LECTURE № 4 Adaptation

☐We differentiate ***physiologic adaptation*** – cells respond to normal stimulation with hormones or other endogenous biologically active substances and ***pathologic adaptation*** – adaptation of cells or tissues to external or internal environment pathogen components influence.
Adaptation
☐Adaptation is manifested with
☐ -hyperplasia,
☐hypertrophy,
☐ organization,
☐ atrophy,
☐metaplasia,
☐dysplasia.
Hyperplasia

Hyperplasia ***is organ or tissue size increase due to cells amount increase.***
☐ Hyperplasia could be physiologic and pathologic. It is differentiated:
☐reactive or defensive,
☐neurohumoral or hormonal hyperplasia and
☐substitutive compensatory hyperplasia in case blood loss.
Hyperplasia

□Reactive or defensive hyperplasia often takes place in immunocompetent organs: thymus, spleen, lymph system, red bone marrow, tonsils under antigen stimulation, septic conditions, anemias, etc.

□**Hormonal hyperplasia** could be **physiologic** (mammary gland hyperplasia during lactation) as well as pathologic: hyperplasia of prostate gland, endometrium, fibrocystic mastopathy, thyroid gland hyperplasia under hormonal disorders in organism.

□**Pathologic hyperplasia** occurs under the influence of viral infection – epithelium hyperplasia in verruga, etc.

Prostate gland hyperplasia
Specimen is colored with hematoxylin and eosin. Hyperplasia of glands is observed. Their contours are stellate. Stroma is excessively developed, infiltrated with lymphocytes.
Hypertrophy

Hypertrophy **(from Latin hyper – excessive, trophe – nutrition) is cell, tissue or organ volume increase on account of cells reproduction or increase of their quantity and intracellular ultrastructures size.**
Hypertrophy

Hypertrophy is integrally connected with hyperplasia (from Latin plaseo – create), which is manifested in cells reproduction by the way of mitosis (cell hyperplasia), tissues excrescence (tissue hyperplasia) and ultrastrauctures excrescence (intracellular hyperplasia).

Hypertrophy

Classification:

☐-True is characterized with volume increase on the account of functional (parenchymatous) structures

☐-pseudohypertrophy is characterized on the account of support tissues – conjunctive or adipose.

☐-Adaptive processes include neurohumoral hypertrophy (hyperplasia)

☐- and hypertrophy excrescences, compensatory – compensatory hypertrophy.

Hypertrophy

Neurohumoral hypertrophy (hyperplasia)

It occurs on the background of endocrine glands dysfunction.

☐Its physiologic type is uterus hypertrophy and macromastia under pregnancy.

☐In pathologic conditions it is observed endmetrium glands hyperplasia, mastopathy under ovarian dysfunction, mammary gland excretory ducts hyperplasia in males (gynecomastia) under testicles atrophy, enlargement of organs and prominent parts of skeleton (acromegalia) under chromophobe adenoma in adults.

Hypetrophic ***excrescences***

☐They are observed under <u>chronic inflammations</u> of mucus tunics with **polyps formation**, under lymph flow disorders in low extremities and lymphostasis causing conjunctive tissue excrescence (elephantiasis).

☐Adipose and conjunctive tissues can fill the space occupied by organ or tissue causing their atrophy. An example could be cranial bones thickening under cerebral atropy, adipose tissue excrescence in atrophied kidney hilus area. This type of hypertrophy is called ***vacant.***

Compensatory hypertrophy

is divided

☐-into work and

☐-substitutional (vicarious) hypertrophy.

☐Work hypertrophy develops as the respond on enhanced work of the organ.

☐ In *physiologic conditions* it is observed in people occupied with heavy manual labor and sportsmen (Hypertrophy of skeleton muscles, heart).

☐ In *pathologic conditions* it occurs in heart, gastrointestinal tract, urinary tracts, when defect existing in these organs are compensated with enhanced work of preserved structures.

Cardiac hypertrophy

☐reaches the highest level under **congenital** and **acquired** ventricles malformations accompanied with stenosis, as well as under hypertensions, aorta lumen narrowing, vascular sclerosis. The part of the heart undertaking functional load is subject to hypertrophy in the first turn. In these cases heart weight reaches 1 kg. Structural manifestation of compensation is heart length increase as well as its cavity dilation determined as active, compensatory, *tonogenous.* However in case prime cause persists ventricular cavity reduces with time passing by. Hypertrophy of cavitary organ (heart, bowel, urinary bladder) under which its lumen decreases is called *concentric*.

<u>Concentric hypertrophy of heart.</u>

On horizontal section of the heart it is seen thickened wall of the left ventricle and interventricular septum, ventricle lumen is concentrically narrowed.

Morphology of **Cardiac hypertrophy**

☐-Left ventricle thickness can reach 2 cm, and right – 1 cm.

☐-Microscopically is observed considerable thickening of cardic hystiocytes and their nucleus enlargement.

☐- Hyperplasia of stroma's fibrous structures, intramural vessels, nerve apparatus components responsible for enhanced function' neurohumoral support, is considerable behind the tempo of cardic hystiocytes' intracellular ultrastructures hyperplasia.

<u>Myocardial hypertrophy.</u>

☐Specimen is colored with hematoxylin and eosin. Cardiac hystiocytes' sarcoplasma is enlarged in volume. Nucleus are enlarged, hyperchromic, their contours are saw-edged. Excessive development of stroma.

Decompensation Cardiac hypertrophy

Thus contributing in compensation phase is fictitious, in its bud it is already has the features of decompensation. In case prime cause is not removed, unbalance occurs between increased demands of hypertrophied myocardium and the level of its blood supply, innervation, energy supply, exchange area of newly formed ultrastructures' membranes. Adipose and albuminous degenerations occurs in hypertrophied cardic hystiocytes weakening cardiac beating activity. In the result of tonus lose by cardic hystiocytes passive *myogenous* dilation of ventricles cavities takes place. Concentric hypertrophy converts into *eccentric* with cavitary organ dilation, which is morphologic feature of cardiac decompensation.

Decompensation hypertrophy

Thus contributing in compensation phase is fictitious, in its bud it is already has the features of decompensation. In case prime cause is not removed, unbalance occurs between increased demands of hypertrophied myocardium and the level of its blood supply, innervation, energy supply, exchange area of newly formed ultrastructures' membranes. Adipose and albuminous degenerations occurs in hypertrophied cardic hystiocytes weakening cardiac beating activity. In the result of tonus lose by cardic hystiocytes passive *myogenous* dilation of ventricles cavities takes place. Concentric hypertrophy converts into *eccentric* with cavitary organ dilation, which is morphologic feature of cardiac decompensation.

Eccentric hypertrophy of the heart

Enlarged in two times clearance of ventricle is seen on a horizontal cut of heart. If not remove cause, which predetermines process of hypertrophy, dystrophic changes in hypertrophied cardiomyocytes and sclerotic in stroma, which also weaken contractive activity of myocardium, appears. Thus cardiac decompensation develops at which muscle is unable to execute intensive work. At decompensation of hypertrophied myocardium transversal, passive or myogenous extend (dilatation) of ventricles take place.

Decompensation hypertrophy

Gastric or bowel muscle layer hypertrophy occurs, naturally, upward stenosis which impedes evacuation. This can take place under ulcers healing, tumors presence. Urinal bladder hypertrophy is observed under prostate gland adenoma, narrowing urethra, as well as in connection with the other impediments of bladder emptying. Functional insufficiency of above named organs occurs under leiomyocytes degeneration and manifests in their cavities dilation.

Vicarious (substitutional) hypertrophy

compensate the function of one of the dead or surgically removed paired organs (lungs, kidneys, adrenal glands). By its pathological essence it is close to regenerative hypertrophy. Significant role in its occurrence plays the complex of reflex and hymoral influences, the same with compensatory hypertrophy.

Atrophy

Atrophy *is lifetime change of organs', tissue's and cells' volume, accompanied with their functions weakening or their functions termination.* ***Physiologic*** *and* ***pathologic*** *atrophies are differentiated.*

Physiologic **atrophy**

is observed during the whole lifetime of human being**.** Upon the birth umbilicial arteries, arterial (Botallo's) duct atrophy and obliterate, aged people face with genital glands atrophy, old people – with bones and intervertebral cartilages atrophy

Pathologic atrophy

is observed in any age and can be caused by various reasons

- insufficient feeding,
- endocrine glands dysfunction,
- central and peripheral nervous system lesions,

- intoxications. Pathologic atrophy is reversible process. In case the cause is removed under condition that atrophy didn't reach high level, organ structure and function can be completely rehabilitated.

Classification of Pathologic atrophy

-general and local.

General atrophy or *Cachexia or emaciation* :

-alimentary cachexia

- emaciation under cancerous cachexia,

- emaciation under cerebral cachexia,

-emaciation under other diseases.

Concept of "emaciation" and "cachexia" are not identical. Cachexia in primary stages can be free from emaciation and be manifested with progressive degenerative changes of the organs, for example, with osteoporosis.

Alimentary emaciation

occurs during starvation.

Morphogenesis

-Gradually fat stock decreases,

-skeleton muscles atrophy,

-Atrophied adipose (fatty) tissue becomes ochre-yellow color due to lipochrome pigment accumulation.

-Fatty tissue of atrium and fatty marrow impregnate with serous fluid and become dropsical (serouse atrophy of fatty tissue).

-Pigment melanin accumulates in the skin of starving, so it colors in grey-brown color.

- Heart, liver and other organs decrease in size.

-Pigment lipofuscin, (wear-and-tear pigment) accumulates in cardic hystiocytes, hepatocytes and myocytes of skeleton muscles, as the resuly of which organs become of brown color (*brown atrophy of organs*).

Emaciation under cancerous cachexia

is characteristic for cancerous growth of any localization.

The most fast it develops in patients ill with cancer of

-esophagus,

-gastric carcinoma or intestine cancer caused by digestion disorders.

Emaciation under cerebral and hypophysial (Simmonds' and Schigens' diseases) cachexia

occurs due to hypothalamus' or hypophysis' injury with inflammatory process or tumor.

Emaciation under the other diseases takes place in case long term chronic infections:

-tuberculosis,

- dysentery,

- chronic sepsis.

It is caused by severe disorder of metabolism.

Morphology of general emaciation

-subcutaneous fatty tissue is absent,

-eyes are hollow,

-skin is dry,

-abdomen is scaphoid.

-Starvation edemas sometimes take place.

Local atrophy

occurs by various reasons. The following types of it are differentiated:

-dysfunctional,

- caused by inadequate blood supply,
- compression,
- -trophoneurotic,
- -caused by physical and chemical agents influence.

Dysfunctional atrophy

or atrophy caused by inactivity occurs because of organ function decrease:

- muscles atrophy under bones fracture,
- optic nerve atrophy after eye ectomy. Atrophy development in patients with ruptures could be slow down in case massage and physical exercises are applied.

Atrophy caused by inadequate blood supply

occurs caused by narrowing of arteries feeding organ.

Exsanguination leads to hypoxia in the result of which parenchimatous elements' functions fall and cells size reduces Hypoxia stimulates fibroblasts proliferation (reproduction), so sclerosis develops under inadequate blood supply. Patients with atherosclerosis suffer from this process in myocardium, kidneys, cerebrum, legs.

Atrophy from compression

occurs in organs subject to compression by -tumor or aneurysm (local evagination of aorta). Even the bones of spinal column and breast bone atrophy because of their compression by aneurysm.

Under urinary tracts obstruction with calculus urine stretches renal pelvis and cups (hydronephrosis) causing kidney parenchyma atrophy.

In case liquor outflow hindrance ventricles of brain dilate (hydrocephalus) and cerebrum atrophy.

Hydronephrosis kidney

It is enlarged and looks like thin-walled sack which is filled with a liquid. Develops as a result of hampered outflow of urine, the cause of which can be presence of stone with obturation of ureters, Urine, accumulating, stretches clearance of pelvis major and minor calyces, squeezes tissue of kidney, that result in atrophy of parenchyma of kidney caused pressure.

Pulmonary emphysema

Specimen is colored with hematoxylin and eosin. Bronchiole is in spasm condition. Alveoli lumen is enlarged. Alveolar septums are thinned, straightened.

Hydrocephalia.

In ventricles of brain there is great quantity of liquid. Ventricles are enlarged. Parenchyma of cerebrum is thinned.

Trophoneurotic atrophy

is caused by failure of organ connection with central nervous system under peripheral nerves traumatic, tumor or inflammatory injury. Skeleton muscles' atrophy often develops by this scenario.

Atrophy caused by physical and chemical agents influence

occurs, for example,

-in marrow and genital glands under radiation influence. Radioiodine causes thyroid gland atrophy.

- After long term treatment with adrenocorticotropic hormone or glucocorticoids adrenal glands cortex' atrophy develops.

Morphology:

-Organs reduce in size under atrophy.

-Their surface in most cases is smooth (smooth atrophy), in kidneys – granular (granular atrophy). Under hydronephrosis and hydrocephalus organs are enlarged due to liquid accumulating in them and their parenchyma is atrophied.

Metaplasia

Metaplasia is adaptive pathologic process characterized with substitution of one differentiated tissue for the other in the limits of one histiotype: mesenchymal or epithelial.

Metaplasia

Aetiology :

-A-hypovitaminosis
-inflammation and
others could be the causes of metaplasia.
Metaplsia is grounded on the change of genetic program of differentiation on column cells level.

Metaplasia

This phenomenon doe not take place in muscular and nervous tissue. The most wide spread example of metaplasia is one layer prismatic epithelium substitution with multilayer flat epithelium,
observed under bronchi mucous tunic inflammation, gastric epithelium substitution with intestinal epithelium – intestinal metaplasia, or gastric mucus tunic enterolization. Conjunctive tissue metaplasia is observed with cartilage or bone formation in cicatrix, aorta wall under atherosclerosis.
Metaplasia could be the background for malignant growth development.

Dysplasia

Displasia is major failures of proliferation and epithelium differentiation with cellular atypia development and histoarchitectonics change: loss of polarity, loss of epithelium histo- and organo- specificity.

Dysplasia

Basic membrane is not injured under dysplasia. The most often dysplasia develops under inflammatory and regenerative processes. Depending on proliferation stage and condition of cellular and tissue atypia three stage of displasia are differentiated: I – minor (small), II – moderate (middle), III – severe (major). Minor and moderate dysplasia are of reversible character. Cellular and tissue changes under severe dysplasia are rare subject to reversible process and are treated as precancerous process. Sometimes locally they are hard to be differentiated from carcinoma.

Regeneration

Regeneration (from Latin regeneratio – restoration) is the process of living matter self-recovery in injured area.

Regeneration takes place on molecular, subcellular, cellular, tissue and organ levels and reflects the principle of living functions autoregulation. It is grounded on cellular and intracellular hyperplastic processes.
Cellular reproduction is characteristic for cellular form of regeneration, ultrastructures and their components quantity increase (hyperplasia) and their enlargement (hyperplasia) are characteristic for intracellular form. The last form is peculiar for all organs' cells and is universal.

Regeneration

Two phases are differentiated in regeneration morphogenesis – proliferation and differentiation. In the term of the first phase reproduction of non-differentiated (cambial, column) cells or pre-cells are observed. During the second phase young cells mature and specialize.

Regeneration

Regenerative process is regulated with
humoral,
immune,
nervous and
functional mechanisms.

□Humoral mechanisms are realized in cells and tissues at intracellular and tissue regulators participation, and out of them – at participation of hormones, poetines, mediators, growth factors as well as keylones (substances depressing cells division).

□Immune mechanisms are connected with "regenerative information" transfer by leukocytes, nervous – with trophic function of nervous system, and functional – with adequate demands of organs and tissues.

Regeneration

Physiologic ***regeneration***

□

Physiologic regeneration is done in the course of the whole life and reflects endless process of substances' disintegration and synthesis. It is characterized with intracellular renewal of molecules and ultrastructures as well as entire cells, fiber structures and major substance of conjunctive tissue. Intracellular regeneration is the only form of content and function renewal of central nervous system's cardiac hystiocytes and neurocytes. Combination of intracellular renewal with cells mitosis is observed in liver, kidneys, pancres. Continuous change of epidermis, digestive tract mucus tunic epithelium, synovial membranes, marrow, blood elements are done on the account of cells division.

Reparative ***regeneration***

□

Reparative regeneration is organ defect substitution under various pathologic processes. It is grounded on the same mechanisms which refer to physiologic regeneration, moreover injury reparation in each organ is going on the same way as in conditions of physiologic recovery, but more intensive. Intracellular regeneration becomes major form of degenerative changed tissues cells' structure rehabilitation, as well as cellular and intracellular – under their necrosis.

□Final result of reparative regeneration is expressed in restitution or substitution.

Restitution **(complete regeneration)**

□is characterized with tissue defect substitution with tissue identical to dead one. It is attributable to those organs and tissues where regeneration is going on exceptionally in cellular form (marrow, epidermis, mucus tunics epithelium).

Substitution **(incomplete regeneration)**

□is characteristic for the organs healing of which goes on mostly or exceptionally by intracellular reparation (heart, central nervous system).

□For example, in myocardium necrosis focuses are substituted with conjunctive tissue,

□in cerebrum dead neurocytes – with glial cicatrix. Function renewal is provided with nucleus and cytoplasm ultrastructures enlargement in preserved cells which hypertrophy.

□ Incomplete regeneration variation is "distance regeneration". As an example of it could be named qualitative reconstruction various portions of gastrointestinal tract, compensating exocrinous, function of pancreas head or uninjured cerebral hemisphere reconstruction in case the other hemisphere injury.

Pathologic regeneration

□is the type of reparative regeneration going on in conditions of local and general regulatory mechanisms failure, and is characterized with regenerative process distortion, violation of proliferation phase change into differentiation phase. Deficiency of proteins or vitamins, nervous regulation failure, hormonal disorders, immune system depression could seriously influence healing speed and quality. In that way long term nonhealing crus ulcers in patients with chronic cardiac insufficiency could be explained as well as persistent wounds under diabetes mellitus.

□ An example of pathologic regeneration can be conjunctive tissue hyperproduction with keloid formation under radiation or thermal trauma.

Regeneration of Blood

□can regenerate by physiologic, reparative and pathologic type.

□ An example of blood reparative regeneration under anemia can serve extramedullary hematosis.

□Pathologic blood regeneration is observed under radiation, leucosis. Small size ***vessels*** regenerates satisfactory and big vessels regenerate by substitution type – cicatrix formation on the place of mid and external layer portions injury.

Conjunctive tissue regeneration

□starts from young mesenchymal cells proliferation and vascularization with *granulation tissue* formation, that is young conjunctive tissue:

□Morphology:

□- non-differentiated lymphocytine cells of conjunctive tissue,

□-leukocytes,

□-plasmocytes,

□-labrocyte,

□-fibroblasts;

□-loop-like thin wall vessels. Granulation tissue maturing is ended with rough fibered cicatrix tissue formation, sometimes even keloid.

Osteous tissue

□regeneration after uncomplicated rupture of bone goes by the way of primary bony union, which have the following stages:

□-primary conjunctive tissue callus,

□-primary bony callus,

□- final bony callus.

□Under regenerative process failure secondary bony union occurs in bone through osteocartilaginous callus.

Cartilage tissue regeneration

□goes as incomplete regeneration with scar tissue growth.

Muscle tissue **regeneration**

□depends on its type.

□ Unstriped muscles regenerate completely under minor defects. Transversely striated muscles regenerate only in case sarcolemma is preserved.

□Cardiac muscle regeneration goes by the way of cicatrix formation.

□***Epithelium*** regenerates by the way of new cells reproduction, in other words by restitution type.

□***Nervous tissue*** regeneration goes ambiguous. Cerebrum and spinal marrow cells regenerate by substitution, that is glia growth and cicatrix formation.

Organization

□*is protective-adaptive process directed to separate and substitute with granulation tissue ----focus of necrosis,*

□*-hemorrhage or*

□*- exudates as well as thrombi,*

□*- foreign objects and parasites.*

□Its essence comes to conjunctive tissue formation under defects healing in wounds and ulcers, substitution with conjunctive tissue areas of necrosis or thrombotic masses (properly organization) and their encapsulation.

By I.V.Davydovsky the following forms of *wounds healing* are differentiated: epithelium defect immediate closing, healing under eschar, primary intention of wound, secondary intention or healing by granulation.

Epithelium defect immediate closing

provides cells growth on wound sides and its skinning over with cells layer without mitotic cells division. Such simple form of healing is peculiar to surface injuries of cornea, mucus tunics, vessels intima.

Healing under eschar

is also characteristic for minor injuries of epidermis.

For example, under surface excoriation lymph and blood excude fast drying and converting into crust (eschar).

Epidermis regenerate under crust which in the result of rejection process drops away on the 3rd -7th day.

healing with primary intention

. Under phagocytes' proteolytic ferments influence partial lysis of grumes and tissue detritus takes place and wound content is removed in the very first date after injury together with exudate, On the 2nd-3rd day granulation tissue appears which ripens on the 10th-15th day. In the clinic the sides of big wounds connect with sutures and support with dressings. In case distance between the sides equals even 10 mm, in few days this distance will diminish to zero due to tissue edema and fibrin clot reduction which sticks wound edges.

secondary intention

occur when wound sides separated due to suppurative inflammation

It is characterized with wound release of detritus and foreign objects by "outsuppuration".

Necrotic masses rejection takes place during the first 5-6 days (secondary cleansing of the wound) and granulation tissue starts to develop on wounds edges.

Under wounds healing by primary or secondary intention granulation tissue maturing is accompanied with epithelium regeneration. However under secondary intention healing on the place of wound cicatrix forms anyway.

Inflammatory process always precedes ulcers healing. Granulation tissue grows into necrosis area which matures into rough fiber and often subjects to hyalinosis. The latter causes cavitary organ deformation and stenosis. Epithelial layer stratifies conjunctive tissue.

Granulation tissue.

Specimen is colored with hematoxylin and eosin. A lot of capillaries overfilled with blood can be seen in specimen as well as a number of cells: fibroblast /elongated shape/, eosinophils, lymphocytes, neutrophilic leucocytes, situated between immature collagen fibers' layers.

Cicatrix.

Specimen is colored by Van Gizon method. Tissue is represented with fibrous conjunctive tissue. Vessels are sclerosed.

organization of necrotic masses

starts from reactive exudates inflammation in surrounding tissues and necrosis areas lysis. Exudative reaction transfers into productive with mesenchymal cells proliferation. Granularion tissue ingrows from periphery and gradually transforms into cicatrix. This type of organization is peculiar to myocardial infarction healing, as well as kidneys and spleen.

Organization and hypertrophy of kidney.

Postinfarction cicatrix of myocardium.

In the stratum of cut myocardium grey-white cicatrix focuses are seen, substituting injured cardiac hystiocyte on substantial area of transverse section.

Big space-occupying cardiosclerosis.

Specimen is colored by Van Gizon method. Big focuses of conjunctive tissue excrescence could be seen between cardiac hystiocytes and on the places of dead muscle fibers.

Nodular regeneration of liver at cirrhosis

Surface of organ is small nodular, there are large regenerator nodes of parenchyma of liver, greyish-yellow which don't have an ordinary lobular structure. A liver acquires such kind at postnecrotic cirrhosis. That is, in areas of massive necrosis of substitution of it by connective tissue. Parenchyma of liver and well kept hepatocytes forms nodes of regeneration if they are less then 1cm in size, such cirrhosis is named small nodular, if they rich 5 cm – great nodular

Nodular regeneration of liver at cirrhosis and hypertrophy of heart

Thrombus organization

- starts from 2nd-3rd day of its origination, goes parallel with aseptic autolysis and is finalized with thrombotic masses substitution with conjunctive tissue, canals formation and vascularization. Organization of hemorrhage or exudates in intermediate tissue also ends with cicatrization and in serous cavities – with their obliteration or joints formation. Fibrinogenous exudates organization in alveoli under croupous pneumonia results in carnification.
-

Organization of exudates in serous cavities – pericardium with their obliteration.