
EDITORIAL
IMMUNONUTRITION IN PEDIATRICS

Immunonutrition in pediatrics

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A well-functioning immune system is critical to enable both an effective defense against pathogens and the tolerance of unthreatening organisms, food components and the body's own cells and tissues.¹

Many nutrients have a tremendous potential to modulate, whether directly or indirectly, the development and function of innate and acquired immunity. The modulation of the immune system activity through the administration of specific nutrients is known as immunonutrition.

Undernutrition, whether as a result of food shortages in low-income countries or malnutrition arising from periods of hospitalization in high-income countries, is well known to impair immune function. Its extent depends upon the severity of the deficiency, the presence of any infection, the subject's age and the duration of the hospitalization.²

There is growing interest not only in the possibility of treating immune deficiencies related to poor diet, but also in whether specific nutritional interventions can further enhance immune function. For example, it has been shown that taking vitamin C and probiotic supplements for 6 months synergically reduces the incidence and duration of respiratory infections in preschool children.³ Preclinical trials have also provided some evidence that vitamin D supplementation benefits autoimmune disorders such as type 1 diabetes and multiple sclerosis,⁴ while a mix-

ture of *Bifidobacterium animalis subsp. lactis* BB12 and *E. faecium* L3 could reduce the signs, symptoms and need for medication in atopic children.⁵

In addition to the effects of a single nutrient on the immune system, there is growing evidence of the effects of diet as a whole on immune function and development. Recent findings that an increased diversity of food introduced in the first year of life protects against allergic diseases are consistent with the hypothesis that exposure to a variety of food antigens during early life might be important for the development of immune tolerance.⁶

The relationship between nutrition and the immune system is complex. It involves the interplay of genetic background and numerous environmental factors, among which dietary pattern and microbiota play an important role.^{7, 8} Epigenetics, which literally means "above genetics," is one of the most important mechanisms through which environmental factors can influence gene expression, *via* a variety of processes that cause heritable changes without affecting the DNA sequence itself.

Epigenetic modifications are at their most active during the period lasting from conception to the second year of life "the 1000 days period," also known as "window of susceptibility." Maternal and early nutrition in this period seems to be the key to long-term programming, thereby possibly influencing

individual susceptibility to the development of childhood and adult diseases such as obesity, diabetes, and other non-communicable chronic conditions, via epigenetic changes.⁹ Early nutrition thus has a primary role in individual immunity. Human milk consists of nutrients and bioactive substances such as cytokines, growth factors, and immunomodulators as well as oligosaccharides, all of which influence the maturation and function of the immune system.¹⁰ It also contains many anaerobic and lactic acid bacteria, which could confer further antimicrobial protection and improve nutrients absorption. Furthermore, it contains more than two hundred types of non-nitrogen compounds, which improve the functionality of the gastrointestinal mucosa by facilitating iron absorption and intestinal colonization by *bifidobacteria*.

Increasing evidence shows the potential of human milk in modulating the immune system. Prolonged exposure to breast milk alone has been associated with a reduced risk of autoimmunity¹¹ and a preventive effect on the onset of allergic diseases, inflammatory bowel diseases and other non-communicable chronic diseases.¹² Most of these effects are mediated by the complex microbial community of the gut, the microbiome, which plays a key role in driving the development and function of the human immune system, a phenomenon known as the gut microbiome-immune system axis.¹³ The microbiota in a healthy gut contains a preponderance of potentially beneficial species. Dysbiosis is increasingly linked to several disorders.^{14, 15} The role of the microbiome as an epigenetic modulator is gaining increasing attention, and although the underlying mechanisms are not yet fully clear, the current evidence supports a significant correlation between gut microbiome composition and epigenetic changes.¹⁵

The articles in this Special Issue of *Minerva Pediatrics* provide a broad range of evidence on how nutrients and nutrition have a major influence on immune responses in both health and disease. The pivotal role of human milk on immune function and development is discussed, and the effects of maternal diet and early nutrition in modulating the immune system in a selected

subset of autoimmune diseases are presented in the light of the current evidence. The complex interplay between microbiome, epigenetic and nutrition and the potential role of biotics in shaping the microbiome, offering new strategies for prevention and treatment, are addressed.

Although maternal diet, breastfeeding and early nutrition play a part in almost all autoimmune diseases, the field of nutrigenetics is still in its infancy. Each disease seems to have specific epigenetic signatures that are as yet unexplored and require further investigation, paving the way for a personalized nutritional intervention.

Given all this, the clinicians have a duty to motivate and guide their patients towards a healthy diet, educating them on the benefits of a “prevention culture” as a lifestyle. As Hippocrates (460-370 BCE) himself said, long before the term epigenetics had been coined: “let the food be the medicine and medicine be the food.”

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