

General pathology lab cell injury and inflammation.

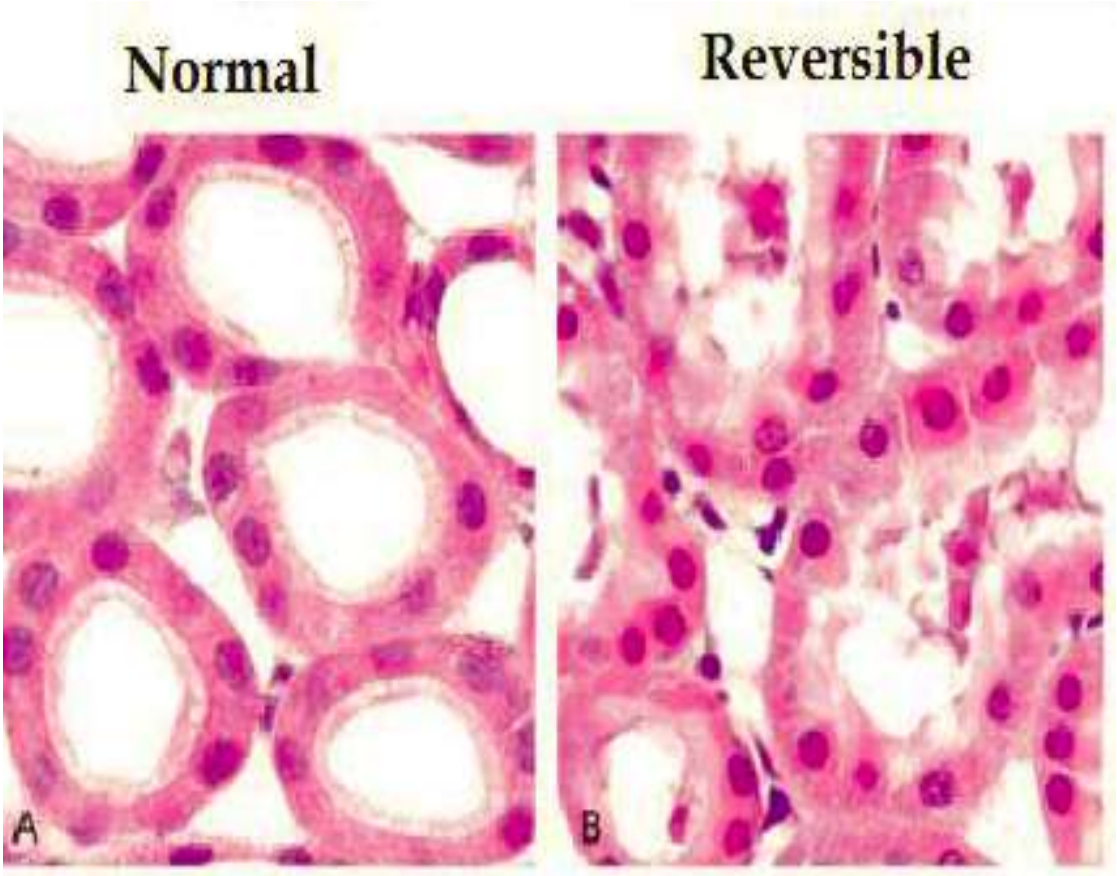
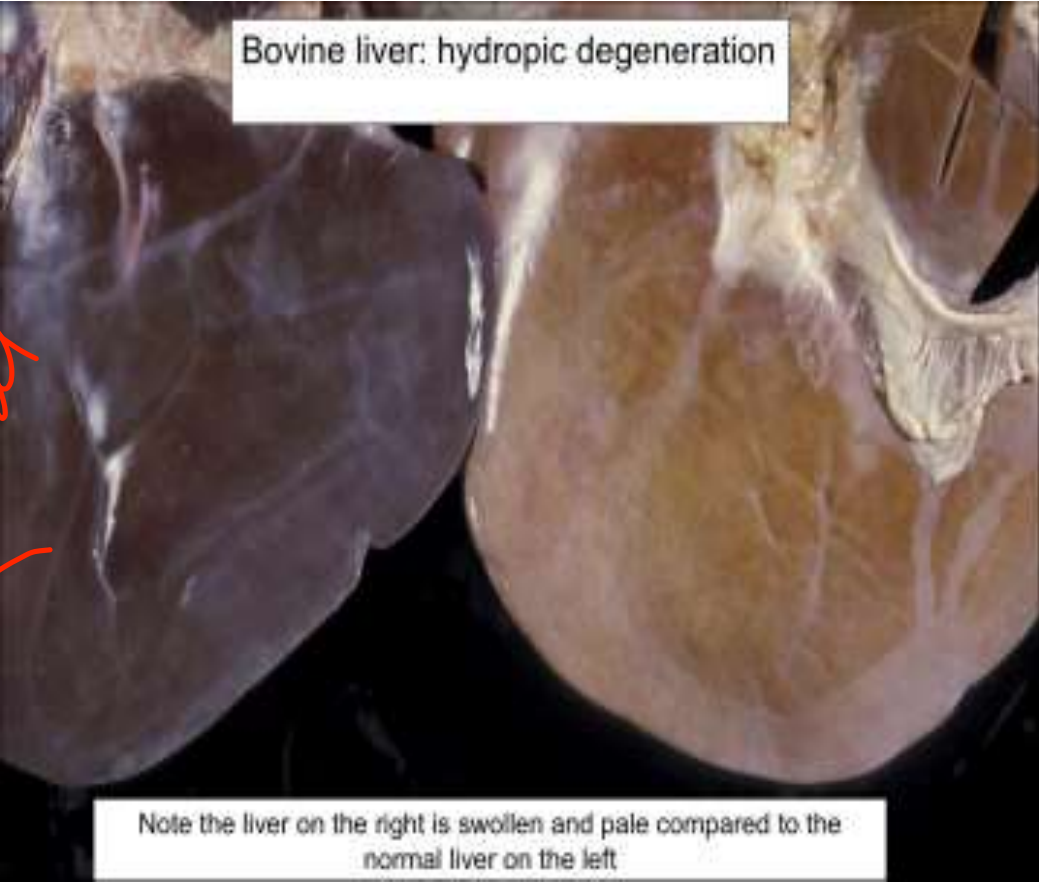


Eman Kreishan, M.D.

4-11-2024.

**Morphological changes of reversible cell injury:
1. Cellular Swelling**

normal



*Renal Tubules
* Swelling*



-mainly
in hypoxic
injury

2. Fatty change

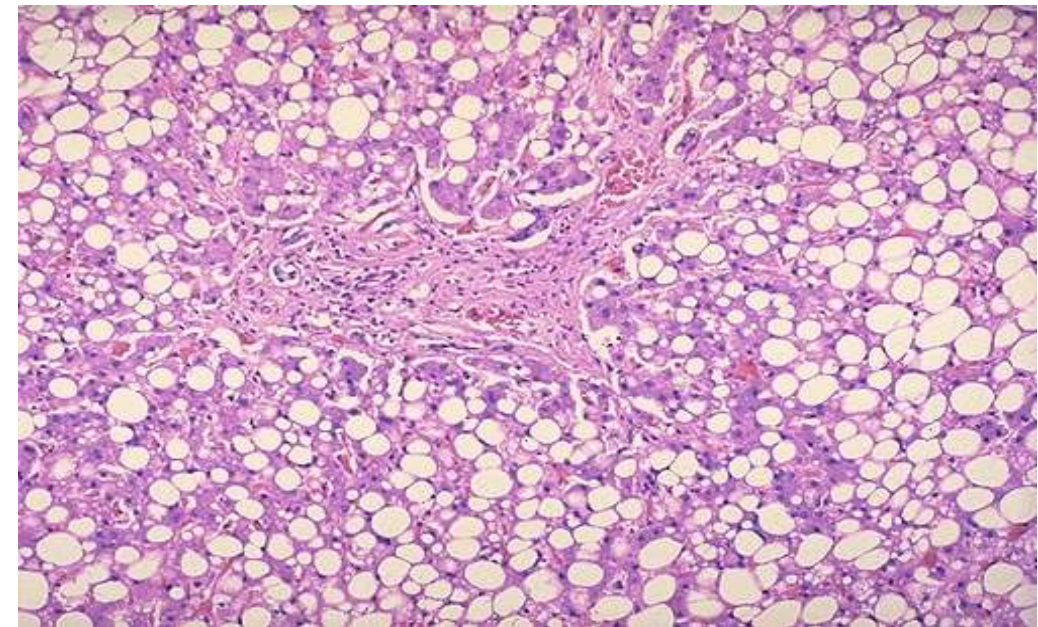
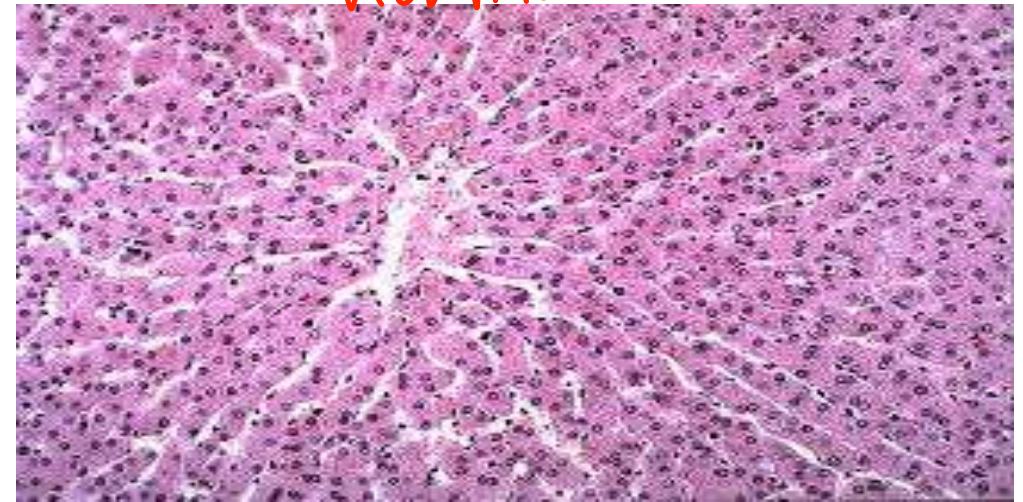
Liver

In Tissues with Fat metabolism
↳ Hepatocytes
& myocardial cells



yellow
oily

normal liver ✓

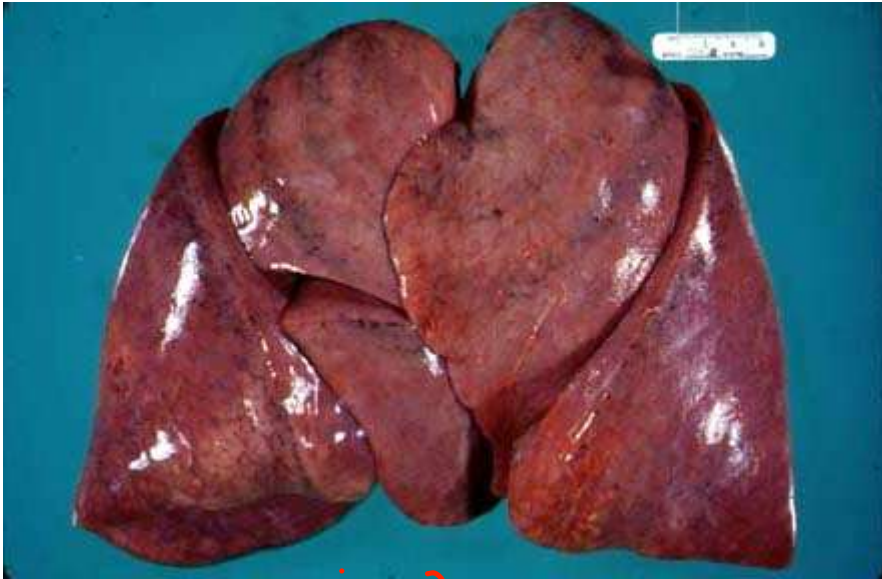


Fat Globules
in Cytoplasm

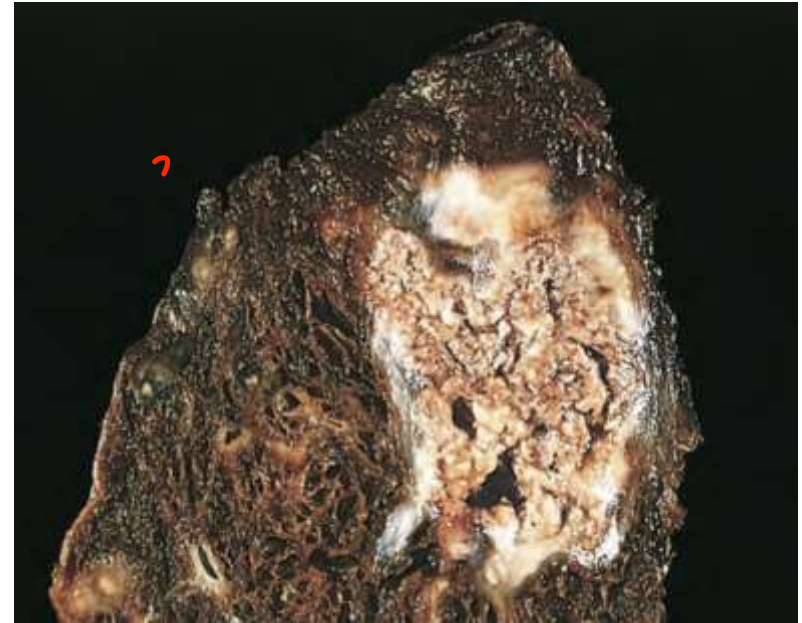


Morphological features of necrosis:

I. Grossly:



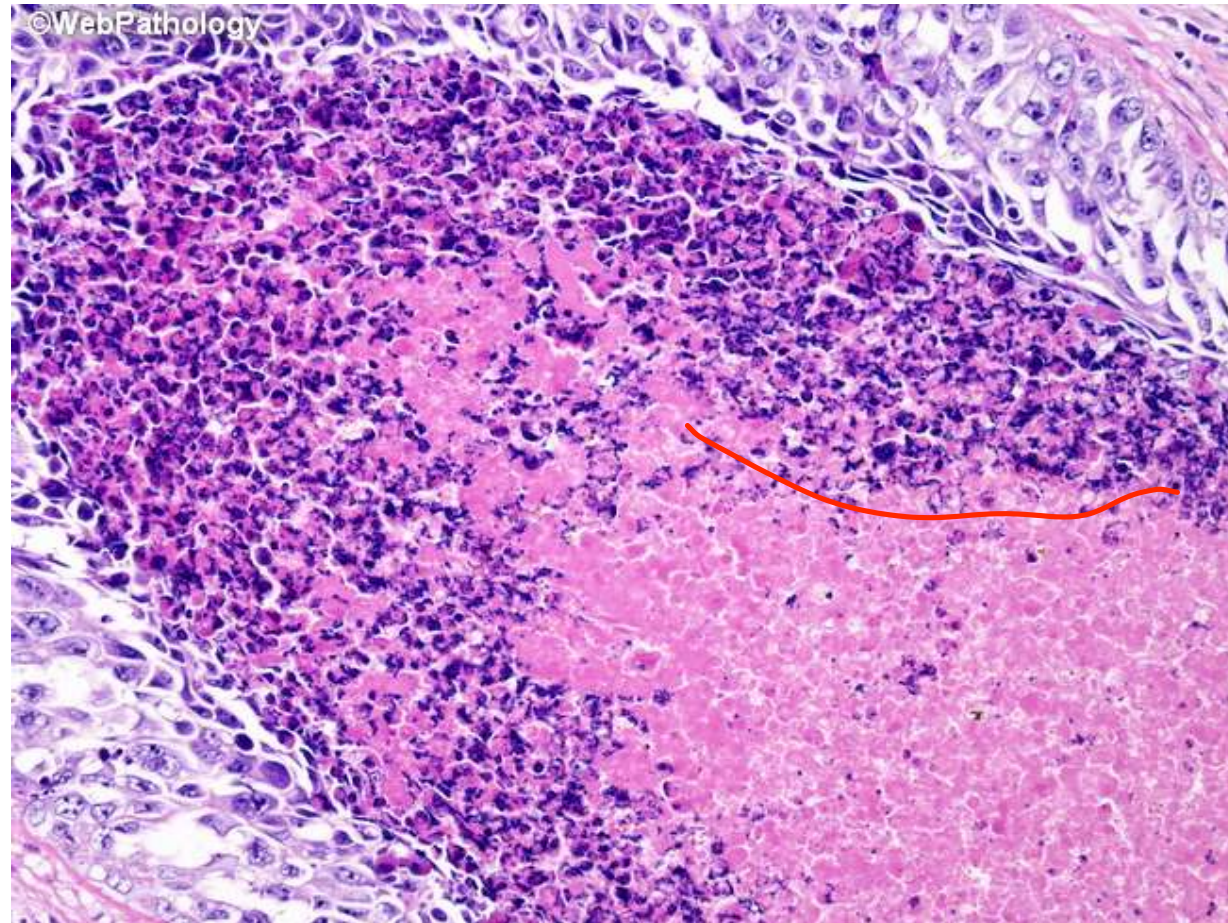
Lung
* shiny



* ill - defined whitish area
* Rough
* pulmonary TB - Caseous necrosis



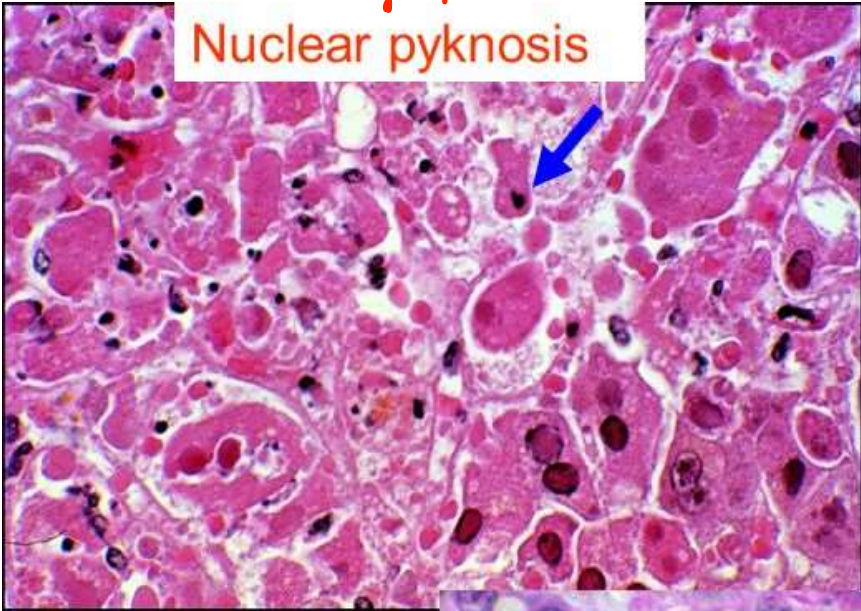
Microscopic appearance of Necrotic dead cells:



- Homogenous
Pink Color
of the Cytoplasm
1. ↑ Binding of eosin to denatured Cytoplasmic Proteins
 2. loss of Glycogen
 3. moth eaten "Enzymatic digestion"

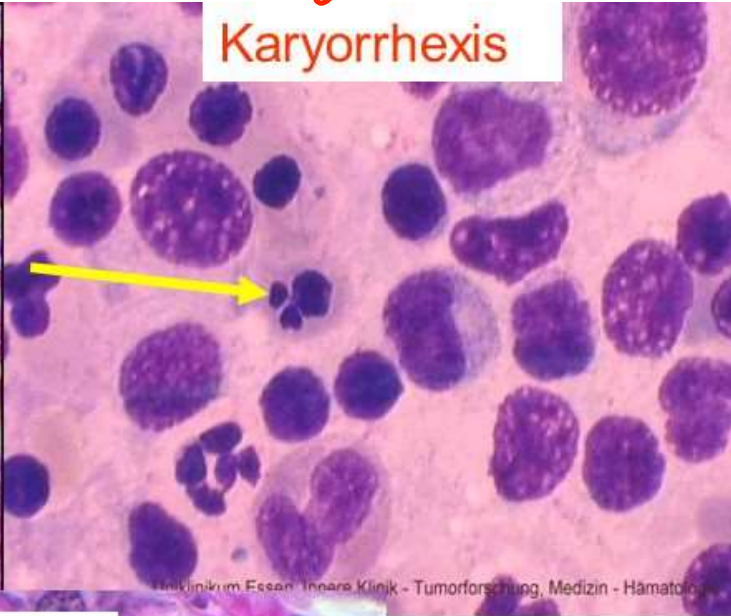


↳ Shrinkage
↑ Basophilia



Nuclear pyknosis

↳ Fragmentation of
Pyknotic nucleus



Karyorrhexis

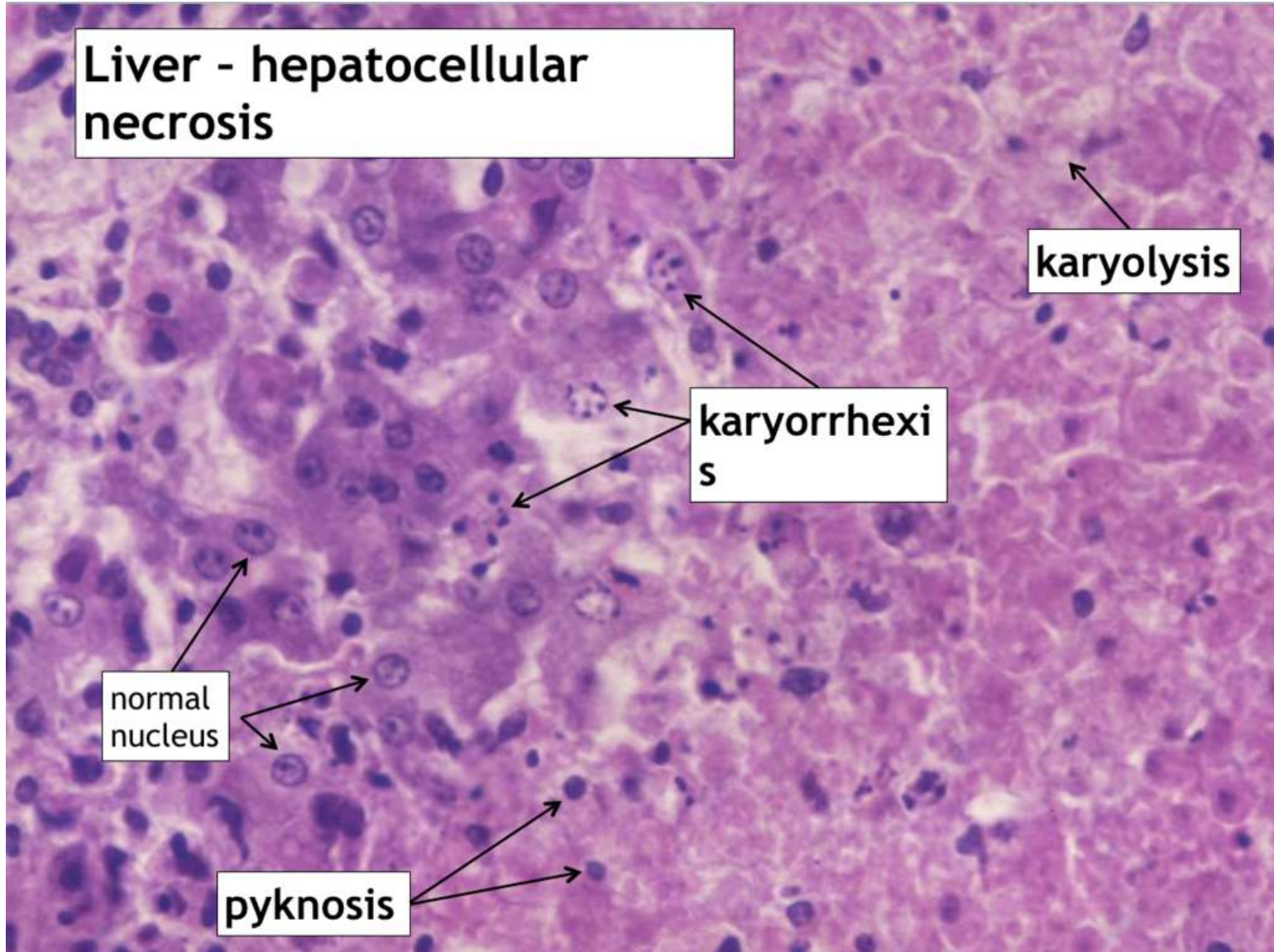


Karyolysis

↓ Basophilia of Chromatin → DNAase



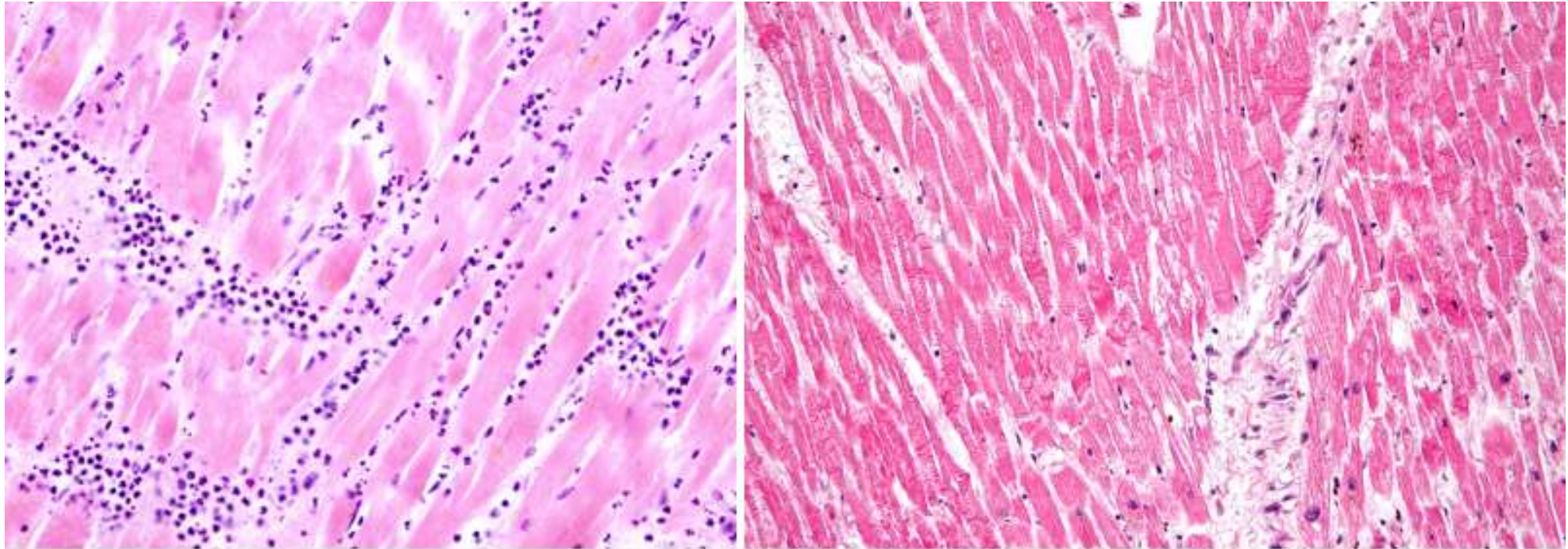
**Liver - hepatocellular
necrosis**



→ Hypoxic cell death

coagulative necrosis in the myocardium after infarction

Not viable وگتلی "Ghost cells"
له بتشبهه ل Normal

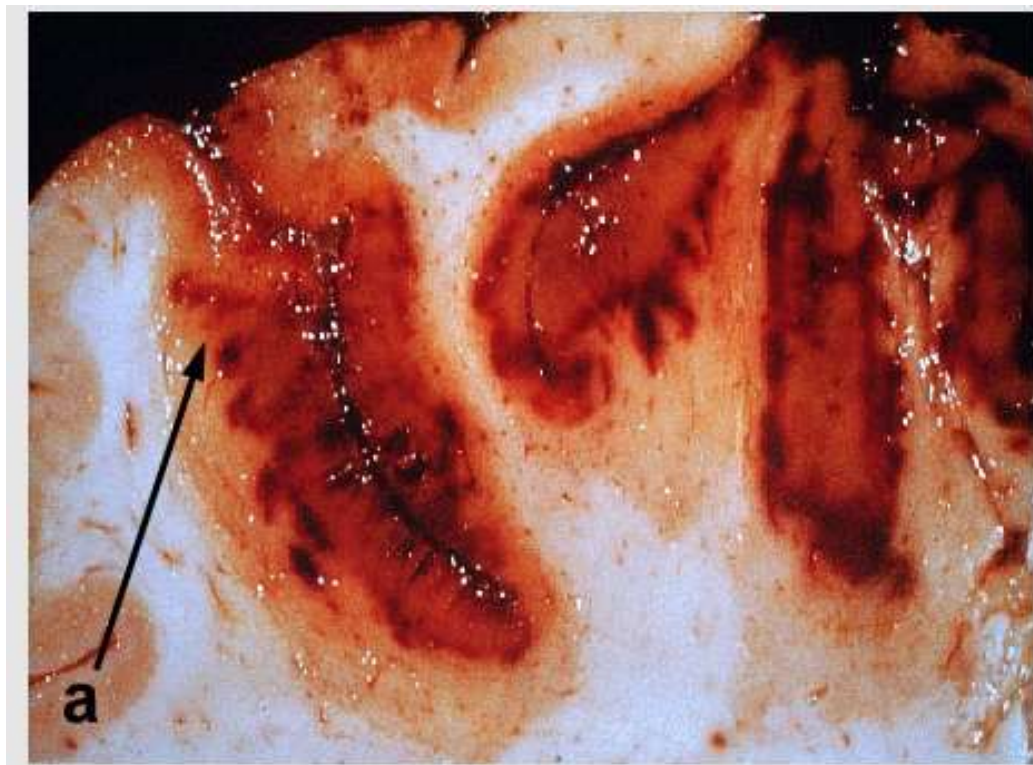


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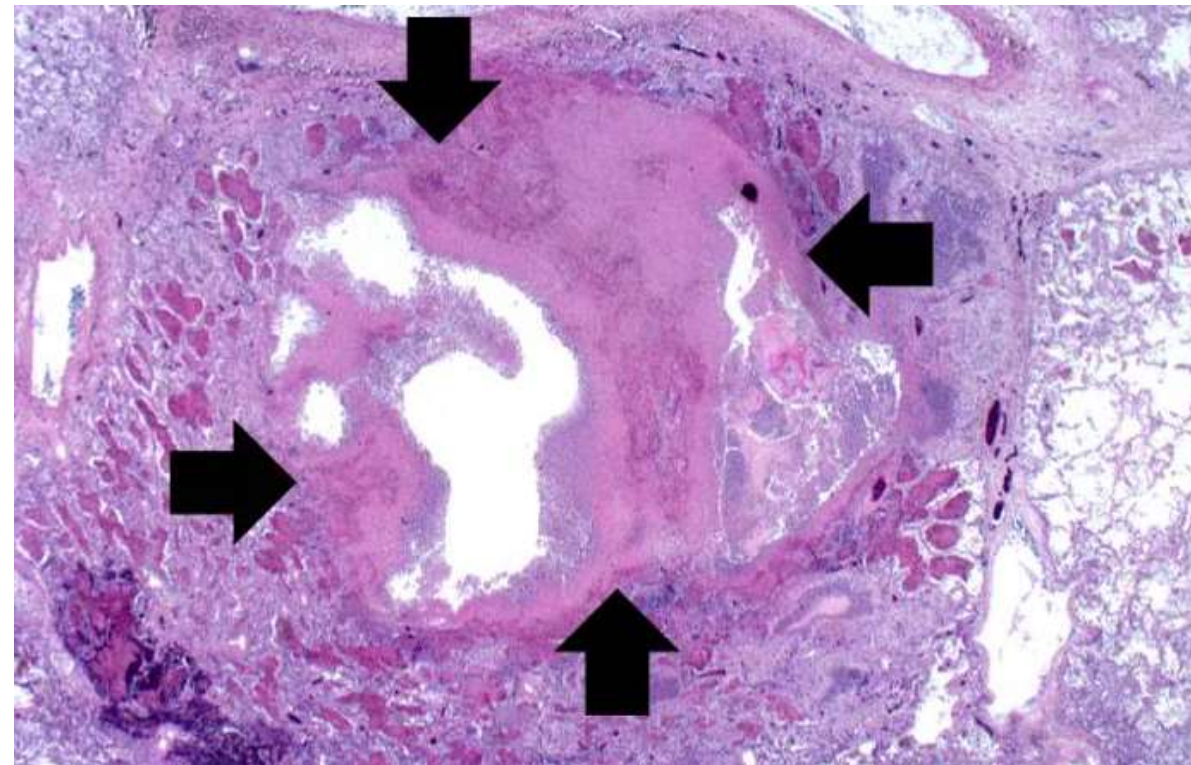
Wet → Because of Enzymatic digestion of lipid by neutrophils

Liquefactive necrosis



Lipid Rich
Tissue

← Brain

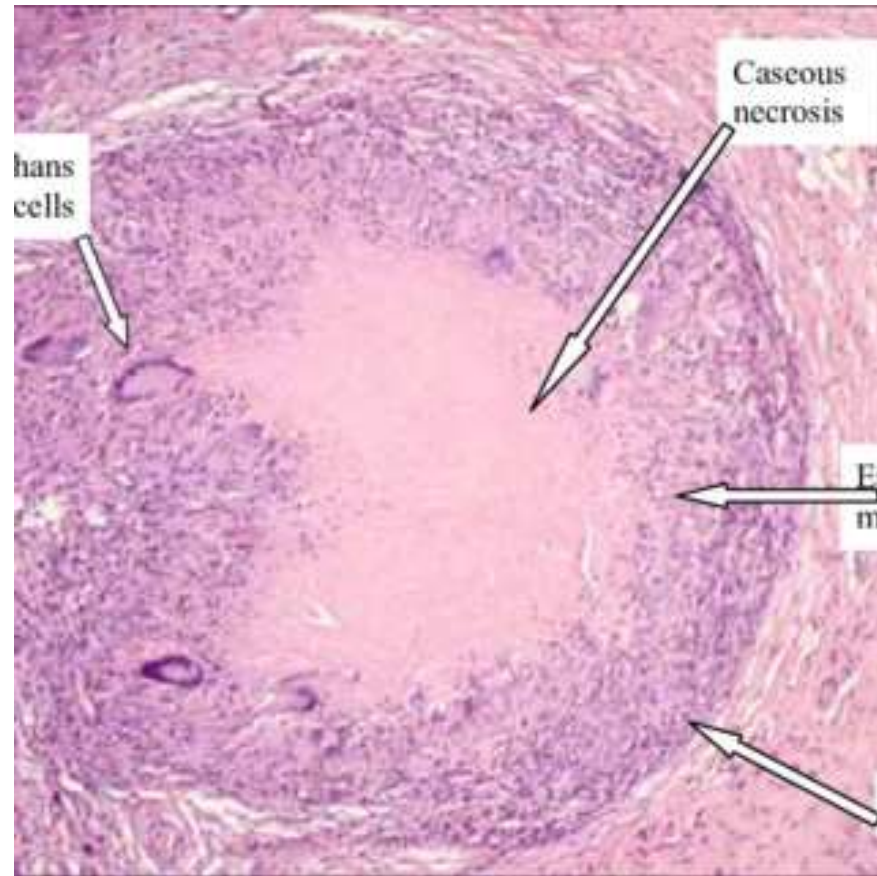


Lung liquefactive
necrosis



Caseous necrosis

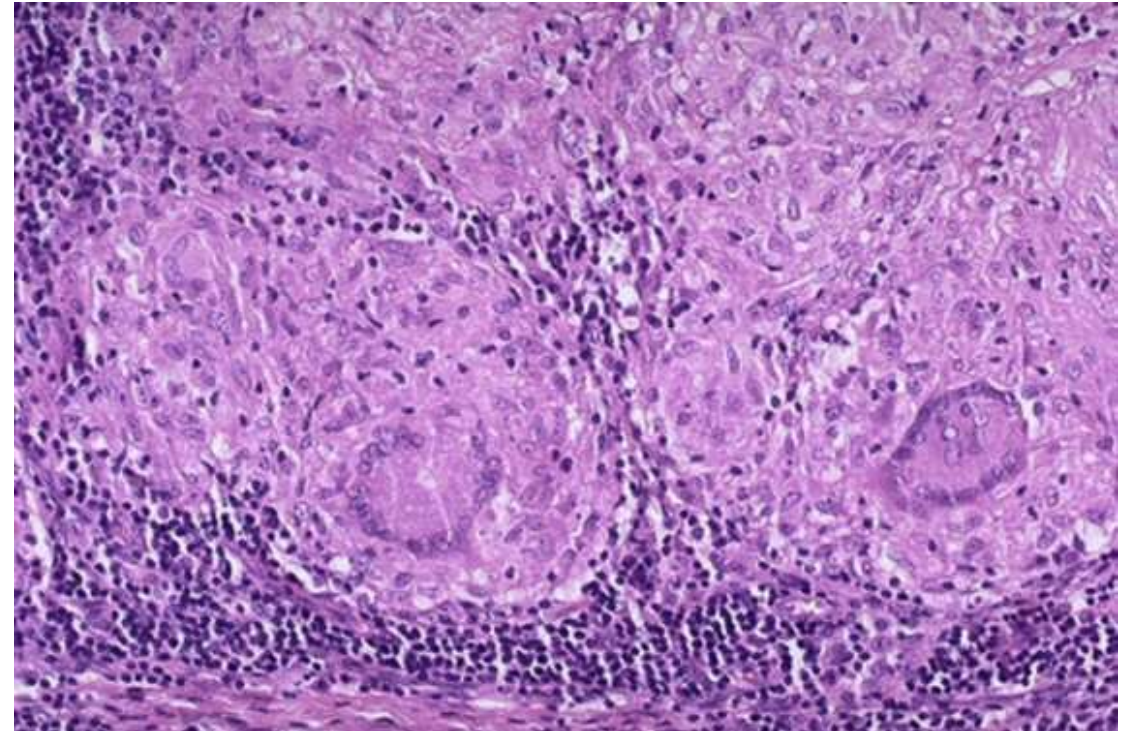
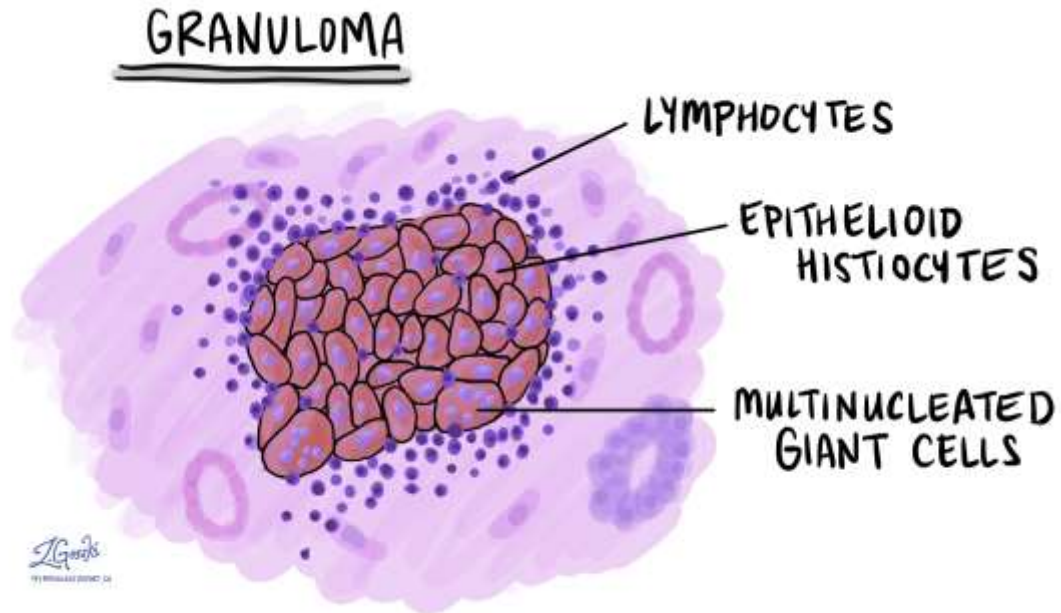
**Cheesy-like appearance*

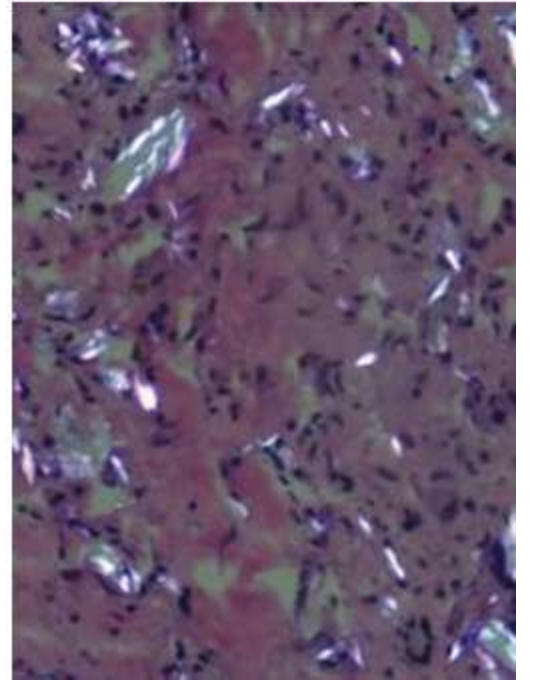
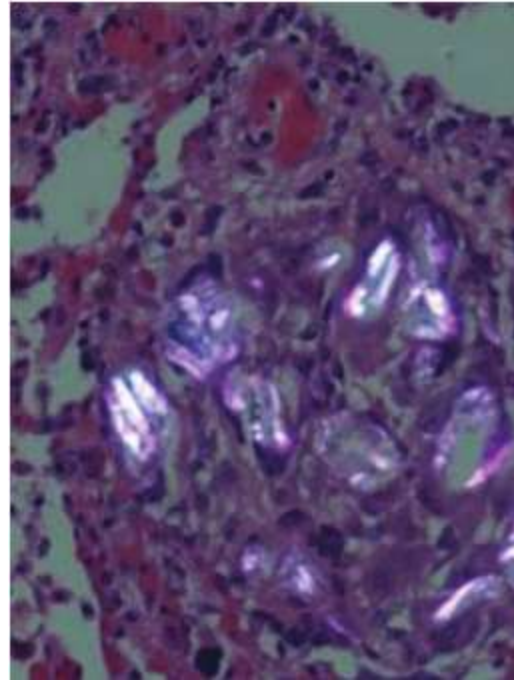
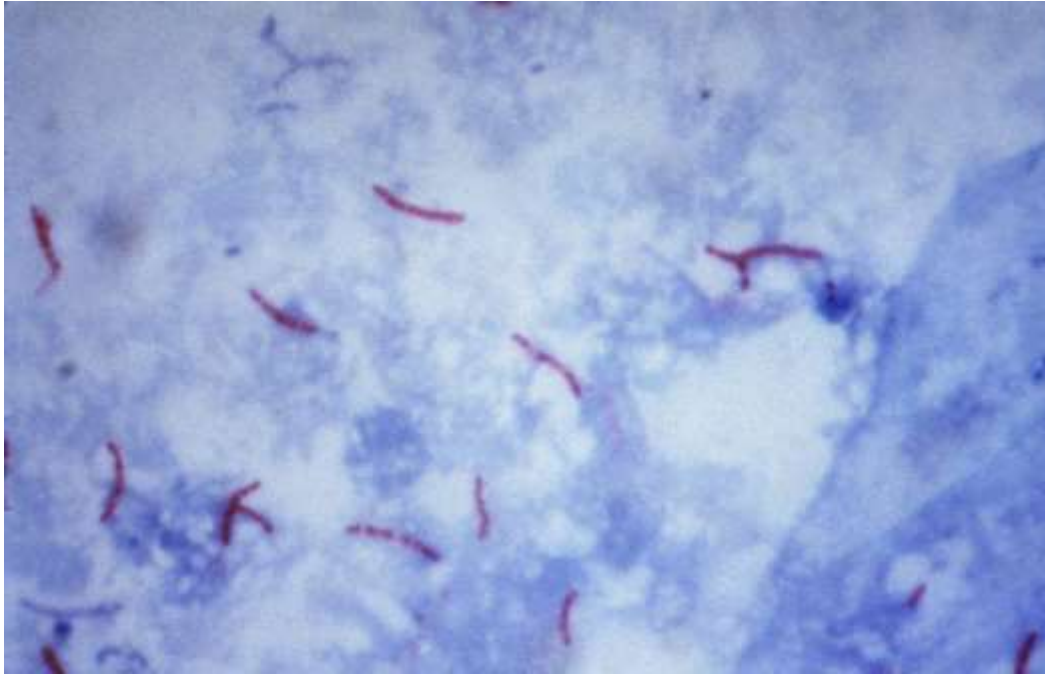


*Caseating
Granuloma!*



Granuloma structure





most common
cause of
Caseating
granuloma

← M.tuberculosis
↳ Ziehl neelsen
Stain

foreign bodies
↳ Polarized
microscope



Fat necrosis

→ Lipase enzyme

↳ Acute pancreatitis

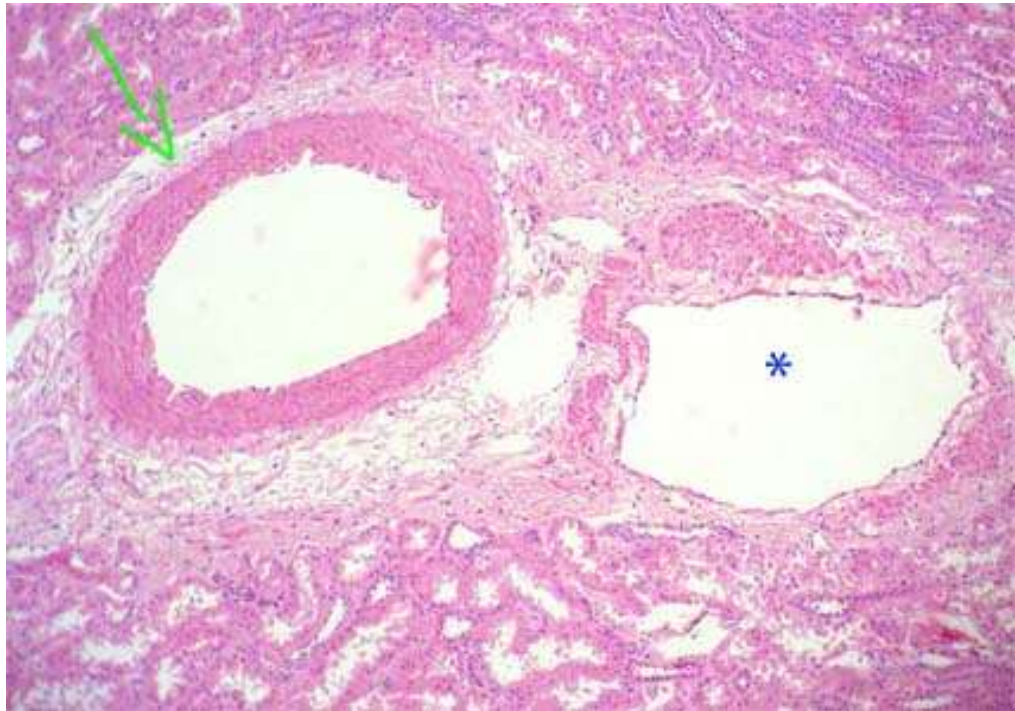


* fatty acids bind and precipitate calcium ions, forming insoluble salts. *"Chalky appearance"* * foamy macrophages adjacent to adipose tissue

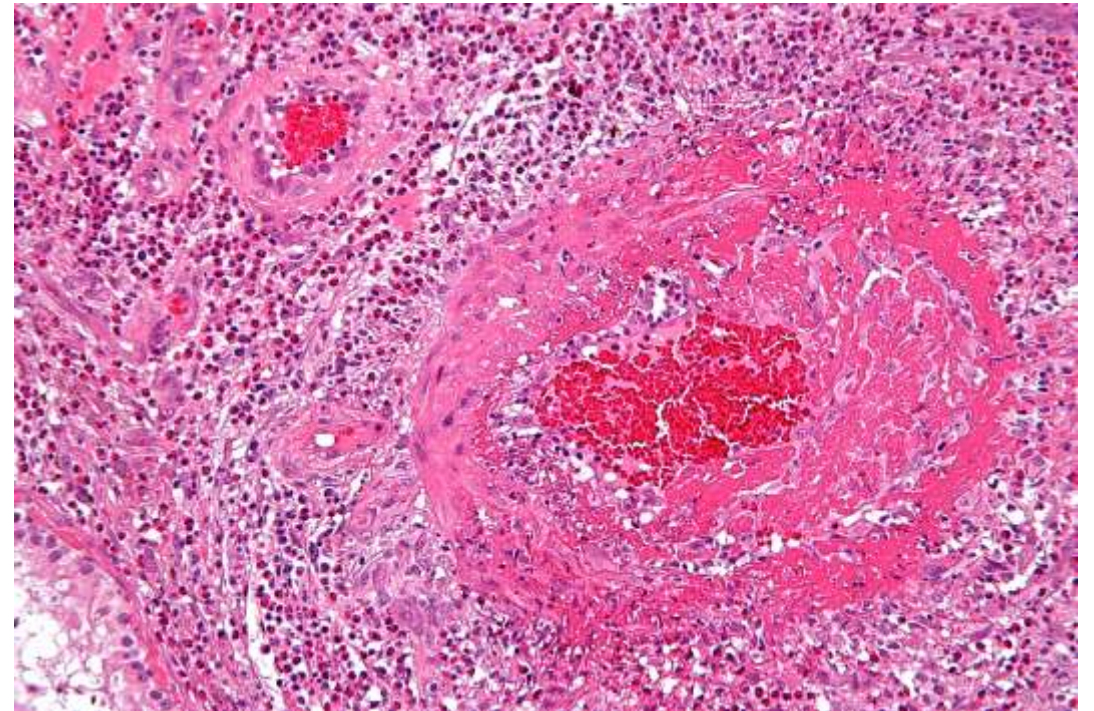


Fibrinoid necrosis

↳ in HTN Patients
↳ Ag-Ab complex with fibrin



Normal B.V



Fibrinoid necrosis



Reactions of Blood Vessels in Acute Inflammation

- Vasodilation:

- induced by histamine, acting on vascular smooth muscle
- first involves the arterioles and then leads to the opening of new capillary beds in the area.
- The result is increased blood flow, which is the cause of heat and redness (erythema) at the site of inflammation.



- Edema
- Edema denotes an excess of fluid in the interstitial tissue or serous cavities.



Lymphangitis and lymphadenitis.



- This streaking follows the course of the lymphatic channels and indicates the presence of lymphangitis

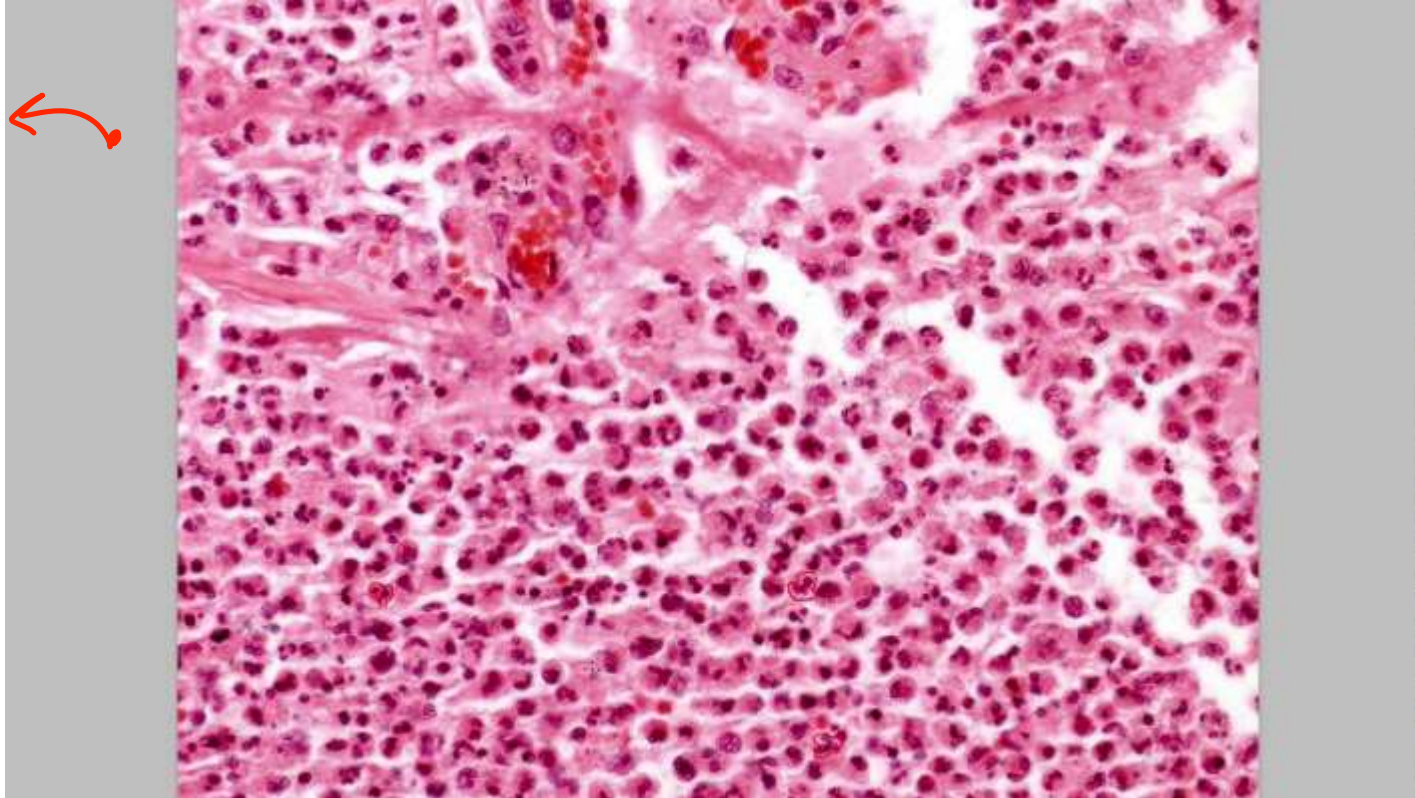


- painful enlargement of the draining lymph nodes, indicating lymphadenitis.



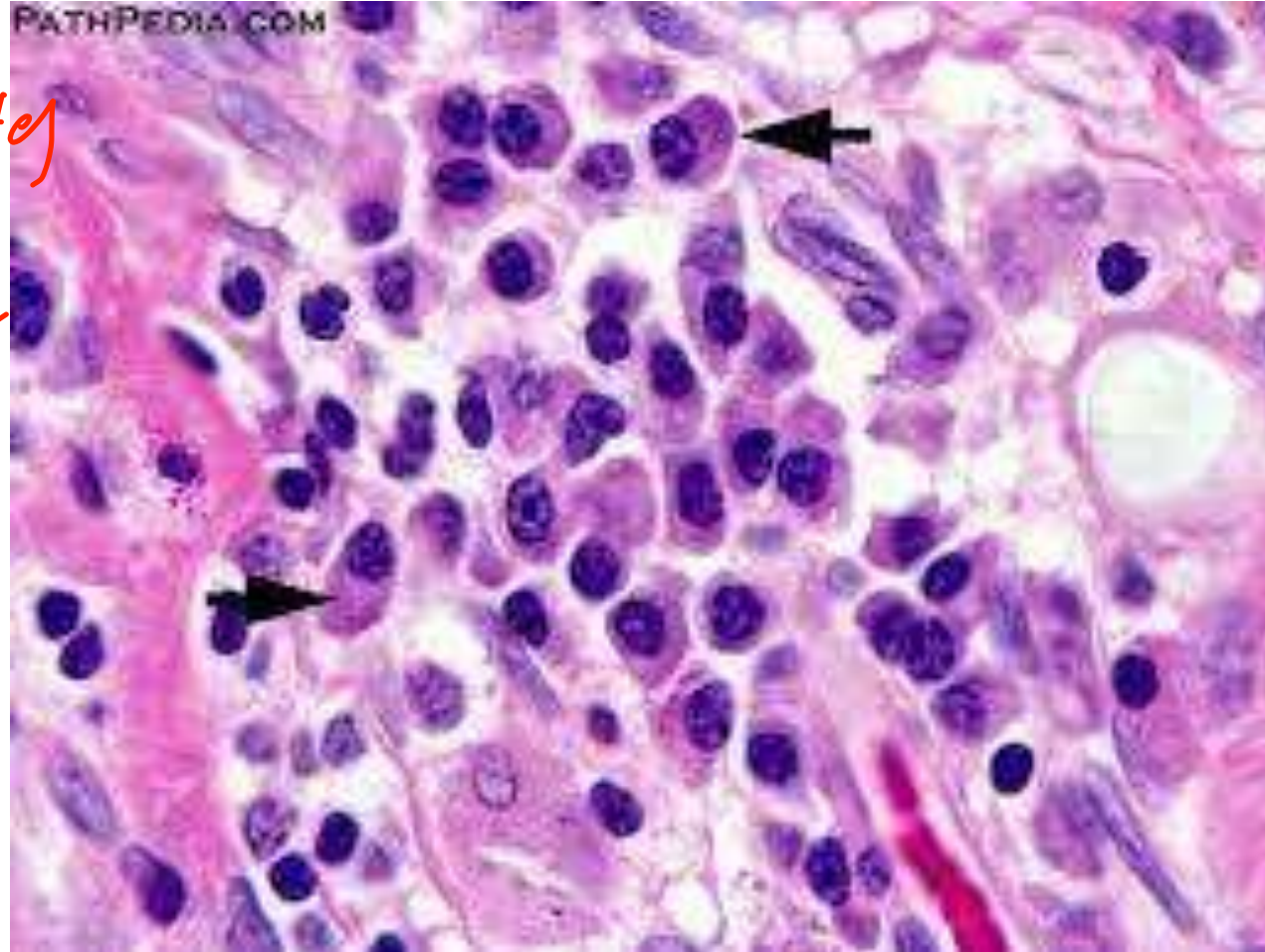
Acute inflammation

Neutrophils
Are the
dominant
cells



Chronic inflammation

Plasma lymphocytes
&
macrophages



cachexia

- Pathologic state characterized by weight loss, muscle atrophy, and anorexia that accompanies some chronic infections and cancers. Explained by sustained production of TNF.



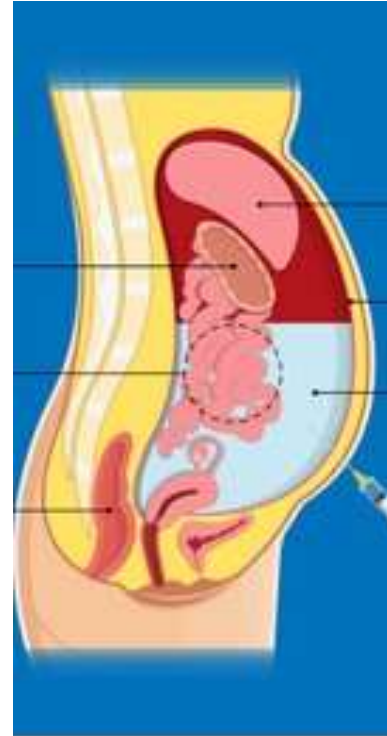
❖ Peritoneal effusion an example of serous inflammation

Clinical
name
↳ Ascites



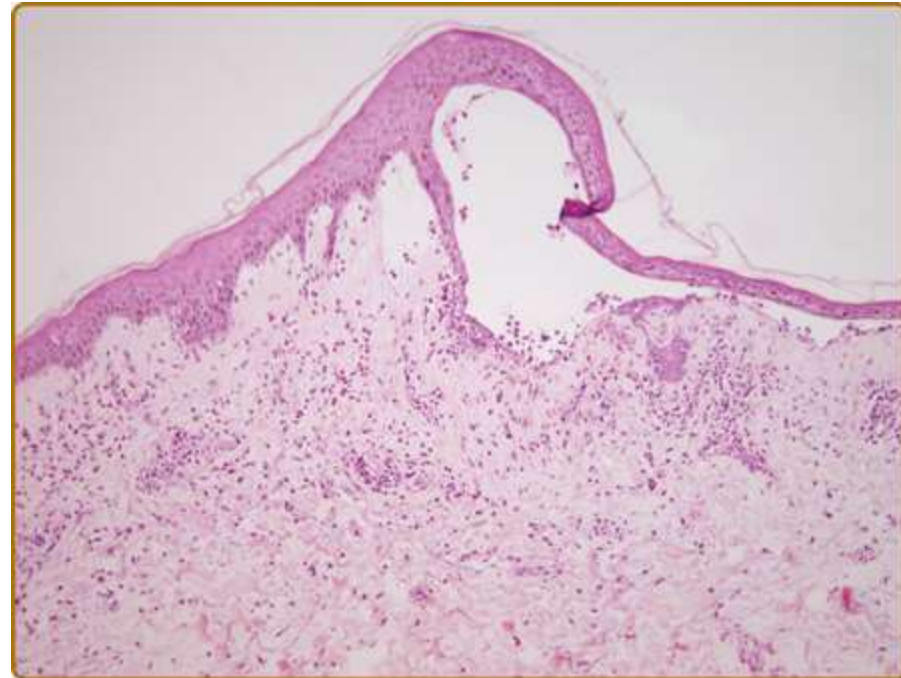
*Sterile → doesn't
contain organisms
nor Leukocytes

لهذا لان زلاله
ما فيه اسي



❖ skin blister

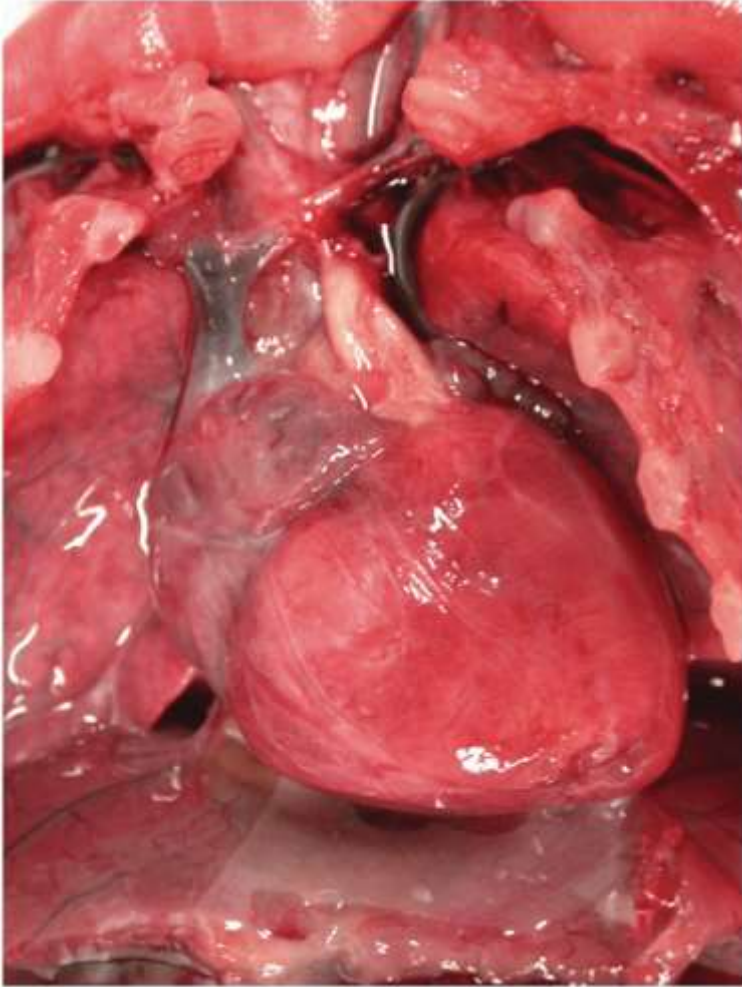
- Resulting from a burn or viral infection.
- Represents accumulation of serous fluid within or immediately beneath the damaged epidermis of the skin



*Between
Dermis
&
Epidermis*



❖ Fibrinous inflammation: → ↑ *Vascular Permeability*
Grossly *Fibrinogen → Fibrin*

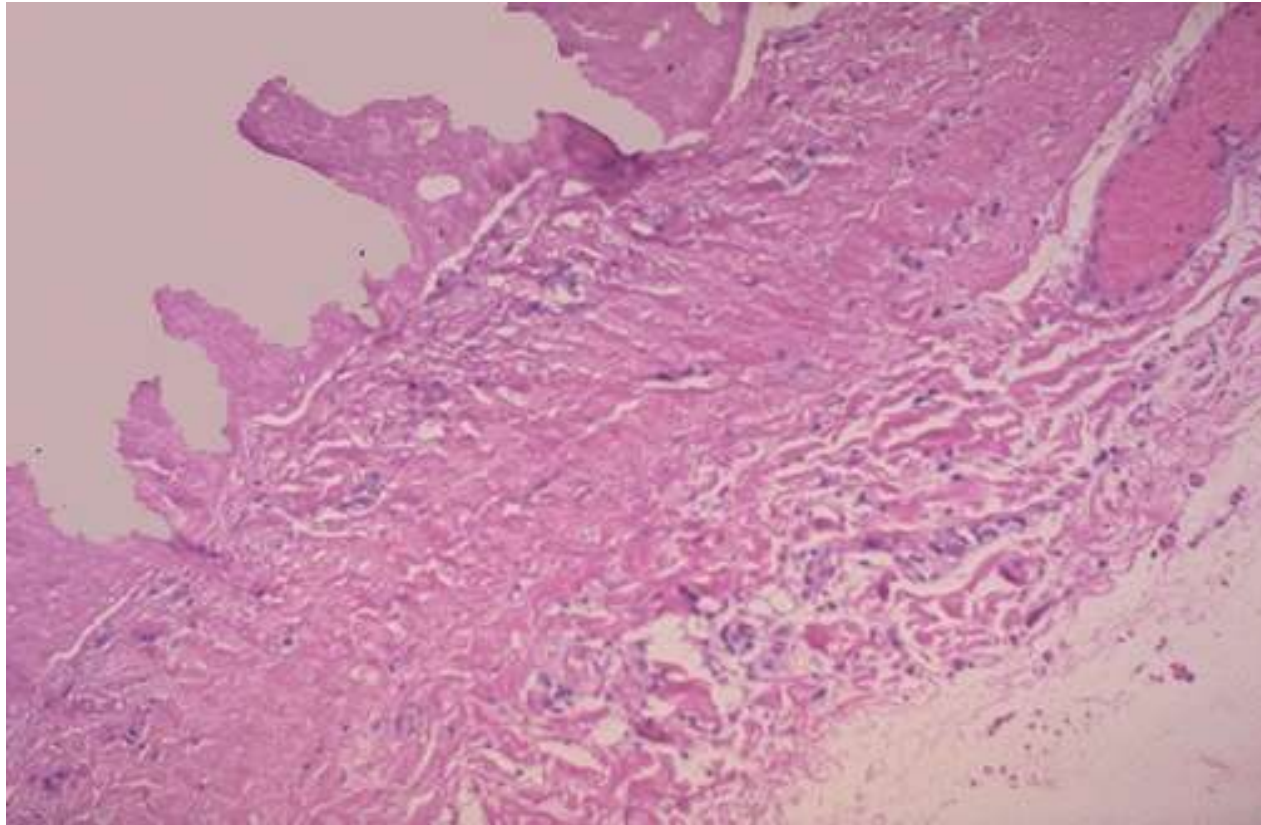


Normally, the visceral pericardium is translucent



The pericardial surface is dry with a coarse granular appearance caused by fibrinous exudate





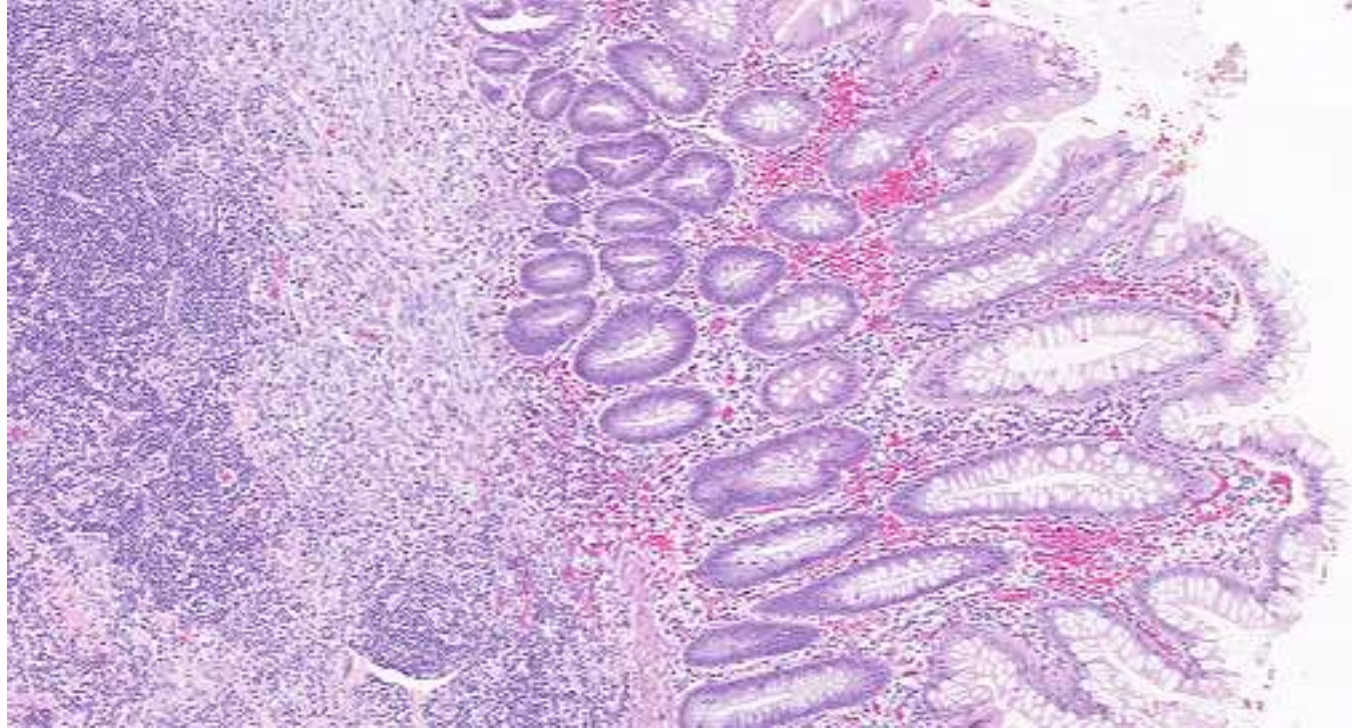
the pericardial surface here shows strands of pink fibrin extending outward. There is underlying inflammation.
fibrin appears as an eosinophilic meshwork of threads



A common example of an acute suppurative inflammation is acute appendicitis



Acute appendicitis



Acute inflammation with predominance of neutrophils; involves some or all layers of the appendiceal wall.



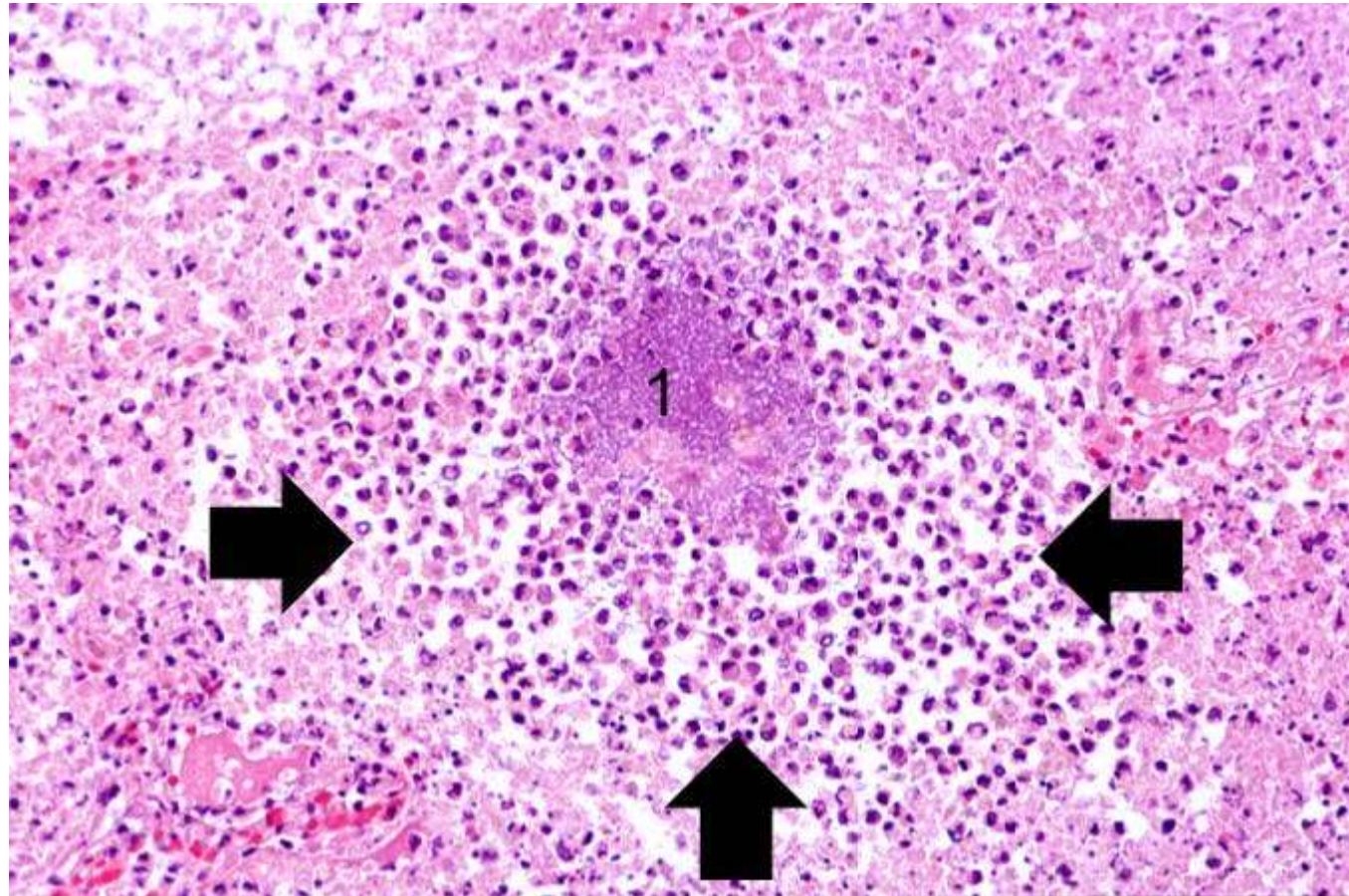
- Abscesses:

- Localized collections of pus caused by suppurative inflammation buried in a tissue, an organ, or a confined space.
- They are produced by seeding of pyogenic bacteria into a tissue . In time the abscess may become walled off and ultimately replaced by connective tissue



Abscesses have multiple areas:

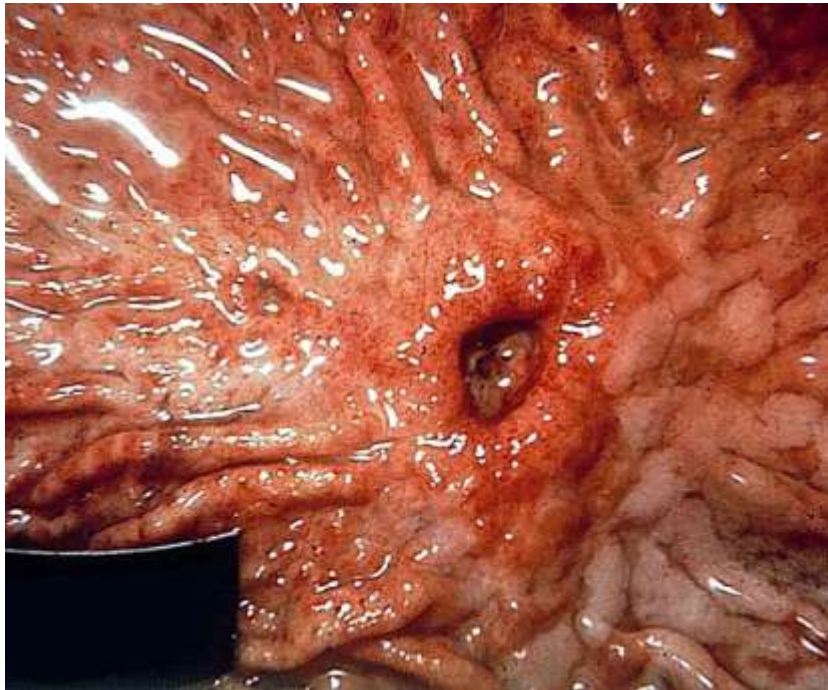
- * central region with necrotic leukocytes and tissue cells.
- * zone of preserved neutrophils around this necrotic focus.
- *vascular dilation, parenchymal and fibroblastic proliferation.



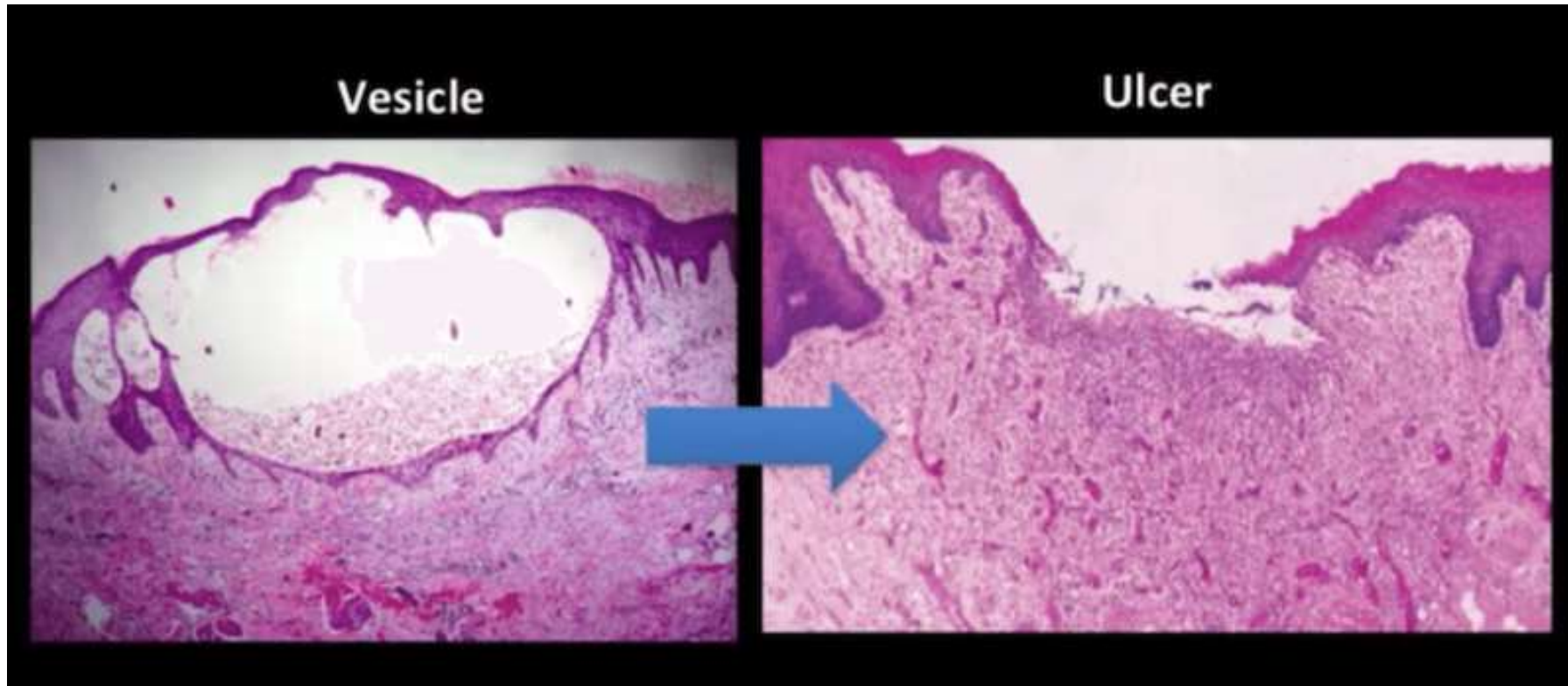
ulcer

- It is most commonly encountered in:
 - (1) the mucosa of the mouth, stomach, intestines, or genitourinary tract.
 - (2) the skin and subcutaneous tissue of the lower extremities in older persons

Stomach
↪



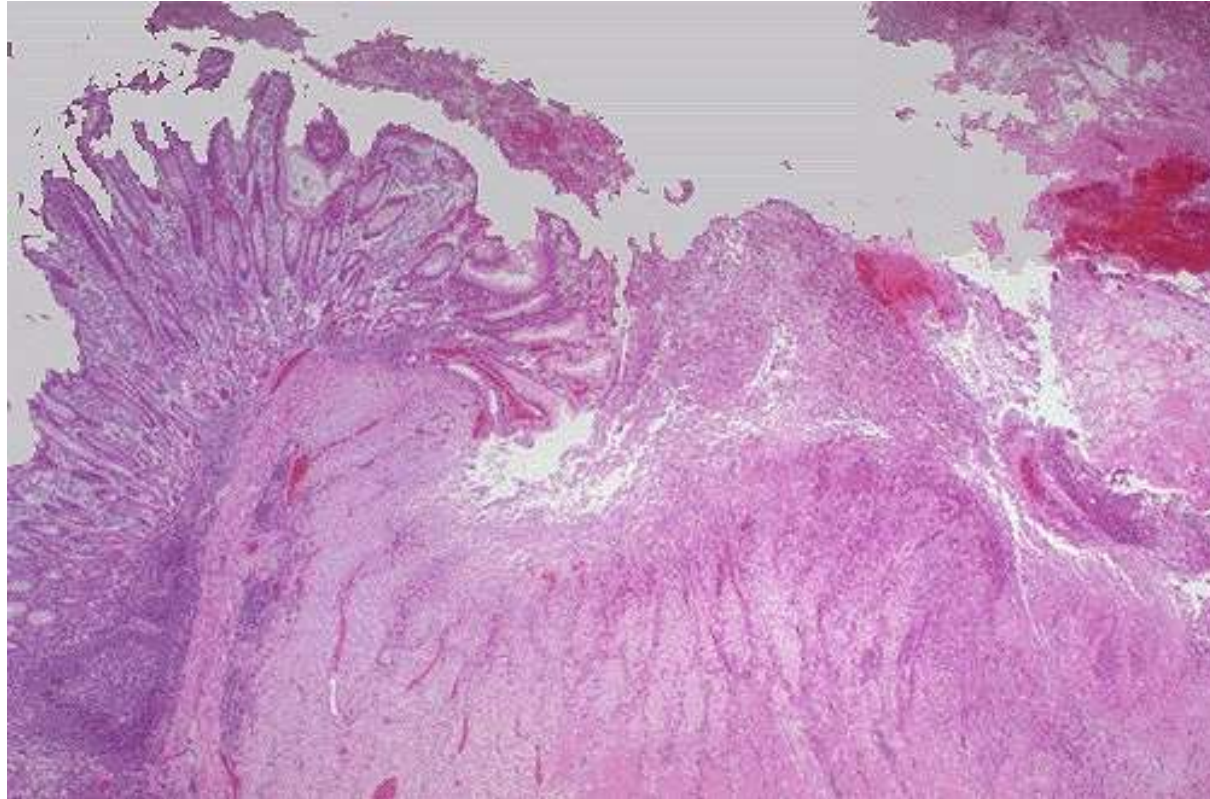
histology



sloughing (shedding) of inflamed necrotic tissue



Microscopic features of Ulcers



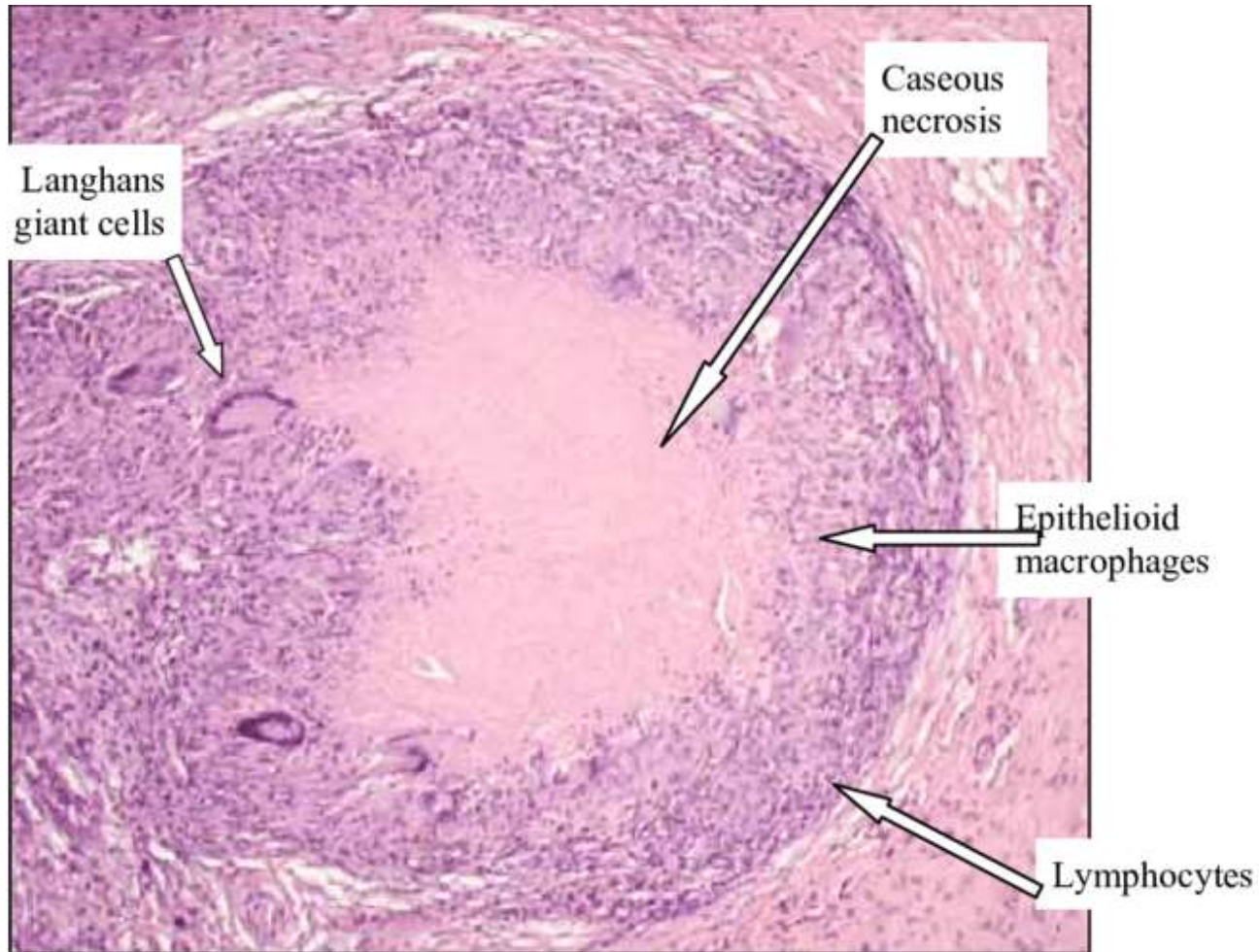
Acute stage:

Intense polymorphonuclear infiltration and vascular dilation in the margins of the defect.

With chronicity:

the margins and base of the ulcer develop fibroblast proliferation, scarring, and the accumulation of lymphocytes, macrophages, and plasma cells.





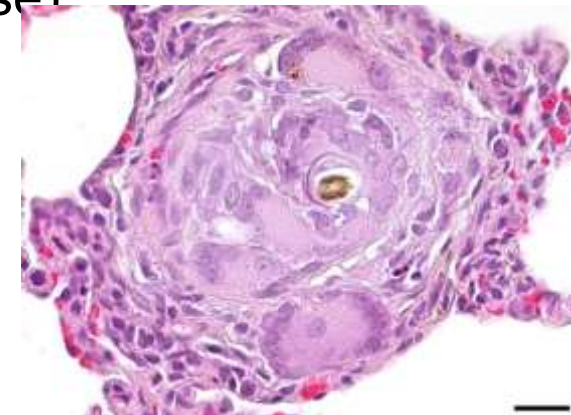
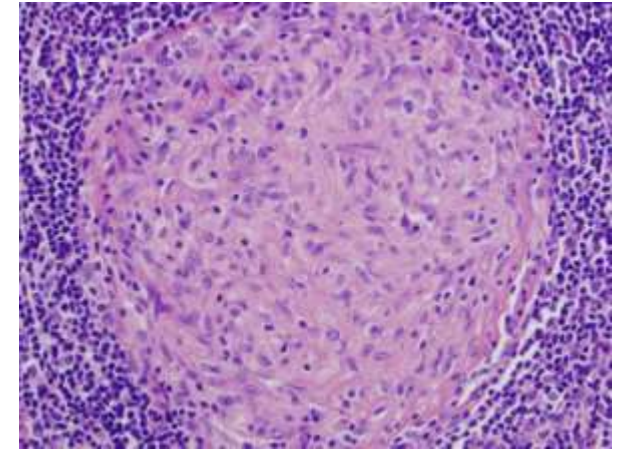
What?
Where??

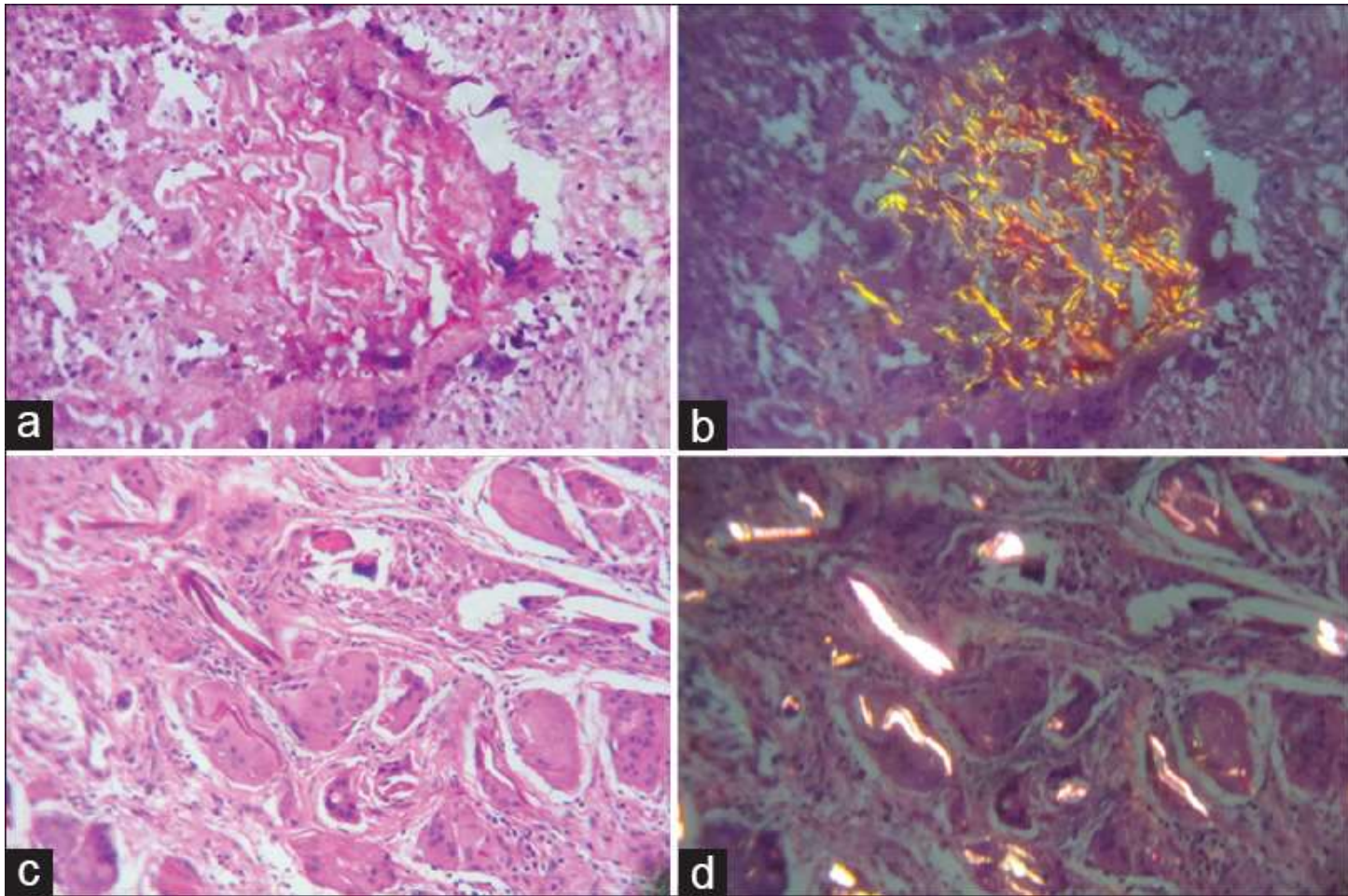
TB



Types of granulomas:

- 1. Immune granulomas:
 - caused by persistent T cell–mediated immune response.
 - when the inciting agent cannot be readily eliminated.
- **2. Foreign body granulomas:**
 - seen in response to inert foreign bodies, in the absence of T cell– mediated immune responses.
 - May form around materials such as talc (associated with intravenous drug abuse), sutures, or other fibers





The foreign material can usually be identified in the center of the granuloma, particularly if viewed with polarized light, in which it may appear refractile.





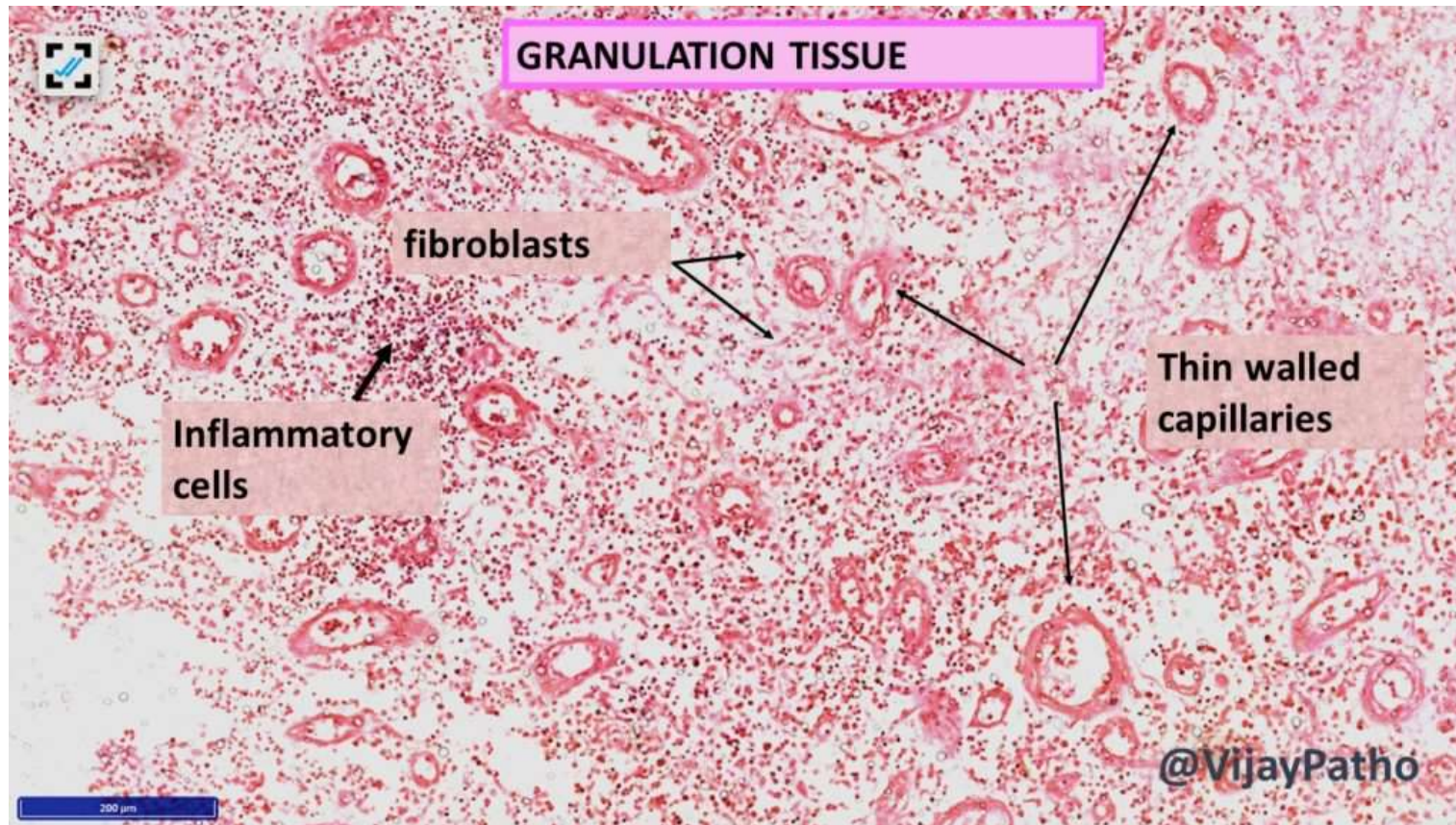
The term [scar](#) is most used in connection to wound healing in the skin.



Replacement of parenchymal cells in any tissue by collagen, as in the heart after myocardial infarction.



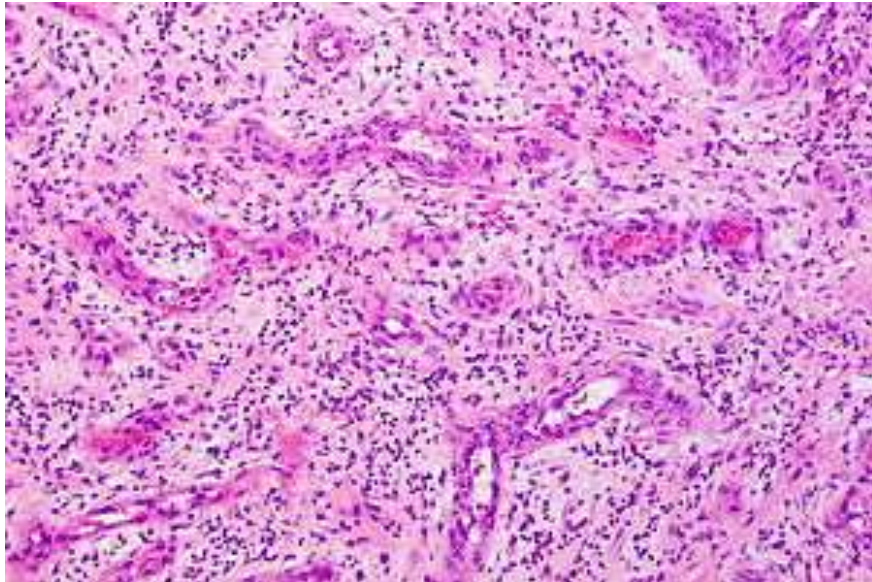
- The combination of proliferating fibroblasts, loose connective tissue, new blood vessels and scattered chronic inflammatory cells, forms a granulation tissue.





Granulation tissue.

pink, soft, granular gross appearance, such as that seen beneath the scab of a skin wound.



proliferating fibroblasts, loose connective tissue, new blood vessels and scattered chronic inflammatory cells



- 1. Venous leg ulcers:

- Seen in elderly people as a result of chronic venous hypertension, which may be caused by severe varicose veins or congestive heart failure.
- These ulcers fail to heal because of poor delivery of oxygen to the site of the ulcer.



2. Arterial ulcers:

- develop in individuals with atherosclerosis of peripheral arteries, especially associated with diabetes.

3. Pressure sores :

- are areas of skin ulceration and necrosis of underlying tissues.
- caused by prolonged compression of tissues against a bone, for example, in bedridden. The lesions are caused by mechanical pressure and local ischemia.



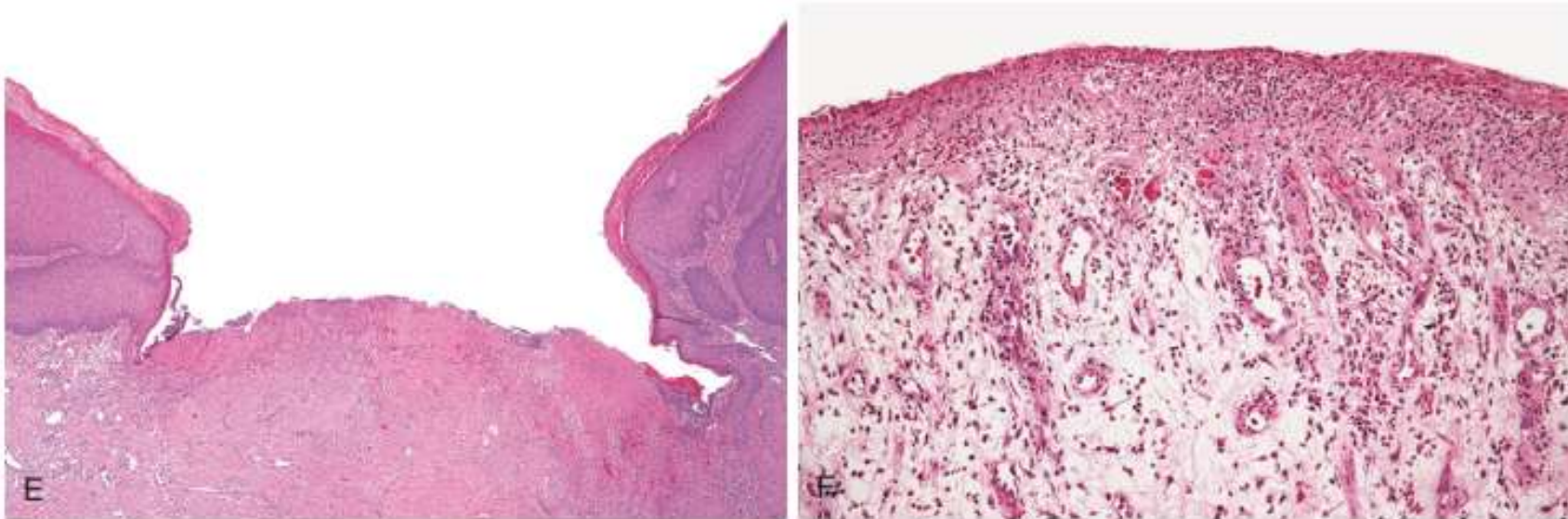
↔ sacrum



4. Diabetic ulcers;

- affect the lower extremities, particularly the feet. Tissue necrosis and failure to heal are the result of small vessel disease causing ischemia, neuropathy, systemic metabolic abnormalities, and secondary infections.





epithelial ulceration and extensive granulation tissue in the underlying dermis



5. wound rupture (dehiscence):

- occurs most frequently after abdominal surgery and is a result of increased abdominal pressure, such as may occur with vomiting or coughing.



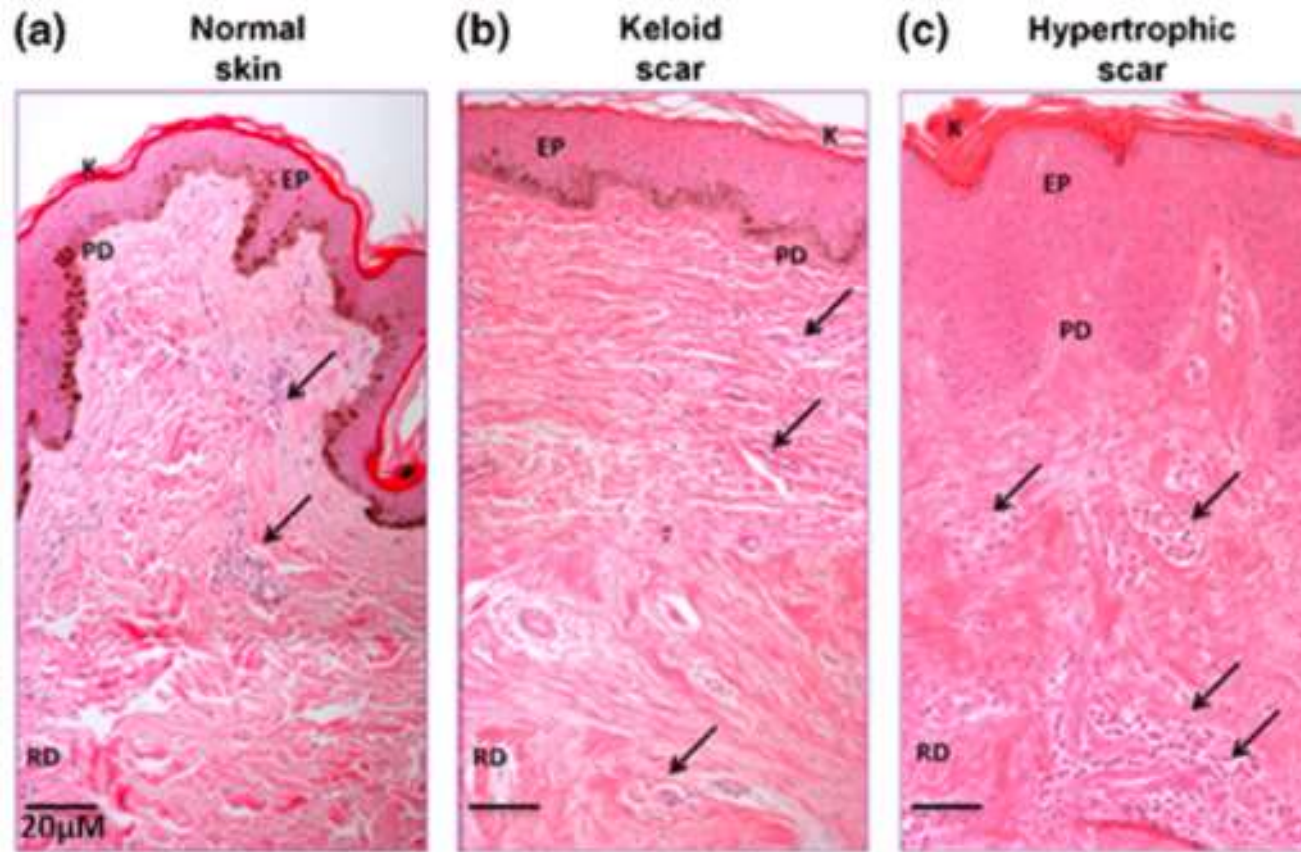


✓ hypertrophic scar.



- keloid:
- It is a hypertrophic scar that grows beyond the boundaries of the original wound and does not regress.





A. In normal skin, the characteristic random orientation and bundle formation of collagen fibres

B. increased number of thick collagen fibres arranged in bundles

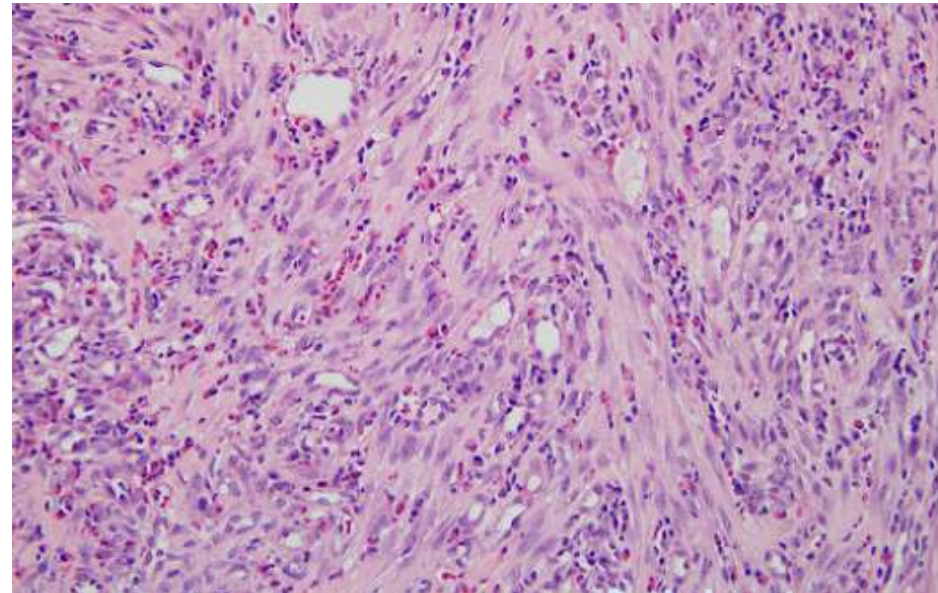
C. The collagen fibres were arranged randomly and showed highly cellular zones

→ حقیقی Bundle



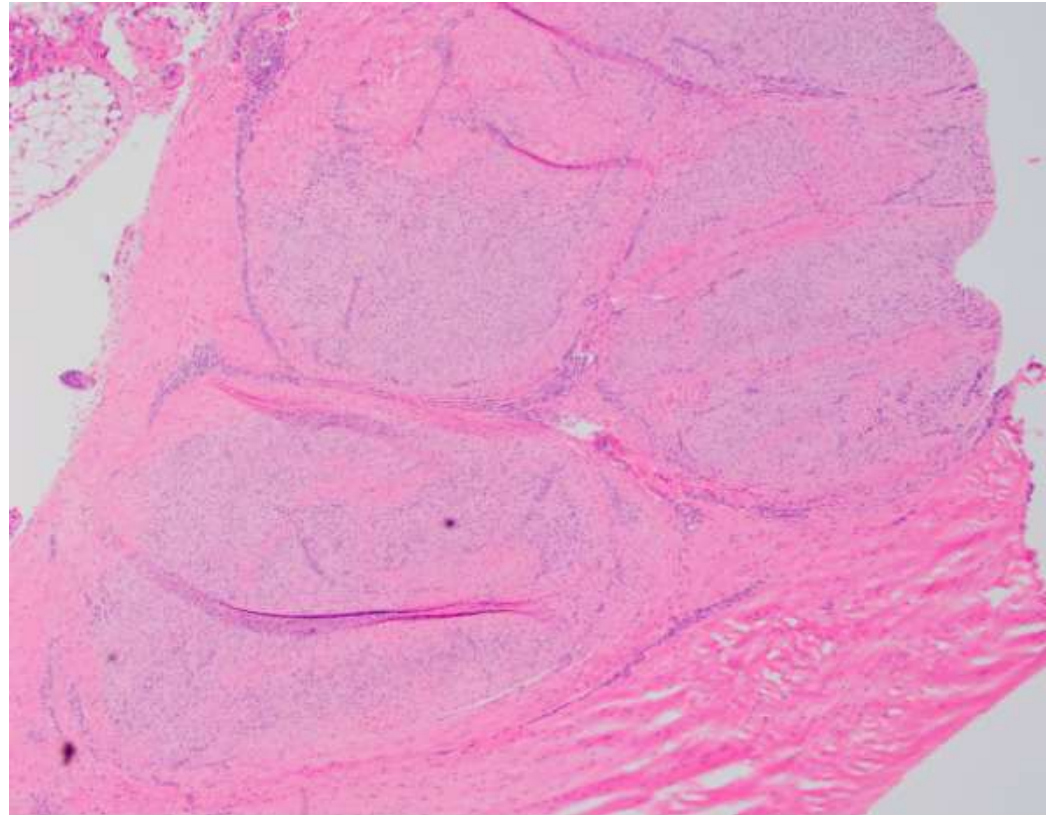
Exuberant granulation

- formation of excessive amounts of granulation tissue, which protrudes above the level of the surrounding skin and blocks reepithelialization .



*Replacing the elastic tissue
with an inelastic tissue

contracture

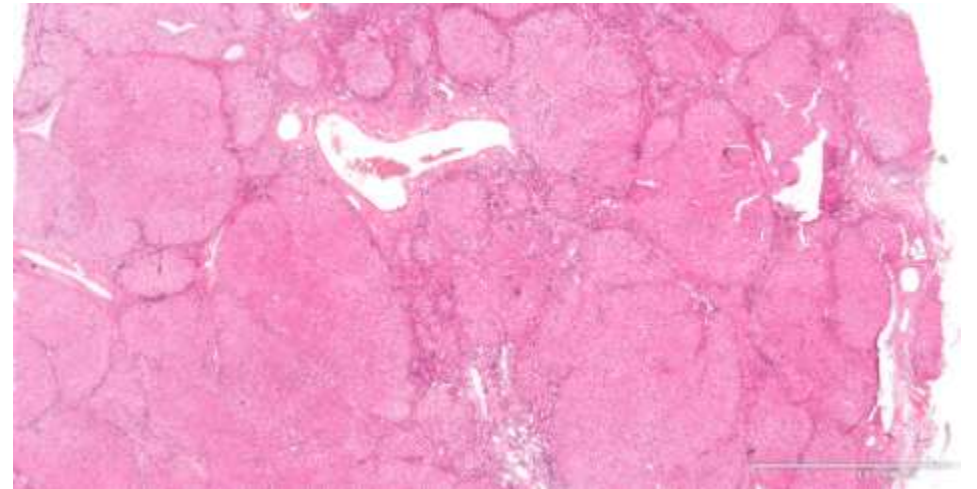


Nodule formation:
Composed of spindle cells (myofibroblasts and fibroblasts)
with dense collagen.



Examples of Fibrotic parenchymal disorders

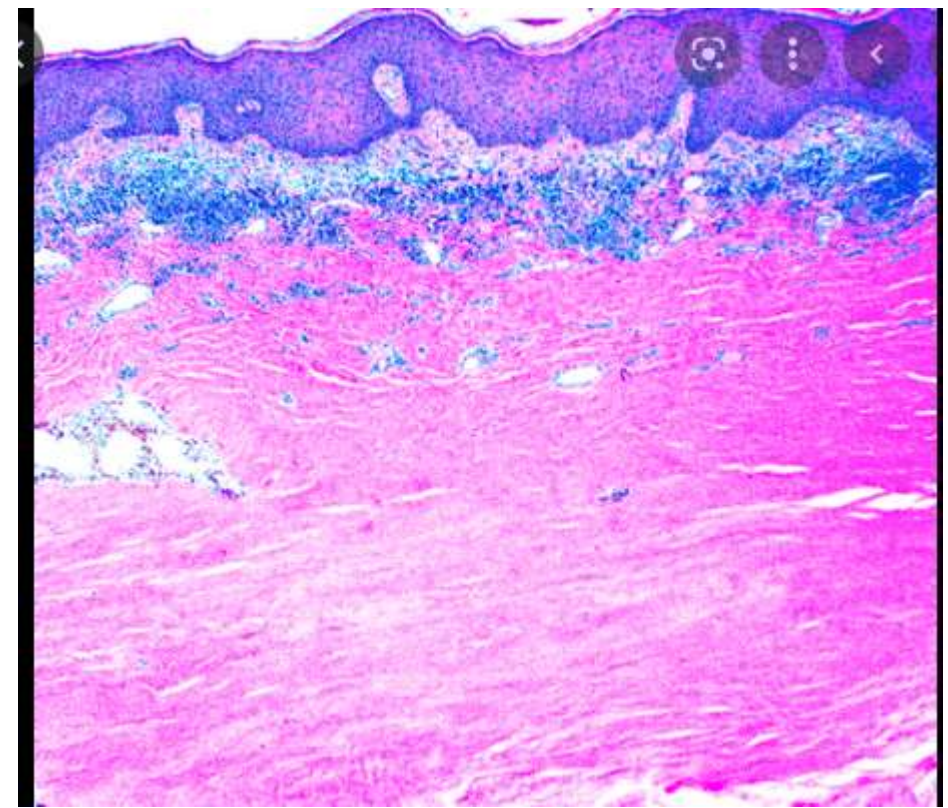
- 1. liver cirrhosis.



2. systemic sclerosis (scleroderma).

* impairment of movement
in joint & skin

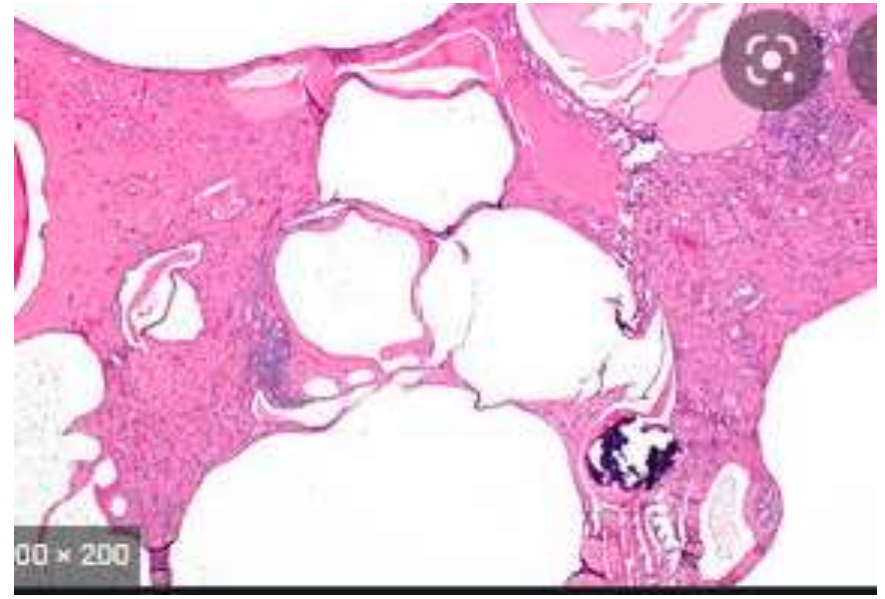
* Excess Collagen in Dermis



3. end-stage kidney disease.

* Replacement of Renal Parenchyma by fibrosis

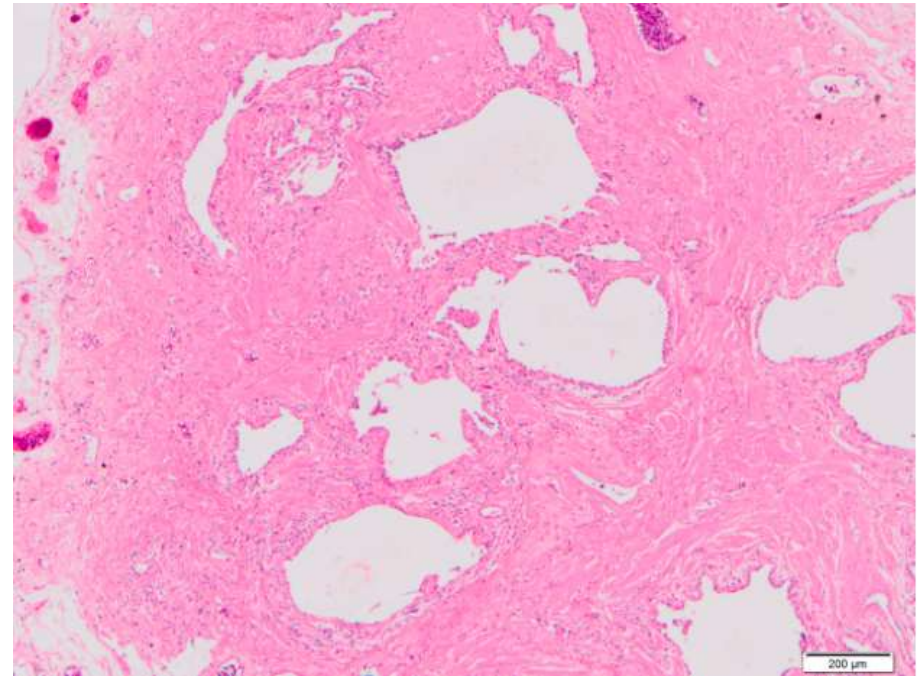
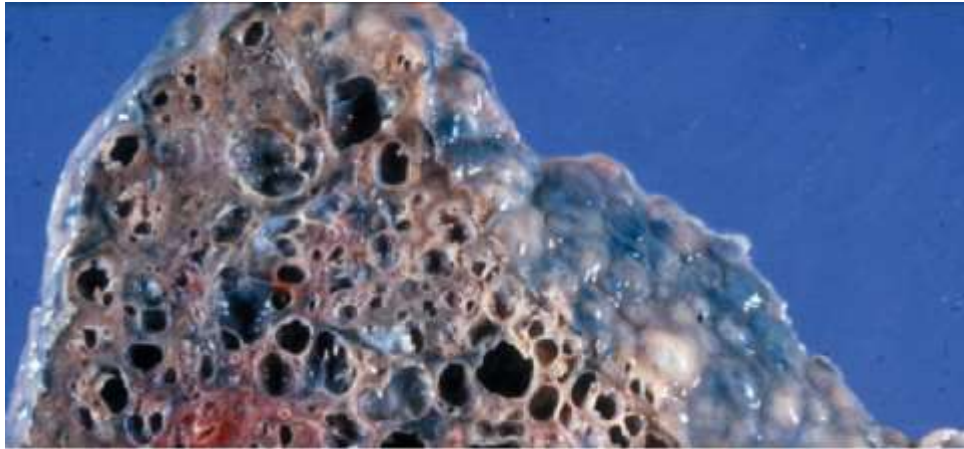
⇒ Renal Failure



❖ fibrosing diseases of the lung.

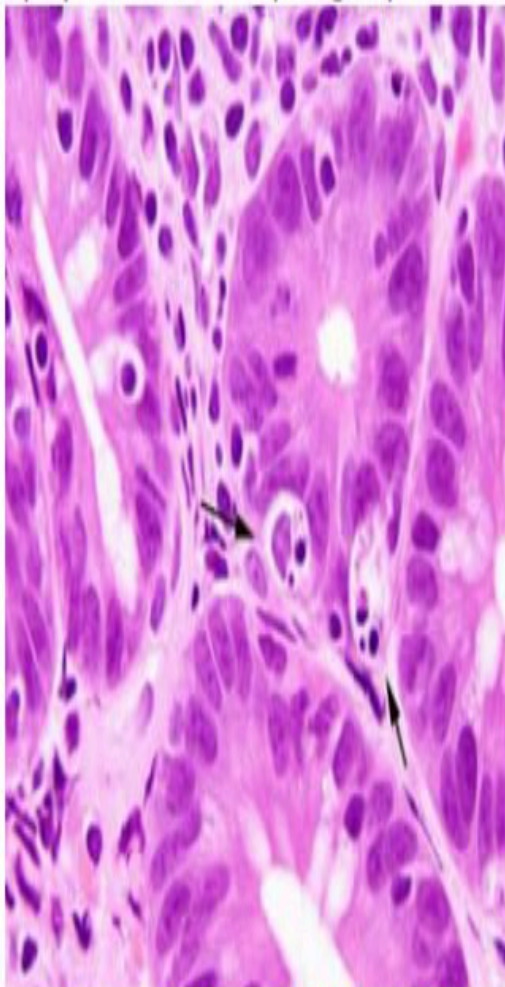
Grossly: Honeycomb, Cystic spaces with fibrotic wall

Histology: cystic spaces lined by bronchiolar epithelium and fibrotic wall

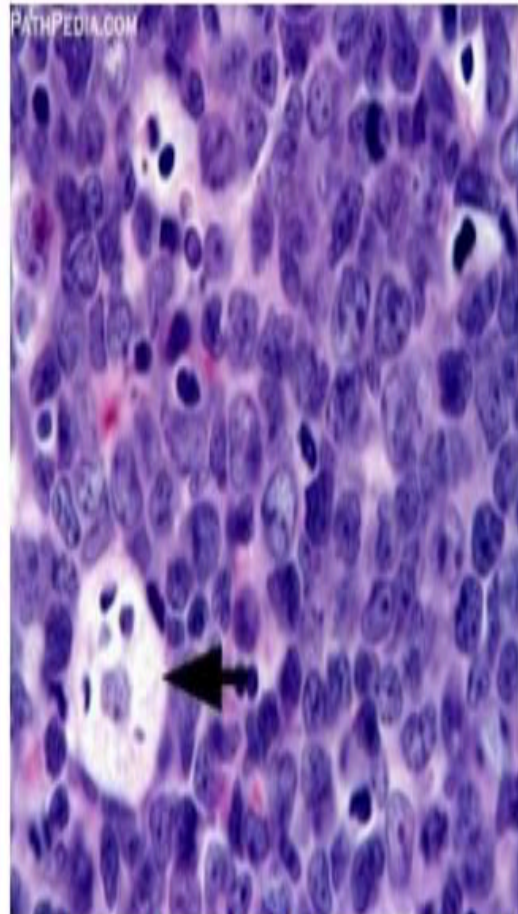


Morphology:

1. Involves single cells or small clusters
2. Cells shrink rapidly, retain intact plasma membrane
3. Formation of cytoplasmic buds
4. Fragmentation into apoptotic bodies
5. Apoptotic bodies phagocytized rapidly before inflammatory response

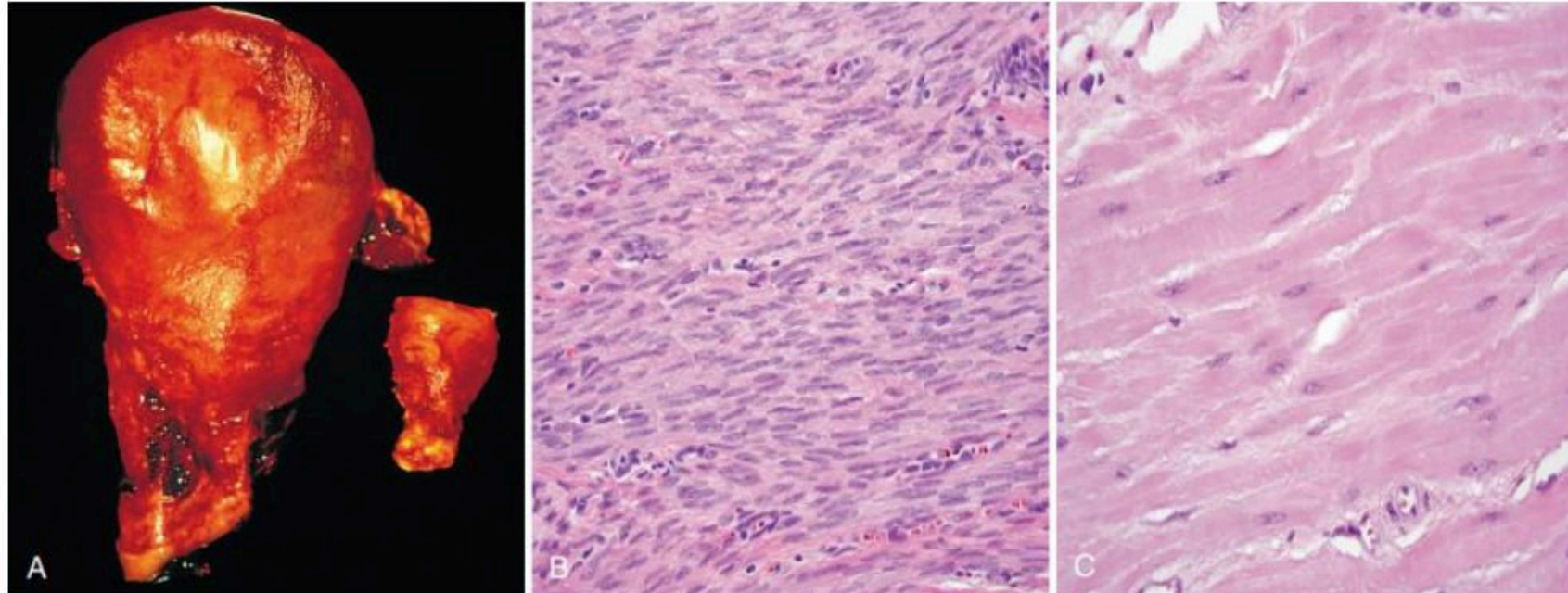


• Intestinal epithelial cells



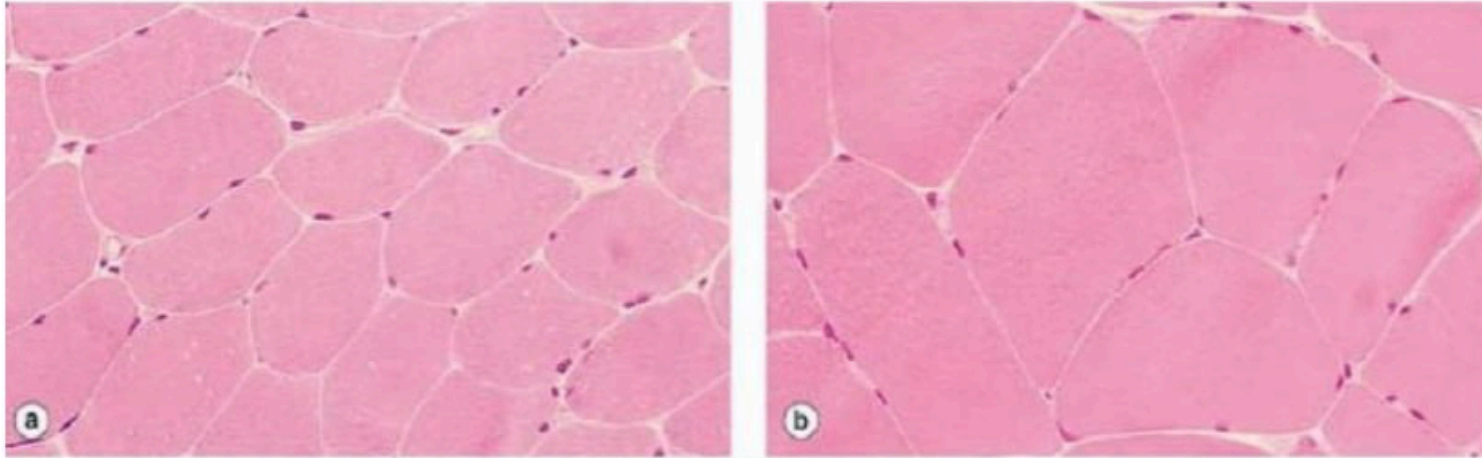
• Lymph node → Macrophage

A. Physiologic-Hypertrophy-Stimulation



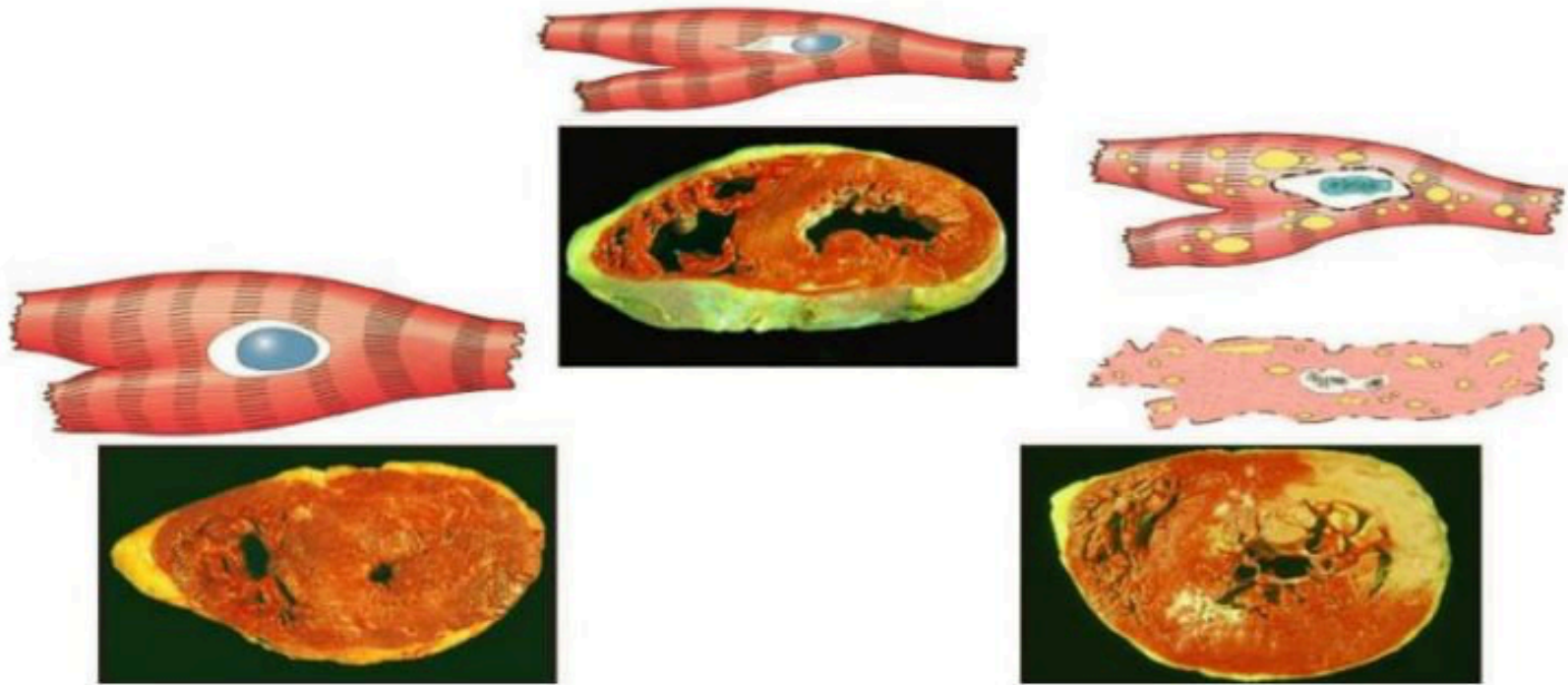
- Physiologic hypertrophy of the uterus during pregnancy. (A) Gross appearance of a normal uterus (right) and a gravid uterus (removed for postpartum bleeding) (left). (B) Small spindle-shaped uterine smooth muscle cells from a normal uterus, compared with (C) large plump cells from the gravid uterus, at the same magnification. – Robbins.

A. Physiologic-Hypertrophy- ↑ Demand



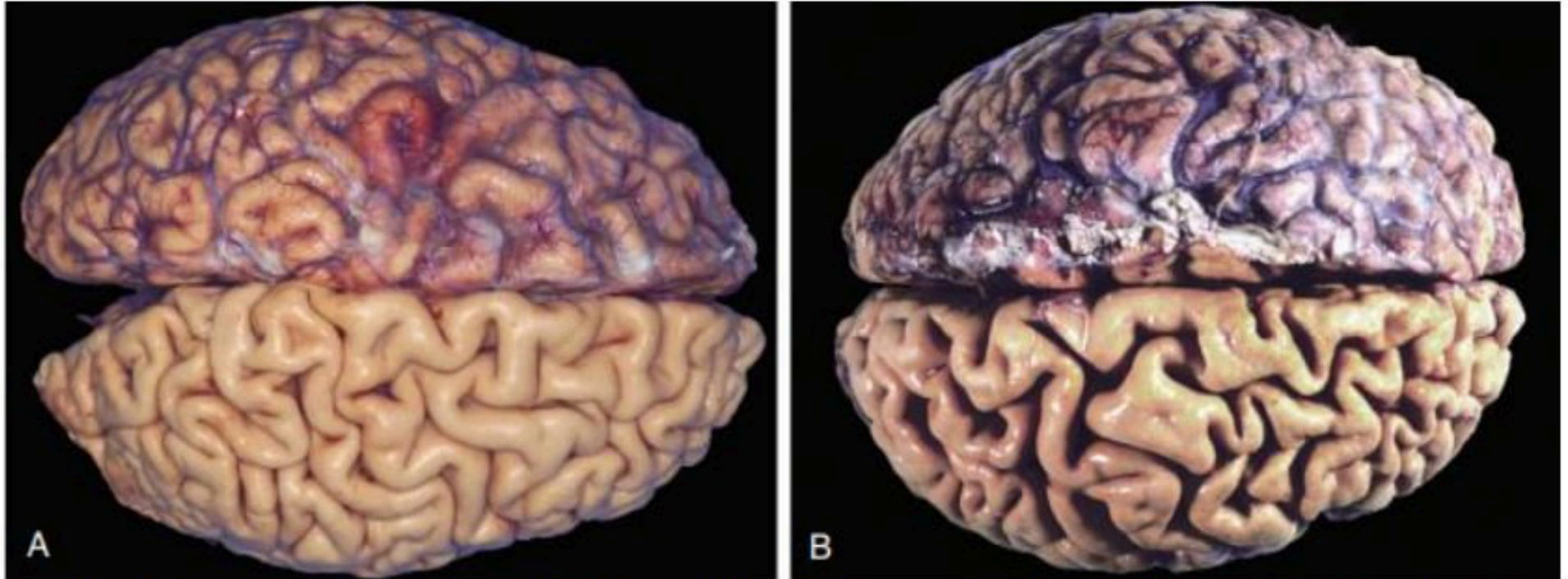
Stevens et al: Core Pathology, 3rd Edition.
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- Hypertrophy of skeletal muscle In response to exercise. Hypertrophy In the absence of hyperplasia is typically seen In muscle where the stimulus Is an increased demand for work. Taken at the same magnification, (a) shows muscle fibers in transverse section from the soleus muscle of a normal 50 year old man, and (b) shows fibers from the same muscle in a veteran marathon runner.
- Note the dramatic increase in the size of the fibers In response to the demands of marathon running.

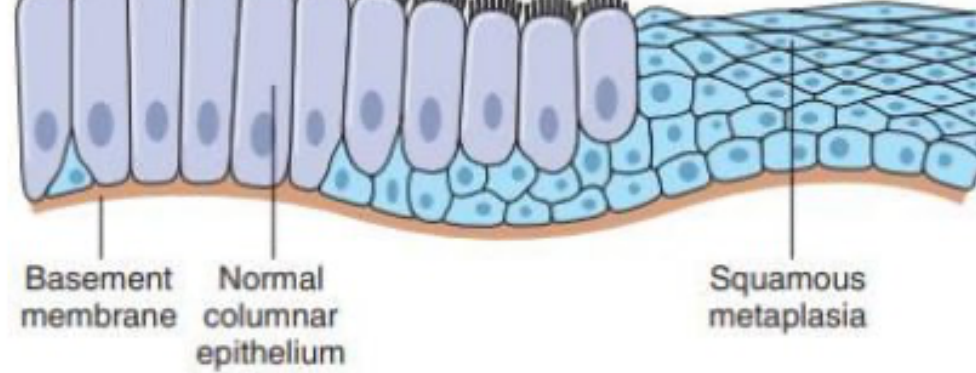


Hypertrophy - pathologic - ↑ demand

In response to increased workload (hypertension or aortic valve disease) myocardial hypertrophy (lower left → to generate the required higher contractile force → heart undergo **only hypertrophy** because cardiac muscles have a limited capacity to divide.



- Atrophy as seen in the brain. (A) Normal brain of a young adult. (B) Atrophy of the brain in an 82-year-old man with atherosclerotic disease. Atrophy of the brain is caused by aging and reduced blood supply. Note that loss of brain substance narrows the gyri and widens the sulci.
- The meninges have been stripped from the bottom half of each specimen to show the surface of the brain



A

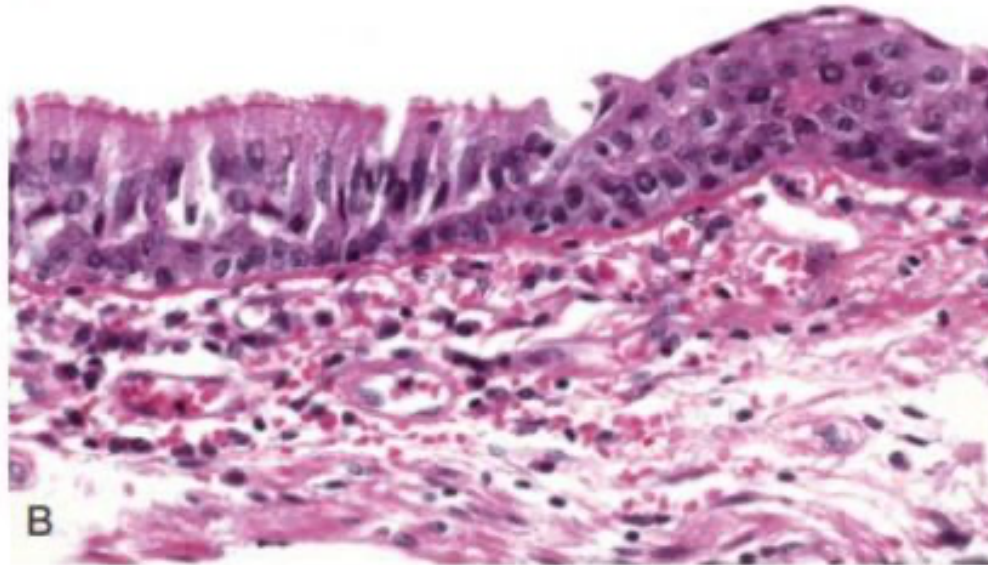
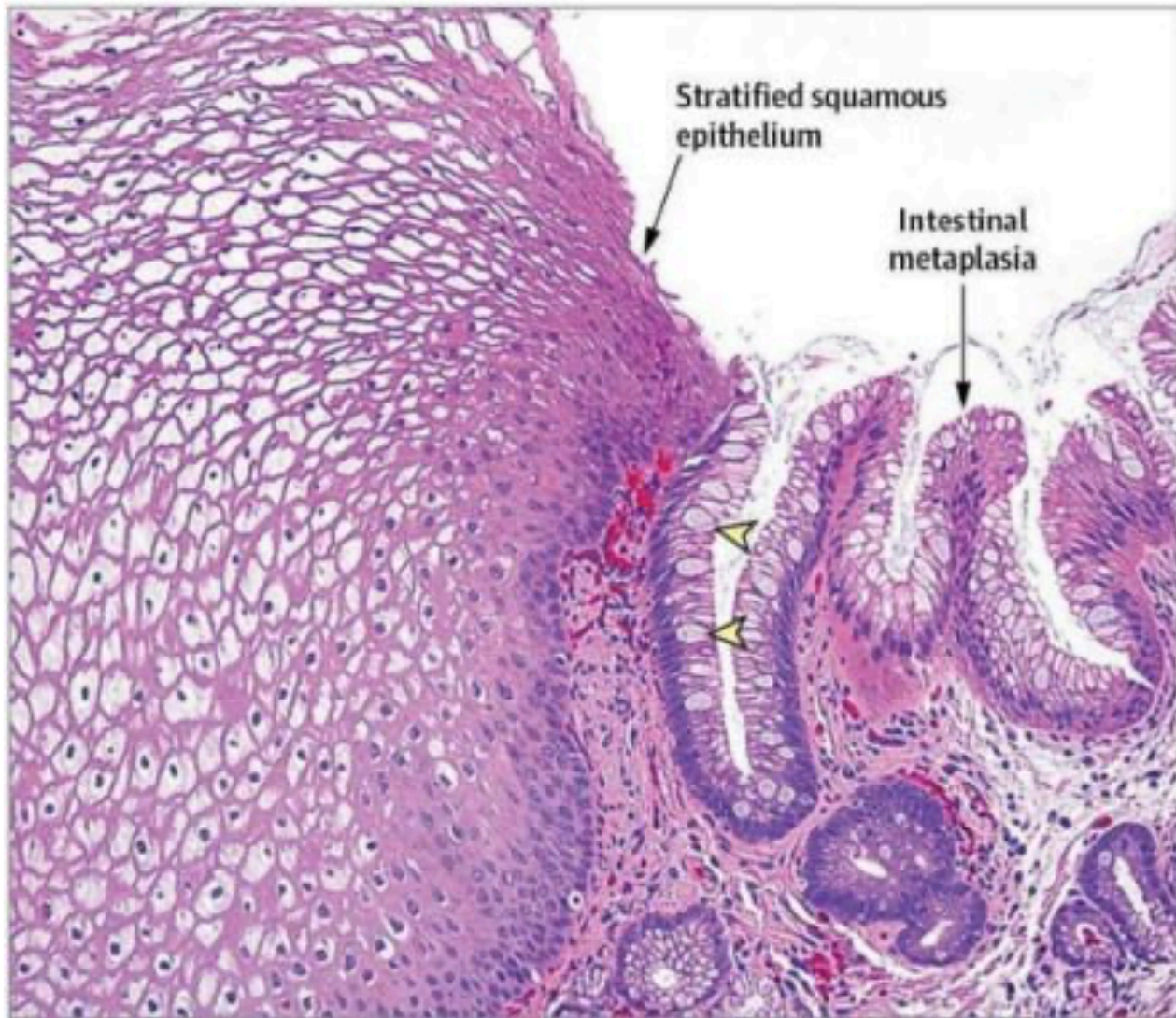
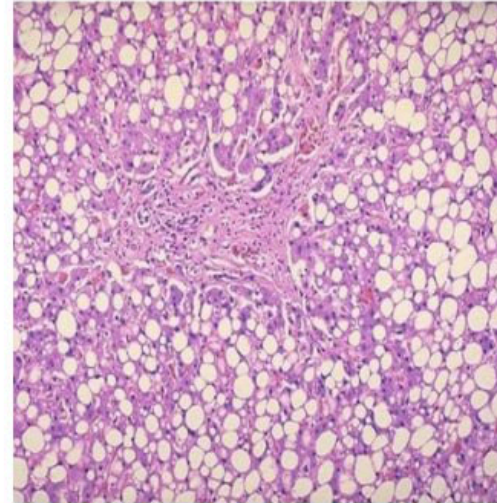


Figure 2.28 Metaplasia of columnar to squamous epithelium. (A) Schematic diagram. (B) Metaplasia of columnar epithelium (*left*) to squamous epithelium (*right*) in a bronchus (as often occurs with smoking).



↳ Lipids → fatty changes

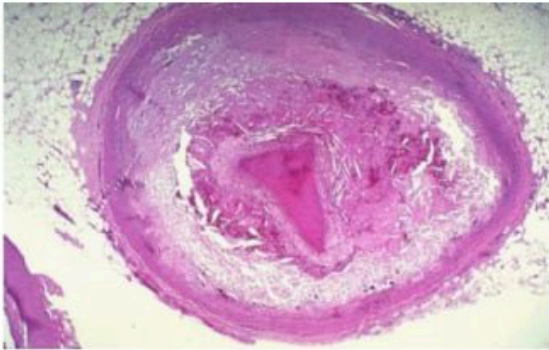
- Fatty change, called **steatosis**.
- Any accumulation of **triglycerides** within parenchymal cells.
- Mostly seen in the liver, (the major organ involved in fat metabolism) , also occur in heart, skeletal muscle, kidney, and other organs.
- Caused by toxins, protein malnutrition, diabetes mellitus, obesity, or anoxia.
- **Alcohol abuse and diabetes associated with obesity are the most common causes of fatty change in the liver.**



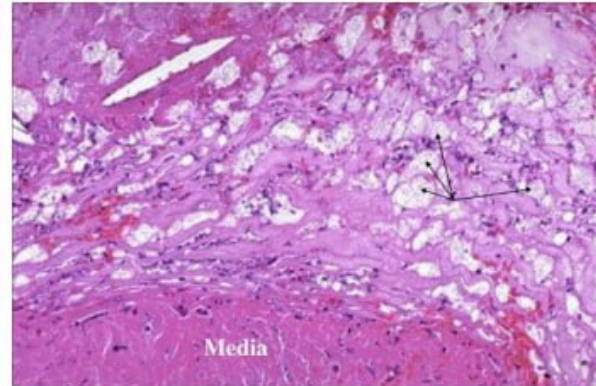
- Clear vacuoles in the cytoplasm displacing the nucleus to the periphery of the cell.

~ Lipids → Cholesterol and Cholesteryl Esters

- Cellular cholesterol metabolism is tightly regulated to ensure normal generation of cell membranes (in which cholesterol is a key component) without accumulation.
- Phagocytic cells may become overloaded in different pathologic processes, mostly increased intake or decreased catabolism of lipids.
- **Atherosclerosis is the most important.**



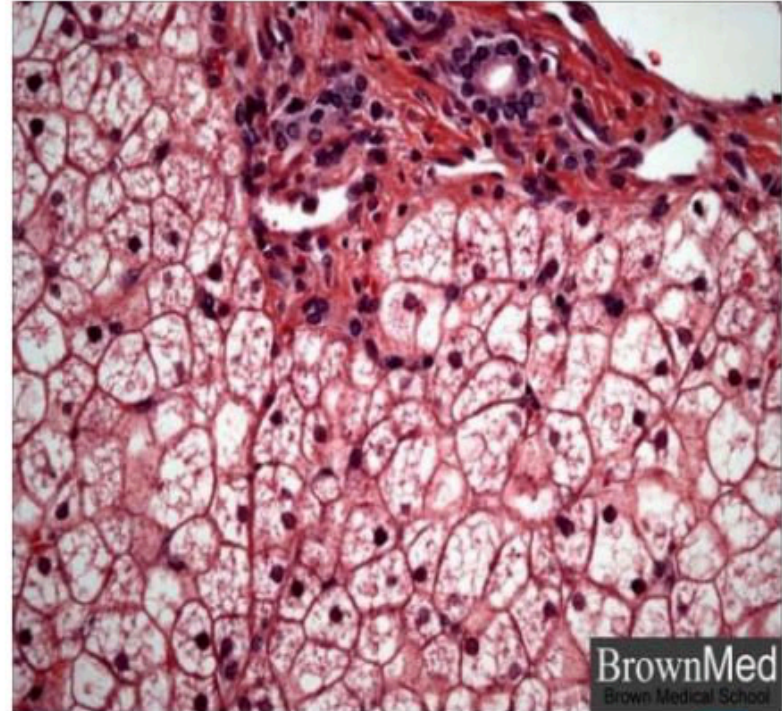
- There is a pink to red recent thrombosis in this narrowed coronary artery. The open, needle-like spaces 'n the atheromatous plaque are cholesterol clefts.



- This high magnification of an atheroma shows numerous foam cells (arrows) and an occasional cholesterol cleft. A few dark blue inflammatory cells are scattered within the atheroma.
-

-w Glycogen

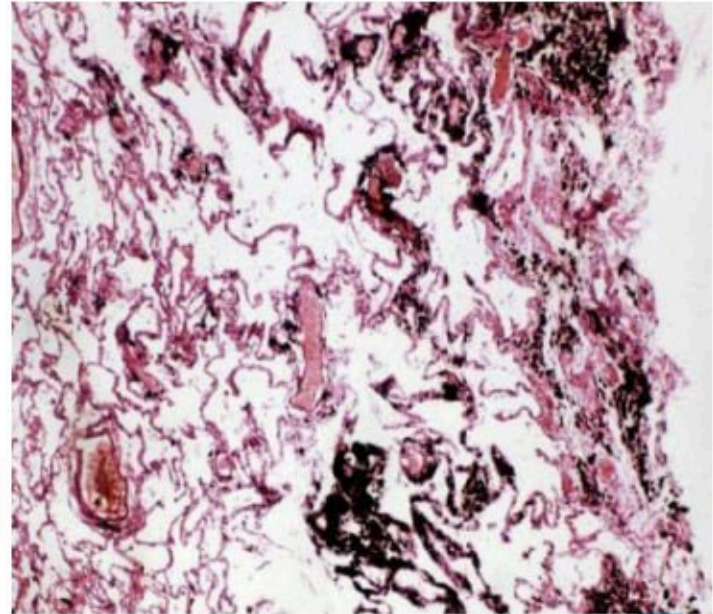
- Excessive intracellular accumulation of glycogen are associated with abnormalities in the metabolism of glucose or glycogen.
- In poorly controlled diabetes mellitus, the prime example of abnormal glucose metabolism, glycogen accumulates in renal tubular epithelium, cardiac myocytes, and β cells of the islets of Langerhans.
- Glycogen also accumulates within cells in a group of related genetic disorders collectively referred to as glycogen storage diseases.



~ Pigments - Carbon

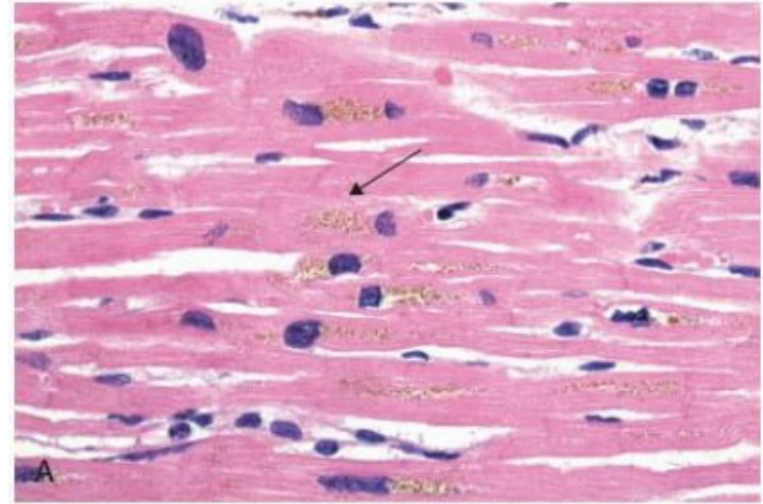


- Pigments are colored substances, they are either exogenous (from outside the body) such as carbon or endogenous (synthesized within the body) itself, such as lipofuscin, melanin, and certain derivatives of hemoglobin.
- The most common exogenous pigment is carbon, a ubiquitous air pollutant of urban life.
- When inhaled → phagocytosed by alveolar macrophages → transported by lymphatic channels to regional lymph nodes.
- Aggregates of the pigment blacken the draining lymph nodes and pulmonary parenchyma (called anthracosis)



~ Pigments - Lipofuscin

- An insoluble brownish-yellow granular intracellular material that accumulates in a variety of tissues (heart, liver, and brain) **with aging or atrophy.**
- Lipofuscin represents complexes of lipid & protein that are produced by the free radical-catalyzed peroxidation of polyunsaturated lipids of subcellular membranes.
- It is **not injurious** to the cell but is a marker of past free radical injury.
- When present in large amounts, imparts an appearance to the tissue that is called **brown atrophy**

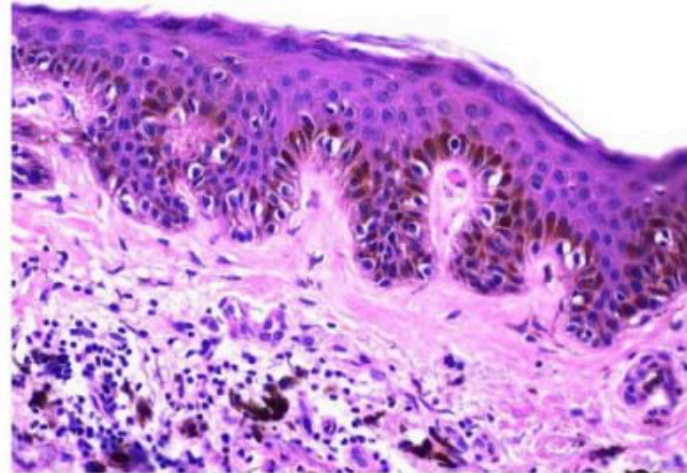


- Lipofuscin granules in cardiac myocytes shown by (A) light microscopy (deposits indicated by arrow)

~ Pigments - Melanin

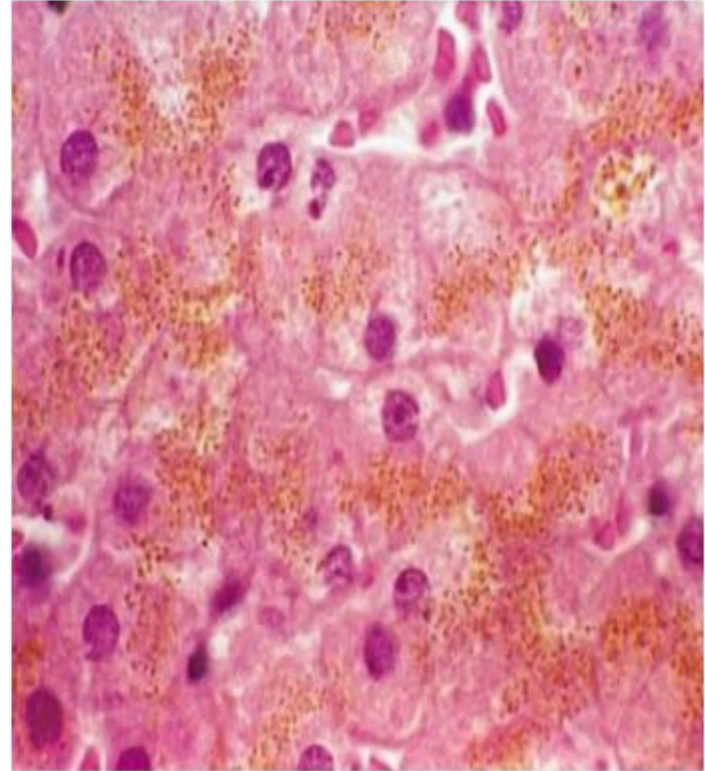


- An endogenous, brown-black pigment that is synthesized by melanocytes located in the **epidermis**.
- **Acts as a screen against harmful UV radiation.**
- Although melanocytes are the only source of melanin, adjacent basal keratinocytes in the skin can accumulate the pigment (e.g., in freckles), as can dermal macrophages.



~ Pigments - Hemosiderin

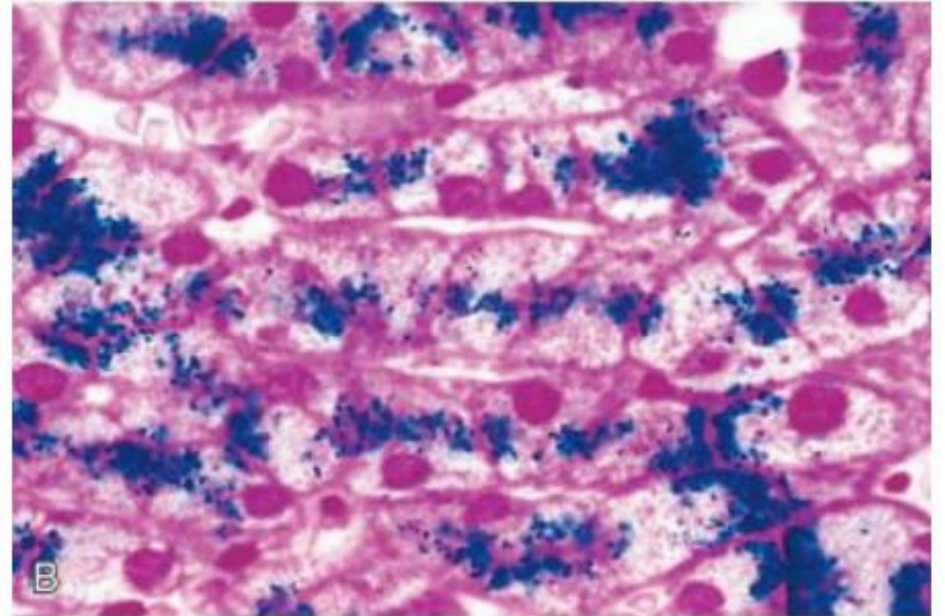
- A hemoglobin-derived granular pigment that is golden yellow to brown.
- Accumulates in tissues when there is a local or systemic excess of iron.
- Iron is normally stored within cells in association with the protein apoferritin, forming ferritin micelles.
- Hemosiderin pigment represents large aggregates of these **ferritin micelles**, readily visualized by light and electron microscopy.



- Hemosiderin granules in liver cells. (A) Hematoxylin-eosin–stained section showing golden-brown, finely granular pigment.

~ Pigments - Hemosiderin

- The iron can be unambiguously identified by the **Prussian blue** histochemical reaction
- Small amounts of this pigment are normal in the mononuclear phagocytes of the bone marrow, spleen, and liver, where aging red cells are normally degraded.
- **Excessive deposition of hemosiderin, called hemosiderosis.**
- More extensive accumulations of iron seen in **hereditary hemochromatosis**



- Hemosiderin granules in liver cells. (B) Iron deposits shown by a special staining process called the Prussian blue reaction