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APPLICATIONS

Fortified Breast Milk Safety

Breast milk is not a sterile product. It contains bacteria commonly found in the environment and on the mothers' and even fathers' breast, nose, and skin. Some of these bacteria reflect the environment in which the mother lives. For example, in a Finnish study, bacteria such as *Staphylococcus epidermidis*, *Streptococcus salivarius*, and *Streptococcal mitis* were found in 30% to 60% of the milk samples. Spanish mothers produced milk with probiotic lactic acid bacteria such as *Lactobacillus gasseri* and *Enterococcus faecium*. In Swedish infants, *Staphylococcus aureus* has been found in 73% of the infants by 2 to 6 months of age, but no symptoms were reported. Human immunodeficiency virus-1 is present in both the milk cells and the fluid phase of breast milk of infected mothers. Other viral pathogens found in the breast milk of infected mothers include cytomegalovirus; hepatitis A, B, and C; rubella; and human T-cell leukemia virus (1).

Other substances in the milk provide protection to the infant. These include lysozyme, secretory immunoglobulin A (IgA), and lactoferrin. Lysozyme is a glycosidase that works with lactoferrin to lyse cell walls and destroy bacteria, especially gram-positive types (2). Secretory IgA is the major antibody in human milk and protects mucosal surfaces, especially in the respiratory and gastrointestinal tract. Lactoferrin has many functions, sometimes acting alone and other times supporting bacteriostatic processes as it does with lysozyme (1). Most frequently, the iron-binding function of lactoferrin is reported to make iron unavailable to iron-requiring bacteria. Lactoferrin has also been reported to cause direct damage to gram-negative bacteria by attacking the outer membrane. It has an additional benefit of providing immune protection without initiating the inflammatory process. It is also known to inhibit several cytokines, including tumor necrosis factor-α and interleukin-1β (3). Lactoferrin also prevents bacterial adhesion and invasion of target host cells. It has both antifungal and antiviral activity and prevents biofilm development (4). There are less-studied components of human milk that also inhibit bacterial growth and immunostimulatory functions. These include κ-casein, lactoperoxidase, haptocirrin, and α-lactalbumin (5).

Although human milk supports normal growth in full-term infants, additional protein and minerals are needed to support preterm growth. Currently, several powdered fortifiers and one liquid fortifier are manufactured. The powdered fortifiers are not sterile and may interfere with the above bacteriostatic properties of breast milk. The liquid fortifier adds extra volume and decreases the amount of breast milk provided to the infant. As reported by Telang and colleagues (6), studies have shown changes in the antimicrobial properties of human milk as a result of the addition of fortifiers. Most of the research has focused on the effect of lysozyme and secretory IgA along with clinical outcomes. A review article by Hawthorne and Abrams on the safety of human milk fortification for very-low-birth-weight infants concludes that current studies support the efficacy and safety of human milk fortification of very-low-birth-weight infants (7). The American Academy of Pediatrics also supports fortification of expressed human milk for many very-low-birth-weight infants (8).

In an institutional setting, there are complicating factors that put infants at risk due to fortification. Contamination of milk can occur at many points before it reaches the infant. These include pumping, storage, transportation, thawing, preparation of the fortifier, and its addition to the milk, along with the setup of the feeding system (9). Once the milk is provided to the infant, the environment, including temperature and time, contribute to the safety of the milk. The Academy of Breastfeeding Medicine provides guidelines for human milk storage, but this is for healthy, full-term infants (10). The storage guidelines suggest that refrigerated fresh breast milk may be stored

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for 5 days. Caution needs to be exercised when dealing with preterm infants.

The study by Telang and colleagues (6) on the growth of *Enterobacter sakazakii* with higher and lower iron-fortified powder provides additional information for the dietetics professional on the safety of fortifiers in the preterm population. It supports the current guidelines of a 4-hour hang time and suggests that even longer may be safe. It also supports the hypothesis that adding iron at the level of 1.44 mg iron/14 kcal does not increase bacterial growth. This study, however, is specific to *Enterobacter sakazakii* and aerobic bacteria that were in this sample. It does not suggest that all bacterial colonies will not be affected by the addition of iron or the length of time at 37°C tested in this study.

There are questions that still remain. What dose of a fortifier affects bacteria growth the most? For example, rather than adding four packets to an infant's human milk feeding, might it be prudent to add only one at a time, wait for a period of time, and then add another? Should fortifiers be added only at the time of the feed, or is it safe to prepare 24 hours of fortified breast milk? Some have suggested that unfortified feeds should be alternated with fortified feeds to allow the bacteriostatic properties of breast milk free reign without the addition of a fortifier (2). Other considerations, including the type of protein used in the fortifier, need to be investigated. Cow's milk protein can initiate an immune response in some infants, especially those with an immature gut, so alternative proteins need to be researched. Quan reported that soy-based formula fortifier did not prevent inhibition of bacteria growth whereas a cow's milk formula additive did prevent inhibition of bacteria (2). The research procedures on the thawing of frozen milk are not standardized, nor is the research done with home refrigerator-freezers. In a preterm population, mothers frequently pump at home due to their infant's long-term hospital stay. This means that milk is frozen and then thawed at the hospital. This adds another opportunity for contamination. The storage of frozen milk in frost-free freezers results in a partial thawing and refreezing to promote the prevention of ice in the freezer. Can this affect the ability of the bacteriostatic compounds to curb bacterial growth? Studies on the use of frozen, thawed milk are necessary using standardized freezing and thawing procedures. Besides measuring lysozyme and secretory IgA activity, it seems that lactoferrin activity is important because of its complementary roles in supporting antibacterial, antiviral, and antifungal activity. Previously listed proteins also need to be studied. Human milk is a complex substance that changes with the stage and length of lactation. Fortification is necessary for preterm infants, and studies such as that by Telang and colleagues provide more information as to its safety. This topic will need further research to give clinicians tools to best provide fortified breast milk safely in an institutional setting.

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