SKIN

The skin (integument) and its derivatives constitute the integumentary system. The skin forms the external covering of the body and is its largest organ, constituting 15% to 20% of its total mass. The skin consists of three main layers:

1) The epidermisis composed of a keratinized stratified squamous epithelium that grows continuously but maintains its normal thickness by the process of desquamation. Epidermis is derived from skin ectoderm.

2) The dermisis composed of a fibrous connective tissue that imparts mechanical support, strength, and thickness to the skin. Dermis is derived from dermatoms of mesoderma somites

The hypodermis containing variable amounts of adipose tissue lies deep to the dermis.

The epidermal derivatives of the skin or epithelial skin appendages include the following structures:

1) Hairs
2) Nails
3) Glands:
   a) sweat glands
   b) sebaceous glands
   c) mammary glands

Major functions of the skin include the following:

1) It acts as a barrier that protects against physical, chemical, and biologic agents in the external environment (i.e., mechanical barrier, permeability barrier, ultraviolet barrier).
2) It provides immunologic information obtained during antigen processing to the appropriate effector cells in the lymphatic tissue.
3) It participates in homeostasis by regulating body temperature and water loss.
4) It conveys sensory information about the external environment to the nervous system.
5) It performs endocrine functions by secreting hormones, cytokines, and growth

factors and converting precursor molecules into hormonally active molecules (vitamin D).

6) It functions in excretion through the exocrine secretion of sweat, sebaceous, and apocrine glands.

The epidermis is composed of five distinct layers:

1) the stratum basale, also called the stratum germinativum;
2) the stratum spinosum, also called the spinous layer or prickle cell layer;
3) the stratum granulosum, which contains numerous intensely staining granules;
4) the stratum lucidum, which there is only in thick skin;
5) the stratum corneum.

According to the thickness and location the human skin is categorized as thick or thin. Thick skin there is in the palms of the hands and soles of the feet. Thick skin is hairless, and have a much thicker epidermal layer than skin in any other location.

Stratum basale

The stratum basale is represented by a single layer of low columnar cells that rests on the basal lamina. It contains the stem cells from which new cells, the keratinocytes, arise by mitotic division. For this reason, the stratum basale is also called the stratum germinativum. As new keratinocytes arise in this layer by mitotic division, they move into the next layer, thus beginning their process of upward migration. This process terminates when the cell riches a skin surface and sloughed off into environment. They are mature keratinized cells.

Basal keratinocytes exhibit extensive cell junctions; they are connected to each other by desmosomes and to the underlying basal lamina by hemidesmosomes.

The cytoplasm of immature keratinocytes appears basophilic in histologic sections because these cells in the basal layer contain numerous free ribosomes, a small Golgi apparatus and rER. Free ribosomes synthesized proteins called keratins, which will later be assembled (əˈsembld) собираться into keratin filaments or tonofilaments. These filaments are classified as intermediate filaments.

Stratum spinosum

Stratum spinosum comprises several layers of large keratinocytes overlying the stratum basale. The cells are cuboidal or polygonal in the deeper layers and slightly flattened in the upper layers of stratum spinosum. They exhibit numerous cytoplasmic processes or spines.The processes are attached to adjacent cells by desmosomes.

In keratinocytes of stratum spinosum the keratin filaments become grouped into bundles called tonofibrils. In the upper part of the stratum spinosum the free ribosomes within the keratinocytes begin to synthesize keratohyalin granules that become the distinctive feature of the cells in the stratum granulosum. As the keratinocytes in the stratum spinosum begin to produce keratohyalin granules, they also produce membrane-bounded lamellar bodies (membrane-coating granules), containing lipids.

Stratum granulosum

The stratum granulosum is the most superficial layer of the nonkeratinized portion of the epidermis. This layer consists of from one to three flattened cells thick. Flattened keratinocytes in this layer contain numerous keratohyalin granules containing the two major intermediate filament–associated proteins called, filaggrin and trichohyalin. Filaggrin and trichohyalin function as promoters in the aggregation of keratin filaments into tonofibrils, thus initiating the conversion of granular cells into cornified cells. This process is called keratinization. The keratin fibrils formed in this process contain soft keratin in contrast to the hard keratin of hair and nails. The transformation of a granular cell into a keratinized cell also involves break down of the nucleus and other organelles and thickening of the plasma membrane.

Spinous and granular keratinocytes synthesize a heterogenous mixture of probarrier lipids containing into lamellar bodies. The content of the lamellar bodies are then secreted by exocytosis into the intercellular spaces between the stratum granulosum and stratum corneum, providing the formation of the epidermal water barrier.

Stratum lucidum

The stratum lucidum is normally only well seen in thick skin. This highly

refractive layer contains unvisible in the light microscope eosinophilic cells in which the process of keratinization is well advanced. The nucleus and cytoplasmic organelles become disrupted and disappear as the cell gradually fills with keratin.

Stratum corneum

The cornified cells in the stratum corneum are the most differentiated keratinocytes. They lose their nucleus and cytoplasmic organelles and become filled almost entirely with keratin filaments. The thick plasma membrane of these cornified, keratinized cells is coated from the outside, in the deeper portion of this layer, with an extracellular layer of lipids together form the water barrier in the epidermis.

The epidermal water barrier thus consists of two structural elements:

1) The cell envelope (CE) is a 15-nm-thick layer of insoluble proteins deposited on the inner surface of the plasma membrane that contributes to the strong mechanical properties of the barrier. They are small prolinerich (SPR) proteins and larger structural proteins. The structural proteins include elafin, filaggrin, involucrin, keratin and loricrin. Loricrin is the major structural protein of the cell envelope.

2) The lipid envelope is a 5-nm-thick layer of lipids attached to the cell surface. The major lipid components of the lipid envelope are a) ceramides, which belong to the class of sphingolipids; b) cholesterol; c) and free fatty acids.

Melanocytes

The less numerous cells of epidermisis are melanocytes. Neural crest–derived dendritic shaped melanocytes are scattered among the basal cells of the stratum basale. The rounded cell body of melanocyte resides in the basal layer and extends long processes between the keratinocytes of the stratum spinosum, forming the contacts with them.

The epidermal melanocytes produce and secrete the pigment melanin. The most important function of melanin is to protect the organism against the damaging effects of nonionizing ultraviolet irradiation. Melanin is produced by the oxidation of tyrosine to 3,4-dihydroxyphenylalanine (DOPA) by tyrosinase and the subsequent transformation of DOPA into melanin.

In melanocytes the pigment melanin there is into membrane-bounded structures called melanosomes. Developing melanosomes and their melanin contents are transferred to neighboring keratinocytes by pigment donation подарок. This process, which involves the phagocytosis of the tips of the melanocyte processes by keratinocytes.

Langerhans' Cells

Langerhans' cells are dendritic, antigenpresenting cells in the epidermis. They originate from common lymphoid progenitor (CLP) cells in bone marrow, migrate via the bloodstream, and enter the epidermis where they differentiate into immunocompetent cells. Langerhans'cells encounter and process antigens entering through the skin. Therefore, they constitute part of the mononuclear phagocytotic system. Once antigen is phagocytized, processed, and displayed on the surface of the Langerhans' cell, the cell migrates from the epidermis to a regional lymph node where it interacts with T lymphocytes.

In epidermis the Langerhans' cells there are in the stratum spinosum. They possess dendritic processes. Nucleus of Langerhans' cell indented in many places, so the nuclear profile is uneven. Also, the cytoplasm of Langerhans' cell contains tennis racquet–shaped Birbeck granules. They represent small vesicles, which appear as rods with a bulbous expansion at their end. Like macrophages, Langerhans' cells express both MHC I and MHC II molecules, as well as Fc receptors for immunoglobulin G (IgG).

Merkel's Cells

Merkel's cells are dendritic cells located in the stratum basale. The origin of Merkel's cells is unknown. Merkel's cells are bound to adjoining keratinocytes by desmosomes and contain intermediate (keratin) filaments and some amount of melanosomes in their cytoplasm. The nucleus Merkel's cell is lobed. In cytoplasm of Merkel's cells there is 80-nm neurosecretory granules that resemble those found in the adrenal medulla. Merkel's cells are closely associated with the expanded terminal bulb of afferent myelinated nerve fibers. Functionally they are sensitive mechanoreceptor.

Hairs

Hairs are elongated a keratinized structures derived from an invagination the epidermal epithelium. They are distributed over the entire полностью body except for the palmar surfaces of the hands, the plantar surfaces of the feet, the lips, and the region around the urogenital apertures.

Each hair has a free visible part called shaft and an invisible part called a root which is embedded in the skin.

The hair consists of epidermal cells arranged in 3 concentric layers:

1) the medulla, forming the central part of the hair and containing large vacuolated cells. The medulla is present only in thick hairs.

2) the cortex, which is located peripherally to the medulla and contains cuboidal cells. These cells undergo differentiation into keratin-filled cells.

3) the cuticle, which is the very thin outermost layer of the hair, containing squamous cells.

Each hair root enclosed by hair follicle which is responsible for the production and growth of a hair.

The hair follicle is divided into three segments:

1) The infundibulum extends from the surface opening of the follicle to the level of the opening of its sebaceous gland.

2) The isthmus extends from the infundibulum to the level of insertion of the arrector pili muscle.

3) The inferior segment of the follicle including the bulb.

Hair follicle consists of 3 sheaths:

1) The external connective tissue sheath, which is a dense irregular connective tissue sheath called the follicular bulge.

2) The internal root sheath which is a multilayered cellular covering that surrounds only the deep part of the hair till the level of the sebaceous gland.

3) The external root sheath which is continuation with epidermal epithelium of the stratum basale and the stratum spinosum.

Epidermal origin the internal root sheath has three layers:

1) The cuticle which consists of squamous cells whose outer free surface faces the hair;

2) Huxley's layer which consists of a single or double layer of flattened cells that form the middle plate of the internal root sheath;

3) Henle's layer which consists of an outer single layer of cuboidal cells. These cells are in direct contact with the external root sheath.

At the end the hair follicle expands to form the hair bulb. The base of the bulb is invaginated by a tuft of vascularized loose connective tissue called a dermal papilla.

Matrix cells immediately adjacent to the dermal papilla represent the germinative layer of the follicle. Division and proliferation of these cells provides the growth of the hair. Scattered melanocytes are also present in this germinative layer. The dividing matrix cells in the germinative layer differentiate into the keratinproducing cells of the hair and the internal root sheath. Thus the hairs are composed of keratinized cells that develop from hair follicles.

Keratinization of the hair and internal root sheath occurs shortly after the cells leave the matrix in a region called the keratogenous zone. By the time the hair emerges from the follicle, it is entirely keratinized as hard keratin. The internal root sheath, consisting of soft keratin, does not emerge from the follicle with the hair but is broken down at about the isthmus level where sebaceous secretions enter the follicle.

Sebaceous glands

Sebaceous glands develop as outgrowths of the external root sheath of the hair follicle. Thus the sebaceous glands are connected with hair follicle. Usually several sebaceous glands drain into a single hair follicle.

Sebaceous glands are located on border between the papillary and reticular layers of dermis. They are alveolar glands, which synthesize the oily substance called sebum, using the holocrine type of secretion. In most sebaceous glands, several alveoli open into a shot wide duct, which empties into the infundibulum of a hair follicle.

Alveoli of sebaceous glands are formed by sebum-producing cells, forming the stratified epithelium. New cells of sebaceous gland are produced by mitosis of the basal cells, lying on basement at the periphery of the gland, and the cells of the gland remain

linked to one another by desmosomes. The basal lamina of these cells is continuous with that of the epidermis and the hair follicle.

The basal cells of the sebaceous gland contain smooth surface endoplasmic reticulum (sER), rER, free ribosomes, mitochondria, glycogen, and a well-developed Golgi apparatus. As the cells move away from the basal layer and begin to produce the lipid secretory product, the amount of sER increases, reflecting отражая the role of the sER in lipid synthesis and secretion. The cells gradually become filled with numerous lipid droplets.

The arrector pili muscle accompanies the sebaceous gland; its contraction assists in gland secretion and discharge into the infundibulum.

Sweat glands

Sweat glands are classified on the bases of their structure and the nature of their secretion into two types:

1) Eccrine sweat glands which are distributed over the entire body surface except for the lips and part of the external genitalia.

2) Apocrine sweat glands which are limited to the axilla, areola, and nipple of the mammary gland; skin around the anus; and the external genitalia. The ceruminous glands of the external acoustic meatus canal and the glands of eyelashes (glands of Moll) are also apocrine type glands.

Eccrine sweat glands are simple coiled unbranched glands that regulate body temperature. It consists of two parts: 1) a secretory portion located deep in the dermis or in the upper part of the hypodermis and a directly continuous, 2) less coiled duct that leads to the epidermal surface.

Three cell types lying on basement are present in the secretory portion of eccrine sweat gland:

1) clear cells;

2) dark cells, both of which are secretory epithelial cells, and

3) myoepithelial cells, which are contractile epithelial cells.

Clear cells are characterized by abundant glycogen, numerous mitochondria, sER, and a relatively small Golgi apparatus. These cells produce the watery component of

sweat.

Dark cells are characterized by abundant rER, relatively large Golgi apparatus and secretory granules in apical cytoplasm of cells. They are features of glycoprotein secretion of these cells.

The duct of eccrine sweat glands composed of stratified cuboidal epithelium, consisting of: 1) a basal cell layer and 2) a luminal cell layer. The duct cells are smaller and appear darker than the cells of the secretory portion of the gland. Also, the duct has a smaller diameter than the secretory portion. In contrast to the secretory portion of the eccrine gland, the duct portion does not possess имеют myoepithelial cells.

Resorption of some of the sodium and water in the duct results in the release of a hypotonic sweat at the skin surface.

Apocrine sweat glands

Apocrine glands are large-lumen tubular glands associated with hair follicles. The connection to the follicle is allowed the secretion of the gland to enter the follicle, typically at a level just above the entry of the sebaceous duct. Like eccrine glands, apocrine glands are coiled tubular glands. They are sometimes branched. The secretory portion of apocrine glands has a wider lumen than that of eccrine glands and is composed of only two types of cells:

1) secretory epithelial cells, and

2) myoepithelial cells, whose contraction facilitates expulsion of the secretory product from the gland.

Apocrine glands become functional at puberty, because their development depends on sex hormones. Apocrine glands produce a protein-rich secretion containing pheromones. Male pheromones (androstenol and androstenone) in the secretion of apocrine glands have a direct effect on the female menstruation cycle. Female pheromones (copulins) influence male perception of females and may also induce hormonal changes in males.

MAMMARY GLANDS

The compound branched tubule-alveolar mammary glands, derived from modified sweat glands in the epidermis, lie in the subcutaneous tissue. The mammary gland is

composed of 15 to 20 irregular lobes separated by fibrous bands of connective tissue.

Until puberty, both females and males mammary glands develop in similar fashion. At the onset с начала of puberty in males, testosterone acts on the mesenchymal cells to inhibit further growth of the mammary gland. In the same time, the mammary glands in women undergo further development under hormonal influence of estrogen and progesterone. Estrogen stimulates mesenchymal cells further development. The mammary gland increases in size, mainly due to the growth of interlobular adipose tissue.

Every lobe of mammary gland further is subdivided into lobules known as terminal duct lobular units (TDLUs). Abundant adipose tissue is present in the dense connective tissue of the interlobular spaces.

By adulthood, the complete ductal system of the gland has been established. Each gland ends in a lactiferous duct that opens through a constricted orifice into the nipple. Each lactiferous duct has a dilated portion, called the lactiferous sinus.

Near the nipple , the lactiferous ducts are lined with stratified squamous keratinized epithelium, which shows a gradual transition to two layers of cuboidal cells in the lactiferous sinus and finally to a single layer of columnar or cuboidal in the intralobular collecting ducts and terminal ductules.

TDLU is structural and functional component of the mammary gland.

TDLU consists of the following components:

1) a cluster of small secretory alveoli (in lactating gland) or terminal ductules (in inactive gland);

2) the intralobular collecting duct which carries alveolar secretions into the lactiferous duct;

3) The intralobular stroma which is specialized hormonally sensitive loose connective tissue that surrounds the terminal ductules and alveoli. The intralobular loose connective tissue contains little adipose cells.

During pregnancy and after birth, epithelium of the terminal ductules, which is lined by secretory cells, differentiates into fully functional secretory alveoli producing milk. Mammary ducts and alveoli are covered by epithelium including two main types of cells:

1) Glandular epithelial cells, producing milk after birth;

2) Myoepithelial cells laying between the glandular epithelial cells and the basal lamina. These cells, arranged in a basketlike network in the secretory portions of the gland. Contraction of myoepithelial cells assists in milk ejection during lactation.

The secretion of mammary glands released in the first few days after childbirth is known as colostrums. This premilk is an alkaline, yellowish secretion with a higher protein, vitamin A, sodium, and chloride content and a lower lipid, carbohydrate, and potassium content than milk. It contains considerable amounts of antibodies (mainly secretory IgA) that provide the newborn with some degree of passive immunity.

Hormonal regulation of the mammary gland during lactation

Production of milk by glandular epithelial cells regulated by hormone called prolactin. Contraction of myoepithelial cells stimulates by hormone called oxytocin.

Nails

A nail is a keratinized plate located on the dorsal aspect of the distal phalanges . The nail plate consists of 2 parts the nail body which is the visible part of the nail and the nail root which is the part hidden in a fold of epidermis. The epithelium of the fold of skin covering the nail root consists of the usual layers of epidermis. The stratum corneum of this epithelium forms the eponychium or cuticle. The nail plate also corresponds to the stratum corneum of epidermis. The nail plate contains closely packed interdigitating corneocytes lacking nuclei and organelles.

The nail plate rests on the nail bed forming by stratum basale and stratum spinosum of epidermis. The epithelium of the nail bed arises from the nail matrix.

The matrix contains a variety of cells, including stem cells. The stem cells of the matrix regularly divide, migrate toward the root of the nail, and there differentiate and produce the keratin of the nail. Nail keratin is a hard keratin, like that of the hair cortex. Unlike the soft keratin of the epidermis, it does not desquamate. It consists of densely packed keratin filaments embedded in a matrix of amorphous keratin with a high sulfur content, which is responsible for the hardness of the nail. The process of hard keratin formation, as with the hair cortex, does not involve keratohyalin granules.