

IRREVERSIBLE CELL INJURY

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II-IRREVERSIBLECELLINJURY(CELLDEATH)

- **Definition: Severe form of cell injury affecting both the nucleus and cytoplasm leading finally to cell death.**
- **Types:**
 - a- Apoptosis**
 - b- Necrosis**

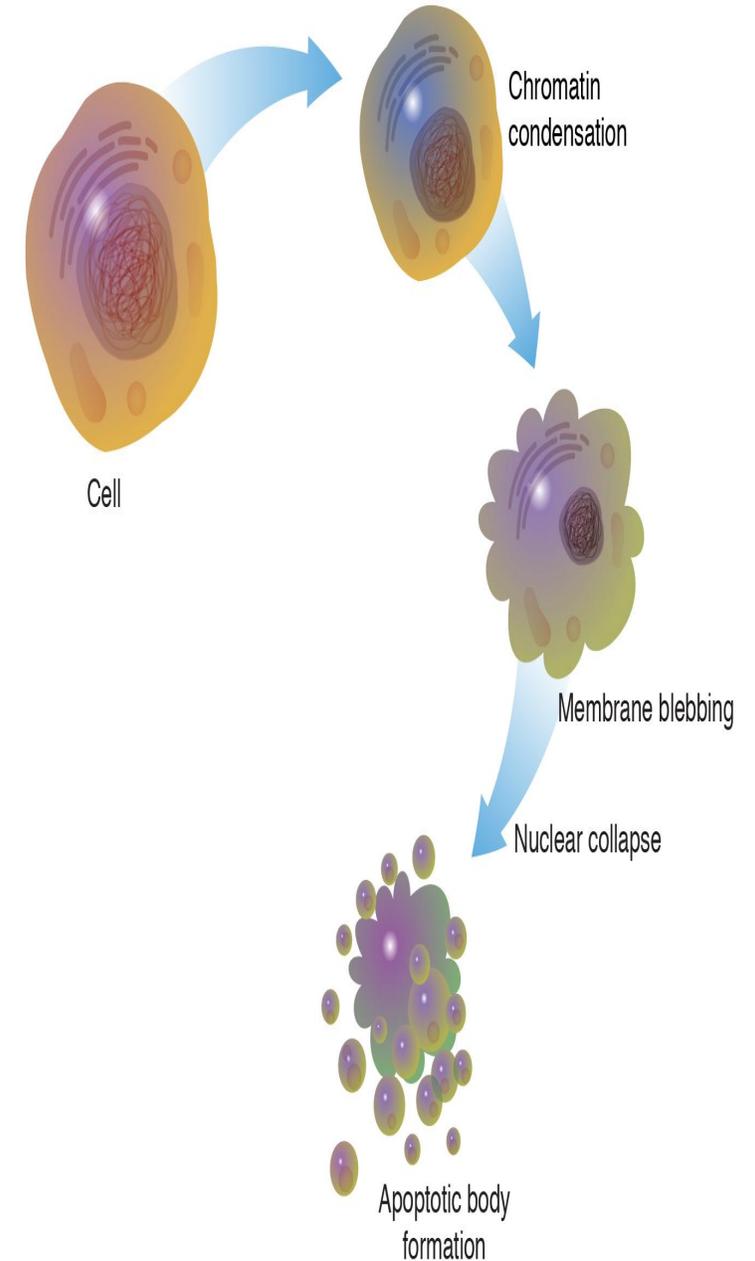
a-APOPTOSIS

Definition: Programmed cell death to eliminate unwanted cells in the living tissues

Types of apoptosis:

Physiologic apoptosis: during embryogenesis.

Pathological apoptosis: viral hepatitis, cytotoxic drugs.



Mechanisms of apoptosis:

- there are **two** phases of apoptosis:

1-Initiation phase: During which caspases become active by:

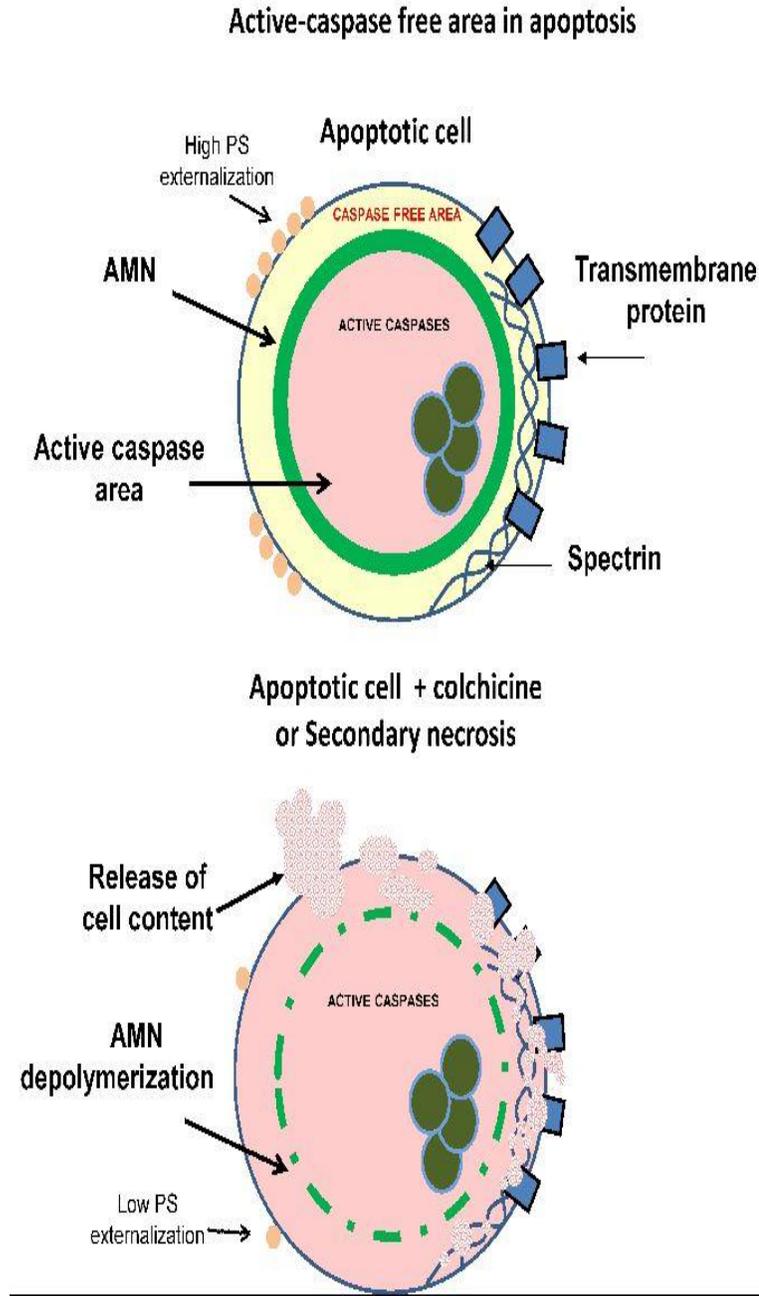
a- Extrinsic pathway (Death receptor-initiated): Stimulation of the cell surface death receptor

eg: **tumor necrosis factor receptors** leads to production of apoptotic signals which finally leads to activation of **the caspases.**

b- Intrinsic (mitochondrial) pathways:

- **Cell injury leads to increased mitochondrial permeability.**
- **Mitochondrial damage leads to release of the pro-apoptotic molecules (as **Bax**) into the cytoplasm which finally activate **the caspases.****

2-Execution phase: Starts after activation of caspases that leads to proteolytic cleavage of cytoskeletal proteins and breakdown of the nucleus with complete cell apoptosis



Morphological changes in apoptotic cells:

Nuclear changes:

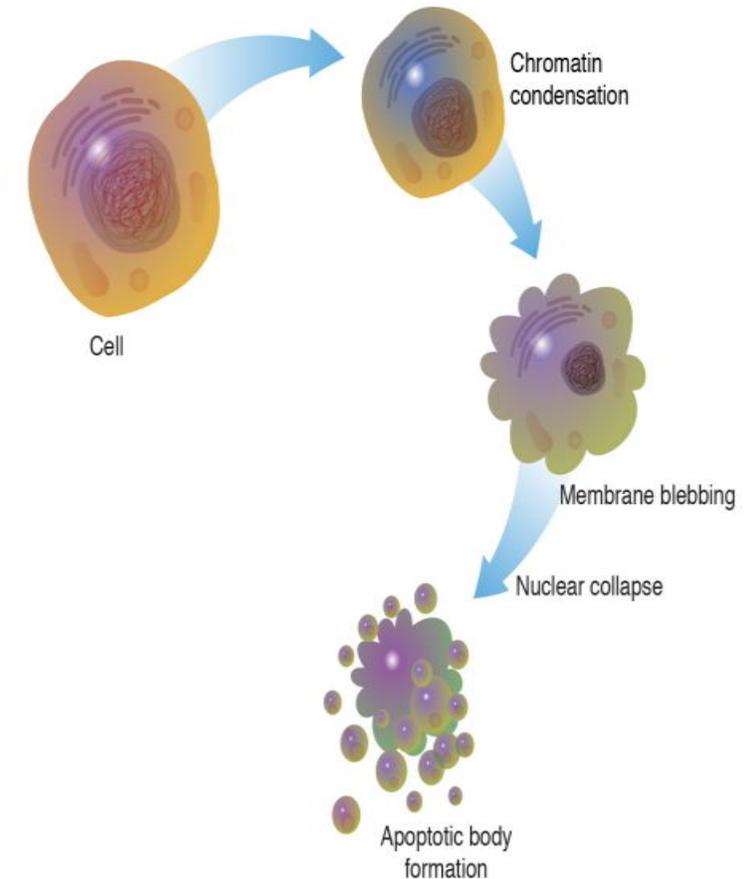
1- Chromatic condensation: The chromatin aggregates under the nuclear membrane then undergo fragmentation.

Cytoplasmic changes:-Cell shrinkage and The cytoplasm becomes dense and eosinophilic. The cells membrane remains intact and form surface blebs. This is followed by fragmentation of the apoptotic cells into apoptotic bodies.

Apoptotic bodies: part of cell membrane enclosing part of the cytoplasm, organelles and nuclear chromatin.

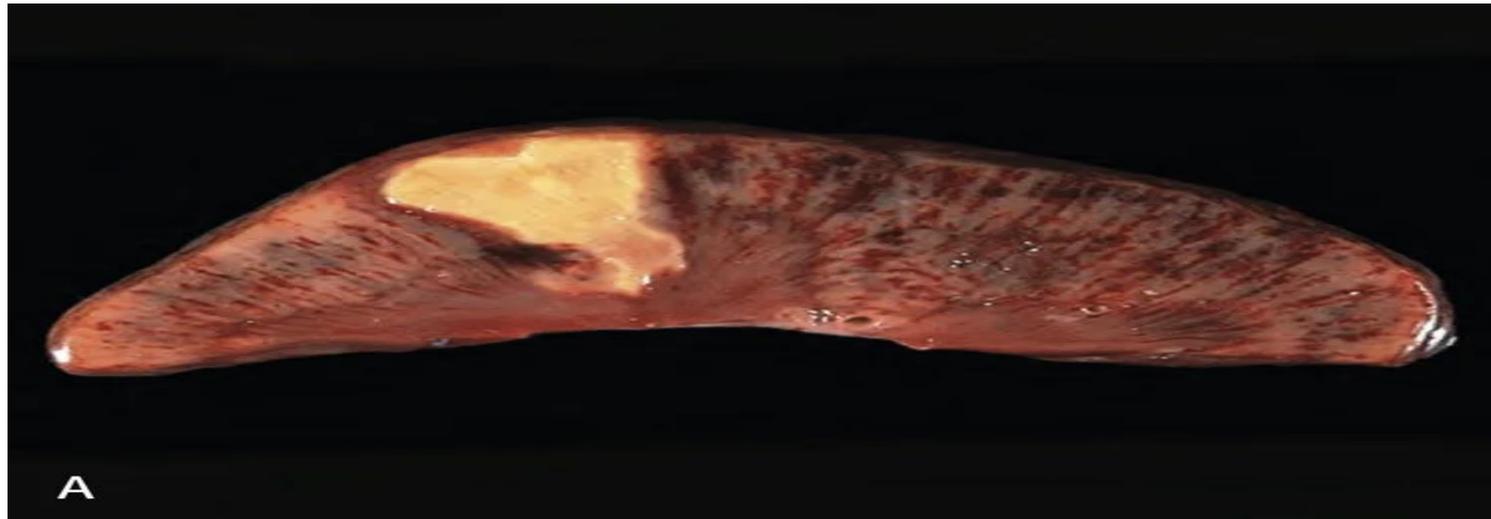
Phagocytosis of apoptotic bodies: apoptotic cells are recognized

and phagocytosed by macrophages



b- Necrosis:

- **Definition: local death of groups of cells in the living tissue**
- **Morphological changes in necrosis:**
- **Gross picture: Necrotic area appears opaque and surrounded by red zone of inflammation.**



Microscopic picture:

1- Cytoplasmic changes:

a- The cells become swollen (cytomegally).

b- Increased eosinophilia.

c- The cytoplasm becomes vacuolated

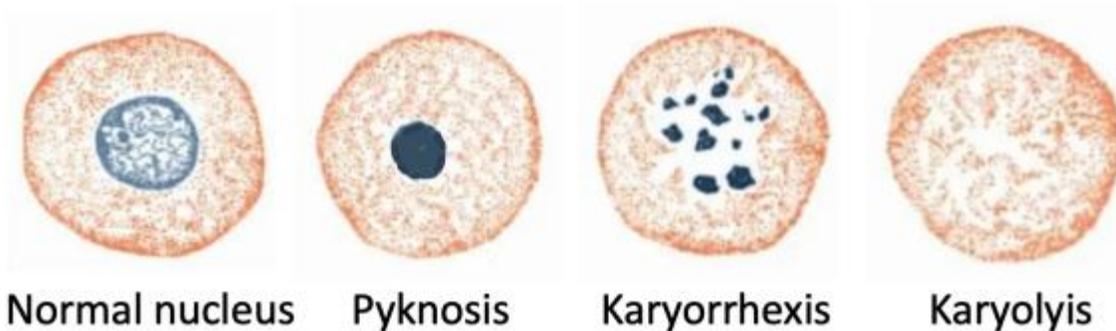
d- Finally the cell membrane ruptures.

2- Nuclear changes:

a- Pyknosis: nuclear shrinkage.

b- Karyorrhexis: Fragmentation of nuclear material

c- Karyolysis: Lysis and dissolution of the nuclear chromatin.



Types of necrosis:

1- Coagulative necrosis.

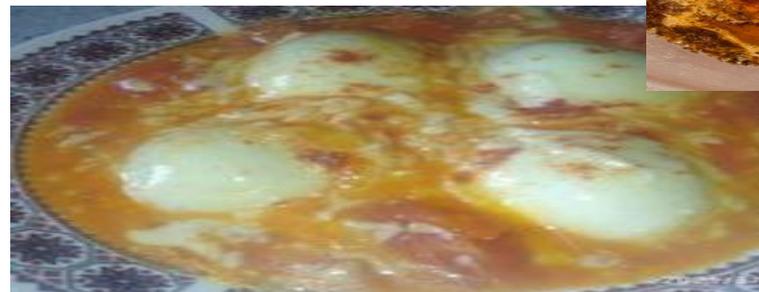
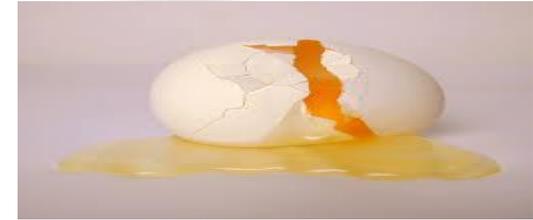
2- Liquifactive necrosis.

3- Caseating necrosis.

4- Fat necrosis.

5- Fibrinoid necrosis.

6- Gangrenous Necrosis



COAGULATIVE NECROSIS

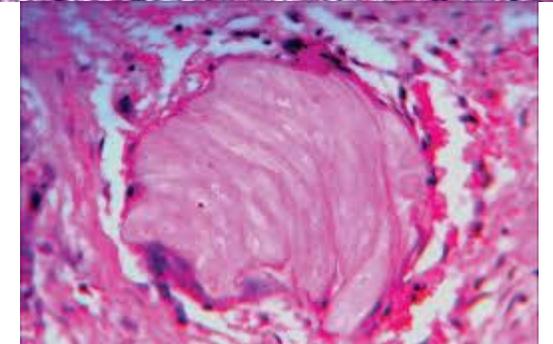
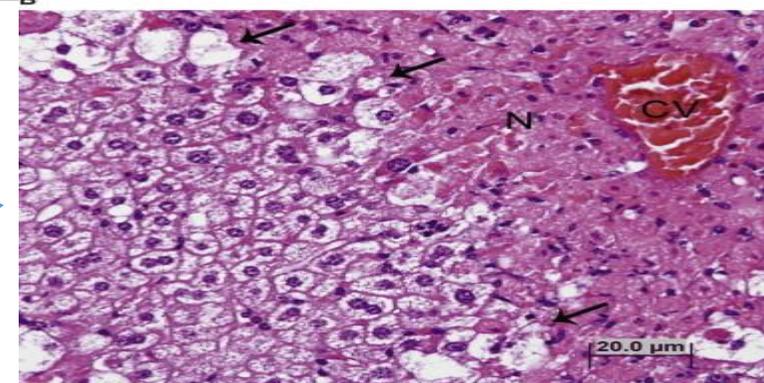
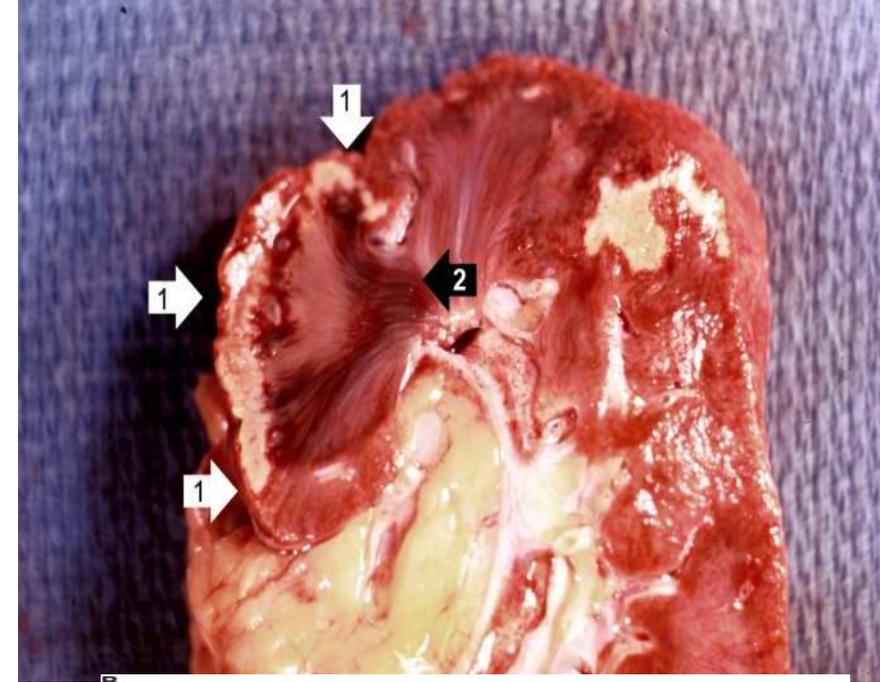
Definition: The most common type of necrosis mainly caused by sudden cut of blood supply. It affects all tissue except the brain.

In this type of necrosis, the injury causes denaturation in both structural proteins and proteolytic enzymes. This delays cell lysis, so the tissue architecture is

preserved and **ghosts of cells remain.**

- **Gross picture: The necrotic part appears firm, swollen, opaque.**

Examples: Myocardial infarction and splenic infarction.



Liquifactive necrosis

Definition:

Type of necrosis characterized by softening and liquefaction of the necrotic tissue.

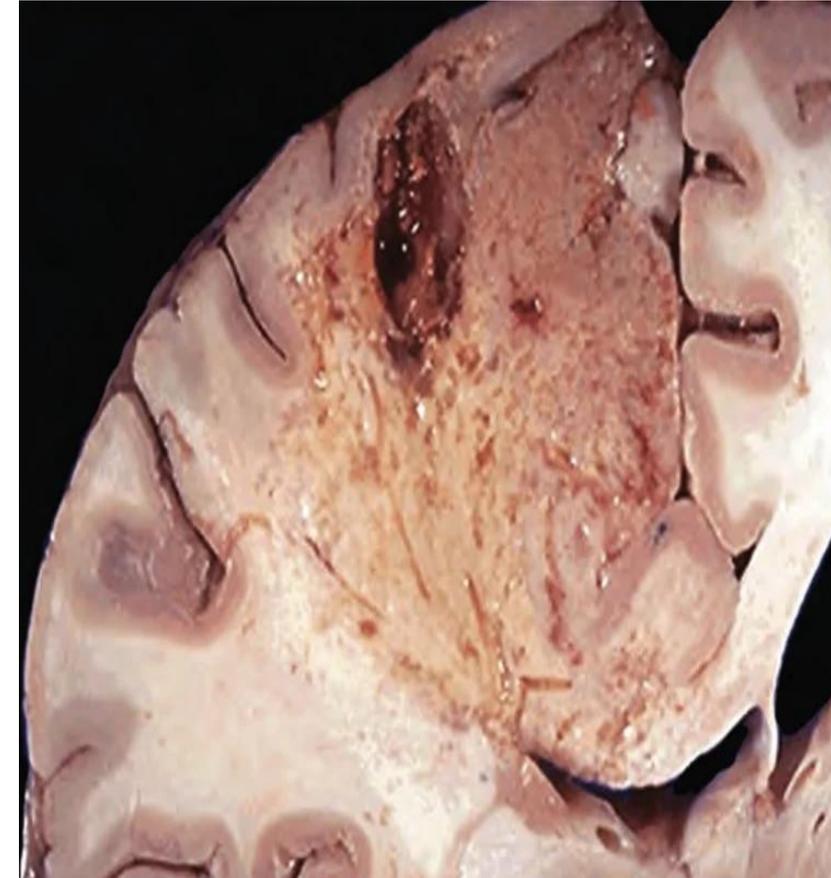
In this type of necrosis, enzymatic digestion is dominant than denaturation.

The necrotic area becomes soft and liquefied.

Examples:

a-Brain infarctions: due to high lipid and fluid content

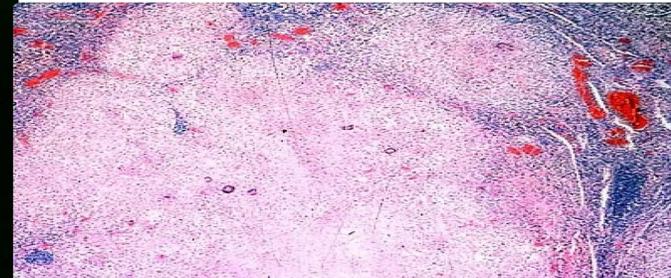
b- Pyogenic abscess due to liquefaction of necrotic tissue by proteolytic enzymes.



CASEATION NECROSIS

Definition: It is a specific type of necrosis characterized by slow partial liquefaction of the necrotic area. It is typically found in caseating

Tuberculosis.



Caseous necrosis with granulomatous inflammation

T.B LUNG :

(Large Area Of Caseous Necrosis)

AREA ,YELLOW-WHITE
AND CHESSY

FAT NECROSIS

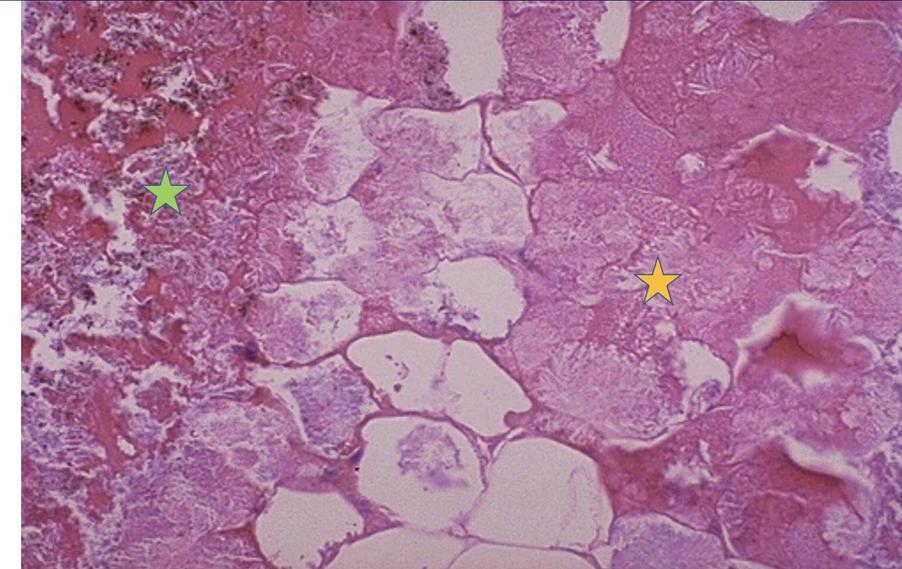
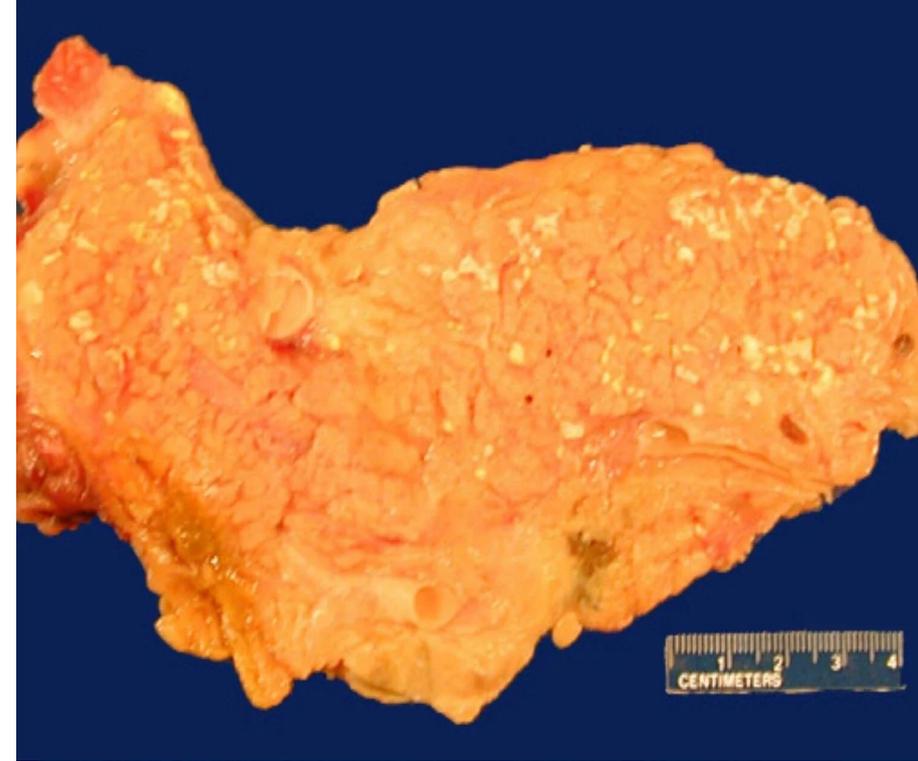
Definition: Local destruction of adipose tissue.

Types of fat necrosis:

a- Traumatic fat necrosis: Mechanical trauma of the adipose tissue

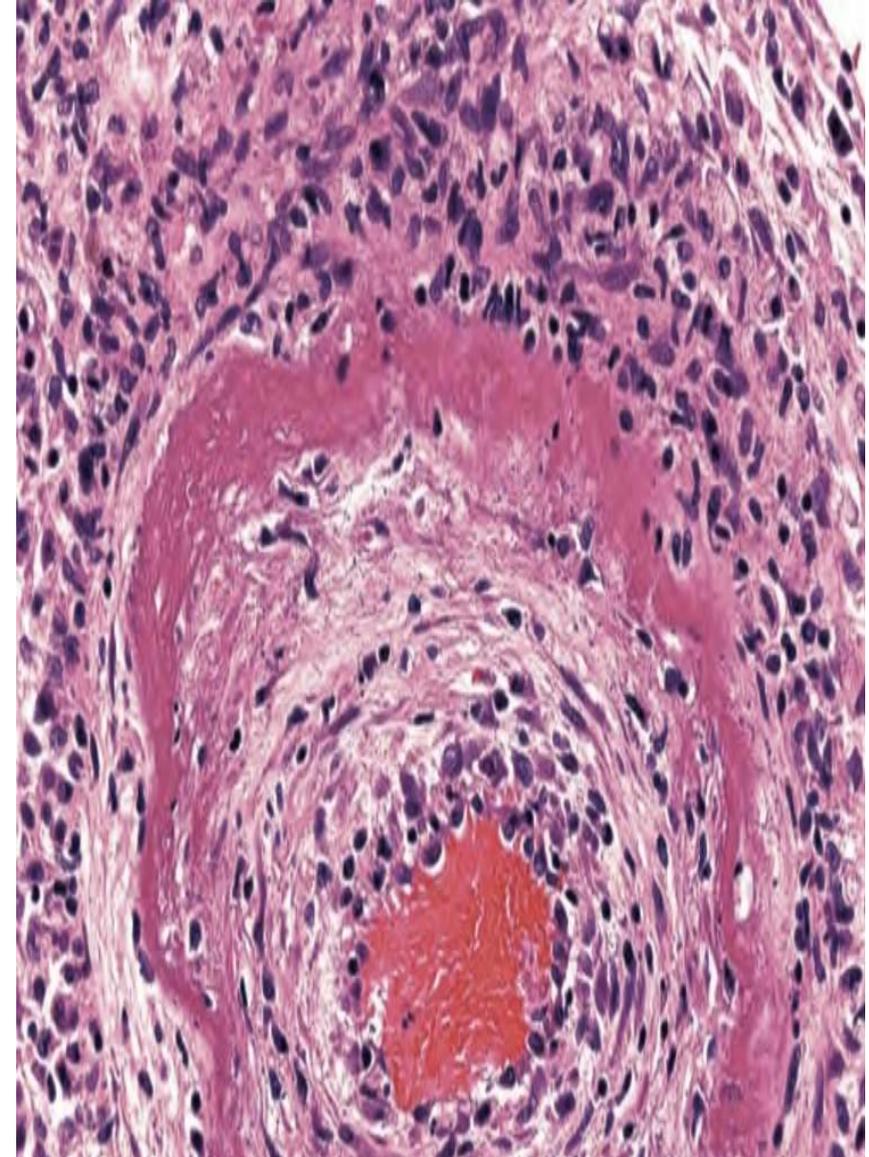
result in splitting of neutral fat with activation of macrophages. It commonly occurs in female breast.

b- Enzymatic fat necrosis: Due to release of lipase enzyme increases of acute hemorrhagic pancreatitis leading to destruction of omental fat



FIBRINOID NECROSIS

Definition: It is a specific type of necrosis affecting the small arteries and arterioles in cases of autoimmune disease and malignant hypertension. The wall of the affected vessel shows homogenous eosinophilic material formed mainly of fibrin with plasma proteins and Ag-Ab complexes which obscure cellular details



GANGRENOUS NECROSIS (Gangrene)

Definition: Tissue necrosis with superadded putrefaction. Necrosis is caused by sudden ischemia. Putrefaction is caused by saprophytic bacteria which breakdown proteins of necrotic tissue liberating hydrogen-sulphide that gives foul odor.

- **Hydrogen sulphide combines with iron of hemoglobin forming iron sulphide that stains gangrenous tissue black color.**



	NECROSIS	APOPTOSIS
Definition	Death of a group of cells in the living tissue	Programmed cell death
Stimulus	Pathologic only	Both physiologic & Pathologic
Associated Inflammation	Present	Absent
Cell size	Enlarged (swelling)	Cell shrinkage
Nuclear changes	Pyknosis, karyorrhexis, karyolysis	Nuclear condensation & Fragmentation
Cell membrane	Disrupted	Intact, altered structure
Energy demand	Does not need energy	Needs energy



Thank
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