American Journal of Medicine and Medical Sciences 2025, 15(8): 2699-2705
DOI: 10.5923/j.ajmms.20251508.59

Cutaneous Microbial Imbalance in Atopic Dermatitis Mechanisms Evidence and Treatment Options

Avazov J. O.[1,*], Ziyadullaev Sh. Kh.[2], Ibragimov Kh. I.[3]

[1]Military Hospital of the Republic of Uzbekistan
[2]Institute of Immunology and Human Genomics of the Academy of Sciences of the Republic of Uzbekistan
[3]Samarkand State Medical University, Samarkand, Uzbekistan

Abstract In the modern world, one of the major medical challenges is atopic dermatitis (AD), a condition that has confounded the medical community with its complexity and many unexplored aspects. AD is known to be a chronic, relapsing inflammatory skin disease characterized by intense pruritus, dysfunction of the epidermal barrier, and impaired immune regulation. In recent years, growing evidence has highlighted the pivotal role of the skin microbiome in the pathogenesis and progression of AD. Dysbiosis-particularly the dominance of Staphylococcus aureus and the loss of commensal microbial diversity-has been consistently associated with disease severity, increased frequency of exacerbations, and resistance to therapy. Recent clinical trials and longitudinal cohort studies have revealed a dynamic relationship between microbial composition and inflammatory processes in both children and adults with AD. Interventions targeting microbial balance-including probiotics, prebiotic emollients, commensal transplants, and live biotherapeutic products-have demonstrated varying degrees of clinical efficacy, offering promising adjuncts to conventional anti-inflammatory therapies. This paper summarizes contemporary findings from high-quality studies, with a focus on the interplay between the skin microbiota and the host immune response. It also highlights emerging microbiome-based therapeutic strategies and the integration of microbial diagnostics into personalized treatment approaches for AD.

Keywords Atopic Dermatitis, Skin Microbiome, Staphylococcus aureus, Microbial Dysbiosis, Microbiome-Targeted Therapy

1. Introduction

The skin is a vital organ that serves as a mediator constantly interacting with the external environment, perceiving it, and maintaining homeostatic relationships with the community of microorganisms that constitute the microbiome. It also contributes to immune responses and tissue repair. Disruption of the microbial balance often leads to inflammation or infection, which can result in various pathophysiological conditions and diseases. According to current statistics, approximately 20% of children and 10% of adults in developed countries are affected by this condition [1].

Moreover, microbial imbalance leads to dysbiosis by reducing the abundance of beneficial species, thereby disturbing microbial homeostasis. This growing disease burden has prompted intensified research into its complex etiopathogenesis and the development of novel therapeutic approaches.

The complexity of the pathophysiological factors in atopic dermatitis (AD) underlies the heterogeneity of its clinical manifestations, such as age of onset, disease severity, natural disease course, and flare cycles, which are marked by significant microbiome alterations and overgrowth of Staphylococcus aureus [2]. Genetically determined deficiencies in structural proteins such as filaggrin (FLG)-particularly loss-of-function mutations-disrupt epidermal homeostasis, facilitating transepidermal water loss and increased allergen penetration [3].

These changes activate innate immune pathways and stimulate adaptive immune responses skewed toward T-helper type 2 (Th2) polarization, characterized by elevated levels of interleukin (IL)-4, IL-13, and IL-31. This further impairs barrier function and sustains inflammation [4]. Additionally, Th17 and Th22 cytokines contribute to disease heterogeneity and chronicity, especially in certain ethnic groups and severe phenotypes [5].

Previously, host–microbe interactions were considered underestimated, but many recent clinical and cohort studies have now demonstrated the critical role of dysbiosis. The aim of this paper is to provide a comprehensive analysis of current understanding regarding the interplay between the skin microbiome and atopic dermatitis (AD), based on recent clinical and translational research, as well as to evaluate the prospects of microbiome-targeted therapeutic interventions.

* Corresponding author:
res.ssmu@gmail.com (Avazov J. O.)
Received: Aug. 2, 2025; Accepted: Aug. 24, 2025; Published: Aug. 26, 2025
Published online at http://journal.sapub.org/ajmms

2. Materials and Methods

Literature Review

A comprehensive literature review was conducted to investigate the role of skin microbiome dysbiosis in the pathogenesis, clinical manifestations, and therapeutic management of AD. The review focused on elucidating microbial alterations associated with AD severity, the interplay between dysbiosis and immune dysregulation, and the emerging microbiome-based interventions. Searches were conducted using electronic databases including PubMed, Scopus, Web of Science, and Google Scholar. Keywords and Boolean combinations used in the search strategy included: “atopic dermatitis”, “skin microbiome”, “dysbiosis”, “Staphylococcus aureus”, “filaggrin mutation”, “Th2 cytokines”, “microbiota-targeted therapy”, “probiotics”, and “microbiome-based interventions in AD”. Preference was given to studies that demonstrated clear methodological quality and direct relevance to the topic.

Inclusion and Exclusion Criteria

The inclusion criteria comprised peer-reviewed original research articles, randomized controlled trials, systematic reviews, and meta-analyses published in English from 2005 to 2025. Studies were included if they addressed at least one of the following: 1) microbial community alterations in AD, 2) immune-microbiome interactions, 3) genetic predispositions affecting skin barrier and microbial susceptibility, or 4) therapeutic strategies targeting the skin microbiota.

Exclusion criteria were: 1) studies not focused on AD or that addressed microbiome dynamics in unrelated dermatologic conditions, 2) non-peer-reviewed materials, 3) case reports without microbiological or immunological correlation, and 4) articles in languages other than English without translation.

Data Extraction

A structured data extraction framework was used to collect information on:

- Microbial composition in lesional and non-lesional skin
- Key taxa associated with disease activity (e.g., S. aureus, C. acnes, S. epidermidis)
- Host factors such as filaggrin mutations, transepidermal water loss, and immune cytokine profiles (e.g., IL-4, IL-13, IL-31)
- Types of interventions targeting microbial dysbiosis, including topical probiotics, emollients with prebiotic effects, bacteriophage therapy, and live biotherapeutic products
- Clinical efficacy outcomes (SCORAD index, flare frequency, corticosteroid use reduction)
- Articles were categorized by research domain: mechanistic studies, clinical observational studies, and interventional trials.

Analysis

The collected data were synthesized thematically to identify consistent microbial signatures of dysbiosis across AD phenotypes, as well as the influence of host genetic and immune factors. Comparative analyses were performed on studies investigating Th2-polarized immune responses, cytokine–microbiome interactions, and therapeutic outcomes. Emphasis was placed on identifying patterns of microbiome restoration associated with disease improvement and reduced inflammation. Mechanistic insights from both pediatric and adult populations were examined separately to reflect age-dependent microbial dynamics.

Ethical Considerations

This review is based entirely on secondary data from previously published research. No human or animal subjects were involved, and ethical approval was not required. All referenced studies were duly cited in accordance with academic standards and publication ethics.

Limitations

This review is subject to limitations inherent in secondary data analyses. Variability in sampling methods (e.g., swab vs. tape stripping), sequencing platforms (e.g., 16S rRNA vs. shotgun metagenomics), and microbial classification algorithms across studies may introduce heterogeneity. Furthermore, a limited number of randomized controlled trials on microbiome-targeted therapies in AD restricts the ability to generalize findings. Future studies employing standardized protocols and integrating multi-omics approaches (metagenomics, transcriptomics, immunophenotyping) are needed to validate microbiome-based stratification and therapeutic strategies.

3. Results

Fundamentals of the Skin Microbiome

The skin is the largest organ of the human body, serving as a protective barrier that prevents infections caused by environmental pathogens. It also regulates body temperature, prevents water loss, and initiates nociceptive responses. This organ hosts a complex consortium of bacteria, fungi, viruses, and mites, which coexist in finely balanced communities influenced by anatomical location, host genetics, immune status, and environmental exposures. In healthy individuals, the skin microbiome is relatively stable over time and contributes to skin homeostasis through various mechanisms, including barrier support, colonization resistance, and modulation of the host immune response [6].

Each microorganism is adapted to the physicochemical characteristics of its ecological niche-a behavior analogous to the flora and fauna of Earth. Given that the skin is a nutrient-poor environment, aside from lipids and proteins, microbial survival depends largely on their ability to utilize resources such as amino acids or urea present in the stratum corneum and/or sebum [7].

The bacterial species commonly found on healthy human skin include Actinobacteria, Firmicutes, Proteobacteria, and Bacteroidetes [8], with Staphylococcus, Corynebacterium, and Propionibacterium species comprising over 60% of the

bacterial population [9]. The composition of the skin microbiota is highly dependent on the physiology of each skin site, and distinct bacterial taxa have been found to inhabit dry, moist, and sebaceous microenvironments [10].

Dry skin areas (e.g., forearms, buttocks, various parts of the arm) exhibit the greatest microbial diversity, reportedly surpassing that of the human gut or oral cavity [11]. These sites harbor a variety of phylotypes, including β-Proteobacteria, Corynebacteria, and Flavobacteriales [9]. Moist areas (e.g., nostrils, axillae, umbilicus, interdigital spaces, inner elbows, groin, antecubital and popliteal fossae, palms, and soles) offer a thermally stable, warm environment where Corynebacteria and Staphylococci dominate due to their ability to withstand moisture [11]. In contrast, sebaceous regions (e.g., forehead, retroauricular area, sides of the nostrils, back) show the lowest bacterial diversity and are mainly colonized by lipophilic species such as Propionibacteria and Staphylococci [9,10,11].

Unlike bacterial communities, fungal communities have been observed to be more uniform across different skin sites despite the varying physiologies [12]. These are predominantly composed of the genus Malassezia, which thrives in sebaceous areas such as the scalp, upper chest, and back [13]. Studies show that Malassezia species dominate healthy human skin, with M. globosa primarily found on the chest and arms, M. sympodialis on the trunk, and M. restricta on facial areas [12,13]. These lipophilic yeasts utilize host lipids for growth and can modulate immune responses by interacting with pattern recognition receptors (PRRs), affecting both Th2 and Th17 pathways [14]. Other genera such as Candida and Cladosporium have been detected sporadically but do not dominate healthy skin communities [15,16,17].

Interestingly, interkingdom interactions between fungi and bacteria-such as those between Malassezia and Staphylococcus aureus-may influence skin inflammation in predisposed individuals [18].

The skin virome adds another layer of complexity and consists primarily of bacteriophages, which regulate bacterial population dynamics and help maintain ecological balance. Unlike bacterial and fungal communities, no conserved core virome has been identified in healthy human skin [19]. However, human-infecting viruses such as human papillomaviruses (HPV), Merkel cell polyomavirus (MCPyV), and Torque teno virus are occasionally detected, especially in immunocompromised individuals or those with malignancies, though their precise role remains poorly understood [20,21].

In addition, microscopic mites-particularly Demodex folliculorum and Demodex brevis-represent micro-eukaryotic skin residents. These arthropods inhabit hair follicles and sebaceous glands, especially on the face, and are typically harmless in small numbers [22]. However, increased mite density can disrupt local immunity and has been associated with inflammatory dermatoses such as rosacea and seborrheic dermatitis. These mites may also indirectly shape the microbial environment by altering sebum composition and influencing microbial colonization [23].

In summary, the skin microbiome is a multilayered, functionally integrated ecosystem where bacteria, fungi, viruses, and mites interact both with one another and with the host to maintain barrier integrity, support immune tolerance, and protect against pathogenic invasion. The following illustrations will provide a clearer depiction of the scientific studies and findings discussed above.

Microbial Dysbiosis in Atopic Dermatitis

Atopic dermatitis (AD) is characterized by a disruption in the symbiotic relationship between the host and its cutaneous microbiome. One of the hallmark features of this dysbiosis is the overgrowth of Staphylococcus aureus (S. aureus), accompanied by a loss of microbial diversity, especially during disease flares. These changes in microbial composition are not merely associative but actively contribute to inflammation and skin barrier dysfunction, creating a pathogenic feedback loop that promotes disease progression. The presence of S. aureus on the skin is associated with disease severity and serves as a major trigger for skin deterioration in AD patients. Cutaneous exposure to S. aureus induces skin inflammation, with the secreted phenol-soluble modulin alpha (PSMα) playing a pro-inflammatory role [24].

Heat-killed S. aureus in AD patients becomes intensely agglutinated within the cytoplasm, stimulating secretion of IL-1α, IL-1β, and IL-18. S. aureus also promotes the release of thymic stromal lymphopoietin (TSLP) from human keratinocytes and mediates type 2 (Th2) inflammation [25,26]. Additionally, it induces rapid IL-33 release from keratinocytes, marking it as a dominant type 2 immune trigger in AD pathogenesis. Th2 cytokines sensitize keratinocytes to S. aureus alpha-toxin–induced cell death, which occurs more frequently in the skin of AD patients compared to healthy individuals [27–29].

S. aureus plays a central role in AD pathogenesis: inflammation leads to rapid neutrophil recruitment, correlating with increased S. aureus colonization. Monocyte -derived Langerhans cells stimulated by AD-associated S. aureus trigger rapid T-cell proliferation, indicating that S. aureus can skew T-cell responses in AD [30].

The role of commensal microbiota in AD pathogenesis is complex and multifaceted. Staphylococcus epidermidis (S. epidermidis), a beneficial commensal organism, enhances the expression of perforin-2, which protects the host from cutaneous infections. It also supports skin barrier integrity by secreting SMase, which elevates ceramide levels and reduces transepidermal water loss. However, some strains of S. epidermidis produce a potent cysteine protease capable of degrading desmoglein-1 and LL-37 in vitro, impairing the physical barrier and causing inflammation in vivo [31,32].

S. aureus secretion of PSMα contributes to skin inflammation and barrier disruption. Coagulase-negative staphylococci (CoNS) on healthy skin suppress S. aureus growth and PSMα expression, suggesting that normal skin microbiota promotes epithelial homeostasis. CoNS strains with antimicrobial properties are prevalent on healthy skin but rarely found in AD lesions. These strains can inhibit S.

aureus quorum sensing, thus protecting against dysbiosis and influencing disease outcomes in AD [33–35].

Commensal fungi such as Malassezia are also implicated in AD pathogenesis. Malassezia selectively induces IL-17 and associated cytokines, enhancing skin inflammation. AD patients show increased Th17 subpopulations induced by Malassezia, which appears to be species-specific. Malassezia globosa secretes MGSAP1, its dominant secreted aspartyl protease, which rapidly hydrolyzes S. aureus protein A and displays anti-biofilm activity against S. aureus [36].

In AD-affected skin, elevated expression of MGSAP1 reduces S. aureus adhesion and disperses cells in both cultured and three-dimensional human epidermal models. MGSAP1 plays a critical role in fungal colonization and barrier disruption [37].

Moreover, excessive colonization by S. aureus can exacerbate AD flares. The initiation and progression of AD may require S. aureus adhesion to the skin, though the precise mechanisms remain unclear [38]. Fibronectin and fibrinogen enhance S. aureus binding to AD skin, while S. aureus stimulates keratinocytes to increase trypsin activity and degrade desmoglein-1 and filaggrin. S. aureus also interacts with corneodesmosin, facilitating adhesion to AD-associated corneocytes [39]. Epidermal barrier impairment in AD may enhance S. aureus penetration into the dermis, worsening inflammation and disease severity. Keratinocytes lacking JunB exhibit higher MyD88 levels, promoting S. aureus colonization. JunB appears to act as a key regulator of microbiota–immune interactions in AD pathogenesis [40].

The skin microbiome differs significantly between children and adults, suggesting that age influences microbial composition. In infants with AD, dysbiotic communities are absent before flare onset, and colonization with S. aureus generally occurs only after disease develops. Reduced microbial diversity is associated with an increased risk of AD in infancy [41]. Commensal staphylococci are less abundant in infants who develop AD by 12 months of age, suggesting a protective role in disease prevention.

In adult AD patients, S. aureus colonization correlates positively with barrier dysfunction and subsequent sensitization to skin-associated microbes, highlighting its importance in eczema pathogenesis. Notably, S. aureus is more prevalent in infants who later develop AD [42]. Infants with early S. aureus colonization develop AD at younger ages compared to non-colonized infants, suggesting a potential role of colonization in triggering early-onset disease [43].

Microbial dysbiosis is a key factor in the development and maintenance of AD, promoting chronic skin inflammation. Staphylococcus aureus overcolonizes the skin, disrupts the barrier, and activates Th2 immune responses. Commensal microbiota maintain epithelial homeostasis by suppressing pathogens and preserving immune tolerance. Reduced microbial diversity weakens the skin's natural defenses. Fungi such as Malassezia can trigger inflammatory responses and contribute to barrier dysfunction in predisposed individuals. Age-related differences in the skin microbiome emphasize the importance of early microbial development in disease pathogenesis. Personalized therapeutic strategies are needed to suppress pathogens and restore microbial balance. Future approaches may include probiotics, bacteriotherapy, targeted microbiome modulation, and reinforcement of the skin barrier.

Microbiome-Targeted Interventions

For a long time, oral and topical antibiotics have been the standard treatment for exacerbations of atopic dermatitis (AD), which are often triggered by secondary infections or significant colonization with Staphylococcus aureus (S. aureus) [44–46]. These agents provide rapid and effective short-term relief by swiftly eliminating pathogenic microorganisms on the skin, thereby reducing erythema, irritation, and the likelihood of further complications. Clinical studies have repeatedly demonstrated the ability of topical mupirocin to eradicate S. aureus in eczematous lesions and alleviate inflammation. Importantly, S. aureus not only infects the skin but actively worsens AD by producing toxins, superantigens, and biofilms that intensify inflammation and impair skin healing [47,48].

However, the long-term or widespread use of antibiotics in AD is now under careful re-evaluation [49,50]. The global public health threat of antibiotic resistance raises significant concerns. Broad-spectrum antibiotics indiscriminately destroy both harmful and beneficial bacteria residing on the skin. This disruption can lead to a substantial reduction in microbial diversity and elimination of commensal bacteria that usually protect against infection, produce antimicrobial peptides, or help regulate immune responses. As a result, patients may experience recurrence of S. aureus colonization or even overgrowth of other undesirable microbes, trapping them in a cycle of dysbiosis and complicating long-term disease management [51].

Probiotics and prebiotics have gained popularity as adjunctive therapies for AD due to increasing awareness of the gut–skin axis and the delicate balance of the skin microbiome. Oral probiotic strains such as Lactobacillus rhamnosus GG and Bifidobacterium have been widely studied for their potential to modulate inflammation and indirectly improve skin health by influencing the immune system through the gastrointestinal tract. However, recent meta-analyses and rigorous clinical trials have reported inconsistent and inconclusive outcomes regarding their overall efficacy in delaying AD onset [52,53].

Synbiotics-formulations combining probiotics with prebiotics, such as prebiotic-enriched emollients-offer a targeted strategy to improve the skin microbiota at the site of disease. These topical agents reinforce the skin barrier by creating an environment less conducive to overgrowth of pathogenic bacteria and more favorable to establishing a stable, balanced microbial ecosystem [54].

Restoring microbial balance in AD through bacterial transplantation and live biotherapeutic products is an emerging and highly targeted approach. The goal is to directly introduce or enhance populations of beneficial commensal bacteria on the skin of AD patients. Research has focused on non-pathogenic commensal staphylococci, such as S. hominis A9. These emollients have shown promising results

in restoring the skin's natural microbial defenses by supplementing or replacing absent protective species [55].

Personalized medicine and predictive biomarkers are also gaining importance in the management of AD. Advanced molecular analysis of the skin microbiome now enables identification of specific alterations, such as reduced microbial diversity, overgrowth of S. aureus, or shifts in key commensal populations, often preceding clinical flares. This deeper understanding facilitates patient stratification for microbiome-targeted therapies, allowing the selection of treatments most likely to benefit individual patients [56].

4. Conclusions

Atopic dermatitis (AD) is a complex and multifactorial disease that significantly impairs quality of life and is often associated with various comorbidities. Advances in our understanding of AD pathophysiology have illuminated the intricate interplay between epidermal barrier dysfunction and immune activation. Technological progress has also expanded our knowledge of cutaneous microbial communities, identifying skin microbiome dysbiosis as a key factor in AD onset and progression. Therapeutic strategies such as probiotics, prebiotics, and skin microbiota transplantation are under active development. However, further high-quality research is needed to assess their efficacy and address practical challenges in clinical implementation.

REFERENCES

[1] Langan SM, Irvine AD, Weidinger S. Atopic dermatitis. Lancet. 2020; 396(10247): 345–60. doi:10.1016/S0140-6736(20)31286-1.

[2] Koh LF, Ong RY, Common JE. Skin microbiome of atopic dermatitis. Allergol Int. 2022; 71(1): 31–9. doi:10.1016/j.alit.2021.11.001.

[3] Elias PM, Schmuth M. Abnormal skin barrier in the etiopathogenesis of atopic dermatitis. Curr Opin Allergy Clin Immunol. 2009; 9(5): 437–46. doi:10.1097/ACI.0b013e32832e7d36.

[4] Facheris P, Jeffery J, Del Duca E, et al. The translational revolution in atopic dermatitis: the paradigm shift from pathogenesis to treatment. Cell Mol Immunol. 2023; 20: 448–74. doi:10.1038/s41423-023-00992-4.

[5] Brunner PM, Guttman-Yassky E, Leung DYM. The immunology of atopic dermatitis and its reversibility with broad-spectrum and targeted therapies. J Allergy Clin Immunol. 2017; 139(4S): S65–76. doi:10.1016/j.jaci.2017.01.011.

[6] Smythe P, Wilkinson HN. The skin microbiome: current landscape and future opportunities. Int J Mol Sci. 2023; 24(4): 3950. doi:10.3390/ijms24043950.

[7] Scharschmidt TC, Fischbach MA. What lives on our skin: ecology, genomics and therapeutic opportunities of the skin microbiome. Drug Discov Today Dis Mech. 2013; 10: e83–9. doi:10.1016/j.ddmec.2012.12.003.

[8] SanMiguel A, Grice EA. Interactions between host factors and the skin microbiome. Cell Mol Life Sci. 2015; 72: 1499–515. doi:10.1007/s00018-014-1812-z.

[9] Grice EA, Kong HH, Conlan S, et al. Topographical and temporal diversity of the human skin microbiome. Science. 2009; 324:1190–2. doi:10.1126/science.1171700.

[10] Grice EA, Segre JA. The skin microbiome. Nat Rev Microbiol. 2011; 9: 244–53. doi:10.1038/nrmicro2537.

[11] Costello EK, Lauber CL, Hamady M, et al. Bacterial community variation in human body habitats across space and time. Science. 2009; 326: 1694–6. doi:10.1126/science.1177486.

[12] Findley K, Oh J, Yang J, et al. Topographic diversity of fungal and bacterial communities in human skin. Nature. 2013; 498: 367–70. doi:10.1038/nature12171.

[13] Vijaya Chandra SH, Srinivas R, Dawson TL Jr, Common JE. Cutaneous Malassezia: commensal, pathogen, or protector? Front Cell Infect Microbiol. 2021; 10: 614446. doi:10.3389/fcimb.2020.614446.

[14] Sparber F, De Gregorio C, Steckholzer S, et al. The skin commensal yeast Malassezia triggers a type 17 response that coordinates anti-fungal immunity and exacerbates skin inflammation. Cell Host Microbe. 2019; 25(3): 389–403. e6. doi:10.1016/j.chom.2019.02.002.

[15] Zhang E, Tanaka T, Tajima M, et al. Characterization of the skin fungal microbiota in patients with atopic dermatitis and in healthy subjects. Microbiol Immunol. 2011; 55: 625–32. doi:10.1111/j.1348-0421.2011.00364.x.

[16] Rafat Z, Hashemi SJ, Ahamdikia K, et al. Study of skin and nail Candida species as a normal flora based on age groups in healthy persons in Tehran-Iran. J Mycol Med. 2017; 27: 501–5. doi:10.1016/j.mycmed.2017.08.007.

[17] Wheeler ML, Limon JJ, Underhill DM. Immunity to commensal fungi: detente and disease. Annu Rev Pathol. 2017; 12: 359–85. doi:10.1146/annurev-pathol-052016-100342.

[18] Yang J, Park S, Kim HJ, et al. The interkingdom interaction with Staphylococcus influences the antifungal susceptibility of the cutaneous fungus Malassezia. J Microbiol Biotechnol. 2023; 33(2): 180–7. doi:10.4014/jmb.2210.10039.

[19] Oh J, Byrd AL, Park M, et al. Temporal stability of the human skin microbiome. Cell. 2016; 165: 854–66. doi:10.1016/j.cell.2016.04.008.

[20] Ursu RG, Damian C, Porumb-Andrese E, et al. Merkel cell polyoma virus and cutaneous human papillomavirus types in skin cancers: optimal detection assays, pathogenic mechanisms, and therapeutic vaccination. Pathogens. 2022; 11(4): 479. doi:10.3390/pathogens11040479.

[21] Joh J, Jenson AB, Moore GD, et al. Human papillomavirus (HPV) and Merkel cell polyomavirus (MCPyV) in non small cell lung cancer. Exp Mol Pathol. 2010; 89(3): 222–6. doi:10.1016/j.yexmp.2010.08.001.

[22] Rather PA, Hassan I. Human demodex mite: the versatile mite of dermatological importance. Indian J Dermatol. 2014; 59(1): 60–6. doi:10.4103/0019-5154.123498.

[23] Paichitrojjana A. Demodex: the worst enemies are the ones

that used to be friends. Dermatol Rep. 2022; 14(3): 9339. doi:10.4081/dr.2022.9339.

[24] Tauber M, Balica S, Hsu CY, et al. Staphylococcus aureus density on lesional and nonlesional skin is strongly associated with disease severity in atopic dermatitis. J Allergy Clin Immunol. 2016; 137: 1272–4. doi:10.1016/j.jaci.2015.07.052.

[25] Moriwaki M, Iwamoto K, Niitsu Y, et al. Staphylococcus aureus from atopic dermatitis skin accumulates in the lysosomes of keratinocytes with induction of IL-1α secretion via TLR9. Allergy. 2019; 74: 560–71. doi:10.1111/all.13622.

[26] Vaher H, Kingo K, Kolberg P, et al. Skin colonization with S. aureus can lead to increased NLRP1 inflammasome activation in patients with atopic dermatitis. J Invest Dermatol. 2023; 143: 1268–78. doi:10.1016/j.jid.2023.01.013.

[27] Nakamura Y, Oscherwitz J, Cease KB, et al. Staphylococcus δ-toxin induces allergic skin disease by activating mast cells. Nature. 2013; 503: 397–401. doi:10.1038/nature12655.

[28] Bitschar K, Staudenmaier L, Klink L, et al. Staphylococcus aureus skin colonization is enhanced by the interaction of neutrophil extracellular traps with keratinocytes. J Invest Dermatol. 2020; 140: 1054–65. doi:10.1016/j.jid.2019.10.017.

[29] Brauweiler AM, Goleva E, Leung DYM. Th2 cytokines increase Staphylococcus aureus alpha toxin-induced keratinocyte death through the signal transducer and activator of transcription 6 (STAT6). J Invest Dermatol. 2014; 134: 2114–21. doi:10.1038/jid.2014.43.

[30] Laborel-Préneron E, Bianchi P, Boralevi F, et al. Effects of the Staphylococcus aureus and Staphylococcus epidermidis secretomes isolated from the skin microbiota of atopic children on CD4+ T cell activation. PLoS One. 2015; 10: e0141067. doi:10.1371/journal.pone.0141067.

[31] Strbo N, Pastar I, Romero L, et al. Single cell analyses reveal specific distribution of anti-bacterial molecule perforin-2 in human skin and its modulation by wounding and Staphylococcus aureus infection. Exp Dermatol. 2019; 28: 225–32. doi:10.1111/exd.13870.

[32] Pastar I, O'Neill K, Padula L, et al. Staphylococcus epidermidis boosts innate immune response by activation of gamma delta T cells and induction of perforin-2 in human skin. Front Immunol. 2020; 11: 550946. doi:10.3389/fimmu.2020.550946.

[33] Cau L, Williams MR, Butcher AM, et al. Staphylococcus epidermidis protease EcpA can be a deleterious component of the skin microbiome in atopic dermatitis. J Allergy Clin Immunol. 2021; 147: 955–66. doi:10.1016/j.jaci.2020.06.024.

[34] Williams MR, Bagood MD, Enroth TJ, et al. Staphylococcus epidermidis activates keratinocyte cytokine expression and promotes skin inflammation through the production of phenol-soluble modulins. Cell Rep. 2023; 42: 113024. doi:10.1016/j.celrep.2023.113024.

[35] Nakatsuji T, Chen TH, Narala S, et al. Antimicrobials from human skin commensal bacteria protect against Staphylococcus aureus and are deficient in atopic dermatitis. Sci Transl Med. 2017; 9: eaah4680. doi:10.1126/scitranslmed.aah4680.

[36] Sparber F, De Gregorio C, Steckholzer S, et al. The skin commensal yeast Malassezia triggers a type 17 response that coordinates anti-fungal immunity and exacerbates skin inflammation. Cell Host Microbe. 2019; 25: 389–403. doi:10.1016/j.chom.2019.02.002.

[37] Li H, Goh BN, Teh WK, et al. Skin commensal Malassezia globosa secreted protease attenuates Staphylococcus aureus biofilm formation. J Invest Dermatol. 2018; 138: 1137–45. doi:10.1016/j.jid.2017.11.034.

[38] Williams MR, Nakatsuji T, Sanford JA, et al. Staphylococcus aureus induces increased serine protease activity in keratinocytes. J Invest Dermatol. 2017; 137: 377–84. doi:10.1016/j.jid.2016.10.008.

[39] Towell AM, Feuillie C, Vitry P, et al. Staphylococcus aureus binds to the N-terminal region of corneodesmosin to adhere to the stratum corneum in atopic dermatitis. Proc Natl Acad Sci U S A. 2021; 118: e2014444118. doi:10.1073/pnas.2014444118.

[40] Uluçkan Ö, Jiménez M, Roediger B, et al. Cutaneous immune cell-microbiota interactions are controlled by epidermal JunB /AP-1. Cell Rep. 2019; 29: 844–59. doi:10.1016/j.celrep.2019.09.042.

[41] Huang C, Zhuo F, Guo Y, et al. Skin microbiota: pathogenic roles and implications in atopic dermatitis. Front Cell Infect Microbiol. 2025; 14: 1518811. doi:10.3389/fcimb.2024.1518 811.

[42] Jinnestål CL, Belfrage E, Bäck O, et al. Skin barrier impairment correlates with cutaneous Staphylococcus aureus colonization and sensitization to skin-associated microbial antigens in adult patients with atopic dermatitis. Int J Dermatol. 2014; 53(1): 27–33. doi:10.1111/ijd.12198.

[43] Shi B, Bangayan NJ, Curd E, et al. The skin microbiome is different in pediatric versus adult atopic dermatitis. J Allergy Clin Immunol. 2016; 138: 1233–6. doi:10.1016/j.jaci.2016.04.053.

[44] George SM, Karanovic S, Harrison DA, et al. Interventions to reduce Staphylococcus aureus in the management of eczema. Cochrane Database Syst Rev. 2019; 2019(10): CD003871. doi:10.1002/14651858.CD003871.pub3.

[45] Lugović-Mihić L, Meštrović-Štefekov J, Potočnjak I, et al. Atopic dermatitis: disease features, therapeutic options, and a multidisciplinary approach. Life (Basel). 2023; 13(6): 1419. doi:10.3390/life13061419

[46] Weiss A, Delavenne E, Matias C, et al. Topical niclosamide (ATx201) reduces Staphylococcus aureus colonization and increases Shannon diversity of the skin microbiome in atopic dermatitis patients in a randomized, double-blind, placebo -controlled Phase 2 trial. Clin Transl Med. 2022; 12(5): e790. doi:10.1002/ctm2.790.

[47] Erwin DZ, Chen P. Mupirocin. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025. Available from: https://www.ncbi.nlm.nih.gov/books/NBK599499/.

[48] Leyden JJ. Mupirocin: a new topical antibiotic. J Am Acad Dermatol. 1990; 22(5 Pt 1): 879–83. doi:10.1016/0190-9622(90)70117-z.

[49] Spellberg B, Blaser M, Guidos RJ, et al. Combating antimicrobial resistance: policy recommendations to save lives. Clin Infect Dis. 2011; 52 Suppl 5: S397–428. doi:10.1093/cid/cir153.

[50] Bowler PG, Duerden BI, Armstrong DG. Wound microbiology

and associated approaches to wound management. Clin Microbiol Rev. 2001; 14(2): 244–69. doi:10.1128/CMR.14.2.244-269.2001.

[51] Helmy YA, Taha-Abdelaziz K, Hawwas HAE, et al. Antimicrobial resistance and recent alternatives to antibiotics for the control of bacterial pathogens with an emphasis on foodborne pathogens. Antibiotics. 2023; 12(2): 274. doi:10.3390/antibiotics12020274.

[52] Rusu E, Enache G, Cursaru R, et al. Prebiotics and probiotics in atopic dermatitis. Exp Ther Med. 2019; 18(2): 926–31. doi:10.3892/etm.2019.7678.

[53] Lee YH, Verma NK, Thanabalu T. Prebiotics in atopic dermatitis prevention and management. J Funct Foods. 2021; 78: 104352. doi:10.1016/j.jff.2021.104352.

[54] Martyniak A, Medyńska-Przęczek A, Wędrychowicz A, et al. Prebiotics, probiotics, synbiotics, paraprobiotics and postbiotic compounds in IBD. Biomolecules. 2021; 11(12): 1903. doi:10.3390/biom11121903.

[55] Alam MJ, Xie L, Yap YA, et al. Manipulating microbiota to treat atopic dermatitis: functions and therapies. Pathogens. 2022; 11(6): 642. doi:10.3390/pathogens11060642.

[56] Litman T. Personalized medicine-concepts, technologies, and applications in inflammatory skin diseases. APMIS. 2019; 127(5): 386–424. doi:10.1111/apm.12934.