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Breast Milk: A Psychoneuroimmunologic Perspective for Mother-Infant Dyads

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ABSTRACT

What's so miraculous about human breast milk (HBM)? Human milk has evolved into an individualized synergist nutritional system that contains elements to protect and support the mother as well as the baby. The evidence is in the details that will be showcased herein to describe the specialized components in HBM that make it a superior nutrition for all babies, including vulnerable infants admitted to the neonatal intensive care unit (NICU). Using a psychoneuroimmunologic perspective on HBM, this review describes the endocrine, immunomodulatory and psychoneurologic benefits to infants and mothers.

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Introduction

What's so miraculous about human breast milk (HBM)? Breast milk feeding provides the mother-infant dyad with a uniquely designed reciprocal synergist nutritional system to balance stress, infection, and healthy development. For infants admitted to the neonatal intensive care unit (NICU), mounting evidence suggests that providing mother's HBM offers powerful benefits to prevent short and long term morbidities commonly seen in this vulnerable population.[1] Psychoneuroimmunology (PNI) is the integrative field that combines three systems (e.g. psychoneurologic, immune, and endocrine). This review was conducted using a PNI lens to examine evidence on the interrelated ability of HBM to provide endocrine, immunomodulatory and psychoneurologic benefits to mother-infant dyads to influence biophysiologic stress, immunity, neurobehavior and improve health outcomes.

Based on findings of many randomized controlled trials (RCTs) citing HBM benefits, the American Academy of Pediatrics (AAP) recommends HBM over synthetic formulas for all healthy and high risk infants (e.g. preterms, very low birth weight (VLBW), extremely low birth weight (ELBW) or infants with complex health needs).[2] Over two decades of evidence supports that HBM decreases several common morbidities seen in babies in NICU (i.e., enteral feeding intolerance, nosocomial infection, necrotizing enterocolitis (NEC), chronic lung disease (CLD), retinopathy of prematurity (ROP) and long term developmental and neurocognitive delay).[3–8]

In 2011, the Surgeon General's Call to Action requested that healthcare professionals be better prepared to understand and promote the benefits of mother and donor HBM to support all mother/infant dyads.[9] In addition, it is recommended that evidenced-based guidelines be established for healthcare professionals to better recognize the vulnerable infants most likely to benefit from exclusive HBM, including donor HBM and/or pasteurized donor milk fortifiers.

Donor HBM is donated by nursing mothers to human milk banks. There are nearly a dozen human milk banks across North American working within the guidelines established by the Food and Drug Administration and the Centers for Disease Control to screen, collect and dispense human milk by prescription. Many infants in NICU may benefit the most from the unique properties of HBM. Some parents of these babies have health conditions that prevent them from being able to breastfeed. Other mothers ready to breastfeed may receive conflicting professional advice that ultimately leads to increased stress and decreased HBM production and duration.[10]

Breast milk provides a superior form of natural nutrition for all infants (e.g. proteins, fats and protective immune and endocrine properties). To this end, this article serves to provide the nurse with a broad overview of a variety of evidence that highlights HBM's nutritional, immunologic, and stress benefits. The goal herein is for nurses to be better prepared to comprehend and share their knowledge about HBM's psychoneuroimmunologic and nutritional benefits to improve clinical practice for mother/infant dyads and their families.

HBM's Protective Immune Molecules

HBM can protect the infant against dangerous bacteria and viruses in several ways. A variety of components in HBM are able to destroy disease-producing cells and fight infection. HBM molecules can weaken or decrease the pathogen's ability to multiple, aid pathogen removal, or directly or indirectly attack the pathogen. For example, the oligosaccharides (i.e., simple sugars) found in HBM can attach to mucosal surfaces to intercept bacteria by forming harmless complexes which are excreted by the baby.[11] Additionally HBM contains a protein, lactoferrin, which can bind to iron making it unavailable to pathogenic bacteria that thrive on it.[11] Lactoferrin also helps decrease pathogenic organisms (i.e., *Staphylococcus aureus*) that cause illness

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and limit bacterial growth by interfering with their ability to digest carbohydrates.[11,12] Free fatty acids found in HBM can wage war on viral membranes (i.e., chicken pox). Mucins in HBM, derived from protein and carbohydrate, adhere to bacteria and viruses to remove them from the body.[12] In a similar way, the B12 binding protein in HBM is capable of weakening microorganisms by depriving them of vitamin B12.[11,12] Bifidus factor is one of the oldest known disease-resistance factors in HBM which promotes healthy growth of *Lactobacillus bifidus*, considered very beneficial to the gut.[11,12]

HBM is superior nutrition as it not only protects the infant against infection but helps the infant's body protect itself. HBM is rich in antibodies also known as immunoglobulins (e.g. IgG, IgA, IgM, IgD, and IgE), of which IgA is the most plentiful. The combination of two joined IgA molecules and a secretory component (SIgA) seems to protect the antibody molecules from being degraded by gastric acid and digestive enzymes.[11,12]

Secretory IgA (SIgA)

In many mammals, the infant is born with a very limited ability to produce immunoglobins and is extremely dependent upon the acquired passive immunity in-utero from the mother and later from the secretory immunity in breast milk feeds.[13] Formula fed infants are less prepared to fight ingested pathogens until up to several months beyond birth when they finally initiate production of their own secretory IgA.[13] However, the SIgA differs between HBM fed infants and formula fed in several ways. First, HBM provides specific antibodies unique to each mother/infant dyad because each mother synthesizes antibodies in her individual environment that are specific to the disease-causing agents she is exposed to via ingestion, inhalation or contact.[13] These specific antibodies will bind to a single protein, or antigen, on the specific disease-causing agent. Because the mother's antibodies are pathogen specific to organisms that she was exposed to, the baby gains special antibody protection that is highly targeted to the surroundings the baby will typically be in early in life.[13] Second, these HBM antibodies support "good bacteria" (i.e., normal flora) in a baby's gut which crowd out potential harmful organisms.[13] Third, secretory IgA molecules in HBM ward off disease without causing inflammation that increases risk for severe harm to the delicate mucosal membranes in the GI system and elsewhere.[13]

Colostrum

Mature HBM differs from colostrum which contains higher concentrations of secretory IgA, growth factors, lactoferrin, anti-inflammatory cytokines, oligosaccharides, soluable CD14, antioxidants and other protective factors (i.e., leukocytes). Interferon, most particularly seen in mother's first milk, has additional antiviral protection.[11,12] Also abundant in colostrum, fibronectin aggravates certain phagocytes into ingesting microbes tagged and untagged antibodies and similar to SIgA diminishes inflammation but also helps repair of tissue damaged by inflammation.[12]

HBM's Protective Immune Cells

HBM is armed with white blood cells (lymphocytes, macrophages, neutrophils, leukocytes). Predominantly these are neutrophils which are interesting as they can either support phagocytes in the infant's gut or protect the mother's breast, but by 6 weeks post birth these neutrophils disappear.[12] Leukocytes activate other defense mechanisms such as macrophages to fight infections and manufacture lysozyme, a bacteria destroying enzyme.[1,12] In the digestive tract, lysozymes call lymphocytes into action. B lymphocytes give rise to antibodies and T lymphocytes directly or indirectly destroy infected cells.[12] Milk lymphocytes, unlike blood lymphocytes, can proliferate in the presence of *Escherichia coli* bacteria, but are less responsive to less threatening germs.[12] Milk lymphocytes can also produce several chemicals (e.g. gamma-interferon, migration inhibition factor and monocyte chemotactic factor) to strengthen an infant's immune response.[12]

Of interest, a fascinating new study identified that HBM leukocytes increased rapidly in number during the course of breastfeeding in response to maternal and infant infection then returned to normal levels when the infection was over.[14] Researchers report that the rise in HBM leukocytes occurred even if the baby had an infection and the mother was asymptomatic.[14]

In essence these new findings align with the PNI model as their research shows a natural synchrony between HBM and the mother/infant dyad that supports both the maternal and infant health while boosting the maturation of the baby's immune system.

HBM and Detected Hormones

Certain endocrine hormones have been described in human breast milk (i.e., cortisol and smaller bio-active milk proteins (i.e., epidermal growth factor, nerve growth factor, insulin like growth factor (IGF-1) and somatomedin C).[12] These act to close up the leaky mucosal linings making it nearly impermeable to unwanted pathogens and other potentially harmful agents.[12] However some other hormones detected in HBM (i.e., leptin, adiponectin, resistin, and ghrelin) reportedly play a complex role in regulating glucose metabolism that scientists conclude may be involved in growth regulation in early infancy and possibly influence development of energy balance later in childhood or adulthood.[15,16]

Also some unknown compounds in HBM stimulate the baby's own production of secretory IgA, lactoferrin and lysozyme and these are found in larger amounts in the urine of HBM fed babies than formula fed babies who cannot absorb these in their gut. Some believe these molecules are produced in the urinary tract to prevent local infections to breastfed babies.[12]

HBM and Necrotizing Enterocolitis (NEC)

In term infants, prior to birth, the gastrointestinal tract function matures to digest HBM and withstand bacterial invasion through production of mucins, defensins and normal cell proliferation, restitution and homeostatis.[17] The normal colonization of the newborn gut can be affected by several factors (e.g. delivery mode, gestational age, NICU admission, antibiotics, opioids, nasogastric tubes, and formula instead of HBM).[18] While inflammatory gut reactions are common in newborn infants, a severe form known as NEC has a high mortality risk in compromised NICU infants (e.g. very preterm, LBW, or those with poor gut perfusion).[17,19,20] Primary risk factors for NEC are prematurity, bacterial colonization, enteral feeds and altered intestinal blood flow.[20]

Walker and Claud hypothesized that NEC is a result of enteral feeds causing pathogenic bacterial colonization in a susceptible immature gut causing mucosal damage that culminates in an exaggerated inflammatory response.[21] More specifically, potential causative factors include reduced peristalisis, impaired epithelial barrier function, gut immaturity, leaky mucosal barriers, dys-colonization, bacterial translocation, reduced mesenteric perfusion and excessive milk feeding.[21] The gut's bacterial colonization and function can be altered by synthetic formula feeds compared to HBM feeds (mother or donor milk).[22] HBM exits the stomach faster,[23] induces lactase activity,[24] provides mucosal immunity,[25] and reduces intestinal permeability faster.[26] In addition, HBM contains multiple factors to stimulate growth, motility, and gut maturation.[27] HBM's protein composition contains a more supportive balance of total proteins, caseins, whey, and growth factors (enzymes, milk fat globule membrane proteins). The unique composition of HBM offers immunologic and anti-inflammatory defense against harmful pro-