NEC NUTRIMENTUM ET CURAE

Nutr Cur 2022; 01: e119
DOI: 10.57625/nec.2022.12

The importance of diet and metabolism: from nutrition to allergy and immunology

Stefania Colantuono, Ilaria Baglivo, Cristiano Caruso

Dipartimento di Scienze Mediche e Chirurgiche, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy

Corresponding Author: Stefania Colantuono, MD, Ph.D;
e-mail: stefania.colantuono@guest.policlinicogemelli.it

ABSTRACT

Food represents not only the source of nutrients for our body, but interacts with the gastrointestinal epithelium, gut microbiome and gut immune system. The diet-immune systems interactions are complex and reciprocal. Various recent studies attempted to explore this complexity in health and in different disease settings in order to untangle the mechanisms and their effects. This short review briefly discusses different aspects of this relationship, focusing on major players. If we consider that diet and microbiome may be modified by healthcare professional intervention, the implication for disease prevention and therapeutics are intriguing.

INTRODUCTION

Food components in our diet provide not only necessary nutrients to our body but also substrates for the mutualistic microbial flora in our gastrointestinal tract, termed the gut microbiome. Thus, what we eat shapes the structure, composition, and function of the gut microbiome, which interacts with the gut epithelium and mucosal immune system and maintains intestinal homeostasis in a healthy state[1].

In this point of view, an increasing interest exists in the potential of diet to impact the immune system, both in preventing disease as a therapeutic option. It has been largely appreciated that nutritional factors played a role in immune system effectiveness in people with nutrient deficiencies or during acute care for critically ill patients. Nonetheless, there has been a recent explosion of interest in understanding how long-term dietary habits impact chronic immune-mediated disorders and responses to infections. Moreover, in many cases, some nutrient excesses could be more dangerous for the immune system than their deficiencies. The diet-immune systems interactions are complex and reciprocal. If the nutritional state and pattern of foods could impact immunity at various levels (i.e., microbiome, epithelial barrier), conversely, the immune system impacts nutrition metabolism and needs and influences the physiological response to food[2].

MICROBIOME

If the relationship between microbiome and host immune systems has implications in healthy individuals, those existing in particular diseases are even more interesting.

Recent advances in metagenomic sequencing and bioinformatics have enabled detailed characterization of the vital microbial communities that constitute the microbiome. Studies in animal models have uncovered unrecognized roles for the microbiota in the normal function of the immune responses and in the pathogenesis of diseases. The composition of gut microbiota can influence local but also systemic inflammation. It is well known that alterations of the gut microbiome are implicated in many intestinal diseases, such as inflammatory bowel disease (IBD), and that diet plays a pivotal role in these diseases. For this

KEYWORDS

IMMUNONUTRITION
FOOD ALLERGY
MICROBIOME
EPITHELIAL BARRIER
NUTRIENT

reason, there is growing interest in nutritional therapy to target the gut microbiome. In recent years[1], literature concerning the dietary effects on the gut microbiome composition flourished. Therapeutic manipulation of the microbiota using fecal microbiota transplantation, probiotics, or engineered probiotics represent effective nontoxic approaches for the treatment or prevention of *Clostridium difficile* infection, allergy, and autoimmune diseases and may enhance the efficacy of certain cancer immunotherapeutics[3].

EPITHELIAL BARRIER AND FOOD

On the opposite point of view, such particular pathological conditions affecting the intestinal surface have taught us how exposure to diverse antigens, such as food antigens, food-borne pathogens, and commensal microbes, cooperate in the pathogenesis. Intestinal epithelial cells prevent the translocation of potentially hostile antigens into the body. The disruption of the epithelial barrier increases intestinal permeability and allows the translocation of commensal microbes into the body, disturbing immune homeostasis and inducing systemic inflammation. Leaky gut syndrome (LGS) represents an example of this process. Interestingly, recent clinical reports have suggested that LGS contributes to autoimmune diseases such as type 1 diabetes, multiple sclerosis, rheumatoid arthritis, and celiac disease. Furthermore, abnormalities of the microbial community, known as dysbiosis, are observed in patients with autoimmune diseases[4].

FOOD ALLERGY

Food allergy represents the best example of causal relationship between food and gut immune system. Allergic diseases, such as respiratory, cutaneous, and food allergies, have dramatically increased in prevalence over the last few decades. The increasing use of antibiotics and dysbiosis are thought to play a role in the enhanced prevalence of allergies and asthma[5]. The immunological processes underpinning allergic diseases present in two phases – the sensitization phase and the effector phase. Sensitization to allergens determines the production of allergen-specific immunoglobulin (Ig)E by B-cells. IgE binds to the receptor on mast cells and basophils. The re-exposure to allergen and its binding to surface-bound IgE determines the cross-linking of two receptors on mast cells or basophils, which finally induces the release of preformed mediators such as histamine and prostaglandin and consequently all typical allergic symptoms. But the link between food and allergy is not only direct. Emerging evidence suggests that nutrition may play a pivotal role in allergy prevention in children. In 2019, the European Academy of Allergy and Clinical Immunology (EAACI) Task Force on Diet and Immunomodulation systematically explored the association between diet diversity and allergy outcomes[6], suggesting that diet diversity in infancy may be associated with reduced allergy outcomes.

NUTRIENTS

Further studies focused on specific nutrients that play a role in the immune response, for example, polyunsaturated fatty acids (PUFAs) of the omega-6 and omega-3 series serve as substrates for the synthesis of signaling molecules, including eicosanoids and docosanoids[7]. Such protective effects have been observed in pregnant and lactating women, whereby increasing maternal and breast milk LCn3PUFA levels are associated with reduced risk of atopic dermatitis and development of food allergies[8]. Fibers, as non-digestible parts of fruits, vegetables and cereals, are an essential energy source for bacteria that, by fermentation, produce short-chain fatty acids (SCFA), essential human nutrients. In numerous studies using different fiber interventions, fibers have been attributed to maintain intestinal homeostasis by enhancing epithelial barrier function, inhibiting pathogen-induced cytotoxicity and preventing colonization with pathogenic bacteria. A high-fiber diet favors microbial diversity and production of SCFA. It prevents the fermentation of less favorable substrates, such as proteins and amino acids, leading to a reduced risk for intestinal diseases such as colorectal cancer and Crohn's disease. But SCFA levels may also impact in pathologies outside the gut, such as asthma, cystic fibrosis and COPD.

During the recent COVID-19 pandemic, a renewed interest in nutrient supplementation and primary prevention of respiratory infection has grown due to the consideration that multiple macronutrients have a recognized role in the immune system. A recent meta-analysis[9] reported that vitamin D supplementation significantly decreased respiratory infections in adults, and zinc supplementation appears to be protective in children.

All the cited topics represent only a few parts of the even more complex immunonutrition, i.e., the study of

the direct and indirect effects of nutrients, including macronutrients, vitamins, minerals, and trace elements on immune system development, functionality and responsiveness. The results of these effects can't be analyzed without considering environmental and lifestyle factors. While the latter remains largely outside the power of the healthcare professional, diet remains a modifiable factor that can be used to prevent or mitigate disease risk and to modify disease course in conjunction with the current standard of care medications and devices[10].

CONCLUSIONS

This brief review discusses different aspects of the complex relationship between nutrition and immune system in health and disease. If we consider that diet and microbiome may be modified by healthcare professional intervention, the implication on disease prevention and therapeutics are intriguing.

Declaration of interest. The authors declare no conflict of interest for this manuscript.

Funding. The authors didn't receive any funding for this paper.

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