

Inside the Tin

Part 2: Advancing the Management of Cow's Milk Protein Allergy

In recent years, there has been a paradigm shift in how cow's milk protein allergy (CMPA) is managed. Previously, the goal was to achieve symptom relief with a focus on allergen avoidance. More recently research has focused on additional nutritional factors that support the gut microbiota and immune system, such as prebiotic oligosaccharides, synbiotics and lactose.^{1,2,3}

Breastfeeding is recommended for the multiple benefits it brings to the mother and the child and should be continued where possible.⁴



Human Milk

Human milk is the gold standard of infant nutrition,⁵⁻⁷ it contains live bacteria, prebiotic oligosaccharides and lactose that stimulate the gut microbiota and immune system.⁸⁻¹¹ Most hypoallergenic formulas (extensively hydrolysed, amino acid and rice protein-based formulas) lack these microbiota stimulating factors.

Breast Milk = Ultimate Synbiotic

- Human milk is the gold standard in infant nutrition^{12,13}
- Breast milk contains live bacteria, prebiotic oligosaccharides and lactose that stimulate the gut microbiota and immune system¹⁴⁻¹⁷
- Hypoallergenic formulas used for the management of CMPA traditionally lack these microbiota stimulating factors

Human milk	Traditional extensively hydrolysed formula	Traditional amino acid based formula
Live bacteria	x	x
Human milk oligosaccharides with prebiotic effect	x	x
Lactose as main carbohydrate	Small amount of lactose	No lactose

Rich in factors that stimulate the gut microbiota & immune system

Limited or complete lack of stimulation of the gut microbiota

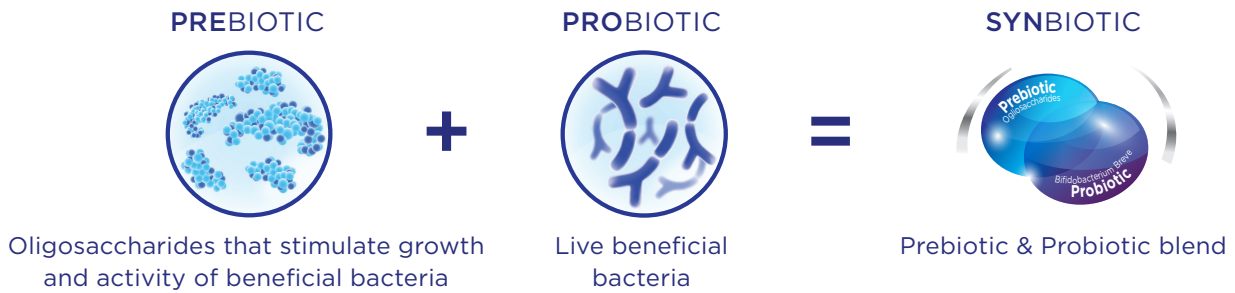
When breastfeeding is not possible using a specialised formula suitable for cow's milk allergy is recommended. A specialised formula with factors to support the gut microbiota and immune system should be considered such as oligosaccharides, synbiotics and lactose.¹⁻³



Role Of Synbiotics In Immune System Development

There is now a greater appreciation of how crosstalk between the gut microbiome and immune system influences allergy development during infancy and diseases later in life.¹¹⁸ Gut microbiota dysbiosis, an imbalance of gut bacteria is often associated with the development of CMPA.¹⁹⁻²¹ It is thought that gut microbiota dysbiosis impacts immune system development, leading to CMPA. As a result, the focus has now shifted from allergen avoidance to supporting healthy immune response via modulation of the gut microbiota.¹⁸ Synbiotics are a combination of a prebiotic oligosaccharides and probiotics that work synergistically to rebalance the gut microbiota. With a growing body of clinical evidence to suggest that synbiotics can have a beneficial effect in infants with CMPA, selected Nutricia products contain the synbiotic, SYNEO, to help rebalance microbiota and support immune system development.²²⁻²⁴

SYNEO - a unique blend of prebiotics and probiotics ²²⁻²⁴



Synbiotics are a combination of prebiotics and probiotics that act synergistically to target gut microbiota dysbiosis in the dietary management of cow's milk protein allergy²²⁻²⁴



Other key ingredients to consider in hypoallergenic formula:

Many formulas are fortified with additional ingredients, what are the key ones for consideration in CMPA hypoallergenic formulas?

Ingredient	Role In CMPA ^{2,26-30}
Lactose	Lactose is the main carbohydrate in human and mammalian milk. Physiological lactose malabsorption in infancy confers beneficial prebiotic effects, including the establishment of Bifidobacterium-rich faecal microbiota. Lactose containing formulas are thought to have improved palatability.
Nucleotides	Nucleotides play a key role in almost all biological processes in the body. Nucleotide supplementation promotes growth, benefits the GI tract and immune functions, and enhances mucosal recovery after intestinal injury.
Medium Chain Triglycerides (MCTs)	An increased supply of MCTs is important to promote growth in infants with malabsorption, such as severe food allergy and preterm infants.
Docosahexaenoic Acid (DHA)	Shown to provide anti-inflammatory effects, beneficial for infants with CMPA and other food allergies. Also promotes normal infant growth as well as visual and mental performance.
Long Chain Polyunsaturated Fatty Acids (LCPUFAS)	Helps to modulate the immune system and reduce allergic sensitisation, thereby reducing acute allergic symptoms.

References:

- D'Auria E, Salvatore S, Pozzi E et al. Cow's milk allergy: Immunomodulation by dietary intervention. *Nutrients* 2019 Jun 21;11(6):1399.
- Heine RG, Alrefaee F, Bachina et al. Lactose intolerance and gastrointestinal cow's milk allergy in infants and children - common misconceptions revisited. *World Allergy Organisation Journal*. 2017 Dec 12. **3**.
- Sorensen K, Cawood A, Gibson G et al. Amino acid formula containing synbiotics in infants with cow's milk protein allergy: A systematic review and meta-analysis. *Nutrients*. 2021, **13** (3), 935.
- Australian Society Clinical Immunology Allergy. Guide for milk substitutes 2020. (Cited 2022 May 5) <https://www.allergy.org.au/hp/papers/guide-for-milk-substitutes-cows-milk-allergy>
- World Health Organisation. Infant and young child feeding. 2003 **6**.
- Jeurink PV, Bergenhenegouwen J, Knippels L et al. A source of more life than we imagine. *Benef Microbes*. 2013;4(1):17-30.
- Martin R, Nauta A, Amor K et al. Early life: gut microbiota and immune development in infancy. *Benef Microbes*. 2010 ;1(4):367-382.
- Walker WA, Shuba Lyengar R. Breastmilk, microbiota and intestinal immune homeostasis. *Pediatric Res*. 2015 77(1):220-28.
- Scholtens P, Oozeer R, Martin R et al. The early settlers: intestinal microbiology in early life. *Annu Rev Food Sci Technol*. 2012;3(1):425-447.
- Hunt KM, Foster J, Forney L et al. Characterisation of the diversity and temporal stability of bacterial communities in human milk. *PLoS One*. 2011;6(8):e21313
- Bergmann H, Rodriguez J, Salminen S et al. Probiotics in human milk and probiotic supplementation in infant nutrition: A workshop report. *British J Nutr*. 2014;112:1119-28.
- World Health Organisation. Infant and young child feeding. 2021 June 9. (cited 2022 May 19) <https://www.who.int/news-room/fact-sheets/detail/infant-and-young-child-feeding>
- Jeurink P., Bergenhenegouwen J, Jimenez E et al. Human milk a source of more life than we imagine. *Benef Microbes*. 2013; Mar 1;4(1):17-30.
- Walker WA, Lyengar R et al. Breast milk, microbiota and intestinal immune homeostasis. *Pediatr Research*. 77 (1-2):220-28.
- Scholtens PAMJ et al. *J Annu Rev Food Sci Technol*. 2012;3(1):425-447.
- Hunt KM et al. *PLoS One*. 2011;6(6):e21313
- Bergman H et al. *British J Nutr*. 2014;112(7):119-28.
- Sackesen C, Ufuk Altintas D, Bingol A et al. Current trends in tolerance induction in cow's milk allergy: From passive to proactive strategies. *Front Pediatr* 2019 Sep 18;7:372.
- Berni Canani R, Sangwan N, Stefka A et al. Lactobacillus rhamnosus G - supplemented formula expands butyrate-producing bacterial strains in food allergic infants. *ISME J* 2016 Mar; 10 3:742-50.
- Ling Z, Li Z, Liu X et al. Altered fecal microbiota composition associated with food allergy in infants. *Appl Environ Microbiol* 2014 Apr;80(8):2546-54.
- Thompson-Chagoyan OC, Vieites J, Maldonado J et al. Changes in fecal microbiota of infants with cow's milk protein allergy - A spanish prospective case - control 6 month follow up study. *Pediatr Allergy Immunol* 2010 March;21:e394-400.
- Candy DCA, Van Ampting M, Oude Nijhuis M et al. A synbiotic containing amino acid-based formula improves gut microbiota in non-IgE mediated allergic infants. *Pediatr Res*; 2018 March;83(3):677-86.
- Fox AT, Woperes H, Van Ampting M et al. A specific synbiotic containing amino acid-based formula in dietary management of cow's milk allergy. A randomised controlled trial. *Clin Transl Allergy* 2019;9:5.
- Van der Aa LB, Heymans HS et al. Effect of a new synbiotic mixture on atopic dermatitis in infants: a randomised controlled trial. *Clin Exp Allergy* 2010;40:795-804.
- Łoś-Rycharska E, Kierszewicz Z, Czerwionka-Szafarska M et al. Medium chain triglycerides (MCT) formulas in paediatric and allergological practice. *Prz Gastroenterol* 2016;11:226-31.
- Maslin K, Fox A, Chambault M et al. Palatability of hypoallergenic formulas for cow's milk allergy and healthcare professional recommendation. *Pediatr Allergy Immunol*. 2018;29:857-862.
- Corkins K, Shurley T et al. What's in the bottle? A review of infant formulas. *Nutrition in Clinical Practice*. 2016. 723 - 729.
- Burks W, Jones S, Berseth C et al. Hypoallergenicity and effects on growth and tolerance of a new amino acid based formula with docosahexaenoic and arachidonic acid. *J Pediatr* 2008;2:P266-71.
- Van den Elsen LWJ, Van Esch B, Hofman G et al. Dietary long chain N-3 polyunsaturated fatty acids prevent allergic sensitization to cow's milk protein in mice. *Clin Exp Allergy* 2013;43:798-810.
- Hoppenbrouwers T, Cvejic Hogervorst J, Garssen J et al. Long chain polyunsaturated fatty acids (LCPUFAs) in the prevention of food allergy. *Front Immunol* 2019;10:1118.

BREASTMILK IS BEST FOR BABIES: Professional advice should be followed before using an infant formula. Partial bottle feeding could negatively affect breastfeeding. Good maternal nutrition is important for breastfeeding and reversing a decision not to breastfeed may be difficult. Infant formula should be used as directed. Improper use of infant formula may affect the health of the baby. Social and financial implications should be considered.

For HCP use only - not for distribution to the general public.

