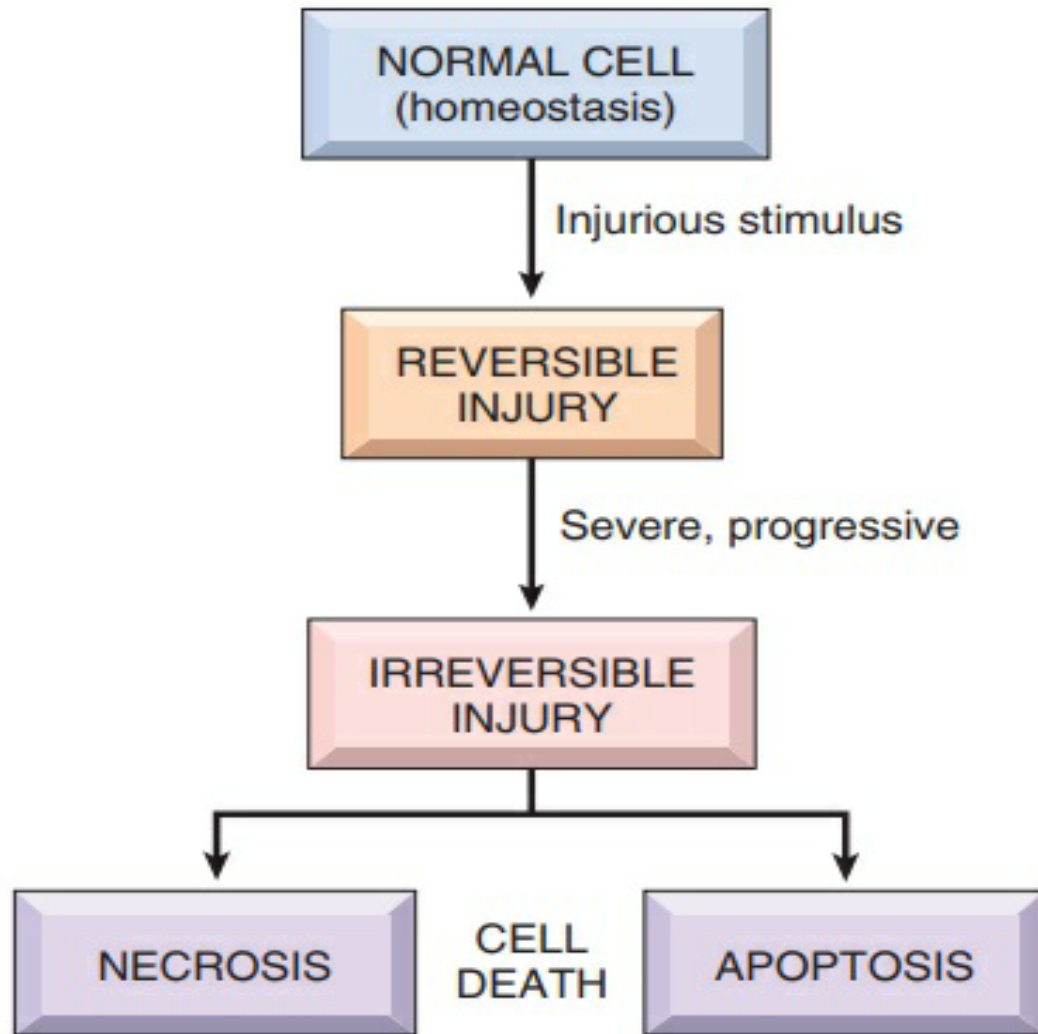


# Cell Injury & Necrosis-2

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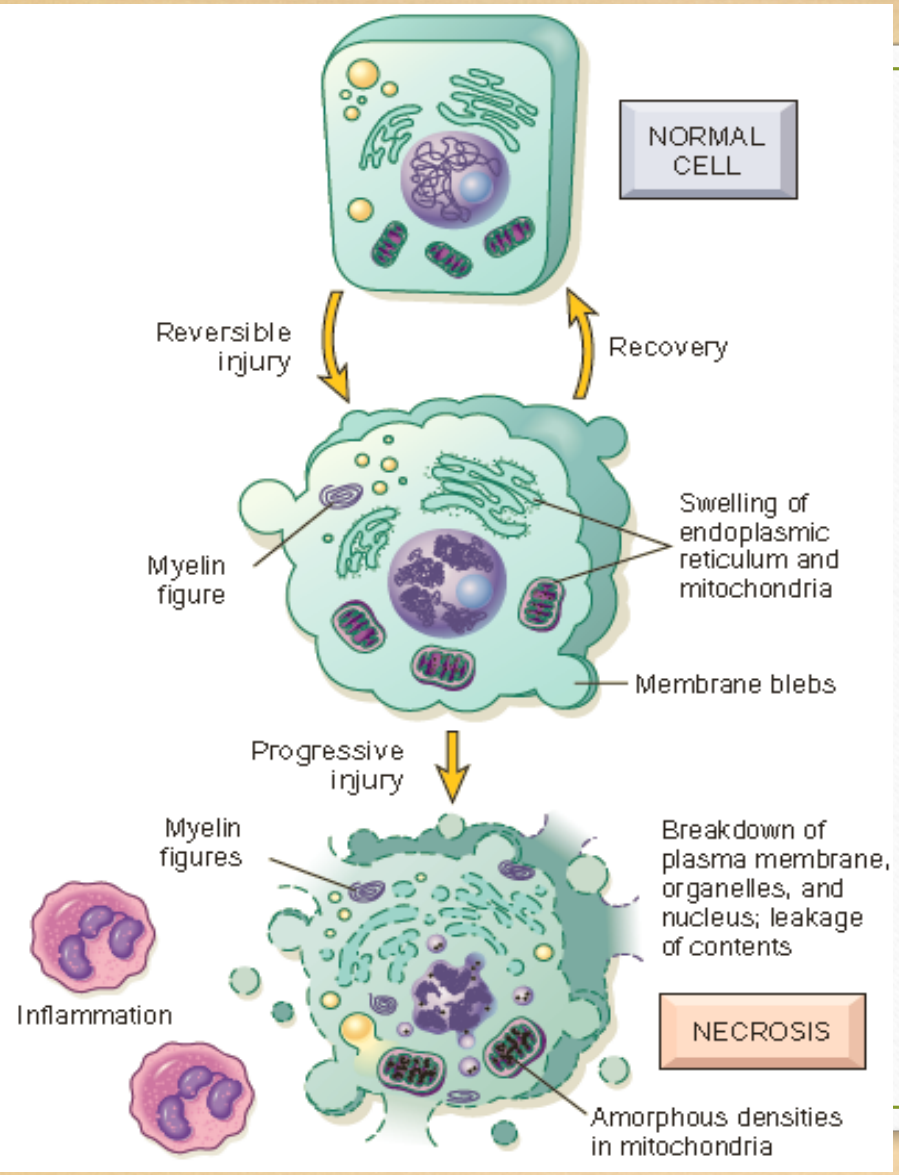


# Cell Death

- Injured cells die by different mechanisms, depending on the nature & severity of the insult:
  - Severe disturbances (loss of oxygen & nutrient supply or toxins) cause a rapid & uncontrollable form of death, called “accidental” cell death because injury is too severe to be repaired → **Necrosis**.  
“Accidental” → not regulated by specific signals or biochemical mechanisms.
  - In less severe injury, or cells need to be eliminated during normal processes → activate a precise set of molecular pathways → culminate in death → **Apoptosis**

# Necrosis

- A form of cell death in which cellular membranes fall apart, and cellular enzymes leak out and ultimately digest the cell.
  - A sequence of morphologic changes that follow cell death in living tissue.
- + often is the culmination of reversible cell injury that cannot be corrected.
- **elicits** a local host reaction, inflammation.



Microscopic appearance of Necrotic **dead cells:**

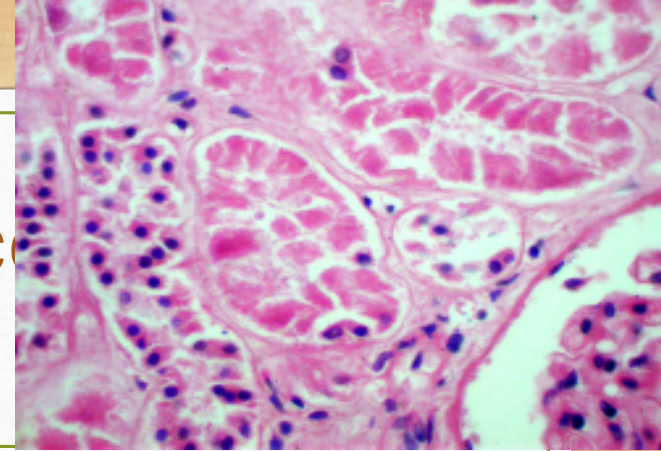
*Cytoplasmic*

*Nuclear*

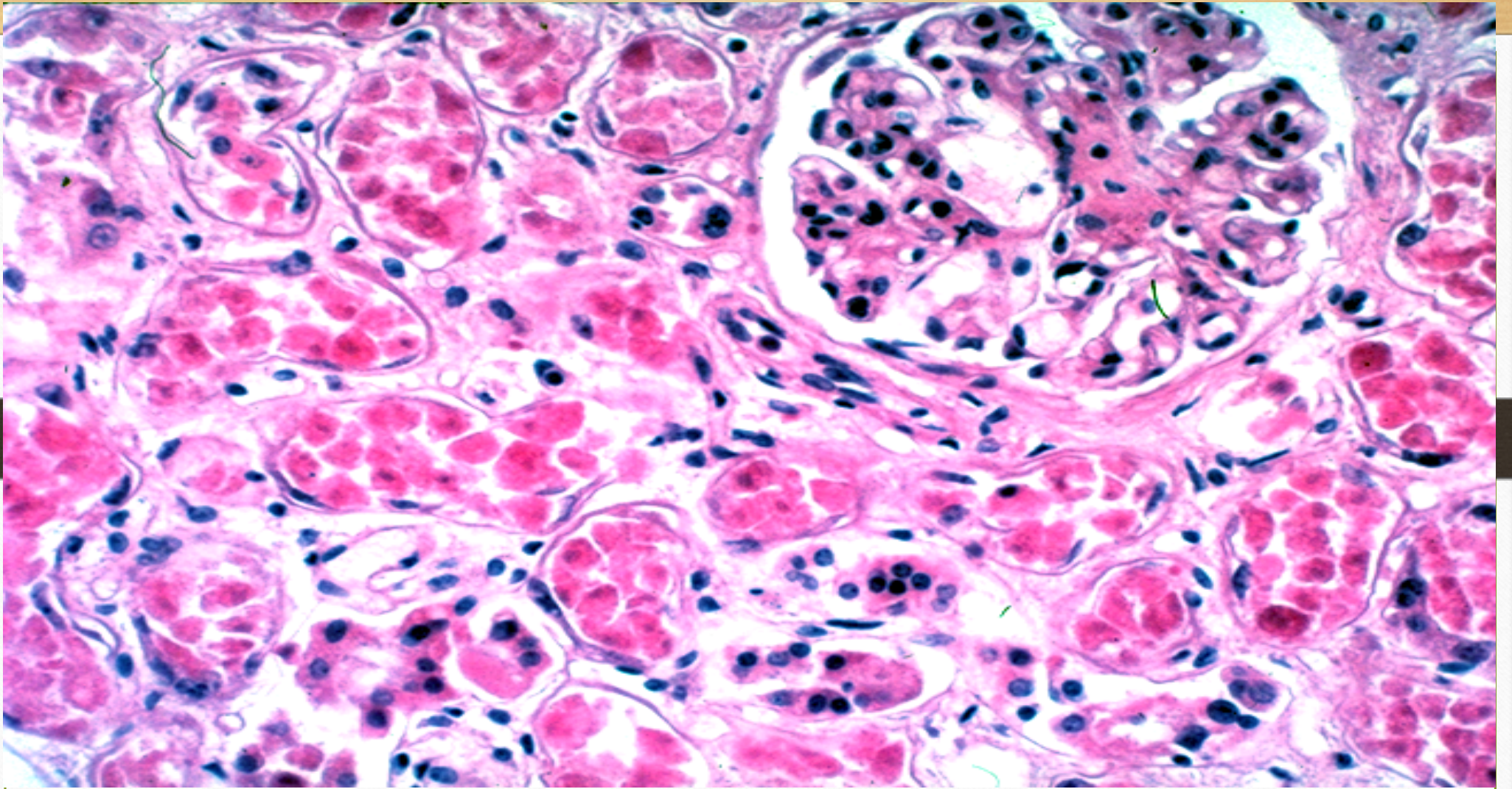
- Eosinophilia: stained red by the dye eosin—the E in [H&E stain)
- Basophilia: stained blue by the dye hematoxylin—the H in [H&E] stain)

# Microscopic appearance of Necrotic cells

## Cytoplasmic



- Increased eosinophilia, attributable to:
  - +increased binding of eosin to denatured cytoplasmic proteins
  - +loss of basophilic ribonucleic acid (RNA) in the cytoplasm.
- A glassy, homogeneous appearance, mostly because of the loss of lighter staining glycogen particles.
- Cytoplasm vacuolated & appears “moth-eaten “; due to enzymes.



Kidney, necrosis of tubular cells



# Microscopic appearance of Necrotic cell: Nuclear

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Nuclear changes → due to break down of DNA; three patterns

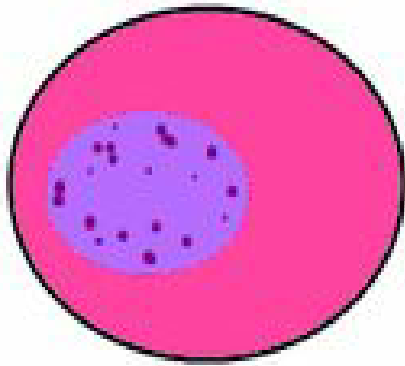
+ *Pyknosis*: shrinkage and increased basophilia.

+ *Karyorrhexis*: fragmentation of pyknotic nucleus.

+ *Karyolysis*: decrease basophilia of chromatin, DNAase:  
(deoxyribonuclease, DNA digestion )

In 1-2 days the nucleus in a dead cell may completely disappear.

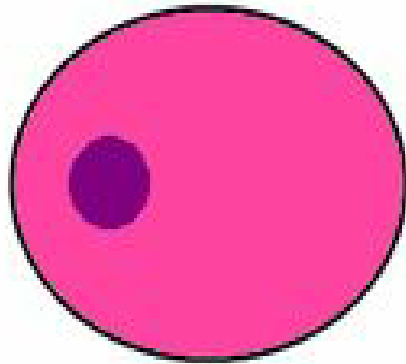
## KARYOLYSIS



### Nuclear fading

*chromatin dissolution due to action of DNAases & RNAases*

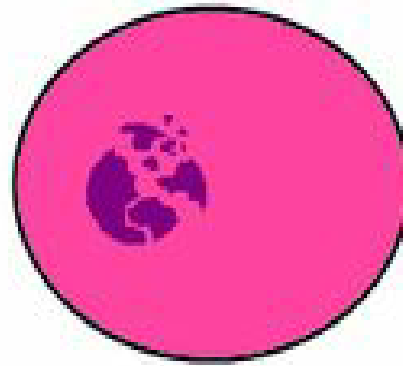
## PYKNOSIS



### Nuclear shrinkage

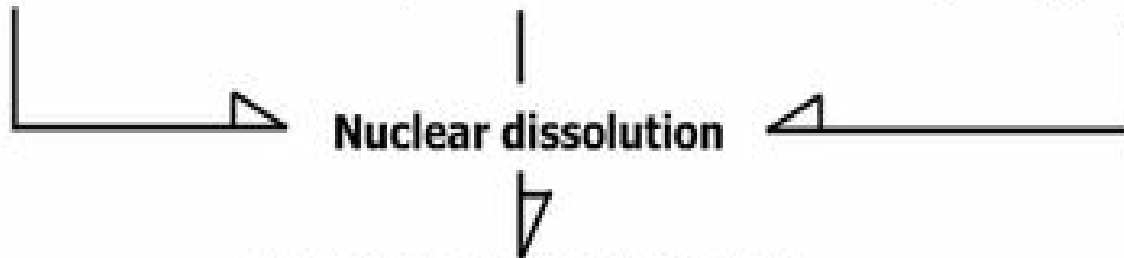
*DNA condenses into shrunken basophilic mass*

## KARYORRHEXIS



### Nuclear fragmentation

*Pyknotic nuclei membrane ruptures & nucleus undergoes fragmentation*



**ANUCLEAR NECROTIC CELL**

# Specific Morphologic Patterns of Necrosis

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- Coagulative necrosis
- Liquefactive necrosis
- Gangrenous necrosis
- Caseous necrosis
- Fat necrosis
- Fibrinoid necrosis

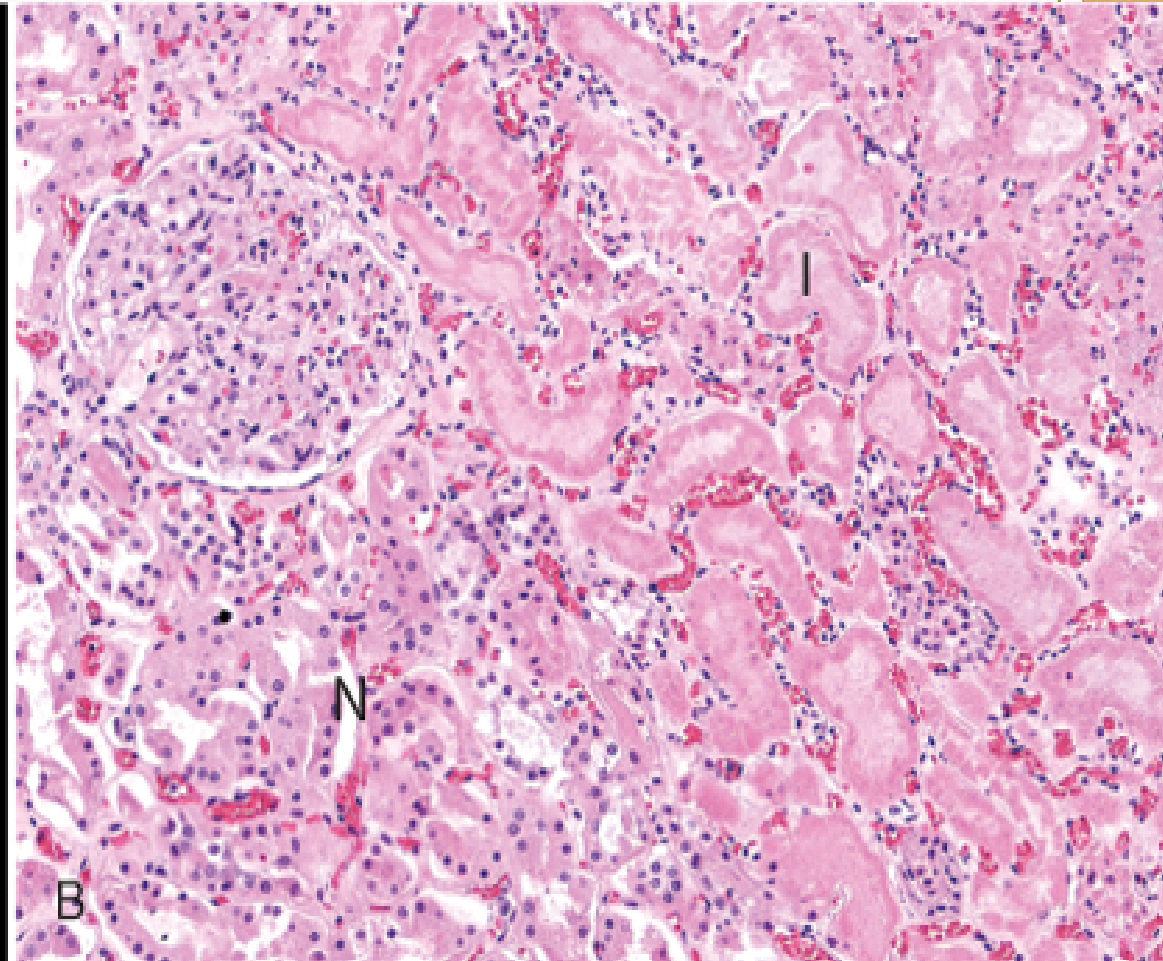
# Coagulative necrosis

- Preservation of the structural outline of the dead (*coagulated*) cell for days
- The *most common* form of necrosis (particularly in myocardium, liver, kidney)
- Characteristic of infarcts (areas of necrosis caused by ischemia) in all solid organs except the **brain**.
- Mechanism: *denaturation* of proteins & enzymes → blocking cellular proteolysis → preserve cell outline.

# Coagulative necrosis



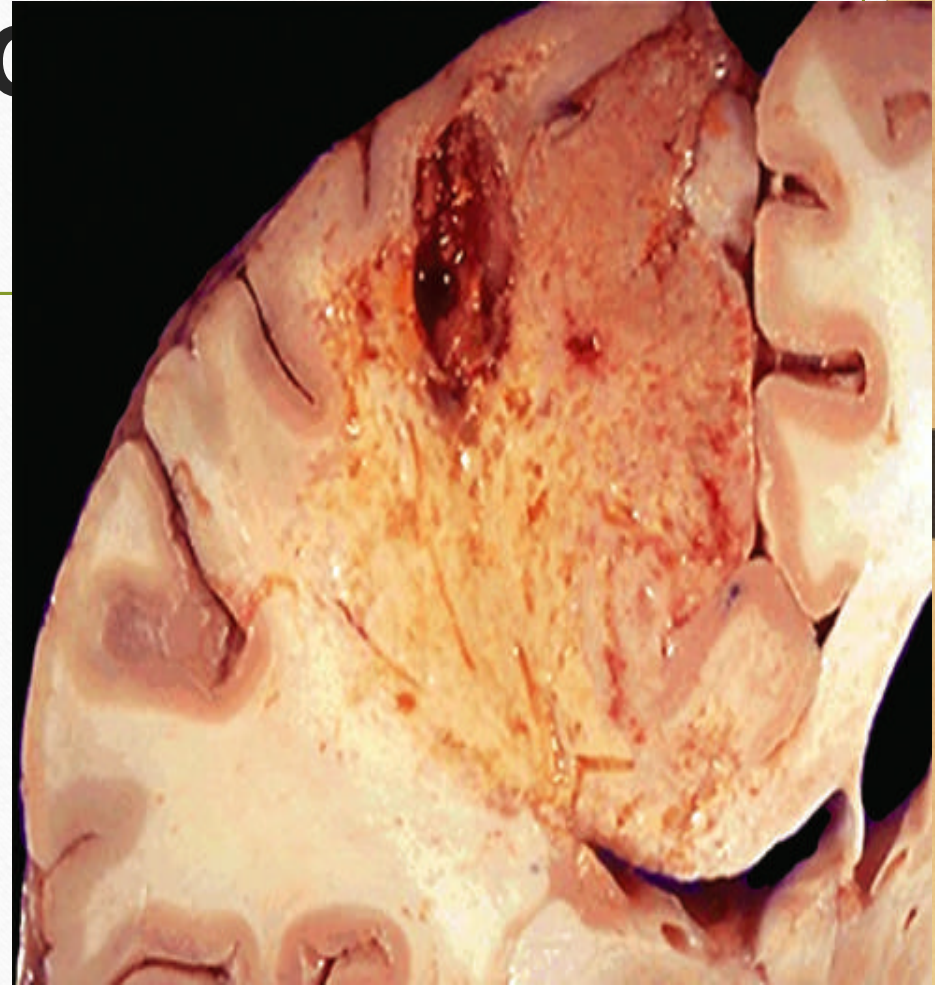
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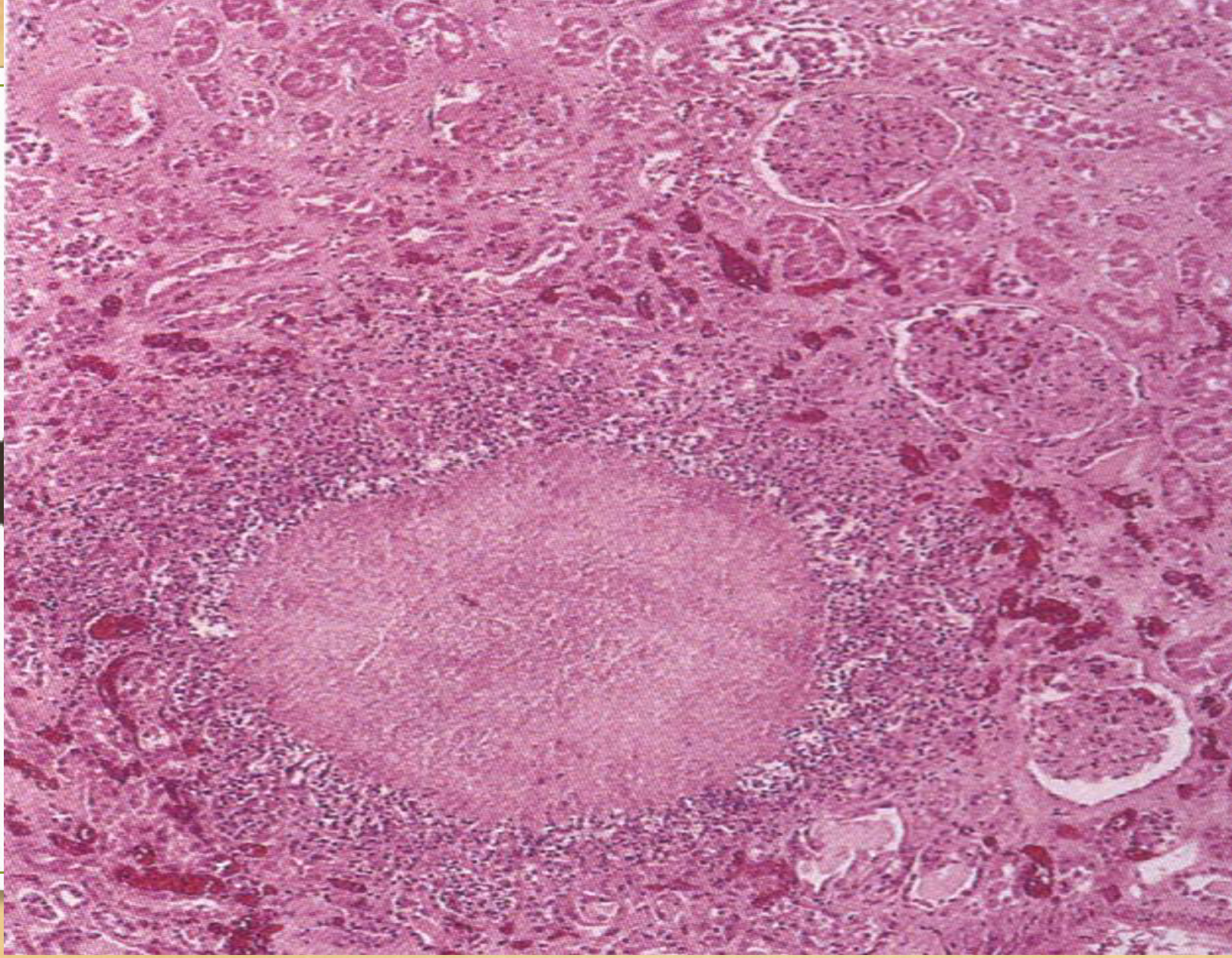


B

# Liquefactive necrosis

- Focal bacterial and fungal infections.
- Hypoxic & death of cells within the central nervous system.
- Microbes -rapid accumulation of inflammatory cells-enzymes of leukocytes digest (“liquefy”) the tissue.
- If acute infection - creamy yellow & is called **pus**





# Caseous Necrosis

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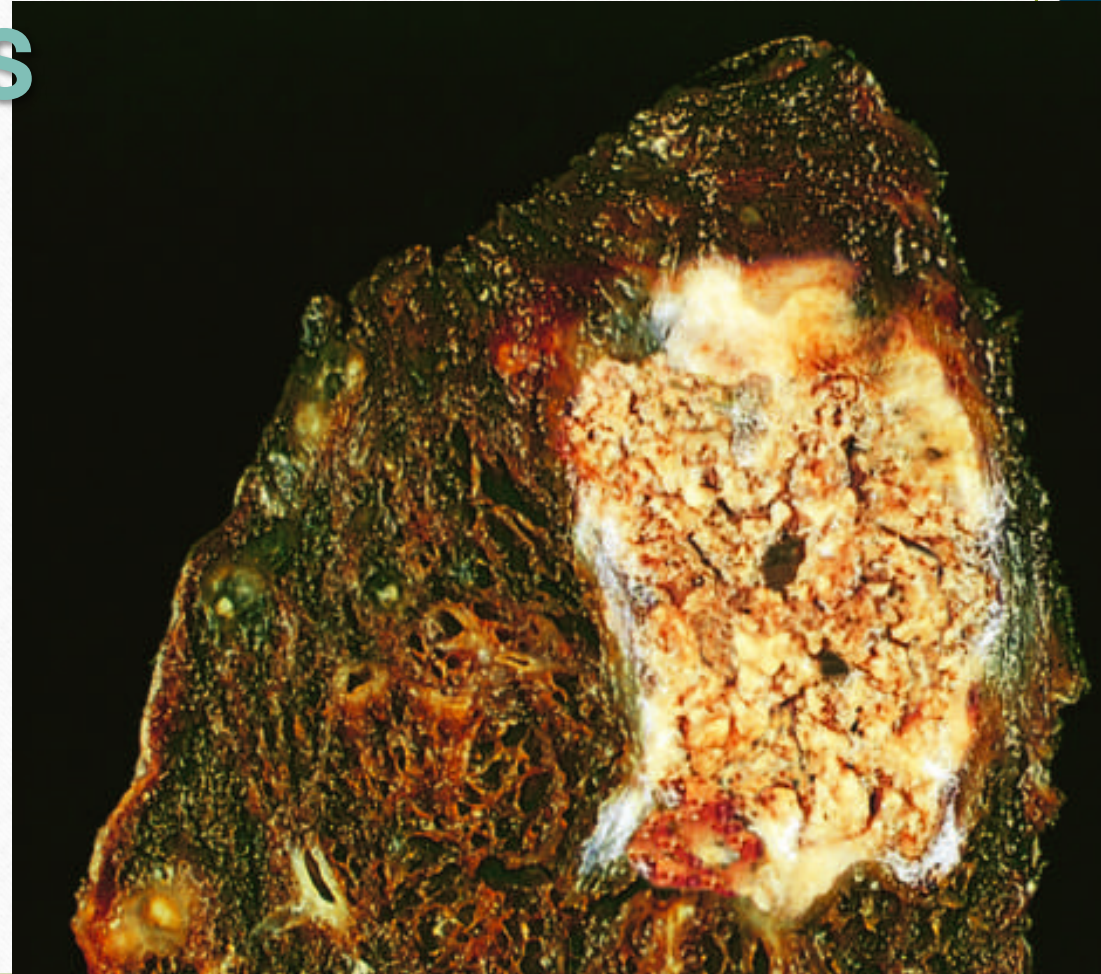
- Most often encountered in foci of tuberculous infection.
- **Caseous** means “cheeselike” : friable yellow-white appearance of the area of necrosis on gross examination.

## Microscopic examination:

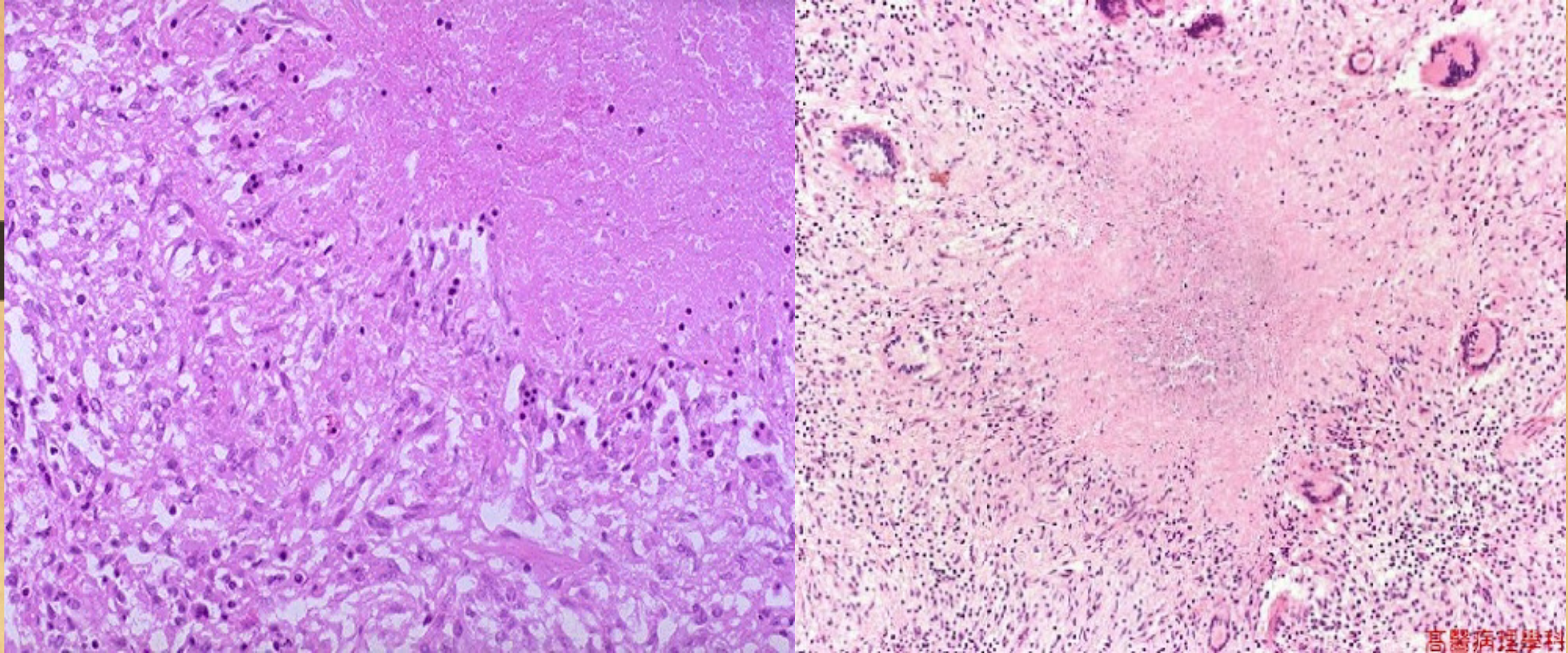
- A collection of fragmented or lysed cells with an amorphous granular pink appearance.
- Architecture -completely **obliterated**, cellular outlines-cannot be discerned
- Surrounded by a collection of macrophages and other inflammatory cells; this is called a **granuloma**



# Caseous Necrosis



# Caseous Necrosis

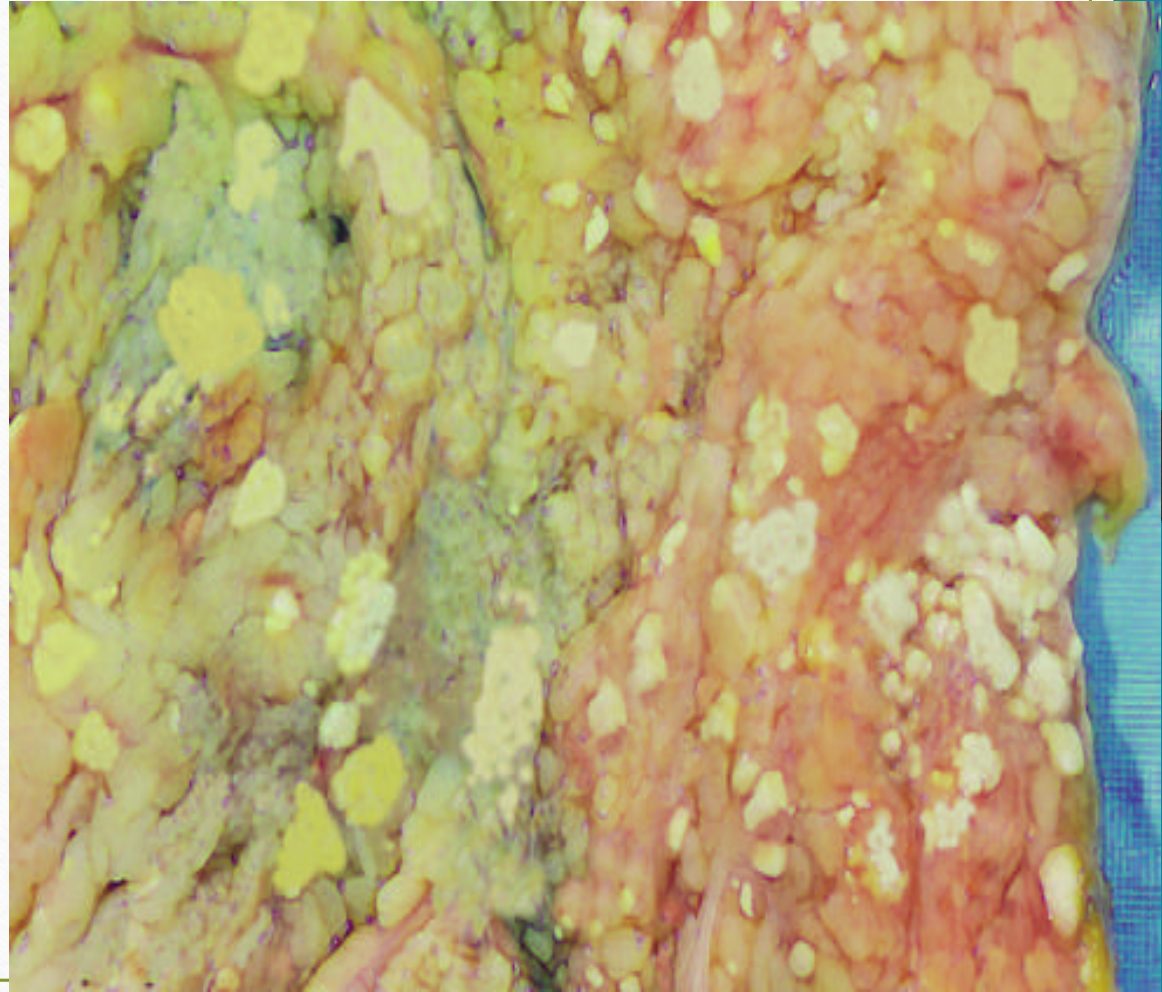


# Fat necrosis

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- Fat destruction.
- the release of activated pancreatic lipases into the substance of the pancreas and the peritoneal cavity (**Acute pancreatitis**)
- lipases + adipose tissue = cleaves triglycerides = fatty acids
- fatty acids bind and precipitate calcium ions, forming insoluble salts.

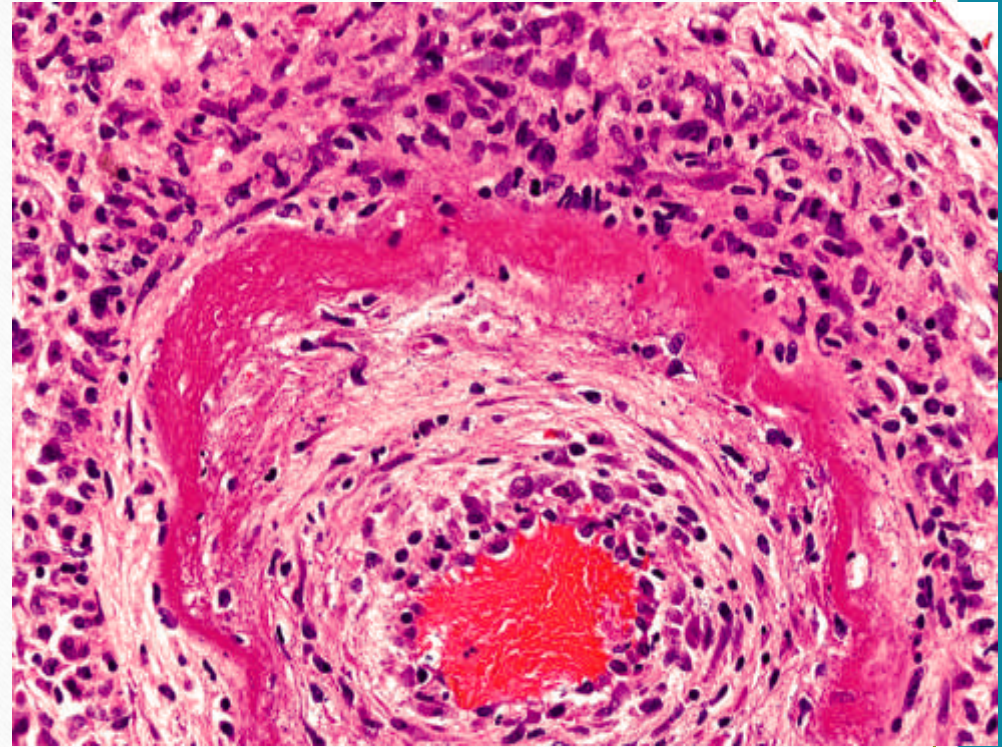
*These salts look:  
+chalky white on  
**gross examination.**  
+ basophilic in  
**histological**  
**sections stained**  
**with H&E***



# Fibrinoid necrosis

- In immune reactions: complexes of antigens and antibodies are deposited in the walls of blood vessels.
- Severe hypertension.
- Deposited immune complexes and plasma proteins that leak into the wall of damaged vessels produce a bright pink, amorphous appearance

A bright pink, amorphous appearance on H&E preparations called fibrinoid (fibrin-like) by pathologists..



# Gangrenous necrosis

- Not a distinctive pattern
- Commonly used in clinical practice.
- Usually refers to the condition of a limb (generally the lower leg) → lost blood supply → coagulative necrosis involving multiple tissue layers.
- Bacterial infection is superimposed → liquefactive necrosis because of the destructive contents of the bacteria & the attracted leukocytes (resulting in so-called “wet gangrene”).





# Fate of Necrosis

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- Most of necrotic tissue is removed by leukocyte (Phagocytosis) combined with extracellular enzyme digestion
- If necrotic tissue is not eliminated → it attracts  $\text{Ca}^{2+}$  salts → dystrophic calcification

**Leakage of intracellular proteins through the damaged cell membrane and ultimately into the circulation provides a means of detecting tissue-specific necrosis using blood or serum samples:**

- Cardiac muscle, isoform of creatine kinase & troponin.
- Hepatic bile duct epithelium, enzyme alkaline phosphatase,
- Hepatocytes contain transaminases

