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Frequently Asked Questions about Prebiotics and Probiotics

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In recent years many baby food companies have advertised that they have added pre and probiotics to their formulas and baby foods. What do we actually know about these additives and is the intensive promotion of products which contain them really justified?

Q1: What are prebiotics and probiotics?

The origin of the term is the Greek word *Bios*, meaning life or living organisms. The prefix *'pre'* means coming before and *'pro'* means supporting. *Prebiotics* thus prepare the way for the *Probiotics* - the live beneficial bacteria which are naturally found in our bodies.

Prebiotics are commonly called 'food for bugs'. Prebiotics are the fiber compounds that pass through the upper part of the digestive tract. Because they are not digested by humans they act instead as a food source to help the essential beneficial bacteria grow and multiply in the infant's gut. Prebiotics are thus not probiotic bacteria, but provide a substrate serving instead to stimulate the growth and activity of the beneficial probiotic bacteria.

Probiotics is the term used for these friendly and harmless bacteria which help move food through the body and fight off all the harmful bacteria that can invade the infant's gut – the digestive system and small and large intestines. Probiotics colonize the large bowel or colon influence and thus inhibit the growth of harmful bacteria, helping to improve digestion and enhance mineral absorption as well as to strengthen the baby's immune system. **In short, pre and probiotics reduce the 'bad bacteria' and increase the 'good bacteria' in the gut.**

Q2: Does breastmilk contain prebiotics and probiotics?

Breastmilk contains both prebiotics and probiotics. Yet breastmilk is far more than a list of ingredients and much more than nutrition. Breastmilk is a living substance; the bioactive components of breastmilk are critical for enhanced growth of babies, as well as their development and immunological protection. This is because breastmilk contains white blood cells called leukocytes, the cells of the immune system which defend the body against infectious diseases and invaders. These live components are active and effective in protecting and promoting the health of infants and young children; some of these components interact to boost their function. *See* http://ibfan.org/issue-scientific-breastfeeding

Breastmilk composition does not remain constant but instead adapts to closely match the changing needs of the infant. Breastmilk is a dynamic substance, individualised and evolving to suit each baby's age and stage of development. As the baby grows older, the mother's breastmilk produces more antibodies and lymphocytes to help the baby resist infections caused by pathogens, the harmful bacteria and viruses present in the environment. Therefore human milk composition uniquely and exactly matches the needs of the infant at every age and stage of development. Hence breastmilk can never be duplicated or copied artificially.

Q3: What prebiotics are found in breastmilk?

Breastmilk contains its own wide variety of **prebiotics, called Human Milk Oligosaccharides (HMOs).** In adults, diets with high-fiber foods such as bananas, onions, garlic, berries and greens contain naturally occurring prebiotics. Newborn babies cannot of course eat any of these foods and thus acquire prebiotics indirectly through breastmilk. HMOs are « abundant and unique to human milk ; research has shown that HMOs are not just 'food for bugs' but in fact have an anti-adhesive and antimicrobial effect that may prevent pathogens from attaching to the surfaces of infant mucosa, thus lowering the risk for viral, bacterial and protozoan parasite infections.» Many other possibilities are listed, including lowering the risk for necrotizing enterocolitis (NEC) in preterm babies.
See 'Human milk oligosaccharides: Every baby needs a sugar mama':
http://www.ncbi.nlm.nih.gov/pubmed/22513036

Q4: What probiotic bacteria are found in breastmilk?

Breastmilk also contains a specific **probiotic *Bifidus* factor** which supports the growth of the beneficial *Lactobacillus* group of bacteria in the infant's intestines. This *Lactobacillus* group is part of the lactic acid bacteria which help to protect the baby against other harmful bacteria by creating an acidic environment in which these toxic invaders cannot survive. At the same time, breastmilk contains lactoferrin, enzymes and other agents to protect the baby against viruses and provide an anti-inflammatory effect.
See American Pregnancy Association: 'What's in Breastmilk?':
http://americanpregnancy.org/firstyearoflife/whatsinbreastmilk.html

Q5: Are any prebiotics and probiotics found in formulas?

All infant formulas (milk-based and soy-based) are industrially processed and therefore inert products, without any of the live cells or anti-infective substances which are found in breastmilk and act as antibacterial, anti-viral or anti-parasitic agents. Formula manufacturers are therefore trying to replicate the prebiotics and probiotics found in human milk, and add them to formula. These companies attempt to try to influence the 'gut flora' of formula-fed infants that is the good bacteria or microbiota in their intestinal tract. As the introduction of prebiotics and probiotics is also closely linked to profits, companies such as Nestlé and Danone apply for patents on isolation and identification of HMOs and *Bifidus* bacteria and on the processes used to incorporate them into formulas. However, attempts to add prebiotics to formula in order to make the gut flora of formula fed babies more closely resemble that of breastfed infants have not met with success. This is because the evidence of a significant health benefit for probiotics through the alteration of the gut microbiota is limited.
See Prebiotics in infant formula: http://www.ncbi.nlm.nih.gov/pubmed/25535999

Q6: When were prebiotics and probiotics first added to formulas?

Scientists are constantly identifying new components in breastmilk, to add to the long list of beneficial substances that are already researched : carbohydrates, proteins and fats, plus vitamins, minerals, digestive enzymes and hormones. As research reveals the incredible complexity and value of breastmilk, formula companies are constantly trying to add the newest constituent to formula. Already beginning in the 1990s, companies such as Nestlé have been researching the role of prebiotics and probiotics and investigating how to add them to formula.
See Hanson L, Yolken R. Nestlé Nutrition Institute Workshops Series, 1997: https://www.nestlenutritioninstitute.org/Resources/Library/Free/workshop/Publication00043/Pages/publication00043.aspx

However, since 2002 there has been a steady increase in the number of promotional claims for the health and nutrition benefits of added prebiotics and probiotics - and claims that formula is 'modelled on' or 'patterned after' breastmilk.

Q7: Who benefits from the addition of prebiotics and probiotics to formulas?

Probably not infants. Companies use health and nutrition claims about the benefits of prebiotics and probiotics to promote their products, expand markets and increase sales. In this way they can be more competitive and reap more commercial benefits. Nestlé claims that its probiotic range contains « Probiotic *Bifidobacteria B. lactis*. Probiotic *B. lactis* contributes to your baby's healthy digestive tract flora. » It is « our closest formula to breastmilk.» Wyeth's S-26 Progress Gold is similarly claimed to contain « Biofactors system, a unique combination of nutrients to support the child's growth at every stage of life. » Such claims allow manufacturers to charge premium prices – up to 10 USD more per container of powdered probiotic formula.

Q8: Is there any evidence that pre and probiotics in formula provide the claimed health and nutritional effects – and justify higher prices?

The short answer is no. In Europe, health claims for probiotics are evaluated by the Panel on Dietetic Products, Nutrition and Allergies of the European Food Safety Authority (EFSA) which examines the evidence and issues Opinions based on scientific data. The article http://www.ncbi.nlm.nih.gov/pubmed/21861940 explains « Despite a substantial amount of basic and clinical research on the beneficial effects of probiotics, all of the evaluated claim applications thus far have received a negative opinion. » An example is the claim for a new product range containing Immunofortis® launched by Danone Baby Nutrition. Immunofortis® is a food constituent mixture of galacto- and fructo-oligosaccharides, which are both prebiotics. Danone made the claim that Immunofortis® acts to "naturally strengthen the baby's immune system" and applied to EFSA for the substantiation of this claim. After a detailed review, in 2010 EFSA published a review of the scientific evidence stating: « The Panel concludes that the evidence provided is insufficient to establish a cause and effect relationship between the consumption of Immunofortis® and the initiation of appropriate immune responses including the defence against pathogens. » **In short, EFSA rejected the claim.**
See http://www.efsa.europa.eu/en/efsajournal/pub/1430.htm

The European Society for Paediatric Gastroenterology, Hepatology and Nutrition, (ESPGHAN) also dismissed the effectiveness of pre and probiotics added to formulas. In 2011, ESPGHAN systematically reviewed published evidence and concluded **« Infant formulae are increasingly supplemented with probiotics, prebiotics or synbiotics (a combination of both) despite uncertainties regarding their efficacy … At present, there is insufficient data to recommend the routine use of probiotic- and/or prebiotic-supplemented formula. »**
See Journal of Pediatric Gastroenterological Nutrition: http://www.ncbi.nlm.nih.gov/pubmed/21150647

This was confirmed in the 2014 Position Paper of the ESPGHAN Working Group on Probiotics and Prebiotics on Use of Probiotics for Management of Acute Gastroenteritis; they concluded that « **the quality of evidence in the studies reviewed was low or very low.»**
See
http://journals.lww.com/jpgn/Fulltext/2014/04000/Use_of_Probiotics_for_Management_of_Acute.30.aspx

Q9: Why are probiotics ineffective in formulas?

Probiotic bacteria have to be alive when administered orally and then remain alive when they pass through the digestive system, so that they improve the balance of other bacteria in the gut. They have to be safe for their intended use and not produce toxins or side-effects. They must also be supplied in adequate amounts to produce sufficient beneficial activity. High numbers are critical for probiotic bacteria to survive during the digestive process and then to arrive in sufficient amounts in the large intestine. The numbers in each dose of added probiotics are thus counted in millions or even billions, but it is uncertain how many actually maintain viability, that is stay alive and remain active when they reach their destination in the large bowel.[1]

In addition, each human body responds differently to probiotics. The Summary of the 2014 ESPGHAN Opinion (see Q8) states «The safety and effects of one probiotic microorganism should not be extrapolated to other probiotic microorganisms « and explains that « Probiotic effects are strainspecific; thus the efficacy and safety of each should be established and recommendations for using these strains should be made accordingly. » This is because each one of the probiotic bacteria not only has a family name but also a species and sub-species name, followed by a series of letters and numbers which identify the particular strain. As stated by S. Bengmark « the (genetic) difference between one probiotic bacterium and the other is larger than the difference between a man and a goldfish. »
See http://www.ncbi.nlm.nih.gov/pubmed/21861940

An example is Nestlé's *Bifidus BL* which is the company's own trade name for the probiotic bacterial strain called *Bifidobacterium lactis* BB-12. This strain was developed from the bacteria classified as *Bifidobacterium animalis* ssp. *lactis* - but what manufacturer would include the word '**animalis'** in the name of bacteria contained in a package of formula? So Nestlé' shortened the name to *Bifidus BL* for the trade name of its product.

[1] Fuller R. 'Probiotics: the Scientific Thesis', London: Chapman and Hall, 1992, provides background information on probiotics in general.
Further publications by Fuller R. provide studies on probiotics in man and animals and in human medicine : http://onlinelibrary.wiley.com/doi/10.1111/j.1365-2672.1989.tb05105.x/abstract;jsessionid=62A2363E8BB50E77B47554AA76812EB2.f04t01

For interesting comparisons, see http://www.foodinfo.net/uk/ff/probiotics.htm

When ESPGHAN reviewed the data to justify the use of Nestlé's *B. lactis* BB-12 as a probiotic, they noted the lack of data and concluded : « No randomized control trial (RCT) evaluated the effect of exclusively administered *B. lactis* Bb12 (sic). »
See
http://journals.lww.com/jpgn/Fulltext/2014/04000/Use_of_Probiotics_for_Management_of_Acute.30.aspx

Q10: Are formulas with added probiotics effective - and are they safe?

Prebiotics and probiotics have complex properties and interactions. It is clear that their benefits are variable and they can be ineffective if they are simply added to a package of formula. Further problems may make products with added probiotics unsafe as well, for example the reduced viability of probiotics due to prolonged shelf life. This is due to the fact that many probiotic species of bacteria are heat-sensitive, meaning that they are inactivated by heat and may lose their properties during prolonged storage at temperatures warmer than 4°C. Formula is kept in grocery stores, pharmacies and homes at room temperature, often for several months if not for years, but how many can maintain temperatures of 4°C over a prolonged period? When baby food is donated to food banks, it may stay on shelves even longer.
See Simpson PJ et al. Intrinsic tolerance of Bifidobacterium species to heat and oxygen and survival following spray drying and storage: http://www.ncbi.nlm.nih.gov/pubmed/16108790

Further serious safety concerns

Parents and care-givers may be led to believe that probiotic bacteria in formula will destroy all harmful bacteria. For example, Nestlé-Gerber's website states that *Bifidus* BL is « probiotic which helps your baby fight against harmful bacteria in his digestive system … it is a mix of probiotics similar to those found in breastmilk. »

However, these product labels and promotional materials fail to warn about the risk of serious infection caused by certain dangerous bacteria, pathogens such as *Enterobacter sakazakii* or *Salmonella* species. Do these claims about probiotic cultures instead foster a false sense of security that the probiotics will reduce any risk of an *Enterobacter sakazakii* or *Salmonella* infection ?

Powdered formula is not a sterile product. *Enterobacter sakazakii*, now renamed *Cronobacter sakazakii*, and certain *Salmonella* species are rare but dangerous bacteria which might be present even in unopened containers of powdered formulas and cause severe invasive infections in infants. In the **2007 Guidelines on safe preparation, storage and handling of powdered infant formula,** the World Health Organization, WHO, states clearly that « Powdered infant formula has been associated with serious death and illness in infants due to infections with *Enterobacter sakazakii*. » In 2005 and 2008, the World Health Assembly urged governments to ensure that manufacturers inform and alert product users through an explicit warning on packaging that powdered formula is not sterile.

Whereas the probiotic bacteria are very sensitive to heat and are killed by high temperatures, *Cronobacter* and *Salmonella* species are resistant to heating and can survive high temperatures. They thrive in the warm milk made from powdered formula, if the formula powder is mixed with lukewarm water or if the water itself is not boiled to kill germs. WHO

therefore recommends a lethal or decontamination step for reconstituting powdered formula: Use water that has first been boiled and then cooled to no less than 70°C before mixing with the formula powder and then cool further to feed to the baby.
See WHO Guidelines for safe preparation, storage and handling of powdered infant formula: http://www.who.int/foodsafety/publications/micro/pif_guidelines.pdf

However, WHO warns that « Some powdered infant formula products may contain probiotics; these would be killed by reconstitution at 70°C. » And Nestlé instructs that « Nestlé Good Start Probiotic must not be warmed above 40°C (100°F) as it will compromise the *B. lactis*. » Although 40°C (100°F) safeguards the probiotic bacteria, it is also the ideal temperature for any *Cronobacter sakazakii* that may be present in the formula container to multiply exponentially.

The key question remains: is formula feeding safe?

All of us should campaign to make formula feeding safer for those infants who are not breastfed. Unlike breastmilk, ready-to-feed and powdered formulas do not provide live anti-infective agents. Furthermore, because these products are processed, packaged and stored before being reconstituted, there is a potential for contamination at every stage.

Pre and probiotics are superfluous and unnecessary additives to formulas that are included for the purpose of increasing sales and charging premium prices. They should not be promoted on the basis of unsubstantiated and misleading claims for health and nutrition benefits, nor on the positive effects which are shown in company-sponsored research and then used in advertising and to convince health workers. Independent and objective scientific bodies such as the Cochrane Reviews have concluded that «There is insufficient evidence to recommend the addition of **probiotics** to infant feeds for prevention of allergic disease or food reactions » and « There is some evidence that a **prebiotic** added to infant formula may prevent eczema and asthma in infants. However, there is some concern about the reliability of the evidence due to not all trials reporting allergy outcomes and trials not reporting the outcome for all infants. »
See
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD006475.pub2/otherversions
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD006474.pub3/abstract

The controversy over the validity of company-sponsored research led the ESPGHAN Committee to make this clear statement : « Because most of the trials (in the review) were company funded, independent trials, preferably financed jointly by national/governmental/European Union bodies and other international organisations, would be desirable. » *See* http://www.ncbi.nlm.nih.gov/pubmed/21150647

It is therefore of critical importance that parents, carers and health professionals do not base their infant feeding decisions on questionable science and unproven claims for added pre and probiotics. Parents need impartial information and sound advice, free from commercial pressures. Mothers need understanding, encouragement and support so that they can breastfeed their babies and be shown how to relactate.
See
http://apps.who.int/iris/bitstream/10665/65020/1/WHO_CHS_CAH_98.14.pdf?ua=1&ua=1
https://www.breastfeeding.asn.au/bfinfo/relactation-and-adoptive-breastfeeding