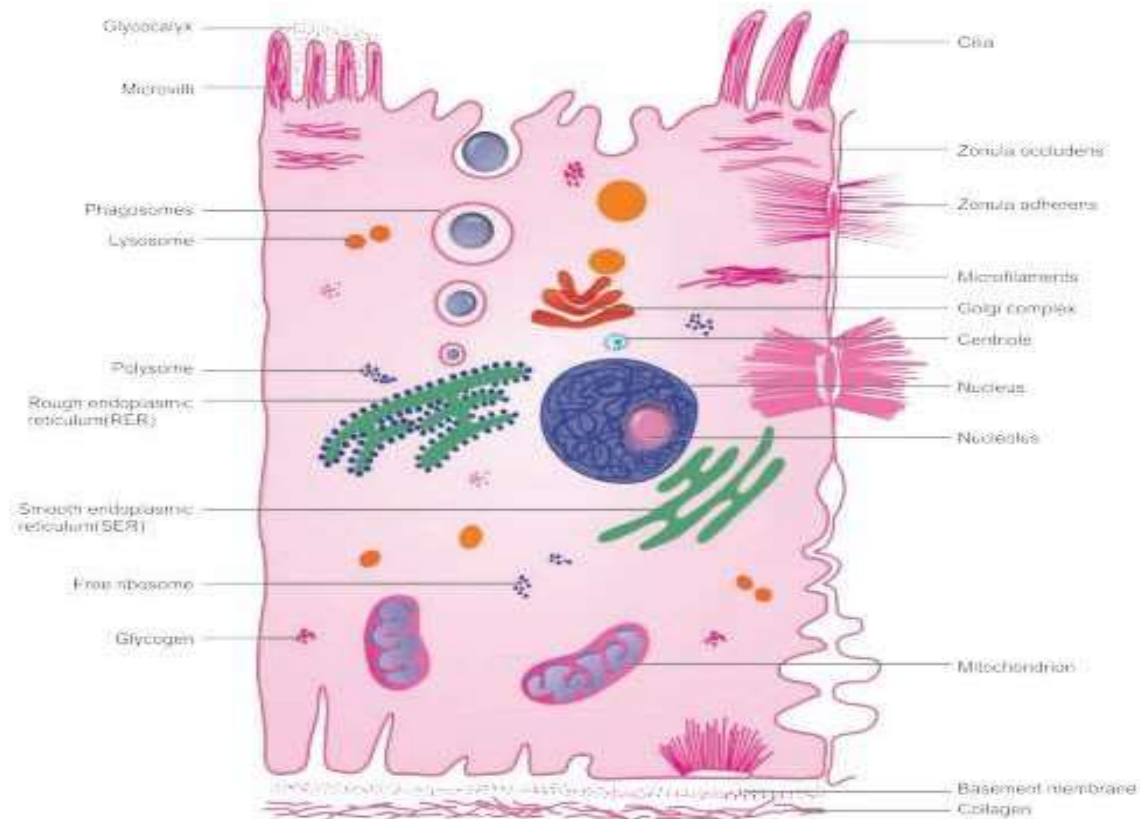


CELL INJURY

Basic Principles of Cell Injury, Adaptation



Introduction to Pathology (Greek Word)

Pathos =Suffering

Logos =Study

Definition:

✓ **It is the scientific study of structure and function of the body in disease.**

(or)

✓ **Pathology consists of the abnormalities that occur in normal anatomy and physiology leading to disease.**

✓ **It mainly involves the investigation of the causes of disease and associated changes at the levels of cells, tissues, and organs, which in turn give rise to the presenting signs and symptoms of the patient.**

Important terms in pathology and medicine:

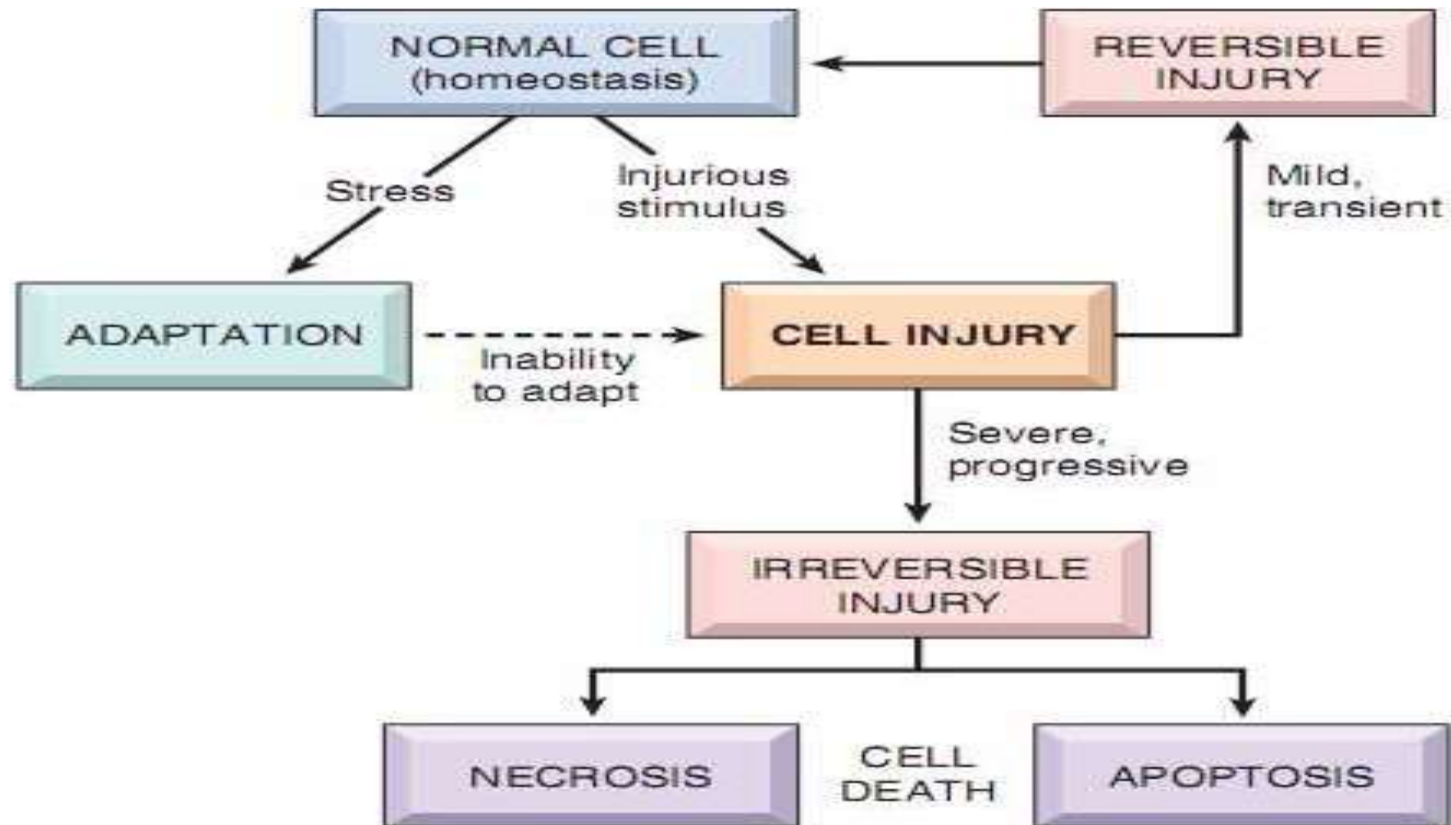
- 1) **Patient:** Is the person affected by disease.
- 2) **Lesions:** Are the characteristic changes in tissues and cells produced by disease in an individual (or) experimental animal.
- 3) **Morphology:** It consists of examination of diseased tissues (Blood & Urine Tests)
- 4) **Etiology:** Includes the underlying causes and modifying factors. (Why of Disease)

Eg: Diseases with unknown etiology: Hypertension, Diabetes, Cancer etc.
- 5) **Pathogenesis:** Refers to the steps in the development of disease. (How of Disease)

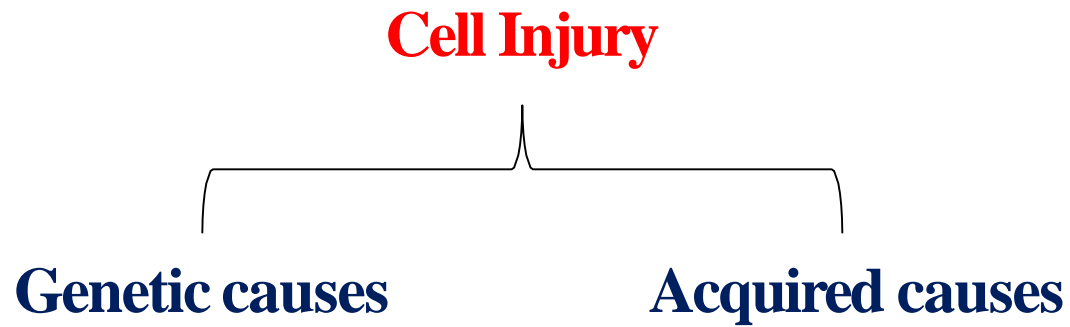
Cell Injury

Definition: It is defined as a variety of stresses a cell encounters as a result of changes in its Internal and external environment.

(Stress may be Physiologic (or) Pathologic stimuli)



Causes (Etiology) of Cell Injury



Examples of Acquired causes:

- ✓ **Hypoxia & Ischemia** : Due to ↓ Blood Supply, Heart & Lung diseases or Anaemia.
- ✓ **Physical Agents**: Eg Road Accidents, Extreme Heat & Cold, Electricity Radiation etc.,
- ✓ **Chemical & Drugs**: Eg Chemical poisons like Cyanide, Arsenic, Mercury, strong acids, insecticides, pesticides, alcohol, narcotic drugs etc.,
- ✓ **Microbial agents**: Eg Bacteria, Viruses, Fungi etc.,
- ✓ **Immunological agents**: Used in Autoimmune disorders.
- ✓ **Nutritional derangements**: Nutritional deficiency (Anaemia, Marasmus, Kwashiorkor etc.,)

✓ **Aging:** Eg Inability to repair in cellular aging.

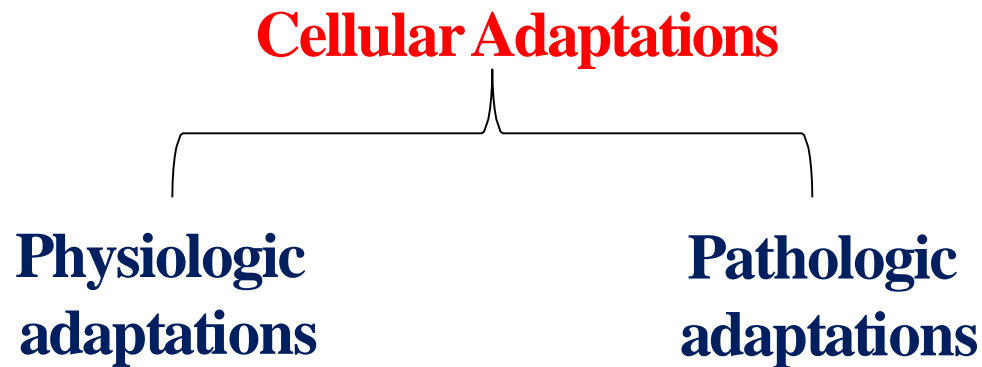
✓ **Psychogenic diseases:** (Depression, Schizophrenia) Eg Drug addiction, Alcoholism, Smoking results in liver damage, Chronic bronchitis, Lung Cancer etc.,

✓ **Iatrogenic Causes:** Errors due to Physician (Unwanted Prescription)

✓ **Idiopathic diseases:** Diseases/Disorders due to Unknown causes
Eg: Hypertension, Cancer, Diabetes etc.,

Cellular Adaptations to Stress:

Adaptations are reversible changes in the number, size, phenotype, metabolic activity, or functions of cells in response to changes in their environment.



✓ **Physiologic adaptations:** Usually represent responses of cells to normal stimulation by hormones (Eg: The hormone-induced enlargement of breast and uterus during pregnancy.)

✓ **Pathologic adaptations:** are responses to stress that allow cells to modulate their structure and function and thus escape injury.

✓ **Types of Cellular adaptations**

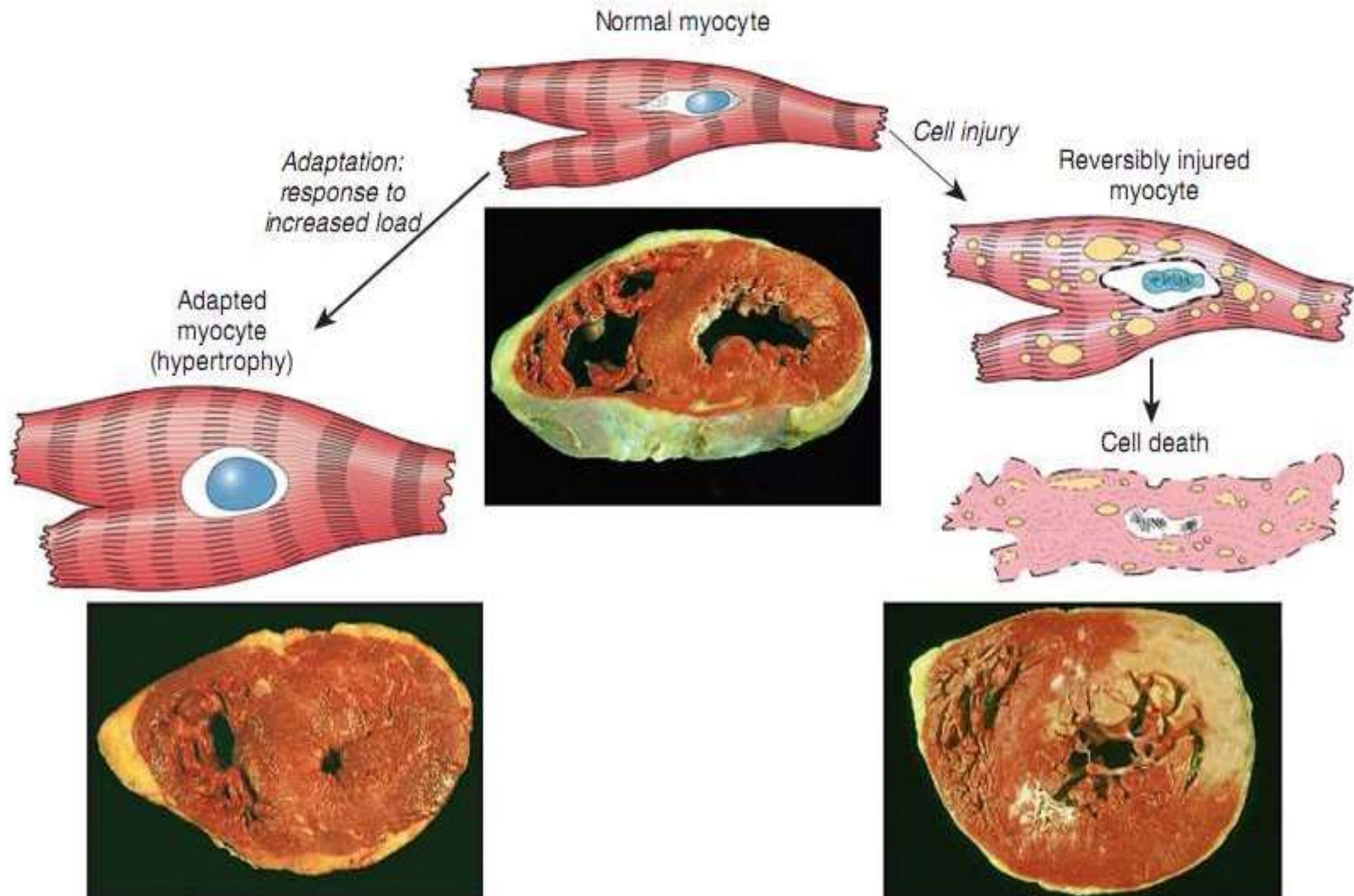
✓ **Hypertrophy** (Increase in Cell size)

✓ **Hyperplasia** (Increase in Cell number)

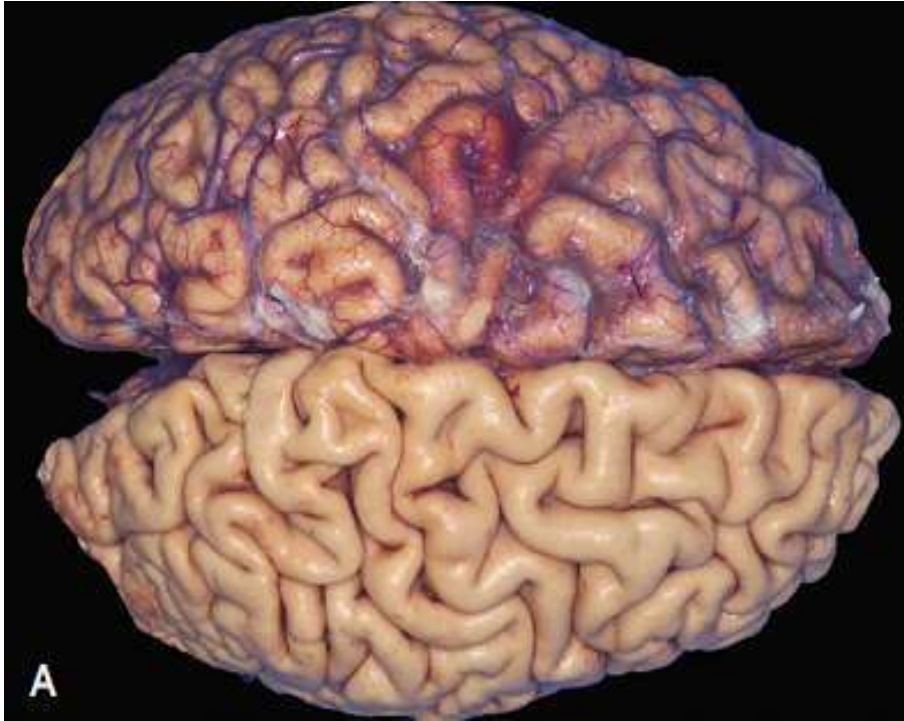
✓ **Atrophy** & (Decrease in Cell size or Cell shrinkage)

✓ **Metaplasia** (Change of one form of cell to other, Eg: Columnar epithelium to Simple Squamous epithelium.)

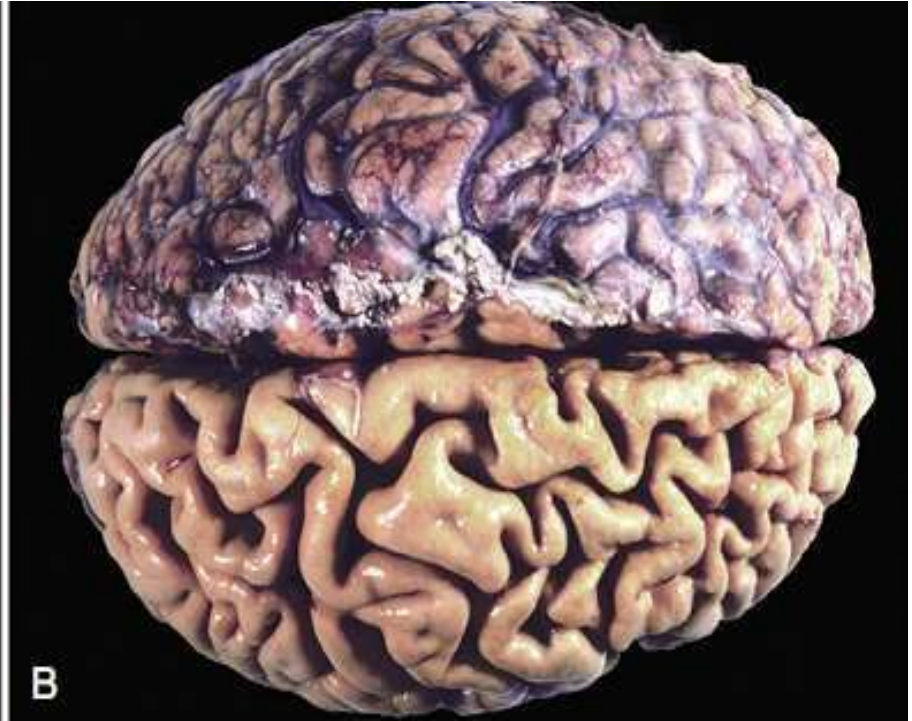
Hypertrophy: E.g. Cardiac hypertrophy & Enlargement of uterus and Breast in Pregnancy.



Atrophy: Due to decreased workload or decreased metabolic activity.

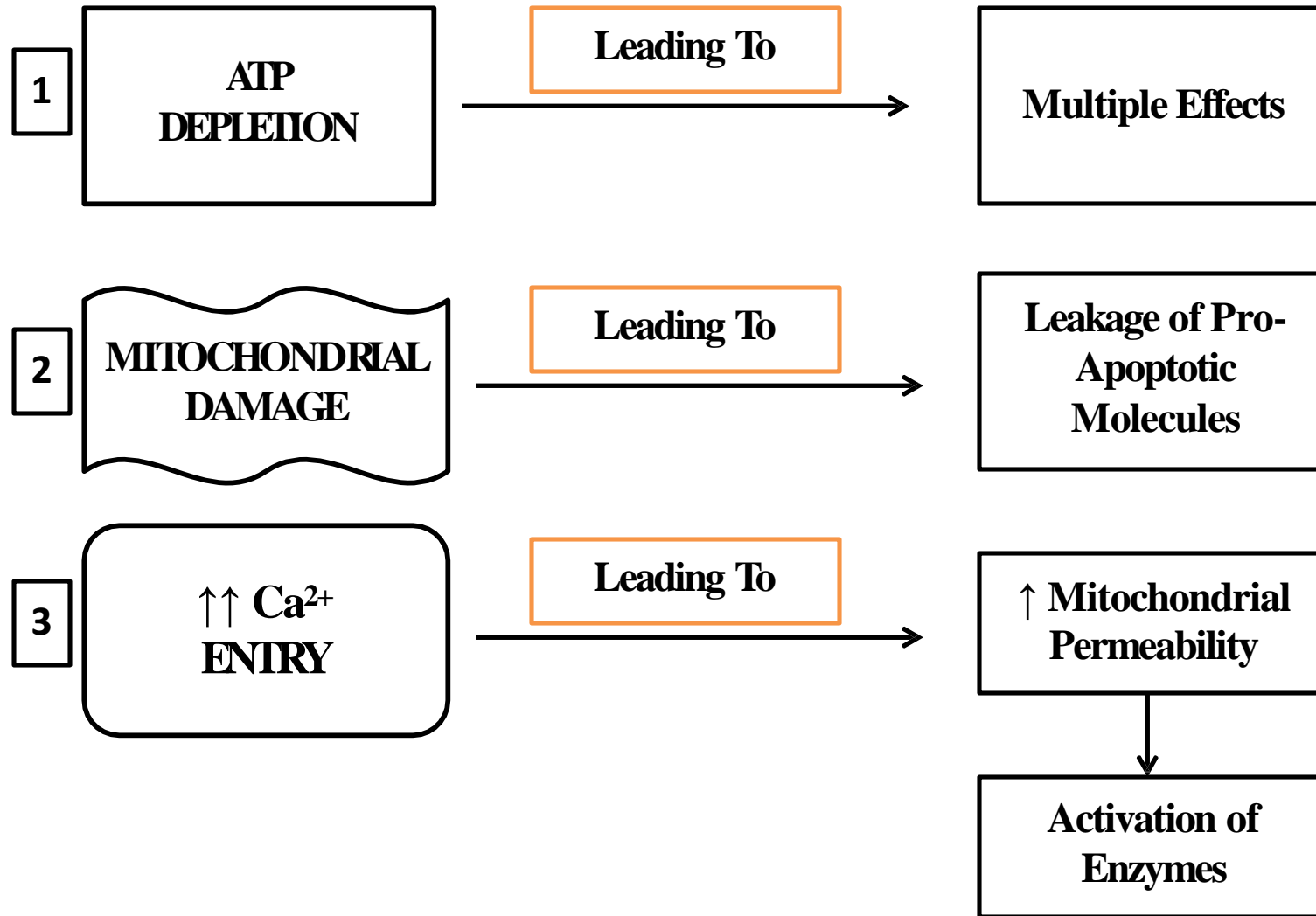


A. Normal Brain

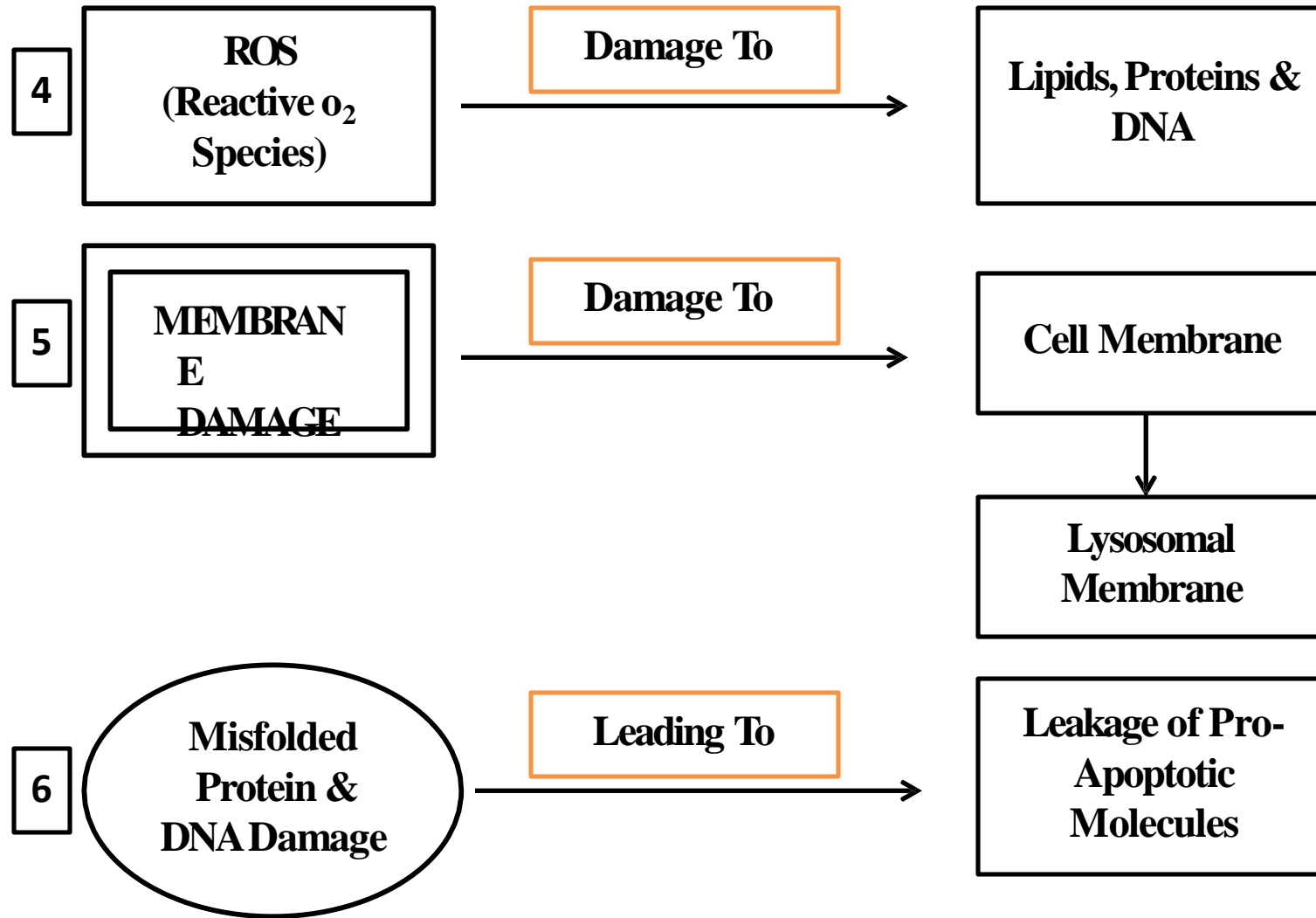


B. Atrophy of Brain

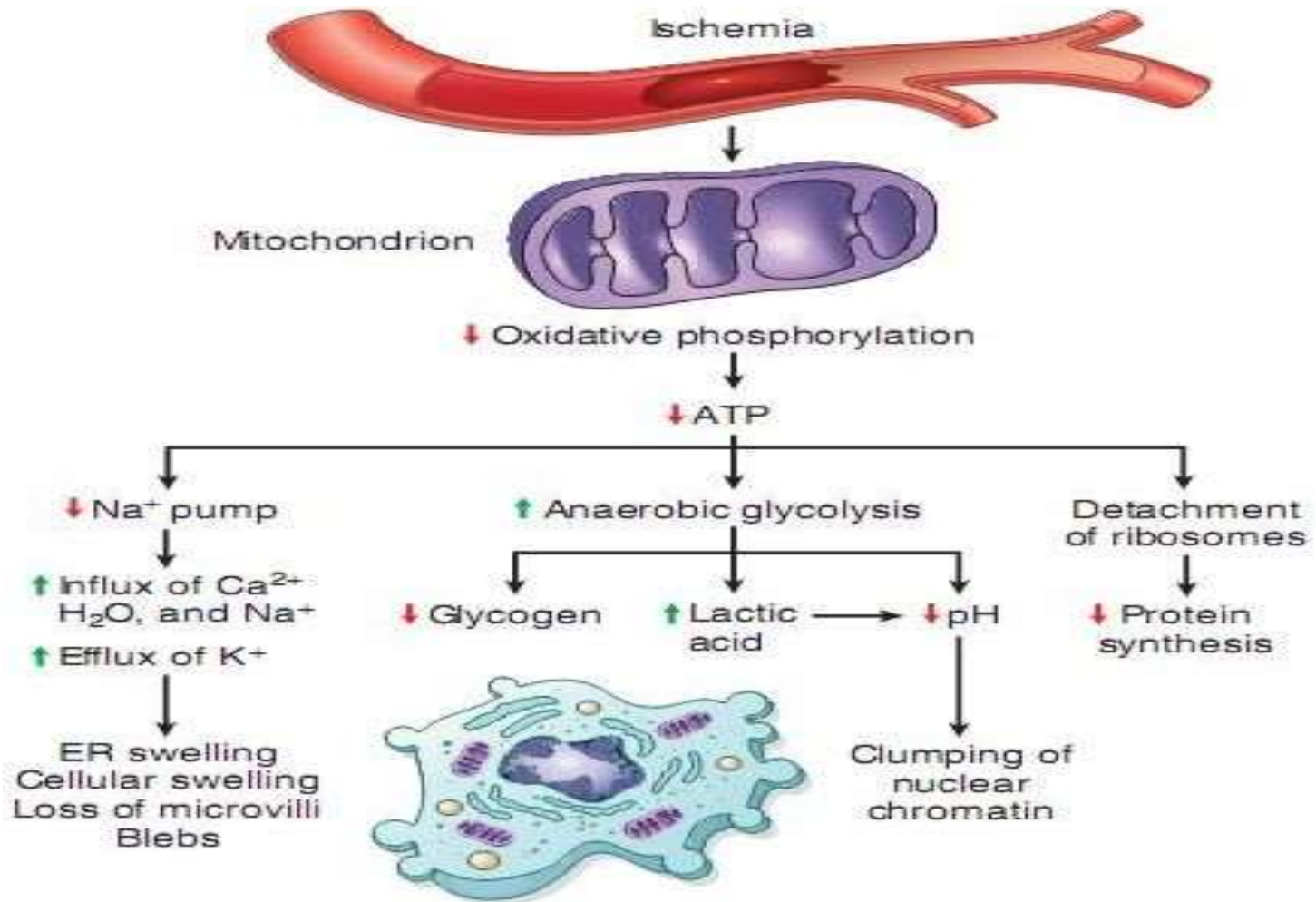
“Mechanisms of Cell Injury”:



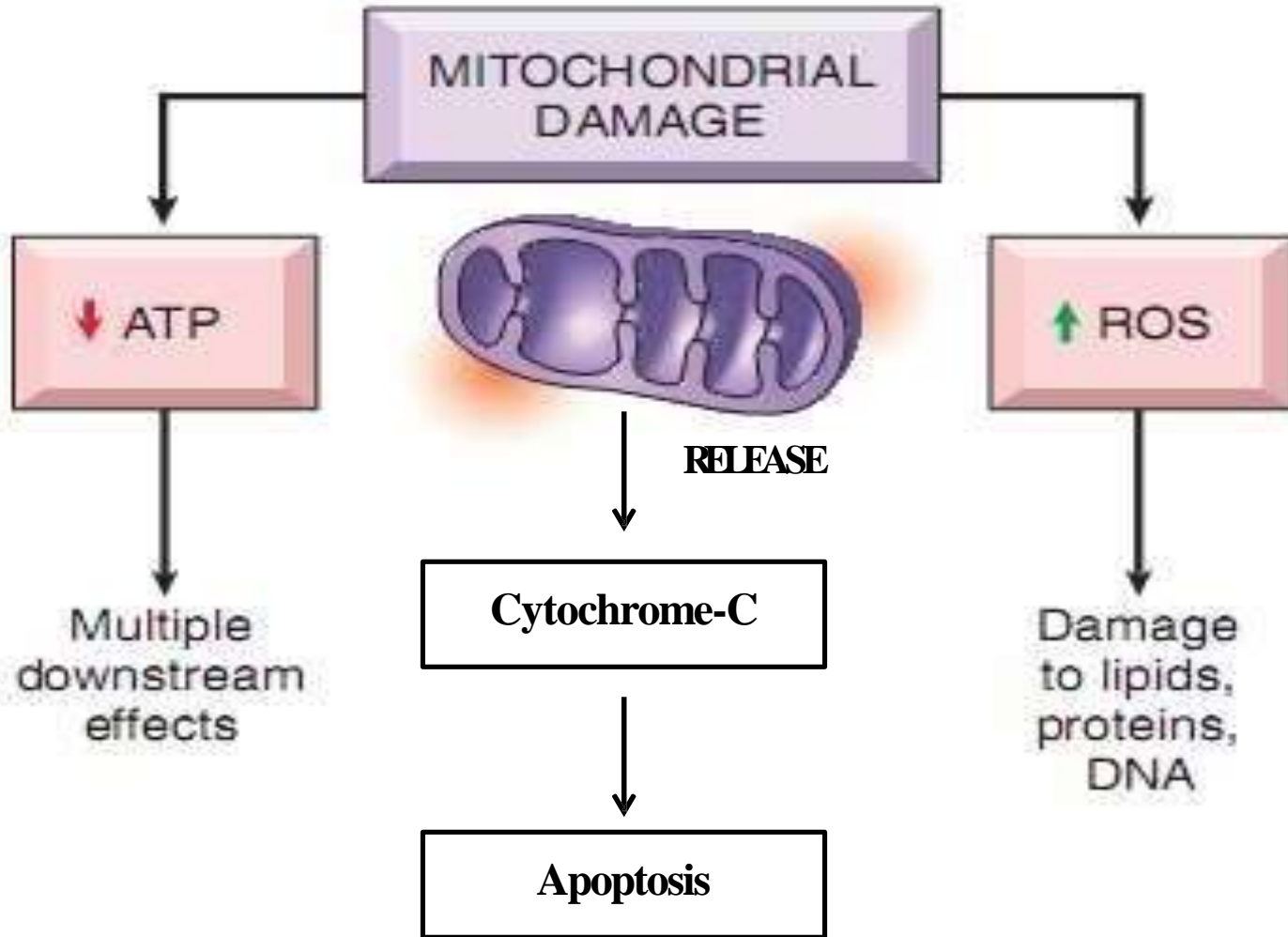
“Mechanisms of Cell Injury”:

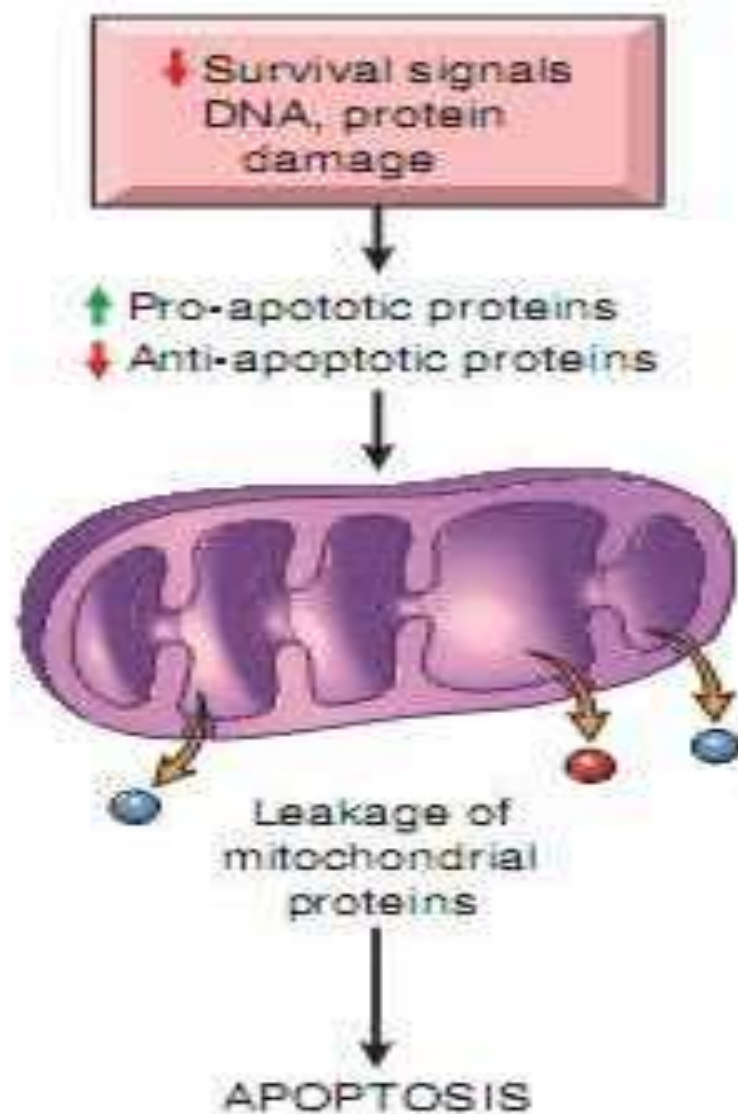
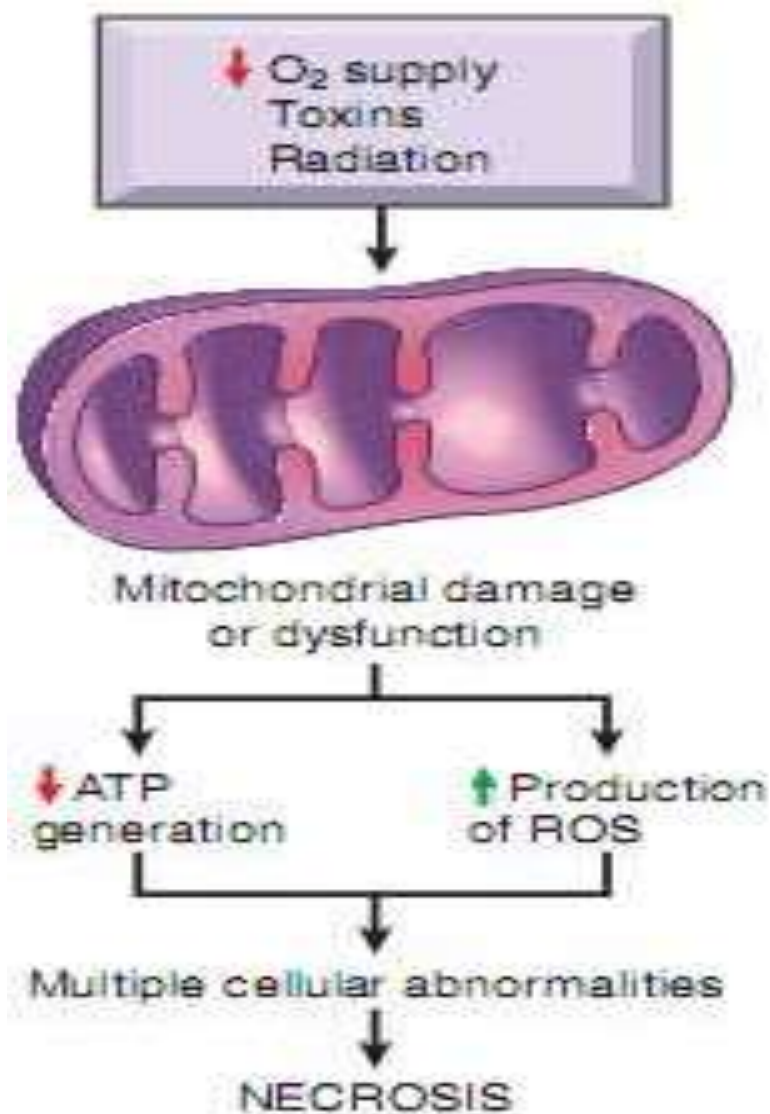


ATP DEPLETION

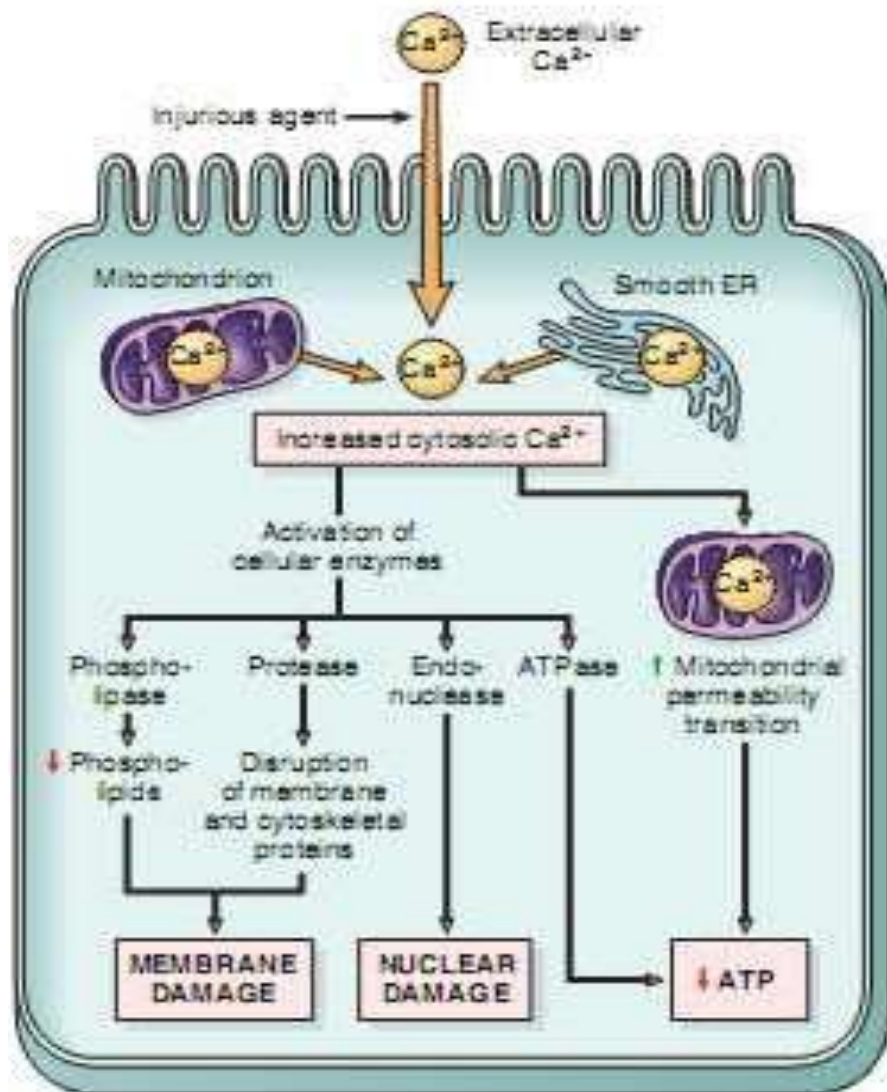
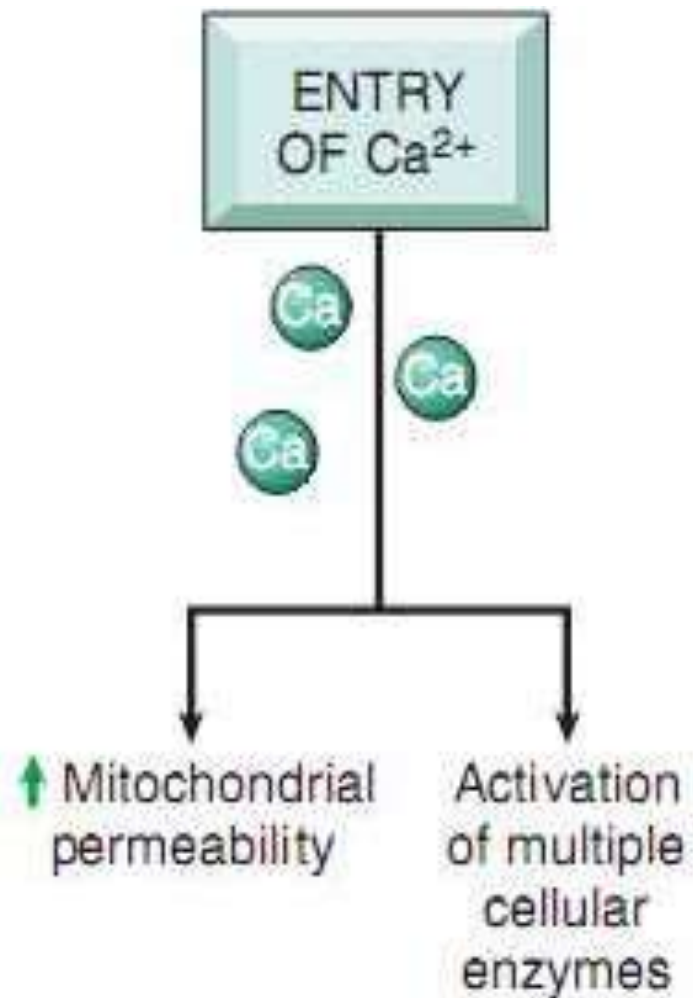


MITOCHONDRIAL DAMAGE





↑↑ CYTOSOLIC Ca^{2+}



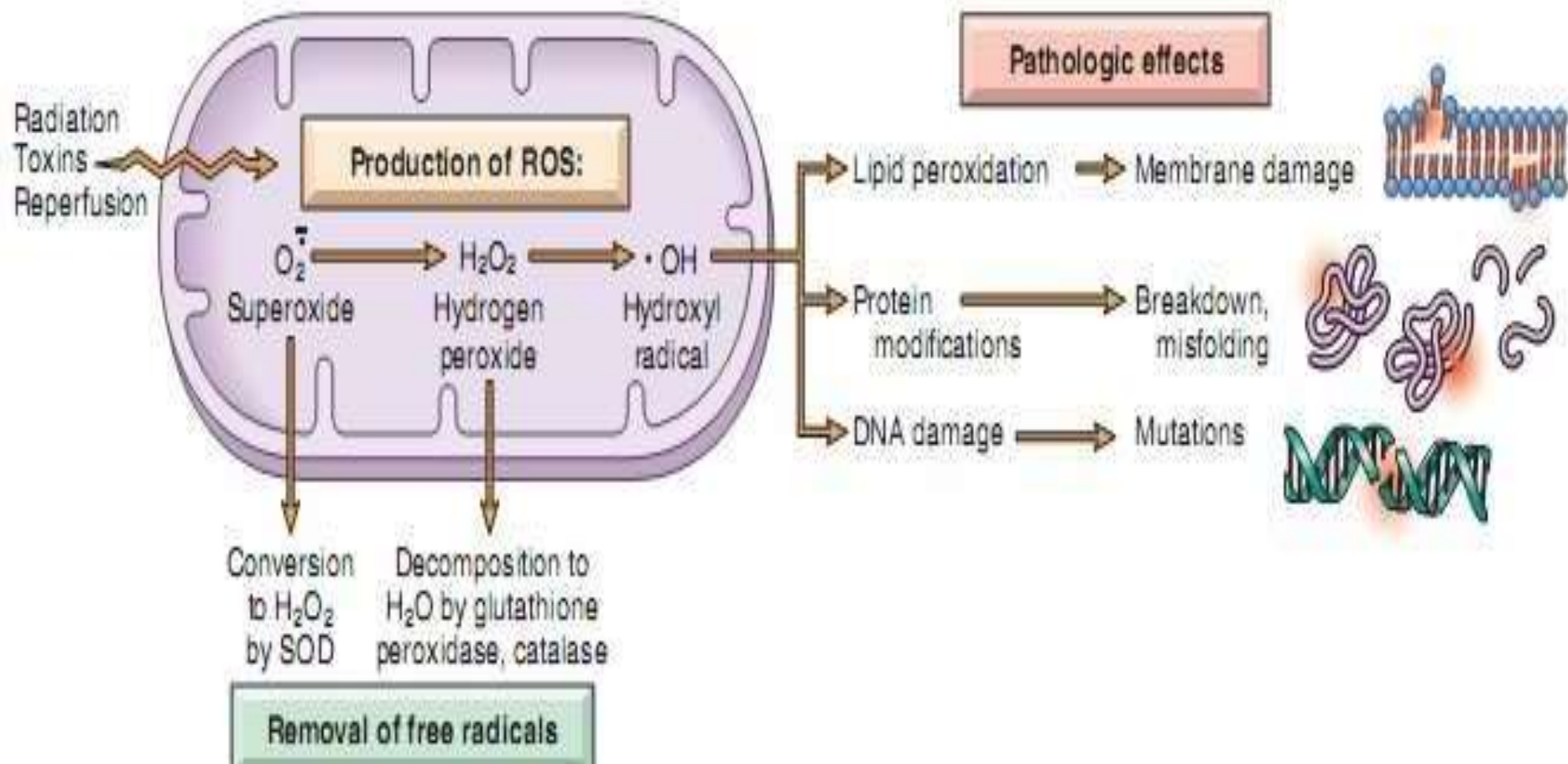
ROS

(Reactive o_2 Species)

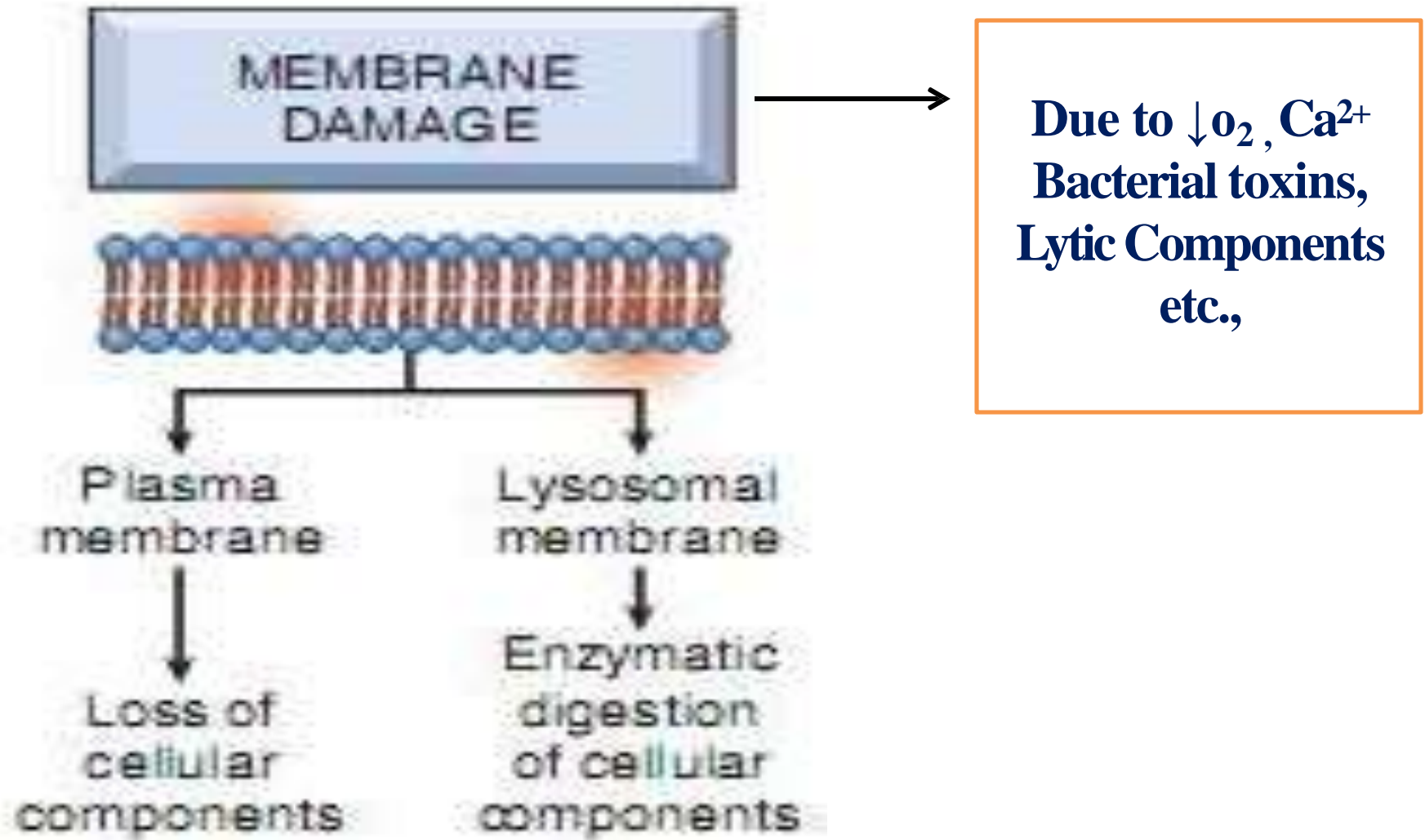
ROS are o_2 derived free radicals (Free radicals are special type of molecules that have an unpaired electron in their outer orbit.)

Causes of free radical generation:

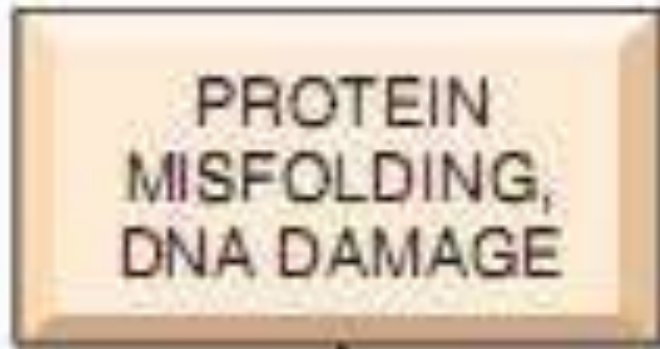
- ✓ **Via normal reduction and oxidation reactions (o_2 , H_2O_2 , OH)**
- ✓ **Ionization radiations .Eg: X-rays etc.,**
- ✓ **Inflammation**
- ✓ **Metabolism of exogenous molecules**
- ✓ **Metals**



MEMBRANE DAMAGE



Misfolded Protein & DNA Damage



Mutations in Genes

Activation of
pro-apoptotic
proteins

Types of Cell Injury

Cell Injury

```
graph TD; A[Cell Injury] --> B[Reversible Cell Injury]; A --> C[Irreversible Cell Injury]; B --> D[Cellular Swelling]; B --> E[Fatty change]; C --> F[Autolysis & Heterolysis]; C --> G[Necrosis]; C --> H[Apoptosis];
```

Reversible Cell Injury

→ **Cellular Swelling**

→ **Fatty change**

Irreversible Cell Injury

→ **Autolysis & Heterolysis**

→ **Necrosis**

→ **Apoptosis**

Morphology of Reversible Cell Injury

The two main morphological correlates of reversible cell injury are:

✓ **Cellular Swelling** :it is the result of failure of energy-dependent ion pumps in the plasma membrane, leading to an inability to maintain ionic and fluid homeostasis. Cellular swelling the first manifestation of almost all forms of cell injury to cells, is a reversible alteration that may be difficult to appreciate with the light microscope, but it may be apparent at the level of the whole organ.

Eg: It causes increase in weight of organ.

✓ **Fatty change:** It occurs in hypoxic injury and in various forms of toxic or metabolic injury and is manifested by the appearance of small or large lipid vacuoles in the cytoplasm.

It is principally encountered in cells participating in fat metabolism (e.g., hepatocytes, myocardial cells) and is also reversible.

✓ **Other morphological characteristic includes:**

- ✓ Plasma membrane blebbing and loss of microvilli,
- ✓ Mitochondrial swelling,
- ✓ Dilation of the ER,
- ✓ Eosinophilia.

Morphology of Irreversible Cell Injury

✓ **Autolysis** (i.e. self-digestion) is disintegration of cell by its own hydrolytic enzymes liberated from lysosomes. Autolysis is rapid in some tissues rich in hydrolytic enzymes such as in the pancreas, and gastric mucosa; intermediate in tissues like the heart, liver and kidney; and slow in fibrous tissue.

✓ **Heterolysis** is disintegration of cell by the hydrolytic enzymes liberated from inflammatory mediators like Neutrophils etc.,

✓ **Necrosis** is a series of morphological changes which occurs in a lethally injured cell.

✓ **Apoptosis** is also known as Programmed Cell death.

Morphology of Necrosis

✓ **Necrosis** is the type of cell death that is associated with loss of membrane integrity and leakage of cellular contents resulting in dissolution of cells, largely resulting from the degradative action of enzymes on lethally injured cells.

(Or)

It is a spectrum of morphological changes that follow cell death in living due to progressive degradation action of enzyme (present with in the cell) on lethally injured cell.

✓ **Morphological changes are due to:**

1) Intracellular protein denaturation.

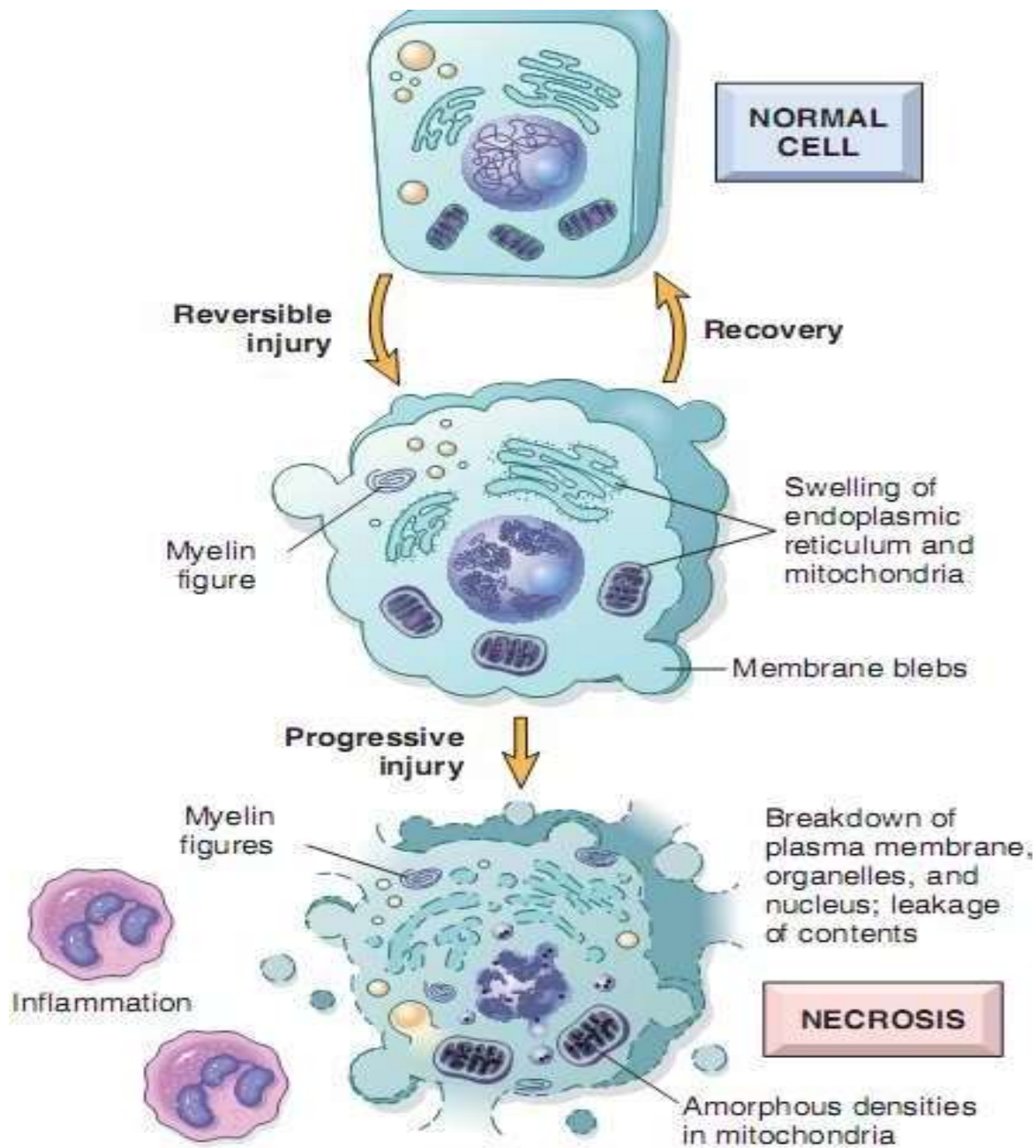
E.g. Both structural and functional proteins.

2) Enzymatic digestion of severely injured cell.

E.g. Leading to Autolysis & Heterolysis.

3) Loss of integrity of plasma membrane of necrotic cell.

✓ **Necrosis is characterized by changes in the cytoplasm and nuclei of the injured cells.**



✓ Cytoplasmic changes: Necrotic cells show increased eosinophilia. Compared with viable cells, the cell may have a more glassy, homogeneous appearance, mostly because of the loss of glycogen particles.

✓ Myelin figures are more prominent in necrotic cells than during reversible injury.

✓ Necrotic cells are characterized by discontinuities in plasma and organelle membranes, marked dilation of mitochondria, disruption of lysosomes.

✓ **Nuclear changes:** Nuclear changes due to breakdown of DNA and chromatin. It includes:

✓ **Pyknosis:** Characterized by nuclear shrinkage and increased basophilia.

✓ **Karyorrehexis:** Fragmentation of Nucleas

✓ **Karyolysis:** Fading of basophilia & chromatin.

✓ **Fates of necrotic cells:**

✓ Necrotic cells may persist for some time or may be digested by enzymes and disappear.

✓ Dead cells may be replaced by myelin figures, which are either phagocytosed by other cells or further degraded into fatty acids.

Types of Necrosis

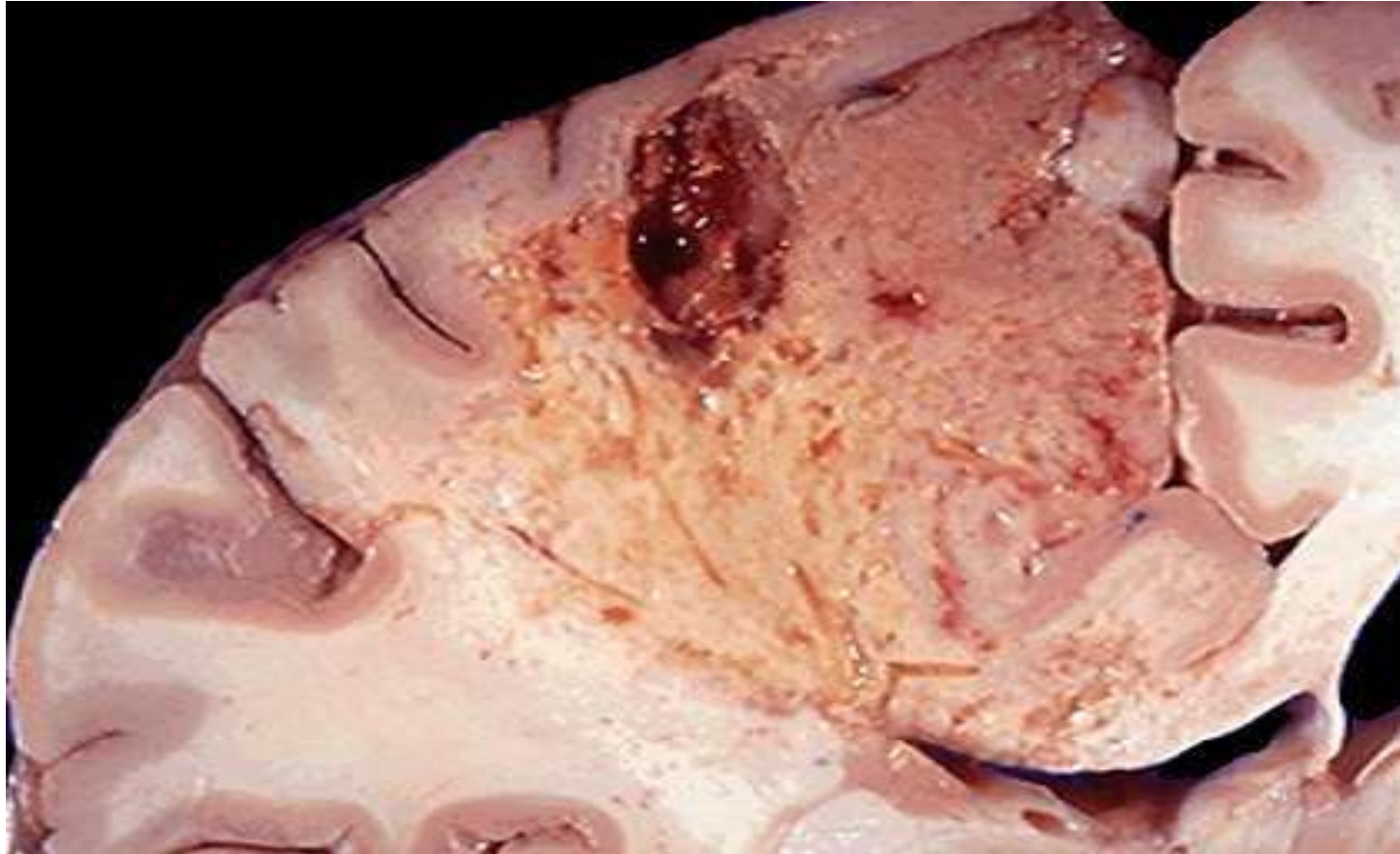
Morphologically, there are six types of necrosis

1) **Coagulative necrosis:** Characteristic of Infarcts



A wedge-shaped kidney infarct (yellow) with preservation of the outlines.

2) Liquefactive necrosis:



Liquefactive necrosis. An infarct in the brain showing dissolution of the tissue.

3) Gangrenous necrosis:

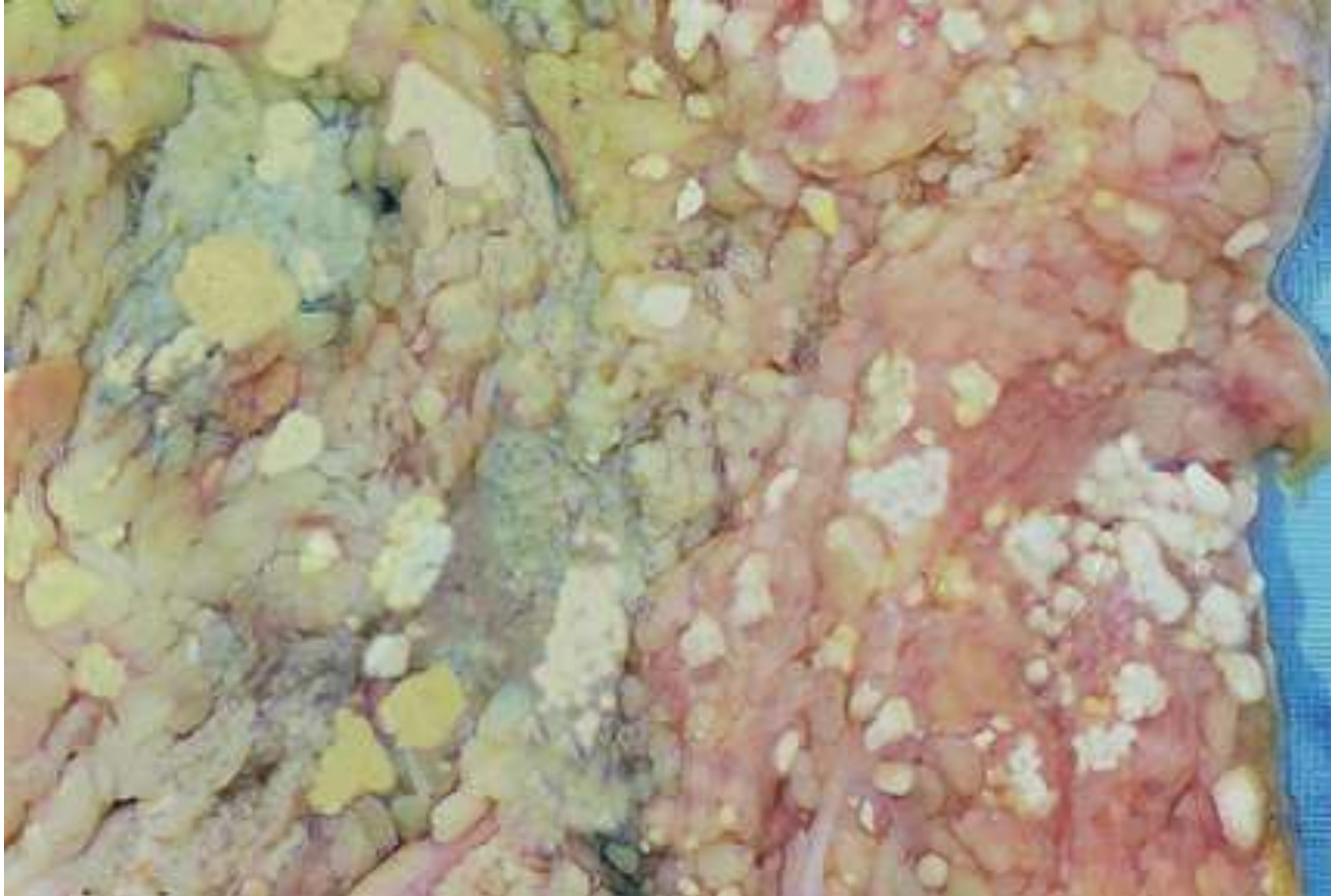


4) Caseous necrosis:



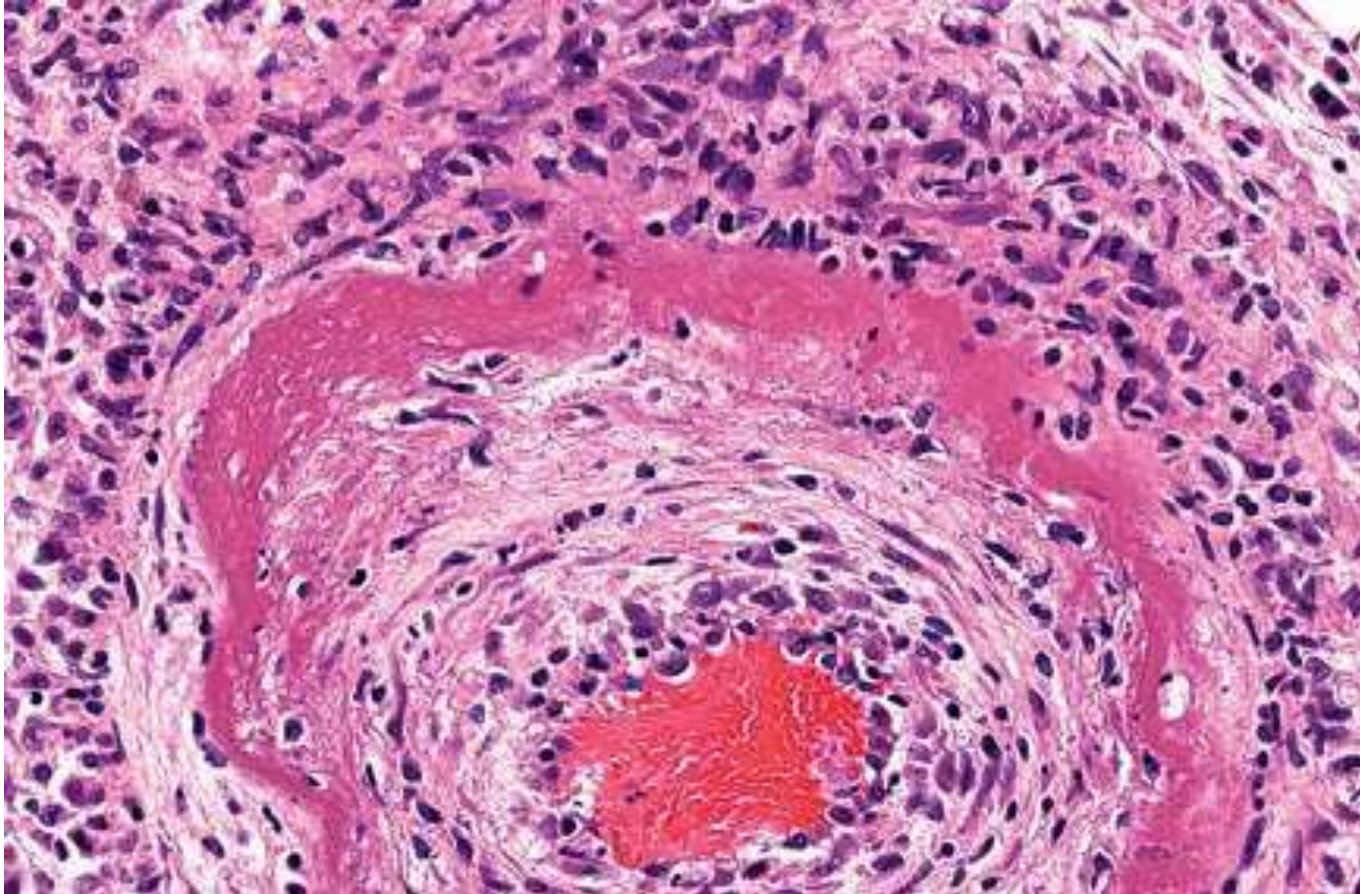
Tuberculosis of the Lung

5) Fat necrosis:



Fat necrosis in acute pancreatitis

6) Fibrinoid necrosis:



Fibrinoid necrosis in an artery in a patient

Apoptosis

- Apoptosis is a pathway of cell death in which cells activate enzymes that degrade the cells' own nuclear DNA and nuclear and cytoplasmic proteins.
- The plasma membrane of the apoptotic cell remains intact, but the membrane is altered in such a way that the cell and its fragments become avid targets for phagocytes.
- Apoptotic cell death does not elicit an inflammatory reaction in the host
- In contrast to Necrosis, Apoptosis takes place in both physiologic and pathologic situations. Necrosis occurs only in pathological conditions.

- This process helps to eliminate unwanted cells by an internally programmed series of events effected by dedicated gene products. It serves several vital functions and is seen under various settings.

- ✓ During development for removal of excess cells during embryogenesis
- ✓ To maintain cell population in tissues with high turnover of cells, such as skin, bowels.
- ✓ To eliminate immune cells after cytokine depletion, and autoreactive T-cells in developing thymus.
- ✓ To remove damaged cells by virus
- ✓ To eliminate cells with DNA damage by radiation, cytotoxic agents etc.
- ✓ Hormone-dependent involution - Endometrium, ovary, breasts etc.
- ✓ Cell death in tumours.



**NORMAL
CELL**



Condensation
of chromatin

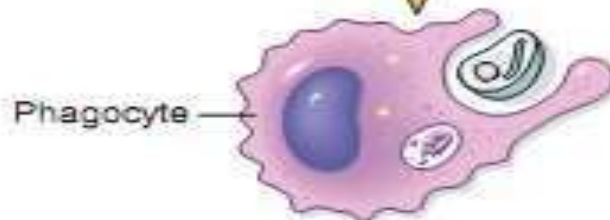
Membrane blebs



Cellular
fragmentation

Apoptotic
body

APOPTOSIS

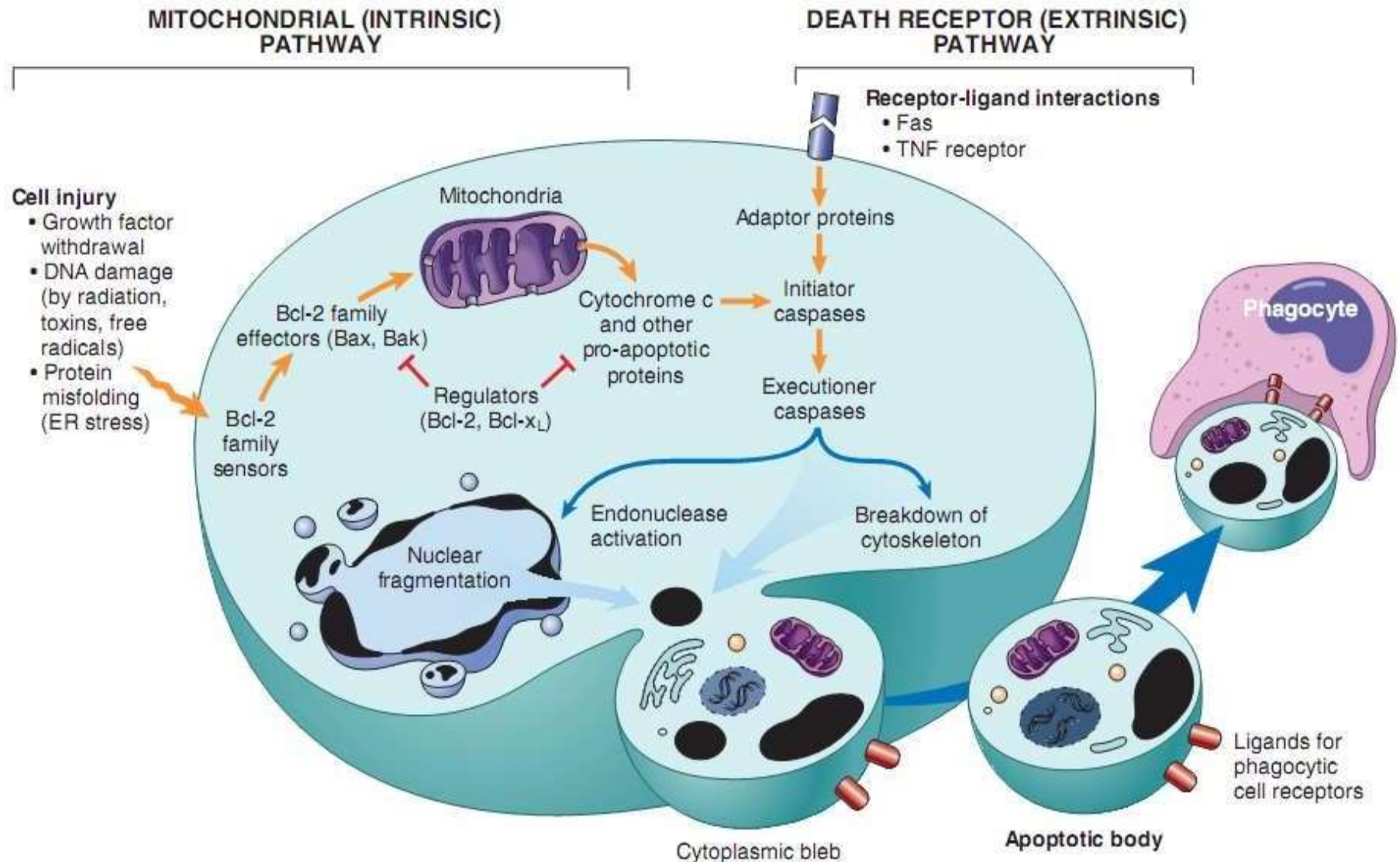


Phagocyte

Phagocytosis
of apoptotic cells
and fragments

Mechanism of Apoptosis

Apoptosis results from the activation of enzymes called caspases.



Comparison between Necrosis and Apoptosis

Feature	Necrosis	Apoptosis
Cell size	Enlarged (swelling)	Reduced (shrinkage)
Nucleus	Pyknosis → karyorrhexis → karyolysis	Fragmentation into nucleosome size fragments
Plasma membrane	Disrupted	Intact; altered structure, especially orientation of lipids
Cellular contents	Enzymatic digestion; may leak out of cell	Intact; may be released in apoptotic bodies
Adjacent inflammation	Frequent	No
Physiologic or pathologic role	Invariably pathologic (culmination of irreversible cell injury)	Often physiologic; means of eliminating unwanted cells; may be pathologic after some forms of cell injury, especially DNA and protein damage

Apoptosis

Asanas with Props

The ancient yogis used logs of wood, stones, and ropes to help them practice asanas effectively. Extending this principle, Yogacharya Iyengar invented props which allow asanas to be held easily and for a longer duration, without strain.



YOGACHARYA IYENGAR IN SETUBANDHA SARVANGASANA

This version of the posture requires considerable strength in the neck, shoulders, and back, requiring years of practice to achieve. It should not be attempted without supervision



Necrosis

