The primary mechanism of transmission is via a mosquito bite. Mosquitoes from the genus *Culex* are primary vectors. The bird-mosquito-bird cycle serves to maintain and amplify the virus in the environment. Humans and horses are incidental hosts. The pathogenesis of the infection is believed to occur via replication of the virus in the skin and lymph nodes, leading to a primary viremia which seeds secondary sites before a second viremia causes the infection of the central nervous system and other affected organs.[39,72] Transmission has been reported in rare instances during pregnancy[5,48] via organ transplant[137] and percutaneously in laboratory workers.[50] West Nile virus transmission occurs via blood and blood product transfusion,[127] and the incidence has been estimated to be as high as 21 per 10,000 donations during epidemics in specific cities.[28] There is no evidence of direct person-to-person transmission without the mosquito vector.

There is one reported case of possible West Nile virus (WNV) transmission via breastfeeding.[49] The mother acquired the virus via packed red blood cell transfusions after delivery. The second unit of blood she received was associated with other blood products from the same donation causing West Nile infection in another transfusion recipient. Eight days later the mother had a severe headache and was hospitalized with fever and a CSF pleocytosis on day 12 after delivery. The mother's CSF was positive for WNV-specific IgM antibody. The infant had been breastfed from birth through the second day of hospitalization of the mother. Samples of breast milk were WNV-specific IgG and IgM positive on day 16 after delivery and WNV-specific IgM positive on day 24. The same milk was WNV-RNA positive by PCR testing on day 16, but not on day 24 after delivery. The infant tested positive for WNV-specific IgM in serum at day 25 of age, but remained well without fever. There was reportedly no clear-cut exposure to mosquitoes for the infant. The cord blood and placenta were not available to be tested. IgM antibodies can be found in low concentrations in breast milk, but this is not common or as efficient as the transfer of IgA, sIgA, or IgG into breast milk. This is the only case currently reported in the literature. Live virus has not been cultured from the samples of breast milk.

Based on the information from this single case in which the infant remained well, and considering the lack of significant disease due to West Nile virus infection in young children, there is no reason to proscribe breastfeeding in the case of maternal West Nile virus infection if the mother is well enough to breastfeed. As with many other maternal viral illnesses, by the time the diagnosis is made in the mother, the infant may have already been exposed during maternal viremia and possible virolactia. The infant can and should continue to receive breast milk for the potential specific immunologic benefit.

SPIROCHETES

Lyme disease

Lyme disease, as with the other human illnesses caused by spirochetes, especially syphilis, is

characterized by a protean course and distinct phases (stages) of disease. Lyme borreliosis was described in Europe in the early 20th century. Since the 1970s, tremendous recognition, description, and investigation of Lyme disease have occurred in the United States and Europe. Public concern surrounding this illness is dramatic.

Lyme disease is a multisystem disease characterized by involvement of the skin, heart, joints, and nervous system (peripheral and central). Stages of disease are identified as *early localized* (erythema migrans [EM], often accompanied by arthralgia, neck stiffness, fever, malaise, and headache), *early disseminated* (multiple EM lesions, cranial nerve palsies, meningitis, conjunctivitis, arthralgia, myalgia, headache, fatigue, and, rarely, myocarditis), and *late disease* (recurrent arthritis, encephalopathy, and neuropathy). The varied manifestations of disease may relate to the degree of spirochetemia, the extent of dissemination to specific tissues, and the host's immunologic response.

The diagnosis of Lyme disease is often difficult in part because of the broad spectrum of presentations, inapparent exposure to the tick, and the lack of adequately standardized serologic tests. Culture of the spirochete, *Borrelia burgdorferi*, is not readily available. ELISA, immunofluorescent assay (IFA), and immunoblot assay are the usual tests. PCR detection of spirochetal DNA requires additional testing in clinical situations to clarify and standardize its utility.

Gardner[98] reviewed infection during pregnancy, summarizing a total of 46 adverse outcomes from 161 cases reported in the literature. The adverse outcomes included miscarriage and stillbirth (11% of cases), perinatal death (3%), congenital anomalies (15%), and both early- and late-onset progressive infection in the infant. Silver[241] reviewed 11 published reports and concluded that Lyme disease during pregnancy is uncommon, even in endemic areas. Although the spirochete can be transmitted transplacentally, a significant immune response in the fetus is often lacking, and the association of Lyme infection with congenital abnormalities is weak.[252,278]

Little published information exists on whether *B. burgdorferi* can be transmitted via breast milk. One report showed the detection of *B. burgdorferi* DNA by PCR in the breast milk of two lactating women with untreated EM, but no evidence of Lyme disease or transmission of the spirochete in the one infant followed for 1 year.[233] No attempt to culture the spirochete was made, so it is not possible to determine if the detectable DNA was from viable spirochetes or noninfectious fragments. In that same study, of 56 women with untreated EM who had detectable *B. burgdorferi* DNA in the urine, 32 still had detectable DNA in the urine 15 to 30 days after starting treatment, but none had it 6 months after initiating therapy. Ziska and associates reported on the management of nine cases of Lyme disease in women associated with pregnancy; seven of the nine women were symptomatic at conception and six received antibiotics throughtout pregnancy. Follow-up of the infants, showed no transmission of Lyme disease, even in the seven infants who had been breastfed.[294]

The lack of adequate information on transmission of *B. burgdorferi* via breast milk cannot be taken as proof that it is not occurring. If one extrapolates from data on syphilis and the *Treponema pallidum* spirochete, it would be prudent to discuss the lack of information on the transmission of *B. burgdorferi* via breast milk with the mother or parents and to consider withholding breast milk at least until therapy for Lyme disease has begun or been completed. If the infection occurred during pregnancy and treatment has already been completed, the infant can breastfeed. If infection occurs post partum or the diagnosis is made post partum, infant exposure may have already occurred. Again, discussion with the mother or parents about withholding versus continuing breastfeeding is appropriate.

After prenatal or postnatal exposure, the infant should be closely observed and empiric therapy considered if the infant develops a rash or symptoms suggestive of Lyme borreliosis. Treatment of the mother and infant with ceftriaxone, penicillin, or amoxicillin is acceptable during breastfeeding relative to the infant's exposure to these medications. Doxycycline should not be administered for more than 14 days while continuing breastfeeding

because of possible dental staining in the neonate. Continued surveillance for viable organisms in breast milk and evidence of transmission through breastfeeding is recommended.

A large body of information is available on various "Lyme vaccines" used in dogs, but these vaccines are only partially protective and must be repeated yearly. Preliminary information suggests that a vaccine for use in humans safely produces good serologic responses, but protective efficacy has not been demonstrated, and no information exists on its use during pregnancy or breastfeeding.

Syphilis

Syphilis is the classic example of a spirochetal infection that causes multisystem disease in various stages. Both acquired syphilis and congenital syphilis are well-described entities. *Acquired syphilis* is almost always transmitted through direct sexual contact with open lesions of the skin or mucous membranes of individuals infected with the spirochete, *Treponema pallidum. Congenital syphilis* occurs by infection across the placenta (placentitis) at any time during the pregnancy or by contact with the spirochete during passage through the birth canal. Any stage of disease (primary, secondary, tertiary) in the mother can lead to infection of the fetus, but transmission in association with secondary syphilis approaches 100%. Infection with primary syphilis during pregnancy, without treatment, leads to spontaneous abortion, stillbirth, or perinatal death in 40% of cases. Similar to acquired syphilis, congenital syphilis manifests with moist lesions or secretions from rhinitis (snuffles), condylomata lata, or bullous lesions. These lesions and secretions contain numerous spirochetes and are therefore highly infectious.

Postnatal infection of the infant can occur through contact with open, moist lesions of the skin or mucous membranes in the mother or other infected individuals. If the mother or infant has potentially infectious lesions, isolation from each other and from other infants and mothers is recommended. If lesions are on the breasts or nipples, breastfeeding or using expressed milk is contraindicated until treatment is complete and the lesions have cleared. Spirochetes are rarely identified in open lesions after more than 24 hours of appropriate treatment. Penicillin remains the best therapy.

Evaluation of the infant with suspected syphilis should be based on the mother's clinical and serologic status, history of adequate therapy in the mother, and the infant's clinical status. Histologic examination of the placenta and umbilical cord, serologic testing of the infant's blood and CSF, complete analysis of the CSF, long bone and chest radiographs, liver function tests, and a complete blood cell count are all appropriate given the specific clinical situation. Treatment of the infant should follow recommended protocols for suspected, probable, or proven syphilitic infection.[62]

No evidence indicates transmission of syphilis via breast milk in the absence of a breast or nipple lesion. When the mother has no suspicious breast lesions, breastfeeding is acceptable as long as appropriate therapy for suspected or proven syphilis is begun in the mother and infant.

PARASITES

Toxoplasmosis

Toxoplasmosis is one of the most common infections of humans throughout the world. The infective organism, *Toxoplasma gondii*, is ubiquitous in nature. The prevalence of positive serologic test titers increases with age, indicating past exposure and infection. The cat is the definitive host, although infection occurs in most species of warm-blooded animals.

Postnatal infection with toxoplasmosis is usually asymptomatic. Symptomatic infection typically manifests with nonspecific symptoms, including fever, malaise, myalgia, sore throat, lymphadenopathy, rash, hepatosplenomegaly, and occasionally a mononucleosis-like illness. The illness usually resolves without treatment or significant complications.

Congenital infection or infection in an immunodeficient individual can be persistent and severe,

causing significant morbidity and even death. Although most infants with congenital infection are asymptomatic at birth, visual abnormalities, learning disabilities, and mental retardation can occur months or years later. There is a clearly defined syndrome of *congenital toxoplasmosis*, with the most severe manifestations involving the CNS, including hydrocephalus, cerebral calcifications, microcephaly, chorioretinitis, sei-zures, or simply isolated ocular involvement. The risk of fetal infection is related to the timing of primary maternal infection, although transmission can occur with preexisting maternal toxoplasmosis. In the last months of pregnancy the protozoan is more readily transmitted to the fetus, but the infection is more likely to be subclinical. Early in pregnancy the transmission to the fetus occurs less frequently but does result in severe disease. Treatment of documented congenital infection is currently recommended, although the duration and optimal regimen have not been determined, and reversal of preexisting sequelae generally does not occur.[215]

Prevention of infection in susceptible pregnant women is possible by avoiding exposure to cat feces or the organism in the soil. Pregnant or lactating women should not change cat litter boxes, but if they must, it should be done daily and while wearing gloves. The oocyst is not infective for the first 24 to 48 hours after passage. Mothers can avoid ingestion of the organism by fully cooking meats and carefully washing fruits, vegetables, and food preparation surfaces.[62]

In various animal models, *T. gondii* has been transmitted through the milk to the suckling young. The organism has been isolated from colostrum as well. The newborn animals became asymptomatically infected when nursed by an infected mother whose colostrum contained *T. gondii*. Only one report has identified *T. gondii* in human milk, and some question surrounds the reliability of that report.[156] Transmission during breastfeeding in humans has not been demonstrated. Breast milk may contain appropriate antibodies against *T. gondii*. Given the benign nature of postnatal infection, the absence of documented transmission in human breast milk, and the potential antibodies in breast milk, no reason exists to proscribe breastfeeding by a mother known to be infected with toxoplasmosis.

Giardia lamblia

Giardiasis is a localized infection limited to the intestinal tract, causing diarrhea and malabsorption. Immunocompetent individuals show no evidence of invasive infection, and no evidence exists documenting fetal infection from maternal infection during pregnancy. Giardiasis is rare in children under 6 months of age, although neonatal infection from fecal contamination at birth has been described.[18] Human milk has an in vivo protective effect against *G. lamblia* infection, as documented by work from central Africa, where the end of breastfeeding heralds the onset of *Giardia* infection.[100] This has been reaffirmed in undeveloped countries around the world.

The protective effect of breast milk has been identified in the milk of noninfected donors.[104] The antiparasitic effect does not result from specific antibodies but rather from lipase enzymatic activity. The lipase acts in the presence of bile salts to destroy the trophozoites as they emerge from their cysts in the gastrointestinal tract. Hernell and associates[118] demonstrated that free fatty acids have a marked giardiacidal effect, which supports the conclusion that lipase activity releasing fatty acids is responsible for killing *G. lamblia*.

G. lamblia have also been reported to appear in the mother's milk, and the parasite has been transmitted to newborns via that route. The exact relationship of breastfeeding to transmission of *G. lamblia* and the effect on the infant continue to be studied, even though symptomatic infection in the breastfed infant is rare.[104] Breastfeeding by mothers with giardiasis is mainly problematic because of the medications used for therapy. Metronidazole's safety in infants has not been established, and little information is available on quinacrine hydrochloride and furazolidone in breast milk. Paramomycin, a nonabsorbable aminoglycoside, is a reasonable alternative recommended for treatment of pregnant women. Breastfeeding by the

mother with symptomatic giardiasis is acceptable when consideration is given to the presence of the therapeutic agents in the breast milk.

Trichomonas vaginalis

Trichomonas vaginalis is a flagellated protozoan that can produce vaginitis (see Chapter 16) but frequently causes asymptomatic infection in both males and females. The parasite is found in 10% to 25% of women in the childbearing years. It is transmitted predominantly by sexual intercourse, but it can be transmitted to the neonate by passage through the birth canal. This parasite often coexists with other STDs, especially gonorrhea.

Infection during pregnancy or while taking oral contraceptives is more difficult to treat. Some evidence suggests that infection with and growth of the parasite are enhanced by estrogens or their effect on the vaginal epithelium. No evidence indicates adverse effects on the fetus in association with maternal infection during pregnancy. Occasionally the female newborn has a vaginal discharge during the first weeks of life caused by *T. vaginalis*. This is thought to be influenced by the effect of maternal estrogen on the infant's vaginal epithelium and acquisition of the organism during passage through the birth canal. The organism does not seem to cause significant disease in the healthy infant. No documentation exists on transmission of *T. vaginalis* via breast milk.

The difficulty encountered with maternal infection during lactation stems from metronidazole (Flagyl), the drug of choice, being contraindicated for infants. Case reports describe treatment of neonates with metronidazole without adverse effect. Although topical agents containing povidone-iodine (Betadine) or sodium lauryl sulfate (Trichotine) can be effective when given as douches, creams, or suppositories, metronidazole remains the treatment of choice. The AAP advises using metronidazole only with the physician's discretion and considers its effect on the nursing infant unknown but possibly a concern. The potential concerns are metronidazole's disulfiram-like effect in association with alcohol, tumorigenicity in animal studies, and the leukopenia and neurologic side effects described in adults. On the other hand, metronidazole is given to children beyond the neonatal period to treat serious infections with various other parasites, such as *Entamoeba histolytica*.

The current recommendation for lactating women is to try local treatment first, and if these fail, then to try metronidazole. A 2-g single-dose treatment produces peak levels after 1 hour, and discarding expressed breast milk for the next 12 to 24 hours is recommended. If this treatment also fails, a 1-g twice-daily regimen for 7 days or a 2-g single daily dose for 3 to 5 days is recommended, with discarding of some breast milk close to the dose and timing of feedings distant from the dose. Infants who exclusively breastfeed are presumed at greater risk from exposure to metronidazole than those who are only partially breastfed.

Malaria

Malaria is recognized as a major health problem in many countries. The effect of malaria infection on pregnant and lactating women and thus on the developing fetus, neonate, and growing infant can be significant. The four species of malaria, *Plasmodium vivax, P. ovale, P. malariae*, and *P. falciparum*, vary in the specific aspects of the disease they produce. *P. vivax* exists throughout the world, but *P. falciparum* predominates in the tropics and is most problematic in its chloroquine-resistant form. Malaria in the United States is most often seen in individuals traveling from areas where malaria is endemic. The parasite can exist in the blood for weeks, and infection with *P. vivax* and *P. malariae* can lead to relapses years later. Transmission occurs through the bite of the anopheline mosquito and can occur via transfusion of blood products and transplacentally.

Congenital malaria is rare but seems to occur more often with *P. vivax* and *P. falciparum*. It usually presents in the first 7 days of life (range 1 day to 2 months). It may resemble neonatal sepsis, with fever, anemia, and splenomegaly occurring in the most neonates and hyperbilirubinemia and hepatomegaly in less than half.

Malaria in infants younger than 3 months of age generally manifests with less severe disease and death than in older children. Possible explanations include the effect of less exposure to mosquitoes, passive antibody acquired from the mother, and the high level of fetal hemoglobin in the infant at this age.[18] The variations in the infection rates in children under 3 months of age during the wet and dry seasons support the idea that postnatal infection is more common than congenital infection. No evidence indicates that malaria is transmitted through breast milk. The greatest risk to the infant is exposure to the anopheline mosquito infected with malaria.

The main issues relative to malaria and breastfeeding are how to protect both the mother and the infant effectively from mosquitoes and what drugs for treating malaria in the mother are appropriate during lactation. Protection from mosquito bites includes screened-in living areas, mosquito nets while sleeping, protective clothing with or without repellents on the clothes, and community efforts to eradicate the mosquitoes. Chloroquine, quinine, and tetracycline are acceptable during breastfeeding. Sulfonamides should be avoided in the first month of the infant's life, but pyrimethamine-sulfadoxine (Fansidar) can be used later.

Mefloquine is not approved for infants or pregnant women. However, the milk/plasma ratio for mefloquine is less than 0.25, there is a large volume of distribution of the drug, high protein binding of the drug limits its presence in breast milk, and the relative importance of breastfeeding in areas where malaria is prevalent shifts the risk/benefit ratio in favor of treatment with mefloquine. The single dose recommended for treatment or the once-weekly dose for prevention allows for continued breastfeeding with discarding of the milk for short periods after a dose (1 to 6 hours). Maternal plasma levels of primaquine range from 53 to 107 ng/mL, but no information is available on levels in human milk. Primaquine is used in children, and once daily dosing in the mother would allow discarding milk with peak levels of drug. Therefore, breastfeeding during maternal malaria even with treatment is appropriate with specific medications.

CANDIDA INFECTIONS

Candida consists of multiple species. The most common species affecting humans include *C. albicans* as the dominant agent and *C. tropicalis, C. krusei*, and *C. parapsilosis*, as well as many other uncommon species. In general, *Candida* exists as a commensal organism colonizing the oropharynx, gastrointestinal tract, vagina, and skin without causing disease until some change disrupts the balance between the organism and the host. Mild mucocutaneous infection is the most common illness, which can lead to vulvovaginitis, mastitis or uncommonly oral mucositis in the mother, and thrush (oral candidiasis) and candidal diaper rash in the infant.

Invasive candidal infection occurs infrequently, usually when the individual has other illness, impaired resistance to infection (HIV, diabetes mellitus, neutropenia; decreased cell-mediated immunity in premature infants or low birth weight or very low birth weight infants), or disrupted normal mucosal and skin barriers and has received antibiotics or corticosteroids. Invasive disease can occur through local spread, as may occur more often in the genitourinary tract (urethra, bladder, ureters, kidneys), but usually develops in association with candidemia. The bladder and kidney are more frequently involved, but when dissemination occurs via candidemia, a careful search for other sites of infection should be made (e.g., retina, liver, spleen, lung, meninges).[179]

Transmission usually occurs from healthy individuals colonized with *Candida* through direct contact with them or through contact with their oral or vaginal secretions. Intrauterine infection can occur through ascending infection up through the birth canal but is rare. No distinct syndrome of congenital candidal infection exists. Most often the infant is infected in passing through the birth canal and remains colonized. Postnatal transmission can occur through direct contact with caregivers.

The mother and infant each serve as an immediate source of recolonization for one another, especially during the direct contact of breastfeeding. For

this reason, the infant and breastfeeding mother should be treated simultaneously when treating thrush, vulvovaginitis, diaper candidiasis, or mastitis. Colonization with this organism usually occurs in the absence of any clinical evidence of infection. Simultaneous treatment should occur even in the absence of any clinical evidence of *Candida* infection or colonization in the apparently uninvolved individual of the breastfeeding dyad.

There are no well-controlled clinical trials defining the most appropriate or most effective method(s) of treatment for candidal infection in the breastfeeding mother-infant pair. The list of possible treatment products is extensive and includes many anecdotal and empirical regimens followed. In the face of this absence of data, Dr. Brent has conducted a survey of members of The Academy of Breastfeeding Medicine concerning the respondents' approach to diagnosis and treatment of thrush in the breastfeeding dyad.[34] Most of the respondents relied on the history and physical examination of the infant, but only a third rated the examination of the mother as very important in making a diagnosis. Only 7% reported using laboratory testing to make the diagnosis. Twenty-one percent of the respondents reported using only oral nystatin for the infant when the mother was asymptomatic. Almost half treated the infant and the mother with topical nystatin, and 13% used oral nystatin for the infant and oral fluconazole for the mother when the mother had breast pain. Less than 5% used oral fluconazole for both infant and mother and other therapies were used by about 15% of the respondents. For recurrence of persistence of the thrush, more respondents reported treating the mother or both the infant and mother with fluconazole, and almost a quarter reported using other therapies.

Treatment of mucocutaneous candidiasis should probably begin with a topical agent, such as nystatin, clotrimazole, miconazole, econazole, butaconazole, terconazole, or ciclopirox. Treatment should continue for at least 2 weeks, even with obvious improvement in 1 or 2 days. Failures most often result from inadequate therapy involving the frequency of application, careful washing and drying before application, or in the case of diaper candidiasis, decreasing the contact of the skin with moisture as well. There have been reports that nystatin oral suspension is less effective for the treatment of oral candidiasis in infants, now as compared to the past, supposedly due to increasing resistance.[106] Gentian violet (diluted to 0.25% to 1.0%) applied to the breast or painted onto the infant's mouth is being recommended more frequently. Other topical preparations have been recommended for the mother's breast including mupirocin, grapefruit-seed extract, or mixtures of mupirocin, betamethasone ointments, and miconazole powder. Again controlled clinical trails for efficacy and toxicity are not available.

When good adherence to the proposed regimen with topical agents fails, or when the infant or mother are severely affected by pain and decreased breastfeeding, systemic therapy is appropriate. Fluconazole and ketoconazole are the most commonly used systemic agents for oral or diaper candidiasis and vulvovaginitis or mastitis. Fluconazole has a better side effect profile than ketoconazole, and there is more available data concerning its safe use in children younger than 6 months of age and even neonates and premature infants.[57,106,143] Fluconazole is not currently approved for use in infants under 6 months of age. For severe invasive infections in the infant amphotericin B with or without oral flucytosine, intravenous fluconazole, or voriconazole are reasonable choices in different situations. Use of itraconazole or caspofungin in infants has not been adequately studied to date. Maternal use of fluconazole during breastfeeding is not contraindicated because only a small amount of medicine compared with the usual infant dose would reach the infant in breast milk. Amphotericin or caspofungin therapy in the mother is also not contraindicated because these are both poorly absorbed from the gastrointestinal tract. Whenever the mother is treated for candidal mastitis or vulvovaginitis, the infant should be treated simultaneously at least with nystatin oral suspension as the first choice of medication.

Any predisposing risk factors for candidal infection in the mother and infant should be reduced or

eliminated to improve the chance of rapid, successful treatment and to decrease the likelihood of chronic or recurrent disease. For the mother, such interventions might include decreasing sugar consumption, stopping antibiotic use as soon as possible, and consuming some form of acidophilus (yogurt, milk, or pills) to establish a normal colonizing bacterial flora. For the infant, breastfeeding can help enhance the growth of specific colonizing bacterial flora such as lactobacillus, which can successfully limit fungal growth. Breastfeeding should continue with appropriate support and problem solving with a professional knowledgeable about breastfeeding.

SUMMARY

HIV-1, HIV-2, HTLV-I, and HTLV-II are the only infectious diseases that are considered absolute contraindications to breastfeeding in developed countries. When the primary route of transmission is via direct contact or respiratory droplets/particles, temporary separation of the mother and infant may be appropriate (whether the infant is breastfed or formula fed), but expressed breast milk should be given to the infant for the organism-specific immunologic benefits in the mother's milk. In most instances, by the time a specific diagnosis of an infection is made in the mother, the infant has already been exposed to the organism and providing expressed breast milk to the infant should continue. (Refer to Appendix E for specifc exceptions, such as Lassa fever.) Relative to antimicrobial therapy for the mother and continued breastfeeding, the majority of the medications commonly used in adults can be used to treat the same infection in the infant. The additional amount of medication received by the infant via the breast milk is usually insignificant. In almost all instances, an appropriate antimicrobial agent for treating the mother can be chosen which is also compatible with breastfeeding.

Unless there is a documented risk to the infant for transmission of an infectious agent via breast milk which leads to a clinically significant illness in the infant, breastfeeding should continue.

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