The Microbiome – New Insights Into the Skin's Own Ecosystem

Alexander Salava, MD and Antti Lauerma, MD, PhD
Department of Dermatology and Allergology, Helsinki University Central Hospital, Meilahdentie 2, FIN-00250 Helsinki, Finland. E-mail: alexander.salava@hus.fi

An ecosystem on the skin

Human skin can be considered as a complex ecosystem and, because it is primarily an interface to the outside environment, the skin is inhabited by an abundant number of micro-organisms such as bacteria, fungi, mites and viruses.

Our current theories point out, that most of the skin's micro-organisms are harmless and are likely to provide protection. However, the interaction between our skin and the microbiome should also be viewed as a symbiosis. One's individual commensal microbial flora receives as compensation for the defense from pathogens an area of skin surface to colonize and, in other words, an ecological niche in the host, i.e. on our body.

This cohabitation between our microbes and ourselves is not isolated. Skin microbes have showed to play a significant role in the modulation of our cutaneous native and adaptive immune system. There is lively communication between apathogenic commensals and our immune system, which contribute to the lifelong training of our cutaneous T cells to recognize correct antigens and develop an adequate immune response (1).

Our current understanding

Seen simplified, mostly the physical and chemical characteristics of a particular skin area determine the microbial flora. Skin thickness, number of skin folds as well as the amount of cutaneous appendages, i.e. sweat and sebaceous glands, hair follicles and their activity all have a considerable effect. On the other side, host characteristics like age, gender and moreover immunological factors have an influence on the composition of the microbiome. Recent studies emphasize the balanced interaction and relationship (symbiosis) between microbes and the host (2).

Nevertheless, the normal resident commensal flora has been shown to vary significantly at different sites and in different individuals. The colonization takes place immediately after birth and a promising area for future research will be the formation and evolution of the cutaneous microbiome during the first years of life and possible connections to skin diseases (3).

New molecular approaches

New innovations in molecular diagnostic methods have dramatically changed our understanding of the cutaneous microbial flora in the last decade. It has been a pleasure to see and use these methods, which have enabled explorations of the complexity of the human-associated microbiota in recent years (4).

Based on genomic studies with 16S ribosomal RNA metagenomic sequencing it has become evident, that the skin colonization of microorganisms has a much greater diversity and variability than previously assumed. Furthermore, there have also been exciting reports of detection of 16S ribosomal RNA in deep skin layers, indicating that the microbiome actually extends to subepidermal compartments of normal skin (5).

Another interesting example is, that the proportions of e.g. the most abundant different bacterial phyla (*Actinobacteria, Firmicutes, Proteobacteria* and *Bacteroidetes*) seem to vary substantially in different locations. Could the microbiome be a possible explanation of the, hitherto not completely understood, prominent sites of predilection of skin diseases?

Howsoever, current knowledge indicates definitely that the proportions and the established microbiome remain surprisingly stable during the life span of an individual.

Atopic dermatitis as a prime example

Changes in the balance of the microbiome and the host's cutaneous immune response have been shown to aggravate atopic dermatitis and lead to secondary skin infections (Fig. 1). During exacerbation, patients with atopic dermatitis show an altered skin microbiome with a decrease of the microbial diversity (Figs 2 and 3). After adequate therapy (topical corticosteroids or calcineurin inhibitors) the skin microbiome has been shown to regenerate and find its way back to diversity

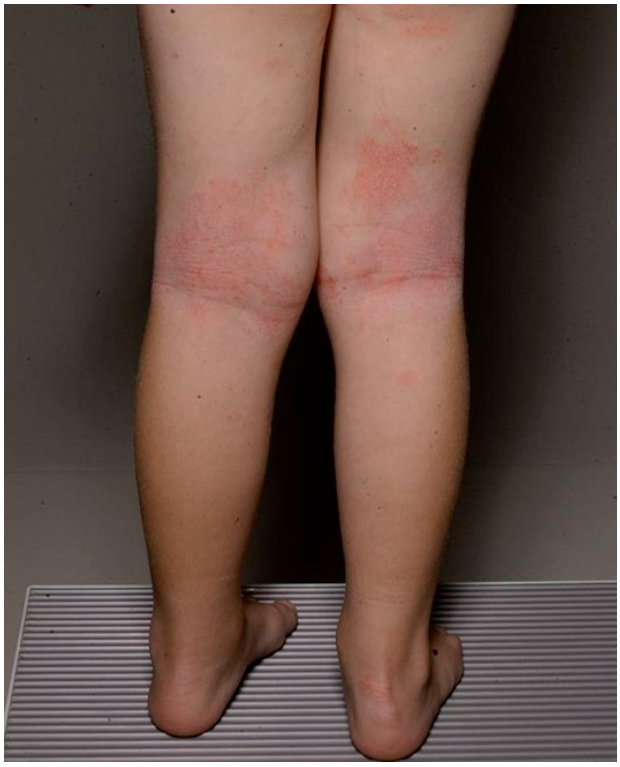

Fig. 1. Atopic dermatitis in the knee folds of a 10-year old patient, a typical site of predilection.

(6). There have been also investigations of the effect of other therapeutic modalities, e.g. phototherapy. In atopic dermatitis the effect of narrowband UV therapy has been documented quite well and shows an increase in microbial diversity.

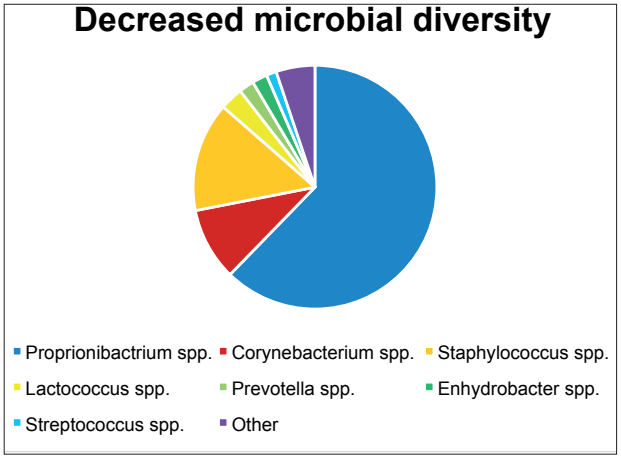

Fig. 2. Atopic dermatitis, disease flare, dry microenvironment (neck), mean relative abundances of the 8 most common genera of the cutaneous microbiome.

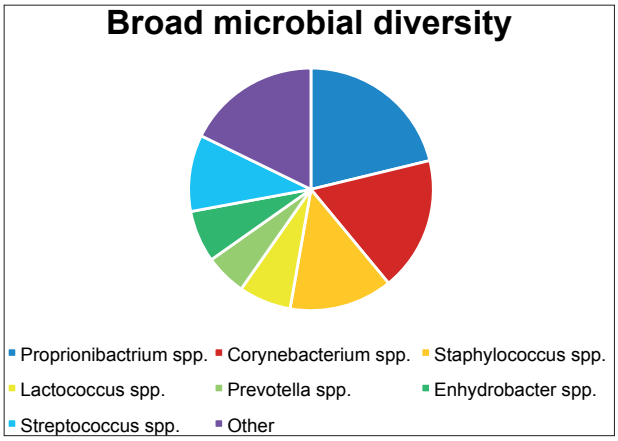

Fig. 3. Atopic dermatitis, under treatment, disease stable, dry microenvironment (neck), mean relative abundances of the 8 most common genera of the cutaneous microbiome. Copyright of figures: Alexander Salava.

It remains however largely unclear whether the changes seen in the skin microbiome of are due shifts in the balance of the immune response or occur secondarily because of permeability barrier changes (7).

Many dermatologic disorders present with a typical clinical distribution and atopic dermatitis can be considered as a prime example. Here the site specificity of skin bacterial communities proposes that not only do particular ecological niches of the skin favor the growth of certain bacteria, but that the local skin microbiome is important in the initiation and continuance of a dermatologic disease (8).

Future perspectives

Our understanding about the cutaneous microbes has changed. As traditionally the species of micro-organisms were considered separate causative agents, we are seeing new concepts rising. These see the microbiome in a captivating dynamic and complex host-microbe context.

The cutaneous micro-organisms exist on our skin within a rich milieu of species that can influence pathogenicity. Additionally to the known dysfunctions in barrier function of the skin and immunologic disturbances, evidence is increasing that inflammatory skin diseases, e.g. atopic dermatitis, are also connected to a dysbiosis of the microbial community without an invading dominant pathogen (9).

Novel fields in skin microbiome research include the role of micro-organisms in cutaneous neoplasms, which our group has been recently investigating (10). Also the development of the skin microbiome in early life has emerged as a new fascinating topic.

Conclusions for the dermatologist

Changes in the microbiome have been quite characteristic for a particular disease state (e.g. in atopic dermatitis stable or exacerbated) and therefore may compose a potential diagnostic tool for the dermatologist in the future (11).

Novel molecular techniques to identify and quantify microbial organisms have to date proved to be sensitive and less-biased thus representing a possible supplement to microbiological and microscopic diagnostics. Our cutaneous ecosystem has proven to more complex than expected and future studies may solve several aspects of the pathogenesis of skin diseases.

And lastly, in the hand of the dermatologist, the investigation of the patient's skin microbiome may even have a foothold in the clinician's diagnostic and therapeutic repertoire.

The authors declare no conflicts of interest.

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