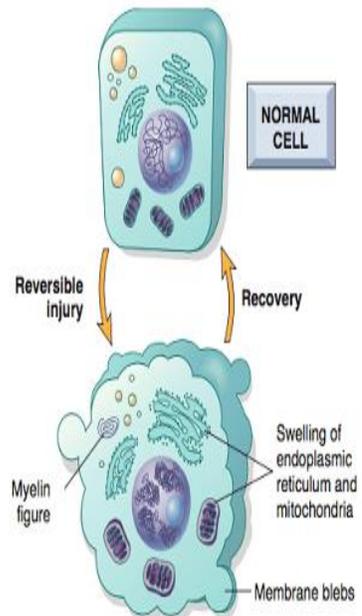
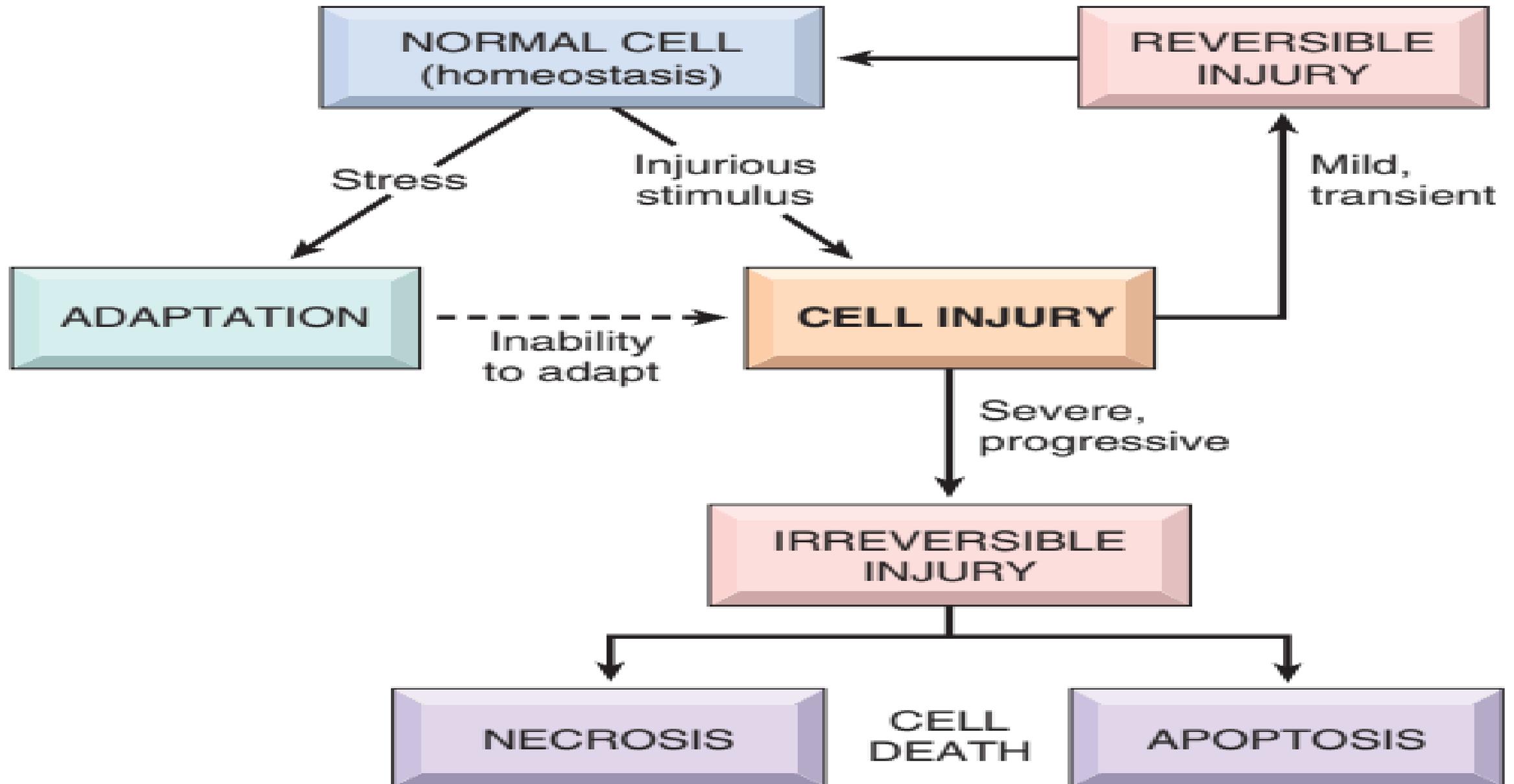


# CELL INJURY

**omyma Meabed**





**Figure 2-1** Stages of the cellular response to stress and injurious stimuli.

# CELLULAR ADAPTATION

- **Definition: Reversible changes in number, size, and function of cells to-overcome adverse environmental changes.**

**Types:**

**1- Hypertrophy**

**2- Hyperplasia**

**3- Atrophy**

**4- Metaplasia**

# **1-HYPERPLASIA:**

- **is the Increase in size and weight of organ or tissue due to increased number of its specialized cells.**
- **Mechanism of hyperplasia:**
  - **Increased local production of growth factors.**
  - **Increased level of growth factor receptors.**
  - **Development of new cells from the stem cells**

# Types of hyperplasia:

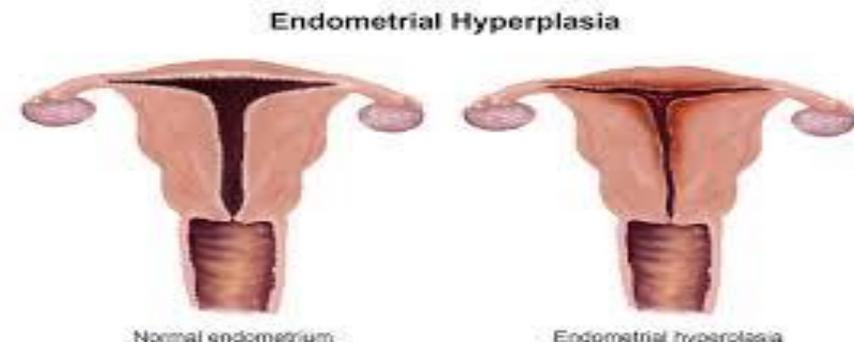
## 1- Physiological

- Mammary gland at puberty, pregnancy and lactation.

## 2- Pathological

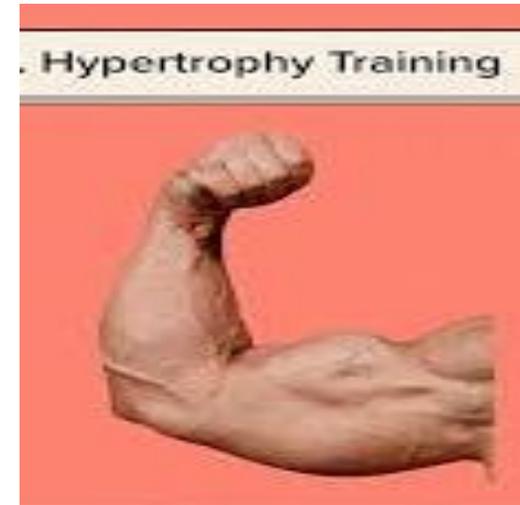
- **Compensatory** hyperplasia: Hyperplasia of bone marrow after hemorrhage.

- **Hormonal** hyperplasia: Endometrial hyperplasia and mammary cystic hyperplasia in response to excess **estrogen** stimulation.



# 2-HYPERTROPHY

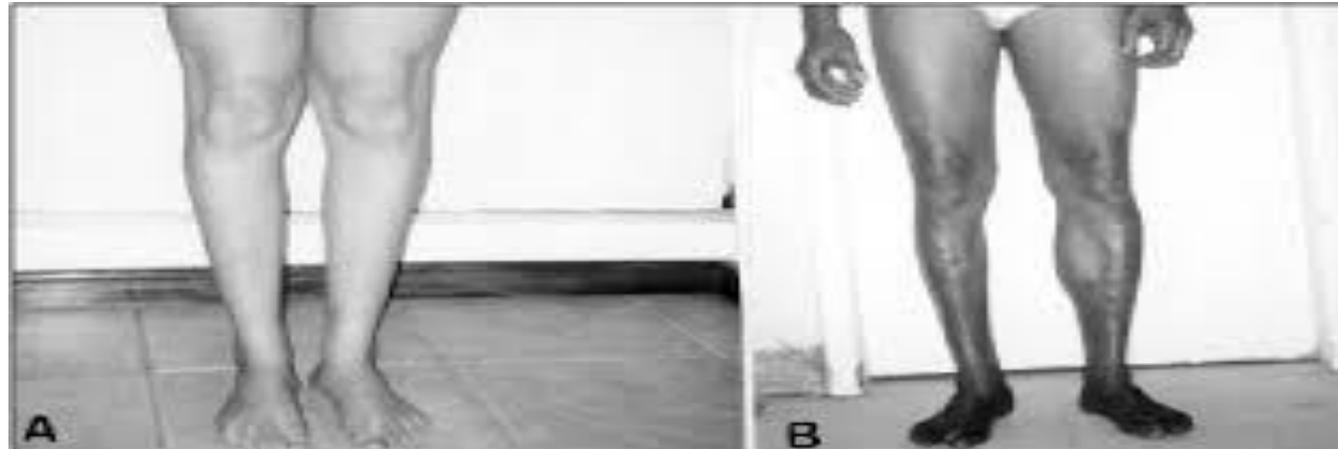
- is the increase in size and weight of an organ due to increased size of its specialized cells.
- **Causes:** increased protein demand causes increased protein synthesis
- **Types of hypertrophy:**
  - 1- Physiological**
    - Uterine muscle in pregnancy.
    - Skeletal muscle in athletes.
  - 2- Pathological**
    - **compensatory:** Hypertrophy of one kidney after nephrectomy of the other one
    - **adaptive:** Left ventricular hypertrophy in systemic hypertension



# 3-ATROPHY

Definition: Decrease in size and weight of an organ or tissue due to decrease number and/or size of its specialized cells.

- **Mechanism of atrophy:**
- It is due to increased protein degradation by increased activity of proteolytic-enzymes in the lysosomes.



# Types of atrophy:

## 1- Physiological atrophy:

- Breast after lactation & ovary after menopause.

## 2- Pathological atrophy:

### a) Generalized:

- Starvation and malnutrition





## **b) Localized:**

- **Ischemic atrophy: Brain in atherosclerosis.**
- **Pressure atrophy: Meningioma-localized brain atrophy.**
- **Neuropathic atrophy: Skeletal muscle atrophy after cutting nerve supply.**
- **Disuse atrophy: Muscle atrophy in an immobilized limb.**

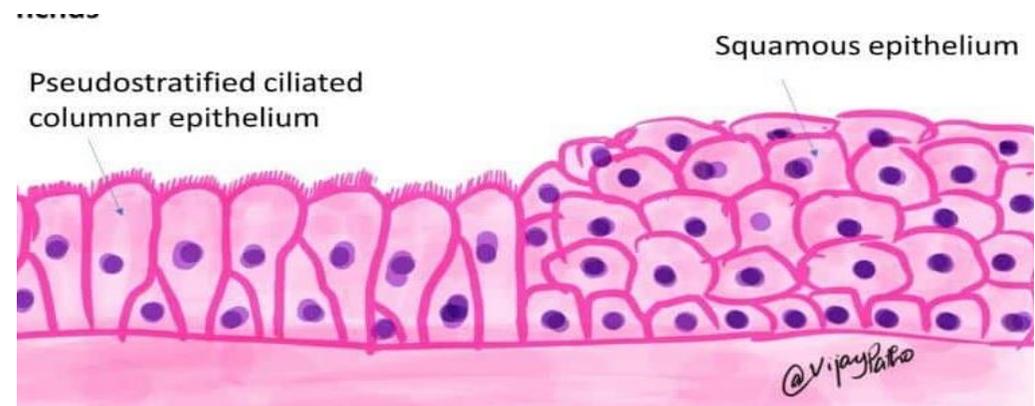


@VijayPatho

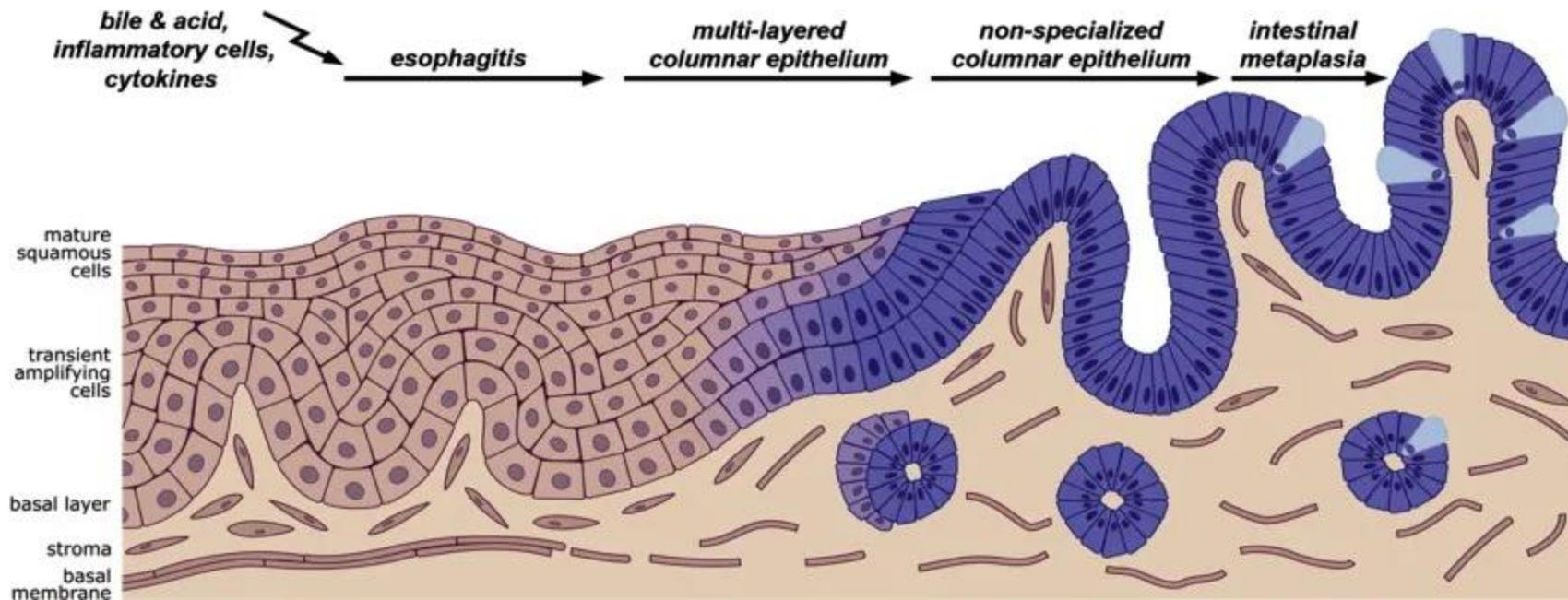


# 4-METAPLASIA

- **Definition:** Change of one type of differentiated tissue to another type of differentiated tissue within the same category.
- **This tissue change helps to adapt changes in environment**
- **Etiology:** chronic irritation
- **Examples:**
  - a- **Epithelial metaplasia:- Respiratory pseudostratified columnar ciliated epithelium change to stratified squamous epithelium due to smoking.**

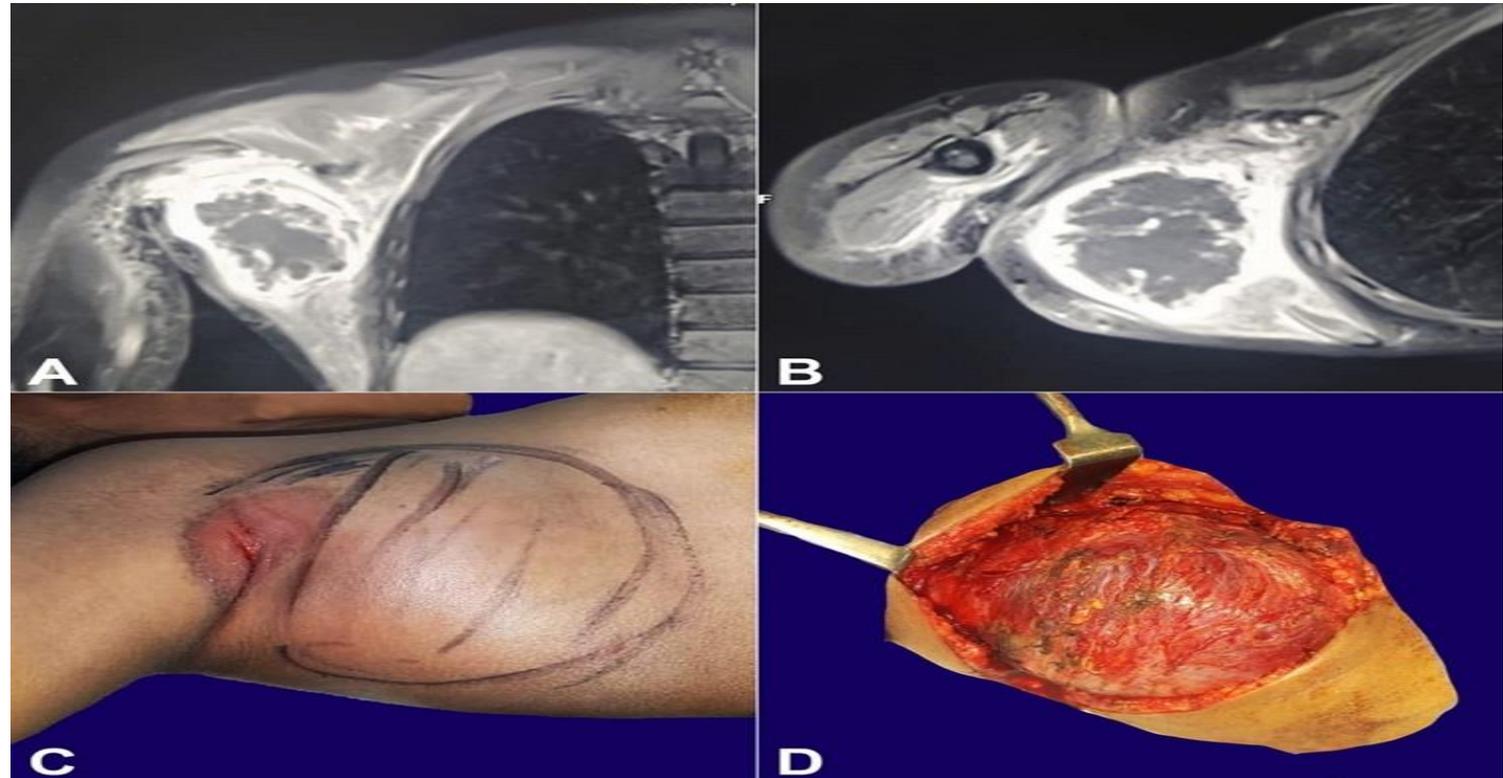


b- Barrett's esophagus: stratified squamous epithelium of the lower third of the esophagus is changed to columnar epithelium due to gastric reflux hyperacidity



## **b- Connective tissue metaplasia**

- **Myositis ossificans: Trauma to muscle with hematoma formation.**
- **Then, Organization occurs and fibroblast change to osteoblasts which lay down osteoid tissue with bone formation.**



# NOTE

**Metaplasia represents an adaptive change during which the cells that are sensitive to stress are replaced by more resistant cell type. Persistence of the etiology of metaplasia may be followed by malignant transformation of metaplastic tissue**

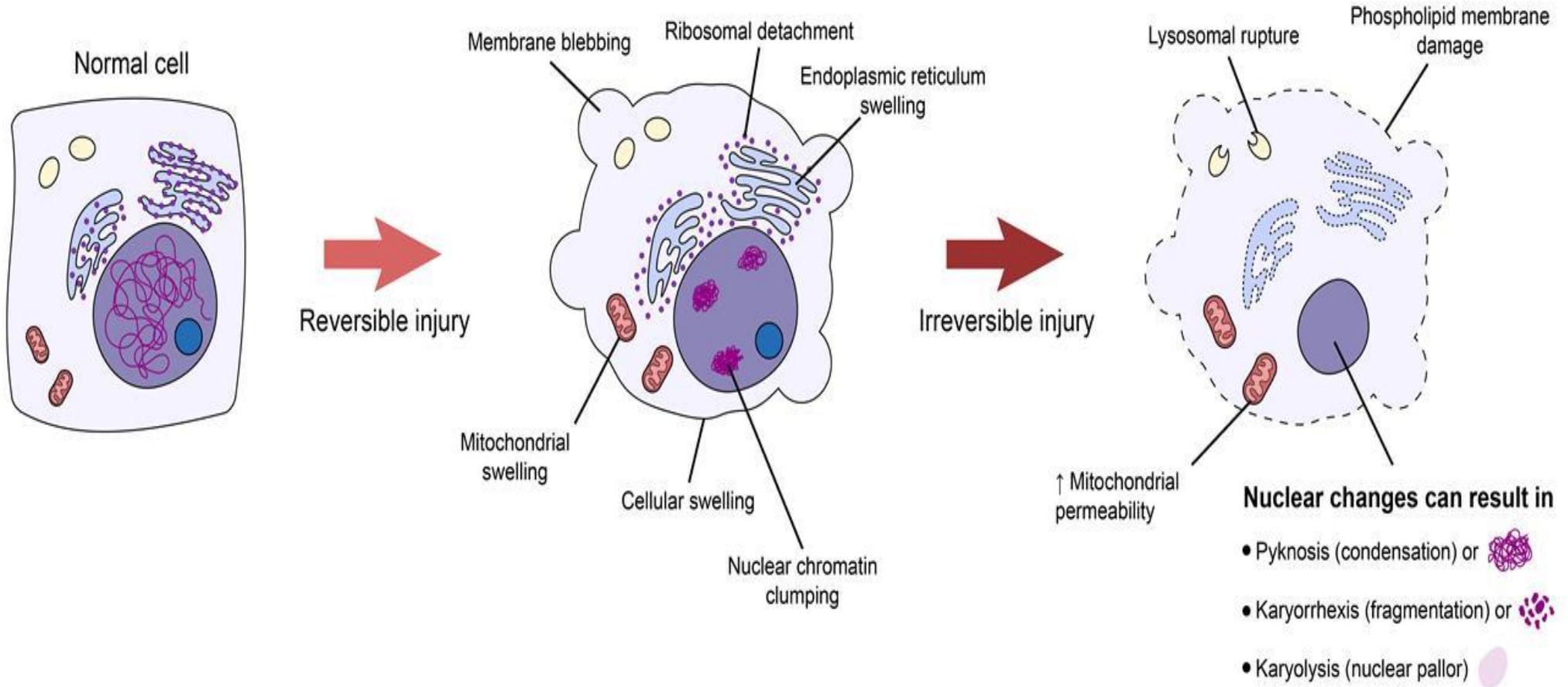
# **Reversible cell injury (Degeneration).**

## **Irreversible (Cell death).**

### **Causes of cell injury:**

- 1- Hypoxia: Oxygen deficiency**
- 2-Ischemia: loss of arterial blood supply leads to reduction of both oxygen & glucose.**
- 3- Physical agents: Mechanical trauma (burns & deep cold),radiation and electric shock.**
- 4- Chemical agents: Strong acids & alkalis.**
- 5- Infectious agents: Viruses, bacteria, fungi and parasites.**
- 6- Immunological reaction: autoimmune diseases, Hypersensitivity reactions**

# Cell Injury



# Mechanisms of cell injury:

**1-ATP depletion:** reduce the activity of Na/K ATPase pump with defect in membrane transport and intracellular accumulation of Na with osmotic gain of water and k diffusion out of the cell.

**ATP depletion result in decrease in protein synthesis and reduction in other metabolic activities of the cells**

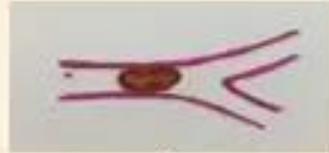
**2-Mitochondrial damage: Leads to decrease energy production and defects in all vital cellular processes.**

**3- Loss of calcium homeostasis: Ischemia or toxins cause increase in intracellular  $\text{Ca}^{+}$  which activate:**

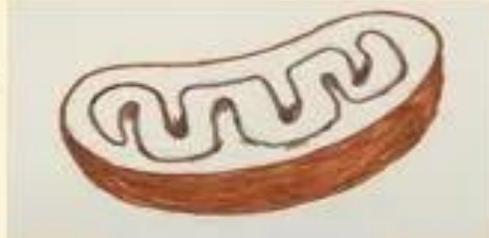
- ATPase (ATP depletion)**
- phospholipase (cell membrane damage)**
- protease (breakdown membrane and cytoskeletal proteins)**
- endonuclease (DNA damage).**

# EFFECTS OF DEPLETION OF ATP

ISCHEMIA



↓ ATP



MITOCHONDRIA

Decreased activity of Na pump

- Intracellular
  - Increased  $\text{Na}^+$
  - Decreased  $\text{K}^+$
  - Increased  $\text{Ca}^{2+}$
  - Increased  $\text{H}_2\text{O}$

Anaerobic metabolism

Decreased Glycogen

Decreased pH

- Decreased activity of cellular enzymes
- Clumping of chromatin

Failure of  $\text{Ca}^{2+}$  pump

Increase in intracellular calcium

- Activation of enzymes leading to damaging effects on cell constituents

Misfolding of proteins

Cell death

Detachment of ribosomes

Decreased protein synthesis

# I- REVERSIBLE CELL INJURY

## **I- REVERSIBLE CELL INJURY**

**Definition: Reversible structural and biochemical changes in cells after exposure to an injury not severe enough to kill the cell(mild stimulus short duration)**

**Types of reversible cell injury:**

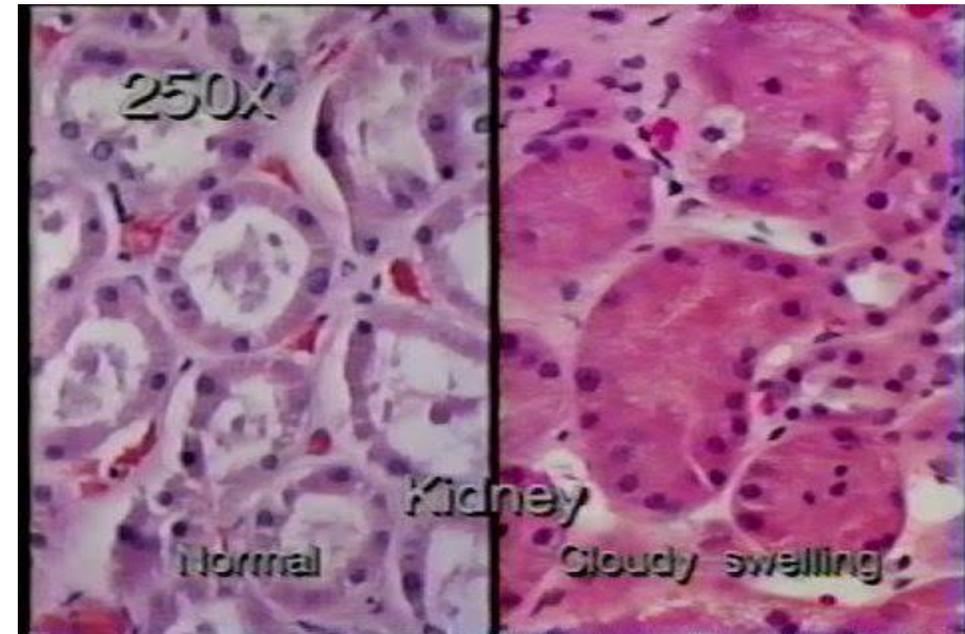
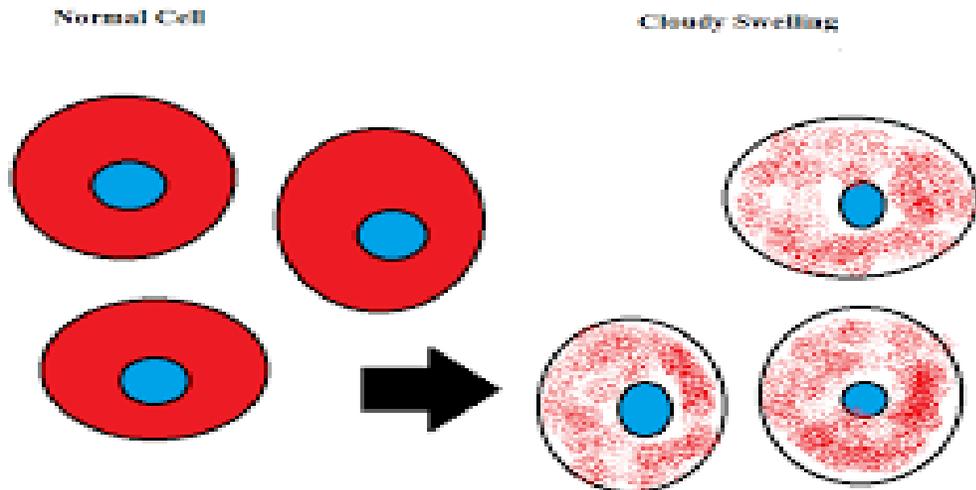
- 1- Disturbance of water metabolism**
- 2- Disturbance of lipid metabolism**

# 1- Disturbance of water metabolism:

## a) Cloudyswelling

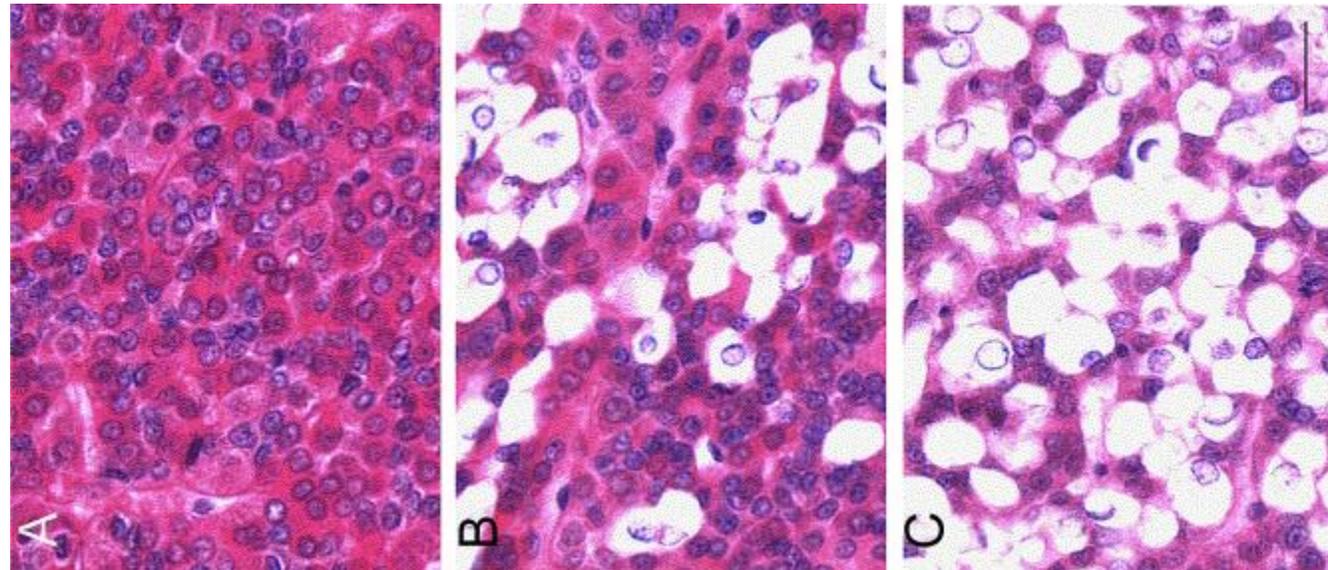
## B) Hydropic degeneration

- **a) Cloudyswelling:** IS the reversible cell damage characterized by accumulation of water inside the cells



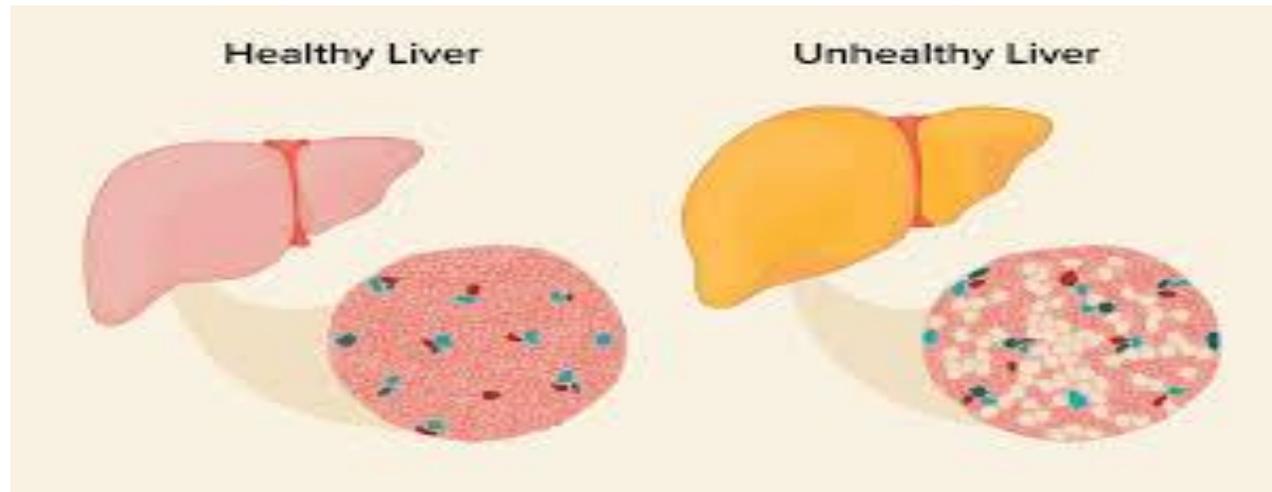
- **Causes:** bacterial toxins e.g., Typhoid.
- **Chemical poisons** e.g., phosphorus and chloroform
- **Pathogenesis:** Damaged mitochondria decrease ATP production causing failure of Na/k pump with retention of Na and water inside the cell.
- **Pathologic features:** usually affect the **parenchymatous organs (site)** e.g., Liver, renal convoluted tubules and heart muscle.
- **Gross:** the affected organ become slightly increased in **size**, pale in **color** soft in **consistency** with round **borders**.
- **Mic:** the cells are swollen due to entry of water, the **cytoplasm is granular**. This is due to accumulation of water and **mitochondrial fragmentation**.
- **The nucleus is normal**

**B) Hydropic degeneration:** is a marked increase in the permeability of cell membrane with influx of excess amount of water and formation of cytoplasmic vacuoles e.g., epidermal cells in burn.



## 2- Disturbance of lipid metabolism

- **Fatty change Def: Pathologic accumulation of fat (triglycerides) in parenchymal cells.**
- **Causes:**
  - Bacterial toxins**
  - Chemical toxins: eg. phosphorus and chloroform.**
  - Severe anemia.**



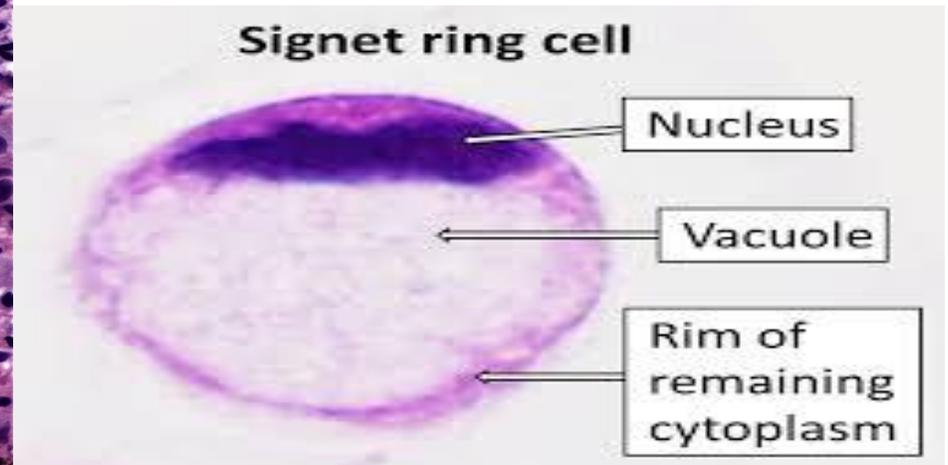
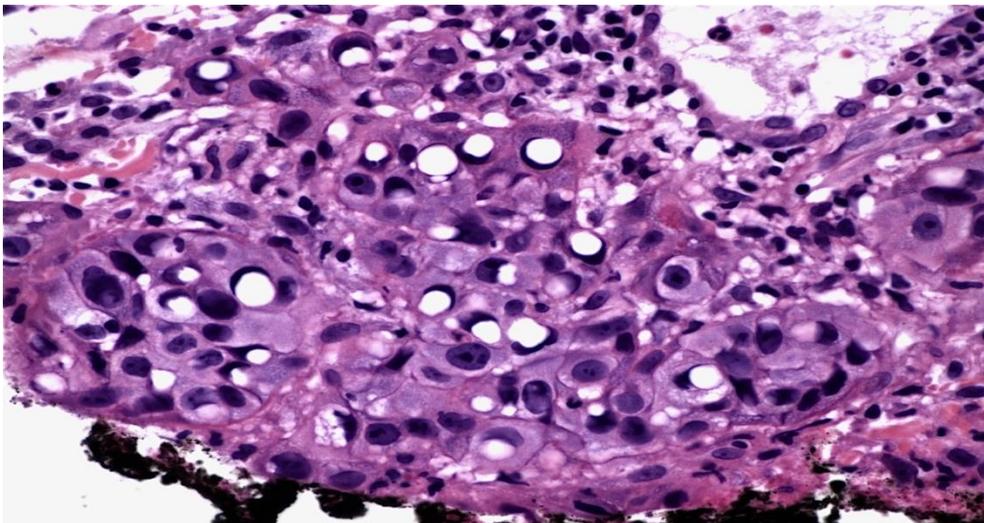
- **Pathogenesis:**

- Excess entry of free fatty acids into the cells.

- **Pathologic features:** usually affect the liver, kidney and heart.

- **Gross:**the organ is enlarged, soft consistency, yellow pale in color, with round borders. Capsule is tense and stretched.

**MIC:** The cells are swollen with fat globules in the cytoplasm. They fuse together forming single large globule that push the nucleus against the cell membrane (signet ring cells).





*Thank You*