

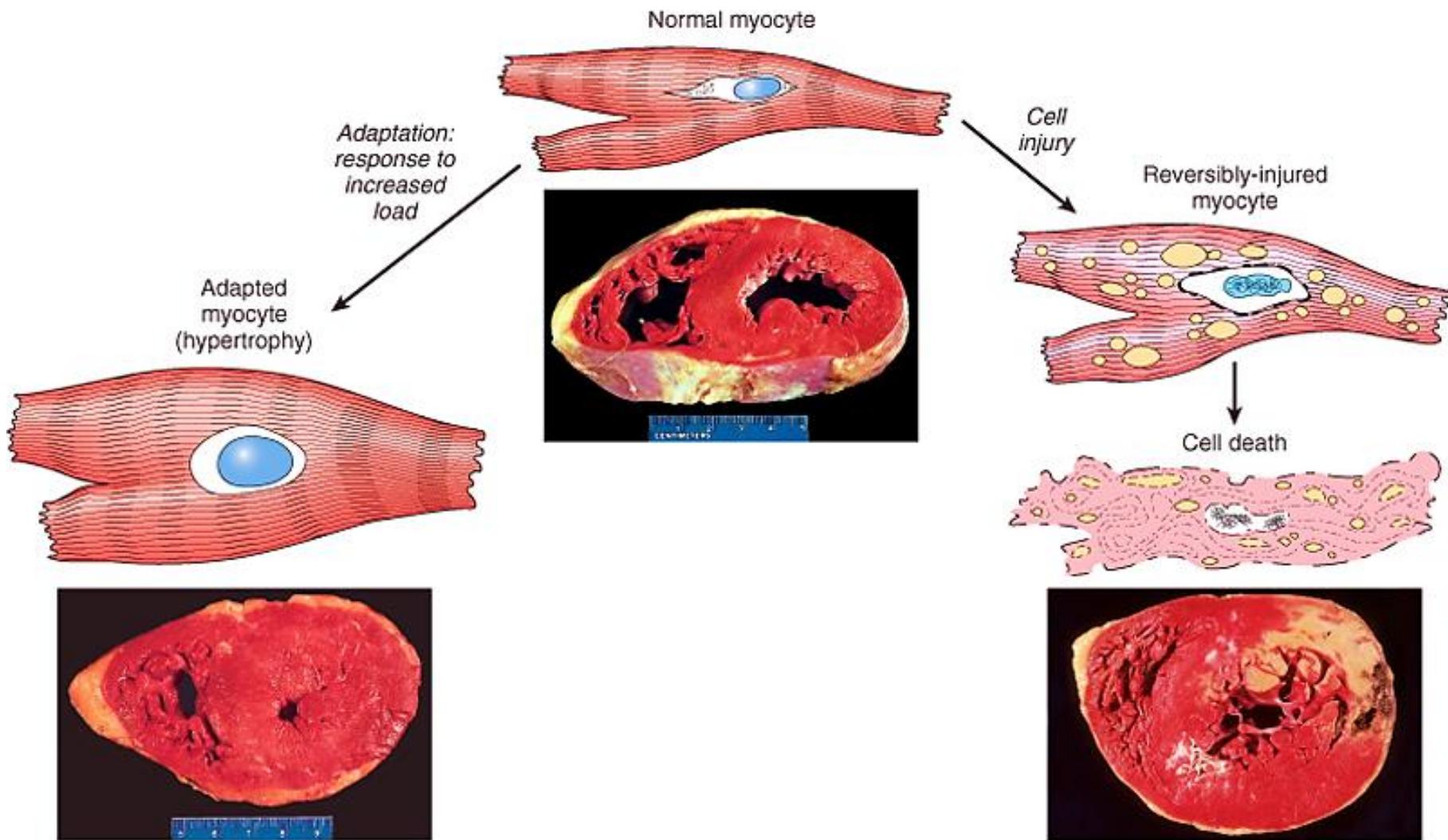
Morphology of metabolic disorders

Lecture #2
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Damage (injury)

- Under the influence of excessive physiological and pathological stimuli cells process of adaptation develops.
- If the limits of the adaptive response of cells are exhausted, cell damage occurs.
- Up to a certain limit cell damage is reversible.
- If unfavorable factor is permanent or its intensity is very large, it leads to irreversible cell damage and death.

Cell injury



Reversible damage

- In the classic pathology reversible (non-lethal) damage is called dystrophy (in english sources - degeneration).
- **Dystrophy - a pathological process, which is based on a violation of the tissue (cell) metabolism, leading to structural changes.**
- This type of cell damage can be manifested by intracellular or extracellular accumulations of abnormal amounts of various substances:
 - water, lipids, proteins and carbohydrates;
 - abnormal substances, including exogenous, such as ions, impaired metabolism products;
 - pigments.

Morphogenetic mechanisms

■ Infiltration

- Excessive penetration of metabolic products from blood and lymph into cells and intercellular substance.
- For example, fatty liver degeneration in hyperlipidemia.

Morphogenetic mechanisms

■ Decomposition

- The disintegration of cell ultrastructures and intercellular substance, leading to disruption of the tissue (cell) metabolism and the accumulation of disturbed metabolic products in tissue (cell).
- For example, fatty degeneration of the myocardium in diphtheria.

Morphogenetic mechanisms

■ **Perverted synthesis**

- Synthesis of substances, which do not occur in normal conditions.
- For example, alcoholic hyaline (Mallory corpuscles) in the liver of alcohol abuse person.

Morphogenetic mechanisms

■ Transformation

- Formation of products of one type from common materials that are used for the construction of proteins, fats and carbohydrates.
- For example, the accumulation of glycogen in the nuclei of hepatocytes in patients with diabetes mellitus.

Classification of dystrophies

- **Depending on the prevalence of morphological changes in the specialized or stromal cells and blood vessels:**
 - Parenchymal,
 - Stromal-vascular (mesenchymal)
 - Mixed
- **Depending on the type of metabolic disorder:**
 - Protein (disproteinosis)
 - Fatty (lipidosis)
 - Carbohydrate
 - Mineral

Classification of dystrophies

- **Depending on the prevalence of process:**
 - Local
 - Systemic
- **Depending on the etiology:**
 - Acquired
 - Hereditary

Parenchymal degeneration

- **Parenchymal dystrophies** are specific for metabolic disorders of highly functionally active cells of parenchymal organs - heart, kidneys, liver.

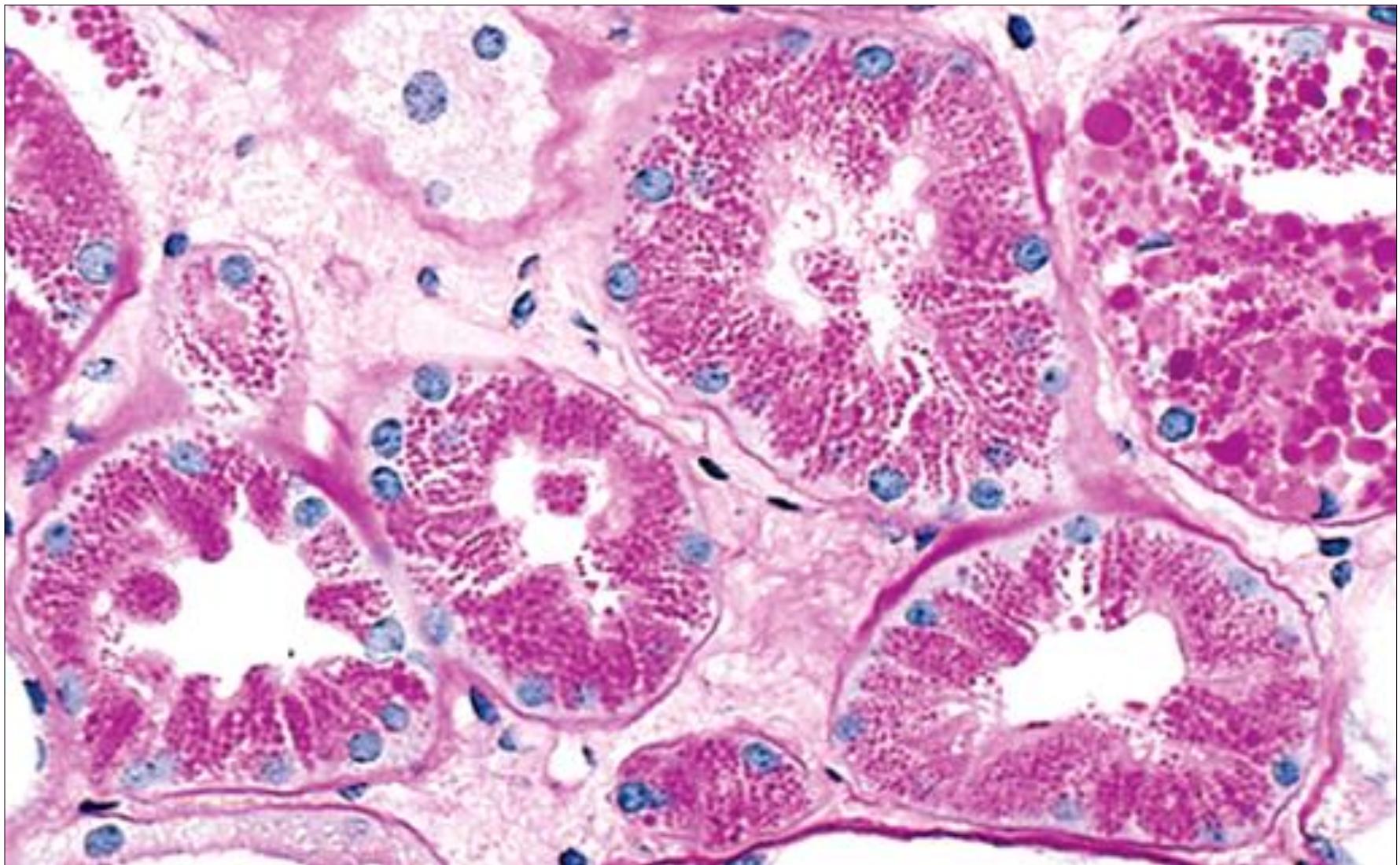
Parenchymal disproteinoses

- Accompanied by the appearance in the cell cytoplasm inclusions of protein nature.
- Parenchymal disproteinoses are morphologically represented by:
 - Hyaline-droplet dystrophy,
 - Hydropic dystrophy.

Hyaline-droplet dystrophy

- **Macroscopically** organs are not changed.
- **Microscopically** in the cytoplasm of cells appear large protein mostly hyaline droplets merging with each other.
- **Outcome:** cell death (focal / total coagulation necrosis).

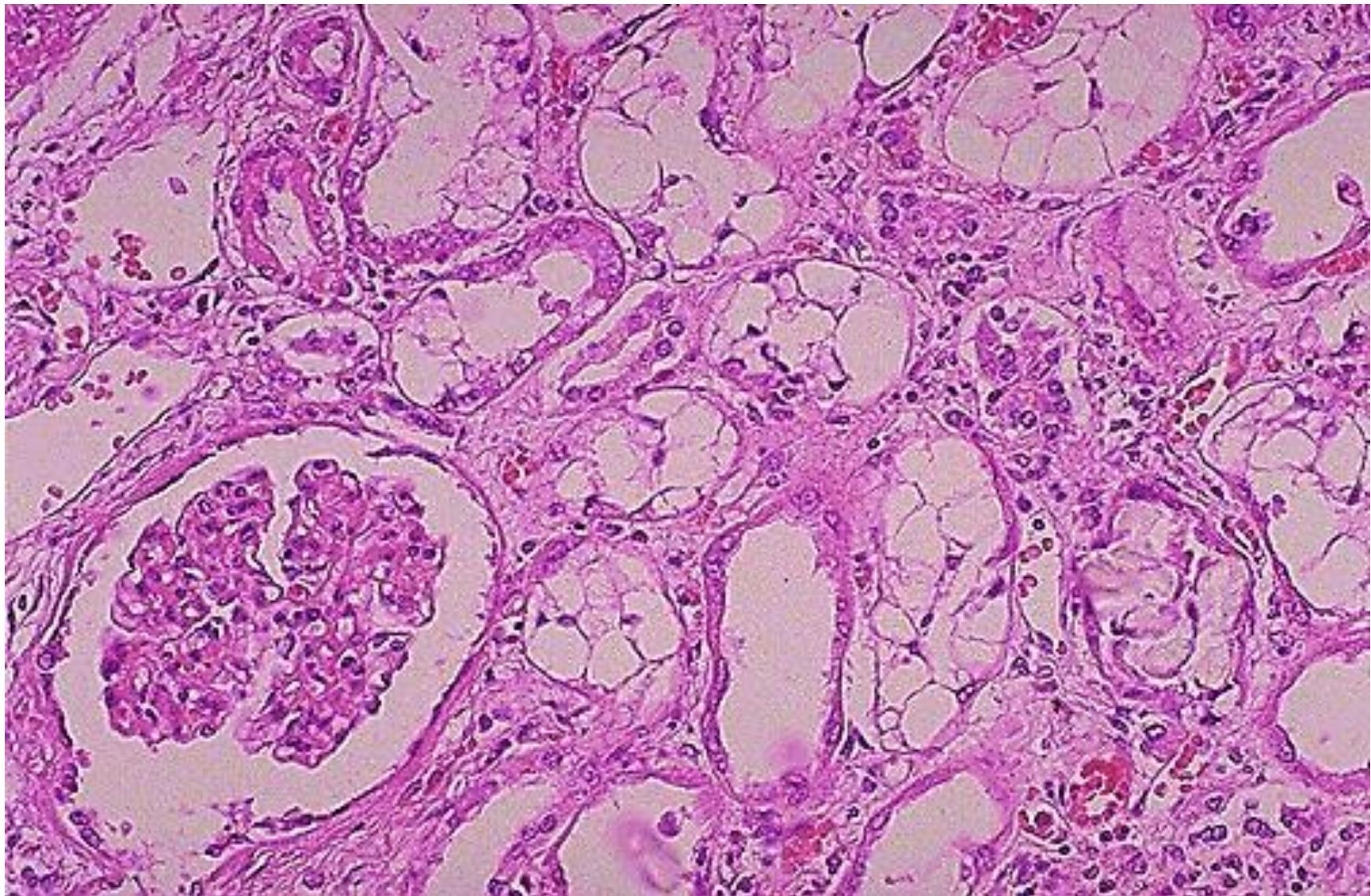
Hyaline-droplet dystrophy



Hydropic dystrophy

- **Macroscopically** organs are not changed.
- **Microscopically** in the cytoplasm appear vacuoles filled with cytoplasmic fluid.
- **Outcomes:**
 - ballooning degeneration (focal colliquative necrosis)
 - cell death (total colliquative necrosis).

Hydropic dystrophy



Parehchymal lypidoses

- Characterized by impaired metabolism of cytoplasmic fat.
- Morphologically manifest with accumulation of drops of neutral fats in the cell cytoplasm.
- To identify the lipids Sudan III stained frozen sections (orange-red) are used.

Fatty liver degeneration («goose liver»)

- **The most common fatty liver degeneration is accompanied by the following diseases and conditions:**
 - Diabetes mellitus,
 - Chronic alcoholism,
 - Malnutrition, starvation
 - Obesity,
 - Intoxication,
 - Anemia.

Fatty liver degeneration («goose liver»)

■ Macroscopic picture ("foie gras"):

- The liver is enlarged
- Flabby consistency
- In the section – yellow with swoop of fat.

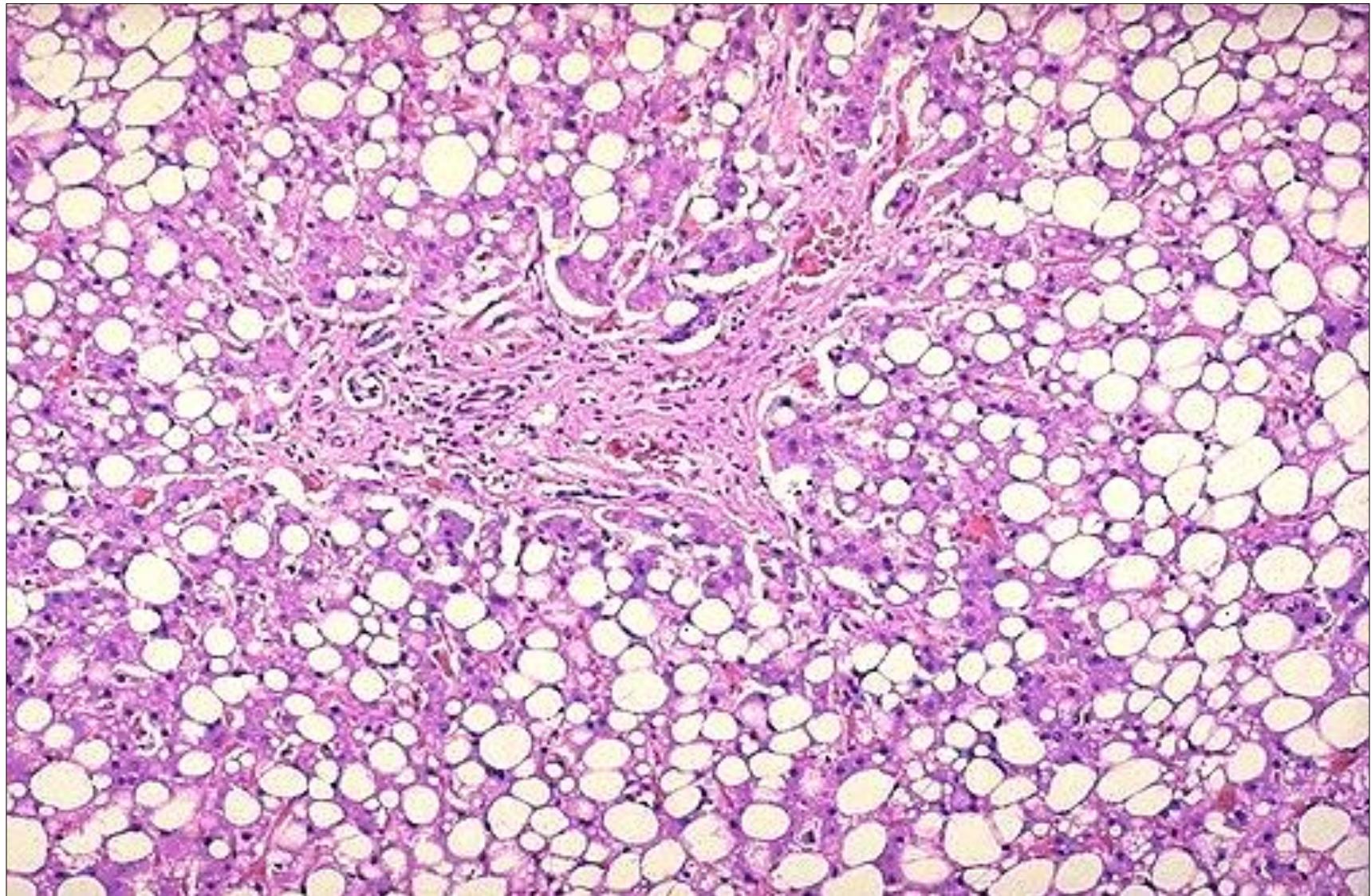
■ Microscopically:

- When stained with hematoxylin and eosin in the cytoplasm of hepatocytes vacuoles in place of the dissolved during processing fat droplets are seen;
- Sudan III staining of fat droplets is orange-red.

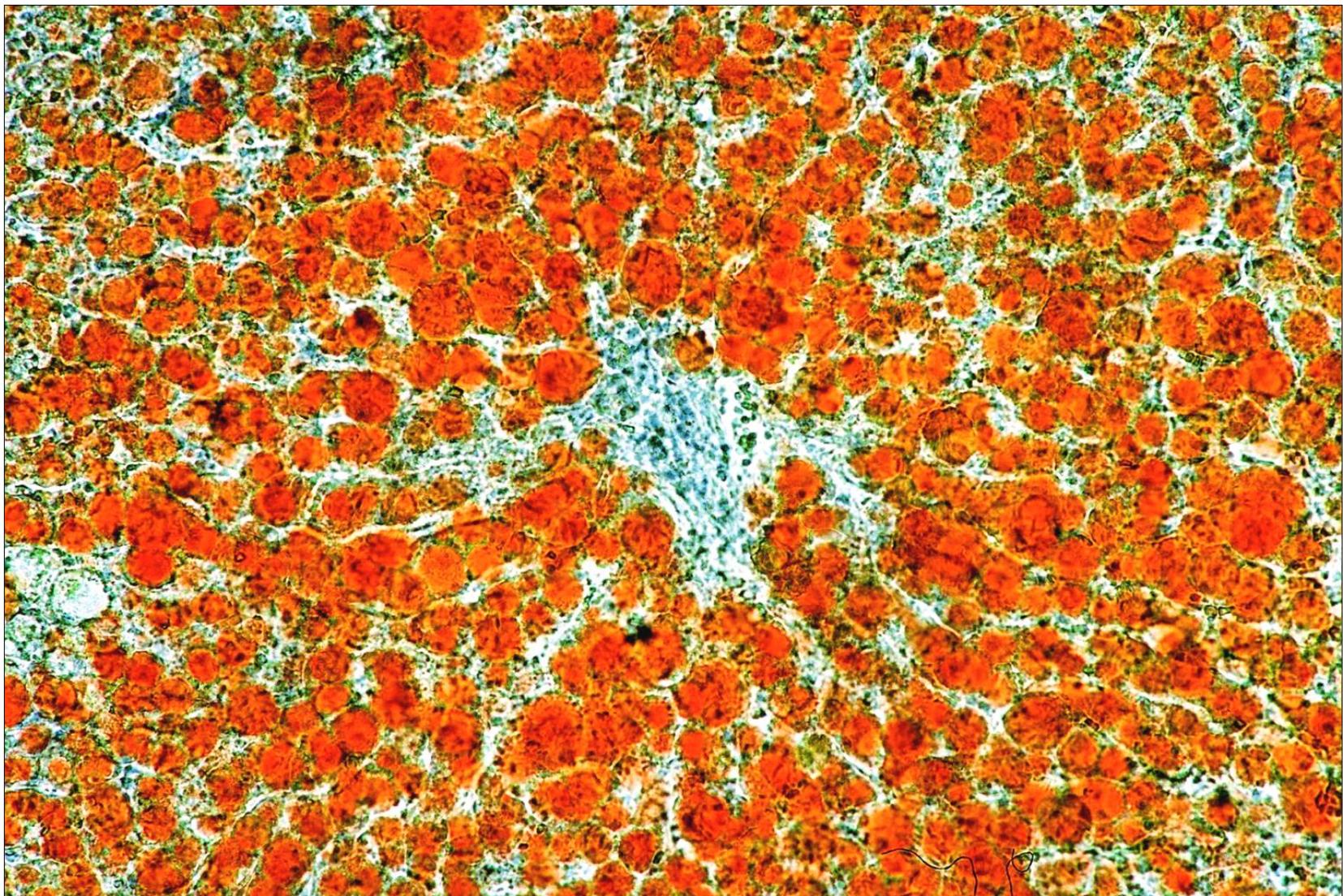
Fatty liver degeneration



Fatty liver degeneration



Fatty liver degeneration (Sudan III)



Fatty myocardium degeneration («tiger heart»)

■ Reasons for development:

- Hypoxia - the most common cause (anemia, heart failure),
- Intoxication (diphtheria, alcohol, phosphorus, arsenic).

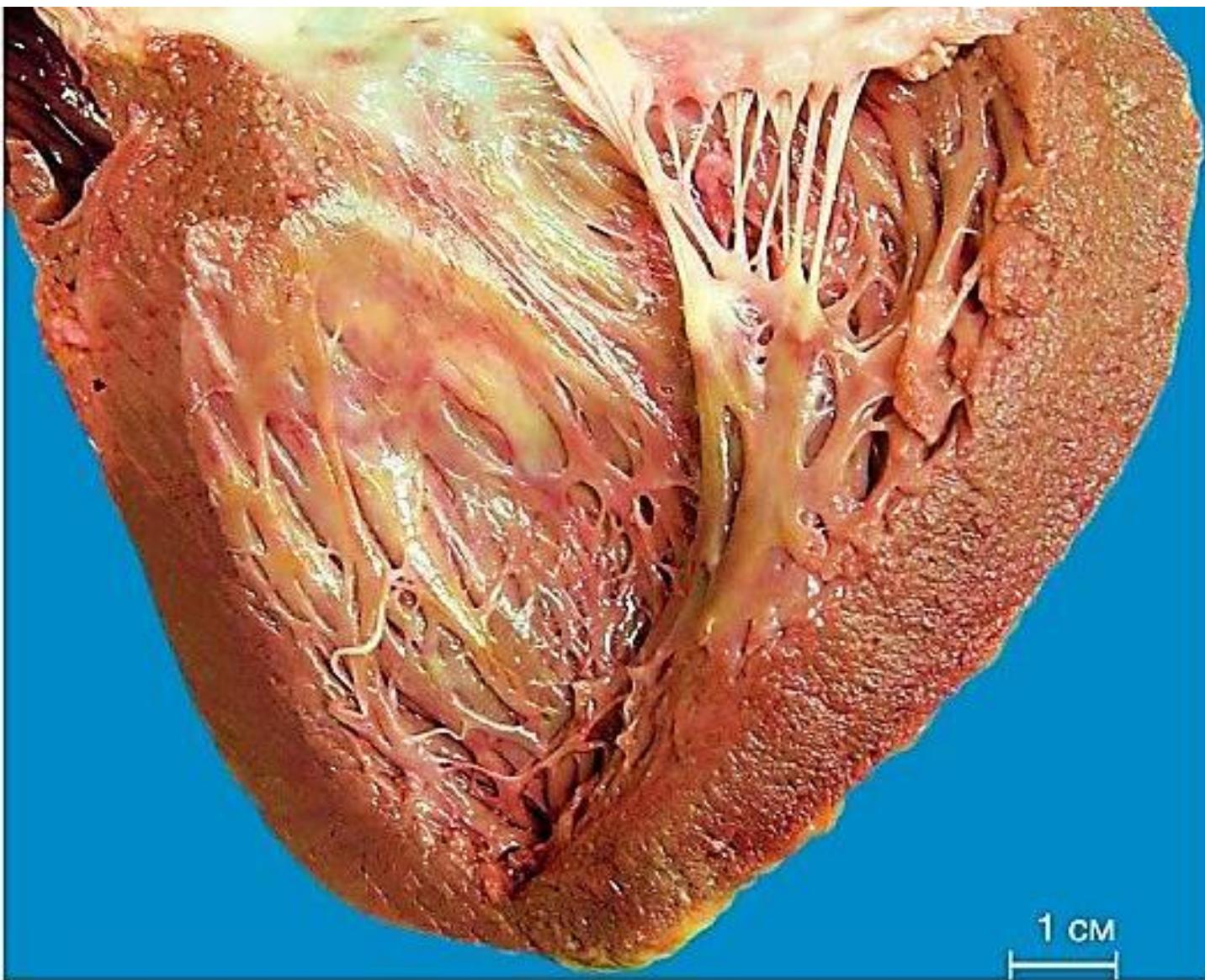
■ Macroscopic picture (tiger heart):

- Heart enlarged, chambers are stretched
- The myocardium flabby, pale yellow (clay) color
- From the endocardium, especially in the field of papillary muscles, yellow and white striations are visible.

■ Microscopically:

- Fatty degeneration is focal.
- Fat containing cardiomyocytes are located mainly along the veins.

Fatty myocardium degeneration



Mesenchymal dystrophies

- **Stromal-vascular or mesenchymal degenerations - structural manifestations of metabolic disorders in the connective tissue being detected in the stroma of organs and vessels walls.**

Mesenchymal dysproteinooses

- **Among the stromal-vascular dysproteinooses distinguished:**
 - Mucoid swelling
 - Fibrinoid swelling
 - Hyalinosis.

Mucoid swelling

- **Superficial and reversible disorganization of connective tissue**
- **Causes:**
 - rheumatic diseases;
 - atherosclerosis;
 - hypertonic disease;
 - hypoxia.
- It is characterized by the accumulation of glycosaminoglycans in the ground substance of connective tissue.

Mucoid swelling

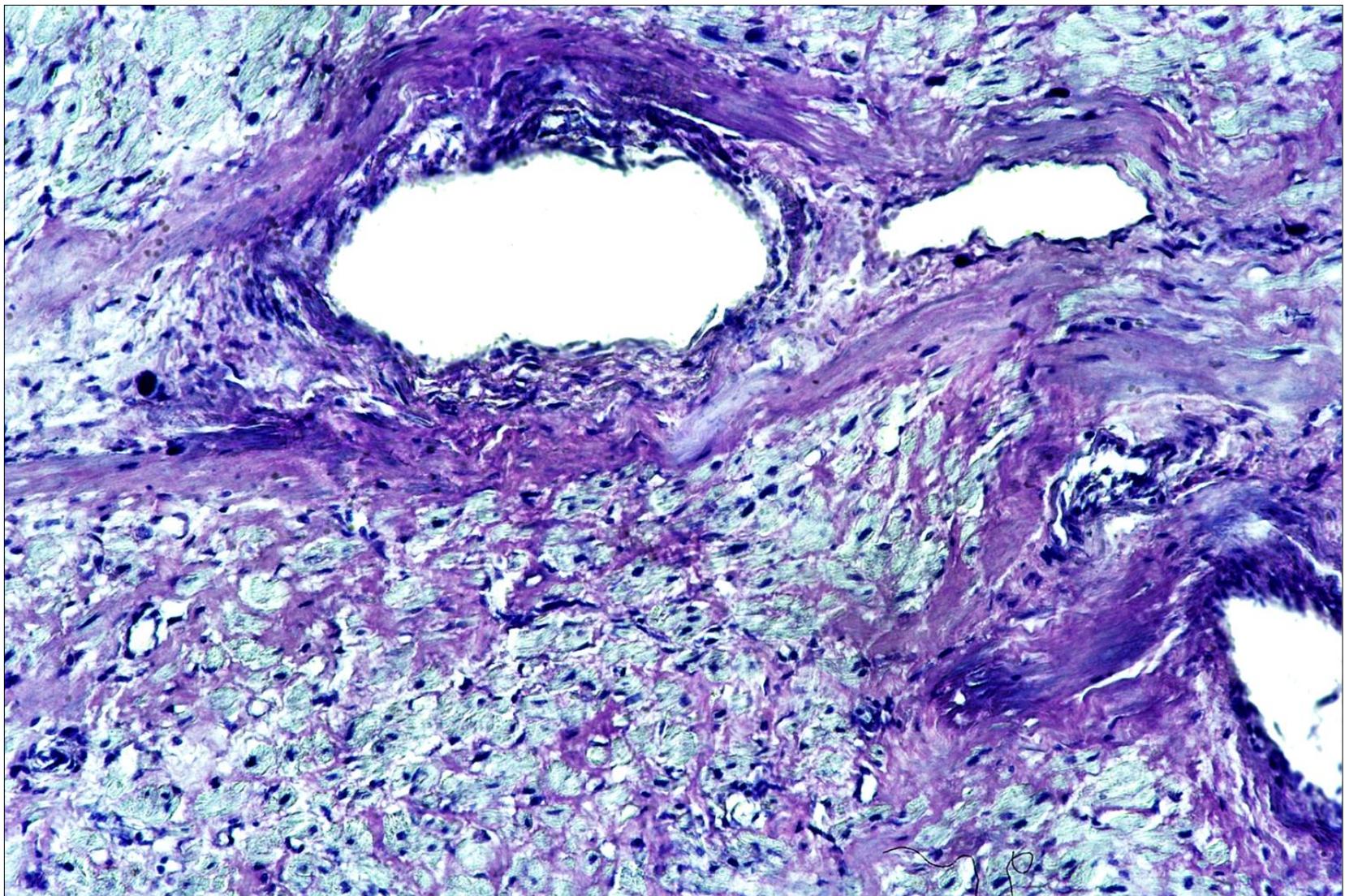
- **Macroscopic picture:**

- Organ or tissue usually do not change.

- **Microscopically:**

- The phenomenon of *metachromatic staining* (especially with toluidine blue): in foci of mucoid swelling the accumulation of glycosaminoglycans are seen, giving violet metachromatic staining.

Mucoid swelling



Fibrinoid swelling

- Deep and irreversible disruption of the connective tissue.
 - Causes:
 - infectious and allergic diseases;
 - autoimmune diseases.
- It is based on the destruction of the basic substance of the connective tissue fibers and accompanied by the release and conversion of fibrinogen to fibrin.

Fibrinoid swelling

- **Macroscopic picture:**
 - the affected organs and tissues slightly changed.
- **Microscopic picture:**
 - bundles of collagen fibers are homogeneous, eosinophilic, indicating a significant increase in the number of glycoproteins.
 - metachromasy by staining with toluidine blue is absent.

Hyalinosis

- It is characterized by the accumulation of translucent dense mass (hyaline) in tissues, reminiscent of hyaline cartilage.
- There are the following types of hyalinosis:
 - Vessels hyalinosis (common, local).
 - Hyalinosis of proper connective tissue (common, local).

Vascular hyaline

■ Ordinary hyaline:

- It arises from plasmorrhage of unaltered plasma components;
- more common in hypertension, atherosclerosis;

■ Lipohyaline:

- It contains lipids and b-lipoproteins;
- the most common for diabetes;

■ Complex hyaline:

- consists of immune complexes, fibrin and collapsing structures;
- Common for the rheumatic diseases and other immunopathologic states.

Vessels hyalinosis

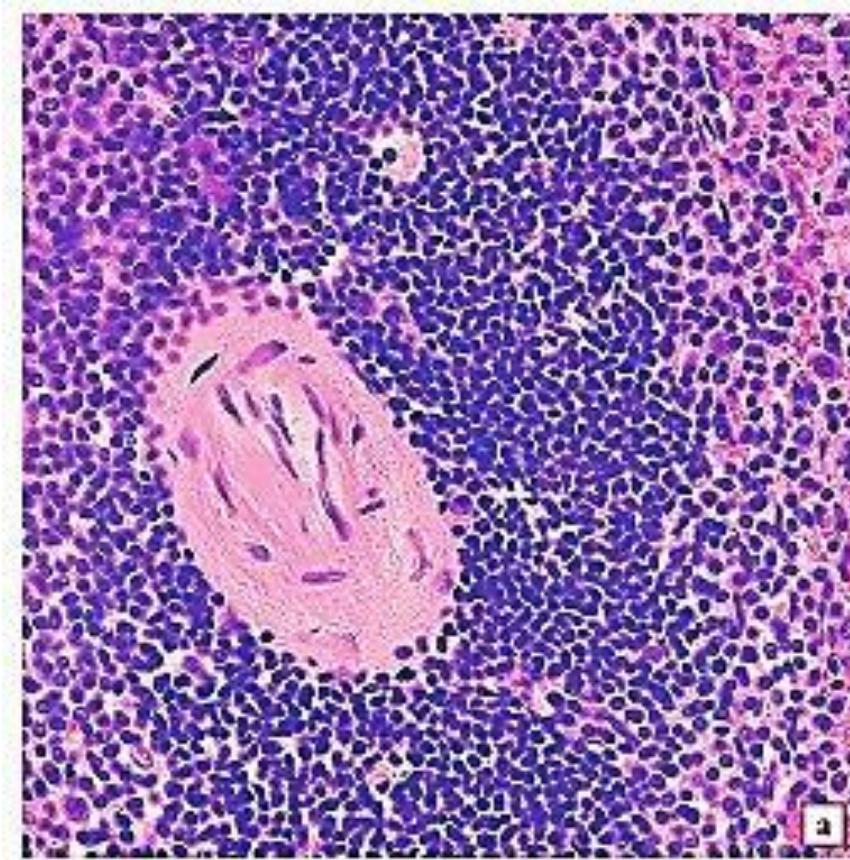
■ Microscopically:

- arterioles become thick glassy tubes with a sharply narrowed or completely closed lumen.

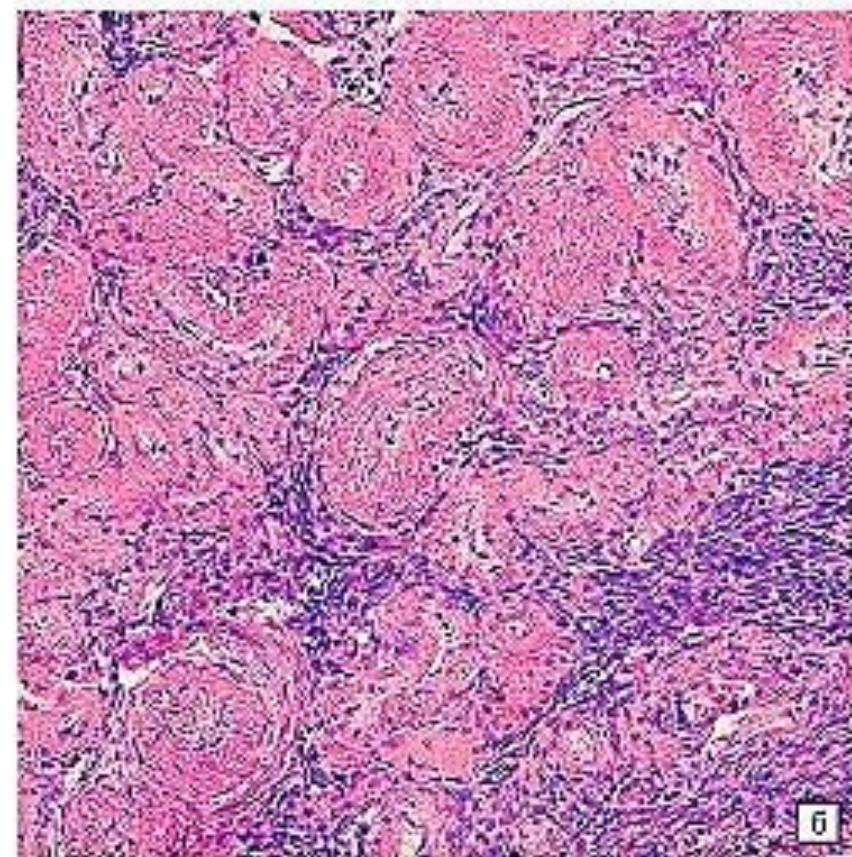
■ Outcomes:

- in most cases unfavorable because the process is irreversible

Spleen vessels hyalinosis



a



b

Connective tissue hyalinosis

■ Macroscopic picture:

- fibrous connective tissue becomes dense, cartilaginous, whitish, translucent.

■ Microscopic examination:

- bundles of collagen fibers lose fibrillarity and merge into a uniform dense chondroid mass;
- cell elements are compressed and undergo atrophy.

Spleen capsule hyalinosis («sugar-coated spleen»)



Mesenchymal lipidoses

- **Obesity - an increase of fat amount in the adipose tissue.**
- **Is general in nature and is expressed in excessive deposition of fat in the subcutaneous tissue, omentum, bowel mesentery, mediastinum, the epicardium.**
- **Obesity is the most dangerous in the heart, which is accompanied by heart failure and can lead to rupture of the right ventricle.**
- **Obesity degree depending on the percentage of excess body weight:**
 - Grade I - 20 - 29%
 - Grade II - 30 - 49%
 - Grade III - 50 - 59%
 - Grade IV - more than 100%.

Types of obesity

■ Depending on the mechanism:

- Alimentary
- Cerebral (trauma, brain tumors)
- Endocrine (at Froehlich's syndrome and Cushing's, hypophyseal syndrome, hypothyroidism, etc.)
- Inherited

■ By appearances:

- Symmetric type - symmetric distribution of fat
- Upper type - face, neck, upper limbs girdle
- Middle type - the abdomen,
- Bottom type - area of the thighs and shins.

Types of obesity



Male type

Female type

Types of obesity

- **Depending on the number and size of adipocytes:**
 - Hypertrophic type:
 - Number of adipocytes not changed,
 - Adipocytes are enlarged and contain several times more triglycerides
 - Course of disease is malignant.
 - Hyperplastic type:
 - Number of adipocytes increased,
 - Function of adipocytes is not disrupted,
 - Course of disease is benign.

Mixed dystrophies

- Mixed dystrophy - a morphological manifestations of impaired metabolism detected in the parenchyma and in the stroma of organs and tissues, as result of violation of the complex proteins exchange - endogenous pigments (chromoproteids), nucleoproteins, lipoproteins, and minerals.

Endogenous pigmentations

- Endogenous pigmentations are commonly associated with excessive accumulation of pigments (chromoproteids) which are formed normally, less frequent - with the accumulation of pigments occurring only in pathological conditions.
- Endogenous pigments are:
 - Hematogenous,
 - Proteinogenic (tyrosinogenous)
 - Lipidogenous

Hematogenous pigments

- They represent various hemoglobin derivatives, arising during the synthesis or breakdown of erythrocytes.
- The normal are:
 - Ferritin,
 - Hemosiderin
 - Bilirubin
 - Porphyrins
- In pathological conditions formed:
 - Hematoidin
 - Hematin

Hemosiderin

- Aggregate of ferritin molecules produced in the cell in excess of iron (e.g., enhanced hemolysis or elevated admission of exogenous iron).
- Accumulation of pigment formed by hemolysis is called gemosiderosis.
- Massive deposition of hemosiderin arising as a result of increased iron uptake is called hemochromatosis
- It is detected in the form of brown granules in the cells, rarely extracellularly.
- In Perls Prussian Blue staining (qualitative reaction for iron) the beads of hemosiderin are blue-green.

Local hemosiderosis

- It occurs by the extravascular hemolysis at foci of hemorrhage:
 - Hemosiderin accumulates in the cells surrounding the hemorrhage: macrophages, leukocytes, endothelium, epithelium.
 - Sequential breakdown of hemoglobin and formation of pigments leads to hemorrhage discoloration ("bloom bruise"): purple-blue color (hemoglobin) is replaced by green-blue (biliverdin), green-yellow (hematoidin) and rusty-brown (hemosiderin).
- An example of local hemosiderosis may be brown induration of the lungs that occurs in chronic venous stasis in patients with chronic heart failure (heart disease, cardiosclerosis, etc.)

Brown induration of the lungs

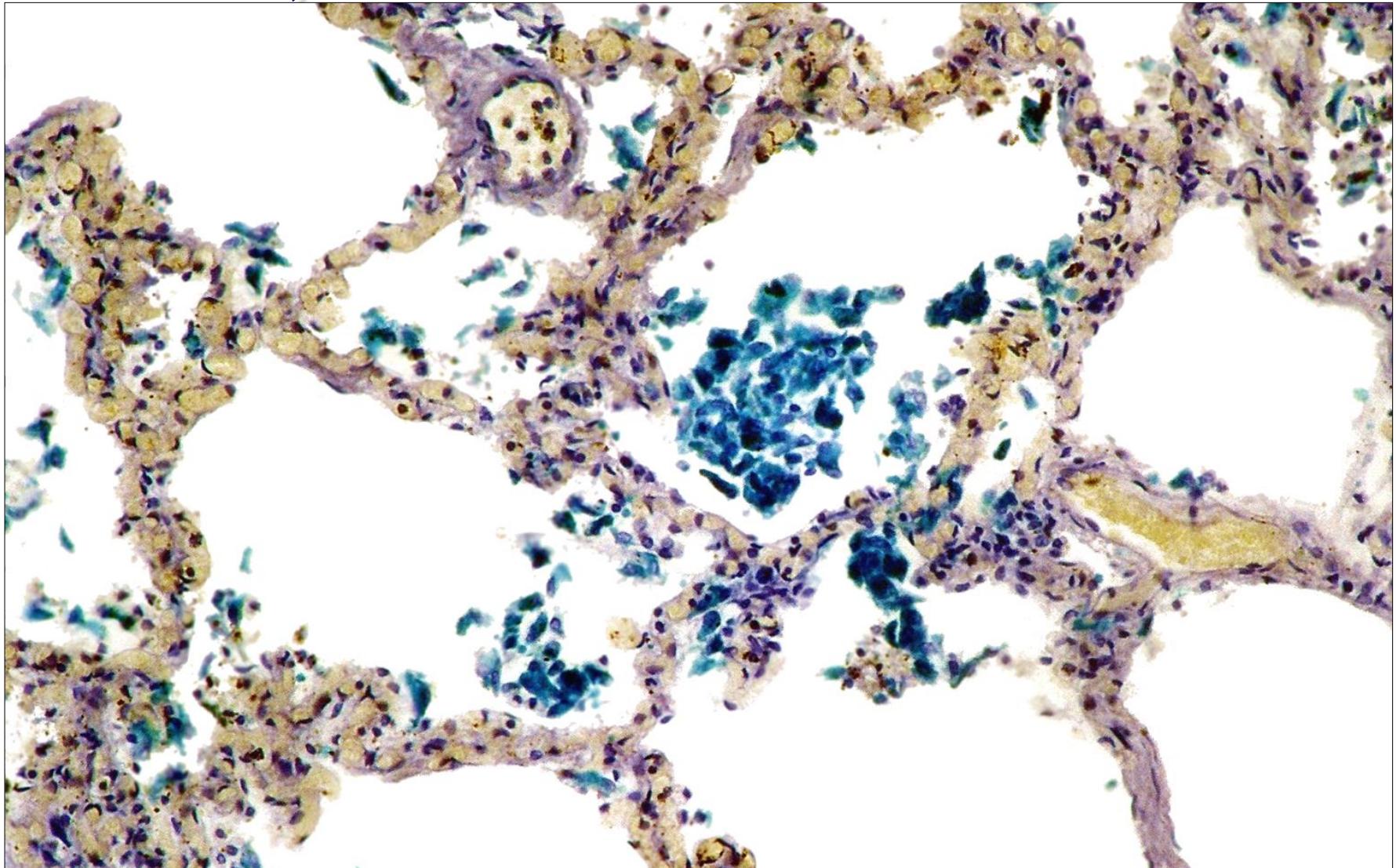
■ Macroscopic picture:

- Lungs enlarged
- Dense consistency
- On section - numerous brownish granules and connective tissue insertions.

■ Microscopically:

- A large number of cells containing a brown pigment in the stroma of the lung, and in the alveoli and bronchi lumens.
- Alveolar septa are significantly thickened due to excrescence of connective tissue.

Brown induration of the lungs (Perls' reaction)



General hemosiderosis

- **It occurs after intravascular hemolysis developed as result of:**
 - Blood diseases (anemia, leukemia)
 - Poisoning with hemolytic poisons,
 - Infectious diseases (malaria, sepsis, relapsing fever, and others.)
 - Transfusion of incompatible blood and rhesus conflict.
- **With the accumulation of pigment organs become rusty-brown.**

Bilirubin

- Bilirubin - the main bile pigment.
- Formed in the cells during hemoglobin cleavage, does not contain iron.
- In the blood is associated with albumin.
- In hepatocytes conjugation occurs - the binding of bilirubin to glucuronic acid, thereafter it is excreted into the bile.
- Excessive accumulation of bilirubin in the blood leads to jaundice (jaundiced coloration of sclera, skin and mucous membranes appear).

Types of jaundice

■ **Suprahepatic (hemolytic) jaundice:**

- Occurs after intravascular hemolysis, is associated with the general hemosiderosis,
- the content of unconjugated bilirubin in the blood is increased

■ **Hepatic (parenchymal) jaundice:**

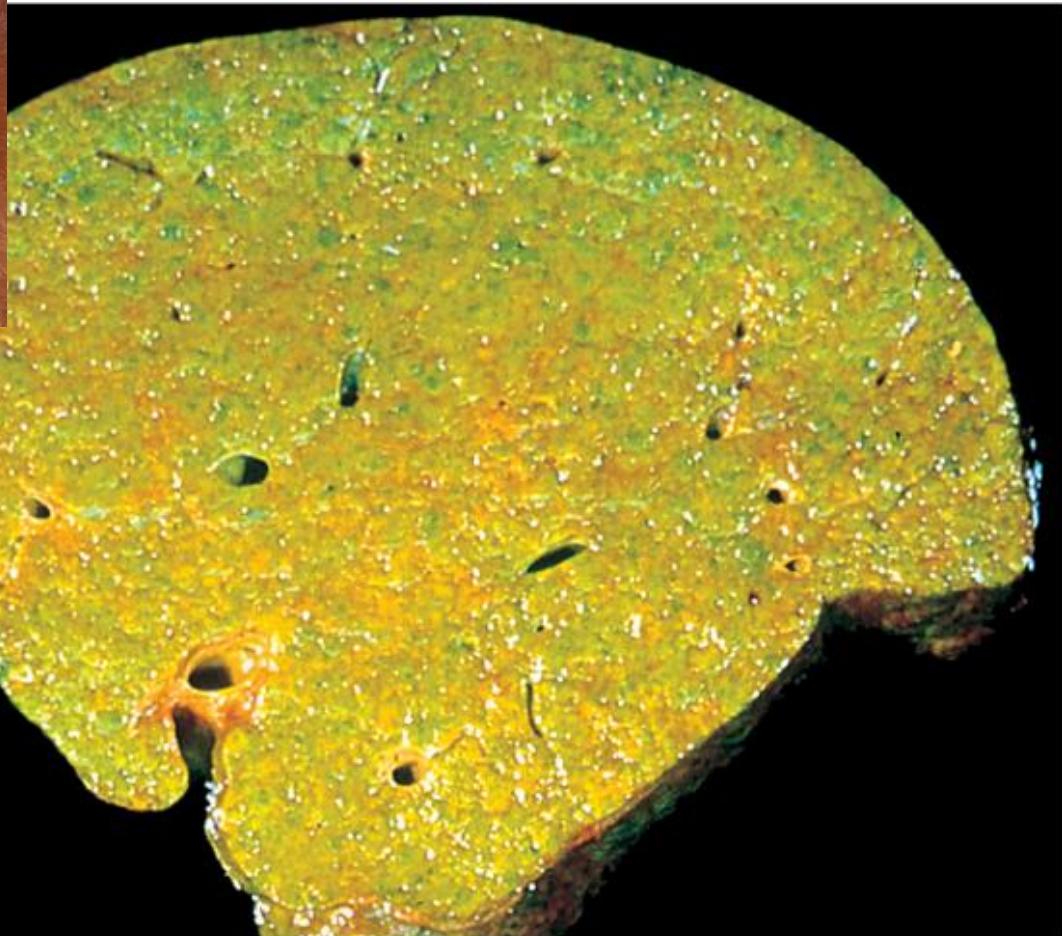
- Symptom of liver diseases (hepatitis, hepatosis, cirrhosis)
- Violated capture and conjugation of bilirubin by damaged hepatocytes,
- the content of conjugated and unconjugated bilirubin is increased.

Types of jaundice

■ **Subhepatic (mechanical) jaundice:**

- The reason is the obstruction of the biliary tract (pancreatic head tumor, a tumor of the biliary tract, liver cancer, cancer metastasis to the liver, the stone in cholelithiasis, helminths)
- Violated bile excretion, conjugated bilirubin passes into the blood,
- It is accompanied by cholestasis.

Jaundice



Proteinogenous pigments

■ Proteinogenous (tyrosinogenous) pigments include:

- Melanin,
- Pigment from granules of enterochromaffin cells
- Adrenochrome

Melanin

- The pigment is brownish-black, is synthesized from tyrosine by the action of tyrosinase in melanocytes specialized structures - melanosomes.
- Melanocytes - cells of neuroectodermal origin, found in the basal layer of epidermis, retina and iris, meninges.

Hyperpigmentations (hypermelanooses)

- **Acquired common hypermelanosis develops in Addison's disease:**
 - The disease is associated with damage of the adrenal glands (tuberculosis, tumors, amyloidosis, an autoimmune disease).
 - Melanin synthesis is enhanced in the skin, it becomes brown, dry, flaky.

Hyperpigmentations (hypermelanooses)

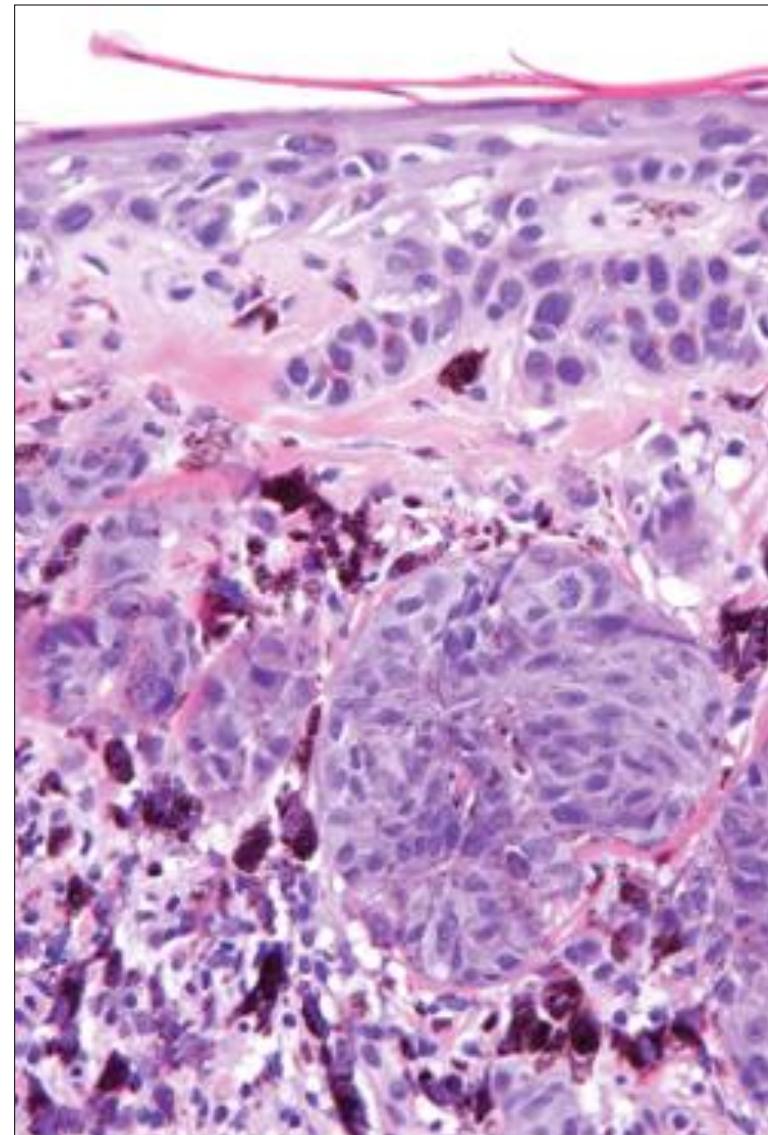
■ Local hyperpigmentation:

- Freckle
- Lentigo (dark brown spots)
- Nevus (benign melanocytic mass)
- Melanoma (malignant tumor)

Lentigo



Hypermelanosis (melanoma)



Hypopigmentations (hypomelanoses)

■ Common hypomelanosis or albinism

- Associated with hereditary deficiency of tyrosinase,
- Skin white, discolored hair, red eyes.

■ Local hypopigmentation

- Most acquired, rarely congenital.
- Are called vitiligo or leukoderma.

Vitiligo



Lipogenous pigments

- **Lipofuscin** - insoluble pigment, also known as the aging pigment.
- It forms golden brown granules in the cell.
- The accumulation of lipofuscin in the cells is called lipofuscinosi
- Lipofuscin accumulates mostly in myocardial cells, liver, skeletal muscle during aging and is accompanied by the development of brown atrophy of organs.

Brown atrophy of heart

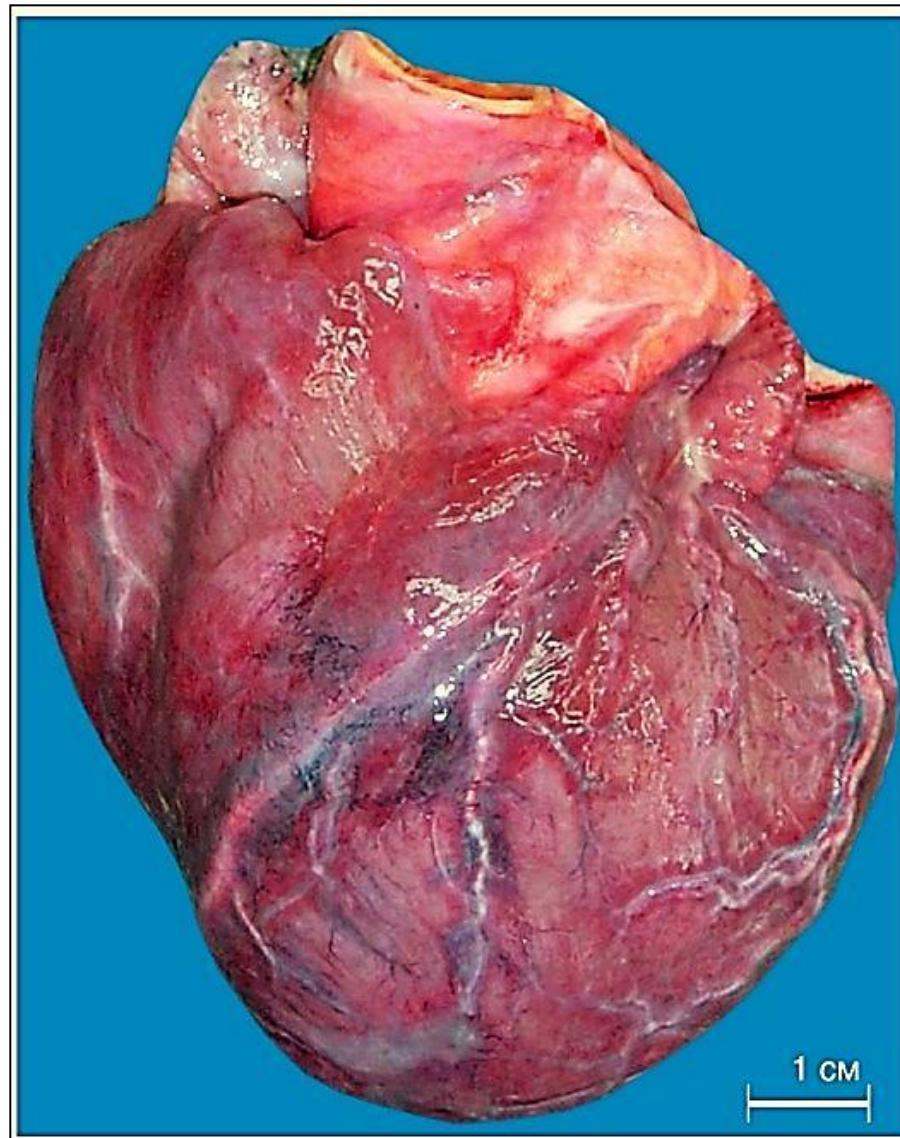
■ Macroscopic picture:

- Heart greatly reduced in size,
- Fatty tissue under the epicardium is virtually absent,
- The vessels become tortuous course,
- In the section myocardium tight, brown.

■ Microscopically:

- Cardiomyocytes are reduced in size
- Brown lipofuscin pigment granules in the cytoplasm of cardiomyocytes.

Brown atrophy of heart



Calcification

- Characterized by the deposition of calcium salts in the tissues.
- may be systemic and local.
- On the mechanism of development are distinguished:
 - Metastatic
 - Dystrophic
 - Metabolic

Metastatic calcification

- The main role is played by hypercalcemia that occurs in case of:
 - Hyperparathyroidism (adenoma, hyperplasia)
 - Massive bone resorption (multiple myeloma, bone metastases, multiple fractures, prolonged immobilization of bones, etc.)
 - Systemic sarcoidosis
 - Hypervitaminosis D
 - Milk-alkali syndrome, chronic administration of antacids,
 - CRF

Metastatic calcification

- **It is systemic:**
 - Affects the kidneys, myocardium, large arteries, lungs.
 - Calcium phosphates (apatite) falls primarily on mitochondrial cristae and in the lysosomes, which are matrix for calcification.
 - After cell death calcification applies to fibrous structures.

Calcareous metastases

- These are focuses of metastatic calcification.
- Macroscopically usually not detectable.
- Microscopically are detectable as numerous small dark purple foci, presented by necrotic cells encrusted with salts of calcium, often with adjacent portions of the stroma surrounded by inflammatory infiltration and sclerosis.
- Specific staining for the detection of foci of calcification is the silvering by Kossa, in which they are stained black.

Dystrophic calcification

- The level of calcium in the blood does not change.
- It occurs locally in necrosis, dystrophy, sclerosis.
- For the development are relevant: alkalinization of environment and increased activity of phosphatases released from damaged tissues .

Petrifications

- These are foci of dystrophic calcification.
- Petrification can occur in separate necrotic cells (psammous cells) and large areas of necrosis.
- The most common manifestations of dystrophic calcification are the following:
 - Petrifications in the lungs as a result of the healing of foci of caseous necrosis in tuberculosis - lesions are white, have rocky density, are surrounded by a connective tissue capsule.
 - Calcification of atherosclerotic plaque (aterocalcinoses).

Metabolic calcification

- **Synonyms: interstitial calcification, calcareous gout.**
- **The level of calcium in the blood does not change.**
- **In the development the role of the following factors is being discussed:**
 - Unstable buffer systems, retaining calcium in a dissolved state
 - Calciphylaxis - increased sensitivity of tissues to calcium.
- **It may be systemic or limited:**
 - In the systemic calcification salts fall in the skin, subcutaneous tissue, along the tendons, fascia, muscles, blood vessels.
 - In a limited calcification deposits of lime in the form of plates in the skin of the fingers are common.



Thank you for attention!