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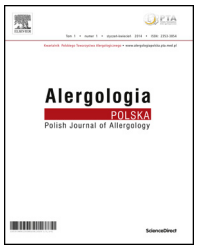

Review/Praca poglądowa

The role of microbiota in allergy development

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ABSTRACT

The increase of allergic diseases incidence has been noticed in industrialized countries. The reason for that is sought in increasing environment pollution and hygienisation of life. Diseases including asthma, hay fever, eczema and food allergies have dramatically increased over the last century. Microbiota (intestinal microflora) is a community of microorganisms, mainly bacteria that forms in the human digestive system a complex ecosystem. Recently more and more attention is paid to the connection of intestinal microflora with the occurrence of allergic diseases. Microbiota and the beneficial effects of probiotic bacteria on human health is becoming increasingly important in allergy development. However, the importance of probiotics in the prevention of these diseases has not been proven. It is a necessity to design and carry out thorough and detailed research to confirm significance of treatment with using probiotics strains.

Human microbiota

The correct composition of the intestinal ecosystem, a group of physiologically bacteria inhabiting the human digestive tract – microbiota, is necessary to maintain the health and proper functioning of our body [26]. The impact of intestinal bacteria is not restricted strictly to the gastrointestinal tract, but it affects the proper functioning of virtually the entire organism. So versatile activity of described ecosystem is due to the multiplicity of functions performed by him. The most important tasks of intestinal bacteria should include protective, immune and digestive function [20].

The hygiene hypothesis of allergic diseases

The increase in the number of cases of allergy diseases, observed in recent years, has become an inspiration to explore new concepts to explain the development of this group of diseases. In the populations affected by this phenomenon the role of environmental factors was revealed. Especially interesting topic is the relationship between an increased incidence of allergic diseases and the increased hygienization of life [22]. Hygiene hypothesis was proposed by Strachan et al. and it says that increase in sterility of our surroundings, the widespread availability of antibiotics and simultaneous migration of population from rural to urban

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areas significantly reduced human contact with the microbial world – bacteria, viruses or parasites [24]. These in turn are the main target of the immune system. As a result, our immune system, looking for new "enemies" began to actively respond to basically harmless particles of food or pollen. Because the normal intestinal ecosystem regulates the immune system, the risk of allergy or atopy is probably the higher, the stronger the dysbiosis of the gastrointestinal tract is. It is known that intestinal bacteria play a significant role in shaping the normal immune response. When the composition of the microbiota is correct, we observe generally balanced ratio of Th1/Th2 and tolerance of food intake. In patients with impaired intestinal ecosystem ratio of Th1/Th2 moves in a direction of decreasing in the activity of Th cells 1. Consequently, there is a mental process of capturing food allergens, so that they penetrate into the blood. Following are produced IgE antibody associated with type I food allergy, so-called immediate type reactions. The strong correlation between the composition of the intestinal ecosystem incidence of food or inhaled allergies has been shown in many scientific studies [22–24].

The intestinal microflora in allergic Estonian and Swedish 2-year-old children

Research conducted by a team of researchers from Estonia pointed to a relationship between the occurrence of allergic disease and the composition of the intestinal ecosystem [1]. In the study of Bjorksten, which the composition of the microbiota of children from the richer, more highly developed economically country (Sweden) with children in a developing country (Estonia). In Swedish children researchers found out strong disorders microflora, primarily lower number *Lactobacillus* sp. and higher numbers of aerobic bacteria especially *Enterobacteriaceae* and *staphylococci*, as well as lower counts of *Bacteroides* in the gastrointestinal tract, which was associated with a higher incidence of allergies [1].

Children who developed atopic dermatitis in their two first years of life were find out to be less often colonizes with *enterococci* during the first month of life and *bifidobacteria* during the first year of life. In addiction higher amount of clostridia at 3 months of age and lower counts of *Bacteroides* at 12 months were observed for allergic infants. Higher spread of colonization with Staphylococcus aureus in allergic children was established in comparison to reference group at 6 months old [2]. Differences of the gut microbiota composition between allergic and healthy subjects were confirmed in case-control studies and concerned various particular genera and species, especially *Bifidobacterium*, *Clostridium*, *Bacteroides*, *Lactobacillus* and *Enterobacteriaceae*. Higher concentration of icaproic acid, due to presence of *Clostridium difficile* and higher *C. difficile* IgG antibody levels, was detected in fecal of allergic infants at one year than non-allergic infants [3, 4]. On the other hand the FISH analysis carried out in order to count bacteria indicated that colonization by *Clostridium sp.* was lower in allergic than reference subjects [5] and no significant difference in *Clostridium* counts were found between preschool controls and children with allergy-associated atopic eczema/dermatitis syndrome (AAEDS) and non-allergic atopic eczema/dermatitis syndrome (NAAEDS) [6]. Colonization with Bifidobacterium, which is a dominant genus in infant fecal microbiota and may have beneficial effect, was proven to have quantitative differences by many studies [7]. Also, prevalence of *Bifidobacterium* has been found to be similar in healthy and allergic subjects, with no regard to allergic diseases, atopic dermatitis or wheezing [8–11]

Food allergy and the role of microbiota

The mucous membrane of the gastrointestinal tract is constantly exposed to a large amount of food and bacterial components. Healthy digestive immune system maintains a balance between immunological defense of mucous membranes and systemic tolerance [14, 27, 28]. In the case of food allergy this balance is disturbed and the body develops tolerance for input from food allergens or it is insufficient. Development of food allergy is caused by risk factors, immature gut barrier and type 2 T-helper (Th2) cell-skewed cytokine profile, which are present in early childhood. The antigen uptake is aberrant and Th2 cells further produce interleukin (IL)-4, a cytokine essential for B-cell differentiation into immunoglobulin (Ig)E-producing cells, and IL-5, which is important for the activity of eosinophils which promotes the development of food allergy [14]. Bacteria colonization of mucous membranes of the digestive tract begins after birth, however, the development of normal microflora is gradual, initially depends, among the composition of the intestinal flora of the mother and the surrounding environment, as well as possible genetic factors [29, 30].

Bacterial flora of the gastrointestinal tract counterbalance the activity of Th2 cells and promotes the development of food tolerance [31, 32]. Studies on germ-free mice (sterile, devoid of microflora) indicate that normal flora of the digestive tract also affects many other parameters of the immune response [14, 33]. In these animals noticed reduced non-specific immune response and reducing the amount of Peyer's tufts, decreased concentration of sIgA and disturbances in the production of microvilli [34, 35]. Furthermore, colonization of mice germ-free mixture of three bacterial strains of the genus *Lactobacillus* significantly affected the increase in integrity of the small bowel mucosa and the induction of antibody production IgA12 [34]. Numerous studies indicate that the dysbiosis intestinal, or qualitative and quantitative abnormalities in the composition of the microflora may be one of the factors involved in the pathogenesis of a number of disorders such as necrotizing enterocolitis newborns (NEC), celiac disease, inflammatory bowel disease, irritable bowel syndrome, atopic dermatitis, allergic disorders, depression, cancer and other [1, 34, 35, 36].

The connection between prevalence of food allergy and abnormal intestinal microflora was suspected in the early 80s [37]. Russian scientists reported that the administration of a mixture containing *Propionibacteria* and *Lactobacillus acidophilus* bacteria hastened the disappearance of food

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