

# The Role of Breast Milk in Infectious Disease



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## KEYWORDS

- Human milk • Breastfeeding • Infectious disease • Contamination
- Misadministration

## KEY POINTS

- Human milk has many advantageous anti-infective and immunologic properties, making it the ideal nutritional source to optimize the well-being of infants.
- There are certain infectious circumstances where breast milk feedings should be withheld or strict precautions followed; however, these are rare events.
- Contamination and misadministration when handling human milk is a safety concern, especially when caring for vulnerable preterm infants, but there are ways to minimize these occurrences.

## BACKGROUND

Human milk is the preferred nutritional source for all infants, especially ill and premature neonates, owing to the many well-established short- and long-term benefits that human milk provides. One of the major benefits of human milk is its protection against different pathogens and infectious illnesses. The American Academy of Pediatrics thus recommends exclusive breastfeeding for the first 6 months of life for all infants.<sup>1</sup> Despite protecting against disease, human milk can, in rare instances, also be the source of transmission of infection to the neonate. Whether owing to maternal illness, human milk mishandling, or misadministration, there is the potential for inadvertent exposure to certain pathogens that can place the neonate at risk. This review describes the potential of human milk to transmit infection to the neonate and discuss ways to reduce these occurrences in the hospital-based setting. Alternatively, it also reviews the many anti-infective benefits that human milk has to offer, which far outweigh any potential risks.

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## BREAST MILK ANTI-INFECTIVE PROPERTIES

Although this section focuses on the prevention of rare transmissible pathogens through human milk, it cannot be overstated that human milk, through numerous mechanisms, is protective against infectious diseases of bacterial, viral, and parasitic origin. Human milk contributes to the infant's immune function by promoting the growth of nonpathogenic flora, decreasing colonization with enteropathogens, and enhancing the development of mucosal barriers. Human milk can provide the passage of immune cells and other anti-infective proteins and enzymes.<sup>2</sup> Human milk is not sterile and consists of normal gut flora (such as *Bifidobacteria* and *lactobacilli*) that help to populate the developing neonatal gut microbiota, which confers gut protection and health.

Although macronutrients of human milk are generally thought to provide nutritional benefits to the neonate, each also helps protect against disease processes. Milk lipids, for instance, inactivate numerous pathogens *in vitro*.<sup>3</sup> Milk proteins are an important source of bioactive components and the building blocks of anti-infective properties that all confer immunity and anti-infective protection to the neonate.<sup>4</sup> Human milk oligosaccharides are indigestible carbohydrates that are abundant in human milk. They act as prebiotics, forming the necessary substrates for the replenishment of native intestinal microflora and are inhibitory against some pathologic bacteria. Human milk oligosaccharides have also been shown to provide protection against numerous viruses.<sup>5</sup>

Other important entities, such as immunoglobulins (eg, secretory IgA), functioning immune cells (eg, neutrophils, macrophages, and lymphocytes), lactoferrin, lysozyme, cytokines, and other anti-inflammatory factors aid in the development of the immature immune system and confer antimicrobial properties to the breast milk-fed infant.<sup>6</sup> A study from Australia found that human milk leukocytes increased significantly from baseline in a mother's milk in response to her infected infant, suggesting that a mother's mammary gland can respond directly to an acute neonatal infection.<sup>7</sup>

In a dose-dependent manner, human milk decreases the rates of certain chronic illnesses and decreases the rates of respiratory infections, otitis media, and gastroenteritis, as well as decreases the risk for late-onset sepsis and the risk of necrotizing enterocolitis in premature infants.<sup>1,2</sup> The many innate benefits of breast milk make it superior to infant formula, especially for premature infants who are at a greater risk of invasive infections. Mother's own milk is preferred over donor milk because the pasteurization process required for the inactivation of microbial contaminants and the multiple freeze-thaw cycles required for transport minimizes many of the anti-infective properties and nutritional components of the donor milk.<sup>8</sup> However, in situations where mother's expressed milk is not available, donor milk is preferred to formula in the preterm population.<sup>1</sup> Processes should be in place to support lactation via improved multidisciplinary and societal supports and increase access to donor milk when mother's own milk is not an option.

## TRANSMITTED INFECTIONS AND HUMAN MILK

This article focuses on the most common pathogens that can be transmitted rarely through human milk or direct breastfeeding. It is important to understand that human milk is just one of the many potential vehicles for postnatal transmission of infections and excluding other more common mechanisms (eg, caregivers, environment, invasive interventions in a hospital setting) can be challenging. Additionally, human milk can help to prevent or ameliorate illness owing to the many

benefits discussed elsewhere in this article. Therefore, human milk administration should only be discontinued in very rare circumstances as outlined elsewhere in this discussion.

All neonatal units should have policies in place to address infection-related precautions and contraindications to breastfeeding. The development of these policies should be via a multidisciplinary approach involving neonatologists, pediatric infectious disease physicians, infection control specialists, and epidemiologists. In specific or rare cases, decisions regarding breastfeeding safety should be made in consultation with an infectious disease specialist. We review how human milk feeding is impacted by infections transmitted through various modes, and take a deeper dive into specific infectious agents.

### **Airborne Diseases**

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In cases where mothers have active diseases that are transmitted through the airborne route, such as measles, varicella, disseminated zoster, and tuberculosis (TB), infants may need to be separated from their mothers temporarily, until deemed noninfectious. During separation, infants can receive mother's expressed milk because the potential route of transmission is via the mother's airborne droplets and not her expressed milk, as long as there are no active lesions on the breast (such as with varicella zoster [VZV] or TB), in which case the milk expressed from the affected side should be discarded. Direct breastfeeding may resume when all of the following conditions have been met: the infectious period is over, any active breast lesions healed, and, in the case of measles, after infant has received immunoglobulin.<sup>9</sup>

### **Droplet Diseases**

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Pathogens transmitted through larger respiratory droplets such as adenovirus, diphtheria, influenza, *Haemophilus* spp, mumps, mycoplasma, *Neisseria* spp, pertussis, other respiratory viruses such as respiratory syncytial virus, coronaviruses, rubella, and *Streptococcus* spp are not shed in human milk and, thus, an infant can continue to receive expressed milk from a woman with one of these infections.<sup>9</sup> Breastfeeding should be continued as long as proper precautions are in place, such as meticulous hand hygiene and surgical mask donning while contagious.

### **Contact Diseases**

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Contact precautions (gloves and gown) are used for diarrheal diseases, multidrug-resistant organisms, staphylococcal skin and soft tissue infections, and viral skin infections. The use of expressed breast milk and breastfeeding is acceptable in most situations where contact precautions are, recommended except when the breast is affected directly by active, open skin lesions, in which case breastfeeding and expressed milk feedings from the affected breast can be resumed once the lesions have healed.<sup>10</sup>

**Table 1** presents breastfeeding issues for selected maternal infections that are transmitted by contact and/or droplets but not necessarily transmitted through human milk.

## **COMMON VIRAL INFECTIONS**

The transmission of viral infections through breast milk is well documented for HIV, cytomegalovirus (CMV), and human T-lymphotropic virus (HTLV) (**Table 2**). Exposure to small amounts of virus in human milk multiple times a day over the period of breastfeeding (months to years) likely contributes to transmission from a breastfeeding

<b>Organism</b>	<b>Predominant Modes of Transmission</b>	<b>Usual Timing of Infant Infection</b>	<b>Impact of Maternal Infection on the Breastfed Infant</b>
<i>Bacillus anthracis</i> (anthrax)	Contact with skin eschar (airborne if bioterror event)	NA	Separate infant from infected mother and no BF/EBM from affected breast until 48 h after appropriate treatment
<i>Candida</i> species	Contact	Postnatal	Express milk, and can BF from unaffected side while mother and infant receive treatment
HSV-1 or HSV-2	Contact	Postnatal	No BF/EBM from affected breast until lesions healed but infant can BF/receive EBM from unaffected breast; must cover lesions
<i>Mycobacterium tuberculosis</i>	Airborne	Postnatal	Separate infant from mother with active pulmonary disease until completed 2 wk of treatment; infant can receive EBM during this time, except when TB mastitis present
<i>Staphylococcus aureus</i>	Contact	Postnatal	No BF/EBM if uncontained draining or open breast lesions but pumping/dumping encouraged; BF/EBM from unaffected side allowed when lesions covered
<i>Treponema pallidum</i> (syphilis)	Blood and body fluids, skin lesion contact	Congenital/perinatal	If syphilitic lesions on breast/nipple then avoid BF/EBM until treated and lesions healed, otherwise no contraindication to BF/EBM
Primary varicella (chickenpox)	Airborne and contact	Postnatal/perinatal	Isolate separately from mother if possible until lesions crusted; can receive EBM. Keep lesions covered. Provide varicella zoster immunoglobulin to high-risk infants
Varicella-zoster virus (shingles)	Contact and droplet	Postnatal	Avoid contact with lesions-keep covered; if lesions on breast, no BF/EBM on affected side until crusted over but can BF from unaffected side

*Abbreviations:* BF, breastfeeding; EBM, expressed breast milk; NA, not applicable.

<b>Pathogen</b>	<b>Transmissible via Human Milk?</b>	<b>Human Milk Feedings Contraindicated?</b>
HIV	Yes	Yes, contraindicated when safe feeding alternatives exist
Hepatitis B virus	Yes	No, transmission risk low especially after neonatal administration of recommended immunoglobulin and vaccine
Hepatitis C virus	No, but theoretical transmission if woman is viremic and if nipples are cracked and bleeding	No, unless cracked and bleeding nipples
CMV	Yes—risk of clinically significant infection in neonate is variable	No, although can be considered in high-risk infant (premature, immunocompromised, etc) with primary maternal infection
Human T-cell lymphotropic virus type I or type II	Yes	Yes, contraindicated when safe alternatives exist
Viral hemorrhagic fevers (eg, Ebola)	Yes	Yes, contraindicated in suspected or active disease

woman to her infant. The subsequent sections address the more common viral illnesses for which human milk ingestion may pose a risk for transmission.

### **HIV**

HIV may be detected in both cell-free and cell-associated portions of human milk. Many studies have shown that the rate of transmissibility is associated with maternal viral load and is drastically decreased in women who are virologically suppressed on highly active antiretroviral therapy. Maternal receipt of antiretroviral therapy is likely to decrease the levels of free HIV in human milk, but the presence of cell-associated virus (intracellular HIV DNA) may remain and may continue to pose a transmission risk.<sup>10</sup>

In settings where alternatives are available, it is not recommended for HIV-infected mothers to breastfeed or provide their expressed milk under any circumstances.<sup>9,11</sup> This practice is an important component of preventing mother-to-child transmission. However, in settings where potable water and formula are not readily available, infants who are not breastfed are at an increased risk of morbidity and mortality owing to malnutrition and infectious diseases, and thus breastfeeding may outweigh the risk of potentially acquiring HIV. In these settings, compliance with maternal antiretroviral therapy and exclusive breastfeeding has been associated with lower rates of acquiring HIV compared with mixed feedings of formula and human milk.<sup>12</sup>

### **Cytomegalovirus**

Postnatally acquired CMV rarely results in clinically significant disease in full-term infants owing to a more developed immune system and the acquisition of transplacental

maternal antibodies; however, in premature and immunocompromised neonates, CMV can range from mild disease to clinically significant disease manifesting as hepatitis, pneumonitis, and a sepsis-like picture with leukopenia, thrombocytopenia, and possibly death.<sup>13,14</sup>

Postnatal CMV can be acquired via personal contact, saliva, or human milk from a seropositive woman during a primary or reactivated infection.<sup>15</sup> Rates of transmission from the milk of CMV IgG-positive mothers to preterm neonates ranges from 6% to 58%, with the median rates of symptomatic disease being 3.7% and severe disease 0.7%, with the more immature infants being greatest at risk.<sup>16</sup> Freeze-thaw cycling may decrease viral titers and pasteurization may eliminate CMV viral particles from human milk<sup>14,16</sup>, however, these treatments must be weighed against the simultaneous concern of reducing important anti-infective properties of the milk. Although breastfeeding is not contraindicated, whether to continue or discontinue providing human milk from a known CMV seropositive mother to her premature infant is debated, and must be weighed carefully, taking into consideration the immune benefits of human milk.

### ***Hepatitis B Virus***

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Chronic hepatitis B virus (HBV) infection develops in 90% of infants infected before or during birth. If infected after birth, about 30% develop chronic HBV, which can manifest as chronic active infection, chronic persistent hepatitis, cirrhosis, and a later risk of hepatocellular carcinoma.<sup>9</sup>

HBV can be found in breast milk from a chronically infected mother, but the risk of transmission is low, and HBV infection is not considered a contraindication to breastfeeding.<sup>17</sup> In this situation, the benefits of human milk outweigh the theoretical risk of transmission. Furthermore, infants born to women who are hepatitis B surface antigen positive should receive HBV immunoglobulin and the first dose of monovalent HBV vaccine within 12 hours of birth, per standard guidelines.<sup>9,17</sup> Breastfeeding need not be delayed during this time.

### ***Hepatitis C Virus***

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Chronic hepatitis C virus (HCV) infection results in the same potential sequelae as does HBV, and develops in more than 75% of infected adults. Limited data suggest a more indolent course in children with chronic infection and cirrhosis occurring less often with most cases being asymptomatic.<sup>9</sup> HCV has been detected in human milk, but there have been no documented cases of human milk transmission from an infected woman to a neonate via human milk feeding, except with HIV coinfection. In the United States, women who have cracked or bleeding nipples, especially when high HCV loads are present, are advised to temporarily refrain from breastfeeding or feeding human milk expressed from the affected side.<sup>9</sup> Otherwise, women with HCV infection are encouraged to breastfeed or express human milk, with the understanding that there may be a theoretical risk of transmission.

### ***Human T-Lymphotropic Virus***

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Although uncommon in women born in the United States and not routinely screened for in pregnant mothers, women who are HTLV type I or II infected should not breastfeed or provide expressed milk.

HTLV type I is associated with the development of malignant neoplasms and neurologic disorders among adults and is endemic in Japan, the Caribbean, and parts of South America and Africa. Early life transmission is associated with higher risks of leukemia. Studies suggest that infant transmission occurs primarily through

breastfeeding.<sup>18</sup> Although the freezing and thawing of expressed human milk may decrease infectivity, currently it is not recommended that HTLV-I–seropositive women breastfeed or provide expressed breast milk if a viable alternative (eg, formula or donor milk) is available.<sup>1,9</sup>

HTLV type II is a retrovirus that causes chronic ataxia and other multisystem illnesses. It has been detected among American and European injection drug users and some American Indian/Alaska Native groups. HTLV-II has been detected in human milk and maternal–infant transmission has been documented, but few data are available.<sup>18</sup> Thus, similar to HTLV-I, it is not recommended that HTLV-II seropositive women breastfeed or provide expressed milk.<sup>1,9</sup>

### ***Herpes simplex virus***

Herpes simplex virus (HSV) types I and II cause severe perinatal infections and, less frequently, prenatal and postnatal infections. HSV infections in infants attributed to maternal HSV breast lesions have been documented, but there has been no evidence to support HSV transmission in human milk.<sup>9</sup> Breastfeeding or expressing milk in the absence of breast lesions is appropriate in women experiencing an HSV infection when contact precautions are followed, including covering the lesions, remaining clothed or gowned, and careful handwashing. Feeding breast milk, directly or expressed, from the affected breast is contraindicated until lesions healed.<sup>19</sup>

### ***Varicella Zoster***

Primary VZV infection as chicken pox and reactivation as zoster or shingles has been associated with neonatal varicella infections. Postnatal transmission occurs primarily through respiratory droplets and contact with skin lesions. VZV DNA and antibodies have been identified in breast milk, but there have been no data to support the transmission of VZV or attenuated vaccine virus through human milk ingestion.<sup>9</sup> In VZV-exposed infants, VZV immunoglobulin should be given to those deemed at high risk, to include immunocompromised, premature, or development of maternal primary VZV infection within 5 days before or 2 days after delivery.<sup>1,9</sup> If a lactating woman develops VZV, the American Academy of Pediatrics and the Centers for Disease Control and Prevention (CDC) recommend that the infant be isolated separately until the maternal vesicles have dried, despite infant VZV immunoglobulin administration.<sup>1,19</sup> Infant can receive expressed milk as long as the lesions are covered and the breast pump avoids vesicles.<sup>9</sup> Others suggest mother–infant separation can harm successful breastfeeding and thus may not be warranted if lesions can be covered adequately.<sup>20</sup> If a lactating woman is exposed to VZV, varicella vaccine can be administered and human milk feeding can continue.

With varicella reactivation or shingles, breastfeeding can continue as long as the lesions do not involve the breast and are covered. If there is breast involvement in the area where the infant's mouth may contact a lesion, avoid breastfeeding or supplying expressed milk from the affected side until the lesion is crusted is appropriate.<sup>19</sup>

### ***Other Viruses***

Viral hemorrhagic fevers (eg, Ebola virus) are a deadly and highly contagious group of viruses that are transmitted via blood and body fluids, including breast milk; thus, breastfeeding in confirmed or suspected maternal cases is contraindicated. Viruses detected in low levels in human milk but do not pose a contraindication to breastfeeding include hepatitis A virus, rubella, West Nile virus, and Zika virus. In these instances, transmission to an infant is extremely uncommon, and benefits of breastfeeding are felt to outweigh the risks.<sup>9,21,22</sup> There is no evidence for transmission through human

breast milk of any of the following: parvovirus B19, respiratory syncytial virus, severe acute respiratory syndrome novel coronavirus 1 (SARS-CoV 1), and Dengue virus. See the “Emerging Infections” section elsewhere in this article, which addresses SARS-Co-V 2 and human milk feeding.

## BACTERIAL INFECTIONS

Transmission of bacterial organisms from mother to child through human milk is relatively rare compared with other more common routes of transmission (eg, perinatal or contact exposures). Bacteria are present in human milk and pumping or other methods of expressing milk are not sterile procedures. The innate antibacterial and anti-infective properties of human milk decrease the opportunity for transmission of pathogens to the neonate. In select maternal systemic infections, mastitis with open or draining lesions, or breast/nipple lesions, women may be advised to replace direct breastfeeding with expression of human milk, select an unaffected breast for direct breastfeeding or human milk expression, or express but not feed their milk to their neonate. There are no data to support the routine culturing of milk for the presence of bacteria, viruses, or other organisms.<sup>23,24</sup>

### *Escherichia coli*

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*E coli* is a common cause of neonatal systemic bacterial infection as well as urinary tract infections and bacteremia in infants and is ubiquitous in the environment. It is generally thought that breast milk is not a source of neonatal *E coli* infection owing to its anti-infective properties<sup>25</sup>; however, there has been recent documentation of an outbreak in a Japanese neonatal intensive care unit (NICU) likely attributed to contaminated unpasteurized milk sharing, which is not a recommended or routine practice.<sup>26</sup> If a woman has an *E coli* infection, breastfeeding can continue as long as proper contact precautions are maintained.

### *Haemophilus influenzae*

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*H influenzae type b* (Hib) infections have decreased significantly owing to widespread vaccination. There is no evidence of Hib transmission through human milk, and human milk ingestion may actually prevent oropharyngeal infant Hib colonization.<sup>27</sup> If a breastfeeding woman has invasive Hib disease, then chemoprophylaxis is indicated for all household members, especially the incompletely or partially immunized infant.<sup>9</sup> Given that Hib is spread via respiratory droplets, the continuation of breastfeeding with careful masking and hand hygiene is appropriate.

### *Staphylococcus Species*

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*Staphylococcus aureus* is the most common etiology associated with soft tissue and musculoskeletal infections in children and colonizes up to half of all healthy children. Both methicillin-susceptible and methicillin-resistant *S aureus* are associated with health care-associated colonization and infection, with difficulty in eradication and treatment, especially with methicillin-resistant *S aureus*. Postnatal contact with family members, health care workers, and contaminated surfaces or equipment are the likely source of colonization and invasive infection in the health care setting.<sup>9</sup> *S aureus* is also one of the most common causes of mastitis in lactating women. Per the CDC recommendations, continued breastfeeding while being treated for staphylococcal mastitis is generally encouraged to promote drainage and infection resolution. Additionally, there are no data to support staphylococcal bacteria transmissibility via human milk. If, however, there is purulent drainage or open skin



lesions on the breast that are unable to be contained by covering, or the infant is premature or at risk for invasive infections, then expressing and discarding milk from affected breast is warranted while continuing to breastfeed from unaffected side.<sup>19</sup>

Coagulase-negative staphylococcal infection is a common cause of late-onset disease in premature, low birth weight infants who require invasive devices for monitoring or therapy, prolonged antibiotic use, and prolonged hospitalization. There is no evidence to support that a coagulase-negative staphylococcal infection is transmitted via human milk and, given the anti-infective properties of human milk, breastfeeding and expressed human milk are encouraged.

Group B *Streptococcus* (GBS; *Streptococcus agalactiae*) is transmitted primarily during delivery and remains the most common cause of neonatal early-onset sepsis despite intrapartum maternal prophylaxis significantly decreasing the early-onset disease burden. GBS infection is also a significant cause of neonatal late-onset sepsis. Although there is evidence that GBS can colonize human milk, it remains unclear if this is an infection source or a marker of heavier colonization load.<sup>28</sup> Routine culturing of the breast or human milk and therapy to eradicate colonization have not proven beneficial. Based on the available data, continuation of breast milk feedings should be encouraged owing to its anti-infective properties, although some investigators suggest that, in recurrent episodes of late-onset GBS disease in the preterm neonate, cessation of maternal breast milk feedings may be considered until the disease is resolved.<sup>29</sup>

### **Listeria**

*Listeria monocytogenes* is a food-borne illness, and infection during pregnancy infrequently results in stillbirth, premature delivery, or severe disease in the neonate through perinatal acquisition. No published information documents transmission of *L. monocytogenes* through human milk; thus, breastfeeding or the use of expressed breast milk from an infected individual is not contraindicated.

### **Chlamydia**

Chlamydial infection is the most frequent sexually transmitted disease in the United States. Perinatal infection acquired from passage through the birth canal of an infected woman results in neonatal conjunctivitis and pneumonitis. Specific secretory IgA has been identified in colostrum and breast milk, but there is no evidence for transmission through human milk.<sup>24</sup>

### **Gonorrhea**

*Neisseria gonorrhoea* is transmitted during passage through the birth canal and infrequently from postnatal contact with an infected person. Transmissions of *N. gonorrhoea* via human milk have not been documented. Breastfeeding can continue while an infected woman is treated with ceftriaxone.<sup>24</sup>

### **Tuberculosis**

Postnatal exposure through aerosolized droplets or droplet nuclei by a family member with active pulmonary TB is possible or, rarely, from a breastfeeding woman with TB mastitis. When a breastfeeding woman has active pulmonary disease, it is recommended to start isoniazid prophylaxis in her infant and separate until a minimum of 2 weeks of appropriate treatment and no longer contagious, per American Academy of Pediatrics and CDC recommendations.<sup>1,19</sup> There have been no documented cases of transmission of TB through breast milk other than with TB mastitis; thus, an infant can receive expressed milk during separation as long as there is no documented

TB mastitis and proper precautions in place (eg, mask and sterile equipment while pumping). With asymptomatic TB, separation of the infant is not indicated and breastfeeding can be continued.<sup>9</sup>

### ***Brucella Species***

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Mothers with untreated brucellosis should not breastfeed or provide expressed milk to their infants until their infection is eradicated.<sup>1,19,30</sup>

## **OTHER INFECTIONS**

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

### ***Lyme Disease***

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*Borrelia burgdorferi* is the spirochete that causes Lyme disease, a multisystem disease presenting in various stages, and is primarily arthropod-borne and -transmitted. Although *B burgdorferi* DNA has been reported in breast milk, there is no evidence for illness in the infant or transmission of the spirochete to the infant through breast milk.<sup>31</sup>

### ***Candidal Infections***

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*Candida* can readily colonize most infants without producing significant illness, but can also be associated with invasive disease in hospitalized neonates. Mucocutaneous candidal disease is the most common form of illness in infants, causing thrush and diaper rash. Invasive candidal infection occurs primarily in individuals with altered immunity or altered skin or mucosal barriers and after the use of broad-spectrum antibiotics. Transmission occurs through direct contact, including breastfeeding.<sup>24</sup> With either maternal candidal mastitis or neonatal oral candidiasis, the simultaneous treatment of both conditions may be considered. Nursing directly from the unaffected breast and milk expression from the affected side is generally advised, with continuation of expressed milk feedings in otherwise healthy neonates.

### ***Toxoplasmosis***

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*Toxoplasma gondii* is a protozoan associated with a congenital syndrome manifest by severe central nervous system and ocular sequelae. Postnatal neonatal infection is usually asymptomatic or can present as mild disease. *T gondii* has been transmitted through maternal milk in animal models, but this finding has not been demonstrated in human milk.<sup>32</sup> Breastfeeding and expressed human milk may be provided during maternal toxoplasmosis infection.

### ***Syphilis***

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*Treponema pallidum* is a spirochete that is generally contracted as a sexually transmitted disease and can cause multisystem disease in stages similar to Lyme disease. Postnatal infection may occur in the infant through contact with open lesions or secretions from an infected person. There is no evidence for transmission of *T pallidum* in human milk in the absence of breast or nipple lesions.<sup>24</sup> In the rare circumstance that syphilitic lesions involve the breast or nipples, then direct breastfeeding or providing milk expressed from the affected breast should be avoided until maternal treatment has been completed and the lesions have healed.

## Botulism

There is no evidence that *Clostridium botulinum*, its spores or its toxin can be transmitted through human milk; there may be a protective effect of human milk against the development of infant botulism.<sup>24</sup>

## EMERGING INFECTIONS: HUMAN MILK AND SEVERE ACUTE RESPIRATORY SYNDROME NOVEL CORONAVIRUS 2

Early in the SARS-CoV-2 pandemic, several studies from Wuhan, China, assessed the transmission of SARS-CoV-2 from nursing mothers to their infants. There were a few instances of transmission, although it is unclear if human milk and/or contact through breastfeeding was the source of positive viral tests.<sup>33,34</sup> As the pandemic progressed, more data have accumulated about the risk of human milk as a source of transmission.<sup>35</sup> A few case reports cite the detection of SARS-CoV-2 RNA in expressed human milk; however, the viability and transmissibility of detected virus were not described. In 1 study, samples of expressed milk from 1 of 2 mildly symptomatic women with confirmed SARS-CoV-2 had viral RNA detected on days 4 to 7 of illness, but this study did not test for viable virus.<sup>36</sup> In another report, viral RNA was detected from the expressed milk of a mildly symptomatic SARS-CoV-2–positive mother intermittently over 10 days, but viable virus was not demonstrated; her infant did test positive and was only mildly symptomatic with a cough.<sup>37</sup>

Forty-nine case reports or series published through June 2020 found that human milk-fed versus formula-fed infants acquired coronavirus disease 2019 (COVID-19) at similar rates (4.7% vs 5.3%).<sup>38</sup> A US study assessing donated human milk from 18 SARS-CoV-2–positive women, 17 of whom were symptomatic, found no detectable replication-competent virus from any human milk sample, including 1 sample from which viral RNA was detected.<sup>39</sup> This report supports the very low risk of clinically significant transmission of SARS-CoV-2 from mothers with COVID-19 to their infant via human milk.

Additionally, there is evidence to suggest that human milk can provide immune protection. A case report of a SARS-CoV-2 polymerase chain reaction–positive, mildly symptomatic mother with an unaffected breastfed newborn had both IgG to and IgA to SARS-CoV-2 detectable in her expressed milk.<sup>40</sup> A recent study of 15 human milk samples (8 SARS-CoV-2 polymerase chain reaction–positive and COVID-19-recovered donors; 7 untested but COVID-19–suspected donors) exhibited significant specific IgA reactivity to the full SARS-CoV-2 spike protein in all samples and a majority exhibited significant IgA, secretory Ab, IgG, and/or IgM binding to the receptor-binding domain.<sup>41</sup>

Although additional research is needed regarding the immune response to SARS-CoV-2 in human milk, the feeding of human milk should be encouraged, either via direct breastfeeding or via expressed human milk if direct breastfeeding is not possible. Standard infection prevention guidelines should be followed for handling and cleaning of pumping and the corresponding apparatus, containers of expressed milk, and storage.<sup>19</sup> There is no recommended postexposure prophylaxis or testing of a neonate who receives human milk from a COVID-19 positive woman, whether planned or accidental administration, because there is no evidence of transmissible viable virus in human milk.

## MATERNAL VACCINATION DURING LACTATION

Lactating nonpregnant women may be immunized similarly to other nonpregnant adults because there is no evidence to support the presence of live virus vaccine in human milk, with the exception of yellow fever vaccine. Lactation is a precaution for

yellow fever vaccine administration owing to 3 serious adverse events in breastfeeding neonates after recent yellow fever vaccination of their mothers. However, if travel to an endemic area is unavoidable or an outbreak occurs, a lactating woman should be vaccinated against yellow fever.<sup>9</sup>

Data are being accrued on the safety of mRNA COVID-19 vaccines in lactating women, the impact on milk production and excretion, and the effects on the breastfed infant. Recently, antibody transfer into the breastmilk of lactating women 1 week after initial dose of mRNA COVID-19 vaccination has been demonstrated suggesting the possibility of passive protection to the breastfed infant after maternal vaccination.<sup>42</sup> The mRNA vaccines are not presumed to be a risk to an infant receiving human milk per the CDC, the Society of Maternal-Fetal Medicine, and other national and international organizations.<sup>43,44</sup> Thus, COVID-19 vaccination of lactating women should not be delayed and human milk feeding should be continued.

### **SPECIAL CONSIDERATIONS: DONOR MILK**

Many NICUs provide donor human milk for infants in whom mother's own milk is unavailable or in low supply. Recent studies have demonstrated numerous benefits of providing donor milk as opposed to formula to preterm infants to prevent acute and long-term adverse events.<sup>45,46</sup> For this reason, the use of donor milk and the number of human milk banks worldwide are increasing. Most US hospitals procure pasteurized donor milk from nonprofit milk banks affiliated with the Human Milk Banking Association of North America or from several for-profit commercial milk banks. These milk banks have established strict policies for health screening and blood serologic testing of donor women (primarily for HIV, HTLV, syphilis, and hepatitis B and C) as well as for the safe collection, storage, shipping, handling, pooling, and pasteurization of milk.<sup>47,48</sup> Although it is still possible for donor milk to be contaminated with infectious agents, pasteurization is highly effective in rendering viruses and most bacteria inert.<sup>49</sup> Furthermore, bacteriologic screening is performed after pasteurization and those batches with abundant bacterial loads are discarded. There have been no reported cases of infant illness attributed to improper screening, handling or shipping by donor banks, although there was a report of 3 *Pseudomonas*-related deaths in preterm infants at a single NICU that were attributed to improper donor milk preparation at the receiving hospital.<sup>50</sup>

In contrast, informal direct milk sharing from other mothers or from the internet is not considered safe and, therefore, not recommended.<sup>19</sup> Owing to minimal oversight, the chances of contamination with organisms and other substances or intentional dilution for the purposes of monetary gain, informal direct human milk sharing is strongly discouraged.

### **BREAST MILK HANDLING CONSIDERATIONS**

The safe collection and proper storage of expressed human milk is invaluable to the health of the recipient infant. Whether from the biological mother or from human donors through an established human milk bank, hospitals with nurseries and those that provide care to infants and children must have processes in place for safe collection, handling, storage, and administration of human milk to infants.

When handling expressed milk in the health care setting, there are multiple opportunities for exposure to both pathogenic and nonpathogenic organisms. Once contaminated, human milk provides the substrate and environment supporting microbial growth. Infant feedings, both human milk and formula, have been linked to sepsis and necrotizing enterocolitis.<sup>51-53</sup> Therefore, it is imperative that proper hygiene and

sanitation of workspace and equipment, use of sterile additives, and maintaining appropriate storage conditions and administration techniques be applied with human milk and formula preparation and administration.

### **Hand Hygiene**

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Hand hygiene is by far the most important aspect of infection prevention in the NICU. Handwashing is recommended before and after handling or preparing an individual's milk, and immediately if visibly soiled. Handwashing is preferred over hand sanitizers because these are not as effective against spores, norovirus, and other select contaminants.<sup>54,55</sup> Compliance with proper handwashing should be monitored and re-education undertaken on a routine basis for all staff members handling milk. Gloves should be worn at appropriate times to prevent hand soiling, but owing to the possibility of contamination, donning gloves should not replace proper handwashing. Hospitals should use policies limiting artificial nails, long natural nails, chipped or cracked polish, and hand jewelry for all staff and families, because these items have been linked to gram-negative bacteria, staphylococcal species, and yeast outbreaks in NICUs.<sup>54</sup> Additionally, pumping mothers should be instructed on proper hand hygiene when expressing or handling their milk.<sup>19,55</sup>

### **Workplace and Equipment Considerations**

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Policies and staff education should be in place to ensure appropriate cleaning, sanitizing and/or sterilizing of milk handling areas and equipment needed for milk preparation.<sup>56</sup> Many health care facilities use the Hazard Analysis Critical Control Point principles to build their practices and policies. A separate work space for milk handling that is distinct from the patient care area (eg, mixing room or milk room) and dedicated, trained staff to handle human milk and milk mixing (eg, milk technicians) are essential.<sup>55</sup> The episodes that were attributed to the *Pseudomonas*-related deaths of 3 preterm infants were associated with contaminated equipment used in measuring human milk,<sup>50</sup> highlighting the extreme outcomes that can result from inadequate cleaning. Additionally, women expressing human milk should be instructed on the proper cleaning procedures for their pumping and collection supplies.

### **Human Milk Additives**

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Human milk is insufficient to support the optimal growth and bone health in the premature infant; thus, nutritional supplementation of expressed human milk with bovine- or human milk-derived additives.<sup>1</sup> The US Food and Drug Administration regulates the manufacturing, distribution, and recall of infant formulas and most human milk additives. Additives should be inspected visually for integrity (intact seal, undamaged container or package, normal-appearing product) and should not be used past the expiration date. They should be stored unopened and per manufacturer's recommendations, usually in a low humidity, room temperature-controlled area.<sup>57</sup>

Liquid formula additives and preparations are sterile; however, powdered additives and formulas are not leading to greater potential for contamination. Therefore, liquid formulations should preferably be used for at-risk populations per the CDC recommendations.<sup>57</sup> This recommendation followed a cluster of fatal *Cronobacter sakazakii* infections attributed to contaminated powdered formula.<sup>58</sup> Additionally, powdered fortifier has been shown to inactivate some of human milk's innate antibacterial activity.<sup>59</sup> Owing to the potential risk and the concern for underreporting, ready-to-feed human milk additives are preferred over powdered additives and formulations.

### ***Human Milk Storage and Administration***

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In general, expressed human milk and prepared human milk should be stored in glass or food-grade plastic containers with tight-fitting lids, or in plastic bags designed specifically for human milk storage. Each container should be labeled with the infant's full name, medical record number, the date and time of expression, and the inclusion of additives, if relevant. The temperatures of refrigerators and freezers used for human milk storage should be monitored with access only to clinical staff.<sup>55</sup> Freshly expressed human milk may be refrigerated at 4°C for up to 96 hours, or frozen for up to 6 months; thawed human milk must be kept refrigerated and administered within 24 hours.<sup>60</sup>

No more than a 24-hour supply should be prepared at one time, and prepared feedings should be dispensed in single-dose units to the clinical area.<sup>61</sup> Heating prepared human milk may impact the immunologic and nutritional components; thus, it is recommended to warm to no higher than body temperature using acceptable methods (warm water baths, heating units, or bead baths).<sup>48,61</sup> There is a suggested maximum 4-hour hang time for neonates receiving prepared human milk with recommended feeding tube changes.<sup>55</sup> Feeding tube colonization is possible, either from the feed itself or from retrograde reflux from the infant, and has been associated with feeding intolerance and necrotizing enterocolitis.<sup>53</sup> Transpyloric feeding tubes pose an additional risk because they bypass the protective acidic gastric secretions that can help to neutralize pathogenic organisms.<sup>53,55</sup>

### ***Human Milk Misadministration***

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Despite having established protocols in place, human milk misadministration events occur within the hospital setting with an incidence ranging from 1 error for every 10,000 feeding opportunities<sup>62</sup> to 0.7 errors per month in 1 NICU study conducted over a 10-year period.<sup>63</sup> Errors can occur for multiple reasons, including mislabeling and not following procedures to ensure appropriate human milk administration.

Infectious risks from a single misadministered feeding of human milk are very minimal. When evaluating risk, the gestational and chronologic age of the infant, and the health and infectious status of the donor woman (the woman whose human milk was inadvertently administered to the wrong infant) as well as the recipient woman (the woman whose infant received an incorrect human milk feeding), should be explored. The more common infectious agents that are transmissible via human milk with potential adverse health outcomes, as shown in **Table 2**, include HIV, hepatitis B and C viruses, and CMV.<sup>9</sup>

Although exposure to another woman's milk can cause a great deal of anxiety and may have a notable nonclinical impact (eg, lack of trust in care team), the infectious risk to the recipient infant is almost negligible.<sup>64</sup> As soon as the error is recognized, the feeding should be discontinued, and both families should be informed and reassured about the extremely low risk of pathogen transmission. Current CDC recommendations no longer require the donor or recipient mother to undergo serologic tests for HIV or hepatitis B and C,<sup>19</sup> although in high-risk situations this testing may be considered. The costs of any screening should be covered by the institution as part of the risk management and mitigation of error policy. Testing neonates is discouraged, because this practice does not address the theoretic transmission risk. Questions to ask donor mother are expression time and handling of the misadministered breast milk, including the presence of cracked or bleeding nipples, and willingness to share recent infectious disease history and medication use with the other family and the care team. A discussion with the family of the recipient infant should

include reassurance of the minimal risk of infectious disease transmission, information about the misadministered milk, and pertinent medical information that the donor mother is willing to share.<sup>19</sup> To the extent feasible, the confidentiality of both mothers must be maintained. Ongoing psychosocial support for the families and staff should be offered, and discussions with the families should be documented per each institution's policy.

### ***Prevention of Future Errors and Exposures***

Many human process errors can be the cause of human milk misadministration in the hospital setting. These often involve the misidentification or mislabeling of the bottle, but occasionally a mother is misidentified. A recent report describes an infant being given to the wrong mother for direct breastfeeding.<sup>65</sup> A study found that more than 75% of human milk misadministration errors happened during evening and night shifts.<sup>66</sup> Other types of errors with human milk misadministration are rare but potentially more serious, such as mistaken intravenous administration of human milk.<sup>67</sup>

A root cause analysis should be pursued in all cases so that measures can be implemented to prevent future occurrences. A review of current policies and procedures, along with re-education of staff is warranted. Potential causal factors, including but not limited to overcrowding, increased patient to staff ratios, and nonadherence to the verification of identity, should be addressed. Large nursery services have determined that hiring human milk technicians to assist with storage, labeling, handling, fortifying, and dispensing expressed human breast milk is cost effective, because it decreases errors, improves quality, and enhances family satisfaction.<sup>68</sup> Point-of-care human milk bar code scanners as check point systems have been implemented in many facilities to prevent misadministration. Bar-coded labels are given to mothers to label their expressed milk bottles for storage and, at the time of feeding, the milk and the designated neonate's identity band should be scanned.<sup>69</sup> Human milk administration errors are preventable and may be addressed by reinforcing the understanding that expressed human milk is a biological product and although the clinical consequences of misadministration are minimal, the psychosocial impact is tremendous.

### **SUMMARY**

Owing to the many advantages of human milk, including its anti-infective and immunologic properties, human milk feeding should be encouraged and supported, except in rare circumstances. Noninfectious contraindications to human milk feeding include active maternal illicit substance abuse, certain maternal medications, and infant galactosemia. Infectious contraindications to direct or expressed human milk feeding include maternal infection with HIV, HTLV, Ebola virus, untreated brucellosis, and active breast lesions (eg, HSV, TB mastitis) from the affected side only. The safety of human milk through the prevention of contamination and misadministration should be reinforced by policies and practices that support the perception that human milk is a biological fluid. In instances where human milk feeding is not indicated, counseling of the family and offering safe feeding alternatives should be undertaken.

### **CLINICS CARE POINTS**

- Human milk should be promoted as the ideal source of nutrition for all infants due to its multitude of benefits, which include its many anti-infective and immunologic properties that help improve overall health. Mother's own milk is superior to donor milk or formula, especially for the vulnerable preterm population.



- There are rare instances when breast milk feedings should be withheld. Infectious-related contraindications are maternal HIV, HTLV, viral hemorrhagic fevers, and untreated brucellosis; avoidance of milk from affected breast is recommended with certain active breast lesions (eg, HSV, TB mastitis) and cracked/bleeding nipples with Hepatitis C. The CDC and AAP Red Book, as well as peer-reviewed research, are quality resources to help guide clinicians in these situations.
- Contamination and misadministration of human milk is possible in the hospital setting which can put infants at risk. Evidence-based practices and policies regarding the safe handling of human milk should be in place to minimize these occurrences.
- In the vast majority of cases, the benefits of mother's milk feeding far outweigh any potential yet rare risks of infectious illness passed to an infant through breastfeeding. Support for lactating mothers should be optimized to help initiate and maintain supply.

### Best practices

*What is the current practice for human milk feeding and infection prevention?*

Best Practice/Guideline/Care Path Objective(s)

Human milk feedings should be promoted for all infants due its multitude of benefits, with consideration for the rare yet possible occurrence of contamination through certain maternal infections or milk mishandling. Practices and policies should be in place to minimize these potential risks to help maintain human milk's natural anti-infective properties.

*What changes in current practice are likely to improve outcomes?*

There have been no major advances in this area other than building evidence of the natural immunologic benefits of mother's own milk. Centers that support safe administration of human milk feeding are likely to have improved neonatal outcomes.

Is there a Clinical Algorithm? If so, please include [either create your own, use from article or search from an Elsevier application] See Table 2 for pathogens associated with human milk transmission.

*Major Recommendations*

Promotion of the safe administration of mother's own milk to all infants and avoidance of human milk in only rare, evidence-based situations where risks outweigh benefits

*Rating for the Strength of the Evidence*

Moderate

*Bibliographic Source(s): This is important list current sources relevant to evidence*

Reference numbers: <sup>1,19</sup>

## DISCLOSURE

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