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Morphology and histology of skin

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Annotation: The article presents lecture material on the study of the morphological and functional characteristics of the skin and its derivatives, which are included in the modern range of active and interactive forms of teaching histology in order to effectively form the professional competence of future doctors in the specialties "General Medicine", "Pediatrics" and "Stomatology", as well as students of biological sciences faculties.

Key words: histophysiology, histochemistry, skin, epidermis, dermis

The skin covers the surface of the body and is the largest organ. Skin functions: protective (mechanical, radiation, chemical, biological); receptor; participation in water-salt metabolism (through sweating); excretory; participation in thermoregulation; metabolic; depositing, etc. The importance of the barrier function of the skin is clearly demonstrated in case of its insufficiency. For example, large area burns lead to increased transepidermal water loss, dehydration, kidney failure and shock, sometimes these consequences are not compatible with life [1; 2].

Sources of development in embryogenesis. The skin ectoderm gives rise to the epidermis, the mesenchyme is the source of development for the dermis, blood and lymphatic vessels, and the neuroectoderm gives rise to nerve structures, receptors, and some cells of the epidermis (melanocytes and Merkel cells).

Morphofunctional characteristics of the skin

1. Anatomy. The total area is

1.5 - 2 m2, weight - 3 - 5 kg (the heaviest organ in the human body). Consists of two parts - epidermis and dermis. Under the skin is the hypodermis, which is formed by adipose tissue, organized in the form of lobules, separated by layers of loose connective tissue. Provides skin mobility. It plays the role of a depot for lipids, hormones, vitamins. Takes part in thermoregulation (limits heat loss by the body).

2. Histology. The epidermis is a stratified squamous keratinized epithelium, in which 5 layers are distinguished: basal (contains cambial elements), prickly, granular, shiny and horny (formed by flat horny scales).

The epidermis is formed by several types of cells: keratinocytes (in the process of differentiation they turn into horny scales), melanocytes (synthesize and accumulate melanin pigments), Merkel cells (perform the function of mechanoreceptors), Langerhans cells (which are part of the skin's immune system) and resident CD8 + T cells memory [3; four; five]. The basement membrane has a tortuous contour (epidermal ridges alternate with dermal papillae). This increases the strength of the connection between the epidermis and the dermis and increases the area of mutual exchange of substances. An important component of the epidermis is CD44, an epidermal transmembrane glycoprotein thought to play a regulatory role in keratinocyte proliferation and maintain local hyaluronic acid homeostasis. With age, its content decreases, which leads to thinning of the epidermis and a decrease in skin elasticity. During natural aging, the basement membrane thickens, while the collagen content in it decreases, which in turn leads to skin fragility [6]. The renewal period of the epidermis is 20-90 days (depending on the area of the skin, age, and other factors).

Derivatives of the epidermis are sebaceous and sweat glands, nails, hair.

The dermis includes two layers: papillary (formed by loose connective tissue) and reticular (made of dense, unformed connective tissue, which gives strength to the skin). Cellular composition: fibroblast cells, macrophages, immature dendritic cells (DC), mast cells and some resident CD4+ memory T cells. It also contains sebaceous and sweat glands, blood and lymphatic vessels, fat cells, most receptors, nerve fibers. Recently, a previously unknown type of cells, telocytes, was discovered in the dermis. The characteristic features of these cells are small size, large elongated nucleus, a small amount of cytoplasm and the presence of several long thin and thick processes - telopodia and the ability to express CD34 and

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PDGFRα antigens (which allows them to be distinguished from fibroblasts and Langerhans cells, with which they have an external resemblance) . There are reasons to believe that telocytes perform a trophic function in relation to the stem cells of the epidermis, and also take part in the regulation of fibroblasts and other cells of the connective tissue of the dermis.

With age, significant changes are observed in the dermis both in the organization and in the architecture of most of the component molecules of the extracellular matrix.

Skin aging is also characterized by elastosis, an aberrant deposition of dystrophic elastic fibers in the papillary and reticular dermis, more often due to loss of oxytalan [7].

It is now well known that ultraviolet and infrared radiation affects gene expression both in keratinocytes and in fibroblastic cells, leading to the formation of wrinkles [8].

Genes encoding matrix metalloproteinases (MMPs), zinc-dependent endopeptidases, are able to remodel the main components of the extracellular matrix of the ECM dermis [9]. When these genes are inhibited, at least three signaling pathways are activated: the mitogen-activated kinase pathway (MAPK), the stress-activated kinase pathway (SAPK), and the p38 pathway. MAPK activation induces increased transcriptional expression of activator protein 1 (AP-1), which regulates the expression of MMP genes [10].

Normal human skin, containing the two pro-oncogenes c-jun and c-fos, constantly expresses high levels of c-fos and junD. Under UV and IR irradiation, as well as the development of oxidative stress, an increase in the number of amino acid chromophores (Trp, Tyr, Phe, His and Cys) is observed.

The color of the skin and hair is due to melanin pigments - pheomelanin (yellow, red, brown) and melanin (black).

3. The structure of the hair. There are three types of hair: vellus, bristly and long. The hair consists of a shaft and a root, located respectively above and below the surface of the skin. The rod is covered on the outside with horny scales that form the cuticle. The cambial elements responsible for hair growth and regeneration are localized mainly in the lower part of the hair root near the hair papilla. Graying of hair is associated with a decrease in the content of pigments and the accumulation of air bubbles in the medulla.

The muscle that raises the hair is formed by smooth muscle tissue. One end is attached to the hair bag, the other is woven into the connective tissue of the papillary dermis.

4. Innervation of the skin. Afferent (sensitive). Skin receptors are divided into three groups according to their functional characteristics: tactile, thermoreceptors, pain.

A. Tactile receptors recognize different types of stimuli (touch, pressure, vibration, tickling), and also provide touch in areas of the hairless part of the skin. Types of tactile receptors: 1) free nerve endings; 2) Merkel disks; 3) Meissner bodies; 4) Vater-Pacini bodies; 5) hair follicle receptors.

Receptor apparatuses of various specializations are unevenly distributed over the entire skin surface: there are an average of 25 tactile receptors per 1 cm2, 150–200 pain receptors, 10–13 cold receptors, and 1–2 thermal receptors.

Studies carried out in recent years have demonstrated the important role of papillary lines in the functioning of the skin analyzer. Thus, it was found that the skin, while maintaining papillary patterns, distinguishes a distance between two points equal to 0.01 mm, while skin devoid of papillary patterns registers a change in external pressure between two points only at a distance of 1 mm. It is assumed that the mechanism of this phenomenon lies in the fact that regular lines on the surface of the skin work as a frequency filter, due to which the signal from an external stimulus to tactile receptors is transmitted in the optimal frequency range for perception. In this case, the greatest efficiency of the system functioning is achieved when the stimulus object moves perpendicular to the papillary lines. It is with this circumstance that the fact of their organization in the form of loops is associated (when moving the fingers in any direction, part of the lines will necessarily be oriented at a right angle with respect to the stimulus).

B. There are two types of thermoreceptors: thermal (40 - 420°C), represented by Ruffini bodies; structure: encapsulated, multiply branching nerve endings; cold (25 - 300°C), represented by Krause flasks; structure: encapsulated branching nerve endings; free nerve endings.

It has been shown that accumulations of thermoreceptors form in the skin a mosaic of heat and cold spots (approximately 1 mm in diameter), the highest concentration of which is observed in certain areas

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of the face (lips, nose, forehead). In this case, cold receptors are located mainly in the superficial layers of the skin (about 0.17 mm), while heat receptors are somewhat deeper (about 0.3 mm).

B. It is believed that there are no specific pain receptors. Their function is performed by free nerve endings - nociceptors (from Latin nocens "harmful"), widely distributed in the skin, muscles, joints, periosteum, internal organs, which are the dendrite terminals of a sensitive neuron. A characteristic feature of pain receptors is their high sensitivity to specific humoral factors - algogenic substances that are released when tissues are damaged or inflamed. These factors are divided into tissue (histamine, serotonin, acetylcholine, hydrogen, potassium, calcium ions, etc.), plasma (bradykinin, etc.), neurogenic (substance P, neurokinin, etc.). These humoral agents are thought to alter the ion permeability of the nerve ending membrane.

Efferent (motor) innervation is represented by sympathetic postganglionic fibers of the autonomic nervous system, ending in the smooth muscles of the vessels, the muscles that raise the hair, and the sweat glands. It is believed that the latter have dual innervation - sympathetic and parasympathetic.

5. Blood supply to the skin. Arterial and venous vessels form three networks - under the hypodermis, at the border of the dermis and hypodermis, and at the border of the reticular and papillary layers of the dermis. Lymphatic plexuses have the same localization. The vascular network of the skin is organized according to a discrete principle: each of its sections contains its own relatively autonomous microvascular module. Due to this structure of the microcirculatory bed, the presence of numerous arteriolo-venular anastomoses, it is possible to quickly and effectively redistribute blood flow between different regions of the skin (horizontally) or (and) its different layers (vertically), which seems important for the implementation of the thermoregulatory function. The leading role in thermoregulation belongs to the deep venous network of the skin.

Morphological methods for evaluating the skin and its derivatives.

A general morphological assessment of the surgical, biopsy and autopsy skin material with light microscopy is carried out using a routine staining method - hematoxylin and eosin. For the specific identification of cellular and extracellular components of the skin, special methods of histochemical staining can be used (for example: staining with picrosirus red and staining according to Van Gieson for collagen fibers; staining with orcein and Weigert for elastic fibers of tissues [11].

Transmission and scanning electron microscopy is used to analyze the ultrastructural structure of cells, intercellular communications, and the basement membrane (lamina lucida, lamina densa, etc.) [9].

In the last decade, to understand the biology and proteomics of skin components, as well as to visualize the expression of various proteins in normal and in some malignant neoplasms, the immunohistochemical method, FISH, RT-PCR, scRNAseq, etc., have been widely used, the results of which are recorded in public maps of The Human

Protein Atlas.

Participation of the skin in immune and inflammatory reactions in normal and pathological conditions.

Unlike CD4+ T cells, CD8+ T cells are cytotoxic, capable of destroying malignant or infected cells.

They contain MHCI antigens that can secrete cytolytic molecules, including perforin and granzymes, or induce Fas-mediated apoptosis [12]. During memory formation, most cytotoxic CD8+ T cells express the transcription factor T-bet and secrete high levels of IFN-γ. However, some CD8+ T cells synthesize Gata3 and exhibit a type II cytotoxic T cell (Tc2) phenotype with secretion of IL-4, IL-5 and IL-13. In many skin lesions (eg, psoriasis), effector CD8+ memory T cells produce IL-17, IL-22, and IL-17/IFN-γ. The expression of chemokine receptors, the influence of effector lymphocytes, and the absence of cytotoxicity (a decrease in CD49a expression against a background of an increase in IL-17 expression) ensure the maintenance of tissue homeostasis at the site of skin injury.

In an experiment on the skin of mice, it was found that Tc17 promotes wound healing by releasing IL-13 upon recognition of non-classical peptides represented by MHCI (H2-M3) derived from commensal bacteria [14]. In general, CD4+ and CD8+ T cells provide a wide range of highly specific functions, compensatory-adaptive reactions to various types of injuries of an infectious or oncological nature, as well as to the wound process.

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The cytokine imbalance described above is also the reason for the decrease in the production of antimicrobial proteins (AMP) and antiviral proteins (AVP) in the epidermis in atopic dermatitis. This is due to an increase in the level of cytokine T2 against the background of a decrease in IL-17, which leads to low production of AMB by keratinocytes [10], breaking the protective barrier and contributing to the colonization of Staphylococcus aureus, the penetration of microbial pathogens and their immunostimulatory components into the skin and infections caused by this pathogen [9]. Therefore, patients with atopic dermatitis are also at increased risk of developing skin infections caused by viral pathogens, including human papillomavirus, herpes simplex virus, molluscum contagiosum virus, and herpetic eczema [10].

Importantly, impaired skin barrier function also contributes to increased epicutaneous sensitization to allergens and may explain the high incidence of allergy in patients with chronic immune skin diseases.

Melanoma is considered one of the most immunogenic types of cancer, as several specific antigens, antibodies, and functionally active lymphocytes have been identified [22; 23; 24]. Metastatic melanoma responds to immunostimulatory agents such as IFNs and IL-2, and also induces cytotoxic T-lymphocytes associated with antigen-4 (CTLA-4) and PD-1 [11].

The factors of immune antitumor activity include: (1) Treg cells and suppressive cells of myeloid origin; (2) anti-inflammatory cytokines such as tumor growth factor (TGF)-β and IL-10; (3) disruption of tumor antigen presentation by cells, antigen expression, and defects in antigen processing; (4) immune inhibitory molecules such as CTLA-4 and PD-1; (5) amino acid catabolizing enzymes such as arginase and indolamine-2-3-dioxygenase (IDO) [12].

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