Cell death
Apoptosis and Necrosis

Lecture 3

2023-2024

Life cannot exist without cellular death

Two main mechanism of cell death

- Apoptosis = “normal” or “programmed” cell death
- Necrosis = “accidental” or “pathologic” cell death

Apoptosis

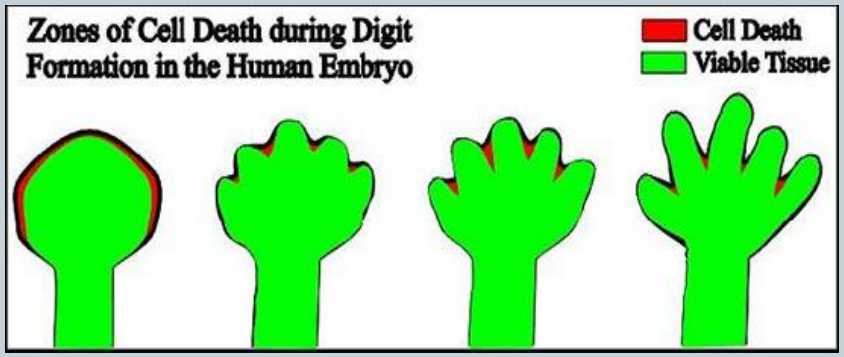
- Apoptosis or programmed cell death (PCD) is a mode of cell death that occurs under normal physiological conditions and the cell is an active participant in its own demise (“cellular suicide”).
- It is important for the development of multicellular organism (embryonic development) and homeostasis of their tissues (adult).

Importance of apoptosis

Apoptosis is a beneficial and important phenomenon:

- In embryo

1. During embryonic development, help to digit formation.



- Lack of apoptosis in humans can lead to webbed fingers called “ syndactyly ”.

Morphological features of apoptosis

Light Microscopy:

A. The apoptotic cells appear as round or oval mass having intensely eosinophilic (dark-red color) cytoplasm.

B. The nuclei appear as fragments of dense nuclear chromatin and shows pyknosis or condensation.

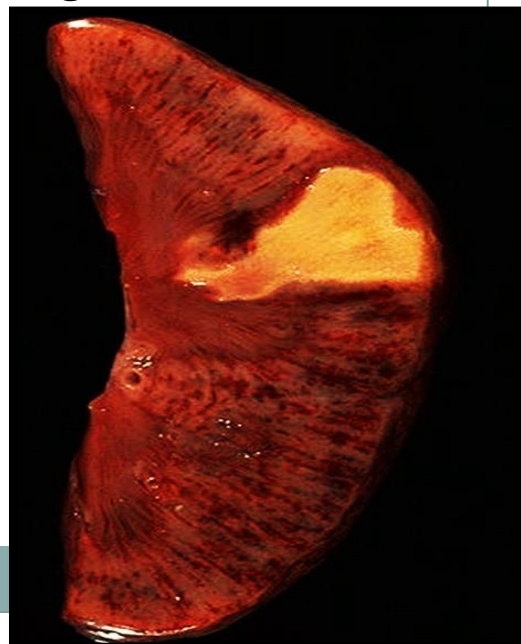
C. Apoptosis does not elicit an inflammatory reaction in the host.

Necrosis

- Necrosis is death of cells and tissues in the living organism.
- Necrosis is an “accidental” and unregulated form of cell death.
- It results from damage to cell membranes and loss of ion homeostasis.
- The necrotic cells cannot maintain integrity of membrane and their contents leak out. This bring out acute inflammatory reaction in the surrounding tissue

Gross appearance or lesion:

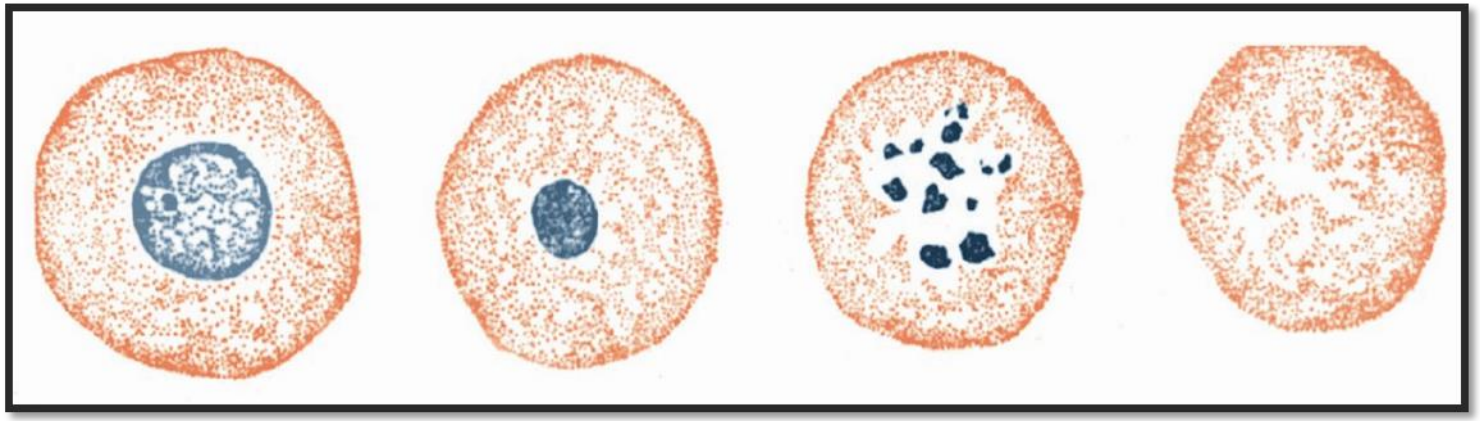
- ✓ Affected areas white, gray or yellow in colour.
- ✓ Have a cooked meat appearance.
- ✓ Sharply demarcated (by red zone) from healthy tissue.
- ✓ In case of gangrene the area is green, orange or black (iron sulphide)

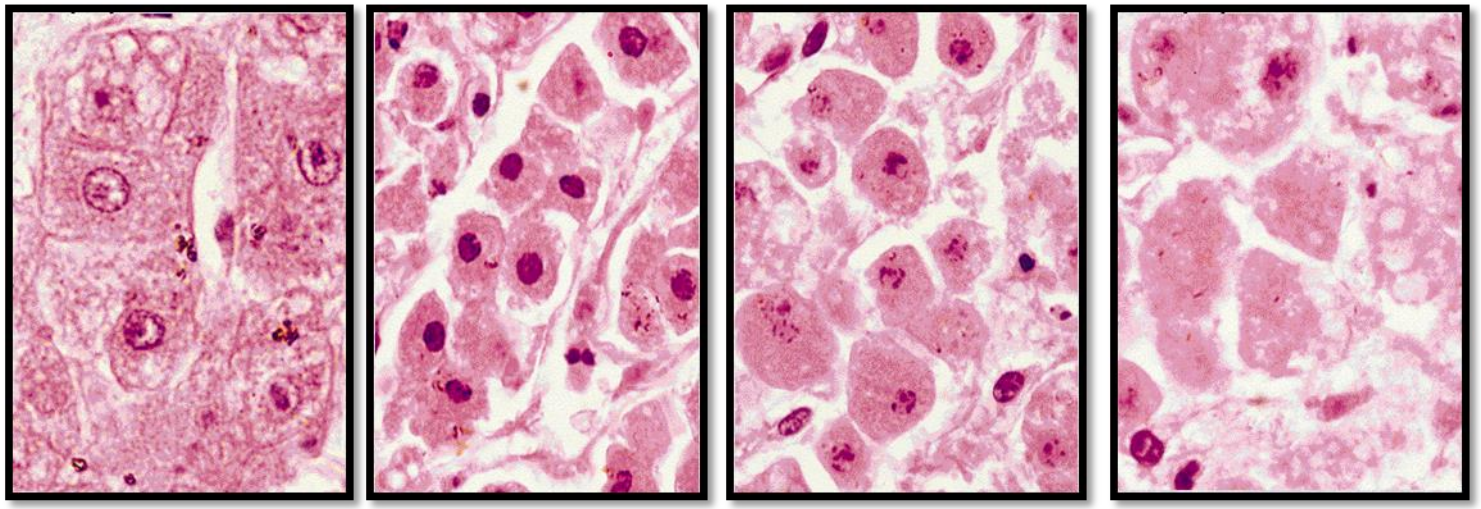


Microscopic appearance:

The microscopic changes of necrosis vary with the type of necrosis. Some general changes of necrosis in the cytoplasm and nucleous are:

- Eosinophilia: The cytoplasm stains darker red in colour.
- Swelling and vacuolation: The cells are swollen and contain different types of vacuoles.
- Changes in the nucleus: The nucleus may show condensation **(Pyknosis),** fragmentation **(karyorrhexis)** and may disappear **(karyolysis).**



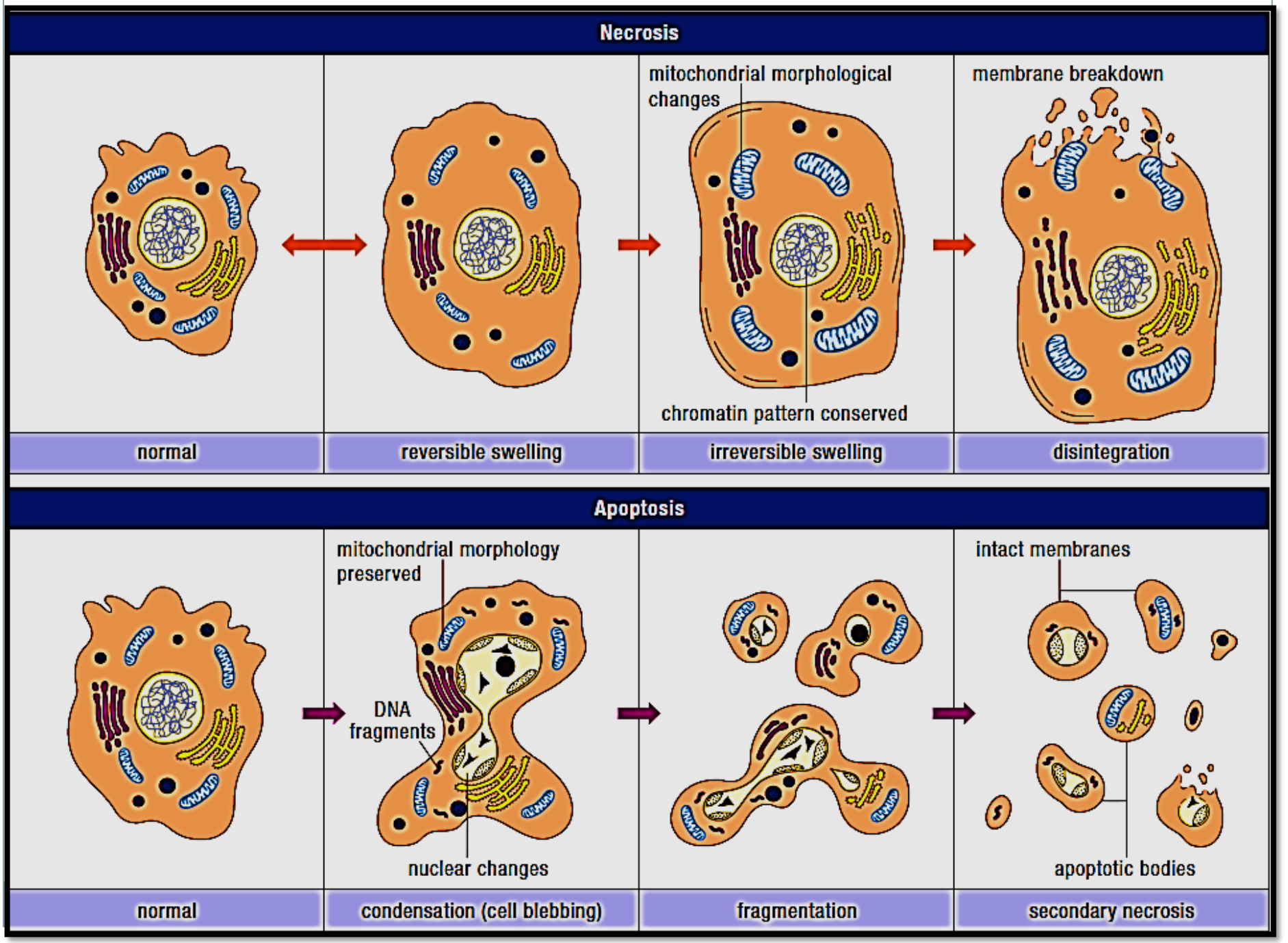


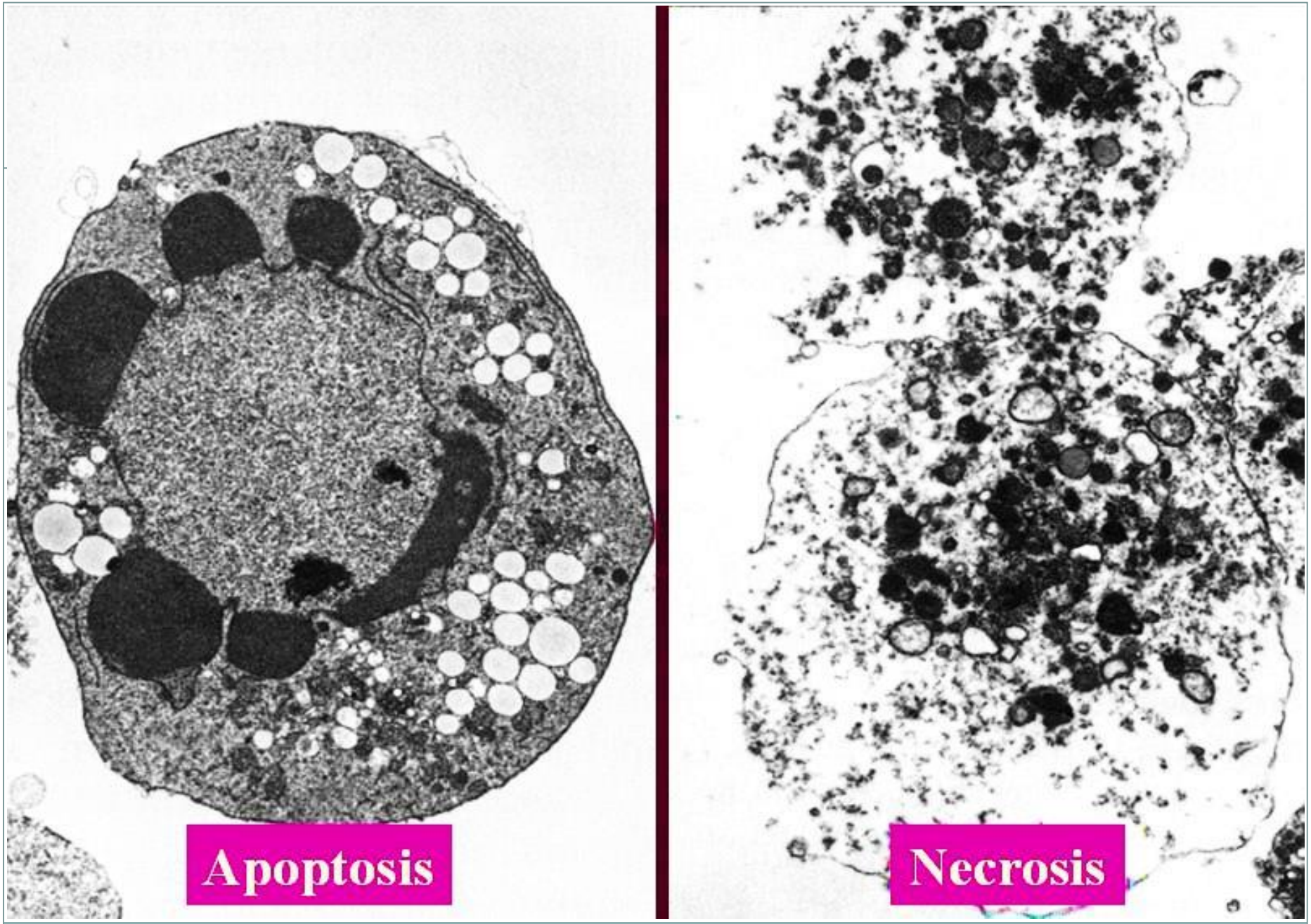
Normal Pyknosis Karyorrhexis Karyorlysis

Nuclear and cytoplasmic changes in necrotic cells

Differences between apoptosis and necrosis

Features	Apoptosis	Necrosis
Cause	Often physiological, means of eliminating unwanted cells; may also be pathological	Invariably pathological
Lysosomes	Intact	Leak lytic enzymes
Cell size	Reduced (shrinkage)	Enlarged (swelling)
Nucleus	Fragmentation	Pyknosis → karyorrhexis → karyolysis
Plasma membrane	Intact	Disrupted
Adjacent inflammation	No	Usual


Necrosis
mitochondrial morphological changes
membrane breakdown
chromatin pattern conserved
normal
reversible swelling
irreversible swelling
disintegration
Apoptosis
mitochondrial morphology preserved
intact membranes
DNA fragments
nuclear changes
apoptotic bodies
normal
condensation (cell blebbing)
fragmentation
secondary necrosis


Apoptosis
Necrosis

Patterns of necrosis

1. Coagulative
2. Liquefactive
3. Caseous
4. Fat necrosis
5. Fibrinous
6. Gangrene
7. Infarct
   - Red/haemorrhagic
   - White

Coagulative necrosis

- The term “coagulation necrosis” describes a type of necrosis typically caused by ischemia.
- It is the most common pattern of necrosis which affects all organs except the brain. More frequent in heart, kidney, spleen and limb (dry gangrene).
- Architectural outlines persist but cellular details are lost.
- Type of tissue can be recognized.
- Denaturation (coagulation) of structural and enzymatic proteins blocks proteolysis.

Gross appearance:

Necrotic area is firm, opaque with cooked meat appearance.

It is sharply demarcated from the healthy areas.

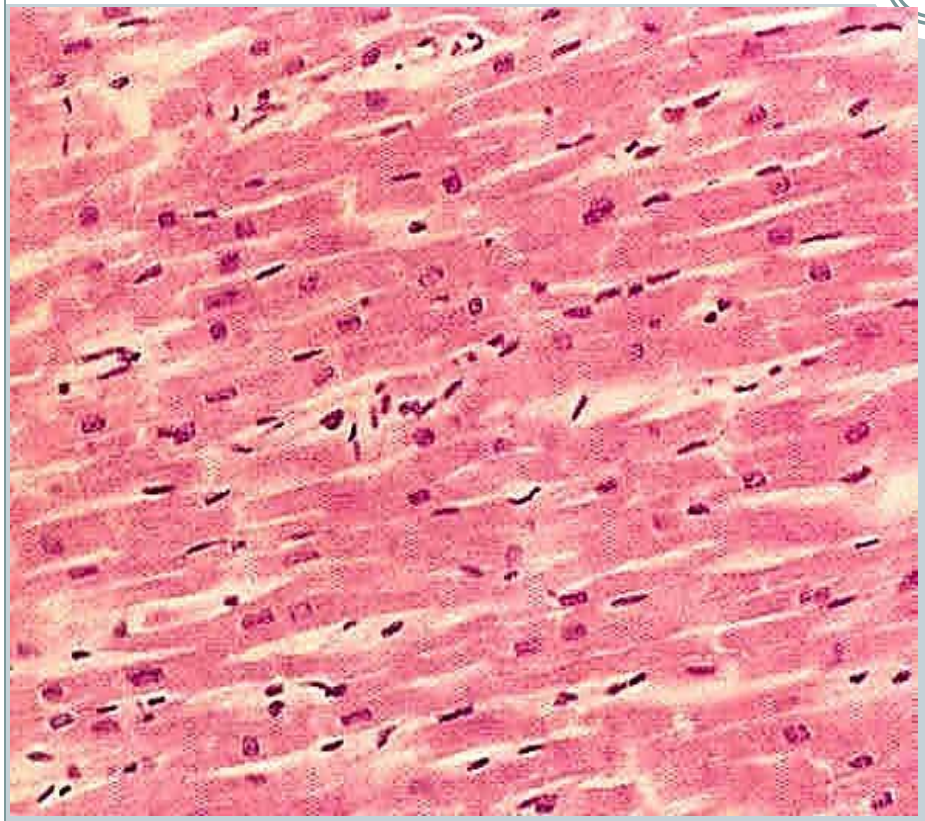
Microscopic appearance:

- Architectural outlines are present; cellular details are lacking.
- The necrotic tissue appears as a **lighter staining tissue** (when stained with H and E).
- The cytoplasm show eosinophilia.
- The necrotic cells **appear containing no nuclei** with very little structural damage giving an appearance of ghost cells.

Result:

Dead tissues remain in the body for a long period, ultimately removed by macrophages.

Coagulative necrosis

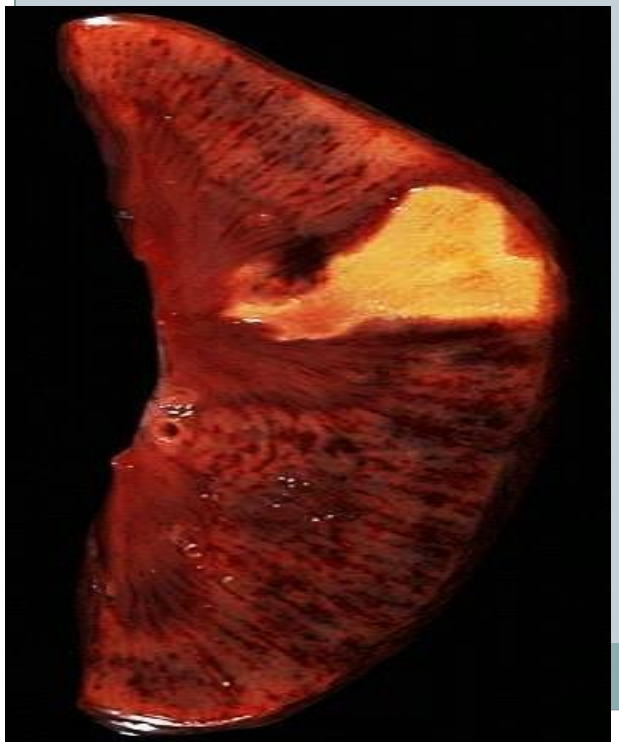


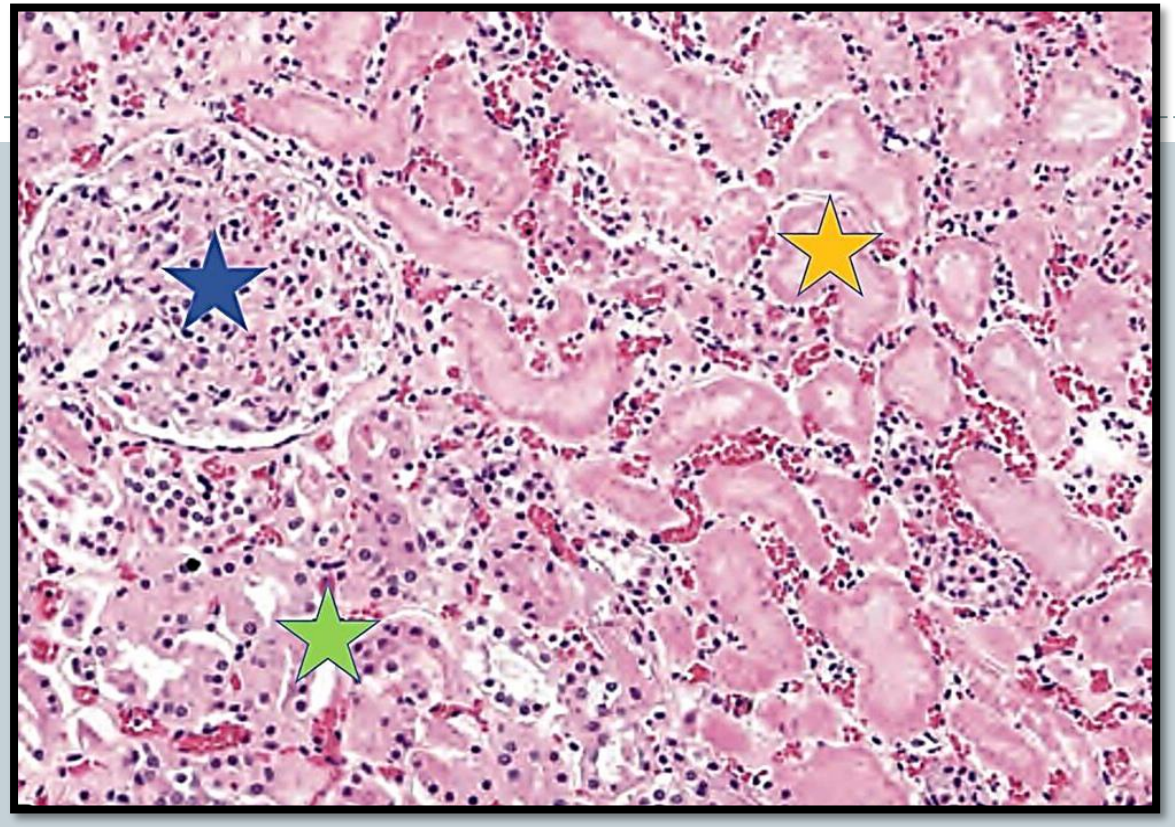
Normal

Necrosis

Coagulative necrosis, kidney infarction

Here, there is a wedge- shaped pale area of coagulative necrosis (infarction) in the renal cortex of the kidney.





The green star shows healthy cells that are less pink and have nuclei present. The blue star is a glomeruli. The yellow star indicates the necrotic portion. Notice that the architectural structure of the cell is still present, but no nuclei can be seen. You could almost draw a line between damaged and non-damaged cells.

Liquefactive necrosis:

There is digestion and liquefaction of necrotic tissue.

Causes:

1.Pyogenic bacterial infections attract neutrophils.

2. Bacterial and leukocytic enzymes liquefy dead cells and tissues.

3.The necrosis in the nervous tissue is mostly liquefactive due to high content of lipids and water.

Gross appearance:

The necrotic tissue is liquefied and filled with semisolid creamy liquid called pus.

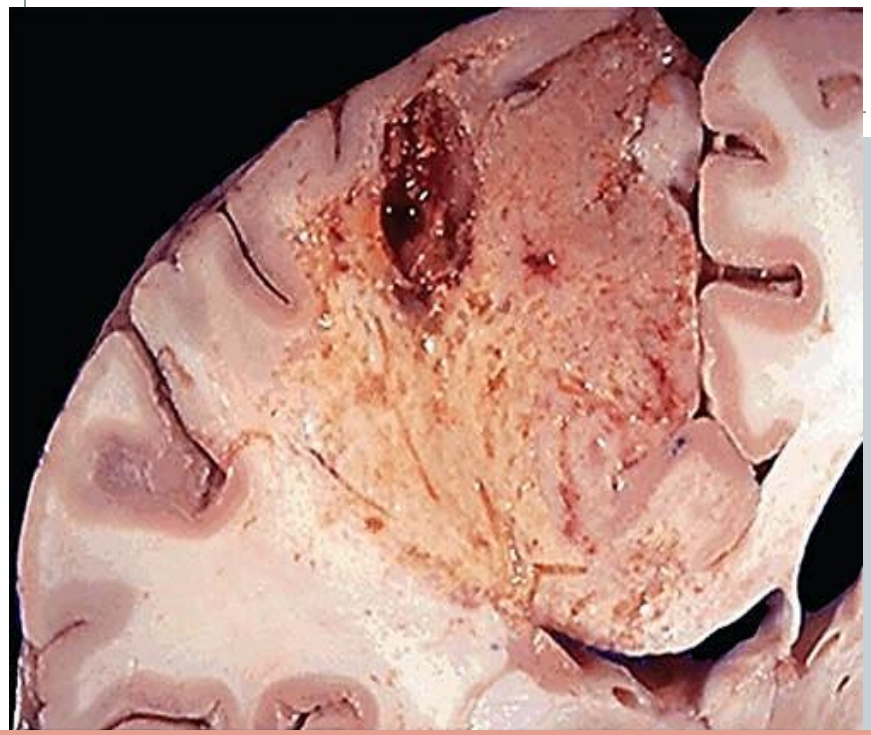
Pus:

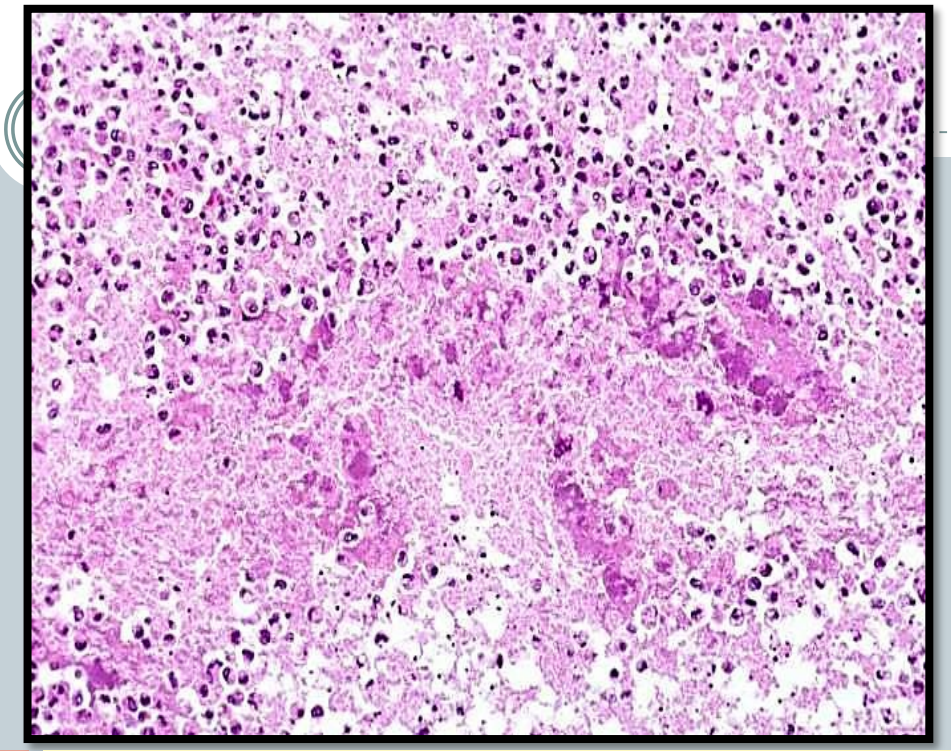
- It is a thick, white or yellow, creamy liquid consisting of exudate of leukocytes, tissue debris and microorganisms (pyogenic).
- Proteolytic enzymes released from neutrophils cause liquefaction of dead cells.

Microscopic appearance:

- No architectural or cellular details are visible in the area of necrosis.
- The necrotic area usually appears as a cavity containing a mass of necrotic neutrophils, bacteria and tissue debris.
- The entire necrotic mass is surrounded by a fibrous connective tissue capsule.

Liquefactive Necrosis





- 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**.

Pus consists of liquefied necrotic cell debris, dead leukocytes and macrophages (inflammatory cells cells).

Caseous necrosis:

Dead tissue is converted into a homogenous, granular mass resembling cheese material.

Cause:

I. Tuberculosis infections caused by *Mycobacterium tuberculosis*

II. Syphilitis

III. Systemic fungi infection.

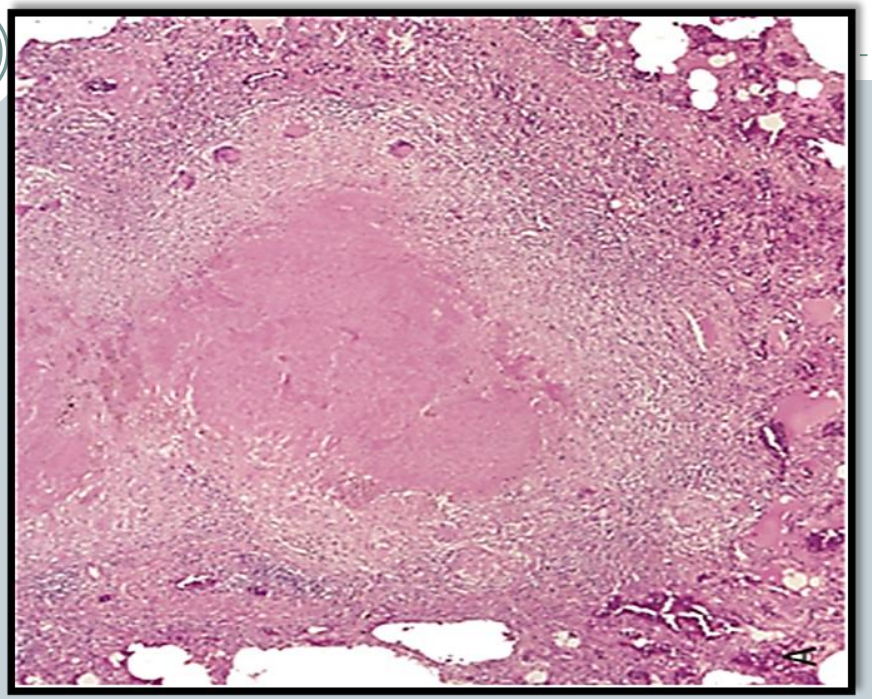
Gross appearance:

- The area of necrosis is amorphous, granular, friable, white-gray resembling cottage cheese.
- The caseous mass is enclosed within a connective tissue capsule.

Microscopic appearance:

- Presence of granuloma.
- The core is necrotic and uniformly eosinophilic, which is surrounded by a border of activated macrophages and lymphocytes.
- There is a fibrous tissue surrounding and enclosing the core.
- No architectural or cellular details are seen.
- Calcification commonly occurs in the necrotic areas.

Caseous Necrosis



"Caseous" (cheeselike) is derived from the friable white appearance of the area of necrosis

Caseous necrosis appears as eosinophilic, coarsely granular material. It is surrounded by macrophages, lymphocytes and fibroblasts.

Granuloma (caseous nerosis)