Breastfeeding: More Than Just Good Nutrition

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Author Disclosure Drs Lawrence and Lawrence have disclosed no financial relationships relevant to this article. This commentary does not contain a discussion of an unapproved/ investigative use of a commercial product/device.

Objectives After completing this article, readers should be able to:

- 1. Discuss the nutritional benefits of breastfeeding and its effects on growth and development.
- 2. Delineate the advantages to the baby of breastfeeding.
- 3. Describe the benefits to the mother of breastfeeding.
- 4. Explain the role that breastfeeding plays in the bonding process.
- 5. List the differences in composition of human milk, colostrum, cow milk, and formula.
- 6. Describe the effects of maternal infection and medication on human milk and infant health.
- 7. List the few contraindications to breastfeeding.
- 8. Review the use of human milk in feeding preterm babies.
- 9. Discuss current recommendations for breastfeeding, including the role of hospitals in promoting the practice.

Introduction

Over the past 50 to 60 years, human milk has been described and recognized as the best first food for human infants; breast is best! Human milk provides substantial nutritional, cognitive, emotional, and immunologic benefits for the infant. Such ongoing acclamation is based on the observations and experiences of mothers, families, midwives, doulas, nutritionists, nurses, physicians, and scientists.

Abbreviations

AAP:	American Academy of Pediatrics
AHRQ:	Agency for Healthcare Research and Quality
ARV:	antiretroviral
BFHI:	Baby Friendly Hospital Initiative
CI:	confidence interval
CMV:	cytomegalovirus
DHA:	docosahexaenoic acid
FFA:	free fatty acid
GBS:	group B Streptococcus
GI:	gastrointestinal
HIV:	human immunodeficiency virus
HTLV:	human T-lymphotrophic virus
lg:	immunoglobulin
NEC:	necrotizing enterocolitis
RID:	relative infant dose
TB:	tuberculosis
TH:	T-helper cell
WHO:	World Health Organization
WNV:	West Nile virus

Over the past 30 years, scientific study and research have accumulated and now constitute a large body of evidence documenting the actual benefits of breastfeeding for the infant and the mother. This article examines and references much of this evidence-based data in describing human milk and how it contributes to the health and well-being of infants and mothers.

Current Evidence: Health Benefits of Breastfeeding

The Agency for Healthcare Research and Quality (AHRQ) Report on Breastfeeding in Developed Countries summarizes evidence (published in English through May 2006) on breastfeeding in maternal and infant health. (1) More than 9,000 abstracts were considered, and data from more than 400 individual studies were included after evidence-based review of meta-analyses, updated systematic review of the data, and newly performed systematic reviews. It is important to emphasize that this report included data from developed countries only. Table 1 presents definitions of breastfeeding that are particularly useful in "quantification" as standard definitions used in clinical studies.

Nineteen specific outcomes were reviewed by the AHRQ

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Table 1. Breastfeeding Definitions

Any Breastfeeding

• Full Breastfeeding

Exclusive: Human milk only; no other nutrients, supplements, or liquids
 Almost Exclusive: No milk other than human milk; minimal amounts of other substances provided infrequently

Partial Breastfeeding

- -High Partial: Nearly all feedings are human milk (≥80%)
- -Medium Partial: A moderate amount of feedings are human milk in combination with other nutrient foods and nonhuman milk (20% to 80% of nutritional intake is human milk)
- Low Partial: Very few feedings are human milk (<20% of nutritional intake)
 Token: Breastfeeding is primarily for comfort (minimal % of total nutritional intake)

Never Breastfed

• Infant has never ingested any human milk

Modified from Lawrence RM, Pane CA. Human breast milk: current concepts of immunology and infectious diseases. *Pediatr Adolesc Health Care*. 2007;37:1-44.

research team, including 13 for term infants and six for mothers. The outcomes for infants were: incidence of acute otitis media, atopic dermatitis, gastrointestinal (GI) infections, lower respiratory tract infections, asthma, obesity, type 1 and 2 diabetes, childhood leukemia, infant mortality, and sudden infant death syndrome as well as cognitive development and the risk of cardiovascular disease. Factors studied in mothers were: return to prepregnancy weight and incidence of type 2 diabetes, osteoporosis, postpartum depression, breast cancer, and ovarian cancer.

For infants, the meta-analyses or systematic reviews strongly favored breastfeeding over not breastfeeding for a reduced risk of acute otitis media, GI infections, asthma (regardless of whether there was a family history of asthma), type 2 diabetes, leukemia, and sudden infant death syndrome. The meta-analysis of GI infections reported a crude odds ratio for 14 cohort studies of 0.36 (95% confidence interval [CI]

0.32 to 0.41) strongly favoring breastfeeding (ever) in reducing the risk of GI infection in infants younger than 1 year of age (Fig. 1). Another analysis reported on two case-control studies demonstrating a summary odds ratio of 0.54 (95% CI 0.36 to 0.80)



Figure 1. The relationship between breastfeeding (BF) and infant outcomes: metaanalysis (MA) results. adjOR=adjusted odds ratio, AOM=acute otitis media, DM=diabetes mellitus, FH=family history, GI=gastrointestinal, LRTI=lower respiratory tract infection, OR=odds ratio, SIDS=sudden infant death syndrome. Adapted with permission from Figure 4 in lp S, Chung M, Raman G, et al. A summary of the Agency for Healthcare Research and Quality's Evidence Report on Breastfeeding in Developed Countries. *Breastfeed Med.* 2009;4:S17–S30, published by Mary Ann Liebert, Inc., New Rochelle, NY.

again favoring breastfeeding. A separate analysis demonstrated that infants breastfeeding exclusively for greater than 3 months' or greater than 6 months' duration had significant reductions in the risk of acute otitis media compared with infants who were never breastfed. The analysis of infants developing atopic dermatitis (who had a family history of atopic disease) demonstrated that the risk for atopic dermatitis was lower in infants breastfed exclusively for longer than 3 months compared with children who were breastfed for less than 3 months. An analysis examining lower respiratory tract infections showed an overall reduced risk of hospitalization due to lower respiratory tract infections in infants (<1 year of age) who were breastfed exclusively for 4 months or longer compared with infants who were never breastfed (Fig. 1).



Figure 2. The relationship between breastfeeding (BF) and maternal outcomes: Metaanalysis (MA) results. adjOR=adjusted odds ratio. OR=odds ratio. Adapted with permission from Figures 2 and 3 in Ip S, Chung M, Raman G et al. A summary of the Agency for Healthcare Research and Quality's Evidence Report on Breastfeeding in Developed Countries. *Breastfeed Med.* 2009;4:S17–S30, published by Mary Ann Liebert, Inc., New Rochelle, NY.

The report presented two meta-analyses and a systematic review demonstrating a reduced risk of breast cancer associated with breastfeeding primarily in premenopausal women. One meta-analysis that included 45 studies showed a 4.3% reduction in risk for each year of breastfeeding. A second meta-analysis that included 23 studies demonstrated a 28% reduced risk of breast cancer for 12 months or more of breastfeeding. The AHRQ team performed a meta-analysis of 9 "fair" quality studies that included 4,387 cases of ovarian cancer and more than 10,000 controls. This new meta-analysis showed an association between breastfeeding and a reduced risk of ovarian cancer. Cumulative lifetime breastfeeding duration of more than 12 months was associated significantly with a decreased risk of ovarian cancer compared with never breastfeeding. This benefit was not seen for cumulative duration of breastfeeding of less than 12 months (Fig. 2). Additional data are needed to confirm a dose-response relationship between breastfeeding and a reduced risk of ovarian cancer.

The analysis for type 2 diabetes, involving two very large cohort studies, showed that breastfeeding was associated with a reduced risk of developing type 2 diabetes in women who did not have a history of gestational diabetes. Each additional year of lifelong breastfeeding was associated with a 4% to 12% risk reduction in the two different cohorts. Breastfeeding did not appear to lead to a reduced risk of developing type 2 diabetes in women who had gestational diabetes. The studies on return to prepregnancy weight, osteoporosis, and postpartum depression were unable to demonstrate an association between breastfeeding and these specific maternal health outcomes due to methodologic issues and the effect of other contributing factors or confounders.

These high-quality, evidencebased data from the AHRQ Report support breastfeeding as providing significant health benefits to both the mother and infant, even in developed countries. A larger body of evidence from developing countries examines the benefits of breastfeeding in locales where the risk of infection in infants and children is high due to poor sanitation, low water quality, contaminated food sources, and other variables. This benefit is well documented for diarrheal disease, respiratory infections, and otitis media.

Beyond the evidence-based he realm of attachment and bond-

medicine measures is the realm of attachment and bonding between infant and mother and the psychological and developmental benefits of breastfeeding for the mother and infant. How these spheres are influenced by breastfeeding has been studied extensively in many different countries and cultures. Close and frequent contact between the mother and infant, especially skin-to-skin contact, affects the mother's attachment to the infant positively. The positive feelings affected by the close (skin-to-skin) and frequent early contact facilitate successful breastfeeding, longer duration of breastfeeding, and more attachment behavior (fondling, kissing, and caressing the infant). Recognition of these effects has led to more direct contact between the infant and his or her parents in the delivery and postpartum areas. Such recognition has supported the recommendation to allow placement of the infant in direct skin-to-skin contact with the mother in the first hour after birth to encourage successful breastfeeding. The multiple contributory factors to infant development makes it difficult to demonstrate a causative connection between early skin-to-skin contact or breastfeeding and overall infant and child development, emotional stability, personality, attachment, or person-to-person interactions.

Breastfeeding to Avoid Allergy

The impact of different methods of feeding infants on the onset of allergy has been researched. A meta-analysis of 18 prospective studies involving term infants who had a family history of atopy found a reduction of 42% (95% CI, 8% to 59%) in the risk of atopic dermatitis for infants breastfed for at least 3 months compared with those who were breastfed for less than 3 months. (1)

Studies on asthma were less definitive. The AHRQ

Component	Human Milk	Similac [®] /Enfamil [®] Formulas	Cow Milk
Calories (kcal/L)	747	700	701
Protein (g/100 mL)	1.1	1.5	2.8
Casein	3.7		25.0
Taurine (mM/100 mL)	25 to 30	Added artificially	<1.0
Phenylalanine (mg/100 mL)	48	390 mM/100 mL	172
Tyrosine	61		179
Fat (g/1,000 mL)	4.5	2.6	4.4
Cholesterol (mg/L)	139	0	120
Carbohydrate (g/1,000 mL)	6.8	7.2	4.7
Minerals ash (weight %)	0.2	0.33	0.7
Calcium (mg/dL)	34	55	118
Phosphorus (mg/dL)	14	44	93
Calcium/phosphorus ratio	2.4:1	1.2:1	1.3:1
Sodium (g/L)	0.512 (7 mL Eq/L)	1.1 (6 mL Eq/L)	0.768 g/L
Vitamin D	4 to 40 IU/L	400 IU	47 to 100 IU
Vitamin K	0.9 to 6.9 mg/L	4 mg/100 kcal	19 mg/L

Table 2. Comparison of Human Milk, Cow Milk, and Infant Formula

Similac® is a product of Abbot Laboratories, North Chicago, IL, Enfamil® is a product of Mead Johnson & Co, Evansville, IN. Data from American Academy of Pediatrics. *Pediatric Nutrition Handbook*. 6th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2009; Walker WA, Watkins JB. *Nutrition in Pediatrics*. Boston, MA: Little, Brown and Co; 1985; and Jensen RG. *Handbook of Milk Composition*. New York, NY: Academic Press; 1995.

reported that breastfeeding for at least 3 months was calculated to provide a 27% (95% CI, 8% to 41%) reduction in the risk of asthma in children who had no family history of asthma compared with children who were not breastfed. Children who had a family history of asthma had a 40% risk (95% CI, 18% to 57%) reduction in the occurrence of asthma before 10 years of age if breastfed for 3 months compared with those not breastfed. The risk for children older than 10 years is less clear. Exclusive breastfeeding for the first 6 months is recommended by the American Academy of Pediatrics (AAP) for many reasons, including reducing the risk of allergy. Further if supplementation is necessary, an amino acid-based formula is recommended (hypoallergenic formula).

Physiologic Consequences of the Differences between Colostrum and Mature Milk

The milk available in the breast after 16 weeks' gestation is called prepartum milk. When the infant delivers and is placed at the breast (or is allowed to find his or her way) to suckle, the milk is colostrum for the next few days. A gradual change from this transition milk to mature milk usually occurs by 14 days. Postpartum colostrum is called "the first immunization" because it contains high concentrations of antibodies and other infectionprotective elements, including cells. Colostrum is high in total protein, low in carbohydrate, and lower in fat than mature milk. The amount of milk produced in the first 24 hours after birth is approximately 50 g, with 190 g produced by the second 24 hours, 400 g by the third 24 hours, and 1,100 g/24 hours by the fourteenth day (800 to 1,000 mL). Human milk and cow milk differ substantially in their composition (Table 2). The proteins differ in quality and quantity. In its unaltered form, cow milk contains too much protein, too much casein, too much sodium, and too much phosphorus and has too high a solute load for a human infant. Formulas have been designed to improve these issues. Cow milk does not contain any taurine, an amino acid that has high concentrations in human milk and is essential to infant brain growth. The profile of amino acids in cow milk differs significantly from human milk, especially phenylalanine and tyrosine, which are at high concentrations in cow milk and formula and contribute to problems in phenylketonuria.

The effect of higher protein in infant formula recently has been questioned by investigators of the obesity epidemic. It has been suggested that a constant intake of high protein in infancy stimulates the metabolic rate and contributes to the long-term obesity of formula-fed infants. After processing, cow milk and infant formulas contain no cells, no enzymes, and no antibodies or other active protective agents and do not support the maintenance of physiologic flora of the infant's GI tract.

Docosahexaenoic acid (DHA) has received considerable attention because studies in preterm infants have demonstrated improved visual acuity and auditory acuity in those fed human milk compared with those fed regular preterm formula. When DHA was added to formula, the acuity improved but did not reach the scores achieved by breastfed infants. DHA and omega-3 fatty acids derived from bacterial culture are added to many formulas, although a benefit has not been proven.

Vitamin concentrations in human and cow milk are comparable, except for vitamin C, which is significantly higher in human milk (100 mg/d). Vitamins in infant formula exceed the concentrations found naturally. Vitamin D has become an important issue because the vitamin D generated in human skin from exposure to sunshine has diminished through the use of sunscreen, wearing of clothing to shade from the sun, pollution of the air by industrial waste, and migration of dark-skinned populations to climates with less sun. Pregnant women have been documented in recent decades to pass less vitamin D to the fetus, so newborns lack sufficient stores at birth. As a result, breastfed infants now are given 400 U daily from birth. Investigative work continues on the benefits of providing pregnant and lactating women with 1,000 U of vitamin D daily. Most, but not all, infant formulas contain 400 U of vitamin D in 26 to 32 oz of reconstituted formula.

Vitamin K content presents an important issue for the newborn who is born with low concentrations, even when the mother receives extra doses at the time of delivery. Hemorrhagic disease of the newborn, with GI or intracranial hemorrhage and generalized bleeding, can present early or up to several weeks after birth and is due to relative deficiencies of vitamin K-dependent coagulation factors. Such deficiency has resulted in all newborns receiving 1 mg of vitamin K intramuscularly at birth, regardless of the proposed mode of feeding. If vitamin K is administered orally, multiple doses should be provided. Formula has extra vitamin K, so an infant who receives 26 to 32 oz per day of formula receives 4 mg of vitamin K orally daily. Concentrations in human milk and cow milk are lower.

Immunologic Considerations of Human Milk

Neonates and infants are immunologically immature and at increased risk for infection. Such developmental immune defects are only some of the factors that place infants at greater risk of infection. In the first 6 postnatal months, phagocyte function is immature, with limited ability to migrate to the site of infection, and reserve production of phagocytes in response to infection is limited. Cell-mediated immunity develops throughout childhood. Defects are particularly apparent in the first 6 months after birth, including decreased cytokine production, decreased natural killer cell function, poor stimulation of B cells for antibody production, and limited numbers of mature functioning T cells. In addition, function of the classical and alternative pathways of complement formation and activation is decreased. Immunoglobulin (Ig) production is limited in amount and repertoire, including poor isotype switching, limited IgG subclass production, and low serum IgA concentrations through 7 to 8 years of age.

Bioactive Factors

Human milk not only bolsters the infant's immature immune response by providing numerous bioactive factors that dynamically affect the innate, adaptive, and mucosal immunity against specific infectious agents but also by influencing immune system development and maturation of the mucosal barrier. A very clear doseresponse relationship has been documented between the amount (full [exclusive], partial, token) and duration of breastfeeding and the benefits gained by the infant and mother. (See Table 1 for the definitions.) Most bioactive factors exert their effects at the level of the mucosal immune system. Igs are the best recognized and studied bioactive components in human milk. Igs in human milk are predominantly secretory IgA, with much smaller amounts of IgM and IgG. Colostrum contains higher amounts of Igs and immunologically competent mononuclear cells than transitional or mature milk. The Igs function by binding directly to specific microbial antigens, blocking binding and adhesion to host cells, enhancing phagocytosis, and modulating local immune response. Table 3 in the online edition of this article lists specific antibodies that have been identified in human milk.

The actual antibodies against specific microbial agents present in an individual woman's milk depends on her exposure and response to the particular agents. Not every mother has antibodies in her milk against every microbe. The predominant action of Igs in human milk is seen at the mucosal level of the infant's mouth, nasopharynx, and GI tract, where they bind to and block the infectious entry of microbial agents through the mucosal barrier. Although best recognized and remembered in association with "specific" protection against individual infectious agents, Igs provide only a small portion of the overall immunologic benefit of human milk.

Other important individual bioactive proteins include lactoferrin, lysozyme, alpha-lactalbumin, and casein. Lactoferrin exerts its effects via iron chelation, which contributes to limiting bacterial growth, blocking adsorption and penetration of viruses and adhesion of bacteria, and enhancing intestinal cell growth and repair. Lysozyme binds to endotoxin, increases macrophage activation, and contributes to bacterial cell wall lysis. Lactalbumin transports calcium and enhances the growth of *Bifidobacterium*, and a modified lactalbumin (in the gut) affects immune modulation. Casein limits adhesion of bacteria and facilitates the growth of *Bifidobacterium*. Carbohydrates are an important nutritional component in human milk, and the specific carbohydrates lactose, oligosaccharides, and glycoconjugates act as bioactive factors. Oligosaccharides act as prebiotics, enhancing the growth of specific probiotic bacteria in breastfed infants, and both oligosaccharides and glycoconjugates bind specific microbial antigens.

Lipids in the form of triglycerides, long-chain polyunsaturated fatty acids, and free fatty acids (FFAs) have a lytic effect on many viruses and are active against Giardia as well. Nucleotides, nucleosides, and nucleic acids comprise more than 15% of the nonprotein nitrogen in human milk. Nucleotides serve many crucial roles in energy metabolism, nucleic acid production, and signal transduction, processes of increased importance during the cellular activation and replication related to an active immune response. Research related to the "essential" nature of nucleotides in protection against infection has led to the addition of nucleotides to some infant formulas. Cytokines and soluble receptors of cytokines are other examples of bioactive factors that serve several functions. Cytokines can act as functional growth factors and have both inflammatory and anti-inflammatory effects in different situations.

Hormones and growth factors, including erythropoietin, epidermal growth factor, insulin, insulin-like growth factor, nerve growth factor, and transforming growth factor-alpha, stimulate the growth and maturation of the GI tract and, to a degree, systemic growth. These bioactive factors are less specific than Igs, but by acting in concert with multiple factors, they provide the major portion of protective effects from human milk.

Anti-inflammatory Factors

The concept of immune protection without an extensive and potentially damaging inflammatory response is gaining in significance in general medicine and in breastfeeding medicine. Many of the same protective bioactive factors act at the mucosal level without stimulating a significant inflammatory response, which indirectly decreases inflammation and possible local tissue damage. Certain factors limit further inflammatory stimulation: lactoferrin blocks activation of complement, and lysozyme inhibits neutrophil chemotaxis and limits formation of toxic oxygen radicals. Various enzymes in human milk break down inflammatory molecules: catalase destroys hydrogen peroxide, histaminase destroys histamine, and arylsulfatase degrades leukotrienes. Various soluble receptors in human milk (IL-1Ra, STNFalpha R1 and R2) bind to specific cytokines, blocking their inflammatory action.

Vitamins A, C, and E, which are present in higher concentrations in human milk than in cow milk, scavenge oxygen radicals. Catalase and glutathione peroxidase as well as lactoferrin serve multiple purposes and have antioxidant properties. Prostaglandins in human milk limit superoxide production. The sum total of these antiinflammatory effects of human milk occurring at the mucosal level limits damage to the mucosal barrier and facilitates its ongoing growth and development to further enhance human milk's protection of the infant.

Infant Microflora, Probiotics, and Prebiotics

The concept that "normal" intestinal microflora influence the development of the local mucosal immunity and even "prime" systemic immunity is being supported by new research. Pathogen-associated molecular patterns in the microflora are recognized by toll-like receptors and may contribute to the expression of toll-like receptors on intestinal epithelial cells as well as lead to "programming" of systemic T-helper cell type 1 (TH1), TH2, and TH3-like T-cell responses. Probiotic bacteria are organisms that live symbiotically in the intestine, conferring additional benefits on the host, which include competition with pathogenic organisms, strengthened tight junctions between cells, production of antimicrobial bacteriocidins, increased mucin production, stimulated peristalsis, increased production of specific nutrients (arginine, glutamine, small-chain fatty acids), and enhanced development of the mucosal immune system.

Prebiotics usually are nondigestible oligosaccharides that, after fermentation, lower the pH of the local environs and increase the amount of available FFAs. Prebiotics enhance the growth of probiotic bacteria in the intestine. Oligosaccharides are the third most common component in human milk in terms of quantity. Cow milk and formula contain less than one tenth of the oligosaccharides in human milk by weight. The microflora of breastfed infants include *Lactobacillus bifidus* and *Bifidobacterium*, which comprise up to 95% of the culturable organisms. The remaining small portion of bacteria include *Streptococcus*, *Bacteroides, Clostridium*, *Micrococcus*, and *Enterococcus* as well as *Escherichia coli* and other organisms in even smaller numbers. The microflora of formula-fed infants are composed primarily of gram-negative organisms (coliforms, Bacteroides, Clostridium, Enterobacter, and Enterococcus) in much larger numbers than in breastfed infants and include very small amounts of Lactobacillus and Bifidobacterium. Lactobacillus and Bifidobacterium ferment oligosaccharides, producing various acids, including FFAs, which lower the pH in the intestine and limit the growth of potential pathogens such as E coli, Bacteroides, and Staphylococcus. New molecular techniques that analyze stool by detecting ribosomal RNA sequences of microbes are expanding the understanding of GI microflora and factors influencing intestinal and immunologic development at the level of the gut. Multiple studies have suggested a protective role of specific intestinal microflora against the risk of developing necrotizing enterocolitis (NEC) in preterm and very low-birthweight infants.

Infectious Disease Considerations

Despite all the evidence for the immunologic benefits of human milk and the protection afforded infants against specific organisms and separate clinical illnesses, data also document the transmission of specific infections through human milk or direct contact with an infected maternal breast. Although only a few infections are transmitted easily through human milk (human immunodeficiency virus [HIV-1], human T-lymphotrophic viruses 1 and 2 [HTLV-1 and -2], and cytomegalovirus [CMV]), these viruses are important because of their potential for causing morbidity or mortality in the infant. In addition, other infections that are uncommonly transmitted by human milk or breast contact should be considered in specific situations.

Transmission of infection through human milk is exceedingly rare compared with the more common mechanisms of transmission for neonates and infants. Prenatal infection is congenital, occurring across the placenta; perinatal infection is due to passage through the birth canal; and postnatal infection occurs via airborne, droplet, or contact transmission other than with the breast. The predominant modes of transmission and the usual timing of infection are important considerations in different clinical situations. (2) Review of the considerations for transmission via human milk for selected organisms can be divided into bacterial, viral, and other. See Tables 4 and 5 in the online edition of this article for summaries of the considerations for selected bacteria and viruses.

Viral Infections

Chronic infection of the mother with HTLV-1 or -2 is considered a contraindication to breastfeeding. Studies on transmission have documented approximately a 30% transmission rate in breastfed infants, 10% rate in "mixed-feeding" infants, and 0% rate in exclusively formula-fed infants. Researchers estimate that 1 mL of human milk can contain 1,000 T cells infected with HTLV-1. Epidemiologic studies from areas of Japan that have high rates of HTLV-1 have reported significant reductions in transmission of the virus from mother to infant with avoidance of breastfeeding or limiting breast-feeding to less than 6 months' duration.

HIV-1 infection in the mother is another chronic infection that can be transmitted readily via human milk to the infant. In the United States and other areas of the world where HIV perinatal transmission prevention is highly successful and safe alternatives to breastfeeding are available, acceptable, feasible, affordable, sustainable, and safe, mothers who have HIV infection have been advised not to breastfeed their infants. In areas of the world where there is an increased risk of infectious diseases, nutritional deficiencies, and significant morbidity and mortality for infants who are not breastfed and replacement feeding is not available, exclusive breastfeeding by an HIV-positive mother can afford the infant the best chance of survival. HIV DNA is detectable easily in human milk and can be categorized as cell-free and cell-associated virus. Factors associated with an increased risk of HIV transmission via breastfeeding include mixed feeding versus exclusive breastfeeding, duration of breastfeeding, maternal illness and high viral loads, lower CD4 lymphocyte counts in the mother, and mastitis or nipple lesions in the mother. Recent studies have documented that effective antiretroviral (ARV) treatment of the HIV-positive mother along with exclusive breastfeeding can lead to lower transmission rates for infants and lower mortality for both mothers and infants. Prophylactic ARV treatment of the infant along with exclusive breastfeeding also has been associated with decreased HIV transmission to the infant. Additional carefully controlled research on exclusive breastfeeding, ARV therapy, and optimizing the infant's nutrition and growth are needed before an optimal regimen can be devised.

Latent CMV infection or even recent CMV infection in a breastfeeding mother is not a contraindication to breastfeeding. Postnatal CMV infection via human milk occurs readily, but viral presence is rarely, if ever, clinically significant in the term infant. In fact, breastfeeding has been described as "natural CMV immunization" in the term infant. Preterm, low-birthweight, and very lowbirthweight infants are at risk for clinically significant postnatal CMV infection via breastfeeding. This postnatal infection is more likely to occur between 3 and 12 weeks postpartum, when virolactia occurs commonly. Pasteurization and freezing-thawing milk can decrease the CMV load in human milk. A reasonable protocol has been outlined for protecting susceptible infants while using human milk in nurseries that include preterm and very low-birthweight infants. (3) The protocol includes screening mothers for CMV before providing human milk to their infants, pasteurizing or freezing-thawing human milk from CMV-positive mothers before its use, and observing infants in the nursery for evidence of acute CMV infection.No prospective, controlled trials document the protective effects of such a protocol.

West Nile virus (WNV) is the only other virus for which there has been evidence for transmission via human milk with any frequency. Several studies document the presence of WNV DNA as well as IgM and IgG antibodies against WNV in human milk, but no clear evidence documents clinically significant illness in infants exposed through breastfeeding by mothers who have WNV infection. The concern about viruses such as herpes simplex virus, varicella-zoster virus, vaccinia virus (smallpox vaccine virus), or variola virus (smallpox virus) is transmission through contact with skin lesions that contain the virus on the mother's nipple or breast, not through virus excreted in the milk. Temporary avoidance of breastfeeding and milk from the mother's breast that has an identified lesion due to one of these viruses may be reasonable. Prophylactic antiviral treatment for the infant along with maternal antiviral treatment usually is adequate to allow breastfeeding to continue.

Viruses commonly transmitted via the respiratory route (influenza, respiratory syncytial virus, severe acute respiratory syndrome-associated coronavirus) are not transmitted through human milk. Most frequently, by the time a specific respiratory illness is diagnosed in the mother, the infant has already been exposed via respiratory secretions. There is no reason to suspend breastfeeding or the use of expressed human milk, except when severe disease in the mother prevents the ability to obtain human milk. The numerous bioactive factors (not Igs if it is early in the maternal infection) in human milk can provide the infant some ongoing protection.

Bacterial Infections

The concern about bacterial infections in the mother is infection of the nipple or breast (mastitis or breast abscess) that introduces the bacteria into the milk or directly into the infant's mouth. (See Table 4 for selected bacterial infections in the mother.) The risk of pulmonary tuberculosis (TB) in the mother is related to transmission via respiratory droplets, which is the same for breastfeeding or formula-fed infants in contact with their mothers. TB mastitis or TB lesions of the breast are rare. Breastfeeding or use of expressed human milk from the mother who has TB can continue once the mother is receiving appropriate antituberculous therapy and the infant is receiving isoniazid prophylactically.

Staphylococcus or group A *Streptococcus* infection of the breast can interfere with breastfeeding. Breastfeeding or use of expressed human milk can continue when the mother is physically comfortable with the process, after a temporary suspension during the mother's initial 24 hours of effective antibacterial therapy. Prophylactic antibiotic therapy for the infant in conjunction with the maternal treatment often allays additional fear.

In general, the same antibiotics used to treat a specific infection in the mother are used and are safe in the infant and in the mother's milk. Antibiotics do enter human milk, but usually in very low concentrations, exposing the infant to a daily dose well below the commonly used therapeutic dose prescribed for infants and children. The exceptions to this principle are doxycycline or tetracycline because of a concern for dental staining or altered bone growth in the infant (short duration of therapy in the mother [<3 wk] generally is considered acceptable) and erythromycin, which has been associated with the occurrence of infantile hypertrophic pyloric stenosis in young infants. Quinolone use has been increasing in children due to the absence of significant adverse effects, and the use of levofloxacin or ofloxacin in breastfeeding mothers appears to be without significant concerns, other than the potential for changing the gut flora of the infant and perhaps bacterial overgrowth with a resistant pathogen.

Additional considerations for group B *Streptococcus* (GBS) infection or colonization of the mother and transmission to the infant include adherence to proposed guidelines for prevention of GBS disease in the infant, the frequent and "back and forth" nature of colonization in mother-infant dyads, the difficulty in eradicating colonization in the mother or infant, and the fact that transmission of GBS from mothers to infants occurs with and without evidence of mastitis in the mother. Acquisition of GBS infection via breastfeeding or human milk remains uncommon compared with transmission via close direct contact between mothers and infants. Close adherence to the guidelines for prevention of early GBS disease in the infant is effective and important.

Other recommendations to decrease possible GBS transmission between mother and infant via human milk include careful instruction of mothers and medical staff on the appropriate techniques for expression, collection, and storage of expressed milk and on the signs and symptoms of mastitis to facilitate early recognition and initiation of effective interventions. Breastfeeding or the use of expressed human milk can continue after a temporary suspension during the initial 24 hours of antibacterial treatment for the mother. Preventive or early empiric antimicrobial therapy for the infant may be indicated in specific clinical situations, along with the continuation of breastfeeding.

Fungal Infections

Candida infection of the breast and mucocutaneous *Candida* infection in the infant are the only pertinent fungal infections related to breastfeeding and human milk. In general, antifungal therapy administered simultaneously to the infant and the mother is the most effective and appropriate treatment because of the ease of colonization or recolonization in both mother and infant. Numerous topical and systemic therapies are effective. Occasionally, persistent or recurrent *Candida* infection adversely affects ongoing breastfeeding. *Candida* infection of the breast is overdiagnosed. Consultation with a professional or physician who has extensive experience supporting and caring for the breastfeeding mother-infant dyad can facilitate effective treatment and ongoing breastfeeding.

Parasitic Infections

Transmission of parasites through breastfeeding or human milk is not a significant concern. Although hookworm infection occurs commonly in young children, and transmammary spread of helminths has been described in veterinary medicine, little substantiated evidence supports the presence of hookworms in human milk or significant infection in the infant due to a hookworm passed via human milk. Giardiasis in infants younger than 6 months of age is rare, and given the various factors active against Giardia in human milk, transmission via this route is highly unlikely. There is no evidence for transmission of malaria via human milk, but the mother and infant both need to be protected from contact with infected mosquitoes. Maternal treatment or prophylaxis for malaria during breastfeeding can be accomplished safely with various agents, such as chloroquine, quinine, pyrimethamine-sulfadoxine, tetracycline, mefloquine, and primaquine, with some attention to the age of the child, the duration of exposure, and short periods of "pumping and dumping" of expressed milk during the use of mefloquine. Transmission of Toxoplasma gondii or Trichomonas via human milk has not been demonstrated.

Breastfeeding and Maternal Medications

The risk of maternal medication to the breastfed infant is a frequent question for the physician. The answer depends on a number of factors that involve the infant, including gestational age at birth, current age, weight, feeding pattern, and total oral intake, and the mother, such as medication dose and dosing pattern, route of administration, drug absorption, peak plasma concentration and timing of that peak, volume of distribution, molecular size of the drug, degree of ionization, pH, solubility in water or lipids, degree to which the drug is protein bound, and oral bioavailability.

A number of questions must be clarified to make an informed decision about the use and the potential risk of the medication. If the drug passes into the milk, what is the concentration in the milk? Is it absorbed by the infant or is it not orally bioavailable as are many drugs that are effective only by the intravenous or intramuscular routes? Is the infant able to detoxify and excrete the drug or does it accumulate in the infant's system? The milk/plasma ratio has been determined for a number of drugs by measuring the concentration in the milk and maternal plasma simultaneously. A single point in time milk/ plasma ratio does not give an accurate determination of how much the infant will receive. A concentration measured in the milk at the time of feeding is the only reliable measure of what the infant receives.

Despite these questions, reliable measures of many common medications have been documented. Considerable research has resulted in valuable estimations of the safety of many, but not all, drugs. The determination of the relative infant dose (RID) has been used to standardize the method that estimates the amount of a given drug that the infant receives. The formula is:

RID (%)=absolute infant dose (mg/kg per day)÷ maternal dose (mg/kg per day ×100)

These calculations assume average metabolism and a maternal dose in the usual therapeutic range. The acceptable RID of a drug is 10% or less for term infants, who have a clearing capacity about one third that of the adult. Preterm infants are less efficient at clearing drugs, with capacity only 5% of the adult capacity at 24 to 28 weeks' gestation and only 10% at 28 to 34 weeks' gestation. After 7 months of age, however, the infant can handle most drugs at adult concentrations. The RID is available for many medications from reference data banks such as the Library of Medicine data bank at http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?LACT. Other resources are *Medications and Mother's Milk* (4) and the University of Rochester Breastfeeding and Human Lactation Study Center Drug Line (585/275-0088).

The AAP Committee on Drugs has published categories of drugs and their safety for use while breastfeeding. If the drug is prescribed normally for term or preterm infants, it is considered safe via human milk. If the infant also needs a drug such as an antibiotic, it must be administered directly to the infant. If the medication is not bioavailable orally, the infant cannot absorb it from the stomach. Large molecules such as insulin, heparin, and many Igs do not pass into milk from maternal plasma.

Drugs of abuse or street drugs are considered contraindicated, and breastfeeding is not recommended. For a mother actively participating in a methadone maintenance program, the potential benefits of breastfeeding and human milk for the mother and infant should be considered strongly. Breastfeeding can be recommended in certain situations in which there has been good prenatal care, maternal compliance with a drug addiction recovery program before birth, and negative maternal urine toxicology screens for 12 weeks before and at delivery. Women who have been stable on a methadone maintenance program should be permitted to breastfeed. Evidence suggests that methadone-exposed infants may have less severe symptoms of neonatal abstinence syndrome when maintained after delivery on human milk.

Immunosuppressant drugs, such as methotrexate, are contraindicated. However, some newer antimetabolites or cancer drugs have very short half-lives. A drug is considered to clear the body within 5 times the half-life. If the half-life is 2 hours, it will clear in 10 hours, during which time the mother can pump and discard her milk. The infant can be fed previously pumped milk or a suitable substitute during that interim period.

Radioactive compounds have been studied widely. The clearance half-life has been measured for most of the radioactive compounds used diagnostically or therapeutically. The same formula ($5 \times$ half-life=clearance time) can be used to determine how long a mother needs to pump and discard her milk. However, when the half-life is longer than 3 days, it is impractical to have a mother pump and discard for 15 days or longer, although this determination is an individual decision. Radioactive iodine falls in this category. Iodine ¹³¹ in therapeutic doses takes 3 to 5 weeks to clear the maternal system.

In summary, drugs that are administered routinely to infants are safe to prescribe for the breastfeeding mother. Important considerations for minimizing the amount of medication to which the breastfeeding infant is exposed include choosing the drug present in the lowest amount in human milk, using a medication in the same classification of drugs that have the lowest RID, avoiding longacting preparations of medications, scheduling dosing so the medication concentration in the milk is lowest when the infant feeds, taking the medication immediately after breastfeeding or breastfeeding just before the next dose when the medication is taken several times a day, and observing the infant for changes in behavior while administering the medication to the mother.

Use of Human Milk in Preterm Infants

All of the benefits of human milk are magnified in the preterm infant. If the infant can receive oral feeding, mother's milk is the safest and best tolerated of all the available feedings. Human milk can be introduced earlier than the foreign protein of formula. All of the infection protection qualities and the antibodies found naturally in human milk protect against infection, especially NEC. The limitations are the ability of the mother to pump her milk and make it available. Milk banks are available throughout the country that can provide pasteurized human milk from approved donors. The concerns of the neonatologist stem from the inability to measure the volume consumed when the infant is at the breast and the need for additional calories in the limited volumes tolerated by extremely immature infants. The quick solution is to add concentrated formula from powder or liquid made from bovine milk, known by the misnomer "human milk supplementer." This preparation contains none of the protective factors of human milk and interferes with those present in any human milk provided. One commercially available supplementer made exclusively from human milk has been shown to promote growth in preterm infants as well as protect against infection, especially NEC.

Because women today commonly are deficient in vitamin D, even while taking prenatal vitamins during pregnancy, their infants have inadequate stores at birth, especially if born preterm. Vitamin D supplementation is required if the preterm infant is receiving mother's milk (400 U daily).

Ideally, preterm nurseries have nursing staff who are also certified lactation consultants and can assist mothers who wish to pump and provide their milk. The consultants can advocate for the mother who is ready and eager to feed her preterm infant at the breast. All neonatal intensive care units should provide electric breast pumps and private accommodations to pump. Freezers and refrigerators should be designated for sole storage of human milk. Pumped milk should be stored in freezersafe containers that can be sealed and labeled with name, unit number, date, and time of collection, so milk can be fed sequentially, beginning with the antibody-rich colostrum. Most neonatal intensive care units have feeding protocols geared to the gestational age and weight of the infant. Mother's milk can be used if these guidelines are followed.

At the time of discharge, some preterm infants still need added calories, which can be provided by "bioengineering," in which the mother pumps 5 mL of milk from the breast first (and saves it frozen for weeks to be used later). She then feeds just the hind milk, which is higher in calories and fat than the foremilk. Some nurseries have the ability to measure the caloric content of mother's milk from a sample taken from each pumping for 24 hours. The average caloric measure is 20 kcal/oz, with a range of 15 to 24 kcal/oz. The milk can be supplemented as necessary or, in the case of high-calorie producers, not at all. The initial milk produced by mothers who deliver preterm has been demonstrated to be higher in protein, calcium, sodium, and calories for the first few weeks. Although an advantage to the infant, lack of bedside technology does not permit factoring in this nutrient variation in the feeding orders.

Current Recommendations

The World Health Organization (WHO), United Nations Children's Fund, AAP Section on Breastfeeding, American College of Obstetricians and Gynecologists, American Academy of Family Physicians, Academy of Breastfeeding Medicine, and many other health organizations recommend exclusive breastfeeding for the first 6 postnatal months. Numerous obstacles to the initiation and continuation of breastfeeding remain within health-care settings, the workplace, communities, and the media.

The goals for Healthy People 2010 for breastfeeding in the United States were: 1) initiation of any breastfeeding in 75% of infants in the early postpartum period, 2) continuation of any breastfeeding in 50% of infants at 6 months of age, 3) continuation of any breastfeeding in 25% of infants at 1 year of age, 4) exclusive breastfeeding in 40% of infants at 3 months of age, and 5) exclusive breastfeeding in 17% of infants at 6 months of age. The Centers for Disease Control and Prevention have reported preliminary survey data on breastfeeding rates in the United States for infants born in 2006. Although rates have improved since 1999, they still fall below the Healthy People 2010 goals. For infants born in 2006, 74% initiated breastfeeding, 43% continued breastfeeding at 6 months, and 23% continued at 12 months of age. An estimated 33% of infants were exclusively breastfed through 3 months of age and 14% through 6 months of age. The Healthy People 2020 goals for breastfeeding were released in late 2010 (http://www.healthypeople.gov/2020/topicsobjectives2020/overview.aspx?topicid=26) and show some changes. Anticipated rates are changed, and methods to reduce barriers are included. The goals are:

- Infants ever breastfed: 82%
- Infants breastfeeding at 6 months: 60.6%
- Infants exclusively breastfed through 3 months: 46.2%
- Infants exclusively breastfed through 6 months: 25.5%

The WHO multicenter growth reference was conducted in six countries (Brazil, Ghana, India, Norway, Oman, and the United States) between 1997 and 2003. The study consisted of a longitudinal follow-up of 882 infants from birth to 24 months of age and a cross-sectional study of 6,669 children ages 18 to 71 months. Children included in the study were healthy infants living in socioeconomic situations favorable to growth, who were breastfed exclusively for at least 4 months and were introduced to complementary foods at 6 months of age, with breastfeeding continuing up through 12 months of age. The tables and charts (www.who.int/childgrowth/ en) created through this study depict normal human growth under optimal environmental conditions. The curves for the six different countries were virtually superimposable on each other for height and weight growth through 60 months of age. These standards now identify breastfeeding as the biologic norm for growth and development and add further evidence for the recommendations of exclusive breastfeeding through 4 to 6 months of age.

Pediatricians and other health-care professionals across the United States should continue to recommend the use of human milk for all infants, with few exceptions (Table 6). A balanced presentation of up-to-date information on the benefits and process of breastfeeding should be provided to all parents to assist them in making an informed decision for the feeding of their infants. Pediatricians and other health-care professionals should adopt and promote the "Ten Steps to Successful Breastfeeding" in all maternity services and facilities providing care to infants and children (Table 7).

In-hospital Breastfeeding Policies: Early and Frequent Contact of Mother and Infant

Hospital management of the mother-infant dyad who plan to breastfeed are clearly spelled out by the WHO-UNICEF ten steps that have been endorsed by the AAP (Table 7). The AAP did take exception to the recommen-

Table 6. Contraindications to Breastfeeding

Infant Conditions

- Classic galactosemia (galactose 1-phosphate uridyltransferase deficiency)
- Maple syrup urine disease
- Phenylketonuria (partial breastfeeding is possible with careful monitoring)

Maternal Conditions

- Human immunodeficiency virus 1 infection (if replacement feeding is acceptable, feasible, affordable, sustainable, and safe)
- Human T-lymphotropic virus 1 and 2 infection (varies by country; in Japan, breastfeeding is initiated)
- Tuberculosis (active, untreated pulmonary tuberculosis, until effective maternal treatment for the initial 2 weeks or the infant is receiving isoniazid)
- Herpes simplex virus infection on a breast (until the lesions on the breast are cleared)
- Medications (those of concern)
- -Most medications are considered safe because little gets into the milk -A few select compounds drugs of abuse and some radioactive compounds that have long half-lives require cessation of lactation

dation on pacifier use with the following footnote: "The AAP does not support a categorical ban on pacifiers due to their role in sudden infant death syndrome risk reduction and their analgesic benefit during painful procedures when breastfeeding cannot provide the analgesia." (6) Pacifier use in the hospital in the neonatal period should be limited to specific medical indications, such as pain reduction or for calming in a drug-exposed infant. Mothers of healthy term breastfeed infants should be

instructed to delay pacifier use until breastfeeding is well-established, usually about 3 to 4 weeks after birth.

Every effort should be made at birth and while in the hospital to keep mother and infant in proximity. Labor-delivery-recovery-postpartum rooms allow care for the dyad to continue in the same room. Birth centers and rooming-in provide the best environment in which to establish lactation. The infant should be put to breast as soon as possible after delivery, ideally in fewer than 30 minutes or, as recommended in the United States, within the first hour after birth. When a mother has her baby nearby, the proximity offers her an opportunity to learn her baby's cues before they are discharged from

the hospital. The Baby Friendly Hospital Initiative (BFHI) promotes the ten steps, and The Joint Commission has introduced them in their review of hospitals that provide delivery services. This support, as recommended by the BFHI, should continue through infancy until weaning.

Weaning involves the introduction of safe and appropriate complementary foods to the infant, beginning at 6 months of age. Weaning is a process, and breastfeeding continues with the introduction of other foods. The

Table 7. Ten Steps to Successful Breastfeeding

Every facility providing maternity services and care for newborn infants should:

- 1. Have a written breastfeeding policy that is communicated routinely to all health-care staff.
- 2. Train all health-care staff in skills necessary to implement this policy.
- 3. Inform all pregnant women about the benefits and management of breastfeeding.
- 4. Help mothers initiate breastfeeding within 30 minutes of birth.
- 5. Show mothers how to breastfeed and how to maintain lactation even if they should be separated from their infants.
- 6. Give newborns no food or drink other than human milk, unless medically indicated.
- 7. Practice rooming-in, that is, allow mothers and infants to remain together 24 hours a day.
- 8. Encourage breastfeeding on demand.
- 9. Give no artificial teats or pacifiers (also called dummies or soothers) to breastfeeding infants.
- 10. Foster the establishment of breastfeeding support groups and refer mothers to them on discharge from the hospital or clinic.

From Evidence for the Ten Steps to Successful Breastfeeding. (5)

Human Milk Banks

stopping breastfeeding.

Human milk banking operates in many countries. Ten approved not-for-profit banks are members of the Human Milk Banking Association of North America (www.HMBANA.org). All the banks follow the association guidelines for collecting and pasteurizing human milk. Women who donate milk are carefully

overall duration of breastfeeding varies significantly according to

the mother's and family's beliefs and cultural practices. The end of

breastfeeding is most frequently

"decided" by the mother and infant

(together or separately), and there

is no predetermined ideal time for

Summary

- Ample evidence documents the clear benefits of breastfeeding for both the mother and the infant.
- Among the very few contraindications to breastfeeding are galactosemia, medications or drugs of concern, and HIV and HTLV infection.
- Pediatricians should recognize that human milk is superior to formula in optimizing each infant's potential for early growth and development.
- Pediatricians should recommend exclusive/full breastfeeding as superior to formula feeding through the first 6 postnatal months and the subsequent timely introduction of adequate, safe, and appropriate complementary foods in combination with continued breastfeeding as optimal nutrition in the first postnatal year.
- Pediatricians should be knowledgeable about important issues concerning breastfeeding and the management of the breastfeeding mother-infant dyad in situations of infant prematurity or illness and maternal illness, infection, and medication exposure.
- Families should be provided with appropriate information about breastfeeding and infant feeding before as well as throughout the pregnancy and infancy.
- Mothers should receive ongoing support for breastfeeding in the hospital, in medical offices and facilities, and throughout communities, paralleling the BFHI.
- Ongoing lifelong education about support for and management of the breastfeeding mother-infant dyad is essential for pediatricians in the 21st century.

tested and screened. Milk is available by doctor's prescription for a fee that covers processing, shipping, and handling. Donors are not paid. At least one forprofit milk bank has investigated the variations in human milk and has produced a concentrated fluid human milk supplementer made only of human milk. The company also provides regular human milk, the calorie and protein content of which is available at 20, 24, and 26 kcal/oz. This milk is also available for a fee.

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Resource

Breastfeeding and Human Lactation Study Center located at the University of Rochester, School of Medicine. Phone Number: 585–275-0088

PIR Quiz Quiz also available online at http://pedsinreview.aappublications.org.

1. Skin-to-skin contact between an infant and mother in the first hour after birth has been associated with:

- A. Calmer personality.
- B. Earlier attachment.
- C. Faster infant development.
- D. Greater emotional stability.
- E. More successful breastfeeding.
- 2. The *most* definitive studies showing a reduction in atopic dermatitis following at least 3 months of breastfeeding involved:
 - A. Children younger than 10 years of age who had a family history of asthma.
 - B. Children older than 10 years of age who had with a family history of asthma.
 - C. Children who had no family history of asthma.
 - D. Infants who had a family history of atopy.
 - E. Infants who had no family history of atopy.
- 3. Vitamin K has been administered routinely to newborns for many years. Which of the following vitamins has also been recommended for supplementation from birth?
 - A. A.
 - B. B.
 - C. C.
 - D. D
 - E. E.
- 4. In the United States, infection with which of the following viruses is a contraindication to breastfeeding?
 - A. Cytomegalovirus.
 - B. Human immunodeficiency virus.
 - C. Respiratory syncytial virus.
 - D. Varicella-zoster virus.
 - E. West Nile virus.
- 5. The earliest age at which most infants can metabolize drugs at adult rates is:
 - A. 1 week.
 - B. 1 month.
 - C. 4 months.
 - D. 8 months.
 - E. 1 year.

HealthyChildren.org Parent Resources from AAP

The reader is likely to find material to share with parents that is relevant to this article by visiting this link: http://www.healthychildren.org/English/ages-stages/baby/breastfeeding/Pages/default.aspx.

Breastfeeding: More Than Just Good Nutrition

Robert M. Lawrence and Ruth A. Lawrence *Pediatrics in Review* 2011;32;267 DOI: 10.1542/pir.32-7-267

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