



Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.

## Breast milk and infection

Robert M. Lawrence, MD<sup>a,\*</sup>, Ruth A. Lawrence, MD<sup>b,c</sup>

<sup>a</sup>*Division of Pediatric Immunology and Infectious Diseases,  
University of Florida College of Medicine, Health Science Center, 1600 SW Archer Road,  
R1-118, Gainesville, FL 32610-0296, USA*

<sup>b</sup>*Division of Neonatology, Departments of Pediatrics and Obstetrics and Gynecology,  
University of Rochester School of Medicine and Dentistry, Rochester, NY, USA*

<sup>c</sup>*The Breastfeeding and Human Lactation Study Center, Strong Memorial Hospital,  
601 Elmwood Avenue, Rochester, NY 14642, USA*

The nutritional, cognitive, emotional, and immunologic benefits of human breast milk and breastfeeding are significant and well documented [1]. Human milk protects against specific pathogens (viruses, bacteria, and parasites) as well as separate clinical illnesses (eg, necrotizing enterocolitis, bacteremia, meningitis, respiratory tract illness, diarrheal disease, and otitis media) [2]. The benefits of breast milk make it one of the most important factors in protecting infants against the morbidity and mortality of infectious diseases [2–8]. Numerous factors within human breast milk act in a complementary fashion to protect against infection. They contribute to the infant's immune protection through various mechanisms, including improved growth of nonpathogenic flora, decreased colonization with enteropathogens, enhanced development of the respiratory and intestinal mucosal barriers, specific factors against individual organisms (eg, secretory IgA [sIgA]), functioning immune cells (eg, neutrophils, macrophages, T and B lymphocytes), decreased inflammatory reaction, and immunomodulation [2,9–11].

Microorganisms also have been identified in colostrum and breast milk. Few are readily transmitted through breast milk to cause clinically significant infections in infants and children (eg, HIV1, human T-lymphotrophic virus I [HTLV-I]). Others have been reported to cause infection in the infant rarely, after transmission through breast milk (eg, group B streptococci). Any decision about possible infection of an infant or child through breast milk should weigh the tremendous benefits of breastfeeding against the potential risk for transmission and the possible severity of the illness.

This article presents an overview of the considerations for breast milk and infection, focusing on the most important organisms that are transmitted through

---

\* Corresponding author.

E-mail address: lawrerm@peds.ufl.edu (R.M. Lawrence).

breast milk (HIV1, HTLV-I, and cytomegalovirus [CMV]) and touching on other organisms that are important in neonates and infants or that have captured public notice. The basic assumption is that breastfeeding is contraindicated rarely during maternal infection. The few exceptions are specific organisms with clear evidence of transmission through breast milk that cause significant morbidity and mortality because of infection through breast milk.

### **Essential concepts**

Several factors must be considered to prove that breast milk is the mechanism of transmission for a clinically significant infection in the infant (Box 1).

Excluding other probable mechanisms of transmission can be challenging, especially in the neonatal period. The organisms that are a concern for transmission through breastfeeding are transmitted more commonly prenatally, perinatally, and postnatally through other mechanisms. Congenital infection can occur in any trimester, depending on the organism. The timing of infection also significantly affects the clinical course of the infection in the fetus or newborn

#### **Box 1. Factors to prove infection transmission through breast milk**

1. Identify the infectious agent in the colostrum or breast milk using culture, nucleic-acid detection, antigen detection, or other methods.
2. Postulate a reasonable mechanism of infection given the current knowledge about the organism and the host's response to it, including timing and pathophysiology.
3. Characterize the clinical manifestations of the illness in the mother and the infant.
4. Demonstrate the occurrence of infection in the mother and the infant by culture, nucleic-acid identification, or immunologic response.
5. Confirm that the organisms identified in the mother and infant are identical based on serotype, sensitivity pattern, nucleic-acid sequence, and other factors.
6. Document that the risk for infection is greater in breast-fed infants than in formula-fed infants.
7. Characterize a dose – response relationship between the quantity of organisms in the breast milk as well as the amount of breast milk ingested and the frequency of transmission or the severity of the infection in the infant.
8. Exclude other possible mechanisms of transmission.
9. Prove the transmission through breast milk by reproducing the process in animal or human studies.

(eg, asymptomatic, fetal demise, prematurity, clinical disease present at birth, or late presentation). Perinatal infections commonly occur from exposure to blood or body fluids and contact with pathogens from the maternal genitourinary and gastrointestinal tracts. The likelihood that the exposed infant will be infected varies significantly with the specific organism and various host factors (eg, passively acquired antibody levels in the infant). Postnatally acquired infections are transmitted most commonly through contact with caregivers (eg, parents, relatives, visitors, health care providers), the environment (eg, medical equipment, other fomites), or breast milk, depending on the organism [12].

The timing of the infection in the mother and the infant is often crucial to documenting the mechanism of transmission. In most infectious situations, the exposure of the infant and mother to child transmission has occurred before the illness is diagnosed in the mother (eg, measles, Coxsackievirus infection) and frequently occurs before the mother becomes ill (eg, chickenpox, hepatitis). Proscribing breastfeeding at that point may not prevent infection in the infant and will diminish significantly the effect of breast milk to limit or modify the illness in the infant. The timing of the infection in the mother can influence significantly the risks to the infant (eg, primary HIV or CMV infection before pregnancy, during pregnancy, or postnatally, ie, during lactation).

The approach to any suspected infection in the breastfeeding mother–infant dyad should be systematic (Box 2). The mother’s initial immunologic response to

### **Box 2. Approach to a suspected infection in a breastfeeding mother**

1. Suspect particular infectious agents based on the clinical presentation.
2. Initiate a directed diagnostic work-up to identify the etiologic cause of the infection.
3. Consider the probable mechanisms of transmission, the known virulence of the likely infectious agents, and the susceptibility of the infant.
4. Institute preliminary infection-control precautions (including temporarily holding or continuing breastfeeding) based on the clinical syndrome, site of infection, probable mode of transmission, and infant’s susceptibility.
5. Start empiric therapy in the mother as indicated by the severity of the mother’s illness.
6. Consider preventive or empiric therapy for the infant when the risks for infection and significant disease are high.
7. Modify the empiric therapies and precautions based on the agent identified as the cause of the infection in the mother.
8. Observe the mother for response to therapy and the infant for signs and symptoms of infection requiring treatment.

the infection may add specific factors to the breast milk that can prevent infection or ameliorate the illness. Many maternal illnesses associated with fever do not require separation of the mother and infant (eg, engorgement of the breasts, atelectasis, nonsuppurative phlebitis, or urinary tract infection) or additional precautions to protect the infant.

Another important consideration relative to breast milk and infection is medications in breast milk. A thorough review of antimicrobial agents and breast milk is outside the scope of this article. Most antimicrobial agents used to treat infection can be used in infants and children. Additional amounts that are ingested by the infant in breast milk are usually insignificant compared with doses used to treat the infant. In almost all cases, an antimicrobial agent that is appropriate for treating the mother and compatible with breastfeeding can be selected.

### Infection-control issues

Infection-control guidelines are intended for hospitals, but the principles of epidemiology can be applied to any infectious situation, even in the home, and can facilitate logical and reasonable use of interventions to prevent transmission of infection to an infant.

Newer concepts and terminology have been proposed recently [13]. *Standard precautions* include avoiding direct contact with blood and body fluids, nonintact skin, and mucous membranes of every patient, regardless of the patient's diagnosis, based on the idea that infection can be transmitted without an identified infection and from unidentified sources. Standard precautions emphasize careful handwashing with every patient contact and the use of appropriate barriers when contamination with body fluids is more likely (eg, gloves, masks, glasses). Breast milk is not considered a potentially infectious body fluid under these guidelines. Careful handwashing before and after breastfeeding is always appropriate, as are selected barriers (mask, gown or clothes, bandages) to prevent infant contact with other body fluids of the mother with a specific infection. Washing the breast before or after breastfeeding is unnecessary and may irritate the breast.

Specific contact, droplet, or airborne precautions are used for certain illnesses and microorganisms based on the predominant mode of transmission [14]. *Airborne precautions* are used to prevent transmission through droplet nuclei (ie, respiratory particles less than 5  $\mu\text{m}$  in diameter that can contain microorganisms). Respiratory protective devices (requiring personal fitting and seal testing) are recommended for illnesses such as measles, varicella, disseminated zoster, and tuberculosis. Because infants cannot wear such devices, infants of mothers with these infections should be separated temporarily from the mother during the infectious period, regardless of the mode of feeding. The infant can receive the mother's expressed breast milk through a bottle (given by another individual), except when there are lesions of varicella-zoster or tuberculosis on the breast, and in the case of measles, where breast milk should be held until the infant has received immunoglobulin.

*Droplet precautions* are used for larger respiratory droplets that travel only short distances in the air and are transmitted more frequently by direct contact with mucous membranes, hands, or objects contaminated with respiratory secretions. Use of a surgical mask (by the individual with the infection) to limit the spray of droplets and touching of mucous membranes as well as careful handwashing are the primary interventions. Droplet precautions should be used for adenovirus, diphtheria, influenza, *Haemophilus* spp, mumps, mycoplasma, *Neisseria* spp, pertussis, respiratory illnesses, rubella, and *Streptococcus* spp. Timing is crucial relative to the institution of such precautions to prevent disease. In the case of parvovirus, a previously well mother is unlikely to be infectious after onset of the rash [15]. Expressed breast milk can be given to the infant in most cases.

*Contact precautions* are used to prevent transmission by direct or indirect contact with potentially pathogenic organisms. Indicated interventions can include the use of gloves and gowns, handwashing before and after using such barriers, and cohorting, separation, or a private room. Contact precautions can be used for many organisms (eg, diarrheal agents, multi-drug-resistant organisms). The use of expressed breast milk is acceptable in most situations where contact precautions are recommended, with Ebola virus infection or Lassa fever as notable exceptions [16].

## Bacterial infections

Bacterial infections in neonates and infants are common. Systemic bacterial infections occur in the neonate with a frequency of one to five episodes in 1000 live births. The timing of infection in the neonate is divided commonly into *early-onset* (before 7 days of age, especially less than 24 hours of age), *late-onset* (7–30 days of age), and *very late-onset* (after 30 days of age). The predominant organisms of early-onset are group B streptococci and enteric bacilli, especially *Escherichia coli*. Less common early-onset pathogens include other streptococci, *Enterococcus* spp, *Listeria* spp, *Haemophilus influenzae*, *Streptococcus pneumoniae*, *Chlamydia* spp, and other organisms in the maternal genital flora. These organisms can cause late- or very late-onset bacterial infections. Additional gram-negative bacilli are resistant frequently to antibiotics, and *Staphylococcus aureus* and coagulase-negative strains become more frequent, especially during hospitalization of a neonate or infant. Transmission of these organisms from mother to child through breast milk is relatively rare compared to the transmission perinatally during delivery, or through direct contact with the mother, family, or health care providers after birth. Table 1 lists selected organisms.

Botulism most frequently occurs between 6 weeks and 6 months of age and primarily before 12 months of age, with the youngest patient in the literature 6 days of age [17]. Botulism is caused by the neurotoxin produced by *Clostridium botulinum*. Arnon and colleagues [18] reviewed 50 patients hospitalized for botulism in California and the breast-fed infants were older at diagnosis than formula-fed infants, and had milder disease. In cases of sudden infant death syndrome

Table 1  
Breastfeeding issues for selected bacterial maternal infections

Organism <sup>a</sup>	Predominant modes of transmission <sup>b</sup>	Usual timing of infection <sup>c</sup>	Evidence for transmission in breast milk	Clinical significance <sup>d</sup>
<i>Clostridium botulinum</i>	Food-borne Toxin-mediated disease	NA	None	BF/BM
<i>Chlamydia trachomatis</i>	Contact-genital, secretions	Perinatal	None	BF/BM
<i>Escherichia coli</i>	Contact—GI tract or stool	Perinatal	None	BF/BM
<i>Haemophilus influenzae</i>	Contact	NA	None	Delay BF 24-hr therapy in mother; BM Rifampin prophylaxis for the infant.
<i>Listeria monocytogenes</i>	Droplets Contact—GI tract	Perinatal	None	BF/BM
<i>Mycobacterium tuberculosis</i>	Food-borne Airborne	Postnatal Postpartum (perinatal and congenital are rare)	Only with TB Mastitis and lesions on the breast	With active TB, delay BF for 14 days; maternal therapy or PI, BM. Infant—isoniazid prophylaxis.
<i>Neisseriae gonorrhoeae</i>	Droplet Contact—genital, oral, rectal Body fluids	Perinatal (postnatal is rare)	None	Ceftriaxone—no delay, BF / BM. Other medications—delay 24-hr maternal therapy, BM.

<i>Staphylococcus aureus</i>	Contact	Postnatal	Lesions on the breast or mastitis Contaminated, stored breast milk	Delay 24-hr maternal therapy, BM. Avoid BM with breast lesions or MRSA.
Coagulase- negative <i>staphylococci</i>	Contact	Postnatal (premature, sick neonates; IV lines, antibiotics)	None	BF/BM
Group B <i>streptococci</i>	Contact—genital tract, secretions	Prenatal Perinatal Postnatal	Case reports, rare	Preventive therapy. Delay 24-hr maternal therapy, BM. Empiric prescription for infant <sup>c</sup>

This is a selected, limited list intended to consider some important bacteria that cause infection in the neonate or infant and possible issues related to breastfeeding and breast milk.

*Abbreviations:* BF, breastfeeding is appropriate; BM, expressed breast milk is appropriate; GI, gastrointestinal; IV, intravenous; NA, Not applicable; PI, period of infectivity; TB, tuberculosis.

<sup>a</sup> Bacteria that cause various clinical illnesses in the infant and the mother; the specific illnesses are too numerous to list.

<sup>b</sup> For breastfeeding and non-breastfeeding situations; does not include all possible or reported modes of transmission (airborne, body fluids, contact, droplet, food-borne).

<sup>c</sup> Does not include all possible times of transmission. If “NA” the timing of infection is not associated frequently with pregnancy, delivery, or neonates and infants.

<sup>d</sup> Notes the appropriateness of breastfeeding or use of breast milk when the mother has specific bacterial infection.

<sup>e</sup> Refer to the text for explanation.



associated with botulism, no infants were breast-fed within 10 weeks of death. An association with the introduction of solid foods has been suggested. Honey and corn syrup often are implicated because they may contain *C botulinum* spores. The apparent immunologic benefit of breast milk may be caused by more acidic stools (pH 5.1–5.4) and increased *Bifidobacterium* species in the stools of breast-fed infants, limiting the presence of *C botulinum* or spores. Botulinum toxin production declines with lower pH. No evidence suggests that the organism or the toxin is transmitted through breast milk.

Chlamydia infection may be the most frequent sexually transmitted disease in the United States. Perinatal infection in the infant produces conjunctivitis and pneumonitis and is caused primarily by colonization of the infant when passing through the birth canal. Specific sIgA has been identified in colostrum and breast milk. There is no evidence for transmission through breast milk.

*Escherichia coli* is a common cause of neonatal systemic bacterial infection as well as urinary tract infections and bacteremia in infants. *E coli* is ubiquitous in the mother and infant's environment. Breast milk has never been documented as a source of *E coli* infection.

*Haemophilus influenzae* infections have decreased significantly in countries with widespread use of the *H influenzae* conjugated vaccines (HibTITER, PedvaxHIB, Comvax, ActHIB, OmniHIB) [19]. Transmission is through direct contact and respiratory droplets; there is no evidence for its transmission through breast milk. Breast milk seems to limit colonization of *H influenzae* in the infant's throat [20]. In the unusual situation of infection in a breastfeeding mother with an incompletely immunized infant, then chemoprophylaxis is indicated for all household members, including the infant [21]. Temporary separation of the infant and mother is appropriate during the first 24 hours of the mother's antimicrobial therapy, after which breastfeeding can resume. Expressed breast milk can be given to the infant in the interim.

Listeriosis during pregnancy infrequently causes premature delivery or still-birth. Perinatal infection is an uncommon cause of severe disease in the neonate with transmission through transplacental spread, infected amniotic fluid, or contact with the organism in the maternal genital tract. No published information suggests transmission of *Listeria monocytogenes* through breast milk. Breastfeeding or use of expressed breast milk from the mother with *Listeria* infection is appropriate, including the selection of antimicrobial agents that are compatible with breastfeeding to treat the mother.

*Neisseria gonorrhoeae* is transmitted during passage through the birth canal and infrequently from postnatal contact with the mother or her partner. There is no documented risk for transmission in breast milk. Breastfeeding can continue when the mother is treated with ceftriaxone (Rocephin), but a temporary cessation (first 24 hours of maternal therapy) of breastfeeding and breast milk should occur when other antibiotics are used.

Staphylococcal infection usually occurs late in the neonatal period. Forty to ninety percent of infants in the nursery at 5 days of age will be colonized with *Staphylococcus aureus* [22]. *Staphylococcus aureus* caused nursery outbreaks in

the past. Postnatal contact with mothers, health care workers, and contaminated, unpasteurized, banked breast milk were the identified sources of infection [23]. *Staphylococcus aureus* is a common cause of mastitis in the mother. There is one reported case of staphylococcal scalded skin syndrome in an infant whose mother had a skin lesion caused by staphylococcus on her areola [24]. No attempt to identify the toxin or the organism in the breast milk was made. This case reinforces close, continued observation of the infant (breast- or formula-fed) when there is a documented maternal infection. In a case of toxic shock syndrome in a mother at 22 hours postpartum, the breast-fed infant remained well through 60 days of age. Staphylococcal enterotoxin F (SEF) was identified in breast milk on days 5, 8, and 11, but *Staphylococcus aureus* was isolated only from the mother's vagina and not the breast milk [25]. SEF is inactivated by pepsin at pH 4.5. It is probably inactivated in the stomach, presenting no risk to the infant. Methicillin-resistant *Staphylococcus aureus* (MRSA) is more frequent than in the past. Skin and nares are the predominant sites of colonization. No treatment regimen to eradicate colonization has proved highly successful. Current regimens include oral systemic therapy with one or two sensitive antibiotics, topical antibiotics twice daily to the nares, and intermittent bathing with hexachlorophene (pHisoHex) or a similar agent. In the face of maternal *Staphylococcus aureus* infection, use of expressed breast milk is appropriate during a temporary 24-hour separation of mother and infant at the initiation of maternal antimicrobial therapy.

Coagulase-negative staphylococcal infection causes late-onset disease in susceptible neonates. Factors associated with increased risk for this infection include prematurity, low birth weight, very low birth weight, invasive therapies (eg, intravenous lines, chest tubes, surgery, dialysis), antibiotic use, and prolonged hospitalization. Colonization rates are as high as 60% to 90% for infants hospitalized at 2 weeks of age, in selected nurseries. There is no difference in the infection or colonization rates for formula-fed and human milk-fed infants. Breast milk can be given and may provide significant other benefits to these susceptible infants.

Group B streptococcus (GBS, *Streptococcus agalactiae*) is transmitted primarily in utero and during delivery. The revised guidelines proposed by the American Academy of Pediatrics committees on Infectious Diseases and the Fetus and Newborn use several variables to identify increased risk for GBS infection in the neonate and recommend intrapartum prophylaxis for those infants at high risk [26]. Colonization of the infant during the postnatal period occurs [27,28]. Although many infants are colonized, few develop disease [29]. Acquisition of GBS through breastfeeding or breast milk is rare, but has been documented in cases of late-onset GBS disease [30,31]. Butter and DeMoor [32] demonstrated GBS in the nose and throat of infants when GBS also was cultured from the mother's breast. It is more likely that transmission occurs through contact rather than the organism passing in the breast milk. A mother or infant colonized or infected with GBS should be managed with standard precautions during hospitalization. Routine culturing of the breast or breast milk and therapy to eradicate colonization have not proved useful. GBS has not been associated

with outbreaks in the nursery. When the mother begins treatment for GBS disease (most often endometritis), temporary, 24-hour separation of the mother and infant should occur with the provision of expressed breast milk for the infant.

Tuberculosis (TB) is uncommon in the United States, but remains a significant and common disease worldwide. Congenital TB is extremely rare, with fewer than 300 reported cases in the literature. TB mastitis is also rare. Starke [33] has summarized the evaluation and treatment of a pregnant woman with a positive tuberculin skin test. The primary concern is the postnatal exposure of the infant through droplets or droplet nuclei by the mother or another household member with active pulmonary TB. Complete evaluation of the suspected person to determine their TB status (active disease with or without positive cultures and smears) and testing of all household contacts are the first steps. Breast-fed and formula-fed infants are equally at risk from respiratory transmission. Separation of the infant from any case of active pulmonary TB is appropriate. Once adequate therapy in the mother has begun and the mother is determined to not be infectious, the infant and mother may have contact. Observation of the mother and infant should continue through the completion of treatment for the mother. Transmission of TB in breast milk has never been documented in the absence of TB mastitis. Expressed breast milk can be given safely to the infant because antituberculous medications can be used in infants. The only contraindication to using breast milk is in the mother who has TB mastitis. Prophylactic isoniazid (Nydrazid, Laniazid) therapy for the infant prevents TB infection in infants. Once both the mother and infant are being treated and closely observed, they can be in contact [34].

## **Viral infections**

Most significant viral infections in neonates or infants occur through transplacental or intrapartum transmission. The risk for transmission from mother to child varies significantly if the maternal infection is a primary infection (eg, herpes simplex virus [HSV], HIV1), a secondary (reactivation) infection (eg, HSV, CMV) or a chronic infection (eg, hepatitis B, HIV1, HTLV-I) during pregnancy or lactation. The transmission of infection through breast milk is well documented for CMV, HIV1, and HTLV-I. Exposure to small amounts of virus in human milk multiple times a day over the period of breastfeeding (months to years) probably contributes to the high rate of transmission of CMV, HIV1, and HTLV-I through breast milk. For most other viruses, transmission through breast milk is rare (Table 2).

CMV is the most common cause of congenital infection in the United States. Approximately 1% of all infants excrete CMV in their urine at or soon after birth (less than 3 weeks of age). About 5% of the CMV congenitally infected infants will manifest disease at birth and 15% will manifest congenital infection later (eg, progressive late-onset hearing loss, learning disability) [35]. Perinatal infection occurs through direct contact or body fluid contact at delivery, but is associated rarely with clinical illness in full-term infants. Postnatal infection occurs through

breastfeeding or contact with infected body fluids, most frequently during play with other infants, especially in day-care settings. Infection through breast milk rarely results in significant disease in full-term infants. The normal acquisition of transplacental maternal antibodies against CMV protects full-term infants of CMV-positive mothers. Rarely, primary CMV infection occurs in the mother around delivery or during lactation, which increases the risk for illness in the infant because of a lack of anti-CMV antibodies available to the infant. CMV is identifiable in breast milk at various rates in CMV-positive mothers, probably because of variation in the testing and sampling techniques and the intermittent nature of reactivation and excretion of the virus. Postnatal exposure of susceptible infants (ie, infants without passively acquired maternal antibodies against CMV: premature infants, infants of CMV-seronegative mothers, and immunodeficient infants) can lead to severe disease (hepatitis, pneumonitis) [36,37].

Vochem and colleagues [38] described CMV transmission in breast milk-fed, premature infants when the mother had viro lactia (17/29, 59%) as compared with infants without CMV identified in the breast milk (0/27). Five of the infants infected before 2 months of age developed an acute sepsis-like picture with apnea, bradycardia, hepatitis, leucopenia, and prolonged thrombocytopenia compared with infants infected after 2 months of age, who exhibited only mild disease. Yasuda and colleagues [39] and Sharland and colleagues [40] demonstrated decreased infection and disease in premature infants who received CMV-positive breast milk when the milk was stored at  $-20^{\circ}\text{C}$  or pasteurized. No prospective, controlled trials have demonstrated the efficacy of such treatments of breast milk in preventing CMV infection in premature infants. CMV-seropositive mothers can breastfeed their full-term infants safely. Exposure of CMV-seronegative or premature infants to CMV-positive blood products or human milk (from donor or mother) should be avoided.

Hepatitis in the pregnant or lactating mother requires complete evaluation and identification of a specific etiologic agent. Many viruses can cause hepatitis, most frequently hepatitis A, B, and C viruses, CMV, and Epstein-Barr virus, and there are several nonviral causes (toxic, autoimmune, and others).

Transmission of hepatitis A virus (HAV) in breast milk has been implicated in one case report [41]. It is uncertain how frequently HAV can be isolated from breast milk. There is no evidence for chronic HAV infection and the infection in infants is usually mild. Exposure of the infant usually has occurred before the diagnosis is made in the mother. There is no reason to stop breastfeeding. The infant of a mother with recently diagnosed HAV infection should receive immunoglobulin and HAV vaccine (Havrix, Vaqta).

Chronic hepatitis B virus (HBV) infection develops in 90% of infants infected before or during birth. Children infected between 1 and 5 years of age develop chronic HBV infection about 30% of the time. The sequelae of chronic HBV infection include chronic active infection, chronic persistent hepatitis, cirrhosis, and hepatocellular carcinoma. Transmission is primarily through blood or body fluids. Transmission of HBV occurs with breast milk and hepatitis B surface antigen has been demonstrated in breast milk. There is no difference in serocon-

Table 2  
Breastfeeding issues for selected viral maternal infections<sup>a</sup>

Virus <sup>a</sup>	Predominant modes of transmission <sup>b</sup>	Usual timing of infection <sup>c</sup>	Evidence for transmission in breast milk	Clinical significance <sup>d</sup>
Cytomegalovirus <sup>c</sup>	Contact—body fluids	Congenital, perinatal, postnatal	Culture; CMV-DNA PCR	Full-term infants: BF/BM. Premature, LBW, VLBW <sup>f</sup> BF/BM
Enteroviruses (coxsackie virus, enterovirus, poliovirus)	Contact—fecal-Oral	Perinatal, postnatal	None	
Hepatitis A	Food; water, contact—body fluids	Postnatal	One case report	BF/BM Immunoglobulin
Hepatitis B <sup>e</sup>	Blood; body fluids; sexual	Perinatal	Hepatitis B Surface Antigen	Routine prevention with HBV vaccine and hepatitis B immunoglobulin, then BF/BM <sup>g</sup>
Hepatitis C	Blood; body fluids	Prenatal, perinatal	? Possible HCV-RNA	BF/BM (increased transmission if coinfectd with HIV)
HSV1, HSV2	Contact	Perinatal (congenital, postnatal)	Transfer only with breast lesions	BF/BM (except with breast lesions)
HIV1	Blood; body fluids; sexual	Perinatal, prenatal, postnatal	HIV-RNA PCR; culture	Avoid BF/BM <sup>c</sup>
HIV2	Blood; body fluids; sexual	Prenatal, perinatal	Limited information	Avoid BF/BM (early weaning may be appropriate)
HTLV-I	Blood; body fluids	Postnatal, prenatal, perinatal	HTLV-I—RNA PCR	Avoid or limit BF/BM to less than 6 mo

Parvovirus	Contact; body fluids	Prenatal	Unknown	BF/BM
Respiratory syncytial virus	Droplets; contact	Postnatal (susceptible neonates and infants)	None; possible benefit of BM	BF/BM Palivizumab <sup>h</sup>
Varicella-zoster virus	Contact; droplets	Postnatal (rare congenital or perinatal)	Only with lesions on breast; VZV-DNA	Avoid BF for PI BM if no breast lesions Varicella-zoster immunoglobulin for infant

This is a selected, limited list intended to consider some important viruses that cause infection in the neonate or infant and possible issues related to breastfeeding and breast milk.

*Abbreviations:* BF, breastfeeding; BM, expressed breast milk; HBV, hepatitis B virus; HCV, hepatitis C virus; LBW, low birth weight; PCR, polymerase chain reaction; PI, period of infection; VLBW, very low birth weight; VZV, varicella-zoster virus.

<sup>a</sup> Viruses that cause a various of clinical illnesses in the infant and the mother; the specific illnesses are too numerous to list.

<sup>b</sup> For breastfeeding and non-breastfeeding situations; does not include all possible or reported modes of transmission (airborne, body fluids, contact, droplet, food-borne).

<sup>c</sup> Does not include all possible times of transmission.

<sup>d</sup> Notes the appropriateness of breastfeeding or use of breast milk when the mother has a specific viral infection.

<sup>e</sup> Refer to the text for more explanation.

<sup>f</sup> CMV-positive breast milk should be avoided in these infants if they lack CMV-IgG. They are at greater risk to develop CMV-related disease.

<sup>g</sup> Breast-fed infants who have received hepatitis B vaccine with or without hepatitis B immunoglobulin as indicated by maternal hepatitis B status are at no greater risk for HBV infection than formula-fed infants (who also should have received hepatitis B vaccine with or without hepatitis B immunoglobulin as indicated by maternal hepatitis B status).

<sup>h</sup> Palivizumab is indicated for certain children at high risk for respiratory syncytial virus infection, regardless of feeding mode [16].

version rates for formula-fed and breast-fed infants [42,43]. The appropriate administration of hepatitis B immunoglobulin (HBIG) and HBV vaccine (Recombinax HB, Engerix-B) at birth for infants born to hepatitis B surface antigen-positive mothers prevents transmission in more than 95% of cases, regardless of the mode of feeding [44]. Breastfeeding can continue along with the administration of HBIG and HBV vaccine.

Hepatitis C virus (HCV) infection leads to chronic infection in 70% to 85% of cases, regardless of the timing of infection, and leads to the same potential sequelae as does HBV. Transmission occurs through blood and blood products, intravenous drug use, probably body fluids contaminated with blood, and sexual transmission when there are other STDs or a high viral load in blood or body fluids. Congenital and intrapartum transmission occurs. Factors that seem to increase risk for such transmission include high maternal viral load, maternal coinfection with HIV, and prolonged rupture of membranes with vaginal delivery [45–53]. The frequency and the easy diagnosis of HCV infection in infants still need to be worked out. Transmission of HCV infection through breast milk has not been proved, and transmission rates seem similar in formula-fed and breast-fed infants. Published studies have not controlled for variables such as maternal HCV-RNA serum viral loads, amount of virolactia, exclusive or partial breastfeeding versus exclusive formula feeding, and duration of breastfeeding [45–47,51–54]. Additional controlled trials are needed to delineate the importance of different factors contributing to or limiting transmission from mother to child. Current Centers for Disease Control and Prevention guidelines do not consider maternal HCV infection a contraindication to breastfeeding, although they suggest that cracked or bleeding nipples may increase risk for transmission [55]. Regardless of the etiologic cause of maternal hepatitis (A, B, or C), the theoretic risks for transmission through breast milk should be discussed balanced with the benefits of breast milk, so the mother and parents can make an informed decision concerning infant feeding.

Herpes simplex virus types 1 and 2 (HSV-1, HSV-2) cause severe perinatal infections and, less frequently, prenatal and postnatal infections. Case reports have demonstrated HSV infections in infants related to maternal HSV-positive breast lesions and inoculation of virus from primary gingivostomatitis in the infant to the mother's breast during breastfeeding [56–58]. Breastfeeding or use of expressed breast milk in the absence of breast lesions in the mother, with other signs of active HSV infection, is appropriate when careful contact precautions are followed, including covering the lesions, remaining clothed or gowned, and careful handwashing. Maternal treatment or prophylactic treatment of the infant may be reasonable in certain situations to decrease shedding, hasten clinical resolution of the lesions, and protect the infant.

Breastfeeding by an HIV1-positive mother increases transmission risk through breast milk 4% to 22%, in addition to the risk for prenatal and perinatal transmission [59–62]. Recent reviews document HIV1 transmission through breast milk [63,64]. Many issues related to HIV1 transmission through breast milk are considered, including the increased risk for transmission with primary HIV1

infection in the mother during lactation, the health of the HIV1-infected, breast-feeding mother, the presence of the virus and potentially immunologically protective factors in colostrum and breast milk, factors that contribute to HIV1 transmission in breast milk, and possible interventions to prevent or limit HIV1 transmission through breast milk. The avoidance of breastfeeding in maternal HIV1 infection is an important component of preventing mother-to-child transmission in the United States and other countries.

In resource-poor situations, where the complete avoidance of breast milk can increase morbidity and mortality because of poor nutrition or other infections, potential interventions can limit HIV1 mother-to-child transmission. Some of the potentially effective interventions include exclusive breastfeeding, early weaning, education and support to decrease the occurrence of mastitis or nipple lesions, antiretroviral therapy for the mother or infant, treating the human milk to decrease the viral burden (ultraviolet light, freezing, and thawing), and stimulating the infant's immune defenses with active or passive immunization. These interventions need to be tested for feasibility, cultural acceptability, preservation of nutritional benefit, and efficacy where they may have the greatest effect. Avoidance of breastfeeding by HIV-positive mothers should continue in countries where an alternative source of nutrition can be provided easily. The World Health Organization, United Nations International Children's Fund, and the Joint United Nations Programme on HIV/AIDS recommend counseling, education, and support for HIV-infected mothers in resource-poor settings where breastfeeding is the norm, and offer vital nutritional and infection-protective effects so they can make an educated decision concerning infant feeding. Mothers making either choice should be provided continuing education, support, and medical care to optimize their infant's and their own health and to minimize the risk of HIV1 mother-to-child transmission.

HIV2 causes clinical disease similar to infection with HIV1, but with a significantly slower progression to immune suppression. Ekpini and colleagues [62] documented infrequent HIV2 vertical transmission, but no cases of late postnatal seroconversion in a cohort of West African mothers and infants (138 HIV1-positive mothers, 132 HIV2-positive women, 69 women seropositive for HIV1 and HIV2, and 274 HIV-seronegative women). HIV2 transmission through breast milk is less common than for HIV1, but the risk and possible factors contributing to transmission have not been quantified adequately. Until additional data are available concerning HIV2 and breast milk, it is appropriate to follow the current guidelines for breastfeeding and breast milk related to HIV1 infection.

HTLV-I causes *adult T-cell leukemia/lymphoma (ATL)*, a chronic, progressive neuropathy called *HTLV-I associated myelopathy* or *tropical spastic paraparesis* associated with various other chronic conditions (uveitis, arthritis, Sjögren's syndrome, infective dermatitis, and a persistent lymphadenitis in children). Early life infection carries the greatest risk for adult T-cell leukemia [62]. HTLV-I occurs endemically in limited areas worldwide, including southwest Japan, the Caribbean, South America, and sub-Saharan Africa [65,66]. Transmission is through sexual contact, blood and blood products, and breast milk. Transmission occurs



more frequently in breast-fed infants than formula-fed infants [67–72]. A longer duration of breastfeeding correlates with greater risk for HTLV-I transmission to the infant [72–74]. Transmission also has been associated with higher maternal provirus levels and a higher HTLV-I antibody titer [75,76]. Complete avoidance of breastfeeding is an effective intervention to prevent mother-to-child transmission [77]. The median time of transmission was estimated at 11 to 12 months of age [78]. In areas of low prevalence, the likelihood of a false positive HTLV-I test is high; therefore repeat testing often is indicated. In a pregnant woman, antibody titer testing and proviral load quantification are appropriate to estimate the risk for transmission to the infant. The risk for mother-to-child transmission should be discussed with the mother and parents. When formula is available readily and culturally acceptable, then avoiding breast milk or recommending early weaning (before or at 6 months of age) is reasonable to decrease the risk for HTLV-I transmission to the infant. Providing the infant with frozen/thawed breast milk may be an acceptable alternative in certain situations, because freezing decreases the amount of viable virus in breast milk for other viruses (eg, CMV, HIV1).

HTLV-II causes at least two forms of chronic ataxia (spastic or tropical) [79]. An association has been noted between HTLV II and several other illnesses: arthritis, glomerulonephritis, myelopathy, T-hairy cell leukemia, and large granulocytic leukemia. The predominant modes of transmission are intravenous drug use, infected blood and blood products, and breastfeeding. The frequency of transmission and the contributing factors to sexual transmission remain uncertain. HTLV-II has been detected in breast milk [80] and transmission is more frequent in breast-fed than formula-fed infants [80–87]. Nyambi and colleagues [85] demonstrated a correlation between duration of breastfeeding and transmission rate. Given the nature of HTLV I and II (ie, early infection, late onset, progressive disease, and no available therapy), it is appropriate to emphasize prevention. In mothers with documented HTLV-II infection, it is reasonable to recommend avoiding breastfeeding or limiting its duration whenever alternative nutrition is available, practical, and culturally acceptable.

Human parvovirus B19 can cause a wide range of clinical illness, but most frequently causes asymptomatic infection or erythema infectiosum. Severe disease is seen most often in individuals with hemoglobinopathy, red blood cell abnormalities, and immune deficiency, and in the fetus or neonate as a result of maternal infection during pregnancy. Transmission is through contact with respiratory secretions (droplets, saliva) and less commonly other body fluids (blood and urine). Seroprevalence data show peak parvovirus infection occurring in school-age children. There is no evidence for parvovirus transmission through breast milk in humans, although it has been identified in rat milk. Continued breastfeeding by a mother with parvovirus infection is reasonable.

Respiratory syncytial virus (RSV) is a frequent cause of respiratory disease (upper and lower tract) in infants and children. In adults, it primarily causes a mild upper respiratory tract infection. There is no evidence of congenital or perinatal infections. Neonates acquire the virus postnatally through droplets or direct contact, often leading to severe disease (bronchiolitis, pneumonia, apnea).

Premature infants and neonates with underlying respiratory disease (hyaline membrane disease, bronchopulmonary dysplasia) or pulmonary hypertension associated with cardiac disease have greater morbidity and mortality with RSV infection. These at-risk infants should receive prophylaxis with either palivizumab (Synagis) or RSV immunoglobulin–intravenous, regardless of the mode of infant feeding. There is no evidence for transmission of RSV through breast milk. There is considerable debate over the measurable benefit of breastfeeding in modifying this disease in neonates. Published studies demonstrate conflicting data about the potential benefit, perhaps because of difficulties controlling for confounding variables (eg, crowding and smoking) [88–90]. Breastfeeding with RSV disease in the mother or the infant can continue as tolerated, and expressed breast milk can be used if the infant is unable to suckle because of respiratory distress.

Varicella-zoster virus (VZV) infection causes chickenpox as the primary infection and zoster or shingles as the recurrent or reactivation infection. Congenital infection can produce distinctive, unilateral malformations of nerve, skin, and other tissues, but is rare. Perinatal infection can be severe when the mother presents with the rash of chickenpox between 5 days before delivery and 2 days after delivery. The severity of the infant's illness may be caused by transmission of the virus to the fetus during maternal viremia before formation and transfer of adequate antibodies to the infant in this narrow window. Postnatal transmission occurs through respiratory droplets and contact or aerosolization of virus from the skin lesions of either varicella or zoster. VZV DNA and antibody against VZV have been identified in breast milk [91,92]. One case of suspected transmission of VZV has been reported without adequate proof to exclude the more common modes of transmission [92]. If a mother develops varicella, breast-fed and formula-fed infants are equally at risk from close contact with her. They should be separated from her and cared for by another individual during the mother's rash (period of infectivity). Expressed breast milk can be given to the infant if no skin lesions involve the breasts or as soon as varicella-zoster immunoglobulin has been given to the infant.

### Other infections

Various other organisms are mentioned in discussions of breastfeeding and infection, a few selected organisms are reviewed here (Table 3).

*Borrelia burgdorferi* is the spirochete that causes Lyme disease. Lyme disease is characterized by multi-organ system involvement (skin, heart, joints, and nervous system) and can occur in three stages (early localized, early disseminated, and late disease). The existence, diagnosis, and treatment of *chronic Lyme disease* remain highly controversial. *B burgdorferi* is primarily arthropod-borne and -transmitted. It is transmitted prenatally uncommonly, even in endemic areas [93], but *B burgdorferi* as the cause of illness in the fetus or congenital abnormalities is debated [94–96]. *B burgdorferi* DNA has been reported in breast milk, but there is no evidence for illness in the infant or transmission of the

Table 3  
Breastfeeding issues for selected maternal infections

Organism <sup>a</sup>	Predominant modes of transmission <sup>b</sup>	Usual timing of infection <sup>c</sup>	Evidence for transmission in breast milk	Clinical significance <sup>d</sup>
<i>Bacillus anthracis</i> (anthrax)	Contact—animals, animal products, cutaneous lesions; airborne	NA	None	BF/BM; cover lesions; medications for therapy and prophylaxis <sup>f</sup>
<i>Borrelia burgdorferi</i> (Lyme disease)	Arthropod	NA	DNA by PCR; no reports of illness in infants	BF/BM
<i>Candida</i> spp	Contact	Postnatal (colonization, susceptible infants)	Contact with breast, not breast milk	BF/BM
Dengue viruses (1–4)	Mosquito	NA	None	BF/BM
SARS-associated coronavirus	Contact; droplet	NA	None	BF/BM
<i>Toxoplasmosis gondii</i>	Animal-borne; soil, fecal-oral	Congenital	None	BF/BM
<i>Treponema pallidum</i> (syphilis)	Body fluids; blood	Congenital, perinatal	None	Delay BF/BM 24-hr after initiating maternal therapy; empiric treatment of infant
Vaccinia virus (smallpox vaccine)	Contact; possibly airborne	NA	One case report, contact with breast lesion	BF/BM <sup>e</sup>
Variola virus (smallpox)	Contact; airborne	NA	None	Avoid BF/BM; separation PI
West Nile virus	Mosquito; blood	NA	One case report (no illness in infant)	BF/BM

This is a selected, limited list intended to consider some important organisms that cause infection in the neonate or infant and possible issues related to breastfeeding and breast milk.

**Abbreviations:** BF, breastfeeding; BM, expressed breast milk; NA, not applicable; PCR, polymerase chain reaction; PI, period of infection; SARS, severe acute respiratory syndrome.

<sup>a</sup> Organisms that cause various clinical illnesses in the infant and the mother; specific illnesses are too numerous to list.

<sup>b</sup> For breastfeeding and non-breastfeeding situations; does not include all possible or reported modes of transmission (airborne, body fluids, contact, droplet, food-borne).

<sup>c</sup> Does not include all possible times of transmission. If “NA,” the timing of infection is not associated frequently with pregnancy, delivery, or neonates and infants.

<sup>d</sup> Notes the appropriateness of breastfeeding or use of breast milk when the mother has an infection with that specific organism.

<sup>e</sup> Refer to the text for more explanation.

<sup>f</sup> Refer to reference [99].

spirochete to the infant through breast milk [97]. In spite of the paucity of data, caution may be warranted. With a confirmed diagnosis of acute Lyme disease in the mother, it is appropriate to discuss the available information with the mother or parents and to recommend temporarily avoiding breastfeeding and breast milk for 24 to 48 hours after beginning maternal antibiotic therapy (amoxicillin [Amoxil, Trimox, and others], penicillin [numerous trade names], or ceftriaxone [Rocephin]).

*Candida* organisms can cause significant late disease in hospitalized neonates and readily colonize most infants without producing significant illness. Mucocutaneous candidal disease is the most common form of illness in infants, causing thrush and candidal diaper rash. Invasive candidal infection occurs primarily in individuals with other illnesses, altered immunity, or skin and mucosal barriers, and after use of broad-spectrum antibiotics. Late-postnatal infection is most common, intrauterine-ascending infection is rare, and there is no evidence for a syndrome of congenital *Candida* infection. Transmission occurs in healthy individuals through direct contact or contact with vaginal or oral secretions. The mother and infant serve as a ready source of *Candida* organisms to recolonize each other, and this is particularly true during breastfeeding. Thrush or diaper candidiasis in the infant and mastitis or vulvovaginitis in the mother should prompt simultaneous treatment of the mother and infant, even when illness or infection is not obvious in the second individual. Many topical and systemic antifungal agents are recommended in different regimens to treat and eradicate *Candida* spp in the breastfeeding mother–infant dyad. Breastfeeding or expressed breast milk is appropriate during treatment, although occasionally maternal mastitis can be so painful that temporary cessation of breastfeeding is necessary for comfort. Management of candidal mastitis requires close adherence to the recommended therapy, careful follow-up, and effective lactation support.

*Toxoplasma gondii* is a protozoan that can cause a congenital infection syndrome with severe central nervous system and ocular sequelae. Postnatal infection is usually asymptomatic; a nonspecific febrile illness, a mono-like illness, lymphadenopathy, or an isolated ocular infection can occur. The cat is the definitive host and transmission is by ingestion of *Toxoplasma* cysts contaminating raw or undercooked meat or inadvertent ingestion of oocysts from soil or contaminated foods. *Toxoplasma gondii* has been transmitted through milk in animal models, but this has not been demonstrated for human milk [98]. Breastfeeding and expressed breast milk can be used in the face of maternal *Toxoplasma* infection during lactation.

*Treponema pallidum*, a spirochete, causes multi-system disease in stages similar to Lyme disease. Transmission is through direct sexual contact and contact with open lesions or secretions from the lesions in the skin and mucous membranes. Congenital syphilis occurs in the fetus through placentitis and perinatal infection occurs in the neonate through contact with the spirochete during passage through the birth canal. Postnatal infection can occur in the infant through contact with open lesions or secretions in the infected mother or another adult.

If syphilitic lesions involve the breast or nipples, then breastfeeding or using expressed breast milk should be avoided until the mother has completed treatment and the lesions have healed. There is no evidence for transmission of *Treponema pallidum* in breast milk without a breast or nipple lesion.

### Potential infections of bioterrorism

Fears of bio-terrorism have exaggerated the importance of various infectious agents to the point of being considered in the routine differential diagnosis of many human illnesses. Breastfeeding has not escaped this concern relative to certain infections, two of which, anthrax and smallpox, are discussed briefly here (see Table 3)

*Bacillus anthracis* causes zoonotic disease worldwide. Transmission in humans occurs through contact with animals or their products (eg, wool) and from person to person by way of cutaneous lesions. Anthrax occurs in three forms: *cutaneous*, *gastrointestinal*, and *inhalational*. There is no evidence for person-to-person spread of inhalational anthrax nor is there evidence of transmission through breast milk. Anthrax lesions of the breast (rare) would necessitate avoiding breastfeeding and breast milk. Contact and standard precautions are appropriate for anthrax. Anthrax, if used as a biological weapon with aerosolization or contamination of the local environment with *B anthracis* spores, would expose breast-fed and formula-fed infants equally.

The primary issue relative to anthrax and breast milk is antimicrobial therapy or prophylaxis after presumed exposure. Clinicians should refer to the published recommendations for treatment and prophylaxis in infants, children, and breastfeeding mothers [99]. The recommendations propose the use of amoxicillin, doxycycline (Vibramycin, Periostat and others), ciprofloxacin (Cipro), and several other agents for 60 days. Little information is available on the prolonged use of doxycycline or ciprofloxacin and their possible effect on infant's teeth and cartilage growth, respectively. Short courses of doxycycline or ciprofloxacin in breastfeeding mothers are acceptable without concern for the infant [100]. Depending on the sensitivity testing of the isolated anthrax strain, amoxicillin or another drug could be used to complete a course of therapy or prophylaxis in a breastfeeding mother or her infant.

Smallpox (variola virus) is highly contagious because of the ease of person-to-person spread by way of droplets, aerosolization from the oropharynx, or direct contact with skin lesions. It also carries a high morbidity and mortality in susceptible populations. For these reasons, it is a potential agent in biological terrorism. The exposure risk of a terrorist act leading to widespread aerosolization, contamination of a closed space, or contamination of the clothes of adults would be the same for breast-fed and formula-fed infants. The high transmission risk from household contact necessitates the separation of any infant from a mother with smallpox. Breast milk should be avoided during the mother's rash because of the possibility of contamination of the milk from the extensive lesions,

even though there is no evidence of transmission of the virus to the infant through breast milk.

Smallpox vaccine (vaccinia virus) presents a possibility of secondary or tertiary spread from the vaccination site. Children over 1 year of age can be vaccinated safely if there is a probable smallpox exposure. The Advisory Committee on Immunization Practices recommends not vaccinating pregnant or breastfeeding women or children less than 18 years old in pre-event smallpox vaccination programs [101]. One case of tertiary contact vaccinia in a breastfeeding infant was reported in 2004. The vaccinee in the household developed an appropriate reaction at the inoculation site and subsequently his wife developed vesicles on both areolae (secondary contact vaccinia). The breastfeeding infant later developed lesions on her philtrum, cheek, and tongue. The mother and infant were observed closely and remained well. Culture and polymerase chain reaction (PCR) testing identified vaccinia virus in the mother and infant's lesions, but the breast milk was not tested [102]. Secondary contact vaccinia from smallpox vaccine is rare, estimated to occur at a rate of 5 to 7 cases per 100,000 vaccinees [103]. Breast-fed and formula-fed infants have the same risk for transmission from close contact with a vaccinee (eg, household contact, close physical contact, or sleeping in the same bed). If the mother has secondary contact vaccinia but her breasts are without lesions, expressed breast milk can be given safely to the infant with the continuation of all other appropriate household precautions after smallpox vaccination.

### **Emerging infections**

Every year seems to bring a new “emerging infectious disease.” Three that have captured public attention in the United States are dengue virus, severe acute respiratory syndrome (SARS), and West Nile virus (WNV).

Dengue viruses (serotypes 1–4) are flaviviruses that cause dengue fever (DF), dengue hemorrhagic fever (DHF), and dengue shock syndrome (DSS) in infants less than 1 year of age, but rarely in neonates less than 3 months of age [104]. Prenatal or perinatal transmission has been reported in 10 instances [105]. Antibody-dependent enhancement, with the presence of certain concentrations of specific antidengue IgG pre-existing in the individual's blood against the infecting strain of virus, reportedly causes more severe disease. There is no evidence for transmission of dengue virus in breast milk, nor more severe disease in breast-fed infants compared with formula-fed infants. There has been no documented person-to-person transmission of dengue virus without a mosquito vector. The mother or infant with dengue disease can continue breastfeeding as they are able.

SARS, as observed in 2003, is caused by a coronavirus different from previously studied coronavirus groups [106,107]. Because the SARS-associated coronavirus was identified recently, much about it is unknown, including whether it is transmitted through breast milk. The SARS virus is transmitted primarily

by respiratory droplets. In the pediatric cases reported in the literature, children had mild respiratory illness, although the severity of the disease in adolescents seemed more similar to that in adults [108–111]. Infants born to mothers with confirmed SARS were born prematurely, presumably because of maternal illness. Two of the five infants described developed severe abdominal disease (coronavirus has been linked to necrotizing enterocolitis), although coronavirus was not identified in any of the infants [112]. It is appropriate to provide expressed breast milk or breastfeed when either the mother or infant has SARS.

WNV infection leads to approximately one case of severe neurologic disease for every 20 cases of nonspecific febrile illness and every 150 to 300 cases of asymptomatic infection (seroconversion) it causes. Although the case fatality rate is high in hospitalized patients or individuals over 70 years of age; children with clinical illness and infants with infection less than 1 year of age have been reported rarely [113]. Transmission occurs through mosquito bite, with mosquitoes of the genus *Culex* being the primary vectors. Transmission also has been reported during pregnancy [114,115], through organ transplant [116], through percutaneous exposure in laboratory workers [117], and through blood and blood product transfusion [118]. One case of possible WNV transmission through breastfeeding has been reported [119]. The mother was infected by a blood transfusion after delivery, became sick 8 days later, and was being hospitalized with a meningoencephalitis-like illness. The infant was breast-fed from birth through the second day of the mother's hospitalization. Samples of the mother's cerebrospinal fluid and breast milk from days 16 and 24 after delivery tested positive for WNV-specific IgM. The breast milk from day 16 was also positive for WNV-RNA on PCR testing. Live WNV was not cultured from the breast milk. The infant remained well. Although this may constitute a case of transmission of WNV through breast milk, the absence of illness in this infant (and most infants/children), the transient nature of maternal viremia with WNV, and the rarity of such a transmission event suggest that there is no reason to avoid breastfeeding or breast milk when a mother is infected with WNV.

## Summary

Three viruses (CMV, HIV, and HTLV-I) frequently cause infection or disease as a result of breast-milk transmission. Reasonable guidelines have been proposed for when and how to avoid breast milk in the case of maternal infection. For other viruses, prophylactic immune therapy to protect the infant against all modes of transmission are indicated (VZV, varicella-zoster immunoglobulin, HAV and immunoglobulin, HBV, and HBIg + HBV vaccine). In most maternal viral infections, breast milk is not an important mode of transmission, and continuation of breastfeeding is in the best interest of the infant and mother (see Tables 2 and 3).

Maternal bacterial infections rarely are complicated by transmission of infection to their infants through breast milk. In a few situations, temporary

cessation of breastfeeding or the avoidance of breast milk is appropriate for a limited time (24 hours for *N gonorrhoeae*, *H influenzae*, Group B streptococci, and staphylococci and longer for others including *B burgdorferi*, *T pallidum*, and *M tuberculosis*). In certain situations, prophylactic or empiric therapy may be advised for the infant (eg, *T pallidum*, *M tuberculosis*, *H influenzae*) (see Table 1). Antimicrobial use by the mother should not be a reason not to breastfeed. Alternative regimens that are compatible with breastfeeding can be chosen to treat the mother effectively.

In most cases of suspected infection in the breastfeeding mother, the delay in seeking medical care and making the diagnosis means the infant has been exposed already. Stopping breastfeeding at this time only deprives the infant of the nutritional and potential immunologic benefits. Breastfeeding or the use of expressed breast milk, even if temporarily suspended, should be encouraged and supported. Decisions about breast milk and infection should balance the potential risk compared with the innumerable benefits of breast milk.

## Acknowledgments

Thank you to Ms. Ruby Kolb for her efforts and careful attention to the details in the preparation of this manuscript.

## References

- [1] Lawrence RA. A review of the medical benefits and contraindications to breastfeeding in the United States. In: Maternal and child health technical information bulletin. Arlington (VA): National Center for Education in Maternal and Child Health; 1997. p. 1–38.
- [2] Lawrence R. Host-resistance factors and immunologic significance of human milk. In: Lawrence RA, Lawrence RM, editors. Breastfeeding: a guide for the medical profession. St. Louis (MO): Mosby; 1999. p. 159–95.
- [3] Beaudry M, Dufour R, Marcoux S. Relation between infant feeding and infections during the first six months of life. *J Pediatr* 1995;126(2):191–7.
- [4] Scariati PD, Grummer-Strawn LM, Fein SB. A longitudinal analysis of infant morbidity and the extent of breastfeeding in the United States [abstract]. *Pediatrics* 1997;99(6):E5.
- [5] Dewey KG, Heinig MJ, Nommsen-Rivers LA. Differences in morbidity between breast-fed and formula-fed infants. *J Pediatr* 1995;126(5 Pt 1):696–702.
- [6] Hanson LA, Korotkova M. The role of breastfeeding in prevention of neonatal infection. *Semin Neonatol* 2002;7(4):275–81.
- [7] Cunningham AS, Jelliffe DB, Jelliffe EF. Breast-feeding and health in the 1980s: a global epidemiologic review. *J Pediatr* 1991;118(5):659–66.
- [8] WHO Collaborative Study Team on the role of breastfeeding on the prevention of infant mortality. Effect of breastfeeding on infant and child mortality due to infectious diseases in less developed countries: a pooled analysis. *Lancet* 2000;355(9202):451–5.
- [9] Goldman AS. The immune system of human milk: antimicrobial, antiinflammatory and immunomodulating properties. *Pediatr Infect Dis J* 1993;12(8):664–71.
- [10] Hanson LA, et al. The mammary gland-infant intestine immunologic dyad. *Adv Exp Med Biol* 2000;478:65–76.
- [11] Pabst HF. Immunomodulation by breast-feeding. *Pediatr Infect Dis J* 1997;16(10):991–5.



- [12] Klein JO, Remington JS. Current concepts of infections of the fetus and newborn infant. In: Remington JS, Klein JO, editors. Infectious diseases of the fetus and newborn infant. Philadelphia: W.B. Saunders; 2001. p. 1–24.
- [13] Garner JS and The Hospital Infection Control Practices Advisory Committee. Guideline for isolation precautions in hospitals. *Infect Control Hosp Epidemiol* 1996;17(1):53–80.
- [14] American Academy of Pediatrics Committee on Infectious Diseases. Infection control for hospitalized children. In: Pickering LK, editor. Red book: 2003 report of the committee on infectious diseases. Elk Grove Village (IL): American Academy of Pediatrics; 2003. p. 146–56.
- [15] American Academy of Pediatrics Committee on Infectious Diseases. Parvovirus B19. In: Pickering LK, editor. Red book: 2003 report of the committee on infectious diseases. Elk Grove Village (IL): American Academy of Pediatrics; 2003. p. 459–61.
- [16] Committee on Infectious Diseases, American Academy of Pediatrics. Hemorrhagic fevers caused by arenaviruses. In: Pickering LK, editor. Red book: 2003 report of the committee on infectious diseases. Elk Grove Village (IL): American Academy of Pediatrics; 2003. p. 305–7.
- [17] Arnon SS. Infant botulism. *Annu Rev Med* 1980;31:541–60.
- [18] Arnon SS, et al. Protective role of human milk against sudden death from infant botulism. *J Pediatr* 1982;100(4):568–73.
- [19] Bisgard KM, et al. *Haemophilus influenzae* invasive disease in the United States, 1994–1995: near disappearance of a vaccine-preventable childhood disease. *Emerg Infect Dis* 1998;4(2):229–37.
- [20] Hokama T, et al. Incidence of *Haemophilus influenzae* in the throats of healthy infants with different feeding methods. *Pediatr Int* 1999;41(3):277–80.
- [21] American Academy of Pediatrics Committee on Infectious Diseases. *Haemophilus influenzae* infections. In: Pickering LK, editor. Red book: 2003 report of the committee on infectious diseases. Elk Grove Village (IL): American Academy of Pediatrics; 2003. p. 293–301.
- [22] Fairchild JP, et al. Flora of the umbilical stump; 2,479 cultures. *J Pediatr* 1958;53(5):538–46.
- [23] Parks YA, et al. Methicillin resistant *Staphylococcus aureus* in milk. *Arch Dis Child* 1987;62(1):82–4.
- [24] Katzman DK, Wald ER. Staphylococcal scalded skin syndrome in a breast-fed infant. *Pediatr Infect Dis J* 1987;6(3):295–6.
- [25] Vergeront JM, et al. Recovery of staphylococcal enterotoxin F from the breast milk of a woman with toxic-shock syndrome. *J Infect Dis* 1982;146(4):456–9.
- [26] American Academy of Pediatrics Committee on Infectious Diseases and Committee on Fetus & Newborn. Revised guidelines for prevention of early-onset group B streptococcal (GBS) infection. *Pediatrics* 1997;99(3):489–96.
- [27] Dillon Jr HC, Khare S, Gray BM. Group B streptococcal carriage and disease: a 6-year prospective study. *J Pediatr* 1987;110(1):31–6.
- [28] Gardner SE, Mason Jr EO, Yow MD. Community acquisition of group B streptococcus by infants of colonized mothers. *Pediatrics* 1980;66(6):873–5.
- [29] Anthony BF, Okada DM, Hobel CJ. Epidemiology of the group B streptococcus: maternal and nosocomial sources for infant acquisitions. *J Pediatr* 1979;95(3):431–6.
- [30] Kenny JF. Recurrent group B streptococcal disease in an infant associated with the ingestion of infected mother's milk. *J Pediatr* 1977;91(1):158–9.
- [31] Schreiner RL, Coates T, Shackelford PG. Possible breast milk transmission of group B streptococcal infection. *J Pediatr* 1977;91(1):159.
- [32] Butter M, DeMoor CE. *Streptococcus agalactiae* as a cause of meningitis in the newborn and bacteraemia in adults. *Antonie Van Leeuwenhoek* 1967;33(4):439.
- [33] Starke JR. Tuberculosis. An old disease but a new threat to the mother, fetus, and neonate. *Clin Perinatol* 1997;24(1):107–27.
- [34] American Academy of Pediatrics Committee on Infectious Diseases. Tuberculosis. In: Pickering LK, editor. Red book: 2003 report of the committee on infectious diseases. Elk Grove Village (IL): American Academy of Pediatrics; 2003. p. 642–60.

- [35] Pass RF. Cytomegalovirus infection. *Pediatr Rev* 2002;23(5):163–70.
- [36] Hamprecht K, et al. Epidemiology of transmission of cytomegalovirus from mother to preterm infant by breastfeeding. *Lancet* 2001;357(9255):513–8.
- [37] Maschmann J, et al. Cytomegalovirus infection of extremely low-birth weight infants via breast milk. *Clin Infect Dis* 2001;33(12):1998–2003.
- [38] Vochem M, et al. Transmission of cytomegalovirus to preterm infants through breast milk. *Pediatr Infect Dis J* 1998;17(1):53–8.
- [39] Sharland M, Khare M, Bedford-Russell A. Prevention of postnatal cytomegalovirus infection in preterm infants. *Arch Dis Child Fetal Neonatal Ed* 2002;86(2):F140.
- [40] Yasuda A, et al. Evaluation of cytomegalovirus infections transmitted via breast milk in preterm infants with a real-time polymerase chain reaction assay. *Pediatrics* 2003;111(6 Pt 1):1333–6.
- [41] Watson JC, et al. Vertical transmission of hepatitis A resulting in an outbreak in a neonatal intensive care unit. *J Infect Dis* 1993;167(3):567–71.
- [42] Beasley RP, et al. Breast-feeding and hepatitis B [letter]. *Lancet* 1975;2(7944):1089.
- [43] Beasley RP, et al. Evidence against breast-feeding as a mechanism for vertical transmission of hepatitis B. *Lancet* 1975;2(7938):740–1.
- [44] American Academy of Pediatrics Committee on Infectious Diseases. Hepatitis B. In: Pickering LK, editor. Red book: 2003 report of the committee on infectious diseases. Elk Grove Village (IL): American Academy of Pediatrics; 2003. p. 318–36.
- [45] Gibb DM, et al. Mother-to-child transmission of hepatitis C virus: evidence for preventable peripartum transmission. *Lancet* 2000;356(9233):904–7.
- [46] Ohto H, et al. Transmission of hepatitis C virus from mothers to infants. The Vertical Transmission of Hepatitis C Virus Collaborative Study Group. *N Engl J Med* 1994;330(11):744–50.
- [47] Dal Molin G, D'Agaro P, Ansaldi F, Ciana G, Fertz C, Alberico S, et al. Mother-to-infant transmission of hepatitis C virus: rate of infection and assessment of viral load and IgM anti-HCV as risk factors. *J Med Virol* 2002;67(2):137–42.
- [48] Ruiz-Extremera A, et al. Follow-up of transmission of hepatitis C to babies of human immunodeficiency virus-negative women: the role of breast-feeding in transmission. *Pediatr Infect Dis J* 2000;19(6):511–6.
- [49] Tajiri H, et al. Prospective study of mother-to-infant transmission of hepatitis C virus. *Pediatr Infect Dis J* 2001;20(1):10–4.
- [50] Yeung LT, King SM, Roberts EA. Mother-to-infant transmission of hepatitis C virus. *Hepatology* 2001;34(2):223–9.
- [51] Lin HH, et al. Absence of infection in breast-fed infants born to hepatitis C virus-infected mothers. *J Pediatr* 1995;126(4):589–91.
- [52] Manzini P, et al. Human immunodeficiency virus infection as risk factor for mother-to-child hepatitis C virus transmission; persistence of anti-hepatitis C virus in children is associated with the mother's anti-hepatitis C virus immunoblotting pattern. *Hepatology* 1995;21(2):328–32.
- [53] Zanetti AR, et al. Mother-to-infant transmission of hepatitis C virus. Lombardy Study Group on Vertical HCV Transmission. *Lancet* 1995;345(8945):289–91.
- [54] Moriya T, et al. Transmission of hepatitis C virus from mothers to infants: its frequency and risk factors revisited. *Biomed Pharmacother* 1995;49(2):59–64.
- [55] American Academy of Pediatrics Committee on Infectious Diseases. Hepatitis C. In: Pickering LK, editor. Red book: 2003 report of the committee on infectious diseases. Elk Grove Village (IL): American Academy of Pediatrics; 2003. p. 336–40.
- [56] Dunkle LM, Schmidt RR, O'Connor DM. Neonatal herpes simplex infection possibly acquired via maternal breast milk. *Pediatrics* 1979;63(2):250–1.
- [57] Quinn PT, Lofberg JV. Maternal herpetic breast infection: another hazard of neonatal herpes simplex. *Med J Aust* 1978;2(9):411–2.
- [58] Sullivan-Bolyai JZ, et al. Disseminated neonatal herpes simplex virus type 1 from a maternal breast lesion. *Pediatrics* 1983;71(3):455–7.
- [59] Bertolli J, et al. Estimating the timing of mother-to-child transmission of human immunodeficiency virus in a breast-feeding population in Kinshasa, Zaire. *J Infect Dis* 1996;174(4):722–6.

- [60] Datta P, et al. Mother-to-child transmission of human immunodeficiency virus type 1: report from the Nairobi Study. *J Infect Dis* 1994;170(5):1134–40.
- [61] Dunn DT, et al. Risk of human immunodeficiency virus type 1 transmission through breast-feeding. *Lancet* 1992;340(8819):585–8.
- [62] Ekpini ER, et al. Late postnatal mother-to-child transmission of HIV-1 in Abidjan, Cote d'Ivoire. *Lancet* 1997;349(9058):1054–9.
- [63] Read JS, American Academy of Pediatrics Committee on Pediatric AIDS. Human milk, breast-feeding, and transmission of human immunodeficiency virus type 1 in the United States. American Academy of Pediatrics Committee on Pediatric AIDS. *Pediatrics* 2003;112(5):1196–205.
- [64] UNAIDS/UNICEF/WHO. HIV and infant feeding. A review of HIV transmission through breastfeeding. New York: WHO/UNAIDS; 1998.
- [65] Fujino T, Nagata Y. HTLV-I transmission from mother to child. *J Reprod Immunol* 2000;47(2):197–206.
- [66] Gotuzzo E. HTLV-I: a new problem for Latin America. *American Society for Microbiology News* 2001;67:144–6.
- [67] Ando Y, et al. Long-term follow-up study of HTLV-I infection in bottle-fed children born to seropositive mothers. *J Infect* 2003;46(1):9–11.
- [68] Ando Y, et al. Long-term follow up study of vertical HTLV-I infection in children breast-fed by seropositive mothers. *J Infect* 2003;46(3):177–9.
- [69] Ando Y, et al. Transmission of adult T-cell leukemia retrovirus (HTLV-I) from mother to child: comparison of bottle- with breast-fed babies. *Jpn J Cancer Res* 1987;78(4):322–4.
- [70] Hino S, et al. Primary prevention of HTLV-I in Japan. *J Acquir Immune Defic Syndr Hum Retroviro* 1996;13(Suppl 1):S199–203.
- [71] Hino S, et al. Breaking the cycle of HTLV-I transmission via carrier mothers' milk. *Lancet* 1987;2(8551):158–9.
- [72] Takahashi K, et al. Inhibitory effect of maternal antibody on mother-to-child transmission of human T-lymphotropic virus type I. The Mother-to-Child Transmission Study Group. *Int J Cancer* 1991;49(5):673–7.
- [73] Takezaki T, et al. Short-term breast-feeding may reduce the risk of vertical transmission of HTLV-I. The Tushima ATL Study Group. *Leukemia* 1997;11(Suppl 3):60–2.
- [74] Wiktor SZ, et al. Mother-to-child transmission of human T-cell lymphotropic virus type I associated with prolonged breast-feeding. *J Hum Virol* 1997;1(1):37–44.
- [75] Hisada M, et al. Virus markers associated with vertical transmission of human T lymphotropic virus type 1 in Jamaica. *Clin Infect Dis* 2002;34(12):1551–7.
- [76] Ureta-Vidal A, et al. Mother-to-child transmission of human T-cell-leukemia/lymphoma virus type I: implication of high antiviral antibody titer and high proviral load in carrier mothers. *Int J Cancer* 1999;82(6):832–6.
- [77] Hino S, et al. Intervention of maternal transmission of HTLV-I in Nagasaki, Japan. *Leukemia* 1993;94:S68–70.
- [78] Furnia A, et al. Estimating the time of HTLV-I infection following mother-to-child transmission in a breast-feeding population in Jamaica. *J Med Virol* 1999;59(4):541–6.
- [79] Lowis GW, Sheremata WA, Minagar A. Epidemiologic features of HTLV-II: serologic and molecular evidence. *Ann Epidemiol* 2002;12(1):46–66.
- [80] Heneine W, et al. Detection of HTLV-II in breastmilk of HTLV-II infected mothers. *Lancet* 1992;340(8828):1157–8.
- [81] Fujiyama C, et al. A new endemic focus of human T lymphotropic virus type II carriers among Orinoco natives in Colombia. *J Infect Dis* 1993;168(4):1075–7.
- [82] Ishak R, et al. Identification of human T cell lymphotropic virus type IIa infection in the Kayapo, an indigenous population of Brazil. *AIDS Res Hum Retroviruses* 1995;11(7):813–21.
- [83] Lal RB, et al. Evidence for mother-to-child transmission of human T lymphotropic virus type II. *J Infect Dis* 1993;168(3):586–91.
- [84] Lal RB, et al. Mother-to-child transmission of human T-lymphotropic virus type II (HTLV-II). *Ann Intern Med* 1994;120(4):300–1.

- [85] Nyambi PN, et al. Mother-to-child transmission of human T-cell lymphotropic virus types I and II (HTLV-I/II) in Gabon: a prospective follow-up of 4 years. *J Acquir Immune Defic Syndr Hum Retrovirol* 1996;12(2):187–92.
- [86] Van Dyke RB, et al. Mother-to-child transmission of human T-lymphotropic virus type II. *J Pediatr* 1995;127(6):924–8.
- [87] Vitek CR, et al. Evidence for sexual and mother-to-child transmission of human T lymphotropic virus type II among Guaymi Indians, Panama. *J Infect Dis* 1995;171(4):1022–6.
- [88] Albargish KA, Hasony HJ. Respiratory syncytial virus infection among young children with acute respiratory tract infection in Iraq. *East Mediterr Health J* 1999;5(5):941–8.
- [89] Bulkow LR, et al. Risk factors for severe respiratory syncytial virus infection among Alaska native children. *Pediatrics* 2002;109(2):210–6.
- [90] Holberg CJ, et al. Risk factors for respiratory syncytial virus-associated lower respiratory illnesses in the first year of life. *Am J Epidemiol* 1991;133(11):1135–51.
- [91] May JT. Antimicrobial factors and microbial contaminants in human milk: recent studies. *J Paediatr Child Health* 1994;30(6):470–5.
- [92] Yoshida M, et al. Case report: detection of varicella-zoster virus DNA in maternal breast milk. *J Med Virol* 1992;38(2):108–10.
- [93] Silver HM. Lyme disease during pregnancy. *Infect Dis Clin North Am* 1997;11(1):93–7.
- [94] Gardner T. Lyme disease. In: Remington J, Klein JO, editors. *Infectious diseases of the fetus and newborn infant*. Boston: Saunders; 2001. p. 519–642.
- [95] Strobino B, Abid S, Gewitz M. Maternal Lyme disease and congenital heart disease: A case-control study in an endemic area. *Am J Obstet Gynecol* 1999;180(3 Pt 1):711–6.
- [96] Williams CL, et al. Maternal Lyme disease and congenital malformations: a cord blood serosurvey in endemic and control areas. *Paediatr Perinat Epidemiol* 1995;9(3):320–30.
- [97] Schmidt BL, et al. Detection of *Borrelia burgdorferi* DNA by polymerase chain reaction in the urine and breast milk of patients with Lyme borreliosis. *Diagn Microbiol Infect Dis* 1995; 21(3):121–8.
- [98] Remington JS, McLeod K, Thulliez P, Desmonts G. Toxoplasmosis. In: Remington JS, Klein JO, editors. *Infectious diseases of the fetus and newborn infant*. Philadelphia: Saunders; 2001. p. 205–346.
- [99] Centers for Disease Control and Prevention. Recommendations for antimicrobial prophylaxis for children and breastfeeding mothers and treatment of children with anthrax. *MMWR Morb Mortal Wkly Rep* 2001;50:1014–6.
- [100] American Academy of Pediatrics Committee on Drugs. Transfer of drugs and other chemicals into human milk. *Pediatrics* 2001;108(3):776–89.
- [101] Wharton M, et al. Recommendations for using smallpox vaccine in a pre-event vaccination program. Supplemental recommendations of the Advisory Committee on Immunization Practices (ACIP) and the Healthcare Infection Control Practices Advisory Committee (HICPAC). *MMWR Recomm Rep* 2003;52(RR-7):1–16.
- [102] Garde V, Harper D, Fairchok MP. Tertiary contact vaccinia in a breastfeeding infant. *JAMA* 2004;291(6):725–7.
- [103] Centers for Disease Control and Prevention. Secondary and tertiary transfer of vaccinia virus among US military personnel—United States and worldwide, 2002–2004. *MMWR Morb Mortal Wkly Rep* 2004;53(6):133.
- [104] Halstead SB, et al. Dengue hemorrhagic fever in infants: research opportunities ignored. *Emerg Infect Dis* 2002;8(12):1474–9.
- [105] Boussemart T, et al. Prenatal transmission of dengue: two new cases. *J Perinatol* 2001;21(4): 255–7.
- [106] Marra MA, et al. The genome sequence of the SARS-associated coronavirus. *Science* 2003; 300(5624):1399–404.
- [107] Rota PA, et al. Characterization of a novel coronavirus associated with severe acute respiratory syndrome. *Science* 2003;300(5624):1394–9.
- [108] Bitnun A, et al. Children hospitalized with severe acute respiratory syndrome-related illness in Toronto. *Pediatrics* 2003;112(4):e261.

- [109] Hon KL, et al. Clinical presentations and outcome of severe acute respiratory syndrome in children. *Lancet* 2003;361(9370):1701–3.
- [110] Hon KL, et al. Personal view of SARS: confusing definition, confusing diagnoses. *Lancet* 2003; 361(9373):1984–5.
- [111] Sit SC, et al. A young infant with severe acute respiratory syndrome. *Pediatrics* 2003; 112(4):e257.
- [112] Shek CC, et al. Infants born to mothers with severe acute respiratory syndrome. *Pediatrics* 2003; 112(4):e254.
- [113] Petersen LR, Marfin AA. West Nile virus: a primer for the clinician. *Ann Intern Med* 2002; 137(3):173–9.
- [114] Alpert SG, Ferguson J, Noel LP. Intrauterine West Nile virus: ocular and systemic findings. *Am J Ophthalmol* 2003;136(4):733–5.
- [115] Centers for Disease Control and Prevention. Intrauterine West Nile virus infection—New York, 2002. *MMWR Morb Mortal Wkly Rep* 2002;51:1135–6.
- [116] Iwamoto M, et al. Transmission of West Nile virus from an organ donor to four transplant recipients. *N Engl J Med* 2003;348(22):2196–203.
- [117] Centers for Disease Control and Prevention. Laboratory-acquired West Nile virus infections—United States 2002. *MMWR Morb Mortal Wkly Rep* 2002;51(50):1133–5.
- [118] Hollinger FB, Kleinman S. Transfusion transmission of West Nile virus: a merging of historical and contemporary perspectives. *Transfusion* 2003;43(8):992–7.
- [119] Centers for Disease Control and Prevention. Possible West Nile virus transmission to an infant through breast-feeding—Michigan, 2002. *MMWR Morb Mortal Wkly Rep* 2002;51(39):877–8.