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# The importance of early life nutrition in the prevention and dietary management of CMA

Nutricia presents the second in a three-part series of discussions around allergies in early life. The following focuses on the role of early life nutrition, exposure to allergens, and how pre- and probiotics have a part to play in the primary prevention and dietary management of cow's milk allergy (CMA).

Food allergies are on the rise, with CMA being one of the most common allergies in infants and young children.<sup>1</sup> Modern lifestyle and environmental factors have contributed to the rising prevalence of food allergies globally.<sup>2,3</sup>

In early life, the infant gut and immune system are rapidly developing. Environmental factors such as mode of delivery, diet and use of antibiotics influence this process. An imbalance in the gut microbiota, known as dysbiosis, is suggested to be one of the key candidates contributing to the current allergy epidemic.<sup>4</sup>

Early life nutrition has a profound effect on a child's immune development, and is key to help avoid and alleviate future allergic diseases

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## The role of early life nutrition

Nutritional support in early life is an essential part of the clinical management of infants at risk of and with food allergies. International guidelines for the management of allergic diseases include recommendations for both primary prevention and dietary management of food allergies.<sup>5,6</sup>

## Allergies – a question of exposure?

Exposure to allergens early in life influences the development of allergen-specific immune responses.<sup>9</sup> Reduced exposure to antigens and a failure to educate the immune system appropriately, may contribute to the increased incidence of food allergy.<sup>10</sup> Food allergy results from a failure to

### Primary prevention

For infants at risk, and if breastfeeding is not possible, international guidelines recommend partially hydrolyzed cow's milk protein formulas for at risk patients.<sup>5</sup> Clinical trials have shown the potential to reduce the risk of developing atopic dermatitis in high risk infants, compared to intact protein formulas.<sup>7</sup> However, since the evidence from the different clinical studies is not fully consistent, in some countries there is debate on these recommendations.

develop oral tolerance, a state of active non-responsiveness to ingested soluble antigens mediated by gut-associated intestinal lymphoid tissue.<sup>11</sup> Several studies strengthen the concept that oral tolerance can be promoted by nutritional intervention by combining the exposure to low dose cow's

### Dietary management

For infants with CMA and in whom breast-feeding is not possible, expert opinion recommends use of hypoallergenic formula such as extensively hydrolyzed cows milk protein-based formula (eHF) and amino acid-based formula (AAF). Whilst an eHF is suitable for the majority of CMA infants, between 10–40% of patients will require an AAF.<sup>8</sup>

milk allergens, in combination with prebiotic oligosaccharides.<sup>12,13</sup> The right environmental conditions, including good nutrition, can support optimal tolerance development, meaning that the immune system recognizes proteins as harmless, preventing an adverse immune response.

## The role of pre- and probiotics in CMA

Gut microbiota dysbiosis has been reported in infants with allergic conditions with low levels of *bifidobacteria* and *lactobacilli* compared with healthy, breastfed infants.<sup>15</sup> Human breast milk contains human milk oligosaccharides (HMOs), which have prebiotic activity, and pass undigested to the colon and serve as substrates to

### What are prebiotics?

A substrate that is selectively utilized by host micro-organisms conferring a health benefit.<sup>24</sup>

### What are probiotics?

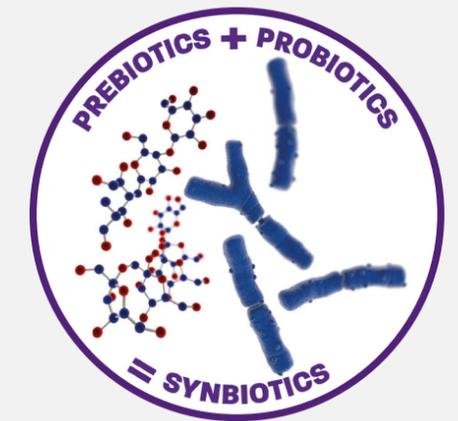
Live micro-organisms which when administered in adequate amounts confer a health benefit on the host.<sup>25</sup>

### What are synbiotics?

A mixture of pre- and probiotics that affects the host by improving the survival and implantation of live microbial dietary supplements in the gastrointestinal tract, by selectively stimulating the growth and/or activating the metabolism of one or a limited number of health-promoting bacteria, and thus improving welfare.<sup>26</sup>

support the developing microbiota.<sup>16</sup> It is now also recognised that human milk contains beneficial bacteria, such as *bifidobacteria*, that provide a continuous supply of bacteria to the infant gut.<sup>17</sup> Given the presence and important role of both HMOs and bacteria in human milk, acting as a natural synbiotic, and recognising that breast feeding is not always possible, ways to positively support the development of the microbiota of formula fed infants by the introduction of pre- and probiotics to the diet have been sought.

Pre- and probiotics aim to influence the immune system directly, or indirectly, via the gut microbiota, thereby aiming to prevent the onset of an allergic disease.<sup>18</sup> Prebiotics are fermented in the large intestine encouraging the growth of beneficial bacteria, changes in short chain fatty acids (SCFA) production and stimulation of intestinal motility.<sup>19</sup> Accumulating clinical evidence indicates that pre- and probiotics can have beneficial effects on infants at risk of, or living with allergies. Recent studies assessing probiotics in allergic children showed that probiotics support gut integrity and function.<sup>20,21</sup> These results



suggest that probiotic supplementation may stabilize the intestinal barrier function and decrease gastrointestinal symptoms in children with allergies such as CMA.

In recognition of the potential benefits of pre- and probiotics the WAO Guideline Panel suggested that pre- and probiotic supplementation be considered for infants at risk of allergy if not exclusively breastfed.<sup>22,23</sup> There are commercially available partially hydrolyzed formulas containing prebiotic oligosaccharides worldwide. Pre- and/or probiotics are now also available in some countries in hypoallergenic formula for the dietary management of infants with diagnosed CMA.

## Future of allergy management for CMA patients

Given:

1. The aberrant gut microbiota associated with allergy and the key role of the gut microbiota on immune system maturation
2. The increasing clinical evidence for providing pre- and probiotics to infants
3. The lack of pre- and probiotic intake by infants with CMA on restricted exclusion diets

there is a strong rationale to supplement the diet of infants at risk of, or with CMA with pre-, pro- or synbiotics.

Nutricia has an extensive clinical trial programme underway investigating the role of these ingredients in the primary prevention and dietary management of CMA.

For more information visit [www.nutriciaresearch.com/allergy/](http://www.nutriciaresearch.com/allergy/)

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