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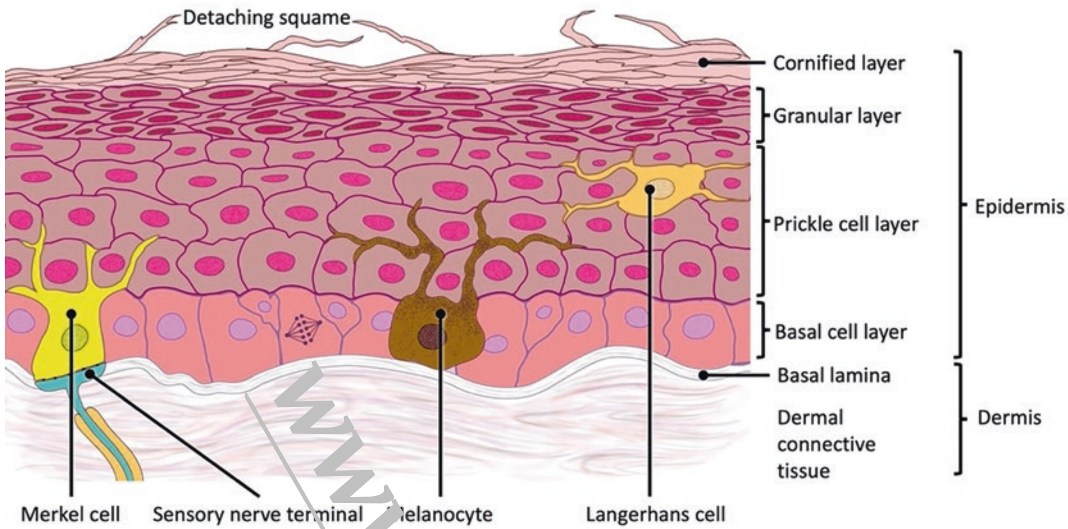

Fig. 1 Fine structure of the epidermis and dermis. Layers, features and characteristic cell types are depicted. (Adapted from [7])

layer, which are required for the elimination of cell components of the resilient anuclear corneocytes as the terminally differentiated keratinocytes [1, 18]. The **lucid layer** (derived from the Latin word 'lūcidus' meaning 'clear') is only present in thick skin areas such as the palm of the hand or the sole of the foot [3]. The keratinocytes of the lucid layer are non-vital and contain the clear intracellular protein eleidin as opposed to the keratin in deeper layers [19]. The **cornified layer** (derived from the Latin word 'cornu' meaning 'horn'; Fig. 1) forms the outermost epidermal layer and consists of flattened anucleated cells that are filled with keratin [3]. The extracellular matrix of the corneal layer contains mainly lipids that are organized within characteristic lamellar bilayers but also enzymes, antimicrobial peptides and structural proteins [20]. Superficial corneocytes are continuously shed off and replaced through an ongoing supply of corneocytes from the granular or lucid layer [3, 9]. This lines up with the fact that corneocytes of deeper layers are more tightly interconnected with desmosomes compared to superficial layers as desmosomes are subjected to proteolytic degradation towards the surface [1].

The Epidermal-Dermal Junction

The epidermal-dermal junction is a transitional zone that anchors the epidermis onto the dermis and can be considered an independent anatomical unit [21]. From superficial to deep, it consists of the following four components:

1. *The dermal surface of the plasma membrane of the epidermal basal cells:* Hemidesmosomes, which describe multiprotein complexes that link the epidermal basal cells to the basal lamina, are the most significant structures of this layer [21, 22].
2. *The lamina lucida as an intermembranous space:* This layer is not to be confused with the epidermal lucid layer. The similar name originates from common microscopic features between the two. In electron microscopy, light can pass through this layer but the space does not occur completely transparent as fine filaments from hemidesmosomes cross on their course between the epidermal basal cells and the basal membrane [21, 23].
3. *The basal lamina:* It is a continuous band of type IV collagen, laminin, nidogen, and per-

lecan [21, 24]. The basal lamina varies in density and is thicker in areas of attaching hemidesmosomes [21]. The basal lamina is of epidermal origin [25].

4. *Fibrous elements of the sub-basal lamina:* Anchoring fibrils connect the basal lamina to the epidermis [21]. They can form a meshwork within the dermis as well as reattach to the basal lamina after looping around collagens [21]. Microfibril bundles can run over considerable distances between the basal lamina and the deep dermis [21]. Also, randomly oriented single collagen fibres with no attachment to the basal lamina can be found in this compartment.

Dermis

The dermis makes up the main body of the skin consisting of dense connective tissue organized in two layers: a superficial thin papillary layer that is tightly connected to the epidermis via the epidermal-dermal junction and a thick deep reticular layer that connects to the hypodermis [3]. The dermal thickness depends on the body site and sex. It is thicker in palms and soles compared to the eyelid and thicker in males compared to females [3]. The **papillary layer** (derived from the Latin word 'papilla' meaning 'nipple') is named after the finger-like elongations that extend towards the epidermis. Thin type I and III collagen fibres can be found in this layer, which are organized in a loose meshwork [26]. Also, fibroblasts, elastic fibres, looped capillaries and tactile corpuscles are located in the papillary layer [3, 27, 28]. The **reticular layer** (derived from the Latin word 'rete' meaning 'network') is composed of dense connective tissue [3]. The main feature of this layer is the presence of thick, coarse type I collagen bundles [26]. Moreover, the reticular dermis contains cells such as fibroblasts and immune cells, elastic fibres, hair follicles, sebaceous and sweat glands, vessels, nerves and sensory receptors such as Pacinian corpuscles and Ruffini corpuscles [1, 3, 27, 29] (Fig. 2). Collagens and elastic fibres of the reticular dermis create tension lines called Langer's lines that are relevant to surgery and wound healing [30]. The boundary between the reticular dermis and the hypodermis is unclear in contrast to the distinct epidermal-dermal junction [3].

Hypodermis

The hypodermis (derived from the Greek words 'hypo' meaning 'under' and 'dérma' meaning 'skin') is located beneath the dermis and describes a layer of loose connective tissue, blood vessels including a rich capillary network and nerves [1, 3]. Simplified, this layer is also referred to as subcutaneous fat as this is the predominant component of this layer, which connects the dermis to the deep fascia, aponeurosis or periosteum [3].

Vascular Supply

The skin has the capacity to alter the regional blood flow almost 20-fold. This vast increase in supply is owing to the thermoregulatory function of the skin. Three sources of supply exist, one direct to the cutaneous tissue, one to underlying musculature and one to the fascio-cutaneous system. The latter two deviate either as muscle perforators under the investing fascia or superficial to it, respectively. A total of six vascular plexus can be found in the dermal layers. Arteriovenous shunts exist especially in the deeper skin layers, which are under autonomic nerve control. Blood supply is influenced by thermal needs and also by emotions. The lymphatics originate in the papillary dermis and receive the interstitial fluid via small vessels into subcutaneous channels. They help transport macrophages, Langerhans cells and lymphocytes to regional lymph nodes [7].

Innervation

The skin forms a major sensory organ, and regional differences exist for both the types and densities of innervation. A number of receptors can be distinguished throughout the layers, which help mediate mechanical, thermal, nociceptive and potentially chemical stimuli. Figure 2 summarizes the locations of these receptors.

- Free nerve endings detect thermal (heat and cold), mechanical stretch or pain and can be found in most of the layers of the skin.
- Meissner [tactile] corpuscles exist in the dermal papillae close to the dermo-epidermal junction. They are rapidly adapting sensors important for the sensation of touch.
- Merkel nerve endings are situated in the epidermis (basal cell layer) and are characterized as slow-adapting mechanoreceptors, detecting continuous pressure. Moreover, they are important for object discrimination.
- Pacinian corpuscles are situated in the dermis or hypodermis predominantly in the digits. They primarily detect vibration and deep pressure.
- Ruffini [Bulbous] corpuscles can be found in the dermis (reticular layer) and are slow-adapting mechanoreceptors responding to ongoing pressure with low capacity to adapt.

Biomechanics of the Skin

Determinants of Biomechanical Properties of Human Skin

Based on the description in the section 'Anatomy of the Skin', it can be concluded that the skin is a composite material of several layers, which are organized into sub-layers with characteristic structural components. That poses the question of which components are responsible for the characteristic biomechanical (load-deformation) behaviour of the skin. Irrespective of the layer, the following two components determine the biomechanics of the skin: cellular components and the extracellular matrix. Tensile tests have demonstrated that predominantly the extracellular matrix forms the mechanical backbone of skin [31, 32]. The epidermis seems less relevant with regard to elasticity and load-bearing of the skin when stretched [32]. However, cells play a role in the strain behaviour of human skin. Following cell removal, skin samples can be strained to a further extent, indicating that cells limit the straining of skin in the native state [32]. The main extracellular matrix components of the skin are collagen, elastin and ground substance [5]. The

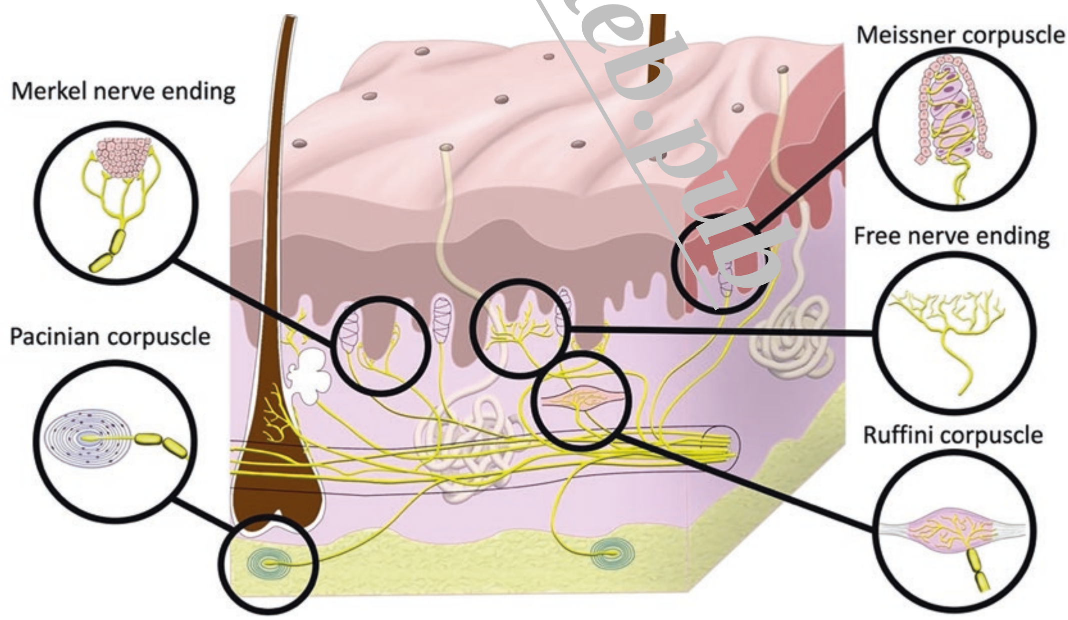

Fig. 2 Skin mechanoreceptor types. Receptor locations are depicted within the layered skin. Each receptor presents unique features, allowing for a broad range of mechanical, thermal and chemical stimuli being transduced

collagen network in the dermis makes up approximately 77% of the dry weight of the skin, forming its key component [1, 5]. Collagen-rich tissues are well known for their mechanical robustness and generally determine the strength of human tissues. Hence, dermal types I and III collagens almost exclusively determine the mechanical strength of human skin under strain [33]. Elastin, which accounts for approximately 4% of the human skin, is predominantly responsible for the recoiling of skin after being stretched with no significant contribution to its strength [34]. Overstretching [5] or mechanical wear of elastic fibres induces a lack of recoiling, which negatively affects the capacity of the skin to regain its initial condition. Ground substance summarizes the physicochemical linkage of the glycosaminoglycans chondroitin, keratin, heparin, dermatan and hyaluronic acid to a protein, which results in so-called proteoglycans [5]. The ground substance likely contributes to the (time-dependent) viscoelastic property of human skin. The ground substance also plays a role in the lubrication of collagens and elastin during movements as well as in the direction of collagen fibre formation [5].

Effects of Ageing on Skin Biomechanics

With age, the skin undergoes changes indicative of mechanical ageing. Eye wrinkles are a common sign of this phenomenon. The section 'Determinants of Biomechanical Properties of Human Skin' outlined that the dermis is the key layer for the mechanical behaviour of the human skin. Thus, age-related structural changes of the dermis will strongly reflect on the biomechanical behaviour of the skin with age. Ageing of the skin can be subdivided into two categories that describe characteristic structural alterations of the skin related to whether these originated within or outside the human body: intrinsic and extrinsic ageing [5]. Intrinsic ageing of the skin describes the atrophy of the dermis that results from a degeneration of collagen and elastin and a decreased tissue hydration with age [5]. Extrinsic ageing, also called 'photoageing', is mainly caused by (types A and B) ultraviolet light and results in an excessive accumulation of abnormal elastin material within the upper and mid-portion of the dermis [5]. This ageing is considered premature. Also, extrinsic ageing of the skin appears to cause an increased collagen degeneration compared to intrinsic ageing [5]. The following characteristic age-related changes in the mechanical properties of the human skin can be observed: Firstly, the skin progressively loses its ability to elastically recover in areas of small stresses, which is related to the elastin network changes in the dermis [35]. Secondly, the time for viscoelastic recovery from larger stresses progressively increases with age, which is thought to be related to changes in the dermal ground substance rather than the proteins [35]. Thirdly, dermal collagen degeneration results in decreased tensile strength of the skin [5]. It has to be noted that the biomechanical behaviour of human skin is complex and might be influenced by other factors such as sex or the way the experimental data was obtained. Therefore, generalizations should be handled with care. For example, a study on human scalp conducted on samples with an age range between 6 and 94 years observed strong age-related decreases in elasticity and tensile strength in females, but none of these were observed in males [33].

Conclusion

The human skin is a composite tissue that is organized into several layers and sub-layers. These are highly adapted to fulfil complex functions. The epidermis is mainly a protective layer that is morphologically structured in different developmental stages of keratinocytes on their progression to the surface. Apart from the protection of deeper body tissues, the collagen-rich dermis is of importance for the thermoregulation, sensation, immune system and biomechanical characteristics of the skin.

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