Ministry of Health of the Republic of Belarus
Educational Institution
“Gomel State Medical University”

Department of Pathological Anatomy

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METHODICAL GUIDELINES

for conducting a practical class
in the academic discipline “Pathological Anatomy”
for students
of the 3rd year, Faculty of International Students (instruction in English),
enrolled in the specialty
7-07-0911-01 “General Medicine”

Topic: “Healing, compensatory, adaptive, and regenerative processes”

Duration: 3 hours

Approved at the meeting of the Department of Pathological Anatomy
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EDUCATIONAL AND INSTRUCTIONAL GOALS, OBJECTIVES, AND MOTIVATION FOR MASTERING THE TOPIC

Educational Goal:

- To provide a definition of physiological and reparative regeneration, as well as complete and incomplete regeneration. To draw attention to the fact that in incomplete regeneration, the restoration of organ function occurs due to cell hyperplasia and hyperplasia of intracellular ultrastructures outside the zone of injury, i.e., through regenerative hypertrophy. To note that the type and form of regeneration are determined by the nature of tissue damage, in particular, the ability of its cells to proliferate.
- To list the local and general conditions that influence the course of reparative processes. To provide examples of pathological regeneration. To analyze the regeneration of individual tissues. To thoroughly examine the structure of granulation tissue, its cellular composition, and the changes occurring during its maturation.
- To define atrophy, noting the adaptive nature of this process that occurs in organs and tissues under altered conditions of existence.
- To discuss the morphological signs of general atrophy. To analyze various types of local atrophy depending on their causes. To draw attention to the different nature of changes occurring in the parenchyma and stroma of an organ during circulatory disorders. To provide examples of various types of local atrophy.
- To define hypertrophy as an increase in organ volume associated with an increase in cell mass, and hyperplasia as an increase in cell number. To identify the types of hypertrophy. When examining work hypertrophy and vicarious hypertrophy, to draw attention to the compensatory significance of these processes, their reversibility, and the inevitability of decompensation in cases where the causative factor continues to act. To demonstrate the particular significance of work hypertrophy of the myocardium in various diseases of the cardiovascular system, and to discuss the signs of cardiac decompensation.
- To examine the etiopathogenesis of metaplasia and dysplasia, note their types, and particularly emphasize their significance as precancerous conditions. To study the processes of organization and note the classifications of sclerotic processes.

Instructional Goal:

- Within the framework of the educational process for this academic discipline, the student must acquire not only theoretical knowledge, practical skills and abilities in the specialty but also develop their personal potential. They should cultivate qualities of responsibility and patriotism, be prepared to actively participate in the economic, socio-cultural, and public life of the country, recognize the social significance of their future professional activity, understand the norms of medical ethics and deontology, and learn to observe academic and labor discipline. In the course of studying the educational

material, students should realize the importance of maintaining a healthy lifestyle and, as an example in the future, when performing professional duties, set an example for those around them and their patients.

Objectives: Upon completion of the practical session, the student must:

***Know*:**

- The essence of adaptation and compensation;
- The stages of compensatory-adaptive processes and provide their morphological characteristics;
- The definition of various types of compensatory-adaptive processes and explain the mechanism of their development;
- The morphogenesis of the regenerative process, its classification, and the features of regeneration of various organs and tissues;
- The diagnostic criteria of hyperplasia and hypertrophy based on microscopic appearance;
- Atrophy as a manifestation of adaptive processes;
- Metaplasia of epithelium and connective tissue, and be able to diagnose it based on microscopic appearance;
- The process of organization as a manifestation of compensatory-adaptive reactions;
- The functional significance of compensatory-adaptive reactions.

Be able to:

- Identify major general pathological processes and diseases using histological specimens under light microscopy;
- Diagnose pathological processes and diseases based on the description of macroscopic and microscopic changes in organs and tissues of the body.

***Master*:**

- Basic techniques for working with a microscope;
- Skills in clinical-anatomical analysis;
- The fundamentals of synthetic generalization of morphological diagnostic signs of diseases and their correct interpretation in cause-and-effect relationships.

Motivation for Mastering the Topic:

The constancy of the internal environment of the organism, known as homeostasis, is an indispensable condition for its existence. This relative stability of biological systems must be maintained during changes in both the external (surrounding) environment and the internal environment (during the development of pathology). Reactions that ensure the adaptation of the organism to the environment and the survival of the species, developed during phylo- and ontogenesis, are called adaptive reactions. When extreme factors cause damage to some structures of the body, reactions aimed at compensating for impaired functions are triggered; these are called compensatory reactions. Compensation is not the opposite of adaptation – it is a particular form of adaptation, its manifestation in a specific individual. These philosophical concepts relate to each other as the general to the particular. In medicine, the concept of compensation is derived purely logically from the concept

of decompensation (and vice versa): it refers to the restoration of disturbed equilibrium. Consequently, the processes that enable the body to restore lost structures and compensate for impaired functions under pathological conditions can be grouped together under the name "compensatory-adaptive processes." Thus, compensatory-adaptive processes are morphological and functional changes in the body aimed at compensating for lost functions. Unlike injuries, which are hypobiotic processes, these processes are accompanied by an increase or normalization of the level of vital activity and ensure the adaptation of the organism to altered conditions of existence under pathological states. The study of the morphology of processes such as regeneration, hypertrophy, atrophy, and metaplasia will subsequently contribute to a deeper assessment of the essence of a number of diseases, the features of their course and prognosis, and will provide assistance in the practical work of a clinical physician.

QUESTIONS

1. Regeneration. Definition. Pathophysiology. Classification. Clinical examples.
2. Hypertrophy. Definition. Pathophysiology. Classification. Clinical examples.
3. Hyperplasia. Definition. Pathophysiology. Classification. Clinical examples.
4. Metaplasia. Definition. Pathophysiology. Classification. Clinical examples.
5. Atrophy. Definition. Pathophysiology. Classification. Clinical examples.
6. Dysplasia. Definition. Pathophysiology. Classification. Clinical examples.
7. Sclerosis and calcification. Definition. Pathophysiology. Classification. Clinical examples.

COURSE OF THE SESSION

Compensation is a complex reaction of the body that occurs in response to the damaging effect of environmental factors and is aimed at compensating for a defect in an organ or tissue (or at maintaining homeostasis).

Adaptation is a general biological concept that unites all life processes that underlie the interaction of an organism with the external environment and is aimed at preserving the species.

Compensatory and adaptive reactions include:

1. Regeneration.
2. Hypertrophy.
3. Hyperplasia.
4. Atrophy.
5. Metaplasia.
6. Organization.
7. Dysplasia.

Regeneration

Regeneration is the restoration of the structural elements of the damaged tissue.

In a biological sense, regeneration is an adaptive process developed in the course of evolution and inherent in all living things. It can be carried out at the molecular, subcellular, cellular, tissue and organ levels. Regulation of the regenerative process can be carried out with the help of humoral, immunological, nervous and functional mechanisms.

There are three types of regeneration: **physiological, reparative, pathological**.

The cells of most organs and tissues continue to divide and differentiate throughout his life. Normally, growth and differentiation are controlled in such a way that the normal structure of a specific tissue is maintained. In tissues that are characterized by a continuous loss of cells (skin, intestinal mucosa, blood), the cambial cells divide and the resulting cells differentiate and replace cells lost during normal life (**physiological regeneration**). Regeneration is the restoration of both structure and function.

Reparative regeneration

Reparative or **restorative regeneration** is the restoration of cells and tissues to replace those that died as a result of various pathological processes. The mechanisms of reparative and physiological regeneration are similar. However, stimulated by pathological processes, reparative regeneration has some qualitative morphological differences from physiological. Reparative regeneration can be complete or incomplete.

Complete regeneration, or **restitution**, is characterized by the replacement of a defect with tissue that is identical to the damaged one. It develops mainly in tissues where cellular regeneration predominates.

With incomplete regeneration, or **substitution**, the defect is replaced by connective tissue, a scar. Substitution is characteristic of organs and tissues in which

the intracellular form of regeneration predominates, or it is combined with cellular regeneration. In such cases, the function is compensated by hypertrophy or hyperplasia of the cells surrounding the defect.

Pathological regeneration

Pathological regeneration is a perversion of the regenerative process, a violation of the change in the phases of proliferation and differentiation. Pathological regeneration is manifested in excessive or insufficient formation of regenerating tissue (hyper- or hyporegeneration). Examples of it are the formation of **keloid scars**, excessive regeneration of peripheral nerves (**traumatic neuromas**), excessive formation of callus during fracture healing, slow wound healing (**chronic trophic ulcers** as a result of venous stasis), etc.

The morphogenesis of the regenerative process consists of three phases:

1) the proliferation of germ cells; 2) cell differentiation; 3) tissue differentiation.

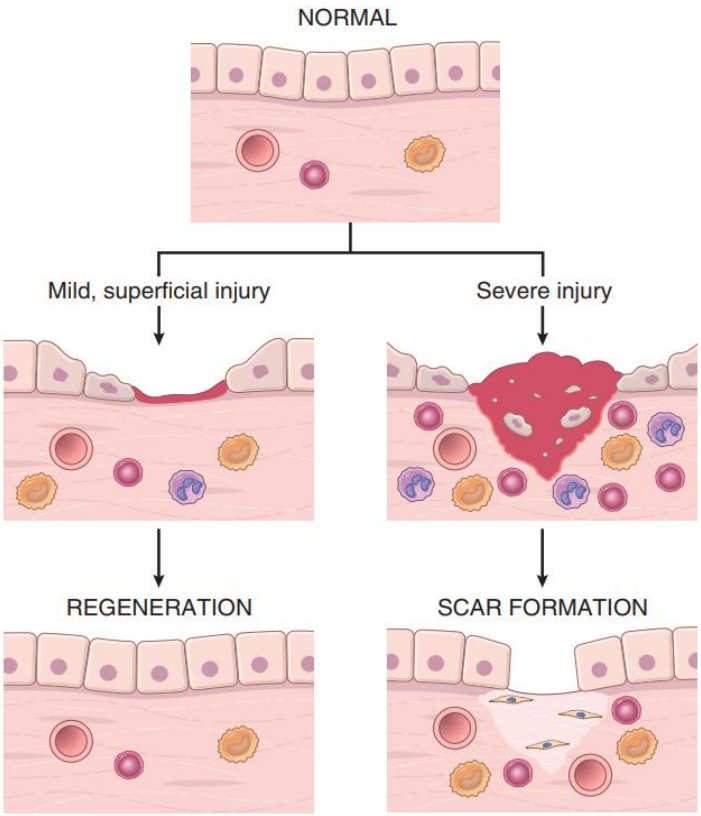
In the proliferation phase, the undifferentiated cells multiply. These cells are called cambial, stem or progenitor cells. Cell division continues until the tissue defect is filled. In the phase of cell differentiation, this young cells mature, their structural and functional specialization occurs, and then tissue differentiation occurs.

Wound healing

There are **4 types** of wound healing:

1. Direct closure of the defect of the epithelial cover (**epithelialization**).
2. Healing under the **scab**.
3. Wound healing by **primary intention**.
4. Wound healing by **secondary intention** (through suppuration).

1) **Epithelialization** is the process of healing small defects in the mucous membranes (mucosa of the stomach, intestines, oral cavity, etc.). During this process, the proliferation of cellular elements occurs along the edge of the wound defect and the defect is closed by this epithelium from the periphery to the center of the wound. In this case, an identical tissue is formed to replace the lost one.



Healing under the scab

The term "scab" is used when a crust has formed by coagulation of blood or exudate. Scabs are found on superficial or partial-thickness wounds. Scab is the rusty brown, dry crust that forms over any injured surface on skin, within 24 hours of injury. Whenever our skin is injured due to any cut or abrasion, it starts bleeding due to blood flowing from the severed vessels. This blood containing platelets, fibrin and blood cells, soon clots to prevent further blood loss. The outer surface of this blood clot, dries up (dehydrates) to form a rusty brown crust, called a scab, which covers the underlying healing tissues like a cap. The purpose of a scab is to prevent further dehydration of the healing skin underneath, to protect it from infections, and to prevent any entry of contaminants from the external environment. Scabs generally remain firmly in place until the skin underneath has been repaired and new skin cells have appeared, after which it naturally falls off.

Healing by primary intention

The condition for enabling primary healing is that the wound edges are sharp and completely clean and free of microbes as is the case with a wound produced via surgical incision (in a sterile environment). It is also possible to close some cuts caused by trauma via primary intention but they need to be sutured within 4 to 6 hours after the incident in order for the wound edges not to have become too inflamed, colonised or necrotic. The advantage of primary healing is that the time to closure is short which reduces the risk of infection and, furthermore, the scarring is limited. If the wound edges cannot be approximated, the wound will need to heal by secondary intention.

Healing by primary intention

A small gap in the epidermis and dermis is filled with clotted blood, which forms a scab and seals the skin for 24 hours, preventing infectious agents from entering the wound.

The epidermis regenerates rapidly by dividing the basal cells at the wound margins. These cells grow under the eschar and restore epidermal continuity within 48 hours.

As the epidermal cells mature, the superficial keratinized layers begin to slough off and the eschar detaches, usually at the end of the first week. In the underlying dermis, the wound fills with clotted blood and heals by scar formation. A small amount of convolutions and tissue debris is liquefied by neutrophil enzymes and removed by macrophages by phagocytosis.

Neutrophils appear in the wound within 24 hours, rapidly complete the liquefaction process, and are usually replaced by macrophages by day 3. Growth of fibroblasts and new vessels (granulation tissue) in the dermal cavity begins around 48th hour, and collagen can be found there at 72nd hour after injury. By 5th day, the dermal defect is filled with granulation tissue and a small amount of loose fibrous connective tissue. The amount of collagen increases within about 4-6 weeks. A young scar that becomes visible after eschar detachment initially appears pink due to the highly vascularized dermal granulation tissue.

Over the next few weeks, the scar turns white as a result of the reduction in the number of blood vessels and the increase in the amount of collagen in the maturing scar. Ultimately, the scar takes on a normal skin color as a result of the maturation of the epidermis.

Healing by secondary intention

Secondary intention healing implicates that the wound edges cannot be approximated. This can be the case if there is not enough skin in order to pull the edges together without causing stasis in the area, as is often the case in venous leg ulcers, or if the tissue loss is extensive with a need for considerable new tissue generation as e.g. in fourth degree burns. It is also the case if the wound area is dirty or colonized or the wound edges are not sharp and clean as both would be the case in blast trauma wounds. Secondary intention healing is almost always necessary in dehisced (sprung open) surgical wounds as the tensile strength of the peri-wound tissue (the wound edges and the tissue just next to them) has proven too weak to sustain the tension of e.g. sutures or staples.

Healing by secondary intention

Secondary healing will typically be characterized by visible granulation tissue and the scar will be bigger than in wounds healed by first intention. The simple fact alone that wounds healing by second intention will be open for longer will render them at high risk of infection. Furthermore, as they will typically be colonized and often dirty and infected they will be prone to complications.

Healing by primary intention is impossible under the following circumstances: in lacerated wounds, when it is impossible to match the edges of the wound; when foreign material is present in the wound; when extensive tissue necrosis occurred; when the wound becomes infected. If the infection develops after

matching the edges of the wound, then as a result of acute inflammation with suppuration, the wound ruptures and pus breaks out.

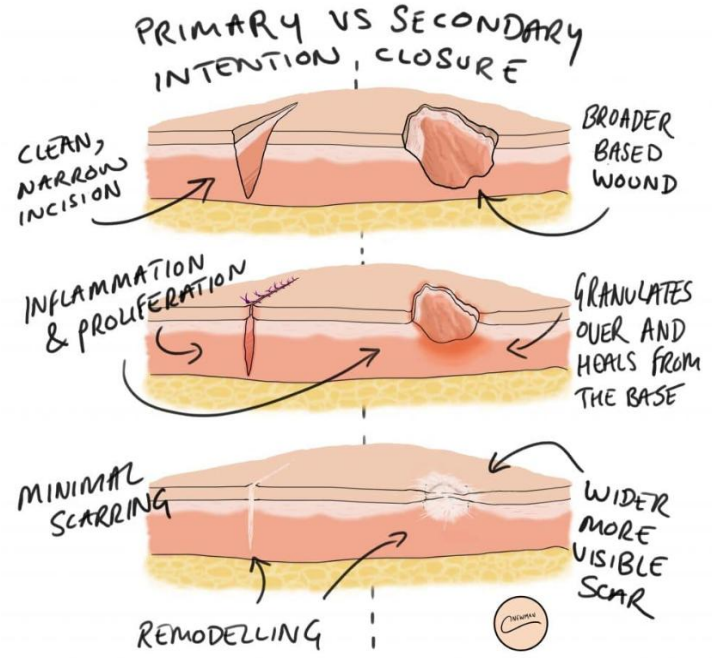
Healing by secondary intention

The processes that cause healing by secondary intention are similar to those that occur during healing by primary intention, but they **last longer** due to extensive tissue damage. The infectious agents are removed by acute inflammation.

Liquid exudate and necrotic tissue are removed by enzymatic liquefaction, lymphatic removal, and phagocytosis. Surgical removal of dead tissue and foreign material from the wound greatly accelerates the process of wound cleansing. Granulation tissue then grows from the healthy tissue at the bottom of the wound and transports the necrotic tissue to the skin surface.

The epidermis regenerates from the basal cells at the wound margin. In large wounds, re-epithelialization may take several weeks. In these situations, surgical skin grafting can speed healing. After completion of the epithelialization of the wound surface, collagenization of the granulation tissue occurs. The final size of a mature scar is smaller than the size of the original wound due to scar reduction. The skin appendages (hair follicles and glands) regenerate if there are enough living cells left. With extensive skin wounds with complete destruction of skin appendages, the resulting skin scar is usually devoid of these structures.

Primary vs secondary intention



Healing by tertiary intention

In tertiary intention healing, there is a need for the wound to be open for a period of time before it can be sutured. Examples can be a wound left open to allow drainage and later is closed or a wound that is left to heal by secondary intention but encounters complications, where after a very thorough debridement is performed followed by an approximation of the wound edges.

Granulation tissue

During wound healing by primary and especially secondary intention, granulation tissue is formed.

It consists of following layers:

1. Superficial leukocyte-necrotic layer.
2. Superficial layer of vascular loops.
3. Layer of vertical vessels.
4. Ripening layer.
5. Layer of horizontal fibroblasts.
6. Fibrous layer.

Organization is a replacement of a site of damaged tissue with connective tissue. Excessive growth of mature dense connective tissue is called **sclerosis**.

Classification of sclerosis considering **etiology and pathogenesis**:

1. Sclerosis as an outcome of chronic productive inflammation.
2. Sclerosis as an outcome of systemic or local disorganization of the connective tissue.
3. The substitutive sclerosis (the outcome of necrosis and tissue atrophy).
4. Formation of scars as a result of healing of wound and ulcer defects.
5. Organization of blood clots, hematomas, fibrin deposits.

Classification of sclerosis according to **morphogenesis**:

1. Neoformation of young connective tissue due to proliferation of fibroblasts (at proliferative inflammation, necrosis).
2. Increased collagen synthesis by fibroblasts without significant hyperplasia of cells; transformation of loose connective tissue into fibrous tissue (at chronic venous congestion).

Hypertrophy is an increase in the size of an organ or tissue by increasing the size of each cell.

According to **pathogenesis**, the following forms of hypertrophy are distinguished:

- compensatory (or functional) hypertrophy
- vicar or substitute hypertrophy
- hormonal or neurohumoral hypertrophy

Hypertrophy

The most common type of hypertrophy is **functional hypertrophy**, which occurs both in physiological and in some pathological conditions. It is caused by an increased function on an organ or tissue. An example of functional hypertrophy under physiological conditions is the hypertrophy of skeletal muscles and the heart in athletes, in persons of heavy physical labor.

Under pathological conditions, compensatory hypertrophy develops in those cases when, as a result of a disease process, an organ or part of an organ has to work hard. In other words, compensatory hypertrophy is the hypertrophy of a heavily functioning organ. This type of hypertrophy is often found in hollow organs that

have a wall of smooth muscles: GIT, bladder. It is also a morphological expression of chronic obstruction. Compensation for the function of these organs occurs due to an increase in the volume of the smooth muscles of the wall above the place of the obstacle.

Cardiac hypertrophy

The causes of **cardiac hypertrophy** may lie in the pathological processes of the heart itself, and in these cases they are referred to as intracardiac. In other cases, they may be associated with the pathology of the small or large circulation, then we are talking about extracardiac causes. Intracardiac causes include heart defects. Heart defects are persistent, irreversible violations of the anatomical structure of the heart, which are accompanied by a violation of its function.

There are **two main mechanisms** for the development of cardiac hypertrophy: an increase in intraventricular pressure (**hypertension in the pulmonary and systemic circulation, stenosis of the valves**) and increased blood filling of the ventricles (**valvular insufficiency with blood regurgitation**). Both of these mechanisms are accompanied by a reflex increase in the strength of heart contractions.

Cardiac hypertrophy

Extracardiac causes of **left ventricular hypertrophy** of the heart are diseases that are accompanied by an increase in blood pressure in the systemic circulation: hypertension, including symptomatic hypertension (glomerulonephritis, thyrotoxicosis, tumors of the adrenal and pituitary gland, etc.); general obesity (due to an increase in the volume of the microvasculature).

Intracardiac causes of **right ventricular hypertrophy** of the heart: stenosis of the pulmonary trunk; pulmonary valve insufficiency; insufficiency of the tricuspid valve; mitral stenosis.

Extracardiac causes of **right ventricular hypertrophy** of the heart can be lung diseases, accompanied by a decrease in the volume of the pulmonary circulation and an increase in blood pressure in the pulmonary artery system:

- chronic diffuse emphysema;
- pneumosclerosis of various etiologies: usual interstitial pneumonia, fibrosing alveolitis, chronic forms of pulmonary tuberculosis, pneumoconiosis
- COPD;
- primary pulmonary hypertension.

Pathological hypertrophy

Pathological hypertrophy occurs in the absence of an appropriate stimulus. Myocardial hypertrophy occurring for no apparent reason (in the absence of hypertension, valvular disease, and congenital heart disease) is regarded as an example of pathological hypertrophy and is called **hypertrophic cardiomyopathy**.

Functional and vicar hypertrophy

Functional hypertrophy is a **reversible** process, provided that the cause is eliminated in time. But in practice this is rarely possible. Often the outcome is decompensation of the hypertrophied heart due to the fact that the process of

hypertrophy is limited by the possibility of blood supply to the organ. Over time, as the mass of the organ increases, a relative insufficiency of blood supply occurs, and chronic ischemia occurs.

The hypertrophy that develops in the organ undoubtedly has a positive value, since it allows the organ function to be preserved despite the disease. This period in the clinic is called the **stage of compensation**. In the future, when dystrophic changes occur in the organ, there is a weakening of the function and, ultimately, when the adaptive mechanisms are exhausted, decompensation of the organ occurs. And in relation to the heart - heart failure develops, which can be lethal for the patient.

Hormonal (neurohumoral) hypertrophy

Vicar or substitute hypertrophy develops in paired organs (eg kidneys) or when a part of an organ is removed (eg in the liver, in the lungs).

An example of **physiological hormonal hypertrophy** is uterine hypertrophy during pregnancy. In pathological conditions, hormonal hypertrophy occurs as a result of dysfunction of the endocrine glands.

An example of such hypertrophy is acromegaly, caused by hyperfunction of the anterior pituitary gland with excessive production of somatotropic hormone, which usually occurs on the basis of eosinophilic adenoma. With acromegaly, there is an increase in organs and protruding parts of the skeleton.

Hyperplasia

Hyperplasia is an increase in the size of an organ or tissue as a result of an increase in the number of their constituent cells. Hyperplasia is observed when the mitotic activity of cells is stimulated, which leads to an increase in their number. There are **reactive** (or protective) hyperplasia, **hormonal** hyperplasia, and **compensatory** (eg after blood loss).

Reactive hyperplasia occurs in immunocompetent organs - in the thymus, spleen, lymph nodes, red bone marrow, tonsils, intestinal lymphatic apparatus, etc. Hyperplasia of the erythrocyte germ of the bone marrow may be associated with increased destruction of erythrocytes (hemolytic processes) or prolonged hypoxia (living in high mountain areas), myeloid - with an increased need for neutrophils in the body, for example, during inflammation. Lymph node hyperplasia is usually a response to antigenic stimulation. Hyperplasia of the spleen is observed in septic conditions.

With hyperplasia, the spleen increases in size, acquires a flabby texture and, if a knife is drawn over the surface of the incision, gives a scraping of the pulp. Lymph nodes increase in size, become juicy, pinkish-red in color. Microscopically observed proliferation of immunocompetent cells. The bone marrow of the femoral diaphysis in septic conditions becomes red due to hyperplasia of myeloid cells.

Hormonal hyperplasia occurs in target organs under the action of hormones. It can also be **physiological**, eg **breast hyperplasia** during pregnancy and lactation.

Examples of hormonal hyperplasia in **pathological conditions** are: **endometrial hyperplasia**, which occurs as a result of increased stimulation of the endometrium by estrogens, and can cause metrorrhagia (irregular, frequent

excessive uterine bleeding); **fibrocystic mastopathy** also occurs as a result of a violation of the hormonal function of the ovaries, manifested by hyperplasia and restructuring of the acini and excretory ducts of the mammary gland.

Hyperplasia of target organs is often accompanied by an increase in their function. So, with hyperplasia of the adrenal glands due to excessive secretion of ACTH, increased secretion of cortisol is observed (**Cushing's syndrome**).

Hyperplasia of the thyroid gland (**Graves' disease**) occurs with an increase in the amount of TSH (thyrotropin) or with the action of autoantibodies that are able to bind to TSH receptors on the membranes of thyroid cells.

Prostate hyperplasia, often occurring in old age, is accompanied by hyperplasia of both glandular tissue and stroma. The etiology of prostate hyperplasia is decreased androgen levels. An enlarged prostate gland is accompanied by stagnation of urine, the formation of stones, and often the development of an ascending infection.

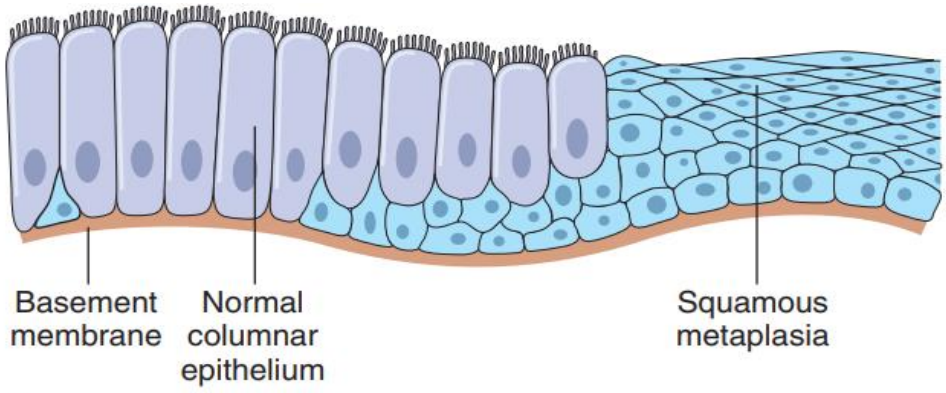
Atrophy is a severe decrease in the volume of cells, tissues of organs, accompanied by a decrease or cessation of their function. Atrophy can be **physiological** or **pathological**, **general** and **local**.

General atrophy (**cachexia**) occurs during exhaustion due to starvation, damage to the pituitary gland, endocrine diseases, long-term severe infectious processes, tumors, etc. It is characterized by a decrease quantity (or disappearance) of adipose tissue in the depot and a brownish coloration of the internal organs (liver, heart, skeletal muscles) due to the accumulation of lipofuscin.

Local atrophy:

1. Dysfunctional (from inactivity).
2. Ischemic (from lack of blood supply).
3. Compressive (**hydronephrosis**; atrophy of the brain tissue when there is a problem in the outflow of cerebrospinal fluid with the development of **hydrocephalus**).
4. Neurotic (due to a violation of the connection of organs with the nervous system during the destruction of nerve conductors).
5. From the impact of physical and chemical factors (eg radioactive radiation).

Metaplasia - is the transformation of one differentiated cell type to another differentiated cell type within the one germ layer. It always appears in connection with the previous proliferation of the cambial elements of the cell tissue, which, upon maturation, turn into tissues of a different type. It often accompanies chronic inflammation that occurs with impaired regeneration and occurs in the epithelium of the mucous membranes.



A

Metaplasia is broadly divided into 2 types: **epithelial** and **mesenchymal**.

(A) **Epithelial metaplasia**. This is more common type. The metaplastic change may be patchy or diffuse and usually results in replacement by less susceptible for damage factors and less specialized epithelium.

1. **Squamous metaplasia**. Various types of epithelium are capable of undergoing squamous metaplastic change due to chronic irritation that may be mechanical, chemical or infective in origin. Some common examples of squamous metaplasia can be seen:

a) in bronchus (normally lined by pseudostratified columnar ciliated epithelium) in chronic smokers

b) in uterine endocervix (normally lined by simple columnar epithelium) in prolapse of the uterus and in old age

c) in prostate (ducts normally lined by simple columnar epithelium) in chronic prostatitis and estrogen therapy

d) in renal pelvis and urinary bladder (normally lined by transitional epithelium) in chronic infection and stones

2. **Columnar metaplasia**. There are some conditions in which there is transformation to columnar epithelium:

1) intestinal metaplasia in stomach and esophagus (**Barrett's esophagus**)

2) conversion of pseudostratified columnar epithelium in chronic bronchitis and bronchiectasis to columnar type

3) in cervical erosion (congenital and adult type), there is variable area of endocervical glandular mucosa everted into the vagina

Metaplasia

(B) **Mesenchymal metaplasia**.

1. **Osseous metaplasia**. Osseous metaplasia is formation of bone in fibrous tissue, cartilage or myxoid tissue:

a) in arterial wall in old age (Monckeberg medial calcific sclerosis / MCS)

b) in soft tissues in myositis ossificans

c) in cartilage of larynx and bronchi in elderly people

d) in scars after hyalinosis

e) in the fibrous stroma of tumors

2. **Cartilaginous metaplasia**. In fractures

Dysplasia is a pathological process characterized by a violation of the proliferation and differentiation of the epithelium with the development of **cellular atypia**.

Epithelial dysplasia is characterized by cellular proliferation and cytologic changes:

1. Hyperplasia of epithelial layers
2. Disorderly arrangement of cells from basal layer to the surface layer
3. Cellular and nuclear pleomorphism
4. Increased nucleocytoplasmic ratio
5. Nuclear hyperchromatism
6. Increased mitotic activity

Historically, grading of dysplasias has followed a **three-tier** system to include **mild**, **moderate** and **severe** dysplasia.

Modern recommendations have introduced a **two-tier** grading scheme to including **low-grade** (mild dysplasia) and **high-grade** (moderate and severe dysplasia/carcinoma in situ) providing for better consensus among pathologists in the interpretation of such dysplastic lesions.

INFORMATIONAL AND METHODOLOGICAL PART

MAIN LITERATURE

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NORMATIVE LEGAL ACTS AND DOCUMENTS

1. Order of the Ministry of Health of the Republic of Belarus No. 111 of 06/01/1993 "On further improvement of the pathological service of the Republic of Belarus"

Access mode: http://patan.by/menyu/administrativnyie-proczeduryi.html - The date fccess: 20.03.2022.

ELECTRONIC DATABASES

1. Physician's consultant. Electronic Medical Library = Consultant of the doctor. Electronic medical library [Electronic resource] / Publishing group "GEOTAR-Media", LLC "IPUZ". – Access mode: http://www.rosmedlib.ru/ . – Access date: 03/15/2022.

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