THE SKIN AS AN ORGAN. STAGES OF SKIN WOUND HEALING

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https://doi.org/10.5281/zenodo.8404806

Annotation. Based on the totality of information presented in the paper, the tasks of reparative regeneration during healing of skin wounds are considered. Regenerative processes depend on the general physiological conditions of the body, which determine the ratio of the components of the extracellular matrix, the proliferation of body tissue by cell division and cell differentiation in the main phases of regeneration. In clinical practice, a large number of drugs acting selectively on tissue repair processes are used. The largest number of drugs among tissue-specific stimulators of regeneration have an effect on the repair of the skin. The final goal of the wound healing process is to restore the external effect of the skin. However, due to individual characteristics, the body cannot always complete wound healing taking into account its aesthetics. The lack of consensus on regeneration issues is one of the reasons for the expansion of the range of tools used, promising not only to heal the wound quickly, but also aesthetically.

This review examines the concepts of skin, as well as the stages of skin wound healing and tissue and cell regeneration.

Keywords: skin, wound treatment, wound healing, regeneration, recovery, regeneration.

Skin as an organ

The skin covers the entire surface of the body of the body and is the largest organ performing various physiological functions. Skin functions: protective (mechanical, radiation, chemical, biological); receptor; participation in water-salt metabolism (by sweating); excretory; thermoregulatory; metabolic; depositing, etc. The importance of the barrier function of the skin can be clearly seen in its insufficiency. For example, burns of a large area lead to increased transepidermal water loss, dehydration, kidney failure and shock, in some cases these consequences are not compatible with life. [1; 2]

Sources of development in embryogenesis. It is known that 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).

According to literary sources, the process of formation of new tissues is the subject of numerous studies and arouses scientific interest in practical medicine. It is proved that almost all tissue structures of the body have the ability to regenerate. The main direction in the issues of tissue regeneration is to identify the factors that stimulate this process and vice versa leading to its suppression. Of particular interest is the restoration of the integrity of the skin in the processes of wound healing. As scientific data and clinical observations accumulate, it becomes clear that all stages of wound healing are interconnected and affect the final functional and cosmetic result [3].

The classic wound healing process

It consists of three phases:

The first phase is exudative or inflammatory. The inflammatory phase lasts about three days. Local reactions of the body are reflected in the form of the release of inflammatory mediators and changes in local microcirculation in tissues. The first vascular reaction consists in stopping bleeding due to vasoconstriction and ends after ten minutes due to activation of the blood clotting system. In this case, platelet aggregation will ensure the initial overlap of damaged vessels. Vasoconstriction is replaced by vasodilation and smooth muscle relaxation occurs in the walls of blood vessels. Platelets stimulate the formation of a blood clot at the site of injury. Due to vasodilation and increased capillary permeability, leukocytes are stimulated to move into the wound area, primarily neutrophil granulocytes and macrophages, whose function is to protect against infection and clean the wound, primarily due to phagocytosis. At the same time, they secrete biologically active substances - mediators that stimulate the cells involved in the implementation of the next phase. At the same time, macrophages play an important role. Their presence in sufficient quantity is necessary for successful wound healing [4].

Monocytes arrive at the site of injury after 24 hours, and then differentiate into macrophages. The main functions of macrophages are phagocytosis, antigen recognition and presentation, immunosuppression, and secretion of immune system mediators [5].

It is macrophages that have a cardinal effect on the course of the secretion of cytokines and growth factors. The duration of the migration is three days. Inflammation is a complex protective reaction of the body, the main task of which is to deactivate the action of the damaging factor. Inflammation is characterized by five symptoms: redness, swelling, pain, fever, dysfunction. Under the action of histamine, serotonin and kinin, arterioles expand, which leads to an increase in local metabolism. The first peak of exudation takes place about ten minutes after the appearance of the wound, the second – about 1-2 hours later. Then there is a local acidosis. It is the shift of the acid-alkaline balance to the acidic side that activates catabolic processes in the wound. Approximately 2-4 hours after the injury, within the framework of inflammatory reactions, the movement of leukocytes begins, which perform phagocytosis of microorganisms. Neutrophil granulocytes predominate in the initial phase of inflammation. The main role of these cells is bacterial phagocytosis. This ensures the primary cleaning of the wound. It is necessary to emphasize the important role of mast cells during wound healing. Mast cells (TC) are a unique cellular element of loose connective tissue. They are located mainly along the blood, lymphatic vessels and nerve trunks, near the glands, as well as under the epithelial layers of the skin and mucous membranes, which are exposed to antigenic influences. Mast cells have broad capabilities to adaptively secrete the necessary amount of biologically active substances depending on the needs of the body, including also mechanisms of regulated gradual degranulation, exocytosis and rapid degranulation [6]. Mast cells are capable of forming various cytokines, lipid mediators that promote the activation of lymphocytes and macrophages, as well as histamine, which affects endothelial cells [7].

The second phase is proliferative, lasts 2-4 weeks. At this stage of reparative regeneration, the extracellular matrix plays the main role. The composition of the extracellular matrix components in the skin is represented by glycosaminoglycans, as well as proteins, collagen, elastin, etc. [4]. This stage is characterized by the formation of a fibrin matrix and fibronectin. Fibronectin regulates the process of structural rearrangement of

extracellular matrix components by binding to procollagen fibrils, takes part in the formation of intercellular contacts through integrins, binding of cells to various substrates. The fibronectin layer is mostly always present in a fresh wound and plays the role of "guiding beams" for migrating fibroblasts to the area of the damaged area, as well as for collagen [8]. Laminin is an adhesive glycoprotein of epithelial and mesenchymal cells, the most important functions of which are acceleration of cell mobility, participation in neoangiogenesis, restoration of the integrity of the basement membrane. Hyaluronic acid promotes water retention in the extracellular matrix, and also functions together with other glycosaminoglycans as a signaling molecule, regulating the synthesis and secretion by fibroblasts and endothelial cells of growth factors and cytokines necessary for further tissue regeneration. Growth factors function as a regular source of cytokines regulating the initial stages of the wound healing process. Angiogenesis begins from the edge of the wound, resulting in the formation of new vascular loops. The permeability of the formed capillaries is slightly higher than that of the other capillaries, due to which an increased metabolism in the wound is maintained. However, these new capillaries have low strength under mechanical loads, so the wound area requires constant protection from injury during recovery [4]. With normal maturation of scar tissue, the vessels subsequently disappear. On day 4, the formation of granulation tissue begins, in the construction of which fibroblasts play an important role. Amino acids serve as a nutrient substrate for fibroblasts. One of the main functions of fibroblasts in the context of reparative regeneration is the production of collagen. Currently, 27 types of collagens are isolated, of which 9 types are found in the skin [9]. Type IV collagen makes up the main part of the basement membranes that delimit the epidermal layer and the dermis. Inhibition of collagen synthesis in case of violations of the assembly of its fibrils inhibits the development of microvessels. Type V collagen is found mainly in the papillary layer of the dermis and around the basal membranes of the vessels. Type VI collagen is defined in the dermis in the form of a dense network. Type VII collagen forms the attachment fibrils of the papillary layer of the dermis. Ultrastructural changes in the extracellular matrix components occur intensively during the wound process. It is known that extracellular matrix molecules bind to growth factors. It is proved that growth factors together with matrix metalloproteinases control the state of the extracellular matrix: growth factors catalyze the production of glycoproteins, while matrix metalloproteinases carry out their destruction of extracellular matrix components, ensuring the existence of the extracellular matrix as a dynamic environment for the existence and movement of cells.

The final phase is the epithelialization phase. During the normal course of the wound process, the number of vascular collaterals decreases and the number of fibroblasts decreases. The wound becomes paler and more inconspicuous. Collagen undergoes constant remodeling. During epithelialization, a balance is established between the process of formation and destruction of collagen fibers. Immediately after the formation of the scar, elastic fibers are formed and the scar is rebuilt. Epithelialization is the process of keratocyte transfer, which occurs at a rate of 1-2 mm / day. Complete epithelialization of the wound occurs within 10-28 days, depending on the nature of the damage. The epidermis serves as a protective barrier for bacteria and reduces the risk of water loss. After epithelialization, there is no longer any need to protect the wound from water. It should be mentioned that newly developed epithelial cells are easily susceptible to injury due to loose fit to the dermis. Bacteria, protein exudate from capillaries and necrotic tissues significantly delay epithelization.

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