

Infant Formula

How to find a fit

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Infant Formula – How to Find a Fit

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I have no conflict of interest in this matter. I have no connection to any infant formula company and I have never received any grants or financial compensation

Eltern stehen im Supermarkt vor einer unübersichtlichen Produktauswahl

In our daily practice, we sometimes come across mothers who cannot (exclusively) breastfeed. This may be due to an inadequate breastfeeding start, treatment for an underlying condition in the mother with incompatible medicine, or an underlying condition in the child that is incompatible with human milk. Additionally, there are mothers who are unable to produce sufficient amounts of milk due to certain chronic conditions (e.g. PCOS, breast surgery) or insufficient glandular tissue. There are breastfeeding dyads where the child has problems and does not induce sufficient milk production in the mother. Sometimes, even after a good breastfeeding start, breastfeeding management is suboptimal, e.g. low breastfeeding frequency or excessive pacifier use, and this renders the milk production inadequate.

Whereas in most cases, donor milk could be an option, we must recognise that in

many European countries, there are few human milk banks and the use of donor milk is poorly established. In practice, we thus often get questions about formula, both in the context of exclusive formula feeding and supplementing breastmilk with formula.

As I work in pharmacy, I have received many questions about infant formula. When I looked for scientifically based answers, I realised quickly that it is very difficult to find independent information about this topic. About seven years ago, I therefore started to do extensive research on the matter. Over the past years, I have taught midwives, physicians and pharmacists about infant formula and currently also teach a class at the University in Brussels, as part of a larger course on infant nutrition. I have written a scientific book about the subject (currently only available in Dutch. I am a breastfeeding advocate and I have given classes on breastfeeding to thousands of my colleagues

working in front-line health care. However, I also strongly believe that women who cannot (exclusively) breastfeed deserve the best information we have.

In this article, I aim to provide lactation consultants with some basic knowledge about standard infant formula. Nowadays, supermarkets and pharmacies often offer an enormous range of infant formulas and it can be difficult to distinguish between them. I would like to point out that the discussion in this article applies only to standard infant formula. When a baby needs medical feeds, for example to treat cows' milk allergy or a metabolic disease, different legislation applies and other benefit-risk ratios need to be taken into account.

Some basic thoughts about formula ^[1]

All infant formulas on the European market are in line with European legislation considering the requirements for infant



- › formula and follow-on formula. This means that every formula, whether you buy it in a pharmacy or supermarket, provides adequate nutrition for growth. However, this does not mean that all formulas are equal. Stating that all formulas are more or less the same, and thus giving the impression that parents can easily switch between them, is malpractice and based on inadequate knowledge of the subject. It should also be noted that expensive formula does not necessarily mean that the quality is better. Let's take a look at the biggest differences and how to choose the best possible 'standard' formula.

Proteins

For the proteins in infant formula, manufacturers mainly use proteins from animal milk, such as cows' milk or goats' milk. There is no physiological advantage of one over the other, however it should be noted that the price of infant formula based on goats' milk proteins is often (a lot) more expensive.^[2,3] Sometimes, infant formula manufacturers use a plant protein source. In Europe, both soy and rice proteins are used for this purpose. According to studies, the growth and development of babies who receive infant formula based on vegetable protein sources is normal compared to the growth and development of babies who receive cow's milk-based infant formula.^[4] The amino acid composition of vegetable proteins is nevertheless different from that of animal proteins, as it has a lower amount of essential amino acids and is thus less aligned with the needs of a human baby.^[5] As a result, infant formulas using plant protein sources compensate by having a higher protein content, which is less desirable. The amount of protein in formula should as far as possible reflect the amount in breast milk (≈ 1.2 g/100ml for infant formula and ≈ 1.0 g/100ml for follow-on formula). There are, however, some situations in which plant sources may be considered, such as allergy to cow's milk protein, religious motives, or the specific wish to ensure a vegan diet for the baby. The latter is however disputable as no formula has an acceptable carbon footprint.^[6,7]

Another topic often discussed when considering protein in infant formula is hydrolysis. I will describe this in a separate section below.

Carbohydrates

Lactose accounts for more than 95 % of the digestible sugars in breast milk. Lactose is a disaccharide with two components: galactose and glucose. In the intestines, lactose is broken down by lactase, an enzyme from the cells of the small intestine. The monosaccharides thus formed provide energy and form building materials for the body's own substances, but lactose also has some functional properties. The (small) surplus that is not digested helps for example to shape the microbiome.^[8]

For infant formula, it is also desirable for the carbohydrate fraction to consist of ≈ 100 % lactose. Manufacturers, however, also use starch and maltodextrins. Starch is mainly added to increase satiety or ease digestion. The rationale behind this is that starch thickens formula in the bottle, thus slowing the drinking pace and increasing satiety.^[9] It is nevertheless possible to obtain similar results by choosing a slow-flow nipple and pausing during feeds.^[10] Considering digestion, it is important to realise that lactose intolerance is very rare in infants and that lactose intolerance mostly only begins after the age of one. Lowering the amount of lactose in infant formula for digestive problems or colic is therefore only very rarely necessary.^[11]

A second carbohydrate that is often used is maltodextrin. There is very little research on the use of maltodextrin in infants, so the recommendations are based on what we know about older children or adults. First, maltodextrin provides the necessary amounts of glucose to maintain levels that are necessary for energy requirements. Therefore, its use is allowed.^[12] When comparing the plasma glucose and insulin responses after the intake of a certain amount of calories in the form of lactose or maltodextrin, however, we observe that the plasma levels increase much more with maltodextrin.^[13] Research in older children and adults show that these frequent spikes in both glucose and insulin responses may be associated with the development of diabetes and/or obesity. Therefore, as a precautionary measure, we recommend avoiding standard infant formulas using maltodextrin as much as possible.

Prebiotics (including oligosaccharides)

Prebiotics are non-digestible carbohydrates that benefit the host by promoting the growth and/or activity of the intestinal flora in the colon. In breast milk, prebiotics are present as human milk oligosaccharides (HMOs). HMO is a collective name for all oligosaccharides that occur in breast milk. More than 200 have already been identified and HMO composition varies greatly between individuals. This has a genetic background, but HMO composition is also strongly related to the mother's environment and nutrition. Besides prebiotic activity, HMOs have multiple other beneficial immunomodulating qualities.^[14,15]

Despite the fact that they have no nutritional value, prebiotics and HMOs are a functional food. In infant formula, the prebiotic galacto-oligosaccharides (GOS) and fructo-oligosaccharides (FOS) are used. Since 2018, HMOs such as 2'-fucosyllactose (2'-FL), 3'-galactosyllactose (3'-GL) and Lacto-N-neotetraose (LnNT) have also been used.^[15] Currently, the ESPHGAN guideline states that the administration of prebiotic oligosaccharides may increase the total amount of bifidobacteria in the stool or soften the stool, but that there is currently insufficient evidence of any clinical benefit.^[16] More and more research is however emerging, showing that the addition of HMOs to formula has immunomodulating effects that are more in line with what we see in breastfed infants.^[17]

Lipids

In infant formula, lipid levels are often lower than in breastmilk. In follow-on infant formula, the lipid fraction is often even lower than in first infant formula. At the very least, one should strive for levels that are as high as possible (≈ 4 g/100ml). However, there are very few infant formulas with lipid levels exceeding 3.5 g/100ml in Europe.

The most abundant fatty acid in breast milk is the saturated palmitic acid. It represents about 20–25 % of all fatty acids. 60–85 % of this palmitic acid is anchored on the middle carbon of the glycerol backbone, the beta position. The total structure is therefore called beta-palmitate (also called beta-palmitic acid or sn-2 palmitic acid).^[18] Most infant formula also contains a high



Why protein hydrolysates shouldn't be your standard choice

WHAT IS HYDROLYSIS?

Hydrolysis is the loss of the protein's primary structure. The protein is broken down into small(er) pieces. The manufacturer may choose to partially hydrolyse, extensively hydrolyse or completely hydrolyse the proteins. In the latter case, we speak of an amino acid formula. It is not legally determined when infant formulas may be called partially or extensively hydrolysed. In partially hydrolysed formulas, however, the size of the molecules mostly varies between 3 and 10 kDalton (for comparison: complete proteins vary between 14 and 67 kDalton). With extensive hydrolysates, 90 % of the proteins remain below 3 kDalton in size. Note that hydrolysis also always renders a certain amount of free amino acids.

WHY HYDROLYSE A PROTEIN FRACTION?

Hydrolysing the protein fraction is done for two reasons: (1) to facilitate digestion or (2) to prevent or treat allergic reactions. Hydrolysed protein fractions are indeed more easily digested than intact proteins as they are slightly "pre-digested". They also pass through the intestinal tract a bit quicker. Most 'comfort' formulas therefore contain a partially hydrolysed protein fraction. [24] They are also often suggested for the prevention of allergies. However, according to a meta-analysis from the British Medical Journal [25] and a Cochrane review [26], there is no evidence that the use of partially hydrolysed formula reduces the risk of developing allergic reactions such as eczema, allergic rhinitis or asthma later in life or that it prevents cows' milk protein allergy. In addition, recent research supports the importance of early allergen exposure to induce immune tolerance. If a cows' milk allergy is diagnosed, however, one should use a formula based on an extensive protein hydrolysate or an amino acid formula for as long as symptoms persist.

CONSEQUENCES OF HYDROLYSIS

Hydrolysis and flavour development [27]

A specific property of free amino acids is that they have a sour and bitter taste. This has both short and long-term consequences for the introduction of infant formula based on extensive hydrolysates and for flavour development. When the taste preferences of children who received diets based on extensive hydrolysates during the first months of life were evaluated at the age of 4–5 years and 10 years, for example, it was found that they are much more likely to prefer sour and bitter tastes than children whose diets were based on intact proteins. They also often develop more unhealthy eating habits.

Hydrolysatation and growth [28]

Several studies report that children who receive infant formula based on extensive hydrolysates or amino acids consume lower volumes than children who receive formula based on intact proteins. This is because the free amino acids enter the bloodstream after absorption and transfer a satiety signal – in this case too early. The intake of lower volumes of infant formula could in turn be the cause of the slower growth observed in children on diets based on extensive hydrolysates or amino acids. Note that you probably won't observe this when these formulas are used to treat cow's milk allergy.

Hydrolysatation and protein content [29]

When a protein is hydrolysed, its nutritional value decreases. As the hydrolysatation is more intensive, the protein content in the milk replacer will therefore have to increase in order to meet the same nutritional requirement. Legally, infant formula based on protein hydrolysates may also contain a higher maximum protein content than formulas based on intact proteins (1.96 g /100 ml versus 1.75 g /100 ml).

Hydrolysis and price

As hydrolysis involves extra steps in the production process of infant formula, these formulas are often 50-100 % more expensive than their counterparts with an intact protein fraction.

amount of palmitic acid. However, it is usually attached to the first or third carbon of the glycerol backbone, the alpha sites. When palmitate is present on the alpha sites, it breaks down and esterifies with calcium, rendering the latter unavailable for absorption. Therefore calcium levels in infant formula need to be higher than in breast milk. [19,20]

According to research, the presence of beta-palmitate in infant formula is favourable (softer stool, better bone density). [20] It is not, however, obligatory. Beta-palmitate is a very expensive material to use. Marketed formulas therefore almost never contain it.

Minerals and vitamins

The requirements for minerals in infant formula are very strictly regulated by European legislation. [1] Therefore, when selecting a formula, you don't need to take account of the mineral and vitamin fraction. Nevertheless, I would like to explain the following. Although the concentrations in infant formula are very similar to those of breast milk, there are some exceptions. In this matter, it is important to realize that 'concentration' does not mean 'bioavailability'.

Infant formula contains for example up to ten times more iron than breast milk. The concentration of iron in breast milk is indeed low, but this iron has a very high bioavailability. Therefore, a very high amount of iron in breastmilk reaches the infant's system. Iron in infant formula on the other hand has a very low bioavailability. Manufacturers need to compensate by increasing the concentration. Another example is calcium. Due to a lower bioavailability, the amounts in infant formula are about double the amount in breast milk. [21]

Infant formula and follow-on formula

According to legislation, infant formula is formula for children from birth up to 6 months. [1] Follow-on formula is aimed at infants from 6-12 months. With breastfeeding, macronutrient composition changes very little after breastfeeding is fully established. The main changes are that over time, the protein fraction decreases (sometimes towards 0.8 g/100ml) and the lipid fraction increases. [22,23] There is therefore no reason to change infant formula at 6 months of age. In addition, follow-on formulas often contain



- › higher protein fractions and lower lipid fractions, the opposite of what we observe physiologically. Lactose is also often unnecessarily replaced by starch. There is however one difference that should be pointed out. It is often stated that follow-on formulas are needed because the iron content is higher than in infant formulas. Parents should be educated about how to provide iron-rich complementary foods to meet the infant's needs rather than encouraged to change the type of formula.

Conclusion

When choosing an infant formula, the aim should be to find a formula whose composition is closest to that of breast milk. When evaluating a food label, you need to pay attention to the following general items:

- › A nutrition label consists of two parts. First, there is the list of ingredients. It lists the ingredients from most common to least common. Then there is the nutritional value table. It contains exact figures about the levels of macro- and micronutrients in the product.
- › Some items, such as the presence or level of beta-palmitate are not legally required to be mentioned. Therefore, you will often not find them on a label;
- › Oligosaccharides (= the prebiotics) are listed under the heading "fibres". To find out the type of oligosaccharide, you have to search the list of ingredients.
- › Lactose, as a disaccharide, falls under the term "sugars". You can always check which sugars were used in the ingredients list. The sooner a sugar is listed, the higher the amount of this sugar in the product.
- › When proteins are hydrolysed, this must be stated on the label. Can't find anything? Then you can assume that the proteins have remained intact.

In terms of content, you can evaluate the general quality as follows:

- › Proteins: Use formula based on intact animal proteins, that has a low protein level (preferably 1.2 g/100ml)
- › Carbohydrates: Use formula that contains 100 % lactose, like human milk.
- › Lipids: Aim for formula that contains a high level of lipids (preferably 3.5 g/100ml or more). DHA-levels do not need to be evaluated as the new legislation sets minimum requirements for this omega-3-fatty acid.
- › Fibre: Evaluate the addition of prebiotics or HMOs. Their absence is not a reason to consider a formula 'bad', however their presence is a nice bonus.



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