Ministry of health Republic of Belarus
Establishment of education “Gomel state medical university”

Department of histology, cytology and embryology

MANUAL

for 1-st year students of faculty of foreign students on gynecology

Topic: 15:

HISTOPHYSIOLOGY OF THE SKIN AND ITS DERIVATIVES

Duration 4 hours

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THE MOTIVATIONAL CHARACTERISTIC OF THE THEME

Skin and its derivatives form an external cover of an organism. It carries out set of different functions. Appearance of skin, temperature, humidity and the hormonal status, deficiency of vitamins, presence and a stage of development of some diseases. Studying of a thin structure of skin and its derivatives forms a basis formation of representation of the doctor about functions of skin in norm and pathology.

THE PURPOSE

Studying of a microscopic and ultramicroscopic structure of skin and its derivatives and their role in functions of protection against harmful influences of an environment and in maintenance of a homeostasis.

PROBLEMS

The student should know:

1) Development of skin and its derivatives.
2) Morphological and biochemical changes during their differentiation.
3) Features of micro-and ultra structures melanocyte, cells of Langerhanse, cells of Merkel. Their origin and functions.
4) Types and a structure of hair.
5) Sweet and sebaceous glands.

The student should be able to be able:

1) Study at a microscopic level layers of skin, their tissue elements and derivative skin, glands and hair).
2) To explain structural features of a skin and its derivatives in various topographical zones in connection with carried out function.

REQUIREMENTS TO THE INITIAL LEVEL OF KNOWLEDGE

For full mastering a theme it is necessary for student to repeat in medical biology and genetics questions on the general cytology.

5. CONTROL QUESTIONS FROM RELATED SUBJECTS

1) The Structure of a cell
2) Life cycle of a cell

CONTROL QUESTIONS ON THE THEME

1) Development and structure of skin.
2) Functions of skin.
3) The Structure of epidermis and its features in various sites of a body.
4) Functions of epidermis
5) The Characteristic of epidermal cells.
6) The Structure and functions derma.
7) Morphological bases skin receptors.
8) The Structure and functions of sebaceous glands.
9) Development and structure of hair.
10) Development and a structure of a nail.
11) Regeneration of skin.

12) The Structure, development and structure of a mammary gland tissue. Cytological bases of a lactation.

THE PRACTICAL PART

1) The Table « the Origin and functions of epidermal cells » – to fill the table (Exercise № 1 in album)

2) The Scheme of a structure of skin – to study and enter designations (Exercise № 2 in album)

3) The Scheme of a structure of a hair follicle – to study and enter designations (Exercise № 3 in album)

4) The Scheme of a structure of a mammary gland – to study and enter designations (Exercise №6 in album)

5) Microscopy and sketch in an album of histological preparations (Exercise 3, 5, 7 and 8 № in album)

SLIDES

1) Skin of the finger

2) Skin with hair

3) Lactating mammary gland

4) Non lactating mammary gland

QUESTIONS FOR SELF-CHECKING KNOWLEDGE

1) Write down in copy-book features of structure of epidermal layers

2) List distinctive features of a structure of a "thick" and "thin" skin.

3) List structural and functional features of the skin glands

HISTOPHYSIOLOGY OF THE SKIN AND ITS DERIVATIVES

The skin is the largest and heaviest organ. It protects against microorganisms, toxic substances, dehydration, ultraviolet radiation, impact, and friction It also acts as a sensory receptor and has a role in excretion, vitamin D metabolism, and regulation of blood pressure and body temperature.

Human skin (the integument) is of 2 types: thick skin, restricted to the palms of the hands and soles of the feet, lacks hairs and has abundant sweat glands, and thin skin, which has hairs, covers the rest of the body. Thick or thin, the skin consists of 2 distinct but tightly attached layers, the epidermis and dermis, which are underlain by the hypodermis [1 – 6].

Epidermis. This outer (superficial) layer of skin, composed of keratinized stratified squamous epithelium, derives from embryonic surface ectoderm. It is avascular, receiving nourishment from vessels in the underlying dermis. Its inner-vation is by unencapsulated (free) nerve endings The epidermal layer is further divided into 5 *strata,* these layers, in order from superficial to deep, are the stratum corneum, stratum lucidum, stratum granulosum, stratum spinosum, and stratum basale. The thickness of these layers differs m thick and thin skin.

The stratum basale is underlain by a basement membrane connecting the epidermis and dermis. It is dermal-epidermal junction. The junction has the appearance of zigzagging interdigitations between upward projections of the dermis-dermal papillae-and downward projections of the epidermis-epidermal ridges [3].

Dermis. This inner (deeper) layer is a vascular connective tissue of meso-dermal origin It can be further divided into a superficial papillary layer and a deeper reticular lay-er The papillary layer contains extensive capillary networks, which nourish the epidermis The reticular layer contains many arteriovenous anastomoses that help regulate blood pressure and body temperature It is richly supplied with free nerve endings, a variety of encapsulated sensory receptors, and autonomic fibers that control the vascular smooth muscle Even in thick skin, the dermis is much thicker than the overlying epidermis

Hypodermis. Although not a part of the skin, this layer of mesoderm-derived loose connective and adipose tissue underlying the dermis flexibly binds the skin to deeper structures Its thickness varies, depending on nutritional status, level of activity, body re-gion, and gender The hypodermis is also called the subcutaneous fascia and, where thick enough, the panniculus adiposus [1 – 3].

Structures associated with the **skin.** Glands (sebaceous and sweat), hairs, and nails arise from epidermal downgrowths into the dermis during embryonic development. These structures, which are mainly of epithelial origin, require epi-thelio-mesenchymal interac-tions between the epidermis and dermis for their formation and maintenance.

Epidermis

The epidermis contains two major and two minor cell populations specialized for specific functions. Major populations include the keratinocytes and melanocytes Minor populations include Langerhans' and MerkePs cells.

The keratinocytes make up most of the epidermis They participate in the continuous turnover (renewal) of the skin surface by passing through several overlapping processes: cell renewal, or mitosis; differentiation, keratinization, cell death and exfoliation (the sloughing of dead cells from the skin surface). The entire process takes 15-30 days and oc-curs in waves. A cell layer produced by a mitotic wave in the basal layer undergoes kerat-inization in synchrony Each wave pushes the cell layers produced in earlier waves toward the surface. The layers from several waves, each at a different depth and step in the pro-cess, give a stratified appearance to vertical sections of the epidermis The 5 layers of the epidermis are distinguished by the shape, staining properties, contents, and orientation of the keratinocytes

Stratum basale (stratum germinativum). This single layer of columnar basophilic keratinocytes rests on the basal lamina that separates epidermis from dermls. These cells divide continuously and give rise to the keratinocytes in all other layers They attach to their neighbors by desmosomes and to the basal lamina by hemidesmosomes. Cytokeratin intermediate filaments (tonofilaments) are important components of both junctions. The cytokeratin content increases as these cells approach the stratum coraeum, where it consti-tutes about 50% of their total protein.

Stratum spinosum. This 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 layer. Tonofibrils (tonofilament bundles) fill the cytoplasm, extend into the numerous cell processes that give these cells their spiny appearance, and insert in-to the desmosomes that attach the tips of these processes to those of adjacent cells The mi-totic rate here is lower than in the stratum basale. Mitosis occurs only in the malphighian layer, which includes the stratum basale and stratum spinosum

Stratum granulosum. This lies above the stratum spinosum and, in thick skin, consists of 3-5 layers of flattened polygonal (often diamond shaped) cells that contain numerous membraneless keratohyalin granules. Cells in this layer also contain small ovoid or rod-like lamellar granules. These fuse with the plasma membrane and release their contents (glycosaminoglycans and phospholipids) into the intercellular spaces This material may be important in sealing the deeper layers of the skin from the external environment and in protection from dehydration

Stratum lucidum. This layer overlies the stratum granulosum and is apparent only in thick skin It is a narrow, acidophilic, translucent band of flattened keratinocytes whose nuclei, organdies, and intercellular borders are not visible The cytoplasm contains dense cytokeratin aggregates embedded in an amorphous electron-dense matrix derived from the keratohyalin granules This intracellular mixture of intermediate filaments and matrix constitutes the immature keratin, sometimes called eleidin.

Stratum corneum. The outermost layer, this consists of many layers of dead, plate-like enucleate keratinocytes with thickened plasma membranes These cells represent the final stage of keratinization and are filled with mature keratin, a birefringent scleroprotein. Keratin's substructure includes tonofiiament subunits formed by 3 coiled and intertwined polypeptide chains. Tonofilaments are embedded in and bound together by the amorphous matrix first found in keratohyalin granules. Dead cells are continuously sloughed (exfoliated) from the surface and replaced, through successive waves of mitosis and differentiation, by ceils from the deeper waves [3, 6].

Mainly the pigments melanin and carotene, the thickness of the epidermis, the number of dermal blood vessels, and the color of the blood in those vessels confer skin color. Melanin synthesized by **melanocytes**. Although they are scattered among the keratinocytes of the stratum basale, they are not attached to them by desmosomes. They have round cell bodies, central nuclei, and long cytoplasmic processes that pass between the cells of the strata basale and spinosum and terminate in small indentations on the keratinocyte surfaces. Melanocytes make up 10-25%of this layer's cells but do not participate in keratimzation. They cytoplasm contains many mitochondria, a well-developed Golgi complex, short cisternae of the RER, and special membrane-bound organelles, melanosomes, in which melanin is synthesized. There is no difference in the number of melanocytes per unit area in the skin of dark- and light-skinned races. Rather, differences in skin color reflect differences in the rates of melanin synthesis, accumulation, and degradation [1 – 4].

Langerhans' cells. These star-shaped cells lack tonofilaments and occur mainly in the stratum spinosum (400-1000 cells/mm^2 of skin surface) They stain selectively with gold chloride and contain numerous rodlike or racket-shaped cytoplasmic granules (Birbeck's granules). They are thought to be antigen-presenting cells that process and present to the lymphocytes any antigenic material that penetrates the skin's surface of mesodermal origin, they arise in bone marrow and may belong to the mononuclear phagocyte system Langerhans'cells also occur in oral and vaginal epithelia as well as in the thymus [1 – 3].

Merkel's cells. Scattered in the stratum basale, these cells are most numerous in thick skin. They resemble basal keratinocytes but have a clearer cytoplasm containing many small dense granules Free nerve endings form a disk-like expansion (Merkel's disk) that covers the basal surface of each Merkel's cell. This arrangement suggest that the cells function as sensory mechanoreceptors, but other evidence suggests that they may have neuroendocrine related functions.

Derm

The dermis, which contains the hair follicles, sebaceous and sweat glands, consists of 2 layers of connective tissue that blend at their common border.

Papillary Layer: This layer of loose connective tissue, rich in elastic fibers, lies directly beneath the epidermal basement membrane. Its projections – dermal papillae – interdigitate with the epidermal ridges, increasing the area of contact. The papillary layer contains immunoprotective cells, a rich capillary network, and abundant free nerve endings, some of which penetrate the epidermis. The tips of many dermal papillae contain encapsulated touch receptors called Meissner's corpuscles.

Reticular Layer. Beneath the papillary layer is a thicker layer of dense irregular connective tissue. Also richly vascularized, this layer contains many arte-riovenous anastomoses, or shunts, that control the amount of blood reaching the papillary capillaries and thus aid in regulating heat loss and blood pressure The reticular layer also contains a rich supply of nerves in both free and encapsulated endings (e.g., Pacinian corpuscles) [2 – 3].

Blood supply to the skin

Although the epidermis is avascular, the skin still receives an extensive vascular supply through the dermal blood vessels, which can hold about 4 5% of the body's total blood volume.

Arterial plexuses. One of the 2 arterial plexuses that provide the skin's blood supply lies at the border between the papillary and reticular layers of the dermis The other lies at the border between the dermis and hypodermis. Both give rise to arterioles that feed the papillary capillaries.

Papillary capillaries. The dermal papillae, which surround the epidermal ridges, contain a rich capillary network that provides oxygen and nutrients to the avascular epidermis.

Venous Plexuses. The capillary bed in each papilla drains, by a single venue, into one of 3 venous plexuses. Two of these lie in the same position as the arterial plexuses, the other lies between them in the middle of the reticular dermis.

Arteriovenous anastomoses (Shunts). Within the dermal plexuses there are many anastomoses-direct cormections-between the arteries and veins. Postgan-glionic autonomic fibers control the opening and closing of these shunts, helping to control blood pressure and body temperature by regulating the amount of blood in the papillary capillaries. When the shunts are closed, more blood flows through the papillary capillaries, when open, they direct blood away from the capillaries, increasing blood volume in the larger vessels and thus increasing the blood pressure. Opening the shunts also reduces the loss of body heat through the skin [1 – 3].

Hairs

Hair occurs only in thin skin, its color, size, shape, and distribution vary according to race, age, sex, and body region. The structures in skin that form hairs and maintain their growth are called hair follicles.

Follicle and Hair Development

Follicles. Early in the third month of human development, local epidermal thickenings form at the sites of future hairs first on the eyebrows, chin, and upper Up and then over the rest of the thin skin. Cells at the base of each thickening invade the dermis, and a small dermal papilla invades the leading edge of the epidermal downgrowth. Interactions between the papilla and the invaginating epidermis induce the differentiation of the hair follicle. Hair begins to form in the hair bulb at the base of the hair follicle as a result of the keratinization of the bulb's epithelial cells. These cells are pushed toward the surface by the mitosis in the germinal matrix (hair bulb epithelium) Some epithelial cells in the walls of the developing follicle divide, forming bulges that differentiate into sebaceous glands.

By the fifth or sixth month of gestation, the fetus is covered by fine hairs (lanugo). Just before birth, most of the lanugo is shed, except for the scalp, eyebrows, and eyelashes. A few months after birth, coarser mature terminal hairs have replaced the remaining lanugo; the rest of the body is covered with a coat of fine short hairs, called vellus. At puberty, coarse terminal hairs replace the vellus in specific body areas. In males, terminal hairs develop in the axilla and pubic region, on the face, and, to some extent, over the rest of the body. In females, they develop mainly in the axilla and pubic regions.

Follicle and Hair Structure. Hair follicles extend from the surface deep into the dermis or hypodermis. The follicle's broad base, or hair bulb, consists of a cap of rapidly dividing epithelial cells (the germinal matrix) overlying a dermal papilla that harbors the nerve and blood supply Cells from the germinal matrix keratinize, forming the concentric layers of the hair shaft as they move toward the surface Near the surface, distinct layers can be seen ensheathing the canal that contains the hair shaft.

Germinal matrix. This cluster of epithelial cells capping the dermal papilla can be divided into 4 indistinct zones that are arranged concentrically around the papilla The zone closest to the papilla resembles the stratum basale of the epidermis In both structure and function. It contains both columnar epidermal cells and the melanocytes that give the hah* its color. This germinal layer gives rise to the poorly keratinized cells of the medulla of the hair shaft and to the cells in the other 3 zones of the germinal matrix Around the base of the bulb, this layer is continuous with the external root sheath that surrounds the entire bulb and shaft, near the surface, it is continuous with the stratum basale Cells in the next layer form the cuticle. The most peripheral layer of the germinal matrix forms the poorly keratinized cells of the internal root sheath [6].

Hair shaft layers. The germinal matrix forms these 3 concentric layers. The cell borders are indistinct, however, and cross sections through hair follicles near the skin surface often do not show the cellular nature of these layers In addition, the hair itself may be dislodged from the canal during tissue processing, leaving only the open space (follicular canal) originally occupied by the shaft The medulla forms the shaft's thin central core It is composed of poorly keratinized and often vacuolated cells. The cortex surrounds the medulla and is composed of several layers of well-keratinized polygonal cells. The cuticle is the shaft's outermost layer. Within the bulb, its cells are cuboidal, farther up the shaft they become tall columnar, fill with keratin, and finally change their orientation to become a few layers of flattened, highly keratinized cells. These cells form the hard, shinglelike cuticle that covers the hair's outer surface.

Root sheaths. The concentric sheaths surrounding the hair shaft are more clearly distinguished m the area between the bulb and the skin surface.

Internal root sheath. The layer closest to the hair shaft, it extends only from the bulb to the level of the sebaceous gland ducts At this point the soft kera tin-filled cells are shed into the follicular canal. There arc 3 component layers the cuticle of the internal root sheath is a layer of flat cells separated from the hair shaft cuticle only by the folHcuIar canal, the middle layer is Huxley's layer, comprising one to 3 layers of low cuboidal cells, the outermost layer is Henie's layer, a translucent layer of flattened to cuboidal cells resembling the epidermal stratum lucidum

External root sheath. This surrounds the internal root sheath and is continuous with the epidermis. Above the level of the sebaceous glands, it includes all the epidermal layers. Below this level, it retains only the granulosum, spinosum, and basale. The granulosum is also tost near the follicle's base, where the spinosum and basale become continuous with the layers of the germinal matrix [2, 3].

Glassy membrane. This is the thickened basal lamina underlying the stratum basale of the external root sheath and separating it from the surrounding connective tissue sheath.

Connective tissue sheath. A layer of condensed connective tissue, this surrounds the entire follicle, including the bulb It extends along the follicle to the surface, where it blends into the looser papillary dermis.

Associated structures. Found near the neck of the root sheath, sebaceous glands always accompany hairs. They empty their secretions via a short duct into the follicular canal. *Arrector pili muscles* are small bundles of smooth muscle fibers that originate in the papillary derails and extend obliquely toward the hair follicle to insert into the follicle's connective tissue sheath below the sebaceous glands When they contract, these muscles cause the hairs to stand upright, giving the appearance of gooseflesh. Their contraction also compresses the sebaceous glands, pushing their secretions into the neck of the follicular canal and out onto the surface of the skin [1 – 3].

Nails

Nails are plates of highly keratinized cells, which are analogous to the stratum corneum. The formation of the nails is similar to that of hair, but involves producing plates rather than cylinders At the end of the third month of embryonic development, a narrow plate of epidermis on the dorsal surface of the terminal phalanges invades the underlying dermis of each finger and toe This invasion continues proximally, forming a furrow called the nail groove. Epithelial cells beneath the groove proliferate to form the nail matrix, whose composition and function are similar to those of the hair's germinal matrix Proliferation |n the nail matrix pushes the upper cells toward the surface. These cells differentiate, becoming highly keratinized to form the nail plate. The plate is gradually pushed out of the groove by further cell proliferation and differentiation in the **nail** matrix. The growing plate slides distally on the dorsal surface of the digit. The epidermis over which it slides becomes the nail bed [4 – 6].

Nail Complex Structure. The nail plate (or nail) consists of 2 parts the nail body (the visible part of the nail) and the nail root – the part hidden in the nail groove. The nail and its supporting structure are surrounded by papillary dermis The nail matrix is a thickened region of epidermis containing proliferating cells in the layer that directly contacts the dermis, and keratinizing cells between this basal layer and the nail plate The nail matrix surrounds the root and extends beyond the nail groove The nail bed lies beneath the nail body, distal to the nail matrix It consists of only the deeper epidermal strata, for which the nail serves as a stratum comeum.

The eponychium (or cuticle) is a thick keratinized layer extending from the upper surface of the nail groove over the most proximal part of the nail body The hyponychium is a local thickening of the stratum corneum underlying the free (distal) end of the tail The lunula is the whitish, opaque, crescent-shaped region on the proximal nail body, adjacent to the nail groove. Its distal border corresponds roughly to the underlying nail matrix [3].

Sebaceous gland

These exocrine glands occur in all thin skin, most often in association with hair follicles into which their ducts empty, but are most numerous in the skin of the face, forehead, and scalp In hairless skin, they open directly onto the surface Their acinar secretory portions contain many large lipid-filled cells that appear pale-staining and foamy.

Function. The acinar cells of sebaceous glands fill with lipid droplets containing a mixture of triglycerides, waxes, squalene, and cholesterol and its esters Their nuclei become pyknotic, and the cells eventually burst, releasing their contents and other cell debris (together termed sebum) into the ducts. The entire cell is shed, a type of secretion known as holocrine secretion. The oily sebum moves through the ducts and Into the hair follicle It covers the hair and moves out onto the surface. Here, it lubricates the skin and may have some antibacterial or antifungal effects. The secretory activity of these glands, which begin functioning at puberty, is continuous and is increased by androgens [1 – 3].

Sweat gland

Two types of sweat glands, eccrine (or merocrine) and apocrine, occur in human skin. Both develop as epidermal invaginations into the dermis, and they differ mainly in their size, distribution, and secretory products.

Eccrine Sweat Glands are the most numerous sweat glands in humans, these average about 3 million per individual. They occur over most of the body, except for the glans penis, glans clitoridis, and the vermillion border of the lips. They are most abundant in thick skin, such as the palms, where there are about 3000 per square inch. They are simply coiled tubular giands.

Ducts. The slightly coiled ducts are lined with simple to stratified cuboidal epithelium, their lining cells are smaller than those in the secretory portions and stain darker Each duct opens directly onto the skin surface.

Secretory portions. These highly coiled parts of the sweat glands are located in deep reticular dermis or shallow hypodermis. Surrounding connective tis sue condenses to form a sheath around the basal 1amina. and there are numerous myoepithelial cells between the basal lamina and the secretory cells. The secretions are released via exocytosis (merocrine secretion). Secretory cells are larger and stain lighter than the duct lining cells. Two secretory cell types are seen. Dark (mucoid) cells are pyramidal and line most of the gland's secretory portion, their bases do not reach the basal lamina They contain rodlike mitochondria, a well-developed Golgi complex, RER, many free ribosomes, and dark glycoprotein-containing granules. Clear cells are also pyramidal. They lack secretory granules, contain abundant glycogen, and surround the inner layer of dark cells. Their basal plasma membranes., which do contact the basal lamina, are highly infolded, suggesting a role in ion and water transport. Eccrine sweat is a watery secretion whose main components (besides water) include NaCl, urea, ammonia, and uric acid. The glands thus assist in excreting by-products of protein metabolism In addition, evaporation of water from the skin surface reduces body temperature by cooling the blood in the papillary capillaries.

Apocrine Sweat Glands

Less numerous than the eccrine type, these glands occur mainly in the axilla, pubic and anal regions, and the areolae of the breasts. Apocrine sweat glands are also simple coiled tubular glands, but are generally larger than eccrine glands

Ducts. These coiled ducts are lined with low cuboidal epithelium and open into hair follicles [3].

Secretory portions. Coiled and embedded in the dermis, each has a wide lumen lined by cuboidal to columnar cells. Myoepithehal cells are present between the secretory cells and the basal lamina. Apocrine sweat is a viscous, odorless fluid that, once secreted, acquires a distinctive odor as a result of bacterial degradation. The term apocrine derives from early evidence that the secretory cells of these glands released their apical cytoplasm along with the secretory product. Recent evidence, however, argues against apical shedding. Therefore, although the secretory products of apocrine and eccrine sweat glands do differ, their mode of secre-tion-merocrine-is similar [4 – 3].

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