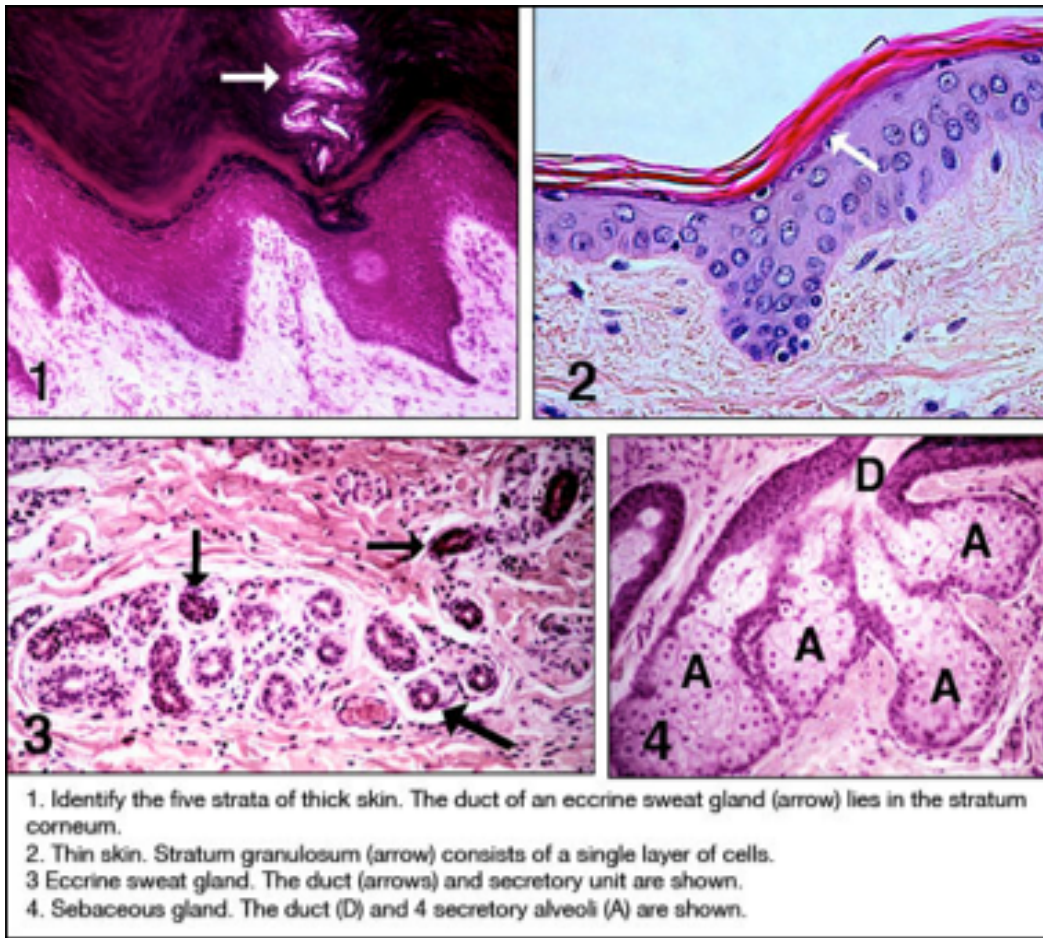


Skin



The skin covers the exterior of the body and constitutes a large organ with several functions. In humans, the skin accounts for about 7% of the total body weight and has a total surface area of about 1.8 square meters. It protects the body from mechanical injury and loss of fluid, acts as a barrier against noxious agents, aids in temperature regulation, excretes various waste products, and through its receptors for sensations of heat, cold, touch, and pain, provides information about the external environment. In addition, the ultraviolet rays of sunlight stimulate the deep epidermis to produce vitamin D (calciferol).

Structure

The skin consists of a surface layer of epithelium called the epidermis and an underlying layer of connective tissue, the dermis (corium). A loose layer of connective tissue, the hypodermis, attaches the skin to underlying structures but is not considered a component of skin. The appendages of the skin – hair, nails, and sweat and sebaceous glands - are local specializations of the epidermis. Together, the skin and its appendages form the integument. The thickness of the skin varies in different parts of the body, and the proportions of dermis and epidermis also differ. Between the scapulas, the dermis is especially thick, whereas on the palms of the hands and soles of the feet, the epidermis is thickened. The terms thick skin and thin skin refer to the thickness of the epidermis and not to the thickness of the skin as a whole. In thick skin the epidermis is especially well developed, whereas in thin skin it forms a

relatively narrow layer. At its junction with the dermis, the epidermis forms numerous ridge like extensions, the epidermal ridges that project into the underlying dermis. Complementary projections of the dermis fit between the epidermal ridges and form the dermal papillae. The surface patterns of the skin, such as the fingerprints, reflect the pattern of the dermal papillae.

Epidermis

The epidermis forms the surface layer of the skin and consists of keratinized stratified squamous epithelium. The cells, keratinocytes, undergo an orderly progression of maturation and keratinization to produce a superficial layer of dense, flattened, dead cells at the surface. A smaller population of cells, the melanocytes, is associated with pigmentation of the skin. The epidermis lacks blood vessels and is nourished by diffusion of material from vessels in the underlying dermis. The epidermis is innervated, however.

The epidermis can be divided into several layers (strata) that reflect the sequential differentiation of keratinocytes as they progress from the base of the epidermis to the surface, where they are exfoliated. In thick skin, the layers are stratum basale, stratum spinosum, stratum granulosum, stratum lucidum, and stratum corneum. In thin skin the layers are narrower and less well defined and stratum lucidum is absent.

Stratum Basale

Stratum basale abuts the underlying dermis, separated from it only by a basement membrane. It consists of a single row of columnar epithelial cells that follows the contours of the ridges and papillae. Stratum basale is the growing layer of the epidermis, and most, but not all, of the mitotic activity occurs in this layer. For this reason, stratum basale often is called the stratum germinativum. Each cell of stratum basale is limited by a typical trilaminar cell membrane and is joined to adjacent cells by numerous desmosomes. At the basal surface, hemidesmosomes aid in attaching the cells to the underlying basement membrane. The basement membrane at the dermoepidermal junction, as elsewhere, consists of three strata: a superficial lamina lucida, a lamina densa, and an underlying fibroreticular lamina. On the dermal side of the basement membrane, anchoring filaments of type VII collagen link the undersurface of the lamina densa to collagen fibers of the papillary dermis. Fibrillin microfibrils attach the lamina densa to elastic fibers. The cytoplasm of the basal keratinocytes is fairly dense and contains many scattered keratin intermediate filaments. Clusters of ribosomes are prominent, and the cells contain a moderate number of mitochondria, some profiles of granular endoplasmic reticulum, and a few Golgi saccules.

Stratum Spinosum

Stratum spinosum consists of several strata of irregular, polyhedral cells that become somewhat flattened in the outermost layers. The cells are closely applied to each other and joined at all surfaces by numerous desmosomes. During tissue preparation, the cells tend to shrink and pull apart except at these points of attachment. Thus, the cells appear to have numerous short, spiny projections that extend between adjacent cells and commonly are called prickle cells. The projections are not areas of cytoplasmic continuity between cells but are sites of typical desmosomes. In addition to the organelles seen in the basal cells, prickle cells in the upper layers of stratum spinosum contain ovoid granules, 0.1 to 0.5 μm in diameter, called membrane-coating granules. These consist of parallel laminae bounded by a double membrane and are rich in glycols and phospholipids that help maintain the barrier function of

the skin. Keratin intermediate filaments are numerous and may form dense bundles that extend into the spinous processes, ending in the dense plaques of desmosomes. Stratum spinosum and stratum basale often are grouped together as stratum malpighii.

Stratum Granulosum

Stratum granulosum of thick skin consists of three to five layers of flattened cells whose long axes are parallel to the surface of the epidermis. In thin skin stratum granulosum consists of a single layer of cells. The cells are distinguished by the presence of amorphous, densely packed dark granules, the keratohyalin granules, that vary in size and shape. The granules are not limited by membranes and are associated closely with bundles of keratin filaments. Chemically, they contain large amounts of sulfur-containing amino acids. The granules increase in number and size in the outermost layers of stratum granulosum, and the cells show evidence of degenerative changes. The nuclei stain more palely, and the contacts between adjacent cells become less distinct. The cells of the granular layer are viable but undergo programmed death as they pass into the succeeding horny layer. Membrane-coating granules increase in number in the cells of stratum granulosum. These rod-shaped granules fuse with the plasmalemma and empty their contents into the intercellular space. The lipid-rich contents act as a barrier between cells of this layer and those toward the surface and contribute to the sealing effect of skin, preventing water loss and entrance by foreign substances between cells. Direct evidence of this can be observed during a deep abrasion or scrape (a strawberry) of the epidermis deep to the stratum granulosum. When this occurs an amber color fluid seeps to the surface that continues to ooze for some time. This is tissue fluid that has passed between keratinocytes toward the surface to meet the nutritional needs of cells deep to stratum granulosum.

Stratum Lucidum

Stratum lucidum forms a narrow, undulating, lightly stained zone at the surface of stratum granulosum. It consists of several layers of cells so compacted together that outlines of individual cells cannot always be made out. Traces of flattened nuclei may be seen, but generally this layer is characterized by the loss of nuclei. Only a few remnants of organelles are present, and the main constituent of the cytoplasm is aggregates of keratin intermediate filaments that now have a more regular arrangement, generally parallel to the skin surface. The plasmalemma is thickened and more convoluted, and the amount of intercellular material is increased. Stratum lucidum is prominent in the thick skin of the palms and soles but is absent from the epidermis in other parts of the body.

Stratum Corneum

Stratum corneum forms the outermost layer of the epidermis and is composed of scalelike cells, often called squames that become increasingly flattened as they approach the surface. Squames are enclosed by a thickened, modified cell membrane due to the continued deposition of an intracellular protein known as involucrin that initially began being expressed in cells occupying the upper layers of stratum spinosum. The squames represent the remains of cells that have lost their nuclei, all their organelles, and their desmosomal attachments to adjacent cells. The cells are filled with keratin, which consists of tightly packed bundles of keratin intermediate filaments embedded in an opaque, structureless material rich in the protein filaggrin. The keratin intermediate filaments of stratum corneum consist of "soft" keratin

as distinct from the "hard" keratin of nails and hair. Soft keratin has lower sulfur content and is somewhat more elastic than hard keratin. The outermost cells of stratum corneum are constantly shed or desquamated; this region often is referred to as stratum disjunctum. Thus, as keratinocytes move toward the surface they are tightly united by desmosomes. As cells pass through the stratum granulosum and approach the surface, specialized proteins some of which are found in the keratohyaline granules interact with the keratin intermediate filaments as well as the plasmalemma to produce a compact mass of keratin. During this migration keratinocytes also produce a complex hydrophobic glycopospholipid, which is released as the superficial keratinocytes die. This material acts to glue the keratin filled squames together as well as making the epidermal surface waterproof for the short term. This water proofing breaks down after prolonged exposure to water as evidenced by placing hands in water for prolonged periods. When this occurs the keratin absorbs water, swells and softens. The keratin layer acts as the main barrier to mechanical damage, desiccation, invasion by bacteria, is inert chemically and relatively impermeable to water. The life span of keratinocytes in their passage from the basal layer to desquamation is between 40 and 55 days. As the keratinocytes progress toward the surface, they become much broader and flatter so that, ultimately, only 4 surface squames are needed to cover the same area as 100 columnar basal cells. Thus, a low rate of mitosis (less than 7 per 1000 basal cells) can maintain the surface layer.

Pigmentation

The majority of keratinocytes forming the epidermis are relatively transparent during life and on exposure to sunlight ultraviolet rays readily pass through the various strata of the epidermis to reach the underlying dermis. As a result, prolonged exposure can not only damage the genetic makeup of nuclei within cells of the stratum basale but also damage elements of the underlying dermis resulting in premature aging and wrinkling of the skin.

Skin color is determined by the pigments carotene and melanin and by the blood in the capillaries of the dermis. Carotene is a yellowish pigment found in cells of the stratum corneum and in fat cells of the dermis and hypodermis. Melanin, a brown pigment, is present mainly in the cells of stratum basale and the deeper layers of stratum spinosum. Melanin is formed in specialized cells of the epidermis, the melanocytes, which originate from cells that emigrated from the neural crest during development. Melanocytes are scattered throughout the basal layer and send out numerous finger-like cytoplasmic processes that extend between the cells of stratum spinosum. Each melanocyte maintains a functional relationship with about 36 keratinocytes in stratum spinosum and basale. The combination of melanocytes and keratinocytes forms an epidermal-melanin unit. In electron micrographs, epidermal melanocytes can be distinguished by the lack of keratin filaments and the content of melanin granules (melanosomes) in various stages of development. Melanocytes also contain the usual array of cytoplasmic organelles. While melanocytes lack desmosomal junctions with neighboring cells, they are affixed to the basement membrane by hemidesmosome-like junctions. Mature melanosomes are transferred from melanocytes via their cytoplasmic processes to keratinocytes of the basal layer and stratum spinosum. In humans, melanosomes frequently aggregate above the nuclei of basal cells, but in the superficial layers of the epidermis the granules are more evenly dispersed and become progressively finer. Since epidermal cells constantly are shed from the surface, melanocytes must provide for continued renewal of melanin. Although melanocytes may die and be replaced by division of neighboring melanocytes, this is a random event, and there does not appear to be a regular cycle of replacement of melanocytes. The number of melanocytes and the size of the melanosomes

are somewhat greater in Negroid and Mongolian skin than in Caucasian, but not sufficiently to account for the differences in skin color. Caucasoid melanosomes are less completely melanized and are packaged in groups, the melanosome complexes, surrounded by a membrane. The larger Negroid melanosomes are more widely dispersed within cells and do not form membrane-bound complexes. The distribution of pigment within the epidermis also differs, being concentrated in the lower zones of the Malpighian layer in Caucasian skin and distributed throughout most keratinocytes of this layer in Negroid skin. The smaller melanosomes of Caucasians are degraded by lysosomes before they reach the upper strata. The degree of pigmentation varies in different parts of the body. The axilla, circumanal region, scrotum, penis, labia majora, nipples, and areola are areas of increased pigmentation. In contrast, the palms and soles contain little or no pigment. Freckles represent local areas of pigmentation resulting from aberrant clones of melanocytes. Pigmentation of freckles and the areolae and nipples may be intensified with pregnancy. A general increase in melanization occurs from exposure to sunlight, at first by darkening of existing melanin and later by increased formation of new melanin. The activated melanocytes produce larger melanosomes. A deficiency of melanin also may occur. The white spotted patterns of piebaldism in humans result from abnormalities in the morphology of melanocytes in which the length and number of the cell processes is deficient. Complete albinism results from an inability of the melanocytes to synthesize melanin, not from an absence of melanocytes.

Other Cell Types

Two other cell types present in the epidermis are Langerhans' and Merkel's cells. *Langerhans' cells* are present throughout the epidermis but are especially numerous in the upper layers of stratum malpighii. In routine sections, the cells have darkly stained, large, convoluted nuclei surrounded by a clear cytoplasm. With special stains they are seen to be stellate cells that extend long cytoplasmic processes into stratum spinosum. In electron micrographs, the nucleus shows a highly irregular outline, and the abundant cytoplasm lacks keratin filaments, desmosomes, and melanosomes but is characterized by membrane-bound, rod-shaped granules with a regular, granular interior. Some of these granules appear to be continuous with the cell membrane. Langerhans' cells trap antigens that penetrate the skin and transport them to regional lymph nodes. These antigen-presenting cells originate in the bone marrow from a monocyte precursor and participate in a type IV delayed-type reaction mediated by T lymphocytes. *Merkel's cells* tend to lie close to naked sensory nerve endings in stratum basale and form Merkel cell-neurite complexes. Like melanocytes, Merkel's cells originate from neural crest. Morphologically, Merkel's cells resemble cells of stratum basale, but in electron micrographs, these lighter-staining cells are distinguished by indented nuclei, prominent Golgi complexes, and numerous dense-cored vesicles.

The vesicles tend to concentrate basally at the site where nerve endings approach. The function of Merkel's cells is unknown, but they may have a mechanoreceptor function. They may play a role in sensory processes and have been compared with polypeptide- and hormone-containing cells, but a definite relationship with these has not been established.

Dermis

The dermis (corium) varies in thickness in different regions of the body. It is especially thin and delicate in the eyelids, scrotum, and prepuce; very thick in the palms and soles; thicker on the posterior than anterior aspects of the body; and thicker in men than in women. The dermis is tough, flexible, and highly elastic and consists of a feltwork of collagen fibers with scattered

elastic fibers in a glycosaminoglycan-containing matrix. The connective tissue is arranged into deep reticular and superficial papillary layers. The reticular layer is the thicker, denser part of the dermis and consists of interwoven bundles of collagen fibers that mostly run parallel to the surface. Below, the reticular layer merges indistinctly into the subcutaneous tissue (hypodermis), which generally contains many fat cells. Collagen in the reticular layer is mostly type I. The reticular layer of the dermis represents a classic example of dense irregular connective tissue. In animals this is the layer used for making leather products (shoes, belts, coats). The reticular layer of the dermis functions as fibroelastic whole-body-stocking that firmly surrounds and encloses the contents of the limbs, trunk, neck and head. The papillary layer lies immediately below the epidermis and extends into it in the form of the dermal papillae. The papillary layer is not clearly demarcated from the reticular layer, but its fibers and bundles of collagen tend to be thinner and more loosely arranged. This layer also contains more ground substance and has a more cellular appearance. Most of the collagen is type III. Just beneath the epidermis, the reticular fibers present have a vertical orientation. Elastic fibers are found deeper in the papillary layer.

Dermal papillae are small, conical projections with rounded or blunt apices that fit into corresponding pits on the undersurface of the epidermis. They are especially prominent on the palmar surface of the hands and fingers, where they are closely aggregated and arranged in parallel lines that correspond to the surface ridges of the epidermis. Capillary loops are present in the papillae, and in some, especially those in the palms and fingers, nerve endings and tactile corpuscles are present. The epidermis, like all epithelia, is avascular and must rely on diffusion through the basement membrane to meet its nutritional requirements. Capillaries within the dermal papillae facilitate this exchange deep within the epidermis. Smooth muscle cells are present in the deeper parts of the reticular layer in the penis, scrotum, perineum, and areola. On contraction, the smooth muscle cells produce wrinkling of the skin in these areas. The arrectores pilorum muscles are small bundles of smooth muscle cells associated with hair follicles. Their contraction results in "goose bumps".

Dermatoglyphics

Skin ridges are normal features on the volar surface of the fingers, hands, feet, and toes. They act as anti-slip devices and also are thought to improve the sense of touch. The ridges form three main patterns: arches, loops, and whorls. Loops are the most common pattern on the fingers and arches the rarest. The ridge patterns on the toes are similar to those on the fingers, but arches are more numerous and whorls are fewer. The ridge pattern is established early in life and is permanent. In any individual the pattern varies from digit to digit, and it is unlikely that in a group of unrelated persons the sequence of patterns would be identical.

Appendages of the Skin

The appendages of the skin are derived from the epidermis and include hair, nails, and sweat and sebaceous glands.

Nails

The nails are hard, keratinized structures that cover the dorsal surfaces of the tips of the fingers and toes. Each nail consists of a visible body (nail plate) and a proximal part, the root, which is implanted into a groove in the skin. The root is overlapped by the proximal nail fold, a fold of skin that continues along the lateral borders of the nail, where it forms the lateral nail

folds. Stratum corneum of the proximal nail fold extends over the upper surface of the nail root and for a short distance onto the surface of the body of the nail, where it forms a thin cuticular fold called the eponychium. At the free border of the nail, the skin is attached to the underside of the nail, forming the hyponychium. The nail is a modification of the cornified zone of the epidermis and consists of several layers of flattened cells with shrunken, degenerate nuclei. The cells are hard, tightly adherent, and throughout most of the body of the nail, clear and translucent. The pink color of the nails is due to transmission of color from the underlying capillary bed. Near the root, the nail is more opaque and forms a crescentic area, the lunule, which is most visible on the thumb, becoming smaller and more hidden by the proximal nail fold toward the little finger. The lunule represents the region from which nail formation occurs. Beneath the nail lies the nail bed, which corresponds to the stratum malpighii of the skin. It consists of prickle cells and a stratum basale resting on a basement membrane. The underlying dermis is thrown into numerous longitudinal ridges that are very vascular. Near the root, the ridges are smaller and less vascular. The nail bed beneath the root and lunule is thicker, actively proliferative, and concerned with growth of the nail; it is called the nail matrix. The nail bed beneath the rest of the nail is thinner and not involved with nail growth. Cells in the deepest layer of the matrix are cylindrical and show frequent mitoses, while above them are several layers of polyhedral cells and flattened squames that represent the differentiating cells of the nail. Nail keratin has higher sulfur content than the keratin of the epidermis and is called hard keratin.

Hair

Hairs are present on almost all surfaces of the skin except for the palmar surfaces of the hands, plantar surfaces of the feet, margin of the lip, prepuce, glans penis, clitoris, labia minora, and inner surfaces of the labia majora. They consist of flexible, keratinized threads that vary in length and thickness in different regions of the body and in different races. From the middle of fetal life, the skin is covered by fine hair called lanugo; this mostly is shed by birth and is replaced by downy vellus hair. Vellus hairs are retained in most regions, where they appear as short, soft, colorless hair such as that on the forehead. In the scalp and eyebrows, vellus hairs are replaced by coarser terminal hair that also forms the axillary and pubic hair and, in men, the hair of the beard and chest.

Structure of Hair

Each hair consists of a root embedded in the skin and a hair shaft projecting for a variable distance above the surface of the epidermis. In cross section the shaft appears round or oval and is made up of three concentric layers. The medulla (core) is composed of flattened, cornified, polyhedral cells in which the nuclei are pyknotic or missing. There is no medulla in thin fine hair (lanugo), and a medulla may be absent in hairs of the scalp or extend only part of the way along the shaft. The bulk of the hair consists of the cortex, which is composed of several layers of intensely cornified, elongated cells tightly compacted together. Most of the pigment of colored hair is found in the cortex and is present in the cells and the intercellular spaces. Variable accumulations of air spaces are present between and within the cells of the cortex. Together with fading of pigment, increase in the number of air spaces is responsible for graying of the hair. The outermost layer is thin and forms the cuticle. It consists of a single layer of clear, flattened, squamous cells that overlap each other, shingle fashion, from below upwards.

The root of the hair is embedded in the dermis. At the lower end, the root expands to form the hair bulb, which is indented at its deep surface by a conical projection of the dermis and called a papilla. Papillae contain blood vessels that provide nourishment for the growing and differentiating cells of the hair bulb. The structure of the root differs somewhat from that of the shaft. In the lower part of the root, the cells of the medulla and cortex tend to be cuboidal in shape and contain nuclei of normal appearance. At higher levels in the root, nuclei become indistinct and finally are lost. The cells of the cortex become progressively flattened toward the surface of the skin.

Hair Follicle

The root of each hair is enclosed within a tubular sheath called the hair follicle, which consists of an inner epithelial component and an outer connective tissue portion. The epithelial component is derived from the epidermis and consists of inner and outer root sheaths. The connective tissue sheath is derived from the dermis.

The inner epithelial root sheath corresponds to the superficial layers of the epidermis that have invaginated from the epidermal surface and undergone specialization to produce three layers. The innermost layer is the cuticle of the root sheath, which abuts the cuticle of the hair shaft. The cells are thin and scalelike and are overlapped from above downward; the free edges of the cells interlock with the free edges of the cells of the hair cuticle. Immediately surrounding the cuticle of the inner epithelial root sheath are several layers of elongated cells that form Huxley's layer. These cells contain granules that are similar to keratohyalin granules but differ chemically; they are called trichohyalin granules. Huxley's layer is surrounded by Henle's layer, a single row of clear, flattened cells that contain keratin filaments. The cells of these three layers are nucleated in the distal parts, but as the inner epithelial root sheath approaches the surface, the nuclei are lost.

The outer epithelial root sheath is a direct continuation of stratum malpighii. The cells of the outermost layer are columnar and arranged in a single row and at the surface become continuous with stratum basale of the epidermis. The inner layers of cells are identical to and continuous with the prickle cells of stratum spinosum.

The connective tissue portion of the follicle consists of three layers. A narrow clear band, the glassy (vitreous) membrane, is closely applied to the columnar cells of the outer epithelial root sheath and is equivalent to the basement membrane. The middle layer consists of fine, circularly arranged collagen fibers. The outermost layer is poorly defined and contains collagen fibers arranged in loose, longitudinal bundles interspersed with some elastic fibers.

A bulbous expansion of the hair root surrounds the papilla. The cells of the hair bulb are not arranged in layers but form a matrix of growing cells. Matrix cells at the tip of the papilla differentiate into the medulla of a hair. Those on the slopes develop into the cortex and medulla. Laterally, cells of the bulb form the inner epithelial root sheath. Pigmentation occurs from the activity of melanocytes present in the matrix.

Hair Cycle

No hair grows forever; each cycle through a proliferative phase (anagen), a period of decreasing growth (catagen), and a resting phase (telogen). The cyclic activity continues throughout life, but the phases of the cycle change with age. At about the fifth month of gestation, all the hairs are in anagen, a uniformity of growth not seen again. Between 8 and 10 weeks before birth, some hair sites have reached catagen and telogen phases. The frontal and parietal scalp areas show the first shedding events; in the occipital region, hairs remain in

anagen until after birth. From about 6 weeks before birth, telogen hairs again appear in the frontal and parietal scalp, indicating a second cycle of hair growth. All hairs usually enter telogen immediately after birth, giving rise to a second period of shedding. After this, the phases are more irregular. About 18 weeks after birth, cycles are associated with individual hairs or groups of hairs. In adults, hair cycles vary with body region. The total hair cycle in the scalp extends over 300 weeks, with telogen occupying 18 to 19 weeks.

Sebaceous Glands

Sebaceous glands occur in most parts of the skin and are especially numerous in the scalp and face and around the anus, mouth, and nose. They are absent from the palms of the hands and soles of the feet. Generally, sebaceous glands are associated with hairs and drain into the upper part of the hair follicle, but on the lips, glans penis, inner surface of the prepuce, and labia minora, the glands open directly onto the surface of the skin, unrelated to hairs. The glands vary in size and consist of a cluster of two to five oval alveoli drained by a single duct.

The secretory alveoli lie within the dermis and are composed of epithelial cells enclosed in a well-defined basement membrane and supported by a thin connective tissue capsule. Cells abutting the basement membrane are small and cuboidal and contain round nuclei. The entire alveolus is filled with cells that, centrally, become larger and polyhedral and gradually accumulate fatty material in their cytoplasm. Nuclei become compressed and pyknotic and finally disappear. Secretion is of the holocrine type, meaning the entire cell breaks down, and cellular debris, along with the secretory product (triglycerides, cholesterol, and wax esters), is released as sebum. Myoepithelial cells are not observed with sebaceous glands, but the glands are closely related to the arrectores pilorum muscle. Contraction of this smooth muscle bundle helps in the expression of secretory product from the sebaceous glands. In the nipple, smooth muscle bundles are present in the connective tissue between the alveoli of these glands. The short duct of the sebaceous gland is lined by stratified squamous epithelium that is a continuation of the outer epithelial root sheath of the hair follicle. Replacement of secretory cells of the alveolus comes mostly from division of cells close to the walls of the ducts, near their junctions with the alveoli. Some replacement comes from cells at the periphery of the alveoli. Collectively, the hair follicle, hair shaft, sebaceous gland, and erector pili muscle are referred to as the pilosebaceous apparatus. The pilosebaceous apparatus produces hair and sebum, the latter of which protects the hair and acts as a lubricant for the epidermis to protect it from the drying effects of the environment. Sebaceous glands become more active at puberty and are under endocrine control: androgens increase activity, estrogens decrease activity.

Sweat Glands

Two classes of sweat glands are distinguished: ordinary or eccrine sweat glands and apocrine glands, such as those of the axilla and perineum. Eccrine sweat glands are distributed throughout the skin except in the lip margins, glans penis, inner surface of the prepuce, clitoris, and labia minora. Elsewhere the numbers vary, being plentiful in the palms and soles and least numerous in the neck and back. Each gland is a simple tubular structure. The deep part is tightly coiled and forms the secretory unit located in the deep dermis. The secretory unit consists of a simple columnar epithelium resting on a thick basement membrane. Two types of cells, clear cells and dark cells are present. The dark cells are narrow at their bases and broad at the luminal surface; in electron micrographs they show numerous ribosomes, secretory vacuoles, and few mitochondria. These cells secrete glycoproteins, which have been identified

in secretory vacuoles. Clear cells are broad at their bases and narrow at the apices. Intercellular canaliculi extend between adjacent clear cells, which contain glycogen, considerable smooth endoplasmic reticulum, and numerous mitochondria but few ribosomes. The basolateral plasmalemma of the cell shows extensive, complex infoldings. Clear cells are thought to secrete sodium, chloride, potassium, urea, uric acid, ammonia, and water.

Myoepithelial cells are present around the secretory portion, located between the basal lamina and the bases of the secretory cells. These stellate cells are contractile and are believed to aid in the discharge of secretions. Eccrine sweat glands are drained by a narrow duct that at first is coiled and then straightens as it passes through the dermis to reach the epidermis. The lining of the duct consists of two layers of cuboidal cells. At their luminal surfaces, the cells of the inner layer show aggregations of filaments organized into a terminal web. The epithelium lies on a basal lamina, and myoepithelial cells are lacking. In the epidermis, the duct consists of a spiral channel that is simply a cleft between the epidermal cells; those cells immediately adjacent to the duct lumen are circularly arranged. When eccrine sweat glands function to regulate body temperature they are regulated by postganglionic sympathetic neurons that release acetylcholine as the neurotransmitter (cholinergic innervation). In contrast, when eccrine sweat glands are involved in emotional sweating they are controlled by postganglionic sympathetic neurons that release norepinephrine (adrenergic innervation). Apocrine sweat glands are enlarged, modified eccrine sweat glands. Their secretions are thicker than those of the ordinary eccrine sweat glands and contain glycoproteins, lipids, glycolipids and pheromones. Their histologic structure also differs from eccrine sweat glands in several respects. Apocrine sweat glands also are simple coiled, tubular glands the secretory units of which are lined by columnar cells. The secretory tubules of these glands are of much wider diameter than those of eccrine sweat glands. Their myoepithelial cells are larger and more numerous, and there is only one type of secreting cell, which resembles the dark cells of the eccrine glands. The ducts are similar to those of ordinary sweat glands but empty into a hair follicle rather than onto the surface of the epidermis. Secretion by apocrine glands is of the merocrine type and involves no loss of cellular structure. Although retained, the term apocrine is misapplied to these glands. Apocrine sweat glands become more active at puberty and are under endocrine control by androgens and estrogens. They also receive innervation from postganglionic sympathetic neurons that release norepinephrine (adrenergic innervation). The ceruminous (wax) glands of the external auditory canal are simple coiled tubular apocrine glands in which the secretory portion and the duct may branch. Glands in the margins of the eyelids (Moll's glands) also are simple coiled tubular apocrine glands but differ in that the terminal portions show less coiling and have wider lumina.