Cell injury

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Topic Covered

- Cellular injury
- Classification of Cellular injury
- Cell Adaptation to Injury
- Reversible and Irreversible Cell Injury

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Cellular injury

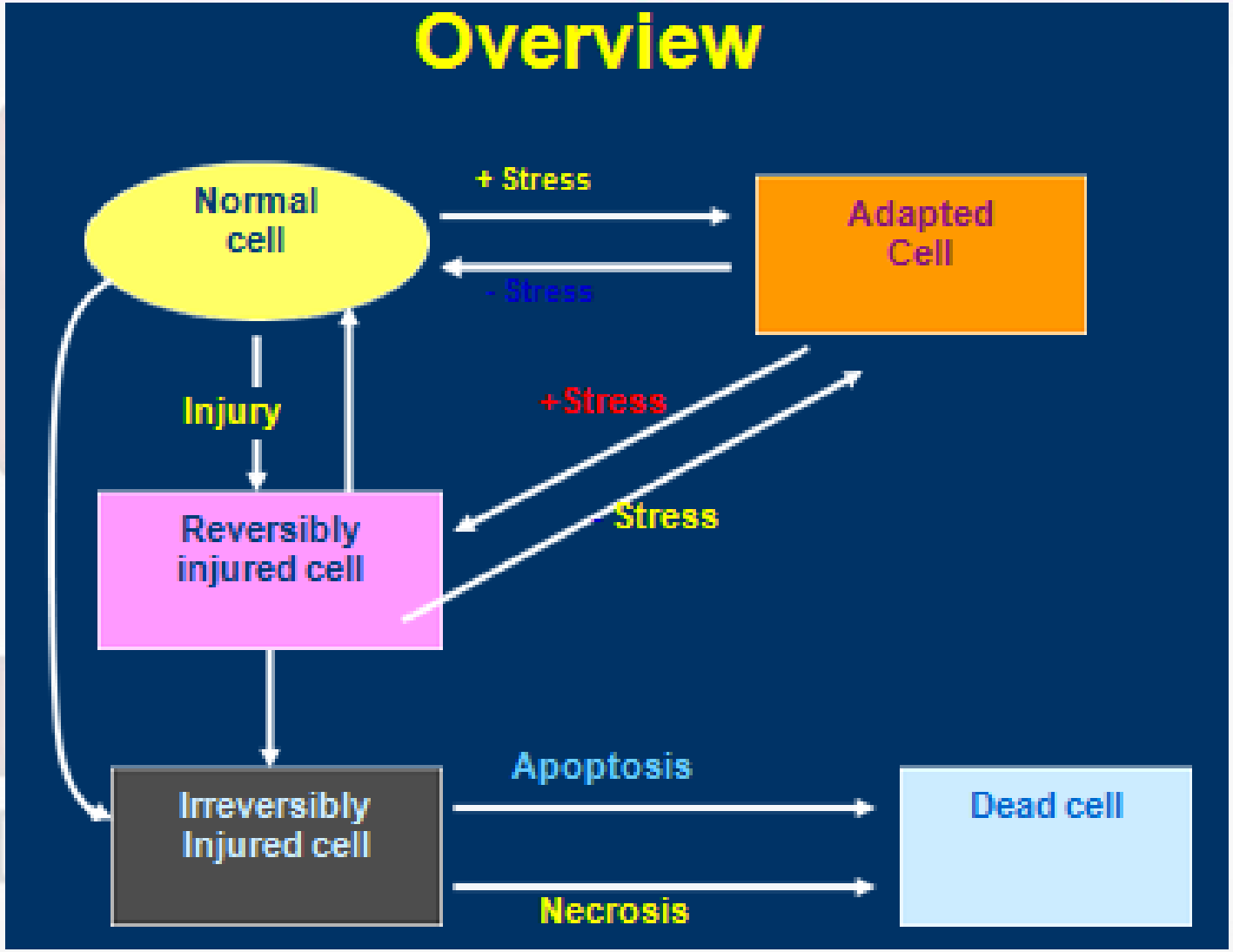
- When the cell is exposed to any injurious agent or stress ,a consequence of events follows, that is loosely termed **cell injury.** Cell injury is reversible up to certain point.

- To survive, cells must have the ability for **adaptation** to variable conditions. This process of adaptation can involve changes in cellular size, number or type.

- If the stimulus persist or severe enough from the beginning , **cell death** occur .

Classification of Cellular injury

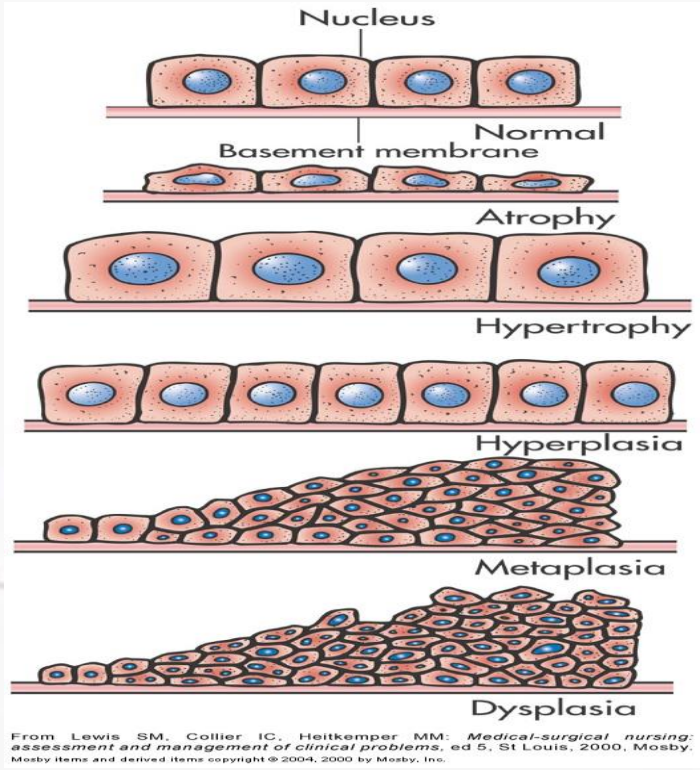
- **Physical injury**
  - Mechanical trauma
  - Temperature extremes (burn injury, frostbite)
  - Electrical current
- **Chemical injury**
  - Chemicals, toxins, heavy metals, solvents, smoke,
  - pollutants, drugs, gases
- **Radiation injury**
  - Ionizing radiation — gamma rays, X rays
  - Non-ionizing radiation — microwaves, infrared, laser
- **Biologic agents**
  - Bacteria, viruses, parasites
- **Nutritional injury**
  - Malnutrition
  - Obesity


Overview
Normal cell
+ Stress
- Stress
Adapted Cell
Injury
+Stress
Stress
Reversibly injured cell
Irreversibly Injured cell
Apoptosis
Necrosis
Dead cell

Cell Adaptation to Injury

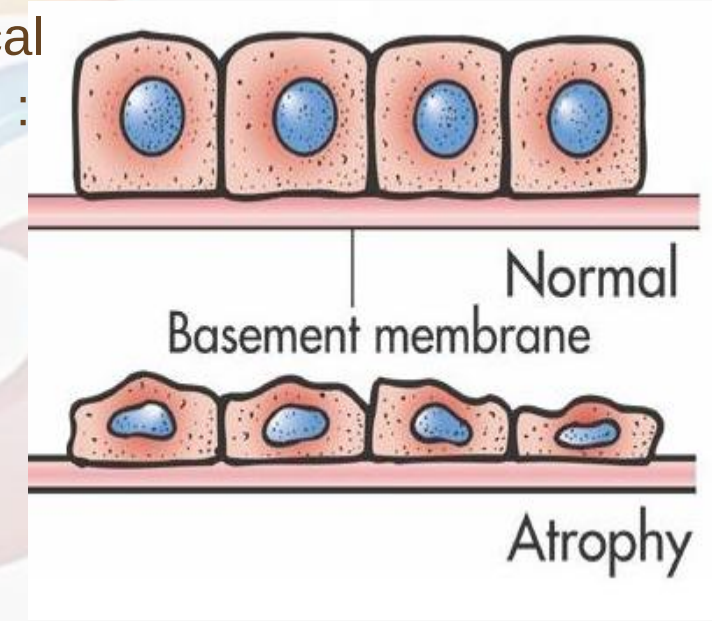
Five Cellular Adaptations to Injury:

1. Atrophy
2. Hypertrophy
3. Hyperplasia
4. Metaplasia
5. Dysplasia



1) Atrophy

- It means Decrease or shrinkage in cellular size.
- That is either Physiological or Pathological
- Pathologic atrophy occur due to ↓↓↓ in :
  - Workload
  - Pressure
  - Use
  - Blood supply
  - Nutrition
  - Hormonal Stimulation
  - Nervous Stimulation



- Atrophy is generally a reversible process, except for atrophy caused by loss of nervous innervations to a tissue.
- Causes of atrophy include prolonged bed rest, disuse of limbs or tissue, poor tissue nutrition and ischemia.

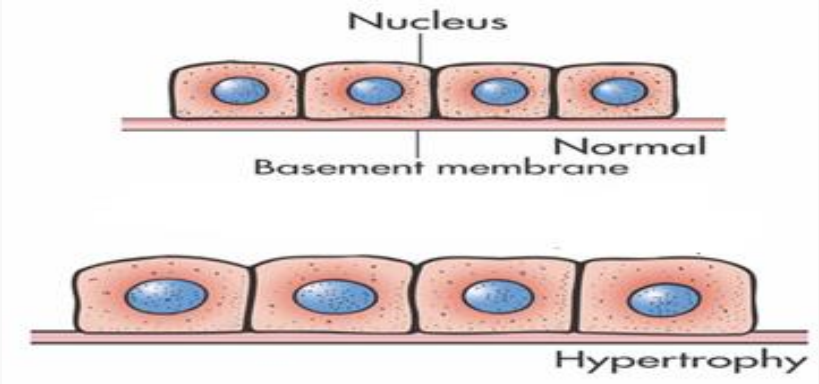
2) Hypertrophy

- Increase in cell size and tissue mass.
- Occurs when a cell or tissue is

exposed to an increased workload.

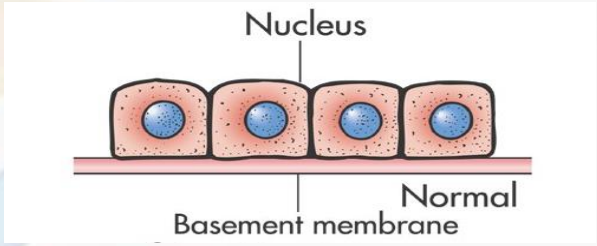
- Occurs in tissues that cannot

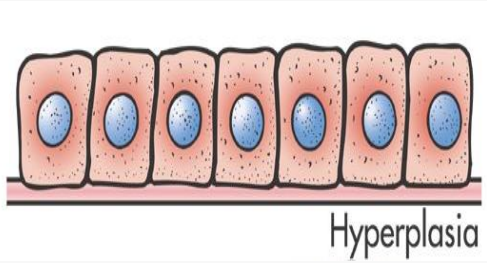
increase cell number as an adaptive response.



- Hypertrophy may be :
  - **normal physiologic** response, such as the increase in muscle mass that is seen with exercise
  - **pathologic** as in the case of the cardiac hypertrophy that is seen with prolonged hypertension.
  - or **compensatory process**, when one kidney is removed, for example, the remaining kidney hypertrophies to increase its functional capacity.

3) Hyperplasia



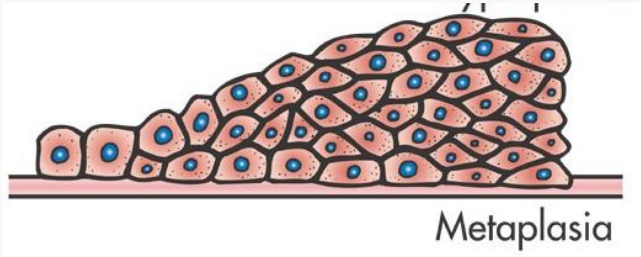


- Increase in number of cells resulting from increased rate of cellular division.

- It is either:
  - **Physiologic process**, as in the breast and uterine hyperplasia that occurs during pregnancy,
  - **Pathologic:** such as Benign Prostatic Hyperplasia (BPH) and gingival hyperplasia (overgrowth of gum tissues) that maybe seen in certain patients receiving the drug phenytoin.
  - or **compensatory mechanism:** for example, when a portion of the liver is surgically removed, the remaining hepatocytes (liver cells) increase in number to preserve the functional capacity of the liver.

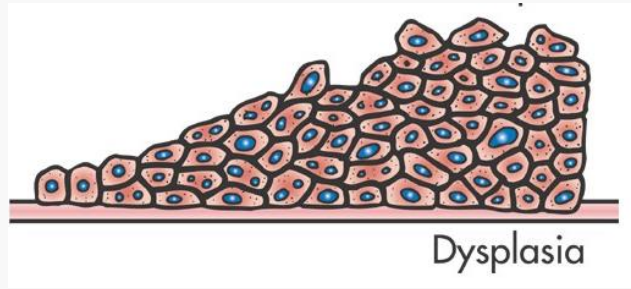
4) Metaplasia

- The conversion of one cell type to another cell type that might have a better chance of survival under certain circumstances.



- Metaplasia occurs in response to chronic irritation or inflammation.
- An example of metaplasia is:
  - **in the respiratory passages of chronic cigarette smokers**, following years of exposure to irritating cigarette smoke, the ciliated columnar epithelium lining the respiratory passages gradually converts to stratified squamous epithelium which although be better to survive to the cigarette smoke, they lack the cilia of the columnar epithelial cells that are necessary for clearing particulates from the surfaces of the respiratory passages.

5) Dysplasia



- A derangement of cell growth that leads to tissues with cells of varying size, shape and appearance.
- Generally **occurs in response to** chronic irritation and inflammation.

Dysplasia may be a **strong precursor to cancer** in certain instances such as in the cervix or respiratory tract. However, dysplasia is an adaptive process and as such does not necessarily lead to cancer. In many cases, the dysplastic cells revert to their former structure and function.

Cellular injury

Pathogenesis or pathophysiology of cell injury

- Hypoxic or ischemic injury
- free radical injury

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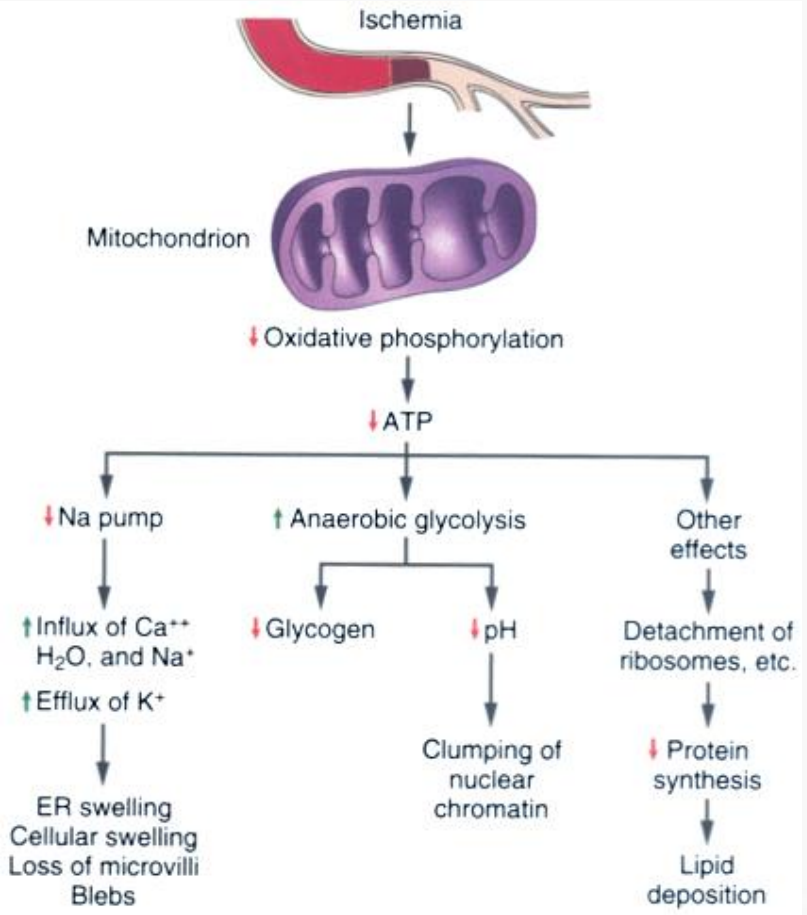
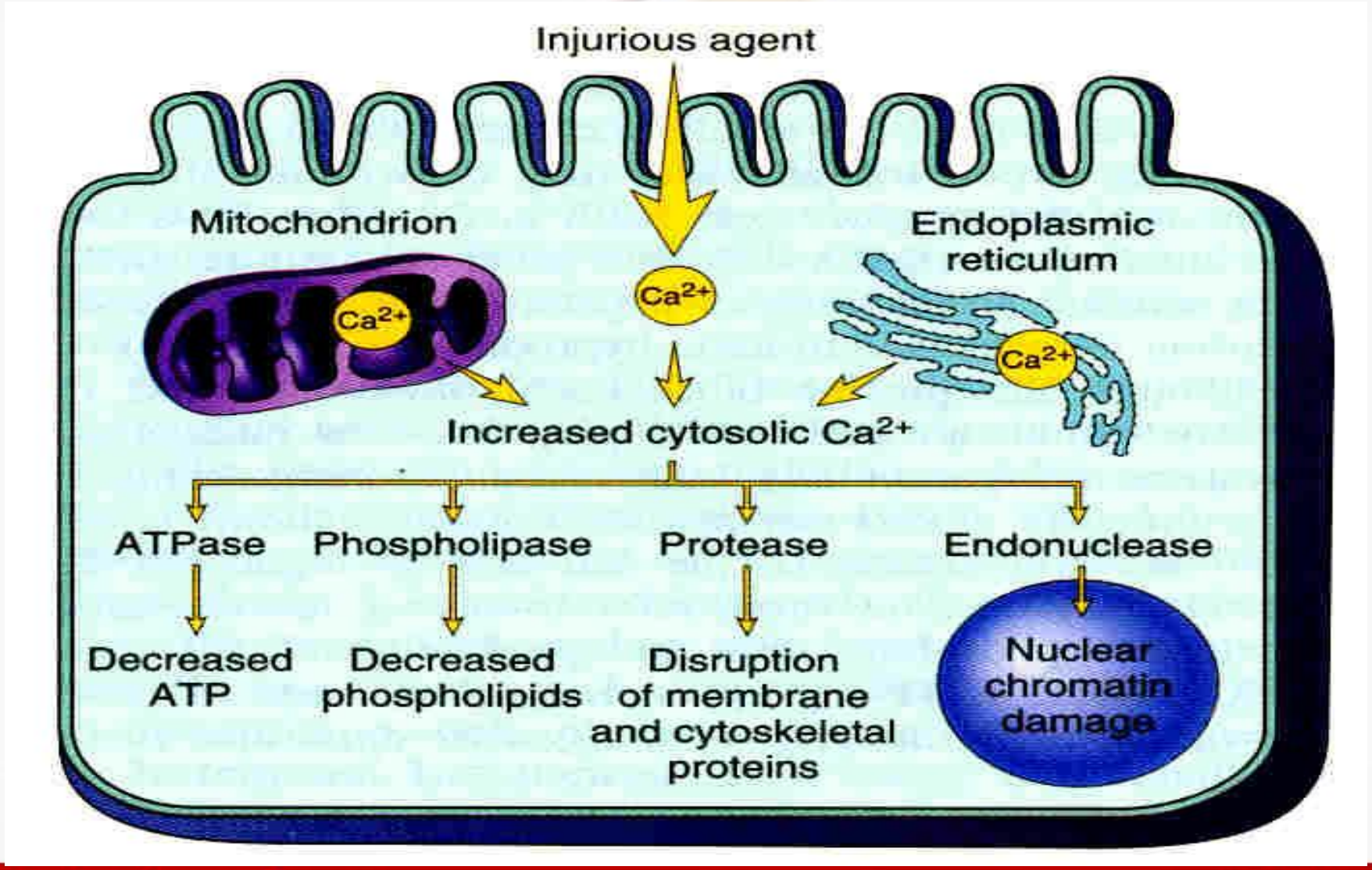
Pathogenesis of cell injury

1.Ischemic and hypoxic injury-




Injurious agent
Mitochondrion
Ca2+
Ca2+
Endoplasmic reticulum
Ca2+
Increased cytosolic Ca2+
ATPase
Phospholipase
Protease
Endonuclease
Decreased ATP
Decreased phospholipids
Disruption of membrane and cytoskeletal proteins
Nuclear chromatin damage

2)Free radical injury

- **Free radicals are** highly reactive chemical species that have one or more unpaired electrons in their outer shell.
- **Examples of free radicals include** *superoxide* **(O^{-2})**,*hydroxyl radicals* **(OH^{-})** and *hydrogen peroxide***(H_2O_2)**.
- **Free radicals are generated as** by-products of normal cell metabolism and are inactivated by free radical–scavenging enzymes within the body such as ***Catalase* and *glutathione peroxidase.***
- **Injury to cells occur when:**
  - excess free radicals are formed from exogenous sources or
  - the free radical protective mechanisms fail.

❖**Free radicals are highly reactive and can injure cells through:**

1. Peroxidation of membrane lipids.
2. Damage of cellular proteins.
3. Mutation of cellular DNA.

❖**Exogenous sources of free radicals include** tobacco smoke, organic solvents, pollutants, radiation and pesticides.

❖**Free radical injury has been implicated as playing a key role in**:

1.The normal aging process.

2.Number of disease states such as diabetes mellitus, cancer, atheroscelrosis, Alzheimer's disease and rheumatoid arthritis.

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Reversible and Irreversible Cell Injury

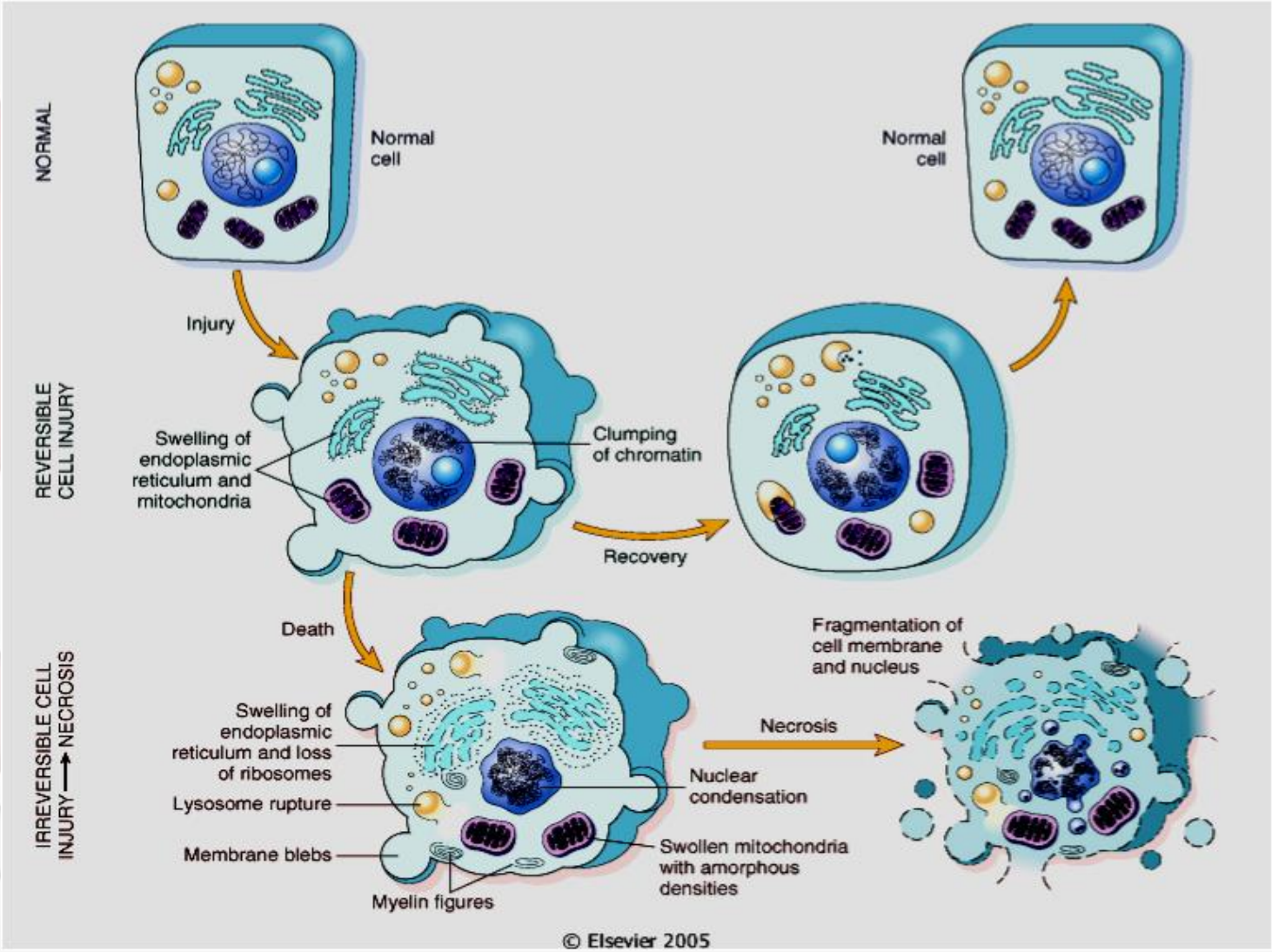
Reversible:

- Decrease generation of ATP
- Loss of cell membrane integrity
- Defects in protein synthesis, and DNA damage
- Defects in protein

Persistent or excessive injury

Irreversible:

- Sever mitochondrial changes
- Extensive damage to plasma membranes
- Swelling of lysosomes
- Defects in protein


NORMAL
Normal cell
Normal cell
Injury
REVERSIBLE CELL INJURY
Swelling of endoplasmic reticulum and mitochondria
Clumping of chromatin
Recovery
Death
IRREVERSIBLE CELL INJURY → NECROSIS
Swelling of endoplasmic reticulum and loss of ribosomes
Lysosome rupture
Membrane blebs
Myelin figures
Nuclear condensation
Swollen mitochondria with amorphous densities
Necrosis
Fragmentation of cell membrane and nucleus
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