

Macronutrients in infant nutrition

Infancy is a period of rapid growth and development, with a gain of approximately 25% in height and 50% in weight. During this period adequate nutrition is crucial for proper growth and development and even has an impact on long-term health. Human milk is known to fulfill all specific needs of infants during early life, it supports the maturation of the digestive tract and immune system and the development of a well-balanced gut microbiome. [1-3] Human milk is composed of macronutrients, micronutrients and bioactive factors. Macronutrients provide the primary nutritional source of energy, playing a vital anabolic role in building tissues and in infants' growth. [4, 5] These are grouped into proteins, carbohydrates, and fats. Infants who cannot be breastfed are reliant on infant formula and the macronutrient requirements in infant formula are strictly regulated. This white paper describes the different groups of macronutrients and their function in infant nutrition.



Human milk: the gold standard

Human milk is considered the most valuable form of nutrition for infants' growth and development. Human milk composition is dynamic, and varies within a feeding, between days, and over the lactation period, to match the specific infants' needs. The major components (macronutrients) of human milk are carbohydrates, followed by fats and proteins (Figure 1) [6, 7]. Each macronutrient has its own important functions in the infants' growth and development. The macronutrient composition of human milk varies within mothers and across lactation but is remarkably stable

across populations despite variations in maternal nutritional status [8]. The composition of human milk is the golden standard for the nutritional composition of infant formulas.

Carbohydrates

Mature human milk contains approximately 7% carbohydrates, with the majority being lactose. Lactose, also known as milk sugar, is a disaccharide and consists of a galactose and a glucose molecule. Lactose is an important source of energy for infants.

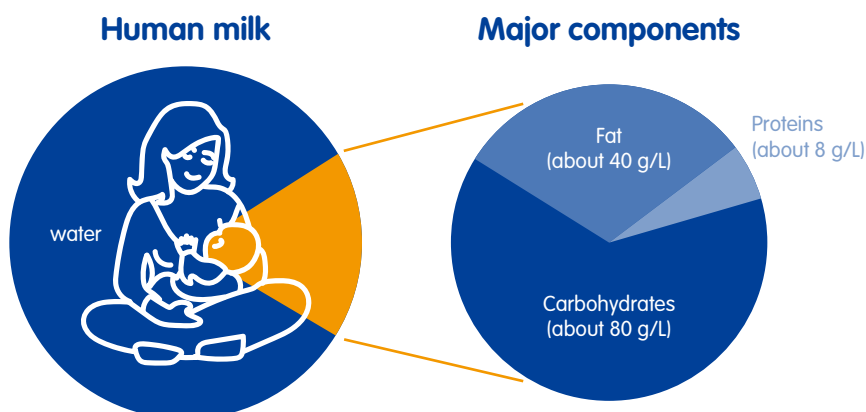


Figure 1 Macronutrient composition of human milk [3, 4]

The enzyme that breaks down lactose is called lactase. Lactase activity is the highest immediately after birth and in the majority of the population the lactase activity declines from childhood to adulthood to about 5-10% of the activity at birth [9].

The second largest group of carbohydrates in human milk are the oligosaccharides (HMOs). They are a structurally and biologically diverse group of complex indigestible sugars that consist of 3-10 monosaccharides. Currently, over 200 different HMOs are identified [10, 11] with 2'-fucosyllactose (2'-FL) as the most abundant human milk oligosaccharide, although this HMO is not secreted by all mothers. 2'-FL is also the most thoroughly studied HMO (for more detailed information see the whitepaper on HMOs -2'-FL). [12, 13] Recently 2'-FL and lacto-N-neotetraose (LNnT), and HMO mixtures have been added to infant formula. [14-16] Other HMOs are currently being studied.

Carbohydrates are ascribed to have different functionalities [17-23]:

- Provide the infant with energy
- Soften the infant's stools
- Assist in the absorption of water, calcium and sodium in the intestinal tract
- Assist in brain development
- Assist in the development of a healthy gut microbiome
- Antibacterial/antiviral by anti-adhesive properties
- Modulation of the immune system

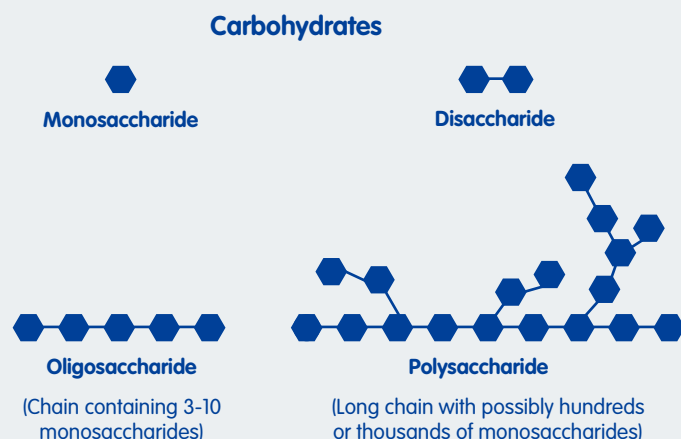


Figure 2 Types of carbohydrates

Lipids

The main difference between lipids and fats is that lipids are a broad group of biomolecules whereas fats are a type of lipids. Fat is stored under the skin and in the adipose tissue. It is mainly used as an energy-storage in the body. Triglycerides, phospholipids, and steroids are different types of lipids found in the body. The two types of triglycerides are fats and oils. [24] An example of how a triglyceride looks like is shown in figure 3, it is composed of a glycerol backbone, with 3 fatty acid chains attached to it.

Around 98% of lipids found in human milk are in the form of triglycerides. Triglycerides are the main constituents of vegetable oils and food lipids. Examples of fatty acids are saturated fatty acids (SFA), that are high in butter and meat, mono unsaturated fatty acids (MUFA), like oleic acid, that are highly present in oils like olive oil, nuts and avocados, and poly-unsaturated fatty acids (PUFA) like docosahexaenoic acid (DHA) (see the whitepaper on DHA and AA), that are mainly present in fish. [25, 26]

Triglycerides are composed of two building blocks

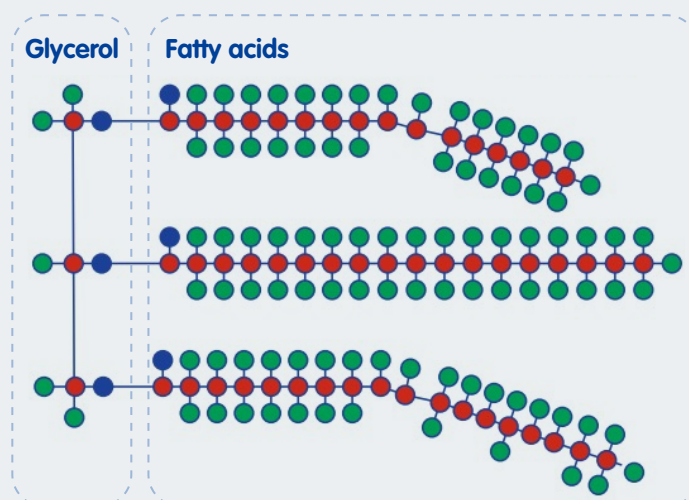


Figure 3 Triglycerides example

Human milk lipids are an important component that provides about 50% of the energy for the infant [27]. While the mean lipid content in human milk is relatively stable during the course of the first months of lactation, there is very wide interindividual and intraindividual variation of milk fat concentrations. Milk lipid content tends to increase with longer duration of breastfeeding and varies during the course of a day. [4, 28-30] Human milk lipids provide essential fatty acids that are important for normal brain and eye development and absorption of the fat-soluble vitamins. The fatty acid profile in human milk is adapted to the infants' specific needs and therefore has a unique and complex composition. [26]

Infant formulas contain a mixture of vegetable oils to meet the fatty acid profile requirements, especially the long chain fatty acids linolenic, α -linolenic acid, DHA and AA are important. [4, 31-34].

To mimic the fatty acid profile of human milk, β -palmitate (or OPO) a structured fat blend used in infant formula, can also be added, which shows positive effects on gut health, growth and stool consistency. [35]

Lipids have multiple purposes for infants [4, 7, 9]:

- Providing the infant with energy
- Promoting neurological development
- Adequate growth
- Providing cholesterol
- Vehicles for transport fat-soluble vitamins (Vitamin A, D, E, K)
- Providing long-chain polyunsaturated fatty acids (e.g. DHA)

Proteins

Proteins are large biomolecules that comprise one or more long chains of amino acids. There are 20 unique amino acids, of which 9 amino acids are essential, meaning that they cannot be synthesized by the human body and must be ingested via the diet. Proteins are the 'building blocks' for the body, serving as a source of amino acids for the development of organs, bones and muscle. Proteins also play an important role in cell repair, hormone production, and pH balance. Protein levels in human milk decrease over the first 4 to 6 weeks of life, regardless of timing of delivery. Human milk protein concentration is not affected by maternal diet, but increases with maternal body weight or height, and decreases in mothers producing higher amounts of milk.

[36, 37]

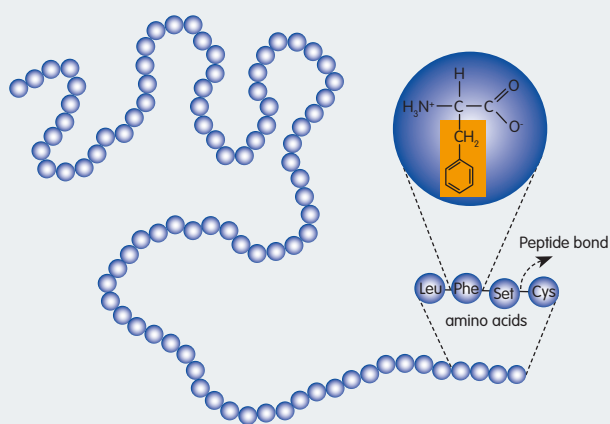


Figure 4 Protein structure

Human milk proteins can be broadly classified into 3 categories: caseins, whey proteins, and milk fat globule membrane proteins. Human milk is whey predominant. The ratio of whey:casein in human milk varies during lactation.

The amount of casein in the first 3-4 days is very low (around 10% of total protein) and increases over the months of lactation. The ratio whey:casein in mature human milk is around 60:40 (whey:-casein). [4, 38, 39] This specific ratio is applied in many available infant formulas to mimic the protein composition of human milk. In some countries this specific whey:casein ratio is regulated, while for other regions also casein-dominated formulas are allowed.

Proteins have multiple purposes for infants [40-42]:

- Serving as a source of amino acids
- Cell repair, hormone production
- pH balance
- Improving bioavailability of micronutrients, including vitamins, minerals, and trace elements
- Supporting immunological defense
- Stimulating intestinal growth and maturation
- Shaping the microbiome
- Enhancing learning and memory

Whey vs casein benefits scheme

Whey proteins

Faster digestion and absorption

"Quick absorption which provides infants with proteins quickly, necessary for growing bodies."



Fast release of nutrients

"High concentration of Branched Chain Amino Acids (BCAA) for muscle growth."



Promotes the immune system and protects against infections

"Rich in bioactive proteins that enhance immune functions."



Casein proteins

Slower absorption and digestion

"Forms a gastric curd, resulting in a sustained release of amino acids, beneficial for infants' growth and development."

Slow release of nutrients

"Helps to maintain a consistent supply of nutrients, increasing the feeling of fullness throughout the day."

Improved solubility of several nutrients

"Casein is rich in calcium, which is essential for bone health."

Figure 5 Whey and Casein Proteins - Benefits and Differences [43-47]

Conclusion

Human milk adjusts specifically to meet infant's nutritional needs at every stage of their development, making it the optimal form of nutrition for infants' growth and development. If breastfeeding is not an option, infant formula is a suitable alternative, as the composition has been adjusted to fulfill infant's nutritional needs on macronutrients, micronutrients (vitamins/minerals) and other (optional) ingredients. Macronutrients have an essential role in optimal growth and development in early life. Human milk has a unique and complex composition, therefore research on the composition and the optimization to mimic human milk in infant formula is an ongoing process, which results in new ingredients that are investigated and regulated to add to infant formula.

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