



## **APOPTOSIS**

Apoptosis is A pathway of cell death induced by a tightly regulated suicidal program, in which the cells destined to die activate enzymes that degrade cells own nuclear DNA and nuclear, cytoplasmic proteins, ‘programmed cell death’ having significance in a variety of physiologic and pathologic conditions (apoptosis is a Greek word meaning ‘falling off’ or ‘dropping off’).

The term was first introduced in 1972 as distinct from necrosis by being a form of cell death which is controlled and regulated by the rate of cell division; when the cell is not needed, pathway of cell death is activated (‘cell suicide’) and is unaccompanied by any inflammation and tissue damage.

### **Causes of apoptosis**

Apoptosis is responsible for mediating cell death in a wide variety of physiologic and pathologic processes as under:

#### **Physiologic Causes :**

1. Programmed destruction during embryogenesis
2. Physiologic involution of cells in hormone-dependent tissues e.g. endometrial shedding.
3. Elimination of cell that serve their useful purpose e.g. RBC

#### **Pathologic Causes:**

1. Pathologic atrophy of organs and tissues on withdrawal of stimuli e.g. atrophy of kidney or salivary gland on obstruction of ureter or ducts, respectively.
2. Cell death in response to infection e.g. viral infection
3. In degenerative diseases of CNS e.g. in Alzheimer’s disease



## MECHANISMS OF APOPTOSIS

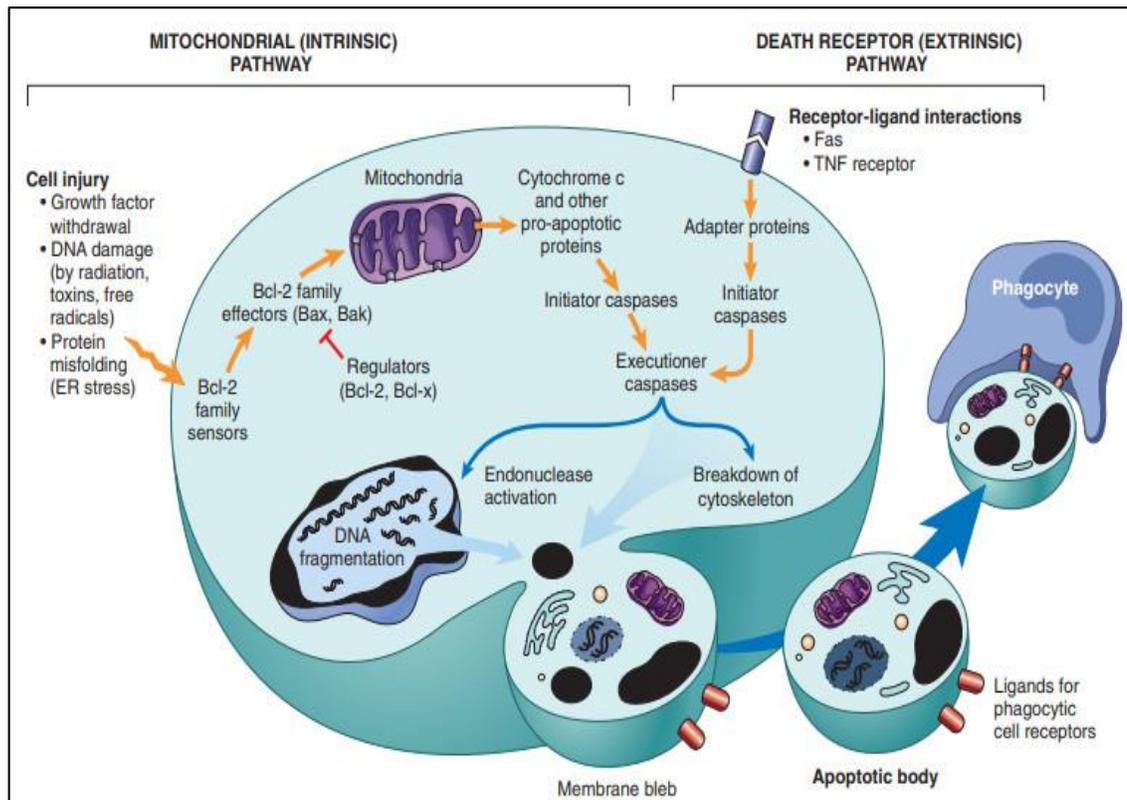
- The Intrinsic (Mitochondrial) Pathway of Apoptosis

The mitochondrial pathway is the major mechanism of apoptosis in all mammalian cells, This pathway of apoptosis is the result of increased mitochondrial permeability and release of proapoptotic molecules (death inducers) into the cytoplasm. Mitochondria are organelles in that they contain proteins such as cytochrome c that are essential for life, but some of the same proteins, when released into the cytoplasm (an indication that the cell is not healthy), initiate the suicide program of apoptosis.

The release of these mitochondrial proteins is controlled by Bcl family . There are more than 20 members of the Bcl family, and most of them function to regulate apoptosis, Bax and Bak, which insert into the mitochondrial membrane and create channels that allow proteins from the inner mitochondrial membrane to leak out into the cytoplasm.

### The Extrinsic (Death Receptor–Initiated) Pathway of Apoptosis

Stimulation from outside of the cell , the cell express molecule called death receptors ,interaction between the stimulus and death receptor lead to activation of caspase inside the cell resulting in caspase cascade that destroys the cell component



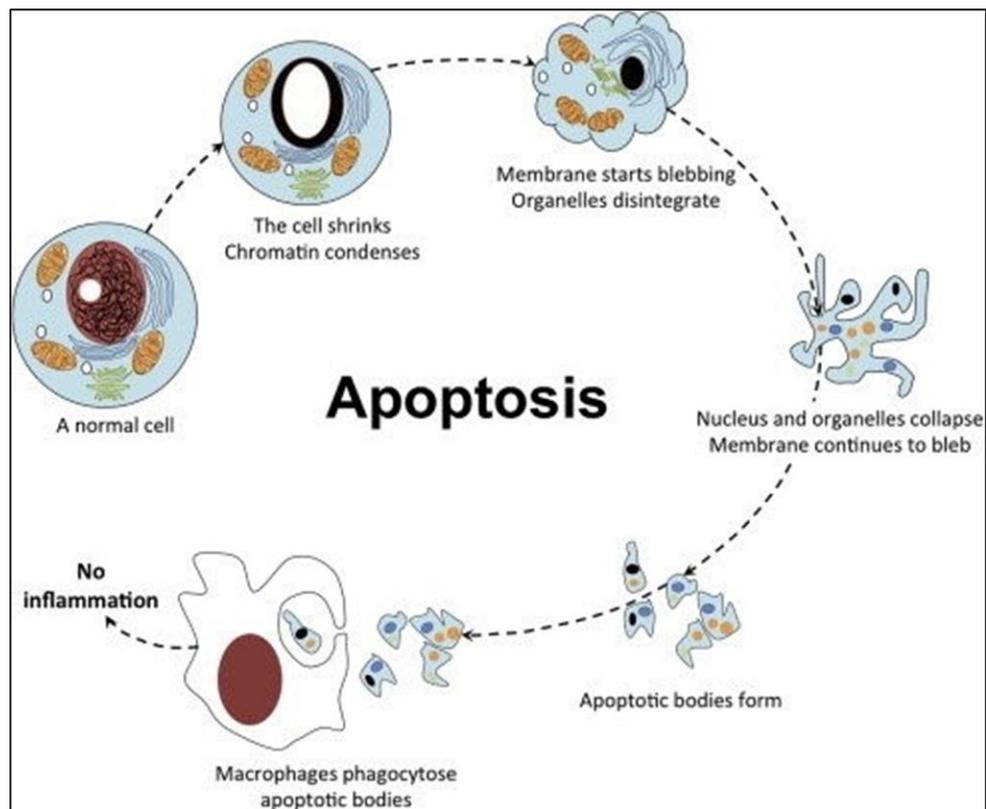
## MORPHOLOGIC FEATURES.

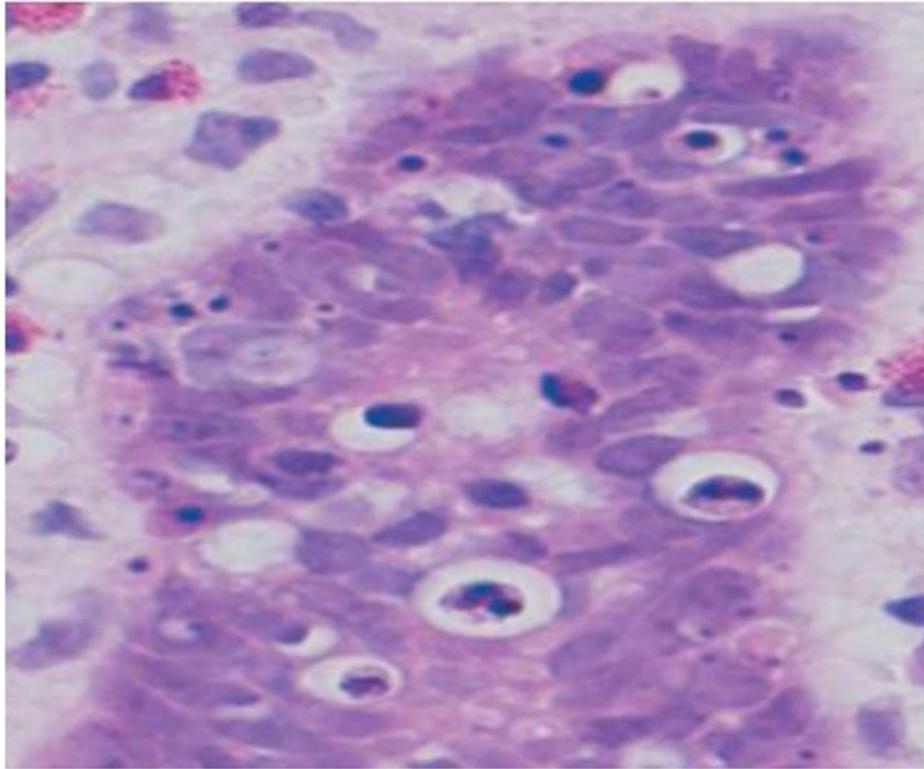
The characteristic morphologic changes in apoptosis seen in histologic and electron microscopic examination are as under

- **Cell shrinkage.** The cell is smaller in size; the cytoplasm is; and the organelles.
- **Chromatin condensation.** This is the most characteristic feature of apoptosis.
- **Formation of cytoplasmic blebs and apoptotic bodies.** The apoptotic cell first shows extensive surface blebbing, then undergoes fragmentation

into membrane-bound apoptotic bodies composed of cytoplasm and tightly packed organelles, with or without nuclear fragments .

- **Phagocytosis of apoptotic cells or cell bodies**, usually by macrophages. The apoptotic bodies are rapidly ingested by phagocytes and degraded by the phagocyte's lysosomal enzymes.



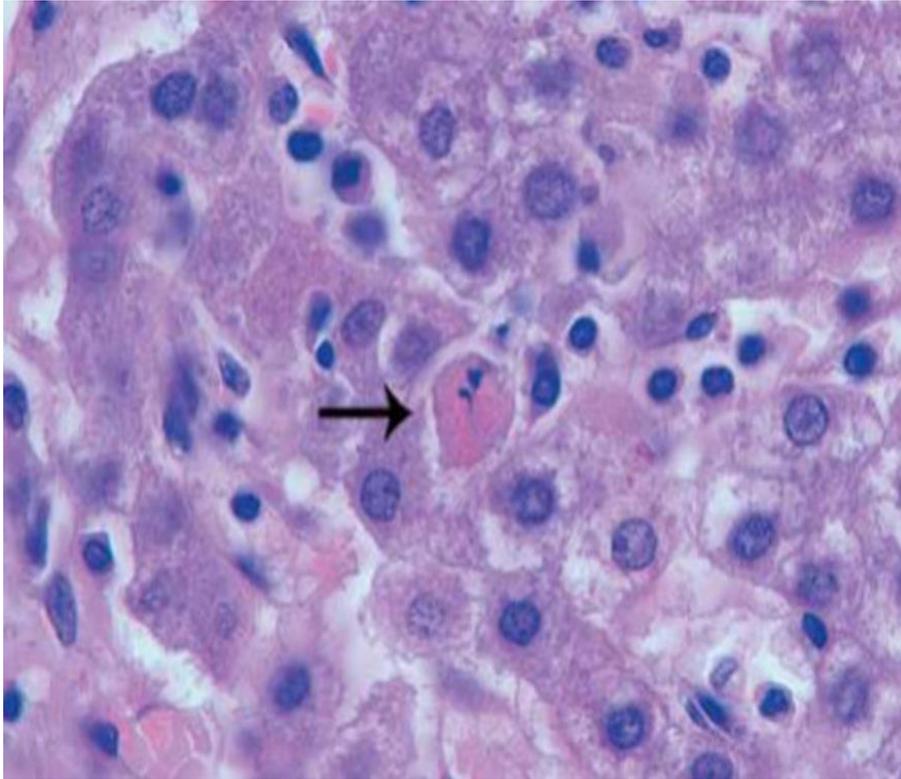


**Organ:** crypt in the colonic epithelium

**Diagnosis:** Apoptosis

**Lesion:**

- 1- cells show various stages of chromatin condensation and aggregation and, ultimately, karyorrhexis
- 2-The cells rapidly shrink, form cytoplasmic buds, and fragment into apoptotic bodies composed of membrane-bound vesicles of cytosol and organelles ,these fragments are quickly phagocytized without eliciting an inflammatory response



**Organ:** liver

**Diagnosis:** apoptosis.

**Lesion:**

- 1- the cell appeared dense eosinophilic with chromatin condensation
- 2- cell shrinkage and loss of cellular junction