A RESEARCH REVIEW™
EDUCATIONAL SERIES

Skin Microbiome and its Role in Skin Barrier Dysfunction and Atopic Dermatitis

Making Education Easy 2018

About the Reviewers

Susan Prescott
BMedSc MB BS PhD (*W.Aust.*) FRACP

Dr. Susan Prescott is an internationally renowned specialist in childhood allergy and immunology. She is Professor of Paediatrics at the University of Western Australia, a paediatric allergist and immunologist at the Perth Children's Hospital, Director ORIGINS Project at Telethon Kids Institute, Founding President of the DOHaD SOciety of ANZ and the Director of *in*VIVO Planetary Health.

Prof Prescott is internationally recognised as one of the leading researchers into the early environmental determinants of health and disease – with a particular focus on immune health, early life nutrition and microbial exposures. She has over 25 years of research experience and is widely published with over 300 scientific papers, as well as being the author of several books: including The Secret Life of Your Microbiome: Why Nature and Biodiversity are Essential to Health and Happiness.

She has received numerous awards and fellowships including a Winston Churchill Fellowship and a prestigious Practitioner Fellowship from the Australian National Health and Medical Research Council (NHMRC).

Louise Reiche
MBChB (Otago) FRACP MD FNZDSI

Dr Louise Reiche is a New Zealand physician trained vocational specialist dermatologist and spent her latter postgraduate advanced training years in the UK, working in High Wycombe, Amersham and Oxford Radcliffe Infirmary, and participated in senior registrar training at St John's London as well as Oxford. After several years of research with L'Oreal she wrote her MD thesis (Self-perceived sensitive skin).

Louise runs general dermatology clinics but in addition has special interests in eczema, patch testing, skin cancer surveillance and Vitamin D. Louise has served on the executive of the NZ Dermatological Society and on the Vitamin D Working Group for the Cancer Society, is a member of Melnet NZ, Clinical advisor for Melanoma NZ and works alongside these groups and on behalf of the NZ Dermatological Society.

This article provides an overview of the human skin microbiome, including its role, origin, and composition. Also discussed is how skin microbiome dysbiosis contributes to the pathogenesis of atopic dermatitis and how moisturisation might benefit the skin microbiome. The intended primary audience for this article is dermatologists, general practitioners, midwives and nurses.

Skin microbiome: origin and composition

The most well understood role of the skin is that it serves as a barrier between the human body and its external environment, preventing loss of moisture at the same time as preventing the entry of UV radiation, toxins, pathogens, allergens, and irritants.[1] However, the skin is also a biologically-active ecosystem in which diverse communities of micro-organisms live in a variety of physiologically and topographically distinct sites.[1,2] These microbial communities and their collective genome are known as the skin microbiome. The specific role of the skin microbiome in human health is unclear but, in addition to protecting against colonisation by pathogenic micro-organisms, the skin microbiome modulates skin barrier function, via the cutaneous immune system.[3]

The formation of the skin microbiome begins at infant birth. This early skin microbiome is characterised by low heterogeneity and is largely determined by delivery mode at birth (vaginal or caesarean).[3] Skin microbiome diversity has also been shown to be positively associated with gestation age during the first month of life.[4] Diversity increases with increasing age and environmental exposure.[3] By adulthood, the skin microbiome has attained a remarkable degree of heterogeneity.

Bacterial gene sequencing studies have revealed that the microbiome on healthy human skin consists of at least 19 phyla, mainly Actinobacteria, Firmicutes, Proteobacteria, and Bacteroidetes.[2,5] Within these phyla, *Propionibacterium*, *Corynebacterium*, and *Staphylococcus* are the three most common genera. It has been estimated that one billion bacteria inhabit just 1cm^2 of human skin.[6] Less is known about other micro-organisms, such as viruses, fungi, and parasites, that also constitute the skin microbiome, but they too are likely to influence immune skin barrier function.[2]

Although human skin can be considered to be a single complex ecosystem it is characterized by three physiologically distinct microenvironments: sebaceous (head, neck, and trunk) moist (underarms, perineum, and toe webs) and dry (forearms and legs).[2,7] The skin microbiome varies topographically from site to site, with different niche-specific communities populating the moist, sebaceous, and dry regions of the skin. For example, it has been shown that *Propionibacterium* species and *Staphylococci* species predominate in sebaceous sites, *Corynebacterium* species predominate in moist sites, and a mixed population of bacteria reside in dry sites.[1] These innate differences in the anatomy of the skin (and hence its physiology) at different sites partially account for skin microbial diversity.[3]

Role of the skin microbiome

The skin microbiome is increasingly recognised as an integral component of the skin ecosystem, with microbial-immune interactions being vital for optimal skin barrier function.[3,8] With skin immune cells involved in both innate and acquired immunity, there is considerable capacity within the cutaneous immune system to react and change in response to its microbial inhabitants.[3] Indeed, the skin contains a variety of immune cells (e.g., keratinocytes, Langerhans cells, and T cells) that can interact with microbes and experimental evidence indicates that specific members of the skin microbiome promote protective immunity via the recruitment and activation of immune cells in the skin.[3,8] Commensal bacteria, such as *Staphylococcus epidermidis*, amplify host immune defence against pathogens and help to maintain host immunity via maintenance of the skin barrier.[3] The evidence also indicates that interaction between commensal microbes and skin immune cells modulates the inflammatory microenvironment.

Skin microbiome dysbiosis

Given increasing evidence that the skin microbiome is a major contributor to normal cutaneous immune system function, a logical assumption is that an imbalance of skin micro-organisms, i.e. microbiome dysbiosis, can be associated with skin pathologies.[3] For example, a dysbiotic skin microbiome can lead to increased colonisation by *Staphylococcus aureus*, which is characteristic of lesional and non-lesional

skin in atopic dermatitis.[8,9] It is unclear, however, whether an imbalance in the composition of the skin microbiome leads to pathologies of the skin or whether underlying host factors or pathologies result in skin microbiome dysbiosis (**Figure 1**).[2,3]

Certainly, a multitude of factors can affect the skin microbiome.[5,9,10] These include: inherent host factors, such as age, skin site, genetics, and underlying medical conditions (e.g., diabetes mellitus); host behavioural/lifestyle factors, such as vaginal or caesarean birth delivery, artificial or breast feeding, the number and relationship of human and animal cohabitants, occupation, diet, sanitation, use and nature of cleaning products (e.g., detergents), application of skin care products (cleansers and moisturisers), and use of medication (e.g., antibiotics); and external environmental factors, such as climate and geographical location. Factors that result in unfavourable conditions within the skin surface microenvironment can lead to an altered community of microbes.[5]

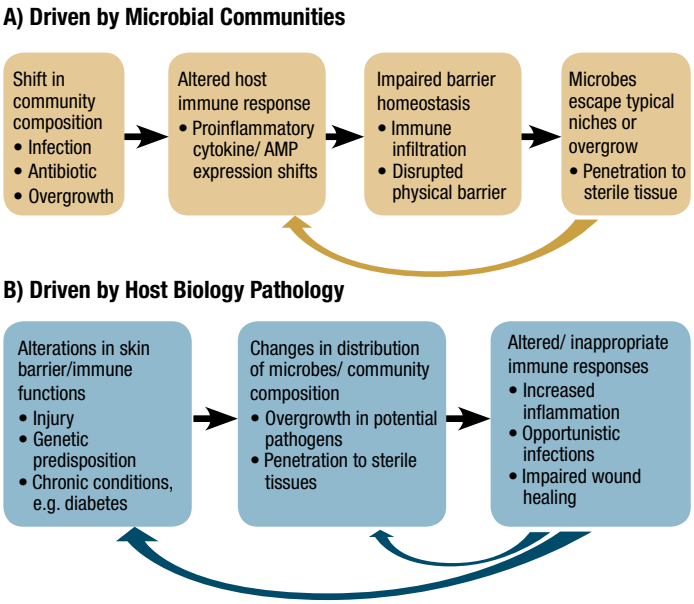

Figure 1. Models of dysbiosis of the skin microbiome, which could explain the development of AD.[3]

Atopic dermatitis

Atopic dermatitis (AD; atopic eczema) is a chronic, relapsing, inflammatory skin disease, which is a cause of substantial patient, family, and societal burden.[11,12] It is a common disorder, with epidemiological estimates suggesting a lifetime prevalence of between 10% and 20% in developed countries.[13] Signs of AD include generalised skin dryness, pruritis, lichenification, and scaling.

The pathogenesis of AD is multifactorial, with genetic predisposition, immune system dysregulation, skin barrier dysfunction, and environmental and lifestyle factors thought to be aggravating factors.[13] Dysregulation of the immune response is a characteristic of AD;[9] however, it remains unclear how dysregulation contributes to and/or results from changes in the skin microbiome.

Association with a dysbiotic skin microbiome

Although the exact cause of AD is unclear, one hypothesis is that skin barrier dysfunction leads to alteration of the composition of the skin microbiome, and subsequent shift in the homeostasis between host and microbiome, which contributes to the pathogenesis of AD.[5] Skin microbiome dysbiosis has been demonstrated to be a factor that can drive eczema-related inflammation.[14]

The results of a study that evaluated the skin microbiome of children with moderate-to-severe AD and healthy controls suggest that homeostasis between the host and microbial community is shifted in the presence of skin barrier dysfunction.[15] Skin barrier dysfunction was associated with reduced skin microbiome diversity characterised by an increased population of *S. aureus*. Marked reductions in skin microbiome diversity (and increased abundance of *S. aureus*) occurred during disease flares in patients with AD and common topical AD treatments restored diversity to the skin microbial community (see **Moisturisation** section). Indeed, observations in birth cohort studies suggest that increased prevalence of *S. aureus* in the skin microbiome contributes to the onset of clinical AD in infancy while an abundance of commensal staphylococci, particularly *S. epidermidis*, protects against the onset of AD.[16,17]

A link between the skin microbiome and AD is also supported by the findings of a study that determined the composition of the skin microbiome on lesional and non-lesional skin of the same individuals.[18] The investigators found that microbial diversity differed between affected and unaffected skin of patients with AD, with the difference in diversity highlighted primarily by an excess of *Staphylococcus* species on affected skin (and corresponding drop in overall microbial diversity). Furthermore, emollient treatment was associated with improvements in clinical symptoms of AD and an increase in overall skin microbial diversity (see **Moisturisation** section).

Other literature confirms the over-representation of *Staphylococcus*, and other Firmicutes species, and under-representation of *Actinobacteria*, *Cyanobacteria*, *Bacteroides*, and *Proteobacteria*, in the (lesional and non-lesional) skin of patients with AD.[5,15]

Further support for a link between the skin microbiome and AD is provided by observations that microbial communities appear to play a role in the observed preferences of AD for certain skin sites. AD has been found to preferentially affect the antecubital fossa (inner elbow) and popliteal fossa (behind the knee), which are regions of the skin that harbour similar groups of micro-organisms and share unique compositions of microbial communities.[1]

Moisturisation

Given the evidence that skin microbiome dysbiosis is associated with AD, restoring microbial balance of the skin may be beneficial in the treatment of AD.[5]

Moisturisers and emollients, for continuous skin barrier repair, form the foundation of treatment for AD.[13,19] There is also emerging evidence suggesting that use of emollients in early life prevents the development of AD.[20] Moisturisers and emollients help to maintain the integrity of the skin barrier, and may affect local microenvironments potentially shifting microbial balances.[5,9] Several published clinical studies have generated initial evidence linking improved clinical symptoms with re-establishment of skin microbiome diversity in AD patients treated with moisturisers.[15,18,21] A recently published study has also investigated changes in the skin microbiome when moisturisation is used as a preventative measure in patients with AD.[22]

In one of these studies, affected and unaffected skin of patients with AD (n=49) was evaluated to provide greater insight into the bacterial communities involved in the skin dysbiosis associated with AD and the potential effects of moisturisation.[18] After 12 weeks of emollient treatment, clinical symptoms had improved in two-thirds of the study population and the microbiome of lesional skin in the treatment responders more closely resembled that of non-lesional skin, as indicated by increased overall diversity and reduced abundance of *Staphylococcus* species compared with baseline.

Another of the studies was a longitudinal evaluation of children with moderate-to-severe AD (n=12) and healthy controls (n=11) that serially analysed bacterial gene sequences from skin samples taken during different disease states.[15] A strong association between lower skin microbiome diversity and increased disease severity was demonstrated. It was also apparent from the study results that topical AD treatments increased the diversity of skin bacteria, which preceded improvements in disease activity. Disease flares were characterised by low bacterial diversity, characterised by a high proportion of *Staphylococcus* species, especially *S. aureus*, in the absence of topical AD treatments.

Contrastingly, intermittent or ongoing topical treatment was associated with higher bacterial diversity and lower *Staphylococcus* species predominance. Based on these findings, the researchers proposed that reductions in microbial diversity and increases in the proportion of *Staphylococcus* species precede worsening of AD (**Figure 2**).

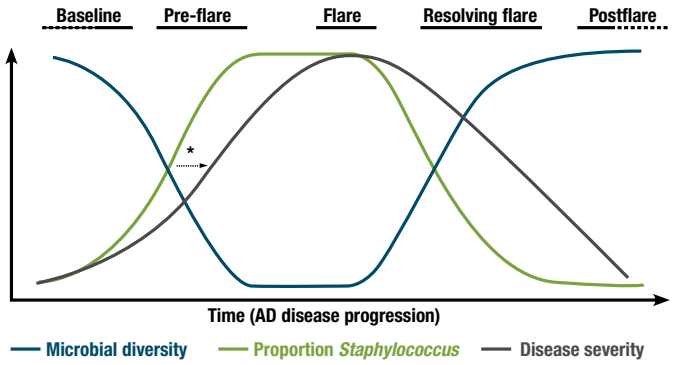

Figure 2. Microbiome progression in AD hypothesis.[15] *Disease states occur with concurrent anti-correlated shifts in microbial diversity and proportion of *Staphylococcus* species.

In a subsequent randomised controlled study, some of the same researchers investigated how longer-term emollient use (once daily for 6 months) alters skin barrier function and the skin microbiome in infants at risk for developing AD.[22] AD developed in one of 11 infants from the emollient group and three of 12 infants from the control group. Skin pH was statistically significantly lower in the emollient group than in the control group while transepidermal water loss (TEWL) was slightly lower and skin water capacitance slightly higher. Analysis of the skin microbiomes in samples from the emollient and control groups revealed that emollient use was associated with higher microbial diversity; in particular, a higher proportion of *Streptococcus salivarius* relative to *S. aureus* was observed. The investigators proposed that lower skin pH and immunomodulatory effects of *S. salivarius* might contribute to the preventative effects of emollients in patients with AD.

Another recent randomised controlled trial measured changes in skin barrier function, skin microbiome, and disease severity in adult patients with mild-to-moderate AD (n=31) during short-term treatment with a proprietary moisturising lotion.[21] At baseline, lesional skin had reduced barrier function (higher pH and TEWL and lower skin hydration) and significantly ($p<0.05$) reduced microbial diversity compared with non-lesional skin.

During a 14-day treatment period, disease severity (ADSI and EASI) and itch severity (VAS scale) improved significantly ($p<0.05$ vs baseline) with use of the moisturising lotion.[21] The improvements in clinical symptoms were accompanied by statistically significant baseline improvements in the pH, TEWL, and hydration of lesional skin. The clinical symptoms improvement was also accompanied by a significant ($p<0.05$ vs baseline) increase in the microbial diversity of lesional skin, which started converging with that of non-lesional skin from day 1 of treatment and remained similar for the rest of the treatment phase and during a 7-day regression phase (**Figure 3**). The results of this study support prior evidence that the microbial species diversity of the skin microbiome is lower on lesional skin and higher on non-lesional skin in patients with AD and that treatment with a topical moisturiser can correct this imbalance and lead to symptomatic improvement.

In summary, preliminary data from prospective clinical studies support the benefit of moisturisation on the skin microbiome in the management and (possibly) prevention of AD. However, there is a need for more well-designed controlled clinical trials, especially studies designed to explore the specific mechanisms by which moisturisation modifies the skin microbiome.

Prebiotic emollients and the skin microbiome

The principle of restoring microbial balance by increasing diversity of the microbiome is supported by the effectiveness of faecal transplantation on gastrointestinal health and earwax transplantation on ear health.[5] Based on the theory of skin dysbiosis in atopic patients, the focus of AD treatment may shift to a moisturiser that also contains the ingredients to directly help restore the skin microbiome (and thus skin barrier function). Indeed, a recent randomised controlled study has demonstrated that use of an emollient containing a biomass of non-pathogenic bacteria was able to normalise the skin microbiome in paediatric and adult patients (n=60) with moderately severe AD, and statistically significantly reduce the number and severity of flares compared with a conventional emollient.[23]

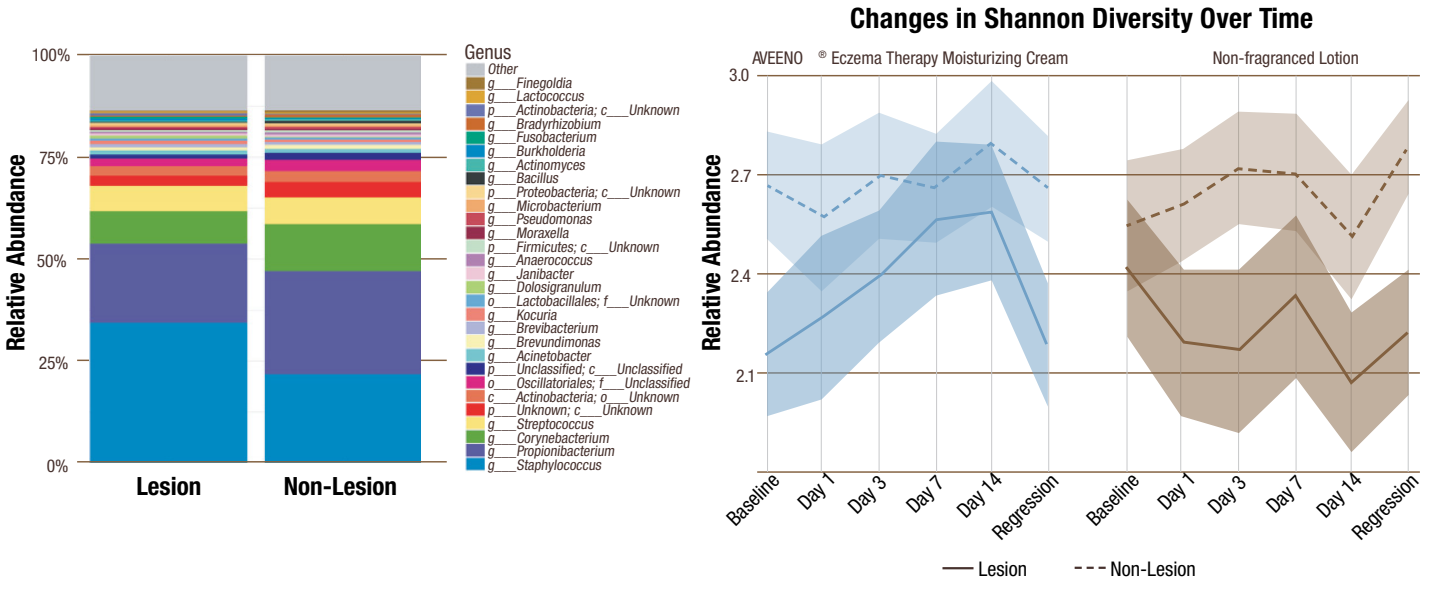

Figure 3. Microbial diversity of the skin microbiome on lesional and non-lesional skin of patients with AD and changes in microbial diversity during a 14-day treatment phase and a 7-day regression phase.[21] The Shannon index characterises species diversity within a community.

EXPERT'S CONCLUDING COMMENTS – LOUISE REICHE

It is well established in clinical dermatology that regular application of moisturisers helps to alleviate AD flares and prevent their recurrences. Restoration of an intact skin barrier function had been considered its mechanism, and, furthermore, an intact skin barrier lessens the impact of *Staphylococcus aureus* causing infection and as a separate fuelling allergen. Patients with AD have long been known to have increased susceptibility to *S. aureus* and virus infection such as herpes. *Staphylococcus epidermidis* is typically the predominant bacteria on skin and produces a variety of antimicrobial peptides, controlling the populations of *S. aureus* and group A streptococci, among other functions.[1] Competition within and between microbial species shapes and preserves a healthy microbiome. When the skin barrier is impaired, there is decreased expression of antimicrobial proteins. An individual's microbial composition is fairly stable over time, although prolonged contact with others, particularly a greater number of other individuals in a close relationship can alter this, but, nonetheless, there is greater variation in the microbial composition between individuals.[2] Pathogenic bacteria and viruses can induce epigenetic changes in host cells, which may influence the course of diseases such as AD. More knowledge in this area will expand our therapeutic potentials.

Like the skin, the gastrointestinal tract as a functional barrier between the environment in the internal body and its microbiome is complex including bacteria, viruses, fungi, and protozoa in extremely large numbers and wider diversity is associated with better health, i.e., reduced infections and reduced autoimmune diseases. Similarly, the bacterial component of the microbiome has been better studied than the other micro-organism groups. Distal gut microbes help to synthesise vitamins, essential amino acids, and metabolic by-products such as short-chain fatty acids. Interestingly, short-chain fatty acid by-products butyrate, propionate, and acetate provide energy for intestinal epithelial cells and strengthen the mucosal barrier.[3] These same short-chain fatty acid by-products are in the chemical structure of topical steroid preparations commonly used in NZ, e.g., clobetasol propionate (Dermol), hydrocortisone butyrate (Locoid), and hydrocortisone acetate (hydrocortisone cream AFT). It is also well recognised in clinical practice that treating eczema with topical corticosteroids is associated with clinical remission and reduced colonisation of *S. aureus*, without concomitant antibiotic use. So, we may well find in future research that the mechanism by which this occurs is via alteration in microbial composition/balance.

Various skin diseases including AD have been associated with inflammatory bowel dysbiosis, disorders and diseases. Changes in dietary protein impact on gastrointestinal microbiome, particularly animal-based or plant-based diets. For example, pure vegetarian pea protein consumption increases the gastrointestinal commensals *Bifidobacterium* and *Lactobacillus* and increases intestinal short-chain fatty acids, which are considered anti-inflammatory and mucosal barrier-enhancing. In contrast, higher levels of potentially pathogenic *Bacteroides* and clostridia are found in subjects consuming a high beef diet. A high animal protein diet is associated with significantly increased risk of inflammatory bowel disease and pro-atherogenic compounds, which increase the risk of cardiovascular disease, cancer, and diabetes mellitus, and overall mortality. Animal milk-based proteins, however, stimulate more favourable microbiome profiles.

Non-digestible carbohydrates are not absorbed through the small intestine but travel intact to the large intestine and provide a good source of carbohydrate for microbiota via fermentation, and, in the process, modify the intestinal milieu and are thus known as prebiotics. A high intake of soybeans, unrefined wheat and barley, fruits, and vegetables provides these favourable prebiotics but typically also provide dietary polyphenols with additional anti-inflammatory and pro-mucosal gut barrier properties. A study examining the anti-bacterial activity of fruit polyphenols resulted in reduced *S. aureus* levels[4] – so this in future may provide insight for other ways of tackling *S. aureus*-associated AD. Overall, a Mediterranean diet (characterised by high levels of varied fruits, vegetables, cereals, legumes, nuts, and olive oil; moderate consumption of fish and poultry; and lower intake of dairy products, red and processed meats, and refined sugars), in contrast to a high animal protein-based or strictly vegan diet, is associated with the greatest microbiome diversity.

In some respects, recent studies showing that a diet rich in plant-based sources and application of emollients to help restore skin health, is not new, but provides greater understanding why this is so and provides scientific evidence to support a lifestyle that our tangata whenua, great grandparents and grandparents were familiar with and recommended. Going beyond personalised prescriptions to personalised advice regarding lifestyle habit recommendations and judicious interaction with our environment, e.g., other people, animals, and so forth, may circumvent concerns regarding growing antibiotic resistance and provide holistic solutions to optimally managing AD.

REFERENCES

1. Schommer NN, Gallo RL. Structure and function of the human skin microbiome. Trends Microbiol. 2013;21(12):660-668.
2. Leung MHY, et al. Individual and household attributes influence the dynamics of the personal skin microbiota and its association network. Microbiome. 2018;6(1):26.
3. Singh RK, et al. Influence of diet on the gut microbiome and implications for human health. J Transl Med. 2017;15(1):73.
4. Su X, et la. Antibacterial effects of plant-derived extracts on methicillin-resistant Staphylococcus aureus. Foodborne Pathog Dis. 2012;9(6):573-8.

EXPERT'S CONCLUDING COMMENTS – SUSAN PRESCOTT

There is now little doubt that microbial exposure early in life is important for the development of competent immune function. While the dominant focus has been on the role of gut and mucosal ecosystems, it is increasingly likely that disruption of skin colonisation can also play a role in both local and systemic propensity for immune dysregulation and chronic inflammation.

The skin microbiome, with complex topographical diversity across human body sites, is critical for the maturation and homeostatic regulation of keratinocytes, specialised antigen presenting cells, and local immune networks. These host microbial interactions appear vital not only for skin barrier integrity, but also for many other functional properties of the skin, including hormonal and neurotransmitter production and immune and metabolic activity – all increasingly recognized for their systemic effects. In essence, this ecological unit provides a complex cutaneous sensory interface that plays a much more dynamic role in sensing and adapting to the external environmental than previously appreciated, with potential whole-body effects.

This means that both exogenous and endogenous factors that influence the skin microbiome and host cell interaction are likely to affect these multifaceted physical and functional aspects of the skin barrier unit. Thus, factors that modify the establishment and health of the skin microbiome have the potential to lead to predispose not to only cutaneous disease, but also other systemic inflammatory conditions. Growing evidence indicates that the biodiversity of skin habitats is influenced by the biodiversity of the ecosystems in which people reside, as well as the patterns of behaviour and interaction with those environments. In particular, environmental biodiversity losses with progressive urbanisation together with indoor behaviour are reducing contact with natural environments, affecting skin microbiomes and ultimately human health. This adds a new dimension to the longstanding 'hygiene hypothesis', better described as the 'biodiversity hypothesis', as an explanation for the increasing prevalence of immune diseases.

This is arguably best exemplified by the dramatic increase in very early onset conditions such as allergic disease, notably AD, which is characterised by early pre-symptomatic defects in skin integrity. Notably, new studies suggest that alterations in the skin microbiome may also precede development of AD in early infancy, reinforcing the importance of this ecological unit for early normal skin function. Disturbances of the stratum corneum have also been observed in psoriasis, rosacea, and acne vulgaris, and with the skin ageing process. Abnormal microbial colonisation of the skin appears to contribute to abnormalities of epithelial development and integrity in these heterogeneous conditions. Remarkably, new research show that strains of *Staphylococcus epidermidis* – a microbe on healthy human skin – can even inhibit the development of melanoma.[1] This microbial strain inhibits UV-induced skin tumour growth in animals when applied topically, and appears to be mediated by specific strains producing 6-N-hydroxyaminopurine (6-HAP). This might lead to probiotic solutions that amplify the effectiveness of pharmaceutical drugs and represents a revolution in the field of skincare and dermatology.

This emphasizes the importance of ecological perspectives in overcoming the factors that drive dysbiosis and the risk of inflammatory diseases across the life course. Understanding these pathways could lead to the development of therapeutic approaches to prevent and treat inflammatory skin disorders and possibly systemic inflammatory conditions. One approach may involve microbial interventions early in life. However, the development of such solutions will require gaining a better understanding of the interconnected ecology of humans, microbes, and the environment. Ultimately personal health solutions will only be successful if we also address the challenges of the built environment, global biodiversity losses, and declining nature relatedness that are contributing to erosion of diversity at a micro-ecological level, including our own microbial habitats.

REFERENCE

1. Nakatsuji T, et al. A commensal strain of Staphylococcus epidermidis protects against skin neoplasia. Sci Adv. 2018;4(2):eaao4502.

TAKE-HOME MESSAGES

- **Diverse microbial communities and their collective genome constitute the skin microbiome.**
- **The skin microbiome prevents pathogen colonisation of the skin and supports cutaneous immune system function.**
- **A diverse skin microbiome is a marker of healthy skin and an altered (dysbiotic) skin microbiome is a marker of atopy and is associated with AD and its severity.**
- **AD flares are characterised by an increased abundance of Staphylococcus species and reduced overall skin microbial diversity.**
- **Resolution of disease flares in AD is preceded by a restoration of microbial diversity.**
- **Preliminary clinical data indicate that moisturisation helps to re-establish the diversity of the skin microbiome in AD concurrent with improvement of clinical symptoms.**
- **More research is needed to substantiate initial findings linking the clinical benefits of moisturisation in AD to restoration of skin microbiome diversity, and to better elucidate the mechanisms involved.**

REFERENCES

1. Grice EA, et al. Topographical and temporal diversity of the human skin microbiome. Science. 2009;324(5931):1190-2.
2. Prescott SL, et al. The skin microbiome: impact of modern environments on skin ecology, barrier integrity, and systemic immune programming. World Allergy Organ J. 2017;10(1):29.
3. Sanford JA, et al. Functions of the skin microbiota in health and disease. Semin Immunol. 2013;25(5):370-7.
4. Pammi M, et al. Development of the cutaneous microbiome in the preterm infant: A prospective longitudinal study. PLoS One. 2017;12(4):e0176669.
5. Lynde CW, et al. The Skin Microbiome in Atopic Dermatitis and Its Relationship to Emollients. J Cutan Med Surg. 2016;20(1):21-8.
6. Grice EA, et al. A diversity profile of the human skin microbiota. Genome Res. 2008;18(7):1043-50.
7. Cundell AM. Microbial Ecology of the Human Skin. Microb Ecol. 2016; 31 May. https://doi.org/10.1007/s00248-016-0789-6
8. Yamazaki Y, et al. Role of the microbiota in skin immunity and atopic dermatitis. Allergol Int. 2017;66(4):539-44.
9. Grice EA, et al. The skin microbiome. Nat Rev Microbiol. 2011;9(4):244-53.
10. Kong HH, et al. Skin microbiome: looking back to move forward. J Invest Dermatol. 2012;132(3 Pt 2):933-9.
11. Avena-Woods C. Overview of atopic dermatitis. Am J Manag Care. 2017;23(8 Suppl):S115-s23.
12. Drucker AM, et al. The Burden of Atopic Dermatitis: Summary of a Report for the National Eczema Association. J Invest Dermatol. 2017;137(1):26-30.
13. Weidinger S, et al. Atopic dermatitis. Lancet. 2016;387(10023):1109-22.
14. Kobayashi T, et al. Dysbiosis and Staphylococcus aureus Colonization Drives Inflammation in Atopic Dermatitis. Immunity. 2015;42(4):756-66.
15. Kong HH, et al. Temporal shifts in the skin microbiome associated with disease flares and treatment in children with atopic dermatitis. Genome Res. 2012;22(5):850-9.
16. Meylan P, et al. Skin Colonization by Staphylococcus aureus Precedes the Clinical Diagnosis of Atopic Dermatitis in Infancy. J Invest Dermatol. 2017;137(12):2497-504.
17. Kennedy EA, et al. Skin microbiome before development of atopic dermatitis: Early colonization with commensal staphylococci at 2 months is associated with a lower risk of atopic dermatitis at 1 year. J Allergy Clin Immunol. 2017;139(1):166-72.
18. Seite S, et al. Microbiome of affected and unaffected skin of patients with atopic dermatitis before and after emollient treatment. J Drugs Dermatol. 2014;13(11):1365-72.
19. Eichenfield LF, et al. Guidelines of care for the management of atopic dermatitis: Section 2. Management and treatment of atopic dermatitis with topical therapies. J Am Acad Dermatol. 2014;71(1):116-32.
20. Lowe AJ, et al. The skin as a target for prevention of the atopic march. Ann Allergy Asthma Immunol. 2018;120(2):145-51.
21. Capone K, et al. Effects of topical lotions on the atopic dermatitis skin microbiome and associations with itch and skin barrier function. [Poster]. Presented at the 76th Annual Society for Investigative Dermatology (SID) Meeting, Portland, OR. 26-29 April. 2017.
22. Glatz M, et al. Emollient use alters skin barrier and microbes in infants at risk for developing atopic dermatitis. PLOS ONE. 2018;13(2):e0192443.
23. Seite S, et al. Clinical efficacy of emollients in atopic dermatitis patients - relationship with the skin microbiota modification. Clin Cosmet Investig Dermatol. 2017;10:25-33.hine: a multicenter, open-label, follow-up study in patients from three short-term clinical trials. Clin Ther. 2006;28(6):943-52.

Aveeno®

Publication of this article was supported by an educational grant from Johnson & Johnson Pacific and the content or opinions expresssed in this publication may not reflect the views of Johnson & Johnson Pacific.