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The Role of the Skin Microbiome in Pathogenesis of Atopic Dermatitis - Current State of Knowledge

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Abstract

Introduction and purpose

The subject of this article is the role of the skin microbiome in the pathogenesis of atopic dermatitis - the current state of knowledge. As is known, the skin plays a key role in protecting the body and maintaining homeostasis, cooperating with the microbiome, which affects its immune functions. The purpose of this article is to provide a comprehensive review of current research on the microbiome's role in the pathogenesis of atopic dermatitis (AD).

Materials and methods

The presented article was developed based on a broad database of peer-reviewed scientific publications obtained from reputable sources such as PubMed, Google Scholar, and literature authored by renowned researchers from both Poland and abroad. In the process of analysis and interpretation of information, only scientific publications with a high impact factor were taken into account. The analyses performed include both clinical and experimental studies, as well as systematic reviews and meta-analyses, which allowed for obtaining a comprehensive view of the current state of knowledge in this field.

Description of the state of knowledge

Atopic dermatitis (AD) is a chronic inflammatory disease, the pathogenesis of which is associated with disorders of the skin microbiome, leading to the dominance of pathogenic microorganisms, such as Staphylococcus aureus. Standard methods of treating atopic dermatitis (AD) often bring only short-term relief. Understanding the role of the microbiome in this disease opens the way to new, more effective therapies, such as probiotics and methods supporting the reconstruction of skin microflora, enabling a more personalized therapeutic approach.

Conclusion

The aim of the article is to draw attention to the role of the microbiome in atopic dermatitis (AD), which is currently one of the most common skin diseases. It affects not only children but also adults, influencing their quality of life.

Keywords

skin, microbiome, atopic dermatitis, dysbiosis, atopic dermatitis treatment, personalized therapy

Introduction

Skin health plays a key role in maintaining the homeostasis of the body, as it provides protection not only against harmful environmental factors or pathogenic microorganisms but also against excessive water loss [1]. The skin performs several functions, such as a physical or immunological barrier. It cooperates with the microbiome, which is both a complex ecosystem of microorganisms and includes bacteria, viruses, fungi, and

archaea. The skin microbiome is not just a passive component but actively participates in protective and regulatory processes, thanks to which it can influence both local immune responses and the stability of the skin barrier [2].

Atopic dermatitis (AD) is a chronic, recurrent inflammatory disease. Its characteristic features include dry skin, itching, and recurrent inflammation [3]. This type of disease has a complex etiology, in which not only genetic or immunological factors but also environmental factors play an important role. Research shows that an important part of the pathogenesis of AD is dysbiosis of the skin microbiome. It is a disturbance of the balance of microflora, which leads to the dominance of pathogenic microorganisms. These include Staphylococcus aureus, appearing at the expense of beneficial commensal bacteria, such as Staphylococcus epidermidis. Therefore, it is important to draw attention to the current state of knowledge regarding the role played by the skin microbiome in the pathogenesis of atopic dermatitis. For this purpose, the focus was on studying the mechanisms of microbiota interaction with the skin immune system, as well as the influence of dysbiosis on the course of the disease and possible therapeutic implications resulting from the modulation of microflora [3, 4].

The aim of this article is to draw attention to atopic dermatitis (AD), which is currently one of the most common skin diseases, affecting not only children but also adults, and which affects their quality of life. Unfortunately, standard treatment methods, including corticosteroids and calcineurin inhibitors, most often provide only short-term relief and may also have side effects. Understanding the role of the microbiome in AD is important, as it can lead to the development of new, more effective, and safer therapeutic strategies, including both probiotics and methods supporting the reconstruction of normal skin microflora. New perspectives are emerging in the treatment of AD thanks to current research on the microbiome. This is becoming possible due to the possibilities of more targeted and personalized therapy.

Skin Microbiome – Definition, Composition, and Functions

The term microbiome (microbiota, microflora) refers to a group of microorganisms (mainly bacteria and fungi) that occur in a given natural habitat. In humans, the microbial habitat is a complex set of ecosystems with distinct species of microorganisms [5]. Several types of microbiomes may occur. Therefore, the inhabited sites include the oral cavity, the digestive tract, the respiratory tract, the urogenital system, and the skin. The most external organ of the human body is the skin, the individual areas of which differ in many respects. The thickness of the epidermis, the distribution of appendages, as well as its moisture and temperature on its surface can be mentioned [5]. All these features have a significant impact on the species and quantitative composition of the microflora [6].

Bacteria, fungi, viruses, and mites accumulate on the skin. It is worth noting that most of the microorganisms that inhabit the skin are harmless and work perfectly in symbiosis with skin cells. Nevertheless, the interactions that occur between microbiomes and skin cells are quite complex and include mutualism, parasitism, and commensalism [7].

However, the species composition of the skin microbiome is not yet fully understood because the reason for the lack of full knowledge about the microorganisms inhabiting the skin lies in the diagnostic possibilities [7].

The cultures and isolation of bacterial strains from clinical materials from sick people encounter a number of limitations. Very often, the growth of microorganisms in vitro depends largely on the technique of collecting the material, the type of transport medium used, the culture conditions, and the type of culture medium, as well as the initial species composition of the material. Therefore, it should be noted that individual species of bacteria and fungi grow in cultures at different rates, and it often happens that one of the cultured species displaces slower-growing species [7, 8]. However, microorganisms that mostly live on the skin surface are not cultured in laboratories. At the same time, there is a chance to introduce molecular methods based on

nucleic acid analysis. These include the analysis of the sequence of the highly conserved 16S rRNA region of bacteria, as well as the complete sequencing of genetic material samples collected from various ecological niches (metagenomics). All this serves to gradually expand knowledge about the skin microbiome [9].

The skin is the largest organ of the human body, which, on the one hand, is responsible for the integration of the body with the external environment, and on the other hand, for its key function; it is also responsible for protecting it from environmental factors. In spite of this, in terms of its structure and biology, it is an exceptionally hostile habitat for the growth of microorganisms. The reason for this is that the surface of the epidermis on a large part of the body is dry, rough, and constantly flaking, which causes regular removal of microorganisms from the skin surface. Therefore, they do not have a chance for unlimited growth, nor for creating a biofilm on the skin surface [4].

An additional difficulty for the growth of microorganisms on the skin surface is the presence of the hydrolipid coat, which is responsible for acidifying the environment from 4 to 6.5 pH. This is also not supported by the presence of antibacterial compounds, such as dermicidin, lysozyme, or sebum [6, 10]. On the other hand, keratinocytes, sebocytes, sweat gland cells, and mast cells have the ability to secrete antimicrobial factors [10].

Studies have shown that there are over 20 antimicrobial peptides (AMPs) on the skin surface. These include cathelicidin (LL-37), defensins – β1 defensin (HBD1), HBD2, HBD3, psoriasins, antimicrobial protein RNase 7 (SAP-2) and SLPI protein. Due to these conditions, the skin can only be inhabited by specific species of microorganisms. At the same time, such conditions have a significant impact on the number of microorganisms present. This makes the skin microbiome not only resistant to changes but also stable in terms of composition and number [11]. The degree of humidity, sebum production, and temperature affect the skin microenvironment, which in turn affects the composition and activity of microorganisms colonizing individual parts of the body. The differences that occur allow us to distinguish three key categories of skin environments: sebaceous areas, moist areas, and dry areas [11].

Seborrheic areas include the skin of the face, i.e., the forehead, nose, and cheeks, the upper back, and chest. These areas are characterized by a relatively high activity of sebaceous glands, which favors the colonization of lipophilic microorganisms. The following can be mentioned here [12]:

the dominant bacteria are Cutibacterium acnes (formerly Propionibacterium acnes) belonging to an anaerobic commensal bacterium that takes part in sebum metabolism. It plays one of the basic roles in the pathogenesis of acne vulgaris; another is a bacterium with immunomodulatory potential, namely Staphylococcus epidermidis,

fungi, namely Malassezia spp., which are lipophilic yeasts that metabolize triglycerides found in sebum. They are associated with the etiology of seborrheic dermatitis,

viruses, these are bacteriophages that regulate C. acnes populations and potentially oncogenic viruses. An example is Human Polyomaviruses.

As for moist areas, they are located in the armpits, groins, and skin folds. They also occupy the interdigital areas, which are niches for microorganisms for which increased humidity plays an important role [12]. On the other hand, characteristic body odor is caused by bacteria such as Corynebacterium spp., Staphylococcus spp. (S. hominis, S. epidermidis, S. lugdunensis). These are bacteria with proteolytic activity that break down proteins present in sweat.

In moist areas, there are also Candida spp. fungi or Malassezia spp. which are opportunistic microorganisms that can cause skin infections in conditions of disturbed homeostasis, and commensal viruses include not only skin viruses but also bacteriophages that regulate the bacterial population [12, 13].

Dry areas, however, are formed by the skin of the forearms, hands, and lower legs. They are characterized by lower moisture and limited sebum production. As a result, this has an impact on lower microbiological density. Here we can list [13]:

bacteria such as Staphylococcus epidermidis, Micrococcus luteus, or Cutibacterium spp. Their characteristic feature is high tolerance to dry conditions,

fungi whose occurrence is significantly limited in relation to seborrheic and moist areas,

viruses, the high diversity of which includes not only DNA viruses but also RNA viruses.

At the same time, under the influence of genetic and physiological factors, i.e., internal, as well as external, i.e., environmental and behavioral, the composition and diversity of the microbiome change [14].

Internal factors include age and genetics. Considering the age of newborns, it should be noted that the skin microbiome is dominated by Staphylococcus spp. and Corynebacterium spp. In turn, puberty causes an increase in the number of Cutibacterium acnes. This is associated with increased activity of the sebaceous glands. The situation is different in elderly people. On the one hand, there is a decrease in the diversity of the skin microbiome, and on the other hand, there is an increase in colonization by opportunistic pathogens. Moreover, genetics includes gene polymorphisms that are associated with both the functioning of the immune system and sebum production, thus influencing the individual specificity of the skin microbiome [14].

External factors include diet, environment, lifestyle, personal hygiene, and social contacts. Diet is associated with the consumption of polyunsaturated fatty acids, probiotics, and fiber, which leads to maintaining the microbiological homeostasis of the skin. In turn, a diet rich in simple sugars and highly processed products can lead to dysbiosis, which will increase inflammatory processes [14.15].

Another external factor is the environment, with polluted air, high humidity, temperature, and exposure to UV radiation. All of this influences the composition of the microbiome [15].

Lifestyle and personal hygiene can also lead to the elimination of beneficial commensal bacteria and an increase in the number of pathogens. This is due to the excessive use of detergents and antiseptics. Local and systemic antibiotic therapy can also cause disruption of the homeostasis of the microbiome, which in turn leads to the selection of resistant bacterial strains [15].

External factors also include social contacts during which the skin microbiome is subjected to dynamic changes that occur as a result of interactions with other people and animals [15].

The role of the skin microbiome in human health

The microbiome plays a key role in the functioning of the skin barrier and the immune system. Thanks to the microbiological balance, it is possible to protect against colonization by pathogens. In turn, its disruption can cause the development of dermatological diseases, such as acne vulgaris, atopic dermatitis, or psoriasis [6].

Thus, the skin microbiome belongs to a dynamic ecosystem of microorganisms that includes bacteria, fungi, viruses, and archaea. They occupy the skin surface along with its structures, i.e., hair follicles and sebaceous glands. The microbiome has a diverse composition that depends not only on anatomical location and environmental conditions but also on individual host characteristics [6]. The task of a healthy microbiome is to perform the most important functions that take care of skin protection against pathogens, modulate the immune system, and maintain skin homeostasis [6, 16].

The key protective mechanisms of the microbiome include the fight for nutrients and biological space. However, commensal bacteria, such as Staphylococcus epidermidis or Cutibacterium acnes, which are basically neutral, play a significant role because it has turned out that their location is important. Their merit is to limit the colonization of the skin with pathogens, which they do by using available nutrients, including lipids and iron ions. At the same time, the tasks of these microorganisms include the production of biofilms that constitute a physical barrier to the invasion of pathogenic bacteria [17]. An additional task of the microbiome is the active synthesis of antimicrobial substances. These include bacteriocins, organic acids, and hydrogen peroxide. All of them have a selective effect on pathogenic microorganisms, thanks to which they

inhibit their growth. An example is Staphylococcus epidermidis, which produces epidermin. This is a peptide with bactericidal activity against Staphylococcus aureus, which plays a significant role in preventing skin infections [17].

The microbiome, in addition to the mechanical and chemical protection of the skin, plays an important role in regulating the immune system. Host cells, including keratinocytes and Langerhans cells, have Toll-like receptors (TLRs) and Nod-like receptors (NLRs), which have the ability to recognize microorganisms and their metabolites by initiating appropriate signaling pathways [18]. An example of such an interaction is the activation of TLR2 by Staphylococcus epidermidis. This leads to the synthesis of antimicrobial peptides, such as β-defensins and cathelicidins, which enhance skin protection [19]. Moreover, thanks to the microbiome, the development of immune tolerance is enhanced by influencing the populations of regulatory T lymphocytes (Treg). In turn, they affect the reduction of excessive inflammatory reactions, thanks to which the skin is protected against autoimmune pathological reactions [18].

The skin microbiome also plays a crucial role in maintaining skin homeostasis, i.e., the stability and proper functioning of the epidermal barrier [18].

It is worth recalling that the previously mentioned commensal bacteria have a significant impact on the synthesis of structural proteins of the skin. These are filaggrin and loricrin, responsible for the integrity of the skin barrier. There are also microorganisms, such as Cutibacterium acnes, which support the metabolism of epidermal lipids. This is achieved by participating in the synthesis of ceramides, the main components of the lipid layer, which prevents transepidermal water loss (TEWL). On the other hand, microbiome disorders can use increased skin permeability, which leads to the penetration of allergens and the induction of inflammation [16].

As for the disturbance of the balance between commensal microorganisms and pathogens, i.e., microbiome dysbiosis, this is the effect of the development of a number of dermatological diseases. For example, in acne vulgaris, not only does excessive proliferation of Cutibacterium acnes lead to the activation of the NLRP3 inflammasome, but it also leads to an increase in the production of proinflammatory cytokines, such as IL-1β and TNF-α, which results in skin inflammation [17]. However, in atopic dermatitis, a reduced diversity of the microbiome and the dominance of Staphylococcus aureus are visible, causing both degradation of the skin barrier and intensification of the inflammatory process [19]. In turn, in psoriasis, the disturbance of the microbiome can lead to excessive colonization of the skin by Streptococcus pyogenes, which can trigger the activation of the IL-17 pathway and the development of an autoimmune inflammatory reaction [20].

In summary, it can be stated that the skin microbiome is one of the most important elements not only of its protection but also of its functioning, because it influences colonization resistance and immune regulation, as well as the homeostasis of the epidermis. Only its proper composition guarantees effective defense against pathogens by supporting the skin barrier function and limiting the inflammatory process. Moreover, when the microbiome is disturbed, it can lead to the development of many skin diseases, which is why conducting research on therapeutic strategies plays an important role. These include probiotics and microbiome modulators, the task of which is to support skin health and prevent its diseases.

The role of the microbiome in the pathogenesis of AD

Atopic dermatitis (AD) is a chronic dermatological condition of an inflammatory nature. It is characterized by periodic exacerbations and remissions of symptoms, as well as erythematous lesions that tend to exfoliate. A troublesome condition is not only the accompanying itching but also the tendency to bacterial, viral, and fungal infections [21–23]. Its first symptoms appear early, most often in the first year of life. It is reassuring that in almost 70% of patients, during puberty, these symptoms partially or completely disappear [24]. However,

about 25% of people start to get sick only after the age of eighteen [21]. In turn, in children, AD is at a level of 4.7% to 9.2% of the population, while in adults this percentage is lower, ranging from 0.9% to 1.4% [21].

To this day, the mechanisms responsible for the development of AD have not been fully identified. It is believed that there are several important causes of the occurrence of this disease. These may include damage to the epidermal barrier, a disorder of the immune response, or changes in the composition of microorganisms inhabiting the skin [3]. It has not been finally explained which of the above factors are primary and which are a consequence of the developing disease [1, 21]. The role of the skin is to protect against external factors, while its top layer, consisting of tightly connected cells, creates a physical barrier against pathogens. An additional protective chemical role is played by peptides and lipids, which are secreted by both epidermal cells and glands [25].

It has been proven that the most important genetic factor influencing the development of atopy is a change in the FLG gene because it encodes a protein called filaggrin, which is involved in the process of organizing keratin structures in the epidermis, with its degradation products being responsible for maintaining the correct level of moisture and skin reaction [25, 26]. If there is a deficiency of this protein, both congenital and acquired, the skin barrier is weakened, not only in terms of structure but also chemically [26]. At the same time, an increased pH of the epidermis favors the colonization of Staphylococcus aureus in the skin [27]. Additionally, when the protective layer of the skin is damaged, the penetration of bacteria into deeper tissues is significantly facilitated, which favors the activation of epidermal cells to produce inflammatory mediators [28].

In the course of atopy, the immune response associated with CD4 lymphocytes differentiating towards Th2 is noticeable. However, when there are too many of these cells, there is an increased synthesis of cytokines IL-4, IL-5 and IL-13, which in turn affects both the production of IgE and the increase in the number of eosinophils in the blood and tissues [21]. As a result, the production of antibacterial peptides, such as defensins and cathelicidins, is weakened, which affects the increased susceptibility of the skin to colonization by pathogenic bacteria [21].

Current research on the skin microbiome in atopic dermatitis

Studies have shown a visible reduction in the diversity of microorganisms inhabiting the skin of atopic patients. The number of bacteria from the genera Cutibacterium, Streptococcus, Acinetobacter, Corynebacterium, and Prevotella is reduced, while at the same time there is an increase in the share of microorganisms from the Staphylococcus group, especially S. aureus [21, 29]. This species constitutes about one-fifth of the skin microbiome in healthy people, while in patients with atopic dermatitis its share may increase to 30–100% [22].

In cases of severe atopic dermatitis, there is a significant reduction in the number of Streptococcus bacteria, which are replaced by Staphylococcus and primarily by S. aureus [21]. At the same time, it has been observed that the greater the colonization of the skin by S. aureus, the more severe the course of the disease. In those areas where there is intense inflammation, compared to the unchanged parts of the skin, we are dealing with a greater number of this microorganism. The presence of these bacteria increases mainly in sick people who have not started treatment [25]. The intensification of the inflammation by S. Aureus occurs primarily due to the activation of B lymphocytes independently of T lymphocytes or the release of cytokines, proinflammatory lipoproteins, and initiation of mast cell degranulation. All this causes the release of substances such as IL-31 which is associated with itching [21]. Through the production of proteolytic enzymes and toxins by this bacterium that weaken the skin's protective barrier, its further penetration is facilitated, which causes an increase in inflammation [25].

Further studies have been devoted to the role of chronic colonization of the nasal cavities by S. aureus in the pathogenesis of atopy. From 19 studies conducted by Totté et al., which included 1,051 patients with AD and 1,263 control subjects, it was found that 57% of patients were carriers of S. aureus in the nasal cavity, while in the control group, this percentage was at the level of 23% [30].

It has been proven that S. aureus is more abundant on the skin of patients with AD, but the number of other species of the Staphylococcus genus is also increasing. These include S. epidermidis and S. haemolyti- cus [3]. S. epidermidis, a natural component of the skin microbiome, participates in both regeneration and wound healing processes. However, in some conditions, its mechanisms may act unfavorably. An example is the production of enzymes that degrade components of the immune system, which allows bacteria to avoid elimination [2].

The analysis of the conducted studies proved that S. epidermidis strains play a dominant role on the skin of patients with less severe symptoms of AD [14, 21]. Additionally, it turned out that Cutibacterium acnes, previously known as Propionibacterium acnes, may not only promote the formation of biofilm but also increase the ability of S. aureus to adhere to the skin [14].

Less interest has been paid to the analysis of fungal microorganisms in AD, where patients have a greater diversity of mycobiome and an increased number of Malassezia, in particular M. globosa and M. restricta. The existence of Aspergillus, Candida albicans, Cryptococcus diffluens, and Cryptococcus liquefaciens has also been detected [31, 32].

Therapeutic Perspectives

The key tasks in the treatment of AD include reducing both the severity of disease symptoms and the frequency of its exacerbations. Therefore, a multifactorial approach plays an important role in its treatment because the disease has a multifactorial basis. During disease exacerbations, the microbiological diversity of the bacterial flora of the skin of patients is strongly correlated with the treatment used. Thus, it turns out that the treatment of atopy diversifies the bacterial flora of the patient's skin, often preceding the clinical improvement in the patient [21].

Currently, the basis of therapy in patients is the local application of emollients every day, thanks to which the goal of restoring the proper functioning of the epidermal barrier will be achieved. Moreover, so-called emollients plus are used, which enrich additional active substances. These include flavonoids, saponins, or bacterial lysates from Aquaphilus dolomiae and Vitreoscilla filiformis. They have a number of advantages because they have anti-inflammatory and antipruritic effects, and it is important that they inhibit the growth of S. aureus while restoring the homeostasis of the disturbed skin microbiome in AD [23].

The study by Glatz et al. included 6-month-old infants with a positive family history of atopic dermatitis. This study showed that there was a greater diversity of skin bacterial flora in children who were treated with emollients than in the control group [33]. In turn, a similar clinical study by Seite et al. conducted on a group of 49 patients showed an increase in the species diversity of the skin microbiome and a decrease in the number of Staphylococcus species [34].

Emollient therapy is not the only basic treatment for atopy. An equally important role is played by local anti-inflammatory drugs, such as glucocorticosteroids (GCs), which reduce the colonization of the skin with S. aureus. However, it should not be forgotten that long-term steroid therapy, even when applied locally, may contribute to the occurrence of adverse effects of GCs. Therefore, intermittent therapy is recommended, which involves the use of local GCs every 2–3 days, alternating with emollients [21]. Local calcineurin inhibitors (tacrolimus, pimecrolimus) also have anti-inflammatory effects, thanks to the inhibition of T lymphocyte activation and the release of inflammatory cytokines [21]. A significant increase in the percentage of commensal species such as Dermacoccus, Pseudomonas, Corynebacterium, Proteus, and a lower frequency of Actinobacteria and Proteobacteria in the skin microbiota was demonstrated by the study conducted by Wongpiyabovorn et al., which included a group of 9 patients with AD. They were subjected to 4 weeks of tacrolimus monotherapy [35].

It is important that in patients with AD, especially during exacerbations, attention is paid to the possible risk resulting from the coexistence of bacterial, viral, or fungal infections, where it may be necessary to use

antimicrobial therapy. To improve the clinical condition by reducing staphylococcal colonization of the skin, significant effectiveness is achieved by using octenidine, chlorhexidine, mupirocin, fusidic acid, and retapamulin, as well as antiseptic baths with the addition of sodium hypochlorite [23]. Nevertheless, when dealing with chronic antibiotic therapy or the negative effect of prolonged antimicrobial treatment on the natural skin microbiome, it is necessary to remember the possible development of antibiotic resistance [21]. However, antibiotic therapy, whether oral or intravenous, should be used only in the case of systemic symptoms of bacterial superinfection [21].

As it results from the currently conducted clinical studies, it is possible that intestinal microflora can influence modulation not only of the systemic inflammatory response but also of immunological processes and thus the development of allergic diseases. A potential measure that could prevent the development of AD may be probiotics, which improve both the integrity of the epithelial barrier and restore the balance between Th1 and Th2 lymphocytes [36]. In turn, Li et al., after analyzing 28 articles, which they conducted in 2019, noticed that in children who were supplemented with probiotics both in the prenatal period and later, the incidence of AD was reduced [37].

Also, another study conducted by Wu et al. in a group of children aged 4 to 48 months suffering from AD included an 8-week therapy with Lactobacillus rhamnosus, which showed a significant improvement in symptoms assessed using the SCORAD (Scoring of Atopic Dermatitis) scale [21]. Virtually identical results were confirmed by Niccoli et al. when they conducted a 4-week therapy using an oral preparation of Lactobacillus salivarius LS01 [38].

Some species of coagulase-negative staphylococci naturally colonizing the skin surface inhibit the growth of their competitors, such as S. aureus, by secreting antimicrobial peptides [39]. It has also been found that strains that produce lantibiotics appear in lower numbers on the skin of people with AD, which is mostly colonized by S. aureus. At the same time, Nakatsuji and his colleagues point to the opportunity that lies in the development of future targeted therapy against microbial atopy, which is based on the use of specific commensal strains of coagulase-negative staphylococci [40].

Conclusion

Atopic dermatitis (AD) is a chronic inflammatory dermatological disease. Its pathogenesis is complex and is associated not only with damage to the epidermal barrier or an abnormal immune response but also with changes in the composition of the skin microbiome. If the patient's skin is dominated by Staphylococcus microorganisms, especially S. aureus, this is a significant factor that worsens the existing inflammation, which leads to an exacerbation of the disease. Disturbances in the composition of the fungal microbiome and skin bacteria may additionally contribute to the exacerbation of the disease.

The goal of treating AD is primarily to restore the integrity of the skin barrier and control inflammation. A significant role in regulating the skin microbiome and reducing the severity of symptoms is played not only by emollients enriched with active substances but also by local anti-inflammatory drugs, such as glucocorticoids and calcineurin inhibitors. Prevention of bacterial and fungal infections also plays an important role in therapy. However, it is important to remember not to conduct long-term antibiotic therapy, as this could disrupt the balance of the microbiome.

Modern research suggests that gut microbiota and probiotics may have the potential to prevent and treat AD by improving skin barrier function and influencing immune response. Further research into the skin microbiome and the role of commensal microorganisms may open the way to new, more targeted therapies for patients with atopic dermatitis.

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Author's Contribution Statement

Conceptualization, Natalia Sidz and Monika Brzozowska; Methodology, Robert Rzenno and Karolina Wojciechowska; Software, Magdalena Tomaszewska; Check, Katarzyna Wicha, Wiktoria Jedlikowska and Natalia Furlepa; Formal analysis, Marcelina Matuszewska; Investigation, Wiktoria Wardal and Robert Rzenno; Resources, Karolina Wojciechowska and Katarzyna Wicha; Data curation, Wiktoria Jedlikowska and Magdalena Tomaszewska; Writing-rough preparation, Natalia Sidz and Marcelina Matuszewska; Writing-review and editing, Wiktoria Wardal; Visualization, Natalia Furlepa; Supervision, Natalia Sidz; Project administration, Monika Brzozowska

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