

The Role of the Microbiome and Probiotics in Food Allergy

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The microbiome

The microbiome consists of all the microorganisms that live inside and on the human body. Each of us have varied types (diversity) and quantities (abundance) of these microorganisms. Each person's microbiota is unique, like his or her fingerprints.' The microbiome has a potentially overwhelming impact on human health.

In exchange for a stable environment and adequate nutrients, the gut microbiota contribute to maturation of the gastrointestinal tract, provides the body with nutrients, and helps safeguard us from harmful microbes. The definition of what comprises a "healthy" microbiome remains to be determined, although low microbial diversity appears to be associated with disease.1

The microbiome & allergy

The 21st century lifestyle, which includes a diet very different from our ancestors', excess antibiotic use and a rise in caesarean section deliveries, have profoundly changed the makeup of microbes in the gastrointestinal tract of people residing in westernised countries.^{2,3}

Interaction between the microbiome and the mucosal immune system appear to play a significant role in the prevention and development of food allergy.4

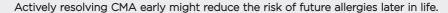
Organisms populating the intestine, skin and lungs during infancy are central to determining how the local and systemic immune systems develop.⁵ Conditions which adversely affect the development of a normal microbiome, such as early exposure to antibiotics and caesarean section, seem to predispose children to the development of allergic diseases.6

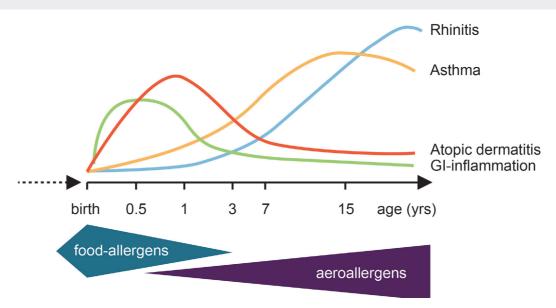
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Cow's milk allergy (CMA)

Cow's milk protein allergy is the leading cause of immediate (IgE mediated) or delayed (non-IgE) mediated food reactions in infants and children younger than three years of age.⁷ An opportunity to intervene and actively resolve CMA early might reduce the risk of developing future allergic manifestations later in life (known as the Allergic March) and positively impact the long-term health of the child.⁸





Adapted from Wahn et al.⁹ 1998, Herz et al. 2005¹⁰

Babies with food allergies are more susceptible to develop future allergies11*

- 4.0 x asthma
- 3.6 x respiratory allergies
- 2.4 x atopic eczema

*Compared to infants without food allergy

It is now recognised that there are two crucial players involved in oral tolerance development in CMA – dietary factors and gut microbiota. 12

Two crucial players are involved in oral tolerance: dietary factors and gut microbiota.

The recommended initial dietary management for CMA is an extensively hydrolysed formula (eHF).¹³ EHF contain cow's milk protein peptides which may help with tolerance acquisition.¹⁴ Conversely, amino acid formula, are completely hypoallergenic and should be reserved for severe cases or where eHF have not resolved symptoms after 2-4 weeks.^{15,16}

Once clear improvement is observed, current recommendations suggest careful re-introduction of the allergenic protein (using a step-wise introduction of baked milk products).¹³ In addition, attention is now turning to the gut microbiota and how early supplementation with probiotics may positively impact the development of food allergy and prevent the progression of the Allergic March.¹⁶ Not all probiotics are the same, however and specific strains of probiotic organisms differ greatly from one another. Optimum use of probiotics requires an understanding of the functions and benefits of each particular strain of bacteria.¹⁷



The role of probiotics in cow's milk allergy

Certain probiotics such as Lactobacillus rhamnosus GG®(LGG®), are able to alter the microbiome and regulate the immune system. Clinical data shows that an extensively hydrolysed casein formula containing LGG® facilitates the development of oral tolerance to dietary antigens at an earlier age compared to other formula in infants with CMA.^{†17}

LGG® is a unique strain of Lactobacillus rhamnosus with properties that regulate the immune system.

LGG® influences tolerance acquisition via a number of suggested mechanisms. A key factor is its impact on shaping the gut microbiome by improving the mucous layer of the lumen which is consumed by beneficial bacteria, which produce butyrate, increasing their growth.18 Butyrate is an anti-inflammation compound involved in the beneficial interaction between bacteria and the immune system resulting in a shift towards tolerance and a decrease in inflammation (via up regulation of the Th1 response and down regulation of the Th2 response)¹⁹ in babies with CMA.¹⁸

Benefits of EHCF+LGG show earlier development of tolerance in CMA and reduction of atopic manifestations.

The longer-term benefits of the promotion of tolerance include a possible reduction in future atopic manifestations in older children. In the most recent study, infants that acquired tolerance earlier also had a reduction in future atopic manifestations up to 3 years of age[‡] and functional gastrointestinal disorders (FGID) up to 4-6 years of age, 920 providing long-term benefits for patients and potential healthcare cost savings.21

- † Versus an eHCF without LGG® probiotics or formulas based on hydrolysed rice, soy or amino acids. ‡ Versus EHCF alone during a period of three years. 8 Versus FHCF alone
- References: 1. Bull MJ, Plummer NT (2014). Part 1: The Human Gut Microbiome in Health and Disease. Integr Med (Encinitas).; 13(6): 17-22. 2. Dunlop JH, Keet CA (2018). Epidemiology of Food Allergy. Immunol Allergy Clin North Am.; 38(1): 13-25. 3. Edwards CA (2017). Determinants and Duration of Impact of Early Gut Bacterial Colonization. Ann Nutr Metab.; 70(3): 246-250. 4, Fieten KB, et al. (2018). Fecal Microbiome and Food Allergy in Pediatric Atopic Dermatitis: A Cross-Sectional Pilot Study. Int Arch Allergy Immunol.; 175(1-2): 77-84. 5, Sampson HA, et al. (2018). Mechanisms of food allergy. J Allergy Clin Immunol.; 141(1): 11-19. 6. MJN Canani Report 2016. Prebiotics and Probiotics in Paediatrics (PPP) International congress. 7. Sicherer SH (2011). Epidemiology of food allergy. J Allergy Clin Immunol.; 127(3): 594-602. 8. Lumia M, et al. (2015). Food consumption and risk of childhood asthma. Pediatr Allergy Immunol.; 26(8): 789-796. 9. Wahn U (1998). 7.6: Allergische Erkrankugen im Säuglings - und Kindesalter (Allergic diseases in infants and children) (p272). In Heppt W et al. (Eds) Allergologie. Springer; IBSN: 3-540-61914-3. 10. Herz U, Petschow B (2005). Perinatal events affecting the onset of allergic diseases. Curr Drug Targets Inflamm Allergy; 4(5): 523-529. 11, Kim KS (2016). Dietary antigens limit mucosal immunity by inducing regulatory T cells in the small intestine. Science; 351(6275): 858-863. 12. Fox A, et al. (2019). An update to the Milk Allergy in Primary Care guideline. Clin Transl Allergy; 9: 40. 13, Meyer R, Groetch M, Venter C (2018). When Should Infants with Cow's Milk Protein Allergy Use an Amino Acid Formula? A Practical Guide. J Allergy Clin Immunol Pract.; 6(2): 383-399. 14. Berni Canani R, et al. (2012). Effect of Lactobacillus GG on tolerance acquisition in infants with cow's milk allergy: a randomized trial. J Allergy Clin Immunol.;129(2): 580-582. 15, Gupta M, Sicherer SH (2017), Timing of food introduction and atopy prevention. Clin Dermatol.; 35(4): 398-405. 16, Berni Canani R, et al. (2013). Formula selection for management of children with cow's milk allergy influences the rate of acquisition of tolerance; a prospective multicenter study. J Pediatr.;163(3): 771-777. 17, Berni Canani R, et al. (2016). Lactobacillus rhamnosus GG-supplemented formula expands butyrate-producing bacterial strains in food allergic infants. ISME J.; 10(3): 742-750. 18, Berni Canani R et al. (2015). Differences in DNA methylation profile of Th1 and Th2 cytokine genes are associated with tolerance acquisition in children with IgE-mediated cow's milk allergy. Clin Epigenet.; 7: 38. 19, Berni Canani R, et al. (2017). Extensively hydrolyzed casein formula containing Lactobacillus rhamnosus GG reduces the occurrence of other allergic manifestations in children with cow's milk allergy: 3-year randomized controlled trial. J Allergy Clin Immunol.; 139(6): 1906-1913. 20. Nocerino R, et al. (2019). Dietary Treatment with Extensively Hydrolyzed

IMPORTANT NOTICE:

Breastfeeding is best for babies. The decision to discontinue breastfeeding may be difficult to reverse and the introduction of partial bottle-feeding may reduce breast milk supply. The financial benefits of breastfeeding should be considered before bottle-feeding is initiated. Failure to follow preparation instructions carefully may be harmful to your baby's health. Parents should always be advised by an independent healthcare professional regarding infant feeding.

Casein Formula Containing the Probiotic Lactobacillus rhamnosus GG Prevents the Occurrence of Functional Gastrointestinal Disorders in Children with Cow's Milk Allergy, J Pediatr.: 213: 137-142, 21. Guest JF, Singh H (2019), Cost-effectiveness of using an extensively hydrolyzed casein formula supplemented

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10/2020 - RB-M-15868

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