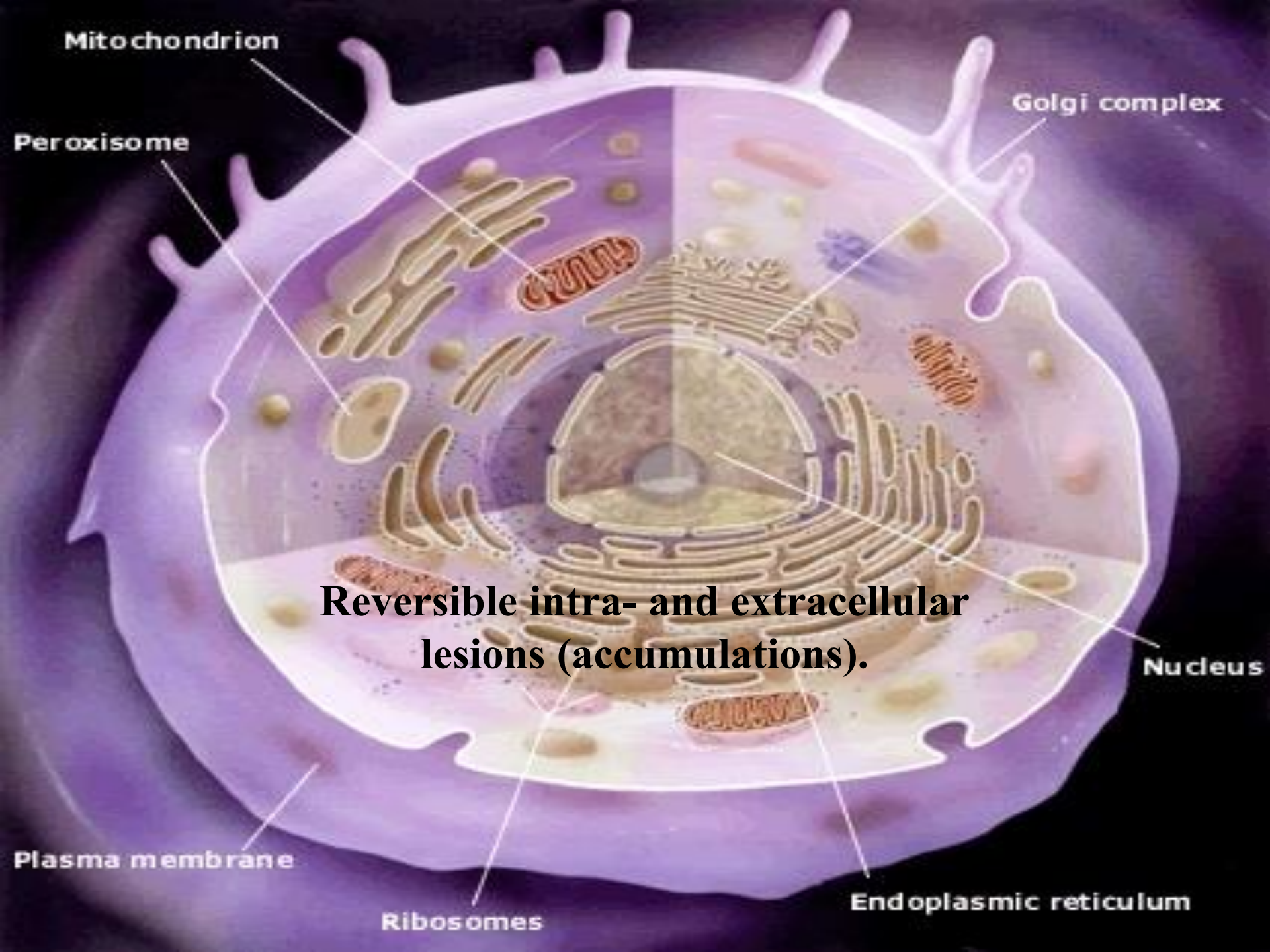


Reversible intra- and extracellular lesions (accumulations).

Reversible intra- and extracellular lesions (accumulations).

I. Microspecimens:

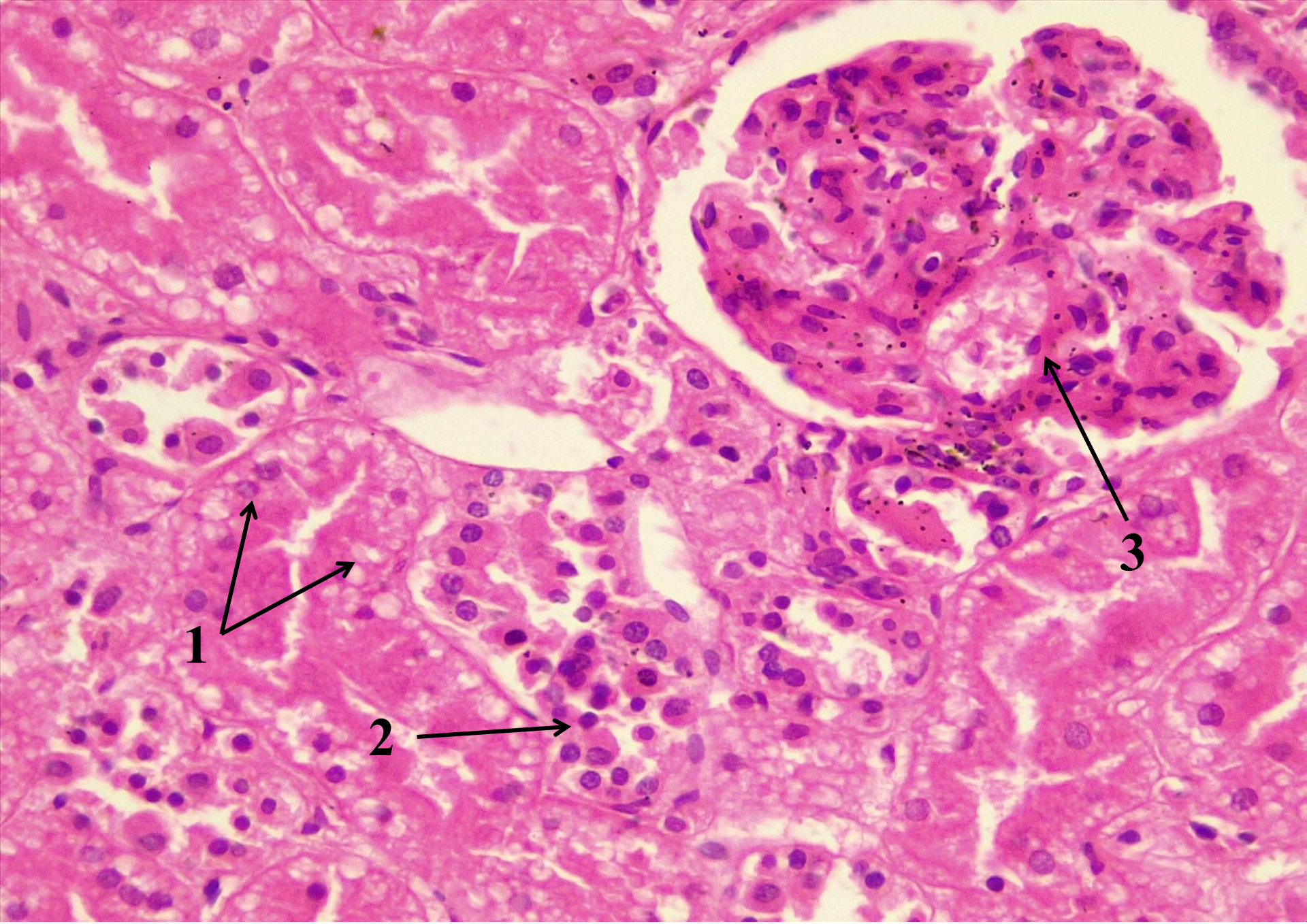
№ 149. **Hydropic (*vacuolar*) degeneration of the renal convoluted tubules epithelium.** *(H-E. stain).*

Indications:

1. Convoluted tubule with hydropic degeneration:
    a. colorless vacuoles in the cytoplasm of the nephrocytes;
    b. poorly colored nucleus.
2. Unchanged tubule.
3. Unchanged glomerulus.

In the nephrocytes of the twisted tubes, a large number of optically empty vacuoles (filled with cytoplasmic fluid) are observed, round or oval in shape, located mainly along the basement membrane; the nucleus of the cells is pale, and the lumen of the tubes – narrowed; in some other parts, in the cells are present the same vacuoles, but larger and located perinuclear.

Hydropic degeneration is found both in the parenchymal organs and in the skin (in the epidermis). Macroscopically the affected organs are slightly altered. The main pathogenetic mechanism consists in the disturbance of the hydro-electrolytic and protein metabolism with the modification of the intracellular colloid-osmotic pressure, which leads to the penetration of water into the cell or to the disorder of the elimination of water formed in the cell during redox processes. Excessive water accumulation conditions the destruction of intracellular ultrastructures and the appearance of vesicles filled with cytoplasmic fluid (cell ballooning). The fluid accumulates in the cisterns of the endoplasmic reticulum and in the mitochondria. The definite diagnosis of hydropic degeneration can be established only after staining microscopic parts for glycogen and lipids (lack of staining confirms the diagnosis). Functional disorders occur in the affected organs, for example, hydropic degeneration of the renal tubule epithelium is more commonly seen in nephrotic syndrome, characterized by pronounced proteinuria and edema. Vacuolar degeneration of the myocardium is manifested by reduced contractile function of the heart. It is observed in infectious diseases (especially in viral hepatitis), intoxications, starvation, avitaminosis, the action of penetrating radiation, etc. At the initial stage, the vacuolar degeneration is reversible, and if the process progresses, the focal or total destruction of the cytoplasmic organelles and the liquefactive necrosis of the cell occur.



№ 149. Hydropic (*vacuolar*) degeneration of the renal convoluted tubules epithelium. *(H-E. stain).*

№ 18. Hyalinosis of the lineal arteries. *(H-E stain).*

Indications:

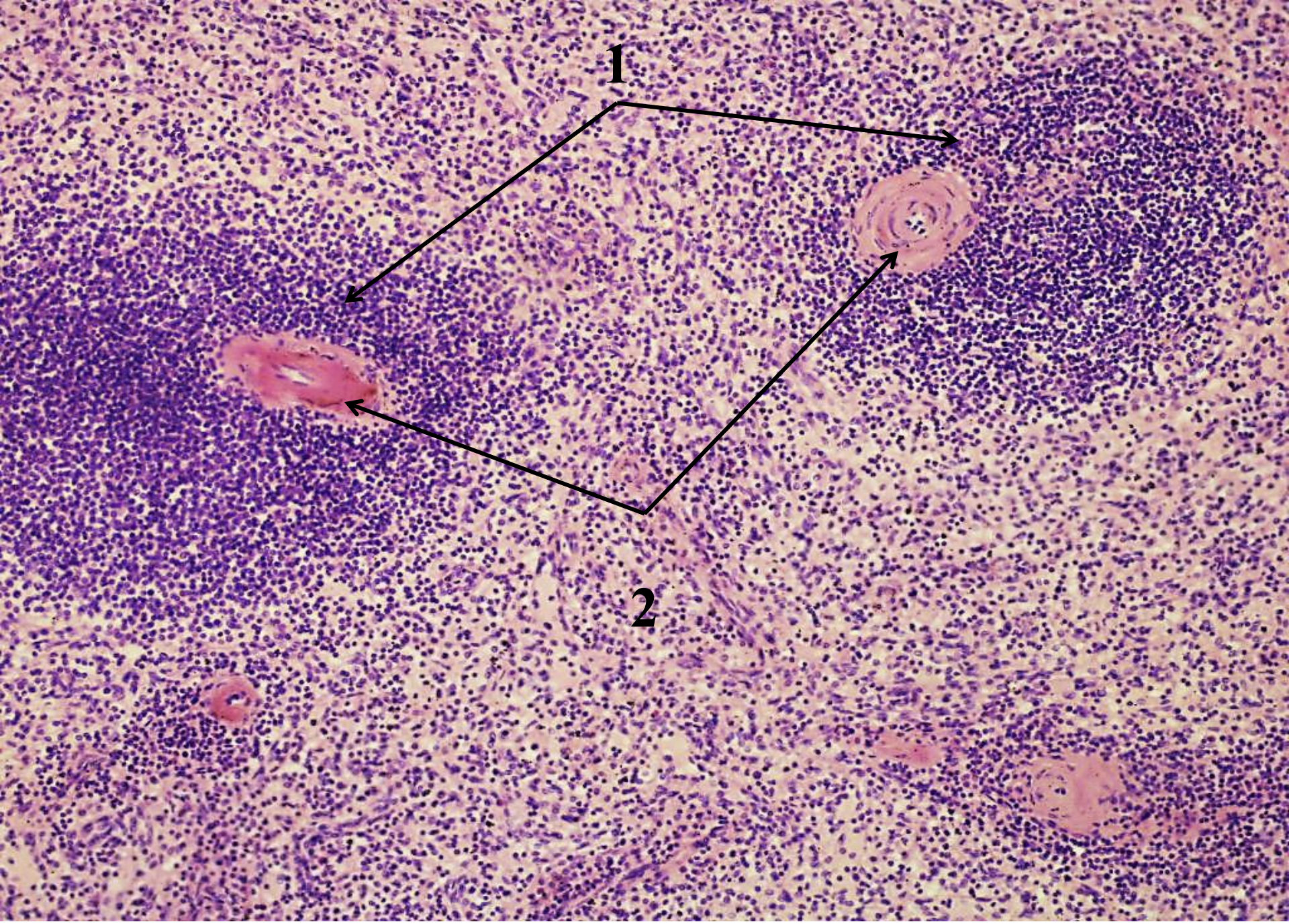
1. Lymph follicle.
2. Central artery of the follicle:
    a. thickened wall;
    b. hyaline masses deposits in the subendothelial layer;
    c. narrowed lumen.

The walls of the central arteries of the spleen follicles are thickened due to diffuse deposits of homogeneous, eosinophilic colored hyaline masses, which accumulate subendothelially; the media is atrophied; tangentially or longitudinally sectioned arteries look like a hyaline tube resembling a narrow-lumen glass tube.

Vessel hyalinosis occurs mainly in small arteries and arterioles, being preceded by increased vascular permeability and plasma imbibition (plasmorrhagia) of vessel walls Vascular hyaline is formed from plasma precursors, especially blood plasma proteins, initially accumulating subendothelially. Smooth muscle cells and fibrillar elements of the vascular walls are gradually atrophied and soaked with fibrin and other plasma components. Over time, the affected vessel turns into a hyaline tube with a thickened wall and a very narrow or even completely clogged lumen. These changes lead to ischemia and hypoxia of the organ, atrophy of the parenchyma and perivascular proliferation of connective tissue.

The lesions are especially characteristic for arterial hypertension and diabetes. Primary are affected small arteries and arterioles of the brain, heart, kidneys, retina, and endocrine glands. In these cases vascular hyalinosis has a generalized character (hyaline arteriolosclerosis or arteriolohyalinosis). Local hyalinosis of the arteries is observed in the spleen, being a physiological process determined by the morphofunctional peculiarities of the spleen as a blood storage organ.

Vascular hyalinosis is an irreversible process, which can lead to functional disorders and serious complications, eg, arteriolosclerotic nephrosclerosis with shedding of the kidneys in arterial hypertension, glomerulosclerosis and diabetic retinopathy.



№ 18. Hyalinosis of the lineal arteries. *(H-E stain).*

№ 25. Fatty liver degeneration. *(H-E. stain).*

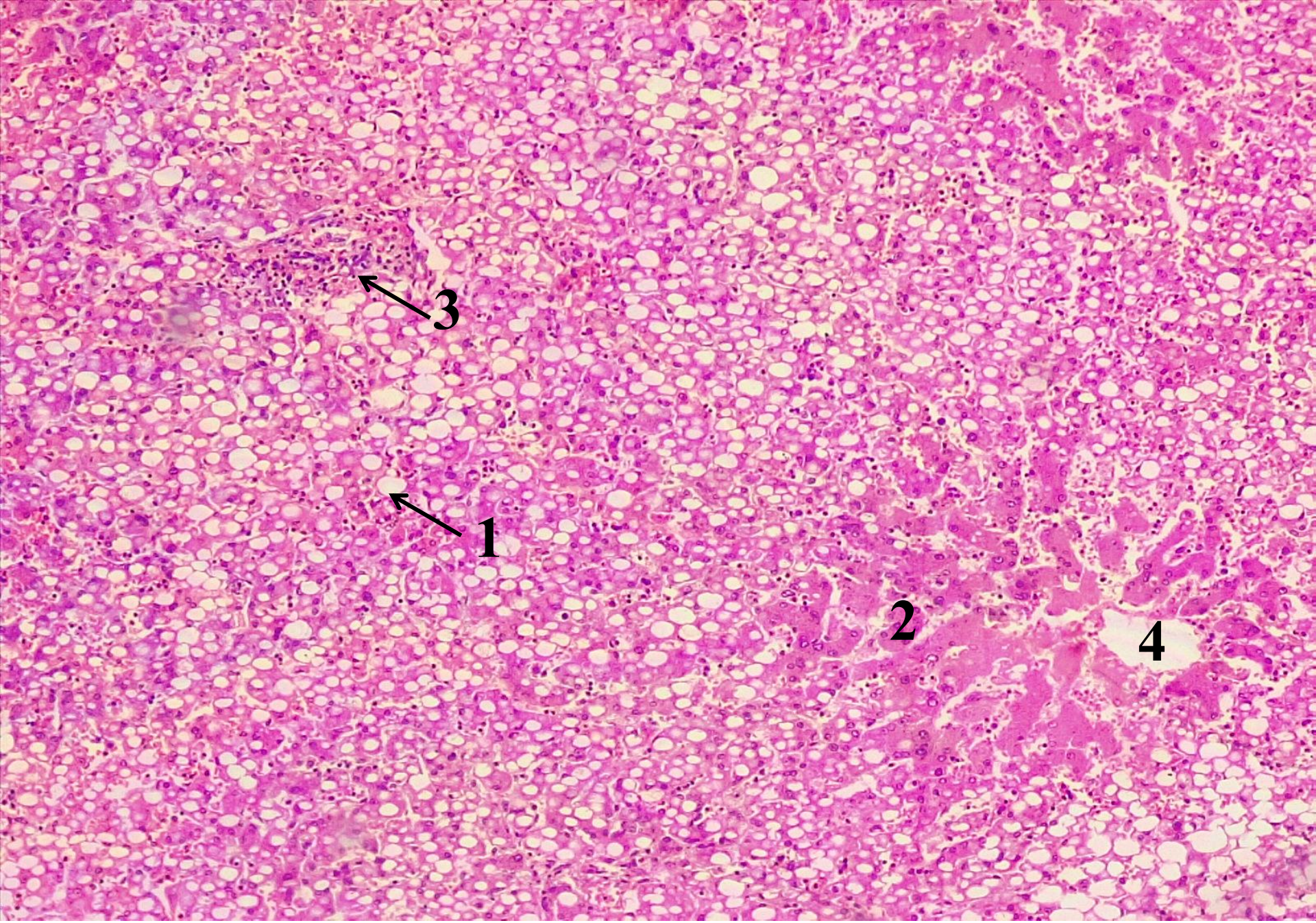
Indications:

1. Colorless lipid vacuoles in the cytoplasm of hepatocytes.
2. Unchanged hepatocytes.
3. Triad (artery, vein, bile duct).
4. Central vein.

The cytoplasm of hepatocytes contains numerous round or oval vacuoles, of different sizes (microvesicular or macrovesicular steatosis), optically hollow, without a limiting membrane, located mainly in the central portion of the hepatic lobe (centrolobular steatosis) or at the periphery of the lobule (peripheral steatosis), or diffuse, occupying the entire lobule (diffuse steatosis); in some liver cells the vacuoles fuse to form a large vacuole, the nucleus being pushed to the periphery, and the hepatocyte becomes similar to the fat cell (adipocyte). Hepatocyte membranes may rupture and lipid cysts may form.

Vacuoles are lipid droplets, which appear optically empty because the lipids dissolve in the process of histological processing of tissue fragments and staining with H-E - procedures, in which lipid solvents (alcohol, chloroform) are used. To store and identify lipids it is necessary to perform sections on ice with the freezing microtome and to process lipophilic dyes with Sudan III (color lipids in orange) or Sudan IV (in black). The most common causes of hepatic steatosis are lipidemia (obesity, excess dietary fat, chronic alcoholism, diabetes, hormonal disorders), hepatic intoxications (with alcohol, phosphorus, carbon tetrachloride, chloroform, etc.), nutritional disorders (deficiencies of proteins or lipotropic factors, avitaminosis, diseases of the digestive tract, etc.), tissue hypoxia (in heart failure, severe anemia, lung disease), etc. In clinical practice, liver steatosis is most important in alcoholism and obesity-associated diabetes.

Liver function in fatty dystrophy remains normal for a long time. In cases where the action of the harmful factor persists, necrosis processes are associated and micronodular cirrhosis (portal type) is gradually installed.



№ 25. Fatty liver degeneration. *(H-E. stain).*

№ 23. Heart lipomatosis. *(H-E. stain).*

Indications:

1. Bundles of fatty tissue that infiltrate the heart muscle.
2. Atrophied muscle fibers.

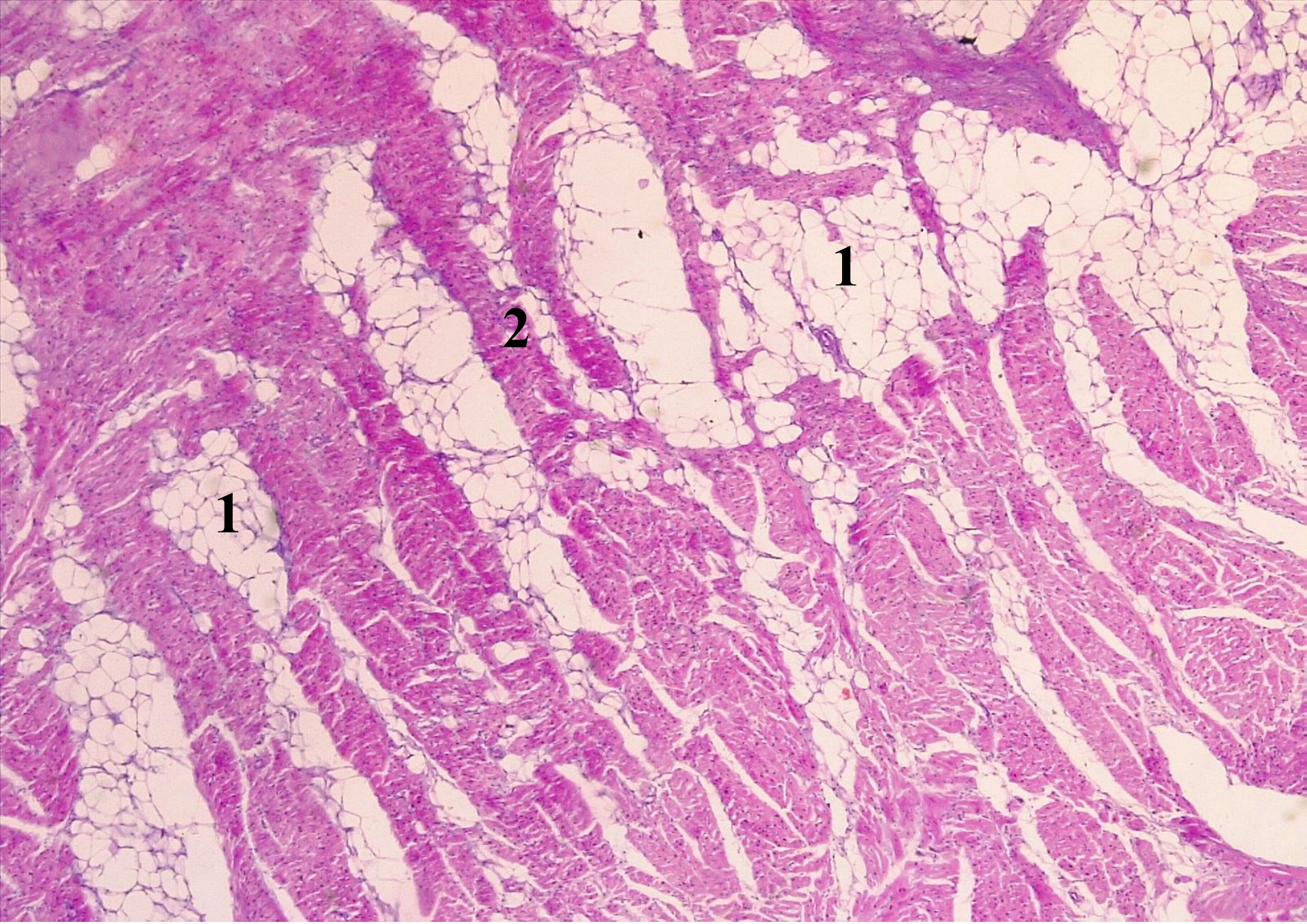
In the microspecimen are present groups of fat cells (adipocytes), which infiltrate the myocardium, dissociating the bundles of muscle fibers, most of which are atrophied.

Heart lipomatosis is a manifestation of obesity - excessive growth of fat deposits. Obesity can be primary, determined by constitutional-hereditary factors (the need for a high-calorie diet is genetically determined) and secondary, which is symptomatic and is observed in some brain, endocrine and hereditary diseases. From this point of view, the following variants of secondary obesity are observed:

a) Alimentary- caused by excess food consumption and hypodynamia (sedentary behaviour)
b) Cerebral - in various brain tumors, trauma, neurotropic infections.
c) Endocrine - in various pathological processes of the endocrine glands, for example:

1. in hypercorticism - hypersecretion of corticosteroid hormones (basophilic adenoma of the anterior lobe of the pituitary gland or hormonally active tumors of the adrenal cortex);
2. in hypothyroidism - decreased thyroid function (myxedema);
3. in hypogonadism - hyposecretion of androgen hormones (inflammatory processes, testicular tumors, in cases of castration, in climax);
4. in hyperinsulinism - insulin hypersecretion (adenoma from the beta cells of the pancreatic islets);
5. hereditary - caused by genetic defects (including hereditary enzymopathies).

Morphologically, obesity is manifested by increased fat deposits in the subcutaneous tissue, omentum, mediastinum, mesentery, retroperitoneal tissue, lodge and stroma of internal organs (heart, pancreas, kidneys, liver). In primary obesity, adipocyte hypertrophy occurs, which leads to a decrease in their insulin sensitivity. Heart lipomatosis is observed in all forms of obesity.



№ 23. Heart lipomatosis. *(H-E. stain).*

II. Macrospecimens:

№ 6. Mitral valve hyalinosis (rheumatic mitral valvulopathy).

The cusps of the mitral valve are thickened, deformed, overgrown with each other, of dense consistency, whitish color, non-transparent (opaque), the cordae tendinae are thickened and shortened; the left atrioventricular orifice is narrowed.

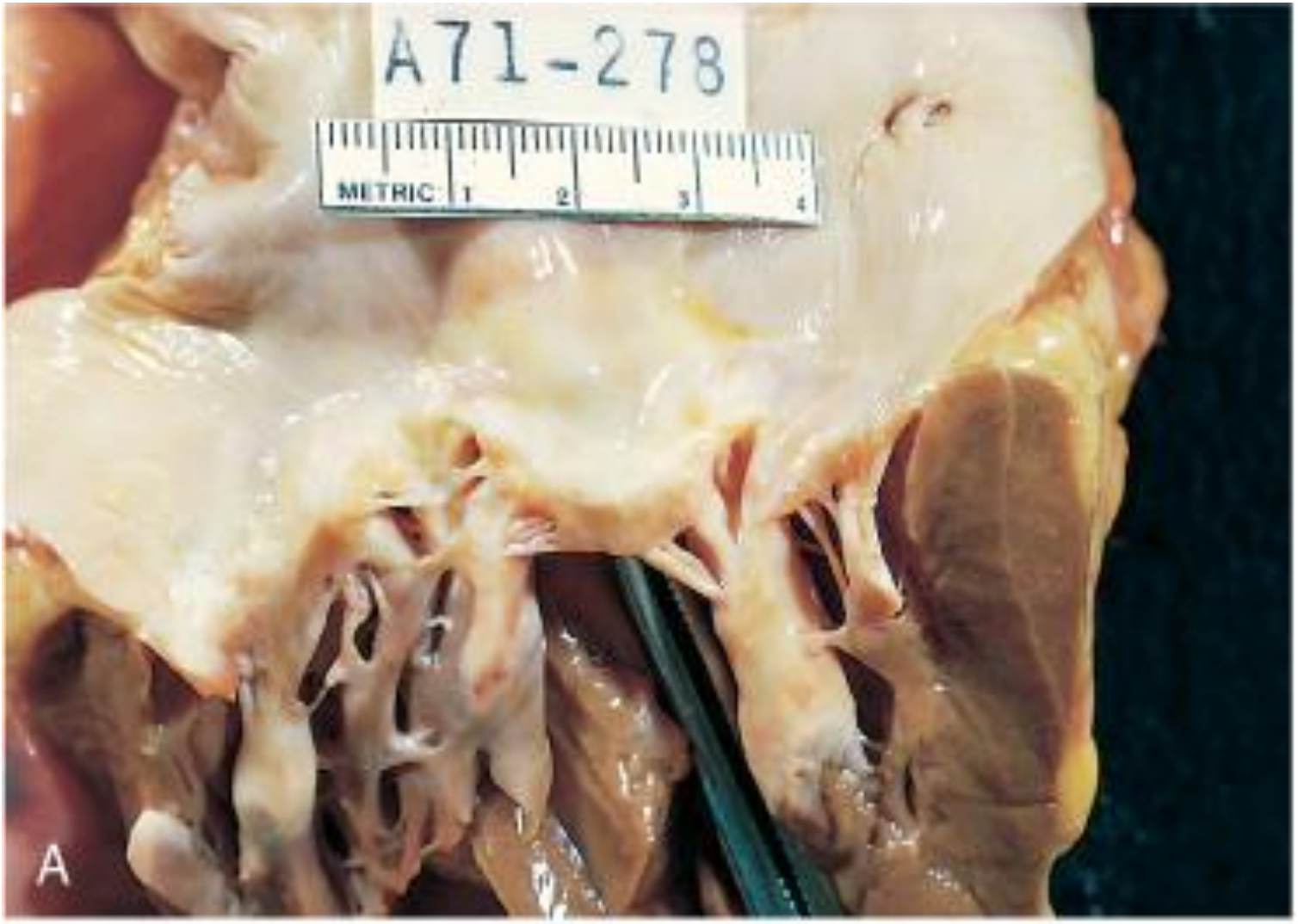
The function of the valve is severely altered, heart valvulopathy develops: stenosis or mitral regurgitation, or, more commonly, mitral valulopathy with the predominance of stenosis or valvular insufficiency. The main complications are heart failure, pulmonary edema, bronchopneumonia, intracardiac thrombosis, thromboembolism, heart attacks, etc. It is mainly a consequence of rheumatism - rheumatic heat disease (rheumocarditis), as a consequence of fibrinoid intumescence of the connective tissue of the valvular apparatus.

№ 19. Heart lipomatosis.

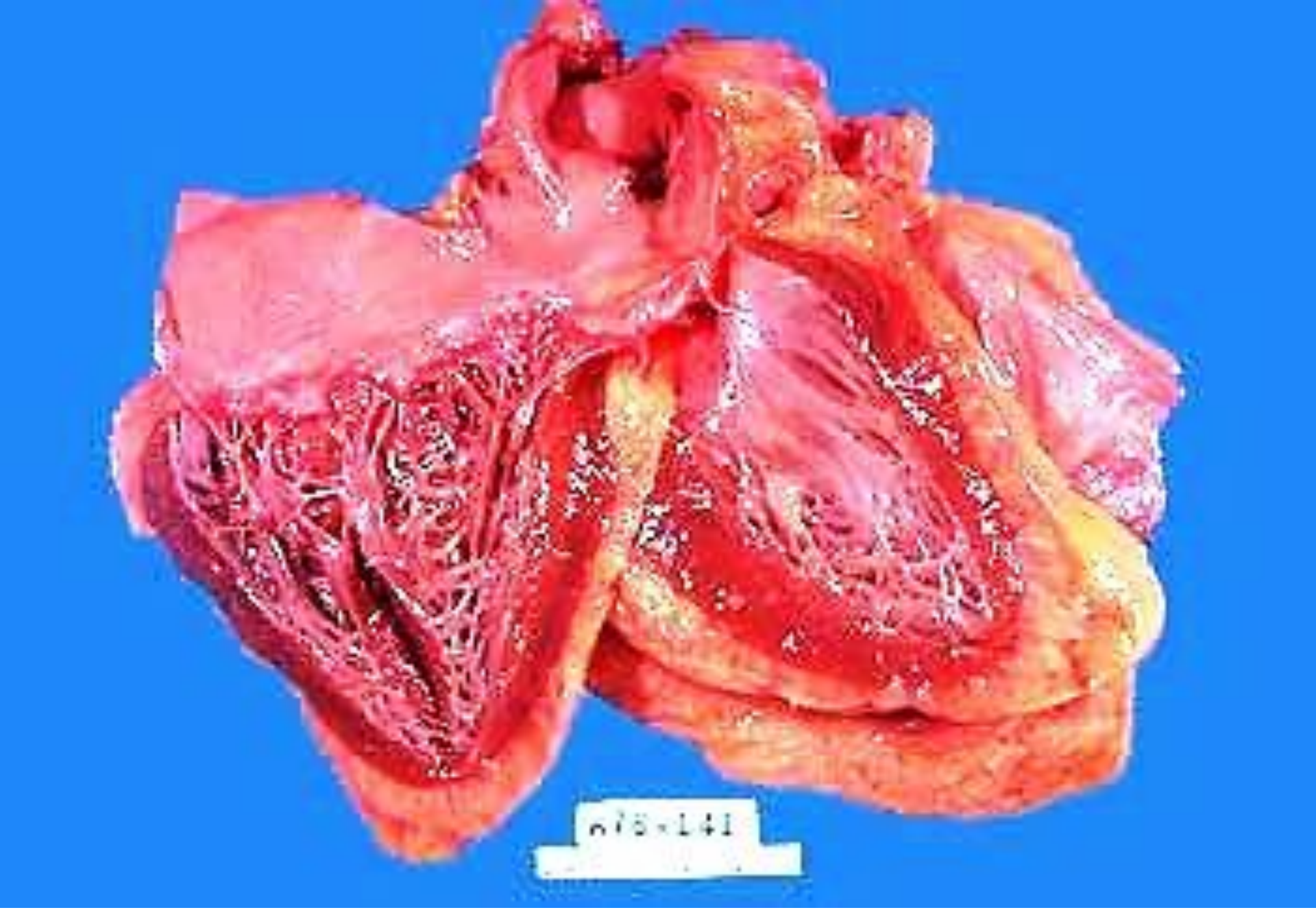
The heart is enlarged, under the epicardium deposits of fat are present, which surround the heart like a sleeve; these manifestations are more prominent in the region of the right ventricle, its thickness can reach 1-2 cm (normal thickness is 2-3 mm).

Heart lipomatosis is present in obesity (microspecimen № 19). Myocardial contraction force is weakened, which can lead to progressive heart failure; the wall of the right ventricle can even rupture, with development of tamponade of the pericardial sac and sudden death.

It should be noted that obesity (including heart lipomatosis) is one of the risk factors for ischemic heart disease (ischemic heart disease).



№ 6. Mitral valve hyalinosis (rheumatic mitral valvulopathy).

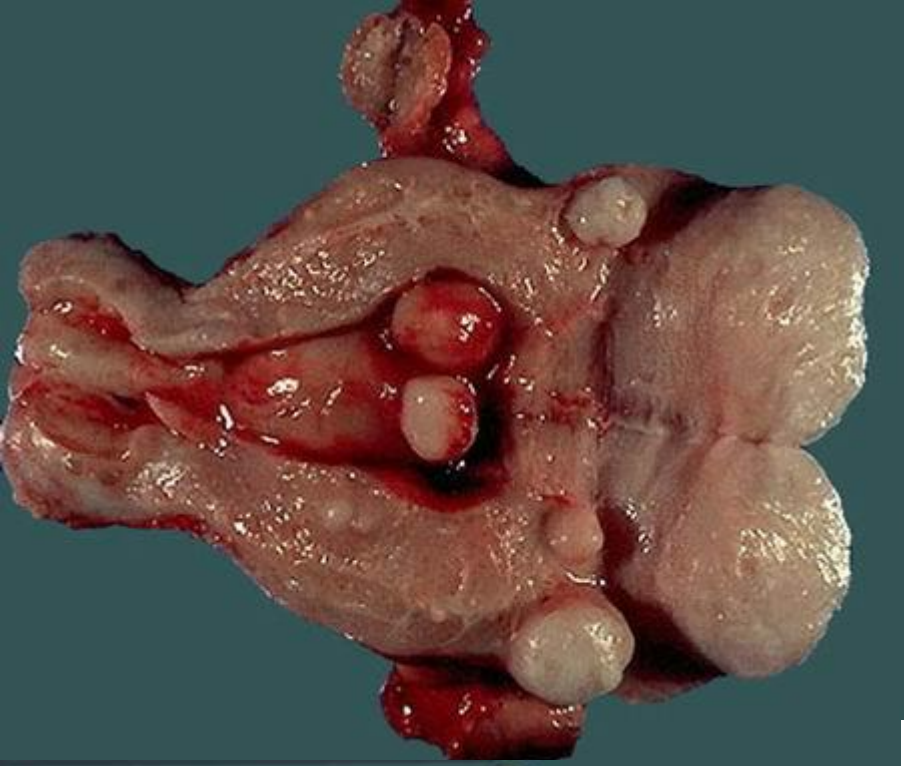


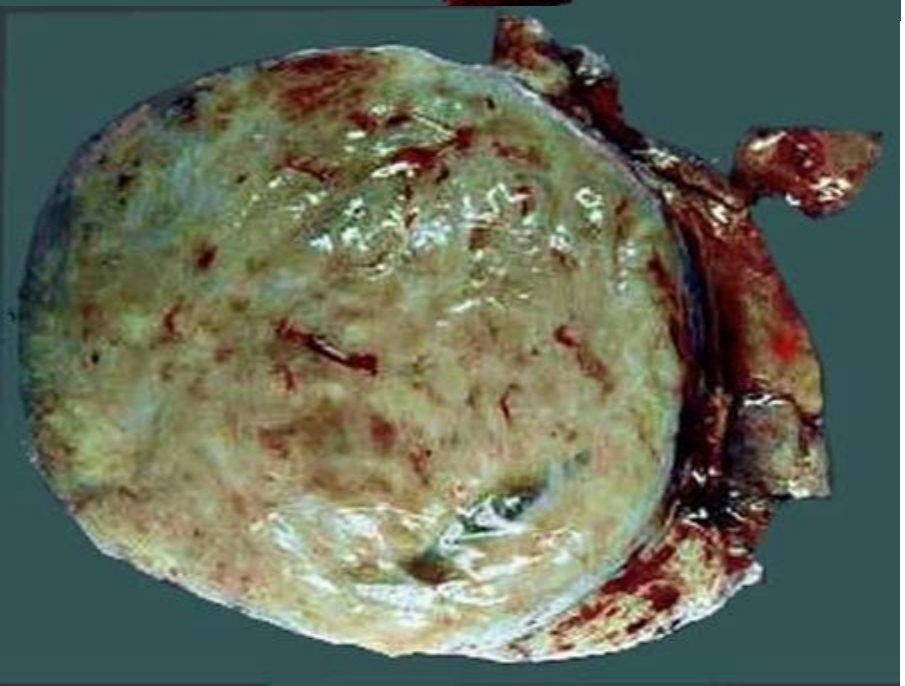
№ 19. Heart lipomatosis.

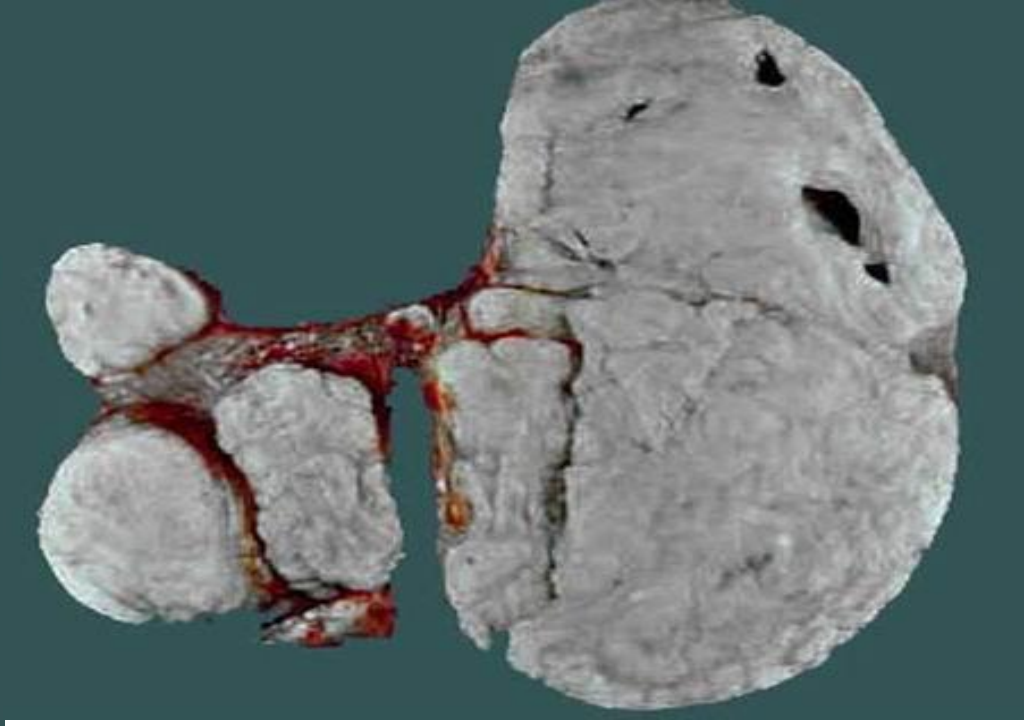
№ 104. Fibroleiomyoma of uterus.

In the uterine wall solitary or multiple tumor nodules are observed, with variable size from 1-2 cm to very large, well-defined, dense, located in subserous layer, intramural (in the thickness of the uterine wall) or submucosal layer; on the cut section they have fibrillar structure, pink smooth muscle bundles and whitish connective tissue have disordered whorled arrangement (tissue atypia). There may be present secondary changes: hemorrhages, foci of necrosis, cystic cavities, foci of hyalinosis, in which fusion and homogenization of collagen bundles takes place; these foci have a smooth, glossy, grayish white appearance.

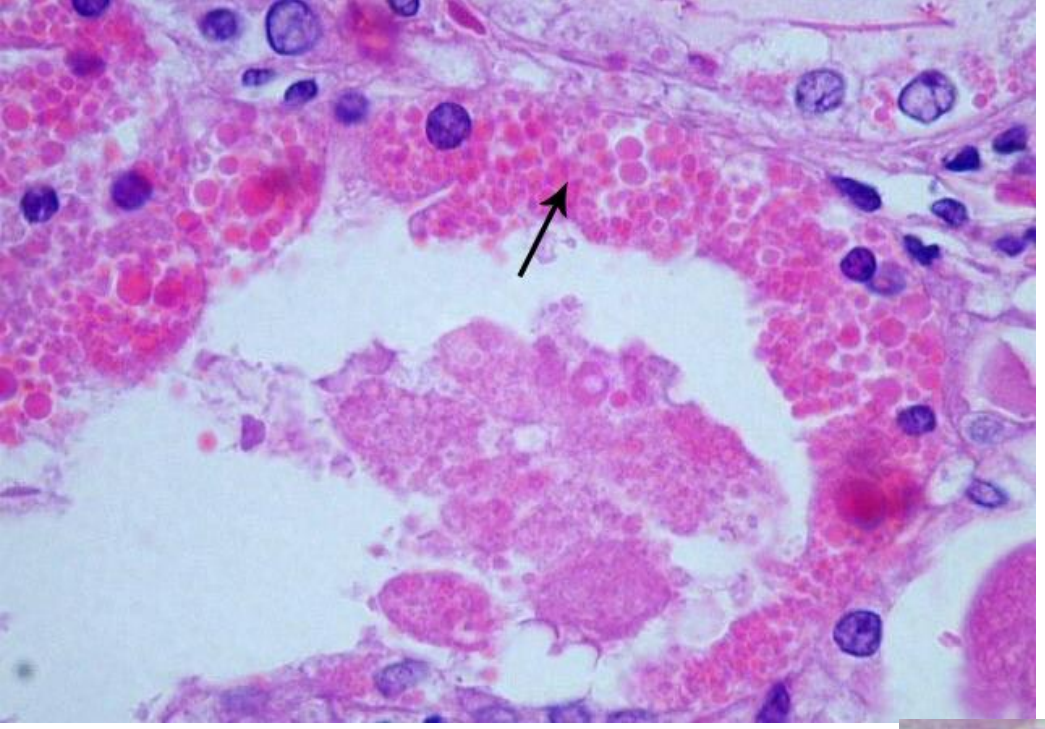
Leiomyoma is a benign tumor of muscular origin, which develops from the smooth muscle tissue itself or from the walls of blood vessels. Because in parallel with the proliferation of the muscle parenchyma, the proliferation of the connective tissue stroma also takes place, the name fibroleomyoma is more correct. Leiomyoma is the most common benign tumor of the uterus, it is clinically manifested by uterine hemorrhage (metrorrhagia).



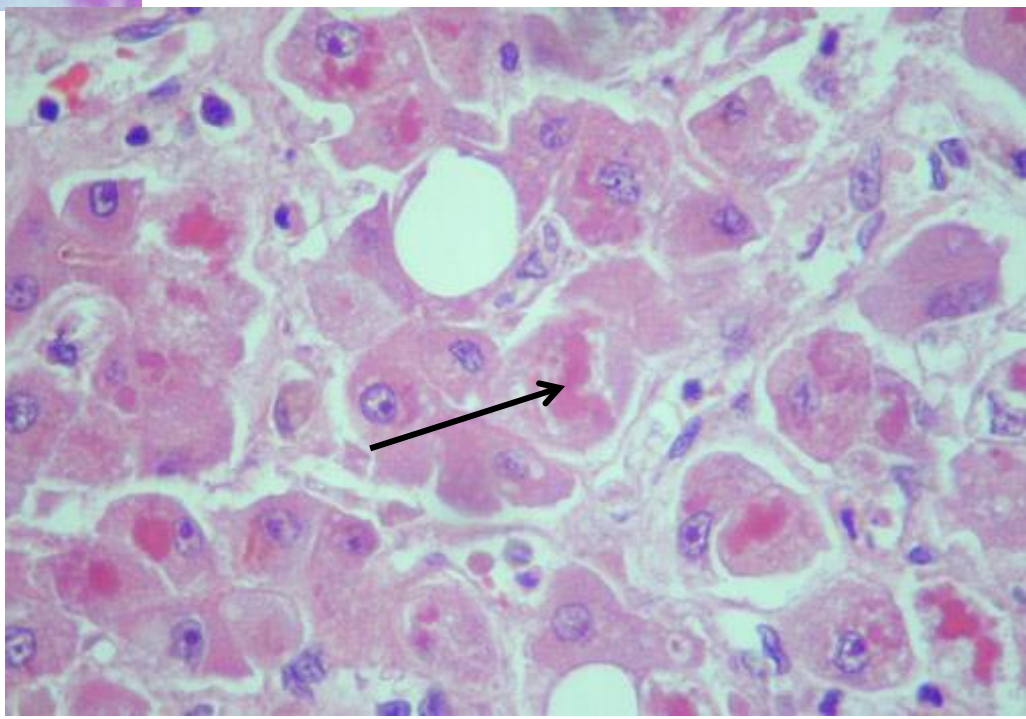




№ 104. Fibroleiomyoma of uterus.

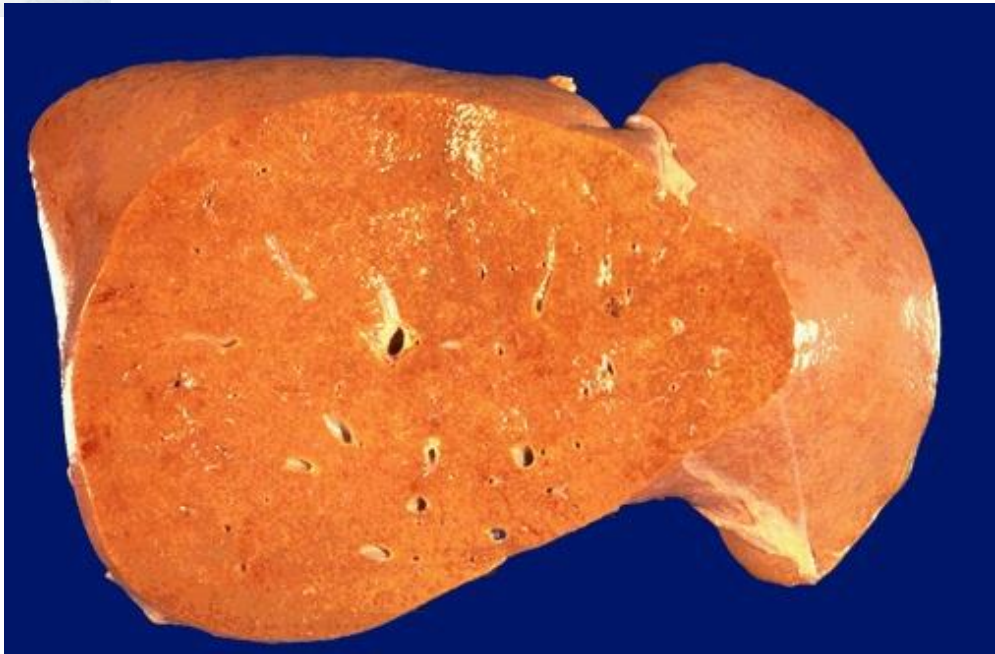


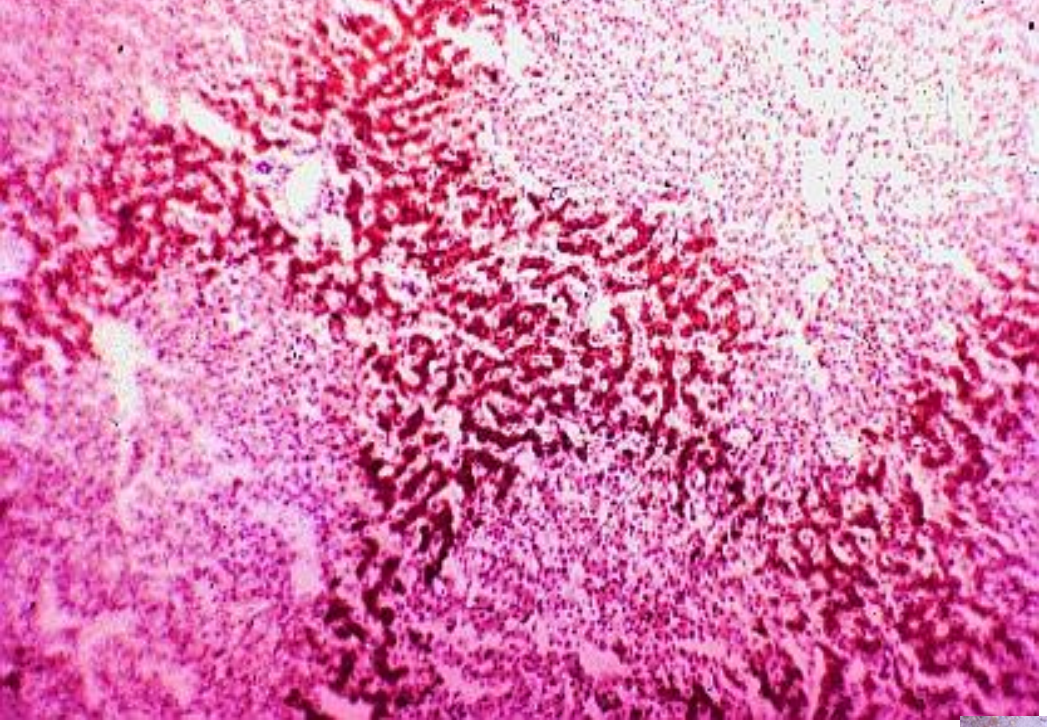
Protein intracellular degeneration of hepatocytes.
(alcoholic hyaline (Mallory bodies)).

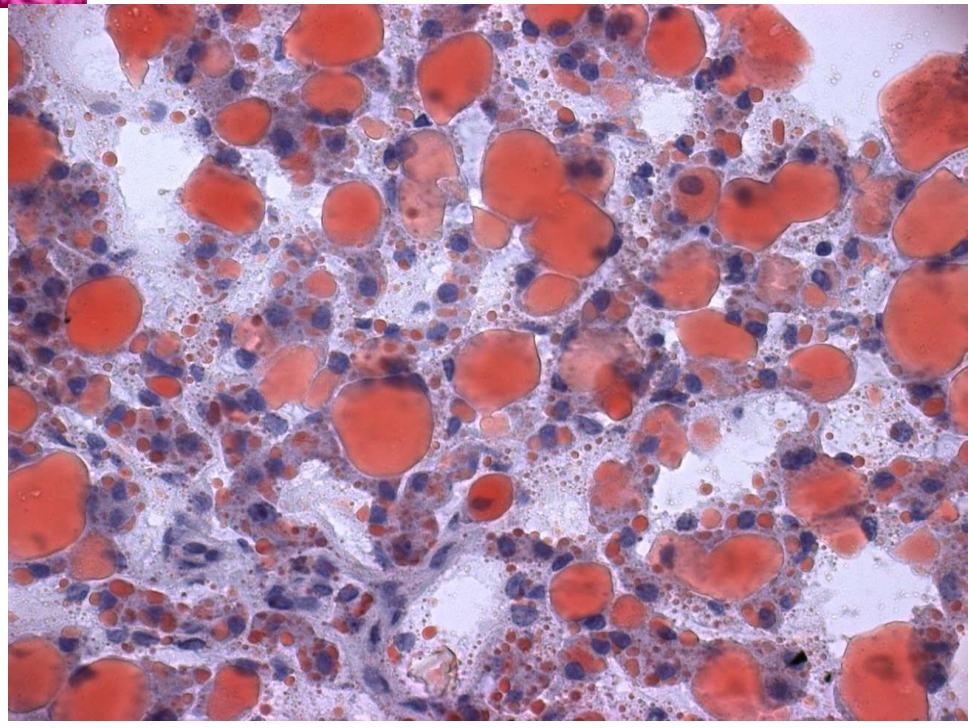


Protein intracellular degeneration of the renal convoluted tubules epithelium

Liver steatosis ("goose liver")

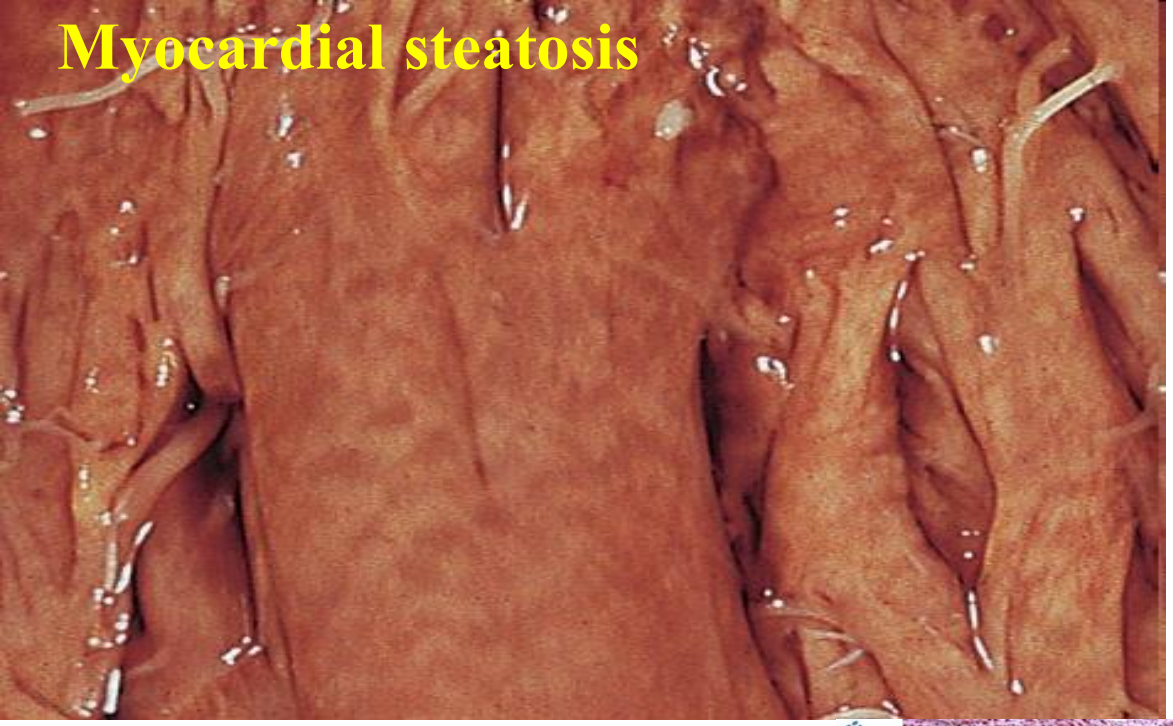






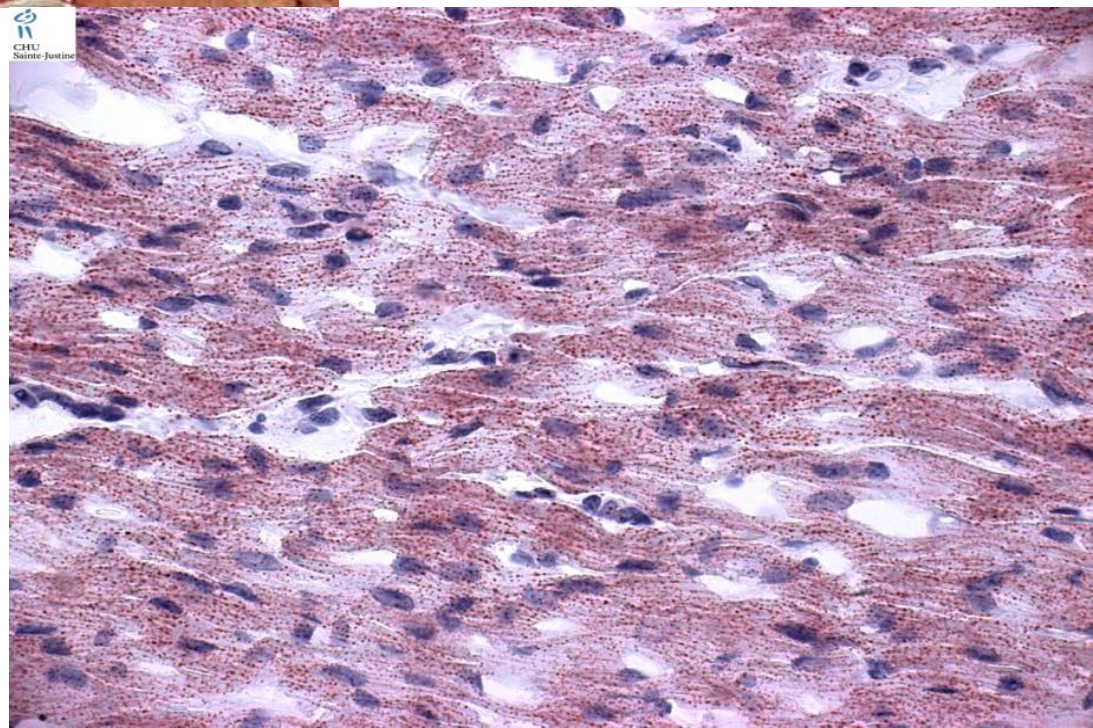
Peripheral steatosis of hepatic lobules in subtotal necrosis of the liver (Sudan III stain).

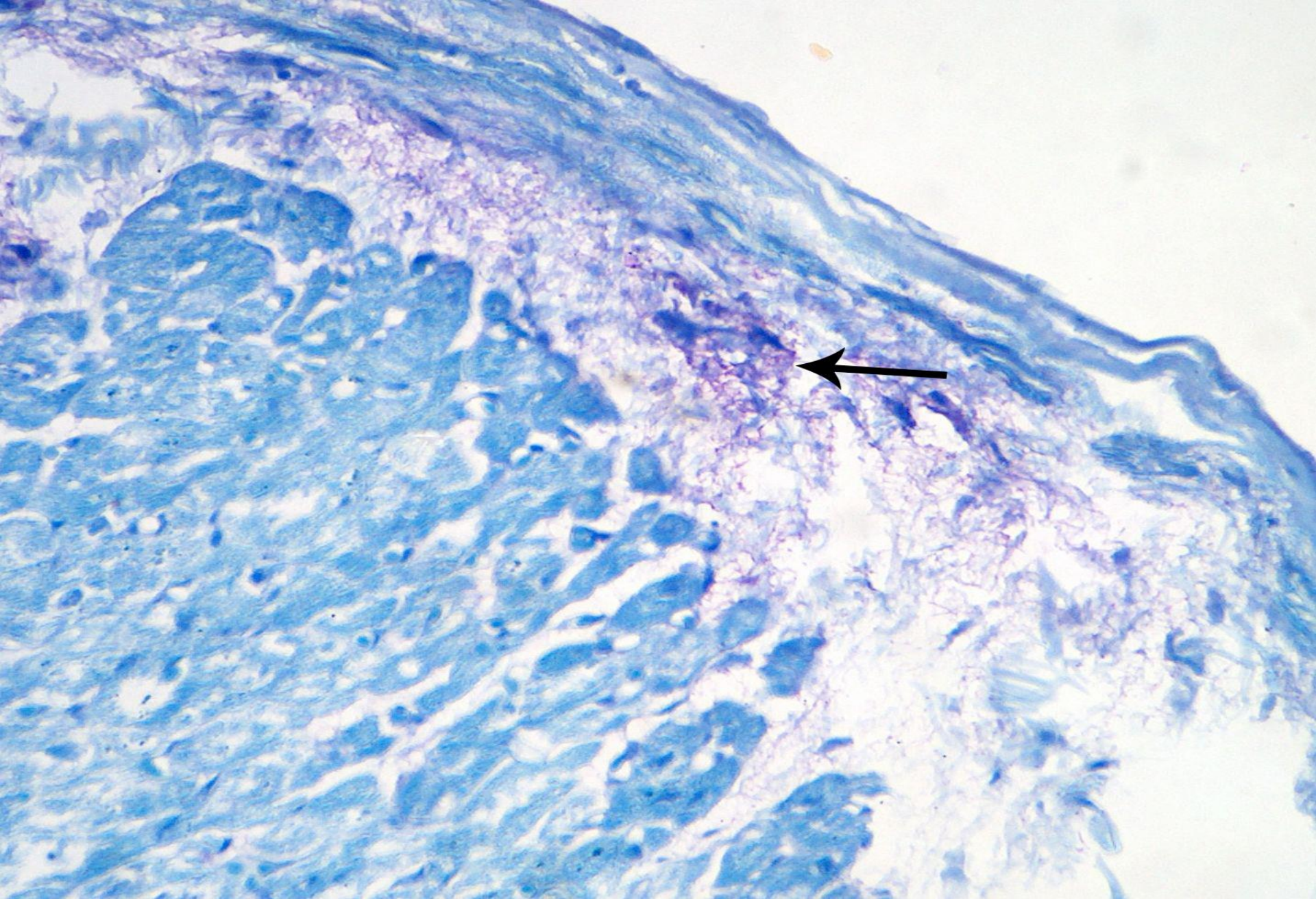
Myocardial steatosis



Micro: Lipids appear as reddish microgranules stained with Sudan III.

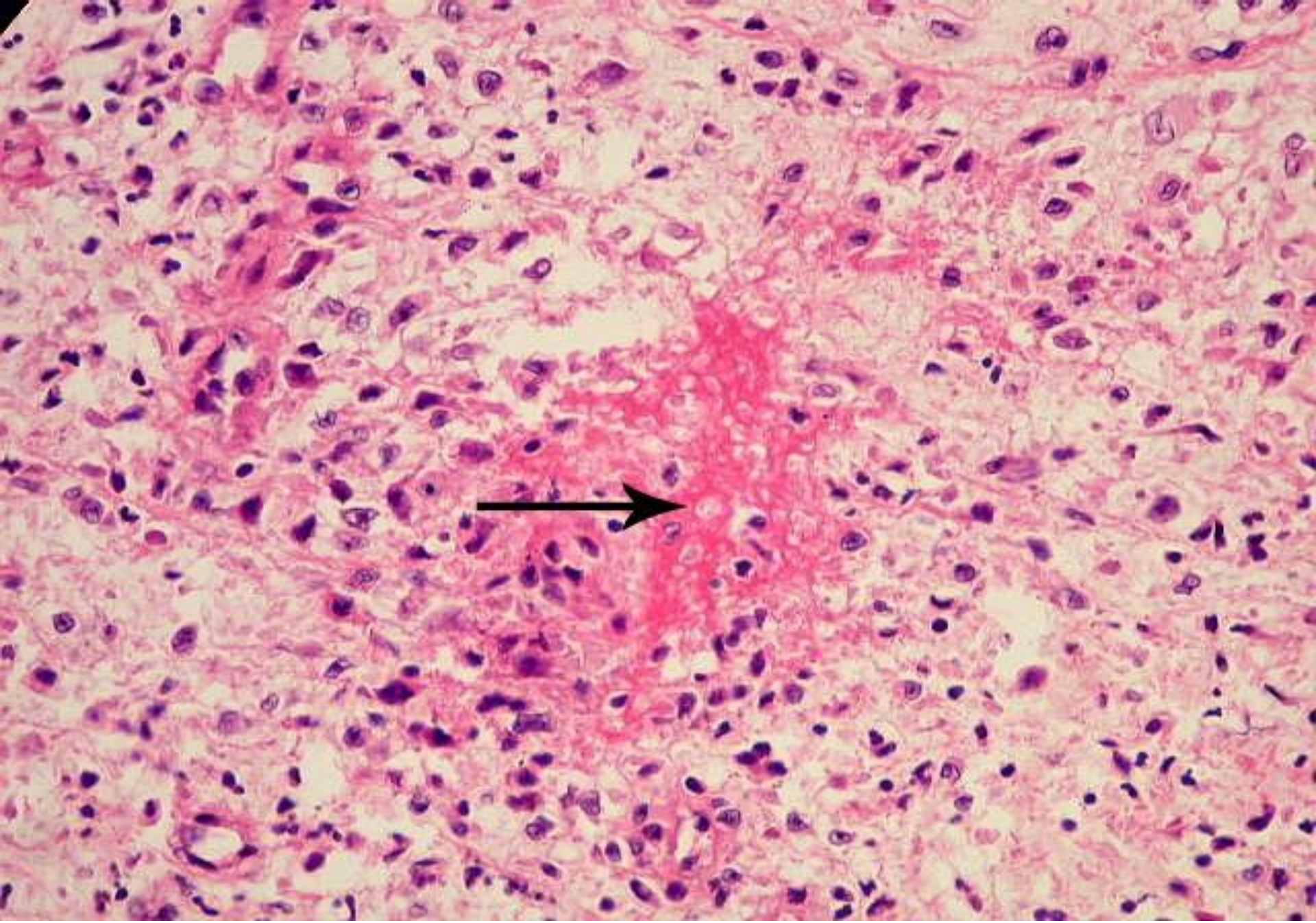
Macro: Intracellular lipid storage creates yellowish lipid strips in the papillary muscles, which alternate with the intact portions (tiger heart).



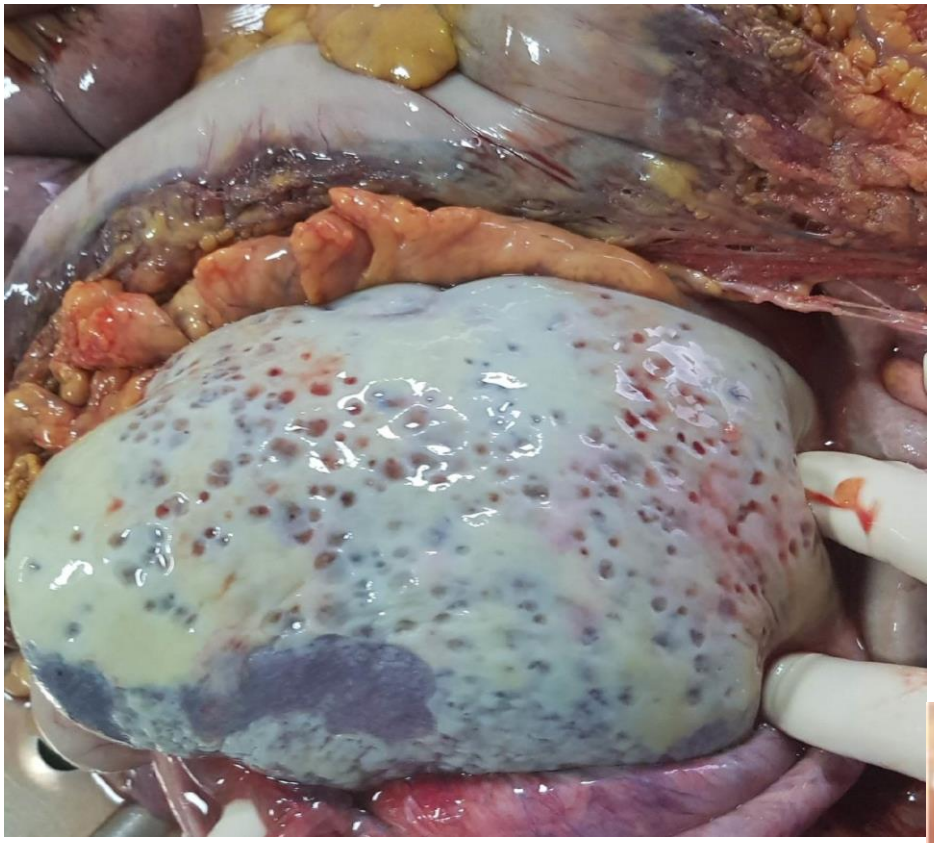


Mucoid intumescence in the heart auricle

(metachromasia with toluidine blue stain)

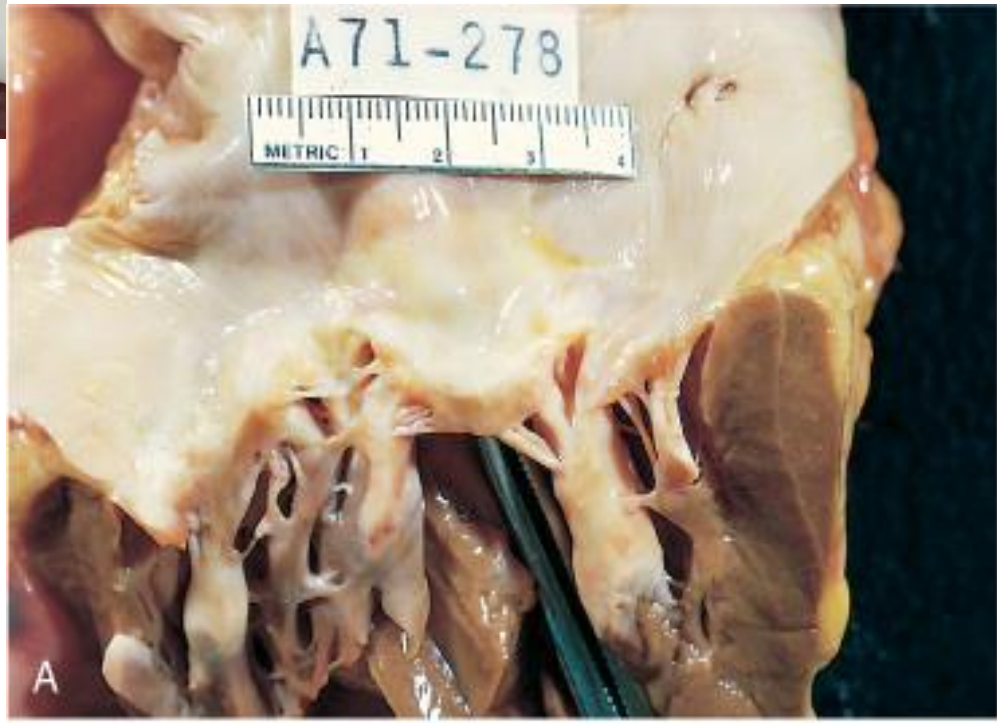


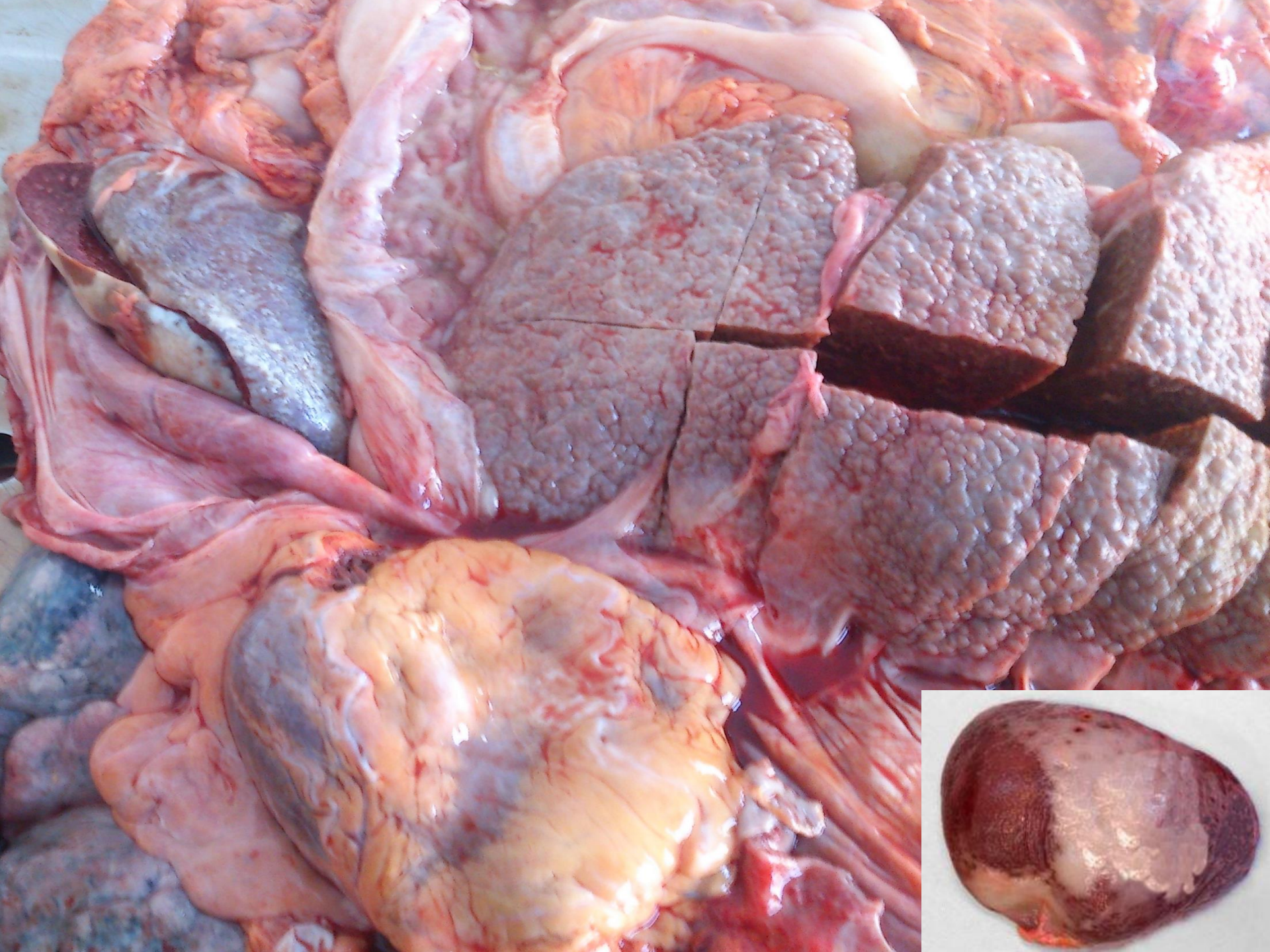
Fibrinoid intumescence of connective tissue in rheumatic fever. *(H-E stain).*

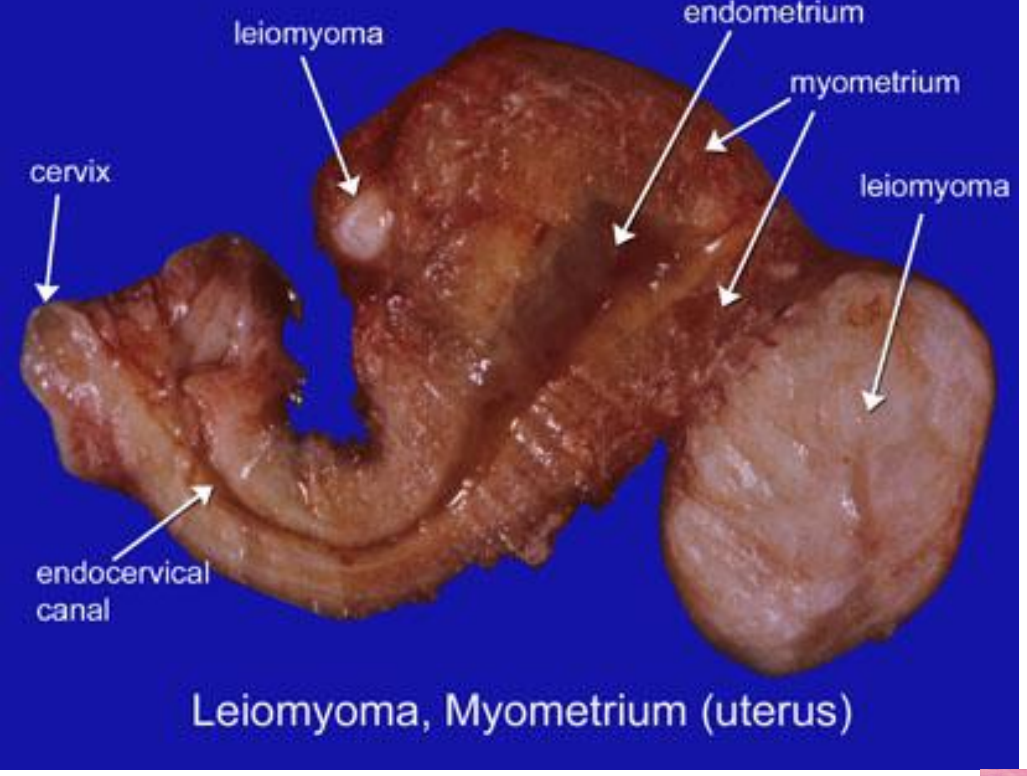


Hyalinosis of the spleen capsule.

Mitral valve hyalinosis in rheumatic fever.

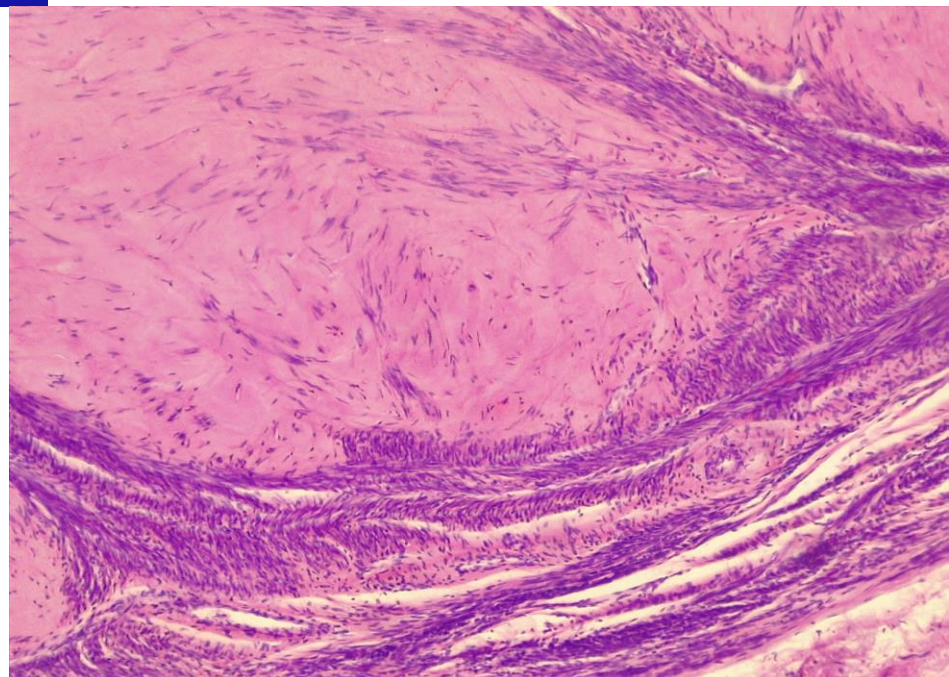


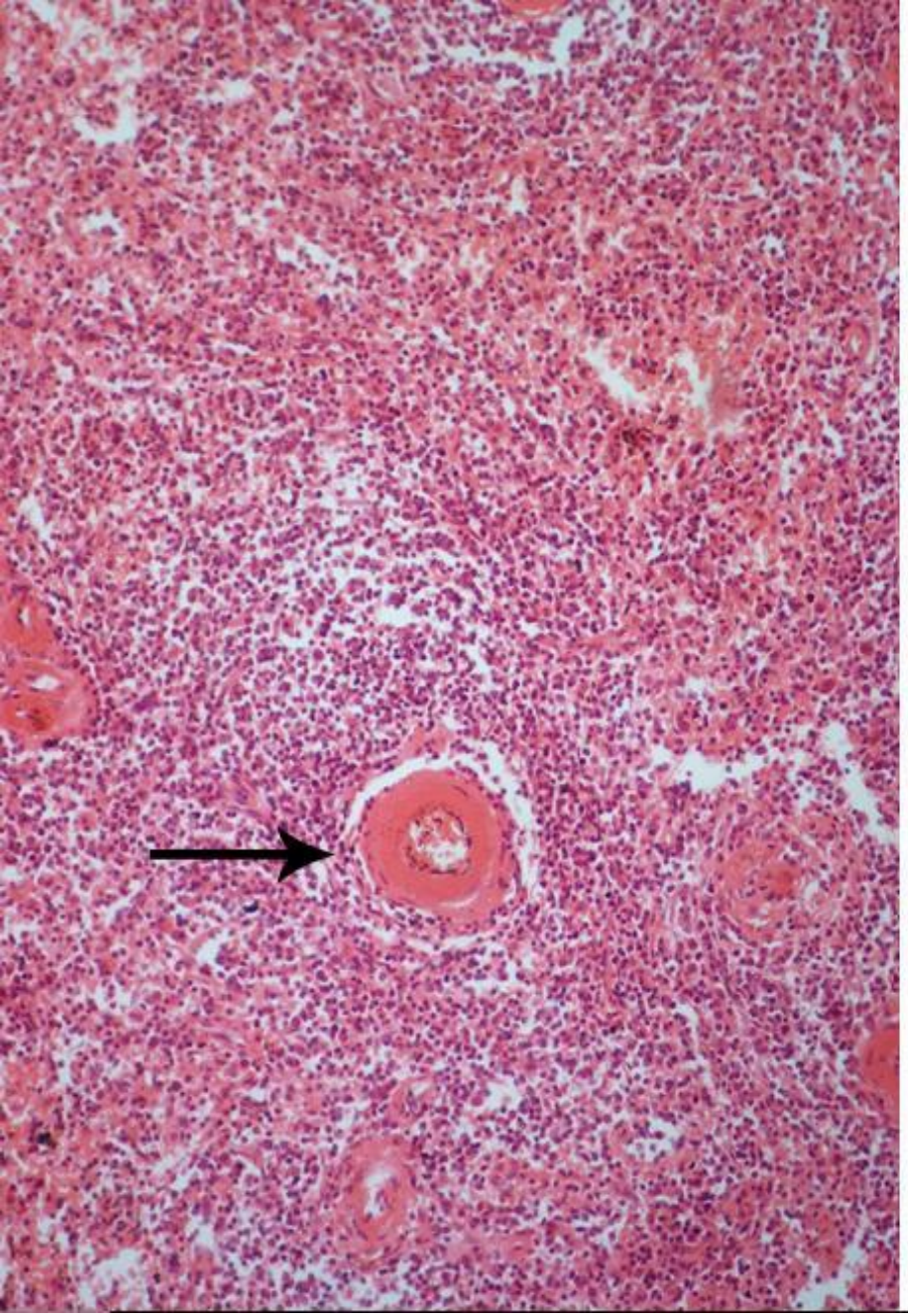


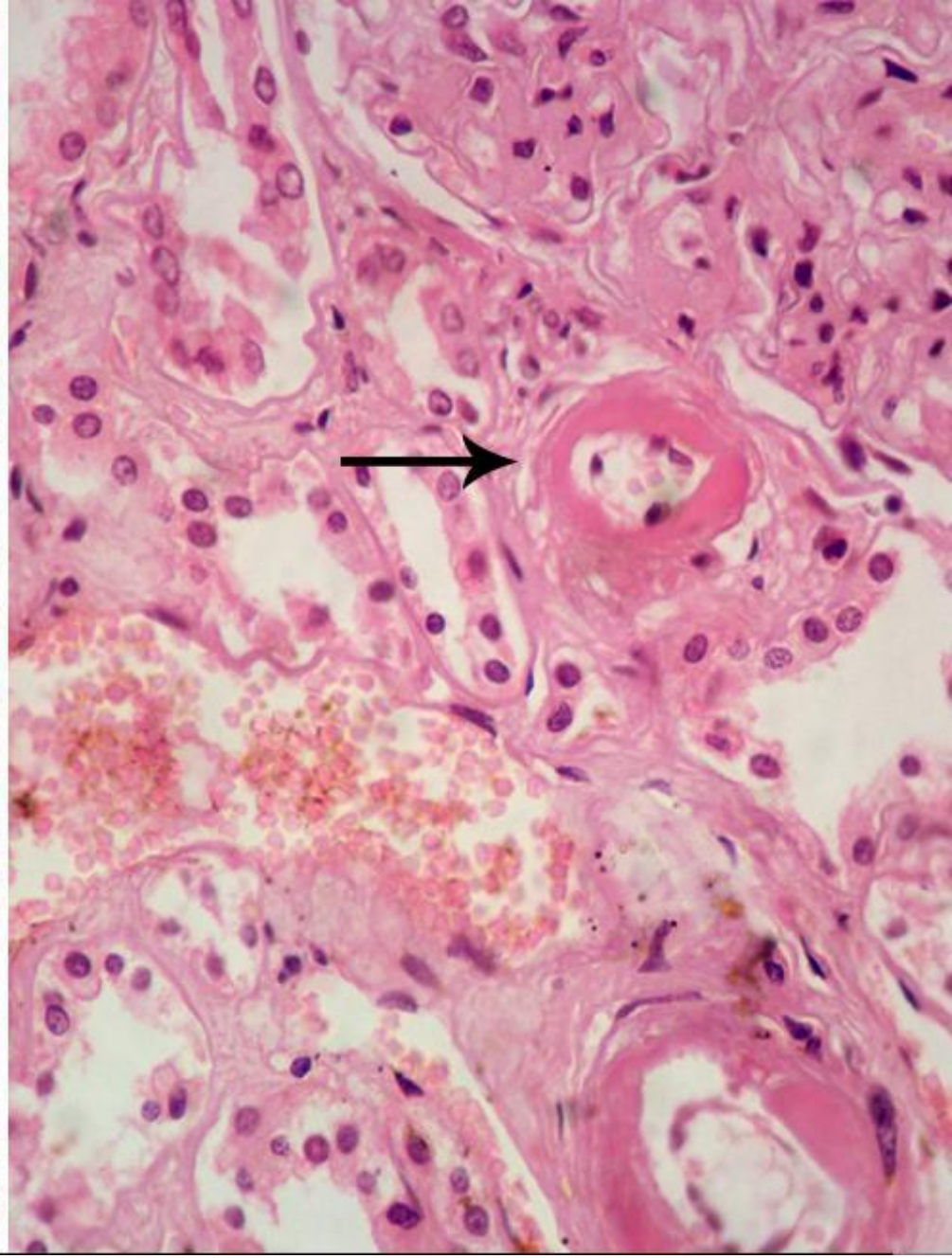


Stroma hyalinosis in uterine leiomyoma.
(H-E stain).

Uterine leiomyoma.







Vascular wall hyalinosis. *(H-E stain).*

Accumulation Process

One of the cellular manifestations of metabolic derangements in pathology is the accumulation of abnormal amounts of various substances

Intracellular and tissue accumulations

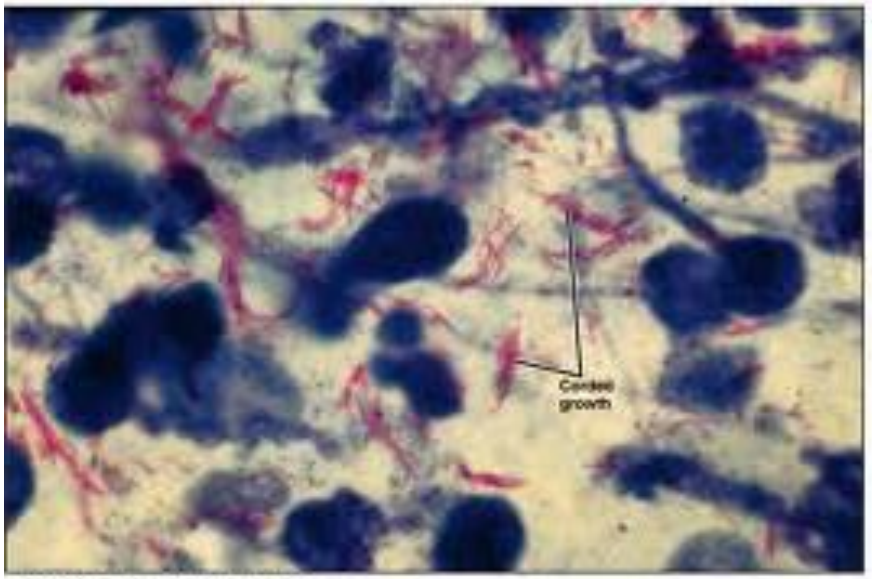
These may be a normal cellular constituent accumulated in excess, such as water, lipid, protein, and carbohydrates

Intracellular and tissue accumulations

These may be an abnormal substance, either exogenous, such as a mineral, or a product of abnormal metabolism

Intracellular and tissue accumulations

These may be a pigment or an infectious product



Intracellular and tissue accumulations

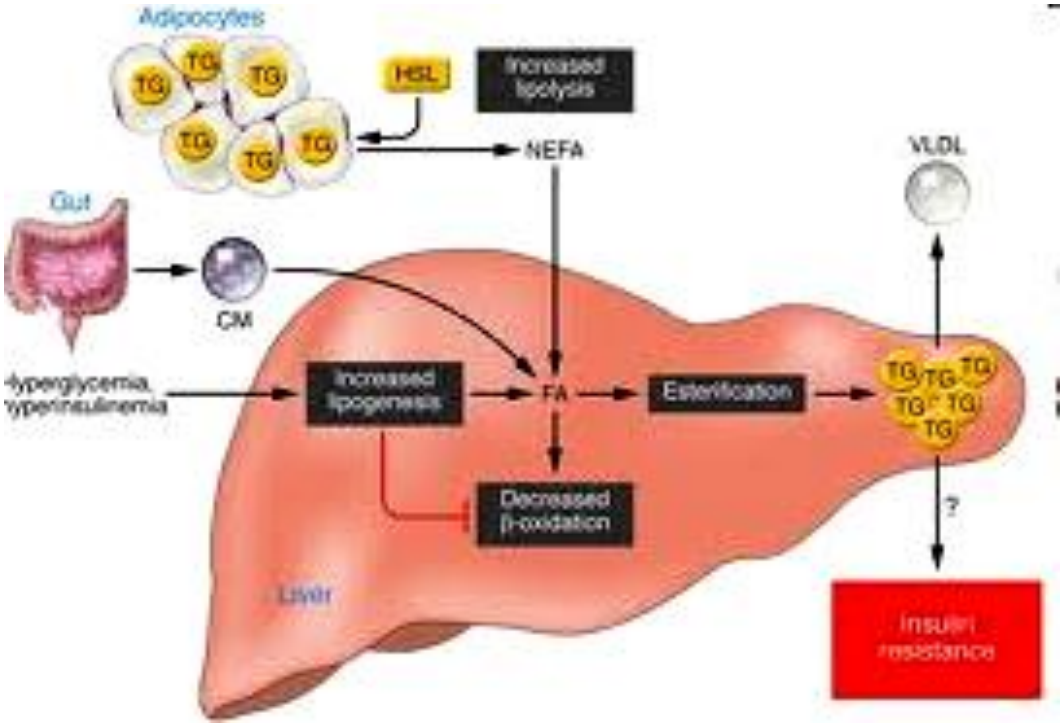
These substances may accumulate either transiently or permanently, and they may be harmless to the cells, but on occasion they are severely toxic.

ClASSIFICATION

- 1) Lipid Accumulation
- 2) Glycogen Accumulation
- 3) Protein Accumulation
- 4) Amyloid and Amyloidosis
- 5) Endogenous Pigments
- 6) Pathologic Calcification (Mineralization)
- 7) Crystals
- 8) Exogenous Pigments
- 9) Parasite Pigments

Lipids

Fatty change is often seen in the liver because it is the major organ involved in fat metabolism, but it also occurs in heart, muscle, and kidney



The causes of steatosis

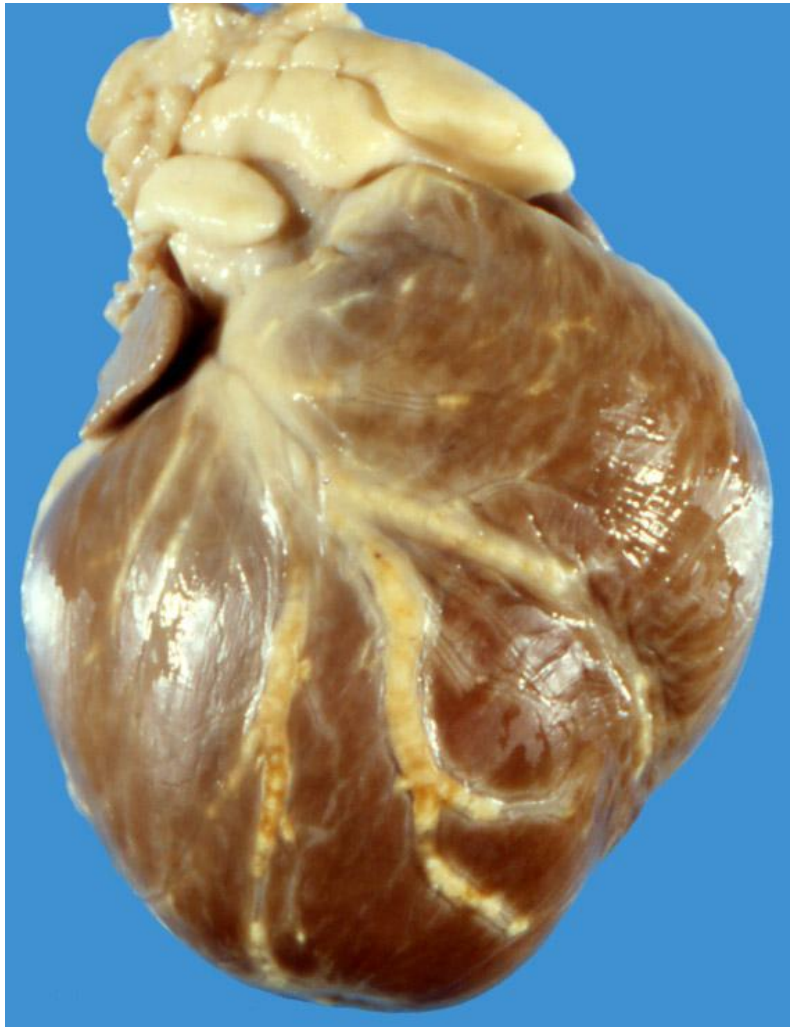
include toxins, protein malnutrition, diabetes mellitus, obesity, and anoxia. In industrialized nations, by far the most common cause of significant fatty change in the liver (fatty liver) is alcohol abuse

Lipids accumulation

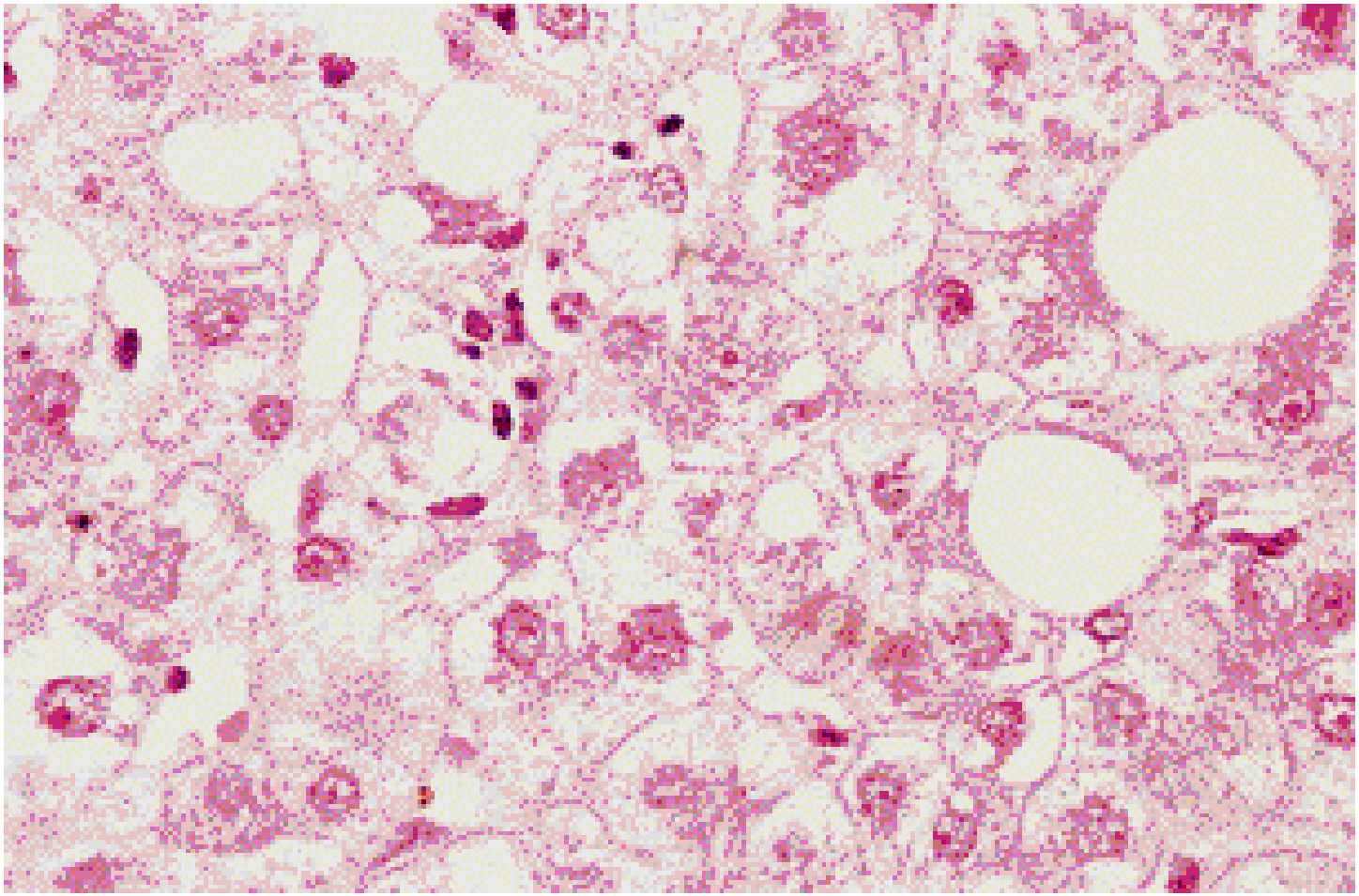
- **Triglycerides (Fatty Change) seen with metabolic / nutritional disorders, toxins, hypoxia, etc.**

- **Inherited Storage Diseases(Lipidosis)**

- **Cholesterol accumulations**
  eg inflammation and necrosis: foamy macrophages.
  eg atherosclerosis: smooth muscle & macrophages.

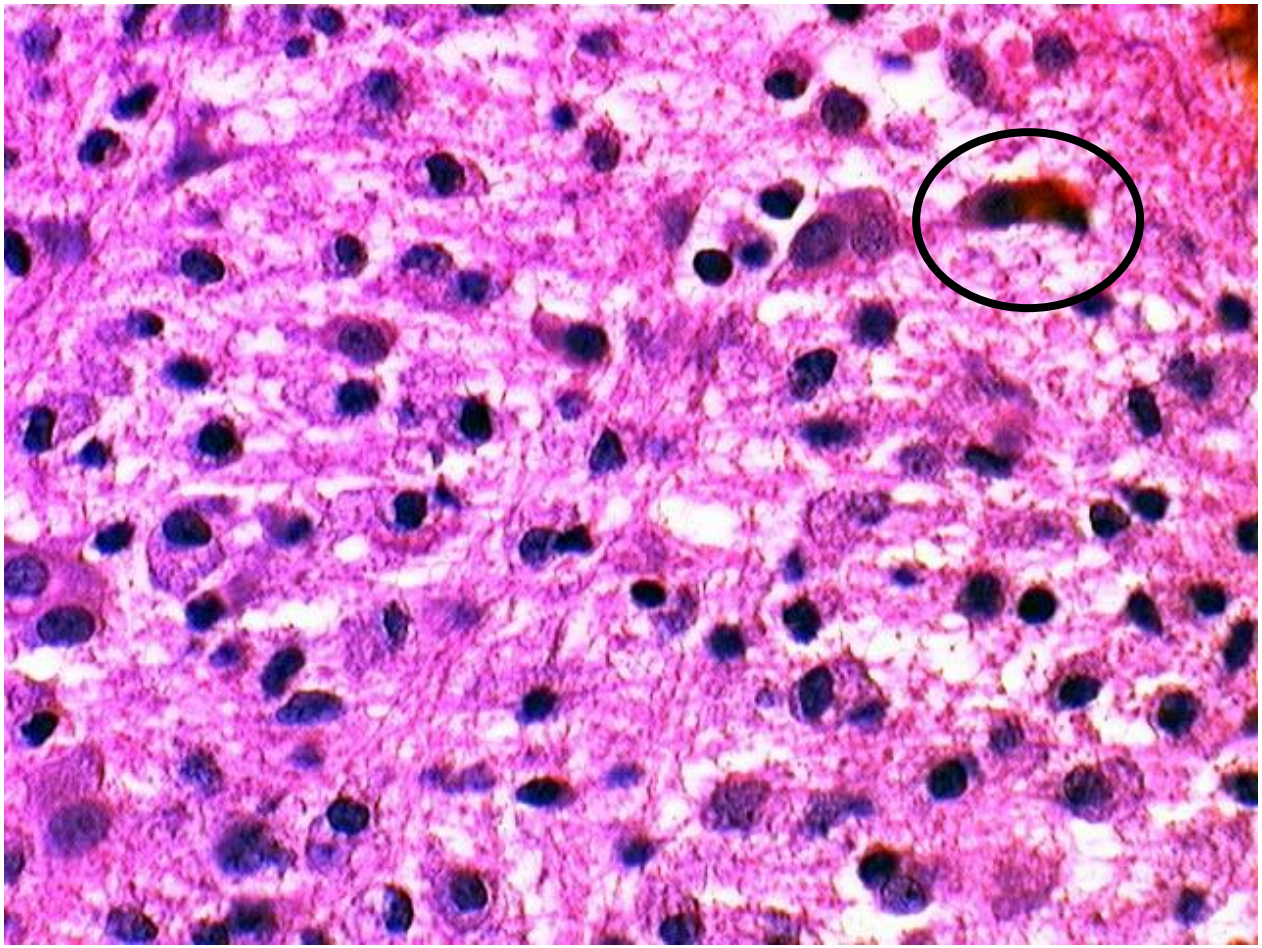


Fatty Change



Alcoholic Liver

Foam Cells

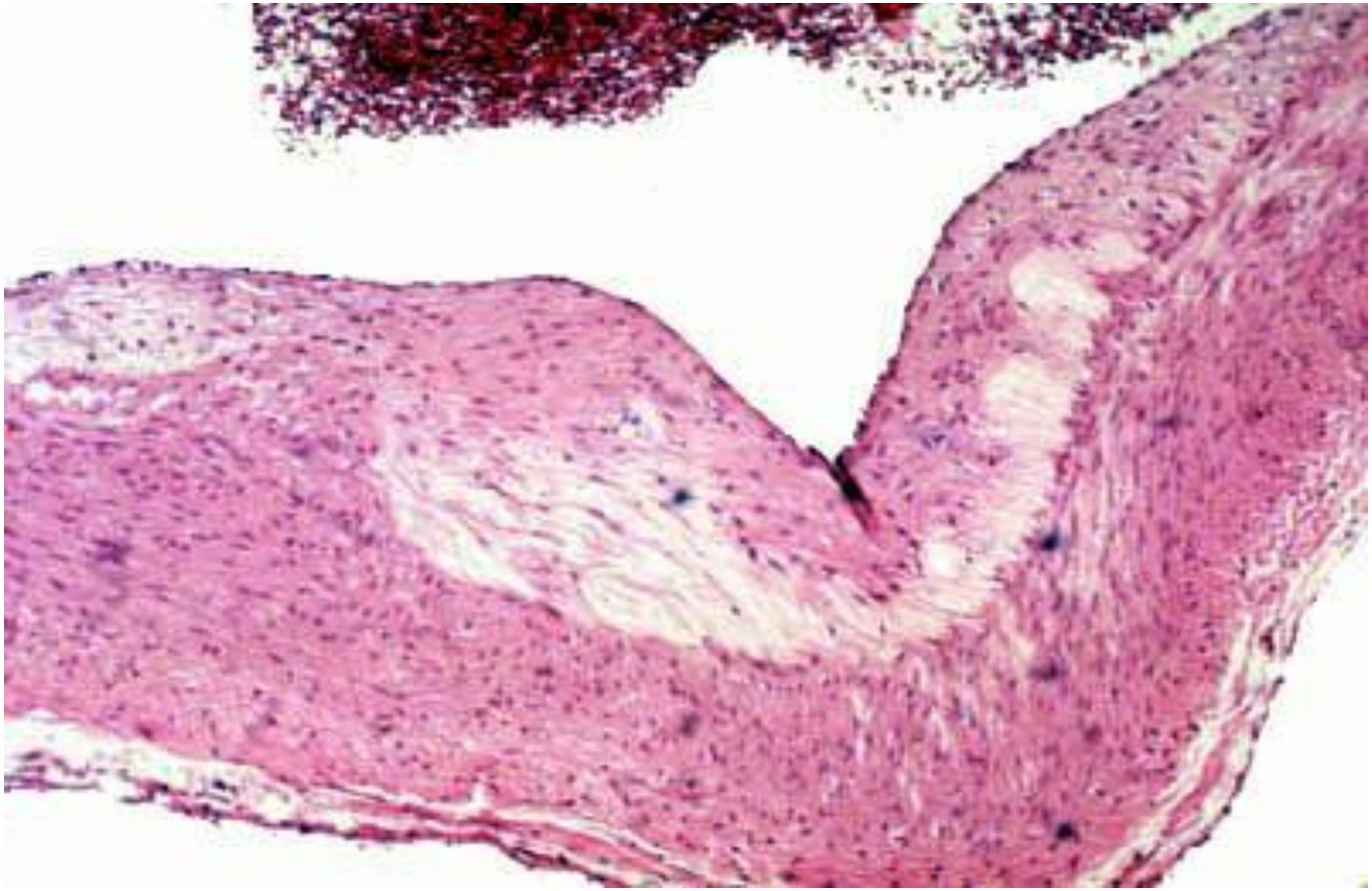


Macrophages filled with lipids

Atherosclerosis

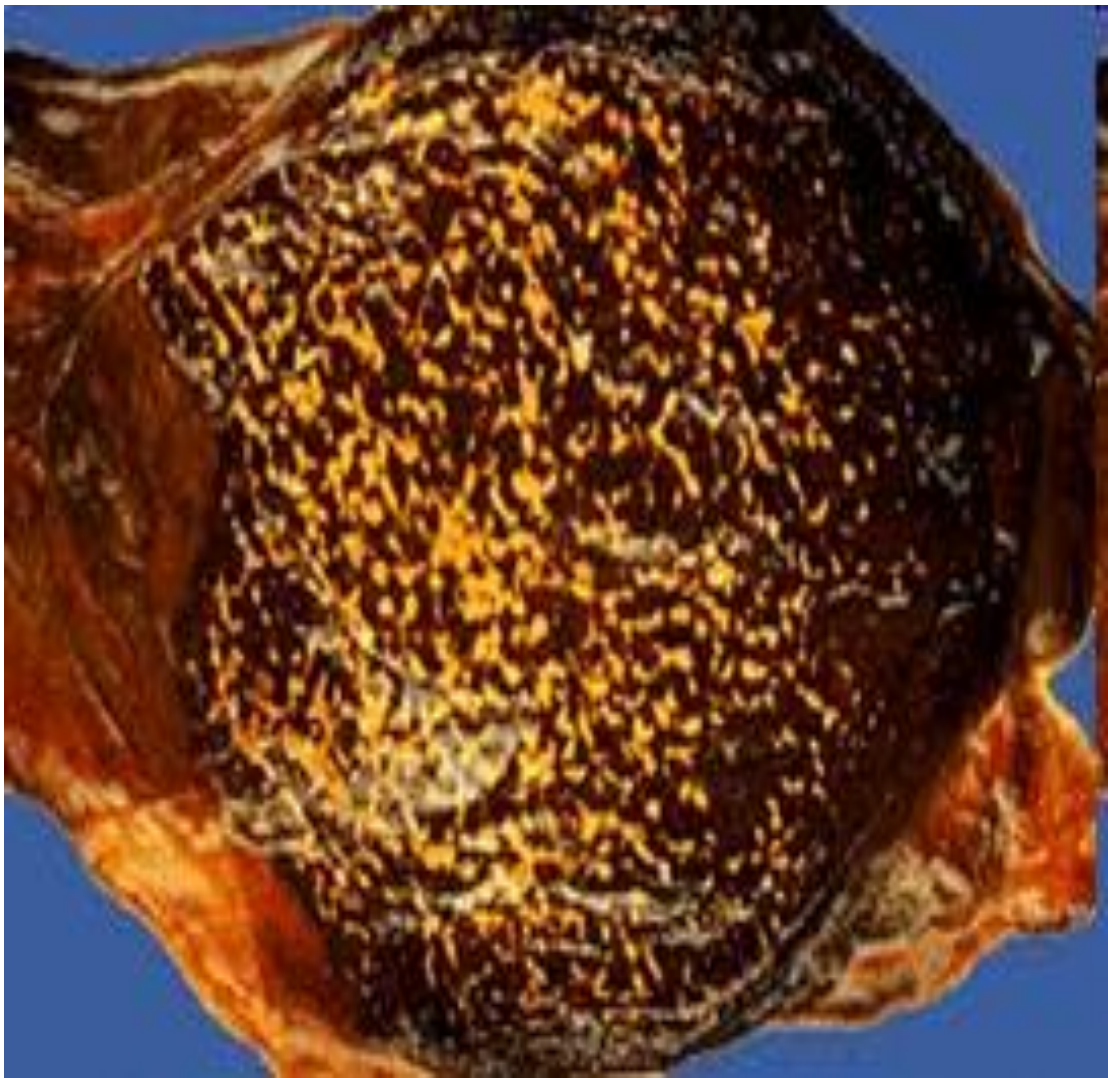
In atherosclerotic plaques, smooth muscle cells and macrophages within the intimal layer of the aorta and large arteries are filled with lipid vacuoles, most of which are made up of cholesterol and cholesterol esters.

Atherosclerosis



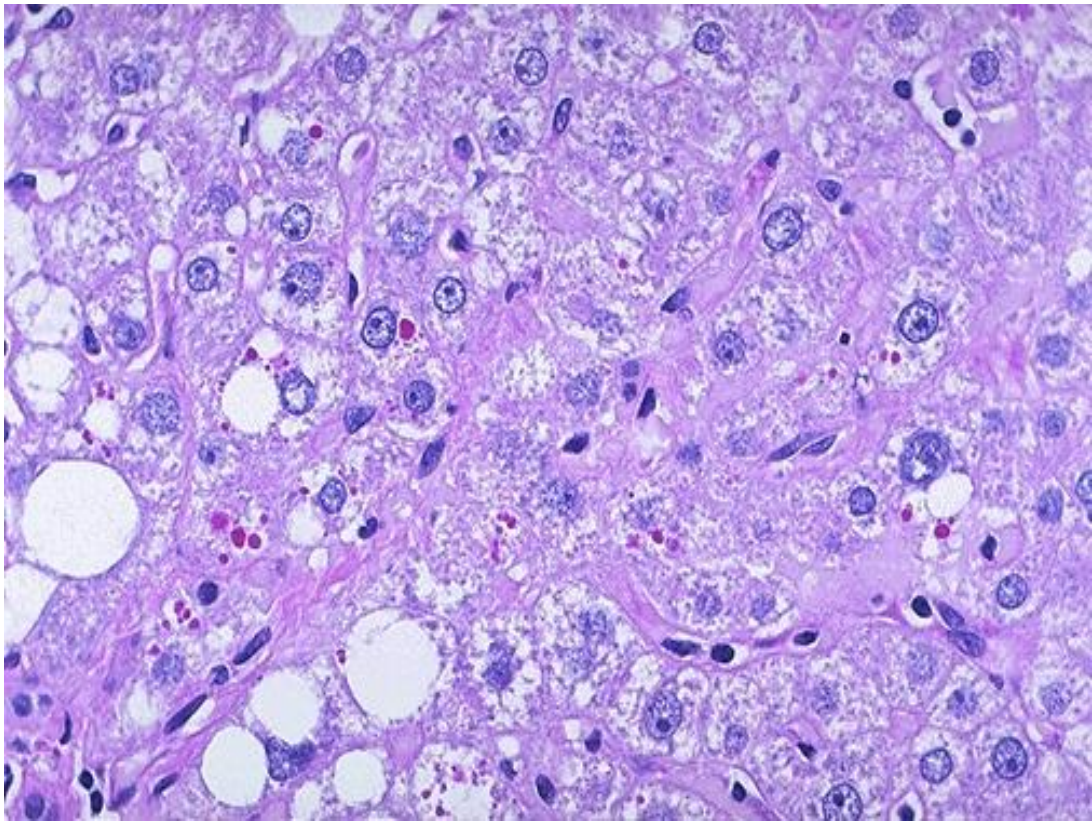
Cholesterolosis

Focal accumulations of cholesterol-laden macrophages in the lamina propria of the gallbladder



Proteins

Excesses of proteins within the cells sufficient to cause morphologically visible accumulation are less common than accumulation of lipids



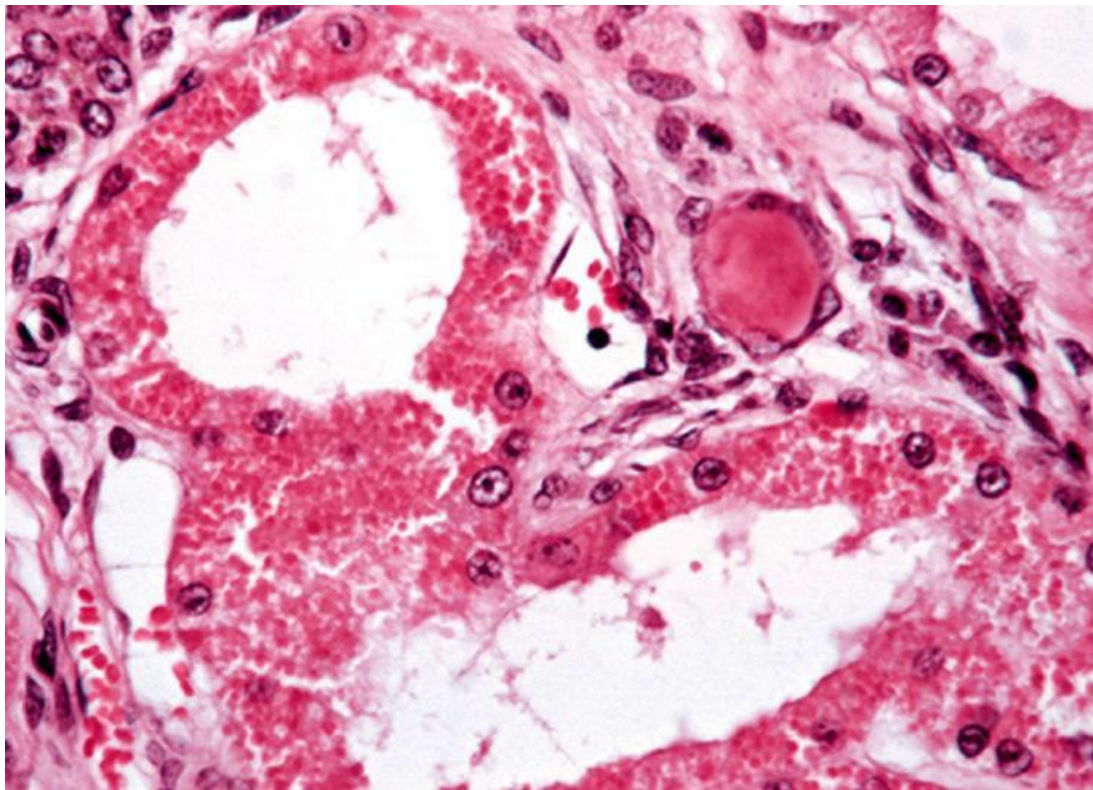
Protein Accumulation

Defects in Protein folding

- **ER stress induced by accumulation of unfolded & misfolded proteins**
- **Genetically defective / misfolded proteins, eg cystic fibrosis.**
- **Aggregation of misfolded proteins (genetic / acquired), eg amyloid, Alzheimer's.**

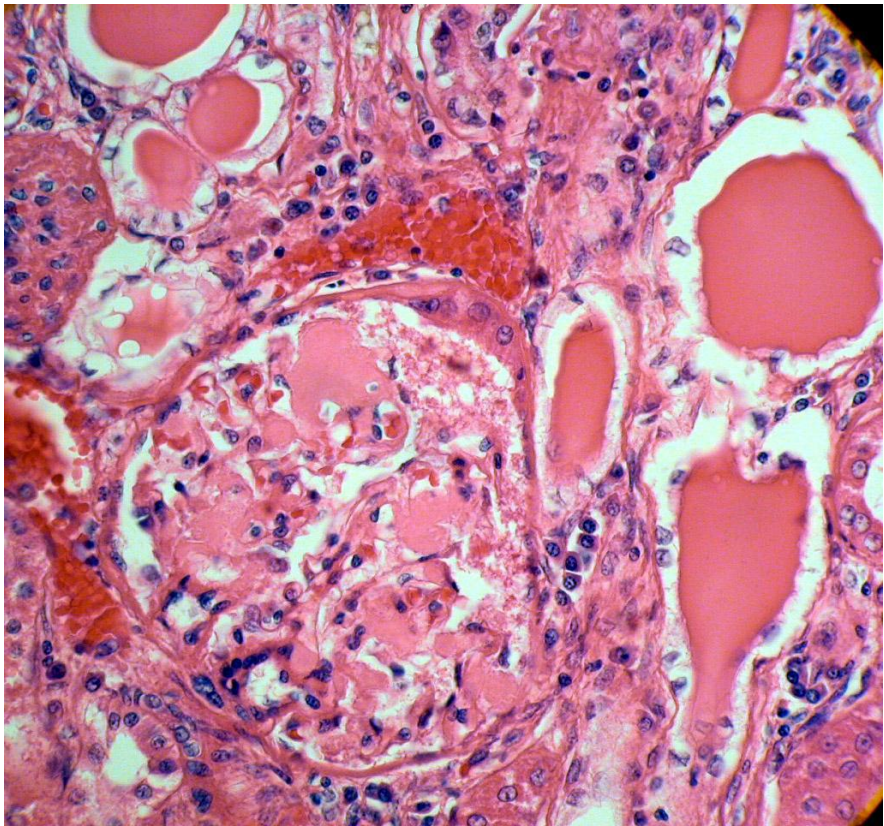
Proteins

Resorption droplets in renal tubular epithelium with proteinuria.



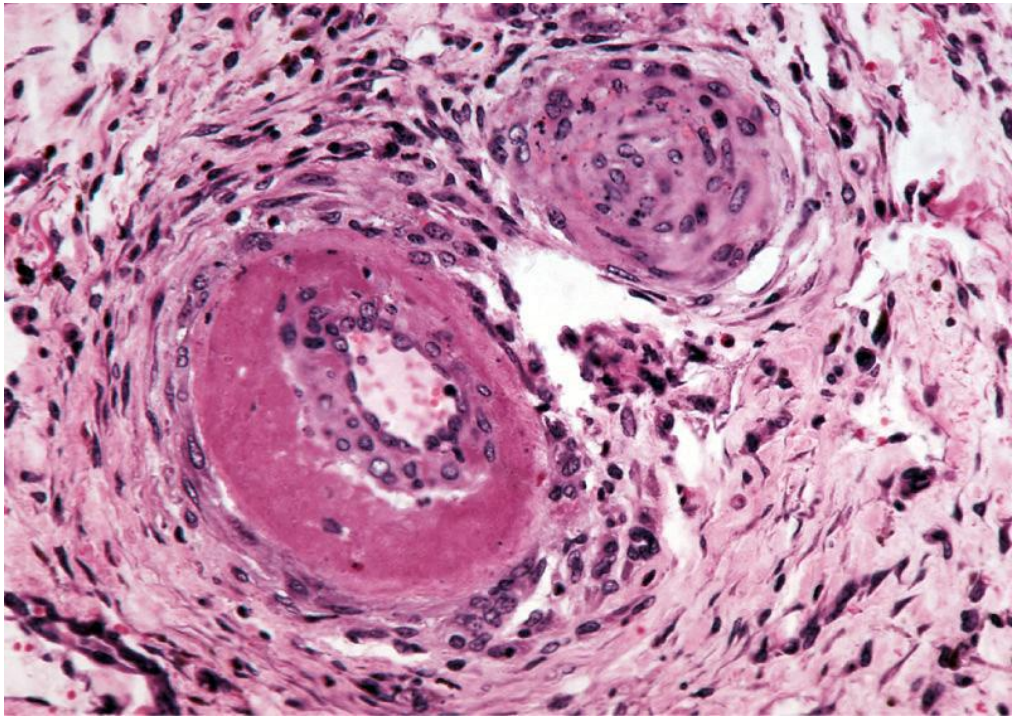
Hyaline Change

- hyaline =any substance (protein), which has a homogeneous, glassy, eosinophilic appearance.
- eg Ig causing thickened BM's, amyloid, protein casts in renal tubules.



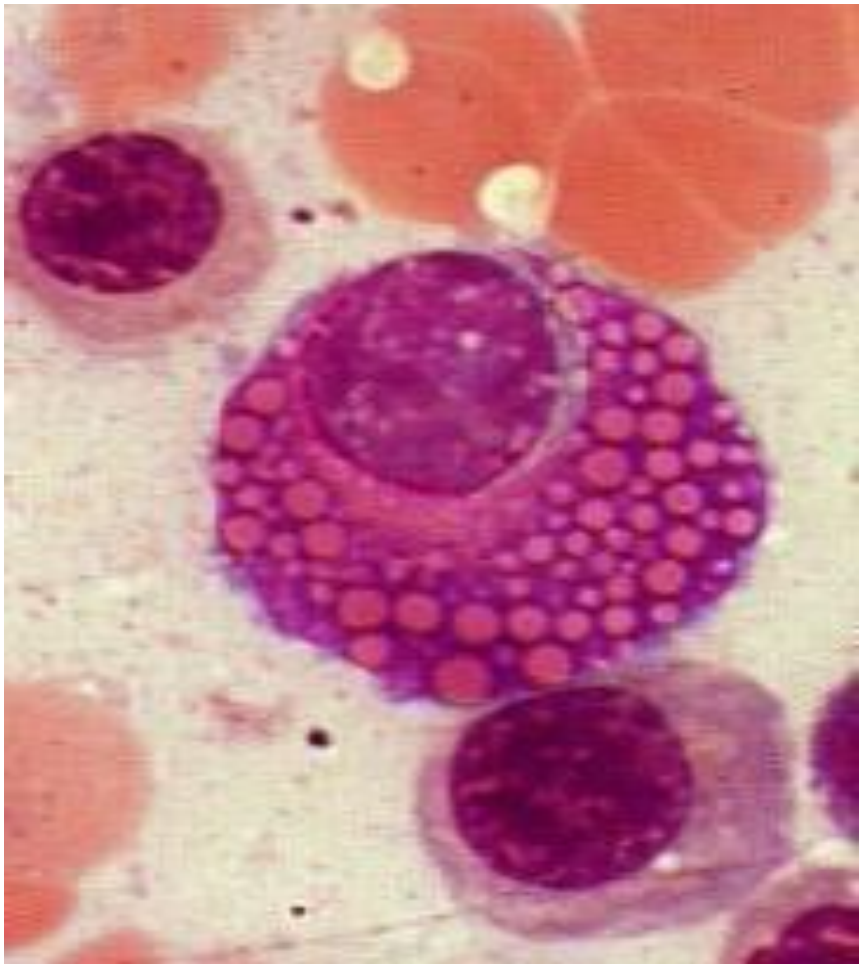
Fibrinoid

- •nonspecific term for hyaline material within an arterial wall.
- •plasma proteins / Ag-Ab / complement in vascular wall →intensely eosinophilic.



Russell bodies

The endoplasmic reticulum of plasma cells engaged in active synthesis of immunoglobulins may become hugely distended, producing large, homogeneous eosinophilic inclusions



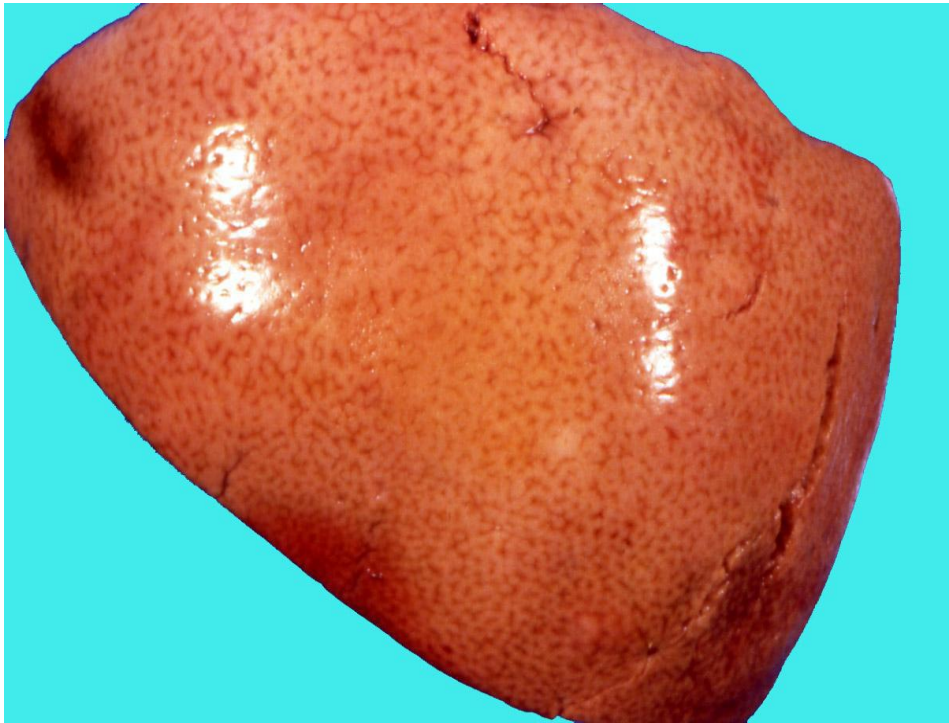
Glycogen

- excessive intracellular deposits with abnormalities of glucose / glycogen metabolism.

-in renal tubular epithelium with diabetes mellitus.

Glycogen Accumulation-in hepatocytes with excess corticosteroids ("steroid hepatopathy").

-in glycogen storage diseases (glycogenoses).

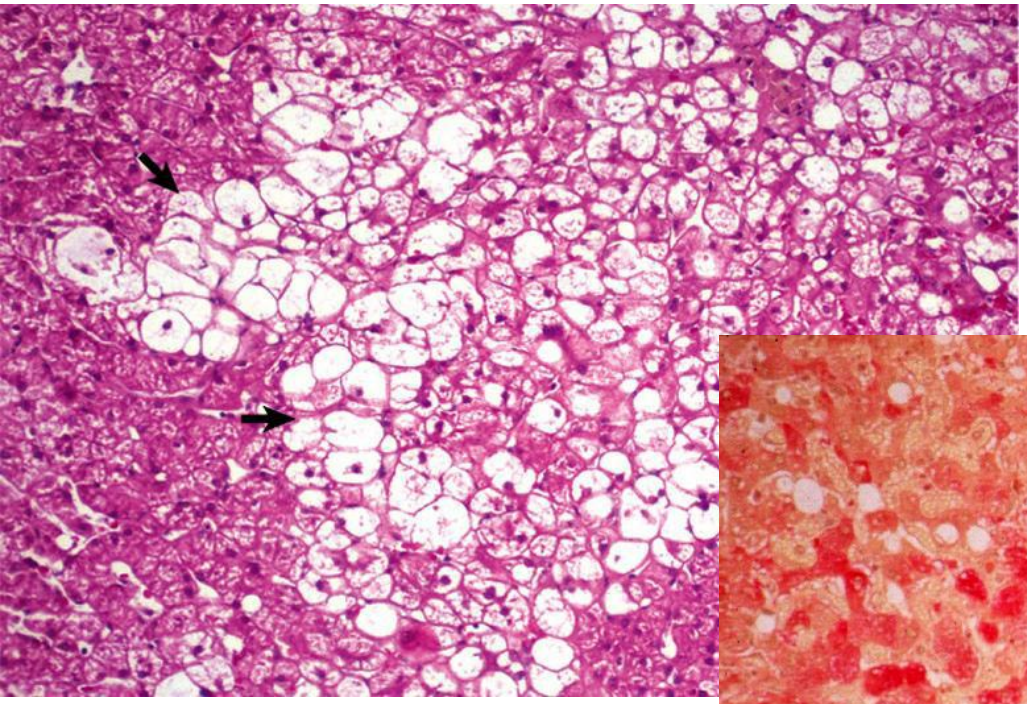


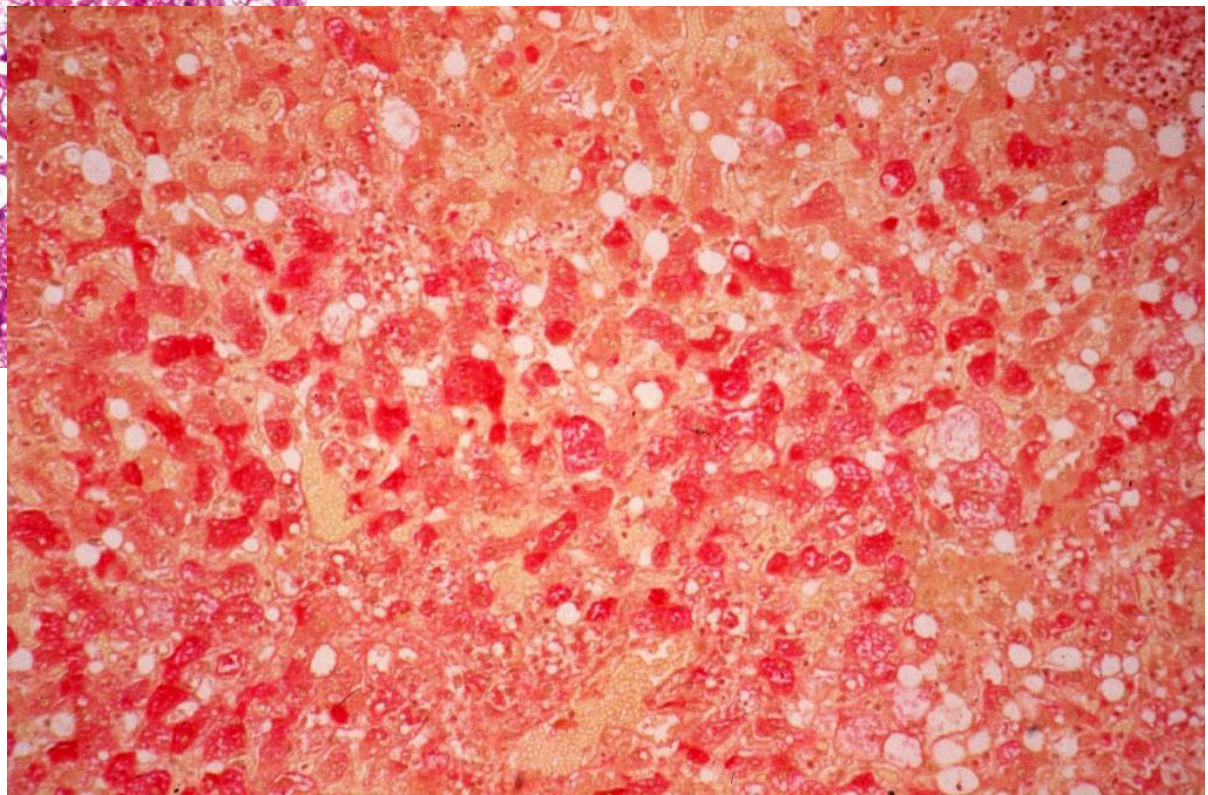
Glycogen

Diabetes mellitus is the prime example of a disorder of glucose metabolism.

Glycogen is found in the renal epithelial cells, within liver cells, beta cells of the islets of Langerhans, and heart muscle cells.

Glycogen storage diseases





Glycogen