

Cell death, Apoptosis, Necrosis and exudates

Cell death

- **Cell death** is the event of a biological **cell** ceasing to carry out its functions.
- There are two forms of cell death, **apoptosis** and **necrosis**.
- **Apoptosis** is controlled (programmed) breakdown of cells occurring in response to damage to DNA or as part of normal growth and development.
- **Necrosis** is uncontrolled breakdown of cells in response to injurious stimuli.

APOPTOSIS

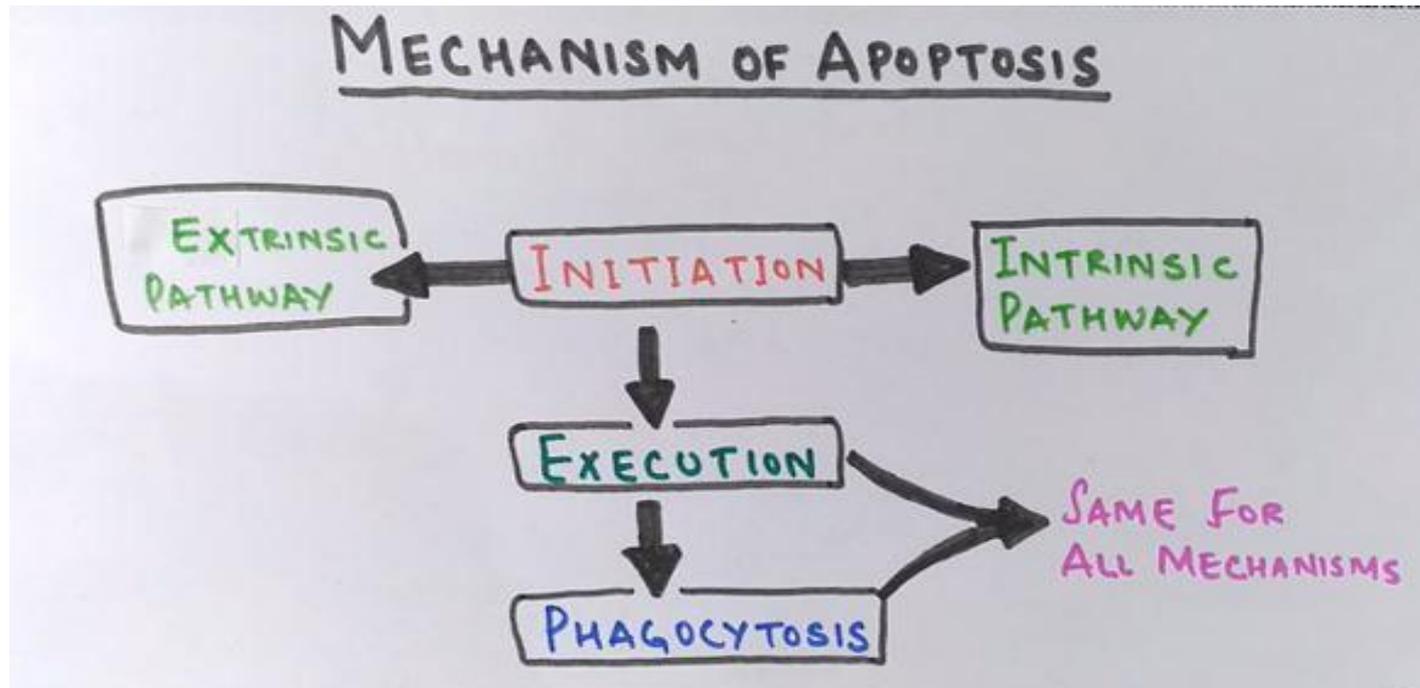
- **Basic description:** Programmed cell death.

Patterns of occurrence of apoptosis

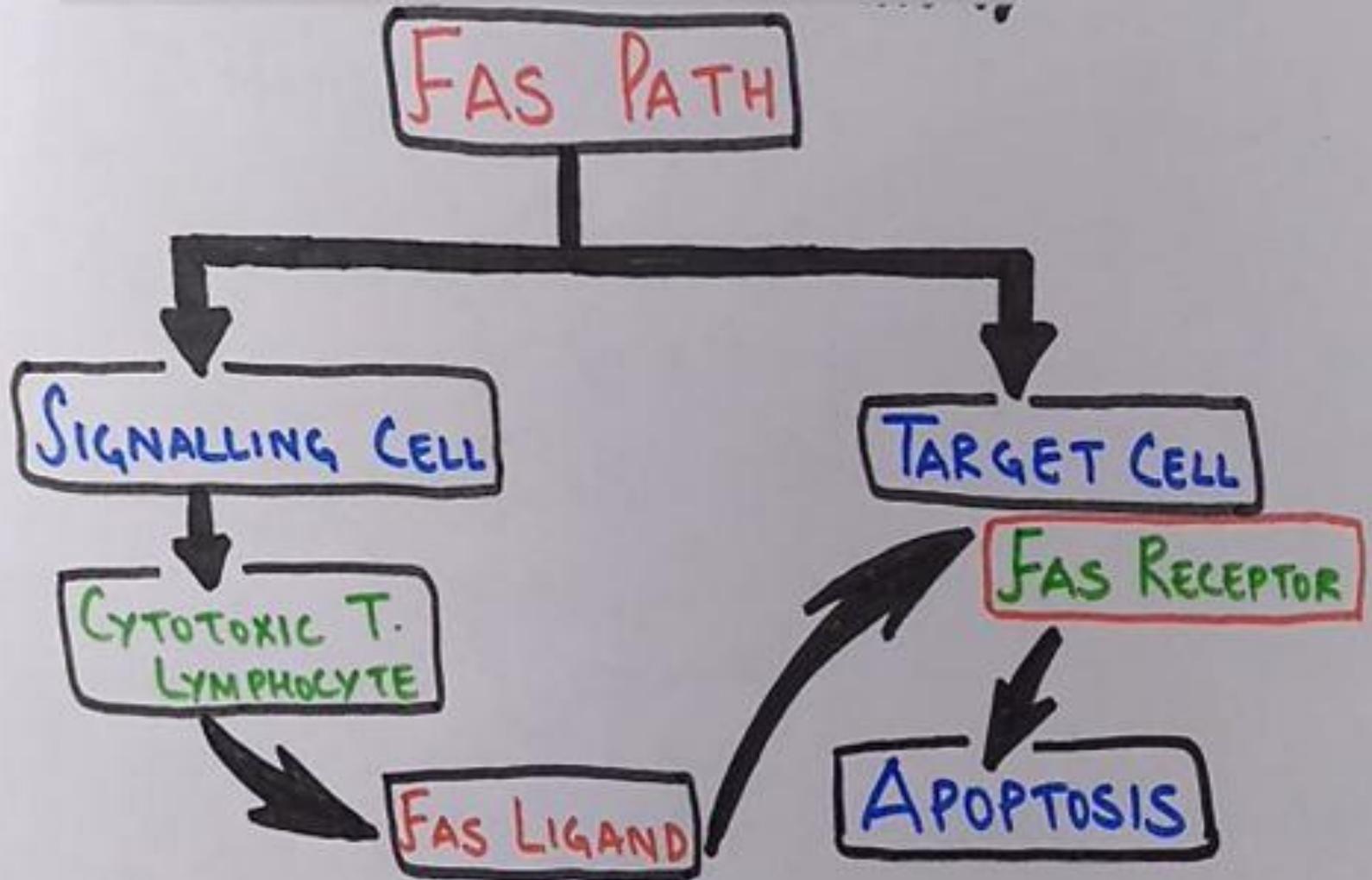
- During growth and development, some cells serve a function in the growth phase but need to be removed after their purpose is fulfilled.
- In neonates, a rapid cell growth rate is necessary; in adults, however, unrestrained cell growth can lead to cancer.
- When DNA sustains irreparable damage (e.g., after low-dose radiation exposure), the cell must be destroyed so mutations that have developed will not be propagated.
- In this manner, apoptosis serves as a safety step by removing damaged cells from the body.

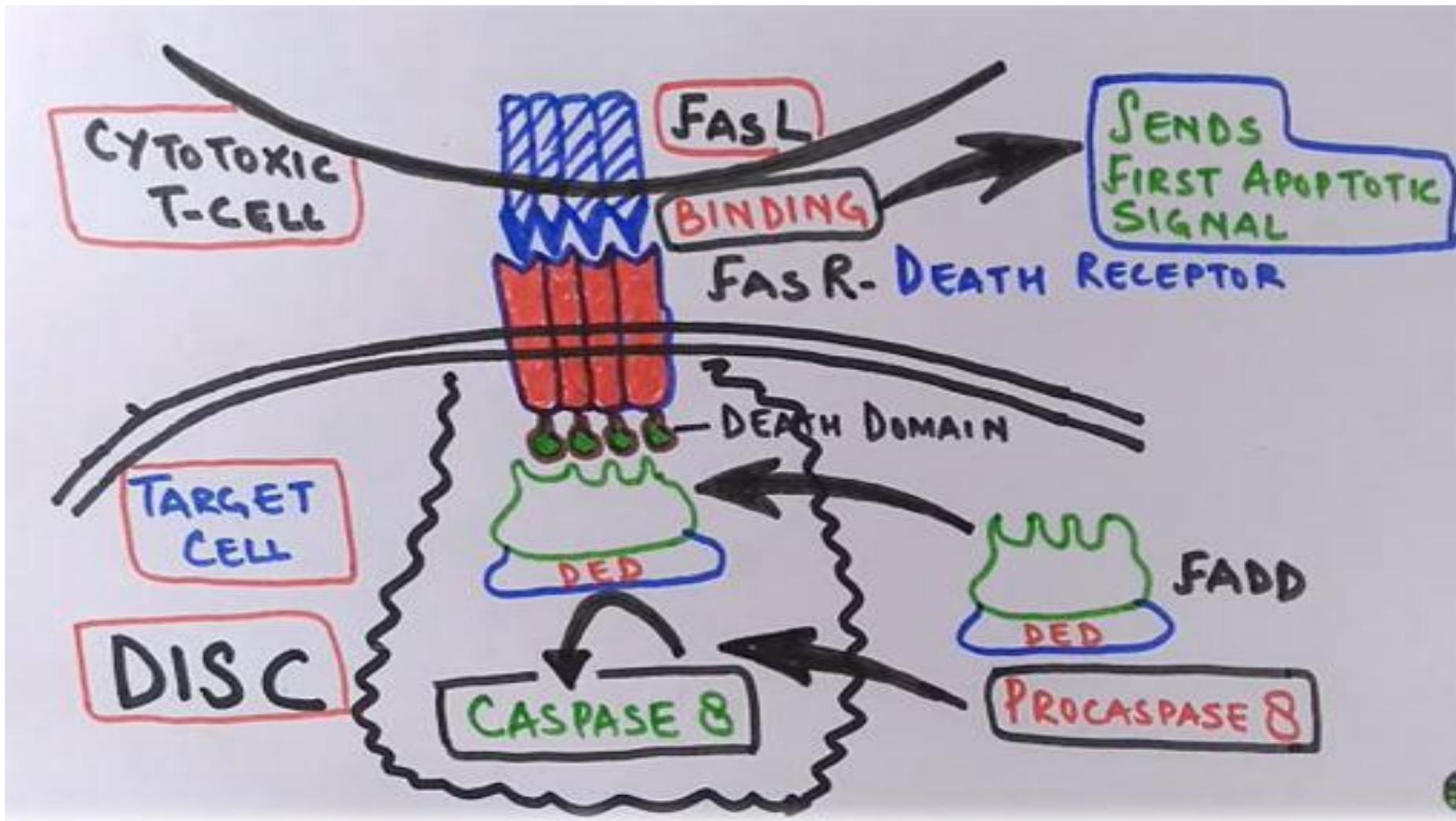
Mechanism of apoptosis

- There are two pathways by which apoptosis is initiated:
- 1. **Extracellular** or **Extrinsic** apoptosis pathway
- 2. **Intracellular pathways** or **Intrinsic** apoptosis pathway



EXTRINSIC PATHWAY,

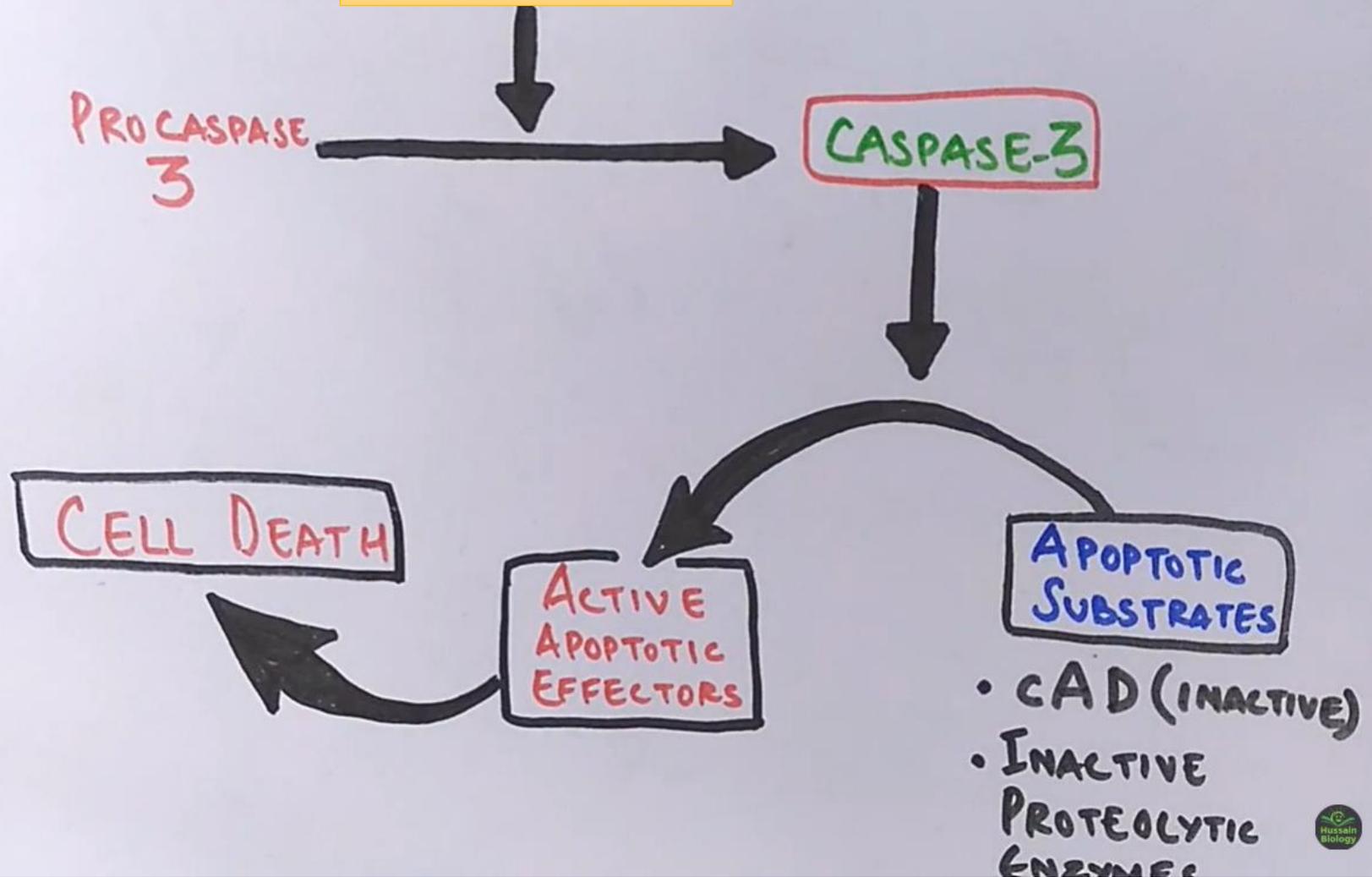




FasL-Fas ligand, **FADD**- Fas-associated protein with dead domain, **DED**-Dead domain, **DISC**- Dead inducing signal complex.

CASPASE- protease enzymes.

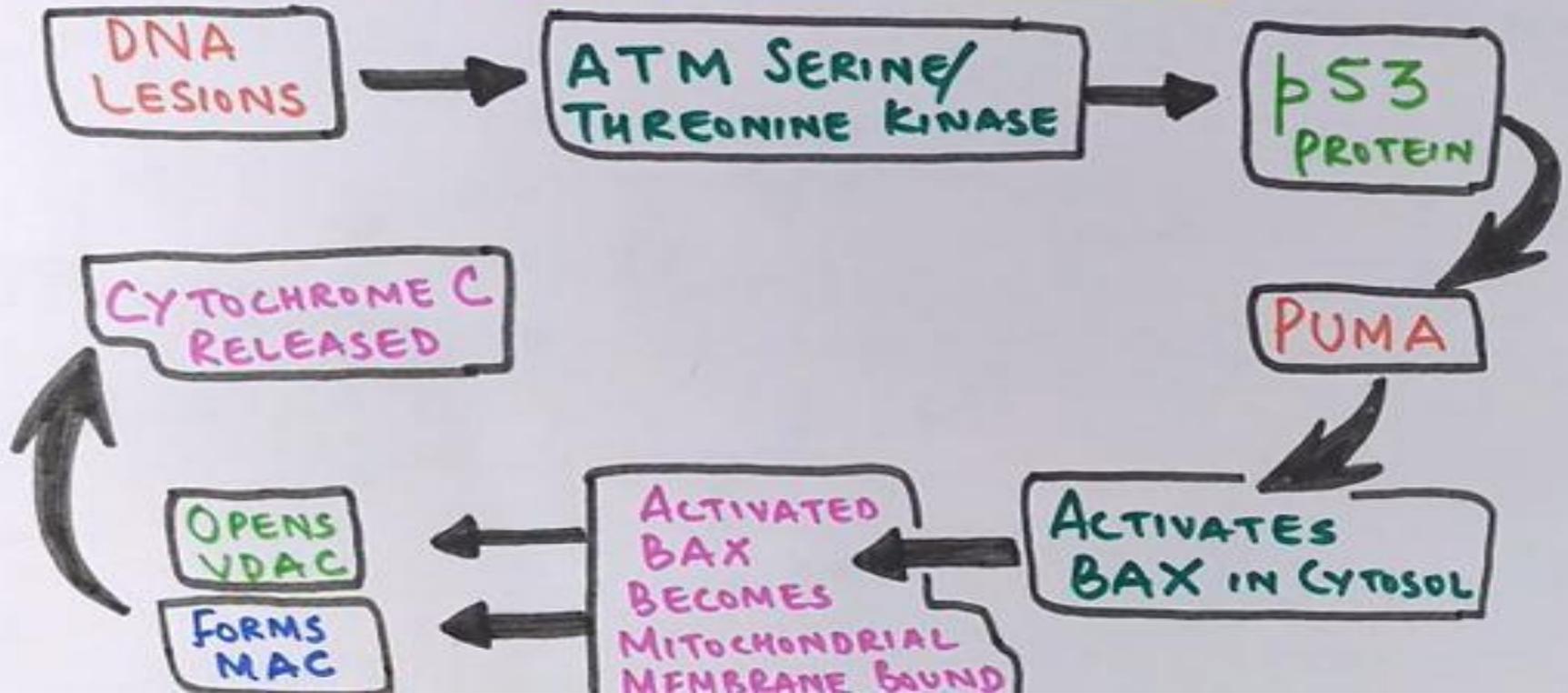
Caspase8



CAD-Caspase Dependent DNase.

Apoptotic effectors- Activated DNase, Activated Proteolytic enzymes

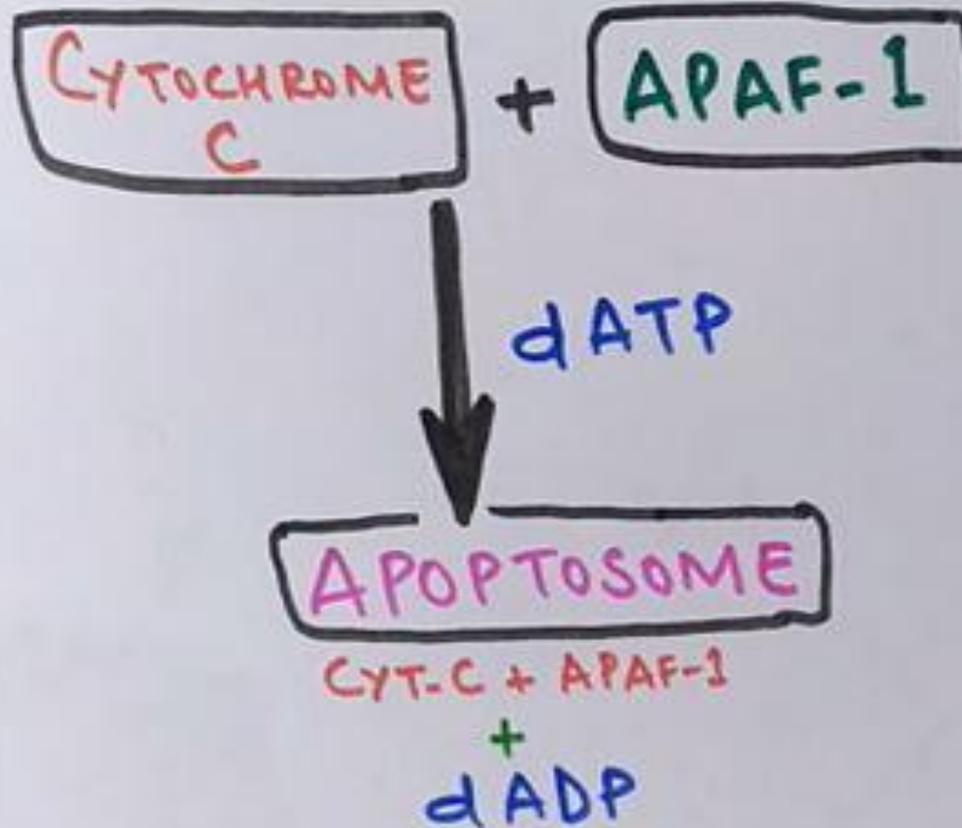
INTRINSIC PATHWAY OR MITOCHONDRIAL PATHWAY



Apoptosis regulator BAX, also known as **bcl-2-like protein 4**, is a protein, functions as an apoptotic activator.

PUMA-p53 Up regulatory Modulator of Apoptosis.

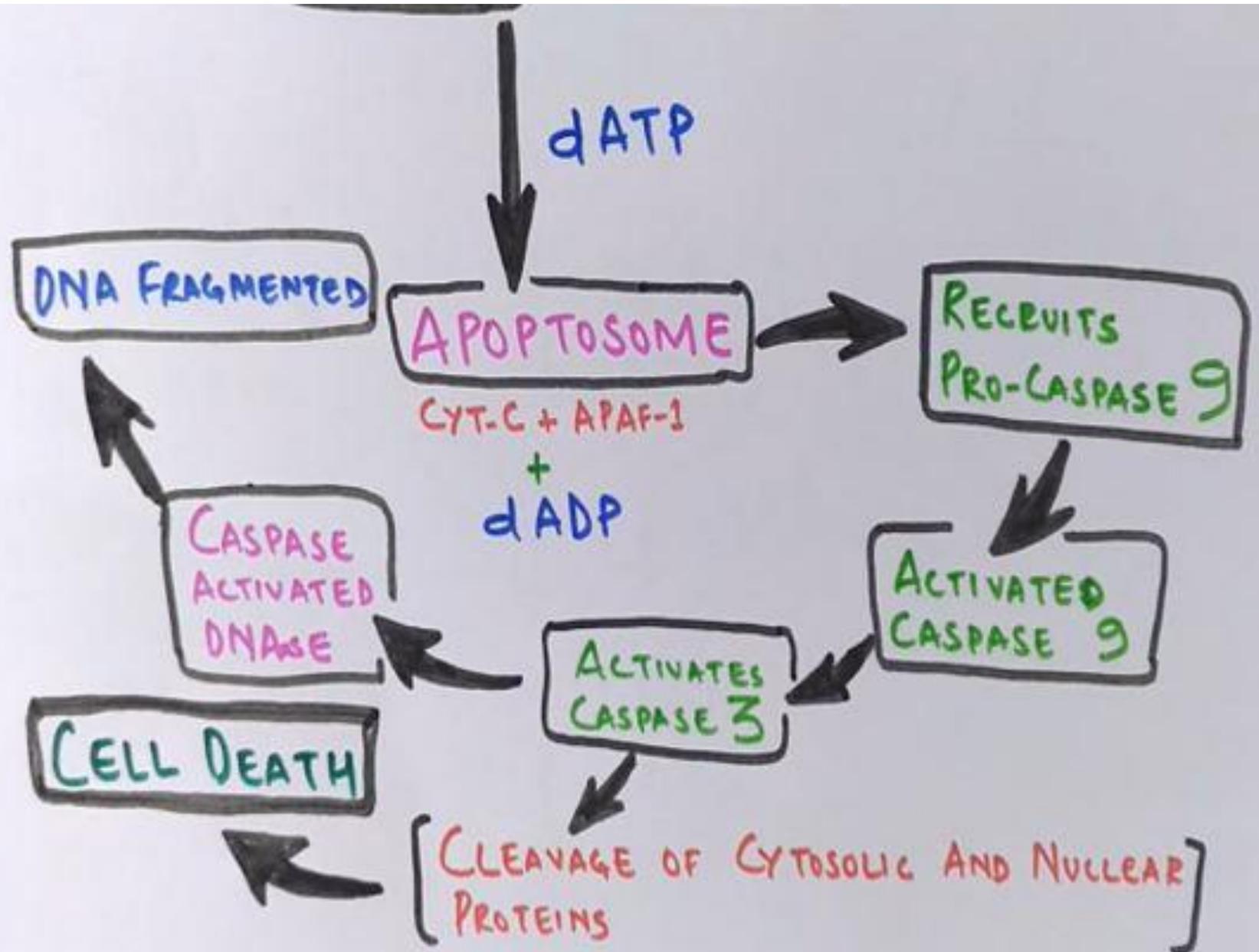
- Farther increase the opening of the mitochondrial voltage-dependent anion channel (**VDAC**), which leads to the loss in membrane potential and the release of cytochrome c.
- **MAC**-mitochondrial Apoptotic inducing channel.



APAF-1: Apoptotic Protease Activating Factor-1

dATP-Deoxyadenosine Triphosphate

dADP-Deoxyadenosine Diphosphate



Necrosis

- **Basic description:** Necrosis is a term used to describe uncontrolled death of cells due to one of the various causes of cellular injury.
- **Gross morphology of necrosis:** Necrosis is typically manifested by softening and discoloration of the organ.

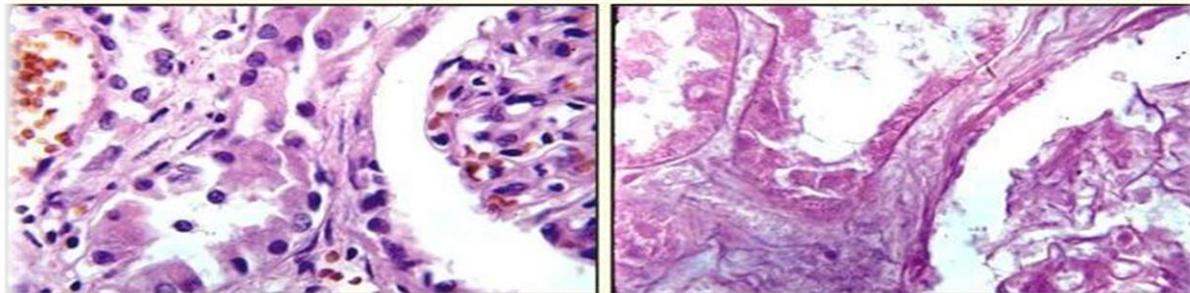
Types of Necrosis

- 1. Coagulative necrosis**
- 2. Liquefactive necrosis**
- 3. Fat necrosis**
- 4. Caseous necrosis**

Coagulative necrosis

- Coagulative necrosis is the type of necrosis in which protein denaturation is more prominent than enzymatic breakdown.
- Coagulative necrosis may occur in any organ.

Coagulative Necrosis - Kidney



Normal

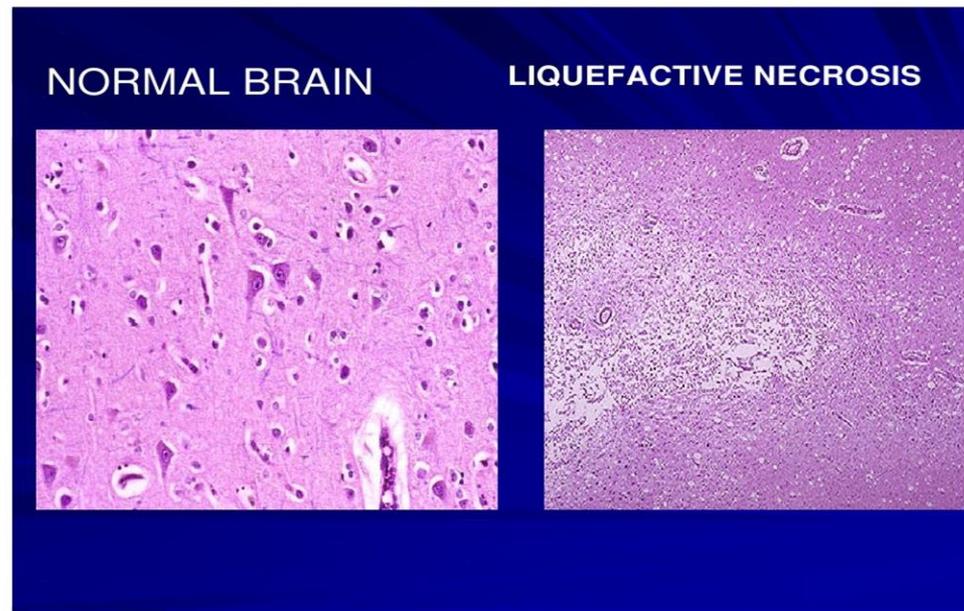
Source: TUSDM

Necrosis

Source: TUSDM

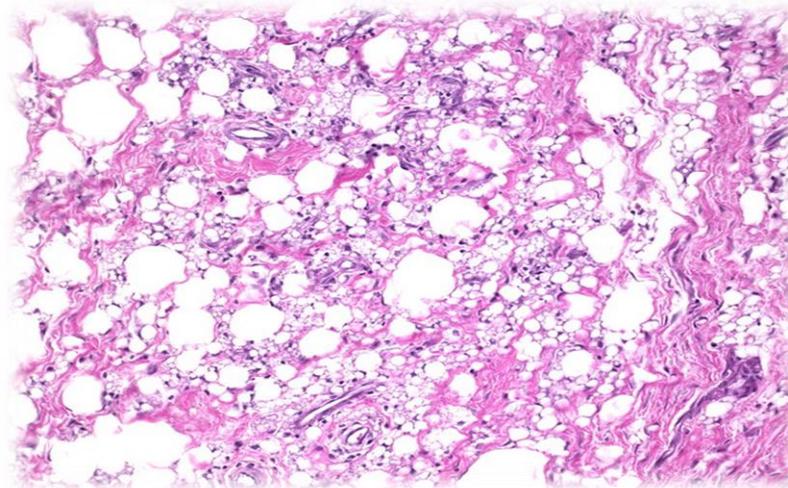
Liquefactive necrosis

- Liquefactive necrosis occurs in situations in which enzymatic breakdown is more prominent than protein denaturation.
- Liquefactive necrosis is most commonly associated with organs that have a high fat and low protein content (e.g., the brain), or those with a high enzymatic content (e.g., the pancreas).



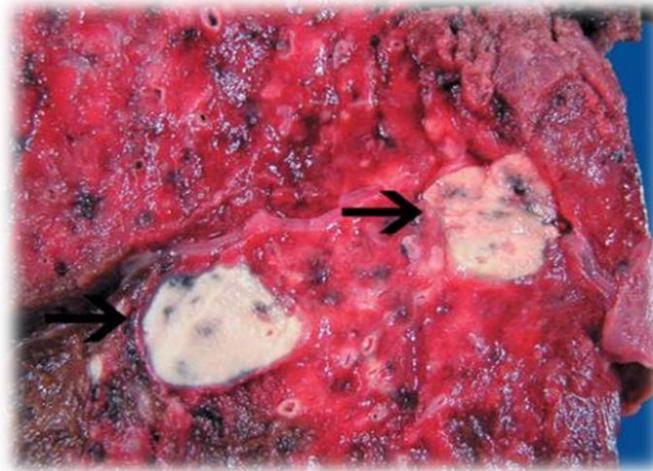
Fat necrosis

- Fat necrosis is a term applied to a change in adipose tissue due to trauma or the release of enzymes from adjacent organs (e.g., the pancreas).
- The trauma or enzymatic action causes a breakdown of lipid and a release of fatty acids, which combine with calcium to form chalky deposits.



Caseous necrosis

- Caseous necrosis is a “cheesy-looking” necrosis associated with tuberculosis infections and other granulomatous disease processes.
- Granulomas are a form of chronic inflammation due to some infections (e.g., mycobacterial), foreign bodies, and other chronic stimuli.

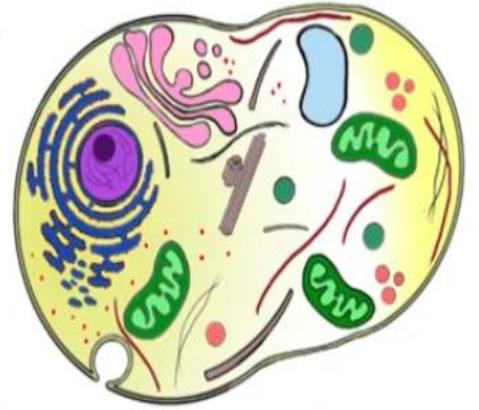


Necrosis

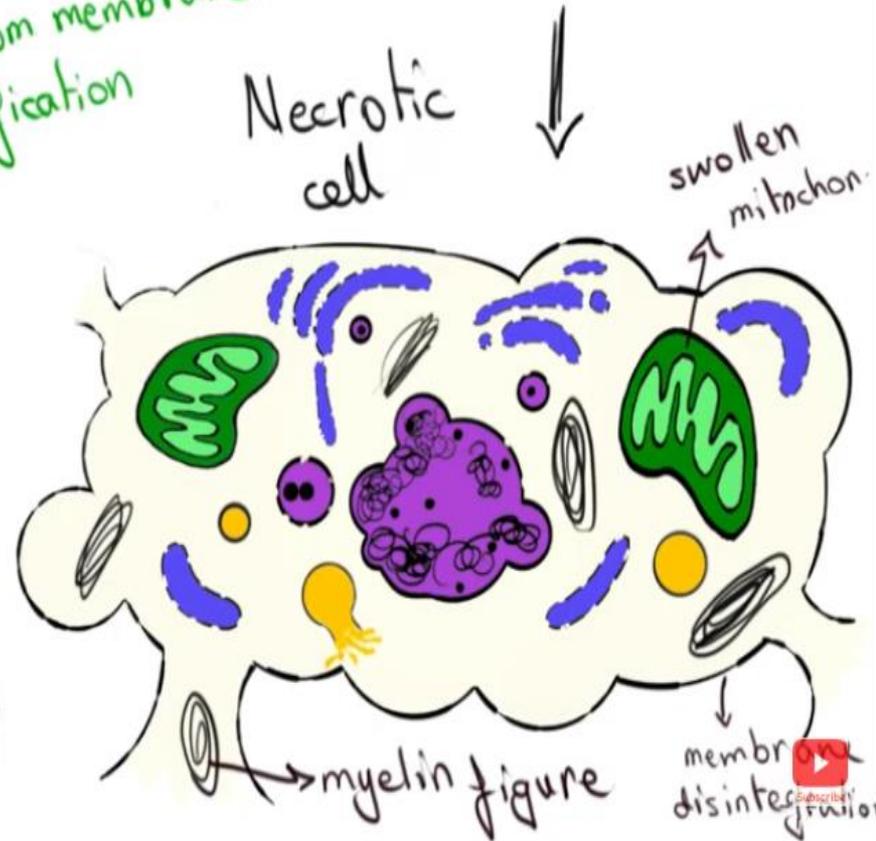
Morphology

- Increased eosinophilia → loss of cytoplasmic RNA
→ denatured cytoplasmic proteins
- Myelin figures → phospholipid masses from membranes
↳ fatty acids → calcification
- Membrane disintegration → hallmark
↳ ROS
- Internal organelle swelling
↳ membrane permeability ↑

Normal cell

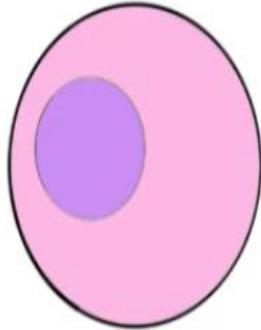


Necrotic cell

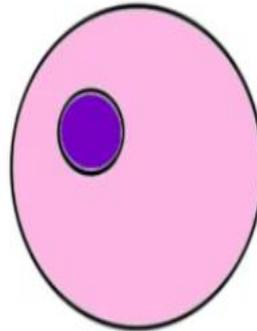


Necrosis

Morphology -> Nuclear Changes



Karyolysis
nuclear fading



Pyknosis
nuclear shrinkage



Karyorrhexis
nuclear fragmentation

Three types of nuclear changes can be seen during cell necrosis

1. Karyolysis
2. Pyknosis
3. Karyorrhexis

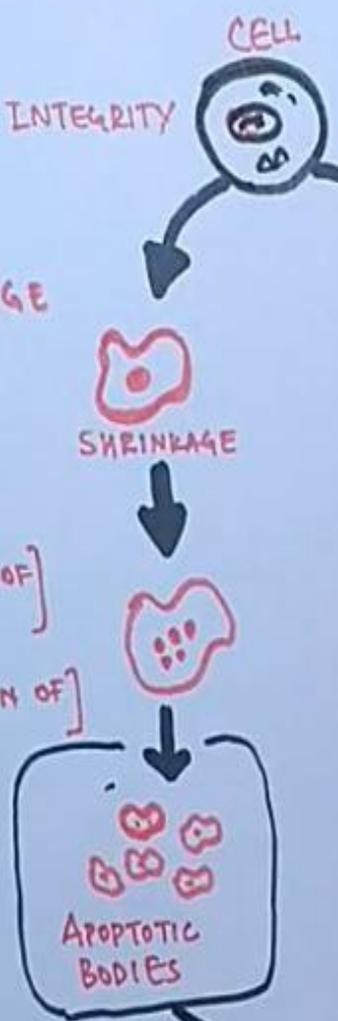
APOPTOSIS

1. INTACT CELL MEMBRANE
↳ NO-LOSS OF MEMBRANE INTEGRITY
BLEBBING OCCURS

2. BEGINS WITH CELL SHRINKAGE AND CONDENSATION OF NUCLEUS

3. PYKNOSIS OCCURS [CONDENSATION OF CHROMATIN]
↓
KARYORRHEXIS [FRAGMENTATION OF NUCLEUS]

4. FORMATION OF APOPTOTIC BODIES



NECROSIS

1. DISRUPTED CELL MEMBRANE
↳ LOSS OF MEMBRANE INTEGRITY

2. BEGINS WITH SWELLING

3. PYKNOSIS + KARYORRHEXIS

↓
KARYOLYSIS ALSO OCCURS
↳ DISSOLUTION OF CYTOPLASM

4. NO VESICLE FORMATION
COMPLETE CELL LYSIS



PHAGOCYTOSIS

Exudate

- An exudate is any fluid that filters from the circulatory system into lesions or areas of inflammation.
- It can be a pus-like or clear fluid.
- When an injury occurs, leaving skin exposed, it leaks out of the blood vessels and into nearby tissues.
- The fluid is composed of serum, fibrin, and white blood cells.

Types of exudate

1. Purulent or suppurative exudate
2. Fibrinous exudate
3. Catarrhal exudate
4. Serous exudate
5. Malignant (or cancerous) exudate

1. Purulent or suppurative exudate

- It consists of plasma with both active and dead neutrophils, fibrinogen, and necrotic parenchymal cells.
- This kind of exudate is consistent with more severe infections, and is commonly referred to as pus.

2. Fibrinous exudate:

- It is composed mainly of fibrinogen and fibrin.

3. Catarrhal exudate:

- It is typical origin from mucous surfaces as in skin.

4. Serous exudate:

- It is usually seen in mild inflammation, with relatively low protein.

5. Malignant (or cancerous) exudate:

- It is effusion where cancer cells are present