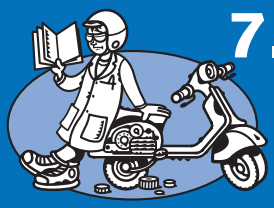


7. Skin

Organization of the skin

The skin is the largest organ in the body, making up 16% of the body's weight, and has a surface area of 1.8 m^2. It has an essential role in both homeostasis and protection of the body from external influences. The skin is composed of three layers:

- The epidermis—stratified squamous epithelium.
- The dermis—supportive connective tissue matrix.
- The subcutaneous layer—loose connective tissue and fat.

The epidermis (ectoderm) develops by the first month of gestation. The dermis (mesoderm) develops at a later stage, usually at around 11 weeks. By 17 weeks' gestation, the skin ridges which cause fingerprints have developed.

The composition of the three separate layers of the skin (see Fig. 1.2) is as follows:

Epidermis

The epidermis is generally around 0.1 mm thick, although it reaches depths of between 0.8 and 1.4mm on the palms of the hand and soles of the feet. The epidermis itself comprises four separate layers: the stratum corneum (horny layer), stratum granulosum (granular cell layer), stratum spinosum (prickle cell layer) and stratum basale (basal cell layer). These four layers are formed by the differing stages of maturation of keratin (Fig. 7.1), a protein produced by keratinocytes, the main cell of the epidermis.

Stratum basale

This layer is composed of keratinocytes (90%) which may be either dividing or non-dividing, melanocytes (5–10%) and infrequent Merkel cells. Keratinocytes are anchored to the basement membrane by hemidesmosomes; condensations of tonofibrils, which in turn are formed by synthesized keratin.

Melanocytes synthesize melanins, which absorb the energy of ultraviolet radiation and act as free radical scavengers. The cells originate from the neural crest and are most numerous on sites exposed to the sun.

Merkel cells appear to have a role in sensation and are found close to the terminal filament of cutaneous nerves.

Stratum spinosum

Here, the keratinocytes change from columnar to polyhedral. Desmosomes, again made of tonofibrils, connect the cells and help to distribute stress equally throughout the epidermis, as well as maintaining a distance of 20 nm between adjacent cells. When seen under a light miscroscope, these desmosomes form the 'prickles' that give the layer its name. Langerhans cells are also found in this layer: these are dendritic cells derived from the bone marrow and play an important role in the cellular immune system.

Stratum granulosum

As the keratinocytes mature, the cells flatten and lose their nuclei. The cytoplasm gains keratohyalin granules and membrane-coating granules which burst their contents into the intercellular spaces.

Stratum corneum

At the end of the maturation process, the keratocytes become overlapping, cornified cells which lack a nucleus—corneocytes. The cytoplasm is replaced by a matrix composed of keratin tonofibrils and keratohyalin granules, glued together by the contents of the membrane-coating granules. This horny layer forms the outermost layer of the skin. The keratin provides flexibility and strength, and the corneocyte layer can absorb three times its weight in water. If the layer becomes dehydrated, however, with the water content falling to below 10%, it is no longer pliable.

Dermis

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

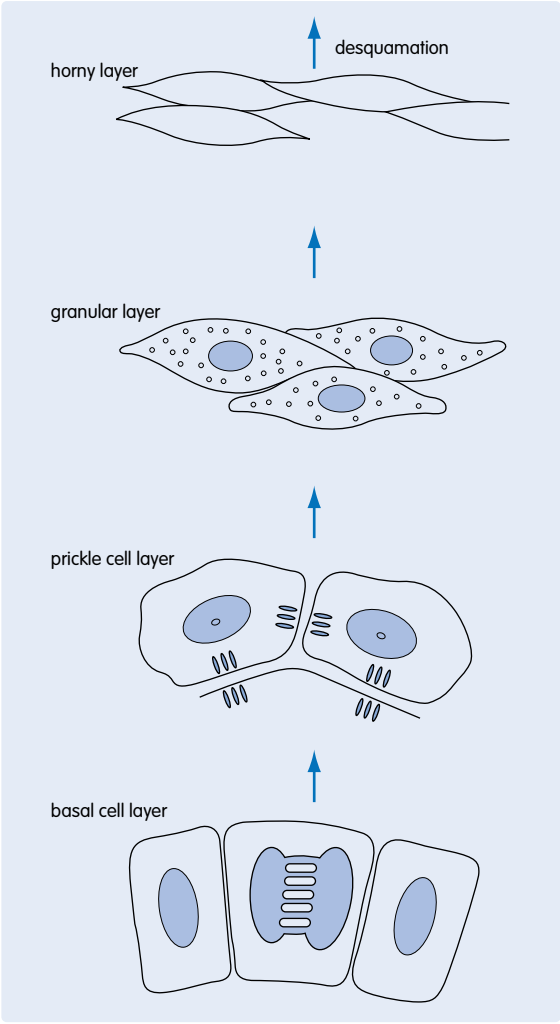


Fig. 7.1 The differing stages of keratinocyte maturation. (Adapted with permission from *Dermatology: an Illustrated Colour Text,* 2nd edn, by D.J. Gawkrodger, Churchill Livingstone, 1997.)

containing fibroblasts, dermal dendrocytes, mast cells, lymphocytes and macrophages.

Subcutaneous layer

Situated directly under the dermis, the subcutaneous layer is made up of loose connective tissue and fat. Most fat cells within the body are housed within this layer and these subcutaneous fat deposits are collectively referred to as adipose tissue.

Skin physiology

Keratinocytes, the basic building blocks of the skin, take around 14 days to mature fully as they travel from the basal layer to the stratum corneum; the dividing cells in the stratum basale replicate every 200–400 h. The dead corneocytes are then shed from the horny layer of the skin in a process called desquamation within a further 14 days. This cell turnover rate of 28 days is dramatically shortened in keratinization disorders such as psoriasis.

Keratinocytes are also involved in the pathology of the blistering skin disorders. Circulating IgG autoantibodies, which are detectable in the serum by indirect immunofluorescence in 90% of affected patients, bind to components within the intercellular epidermal substance, and induce proteolytic enzyme release from the adjacent keratinocytes. These enzymes cause the loss of adhesion between cells and result in splits within the epidermis.

Derivative structures of the skin

Hair

In our now relatively bald state, humans no longer rely on hair to play a vital role in the conservation of heat. Although scalp hair still protects against the harmful effects of ultraviolet radiation and minor injuries, the main role of hair today is as an organ of sexual attraction.

Hair can be found in varying densities of growth over the entire surface of the body: exceptions are the vulval introitus, glans penis and the glabrous skin of the palms and soles of the feet. Follicles are most dense on the scalp and face. Follicles are derived from the epidermis (cells of the cortex matrix and the hair shaft) and the dermis (papilla).

Structure of hair

Each hair follicle is lined by germinative cells, which produce keratin and the other components of the hair shaft. The hair shaft itself consists of an outer cuticle, a cortex of keratinocytes and an inner medulla (Fig. 7.2). The root sheath that surrounds the hair bulb is composed of an inner and outer layer. An arrector pili muscle is associated with the hair shaft, which is the structure behind 'goose pimples'—it contracts with cold, fear and emotion to pull the hair erect.

Classification of hair types

There are three types of hair:

- Lanugo hairs—these are formed at 20 weeks' gestation and are usually shed before the fetus is

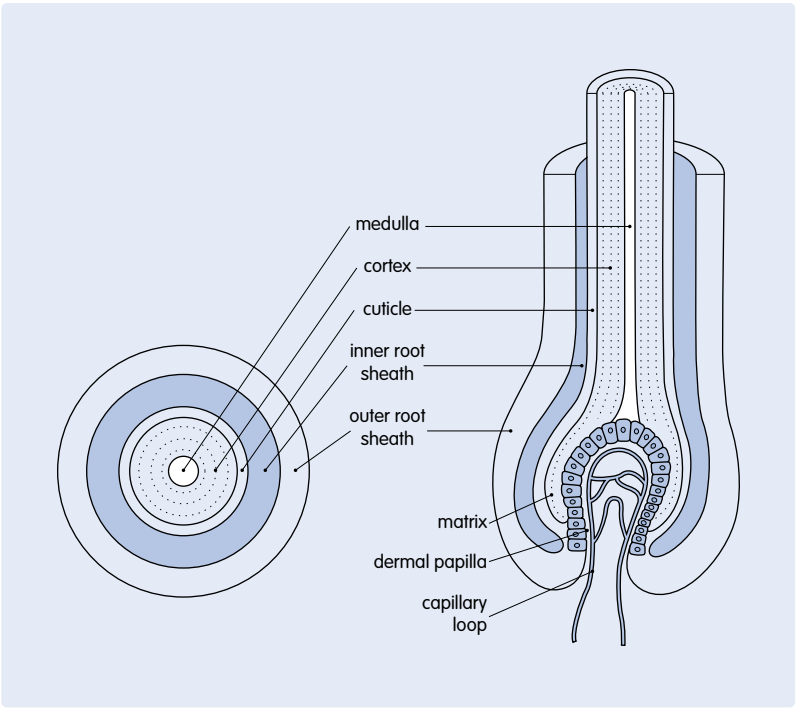


Fig 7.2 Structure of hair follicle. (Adapted with permission from *Dermatology: an Illustrated Colour Text,* 2nd edn, by D.J. Gawkrodger, Churchill Livingstone, 1997.)

born. They can be seen in premature babies, and are fine and long.
- Vellus hairs—this is the most common hair type; vellus hairs cover most of the surface of the body. They are short, fine and light in colour.
- Terminal hairs—there are around 100 000 terminal hairs on the scalp, and they are also found in the eyebrows, eyelashes, and the pubic and axilla regions. They are also the hairs which compose the beard.

Stages of hair development

Hair growth is cyclical, with the normal rate being 0.4 mm per day. There are three different stages of hair development (Fig. 7.3).

Anagen: This is the growth phase; 80–90% of scalp hair is in this phase at any one time. The length of this phase depends on the hair site: it lasts between 3 and 7 years for scalp hair, but only for 4 months for eyebrow hair.

Catagen: The resting phase, which normally lasts for 3–4 weeks. During this stage, the synthesis of the hair follicle stops. 10–20% of scalp hair is in catagen at any one time, with 50–100 follicles entering the phase every day.

Telogen: The shedding phase; less than 1% of scalp hairs are in telogen at any one time. Hairs undergoing telogen are distinguished by a short club root.

Hair growth is not usually in phase, but if synchronized during the resting stage, will be uniformly shed 3 months later (telogen effluvium). This synchronization results from childbirth, high fever, surgery, drugs or other stress. Anagen effluvium (abrupt cessation of hair growth) occurs after ingestion of drugs such as cytotoxins, heparin and warfarin, carbimazole, colchicine and vitamin A. It may also follow ingestion of drugs such as thallium.

Nails

Consisting of a dense plate of hardened keratin between 0.3–0.5mm thick, the nail is a leftover of the mammalian claw. Its function is to protect the tip of the finger and facilitate grasping.

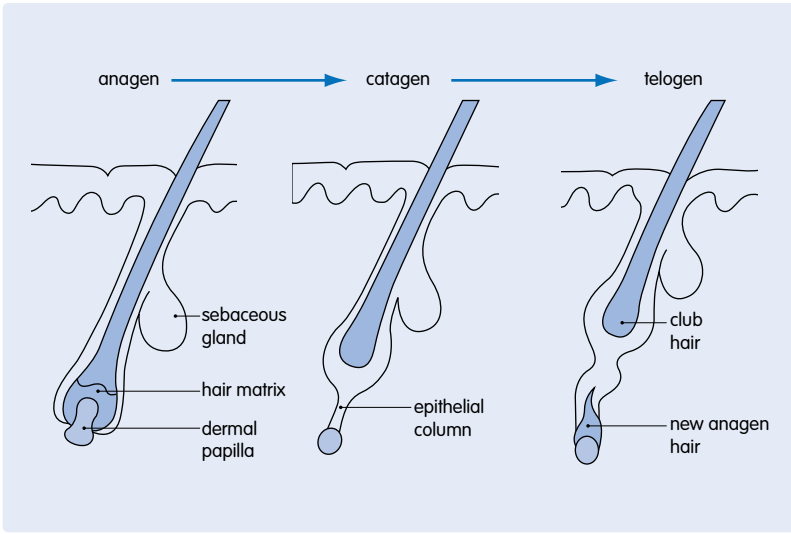


Fig. 7.3 Stages of hair development. (Adapted with permission from *Dermatology: an Illustrated Colour Text,* 2nd edn, by D.J. Gawkrodger, Churchill Livingstone, 1997.)

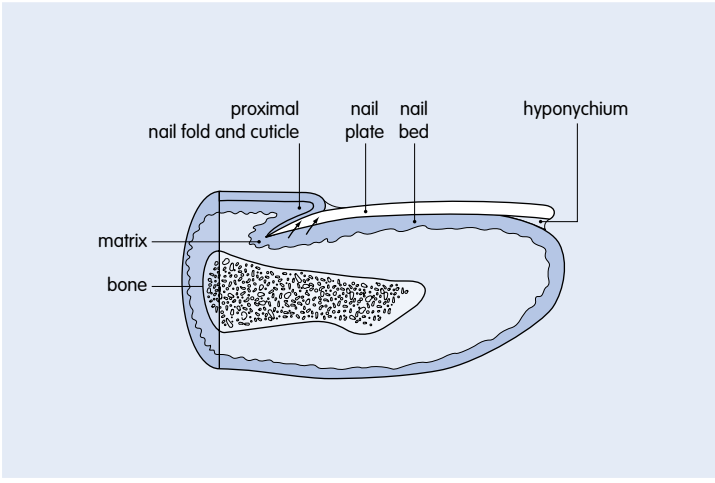


Fig. 7.4 Structure of the nail. (Adapted with permission from *Dermatology: an Illustrated Colour Text,* 2nd edn, by D.J. Gawkrodger, Churchill Livingstone, 1997.)

Structure of the nail

The nail is composed of a nail bed, nail matrix and a nail plate (Fig. 7.4) The nail matrix is composed of dividing keratinocytes which mature and keratinize into the nail plate. Underneath the nail plate lies the nail bed; this structure produces a small amount of keratin. The pink appearance of the nail plate is caused by the dermal capillaries which underlie the nail, and the white lunula at the base of the nail plate is the distal, visible part of the nail matrix. The thickened epidermis which underlies the free margin of the nail at the proximal end is called the hyponychium.

Nail growth

The fingernails grow at 0.1 mm per day; the toenails grow more slowly. Any pathological process which disturbs nail growth leaves visible clinical signs in the nail. Systemic illness may lead to transverse grooves in the nail called Beau's lines, which indicate an interruption to the growth of the nail matrix. Cytotoxic drugs cause black transverse bands in the nail, heavy metal poisoning causes white transverse bands, and trauma to the nail matrix can cause white spots within the nail or splinter haemorrhages.

Clubbing of the nail is caused by many disorders (Fig. 7.5); the nail matrix increases in vascularity and

Fig. 7.5 Some causes of finger clubbing. (Adapted with permission from *Principles of Clinical Medicine*, 2nd edn, P.J. Kumar and M.L. Clarke, Bailliere Tindall, 1990.)

Causes of finger clubbing	
respiratory	lung cancer, cystic fibrosis, interstitial lung disease, idiopathic pulmonary fibrosis, sarcoidosis, lipoid pneumonia, empyema, pleural mesothelioma, pulmonary artery sarcoma, cryptogenic fibrosing alveolitis, pulmonary metastases, bronchiectasis and lung abscess
cardiac	cyanotic congenital heart disease, other causes of right-to-left shunting, and bacterial endocarditis
gastrointestinal	ulcerative colitis, Crohn's disease, primary biliary cirrhosis, cirrhosis of the liver, achalasia and peptic ulceration of the oesophagus
malignancy	thyroid cancer, thymus cancer, Hodgkin's disease and disseminated chronic myeloid leukaemia
miscellaneous	acromegaly, thyroid acropachy and pregnancy

feels fluctuant. In addition, the normal angle between the base of the nail and the nail fold is lost, the nail curvature increases in all directions and the end of the finger may expand.

Sebaceous glands

Derived from epidermal cells, sebaceous glands are closely associated with hair follicles and produce an oily sebum (Fig. 7.6). This sebum flows into the hair follicles, and from there travels to the surface of the skin, where it oils both the hair and the keratinized surface of the skin to help waterproof and protect them from dehydrating and cracking. The secretions are in general highly toxic to bacteria.

The sebaceous glands are sensitive to androgens and become active at puberty. They are most numerous over the scalp, face, chest and back, and are not present on hairless skin.

Location of sebaceous and sweat glands	
Type of gland	**Location**
sebaceous	associated with hair follicles; found on scalp, face, chest and back. Are not found on skin which is hairless
eccrine sweat	widely distributed, but most numerous on palms, soles, axillae and forehead
apocrine sweat	open into hair follicles; profuse around axillae, perineum and areolae

Fig. 7.6 Location of sebaceous and sweat glands. (Adapted with permission from *Principles of Clinical Medicine*, 3rd edn, P.J. Kumar and M.L. Clarke.)

Sweat glands

These glands are located within the dermis, and are present over the majority of the body—there are an estimated 2.5 million on the skin surface. The glands are composed of coiled tubes which secrete a watery substance, and are classified into two different types: eccrine and apocrine.

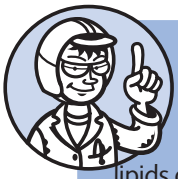
Eccrine glands

These sweat glands are found all over the skin, especially in the palms, soles, axillae and forehead, but are not present in mucous membranes. Eccrine glands are under psychological and thermal control and are innervated by sympathetic (cholinergic) nerve fibres. The watery fluid which the glands secrete contains chloride, lactic acid, fatty acids, urea, glycoproteins and mucopolysaccharides.

Apocrine glands

These are large sweat glands, the ducts of which empty out into the hair follicles. They are present in the axillae, anogenital region and areolae. They become active at puberty and produce an odourless, protein-rich secretion which gives out a characteristic odour when acted upon by skin bacteria. The apocrine glands are a phylogenetic remnant of the mammalian sexual scent gland. Wax in the ears is produced by a modified version of the same gland. Apocrine glands are also present on the

eyelids. These glands are under the control of the sympathetic (adrenergic) nerve fibres.



The slightly acidic pH of the skin (between 6 and 7) is maintained by sebum, sweat and the intercellular lipids of the stratum corneum. This lower pH level discourages microbial growth on the skin's surface.

Nerves in the skin

Functions of the skin include perception of touch and temperature, and so the organ is richly innervated. The densest concentrations of nerve endings are found in areas where sensation is of paramount importance: hands, face and genitalia. There are different types of sensation detectors found in the skin (Fig. 7.7). Free sensory nerve endings are found within the dermis and epidermis, and detect pain, itch and temperature. They contain neuropeptide transmitters such as substance P. Corpuscular receptors which are specialized for certain types of sensation are also found in the dermis: these are Pacinian corpuscles, which detect pressure and vibration, and Meissner's corpuscles, which are sensitive to touch, and are found in the dermal papillae of the feet and hands. Innervation to hair-bearing and non-hair-bearing skin is also different.

Merkel cells are derived embryologically from the neural crest and play a role in sensation by acting as mechanoreceptors. They also contain neurotransmitters.

The sensory nerve fibres that innervate the skin are both myelinated and unmyelinated, and their cell bodies are contained within the dorsal root ganglion.

Vessels in the skin

The skin has 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 singular arterial and venous vessel: arteriovenous anastomoses. The veins drain into mid-dermal and subcutaneous venous plexus.

Dilatation or contraction of the arteriovenous anastomoses plays a direct role in thermoregulation of the skin. The changes in blood flow through the capillary loops help to control direct heat loss through the surface of the skin via convection and radiation (Fig. 7.8). The arteriovenous anastomoses are under the control of the sympathetic nervous system.

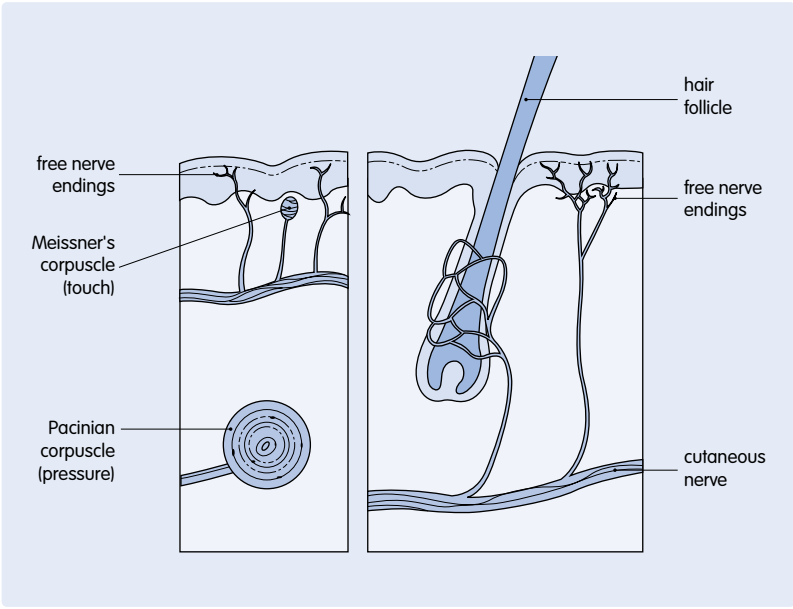


Fig. 7.7 The different types of nerve detectors within the skin. (Adapted with permission from *Dermatology: an Illustrated Colour Text,* 2nd edn, by D.J. Gawkrodger, Churchill Livingstone, 1997.)

Lymphatic drainage of the skin occurs through lymphatic meshes that originate in the papillae and go on to become larger lymphatic vessels which subsequently drain into regional lymph nodes.

Functions of the skin

Skin performs several functions. These include:

- Providing a mechanical barrier to antigens and bacteria, thus forming a protective cover for the body.
- Contributing to thermoregulation.
- Synthesizing vitamin D within the epidermis upon exposure to sunlight.
- Providing protection against excessive water absorption or loss.
- Providing protection, via skin pigmentation, against ultraviolet light.
- Distinguishing between pain, touch and temperature sensations.

Keratinocyte function

The main function of keratinocytes is to produce the high molecular weight polypeptide chains called keratin. The stages of keratinocyte maturation have been described. Each different stage of keratinocyte maturation produces different molecular weight keratins (e.g. 50, 55, 57 and 67 kDa), hence different keratins are found in each separate layer of the epidermis. The hardiness of keratin is caused by the strong covalent bonds which link the cysteine molecules, and the keratin found in the epidermis contains less cysteine and more glycine molecules than the stronger keratin which makes up hair.

Melanocyte function

Melanocytes are found within the basal layer of the epidermis and produce melanin, a brown pigment which protects against harmful ultraviolet rays from the sun—the melanin forms a protective cap over the nuclei of keratinocytes in the epidermis. The hereditary determination of number and size of melanosomes, the membrane-bound storage organelles, is responsible for the varying shades of the skin across different races, not the number of melanocytes. In addition, the amount of melanin in the skin can be temporarily increased in response to exposure to the sun's rays, as pre-formed melanin is photo-oxidized, stimulating melanocytes to produce more melanin, resulting in a 'tan'.

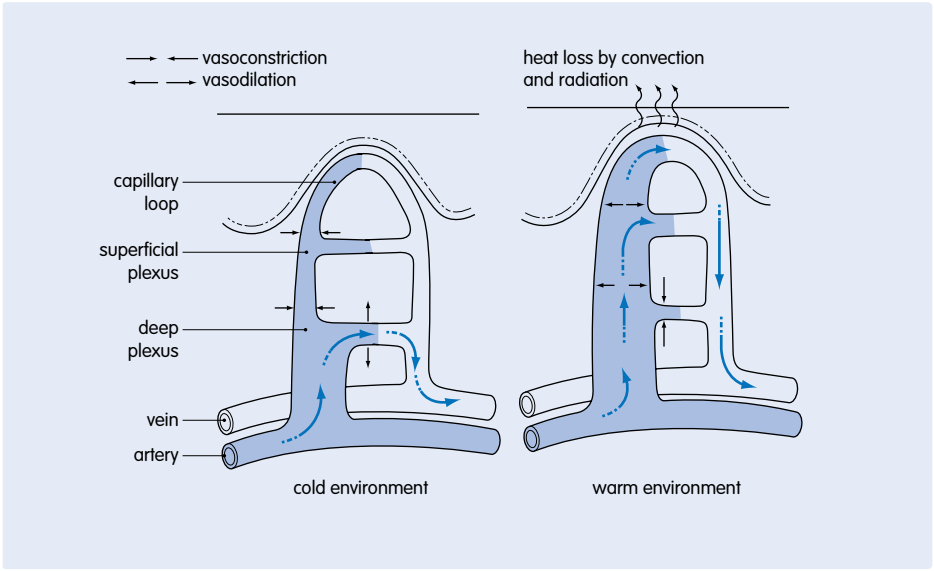


Fig. 7.8 Regulation of temperature by arteriovenous anastomoses. (Adapted with permission from *Dermatology: an Illustrated Colour Text,* 2nd edn, by D.J. Gawkrodger, Churchill Livingstone, 1997.)

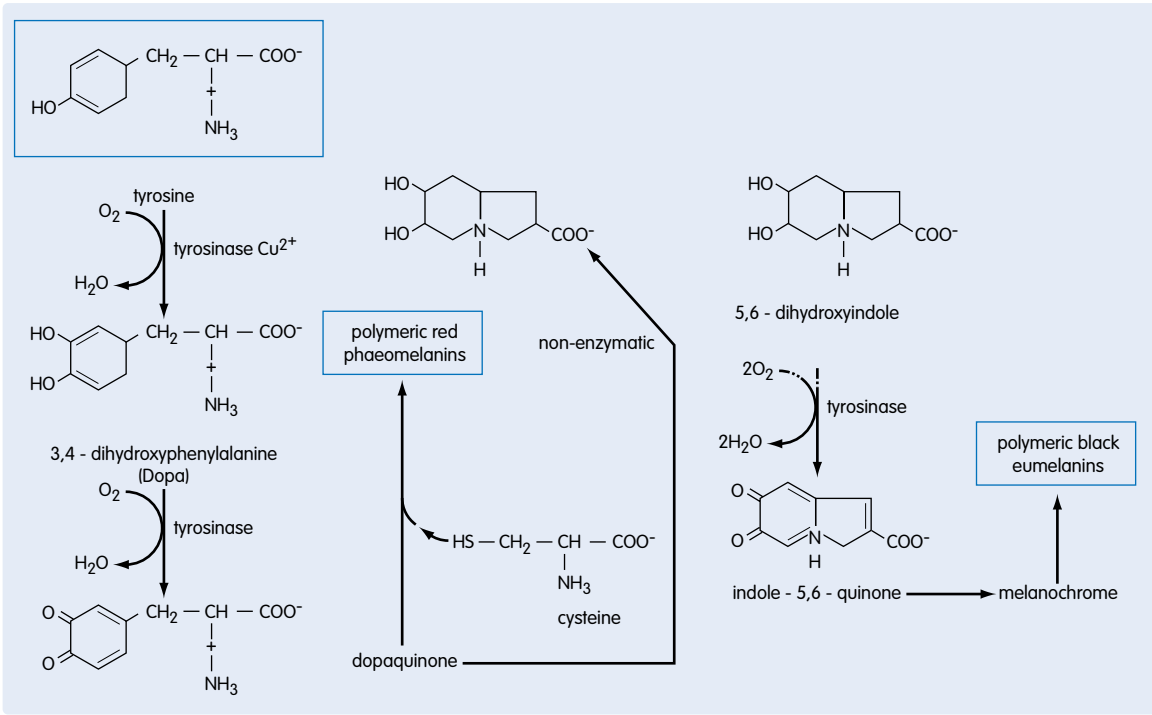


Fig. 7.9 Biosynthesis of melanin from tyrosine. (Adapted with permission from *Dermatology: an Illustrated Colour Text,* 2nd edn, by D.J. Gawkrodger, Churchill Livingstone, 1997.)

As well as absorbing the energy of ultraviolet radiation, melanin also acts as a free radical scavenger and as an energy sink. Melanin itself is produced from tyrosine (Fig. 7.9), and comes in two separate forms, eumelanin and phaeomelanin. Eumelanin is the more common form and pigments the skin a brown–black colour. Phaeomelanin produces a yellow–red coloration, the pigment produced in red-haired people. Most melanins are a mixture of the two different forms.

Fibroblast function

Fibroblasts produce and secrete the components of the extracellular matrix, the intricate meshwork of fibrous proteins embedded in a gel-like substance. The extracellular matrix holds the cells together, so the majority are not in direct physical contact with each other. Nutrients, waste products and other water-soluble materials diffuse through the gelous matrix between the blood vessels and cell tissues.

The main components of the extracellular matrix produced by fibroblasts are collagen, elastin and structural proteoglycans such as glycosaminoglycans (GAGs). Their functions are discussed in Chapter 1.

Types of collagen	Location
type I	reticular dermis
type III	papillary dermis
types IV and VII	basement membrane structures
type VIII	endothelial cells

Fig. 7.10 Types of collagen found in the skin.

Collagen is the major structural protein of the dermis, and makes up 70–80% of its dry weight. Of the 15 different types of collagen, five are found in the skin (Fig. 7.10).

The cable-like structure of collagen fibres provide tensile strength; the collagen is resistant to longitudinal stress. In disorders where there is pathology of the collagen, such as scurvy (a disease caused by vitamin C deficiency), the tissues which rely on collagen for strength become very fragile. In skin the blood vessels are easily damaged, and bleeding is very noticeable in the mucous membranes, especially in the gums.

Elastin is a rubber band-like protein fibre which facilitates the stretching and recoiling of structures. It plays an important role in the inflation and deflation of the lungs: in the skin, it maintains normal elasticity and flexibility.

The structural proteoglycans which make up the ground substance of the skin are mainly GAGs; these proteins provide the viscosity and hydration of the skin.

Thermoregulation

Thermoregulation is dependent on metabolic and physical factors. The evaporation of sweat from the skin's surface aids cooling of the skin, and the variations in the arteriovenous anastomoses also play an important role in temperature regulation (p. 135). Both of these mechanisms help to maintain the body's core temperature of 37°C in differing climates and during physical exertion.

Immune functions of the skin

The skin's structures, cells, functional systems and immunogenetics all play a role in the cutaneous immunity system (Fig 7.11).

Epidermal barrier

This physical structure provides an impenetrable barrier to most micro-organisms that come into contact with it. In addition to this external structure, the vessels of the dermis are important routes through which immune cells can travel to where they are needed.

Langerhans cells

Situated in the epidermis, these dendritic, bone marrow-derived cells are the first line of defence against micro-organisms which penetrate the epidermal barrier. They can be distinguished

Immune components of the skin

Type of defence	Different components	Action
structural	skin	impenetrable physical barrier to most outside organisms
	blood and lymphatic channels	provide transport network for cellular defence
cellular	Langerhans cells	play important role in antigen presentation
	T lymphocytes	facilitate immune reactions, including cell destruction. Self-regulating through the action of suppressor T cells
	mast cells	facilitate inflammatory reaction of the skin
	keratinocytes	produce inflammatory cytokines; have the ability to express surface immune reactive molecules
systematic	skin-associated lymphoid tissue	as skin contains the above immune cells and structural defences, it can be classified as a fully functioning immunological unit
	cytokines and eicosanoids	cytokines are cell mediation molecules produced by components of the cellular defence system; eicosanoids are non-specific inflammatory mediators produced by mast cells, macrophages and keratinocytes
	complement cascade	activation of the complement cascade initiates a variety of destructive mechanisms, including opsonization, lysis, chemotaxis and mast cell degranulation
	adhesion molecules	increase the number of cellular defence facilitators in a particular area by binding T cells
immunogenetic	major histocompatibility complex (MHC)	facilitates immunological recognition of antigens. Located on HLA gene cluster; the appearance of specific HLA genes is associated with certain pathologies, e.g. ankylosing spondylitis is associated with HLA B27

Fig. 7.11 Immune components of the skin.

histologically by Birbeck granules, a cytoplasmic organelle found only in this type of cell. The Langerhans cells play a defensive role in antigen presentation.

Other dendritic cells can be distinguished in the epidermis, which also appear to present antigen. If they lack the Birbeck granules, however, they aren't Langerhans cells.

T lymphocytes

These cells are produced in the bone marrow and mature in the thymus gland; they circulate throughout the body's tissues and come into direct contact with invading foreign antigens. Once activated by this binding process, the T cells proliferate and carry out a cell-mediated immune attack on the antigens.

There are four different types of T cells (Fig. 7.12), distinguished by different functions and varying surface receptors and identified by monoclonal antibodies. The other family of lymphocytes, B lymphocytes, is not normally seen within the skin but can be present in some types of skin pathology.

Mast cells

Mast cells are found within the dermis and are involved in the immediate (Type I) hypersensitivity reaction of the skin. They can be recruited to inflammation sites within the dermis.

Keratinocytes

As well as being responsible for keratin, keratinocytes also produce proinflammatory cytokines, such as interleukin-1 (IL-1). Keratinocytes can also express surface immune reactive molecules such as major histocompatibility complex (MHC) class II antigens (e.g. HLA DR), and intercellular adhesion molecules such as ICAM-1.

MHC class II antigens are also expressed on B lymphocytes, Langherhans cells, some T lymphocytes, macrophages and endothelial cells. They play an important role in immunological recognition, and are also responsible for the mechanism behind transplant rejection. The tissue type antigens of each person are also found within the MHC, which is situated within the HLA gene complex on chromosome 6. Certain HLA genes are associated with an increased risk of developing specific diseases, including some which are classified as 'autoimmune' (Fig. 7.13).

The adhesion molecules, in particular ICAM-1, are found on the cell surface of lymphocytes and some endothelial cells and keratinocytes. They bind with T cells by interacting with leucocyte-functional antigens, and so increase the site's cell traffic.

Lymphoid tissues of the skin

Lymphoid tissue is a term used to describe tissues that collectively store, produce and process lymphocytes. The skin, with its rich blood supply and generous lymphatic drainage, together with the circulating T lymphocytes and *in-situ* immune cells, can be classified as lymphoid tissue.

Cytokines and eicosanoids

The cytokines include γ-interferon, IL-1, IL-2 and IL-3. Produced mainly by T lymphocytes, these soluble molecules mediate actions between cells. They are also produced by Langerhans cells,

T lymphocytes found in the skin	
Helper	Facilitates immune reactions
Delayed hypersensitivity	Specifically sensitized
Cytotoxic	Kills infecting cells
Suppressor	Regulates other lymphocytes

Fig. 7.12 T lymphocytes found in the skin.

NLA antigens associated with skin diseases	
Skin disease	**HLA antigen**
psoriasis	B13, Bw37, Cw23
Reiter's disease	B27
dermatitis herpetiformis	B8

Fig. 7.13 HLA antigens associated with skin diseases.

keratinocytes, fibroblasts, endothelial cells and macrophages.

Eicosanoids are produced from arachidonic acids by mast cells, macrophages and keratinocytes. They are non-specific inflammatory mediators; prostaglandins, thromboxanes and leukotrienes are all eicosanoids.

Hypersensitivity reactions of the skin

A hypersensitivity reaction is one in which the adaptive immune response is exaggerated or inappropriate; an allergy is the acquisition of an inappropriate specific immune reaction to a normally harmless substance in the environment. There are four main types of hypersensitivity response, all of which are exhibited in the skin (Fig. 7.14).

If a patient who has high circulating levels of a certain antibody is injected with the appropriate antigen, an Arthus reaction will occur—a type III hypersensitivity reaction. This involves a red oedematous area which develops over the site of the injection within 4–12 h.

Skin secretions

The components of sweat, sebum and epidermal lipids differ in content (Fig. 7.15). Sweat is a watery isotonic liquid which is delivered to the skin's surface. It has a low pH of between 4 and 6.8 which

Hypersensitivity reactions of the skin	
Type I (Intermediate)	Fc receptors bind IgE to the surface of mast cells; when an antigen is encountered, the IgE molecules cross-link. This action stimulates the release of inflammatory mediators such as histamine, prostaglandins and leukotrienes. The response occurs within minutes, although there is a delayed component present, and results in urticaria in the skin. Massive histamine release can cause anaphylaxis. The most common allergens that provoke an allergic reaction are pollen grains, bee stings, pencillin, certain foods, moulds and house dust mites.
Type II (Antibody-dependent cytotoxicity)	When antigens bind to target skin cells on the basement membrane, a reaction occurs whereby cytotoxic killer-T cells or complement activation destroy the foreign body. The powerful effects of complement cascade activation include opsonization, lysis, mast cells degranulation, smooth muscle contraction and chemotaxis. Haemolytic anaemia and transfusion reactions are examples of type II hypersensitivity, as is the pathology involved in pemphigus: IgG antibodies which are directed against keratinocyte surface-antigens result in lysis of the keratinocytes causing intra-epidermal splitting. This results in characteristic skin blisters of pemphigus.
Type III (Immune complex disease)	When antigens and antibodies bind in the blood, an immune complex is formed which is deposited in the walls of small blood vessels such as those found in the skin. Although these complexes are usually removed by the reticuloendothelial system, a leucocytoclastic vasculitis can sometimes occur; vascular damage caused by complement activation and lysosomal enzymes released from polymorphs. This vasculitis is seen in systemic lupus erythematosus, dermatomyositis and microbial infections such as infective endocarditis.
Type IV (Cell-mediated or delayed)	Pre-sensitized T cells come into secondary contact with the antigen after it has become bound to an antigen presenting cell. The T cells release cytokines which in turn activate other T cells and macrophages—the process takes some time and the damage to tissue is most pronounced after 48–72 hours. Disorders which contain a variant of Type IV hypersensitivity in their pathology include allergic contact dermatitis, leprosy and tuberculosis.

Fig. 7.14 Hypersensitivity reactions of the skin. (Adapted with permission from *Dermatology: an Illustrated Colour Text*, 2nd edn, by D.J. Gawkrodger, Churchill Livingstone, 1997.)

Components of sebum and epidermal lipid		
Component	**Sebum (%)**	**Epidermal lipid (%)**
glyceride/free fatty acids	58	65
wax esters	26	0
squalene	12	0
cholesterol esters	3	15
cholesterol	1	20

Fig. 7.15 Components of sebum and epidermal lipid.

Action of hormones on the skin		
Hormone	**Site of production**	**Action on skin**
corticosteroids	adrenal cortex	vasoconstriction, decreased mitosis of basal cells, anti-inflammatory role
androgens	adrenal cortex, gonads	stimulates growth of terminal hair, stimulates sebum production
oestrogens	adrenal cortex, ovaries	stimulates melanin production
melanocyte stimulating hormone (MSH)	pituitary gland	stimulates melanin production
adrenocorticotrophic hormone (ACTH)	pituitary gland	stimulates melanin production
Epidermal growth factor (EGF)	skin	stimulates cell differentiation, plays a role in calcium metabolism
vitamin D	skin	no effect on skin, plays a role in bone metabolism

Fig. 7.16 Hormones and the skin. (Adapted with permission from *Dermatology: an Illustrated Colour Text*, 2nd edn, by D.J. Gawkrodger, Churchill Livingstone, 1997.)

makes the skin slightly acidic, and this discourages microbial growth. The minimum insensible loss through perspiration per day is 0.5 l, and the maximum daily output is 10 l, which is limited by the body's capability of sweating 2 l/h. Men sweat more than women.

As well as lowering the skin's pH and cooling the skin, sweat hydrates the outer layers of the epidermis and aids the hands and soles of the feet in gripping.

Hormonal production and the skin

The skin manufactures vitamin D in the dermis but is also affected by many other hormones (Fig. 7.16).

- List the four different sections of the epidermis and describe the stage of keratinocyte maturation for each one.
- Define where you would find lanugo, vellus and terminal hair.
- List ten causes of clubbing.
- Differentiate between eccrine and apocrine sweat glands.
- Describe the different functions of Merkel's cells, Meissner's corpuscles and Pacinian corpuscles.
- Differentiate the two forms of melanin.
- List the various products of fibroblasts and their functions.
- Describe the four different types of hypersensitivity reaction.
- List the functions of sweat.
- Explain the systemic importance of vitamin D production.