

# CELL INJURY



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*Shaping Lives...*  
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# CELL INJURY

**Cell Injury** also known as **Cell damage**. It is a variety of changes of stress that a cell suffers due to external as well as internal environmental changes and other causes are physical, chemical, infectious, biological, nutritional or immunological factors.

It is further divided in to two types.

1. Reversible Cell Injury
2. Ir-Reversible Cell Injury

REVERSIBLE CELL INJURY	IRREVERSIBLE CELL INJURY
A type of cell injury that can return to the steady state by altering cellular conditions	One of the severe types of cell injury, which leads to the cell death
Can return to the normal position	Has passed the point of no return
Sub-lethal and short-acting	Lethal and long-lasting
Caused by lack of oxygen (hypoxia or ischemia) or blood flow to the cells	Caused by immunological responses or viral infections
Results in cellular swelling and fat accumulation	Results in necrosis and apoptosis
Can be treated with drugs	Leads to permanent cell loss
	Visit <a href="http://www.PEDIAA.com">www.PEDIAA.com</a>

## ETIOLOGY OF CELL INJURY

1. Genetic
2. Acquired

### GENETIC CAUSES:

- a) **Developmental Defect:** Developmental defect are the group of abnormalities from fetal life.
- b) **Cytogenic Defect:** Abnormalities of chromosomes. These are two types....**Numerical & Structural**

**Numerical:** These abnormalities occurs due to increase or decrease in the number of fetal chromosome.

**Structural:** These abnormalities occurs due to change in appearance of chromosome.

### ACQUIRED CAUSES:

#### a) Hypoxia and Ischemia:

**Hypoxia:** Lack of oxygen supply to the cell.

**Ischemia:** Lack of blood supply to the cell.

- Body cells required oxygen through blood to meet the metabolic needs of the body. If it is not supplied according to the body's requirements, It causes cell injury.

#### b) Physical Agents:

- Mechanical trauma (accident)
- Thermal trauma (hot/cold/humidity/weather)
- Electric current
- Radiation (UV radiation)
- Rapid change in atmospheric pressure

- Pollutes air
- High concentration of oxygen , carbon dioxide etc..

**c) Chemical Agents:**

- Chemical poisoning
- Strong acid and base
- Pesticides, insecticides, herbicide
- Hypertonic salt/glucose
- Alcohol, Narcotic drugs

**d) Microbial Agents:**

- Wide range of microbes such as: bacteria, virus, fungi, protozoa and other parasites cause cell damage or cell injury.

**e) Immunological Agents:**

- Hypersensitivity reactions
- Anaphylactic reactions to a foreign body
- Autoimmune disease

**f) Nutritional Imbalance:**

Dietary insufficiency of different nutrients like protein, vitamins, carbohydrate, lipids and minerals can leads to different disease conditions at the cellular level due to interference in normal metabolic pathways.

**g) Psychological Disorders:**

Parkinson's disease, Epilepsy etc..

## **h) Iatrogenic Disease:**

- Drug interaction
- Drug overdose
- Multi drug prescription
- Side effects of drug
- Complication after radiation
- Complication after surgery

## **PATHOGENESIS OF CELL INJURY**

- 1. Cell Membrane damage**
- 2. Mitochondrial damage through ATP depletion**
- 3. Ribosomal damage**
- 4. Oxidative Stress mediated Nuclear damage**

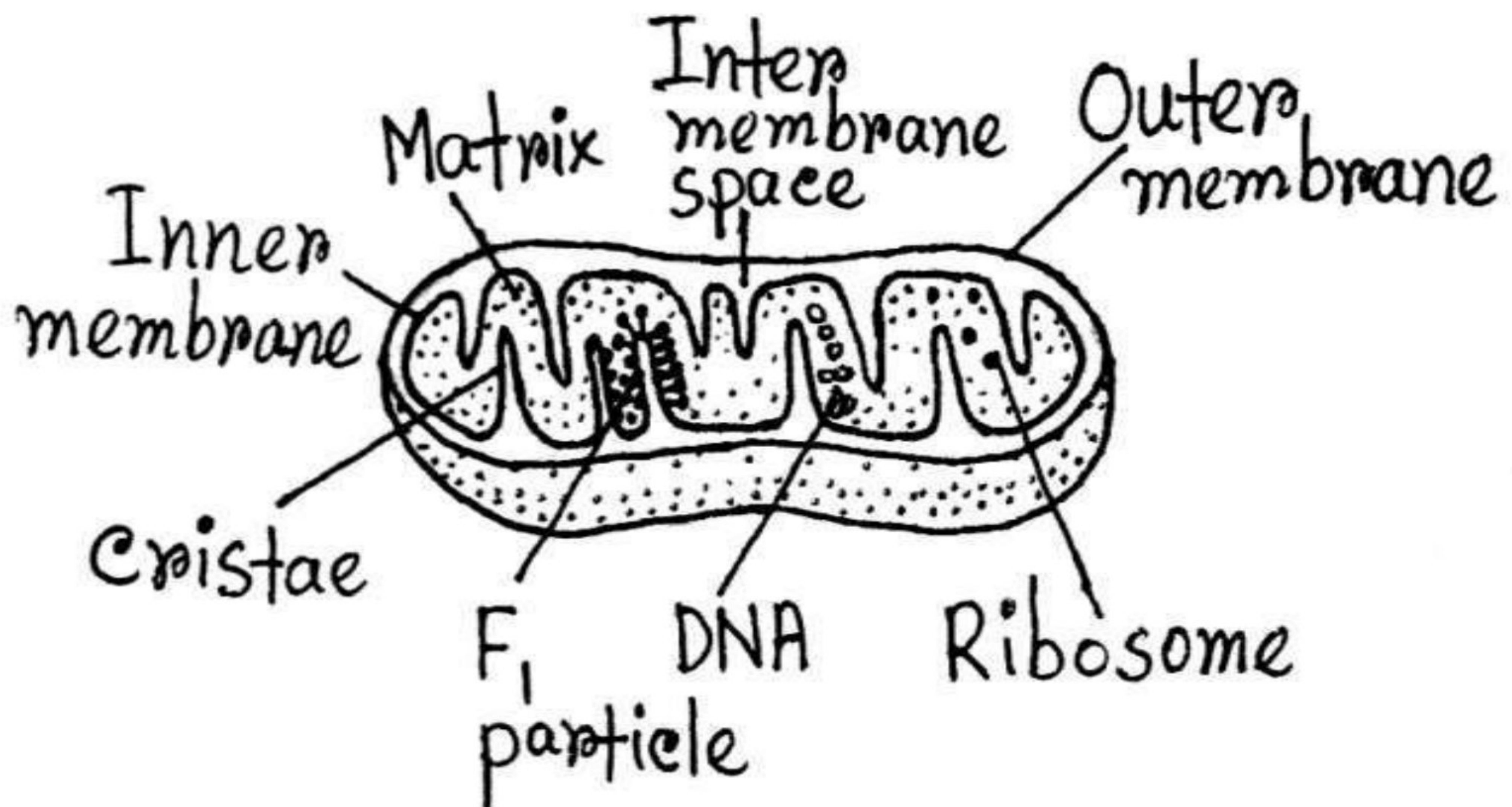
## **CELL MEMBRANE DAMAGE THROUGH**

### **CALCIUM INFLUX:**

- Usually, a cell's extracellular space has a larger concentration of calcium ions than its intracellular space.
- When a cell experiences various types of stress. Endoplasmic reticulum (ER) and mitochondria release calcium ions inside the cell.
- Higher concentration of intracellular calcium ion triggers calcium channel present on the surface of the cell membrane.
- Then, calcium enters the cell through the calcium channel, then it increases the amount of calcium ions inside the cell.
- The mitochondria will get damaged by an increase in calcium ions within cell.
- It mainly triggers three different kinds of cell-based enzymes.
- It triggers proteases, which will break down the proteins in the cell membrane.

- Additionally, it stimulates phospholipases, which will cause plasma membrane (lipid bi layer) rupture.
- Additionally, it stimulates the ATPase enzyme, which results in a drop in ATP levels, as well as endonucleases, which will enter the nucleus and destroy DNA.
- In this manner, calcium influx will harm the cell membrane.

### MITOCHONDRIAL DAMAGE THROUGH ATP DEPLETION:



- Hypoxia, ischemia and any chemical agent will cause mitochondrial damage.
- Normally, mitochondria use blood oxygen molecules to make ATP.
- Oxygen deficiency will interfere with ATP generation, which will lower the amount of ATP or lead to ATP depletion.

- The inter membrane space (IMS) and matrix contain the mitochondrial permeability transition pore (MPT).
- Due to Mitochondrial damage (increase in calcium ions with in cell), MPT will transferred to the mitochondria's outer surface and form a gate or channel.
- Mitochondria releases hydrogen ions and calcium ions through MPT channel, that will cause increase in cytosolic calcium level within the cell.
- Hydrogen ion will reduce the electron transport system (ETS) within the cell.
- (ETS) electron transport system then reduces ATP generation while increasing ROS or free radicals production.
- \*Mitochondria also produce antioxidants.
- Then there will be an influx of water in to the cell.
- It causes the outer membrane of cell to swell, which leads to cell bursts.
- This causes mitochondrial damage through ATP depletion.

### **RIBOSOMAL DAMAGE THROUGH Na<sup>+</sup> K<sup>+</sup> ATPase PUMP:**

- Normally, the Na<sup>+</sup> K<sup>+</sup> ATPase pump allows potassium into the cell and sodium out.
- Na<sup>+</sup> K<sup>+</sup> ATPase does not function properly as a result of ATP depletion.
- Sodium ion accumulation occurs inside the cell, resulting in rising of water level.
- It also causes a drop in the potassium ion level within the cell.
- Then cell swelling occurs as the water level within the cell rises.
- This also leads to swelling of Endoplasmic reticulum (ER).
- The ribosomes then separated from the rough endoplasmic reticulum surface (RER).

- It causes reduction in protein synthesis within the cell (Ribosomes is responsible for protein synthesis), resulting in Ribosomal damage.

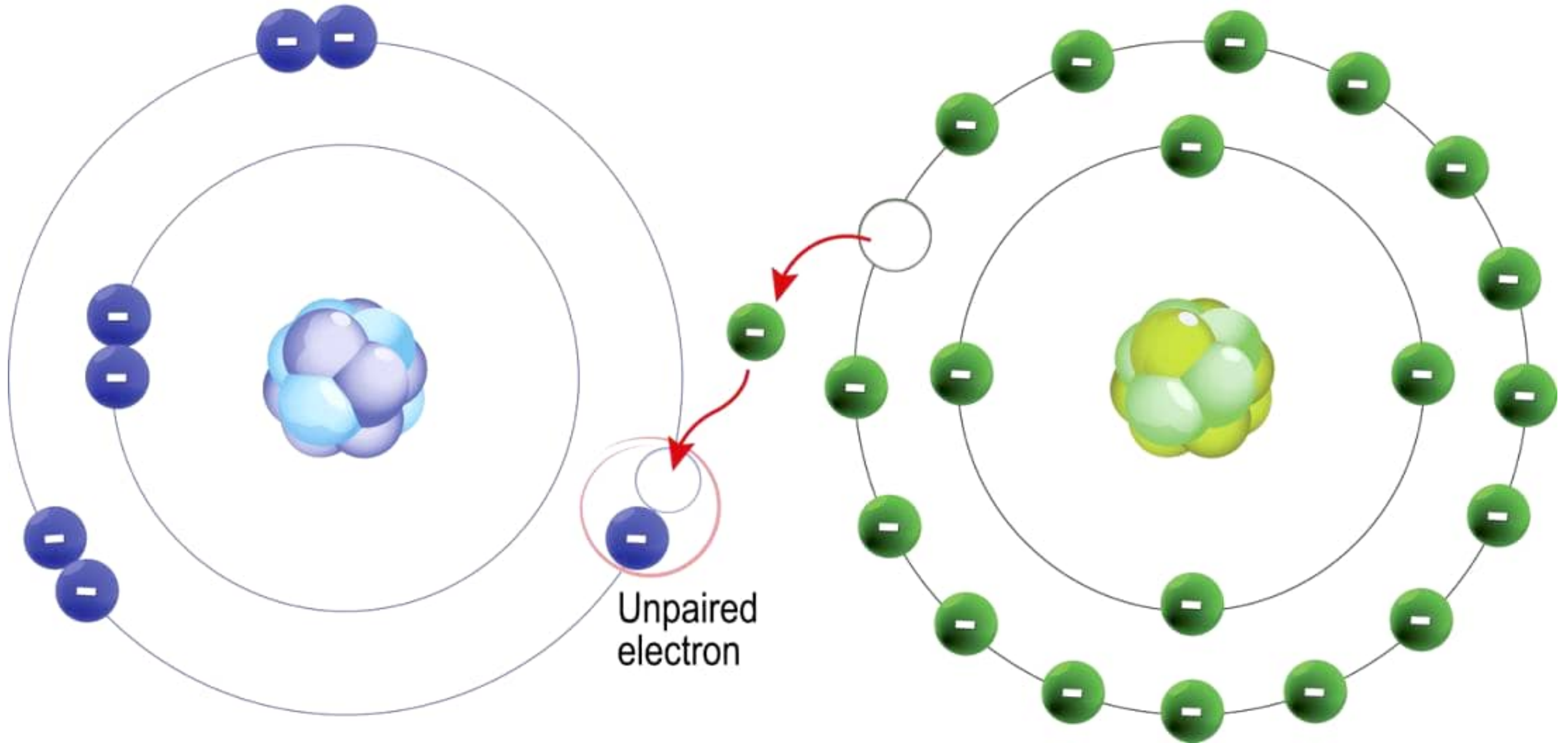
### **OXIDATIVE STRESS MEDIATED NUCLEAR DAMAGE:**

- DNA is a double standard molecule composed of four nucleotide bases. (Adenine, Guanine, Cytosine, Thymine)
- DNA damage occurs as a result of free radical oxidative stress.
- Free radicals are chemical species with a single unpaired electron in an oxygen outer orbit. Inside the mitochondria, free radicals are formed.
- Free radicals cause oxidation of DNA nucleotide bases by damaging the normal DNA molecule.
- Guanine is more oxidized than other nucleotide bases and after oxidation, it form 8-Hydroxy Guanine.
- It resulting in nuclear damage.



# Free radical

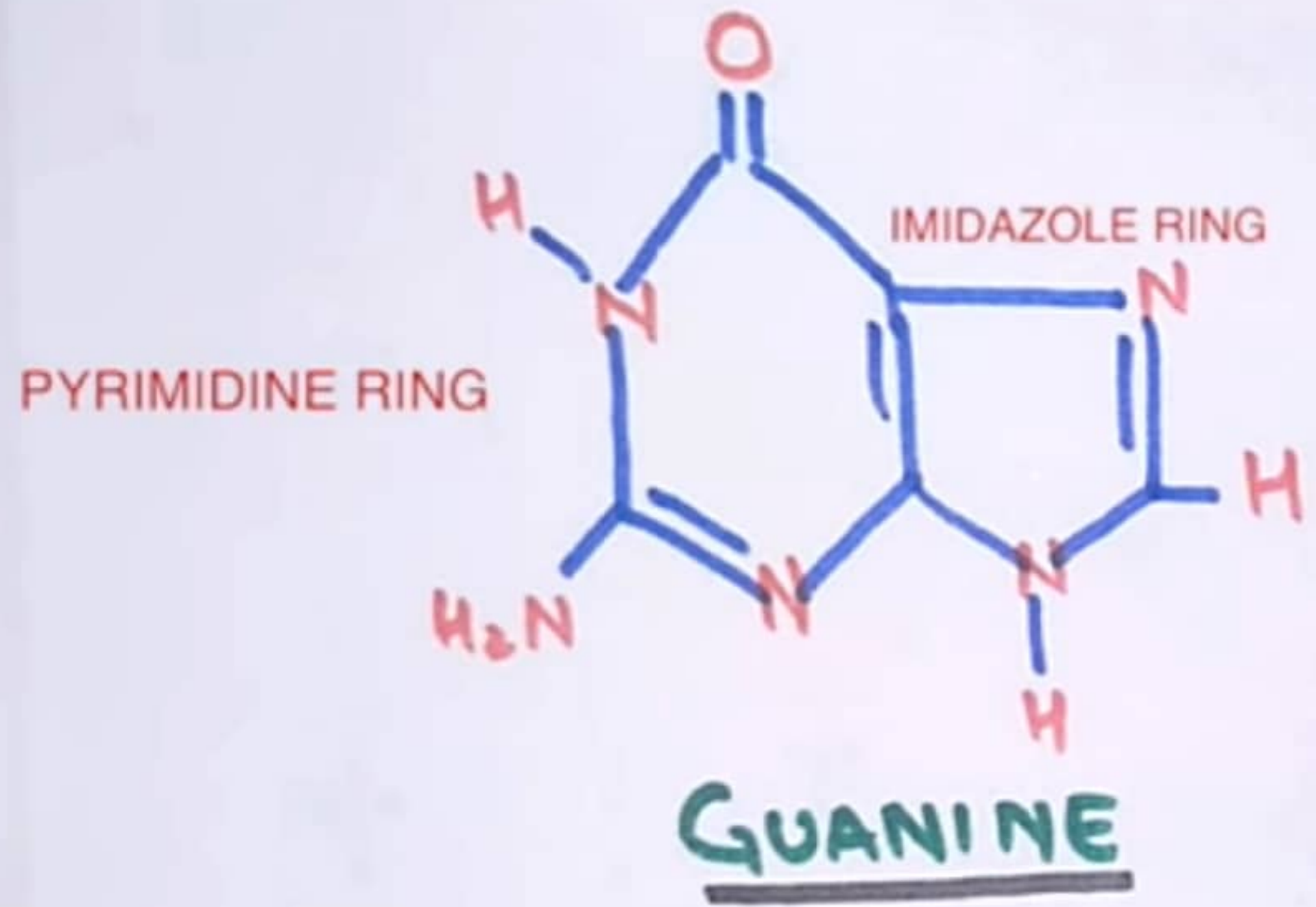
# Antioxidant



# REACTIVE OXYGEN SPECIES

## FREE RADICALS IN BIOLOGICAL SYSTEMS





Rxn WITH  
ROS / FREE  
RADICALS

