

Chapter 2

Infants: Transition from Breast to Bottle to Solids

James K. Friel and Wafaa A. Qasem

Key Points

- Exclusive breastfeeding is recommended for the first 6 months of life.
- Formula feeding is only recommended to mothers who cannot or choose not to breastfeed.
- Breast milk has a degree of bioactivity (effect on cell or tissue), antioxidants, immunological defenses, minerals, and fatty acids not found in formula. These deficient elements may help explain the health benefits associated with breast milk. Formula manufacturers are trying to introduce these missing elements into formula.
- Complementary feeding should begin at 6 months of age with breast milk continuing until at least 1 year of age.
- Complementary feeding should help promote a positive association with hunger, food, appetite, and the person feeding. Infants should also learn gross motor skills and form relationships.

Keywords Infants • Breast milk • Breastfeeding • Complementary feeding • Formula • Growth

What Is the Best Milk for an Infant?

Breastfeeding is recommended for the first year of life [1, 2]. Exclusive breastfeeding is recommended for the first 6 months of life. Formula feeding is recommended only for those women who choose not to or cannot breastfeed. The consumption of whole or reduced-fat cow's milk is not recommended during the first year of life [3]. About two out of three mothers in the United States initiate breastfeeding and one out of five continues to 6 months.

J.K. Friel, Ph.D.

Department of Human Nutritional Sciences, University of Manitoba,
196 Innovation Drive, Winnipeg, MB, Canada, R3T 6C5

Department of Pediatrics, University of Manitoba, Winnipeg, MB, Canada

W.A. Qasem, Ph.D., M.D. (✉)

Department of Human Nutritional Sciences, University of Manitoba,
196 Innovation Drive, Winnipeg, MB, Canada, R3T 6C5

e-mail: qasemw@myumanitoba.ca

Breastfeeding is rarely contraindicated. Infants who have galactosemia or whose mother uses illegal drugs, has untreated active tuberculosis, or has been infected with HIV should not breastfeed. However, neither smoking nor environmental contaminants, moderate alcohol consumption, and the use of most prescription and over-the-counter drugs should preclude breastfeeding.

With all the best intentions and technological expertise, “humanized” infant formulas cannot be compared with mother’s own milk. It is therefore logical and appropriate for health professionals to encourage the consumption of human milk whenever possible. However, once the information is presented, there is no justification for attempting to coerce women into making a feeding choice [4]. Sometimes a formula-fed child and rarely a breastfed infant develop sensitivity to cow’s milk, either cow’s milk allergy (CMA) or lactose intolerance (due to lactase deficiency). While primary lactase deficiency develops as a result of genetic mutation of the intestinal enzyme lactase, secondary lactase deficiency does occur due to lactase shortage most often following surgery or a gastrointestinal disorder.

While human milk is “uniquely superior” for infant feeding and is species specific, the most acceptable alternative is commercial formulas. Manufacturers do their utmost to mimic human milk. A “formula” is just that: an equation that is proprietary, consisting of a composite mix of nutrients, emulsifiers, and stabilizers. Formulas in North America that are marketed for term infants are based on one of the following: (a) cow’s milk (casein or whey predominant), (b) soy protein, or (c) protein hydrolysate. The use of soy-based formulas, special formulas, or formulas for the feeding of the premature infant is beyond the scope of this review.

The success of formula manufacturers is due to (a) aggressive marketing, (b) lack of support for breastfeeding from family, friends, and the medical profession, (c) cultural and public perception, (d) convenience, and (e) some government programs giving infant formula away for free. With the increase in working mothers, formula feeding becomes a practical and attractive alternative. Guidelines for formula composition have evolved over the years to provide not only what must be in a formula but minimum and maximum levels as well. Standards may vary between countries.

Nutrient Content of Breast Milk and Infant Formula

The composition of a formula depends on many factors and differs between manufacturers. For example, cholesterol exists in human milk but is not added to formula because the public perceives it as “bad.” Human milk has a caloric density of 670 kcal/L. Most term formulas are designed to have the same caloric density. Low-iron formulas are marketed even though health professionals do not recommend their use as a standard feed. They remain on the market because the public and some health professionals perceive them as beneficial in dealing with problems such as colic and constipation.

The nutrient composition of milk changes over time. The composition of human milk also changes during feeding so that most of the fat in human milk is concentrated in the latter part of feeding, probably saturating the infant and providing a signal for terminating feeding. It appears that breastfed infants have more control over the amount consumed at a feeding than do formula-fed infants [4]. Frequent feedings with small amounts at each feeding, as is seen in infants who are breastfed ad libitum, may lead to favorable changes in metabolism [5]. These differences may affect feeding habits later in life.

The protein content of human milk is high during early lactation (colostrum) and then gradually declines to a low level of 0.8–1% in mature milk. The high protein concentration of colostrum is largely due to very high concentrations of secretory IgA and lactoferrin. These proteins provide protection against bacteria giving benefits in early life beyond the role of building blocks for tissue synthesis. Indeed, human milk is truly the first and foremost “functional food.”

Milk proteins are separated into various classes, mainly caseins (10–50% of total) and whey (50–90% of total) proteins [6]. Milk fat globule membrane proteins and protein derived from cells

present in milk comprise 1–3%. For some years, manufacturers prepared their formula with either a whey or casein base. For the term infant, there appears to be no advantage nutritionally of whey predominant over casein-predominant formulas. Interestingly, digested fragments of human casein, but not bovine, may exert physiological effects such as enhancing calcium uptake by cells and playing a role in infant sleeping patterns [6]. Little is known about the role of hormones that are present in human milk; they may play a role in the developing infant.

Human milk contains significant amounts of polyunsaturated fats. These include 10–12% linoleic acid (18:2, *n*-6), 1–2% linolenic acid (18:3, *n*-3), and a small but significant amount of other long-chain (*n*-3) and (*n*-6) fatty acids such as docosahexaenoic acid (22:6, *n*-3) and arachidonic acid (20:4, *n*-6) [7]. While the level of total polyunsaturated fats in human milk varies with the intake of the mother, it is generally 13–20%. Long-chain fatty acids present in human milk, and recently in some formula, may confer some developmental advantage. Formula contains more of the shorter-chain fatty acids.

The primary carbohydrate source in formula and human milk is lactose with very small amounts of other sugars. No minimum or maximum level of carbohydrate is set for North America. Corn syrup solids and/or maltodextrin may be used in certain formulas [4].

Minerals can be divided broadly into macro, micro, and ultra-trace elements. Mineral concentrations differ in human milk over the first 3 months of lactation [8]. The levels of Zn, Cu, Rb, and Mo decrease over time, suggesting homeostatic regulation and possible essentiality for human infants [8]. In general, the mineral content of human milk is not influenced by maternal diet, parity, maternal age, time of milk collection, different breasts, or socioeconomic status [9].

The ultra-trace elements (<1 µg/g dry diet) exist naturally in human milk but depend on protein sources in formulas where they occur as contaminants. Although many of these elements have no specified human requirement, we believe that recommendations for ultra-trace elements need to be established.

Human milk has all the essential vitamins required by the infant but is low in vitamins D and K. Vitamin K is given to all infants at birth and vitamin D (also considered to be a hormone) is usually recommended as a supplement for breastfed infants and infants receiving less than a liter of formula. Minimum and maximum levels of vitamins are regulated for formulas so that they are complete. Formula labels state the amount of all nutrients, including vitamins, which must be present when the shelf life expires. Because of this, “overage” is necessary as some vitamins will break down over time. Thus, as much as 60% over label claim might be present for different nutrients, primarily vitamins [10].

The use of supplements for human milk-fed infants is controversial. Some see supplements as undermining the integrity of human milk and implying that milk is not adequate. Nonetheless, human milk is neither a perfect nor a complete food [11]. There are good data to support the administration of vitamin K soon after birth to prevent hemorrhagic disease of the newborn and vitamin D supplements during early infancy to prevent rickets [2, 11].

Current practice is for iron supplements to be deferred until 4–6 months of age. Some authorities [11] recommend iron supplements of 7 mg/day, beginning in the first few weeks of life. A significant increase in iron status has been documented in infants receiving a modest iron supplement (7.5 mg/day) [12]. Fluoride supplements once recommended for all infants are no longer recommended during the first year of life [11].

Formulas that conform to specification of Canadian/American guidelines are complete and therefore do not require supplementation with any minerals or vitamins. A controversial nutrient is iron. The amount of iron fortification required is not yet certain; however, formulas have a low content of iron (<4 mg/L) which may lead to anemia. It was believed that consuming iron-fortified formulas would result in intolerance and gastrointestinal distress, but these theories have been discredited [13]. See Fomon [4] for a review of regulations for the nutrient content of infant formulas.

In general, the content of protein, lipid, carbohydrate, energy, minerals, and most water-soluble vitamins in human milk is not affected by poor maternal nutrition [14]. But fat-soluble vitamins and fatty acids are affected by the maternal diet [14]. It appears that there are mechanisms to ensure

constant supply and stability of nutrients to the breastfed infant. The major difference between a breastfed and a formula-fed infant is that many of the components of human milk also facilitate the absorption of nutrients and have a function beyond nutrient requirements. Adding more of a nutrient to formula is not necessarily as good as having a bioactive component in human milk, even if only present in small amounts (e.g., lactoferrin for both iron absorption and as a bactericide). There are many properties of human milk that attend to such details for the benefit of the infant.

Bioactivity of Human Milk and Formulas

Human milk is “alive,” meaning it has functional components that have a role beyond simply the provision of essential nutrients. Bioactive compounds in human milk can be divided into several broad categories: (1) those involved in milk synthesis, nutritional composition, and bioavailability and (2) those compounds that aid in protection and subsequent development of the infant. To date many bioactive compounds have been identified in human milk including cytokines, immune factors, growth factors, hormones, antimicrobial agents, nucleotides, antioxidants, and enzymes (*see review [15]*). Hormones, enzymes, cytokines for immunity, and cells present in milk have physiologically active roles in other tissues so it is reasonable to assume that they play a role in infant growth and development. Indeed, many bioactive compounds can survive the environment of the neonatal stomach thereby potentially exerting important physiological functions [15, 16].

Early postnatal exposure to flavor passed into human milk from the mother’s own diet can predispose the young infant to respond to new foods. The transition from the breastfeeding period to the initiation of a varied solid food diet can be made easier if the infant has already experienced these flavors. Cues from breast milk can influence food choices and make safe new foods with flavors already experienced in breast milk [17]. Again, this does not happen with formula feeding.

Until recently, human breast milk was thought to be sterile and the only time that bacterial organisms could be identified was when a woman develops “mastitis.” But recent research has shown that breast milk contains various bacterial genera including *Bifidobacterium* and *Lactobacillus* with greater diversity in intra-phylogenotypes than previously thought, forming the microbiome [18, 19]. It is believed that the human milk microbiome plays a major beneficial role in shaping the development of the infant’s intestinal microbiota and their immune system, and may also play a role in other aspects of short- and long-term infant and maternal health [20]. Formula-fed infants have different microbiota profiles compared to breastfed infants; this may favor intestinal pro-inflammatory status thereby leading to negative health outcomes [21].

A variety of other cells exist in human milk. Macrophages, polymorphonuclear leukocytes, epithelial cells, and lymphocytes have been identified in human milk and appear to have a dynamic role to play within the infant gut. These cells may offer systemic protection after transport across the “leaky gut,” particularly in the first week of life [22]. Antiviral and antibacterial factors exist in human milk with secretory IgA produced in the mammary gland being one of the major milk proteins [6]. There may even be a pathway from the infant back to the mother, which tailors production of antibodies against microbes to which the infant has been exposed.

Hamosh [15] classified enzymes in human milk into three categories: (1) those that function in the mammary gland, (2) enzymes that might function in the infant, and (3) enzymes whose functions are unclear. It is only recently that the physiological significance of enzymes in human milk has started to become appreciated. More than just protein, and not present at all in infant formulas, enzymes are another example of why human milk must be seen as alive. These enzymes appear to have a more highly organized tertiary structure than enzymes from other tissues, which may be to protect function by resisting denaturation in the gut [15]. We think that as well as serving an immediate function in the intestine, some enzymes may be transported across the gut or act within the body to offer protection to the infant.

Interestingly, amylase digests polysaccharides that are not present in human milk. Amylase is important after the initiation of starch-containing foods such as cereals [15]. It is as if the mammary gland is “thinking ahead” and assisting the infant gut in the transition to weaning. Milk digestive lipase assists the newborn whose endogenous lipid digestive function is not well developed at birth.

Recent interest has focused on the antioxidant properties of human milk. Several groups have reported the ability of colostrum [23] and mature milk [24] to resist oxidative stress using a variety of end points. This feature of human milk appears to be heterogeneous rather than attributable to a specific compound. Infant formulas appear to be less resistive to oxidative stress than is human milk. This is noteworthy since formulas always have considerably more vitamin E and vitamin C, considered to be two of the more important antioxidants, than are found in human milk. Some have suggested that the attainment of adult levels of some antioxidants during infancy is dependent on human milk feeding [16].

Health Benefits of Human Milk

The health benefits of human milk are significant. Breastfeeding protects against a wide variety of illnesses, particularly the incidence and severity of diarrhea, otitis media, upper respiratory illnesses, botulism, and necrotizing enterocolitis [14, 25]. Prior to advancements in hygiene, infants who were not breastfed did not fare well and mortality rates could be as high as 90% [4, 14]. Even with the use of current formulas, breastfed infants have lower incidences of many illnesses and are generally sicker for shorter times than formula-fed infants [26]. Previous work demonstrated that later in life breastfed infants have decreased risk of diabetes, cancer, and cardiovascular disease [26]. However, the recent results from the National Longitudinal Survey of Youth (NLSY) showed that longer duration of breastfeeding may not necessarily lead to long-term healthier childhood and well-being [27].

The most practical measure of overall infant health and well-being is growth. One would expect that with all the advantages of human milk, a breastfed baby would gain more weight. It is a puzzling phenomenon that growth of the exclusively breastfed infant is lower in weight-for-age than a formula-fed infant. Likely there is more energy intake by a formula-fed infant. However, the relevance of less growth in breastfed infants is questionable as no negative effects on functional outcomes have been observed. We found infants who had consumed home-made formulas of evaporated milk grew more than either formula-fed or breastfed babies [28], yet they did not perform as well as breastfed infants on tests of visual function [29].

There is controversy in the area of cognitive development as it is difficult to carry out the ideal study. Breastfed infants appear to have enhanced cognitive and neurological outcomes in comparison to formula-fed infants [30]. Small differences have been seen even in later childhood [30]. Increased duration of breastfeeding is associated with higher verbal IQ scores. In addition, increasing the period of exclusive breastfeeding appears to enhance infant motor development [31]. We found enhanced visual acuity in full-term breastfed infants compared to formula-fed infants which was related to blood fatty acid levels [29]. The explanation for these consistent observations is highly controversial. Possibly, there are components of human milk that enhance cognitive development. Other factors that may be responsible are the act of breastfeeding itself, maternal education, and social class.

A paper by Allan Lucas [30] reporting improved neurological development in breastfed infants sparked a major debate on which factors really explained increased cognitive development. It is reasonable to assume that the long-chain polyunsaturated fatty acids, enzymes, hormones, trophic factors, peptides, and nucleotides present in breast milk may enhance brain development and learning ability. Further, it would be sensible to feed human milk whenever possible if any or all of the above differences turn out to be true. Whether a breastfed infant has better development because of maternal factors or biological factors does not lessen the value of enhanced development to the infant.

Transition to Solid Foods

During the second 6 months of infancy, breast milk no longer meets all the nutritional needs of the infant. Solid foods should therefore be introduced. However, continuation of breastfeeding is recommended for the first year of life and can be continued until the mother and infant decide to cease. The introduction of solid foods is known as complementary feeding. A proper transition between a liquid diet and a diet with solids is crucial for the development of infants. The WHO gives four goals of complementary feeding: it should be timely, adequate, safe, and properly administered [32].

The timely introduction of complementary foods should begin at 6 months of age. Most infants start consuming complementary foods at 3–4 months. Early introduction of complementary foods was once believed to promote a healthy appetite, food acceptance, and a full night of sleep; however, those theories have been discredited. Delaying the introduction of solid foods till 6 months and thereby extending formula or breastfeeding has been shown to decrease gastrointestinal infections and morbidity rates in infants [14, 26]. Delaying complementary feeding allows for the infant to gain more benefits from breast or formula feeding.

Complementary foods need to meet the infants' growing nutritional needs. These foods need to be nutritionally adequate to provide enough energy, macronutrients, and micronutrients to support normal development [32]. Traditionally, the first solid foods a baby consumes are cereals and other grain-based products. Fruits and vegetables are normally the next food groups introduced, with meats and other protein-rich foods being introduced later. Breast milk is a poor source of iron and zinc; the ideal complementary food would be rich in both of these micronutrients. Some have suggested that iron-rich foods like meat should be one of the first solids consumed [33]. Currently, meats are not consumed regularly until 7–8 months of age, with other food groups starting at 4–6 months.

The physical act of feeding is important to a developing infant. As they age, infants become more aware of feeding methods and eventually learn how to self-feed by mimicry. Development of gross and fine motor skills is encouraged through self-feeding. Formation of emotional connections with other people is facilitated through feeding. Many of the infant's attitudes about food, hunger, and appetite can be affected by the type of relationship the infant forms with his or her feeder. The frequency of feedings should start with 2–3 meals a day from 6 to 8 months and then increase to 3–4 meals per day to the end of toddlerhood. Feeding should promote a positive correlation with food, appetite, hunger, and emotional relationships. Food safety is also a concern for infant nutrition. Food must be prepared in a hygienic environment including clean water, utensils, and storage facilities for the food.

The proper transition to solid foods is key to the growth and development of infants. The type of foods and feeding methods presented to the infant have an impact on food preferences and future eating habits [34]. There have been correlations made between unbalanced diets in infancy and being overweight or obese later in life [35]. The protein content of the infant's diet is of concern for obesity risks. Diets high in protein in infancy have been shown to be associated with obesity in childhood. A balanced amount of all the macronutrients and micronutrients is critical to the health and growth of the infant. Stunting is often the result of inadequate micronutrient intakes and can result in growth and developmental retardation.

Summary

There is no doubt that human milk is the best food for a human infant. The reasons are endless and convincing. However, it is a challenge for the formula industry to make the best alternative to human milk. There are, were, and always will be some women who are unable or choose not to follow recommendations to breastfeed for whatever reason. We have a responsibility to those mothers and their

infants to produce a formula that meets their needs. Future changes in infant formulas are likely to be designed to have a positive effect on physical, mental, and immunological outcomes. Our hope is that formula will include bioactive ingredients that perform some of the same functions found in that exemplary fluid, human milk.

When breast milk is no longer adequate, the correct approach needs to be taken for complementary feeding. Incorporating the themes of timely feeding, nutritionally sound and safe meals, and properly administering meals into complementary feeding will prompt appropriate development and growth [33]. The importance of proper complementary feeding practices is not normally stressed; however, several incentives have been proposed to address the current practices. The lengthening of exclusive breastfeeding to 6 months and delaying complementary feeding until then is recommended for the majority of infants. Benefits for this are similar to the benefits of breastfeeding. Molding the infant's diet to include appropriate amounts of micronutrients, especially iron and zinc, is a primary concern for parents. A suitable transition to a diet of solid foods sets the pace for the rest of the infant's life.

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