

Review on Key Features of Infant Feeding: Human Milk and Infant Formula

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Abstract

Human breast milk (HBM) is the finest source of nutrition for almost all infants. Breast milk as a bodily fluid has many benefits beyond somatic cell growth, including regulation of postnatal intestinal function, immune ontogeny, and brain development. However, breastfeeding is strongly recommended, breastfeeding may not always be possible, suitable or solely adequate¹. Hence, Infant formula is often an alternative source of infant nutrition when breastfeeding is unacceptable or impossible. The composition of infant formula should be as close as possible to the composition of human breast milk, both in terms of content and chemical specification². Infant formulas try to mimic the nutritional composition of breast milk as closely as possible. A number of substitutes to milk-based formula also exist. In this article, we review nutritional information for breast milk and infant formulas to help you better understand the importance of breastfeeding and the use of infant formulas up to 24 months of age when alternative feeding is required. In general, breast milk is the ideal food to ensure that an infant's nutritional needs are met.

Keywords: breast milk; infant formula; type of infant formula; benefits

1. Introduction

Milk is important for babies. For a newborn child, breast milk is the preferred food to nourish a daily requirement for growth and development. There is no supreme composition of human milk and also no easy way to control the complexity of its nutritional quality and the quantity received by breastfed infants³. However, when breastfeeding is not a possibility, infant formula (IF) is the best alternative⁴.

Infant growth chart (weight, head circumference, size) and neurodevelopment criteria is referred by pediatricians and nutritionists to reflect the food that these infants receive. These graphs initially reflect infant physiology and may reflect the composition of breast milk when infants are breastfed. In preterm infants, maternal

physiology partially influences the composition of breast milk. This explains why it is more difficult to correlate infant growth and neurological development with milk composition. Several biomarkers (lipids, oligosaccharides) have been recognized in breast milk, but their roles are not always understood. For better understanding on how human milk could act on infant growth to the mid- and long-term participating thus to nutritional programming is a challenging question for a better management of infants' nutrition, especially for preterm infants who are most fragile³.

Mother's breast milk is considered the gold standard in infant nutrition. Due to its unique

composition, which is individually adapted to the child's needs, it is highly recommended that infants be exclusively breastfed for at least 6 months. Such positions, particularly endorsed by the American Academy of Pediatrics (AAP) and the American Academy of Family Physicians (AAFP), emphasize that breastfeeding reduces the risk of late-life illness⁵. Gregg et al. [4] specify that lactation is the period in which the baby's health is mainly dependent on the mother's milk, and its components influence the baby's metabolic programming⁶. In addition to sufficient amounts of energy and nutrients required for proper growth of young organisms, it also comprises several efficient ingredients with bioactive effects⁷. These ingredients stimulate the immune system, prevent infections in the body, and have a significant impact on the health of newborns⁸. The bioactive constituents of breast milk include proteins, oligosaccharides, polyunsaturated fatty acids (PUFAs), fat-soluble vitamins, hormones, growth factors or probiotics⁹. Lipids play a distinct role in the development of a young organism. During the first month of life, newborns get about 50% of their energy from fat. Thus, lipids are not only an energy source, but also a very important for structural function of the brain and nervous system during this period¹⁰. Breastfeeding is universal and the most precise form of nourishing to the infants up to 6 months of age.

When breastfeeding is not conceivable, alternative sources of nutrients are required for infant. Human milk is significantly different from cows' milk, both in terms of macronutrients and micronutrients. Cow milk comprises high level of proteins and minerals which obstructs digestion. Further, iron, vitamin C and some fats that important for growing babies are not available in cow milk. For this motive, cow milk should not be consider as the main drink before 12 months of age. However, minor volumes may be added to complementary foods¹¹

The choice to breastfeed is highly personal and is often influenced by many aspects. Under certain circumstances, breastfeeding might not be

conceivable, unsuitable or inadequate, which permits an interruption or cessation in breastfeeding. Commercial infant formula is usually used as a nutritional supplement for babies or as a complete breast milk substitute. Infant formulas must be properly formulated to provide adequate nutrition for optimal growth. Milk based or soymilk are most usually used as the base, with supplemental elements added to obtain better approximate the composition to human breast milk and to get health benefits, including iron, nucleotides and compositions of fat blends. The fatty acids of arachidonic acid (AA) and docosahexenoic acid (DHA) are added. Probiotics and compounds, produced by genetic engineering, are either added or currently being considered for addition to formula¹.

Optimal nutrition is very important in the first six months of life for the infants, as nutritional deficiencies can have very serious consequences. The purpose of this article is to review nutritional information on human milk and infant formula and to emphasize the importance of breastfeeding while understanding the use of infant formula.¹

2. Human Breast Milk

Breast milk contains carbohydrates, proteins, fats, vitamins, minerals, digestive enzymes and hormones. In addition to these nutrients, it is rich in immune cells, including macrophages, stem cells, and many other bioactive molecules. Some of these bioactive molecules are derived from proteins and lipids, while others, such as oligosaccharides, are derived from proteins and are indigestible. Human milk oligosaccharides (HMOs) fill the infant's gastrointestinal tract with decoys that bind and keep pathogens away from the intestinal wall and possess anti-infective properties against pathogens in the infant's gastrointestinal tract such as Salmonella, Listeria and Campylobacter [9]. Oligosaccharides also play a key role in the development of a diverse and balanced microbiota that is essential for proper innate and adaptive immune responses,

helping to colonize up to 90% of the infant biome¹².

a. BREASTFEEDING

For both mother and child, breastfeeding can be a wonderful experience. It offers the best nutrition and a unique opportunity for bonding that many mothers treasure. Breastfeeding is advised as the best option for infants by a variety of medical organizations, including the American Academy of Pediatrics (AAP), the American Medical Association (AMA), and the World Health Organization (WHO). Breastfeeding aids in the prevention of allergies, infections, and a number of chronic diseases. Mother milk is the greatest food for the newborn baby¹⁰

Exclusive breastfeeding is normal but not always simple; when there is a problem, such as a delay in the milk supply arriving, inverted nipples, or insufficient milk supply, babies may experience problems. It's not always simple for women who don't have a lot of family or medical assistance, particularly for first-time mothers who feel overburdened, experience sore nipples, and fear that their infants aren't eating enough. Breastfeeding works best when moms have a supportive work environment, as well as a competent and nurturing community to assist them work through the inevitable concerns and issues, but not all mothers have these resources³.

b. Composition of Human Breast Milk

Human breast milk is a complex matrix with a typical composition of 87% water, 3.8% protein, 1.0% protein and 7% lactose. Fat and lactose provide 50% and 40% of the total energy in milk, respectively. Human milk also comprises many minerals (Calcium, Magnesium, Phosphorus, Sodium, Potassium, etc...) and several vitamins. However, the composition of breast milk is dynamic and changes over time to adapt to the changing needs of a growing child. For example, during each feeding, the first milk expressed

(colostrum) is thin, has a high lactose content, and quenches your baby's thirst. Also, the hindmilk after the foremilk is creamier and has a much higher fat content for the baby's needs.

There are also differences related to the stage of lactation (infant's age), maternal diet, maternal health, and environmental exposure. The protein content of breast milk during early lactation ranges from 1.4–1.6 g/100 mL, to 0.8–1.0 g/100 mL at 3 to 4 months, and 0.7–0.8 g/100 mL after 6 months. Becomes¹³. Fat content varies greatly with maternal diet and is also positively correlated with weight gain during pregnancy. Of note, it has been observed that mother's breast milk contains essential nutrients that are almost always sufficient for the growth and development of term infants, even when the mother's own diet is inadequate. The average concentrations of protein, sodium, chloride, and potassium in breast milk of preterm infants are sufficient to meet the estimated requirements of preterm infants, but breast milk of preterm infants requires special nutritional supplementation¹⁴.

In contrast to protein and fat, the lactose content in mature milk (21 days old) is fairly constant. A stable lactose concentration is important to keep the osmotic pressure of milk constant. Lactose also supports the absorption of minerals and calcium. In breast milk, many carbohydrate-based bioactive compounds such as oligosaccharides are bound to lactose. If the small intestine does not produce enough enzyme (lactase) to digest these sugar complexes, lactose malabsorption and intolerance syndrome may be observed. Malabsorption due to lactase deficiency Also, illness is very rare in exclusively breastfed infants.

c. Breastfeeding Challenges

Some moms find breastfeeding to be simple right away, while others find it difficult to adjust to at first. To become accustomed to the rhythm of

nursing, mothers and babies need to be very patient.

In particular, during the first several weeks and months, new mothers frequently worry about:

- **Individual comfort.** Many mothers initially find breastfeeding painful. But most mothers can overcome this with the right training, encouragement, and practice.
- Within the first week to 10 days, latch-on soreness is typical; it should subside after less than a minute with each feeding. Nonetheless, it is advisable for breastfeeding women to seek assistance from a lactation consultant or their doctor if breastfeeding hurts during feedings or if their nipples and/or breasts are uncomfortable. Most of the time, it's only a matter of employing the right method, but pain might occasionally indicate the presence of another condition, such as an infection.
- **Feeding duration and frequency.** Mothers must devote a significant amount of time to breastfeeding, especially in the beginning when babies eat often. Some mothers may find it more difficult to work, conduct errands, or travel due to a breastfeeding schedule or the need to pump breast milk throughout the day.
- Also, because breast milk digests more quickly than formula, breastfed babies do need to eat more frequently than formula-fed ones. In the first few weeks, mom can find herself in demand every two to three hours (or possibly more or less).
- **Diet.** Women who are nurturing need to be alert of what they eat and drink, since these can be passed to the baby through the breast milk. Breastfeeding mothers should avoid eating fish that is rich in mercury and should limit their intake of fish that is lower in mercury.
- A tiny amount of alcohol consumed by a mother may be transferred to the infant through breast milk. To prevent giving alcohol to the child while nursing, she should wait at least two hours after consuming one

alcoholic beverage. Because it can make some babies irritable and restless, caffeine consumption should be limited to no more than 300 mg (about one to three cups of ordinary coffee) daily¹⁰.

d. Nutrient composition

Macronutrients

As is well known, HBM contains approximately 87-88% water and also solid components such as macronutrients such as carbohydrates, proteins and fats. Mature milk typically contains 65-70 kcal of energy per 100 ml, with approximately 50% fat and 40% carbohydrates of the total caloric intake¹⁵.

However, unlike infant formula, which has narrow composition guidelines and is based on strict criteria for health effects on infants, the nutritional composition of HBM is dynamic for several reasons¹⁶.

The composition of HBM depends on maternal diet, mammary gland physiology, maternal health, and many other environmental factors. In addition, it also depends on whether the baby is foremilk, hindmilk, or breastfed for premature birth. Whether it is colostrum, transitional milk or mature milk, it may vary depending on processing conditions such as storage, pasteurization and packaging¹⁷. Foremilk produced by the mammary glands is relatively lean and increases with lactation, whereas hindmilk is fatty. There is no significant difference in protein and lactose content. Colostrum is low in fat, high in protein (10%), and relatively high in immunoprotective components such as immunoglobulin A (IgA) and lactoferrin, which help prevent neonatal infections.

1) Carbohydrates

Carbohydrates are the macronutrients of HBM and play important roles in infant nutrition,

development of physiological function throughout the gastrointestinal tract from birth, and maintenance of gut microbiota composition¹⁸. Most people get their carbohydrates in the form of glucose, but infants whose gastrointestinal tract is not yet developed get their carbohydrates in the form of lactose. Lactose is therefore the main carbohydrate component of her HBM and the most abundant nutrient in breast milk. Lactose is digested by lactase-phlorizin hydrolase (also called lactase) present on the apical surface of intestinal brush border enterocytes. Lactose is readily digested by almost all infants. However, enzyme deficiencies can lead to a variety of conditions, such as lactose intolerance and malabsorption. In contrast to protein and fat, colostrum contains relatively constant levels of lactose over long periods of time.¹⁹

A constant level of lactose is vital for keeping a constant osmotic pressure in HBM. In addition, carbohydrate-based bioactive components, such as oligosaccharides, are attached to lactose; this helps in the absorption of minerals and calcium.¹⁵ The levels of free glucose and other glucose metabolites in HBM are low; thus, their nutritional significance is negligible in infants.²⁰

2) Protein

Proteins are key elements that maintain the function and organization of all cells in the human body, and an adequate supply of proteins is essential for growth, development and function. The proteins in HBM are composed of whey and casein, and a mixture of various peptides. Casein is micellar and forms lumps or curds in the stomach and does not dissolve easily. Whey is in liquid form and is easily digested.¹⁵ The ratio of whey to casein depends on when the milk is produced. In colostrum, the whey/casein absolute ratio is almost 90:10, but in mature milk this gradually changes to 60:40.

However, the percentage of whey in HBM is relatively higher than that in infant formula

(approximately 20%).^{11, 35}. The protein content in HBM is around 14–16 g/L at birth, but decreases to 8–10 g/L at 3–4 months of birth and further decreases to 7–8 g/L after 6 months.

The protein concentration of HBM is not significantly affected by maternal diet but increases with maternal body weight for height. Depending on the stage of breast milk, 80% to 50% of the protein in breast milk is whey. The whey/casein ratio in breast milk varies between 70/30 and 80/20 during early lactation and decreases to 50/50 during late lactation.

This proportion is significantly higher than in other mammalian milks. In milk, whey protein accounts for only 18% of milk protein. Infant formula traditionally contains high levels of casein. Hence, it is more difficult to digest than breast milk. Casein and whey proteins have different amino acid profiles, so the overall amino acid profile of breast milk varies at different stages of lactation. Glutamine, the most abundant free amino acid, is almost 20-fold higher in mature milk than the lowest levels in colostrum¹⁶.

Glutamine is essential for providing ketoglutaric acid for the citric acid cycle, possibly serve as a neurotransmitter in the brain, and helping as a major energy substrate for intestinal cells.

The major whey proteins are alpha-lactalbumin, lactoferrin, and secretory IgA. Other proteins include lysozyme, folate-binding protein, bifidus factor, casein, lipase and amylase, alpha-antitrypsin and antichymotrypsin, and haptocorrin. These proteins are broken down into free amino acids as soon as they are ingested and are absorbed and utilized. Most of these proteins also have bioactive and non-nutritional functions¹⁷. For example, alpha-lactalbumin is essential for the synthesis of lactose and the binding of Ca and Zn ions. Casein helps increase calcium and phosphorus. Lactoferrin and lysozyme prevent the spread of potentially pathogenic bacteria, thereby preventing infant

illness. IgA antibodies destroy bacteria and protect the intestinal mucosal surface.

3) Fat

In HBM, fat is the second largest macronutrient and plays the most important role in infant nutrition (almost 50% of total energy content) and central nervous system development. Colostrum contains 15–20 g/L of fat, but this amount increases over time, with mature milk containing almost 40 g/L. Its levels are two to three times higher in hindmilk than in foremilk.²¹ The main component of HBM fatty acids is triglycerides (approximately 95-98%) and also contains two essential fatty acids, linoleic acid and alpha-linolenic acid.

Linoleic acid and alpha-linolenic acid are precursors of arachidonic acid and eicosapentaenoic acid (EPA) respectively, the latter is further converted to docosahexaenoic acid (DHA), and cannot be synthesized in the human body.

In addition, they are important for inflammatory responses, immune function, and growth as components necessary for the generation of in vivo signal transduction and components of the nervous system and retina.

Fats in HBM are more readily digested and absorbed than fats in infant formula due to the presence of bile salt-stimulated lipase that complements pancreatic lipase and the presence of palmitic acid at the sn-2 position of breast milk triglycerides.²² This position preference has not been well documented in infant formula and influences the infant's plasma lipid profile, including cholesterol concentrations.²³ The fat content of HBM is closely related to maternal diet and weight gain during pregnancy. In addition, there are regional differences in food intake.

Trans fat may be present in HBM when lactating mothers consume foods such as bread, snack

foods, fast foods, and margarine, which account for up to 7.7% of total fat. Concentrations of trans fat vary by region, adversely affect infant growth and development, and are inversely correlated with linoleic and alpha-linolenic acids.²⁴

Arachidonic acid is also correlated with arachidonic acid-rich dietary intake in lactating mothers, and EPA and DHA are also closely related. Therefore, vegetarians have very low DHA in their milk because of the lack of fish or other foods in their diet. Therefore, it is recommended to take up to 300 mg of DHA per day to maintain sufficient amount of DHA in breast milk.²

Fat is the most important component of breast milk, providing energy and supporting central nervous system development. In addition, milk fat is a flavor and aroma carrier. In general, the fat content of breast milk of a lactating human is in range of 3.5%-4.5%.

The major lipid moiety is triglycerides, accounting for approximately 95% of total lipids. Nearly half of milk fatty acids are saturated, with palmitic acid (C16:0) accounting for 23% of total fatty acids. The monounsaturated fatty acid oleic acid (18:1w9) is found in the highest proportion (36%) in milk.¹

Human breast milk also contains two essential fatty acids, 15% linoleic acid (C18:2w6) and 0.35% of alpha -linolenic acid (C18:3w3). These two essential fatty acids are converted respectively to arachidonic acid (AA, C20:4w6) and eicosapentaenoic acid (EPA, C20:5w3), the latter of which is further converted to docosahexaenoic acid (DHA, 22:6w3). AA, EPA, and DHA are important for neonatal growth, inflammatory response, immune function, vision, cognitive development, and regulation of the motor system.¹

Long-chain polyunsaturated fatty acids are transferred from the mother to the fetus through the placenta during the third trimester of

pregnancy and to the infant through breast milk after birth²⁵. During late pregnancy and the neonatal period, brain tissue is synthesized rapidly.

Cell differentiation and development of active synapses in the brain need specific requirements of DHA and AA. Eighty percent of brain DHA is acquired from the 26th week of gestation until birth. Notably, the synthesis of AA and DHA from linoleic acid (18:2w6) and alpha-linolenic acid (18:3w3) is limited in the fetus and neonate due to the premature enzyme activity.

Therefore, the required amount of AA and DHA must be supplied by the mother during pregnancy or in breast milk after delivery. Studies have shown that the fat content and proportion of all polyunsaturated fatty acids in breast milk increases significantly between the 6th week and 6th month of lactation²⁶.

There is evidence that slowly turning-over maternal body pools of AA are the major source of milk AA [21]. The AA concentration in breast milk is dose-dependently associated with the consumption of AA-rich foods in lactating mothers²⁷.

EPA and DHA concentrations in breast milk are also closely related to maternal dietary EPA and DHA intake. It is believed that an intake of approximately 300 mg of DHA per day is required to reach DHA levels of 0.3-0.35% in breast milk²⁸. However, the effects of breast milk fatty acids on neurodevelopment are complex, especially as neurodevelopment is assessed after the first six months of her exclusive breastfeeding.

In premature birth, the transmission of these fatty acids is interrupted from the placenta to the fetus during the critical last trimester. Studies also showed that decreased postnatal docosahexaenoic and arachidonic acid blood levels in premature infants are associated with neonatal morbidities²⁹.

Therefore, premature infants require proper postnatal nutrition to obtain adequate fatty acid levels. Adding her DHA and AA to formula for preterm infants initially had beneficial effects on visual acuity, visual attention, and cognitive development compared to infants who did not receive supplements.

e. Vitamins and minerals

HBM is affected by the diet of lactating women, but in most cases HBM contains sufficient vitamins to ensure normal infant development. However, exclusively breastfed infants may be deficient in vitamins D and K and may require supplementation. Vitamin D is influenced by maternal diet related to climate, season, latitude, skin color and lifestyle, as well as sun exposure. HBM typically contains less than 1 mg or less than 40 IU/L of vitamin D, which is not sufficient to meet the needs of infants. Breastfed infants can receive vitamin D from HBM synthesized by sunlight exposure in lactating mothers or stored during pregnancy. However, the stored vitamin D is rapidly depleted in infants. The Korean Nutritional Society and American Academy of Pediatrics recommend lactating mothers and infants to take vitamin D supplements of 200–400 IU per day in maintenance doses and 2,000 IU/day in deficiency.³⁰

A limited amount of vitamin K is also transferred from the mother to the fetus, so vitamin K deficiency can develop in newborns. Therefore, vitamin K supplementation is recommended after childbirth. Water-soluble vitamins are also strongly influenced by maternal condition. In general, malnourished mothers may be deficient in vitamins B6, B12 and folic acid, but may still have relatively adequate levels of thiamine and riboflavin. More than 20 minerals have been identified in HBM, including iron, copper and zinc, most of which are abundant in colostrum but decrease as lactation progresses.³¹ Unlike vitamins, most minerals are largely unaffected by the maternal condition and do not differ

significantly among maternal nutritional supplements.

The mineral content is lower in HBM than in infant formulas, but due to their high bioavailability, no additional supplementation is required during full breastfeeding. In particular, iron content is 0.5–1.0 mg/L in colostrum and 0.3–0.7 mg/L in mature milk, but its bioavailability is 20%–50%, which is more effective than in infant formula (4%–7%). Therefore, in exclusively breastfed infants, it is generally not necessary to supply iron before 4–6 months of age, and then, it is recommended to supply gradually through iron-enriched solid foods.²

Breast milk contains most vitamins in sufficient amounts to support normal infant growth, with the exception of vitamin D and vitamin K. Exclusively breastfed infants consume less than the recommended minimum intake of vitamin D and much less than the recommended dietary intake. These infants are at risk for diseases such as vitamin D deficiency, lack of bone mineralization, and rickets. However, the overall risk of vitamin D deficiency in breastfed infants is also correlated with overall sun exposure with increasing risk in climates with a lower sun index. Maternal supplementation with 400–2000 IU (International Unit) of vitamin D/day can increase the levels of vitamin D in breast milk, but only a higher dose (2000 IU) achieves satisfactory levels of 25-OH-D in the infant. Normal stores of vitamin D present at birth are depleted within 8 weeks. Sun exposure and vitamin D supplementation are recommended for breastfed infants. Formula-fed infants often have higher serum concentrations of vitamin D metabolites than breast-fed infants. Vitamin K is important as a protein involved in blood clotting. However, only a limited amount of vitamin K is transferred from the placenta to the fetus. Therefore, newborns often have very low vitamin K levels and are at risk of developing bleeding disorders. Vitamin K supplementation is recommended after childbirth.¹

In human breast milk, minerals contribute to a variety of physiological functions, forming essential parts of many enzymes and are of biological importance to molecules and structures. The contents of minerals are comparable between human milk and bovine milk. Many other bioactive components in breast milk have been identified over the decades, including hormones, growth factors and immunological factors.¹

f. HBM components in prematurity infants

Premature babies can experience a variety of problems compared to full-term babies. Nutritional attention and sufficient supply are needed because the risk of growth failure, neurodevelopmental delay, sepsis, and gastrointestinal problems, such as necrotizing enterocolitis, is higher. In addition, deficiency-related complications can occur due to the lack of provision of various nutrients that are transferred from the placenta to the fetus in late pregnancy³².

Even in this case, HBM plays a primary role as an enteral diet. However, HBM in mothers feeding premature infants differs from HBM in mothers feeding term infants. Protein content and bioactive components tend to be richer, with more fat, free amino acids, and sodium in the preterm³³. However, as lactation progresses, these components tend to gradually decrease. Copper and zinc are also higher in the HBM of mothers feeding preterm infants and gradually decrease with breastfeeding, whereas calcium is low in preterm infants and gradually increases with breastfeeding³⁴. Most other minerals have comparable levels at preterm and full term. Lactose is present in small amounts in colostrum and increases as lactation progresses, but is more abundant in preterm milk³³. In addition, lactase in the small intestine is not formed and secreted until 32 weeks of gestation, so it is difficult for premature infants born before 32 weeks of gestation to digest breast milk. HMOs vary in the overall content depending on genetic diversity and the content of fucosylated HMOs.³⁵⁻³⁶

Differences in the content of bioactive molecules, such as growth factors and lactoferrin, between colostrum and early mature milk are greater between HBM mothers with preterm birth and HBM mothers with full-term birth. Donor milk or fortification can be used to compensate for the lack of mother's own milk for long-term growth and prognosis of preterm infants.³³

g. Hormones and growth factors in HBM

Hormones and growth factors in HBM also serve as various bioactive proteins and peptides. The role of hormones in HBM such as parathyroid hormone, insulin, leptin, ghrelin, apelin, nesfatin-1, obestatin, and adiponectin and their effects on infants are poorly understood. Conversely, many growth factors have been relatively extensively studied and are known to have diverse effects on the intestinal tract, vascular, nervous system, and endocrine systems¹⁵. Epidermal growth factors play a critical role in intestinal maturation and repair. Their levels in colostrum are 2,000 times higher than in mature milk and decrease with lactation. Brain-derived neurotrophic factor and glial cell-line-derived neurotrophic factor act on the enteric nervous system and are necessary for the development of immature intestine in infants.³⁷

3. Infant Formulas

a. Formula Feeding

Formula feeding is also a healthy choice for little one. If you use a formula, your little one will get the best possible substitute to breast milk. (You should not try to make your own formula or feed an infant cow's milk or another kind of milk.)

Many mothers preferred formula for a variety of reasons:

- It's easy and convenient. Formula-fed babies can be fed by anyone at any time.
- It's flexible. You don't have to fit pumping into your work schedule. Instead, you can

simply leave formula for your babysitter or day care center.

- Your partner can help out with nighttime feedings and share that bonding experience with your baby.
- Scheduling feedings may be easier. Formula isn't digested as quickly as breast milk, so formula-fed babies don't need to eat as often, especially in the first few months.
- You don't have to worry about what you eat. Moms who breastfeed may have to avoid certain foods that their baby can't tolerate.
- You can have a glass of wine or a cocktail once in a while. Alcohol is a no-no for women who breastfeed because they pass on tiny amounts of it to their babies.

Infant formula is intended to be an effective substitute for breast milk and is formulated to mimic the nutritional composition of breast milk. The recently updated FDA (Food and Drug Administration) rule on current Good Manufacturing Practices for infant formula, 21 CFR 106.96 [6], requires, among other things, that formulas satisfy the quality factors of normal physical growth and a sufficient biological quality of protein component (adequate amounts of protein in a form that can be used by infants). Infant formula is intended only for the health of infants with no medical or nutritional abnormalities. The manufacturing process is highly regulated and monitored to meet national and international quality standards³⁸

b. Guidelines for Manufacturing of Infant Formula

Infant formulas must comprise proper level of water, carbohydrate, protein, fat, vitamins and minerals. The composition of infant formula is strictly regulated, and each manufacturer must follow established guidelines set by government bodies. For example, every major ingredient (protein, fat, carbohydrate) added to a formula has a set of minimum and maximum potency levels. A safe usage history must be available for these components³⁹

The required level of each nutrient must be maintained throughout the shelf life of the product⁴⁰. For amino acids, only L forms of amino acid are permitted to be added, while D forms are not allowable because they may cause D-lactic acidosis⁴¹. Fructose should be avoided due to fructose intolerance. Hydrogenated fats and oils are also not allowed. Ionizing radiation of the formula product is not permitted because it could cause product deterioration.⁴⁰ Furthermore, product reformulation must be based on medical and nutritional findings. The committee of the “Evaluation of the addition of Ingredients New to Infant Formula” has recommended that “manufacturers must demonstrate that the formula containing the new ingredient is capable of sustaining physical growth and development over 120 days when formula is likely to be the sole source of infant nutrition”.

c. Classes of Infant Formula Products

There are three main classes of infant formula: milk, soy formula and specialty formula. This formula varies in nutritional value, calories, taste, digestion and cost. Specific types of formulas are available to meet different needs. Some milk substitutes are amino acid-based or contain extensively hydrolyzed whey or casein proteins. There is also a rice-based formula.¹

1. Milk-Based Formula

Bovine is the basis of most infant formulas. However, compared to human breast milk, animal milk contains a higher proportion of fats, minerals and proteins. Therefore, milk should be defatted and diluted to more closely match the composition of human breast milk³⁹⁻⁴⁰. Milk-based infant formulas contain vegetable oils, vitamins, minerals and iron that most healthy adult infants can consume.

According to the American Academy of Pediatrics, children under the age of 1 should not be given raw, unprocessed, or unpasteurized animal milk in place of breast milk or infant formula. In addition, unfortified animal milk does not provide adequate amounts of vitamin E, iron and essential fatty acids. Additionally, an

infant's body cannot tolerate the high levels of protein, sodium, and potassium found in unprocessed animal milk. Formulas with a protein content 2–2.5 g/100 mL and a protein/energy ratio <3 g/100 kcal are used for normal infants, while with higher protein content (2.9 g/100 mL) and higher protein/energy ratio (3.5 g/100 kcal) are for a very low birth weight or preterm infants⁴². A recent study showed that high protein in infant formula was associated with excessive weight gain in infancy and could be associated with a 20% increased risk of obesity later in life.⁴³

2. Soy-Based Formulas

Soy protein formula is an effective option for infants with galactosemia or congenital lactase deficiency. These can help with colic and cow's milk allergy, but infants who are allergic to cow's milk may also be allergic to soy milk in rare cases. Soy products should not be used in infants under 6 months of age who have food allergies. Because phytoestrogens are present in soy-based formula, the uses of soy-based formulas are limited by the concern of potential harm for the infant, although this remains controversial⁴⁴⁻⁴⁵

3. Hypoallergenic Formulas

Protein hydrolysate formulas are intended for infants and babies who are unable to tolerate cow milk or soy-based formulas. They contain protein that has been hydrolyzed—partially or extensively—into smaller sizes than those found in cow or soy-based products. For infants who have a protein allergy, extensively hydrolyzed formulas are a satisfactory alternative.¹

4. Amino Acid Formulas

Amino acid formulas are another option for infants who have severe cow milk allergy with reactions to or refusal to ingest appropriate amounts of extensively hydrolyzed formula. They provide protein in the form of free amino acids with no peptides.

d. Non-Bovine Milk Sources

Elimination of all cow milk products without appropriately modified and fortified substitutions can lead to malnutrition and/or specific nutrient deficiencies at a time when infants and children are growing. Infant milk formulas from different animals (goat, ewe, mare, donkey, or camel), or formulas based on lamb or chicken, have been widely marketed as substitutes for cow milk in the management of cow milk allergy in infants and children. However, other animal-milk-based formulas are currently not acceptable in many places because there are no robust randomized clinical trials.

e. Probiotics and Prebiotics

The high concentrations and structural diversity of breast milk oligosaccharides are unique to humans. Without probiotic and prebiotic supplementation, the gut microbiota of formula-fed infants is generally not dominated by Bifid bacterium species. Studies have shown that breastfed neonates have a more stable and consistent oligosaccharide population compared to formula-fed neonates⁴⁶. Adding probiotics to the formula reduces incidence and Severity of diarrhea in infants⁴⁷.

f. Fatty Acids and Milk Fats from Different Mammalian Species

The lipid portion of human milk is the major source of energy for growing infants and provides approximately 45% to 55% of total energy. The lipid compositions of mammalian milks (cow, buffalo, donkey, sheep, and camel) were compared with that of human milk on fatty acid profiles and triacylglycerol (TAG), phospholipid, and phospholipid fatty acid compositions, as well as melting and crystallization profiles⁴⁸. The results showed that these milk fats, especially sheep milk fat, had high degrees of similarity to human milk fat in total fatty acid composition. However, other chemical aspects had less similarity. This

outcome indicates that these milk fats do not meet the requirements of human milk fat substitutes, but large amounts of these commercialized mammalian milk fats are good raw materials for infant formula production. Milk fat globule membranes are a fraction that has been previously excluded from infant formulas, but its components are active and prevent infection⁴⁹. Milk fat globule membrane supplementation of infant formula also narrows the gap in cognitive development between breastfed and formula fed infants⁵⁰

g. Bioactive Proteins

Novel dairy fractions from bovine milk have been isolated and are now commercially available. Many of these components are proteins, such as α -lactalbumin, lactoferrin, osteopontin, and milk fat globule membrane proteins. When adding bioactive proteins to infant formulas, it is important to reduce the total protein content of formula. The amino acid composition of formula is also important; serum concentrations of essential amino acids should not be lower than those in breastfed infants. For example, α -Lactalbumin, often the first limiting amino acid in infant formulas, is digested into smaller peptides with antimicrobial and prebiotic activities and has an immunostimulatory effect. It also enhances mineral absorption. Osteopontin is a heavily phosphorylated and glycosylated protein that modulates immune function and stimulates Th1/Th2 switching. It might also affect bone mineralization and growth, and facilitate the biological function of lactoferrin.

h. Conclusions

Breast milk is the optimal food for infant growth and development and is also rich in antibodies, the first source of adaptive immunity in the neonatal intestinal tract. Breast milk is the first choice for preterm or low birth weight infants. If this is not available, donor milk is considered the next best choice. Infant formula is now the first choice for healthy newborns whose mothers

cannot produce enough breast milk or mother milk is not available.

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