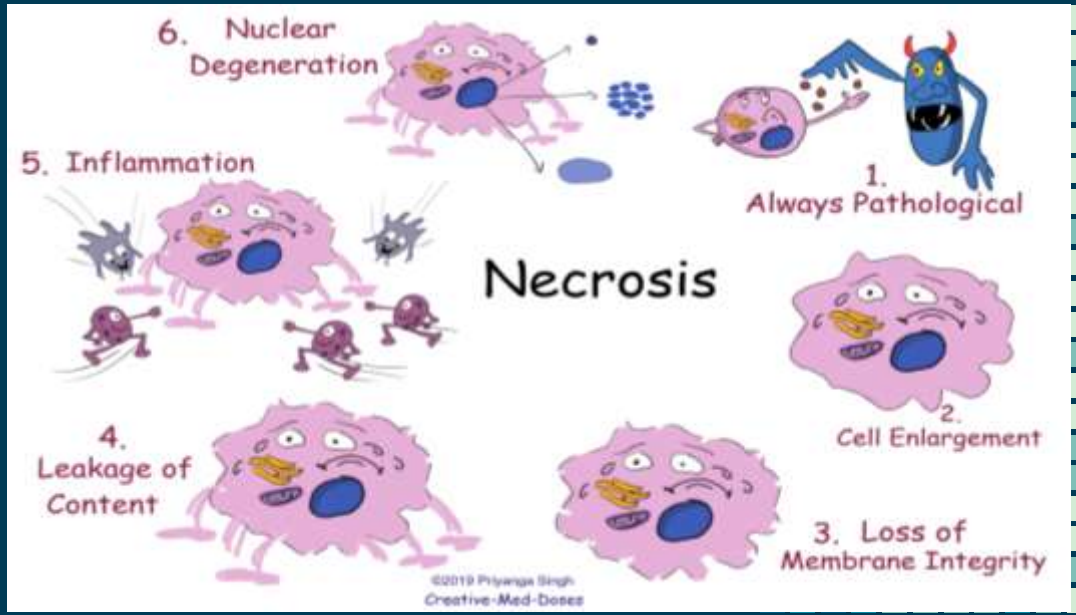
Cell Injury & Necrosis-2



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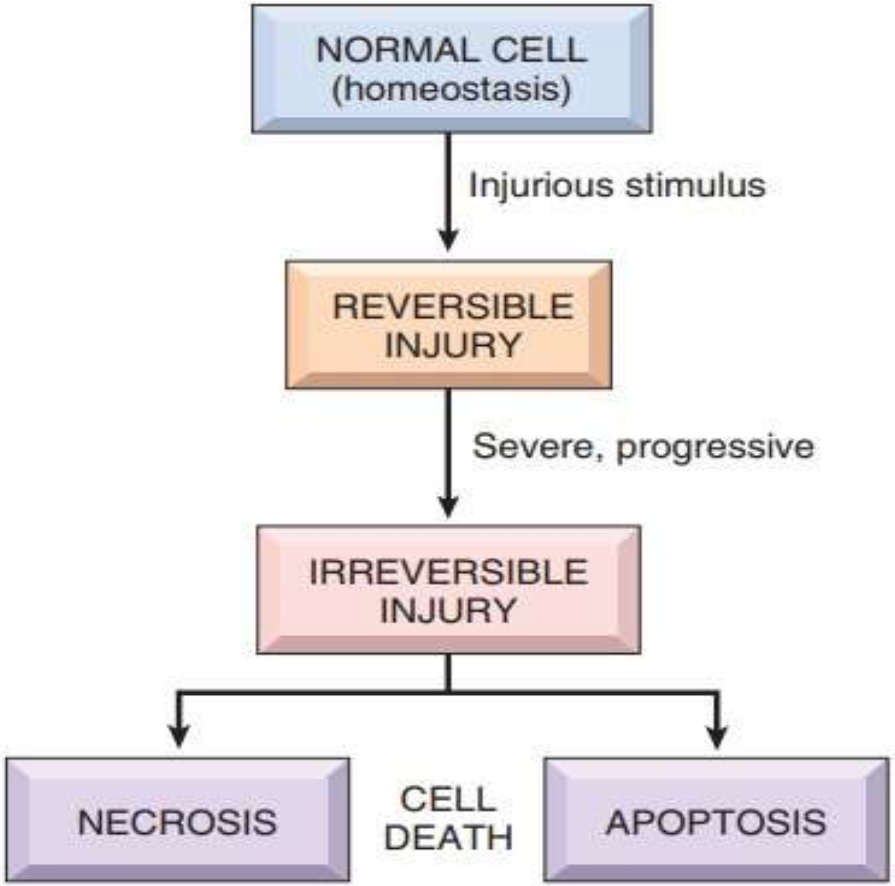
18/10/2021


NORMAL CELL
(homeostasis)
Injurious stimulus
REVERSIBLE
INJURY
Severe, progressive
IRREVERSIBLE
INJURY
NECROSIS
CELL
DEATH
APOPTOSIS

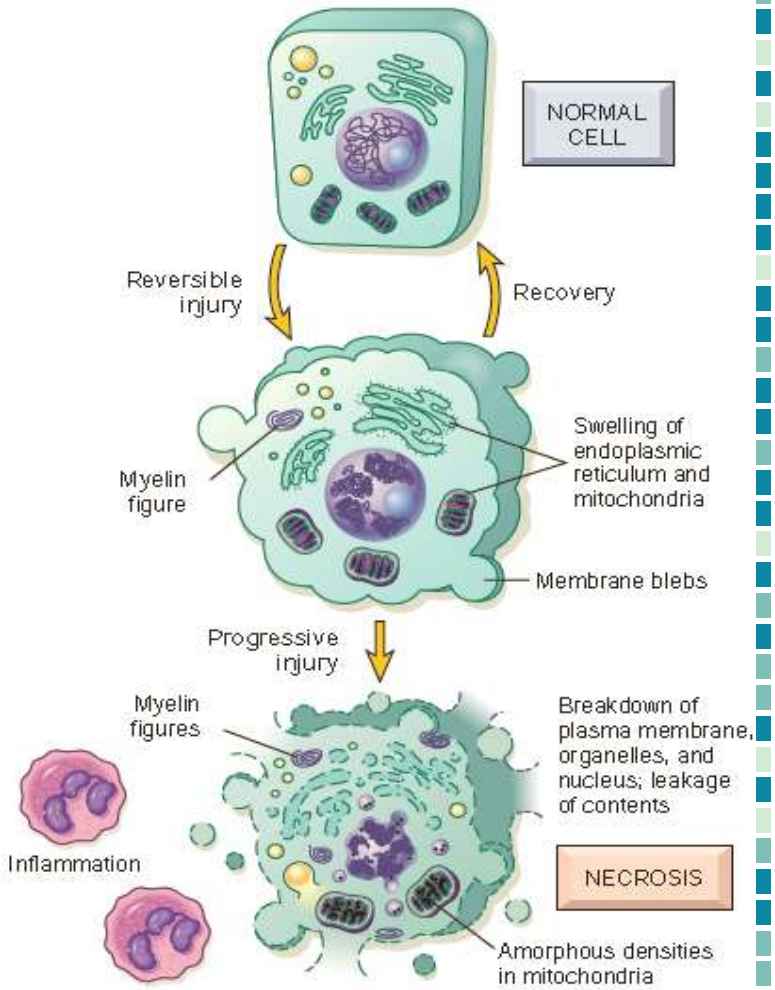
Cell Death

- 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:***

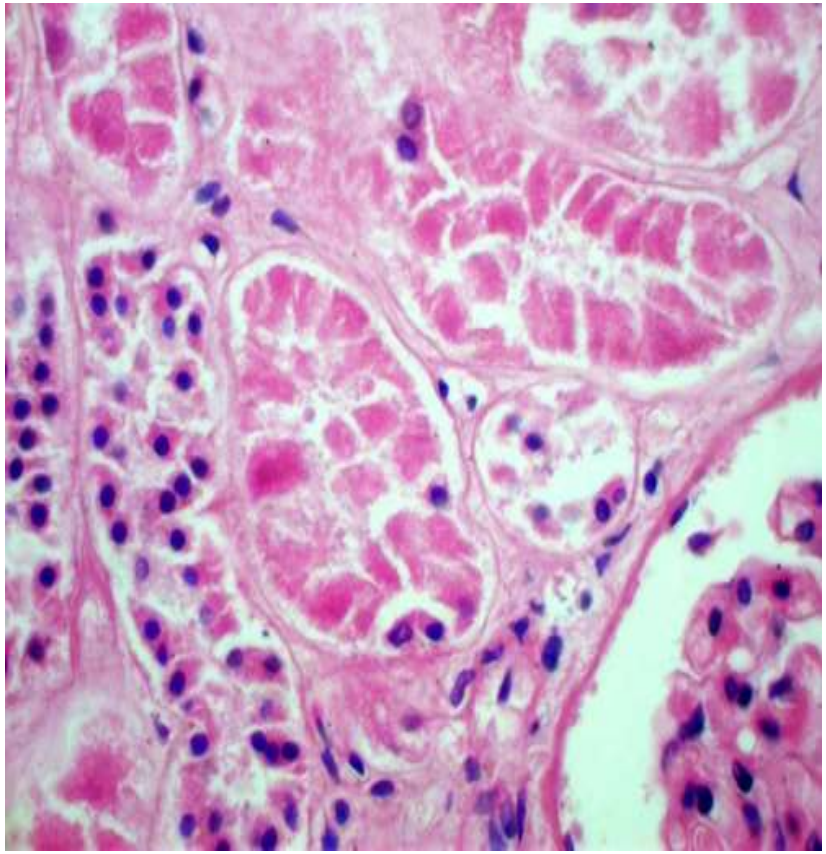
- *Cytoplasmic*
- *Nuclear*

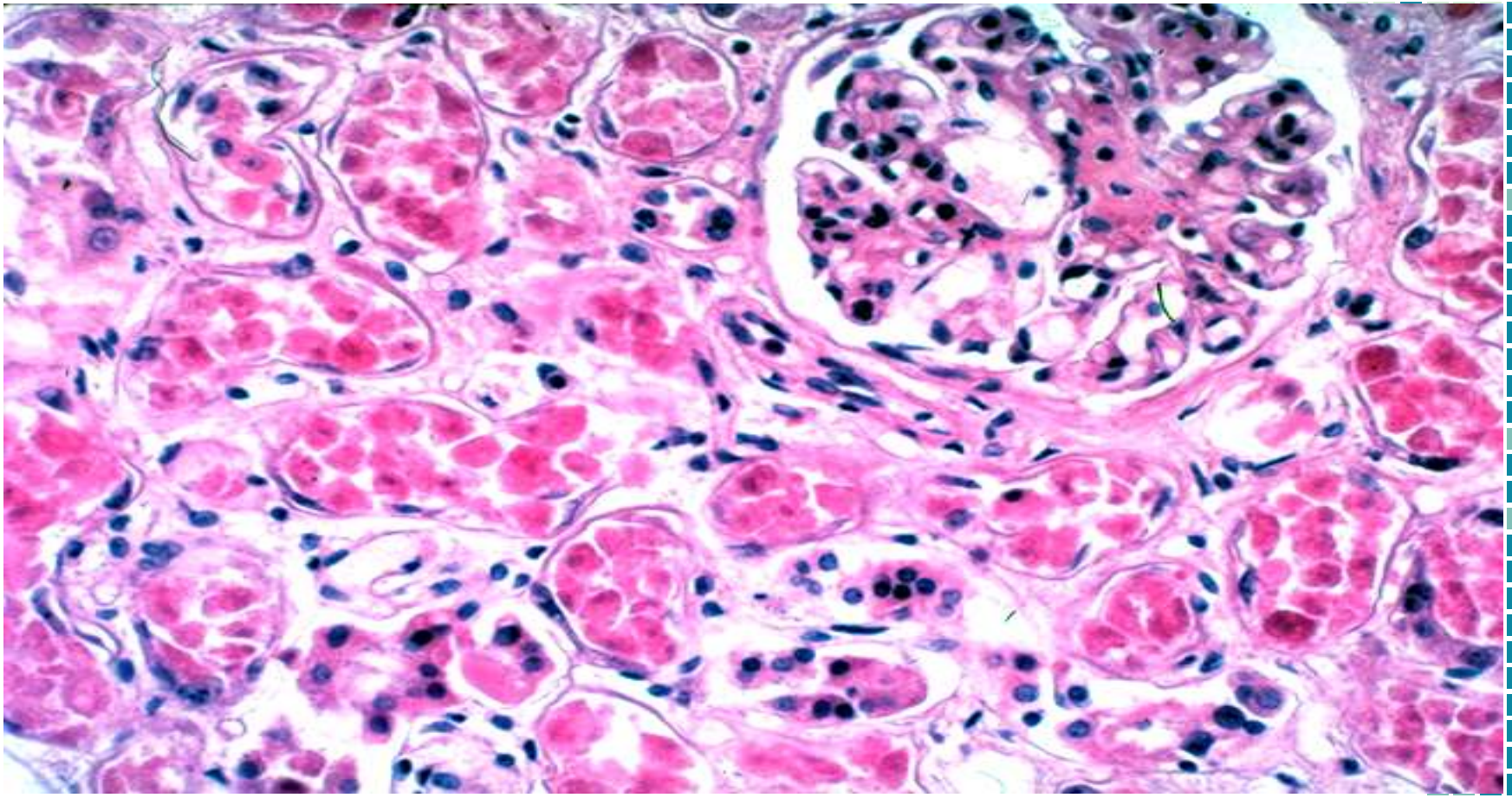
- Eosinophilia: stained red by the dye eosin—the E in [H&E] stain)
- Basophilia: stained blue by the dye hematoxylin—the H in [H&E] stain)

Microscopic appearance of Necrotic cell:

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**

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.

Nuclear fading

chromatin dissolution due to action of DNAases & RNAases

Nuclear shrinkage

DNA condenses into shrunken basophilic mass

Nuclear fragmentation

Pyknotic nuclei membrane ruptures & nucleus undergoes fragmentation

Nuclear dissolution

ANUCLEAR NECROTIC CELL

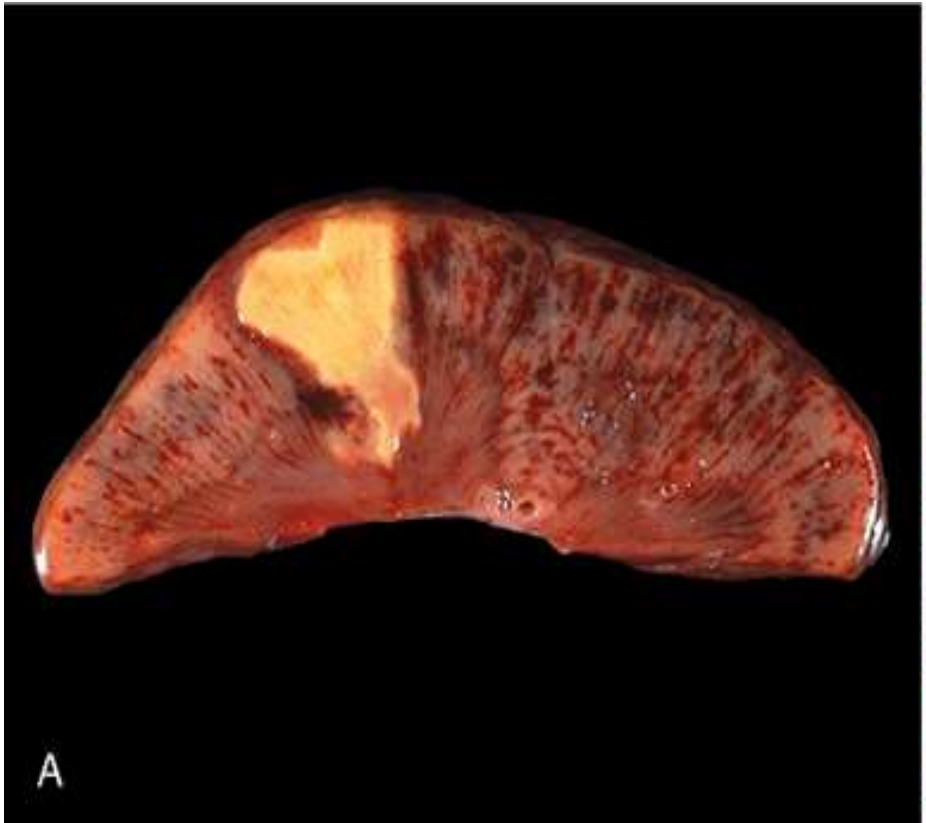
Specific Morphologic Patterns of Necrosis

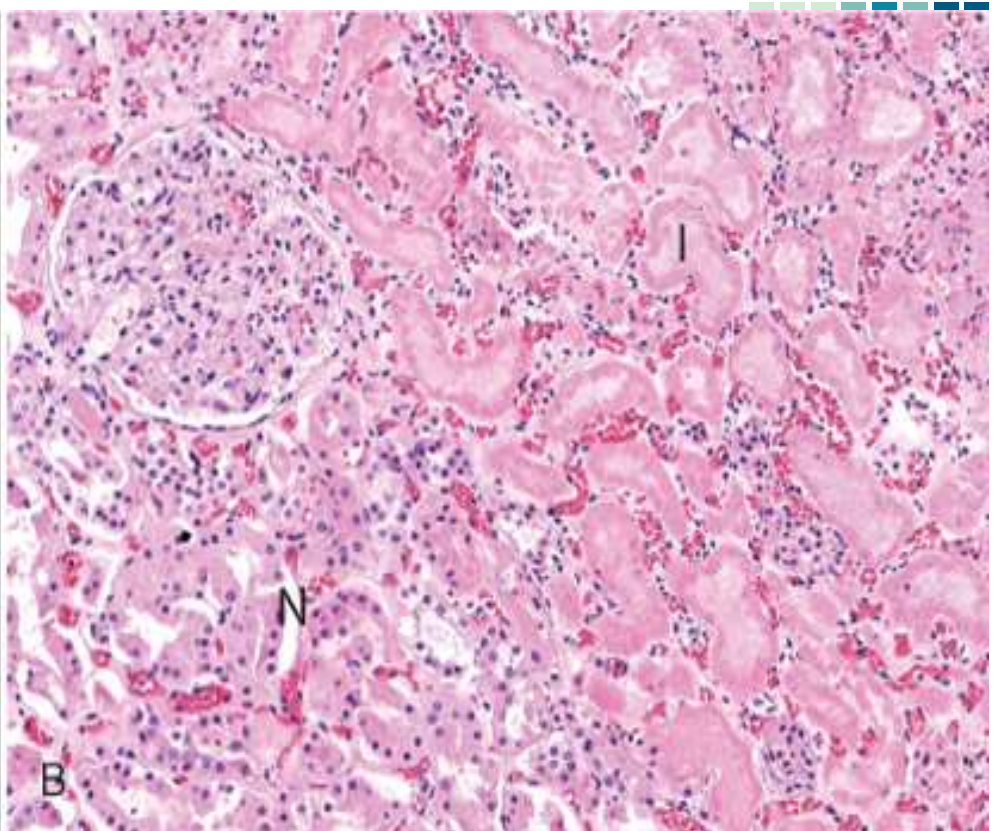
- Coagulative necrosis
- Liquefactive necrosis
- Gangrenous necrosis
- Caseous necrosis
- Fat necrosis
- Fibrinoid necrosis

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.

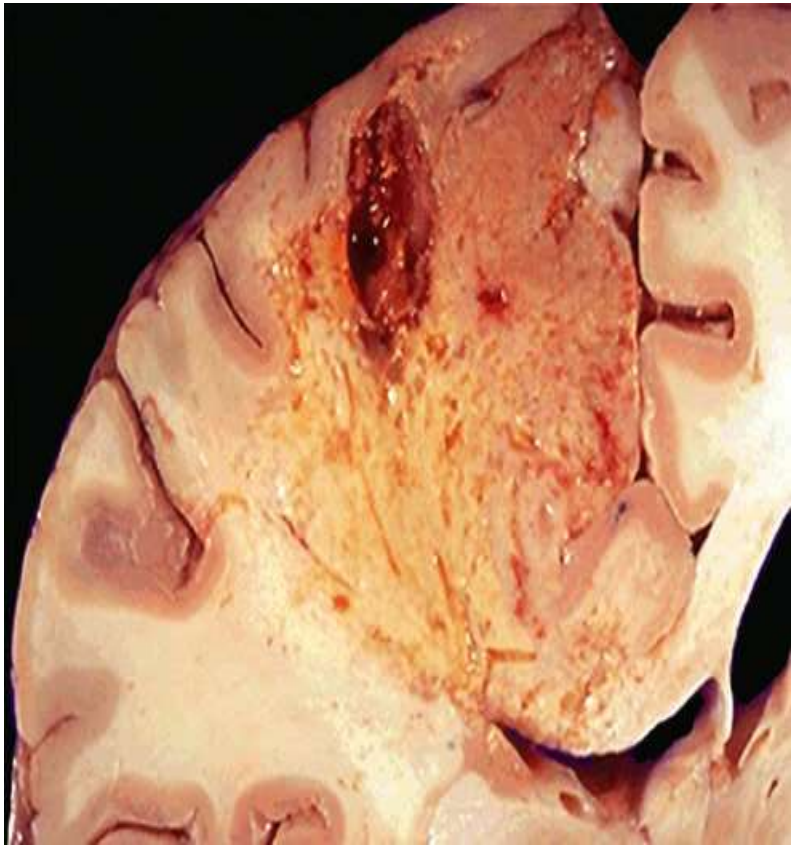
Coagulative necrosis

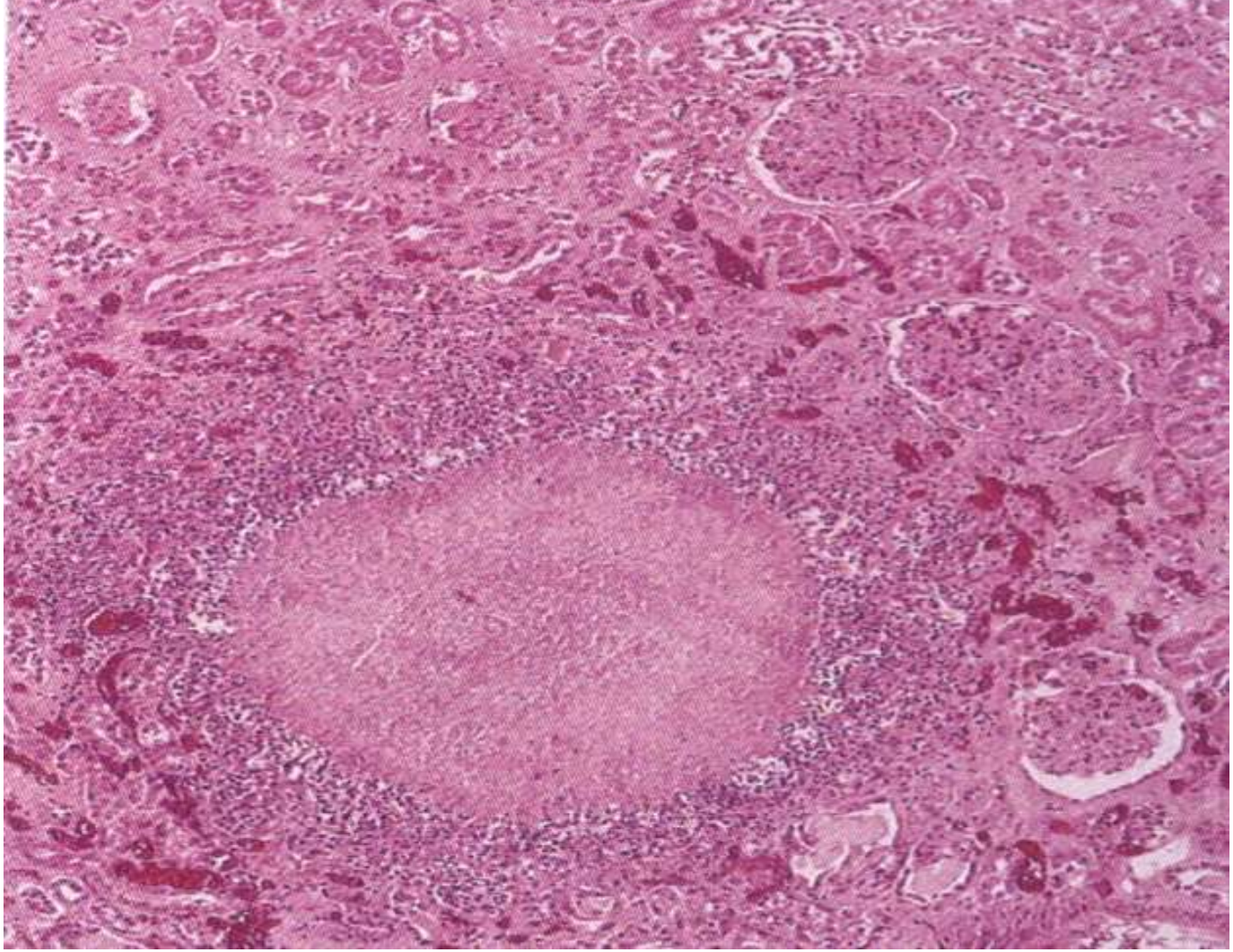




Liquefactive necrosis

- 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**





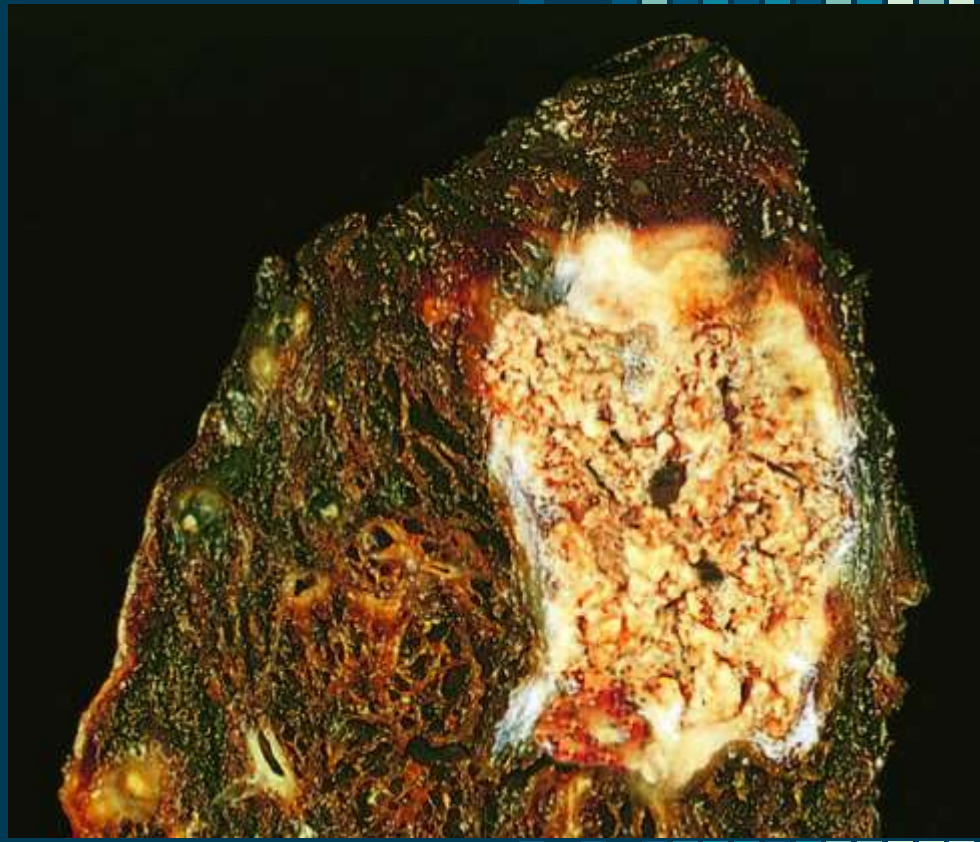
Caseous Necrosis

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

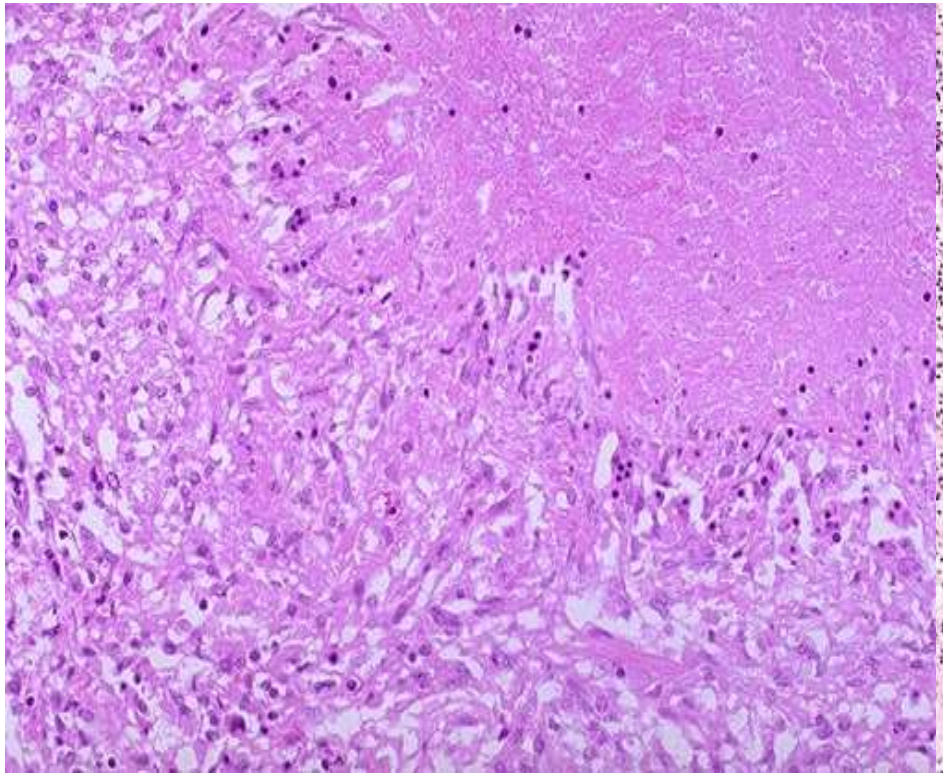
microscopic examination:

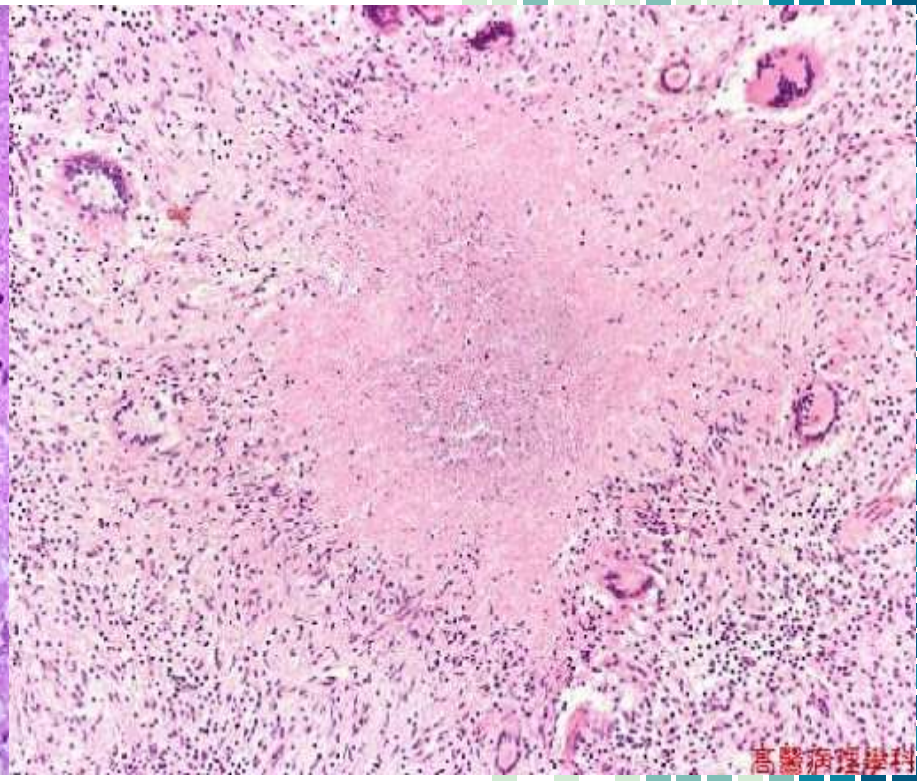
- A collection of fragmented or lysed cells with an amorphous granular pink appearance.
- Architecture -completely **obliterated**, cellular outlines-cannot be discerned
- Surrounded by a collection of macrophages and other inflammatory cells; this is called a **granuloma**

Caseous Necrosis



Caseous Necrosis





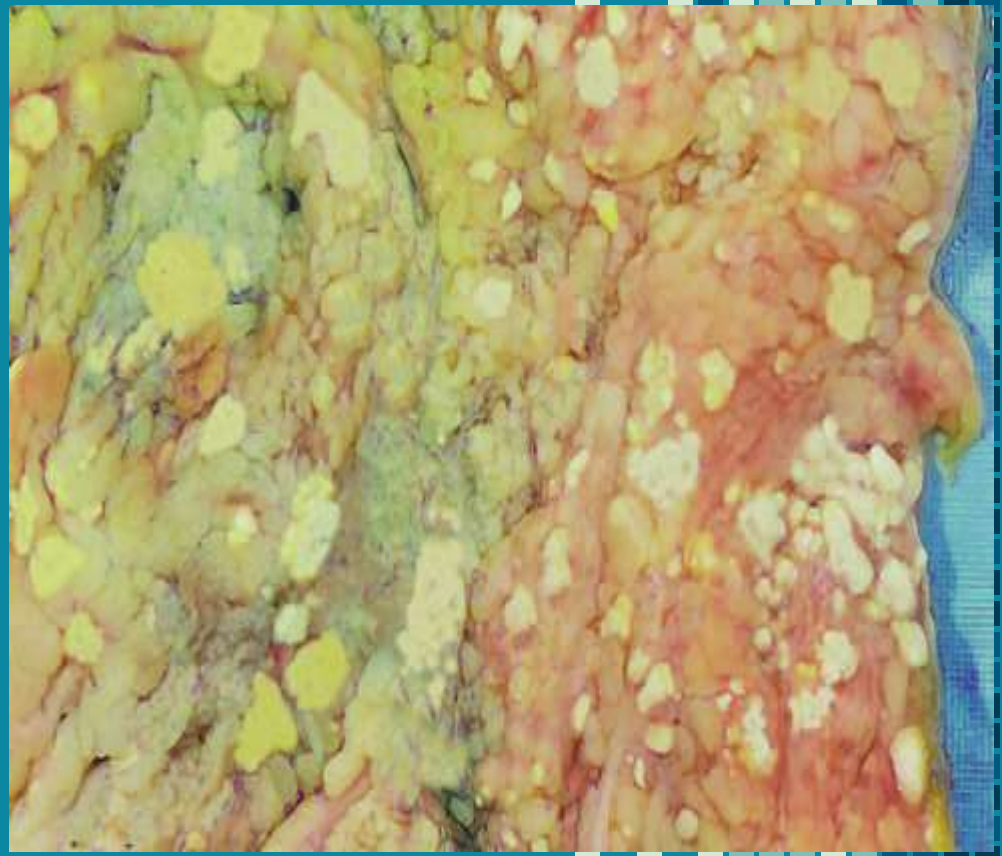
Fat necrosis

- 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*

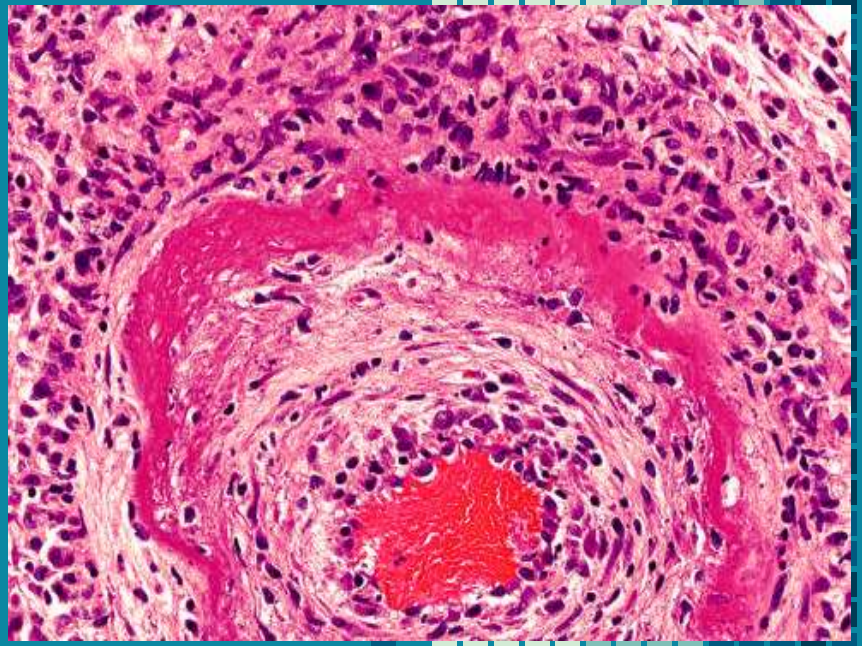


Fibrinoid necrosis

- 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

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

THANKS!

Any questions?