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REVIEW PAPER/*PRACA POGLĄDOWA*

The importance of the gut microbiome in the development of allergic diseases

Znaczenie mikrobiomu jelitowego w rozwoju chorób alergicznych

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ABSTRACT

Allergic reactions leading to food allergies, asthma or atopic eczema symptoms, are significantly impacted by the gut microbiome. Dysbiosis, an imbalance in gut microbiota, can increase the risk of these conditions. Food allergies are caused by dysregulation in IgE synthesis, but commensal bacteria in the human microbiota can regulate the immune response and prevent the development of food allergies. Exposure to microbes during infancy can positively influence allergy development. Treatment options include food allergy immunotherapy, pharmacological treatments, prebiotics and probiotics. Studies show that the gut microbiota composition differs in individuals with allergic and non-allergic asthma compared to healthy individuals, with higher richness but lower diversity of gut microbiome in asthmatic individuals. The relationship between the intestinal microbiota and the occurrence of atopic eczema is clear, with differences in the number of types of bacteria contributing to the activation of the immune system and the appearance of atopic eczema. Understanding the complex interactions between the gut microbiome and the immune system may lead to new therapeutic strategies for the prevention and treatment of allergic diseases, which have a significant impact on patients' lives.

KEY WORDS

allergy, asthma, eczema, food allergies, gut microbiome, microbiome dysregulation, plant-based diet.

STRESZCZENIE

Mikrobiom jelitowy znacząco wpływa na reakcje alergiczne prowadzące do objawów alergii pokarmowych, astmy lub wyprysku atopowego. Dysbioza, czyli brak równowagi mikroflory jelitowej, może zwiększać ryzyko wystąpienia tych schorzeń. Alergie pokarmowe są spowodowane rozregulowaniem syntezy IgE, ale bakterie komensalne w ludzkiej mikroflorze mogą regulować odpowiedź immunologiczną i zapobiegać rozwojowi alergii pokarmowych. Ekspozycja na drobnoustroje w okresie niemowlęcym może pozytywnie wpływać na rozwój alergii. Leczenie obejmuje immunoterapię alergii pokarmowej, leczenie farmakologiczne, stosowanie prebiotyków i probiotyków. Badania pokazują, że skład mikroflory jelitowej różni się u osób z astmą alergiczną i niealergiczną w porównaniu z osobami zdrowymi, z większym bogactwem, ale mniejszą różnorodnością

mikrobiomu jelitowego. Związek między mikrobiomem jelitowym a występowaniem wyprysku atopowego jest wyraźny, przy czym różnice w liczbie rodzajów bakterii przyczyniają się do aktywacji układu odpornościowego i pojawienia się wyprysku atopowego. Zrozumienie złożonych interakcji między mikrobiomem jelitowym a układem odpornościowym może prowadzić do nowych strategii terapeutycznych w zapobieganiu i leczeniu chorób alergicznych, które mają znaczący wpływ na życie pacjentów.

SŁOWA KLUCZOWE

alergia, astma, egzema, alergie pokarmowe, mikrobiom jelitowy, dysregulacja mikrobiomu, dieta roślinna.

ADDRESS FOR CORRESPONDENCE

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INTRODUCTION

The human body houses a diverse and dynamic gut microbiome, which in its essence is a process. This process involves a complex community of bacteria, viruses, fungi as well as parasites. The microbial population is influenced by the development of the host [1]. It participates in a sequence of immune and metabolic activities, is variable and dependent on many stimuli [2].

An infant has a different composition of the intestinal microflora than an adult. Factors determining it include, among others, past infections, antibiotic therapy, stress and diet. The latter factor, among many other processes, affects the interaction between the microbiome and epigenetics (epigenetic modification is one of the mechanisms associated with the development of diseases in response to a modified gut microbiome). Genetics itself also plays an important role in shaping the composition of the gut microbiome [3].

Numerous studies exploring the gut microbiome have confirmed its association with the course and occurrence of many diseases and ailments. A diverse and dynamic microbial population influences, among other things, the occurrence of autoimmune disorders, cancer, infectious diseases or allergies in humans. Cohort studies have shown significant differences in the composition of the microbiome in healthy people compared to those affected by food allergies. It has also been proven that the development of food allergies is one of the consequences of dysbiosis [4].

In addition, it is worth noting that there is a consistency of the gut microflora with the human immune system, as evidenced by processes like regulation of immune functions and inhibition of pro-inflammatory factors by the bacterial community. What is more, studies have confirmed the role of the microbiome in the development of asthma and atopic eczema [5, 6]. The aforementioned ecosystem, composed of trillions of microorganisms, has a significant impact on the human body during both homeostasis and disease [4]. It participates in many physiological functions such as neutralizing toxins and pathogens, producing vitamins, maintaining intestinal cells and obtaining energy from food. Human health depends on its composition and function.

This review summarizes the current state of knowledge on the importance of the gut microbiome in the development of allergic diseases.

RELATIONSHIP BETWEEN GASTROINTESTINAL MICROBIOTA DYSBIOSIS AND FOOD ALLERGIES

Food allergies have become a more prevalent problem over the course of 2 decades. Reasoning behind this phenomenon is yet to be fully established. Food allergies significantly reduce the standard of living of patients, however there is no established cure for treating or preventing food allergies [7].

Currently it is thought that pathogenesis of food allergies is mostly based on immunoglobulin E (IgE)-mediated reactions. Symptoms appear within minutes, and they consist of rash, fever, redness, diarrhea, vomiting and swelling. Severe food allergies may lead to life-threatening anaphylaxis. Symptoms of food allergies are conditioned by the degranulation of basophils and mast cells. Degranulation occurs as a result of the binding of IgE to high-affinity IgE receptor (FcεRI) (Figure 1). However, IgE secretion itself is dependent on Th2 lymphocytes that produce IL-4. It is this interleukin that B cells need to form the IgE isotype. In addition, it is important to re-

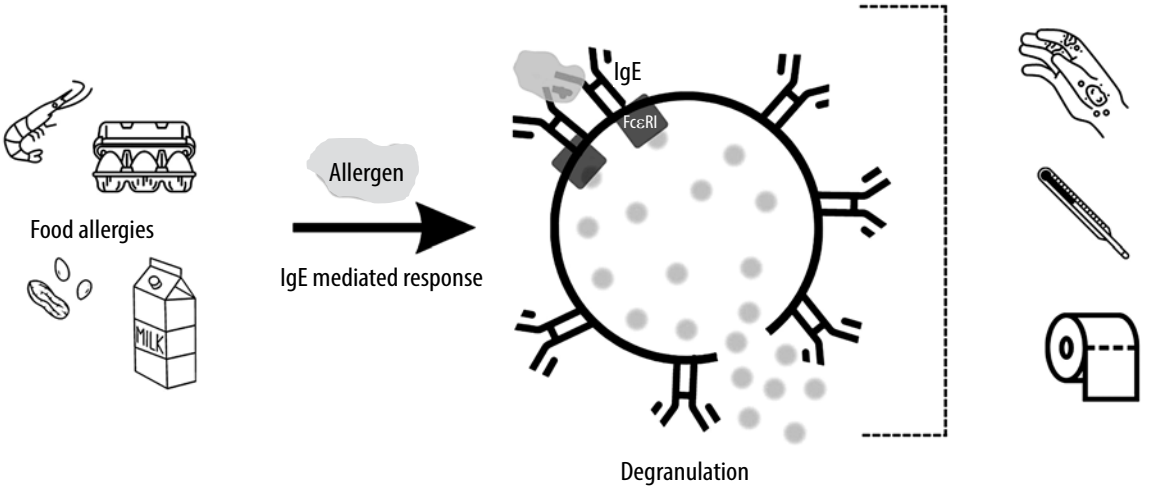

FIGURE 1. IgE-mediated allergic reaction caused by food containing allergens

member the key function of Treg cells, which can stop the generation of Th2 immunity and the production of IgE. It can be concluded that food allergies are likely caused by dysregulation in IgE synthesis, for instance, germ-free mice, or mice treated with antibiotics became increasingly more susceptible to peanut allergy, while showing increased levels of peanut-specific IgE compared to the control groups [8–10].

The human microbiota consists of bacteria, fungi, viruses and protozoa. However, the intestines of healthy people are mainly inhabited by commensal bacteria. The mucosal surface in the digestive tract is constantly exposed to trillions of bacteria with which it forms a symbiotic relationship. The number of bacterial cells far exceeds the number of human cells, which is why maintaining symbiosis is crucial for the proper regulation of the immune response [11]. Short-chain fatty acids (SCFAs) are one example of metabolites produced by the microbiota that are crucial in promoting oral tolerance and barrier integrity to decrease pathogenic reactions to consumed meals. Unfortunately, westernized diet is currently low in fiber, which is the substrate for subsequent production of SCFAs. SCFAs are essential metabolites in the regulation of intestinal Treg cell differentiation and, in addition, cause increased secretion of IL-10. It should also be borne in mind that SCFAs are epithelial barrier enhancers by controlling goblet cell mucus secretion and IL-22 production by ILC3 [12]. Results from multiple studies indicate that production of SCFAs by microbes inhabiting the gut helps in prevention of developing food allergies, therefore dysbiosis in gut microbiome can increase the risk of developing food allergies [13–15].

It is suggested that the first few years after birth are crucial in preventing food allergies. Microbiome colonization is fully completed by the end of the first month, and later changes are observed usually when the infant's diet is introduced to new food groups [16]. Roduit *et al.* discovered that the variety of food consumed in the first year of life has a counter-proportional effect on the development of food allergies [17]. Research provided by Du Toit *et al.* supports the hypothesis that infants should be introduced to allergens as fast as possible. In this study, 640 infants at 4–11 months of age that have been already diagnosed with at least one allergy, were randomly assigned to a group where they were either consuming or avoiding peanuts until 60 months of age. Results confirmed that early introduction to the allergen in high-risk patients, had a great chance of decreasing the risk of development of food allergy targeted toward peanut allergy [18]. Another important factor to take into consideration is "hygiene hypothesis". Once again, in this aspect everything starts in infancy. The term "hygiene hypothesis" was first used in 1989, when David Strachan linked the exposure to the microorganism with development of the immune system in childhood [19]. First studies that were researching this hypothesis were done in Europe and resulted in promising findings. Children living in the farm areas were exposed to much more microbes than children in city areas. This exposure to microbes, positively influenced development of the allergy in children brought up in farm areas. Apart from the exposure to microbes, the mode of delivery, family size, diet, antibiotic exposure and exposure to furry animals also play important roles. All those factors lie under the "hygiene hypothesis" umbrella term, and they are playing a crucial role in composition of microbiome and development of food allergies [20].

Establishing the fact that gut microbiome has in fact modulatory properties when it comes to development of food allergies, can be crucial in finding the proper way to help ameliorate the patient's quality of life. So far, potential methods have focused on specific immunotherapy,

pharmacological treatments, transplant of fecal matter, manipulations with microbiome introducing probiotics and prebiotics. The most promising direction is food allergy immunotherapy. By modifying the immune system, the therapy hopes to permanently stop the body's reactivity to dietary allergies. This involves increasing regulatory B cells, which release IL-10, and converting allergen-specific Th2 lymphocytes into Treg cells, which generate IL-10. These modifications lead to a diminished sensitivity to allergen triggers and a decrease in Th2 inflammation. There are three proposed ways of introduction the food allergy immunotherapy, including the oral, sublingual and transdermal route. For now, the oral route seems to be the most effective, despite having the most side effects. Pharmacological treatments, apart from known adrenaline and antihistamine drugs, one of the biotechnological drugs – omalizumab, seems to be gaining interest as an anti-IgE monoclonal antibody. Prebiotics and probiotics are also considered as helpful, however results from multiple studies are non-homogeneous and further research is needed to establish their full potential. Fecal microbiota transplantation or restoring the composition of the microbiome is also researched due to its promising outcomes in animal model experiments [21–23].

RELATIONSHIP BETWEEN GASTROINTESTINAL MICROBIOTA DYSBIOSIS AND ASTHMA

Asthma is a diverse clinical condition that impacts over 300 million individuals worldwide, making it the most prevalent chronic disease among children. In the United States alone, in 2020, 7.8% of the population was diagnosed with asthma, with women being more susceptible than men according to CDC data. Breathing difficulties in asthma are caused by the constriction of the airways due to spasms and a rise in bronchial secretions, which can be reversed and brought on by allergens or hypersensitivity. Both allergic asthma and non-allergic asthma typically exhibit higher levels of IgE in serum compared to healthy individuals, although IgE levels alone are not reliable indicators for distinguishing between the two. Allergic asthma often manifests when a patient is exposed to allergens and tends to develop in early stages of life, while non-allergic asthma usually occurs later in life. Furthermore, studies have suggested that the gut-lung axis plays a significant role in asthma development, with dysbiosis or other factors potentially contributing to its onset [24–28].

Many studies have shown differences in composition of gut microbiota between patients with allergic asthma, non-allergic asthma, and healthy individuals. Zheng *et al.* [29] conducted a study using fecal samples collected from 57 patients, including 20 healthy children, 10 non-allergic asthmatic children, and 27 allergic asthmatic children. The researchers performed 16s RNA gene sequencing to investigate whether the composition of gut microbiota differed among these groups. The results revealed that the richness of gut microbiome was significantly higher in asthmatic groups compared to healthy controls. However, the diversity of gut microbiome was lower in asthmatic groups compared to healthy controls. Notably, *Proteobacteria* showed the largest difference in abundance, being most abundant in both allergic and non-allergic asthma. *Lactobacillales* were the richest taxa in allergic asthma, while both non-allergic and allergic patients showed lower abundance of genera from *Clostridia*.

Hoffmann *et al.* [30] conducted a study to compare the composition of gut microbiota between patients with asthma and healthy individuals. The study included 20 samples, with 7 from healthy patients and 13 from asthmatic patients. The results of 16s RNA sequencing revealed that at the genus level, asthmatic patients had significantly higher levels of *Lachnoclostridium*, *Parabacteroides*, and *Faecalitalea* compared to non-asthmatic patients. When examining individual groups of bacteria, the abundance of *Bacteroides* was significantly increased in the asthmatic group compared to the control group, while *Prevotella* showed a significant decrease in the asthmatic group. At the species level, there were also notable differences in the gut microbiota composition of asthmatic patients, particularly with *B. vulgatus*, which accounted for approximately 20% of the gut microbiota in asthmatic patients compared to approximately 5% in healthy controls. Conversely, the abundance of *Oscillobacter valericigenes* was higher in the asthmatic group compared to healthy controls. In terms of alpha diversity, the asthmatic group showed lower diversity compared to the healthy control group.

Zou *et al.* [31] attempted to describe the gut microbiota composition in various types of asthma characterized by inflammation. They collected 67 stool samples from patients, including 20 healthy individuals and 47 newly diagnosed asthmatic patients. The results of the study revealed that patients with asthma had lower bacterial richness and diversity in their stool samples compared to healthy controls. Additionally, the study identified three specific bacterial species, namely *R. bromii*, *B. vesicularis*, and *C. disporicum* that were associated with the asthma phenotype.

In conclusion, several studies have shown that there are differences in the composition of gut bacteria between people with allergic asthma, non-allergic asthma, and those who are healthy. These studies used fecal samples and 16s RNA gene sequencing to study the composition of gut microbiota. The results suggest that people with asthma generally have more types of bacteria in their gut (higher richness), but less overall diversity compared to

healthy people. Certain types of bacteria, like *Proteobacteria* and *Lactobacillales*, are more common in people with asthma, while other types, like *Clostridia* and *Prevotella*, are less common. Some studies also found that specific species of bacteria, such as *Bacteroides vulgatus* and *Oscillobacter valericigenes*, are different in people with asthma compared to healthy people. Additionally, patients with asthma were found to have lower bacterial richness and diversity in their gut compared to healthy individuals. Certain bacterial species, like *R. bromii*, *B. vesicularis*, and *C. disporicum*, were also associated with asthma in some studies. These findings suggest that the gut bacteria may play a role in the development and progression of asthma, but more research is needed to better understand how this works and if it can be used for potential treatments.

RELATIONSHIP BETWEEN GASTROINTESTINAL MICROBIOTA DYSBIOSIS AND ECZEMA

Atopic eczema, which may otherwise be called atopic inflammation, is a disease that affects young children, in particular, with most cases reported in affluent societies [32]. The cause of this condition is a disruption of the protective barrier, that is the epidermis and an allergy involving immunoglobulin E. The skin lesions are mostly characterized by itching, leaks and papules, which increases the chances of bacterial or viral infections [33]. More than 80% of people who develop atopic eczema, later struggle with allergic diseases such as allergic asthma or rhinitis [34]. As the etiology of atopic eczema is not completely understood and involves both environmental, genetic and allergenic factors, scientists have begun to look for a link between the disease and changes occurring in the gut microbiome.

Previous studies have confirmed the correlation between the occurrence of atopic eczema and changes in the gut microbiome. A study conducted by Zheng *et al.* aimed to compare the gut bacteria between healthy infants and infants who developed atopic eczema [32]. The feces of 51 sick infants and 50 healthy ones who served as a control group were examined. Interestingly, the infants with atopic eczema had bacteria that were not present in the control group, and *vice versa*. Table 1 shows exactly which bacteria were present in each group [32].

A recent scientific study has confirmed that allergic diseases are linked to the diversity of the gut microbiota. Researchers led by Ismail *et al.* analyzed feces from 98 newborns who had a high risk of allergic disease [35]. They did another analysis after 12 months to study differences in the microbiota. They performed an analysis of microbial diversity through terminal restriction fragment polymorphisms. According to the results, infants who developed atopic eczema soon after birth had lower gut microbiota diversity than children who did not develop atopic eczema [35].

Changes regarding microbiota diversity in a one-year-old child were presented by Doreswamy and Peden [36]. As in previous studies, they confirmed that infants with atopic eczema have reduced microflora. A significant difference was observed in the presence of *Proteobacteria*. This microorganism is courted by Gram-negative bacteria with a built-in endotoxin that induces the immune system through T-helper type 1 cells (Th1). There is an increase in IL-12 and dendritic cells, this process favors the occurrence of atopic eczema.

There was a significant reduction in *Ruminococcaceae* bacteria compared to the control group [37]. These bacteria also activate cells of the immune system and stimulate IL-6, among other things [38, 39]. According to pyrosequencing, the infants without atopic eczema had significantly lower numbers of *Enterobacteriaceae* but this may be due to the fact that the newborns were delivered by cesarean section [40]. Interestingly, the feces of women in the third trimester of pregnancy whose offspring had IgE-associated atopic eczema at birth were studied, and as it turned out, they had elevated numbers of *Streptococcus*

TABLE 1. Differences in composition of the microbiome in healthy infants and in infants with atopic eczema

Infants with atopic eczema	Healthy infants
Bacteroides clarus	*Bifidobacterium bifidum*
Bacteroides plebeius	*Bifidobacterium longum*
Parabacteroides merdae	*Bacteroides fragilis*
Prevotella buccae	*Streptococcus salivarius*
Ruminococcus gnavus	*Eubacterium biforme*
Faecalibacterium prausnitzii	
Gemmiger formicilis	
Akkermansia muciniphila	

Own development based on [32].

compared to mothers whose offspring did not have atopic eczema [40, 41].

A study conducted by Mah *et al.* also found a lower colonization of *Bifidobacterium* in children with atopic eczema compared to the control group [42]. Based on a study conducted in Singapore, it was also found that those exposed to atopic eczema have a significantly higher number of *Enterococci*. It was also confirmed that children with atopic eczema are not deficient in aerobic bacteria such as *Lactobacillus*.

Previous studies conducted for *Clostridium* yielded conflicting results. Kalliomäki *et al.* and Björkstén *et al.* showed a significant number of *Clostridium* bacteria in children with a high risk of atopic eczema [43, 44]. Completely opposite results were obtained by the team of Watanabe *et al.* [6]. However, a study by Mah *et al.* confirmed that children with atopic eczema have significantly fewer of these bacteria [42]. The differences in results may be due to the study of different species of these bacteria.

Another study found significantly higher *Campylobacter* colonization in children with atopic eczema compared to healthy controls. This relationship may be due to the fact that this bacterium can damage the epithelium, facilitating the passage of *Escherichia coli*, which can induce colitis/inflammation [45, 46]. The opposite observation was made for *Roseburia,* a bacterium that has a positive effect on protecting the colon, so its decreased numbers can also lead to inflammation and atopic eczema [46, 47].

The number of *Escherichia coli* is correlated with the presence of IgE. Studies confirm that children suffering with atopic eczema have significantly more of these bacteria than the control group [48, 49]. Through the ability to produce Lipopolysaccharide (LPS), this bacterium is virulent, can cause inflammation, increase the permeability of membranes, allowing the penetration of non-threatening antigens, which can cause an excessive immune response and may reduce the number of beneficial bacteria.

In conclusion, there is a clear relationship between the intestinal microbiota and the occurrence of atopic eczema. This is especially true for differences in the number of types of bacteria, especially the Gram-negative *Enterobacteriaceae* family and the Gram-positive *Ruminococcaceae*. These bacteria largely contribute to the activation of the immune system, which increases the likelihood of the appearance of eczema [40].

RELATIONSHIP BETWEEN GUT FLORA, ALLERGIC DISEASES AND PLANT-BASED DIET

The plant-based diet is based mainly on plants such as vegetables, fruits, seeds, oils and so on. Notably, the plant-based diet has a lot of benefits which influence on our health by reducing cholesterol or saturated fatty acids. However, gut flora plays a crucial role in drug metabolism, nutrient metabolism or maintaining immunomodulation. Gut flora consists mainly of a set of bacteria which are responsible for controlling digestion and absorbing vital nutrients from foods which are necessary for the health. Some of studies have indicated that plant-based diet especially vegan diet, contains more bacteria in gut flora, therefore the gut flora may have more desirable metabolites and other ingredients which will be able to prevent the inflammation. Other studies have shown that plant-based diet especially vegetarian diet indicated a decreased level of IgE which is directly associated with development of allergic disorders. There are many allergic diseases such as asthma and others which have different pro-inflammatory factors; however, they share a common, elevated level of IgE compared to healthy groups [50–52].

For instance, some studies indicate that children and adults that regularly eat fruits and vegetables, had decreased chances of developing asthma. Furthermore, thanks to the consumption of fruits and vegetables, some symptoms of allergic asthma may be relieved. Therefore, patients consuming plant-based diet have a significantly reduced risk of developing allergic asthma. The same studies confirmed that fruits and vegetables contain health-promoting flavonoids, containing antioxidants, which work by inhibiting pro-inflammatory cytokines and influence on not only gut microbiota, but also other cells. Some of antioxidants such as vitamin C or E are able to prevent development of oxidative stress and lipid peroxidation which are involved in cellular damage and initiating an excessive cytokine response [53].

In the case of atopic dermatitis, there is an overproduction of free oxygen radicals, which causes the development of oxidative stress and intensification of inflammation. Therefore, applied plant-based diet can prevent the formation of free radicals because antioxidants are able to inhibit free radicals thereby decreasing the inflammation process in the cells [54].

The mechanism of action is not homogeneous, as antioxidants may use various mechanisms to prevent the development of oxidative stress. One of the mechanisms concerns a chain-breaking mechanism where the antioxidant supplies the electron to free radical thereby neutralizing the action of the free radical. One of the other mechanisms concerns to remove some of reactive oxidative species initiators by silencing the catalyst which is able to induce the electron transport chain. Finally, the antioxidants contain various enzymes and proteases which are able to prevent the action of oxidized proteins which were created by free radicals.

Free radicals overproduction is harmful to human health because they can cause oxidative stress, which con-

tributes to the development of many diseases not only allergic diseases but also other such as cardiovascular, neurodegenerative or cancer diseases.

Therefore, all of diets which contain a lot of plants are vital for human health to prevent the development of oxidative stress [55].

SUMMARY

There is a lot of evidence for the direct impact of the composition of the microbiota on the development of various types of allergic diseases. Any type of response to allergens causes significant discomfort in the lives of patients and in some cases can even be life threatening. The summary of knowledge on the discussed topic highlighted how important and timely this topic is. We still do not know all the answers to these questions, so further and more detailed research into the causes and potential treatments is required.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

REFERENCES

1. Bhattacharjee G, Khambhati K, Gohil N, et al. Gut microbiota in gastrointestinal diseases. Prog Mol Biol Transl Sci 2022; 191: 141-51.
2. Al Bander Z, Nitert MD, Mousa A, Naderpoor N. The gut microbiota and inflammation: an overview. Int J Environ Res Public Health 2020; 17: 7618.
3. Ibay ICV, Poteres E, Isabelli A, Martinez-Guryn K. Diet-microbiome interactions and the regulation of the epigenome. In: Nutritional Epigenomics. Ferguson BS (ed.). 2019; 14: 401-7.
4. Thursby E, Juge N. Introduction to the human gut microbiota. Biochem J 2017; 474: 1823-36.
5. Chan CWH, Leung TF, Choi KC, et al. Effects of gut microbiome and environment on the development of eczema in Chinese infants. Medicine (Baltimore) 2020; 99: e20327.
6. Sullivan A, Hunt E, MacSharry J, et al. The microbiome and the pathophysiology of asthma. Respir Res 2016; 17: 163.
7. Blázquez AB, Berin MC. Microbiome and food allergy. Transl Res 2017; 179: 199-203.
8. Bashir ME, Louie S, Shi HN, Nagler-Anderson C. Toll-like receptor 4 signaling by intestinal microbes influences susceptibility to food allergy. J Immunol 2004; 172: 6978-87.
9. Stefka AT, Feehley T, Tripathi P, et al. Commensal bacteria protect against food allergen sensitization. Proc Natl Acad Sci USA 2014; 111: 13145-50.
10. Hill DA, Siracusa MC, Abt MC, et al. Commensal bacteria-derived signals regulate basophil hematopoiesis and allergic inflammation. Nat Med 2012; 18: 538-46.
11. Nance CL, Deniskin R, Diaz VC, et al. The role of the microbiome in food allergy: a review. Children (Basel) 2020; 7: 50.
12. Stephen-Victor E, Crestani E, Chatila TA. Dietary and microbial determinants in food allergy. Immunity 2020; 53: 277-89.
13. Smith PM, Howitt MR, Panikov N, et al. The microbial metabolites, short-chain fatty acids, regulate colonic Treg cell homeostasis. Science 2013; 341: 569-73.
14. Tan J, McKenzie C, Vuillermin PJ, et al. Dietary fiber and bacterial SCFA enhance oral tolerance and protect against food allergy through diverse cellular pathways. Cell Rep 2016; 15: 2809-24.
15. Björkstén B, Sepp E, Julge K, et al. Allergy development and the intestinal microflora during the first year of life. J Allergy Clin Immunol 2001; 108: 516-20.
16. Bunyavanich S, Berin MC. Food allergy and the microbiome: current understandings and future directions. J Allergy Clin Immunol 2019; 144: 1468-77.
17. Roduit C, Frei R, Depner M, et al.; PASTURE study group. Increased food diversity in the first year of life is inversely associated with allergic diseases. J Allergy Clin Immunol 2014; 133: 1056-64.
18. Du Toit G, Roberts G, Sayre PH, et al.; LEAP Study Team. Randomized trial of peanut consumption in infants at risk for peanut allergy. N Engl J Med 2015; 372: 803-13.
19. Strachan DP. Family size, infection and atopy: the first decade of the "hygiene hypothesis". Thorax 2000; 55 (Suppl 1): S2-10.
20. Prince BT, Mandel MJ, Nadeau K, Singh AM. Gut microbiome and the development of food allergy and allergic disease. Pediatr Clin North Am 2015; 62: 1479-92.
21. De Martinis M, Sirufo MM, Suppa M, Ginaldi L. New perspectives in food allergy. Int J Mol Sci 2020; 21: 1474.
22. Zhao W, Ho HE, Bunyavanich S. The gut microbiome in food allergy. Ann Allergy Asthma Immunol 2019; 122: 276-82.
23. Berni Canani R, Paparo L, Nocerino R, et al. Gut microbiome as target for innovative strategies against food allergy. Front Immunol 2019; 10: 191.
24. Romanet-Manent S, Charpin D, Magnan A, et al., the EGEA Cooperative Group. Allergic vs nonallergic asthma: what makes the difference? Allergy 2002; 57: 607-13.
25. Schatz M, Rosenwasser L. The allergic asthma phenotype. J Allergy Clin Immunol Pract 2014; 2: 645-8.
26. Stern J, Pier J, Litonjua AA. Asthma epidemiology and risk factors. Semin Immunopathol 2020; 42: 5-15.
27. Dharmage SC, Perret JL, Custovic A. Epidemiology of asthma in children and adults. Front Pediatr 2019; 7: 246.
28. Dang AT, Marsland BJ. Microbes, metabolites, and the gut–lung axis. Mucosal Immunol 2019; 12: 843-50.
29. Zheng P, Zhang K, Lv X, et al. Gut microbiome and metabolomics profiles of allergic and non-allergic childhood asthma. J Asthma Allergy 2022; 15: 419-35.
30. Hoffmann A, Strózik T, Wasiak T, et al. Compositional differences between gut microbiotaof adult patients with asthma and healthy controls. Adv Dermatol Allergol 2023; 40: 142-9.
31. Zou XL, Wu JJ, Ye HX, et al. Associations between gut microbiota and asthma endotypes: a cross-sectional study in South China based on patients with newly diagnosed asthma. J Asthma Allergy 2021; 14: 981-92.
32. Zheng H, Liang H, Wang Y, et al. Altered gut microbiota composition associated with eczema in infants. PLoS One 2016; 11: e0166026.
33. Sohn A, Frankel A, Patel RV, Goldenberg G. Eczema. Mt Sinai J Med 2011; 78: 730-9.
34. Chan CWH, Yuet Wa Chan J, Leung TF, et al. Altered gut microbiome and environmental factors associated with development of eczema in Hong Kong infants: a 4-month pilot study. Int J Environ Res Public Health 2020; 17: 7634.

35. Ismail IH, Oppedisano F, Joseph SJ, et al. Reduced gut microbial diversity in early life is associated with later development of eczema but not atopy in high-risk infants. Pediatr Allergy Immunol 2012; 23: 674-81.
36. Doreswamy V, Peden DB. Modulation of asthma by endotoxin. Clin Exp Allergy 2011; 41: 9-19.
37. Abrahamsson TR, Jakobsson HE, Andersson AF, et al. Low diversity of the gut microbiota in infants with atopic eczema. J Allergy Clin Immunol 2012; 129: 434-40, 440.e1-2.
38. Migrujące bakterie jelitowe przyczyną wielu chorób. Nauka w Polsce, 2023.
39. Gillevet PM, Puri P. Intestinal Microbiome and the Liver. Zakim and Boyer's Hepatology: A Textbook of Liver Disease. Boyer TD, Lindor KD (eds.). 7th edition. Elsevier 2016.
40. West CE, Rydén P, Lundin D, et al. Gut microbiome and innate immune response patterns in IgE-associated eczema. Clin Exp Allergy 2015; 45: 1419-29.
41. Koren O, Goodrich JK, Cullender TC, et al. Host remodeling of the gut microbiome and metabolic changes during pregnancy. Cell 2012; 150: 470-80.
42. Mah KW, Björkstén B, Lee BW, et al. Distinct pattern of commensal gut microbiota in toddlers with eczema. Int Arch Allergy Immunol 2006; 140: 157-63.
43. Björkstén B, Sepp E, Julge K, et al. Allergy development and the intestinal microflora during the first year of life. J Allergy Clin Immunol 2001; 108: 516-20.
44. Kalliomäki M, Kirjavainen P, Eerola E, et al. Distinct patterns of neonatal gut microflora in infants in whom atopy was and was not developing. J Allergy Clin Immunol 2001; 107: 129-34.
45. Tang MF, Sy HY, Kwok JS, et al. Eczema susceptibility and composition of faecal microbiota at 4 weeks of age: a pilot study in Chinese infants. Br J Dermatol 2016; 174: 898-900.
46. Lamb-Rosteski JM, Kalischuk LD, Inglis GD, Buret AG. Epidermal growth factor inhibits Campylobacter jejuni-induced claudin-4 disruption, loss of epithelial barrier function, and Escherichia coli translocation. Infect Immun 2008; 76: 3390-8.
47. Kang Y, Cai Y, Pan W. Change in gut microbiota for eczema: implications for novel therapeutic strategies. Allergol Immunopathol (Madr) 2018; 46: 281-90.
48. Wang HB, Wang PY, Wang X, et al. Butyrate enhances intestinal epithelial barrier function via up-regulation of tight junction protein Claudin-1 transcription. Dig Dis Sci 2012; 57: 3126-35.
49. Penders J, Stobberingh EE, Thijs C, et al. Molecular fingerprinting of the intestinal microbiota of infants in whom atopic eczema was or was not developing. Clin Exp Allergy 2006; 36: 1602-8.
50. Losno EA, Sieferle K, Perez-Cueto FJA, Ritz C. Vegan diet and the gut microbiota composition in healthy adults. Nutrients 2021; 13: 2402.
51. Sidhu SRK, Kok CW, Kunasegaran T, Ramadas A. Effect of plant-based diets on gut microbiota: a systematic review of interventional studies. Nutrients 2023; 15: 1510.
52. Han P, Gu JQ, Li LS, et al. The association between intestinal bacteria and allergic diseases-cause or consequence? Front Cell Infect Microbiol 2021; 11: 650893.
53. Alwarith J, Kahleova H, Crosby L, et al. The role of nutrition in asthma prevention and treatment. Nutr Rev 2020; 78: 928-38.
54. Fusano M. Veganism in acne, atopic dermatitis, and psoriasis: benefits of a plant-based diet. Clin Dermatol 2023; 41: 122-6.
55. Lobo V, Patil A, Phatak A, Chandra N. Free radicals, antioxidants and functional foods: impact on human health. Pharmacogn Rev 2010; 4: 118-26.