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Morphological Features of the Skin

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Abstract: The article presents a lecture material on the study of the morphofunctional characteristics of the skin and its derivatives, which are included in the modern spectrum of active and interactive forms of histology education in order to effectively form the professional competence of future doctors of the specialties "Medicine", "Pediatrics" and "Dentistry", as well as students of biological faculties.

Keywords: 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 its insufficiency. For example, burns of a large area 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 cutaneous ectoderm gives rise to the epidermis, the mesenchyme is the source of development for the dermis, blood and lymph vessels, and the neuroectoderm gives rise to nerve structures, receptors, as well as 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). It consists of two parts – the epidermis and the dermis. Under the skin there is a hypoderm, 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. Participates in thermoregulation (limits heat loss by the body).

2. Histology. The epidermis is a multilayered flat keratinizing epithelium, in which 5 layers are distinguished: basal (contains cambial elements), spiny, granular, shiny and horny (formed by flat horny scales). The epidermis is formed by several types of cells: keratinocytes (turn into horny scales during differentiation), melanocytes (synthesize and accumulate melanin pigments), Merkel cells (perform the function of mechanoreceptors), Langerhans cells (which are an element of the skin's immune system) and resident CD8 + memory T cells [3; 4; 5]. The basement membrane has a sinuous contour (epidermal scallops alternate with dermal papillae). This increases the strength of the connection of the epidermis with the dermis and increases the area of mutual metabolism. An important component of the epidermis is CD44, an epidermal transmembrane glycoprotein, which is believed to play a regulatory role in the proliferation of keratinocytes and supports local homeostasis of hyaluronic acid. With age, its content decreases, which leads to a thinning of the epidermis and a decrease in skin elasticity. In the process of natural aging, the basement membrane thickens, while the collagen content in it decreases, which in turn leads to skin fragility [6]. The period of renewal of the epidermis is 20 – 90 days

(depends on the skin area, 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 mesh (made of dense unformed connective tissue, which gives strength to the skin). Cellular composition: fibroblastic 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, and nerve fibers. Recently, a previously unknown type of cells, telocytes, was discovered in the dermis. The characteristic features of these cells are small size, a 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 PDGFRa antigens (which allows them to be distinguished from fibroblasts and Langerhans cells, with which they have an external similarity). There are reasons to believe that telocytes perform a trophic function in relation to epidermal stem cells, 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 component molecules of the extracellular matrix. Skin aging is also characterized by elastosis, aberrant deposition of dystrophic elastic fibers in the papillary and reticular layers of the dermis, more often due to loss of oxytalan [7]. It is now well known that ultraviolet and infrared radiation affects gene expression in both keratinocytes and 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. Activation of MAPK induces increased transcription expression of activator protein 1 (AP-1), which regulates the expression of MMP genes [10]. Normal human skin containing two pro-oncogenes c-jun and c-fos constantly expresses high levels of c-fos and junD. With 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 coloring of the skin and hair is caused by the pigments melanins – pheomelanin (yellow, red, brown) and eumelanin (black).

3. The structure of the hair. There are three types of hair: fluffy, bristly and long. The hair consists of a rod and a root, located respectively above and below the surface of the skin. The rod is covered on the outside with horny scales forming a 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 the hair is associated with a decrease in the content of pigments and the accumulation of air bubbles in the medulla. The muscle that lifts 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 layer of the dermis.

4. Innervation of the skin. Afferent (sensitive). On a functional basis, skin receptors are divided into three groups: tactile, thermoreceptors, pain.

A. Tactile receptors recognize different types of stimuli (touch, pressure, vibration, tickling), and also provide touch in the areas of the hairless part of the skin. Types of tactile receptors: 1) free nerve endings; 2) Merkel discs; 3) Meissner corpuscles; 4) Vater-Pacini corpuscles; 5) hair follicle receptors. Receptor devices of various specializations are distributed unevenly over the entire skin surface: an average of 25 tactile receptors per 1 cm2, 150-200 painful, 10-13 cold, 1-2 thermal. 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 the distance between two points equal to 0.01 mm, while the 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, so that the signal from an external stimulus to tactile receptors is transmitted in the optimal frequency range for perception. At the same time, the greatest efficiency of the system 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 right angles to the stimulus).

B. There are two types of thermoreceptors: thermal (40 – 420 S), represented by Ruffini corpuscles; structure: encapsulated, repeatedly branching nerve endings; cold (25 – 300 S), represented by Krause flasks; structure: encapsulated branching nerve endings; free nerve endings. It is shown that clusters of thermoreceptors form a mosaic of heat and cold spots in the skin (with a diameter of approximately 1 mm), the greatest concentration of which is observed in certain areas of the face (lips, nose, forehead). At the same time, cold receptors are located mainly in the surface layers of the skin (about 0.17 mm), while thermal 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 Lat. nocens "harmful"), widespread in the skin, muscles, joints, periosteum, internal organs, representing the terminals of the dendrite of a sensitive neuron. A characteristic feature of pain receptors is a high sensitivity to special humoral factors – algogenic substances that are released when tissues are damaged or inflamed. These factors are divided into tissue (histamine, serotonin, acetylcholine, hydrogen ions, potassium, calcium, etc.), plasma (bradykinin, etc.), neurogenic (substance P, neurokinin, etc.). It is assumed that these humoral agents change the ionic permeability of the membrane of nerve endings. Efferent (motor) innervation is represented by sympathetic postganglionic fibers of the autonomic nervous system, ending on the smooth muscles of the vessels, muscles that lift the hair, sweat glands. It is believed that the latter have a double innervation – sympathetic and parasympathetic.

5. Blood supply to the skin. Arterial and venous vessels form three networks – under the hypoderm, at the border of the dermis and hypoderm, and at the border of the reticular and papillary layers of the dermis. The lymphatic plexuses have the same localization. The vascular network of the skin is organized according to a discrete principle: each part of it contains its own relatively autonomous microvascular module. Due to this structure of the microcirculatory bed, the presence of numerous arteriol-venular anastomoses, it is possible to quickly and effectively redistribute blood flow between different regions of the skin (horizontally) or (and) its various layers (vertically), which is 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. The general morphological assessment of surgical, biopsy and autopsy skin material under light microscopy is carried out using a routine staining method – hematoxylin and eosin. For specific identification of cellular and extracellular components of the skin, special methods of histochemical staining can be used (for example: picrosirus red staining and Van Gieson staining on collagen fibers; orsein and Weigert staining on elastic tissue fibers [11]. Transmission and scanning electron microscopy are used to analyze the ultrastructural structure of cells, intercellular communications, and the basement membrane (lamina lucida, lamina densa, etc.) [12]. In the last decade, the immunohistochemical method, FISH, PCR-RV, scRNAseq, etc., have been widely used 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 results of which are recorded in the public maps of The Human Protein Atlas. The skin's involvement in immune and inflammatory reactions is normal and pathological. Unlike CD4+ T cells, CD8+ T cells have a cytotoxic effect, capable of destroying malignant or infected cells. They contain MHCI antigens that can secrete cytolytic molecules, including perforin and granzymes, or cause Fas-mediated apoptosis [13]. 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 the phenotype of cytotoxic T cells of the second type (Tc2) with the secretion of IL-4, IL-5 and IL-13. In many skin lesions (for example, psoriasis), effector CD8+ memory T cells produce IL-17, IL-22 and IL-17/IFN-γ. The expression of chemokine receptors, the effect of

effector lymphocytes and the absence of cytotoxicity (a decrease in CD49a expression against the background of an increase in IL-17 expression) ensure the maintenance of tissue homeostasis at the site of skin damage. In an experiment on the skin of mice, it was revealed that Tc17 promotes wound healing due to the release of IL-13 when recognizing non-classical peptides represented by MHCI (H2-M3) obtained from commensal bacteria [14]. In general, CD4+ and CD8+ T cells provide a wide range of highly specific functions, compensatory and adaptive reactions to various types of damage of an infectious or oncological nature, as well as the wound process. The cyotokine imbalance described above is also the cause of a decrease in the production of antimicrobial proteins (AMB) and antiviral proteins (AVB) 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 AMB production by keratinocytes [15; 16; 17], violating the protective barrier and contributing to the colonization of Staphylococcus aureus, the penetration of microbial pathogens and their immunostimulating components into the skin and infections caused by this pathogen [18; 19]. Therefore, patients with atopic dermatitis are also characterized by an increased risk of developing skin infections caused by viral pathogens, including human papillomavirus, herpes simplex virus, mollusc contagious virus and herpitic eczema [20; 21]. It is important to note that a violation of the function of the skin barrier also contributes to an increase in epicutaneous sensitization to allergens and may explain the high incidence of allergies in patients with chronic immune skin diseases.

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