

Skin structure and function

Introduction

The integument or skin is the largest organ of the body, making up 16% of body weight, with a surface area of 1.8 m². It has several functions, the most important being to form a physical barrier to the environment, allowing and limiting the inward and outward passage of water, electrolytes and various substances while providing protection against micro-organisms, ultraviolet radiation, toxic agents and mechanical insults. There are three structural layers to the skin: the epidermis, the dermis and subcutis. Hair, nails, sebaceous, sweat and apocrine glands are regarded as derivatives of skin (see Figure 1.1). Skin is a dynamic organ in a constant state of change, as cells of the outer layers are continuously shed and replaced by inner cells moving up to the surface. Although structurally

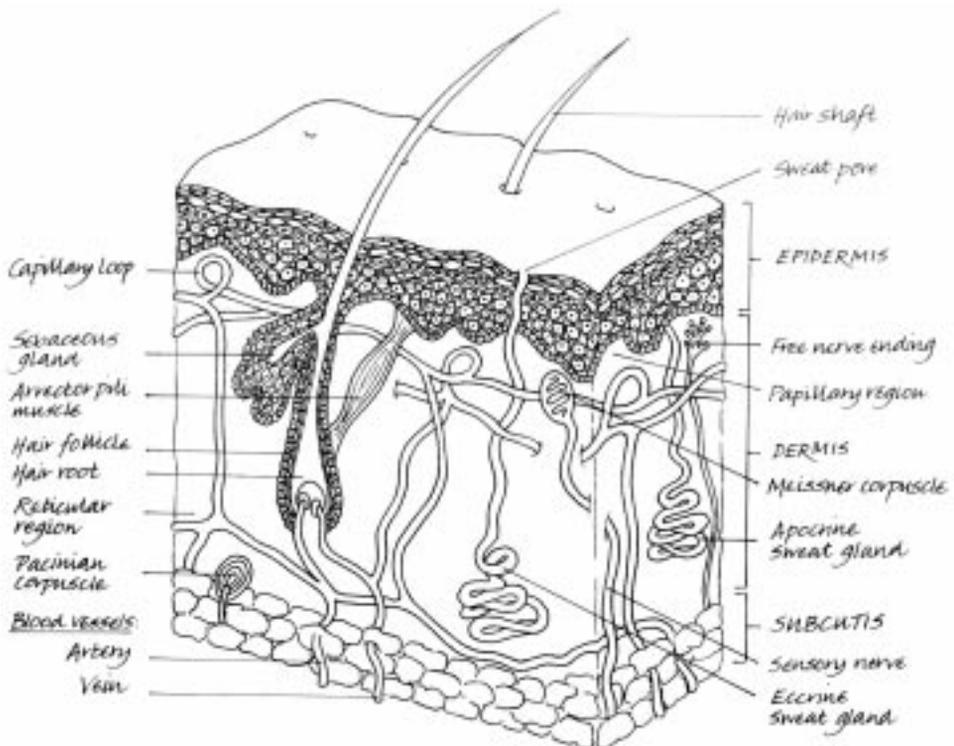


Figure 1.1 Cross-section of the skin.

Table 1.1 Layers of the skin.

<i>Skin layer</i>	<i>Description</i>
Epidermis	The external layer mainly composed of layers of keratinocytes but also containing melanocytes, Langerhans cells and Merkel cells.
Basement membrane	The multilayered structure forming the dermoepidermal junction.
Dermis	The area of supportive connective tissue between the epidermis and the underlying subcutis: contains sweat glands, hair roots, nervous cells and fibres, blood and lymph vessels.
Subcutis	The layer of loose connective tissue and fat beneath the dermis.

consistent throughout the body, skin varies in thickness according to anatomical site and age of the individual.

Skin anatomy

The epidermis is the outer layer, serving as the physical and chemical barrier between the interior body and exterior environment; the dermis is the deeper layer providing the structural support of the skin, below which is a loose connective tissue layer, the subcutis or hypodermis which is an important depot of fat (*see* Table 1.1).

Epidermis

The epidermis is stratified squamous epithelium. The main cells of the epidermis are the keratinocytes, which synthesise the protein keratin. Protein bridges called desmosomes connect the keratinocytes, which are in a constant state of transition from the deeper layers to the superficial (*see* Figure 1.2). The four separate layers of the epidermis are formed by the differing stages of keratin maturation. The epidermis varies in thickness from 0.05 mm on the eyelids to 0.8–1.5 mm on the soles of the feet and palms of the hand. Moving from the lower layers upwards to the surface, the four layers of the epidermis are:

- stratum basale (basal or germinativum cell layer)
- stratum spinosum (spinous or prickle cell layer)
- stratum granulosum (granular cell layer)
- stratum corneum (horny layer).

In addition, the stratum lucidum is a thin layer of translucent cells seen in thick epidermis. It represents a transition from the stratum granulosum and stratum corneum and is not usually seen in thin epidermis. Together, the stratum spinosum and stratum granulosum are sometimes referred to as the Malpighian layer.

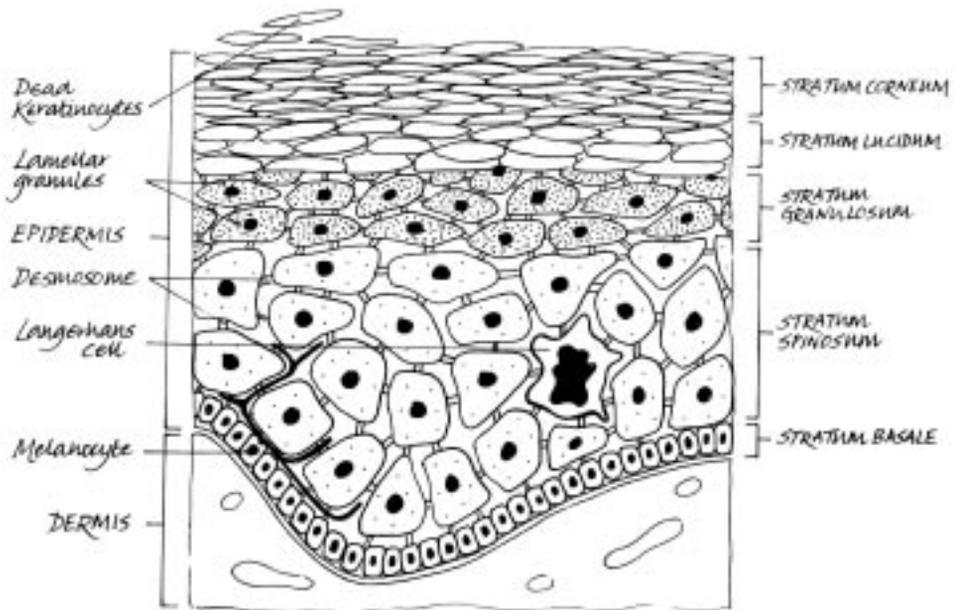


Figure 1.2 Layers of the epidermis.

Stratum basale

The innermost layer of the epidermis which lies adjacent to the dermis comprises mainly dividing and non-dividing keratinocytes, which are attached to the basement membrane by hemidesmosomes. As keratinocytes divide and differentiate, they move from this deeper layer to the surface. Making up a small proportion of the basal cell population is the pigment (melanin) producing melanocytes. These cells are characterised by dendritic processes, which stretch between relatively large numbers of neighbouring keratinocytes. Melanin accumulates in melanosomes that are transferred to the adjacent keratinocytes where they remain as granules. Melanin pigment provides protection against ultraviolet (UV) radiation; chronic exposure to light increases the ratio of melanocytes to keratinocytes, so more are found in facial skin compared to the lower back and a greater number on the outer arm compared to the inner arm. The number of melanocytes is the same in equivalent body sites in white and black skin but the distribution and rate of production of melanin is different. Intrinsic ageing diminishes the melanocyte population.

Merkel cells are also found in the basal layer with large numbers in touch-sensitive sites such as the fingertips and lips. They are closely associated with cutaneous nerves and seem to be involved in light touch sensation.

Stratum spinosum

As basal cells reproduce and mature, they move towards the outer layer of skin, initially forming the stratum spinosum. Intercellular bridges, the desmosomes, which appear as 'prickles' at a microscopic level, connect the cells. Langerhans cells are dendritic, immunologically active cells derived from the bone marrow,

and are found on all epidermal surfaces but are mainly located in the middle of this layer. They play a significant role in immune reactions of the skin, acting as antigen-presenting cells.

Stratum granulosum

Continuing their transition to the surface the cells continue to flatten, lose their nuclei and their cytoplasm appears granular at this level.

Stratum corneum

The final outcome of keratinocyte maturation is found in the stratum corneum, which is made up of layers of hexagonal-shaped, non-viable cornified cells known as corneocytes. In most areas of the skin, there are 10–30 layers of stacked corneocytes with the palms and soles having the most. Each corneocyte is surrounded by a protein envelope and is filled with water-retaining keratin proteins. The cellular shape and orientation of the keratin proteins add strength to the stratum corneum. Surrounding the cells in the extracellular space are stacked layers of lipid bilayers (*see* Figure 1.3).

The resulting structure provides the natural physical and water-retaining barrier of the skin. The corneocyte layer can absorb three times its weight in water but if its water content drops below 10% it no longer remains pliable and cracks. The movement of epidermal cells to this layer usually takes about 28 days and is known as the epidermal transit time.

Dermoepidermal junction/basement membrane

This is a complex structure composed of two layers. Abnormalities here result in the expression of rare skin diseases such as bullous pemphigoid and epidermolysis bullosa. The structure is highly irregular, with dermal papillae from the papillary dermis projecting perpendicular to the skin surface. It is via diffusion at this junction that the epidermis obtains nutrients and disposes of waste. The dermoepidermal junction flattens during ageing which accounts in part for some of the visual signs of ageing.

Dermis

The dermis varies in thickness, ranging from 0.6 mm on the eyelids to 3 mm on the back, palms and soles. It is found below the epidermis and is composed of a tough, supportive cell matrix. Two layers comprise the dermis:

- a thin papillary layer
- a thicker reticular layer.

The papillary dermis lies below and connects with the epidermis. It contains thin loosely arranged collagen fibres. Thicker bundles of collagen run parallel to the skin surface in the deeper reticular layer, which extends from the base of the papillary layer to the subcutis tissue. The dermis is made up of fibroblasts, which produce collagen, elastin and structural proteoglycans, together with immunocompetent mast cells and macrophages. Collagen fibres make up 70% of the dermis, giving it strength and toughness. Elastin maintains normal elasticity and flexibility while proteoglycans provide viscosity and hydration. Embedded

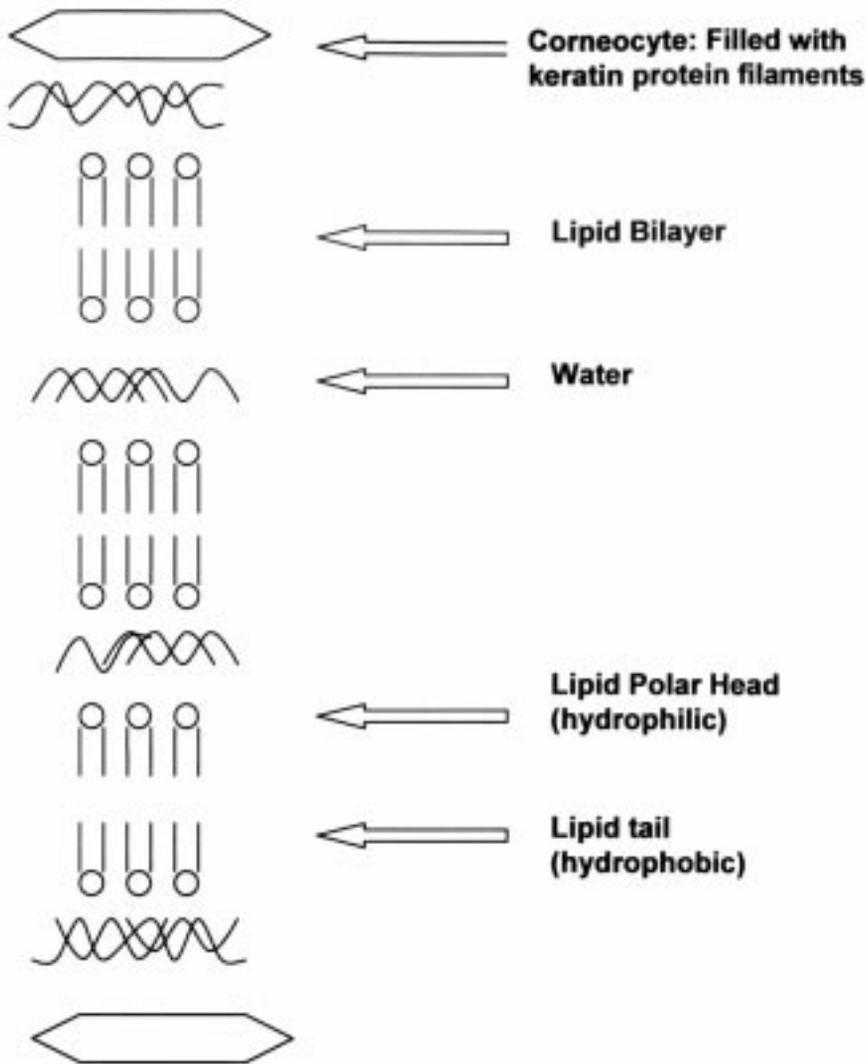


Figure 1.3 Corneocyte lipid bilayers.

within the fibrous tissue of the dermis are the dermal vasculature, lymphatics, nervous cells and fibres, sweat glands, hair roots and small quantities of striated muscle.

Subcutis

This is made up of loose connective tissue and fat, which can be up to 3 cm thick on the abdomen.

Blood and lymphatic vessels

The dermis receives a rich blood supply. A superficial artery plexus is formed at the papillary and reticular dermal boundary by branches of the subcutis artery.

Branches from this plexus form capillary loops in the papillae of the dermis, each with a single loop of capillary vessels, one arterial and one venous. The veins drain into mid-dermal and subcutaneous venous networks. Dilatation or constriction of these capillary loops plays a direct role in thermoregulation of the skin. Lymphatic drainage of the skin occurs through abundant lymphatic meshes that originate in the papillae and feed into larger lymphatic vessels that drain into regional lymph nodes.

Nerve supply

The skin has a rich innervation with the hands, face and genitalia having the highest density of nerves. All cutaneous nerves have their cell bodies in the dorsal root ganglia and both myelinated and non-myelinated fibres are found. Free sensory nerve endings lie in the dermis where they detect pain, itch and temperature. Specialised corpuscular receptors also lie in the dermis allowing sensations of touch to be received by Meissner's corpuscles and pressure and vibration by Pacinian corpuscles. The autonomic nervous system supplies the motor innervation of the skin: adrenergic fibres innervate blood vessels, hair erector muscles and apocrine glands while cholinergic fibres innervate eccrine sweat glands. The endocrine system regulates the sebaceous glands, which are not innervated by autonomic fibres.

Derivative structures of the skin

Hair

Hair can be found in varying densities of growth over the entire surface of the body, exceptions being on the palms, soles and glans penis. Follicles are most dense on the scalp and face and are derived from the epidermis and the dermis. Each hair follicle is lined by germinative cells, which produce keratin and melanocytes, which synthesise pigment. The hair shaft consists of an outer cuticle, a cortex of keratinocytes and an inner medulla. The root sheath, which surrounds the hair bulb, is composed of an outer and inner layer. An erector pili muscle is associated with the hair shaft and contracts with cold, fear and emotion to pull the hair erect, giving the skin 'goose bumps'.

Nails

Nails consist of a dense plate of hardened keratin between 0.3 and 0.5 mm thick. Fingernails function to protect the tip of the fingers and to aid grasping. The nail is made up of a nail bed, nail matrix and a nail plate. The nail matrix is composed of dividing keratinocytes, which mature and keratinise into the nail plate. Underneath the nail plate lies the nail bed. The nail plate appears pink due to adjacent dermal capillaries and the white lunula at the base of the plate is the distal, visible part of the matrix. The thickened epidermis which underlies the free margin of the nail at the proximal end is called the hyponychium. Fingernails grow at 0.1 mm per day; the toenails more slowly (*see* Figure 1.4).

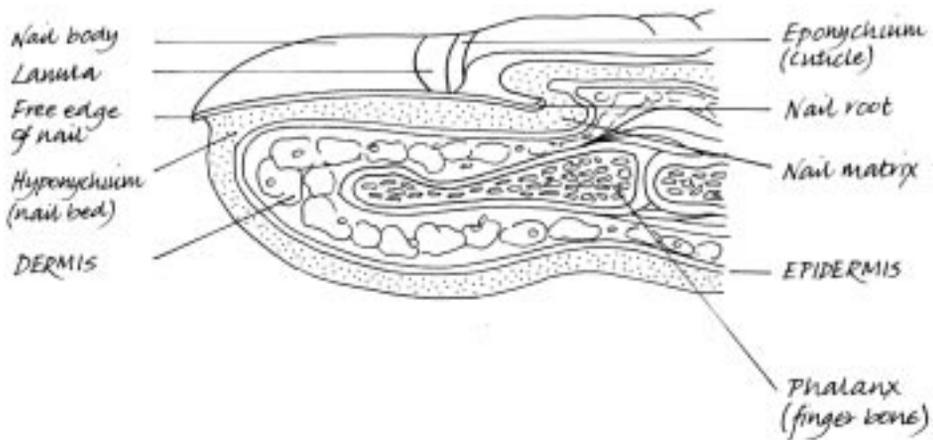


Figure 1.4 Nail structure.

Sebaceous glands

These glands are derived from epidermal cells and are closely associated with hair follicles especially those of the scalp, face, chest and back; they are not found in hairless areas. They are small in children, enlarging and becoming active at puberty, being sensitive to androgens. They produce an oily sebum by holocrine secretion in which the cells break down and release their lipid cytoplasm. The full function of sebum is unknown at present but it does play a role in the following:¹

- maintaining the epidermal permeability barrier, structure and differentiation
- skin-specific hormonal signalling
- transporting antioxidants to the skin surface
- protection from UV radiation.

Sweat glands

There are thought to be over 2.5 million on the skin surface and they are present over the majority of the body. They are located within the dermis and are composed of coiled tubes, which secrete a watery substance. They are classified into two different types: eccrine and apocrine.

- Eccrine glands are found all over the skin especially on the palms, soles, axillae and forehead. They are under psychological and thermal control. Sympathetic (cholinergic) nerve fibres innervate eccrine glands. The watery fluid they secrete contains chloride, lactic acid, fatty acids, urea, glycoproteins and mucopolysaccharides.
- Apocrine glands are larger, the ducts of which empty out into the hair follicles. They are present in the axillae, anogenital region and areolae and are under thermal control. They become active at puberty, producing an odourless protein-rich secretion which when acted upon by skin bacteria gives out a characteristic odour. These glands are under the control of sympathetic (adrenergic) nerve fibres.

Table 1.2 Functions of the skin.

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- Provides a protective barrier against mechanical, thermal and physical injury and noxious agents.
 - Prevents loss of moisture.
 - Reduces the harmful effects of UV radiation.
 - Acts as a sensory organ.
 - Helps regulate temperature control.
 - Plays a role in immunological surveillance.
 - Synthesises vitamin D₃ (cholecalciferol).
 - Has cosmetic, social and sexual associations.
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Skin functions

The skin is a complex metabolically active organ, which performs important physiological functions that are summarised in Table 1.2.

Barrier function and skin desquamation

As the viable cells move towards the stratum corneum they begin to clump proteins into granules in the granular layer (*see* Figure 1.5). The granules are filled with the protein fillagrin, which becomes complexed with keratin to prevent the breakdown of fillagrin by proteolytic enzymes. As the degenerating cells move towards the outer layer, enzymes break down the keratin-fillagrin complex. Fillagrin forms on the outside of the corneocytes while the water-retaining keratin remains inside.

When the moisture content of the skin reduces, fillagrin is further broken down into free amino acids by specific proteolytic enzymes in the stratum corneum. The breakdown of fillagrin only occurs when the skin is dry in order to control the osmotic pressure and the amount of water it holds: in healthy skin the water content of the stratum corneum is normally around 30%. The free amino acids, along with other components such as lactic acid, urea and salts, are known as ‘natural moisturising factors’ (NMF) and are responsible for keeping the skin moist and pliable due to their ability to attract and hold water.

Lipids

The major factor in the maintenance of a moist, pliable skin barrier is the presence of intercellular lipids. These form stacked bilayers that surround the corneocytes and incorporate water into the stratum corneum. The lipids are derived from lamellar granules, which are released into extracellular spaces of degrading cells in the granular layer; the membranes of these cells also release lipids. Lipids include cholesterol, free fatty acids and sphingolipids.

Ceramide, a type of sphingolipid, is mainly responsible for generating the stacked lipid structures that trap water molecules in their hydrophilic region. These stacked lipids surround the corneocytes and provide an impermeable barrier by preventing the movement of water and NMF out of the surface layers of the skin. After the age of 40 there is a sharp decline in skin lipids thus increasing our susceptibility to dry skin conditions.

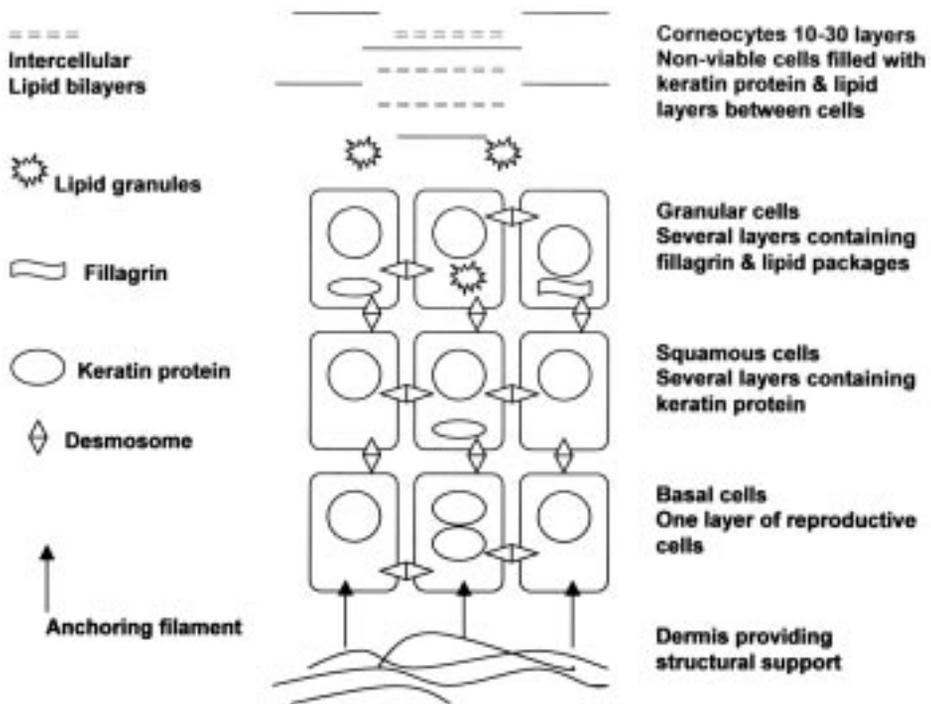


Figure 1.5 Barrier function of the epidermis.

Shedding (desquamation) of skin cells

Shedding the cells of the stratum corneum is an important factor in maintaining skin integrity and smoothness. Desquamation involves the enzymatic process of dissolving the protein bridges, the desmosomes, between the corneocytes, and the eventual shedding of these cells (*see* Figure 1.2). The proteolytic enzymes responsible for desquamation are located intracellularly and function in the presence of a well-hydrated stratum corneum. In the absence of water the cells do not desquamate normally and the skin becomes roughened, dry, thickened and scaly. In normal healthy skin there is a balance in the production and shedding of corneocytes. In diseases such as psoriasis, which involve increased corneocyte production, and where decreases in shedding occur, the result is dry, rough skin as the cells accumulate on the skin.

Remaining functions

UV protection

Melanocytes, located in the basal layer, and melanin have important roles in the skin's barrier function by preventing damage by UV radiation. In the inner layers of the epidermis, melanin granules form a protective shield over the nuclei of the keratinocytes; in the outer layers, they are more evenly distributed. Melanin

Table 1.3 Immune components of the skin.

<i>Defence type</i>	<i>Component</i>	<i>Immune action</i>
Structural	Skin	Impenetrable physical barrier to most external organisms.
	Blood and lymphatic vessels	Provision of transport network for cellular defence.
Cellular	Langerhans cells	Antigen presentation.
	T lymphocytes	Facilitate immune reactions. Self-regulating through the action of T suppressor cells.
	Mast cells	Facilitate inflammatory skin reactions.
	Keratinocytes	Secrete inflammatory cytokines; have ability to express surface immune reactive molecules.
Systemic	Cytokines and eicosanoids	Cytokines: cell mediation chemicals produced by components of the cellular defence system.
		Eicosanoids: non-specific inflammatory mediators produced by mast cells, macrophages and keratinocytes.
	Adhesion molecules	Increase the number of cellular defence facilitators in an area by binding to T cells.
	Complement cascade	Activation of this initiates a host of destructive mechanisms, including opsonisation, lysis, chemotaxis and mast cell degranulation.
Immunogenetic	Major histocompatibility complex (MHC)	Enables immunological recognition of antigens.

absorbs UV radiation, thus protecting the cell's nuclei from DNA (deoxyribonucleic acid) damage. UV radiation induces keratinocyte proliferation, leading to thickening of the epidermis.

Thermoregulation

The skin plays an important role in maintaining a constant body temperature through changes in blood flow in the cutaneous vascular system and evaporation of sweat from the surface.

Immunological surveillance

As well acting as a physical barrier, skin also plays an important immunological role. It normally contains all the elements of cellular immunity, with the exception of B cells.² Immune components of the skin are given in Table 1.3.

References

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- 2 Gawkrödger DJ. *Dermatology, An Illustrated Colour Text*. 3rd ed. Edinburgh: Churchill Livingstone; 2002.