МІНІСТЕРСТВО ОХОРОНИ ЗДОРОВ'Я УКРАЇНИ
Харківський національний медичний університет

Module 1.
Clinical immunology and allergology.
Theme 6.
IMMUNOLOGY AND PROCESSES OF REGENERATION OF ORGANS AND TISSUES OF MAXILLO-FACIAL AREA

Manual for practical lessons students having higher Medical education in English majoring in dentistry

Модуль 1.
Клінічна імунологія та алергологія.
Тема 6.
ІМУНОЛОГІЯ ТА ПРОЦЕСИ РЕГЕНЕРАЦІЇ ОРГАНІВ ТА ТКАНИН ЩЕЛЕПНО-ЛИЦЕВОЇ ДІЛЯНКИ

Методичні вказівки до практичних занять студентів медичних вузів з англійською мовою навчання за спеціальністю "Стоматологія"

Затверджено
вченою радою ХНМУ.
Протокол № 1 від 16.01.2014.

Харків
ХНМУ
2015

Module 1. Clinical immunology and allergology. Theme 6. Immunology and processes of regeneration of organs and tissues of maxillo-facial area : manual for practical lessons students having higher medical education in English majoring in dentistry / compl. P. G. Kravchun, V. D. Babadzhan,. I. I. Sokolova, V. I. Zolotaykina. – Kharkiv : Kharkiv State Medical University, 2015. – 16 p.

Compliers P. G. Kravchun,
V. D. Babadzhan,.
I. I. Sokolova,
V. I. Zolotaykina

Модуль 1. Клінічна імунологія та алергологія. Тема 6. Імунологія та процеси регенерації органів та тканин щелепно-лицевої ділянки : метод. вказ. до практ. занять для студентів мед. вузів з англ. мовою навчання за спеціальністю "Стоматологія" / упор. П. Г. Кравчун, В. Д. Бабаджан, І. І. Соколова, В. І. Золотайкіна. – Харків : ХНМУ, 2015 – 16 с.

Упорядники П. Г. Кравчун
В. Д. Бабаджан
І. І. Соколова
В. І. Золотайкіна

I. Actuality of theme

Withing last two decades modern sciense has considerable progress in the of treatment of different injures: the biological mechanisms of healing are set on anatomic, biochemical and molecular levels; the enterprises of medical industry made impact in the benefit of developments of more effective methods of treatment of wounds and, thus, in the necessity of supporting of researches new ways of their healing. Development of new pharmacological drugs in industry of molecular biology and immunology will assist more effective impairment both ordinary and resistant wounds; possibilities of reconstructive surgery became better with development of methods of transplantation of muscular and musculocutaneous shreds, and also microvessel technique for transplantation of free tissue transplants; surgical methods occupy leading direction in treatment of diseases of paradontium. Thus, dentist must use knowledge from clinical immunology in everyday practical work for providing of more high-quality treatment of patients and necessary prophylaxis of complications.

II. Educational aims

General:

1. Learning to evaluate the status of the immune system for patients with different stomatological diseases which require surgical interference.
2. Learning to determine the necessity of setting of immune therapy for treatment of generalized periodontitis (GP) depending on a degree and character of disease.

The preparatory stage

At the beginning of class, the instructor reveals the importance of the subject, defines the main goals and objectives of the lesson, assess the initial level of knowledge by solving tests and oral interviews. Students are given a task to work with patients.

Concrete aims:

To know:

1. By the mechanisms of healing of postoperative wounds of skin, mucous membranes, tissue of alveolar bone (α-II).
2. Mechanisms of adjusting of regeneration and immunocorrection (α-II).
3. Postoperative treatment of patients (α-II).
4. Classification of stimulators of reparative osteogenesis (α-II).
5. Content, indications and stages of guided tissue regeneration (α-II).

To be able

1. From data of clinico-laboratory inspection of GP patient to appoint a coplex treatment in a postoperative period (α-III).
2. To define the necessity of inspection for a clinical immunologist and setting of immune therapy in before- and postoperative period for optimization of regeneration (α-III).

Tests to check the initial level of knowledge:

1. Progressive decrease in the number of microvessels, reduced macrophages and fibroblasts is typical for what phase of wound healing?

A. preparatory *B. regeneration* *C. scarring*

2. Can the periodontal guided tissue regeneration?

A. yes *B. no*

3. Hypertonic solution of sodium chloride, water-soluble ointment base, proteolytic enzymes and drainage can be used for the treatment in which phase of purulent wounds of the maxillofacial area?

A. in the first (preparatory) *C. the third (scarring)*

B. a second (refresh rate)

4. The negative impact on the defense mechanisms prosthesis in the mouth is the following

A. Metal ions (prosthetic alloys) can influence the resident microflora of the mouth

B. Plastics reduce the migration of leukocytes into the oral cavity

C. Molecules of some prosthetic materials capable of combining with proteins and cells to cause allergic antibody synthesis

D. Mechanical effects of prostheses reduces the local protection of the oral mucosa

E. All of the above is true

5. Prosthesis patient who has completed a course of radiation therapy, it is advisable

A. immediately after treatment

B. a year later, after a course of radiotherapy

C. normal (clinical blood test, immunogram) blood picture

D. two months after the end of radiotherapy

E. 6–8 months

6. Immunological processes in the oral cavity can affect the results of

A. cryogenic effect on tissues

B. the action of high temperature on the fabric

C. Ultrahigh frequency therapy

D. radiotherapy

E. all of the above

7. Wound process - is:

A. collection of clinical pathophysiology, biochemical, biological and morphological changes associated with wound healing dynamics

B. damage to tissues and organs in violation of the integrity of their cover, caused by mechanical action

8. What contributing factors can be called decisive in the development of purulent wounds of the maxillofacial region:

A. the number of microorganisms in the wound

B. view microflora in wound detritus

C. structural features of the damaged tissue

D. specificity of reparative processes

9. What bioactive substances secreted by neutrophils possess a higher bactericidal in the wound?

A. cationic proteins *C. lactoferrin* *E. lysozyme*
B. kallikrein *D. ferritin*

10. What inducers of acute inflammation in the oral cavity can stimulate polymorphonuclear leukocytes?

A. immune complexes *C. histamine*
B. microbial toxins *D. norepinephrine*

Correct answers to the test tasks: 1 – C. **2** – A. **3** – A. **4** – E. **5** – C. **6** – E. **7** – A. **8** – A, D. **9** – A, C. **10** – B.

BASIC CONTENT OF THEME

A regeneration (from lat. Regeneratio is a revival) is proceeding (compensation) in the structural elements of tissue instead of lost one. In the biological sense, regeneration is the adaptive process produced in the course of evolution and is inherent in all living. Every living organism requires a functional administration costs substrate material and its recovery. Consequently, the recovery is self-reproduction of living matter, and a reproduction of living reflects the principle of autoregulation and automations of vital functions.

Regenerative restoration of the structure can occur at different levels - molecular, subcellular, cellular, tissue and organ, but always it would be a compensation of structure that is able to perform a specialized function. Regeneration is a restoration of both structure and function. The value of regenerative processes is in the containing of homeostasis.

Restoration of the structure and function can be performed by cellular or intracellular hyperplastic processes. On this basis we distinguish cellular and intracellular forms of regeneration.

For the cellular form of regeneration it is characteristically regeneration by mitotic and amitotic way for intracellular form of regeneration that can be orhanic and intraorhanic, increase in number (hyperplasia) and size (hypertrophy) ultrastructure (nucleus, nucleolus, mitochondria, ribosomes, complex, etc.) and their components. Intracellular form of regeneration is universal because it is inherent in all organs and tissues. However, the structural and functional specialization of organs and tissues in filogenesis and ontogenesis is "selected" for some predominantly cellular form, for others - mainly or exclusively intracellular, for the third - both forms of regeneration.

The prevalence of some form of recovery in certain organs and tissues is determined by their functions, structural and functional specialization. The need to preserve the integrity of the integument explains, for example, the prevalence of cell shape regeneration of the epithelium as a skin and mucous membranes. Specialized feature pyramidal cells of the brain, as well as heart muscle cells, precludes the distribution of these cells and allows us to understand the need for selection in filogenesis and ontogenenesis of intracellular regeneration as the only forms of recovery of the substrate.

These data deny that existed until recent time, the loss of certain organs and tissues of mammals the ability to regenerate, the "bad" and "good" regenerating human tissue, that there is the law of inverse relationship between the degree of differentiation of tissues and their ability to regenerate. It is now established that during the evolution of the ability to regenerate some tissues and organs has not gone away, and took the form (cellular or intracellular), corresponding to their structural and functional identity. Therefore, all tissues and organs are able to regenerate a variety of forms depending on the structural and functional specialization of tissue or organ.

Morphogenesis of regeneration process consists of two phases – proliferation and differentiation. Especially good these phases are expressed in the form of cell regeneration. In the proliferative phase young, undifferentiated cells multiply. These cells are called cambial (from Lat. Cambium – exchange, change), stem cells and progenitor cells.

Each tissue has its cambial cells that differ in proliferative activity and degree of specialization, but one stem cell can be several types of progenitor cells (eg, hematopoietic stem cell system, lymphoid tissue, some representatives of the cellular connective tissue).

In the differentiation phase of young cells mature, they undergo structural and functional specialization. The same replacement of the hyperplasia of ultrastructure by differentiation (maturation) is the basis of the mechanism of intracellular regeneration.

Adjust of the regenerative process

Among the regulatory mechanisms of regeneration we distinguish humoral, immune, nervous, functional.

Humoral mechanisms are implemented both in cells damaged organs and tissues (cellular and intracellular regulators) and beyond (hormones, poetyns, neurotransmitters, growth factors, etc.). Humoral regulators contain keylons (from the Greek. Chalaino – relax) – substances that can inhibit cell division and DNA synthesis, they have tissue specificity.

Immunological mechanisms of regulation are associated with "regeneration information" that carry by lymphocytes. So it should be noted that the mechanisms of immunological homeostasis determine the structural homeostasis also.

Neural mechanisms of regenerative processes associated primarily with the trophic function of the nervous system, and ***functional mechanisms*** – with a functional "demands" of the body tissue, which is seen as a stimulus for regeneration.

Development of regenerative process depends on a number of general and local conditions or factors. The general ones include age, constitution, nutrition, metabolism and hematopoiesis state, local – condition of innervation, blood and lymph tissue proliferative activity of cells, the nature of the pathological process.

Classification.

There are three types of regeneration:

- physiological,
- reparative,
- pathological.

Physiological regeneration occurs throughout hole life and is characterized by constant renewal of cells, fibrous structures, the basic substance of connective tissue. There are no such structures that have not been subjected to physiological regeneration. Where the dominant form of regeneration is cellular, there cell renewal takes place. So there is constant change in surface epithelium of the skin and mucous membranes of the secretory epithelium of the exocrine glands, cells lining the serous and synovial membranes, cellular elements of connective tissue, red blood cells, white blood cells and blood platelets, etc. In the tissues and organs where cell regeneration is absent, such as the heart, the brain, it updates by the intracellular structures. Along with updating cells and subcellular structures there is constant biochemical regeneration, i.e. updating the molecular composition of all components of the body.

Restorative or reparative regeneration observed in various pathological processes that lead to damage of cells and tissues. Mechanisms of physiological and reparative regeneration are the same; reparative regeneration is enhanced physiological regeneration. However, due to the fact that reparative regeneration caused by pathological processes, it is qualitative morphological differences from physiological process. Reparative regeneration can be full and complete.

Complete regeneration or restitution, is characterized by regeneration of the tissue that is identical to the deceased. It develops mainly in tissues where the predominant cell regeneration exists. Thus, in the connective tissue, bones, skin and mucous membranes even relatively large defects body can be replaced by cell division that is identical to died.

Incomplete recovery, or substitution, occur when the defect is replaced by connective tissue scar. Substitution is characteristic of organs and tissues in which intracellular form of regeneration is predominant, and it is combined with cell regeneration. Since the recovery is a restoration of the structure, able to perform specialized functions, sense of incomplete recovery is not in substitution scar defect, but in compensatory hyperplasia of items remaining in the specialized tissue, i.e. there is hypertrophy of the tissue.

Incomplete regeneration is healing scar tissue, hypertrophy occurs as an expression of regenerative process, so it is called regeneration, it - biological sense reparative regeneration.

Regenerative hypertrophy can be done in two ways – by using cell hyperplasia and hypertrophy or hyperplasia of cellular ultrastructure, ie cell hypertrophy.

Restore the initial mass body and its functions mainly through cell hyperplasia occurs in regenerative hypertrophy of the liver, kidney, pancreas, adrenal, lung, spleen, etc.

Regeneration hypertrophy due to hyperplasia of cellular ultrastructure characteristic of the myocardium, brain, i.e. those of a predominantly intracellular form of regeneration. In the myocardium, for example, on the periphery of the scar, which replaced the infarct size, muscle fibers increase significantly, providing their hypertrophy by the hyperplasia of subcellular elements. Both ways of the regenerative hypertrophy are not mutually exclusive, but rather are often combined. Thus, the regeneration of liver hypertrophy is not only by increasing of the number of cells after damage of the body, but also by their hypertrophy. We can not exclude that the regeneration of heart muscle by hypertrophy can occur not only in the form of fiber hypertrophy but also by increasing the number of their constituent muscle cells.

The recovery period usually is not limited by the fact the damaged organ's repratiregeneration takes place. If the effect of pathogenic factors cease to cell death, there is a gradual recovery of damaged organelles. Thus, the expression of reparative reactions should be expanded to include recovery of intracellular processes in dystrophic organs. The conventional idea of regeneration only is a final stage of the pathological process is eparative regeneration is not local, and the overall reaction, covering various organs, but realized fully only in one or another of them.

About a pathological regeneration it is talked in those cases, when as a result of those or other reasons there is perversion of regenerator process, violation of change of phases of proliferation. A pathological regeneration shows up in excessive or insufficient formation of regenerating tissue (hyper- or hyporegeneration), and also in transformation during the regeneration of one type of tissue in other. Examples can be as hyperproduction of connecting tissue during formation of keloid, healing of wounds and metaplasia of epithelium in the cell of chronic inflammation. A pathological regeneration usually develops at violations of general and local conditions of regeneration (violation of innervation, albuminous and vitamin starvation, chronic inflammation and so on).

Mechanisms of wound healing

In the process of healing three biological mechanisms are involved.

Epithelialization – a process in which cells of stratified squamous epithelium move and proliferate, cover defects (with no damage to the depth) of the skin or mucous membranes. Examples - epithelialization of wound healing in place of taking partial depth donor grafts for transplantation of skin, healing abrasions, blisters, burns of I and II grades.

Collection (convergence) wound – a process in which spontaneous closure of skin wounds (with lesions on the depth) or decrease after injury lumen of tubular organs, such as the common bile duct and esophagus.

The deposition of collagen – a process in which fibroblasts are transferred to the injury site and produce a new connective tissue matrix. Intertwined in various ways collagen fibers provide strength and integrity of the scar and well healed all wounds.

Phases of the wound healing.

Coagulation

The emergence of wounds due to trauma or surgical exposure is accompanied by bleeding from damaged vessels. Spasm of the blood vessels occurs almost immediately, resulting in the selection of wound catecholamines. Other vasoactive substances are bradykinin, serotonin and histamine, which are released from mast cells in the surrounding tissue. These chemicals trigger the process of diapedesis, exit the wound blood cells, of which formed a clot.

Clotting factors, released from platelets contribute to the formation of fibrin, which provides hemostasis and serves as a kind of network, which then migrate to the cells involved in inflammation and fibroblasts. Fibrin is the result of running the processes of blood coagulation cascade. No fibrin mesh frame healed scar in place of the wound is not strong. Platelets also produce key cytokines that influence the process of wound healing.

Inflammation

The phase of inflammation is begun with migration in the wound of leucocytes. In the first 24 hours the wound is dominated by polymorphonuclear leukocytes, and later - macrophages and lymphocytes. These cells regulate the creation of emerging scar connective tissue matrix by providing a variety of cytokines that were previously designated as "growth factors".

Fibroplasia - a phase of wound healing is characterized by the synthesis of collagen. It begins in the first 24 hours after injury, but reaches its peak until the 5th day. After a 7-th day collagen gradually decreases. Reconstruction of the wound depends on the balance between the formation of collagen and its degradation. While old collagen fibers break down tissue collagenase, new fibers are synthesized and more tightly intertwined. This process increases durability of the unformed scar.

Cytokines

Cytokines provide mutual communication and cooperation cells. They can play an important role as pharmacological agents used to enhance wound healing. For example, it is known that cytokines control and regulate the formation of connective tissue, healing wounds that do not heal for a long time, engraftment of skin grafts, vascularization, increased bone strength and tendon after restoring their integrity and perhaps even influence the process of malignancy.

PdGF(platelet - derived growth factor) is one of a series of platelet cytokines that trigger several processes involved in wound healing. Moreover,

it stimulates the production of various other wound cytokines. PdGF provides chemotaxis of fibroblasts, macrophages and smooth muscle cells.

TGF-β (transforming growth factor-β) produced by platelets and some other cells, including fibroblasts and macrophages. This important cytokine release collagen synthesis by enhancing the expression of specific matrix genes and by inhibiting production and collagenolytic activity. The result is a significant stimulation of collagen deposition.

Basic FGF (basic fibroblast growth factor) is another cytokine that binds to heparin and heparin-like glycosaminoglycans. This is a potential factor of neoangiogenesis which also causes migration of epithelial cells and accelerates wound contraction.

EGF (epidermal growth factor) – a cytokine that stimulates the division and migration of epithelial cells. It is shown that this cytokine accelerates epithelization of skin wounds in place of taking donor graft for transplantation. These recent data suggest that the activity of EGF can inhibit wound protease and suppression of these proteases allows EGF function.

Metabolism of extracellular matrix.

Extracellular matrix is a complex structure, which interacts variety of different types of cells and other components. Collagen is the main component of the extracellular matrix of the soft tissues, tendons, ligaments and bone matrix. In addition to collagen in the matrix are also present glycosamino-glycans, proteoglycans, fibronectin, laminin and elastin.

Synthesis of collagen

Collagen synthesis begins with the formation of DNA-based corresponding RNA. The second stage of the genetic information in the cell - Stream – occurs on ribosomes rough endoplasmic reticulum. In its final form the collagen molecule consists of three polypeptide chains. In the sequence of amino acids is very common combination "glycine – proline -s ". After assembly of polypeptide chains of specific molecules proline involve in process of hydroxylation. This point is very important because the lack of hydroxylation of proline leads to the formation of unstable collagen fibers. For hydroxylation different cofactors and the presence of a number of substances requires. Lack of ascorbic acid or oxygen gives collagen production leads to insufficient strength of the scar is formed. Collagen is different from all other proteins that undergoes various modifications after its entry into the extracellular space. There is the formation of fibrils and fibers, structural glycoprotein component of which is collagen. Necessary for this process is lysyl oxidase enzyme.

Degradation of collagen

For normal wound healing collagen must not only synthesize but also destroyed. Degradation of collagen gets highly enzyme called tissue collagenase

are synthesized by various cells, including inflammatory cells, fibroblasts and epithelial cells. Collagenase exists in an inactive form, which should be transferred to other active proteases such as plasmin. After collagenase activated, it can be inactivated by complex formation with plasma proteins and tissues a2-macroglobulin.

The main substance of connective tissue.

The main substance of connective tissue composed of proteoglycans and glycosaminoglycans. In recent studies it have been shown that the role of the base material in the process of wound healing is more important than was assumed. Proteoglycans in combination with cartilage act as molecular "shock" absorbers. They provide moisture retention in tissues and are also involved in cytokine production. Hyaluronic acid belongs to a specific glycosaminoglycan. It is very unusual, because it is exposed to sulfates and is not associated with the protein. Glucuronic acid has a higher molecular weight and maintains fluid in the tissues, which contributes to the rapid movement of cells in the matrix and cell differentiation. In adults, it appears early and transient decreases after tissue injury, whereas in the skin and in fetal wounds kept much longer.

Wound contraction

Wound contraction represents one of the most powerful mechanical forces in the body. Regarding the exact biological mechanism underlying this process, there are different, often conflicting, points of view. In addition, surgeons consider the process of wound contraction both a favorable and an unfavorable factor. Even the ancient doctors knew that open skin wounds heal if kept clean and protected with bandages. In the process of healing the wound edges closer together until contact with each other, providing a scarring of wounds.

In many cases, wound contraction, which is a normal active biological process that leads to the formation of contractures - resistant strains involving both cosmetic defect, or dysfunction of the patient. The most dramatic is the contraction of skin and hollow organs. Loss of skin resulting from burns or mechanical injury may be accompanied by contracture, because the process of wound healing edge skin drawn together to close it. If transplanted skin was not used, contracture is formed. This is especially seen in flexion surface of joints, such as the neck or palmar surface of the fingers. But the process is not limited to the skin. Any type of damage of hollow organs such as the esophagus or the common bile duct can start the process of healing contraction, leading to the development of strictures that mechanically break feature a hollow body. Researchers have noted the presence on an open skin wound fibroblast cells, which are components of the cytoplasm, typical for fibroblasts and for smooth muscle cells. These cells are called " myofibroblasts". If strips of granulation tissue from an open wound placed in a tub of water, they are reduced in the presence of agonist function of smooth muscle cells and relax in the presence of

antagonists. Moreover, a large number of myofibroblasts found in human tissues under certain conditions, such as Dupuytren's contracture, burn contracture and contracture capsules around silicone breast implant. Peak number of cells observed during contraction of the scar and after its completion.

All attempts to use pharmacological agents for correcting of wounds convergence were failed. For example, some researchers have tried to slow down the contraction of open wounds with inhibitors of smooth muscle function, such as trotsinat which gave effect only as long as was on the wound surface. Fitting the tires in emerging contracture does not prevent its formation. Once the splint is removed, the powerful biological forces moved wound edges in a position where they would be, if the tire is not imposed. In the surgical treatment of contractures there are some justified principles. First, you must determine whether mature or immature rumen. Mature scar is a soft and malleable, whereas immature scar can not be moved, sealed, hypertrophic and even stressful. Residual myofibroblasts and inflammatory cells try to create contracture during cutaneous graft, as well as with other attempts to close the immature scar. In combat contractures is better to replace defective patches, consisting of skin and subcutaneous tissue, and in some cases - the muscle tissue. Since the flap consists of several components and replaces all soft tissue defect in wound contracture after such transplants are rare. On incomprehensible reason contractures meet rarer after closing of open wounds by a whole skin transplant, than split. In any case before transplantation it follows a splint for the complete opening of wound. It can demand a few months. Splintage it is necessary until in a wound all myofibroblasts will not disappear and the used for setting fire cages. Time during which it must remain imposed tire is determined by means of «clinical estimation», no scientific recommendations on this occasion do not exist.

Epithelialization

All surfaces contacting with the external environment are covered with epithelium. An example is the skin, although the mechanisms of epithelialization are the same throughout the body. The skin is covered with epidermis, which is a stratified squamous epithelium that protects the body from water loss, invasion of microorganisms and injury. Wounds with partial depth of skin damage heal by epithelialization. In this case, there are two basic phenomena: migration and proliferation of epithelial cells. After the destruction of the epithelium forming a blood clot begins. When it dries, a scab forms that protects the deeper layers of the wound. The healing process begins with the migration of epithelial cells, independent of their proliferation. Migration is the dominant process. Epithelial cells grow from the wound edges and the epithelium of hair follicles and sebaceous glands, remaining on the bottom of the wound. Superficial wounds without damaging the basement membrane regenerate very quickly. Deeper

wounds with damage of the dermis, such as, for example, burns, in which the basement membrane is destroyed, can also heal by epithelialization and although it takes longer, the outcome is often satisfactory.

Regardless of the type of damage, migration begins in the basal layer of the epidermis and deep-seated hair follicles and sweat glands. Cells were flattened and send their cytoplasmic processes which penetrate into the surrounding tissue. These cells also lose contact with neighboring cells of the basal layer and begin to migrate. A few days after migration shifted cells begin to divide.

The presence of fibronectin and vitronectin supports migration of epithelial cells. Moreover, a number of growth factors stimulate the migration and division of cells of the epithelium. These are basic fibroblast growth factor, platelet -derived growth factor, T-cell growth factor and epithelial growth factor. Obviously, epithelial cells have a cytoskeleton and can migrate with actin- myosine contractile system. Once the surface is covered with epithelial cells, they return to their typical phenotypic behavior. This return to a normal state can be as a key to understanding the loss of cell contact inhibition in cancer. Epithelialization is most successful with the support of the wound surface when it is wet than dry. Typically, these conditions provide a scab, but those bandages that do not adhere can maintain a moist environment in the wound and make a specific action to strengthen the process of epithelialization.

Bone grafts obtained from donor sites such as the crest of the ilium, femur, containing osteocompetent cells, islets of mineralized cancellous bone, blood clot fibrin and platelets, which are in the bunch. Within hours after transplantation graft begins degranulation of platelets, which are in the bunch, which leads to the release of platelet derived growth factor (PdGF) and transforming growth factor β-1 and β-2 (TGF β-1 and TGF β-2). These factors initiate the process of bone regeneration.

During the first three or four weeks after transplantation graft developing biochemical and cell phase regeneration, clinically expressed in the graft consolidation by combining individual islets and osteoid surface osteoid spongy bone with the host bone bed. In addition, a process of bone formation and osteoconduction. This cell phase is often called the first stage of bone regeneration step or stage of loose bone.

During the first phase cellular regeneration leads to the formation of disorganized loose bone that is structurally very tight formation, but not mature. The bone will be exposed to imminent resorption and replacement in the remodeling. In the end, the first phase of bone regeneration is changing by the second, during which bone cells contains less mineralized and becomes more and more organized structure that resembles lamellar bone.

Osteoclast initiate bone substitution of the first phase on the bone, characteristic to the second phase. Theoretically, the first phase of bone

resorbed by osteoclasts under cycle during normal remodeling and replacement. Histologically, these grafts are long remodeling phase, which resulted in the renewal of the skeleton is normal. During this cycle periosteum is formed and endosteal layer, and the graft is replaced by dense, spongy structure.

Growth and differentiation factors are a class of biological mediators that play a critical role in stimulating and regulating the process of wound healing in the body. Specific growth factors and differentiation regulate key cellular processes, including mytogenesis, chemotaxis, differentiation and metabolism.

All these factors play a major role in the process of osseointegration. Theoretically, the use of growth factors in combination with bone material can enhance and even accelerate the normal process of bone regeneration.

One method, which uses valuable properties possessed by growth factors is to deliver platelet rich plasma (PRP) to the bone graft. Platelets are a rich source of PdGF, TGF β-1 and TGF β-2. Studies have shown that bone marrow cells present in the bone graft to contain such growth factors. In addition, radiographic evidence were obtained that the use of PRP can significantly reduce the time of consolidation and maturation of bone and increase its density.

Mixing PRP with bone material allows the impact PdGF, TGF β-1 and TGF β-2 in the initial stages of regeneration. During the degranulation of platelets PdGF and TGF β are released. It is known that all platelets are destroyed in the wound during the first three to five days, and initial activity of growth factors are exhausted within 7–10 days.

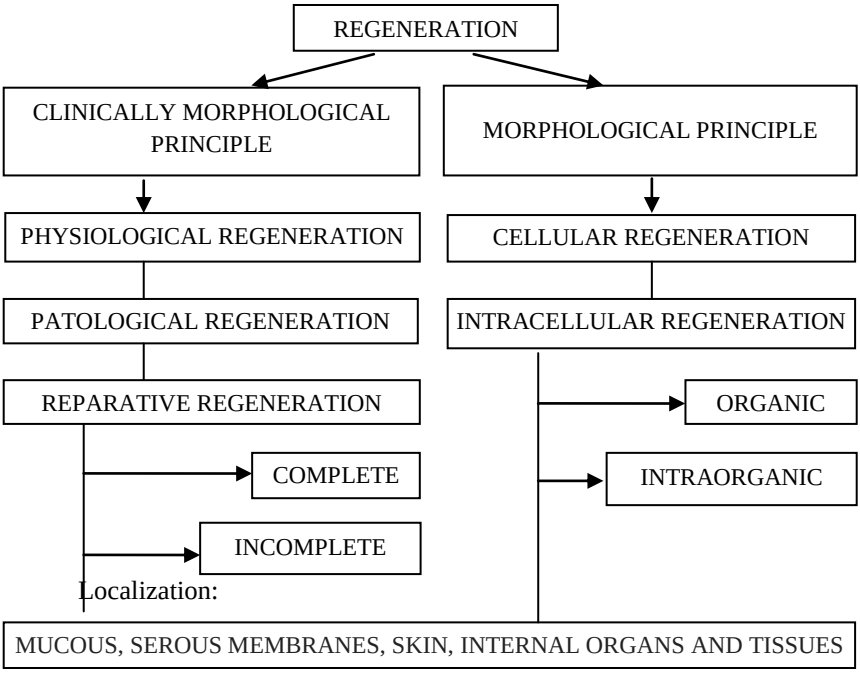
Initial push of PRP initiates "launching" stage of the regeneration cycle, which continues to form the mature graft.

PdGF is one of the most important hormone that is present in all wounds. It initiates the healing of connective tissue, including bone regeneration. PdGF has a strong mitogenic and angiogenic activity, and regulates the activity of other growth factors. Mitogenic effect leads to the formation of a large number of cells involved in the healing and angiogenic promotes the construction of new capillaries.

Activation of other growth factors leads to the induction of fibroblast and osteoblast function, accelerates differentiation of cells and also affects the function of other cells, such as macrophages. In addition, there is evidence that PdGF increases the rate of stem cells proliferation.

TGF β-1 and TGF β-2 are involved in the overall process of tissue repair and regeneration of bone. Their main effect is in the regulation of chemotaxis and mytogenesis progenitor cells and osteoblasts deposition, ability to stimulate collagen matrix for wound healing and bone regeneration. Furthermore, these growth factors accelerate bone formation through the growth rate of proliferation of stem cells and inhibitionof the osteoclasts formation, i.e. bone resorption.

REGENERATION CLASSIFICATION



Fibrin component provides PdGF binding particles of bone material and promotes osteoconduction help create a network that acts as a skeleton that supports the growth of new bone. Moreover, PdGF modulates and improves the functioning of some growth factors in the presence of others.

This ability distinguishes growth factors contained in PdGF from other growth factors that have an independent effect, and meet only a single aspect of regeneration.

The pathogenesis of periodontal diseases are violations of the physiological regeneration of bone of the alveolar process. At a certain stage of ontogeny physiological regeneration of moving to an alternative path – reparative (adaptive) or pathological. Pathological periodontal regeneration is the way a particular outline nosological unit.

Physiological regeneration process occurs on several organizational and structural levels of the body – the intracellular, cellular, tissue and organ. Intracellular physiological regeneration is the primary material basis of all manifestations of life, reflecting the continuously ongoing process of decomposition and synthesis of substances at the molecular and ultrastructural levels. Along with the

continuous renewal of intracellular physiological regeneration inherent in cell shape, in which a change in the cellular composition of tissue by proliferation and differentiation of its components from stem cells to mature. This occurs during the replacement of old forms and osteocytes fybroblasts cells into mature osteoblasts and fibroblasts.

V. Questions to control the preparatory knowledge:

1. What are the anatomical and histological features of periodontal tissue complex?
2. Features of the structure of the epithelium and gingival groove connection?
3. Features of innervation and vascularization of periodontal tissues.
4. What is the purpose of surgical treatment of GP?
5. Indications and stages of gingivectomy
5. Indications and stages of gingivotomy.
6. Indications and stages of gingivoplastic.
7. The method of directed tissue regeneration.

Tests for verification final level of knowledge

1. Phagocytes may be involved in the damage of periodontal own cells as well as in the purification chamber of acute inflammation from infection, is it true?
A. yes *B. no*

2. Wound cleansing of necrotic tissue and microorganisms is the result:
A. phagocytosis *C. fibrillogenesis*
B. extracellular proteolysis *D. wound contraction*

3. Failure to replace the neutrophils monocytes in the wound is accompanied by:
A. amplification process fibroplastic *C. increased tissue decay*
B. fibroplastic braking process *D. limitation of tissue decay*

4. Which cells play a crucial role in the regeneration phase of wound healing?
A. neutrophils *B. eosinophils* *C. fibroblasts* *D. endothelial cells*

5. What phases are isolated in the healing process of face skin wounds?
A. wound contraction (contraction of the edges)
B. wound epithelialization
C. out of the wound gusset growth
D. wound fibrillogenesis
E. the formation of new tissue in the defect and transform them into reclaim

6. Ointments and himopreparatami antiseptics may be used in which phase of festering wounds of the maxillofacial area?
A. in the first (preparatory) *C. the third (scarring)*
B. a second (refresh rate)

Correct answers: 1 – A. **2** – A, D. **3** – B, C. **4** – C. **5** – A, C, E. **6** – B.

Навчальне видання

Модуль 1.
Клінічна імунологія та алергологія.
Тема 6.
ІМУНОЛОГІЯ ТА ПРОЦЕСИ РЕГЕНЕРАЦІЇ ОРГАНІВ ТА ТКАНИН ЩЕЛЕПНО-ЛИЦЕВОЇ ДІЛЯНКИ

Методичні вказівки до практичних занять студентів медичних вузів з англійською мовою навчання за спеціальністю "Стоматологія"

Упорядники Кравчун Павло Григорович
Бабаджан Володимир Данилович
Соколова Ірина Іванівна
Золотайкіна Вікторія Ігорівна

Відповідальний за випуск П. Г. Кравчун

Комп'ютерний набір В. І. Золотайкіна
Комп'ютерна верстка О. Ю. Лавриненко

План 2015, поз. 35.
Формат А5. Ризографія. Ум. друк. арк. 1,0.
Зам. № 15-3251.

Редакційно-видавничий відділ
ХНМУ, пр. Леніна, 4, м. Харків, 61022
izdatknmu@mail.ru, izdat@knmu.kharkov.ua

Свідоцтво про внесення суб'єкта видавничої справи до Державного реєстру видавництв, виготівників і розповсюджувачів видавничої продукції серії ДК № 3242 від 18.07.2008 р.

Module 1.
Clinical immunology and allergology.
Theme 6.
IMMUNOLOGY AND PROCESSES OF REGENERATION OF ORGANS AND TISSUES OF MAXILLO-FACIAL AREA

Manual for practical lessons students having higher Medical education in English majoring in dentistry