

IMMUNOLOGY OF THE SKIN

What is the largest organ in the body? The bowel? No, it's the skin.

The average human body is covered by 1.8m² of skin (up to 15% of body weight), providing a primary barrier against physical insults and microbial entry. As with any interface between the body and its environment, the skin must not only provide passive protection, but must also actively sense and respond to changes in environmental factors, as well as alterations in the organisms ("flora") lining the skin. In this sense, the skin "communicates" with the environment and the interaction runs both ways – the skin's immune system controls microbial burden, but at the same time, colonising microbes "educate" the immune system. As you may know, there is at least one microbe for every body cell, so we could be thought of as "walking colonies" as much as individual human entities.

The skin is an immunological organ, consisting of a variety of specialised cellular and soluble mediators, including skin cells (keratinocytes), Langerhans cells, dermal dendritic cells, resident T cells, monocytes, complement, antibodies, and antimicrobial peptides. The skin holds an estimated 20 billion T cells! The diverse and functionally specialized components of the immune system sense and respond to infection or various barrier breaches to activate an immune response and eventually return to homeostasis (steady state). However, poorly regulated immune responses can also cause inflammatory skin disorders.

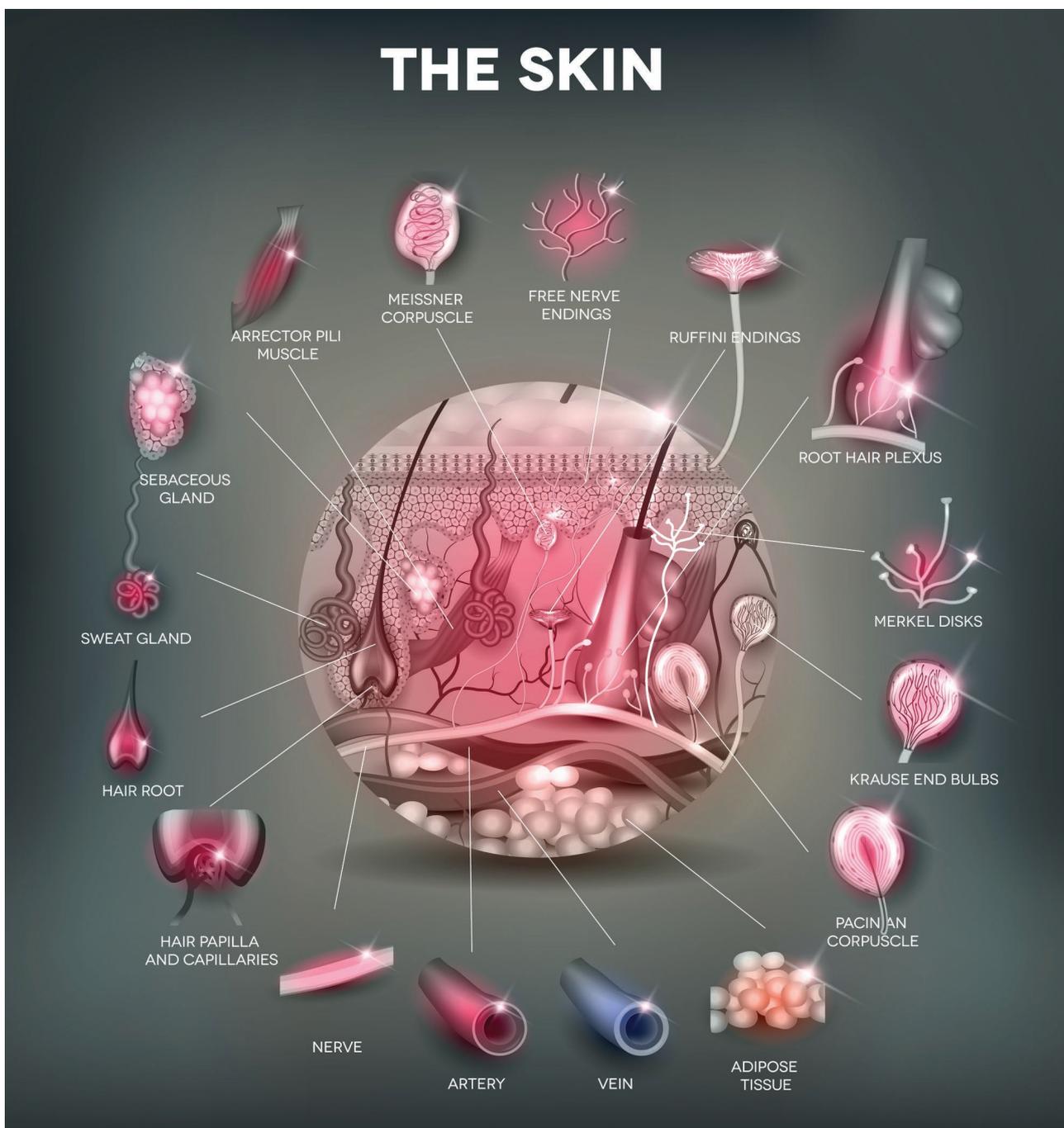
There are a number of connections between the skin and the immune system:

- Skin infections result from inadequate immune control of colonising microbes. - - - Seborrhoeic dermatitis is an itchy skin condition with a tendency to affect the scalp and face, and is thought to represent a host response to the fungal agent *Malassezia*.
 - Acne is often caused by the commensal (colonising) organism *Propionibacterium*
 - Staphylococci and streptococci can invade the skin, causing skin infections such as cellulitis and impetigo.
- Microbe responses - The skin is lined by many organisms (fungi, bacteria, viruses), and disturbances in the flora or the immune system's response to these bugs can cause disease. Different bodily sites display varied microbial "signatures", depending upon local oiliness, dampness and light exposure. Exaggerated

responses to staphylococci, which are carried on the skin in most individuals, can (in genetically disposed individuals) contribute to inflammatory skin conditions such as eczema and psoriasis. The incidence of these skin problems has doubled over the last thirty years, in parallel with decreased exposure (or altered diversity) of skin organisms, especially in early life (and even influenced by whether delivery is vaginal or caesarean).

- Immune "hypervigilance" - the skin senses "danger". An uncommon condition called Bechet's represents an inherent exaggerated sensitivity of the body's immune response to microbes as well as non-specific trauma. This is best illustrated by the phenomenon of "pathergy", where a trivial trauma to the skin results in localised inflammation, manifesting as a pustule. Pathergic phenomena can also occur on the skin or the bowel in individuals with inflammatory bowel disease (ulcerative colitis, Crohn's disease), and might translate into poor wound healing, non-infective inflammatory skin lesions, and even "dehiscence" (falling apart) over surgical suture sites.
- Allergic responses can be started in the skin. This may take the form of immediate hypersensitivity (so-called "Type I allergy", mediated by IgE antibodies), such as the contact urticaria ("hives") seen in some individuals when grass or animal proteins contact the skin surface. Alternatively, skin cells may be activated by various agents in prolonged contact with the skin (e.g. watches, jewellery), resulting in "contact" (delayed, Type IV hypersensitivity) dermatitis. Scratch and patch tests can define these conditions more precisely. Skin contact with peanut-derived products such as ointments and creams (especially in infancy) appears to increase the likelihood of allergy to ingested peanut, which may manifest as anaphylaxis.
- Scleroderma is a group of conditions characterised by skin thickening (from the Greek "sclero" thick, "derma" skin). There are limited and diffuse forms of the condition, representing the degree of skin involvement, with diffuse varieties demonstrating thickening extending past the elbows, plus a greater propensity for internal organ involvement. Scleroderma is almost always associated with "Raynaud's phenomenon", the term describing triphasic colour changes (white, blue, red) on exposure to cold and stress, in the hands and extremities. Our centre is implementing the use

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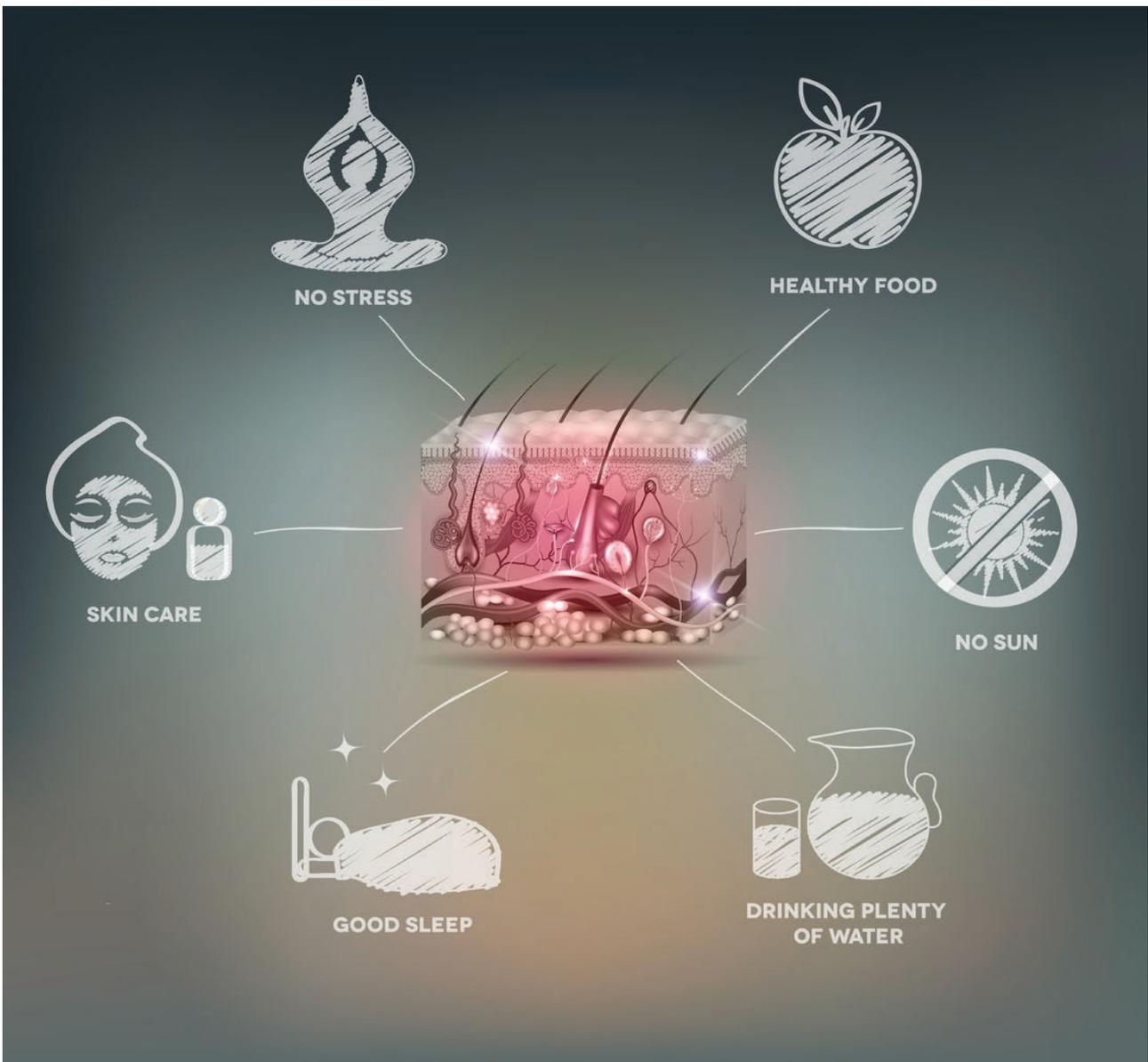


of capillaroscopy (an instrument that studies the skin's blood vessels at the fingernail beds) to define the likelihood of scleroderma developing in people with Raynaud's, as well as in subtyping subsets of patients with established scleroderma to allow prediction of complications such as ulceration and even organ involvement (e.g. lung fibrosis). Raynaud's phenomenon is common, affecting up to 10% of women, but only a small minority of these people will ever go on to develop scleroderma or other autoimmune conditions, and the performance of capillaroscopy and antinuclear antibody (ANA) testing can define this small subset.

- Itching of the skin is a common medical problem, and, despite popular wisdom that this must represent some form of body allergy or sensitivity, the yield for allergy is very low, and drops exponentially the longer the itch has been present. We urge the itch sufferer not to undertake

arduous and expensive trials of complementary allergy testing, dietary elimination, or other questionable approaches. Whilst skin itch may rarely be the manifestation of some internal bodily ill (renal, thyroid, liver conditions, blood problems), the commonest cause is dry skin, aggravated by the growing inability of the skin to cope with drying soaps and shampoos with the passage of time. Moisturisation and antihistamines can be helpful here. Sjögren's, an autoimmune syndrome causing dry eyes and mouth, can also result in dryness of the skin, and aggressive skin moisturisation is also important in this condition.

- Skin rashes are common. Usually, they reflect a passing hyperactivity of the immune system to an infective (usually viral) challenge; various drugs can aggravate the immune hyperreactivity seen in these settings, particularly anti-inflammatory drugs and codeine. Occasionally,



hives (“urticarial”) can be seen in response to such infective or drug triggers, and all these rashes will be exaggerated by stress and sleep deprivation. Sometimes, infections can trigger a type of immune problem that results in inflammation of the linings of the blood vessels, particularly the small blood vessels that supply the skin with nutrients and oxygen. The process, called “vasculitis”, is usually secondary to an infection or drug, although there are rarer syndromes where the body spontaneously becomes activated and inflamed, and, if larger blood vessels become involved, then problems such as arthritis and inflammation of the kidney, lungs and other organs may occur. This is one example of the skin providing a “window” to the behaviour of the body’s immune system, signalling that something is amiss.

- An uncommon autoimmune condition called pemphigus features the production of antibodies to the “cement” that holds the “bricks” (skin cells – keratinocytes) together. This causes a blistering rash. Coeliac disease, whilst best known for its association with gut

problems (malabsorption, diarrhoea, bloating) in response to gluten, can also cause an intensely itchy blistering skin rash called dermatitis herpetiformis, and, in some coeliac patients, this may be the sole clinical manifestation.

As you can see, the skin is more than a barrier – it is a complex, dynamic organ, the largest one we have! Whilst the skin may not always behave as it ought to, I trust that, with careful attention and consultation where appropriate, you’ll be comfortable in your own skin.



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