Irreversible tissue / cellular lesions: necrosis, apoptosis.

Irreversible tissue / cellular lesions: necrosis, apoptosis.

I. Microspecimens:

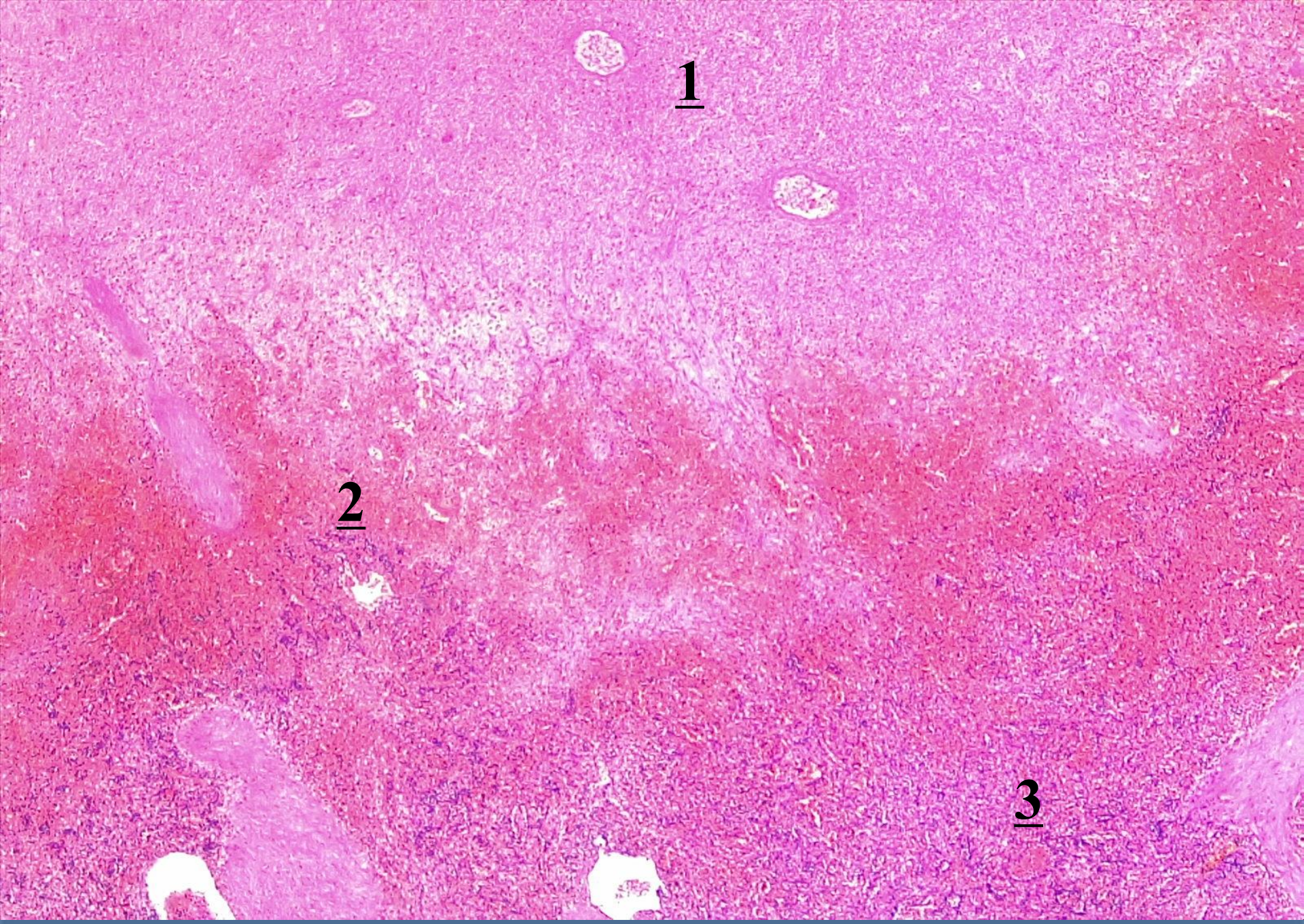
№ 6. Ischemic infarction of the spleen. *(H-E stain).*

Indications:

1. Necrosis area without nuclei *(karyolysis).*
2. Demarcation zone:
   a. hyperemic vessels;
   b. leukocyte infiltration.
3. Adjacent spleen tissue.

In the microspecimen a homogeneous, structureless area, with eosinophil stain - pink colour (detritus), the cells are fragmented or disintegrated (cytorexis and cytolysis), the nuclei are absent (caryolysis); at the periphery of this area fragments of disintegrated nuclei can be noted (cariorexis); from the initial structures in the area of infarction only slightly colored connective tissue tracts are preserved; at the periphery of the infarction there is an area of edema, hyperemia and infiltration with neutrophil leukocytes - demarcation inflammation, which delimits the area of necrosis; the adjacent spleen tissue is hyperemic.

Spleen infarction is a white infarct, ischemic infarction due to insufficient collateral circulation; the main causes are thrombosis or embolism of a branch of the slepnic artery. It can happen in atherosclerosis of the splenic artery complicated by thrombosis, in aortic atherosclerosis - embolism with thrombi or atheromatous masses, in cases of thrombosis of the left ventricle, which can lead to thromboembolism, for example in rheumatic or infectious endocarditis, cardiac infection, cardiomyopathies. The most common consequence of a splenic infarction is organization (scarring), the capsule in the infarcted region becomes thickened, sclerosed.



№ 6. Ischemic infarction of the spleen. *(H-E stain).*

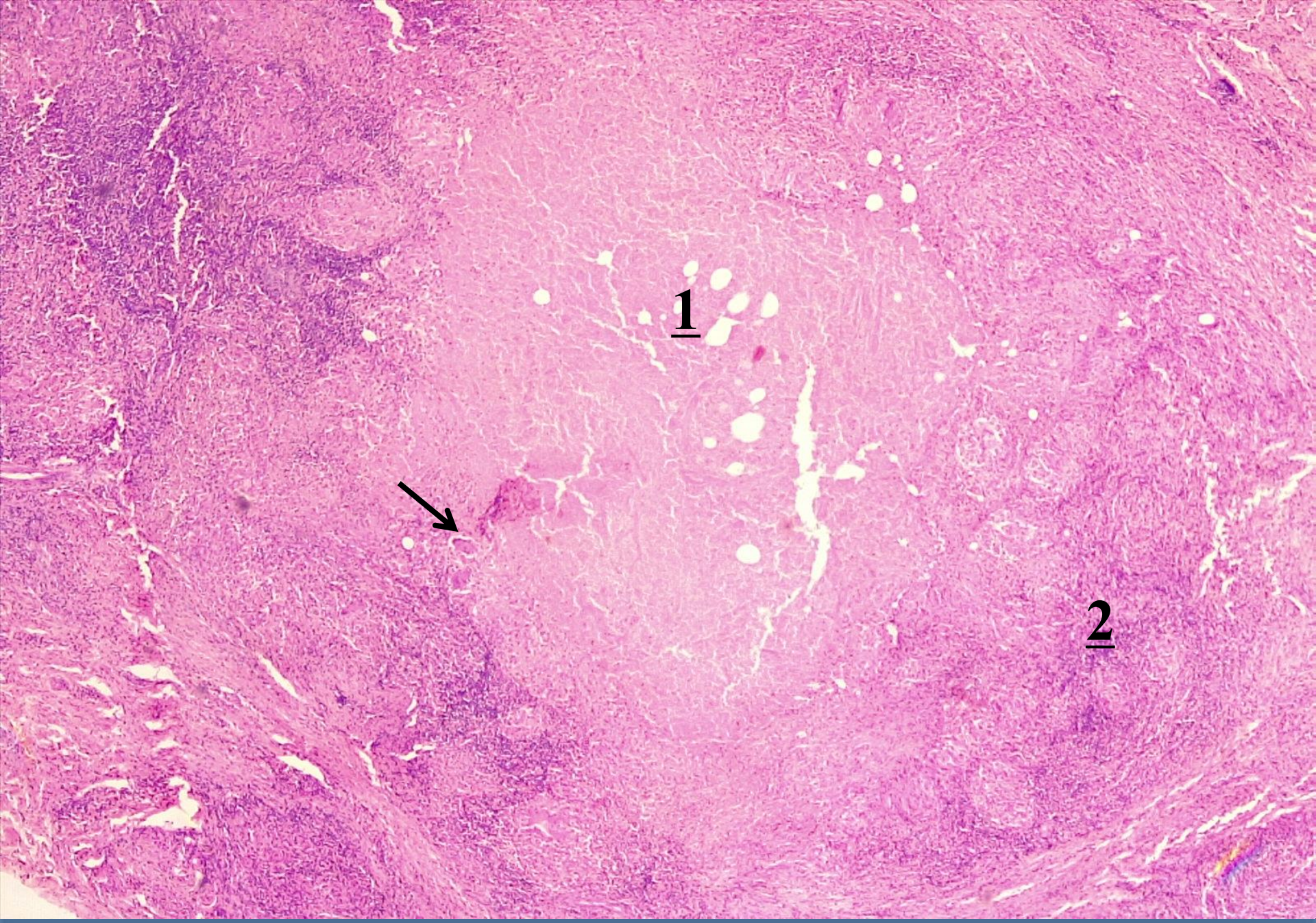
№ 81. Caseous necrosis of lymph node in tuberculosis. *(H-E stain).*

Indications:

1. The focus of caseous necrosis.
2. Inflammatory infiltrate (lymphocytes, epithelioid cells, giant cells).

In the microspecimen an extensive pink-red area can be observed with the naked eye, at the low magnification, this area is homogeneous, microgranular, structureless, intensely eosinophilic, the nuclei are missing (caryolysis), at the periphery of the necrosis area fragments of nuclei can be observed (cariorexis); in the surrounding tissue tuberculous granulomas are detected in the stage of fibrosis, giant polynuclear cells Langhans can be noted.

Caseous necrosis is most common in tuberculosis, but is also seen in syphilis, Hodgkin's lymphoma, leprosy, in some fungal granulomas. It is a type of coagulative necrosis. The necrotic masses have a dense consistency, whitish-yellow color, are friable, have a "cheesy" appearance. Histologically, the necrosis area appears amorphous, structureless eosinophilic. It is characterized by the complete loss of tissue architecture, cellular and tissue structures disappear completely. The most common consequences are calcification (petrification), encapsulation and organization.



№ 81. Caseous necrosis of lymph node in tuberculosis. *(H-E stain).*

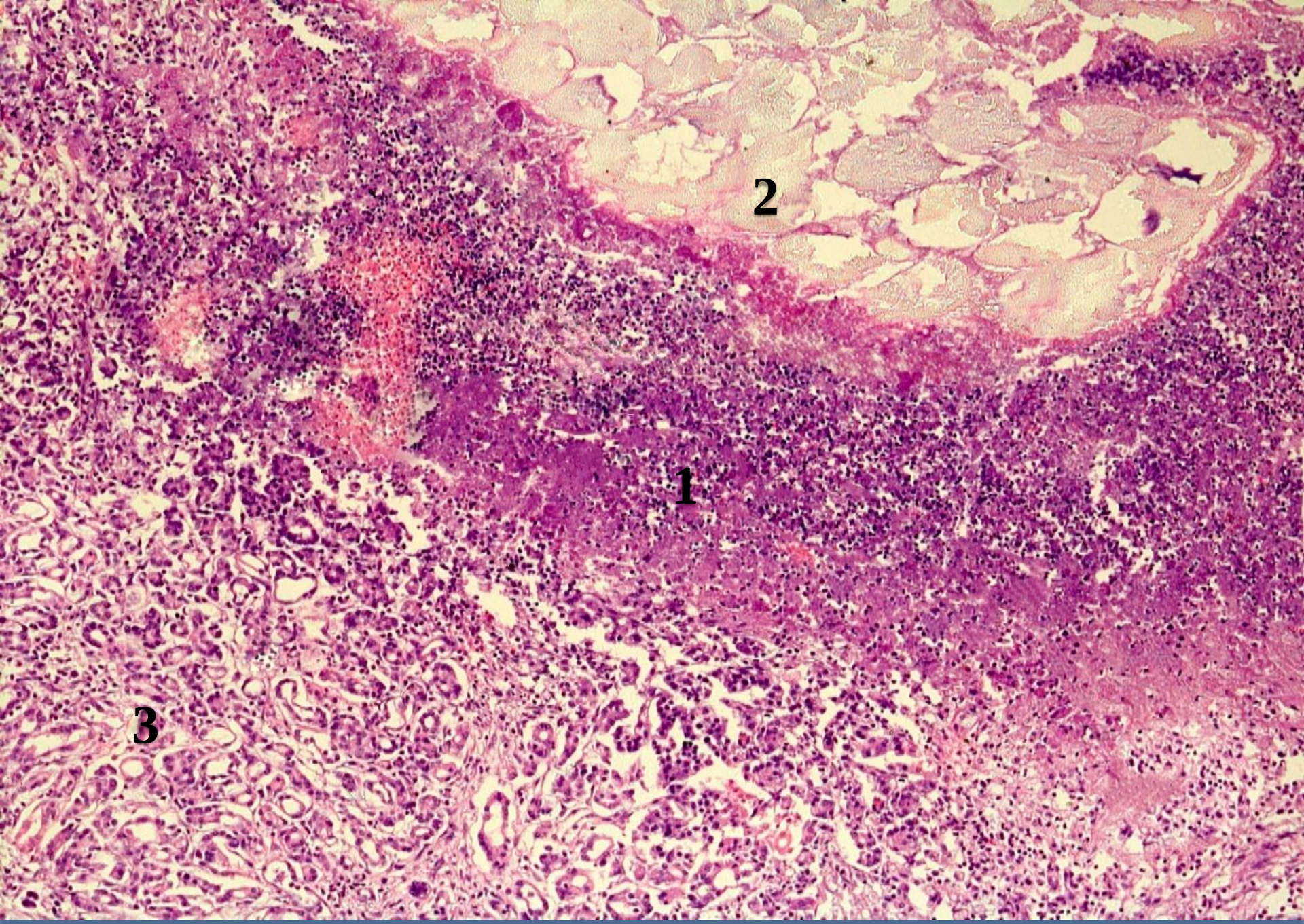
№ 153. Pancreonecrosis. *(H-E stain).*

Indications:

1. Focus of the glandular tissue necrosis.
2. Focus of the adipose tissue necrosis.
3. Adjacent pancreatic tissue.

The microspecimen contains foci of necrosis of the pancreatic parenchyma which are intensely colored, the structure is unclear, the structural elements are disintegrated, necrotic remains are infiltrated with neutrophilic leukocytes, fragments of nuclei (cariorexis) are observed, in foci of necrosis the pancreatic adipocytes have basophilic cytoplasm, are swollen and poorly contoured, the surrounding pancreatic tissue is edematous, hyperemic.

Steatonecrosis (fatty necrosis) - necrosis of adipose tissue. It is a form of enzymatic necrosis caused by the action of lipase and trypsin, which are released from the pancreatic acinar cells in cases of acute pancreatitis (pancreonecrosis). Lipase penetrates adipocytes, induces their necrosis and the transformation of lipids into soaps (calcium salts of fatty acids), which macroscopically give necrotic foci the appearance of white-yellow clearly defined stearin spots, with dense consistency. In acute pancreatitis foci of steatonecrosis are observed in the pancreas, peripancreatic tissue, omentum and adipose tissue in other areas. Microscopically the adipocytes become blurred, with unclear contours, they are basophilic (stained in blue) due to the high concentration of calcium salts. It can also be observed in adipose tissue trauma, for example, of the mammary gland.



№ 153. Pancreonecrosis. *(H-E stain).*

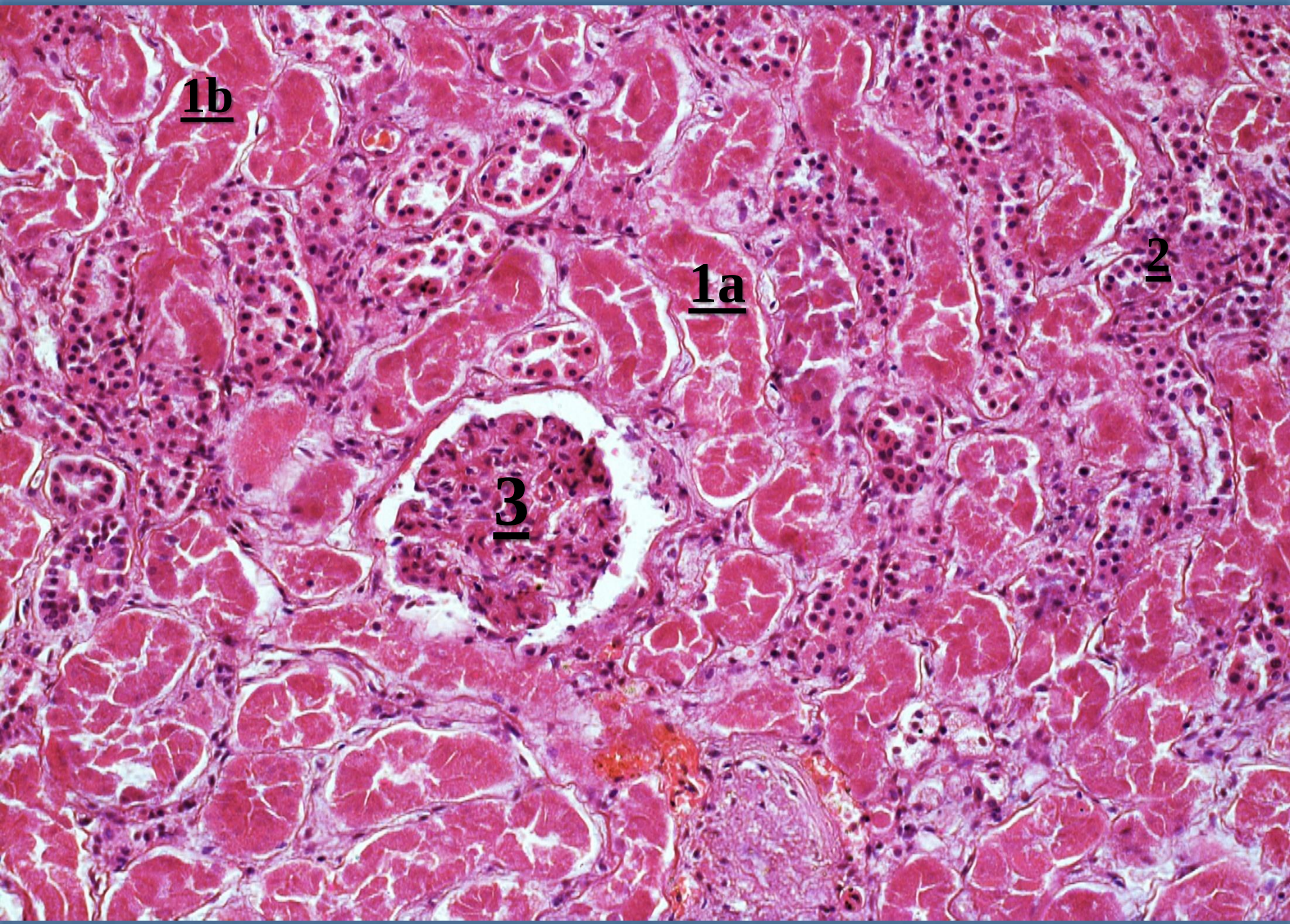
№ 2. Acute tubular necrosis. *(H-E stain).*

Indications:

1. Necrosed tube :
   a. epithelial cells without nuclei *(karyolysis);*
   b. narrowed lumen.
2. Unchanged tube.
3. Unchanged glomerulus.

The epithelial cells of the proximal and distal convoluted tubules are swollen, lack nuclei (caryolysis), the cytoplasm is homogenized, pink (eosinophilic); the lumen of the tubes is narrowed, and in some cases are missing completely due to the blockage with masses of cellular detritus (plasmorexis and plasmolysis); the blood vessels are dilated and hyperemic, the cellular structure of the glomeruli, Henle loops and straight tubes and collectors is preserved.

Necrosis of the epithelium of the convoluted renal tubules (necrotic nephrosis) occurs as a result of hemodynamic disorders (cortical ischemia of the kidneys) or direct toxic action on nephrocytes of various chemicals (mercury dichloride, ethylene glycol, etc.). Clinically it is manifested by acute renal failure (oliguria or anuria). It is found in states of shock (traumatic, cardiogenic, toxic, bacterial, hemorrhagic, posttransfusional, etc.). Possible consequences of necrotic nephrosis: healing (regeneration of the renal tubules) and restoration of diuresis or lethal due to uremia.



№ 2. Acute tubular necrosis. *(H-E stain)*.

II. Macrospecimens:

№ 141. Ischemic infarction of the spleen.

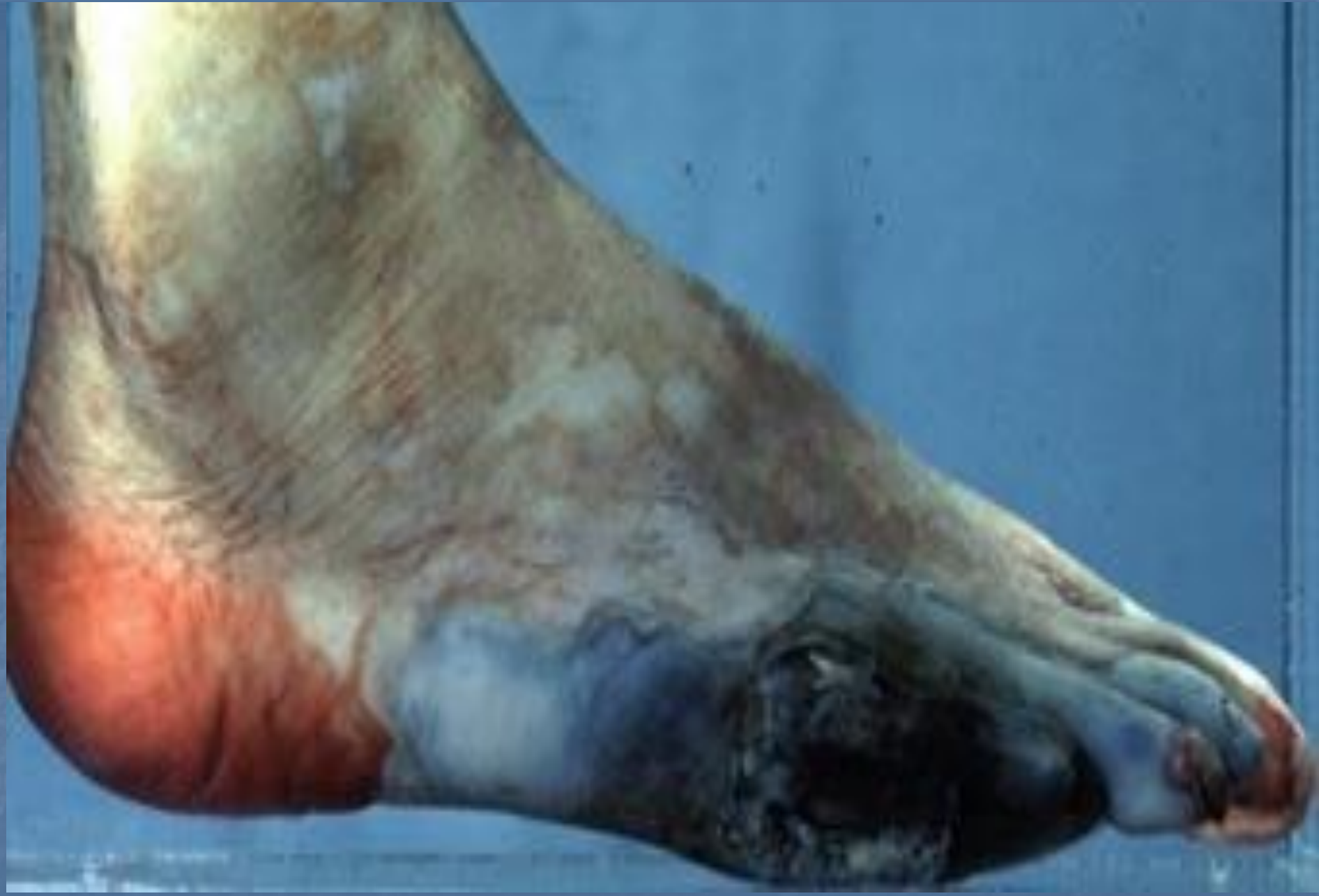
On the cut surface of the spleen areas of triangular (conical) necrosis, whitish-yellow in color and dense in consistency, clearly delimited by the adjacent tissue, with the base oriented towards the organ capsule and the tip towards the hilum due to the "fan" branching of the splenic artery. the spinal artery); the capsule is covered with deposits of fibrin (fibrinous inflammation), which clinically causes pain in the left hypochondrium [microscopic appearance - micropreparation № 6].

№ 151. Low (upper) extremities gangrene.

The soft tissues of the foot (or hand) are dry, wrinkled, mummified, black, with dense consistency; between the viable tissue and the gangrene area, the demarcation line (demarcation inflammation) is highlighted.

Gangrene develops in the tissues (organs) that have contact with the external environment. The black color is due to iron sulfite, which is formed by the contact of hemoglobinogenic pigments with atmospheric air and hydrogen sulfide produced by bacteria in mortified tissues. During the demarcation inflammation progressive erosion of the necrotic tissue with its complete detachment - self-amputation can happen. The most common causes of limb gangrene, primarily of the lower ones, are thrombosis or thromboembolism of the arteries in atherosclerosis, diabetes, endarteritis obliterans, as well as trauma, burns, frostbite. When associated with a bacterial infection, dry gangrene can turn into wet gangrene due to tissue liquefaction under the action of proteolytic enzymes of bacteria and leukocytes.

№ 141. Ischemic infarction of the spleen.



№ 151. Low (upper) extremities gangrene.

№ 131. Pancreonecrosis (acute necrotic pancreatitis).

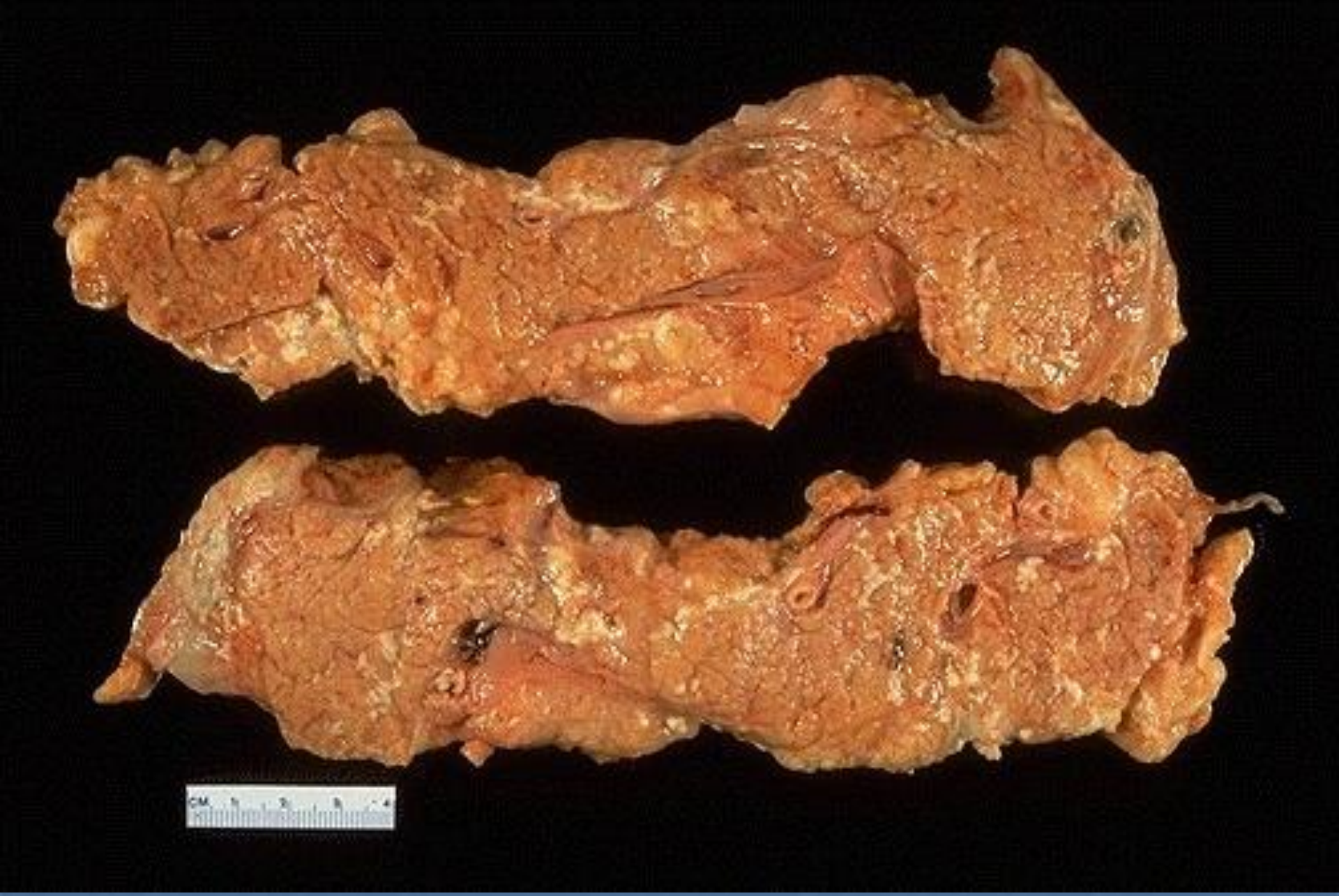
In the pancreas there are foci of dark red hemorrhage and foci of whitish-yellow necrosis of intra/peripancreatic adipose tissue, which resemble stearin (foci of steatonecrosis).

Pancreonecrosis or acute necrotic pancreatitis is an acute pathology in the field of medical emergencies ('acute abdomen'), in which the proteolytic destruction of pancreatic tissue and adipose tissue (steatonecrosis) occurs under the action of hyperactivated pancreatic enzymes and primarily trypsin and lipase (self-digestion). The most common causes are bile duct disorders and alcoholism. The most serious complication is enzymatic shock, which can cause death.

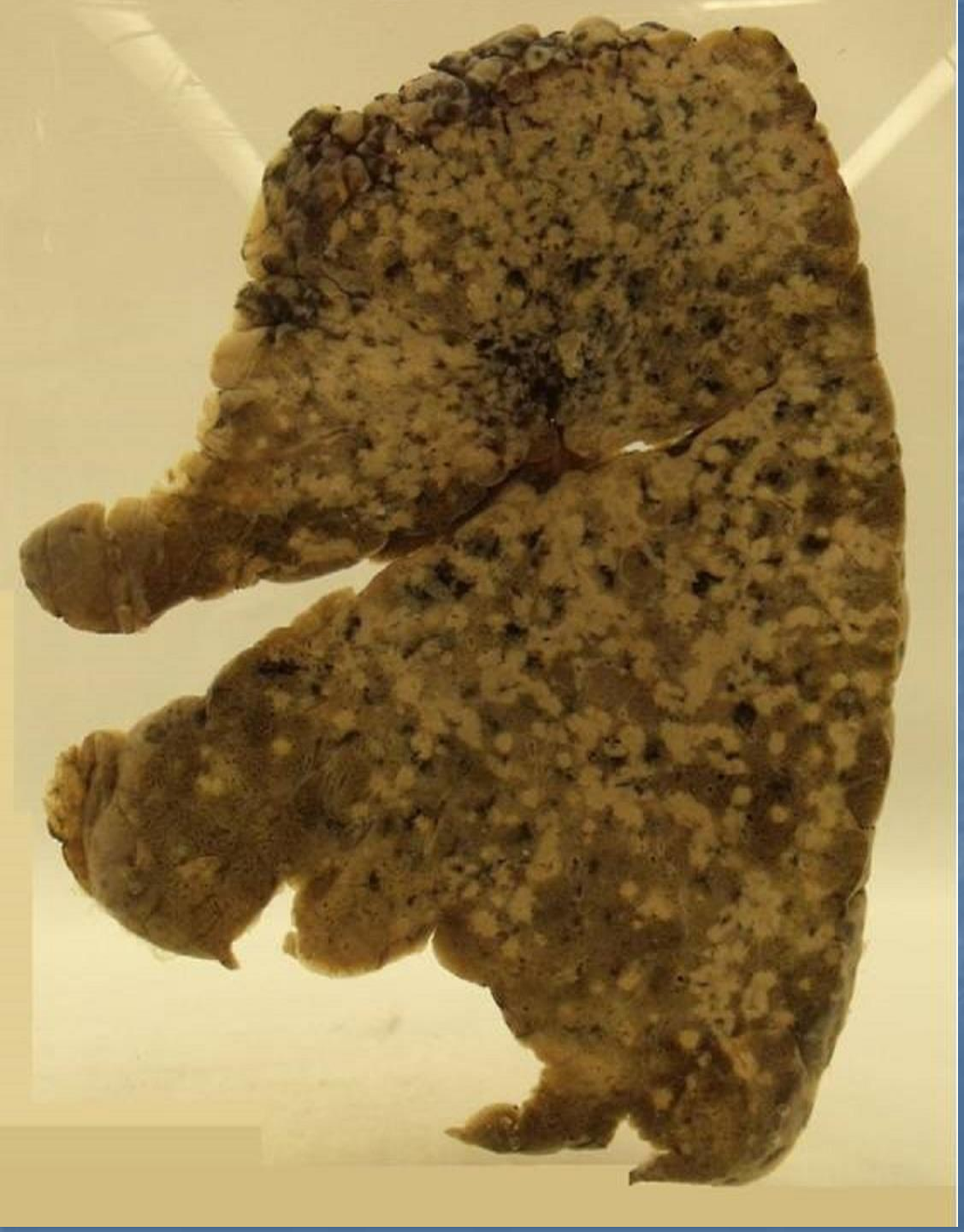
№ 43. Caseous necrosis in tuberculosis *(caseous pneumonia).*

In the lung there is an extensive, non-aerated, whitish-yellow area, with a friable, that can easily be fragmented, similar to dry cheese, hence the name of caseous pneumonia (lat. Caseum - cheese).

Caseous necrosis is characteristic of tuberculosis. Caseous pneumonia is more common in secondary tuberculosis, but can also be in primary tuberculosis. There are deposits of fibrin in the pleura. The caseous masses can be subjected to purulent lysis and liquefaction with the appearance of decomposition cavities - caverns (cavernous tuberculosis).



№ 131. Pancreonecrosis (acute necrotic pancreatitis).

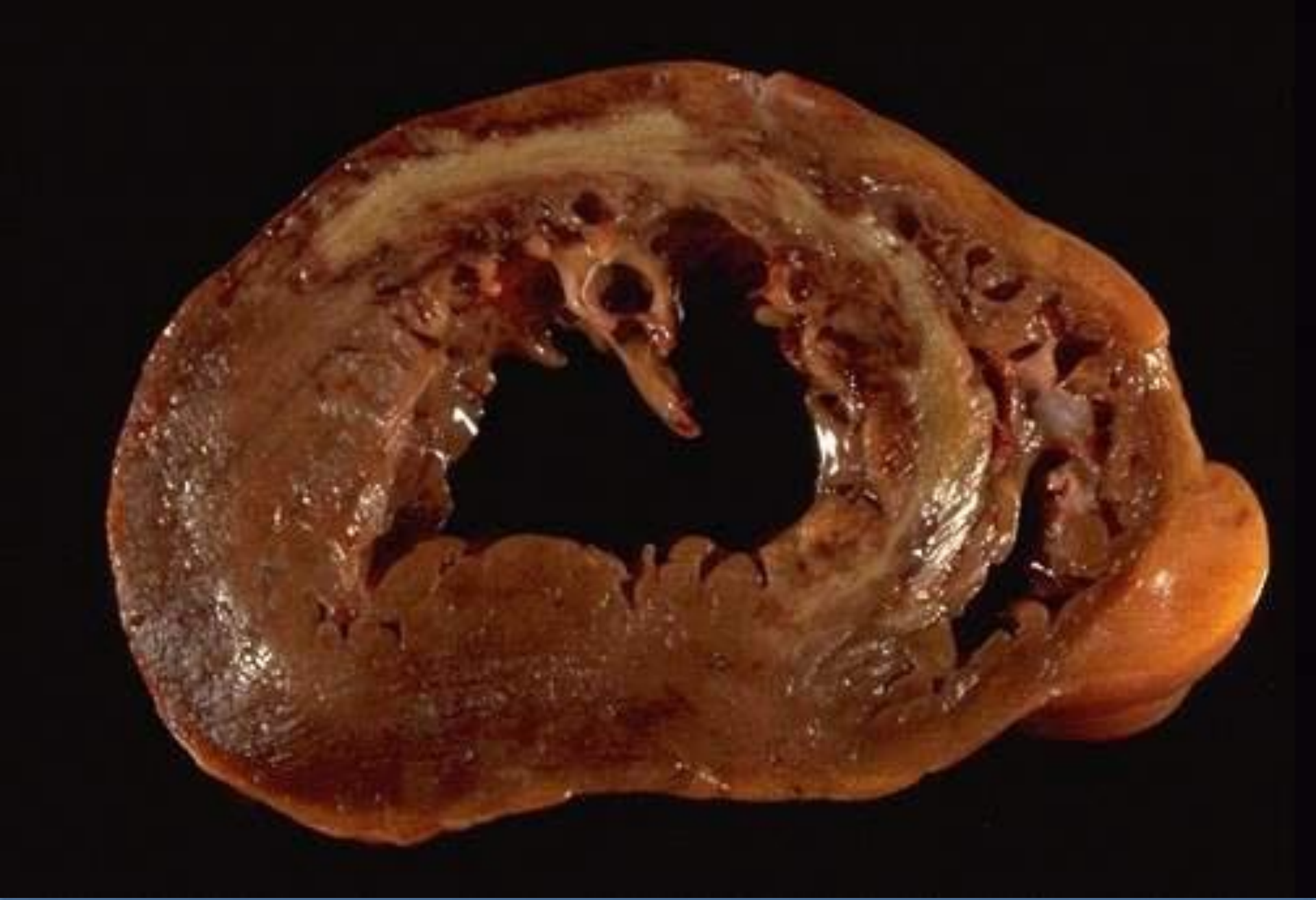


№ 43. Caseous necrosis in tuberculosis *(caseous pneumonia)*.

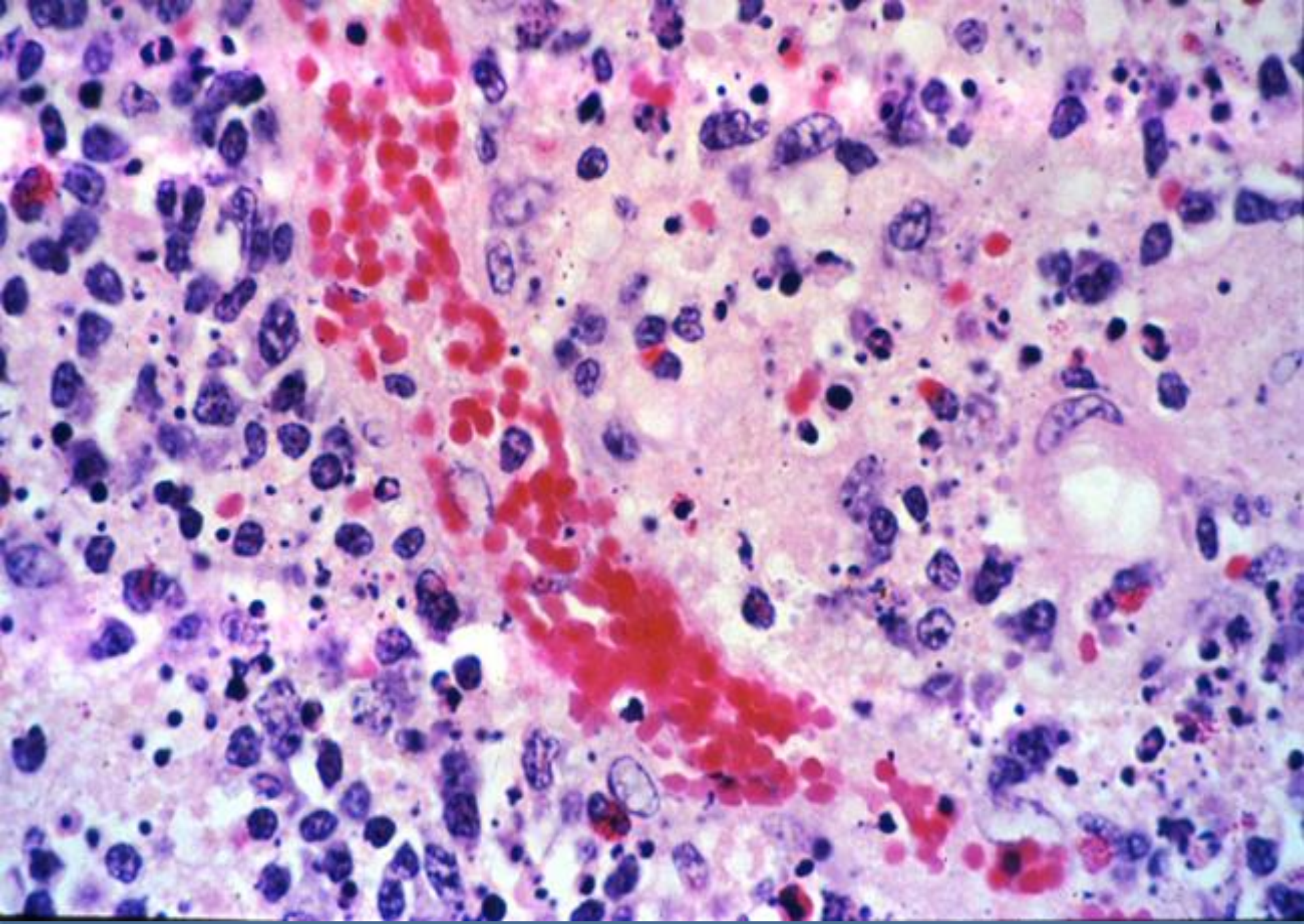
№ 13. Macrofocal postinfarction cardiosclerosis.

On the cut section of the left ventricular wall there is an area of scar-fibrous connective tissue, white-gray, with cartilaginous appearance, hard consistency, the ventricular wall is thickened, hypertrophied.

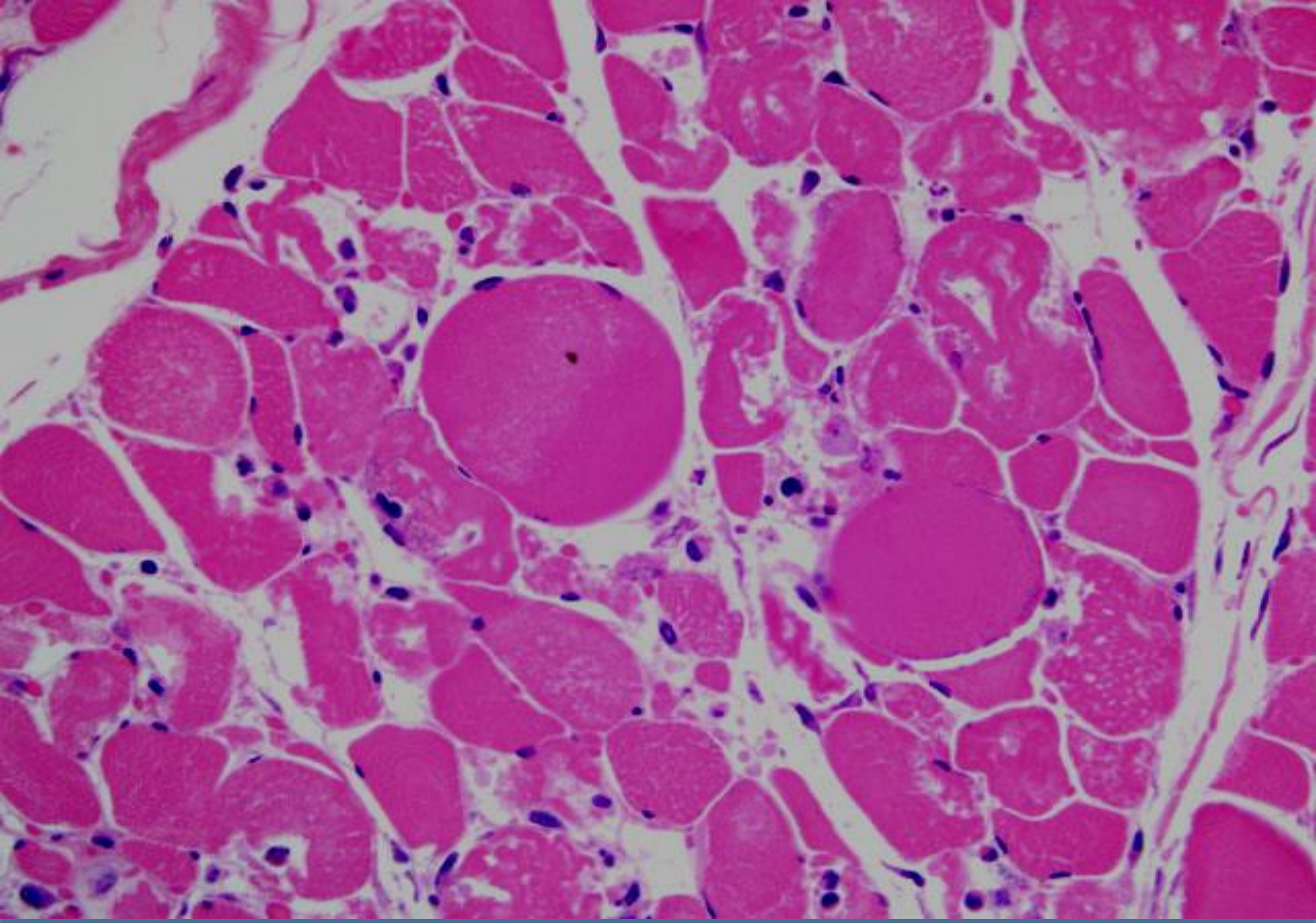
Macrofocal cardiosclerosis is a consequence of myocardial infarction, occurs after the organization of the infarct area, which occurs within 6-7 weeks from the onset of the disease. Calcium salts can be stored in the area of the post-infarct scar, compensatory hypertrophy is observed in the adjacent heart muscle. Possible complications: congestive heart failure, rhythm and conduction disorders, chronic heart aneurysm.



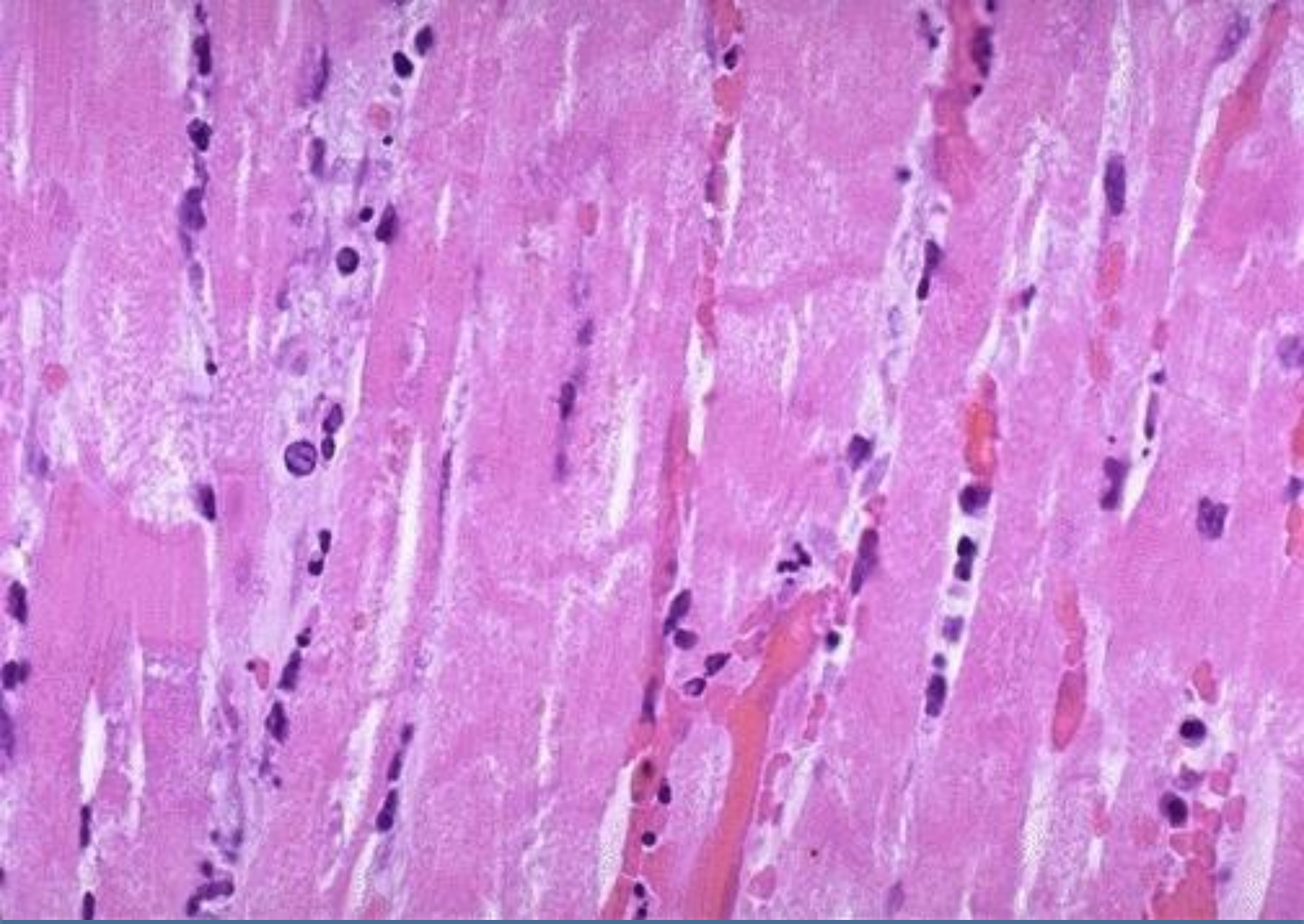
№ 13. Macrofocal postinfarction cardiosclerosis.



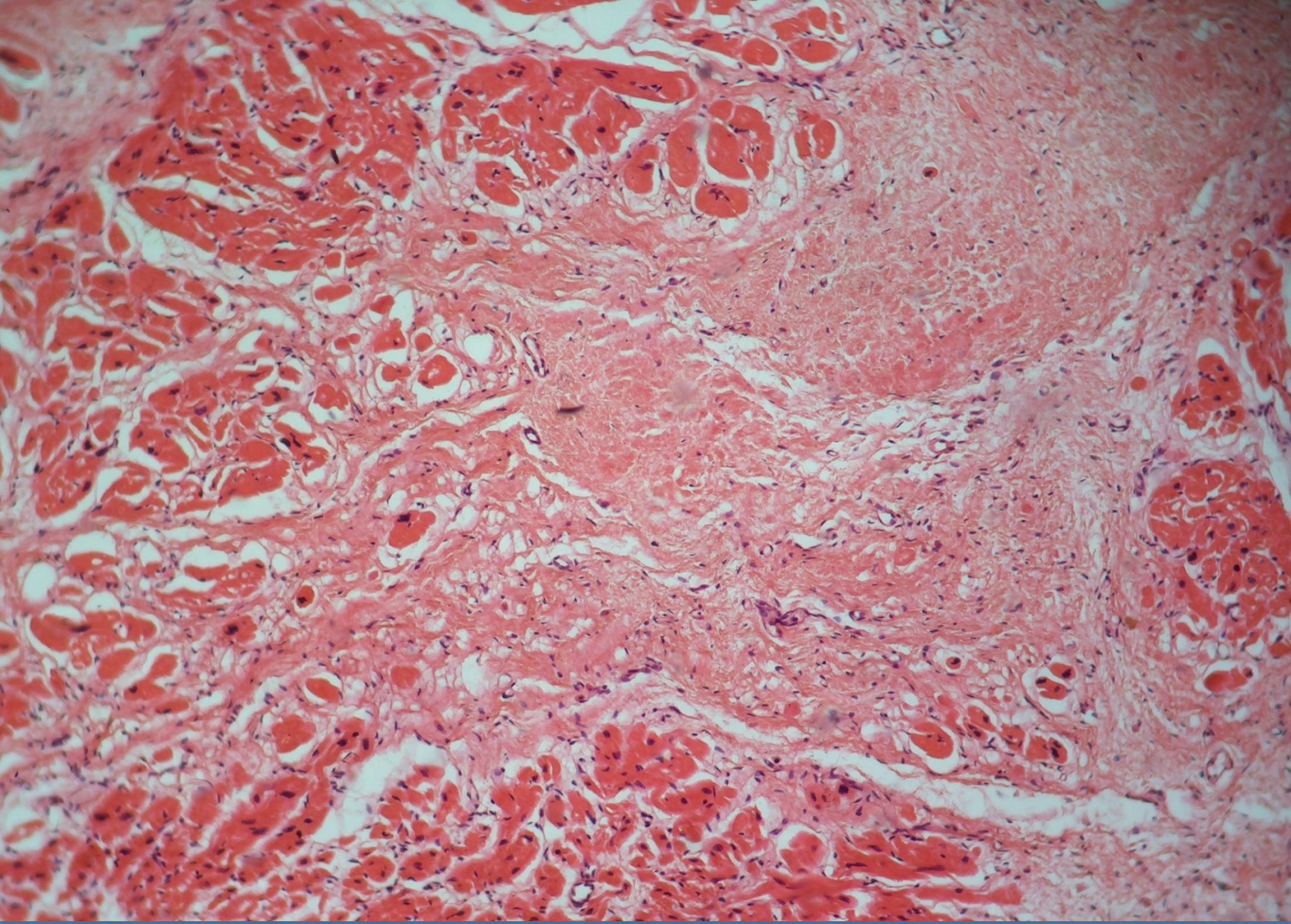
Karyopyknosis and karyorrhexis of lymphoid tissue.



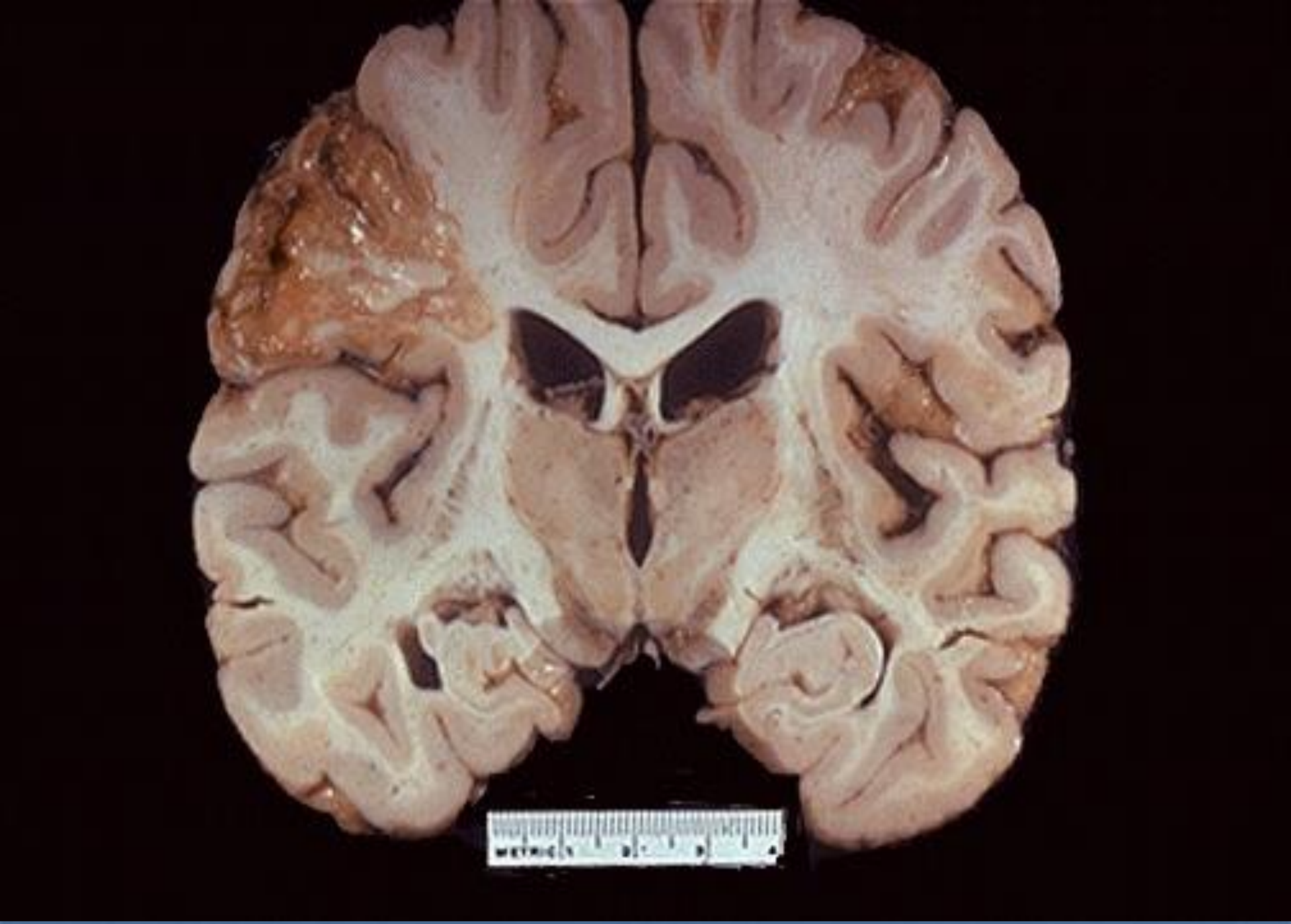
Waxy necrosis (Zencker) of striated muscle. (H-E stain).



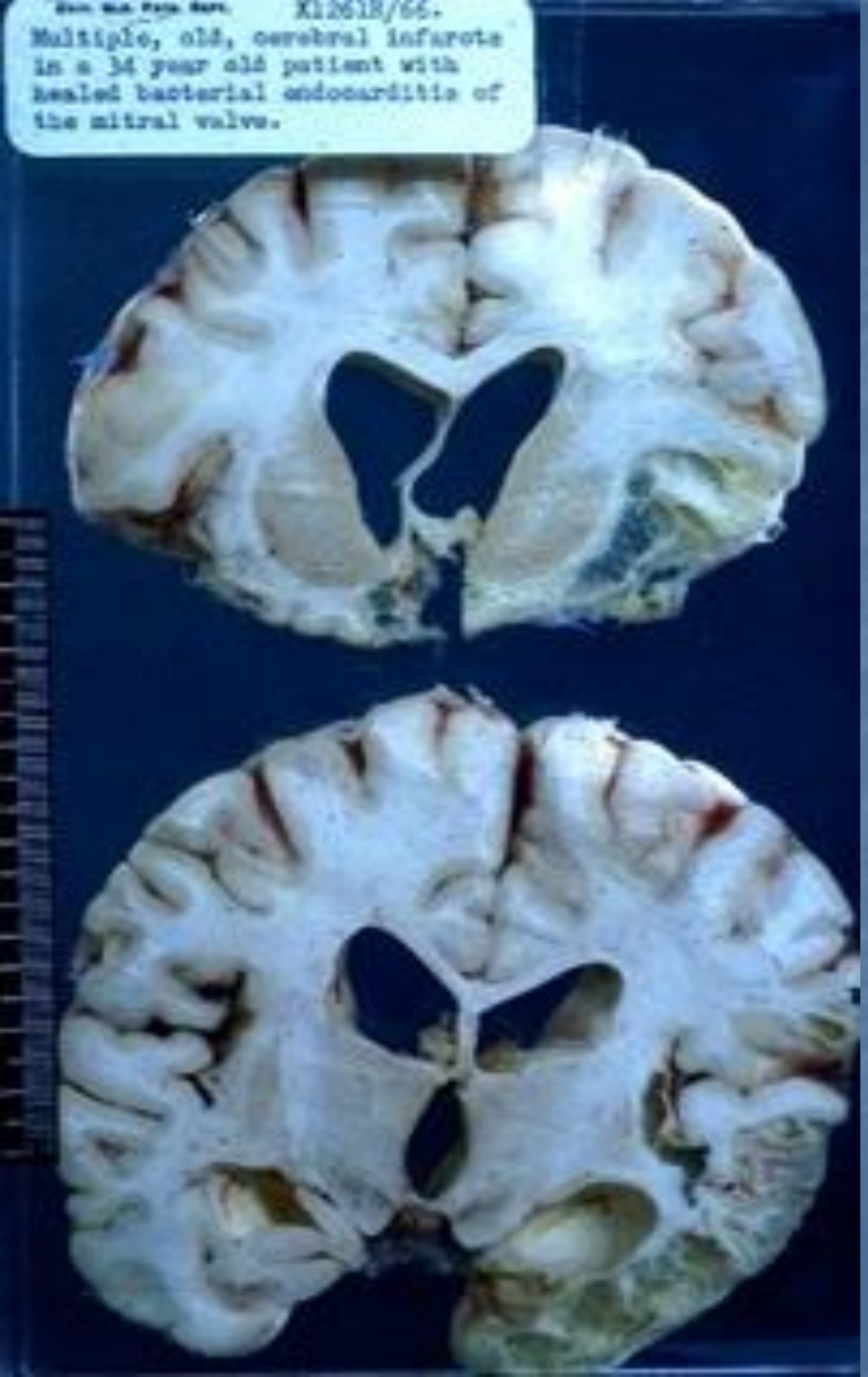
Coagulative necrosis of the myocardium.



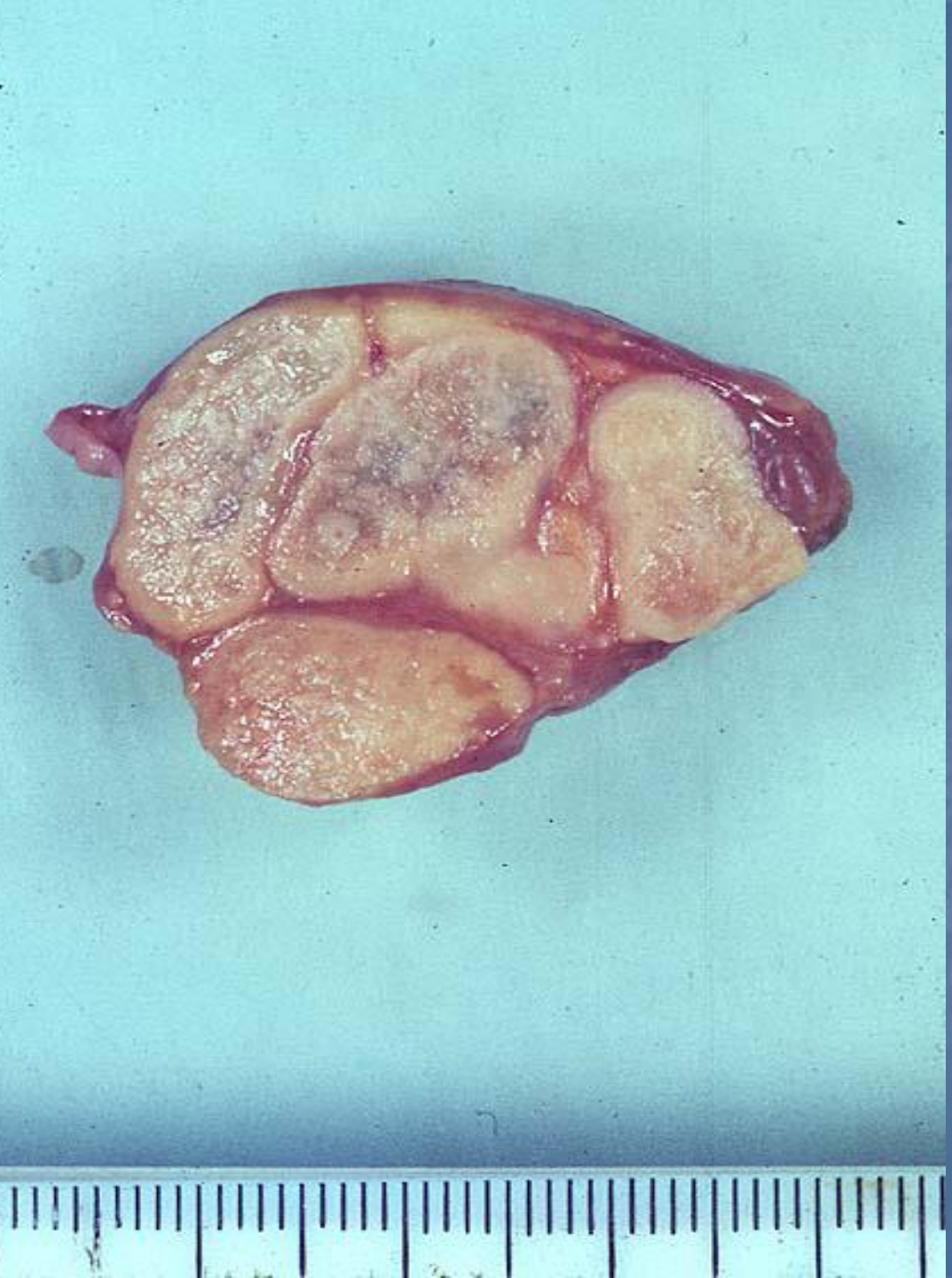
Sequelae of myocardial coagulation necrosis.



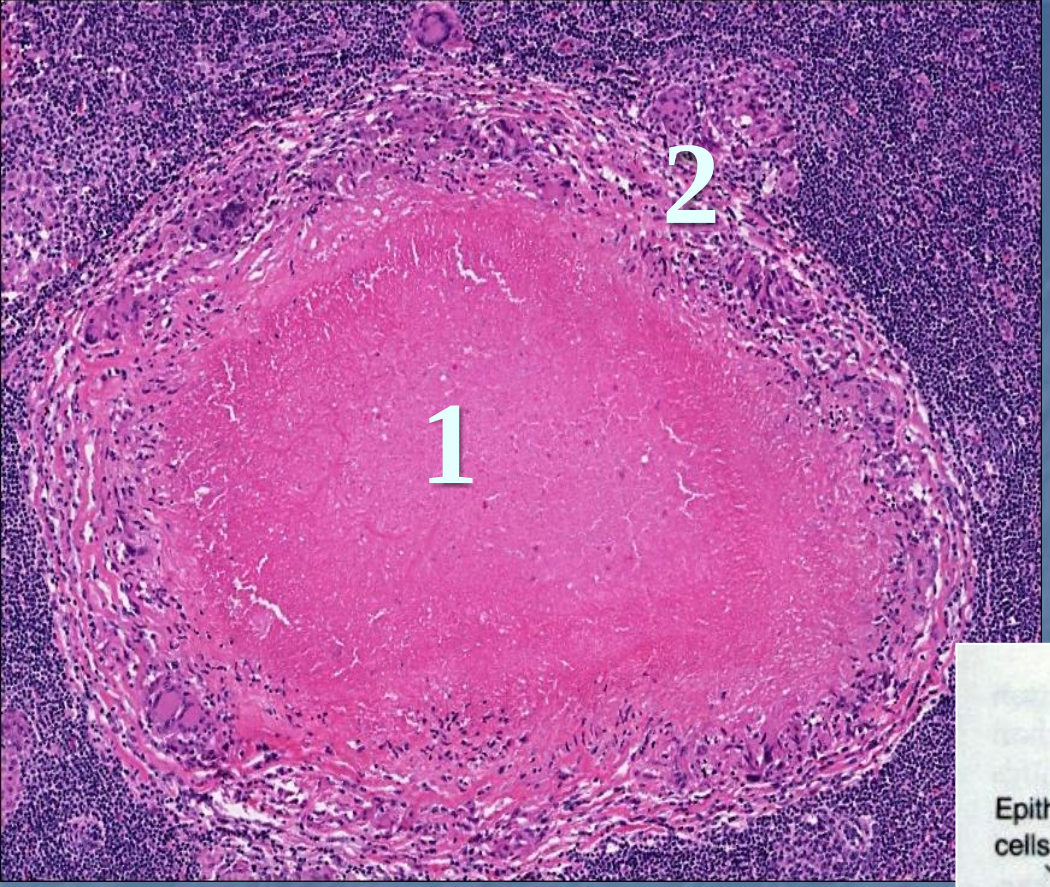
Cerebral ischemic softening.



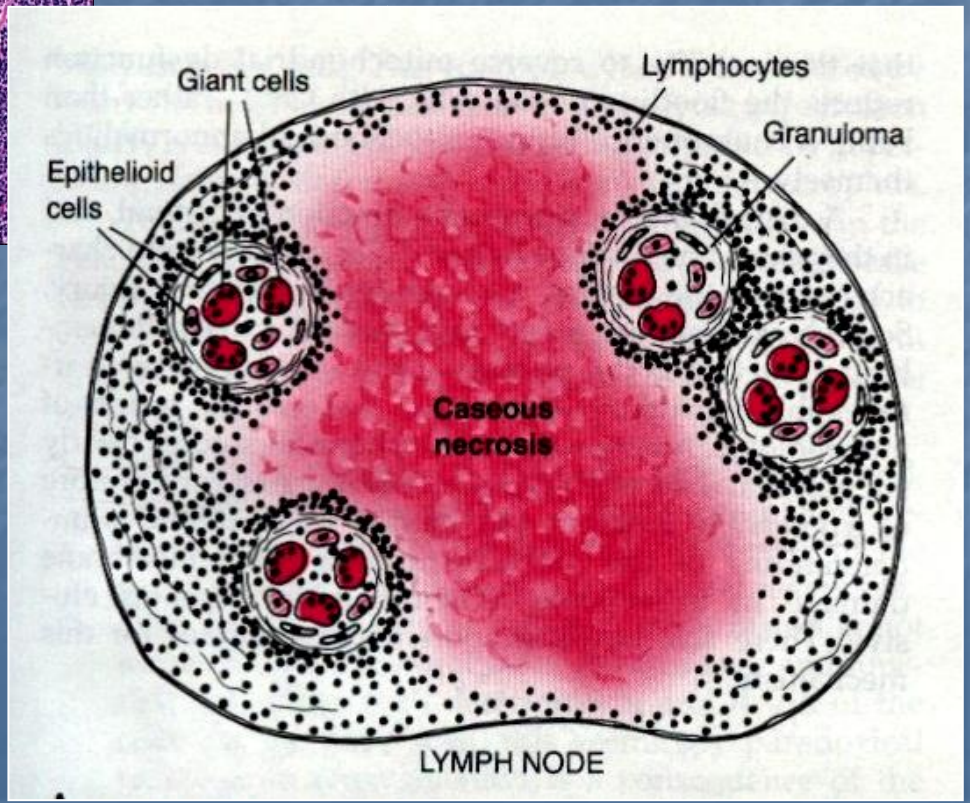
Sequelae of cerebral infarction.

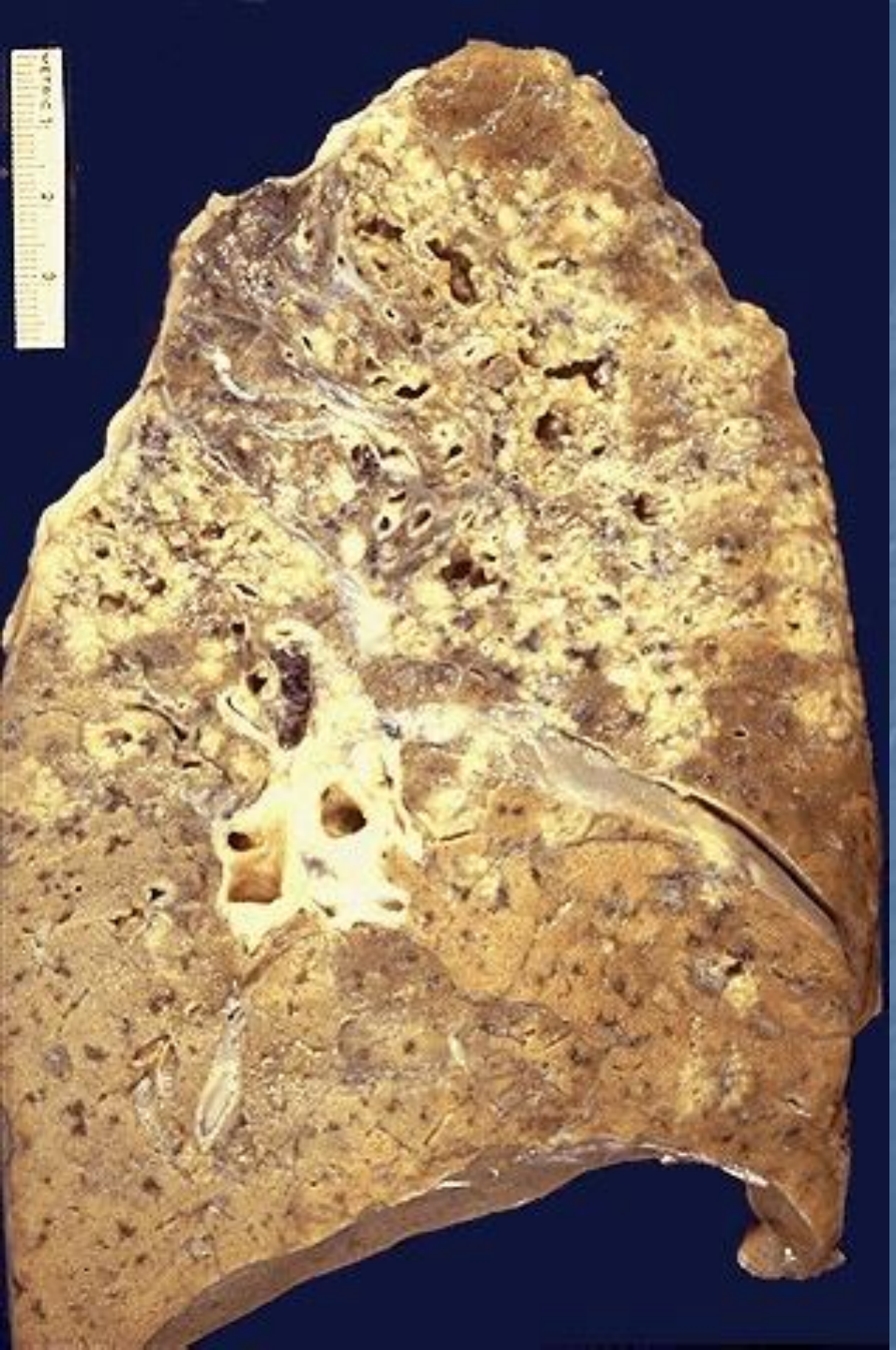


Caseous necrosis of the lymph node in tuberculosis.

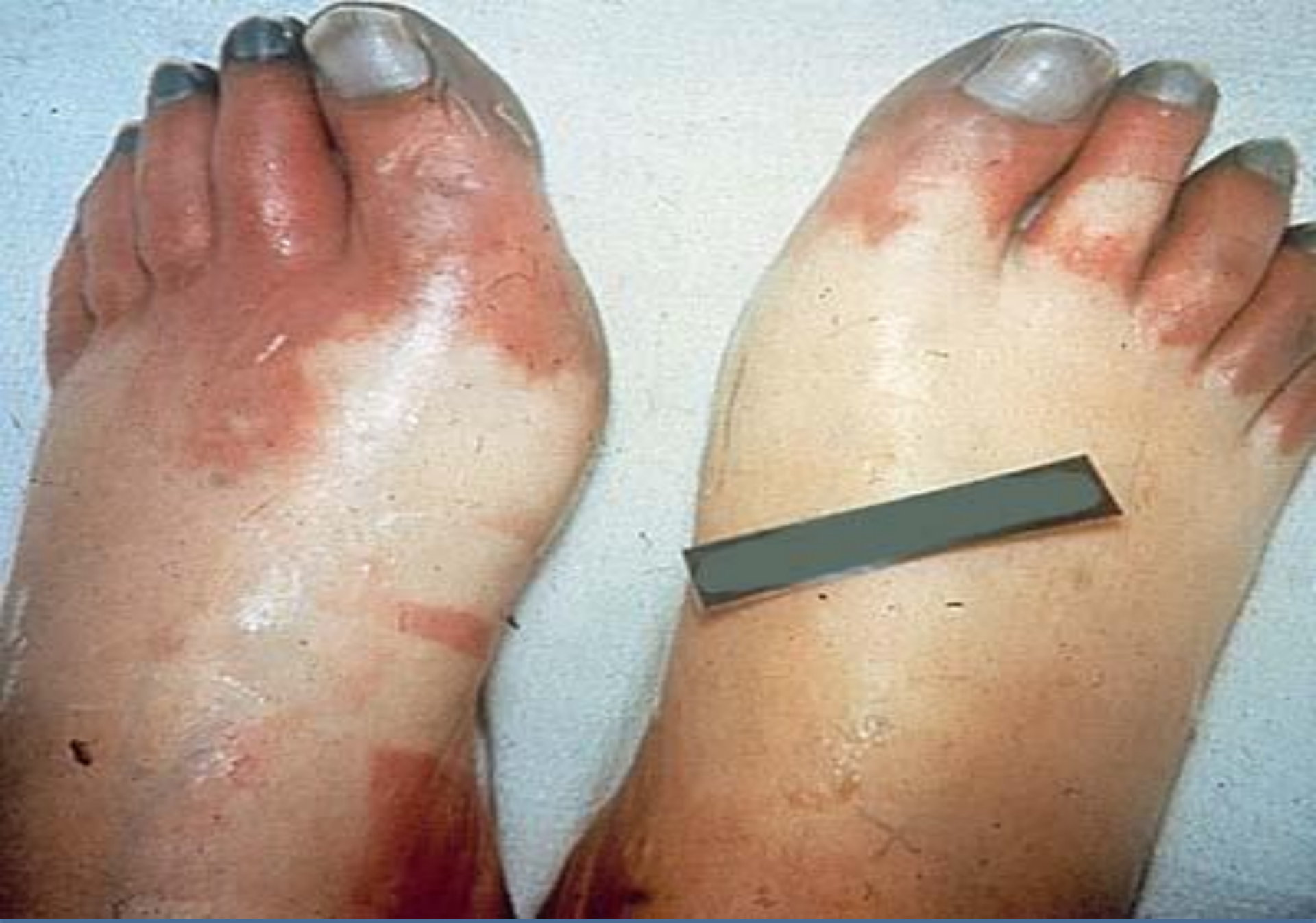


Caseous necrosis of the lymph node in tuberculosis. (H-E stain).

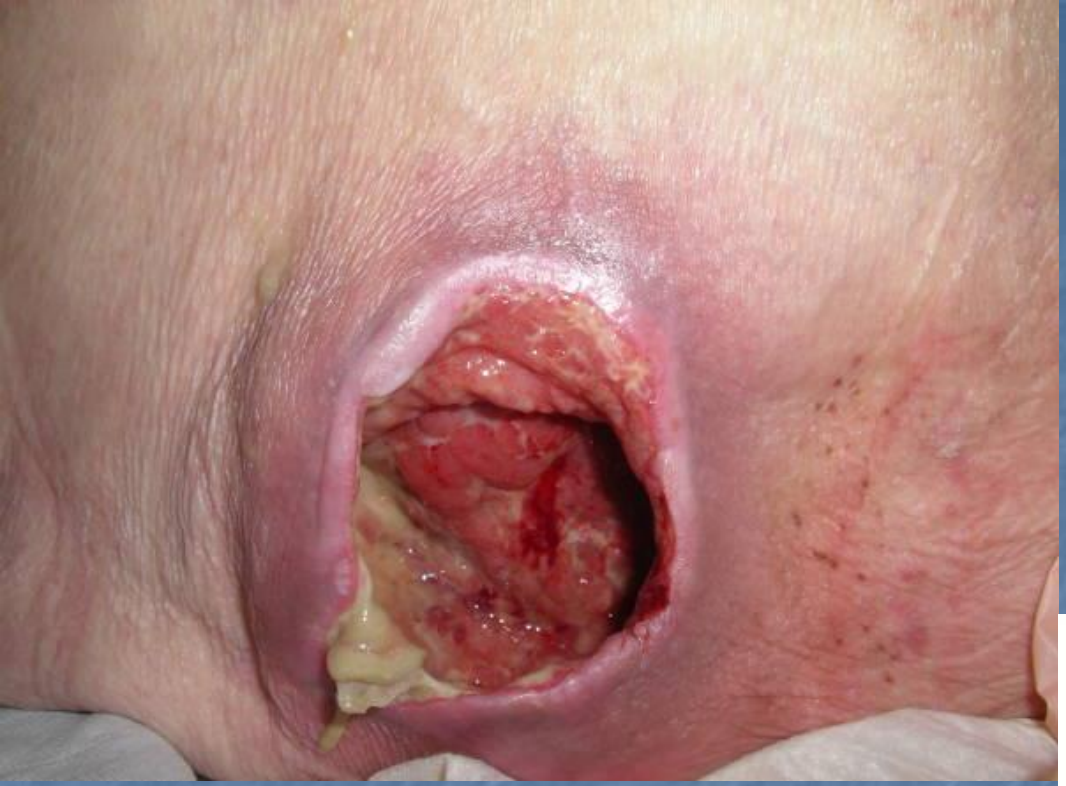




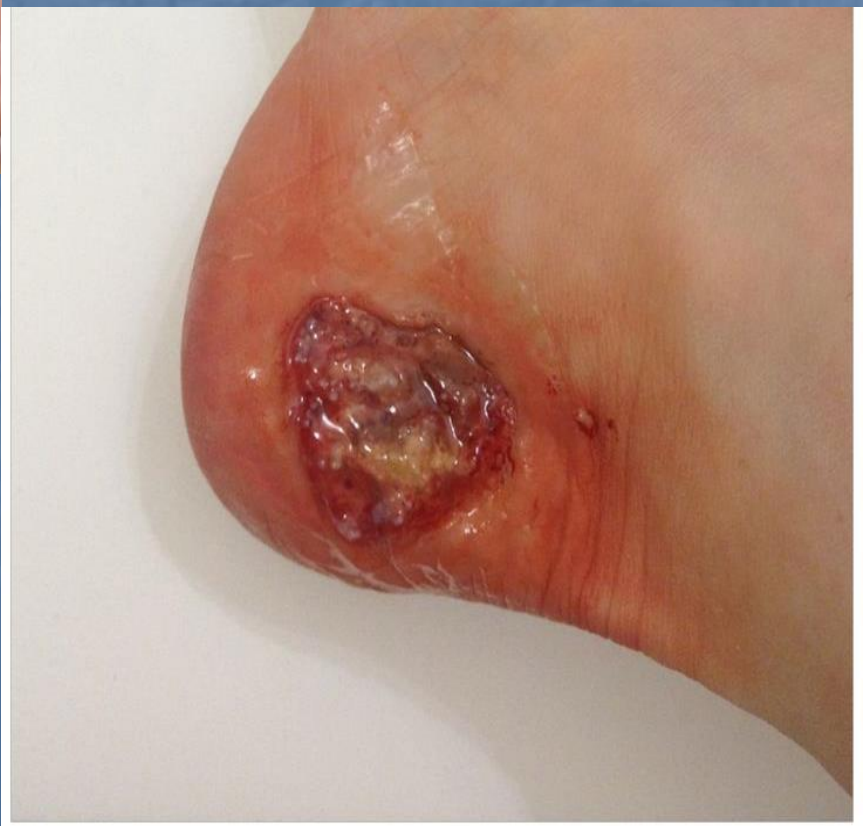
Caseous necrosis in the lungs.

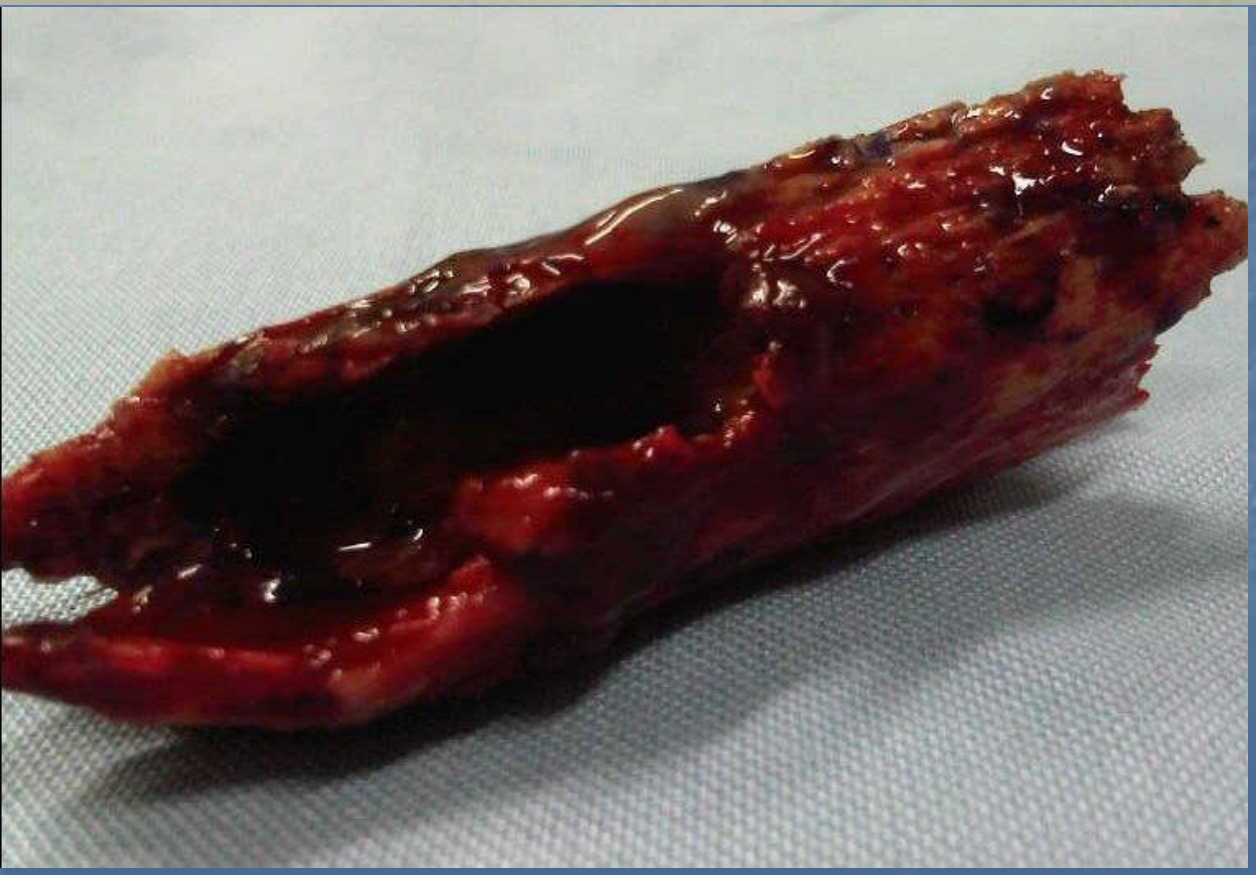


Wet gangrene of the foot.

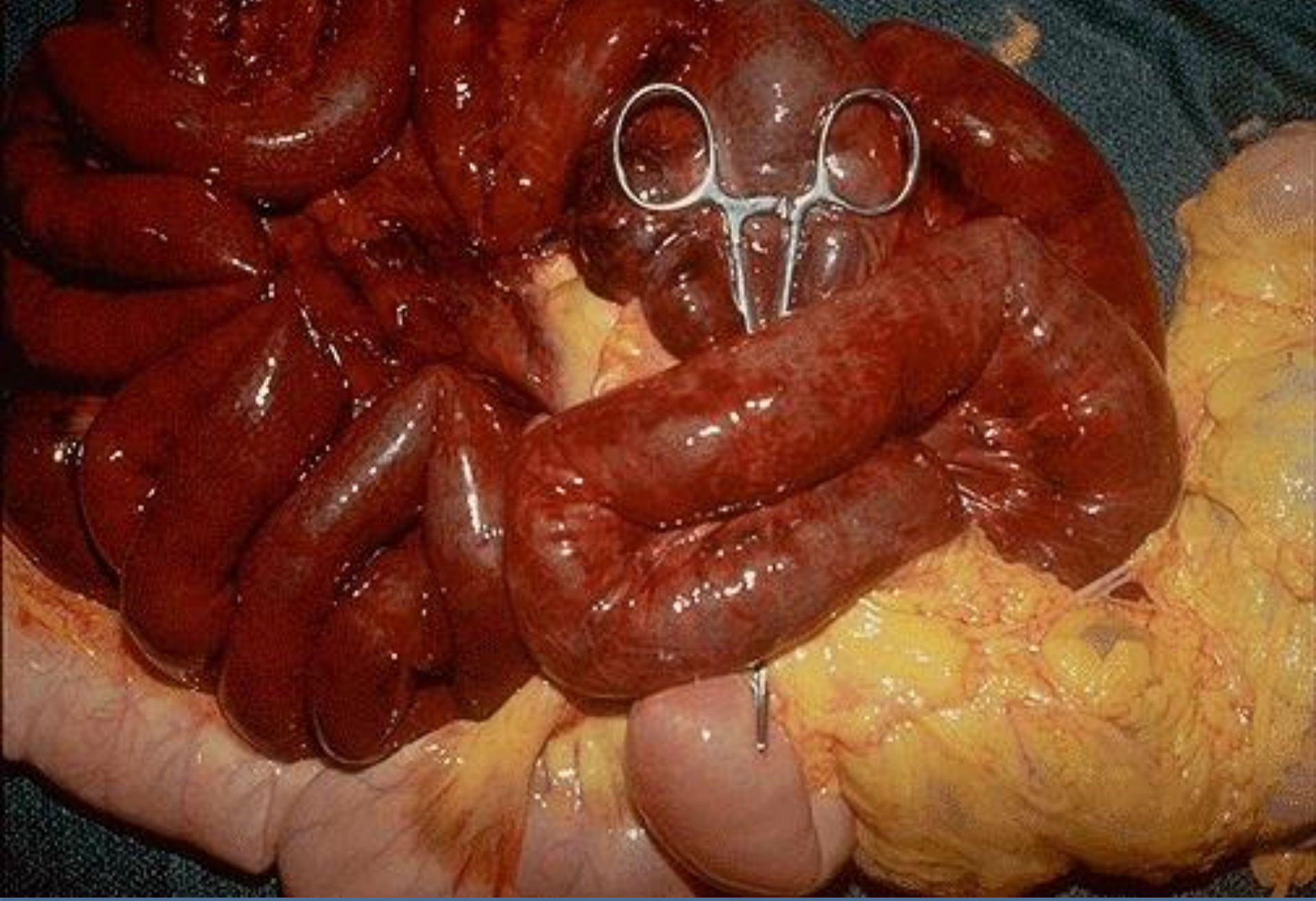


Decubitus ulcers

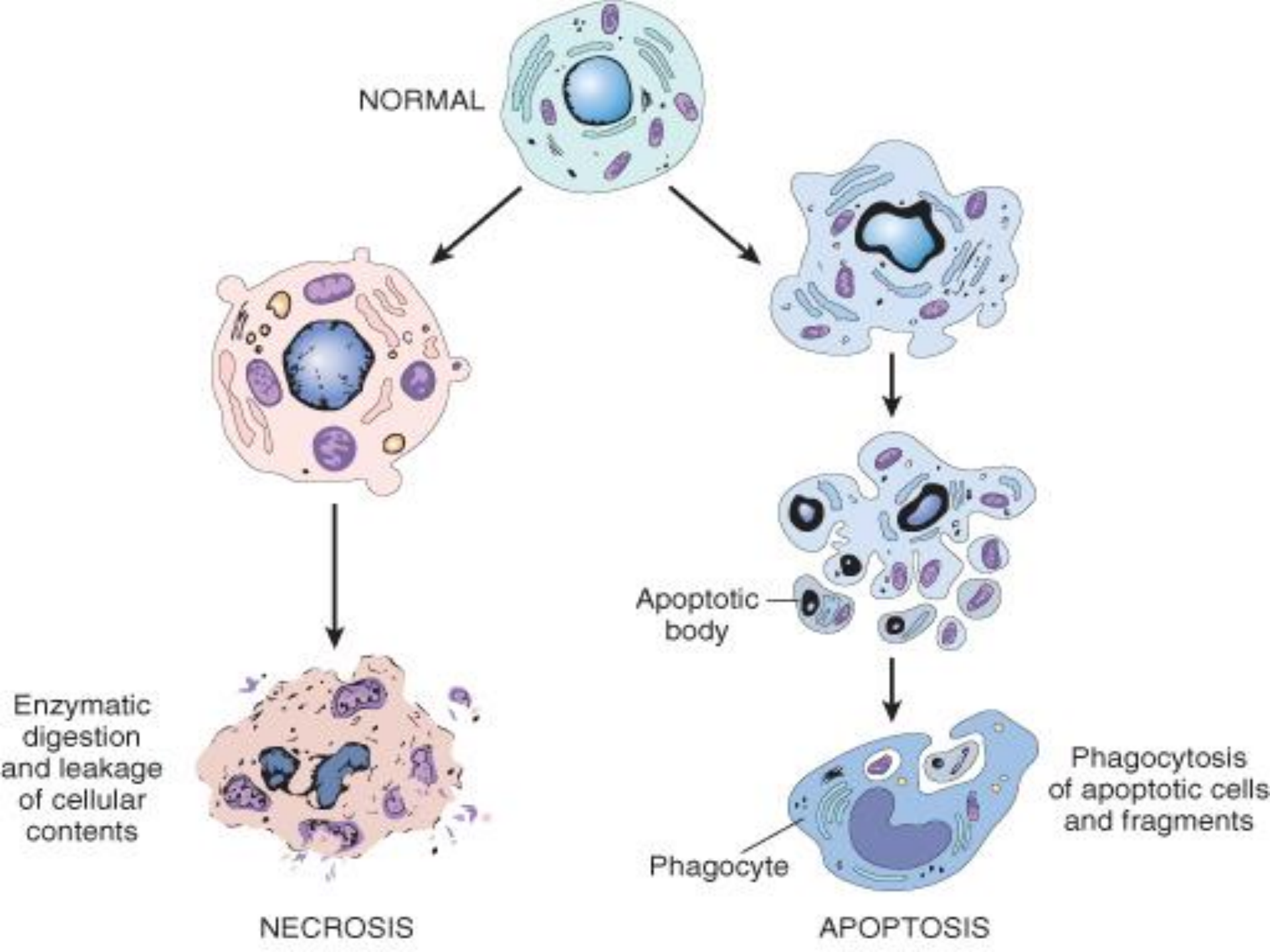




Bone sequester



Gangrene of the small intestine.


NORMAL
Enzymatic digestion and leakage of cellular contents
Apoptotic body
Phagocytosis of apoptotic cells and fragments
Phagocyte
NECROSIS
APOPTOSIS

Medicine, to produce **HEALTH**

must study **disease**

And music, to produce **HARMONY**

must study **discord**

by Plutarch

CELL INJURY

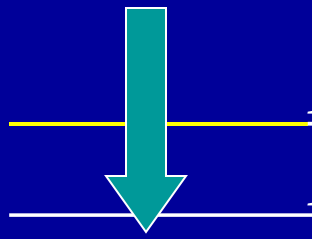
Homeostasis

Cells maintain normal structure and function in response to physiologic demands.

- **Under normal conditions, the cells are in:**
- ***homeostastatic „steady" state.*** **Normal cell is confined to relatively narrow range of functions and structure by its genetic programme to handle normal physiologic demands.**
- **Cells react to *adverse influence* by**
- **1- adapting**
- **2- sustaining reversible injury**
- **3- suffering irreversible cellular injury- cell death**

Structures of living systems are not constant. They are restructured and restored continuously. All living organisms absorb and extract proteins, lipids (fats), carbohydrates, and their components as well as water, ions, and pigments

Cells *Homeostasis*

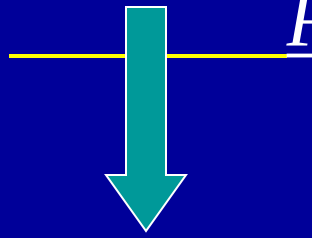


Physiologic stress

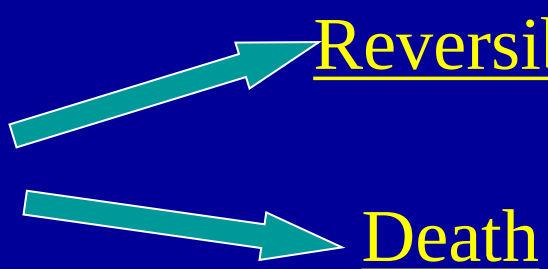
Pathologic stimuli

Adaptation

Failure to adapt



Cell Injury



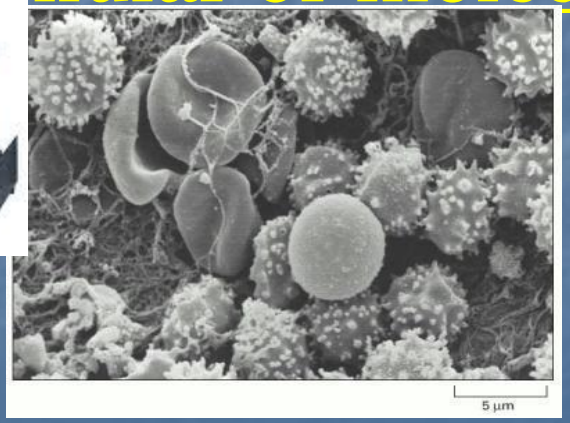
Reversible

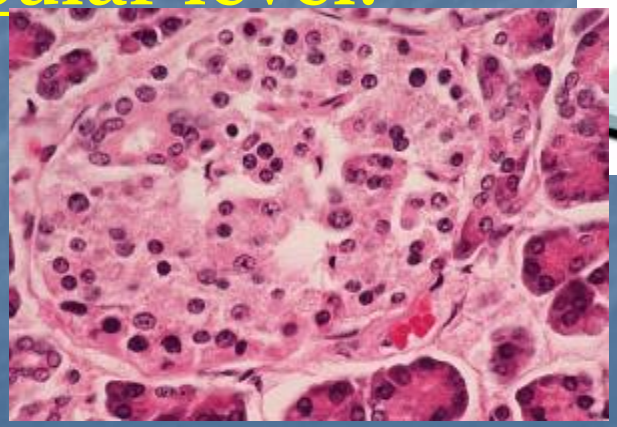
Death

cell injury initiation

"All organ injuries start with structural or molecular alterations in cells" concept began by Rudolf Virchow in 1800's

study of disease attempts to
nd how cells react to injury, of
llular or molecular level.





CELLULAR INJURY ETIOLOGY

The basis of all diseases is INJURY to the smallest living unit of the body, namely the cell. Cell encounters many stresses as a result of changes in their internal and external environments. However, the normal cell is in steady state able to handle physiologic demand according to its adaptive capacity.

Causes of cell injury:

1. Hypoxia (deficiency of oxygen) due to: (1) Ischemia (2) decrease of oxygen carrying capacity of blood due to anemia, cardiac or respiratory failure and CO poisoning.
2. Physical agent: burns, deep cold, radiation, mechanical trauma and electric shock.
3. Biological agents e.g. viruses, bacterial toxins, fungi and parasites.
4. Chemical agents and drugs e.g. alkalis, acids, insecticides, alcohol and narcotic drugs & air pollutants et..
5. Endogenous toxins as in case of uremia, jaundice and diabetic ketosis.
6. Immunologic reactions (hypersensitivity).
7. Nutritional imbalance such as protein calorie malnutrition, starvation, obesity, diabetes mellitus and deficiency of other substances and vitamins.
8. Genetic abnormalities as in Down syndrome & sickle cell anemia.

Cellular injury depends on cell:

- **1. type (myocardial cells dies in 20- 30 min, but epidermis cells dies in weeks, after cause (etiologic agents) acted**
- **2. genetic makeup**
- **3. adaptability (hepatic cells are more adaptive cells, then neurons)**
- **4. status (normal or hypertrophic)**

Cellular injury depends on injury:

- **1. type (ischemia or infective agent)**
- **2. its duration**
- **3. its severity**

GENERAL MECHANISMS OF CELL INJURY.

- Four intracellular systems are particularly vulnerable to cell injury:
- 1. maintenance of the integrity of *cell membrane* (upon which the osmotic homeostasis of the cell is dependent)
- 2. aerobic respiration involving oxidative phosphorylation and production of ATP (*mitochondria*)
- 3. synthesis of functional and structural proteins (*Golgi)*
- 4. preservation of the genetic apparatus of the cell (*nucleus)*

Cell Injury

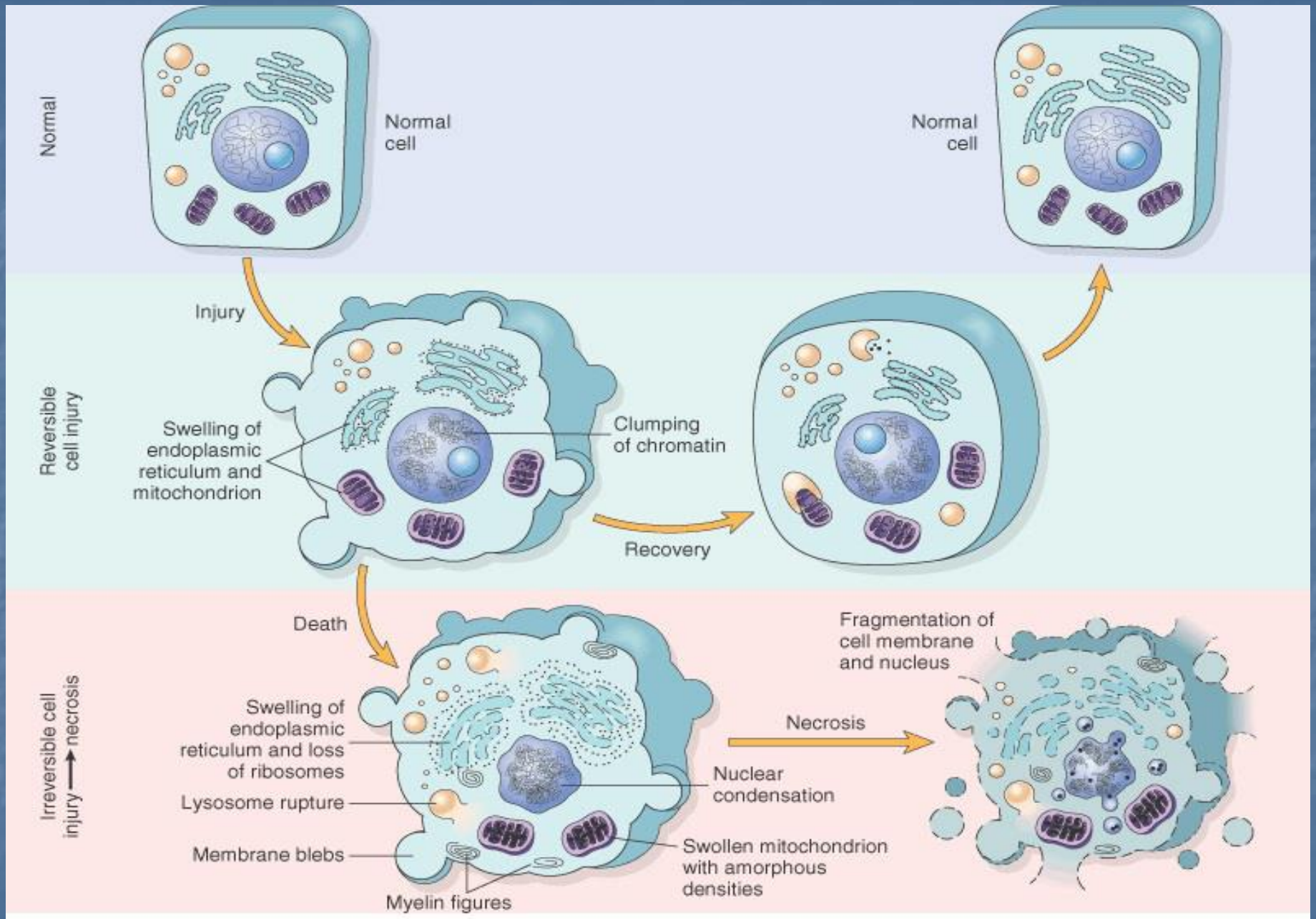
- if limits of the adaptive response are exceeded or if adaptation is not possible, a sequence of events called cell injury occurs.

a) Reversible Cell Injury

- removal of stress results in complete restoration of structural and functional integrity.

b) Irreversible Cell Injury / Cell Death

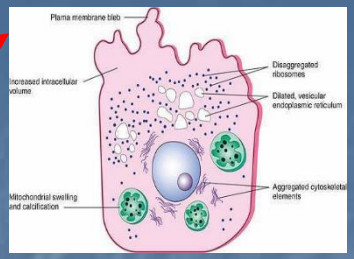
- if stimulus persists or is severe enough from the start, the cell suffers irreversible cell injury and death.

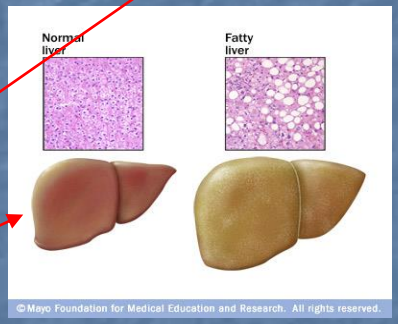


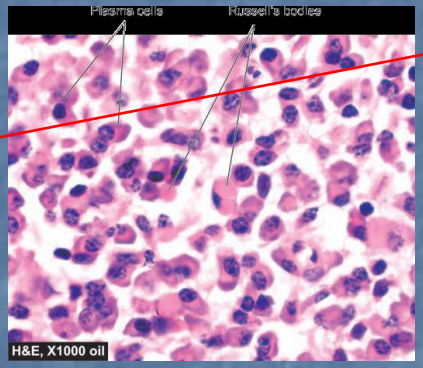
(From Kumar V, Abbas A, Fausto N: Robbins & Cotran pathologic basis of disease, *ed 7, Philadelphia, 2005, Saunders.)*

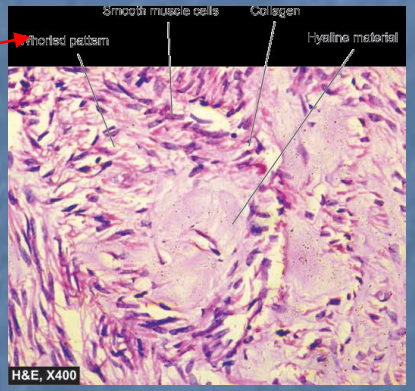
Reversible cell injury

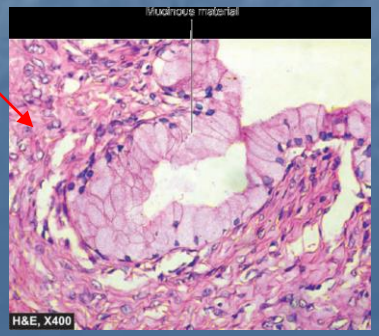
- Following morphologic forms of reversible cell injury are
- included under this heading:
- 1. Hydropic change (cloudy swelling, or vacuolar
- degeneration)
- 2. Fatty change
- 3. Hyaline change
- 4. Mucoid change











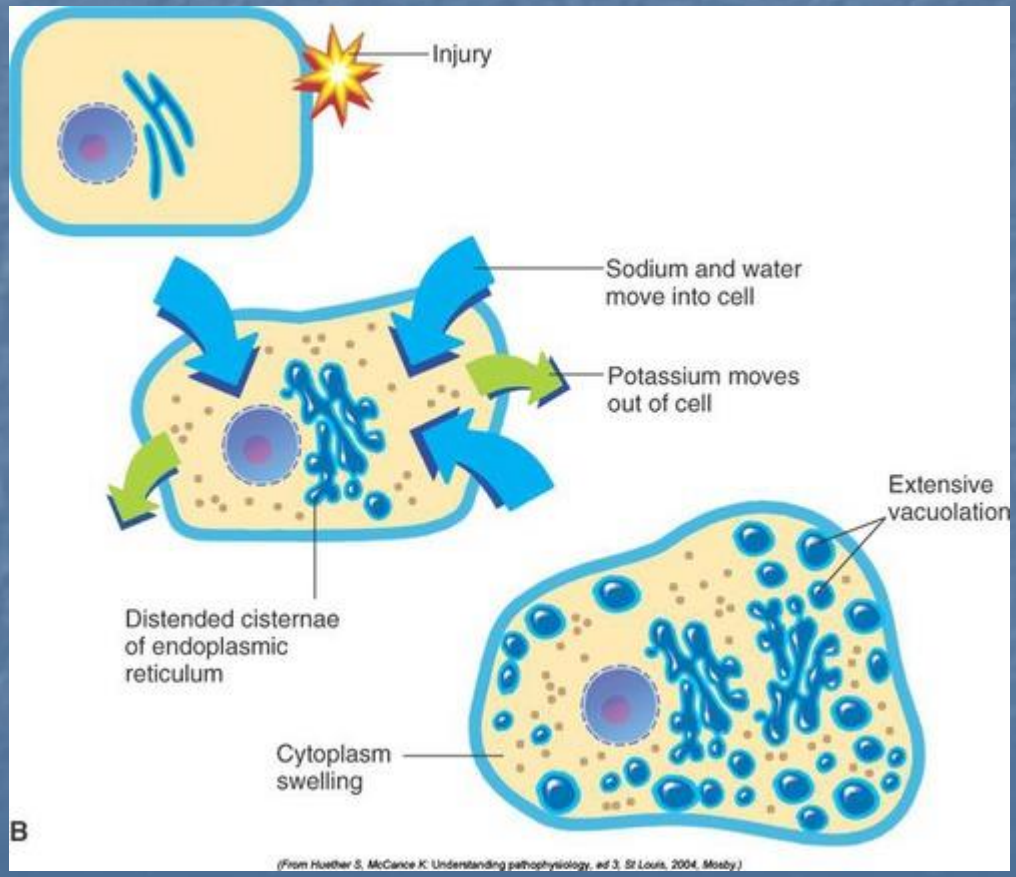
Hydropic swelling

Hydropic swelling is an acute stress cell injury caused by a variety of agents leading to swelling in the cells.

<u>Pathogenesis</u>:

Hydropic swelling results from impairment of the *process controlling ionic sodium* concentration in the cytoplasm. This regulation is controlled by:

1) **Plasma membrane itself,**
2) **Plasma membrane sodium pump,**
3) **The supply of ATP.**



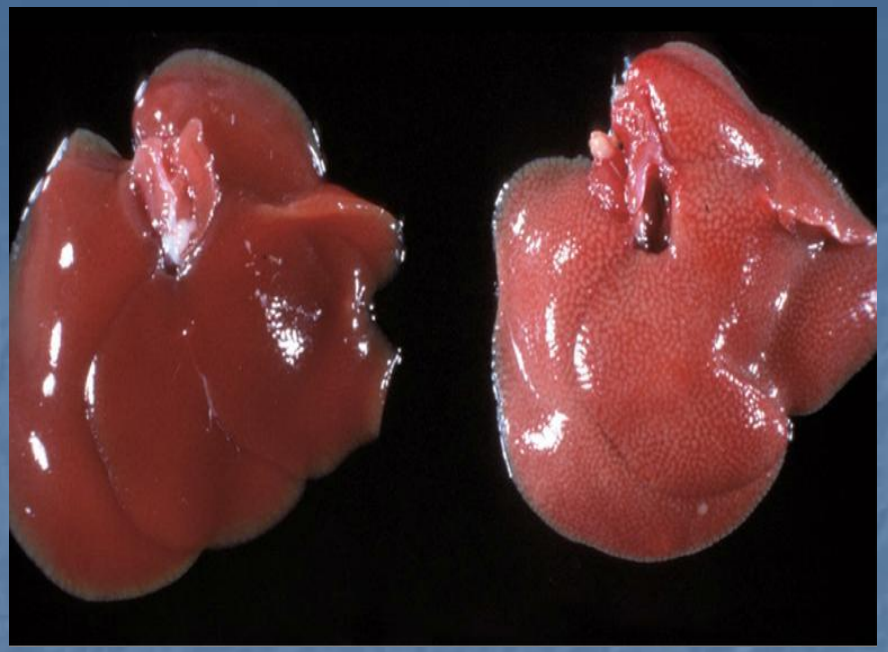
Structural changes:

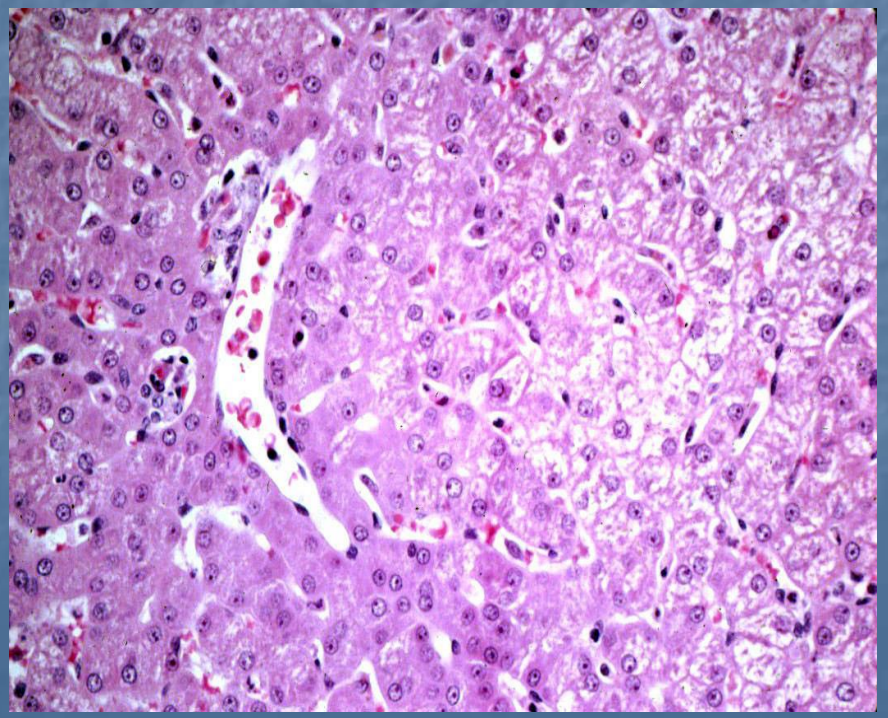
Grossly, the affected organ increases in size becomes pale, bloodless, having sharp edge which bulge over the capsule on cut section of that organ.

Microscopically, the cell becomes large with pale cytoplasm and normally located nucleus.

Examples of hydropic swelling:

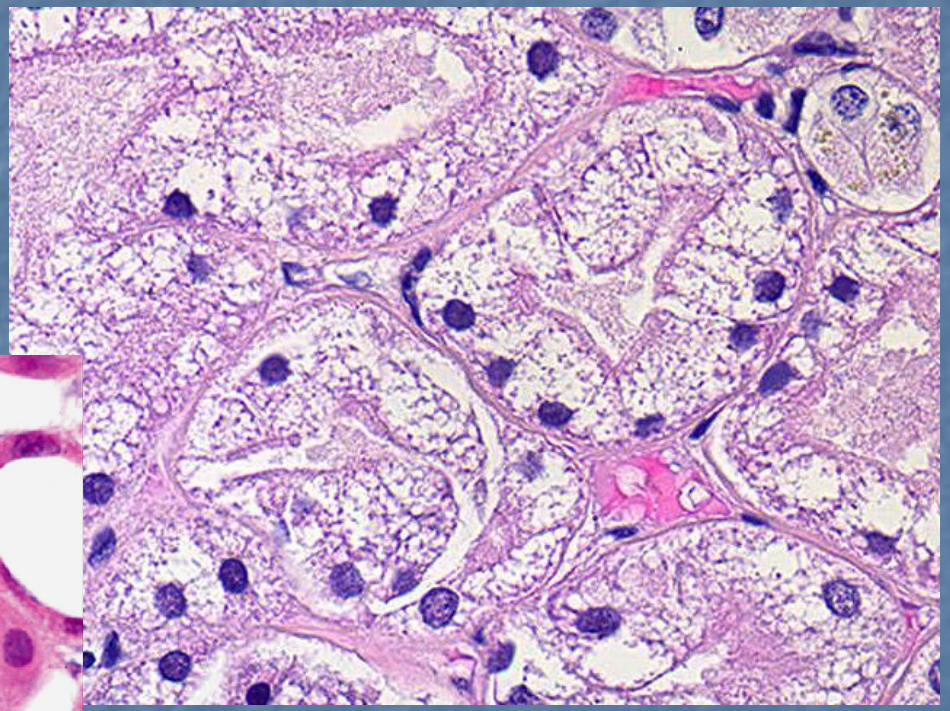
Ballooning of hepatocytes in cases of acute *viral hepatitis*, epidermal cells in burns, *Mickulicz cell*(Histiocytes) in Rhinoscleroma

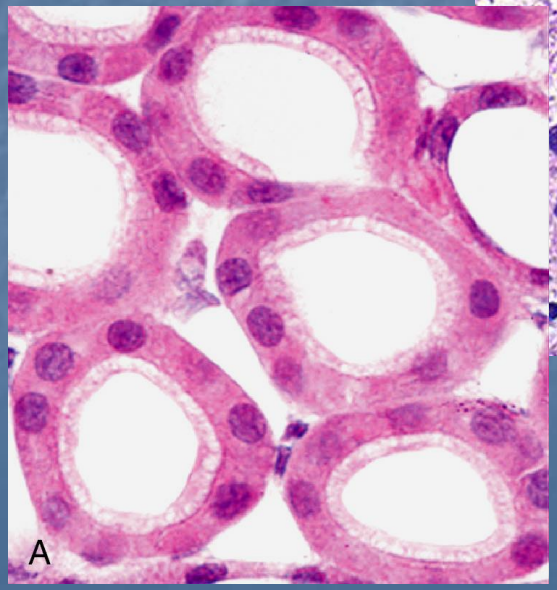




Cellular swelling or hydropic dystrophy

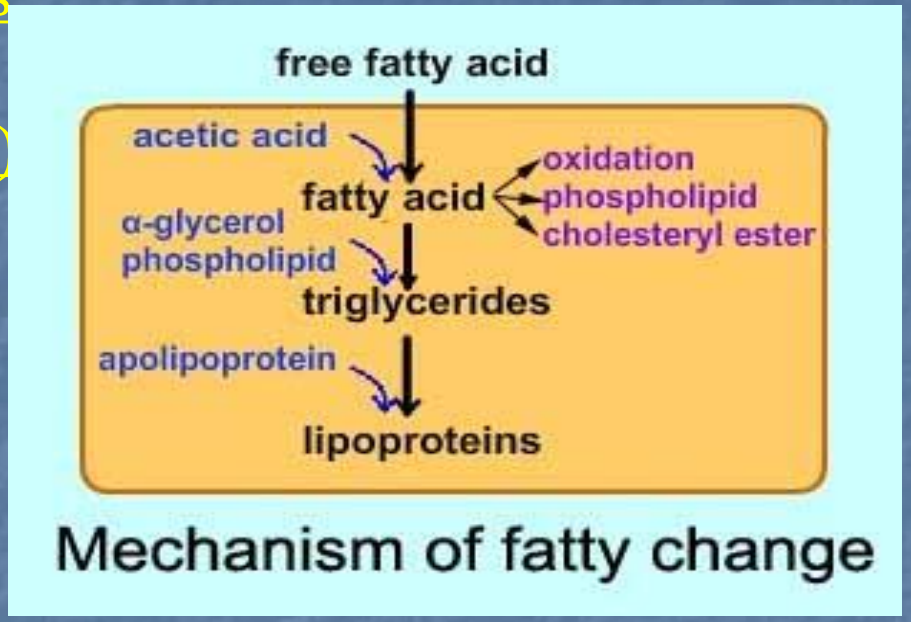
The tubular vacuolization and tubular dilation here is a result of the toxic effect of ethyleneglycol poisoning





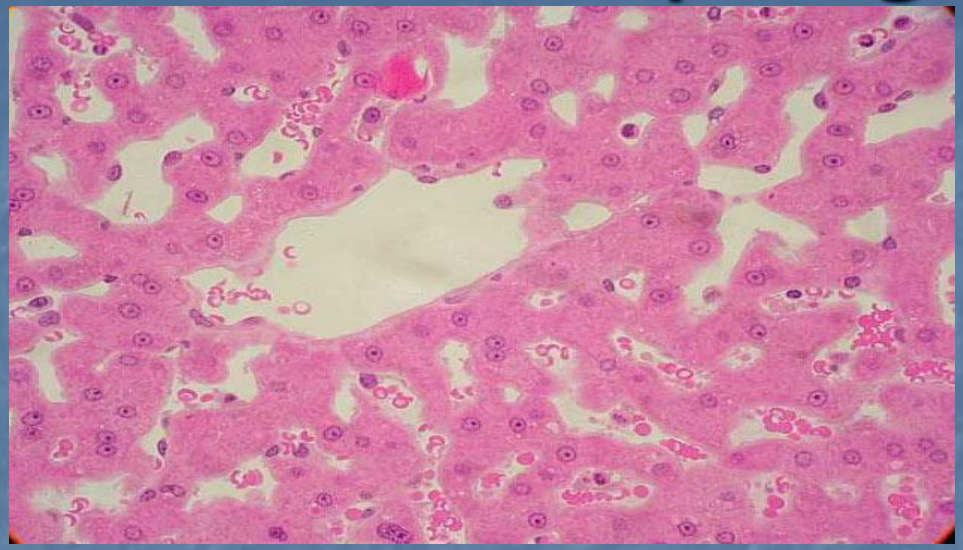
FATTY CHANGE

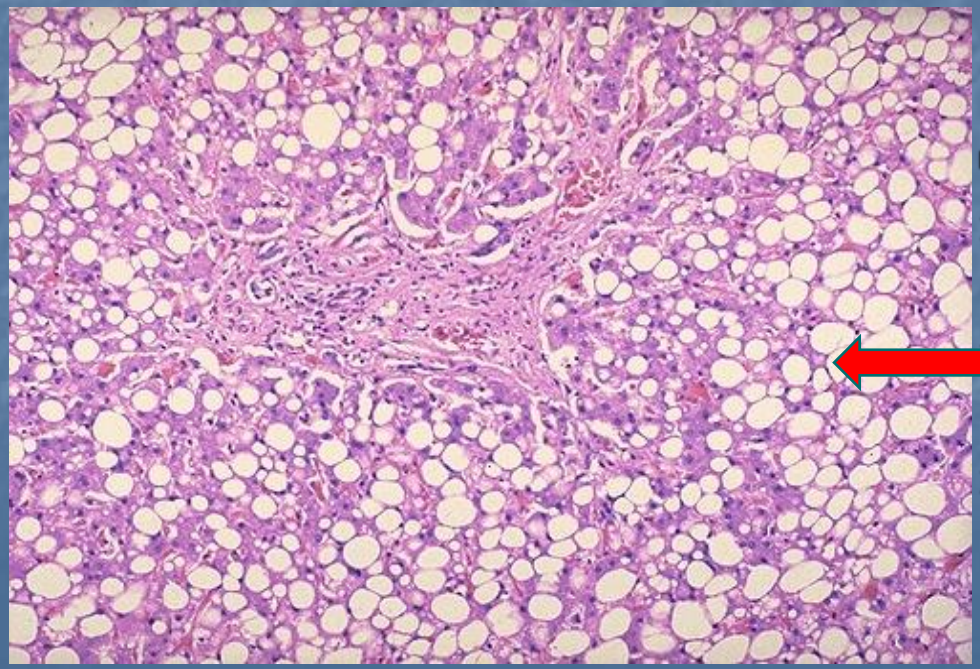
- Excessive entry of free fatty acids into the liver (starvation, corticosteroid therapy)
- Enhanced fatty acid synthesis.
- Decreased fatty acid oxidation.
- Increased esterification of fatty acid to triglycerides (alcohol).
- Decreased apoprotein synthesis (CCl_4).
- Impaired lipoprotein secretion from the liver (alcohol).



Mechanism of fatty change

Fatty Degeneration





- Fatty degeneration or fatty metamorphosis, steatosis is the abnormal appearance of fat within parenchymal cells.
- It results from hepatotoxic agents such as $C_2 H_5OH$, chloroform, CCl_4, during sever infections, in prolonged anemia and in toxemia of pregnancy.
- Fatty liver is due to:
  - inability of the liver to synthesize phospholipids
  - decreased lipoprotein release from hepatocytes
  - Increased triglyceride production

Hyaline Change

INTRACELLULAR HYALINE. Intracellular hyaline is mainly seen in epithelial cells. A few examples are as follows:

1. *Hyaline droplets* in the proximal tubular epithelial cells in cases of excessive reabsorption of plasma proteins.
2. *Hyaline degeneration* of rectus abdominalis muscle called Zenker's degeneration, occurring in typhoid fever. The muscle loses its fibrillar staining and becomes glassy and hyaline.
3. *Mallory's hyaline* represents aggregates of intermediate filaments in the hepatocytes in alcoholic liver cell injury.
4. Nuclear or cytoplasmic *hyaline inclusions* seen in some viral infections.
5. *Russell's bodies* representing excessive immunoglobulins in the rough endoplasmic reticulum of the plasma cells

EXTRACELLULAR HYALINE. Extracellular hyaline is seen in connective tissues. A few examples of extracellular hyaline change are as under:

1. Hyaline degeneration in *leiomyomas* of the uterus
2. Hyalinised *old scar* of fibrocollagenous tissues.
3. *Hyaline arteriolosclerosis* in renal vessels in hypertension and diabetes mellitus.
4. Hyalinised glomeruli in *chronic glomerulonephritis*.
5. *Corpora amylacea* are rounded masses of concentric hyaline laminae seen in the prostate in the elderly, in the brain and in the spinal cord in old age, and in old infarcts of the lung.

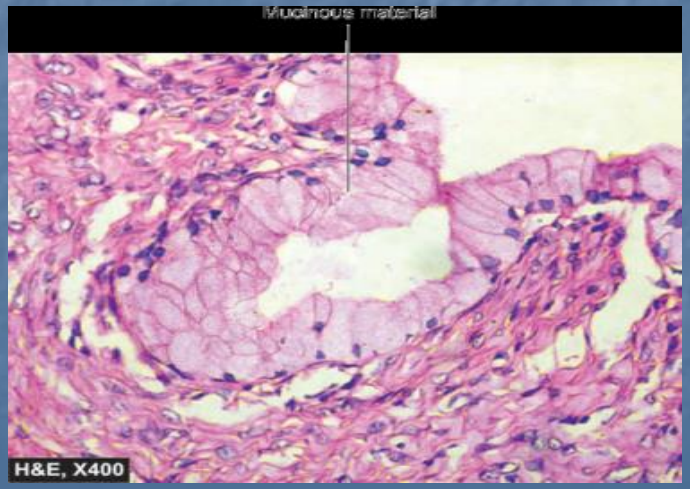
Mucoid Change

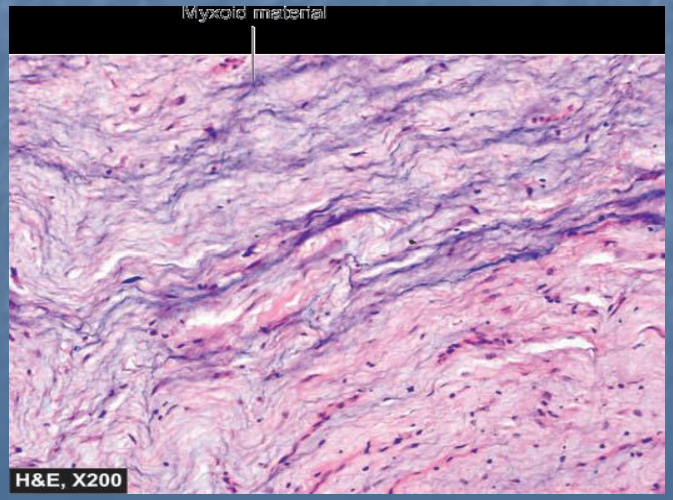
EPITHELIAL MUCIN.

1. Catarrhal inflammation of mucous membrane (e.g. of respiratory tract, alimentary tract, uterus).
2. Obstruction of duct leading to mucocele in the oral cavity and gallbladder.
3. Cystic fibrosis of the pancreas.
4. Mucin-secreting tumours (e.g. of ovary, stomach, largebowel etc)

CONNECTIVE TISSUE MUCIN.

1. Mucoid or myxoid degeneration in some tumours e.g.myxomas, neurofibromas, fibroadenoma, soft tissue sarcomas etc
2. Dissecting aneurysm of the aorta due to Erdheim's medial degeneration and Marfan's syndrome.
3. Myxomatous change in the dermis in myxoedema.
4. Myxoid change in the synovium in ganglion on the wrist.

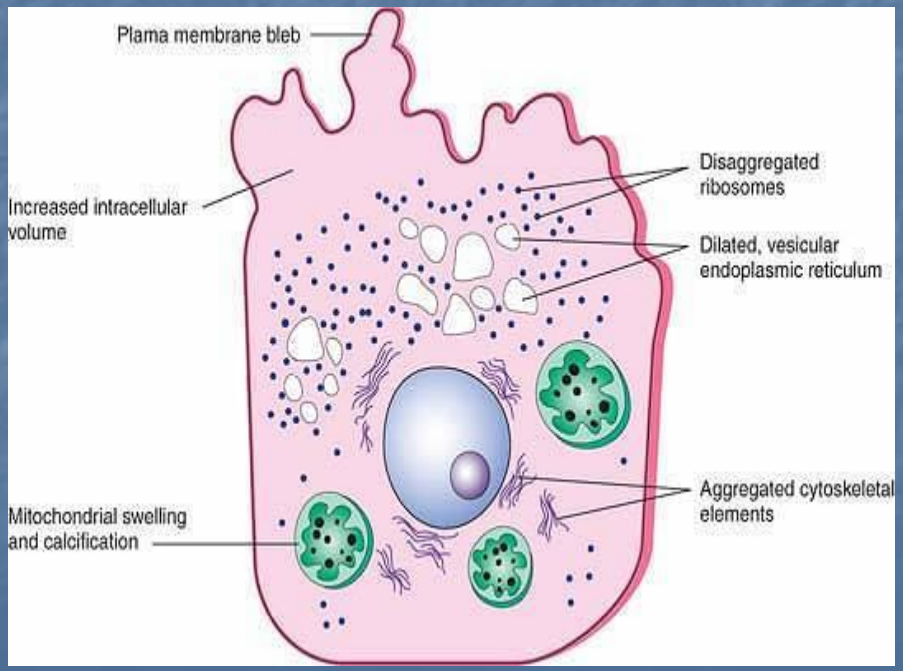


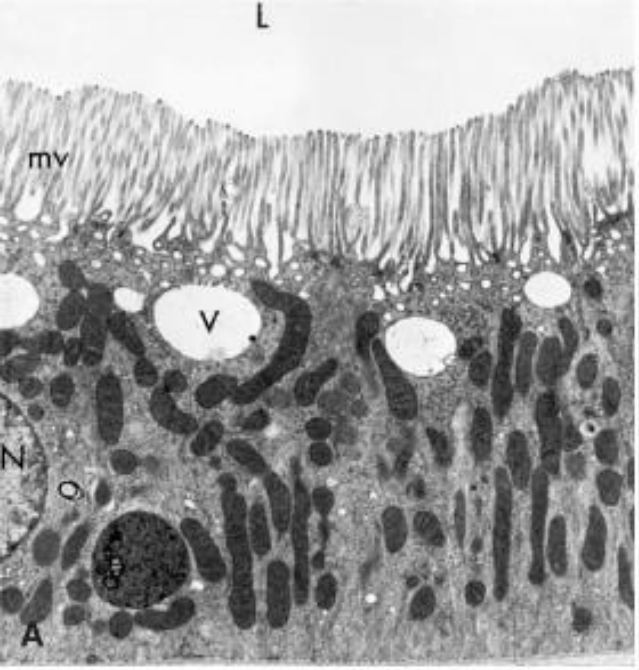


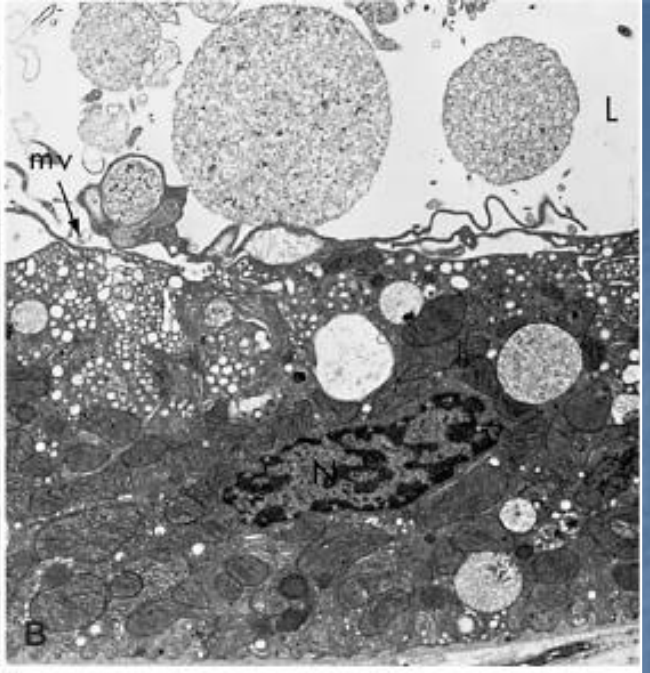
REVERSIBLE Cellular injury at the subcellular level

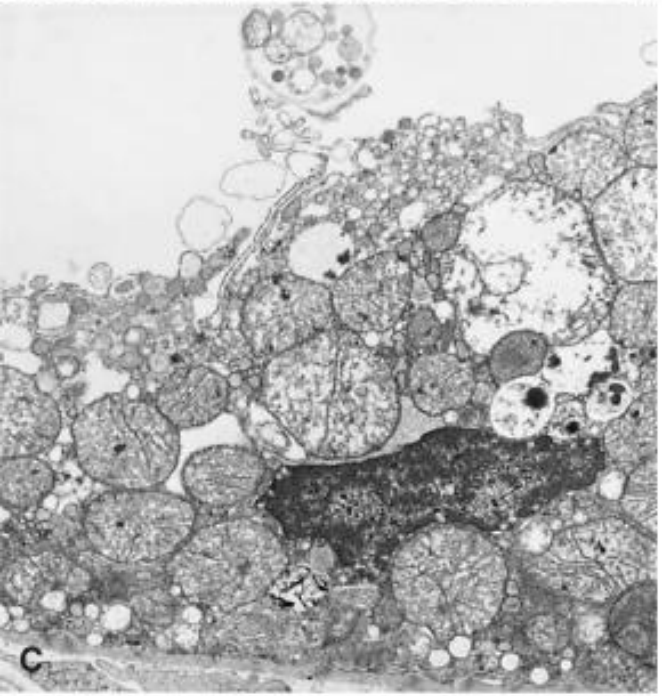
INTRACELLULAR RESPONSE INCLUDS

- Aggregation of intramembranous particles
- Endoplasmic reticulum swelling
- Dispersion of ribosomes
- Cell swelling
- Clumping of nuclear chromatin
- Mitochondrial swelling
- Small densities within mitocondria









Cell Membrane Injury

A. Normal cell membrane

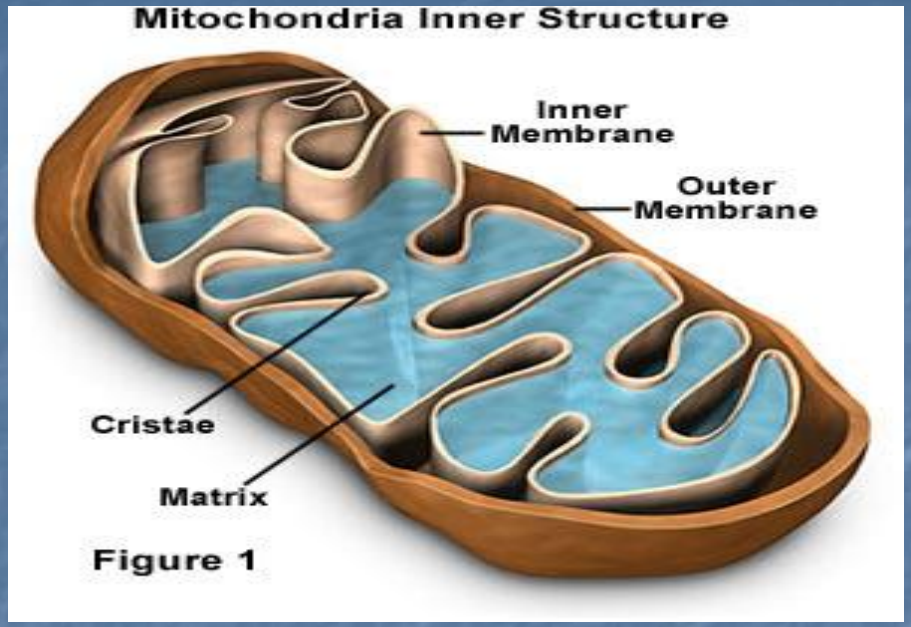
B. Reversible membrane injury

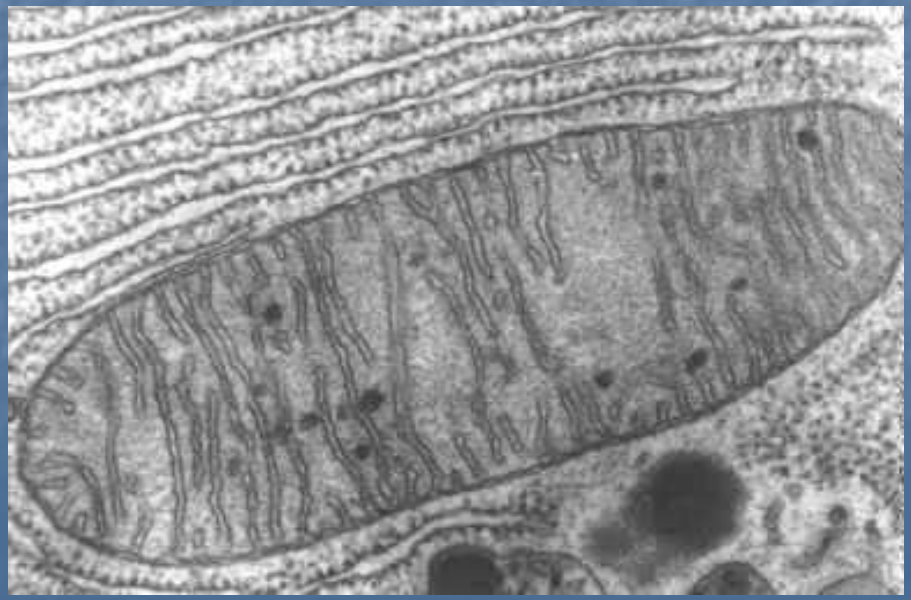
C. Necrosis

Injured membranes are leaky

Enzymes and other proteins that escape through the leaky membranes make their way to the bloodstream, where they can be measured in the serum

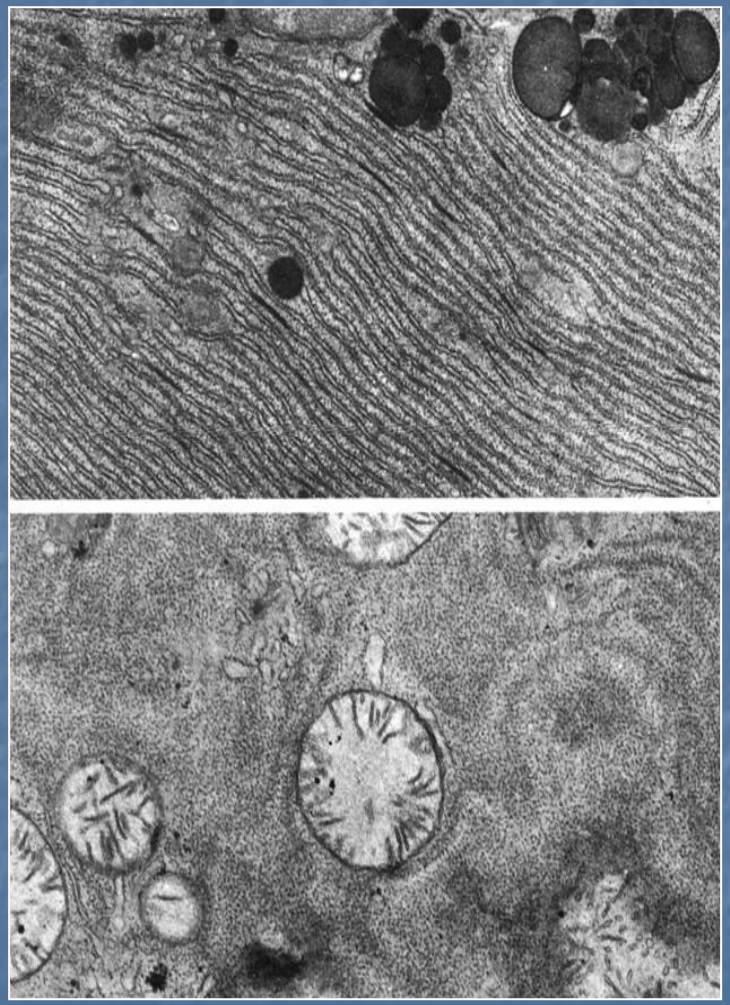
Mitochondrial Changes



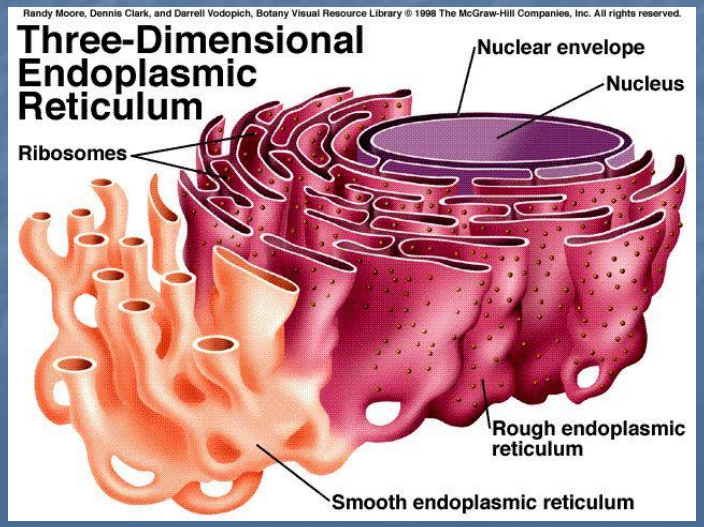


- Early, appears condensed as a result of loss of matrix protein following loss of ATP
- Followed by swelling due to ionic shifts
- Amorphous densities which correlate with the onset of irreversibility
- Finally, rupture of membrane followed by progressing increased calcification

Endoplasmic reticulum changes



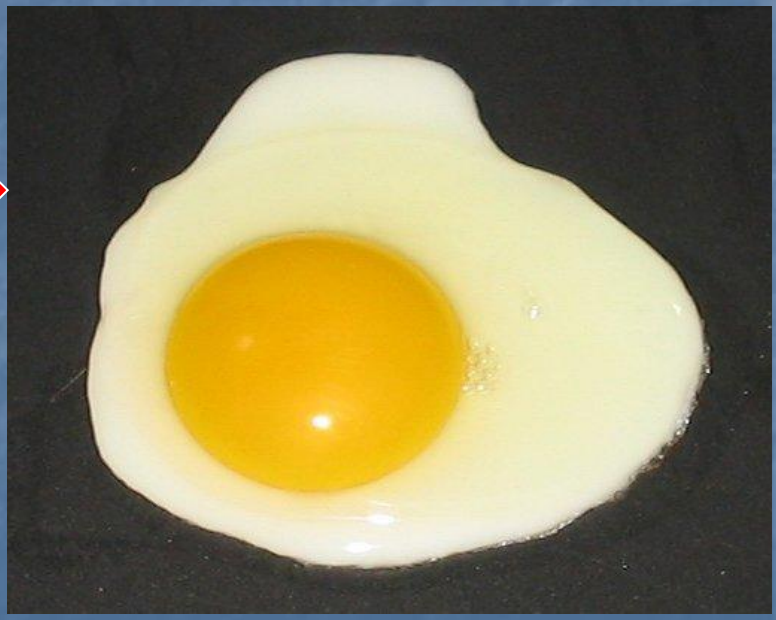
- Dilatation
- Detachment of ribosomes and disaggregation of polysomes with decreased protein synthesis
- Progressive fragmentation and formation of intracellular aggregates of myelin figures



Consequences of Injury

1. **No long term effects- - the cell damage is repaired, the effects of the injury are reversible.**
2. **The cell "adapts" to the damaging stimulus.**
3. **The cell dies, undergoing necrosis. The damage is irreversible.**

IRREVERSIBLE CELL INJURY



the morphologic appearance is due to 2 concurrent processes:

1. denaturation of proteins
2. enzymatic digestion

IRREVERSIBLE CELL INJURY

NECROSIS

Definition:

NECROSIS is local death of cells while the individual is **a life** followed by morphological changes in the surrounding living tissue, (cell placed immediately in fixative are dead but not necrotic).

Causes of cell necrosis: See before, but the most common causes of cell death are ***viruses, ischemia, bacterial toxins, hypersensitivity, and ionizing radiation.***

Morphologic change in necrosis:

The changes don't appear in the affected cells by light microscopy before 2-6 hours according to the type of the affected tissue.

AUTOLYSIS

- Enzymatic digestion by lysosomal enzymes of the dead cells themselves.

HETEROLYSIS

- Digestion by lysosomal enzymes of immigrant leukocytes.

DEAD CELL MORPHOLOGY:

- *cytoplasm*- increased eosinophilia-attributable in part to the loss of normal cytoplasmic basophilia caused by the RNA and in part by increased binding of eosin to denatured intracytoplasmic proteins
- more glassy appearance of the cell cytoplasm-due mainly to the loss of glycogen particles
- *nucleus*- nuclear changes can be *reversible* -clumping of the chromatin with large aggregates attached to the nuclear membrane *or irreversible-*

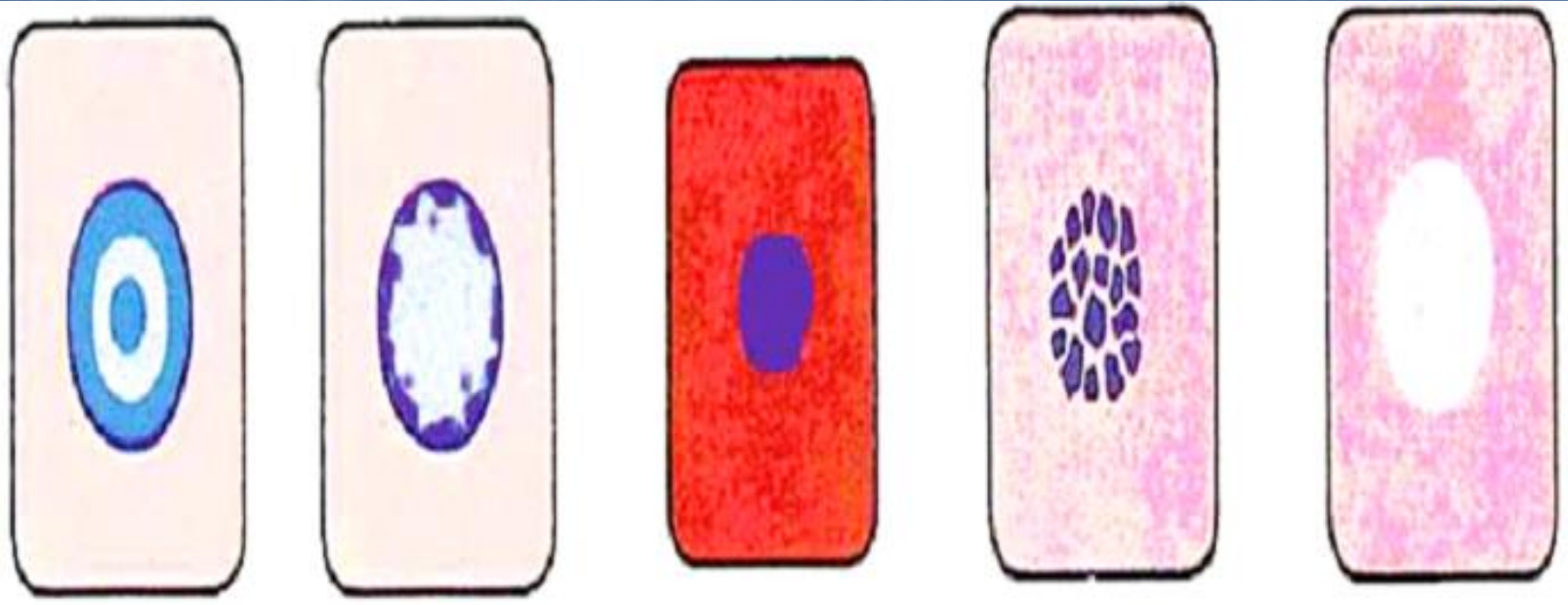
1.- pyknosis = nucleus progressively shrinks and becomes dense mass of tightly packed chromatin

2.- karyorrhexis = nucleus may break up to many clump

3.- karyolysis = progressive dissolution of nuclear chromatin due to action of DNAases of lysosomal origin

Basic Pathologic Change of Necrosis

1) Nucleus changes:



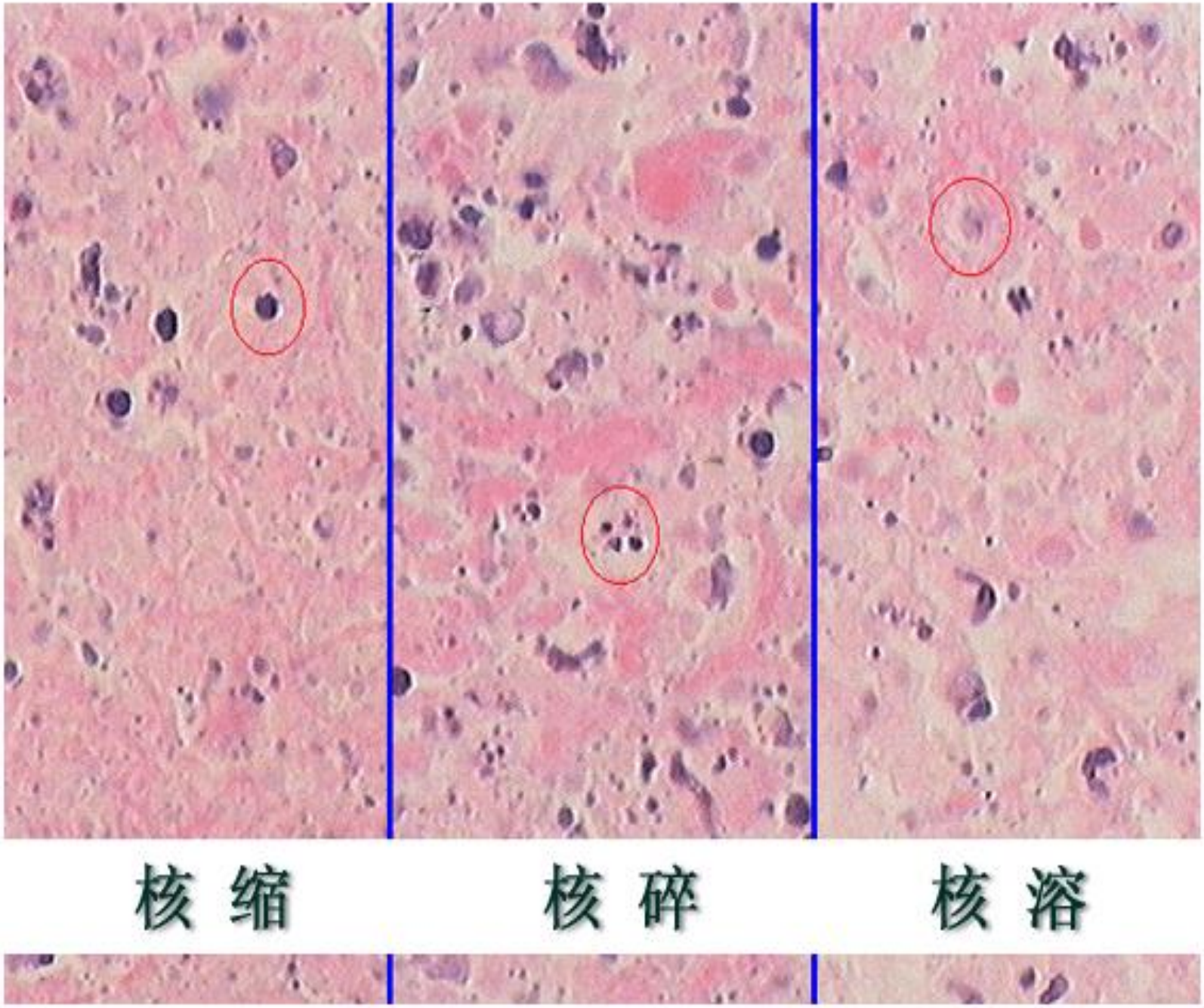
Normal cell

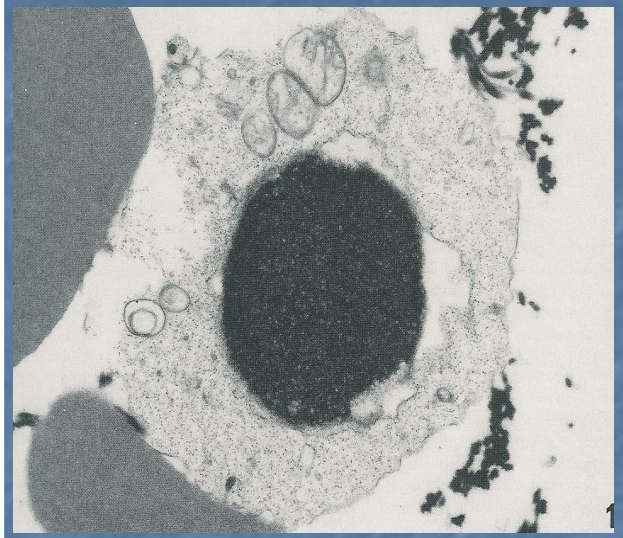
Chromatin margination

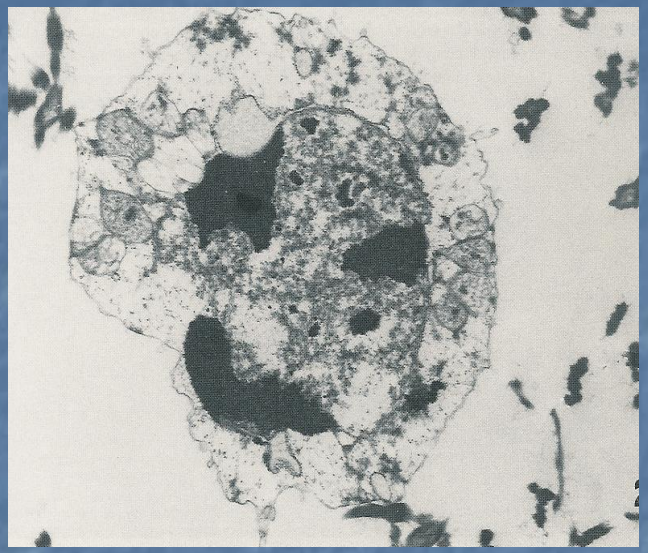
pyknoss

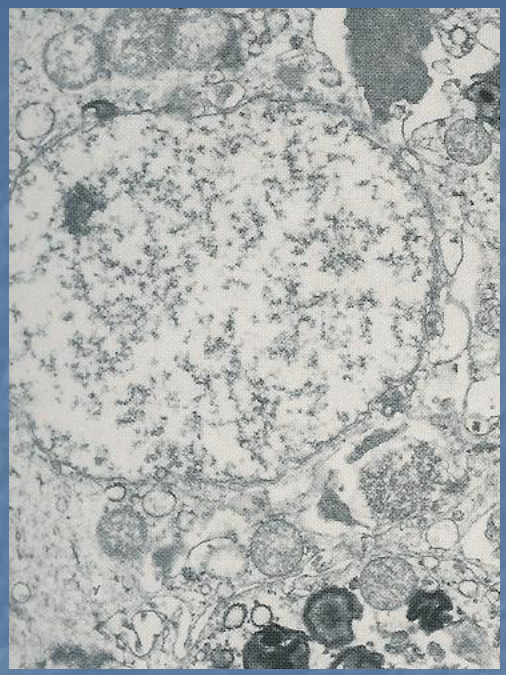
karyorrhexis

karyolysis


核缩
核碎
核溶







Pyknosis Karyorrhexis Karyolysis

Healthy cell

Necrosis morphological classification

- Coagulation Necrosis
- Liquefactive Necrosis
- Caseous Necrosis
- Fibrinoid necrosis
- Fat Necrosis
- Gangrenous Necrosis

Types of necrosis

The variable types of necrosis differ as regards *causes*, *gross* and *microscopic pictures*.

(1) Coagulative necrosis:

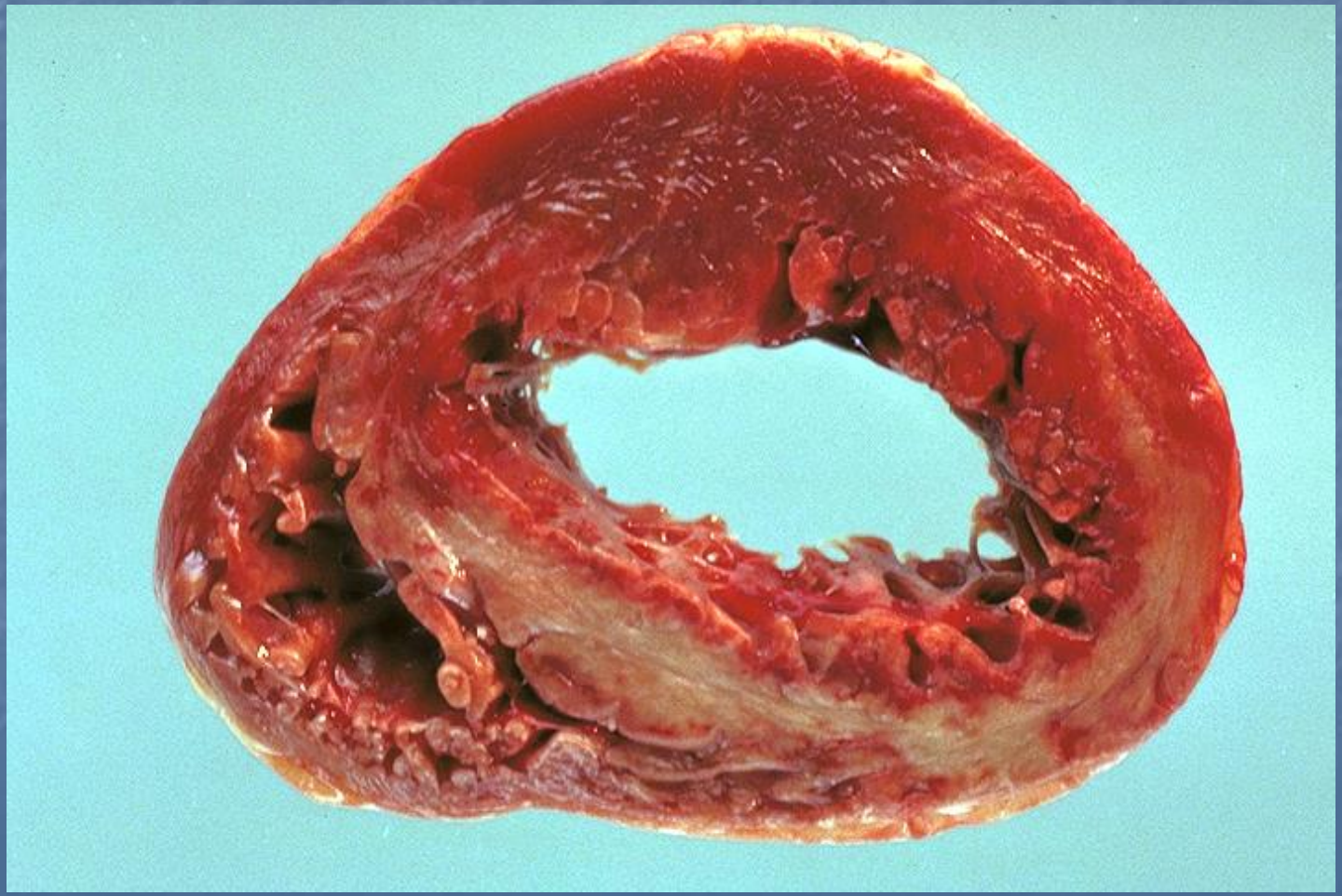
It is mainly caused by sudden ischemia e.g. **infarction** of **heart, kidney and spleen. The protein of the affected tissue becomes denaturated.**

***Grossly*, it appears dry pale opaque. It is triangular ? subcapsular with the base towards the capsule of the affected organ. This is due to the fan like distribution of the supplying blood vessels. The infarct area is surrounded by narrow zone of inflammation and congestion.**

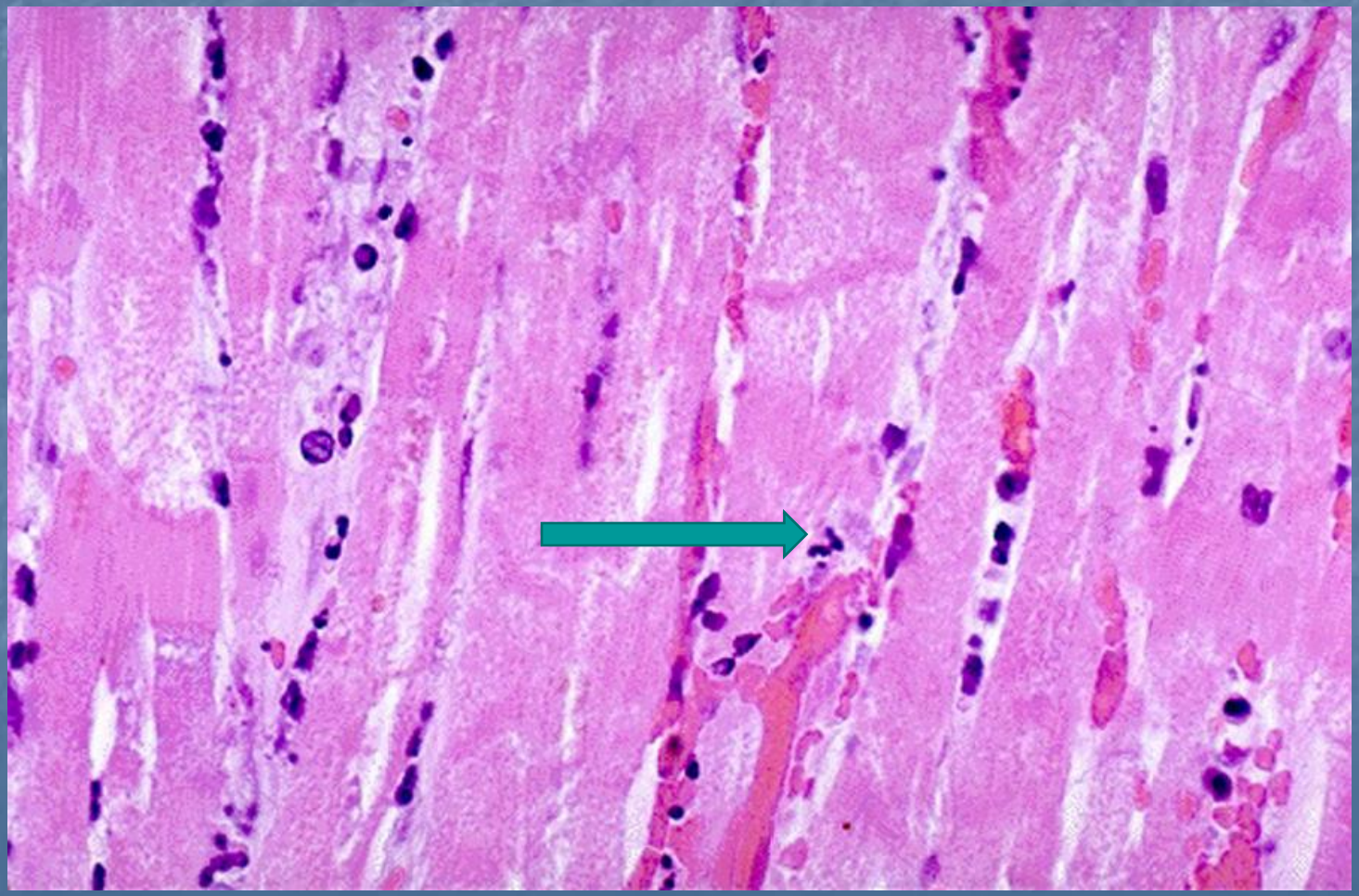
***Microscopically*, the structural outline of the affected tissue is preserved but the cellular details are lost.**

Large pale area of coagulation necrosis in the interventricular septum

ACUTE INFARCT



Acute coagulation necrosis of myocardium. Cell outlines are mostly visible but there is loss of most striations. Fading or absent cardiomyocyte nuclei. A few infiltrating neutrophils (arrow).

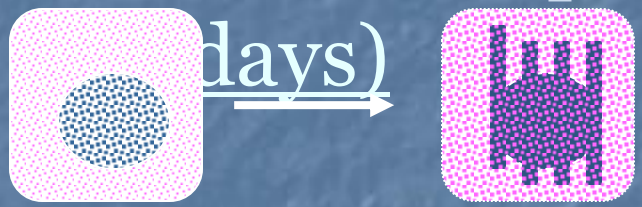


The features of coagulative necrosis

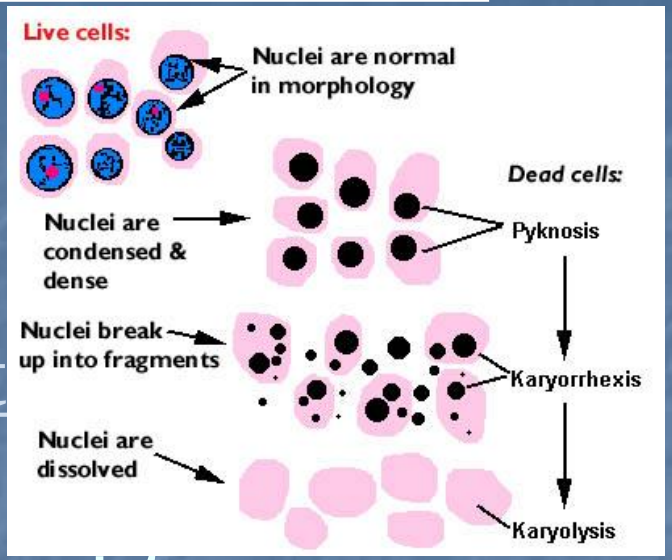
Karyolysis becomes complete

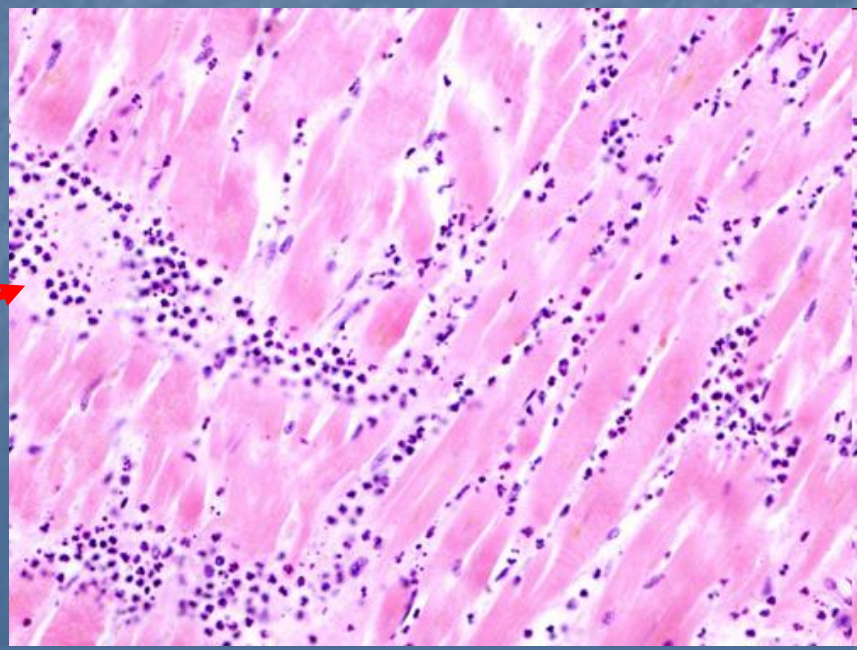
Loss of nucleic acids: pink cyt

Cell outline is preserved (at least for a
days)

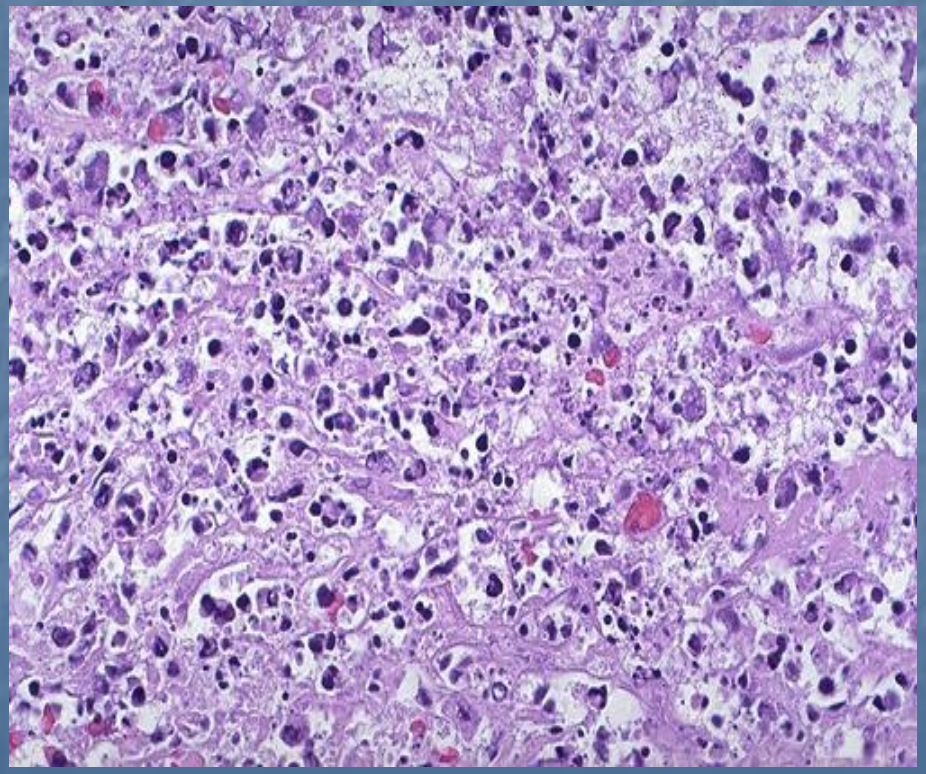


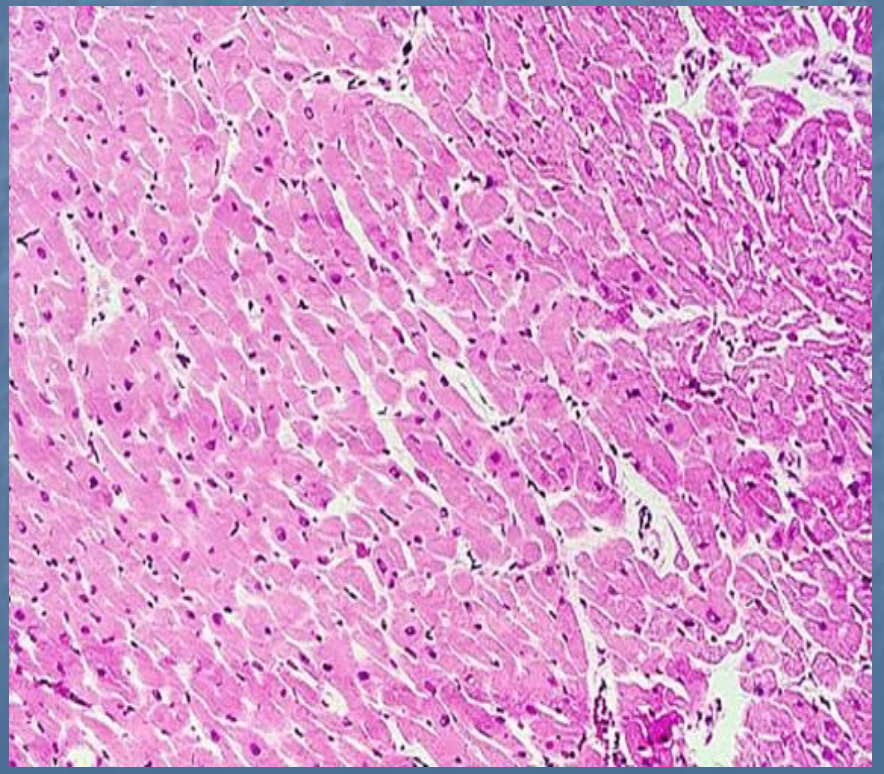
Neutrophils as part of the inflammatory response





When there is marked cellular injury, there is cell death. This microscopic appearance of myocardium is a mess because so many cells have died that the tissue is not recognizable. Many nuclei have become pyknotic (shrunken and dark) and have then undergone karorrhexis (fragmentation) and karyolysis (dissolution). The cytoplasm and cell borders are not recognizable.

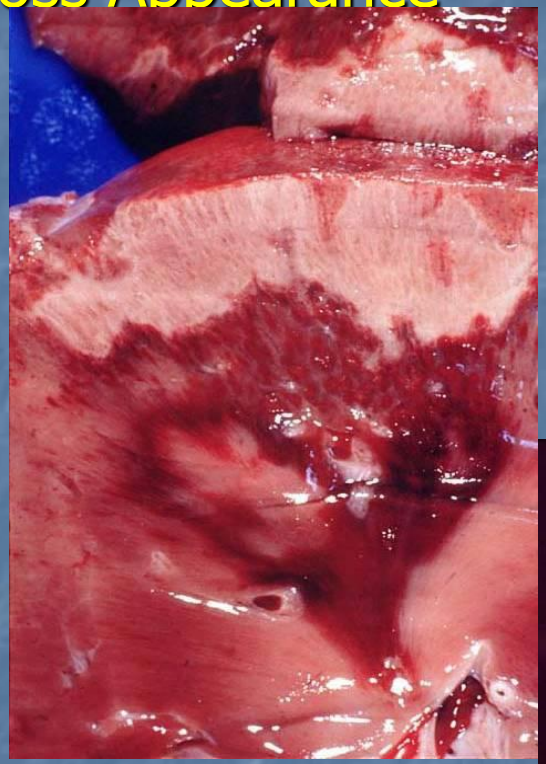


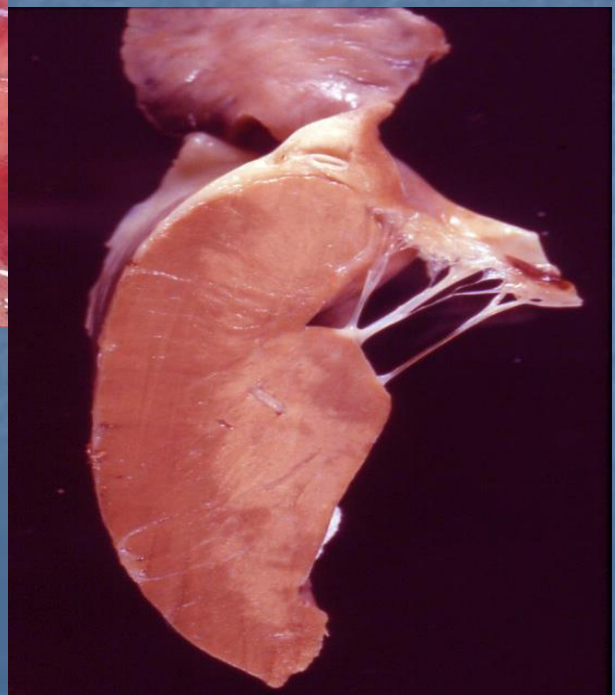


Coagulation Necrosis

Gross Appearance

- architecture resembles normal tissue, but colorant texture are different.
- lighter in color (pale) -due to coagulation of cytoplasmic proteins and decreased blood flow (eg infarcts).
- usually firm.
- tissue may be swollen or shrunken.
- may see a local vascular / inflammatory reaction to necrotic tissue.

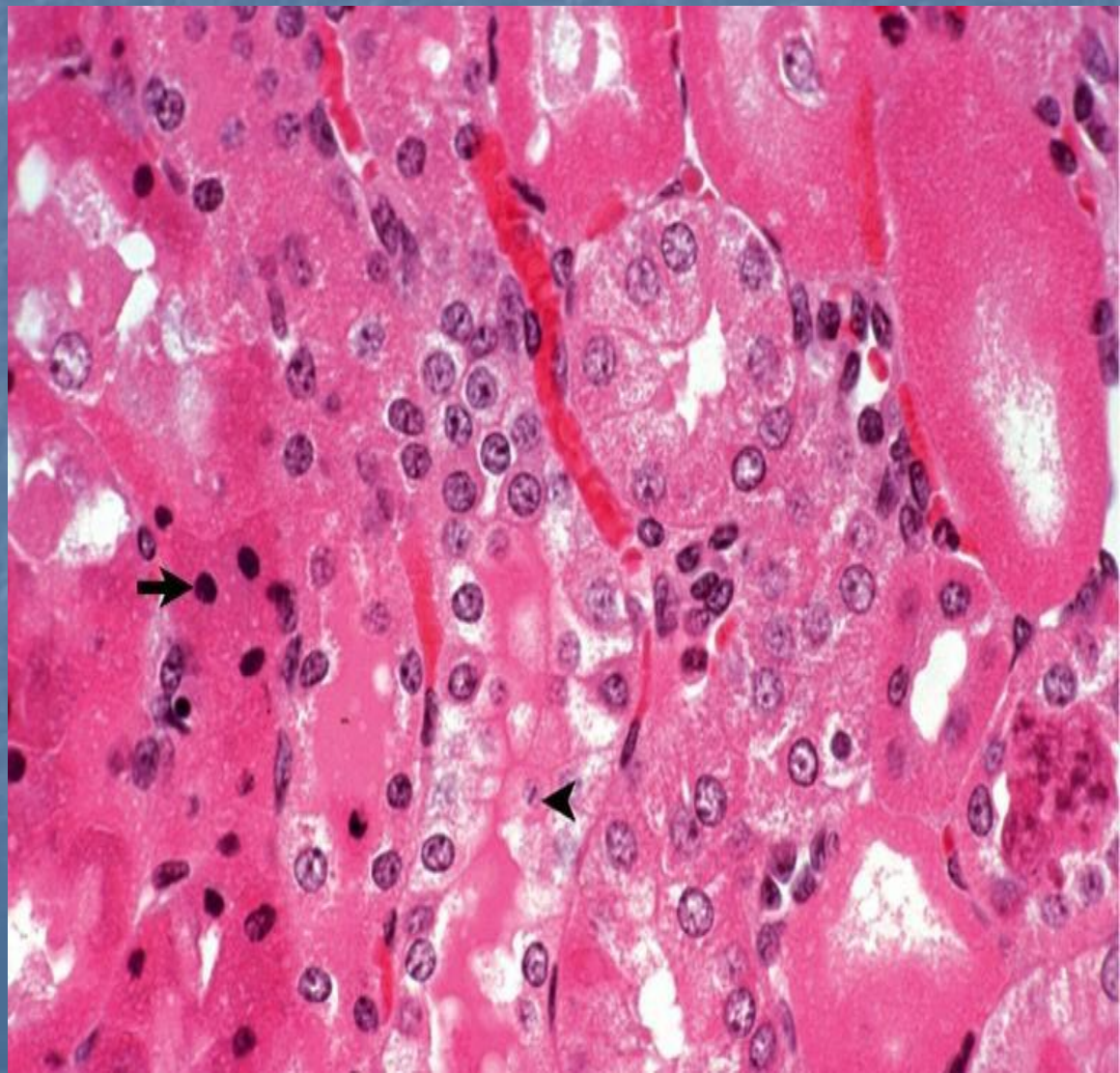




Coagulation Necrosis

Microscopic Appearance

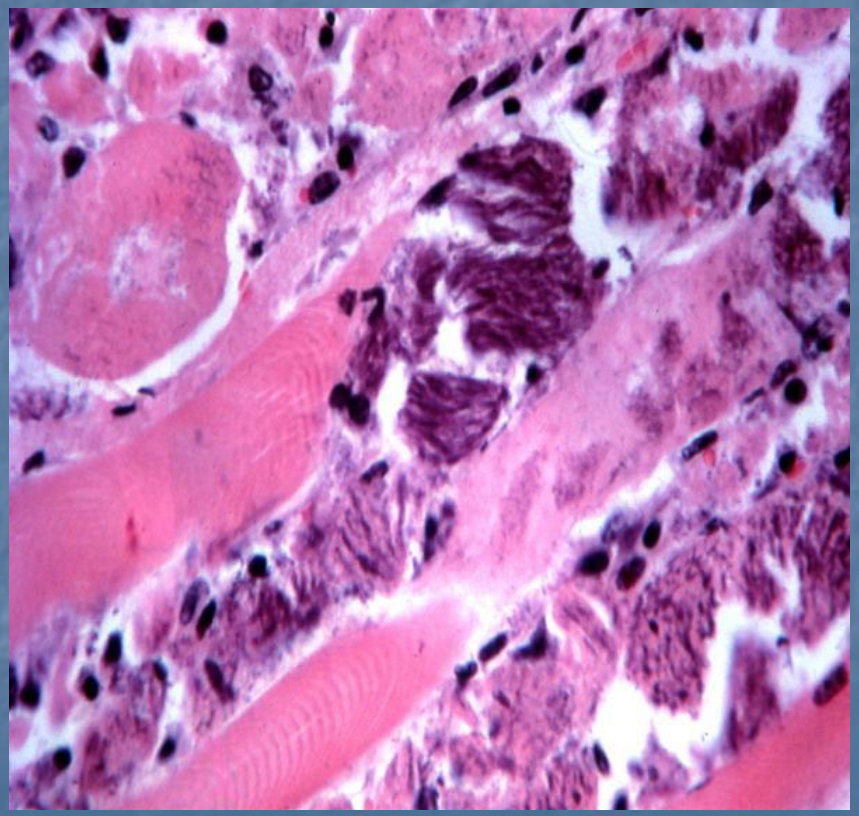
- original cell shape & tissue architecture is preserve die. Dead cells resemble an eosinophilic "shadow" of the original cells.
- cytoplasm: increased eosinophilia (H&E stain)usually hyalinized (homogeneous glassy appearance) may be mineralized.



Zenker's necrosis:

Of the rectus abdominus muscle and diaphragm as a complication of :

- ***bacterial infection*** *particularly* ***typhoid*** *fever. The striated muscles lose its striation, swell and fuse together in homogeneous structureless mass.*



(2) Liquifactive necrosis

The necrosed tissue undergoes rapid softening e.g. infarction of the nervous tissue which has abundant lysosomal enzymes. Also, this type of necrosis occurs in case of suppurative inflammation (Abscess) where liquefaction occurs under the effect of proteolytic enzymes of PNLs liquefaction of the amoebic abscess occurs due to the effect of strong proteolytic enzymes and hyaluronidase secreted by E. Histolytica.

Grossly: the affected tissue appears as homogenous amorphous substance.

Microscopically: it appears as homogenous eosinophilic structure.

Liquefactive Necrosis

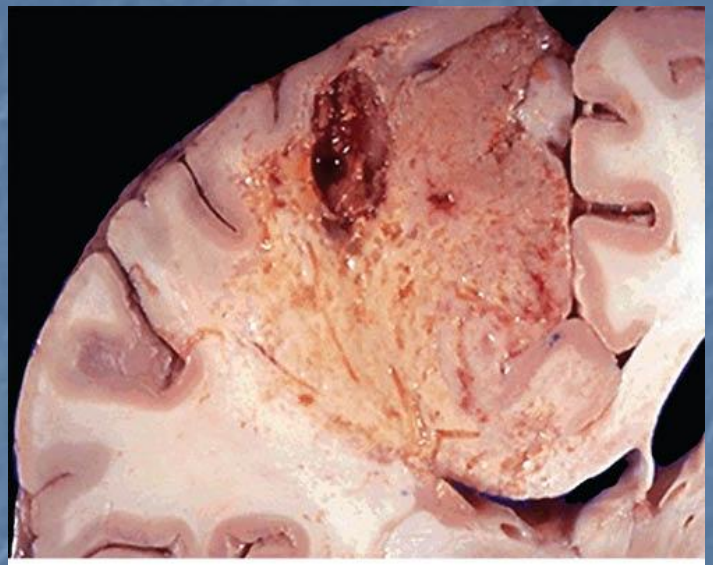
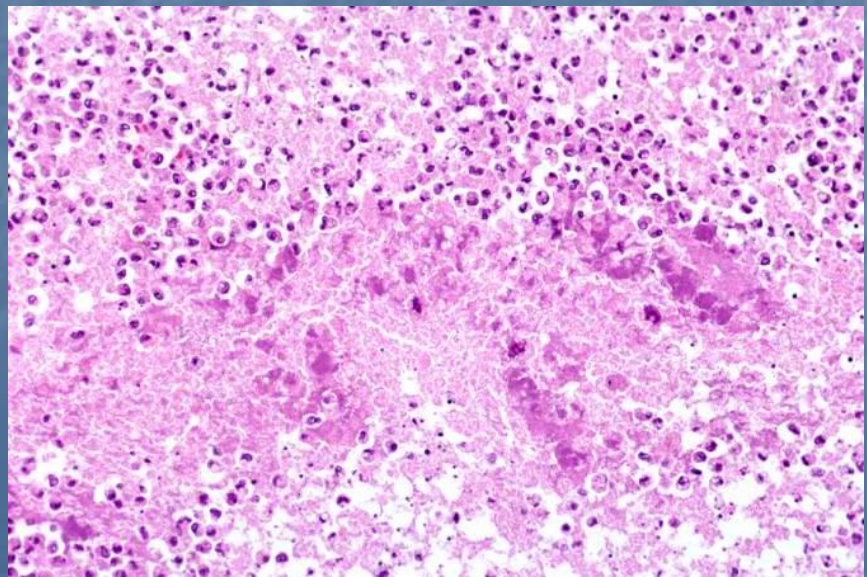


FIGURE 1–12 Liquefactive necrosis. An infarct in the brain, showing dissolution of the tissue.

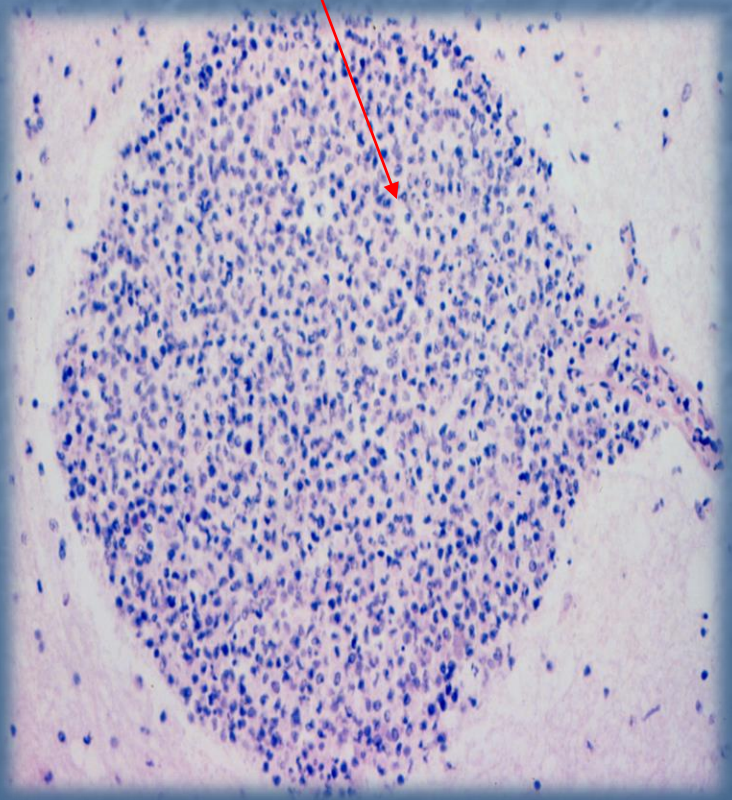
Digestion of the dead

Transformation of the tissue into a liquid viscous mass.

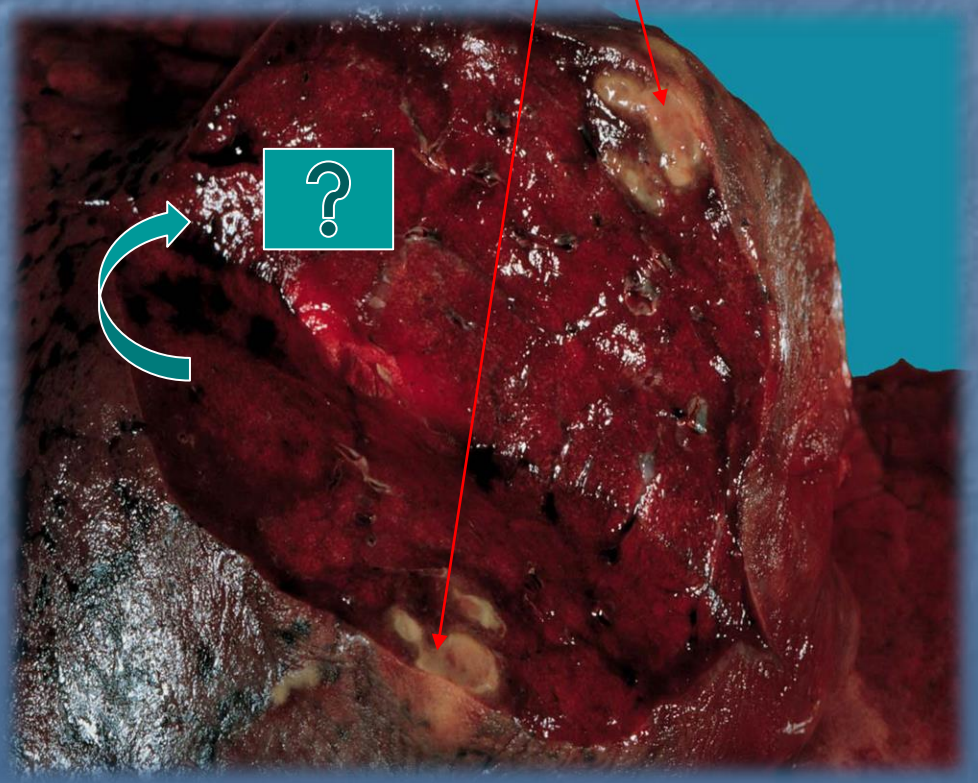
The necrotic material is frequently creamy yellow because of the presence of dead leukocytes and is called pus.



Localized collection of pus; no fibroblastic rim



The two lung abscesses seen here are examples of liquefactive necrosis in which there is a liquid center in an area of tissue injury.



(3) Caseous necrosis:

- It is characteristic of **tuberculosis.** The necrotic tissue undergoes slow partial liquefaction forming yellow cheesy material.
- ***Microscopically,*** it shows amorphous granular eosinophilic material lacking the cell outlines.
- Unlike coagulative necrosis, the necrotic cells do not retain their cellular outlines, and do not disappear by lysis, as in liquifactive necrosis

- ***Grossly,*** the caseous material resembles clumpy cheese, hence the name caseous necrosis.
- **The cause of necrosis** in TB is **hypersensitivity** reaction caused by the tuberculoprotein content of the cell wall of Mycobacterium..

The features of caseous necrosis

Cell outlines: lost

Liquefaction: does *not* occur (caseous necrosis – solid)

Used clinically when describing granulomas

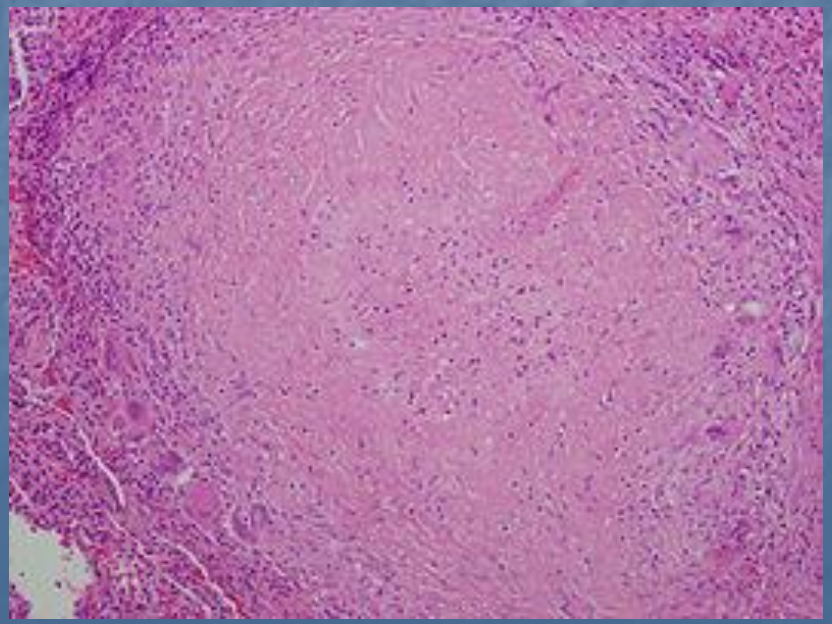
- caseating versus noncaseating granulomas

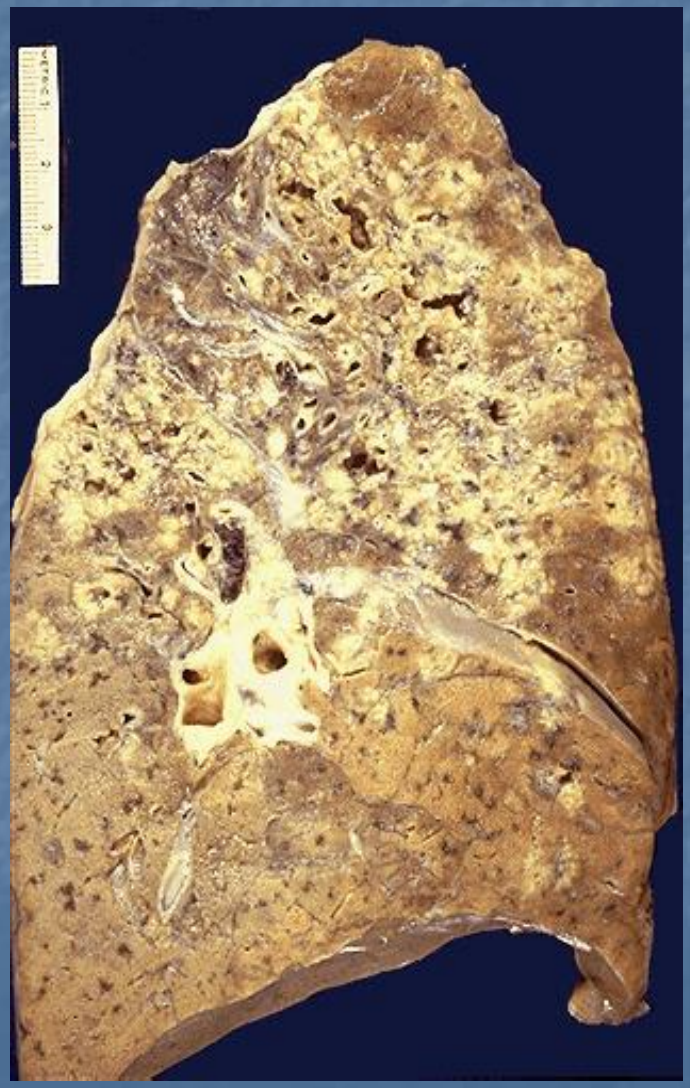
- granuloma: a type of chronic inflammatory reaction

- spherical: +/- central necrosis

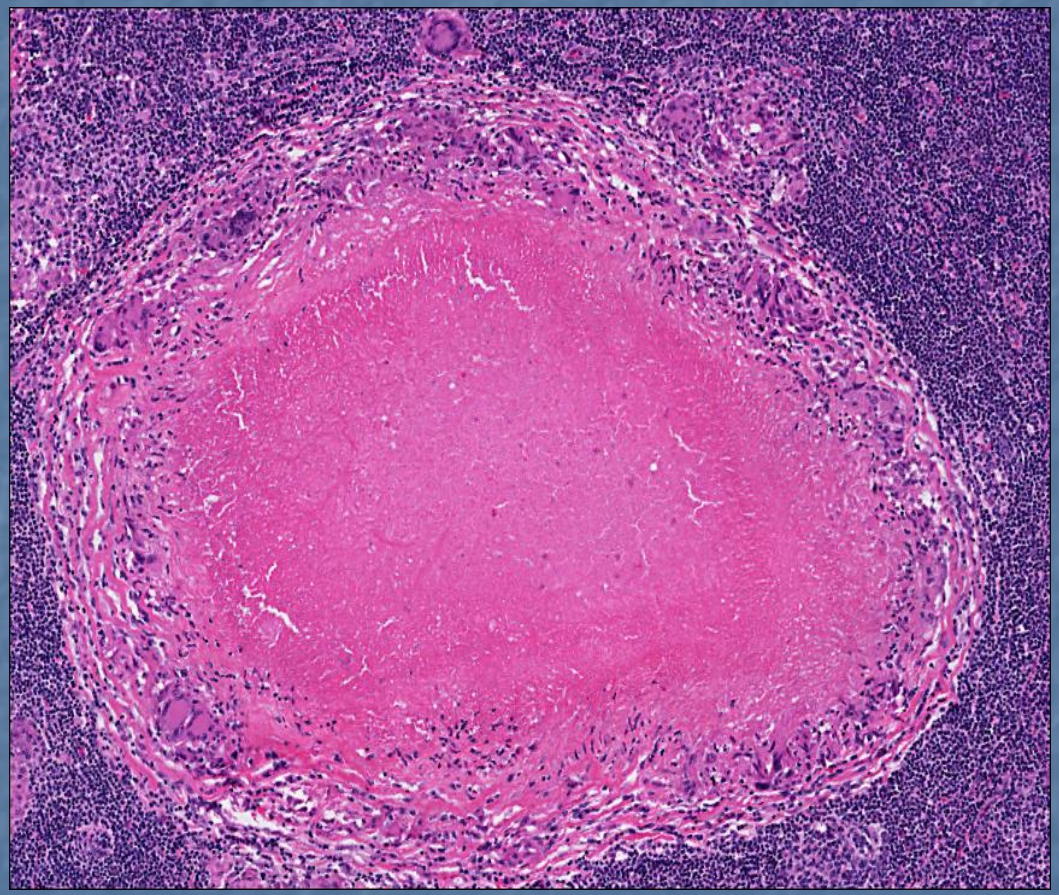
Caseous Necrosis

"Caseous" (cheeselike) is derived from the friable white appearance of the area of necrosis. Necrotic area appears as a collection of fragmented or lysed cells and amorphous granular debris enclosed within a distinctive inflammatory border; this appearance is characteristic of a focus of inflammation known as a granuloma.

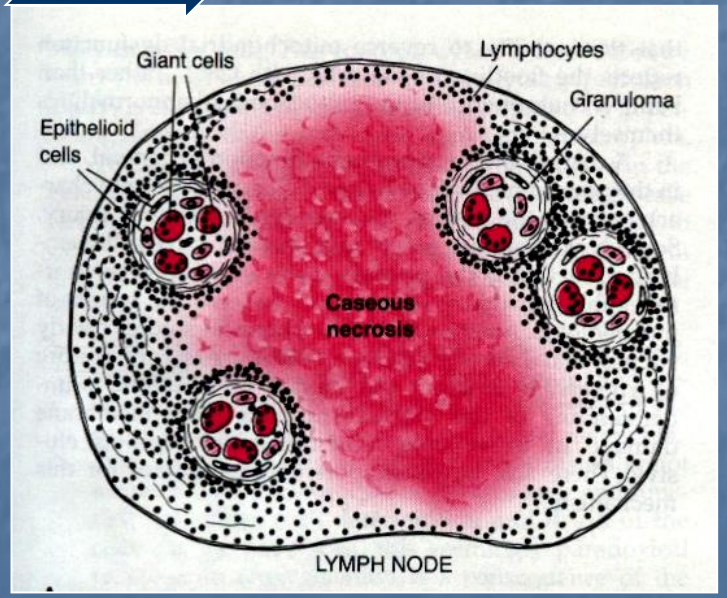




Caseous necrosis in lymph node

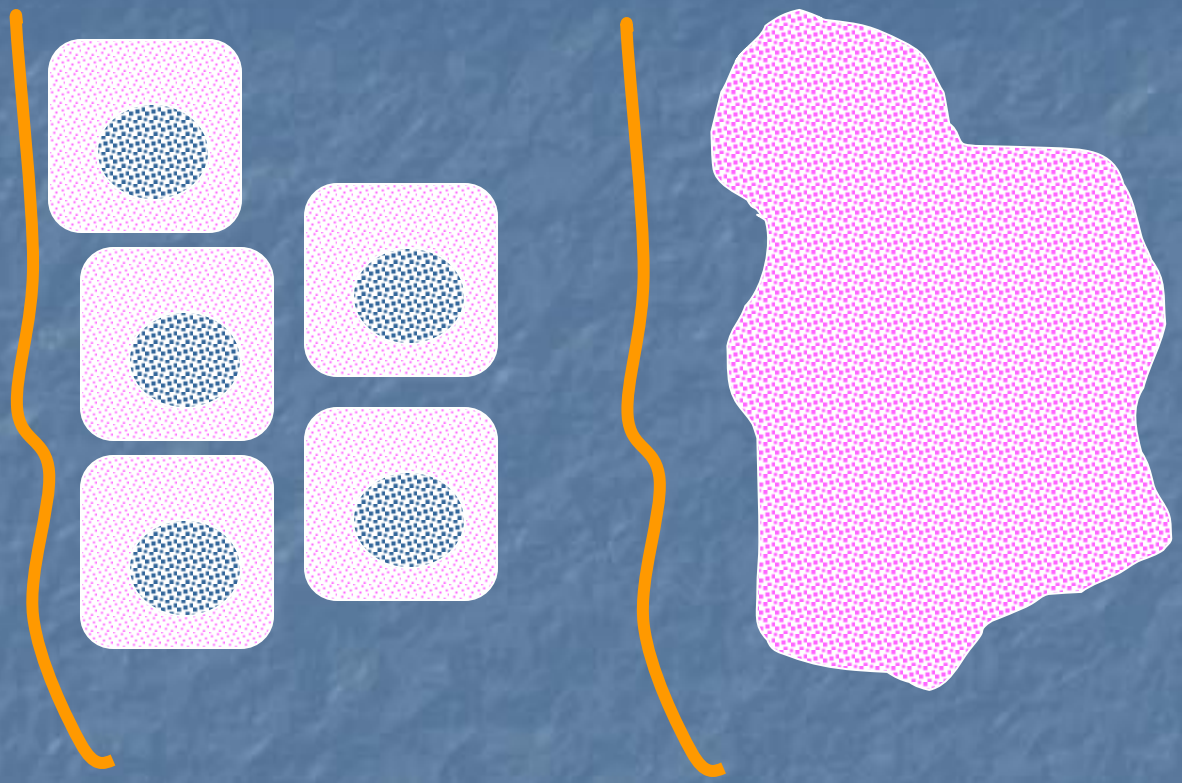


Amorphous ,granular ,eosinophilic ,necrotic center is surrounded by granulomatous inflammation.

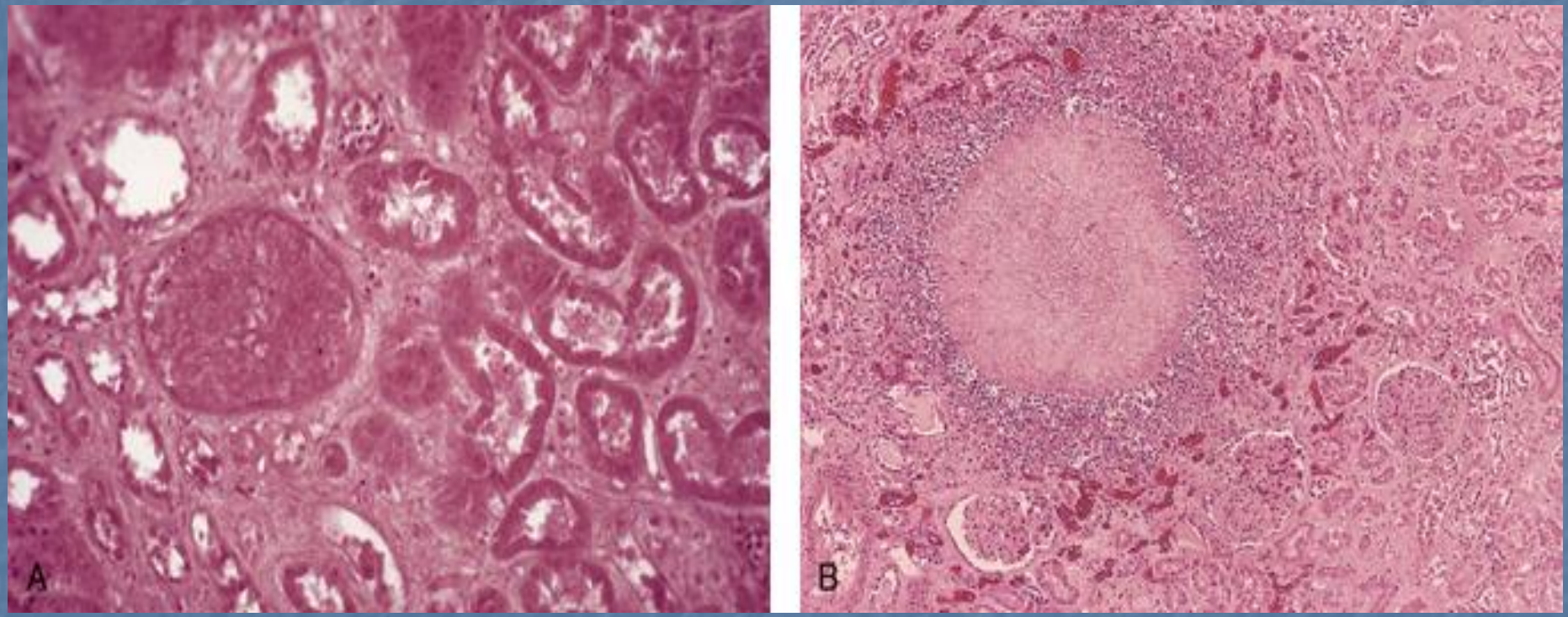


Living cells

Caseous necrosis (solid)



Left: coagulation necrosis of renal cortex. Right: liquifactive necrosis in renal cortex.



Coagulation necrosis

Liquifactive necrosis (abcess)

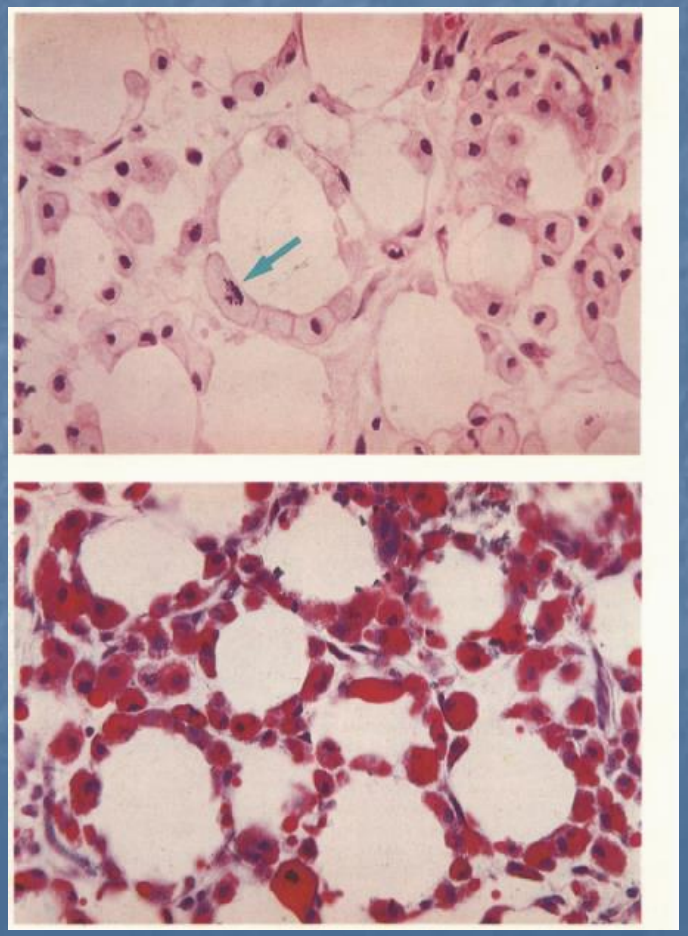
(4) Fat necrosis

it is necrosis of adipose tissue including two types:

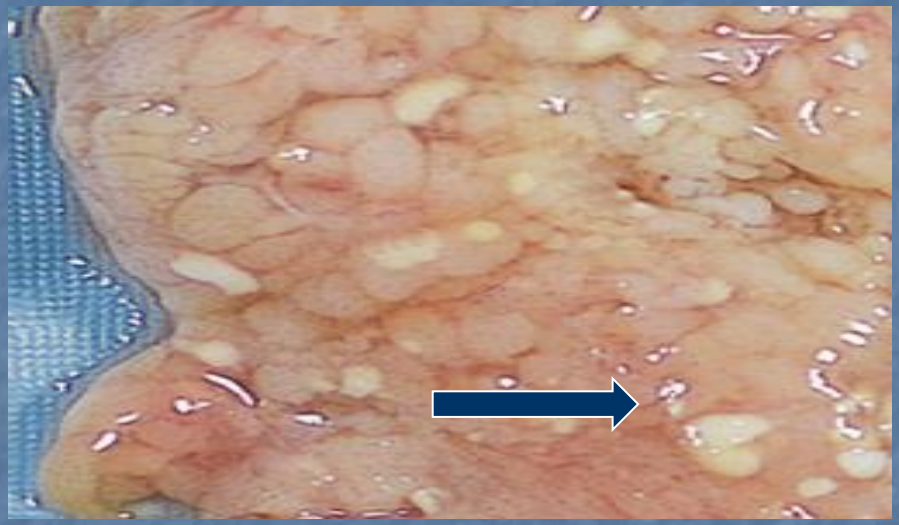
a)**Traumatic:** caused by trauma to adipose tissue e.g. breast and subcutaneous tissue.

b) **Enzymatic:** which occurs in case of acute haemorrhagic pancreatitis.

- Obstruction of the pancreatic duct leads to release of lipase which splits the fat cells of the omentum into fatty acid (combine with Ca giving chalky white calcification) and to glycerol which is absorbed in the circulation.

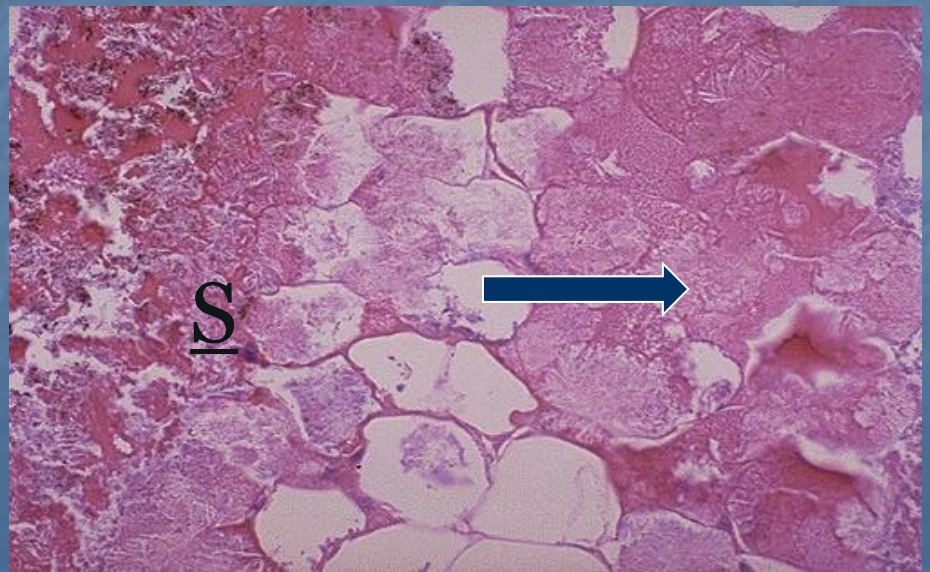


Enzymatic fat necrosis



Fat cells

This is fat necrosis of the pancreas. Cellular injury to the pancreatic acini leads to release of powerful enzymes which damage fat by the production of soaps, and these appear grossly as the soft, chalky white areas (Arrow) seen here on the cut surfaces.



Microscopically, fat necrosis adjacent to pancreas is seen here. There are some remaining steatocytes at the left (S) which are not necrotic. The necrotic fat cells at the right (Arrow) have vague cellular outlines, have lost their peripheral nuclei, and their cytoplasm has become a pink amorphous mass of necrotic material.

(5) Fibrinoid necrosis

This is characterized by swelling, fragmentation, increased eosinophilia of collagen fibers and accumulation of mucopolysaccharides and fibrin due to vascular exudation of fibrinogen at the site of lesion, e.g.:

a) Collagen diseases (Rheumatic fever, Rheumatoid, Sclerodermia, Lupus erythematosus and Polyarteritis nodosa).

b) In the wall of blood vessels in malignant hypertension

Fibrinoid Necrosis

- **Glassy, eosinophilic fibrin-like material is deposited within the vascular walls**

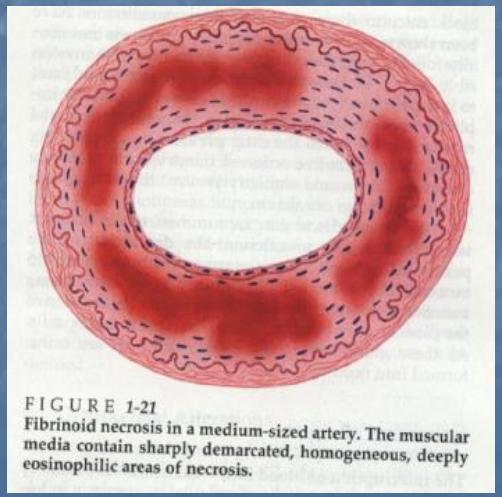
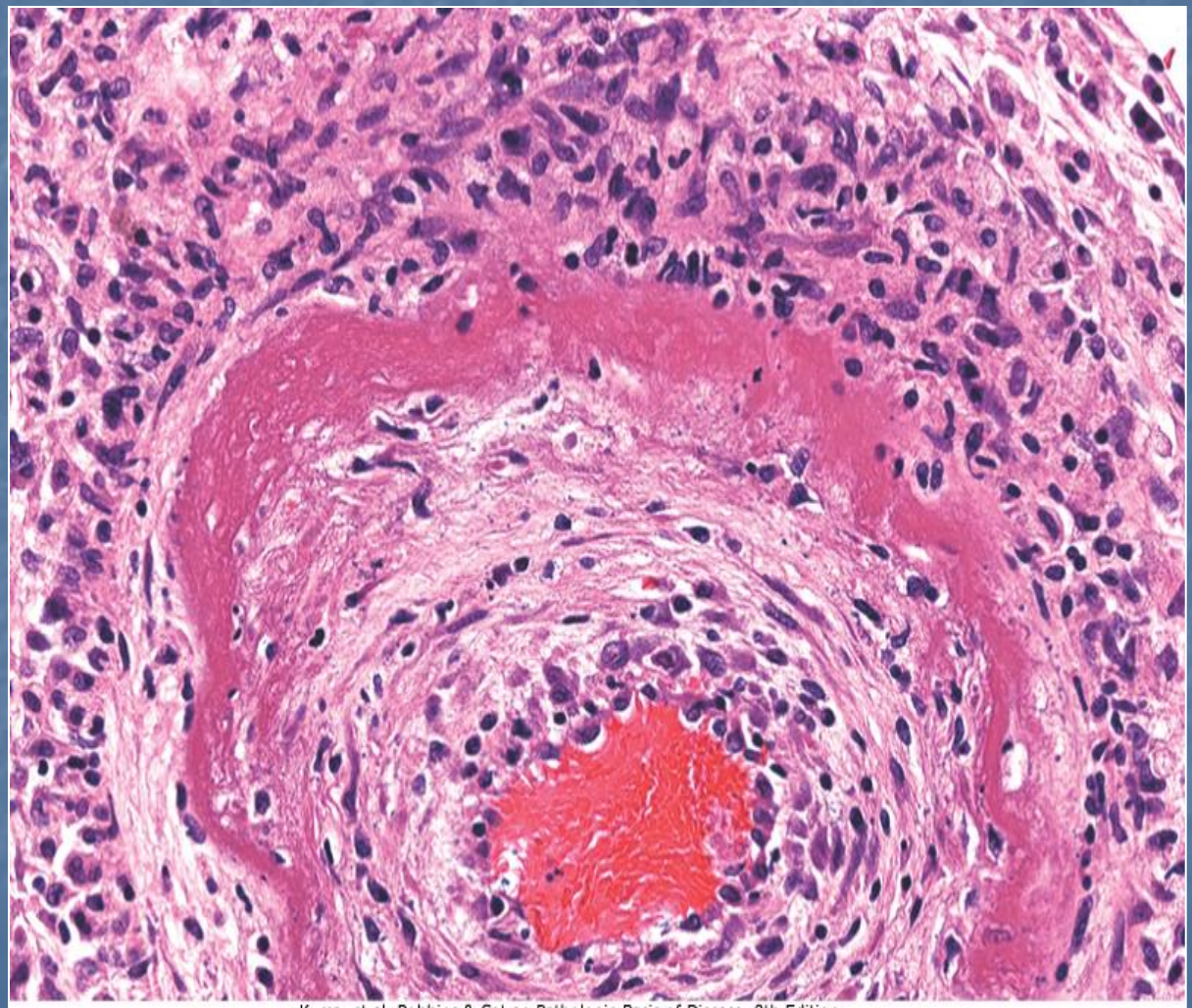


FIGURE 1-21
Fibrinoid necrosis in a medium-sized artery. The muscular media contain sharply demarcated, homogeneous, deeply eosinophilic areas of necrosis.



(6) Gangrenous necrosis:

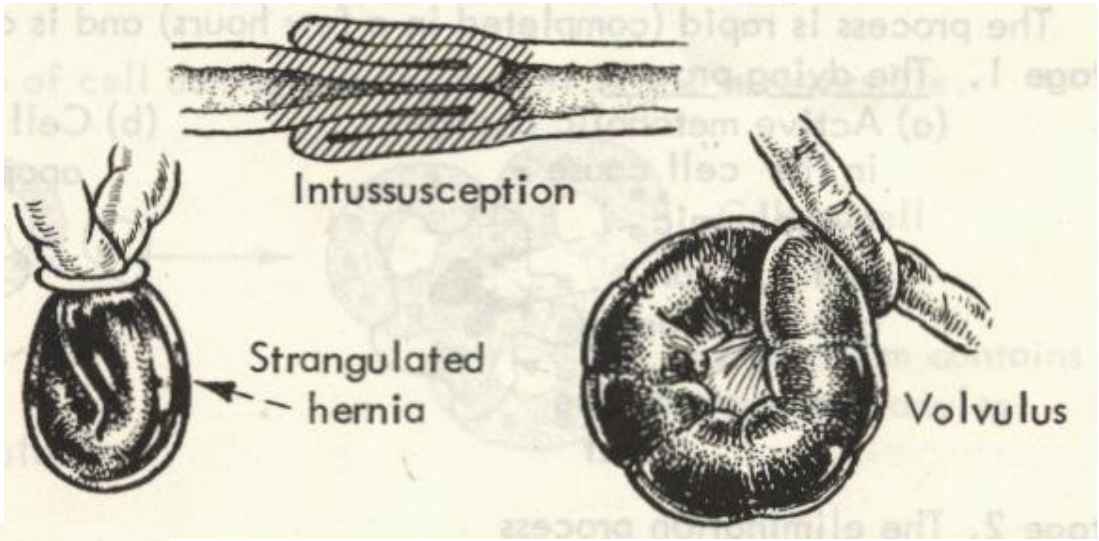
The tissue in this case have undergone ischemic cell death and **coagulative** necrosis followed by **liquifactive** action of putrefactive organisms.

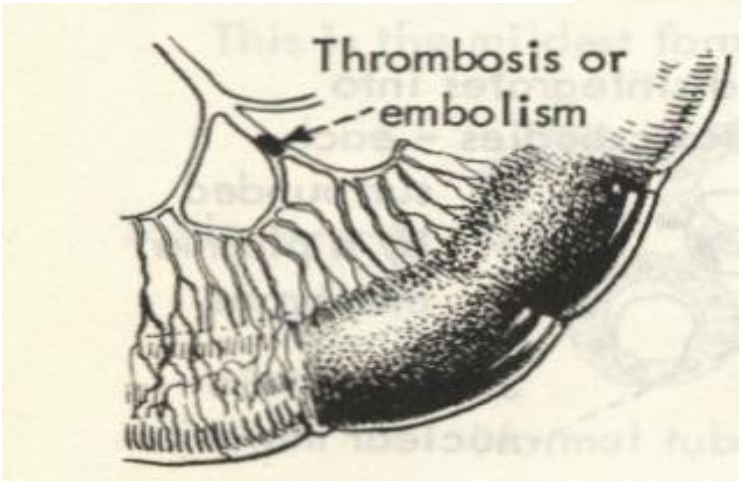
When coagulative pattern is dominant the process is termed ***dry gangrene***.

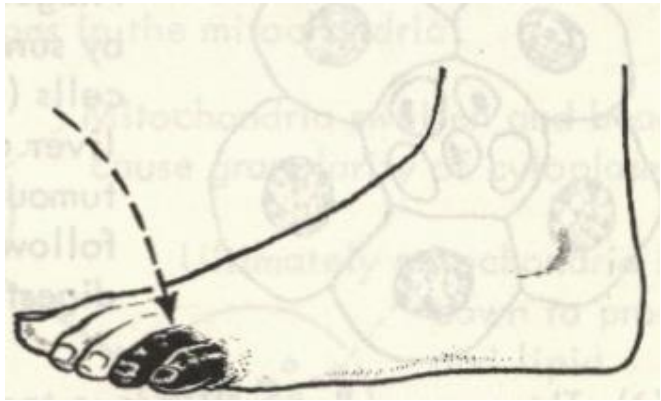
When the liquifactive action of the bacteria is more pronounced it is called ***wet gangrene***.

Obstraction of blood supply to bowel is alrmost followed by

Gangrene

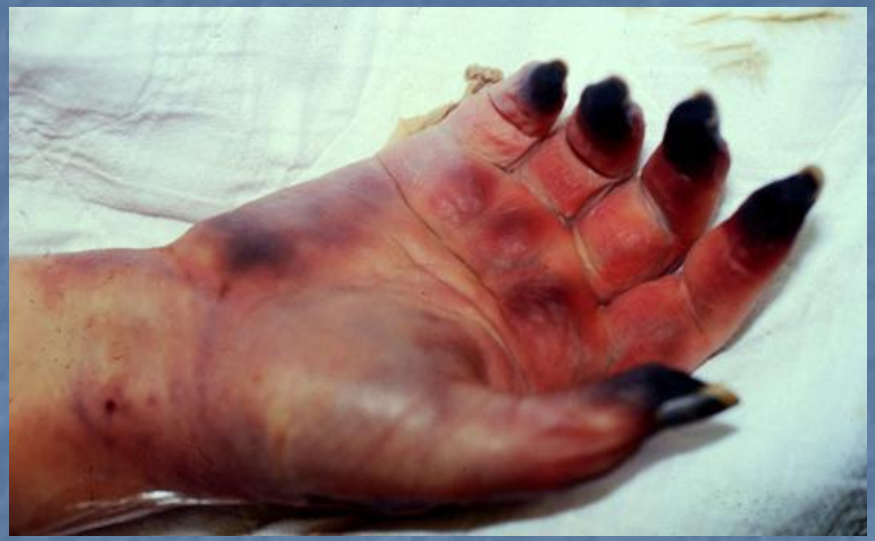






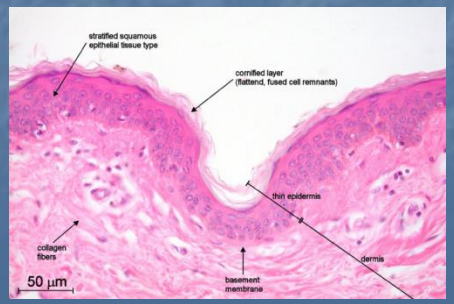
Gangrenous Necrosis

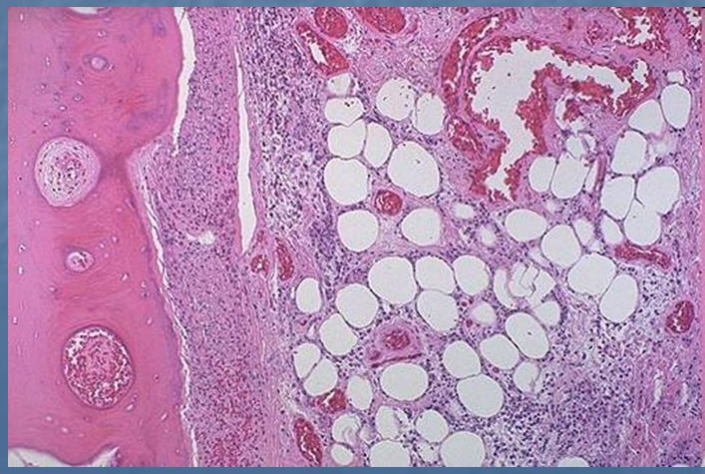
- **•definition= necrosis (usually ischemic) of extremities, eg digits, ear tips.**
- Not a specific pattern.
- Term is commonly used in clinical practice. U
- Upper extremitiy, that has lost its blood supply
- and has undergone, typically,
- coagulative necrosis



•dry gangrene= coagulation necrosis of an extremity.

•wet gangrene= when the coagulative necrosis of dry gangrene is modified by liquefactive action of saprophytic/putrefactive bacteria.





Fate and local effects of NECROSIS :

1. A small area undergoes repair:

A) The products of the necrotic cells irritate the surrounding tissue forming a zone of inflammation.

B) The accumulated neutrophils in the zone of inflammation soften the necrotic tissue and make its removal by macrophages and blood stream easy and help the process of healing.

C) Repair by regeneration or fibrosis depends upon the type of cells affected (labile-stable-permanent).

2. *If the necrotic area is wide*, its products can't be removed and a fibrous capsule form around it in order to separate it from the living tissue. Areas of necrotic softening in the brain become surrounded by **proliferated neuroglia (gliosis).**

3. *Old unabsorbed* caseous lesions and fat necrosis usually becomes heavily calcified (dystrophic calcification).

4-when the necrotic tissue is infected with putrefactive Organism----- Gangrene

General effects of necrosis

1. Release of enzymes from the breakdown tissue into the blood forms the basis of clinical tests for diagnosis e.g. detection of transamenase in myocardial infarction and liver necrosis in hepatitis.
2. Absorption of dead products into the circulation leads to leukocytosis and fever (Not diagnostic).

Exercises

1. Why should you study cell injury?
2. Mention some of the causes of each of the various types of necrosis.
3. Know the differences between reversible & irreversible forms of cell injury.

4. Describe the mechanisms of necrosis.
5. Describe the various types of necrosis & know some of their causes.
6. Compare & contrast necrosis & apoptosis.