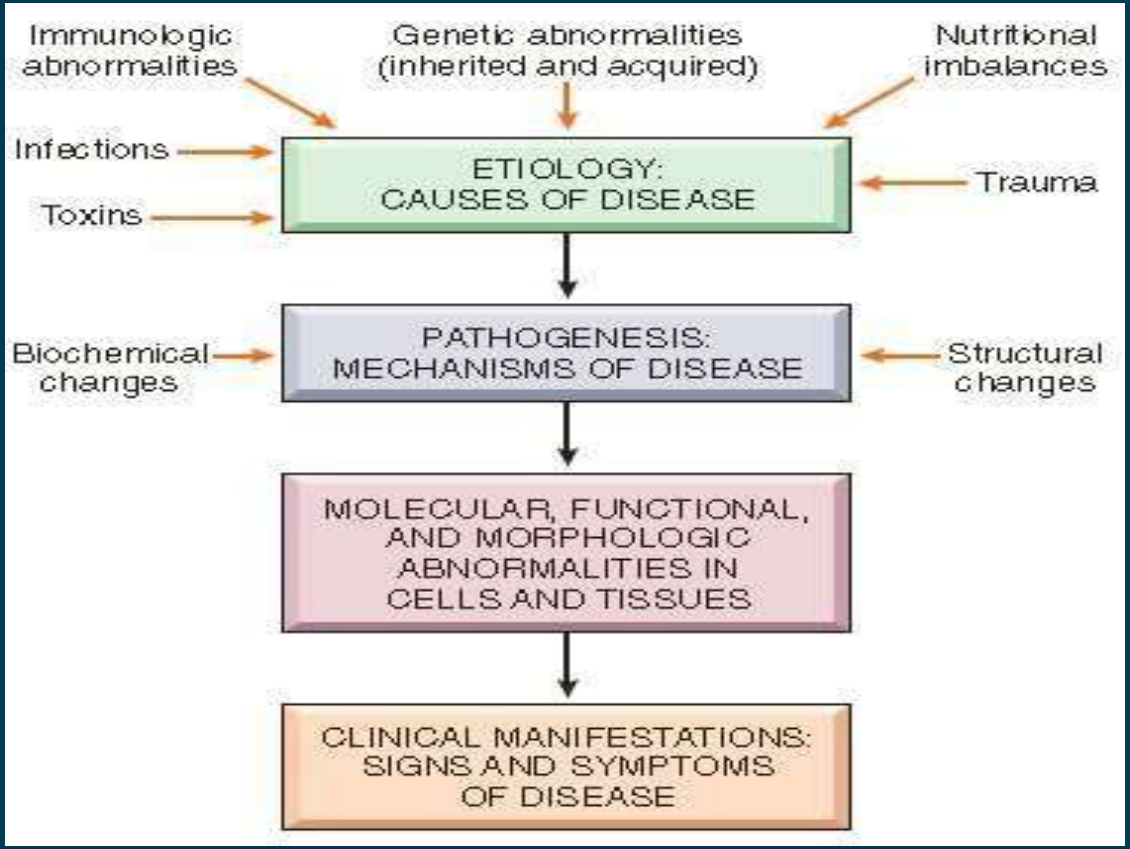
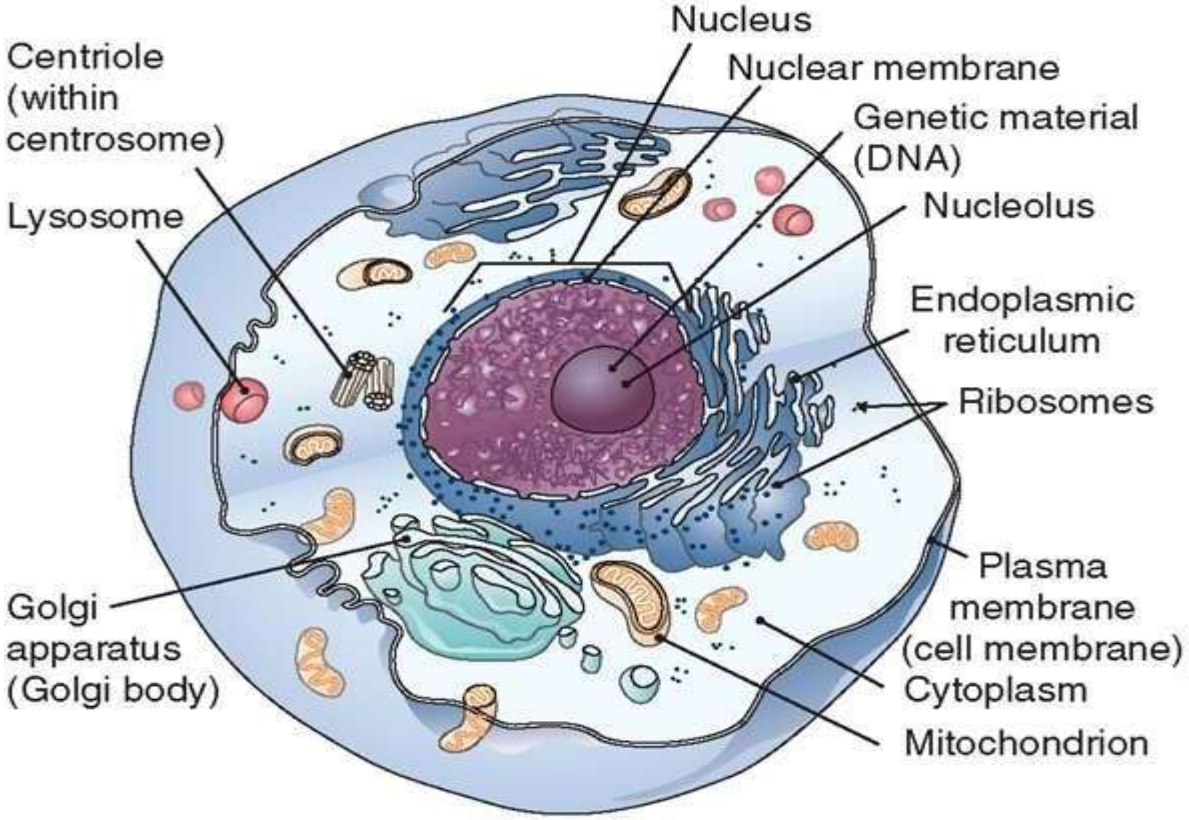
Cell Injury and Necrosis -1

The evolution of disease

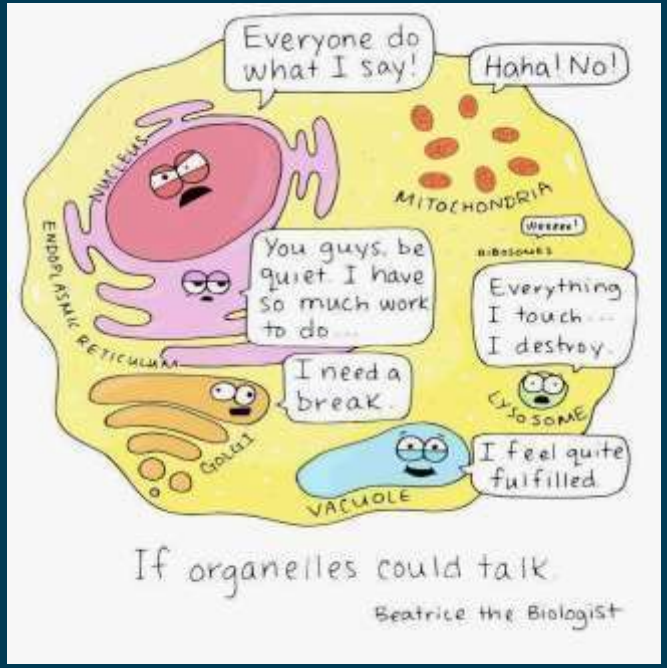


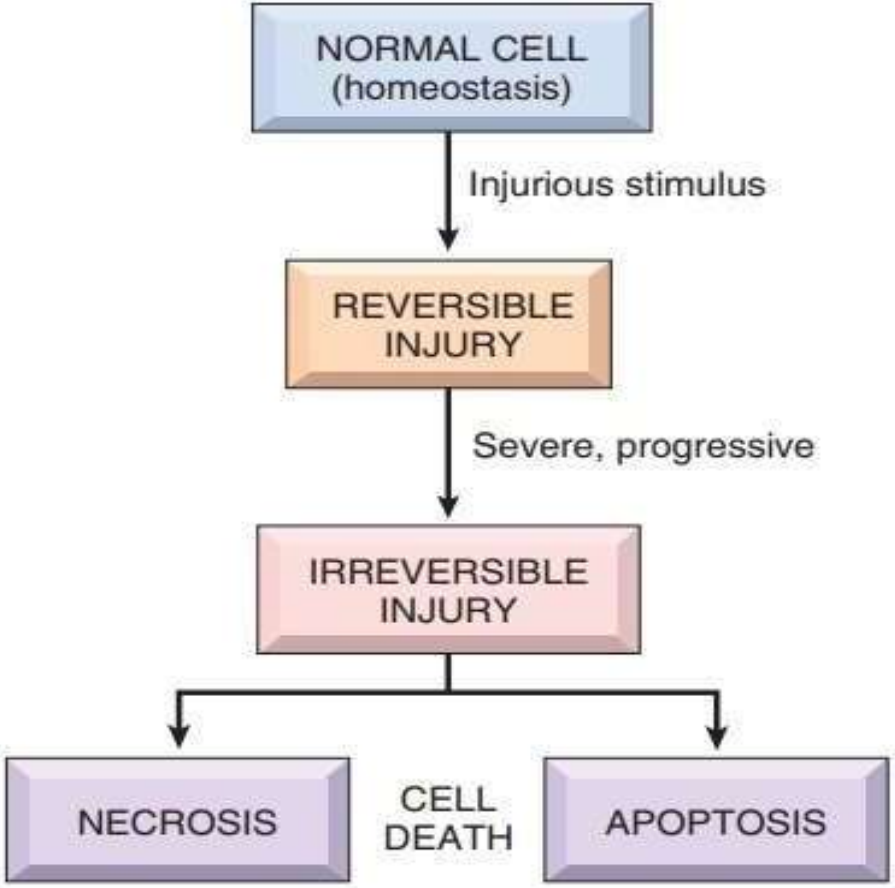
Normal cell


Nucleus
Nuclear membrane
Genetic material (DNA)
Nucleolus
Endoplasmic reticulum
Ribosomes
Plasma membrane (cell membrane)
Cytoplasm
Mitochondrion
Golgi apparatus (Golgi body)
Lysosome
Centriole (within centrosome)

Homeostasis..

+ constant internal environment.
+ The intracellular milieu is normally tightly regulated.
+ In order for the cell to function.
+ Such as; Body Temperature, sugar level




NORMAL CELL
(homeostasis)
Injurious stimulus
REVERSIBLE
INJURY
Severe, progressive
IRREVERSIBLE
INJURY
NECROSIS
CELL
DEATH
APOPTOSIS

Causes of cell injury

- **Genetic causes**

- **Acquired causes**
  - -Hypoxia and ischemia
  - -Physical agents
  - -Chemical agents and drugs
    - -Microbial agents
    - -Immunological agents
    - -Nutritional derangements
    - -Psychological factors

Acquired causes

1. Oxygen Deprivation

- **Ischemia** (loss of blood supply from impeded arterial flow or reduce venous drainage)
  - Local e.g. embolus
  - Systemic e.g. cardiac failure
- **Hypoxia** (deficiency of oxygen causing cell injury by reducing aerobic oxidative respiration)
  - Oxygen problems e.g. altitude
  - Haemoglobin problems e.g. anaemia

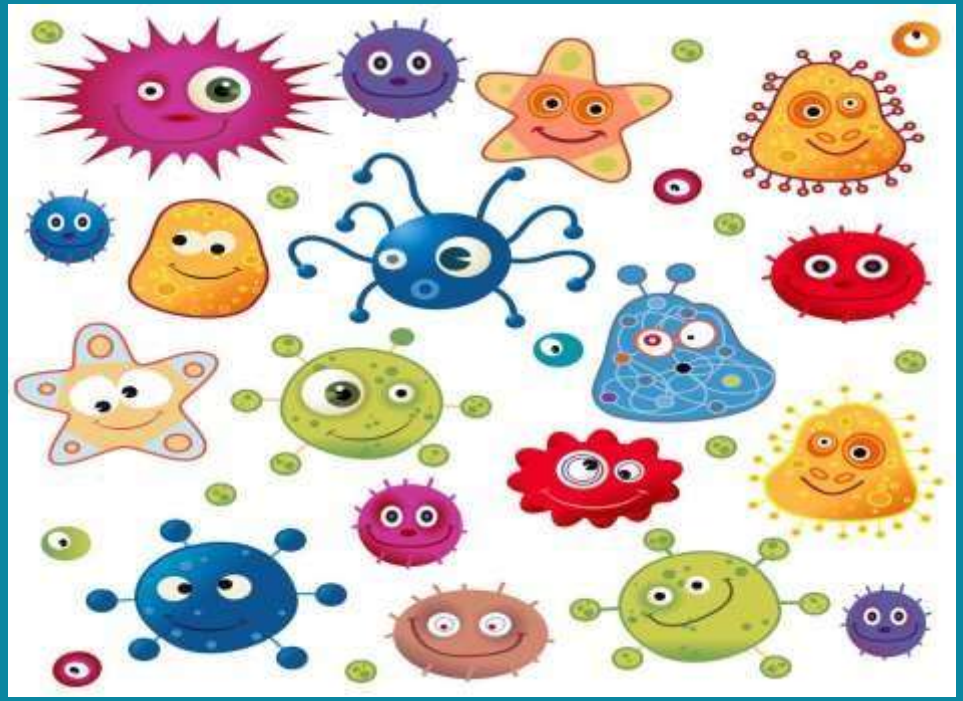
Toxins

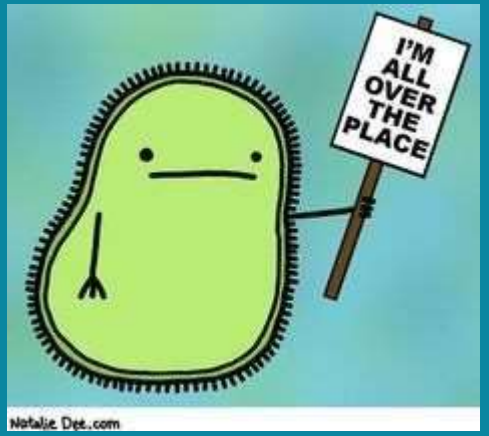
+air pollutant, CO, asbestos, cigarette smoke, & ethanol

+ drugs: susceptible patients, excessively and inappropriately.

+Innocuous substances: Water, salt, glucose, and oxygen.

Infectious Agents





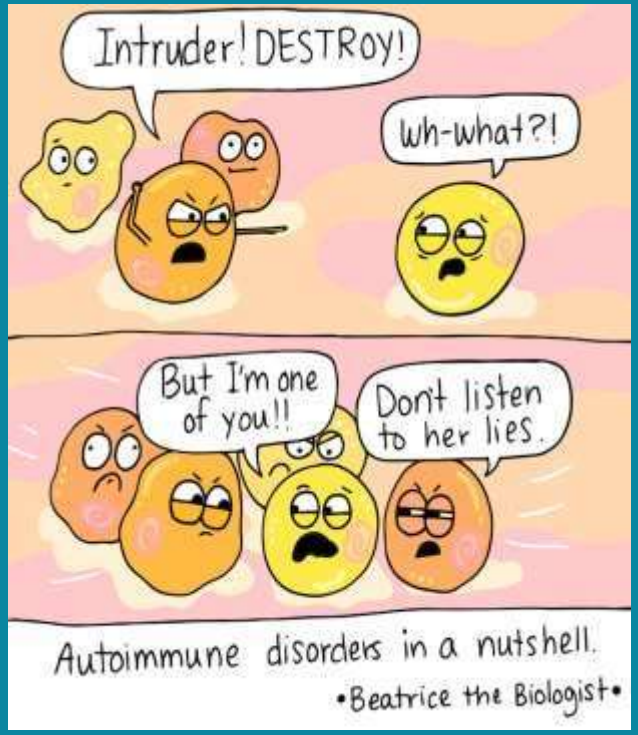
Immunologic Reactions

+ Autoimmune reactions

+ Allergic reactions: innocuous environmental substances.

+excessive response to microbes

.. Inflammatory reaction that damage cells and tissue



Nutritional Imbalances

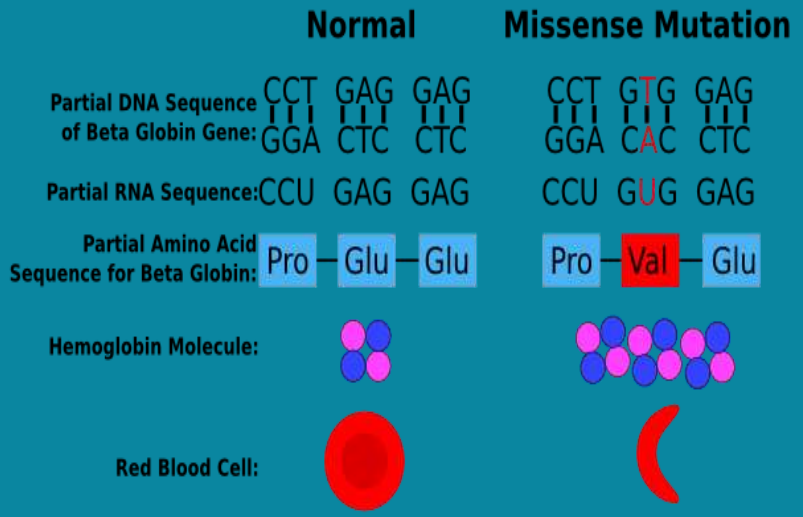
+ Protein-calorie insufficiency: countries in Poverty

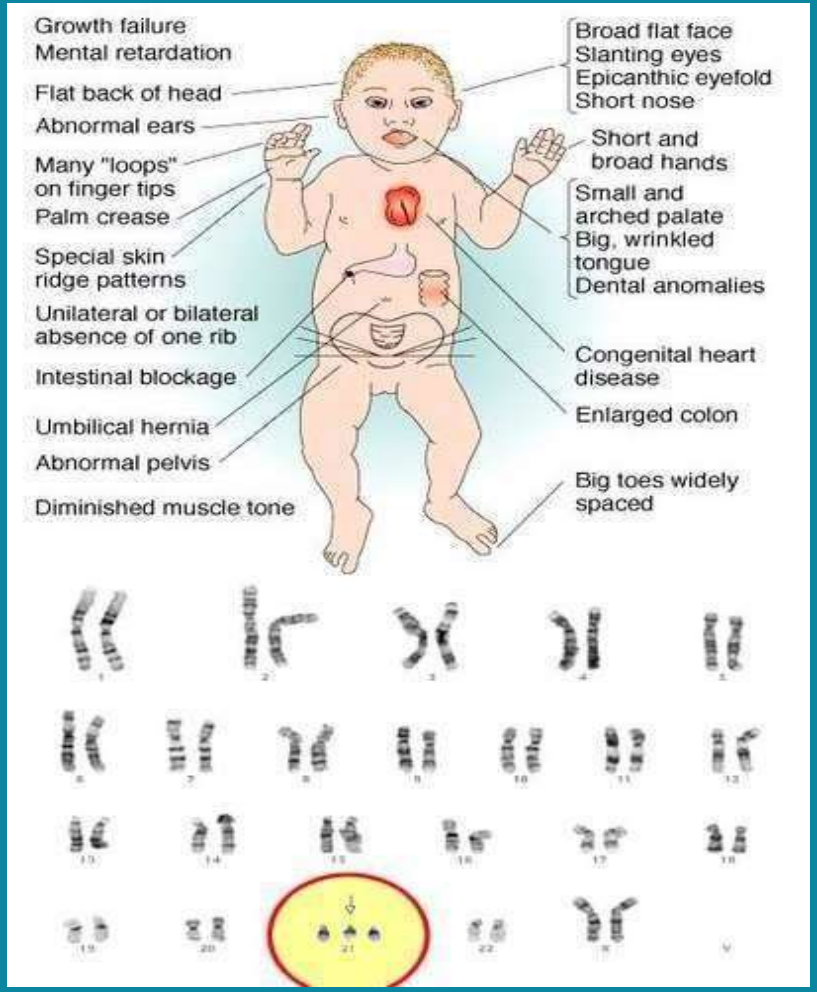
+ Specific vitamin deficiencies

+ Excessive dietary intake may result in obesity; DM-2 atherosclerosis (MI , stroke)

Physical Agents

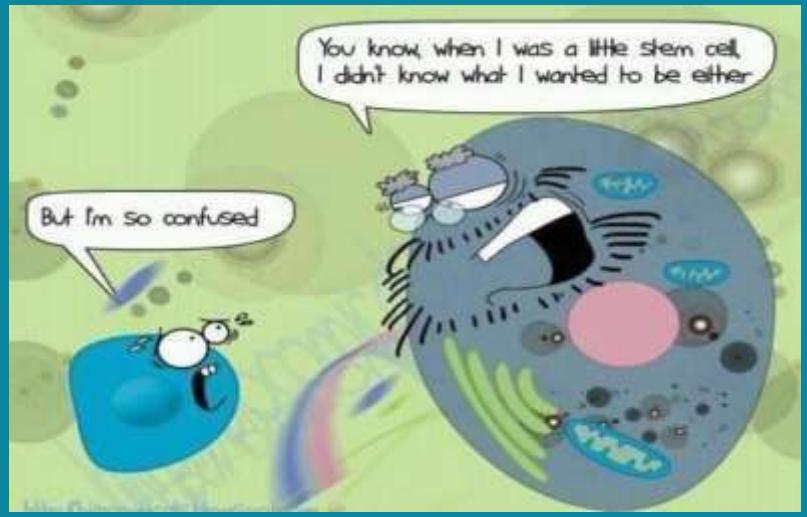
Genetic abnormalities





Aging

+ diminished ability of cells to respond to stress eventually.



SEQUENCE OF EVENTS IN CELL INJURY AND CELL DEATH..

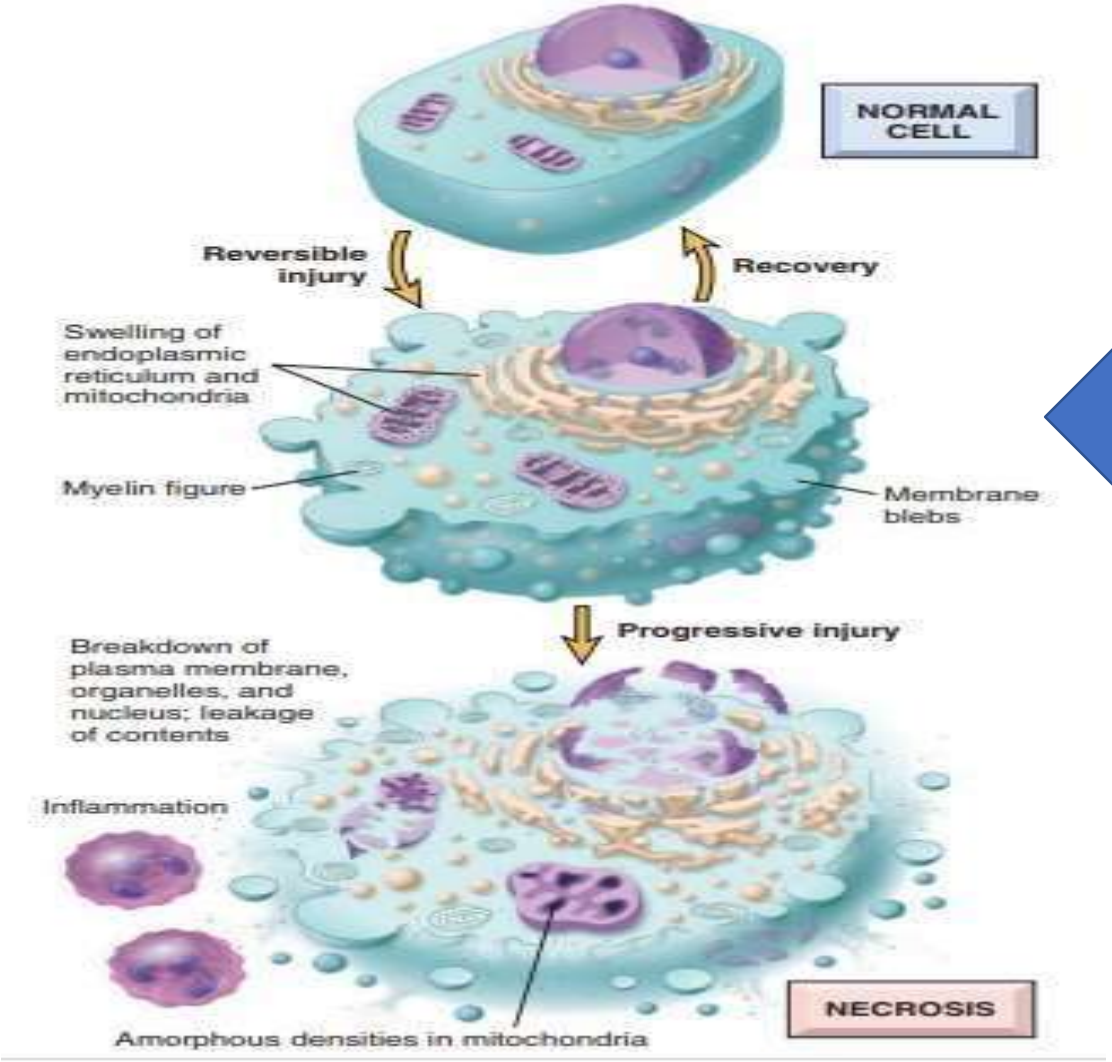
Cellular responses:
Reversible & Irreversible cell injury

Cell injury :
If the cell's adaptive capability is exceeded or if adaptive response is not possible, cell injury develops.

- Two types

1. **Reversible cell injury (Degeneration):** stress is mild to moderate ; injured cell may recover.

2. **Irreversible cell injury (Necrosis) :** Persistent & severe form of cell injury leads to cell death.

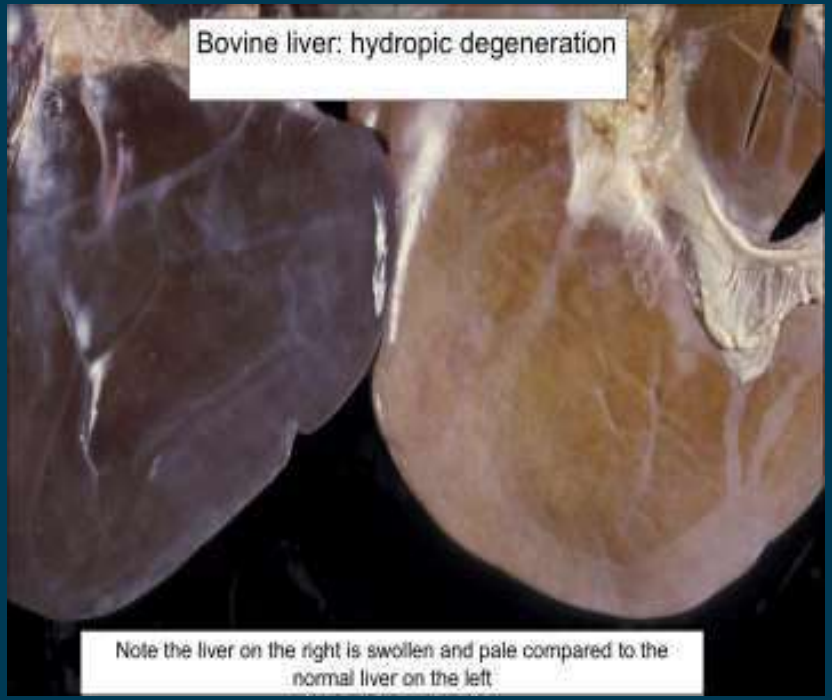


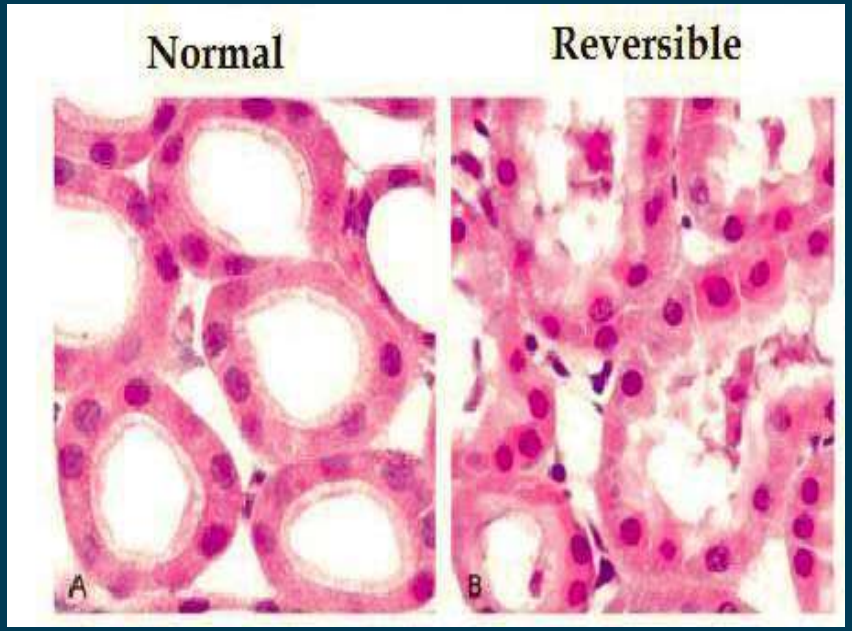
Reversible injury

Two main morphological abnormalities in reversible cell injury:

1. Cellular swelling

- Results from failure of the sodium potassium pump due to ATP depletion
- It is reversible
- Microscopy: small clear vacuoles within the cytoplasm (hydropic change or vacuolar degeneration)
- The organelles within the cells are also swollen

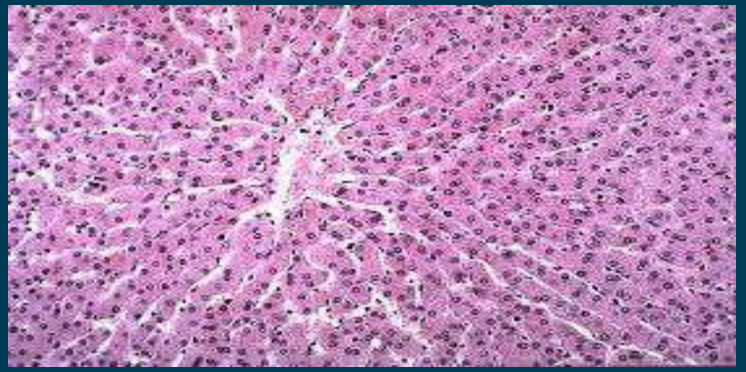

Bovine liver: hydropic degeneration
Note the liver on the right is swollen and pale compared to the normal liver on the left

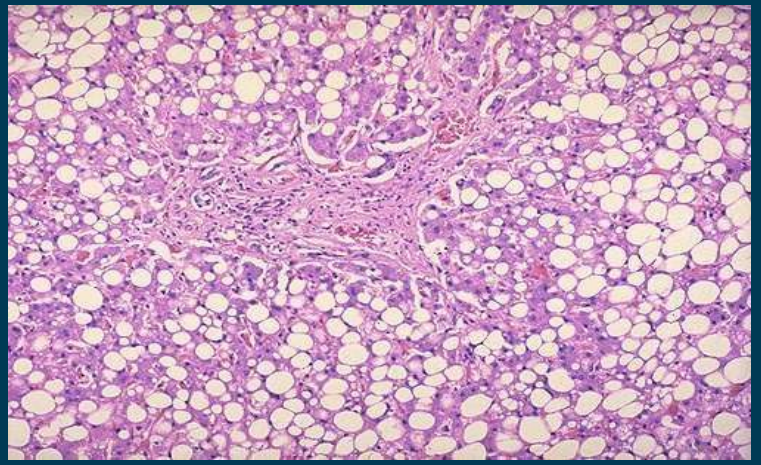

Normal
Reversible
A
B

2. Fatty change

- Occurs mainly in hypoxic, toxic and metabolic injuries.
- Microscopy: lipid (triglyceride) vacuoles in the cytoplasm
- Seen mainly in organs that involved in fat metabolism like hepatocytes (LIVER) and myocardial cells (HEART)
- It is reversible.

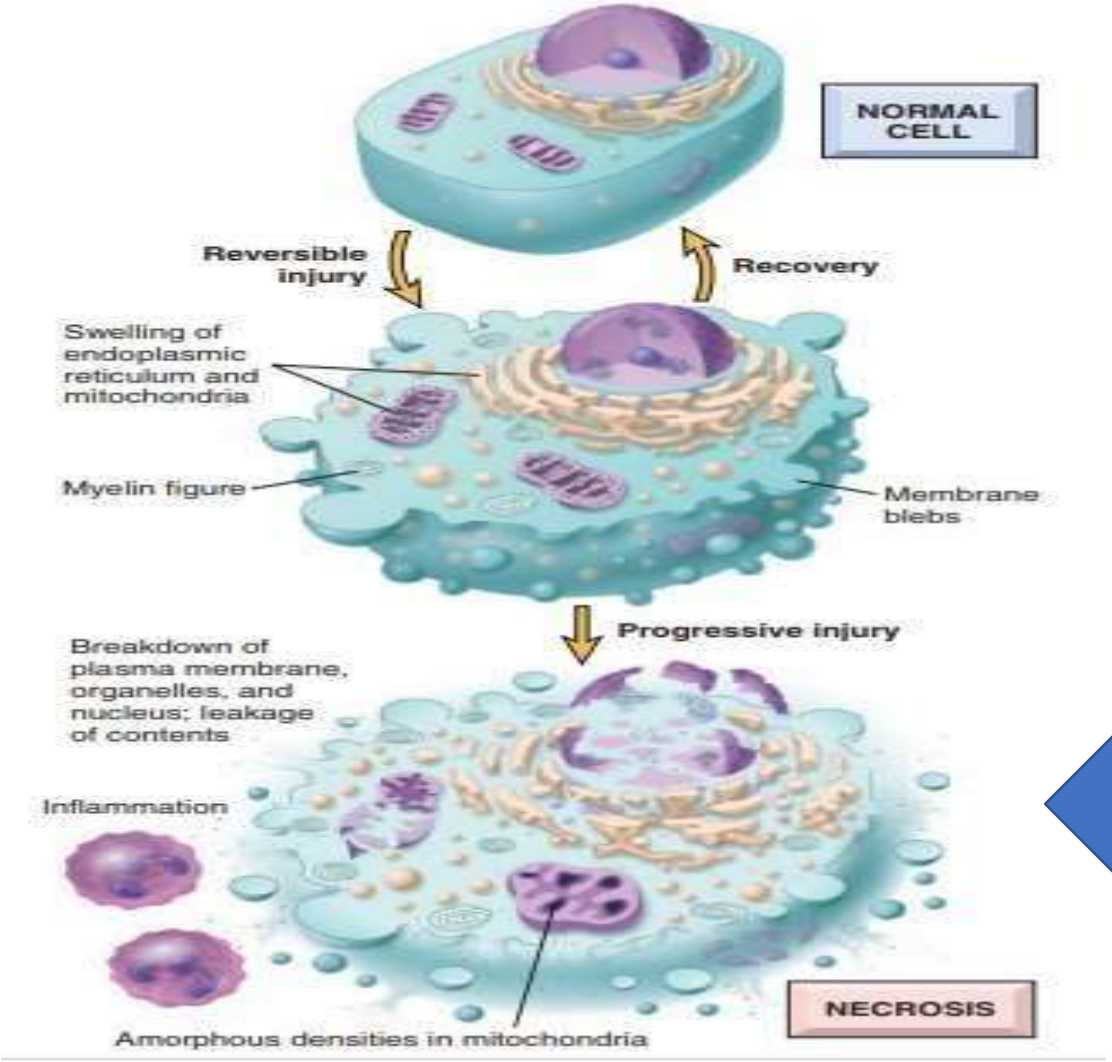

Healthy
Fatty
Cirrhosis





ULTRA-STRUCTURE

- Plasma membrane alteration; blebbing and blunting.
- Mitochondrial swelling and amorphous densities.
- Dilation of ER and detachment of ribosomes.
- Clumping of nuclear chromatin.
- Cytoplasmic Myelin figures.



Irreversible injury

IRREVERSIBLE Cell injury

+ if the stress is severe, persistent, or rapid in onset.

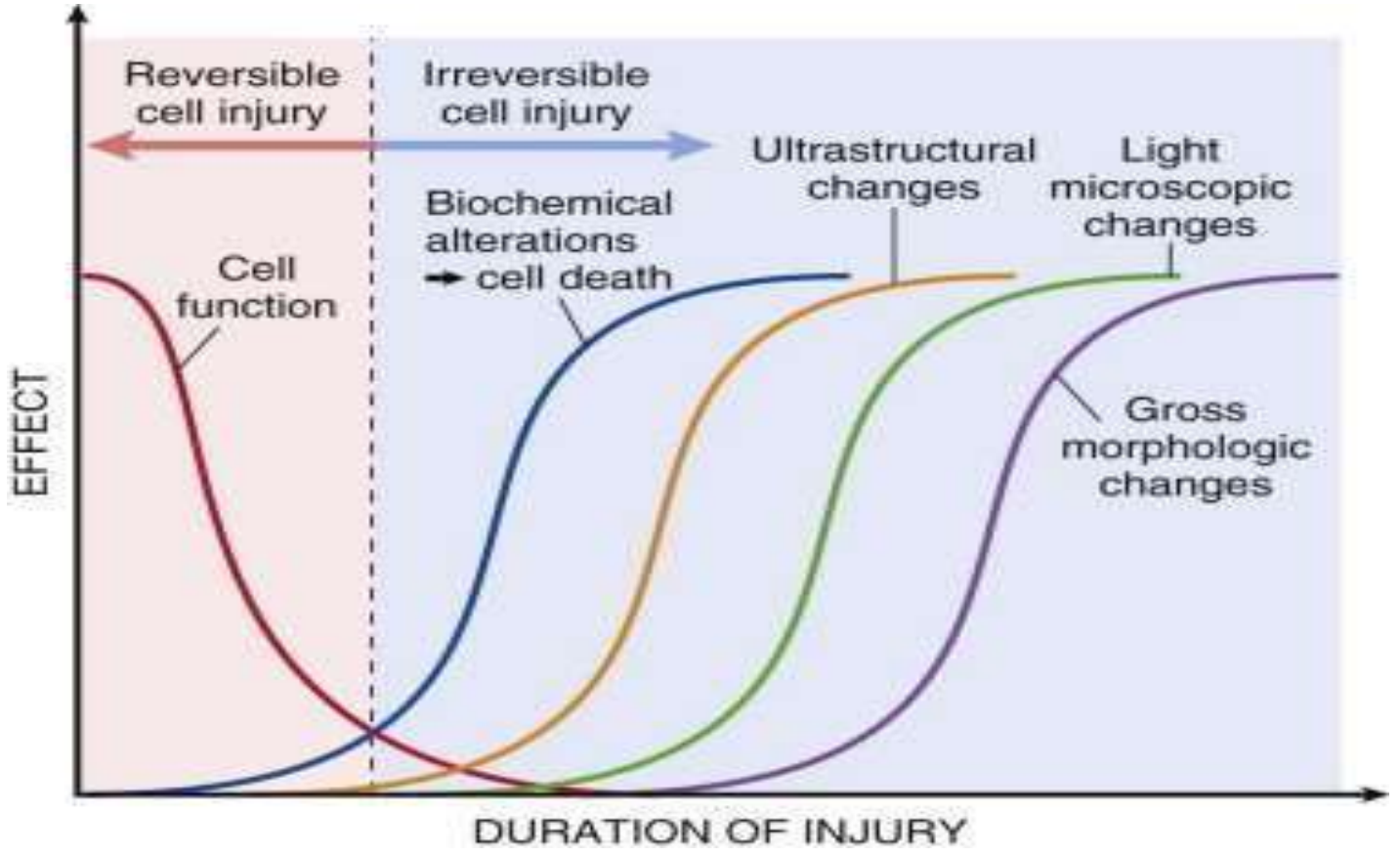
+ injured cells pass a nebulous "point of no return" and undergo cell death.

Irreversible injury:

Although there are no definitive morphologic or biochemical correlates of irreversibility, it is consistently characterized by three phenomena:

- **The *inability to restore mitochondrial function* even after resolution of the original injury**
- **The *loss of structure and functions of the plasma membrane and intracellular membranes***
- **The l*oss of DNA and chromatin structural integrity*.**

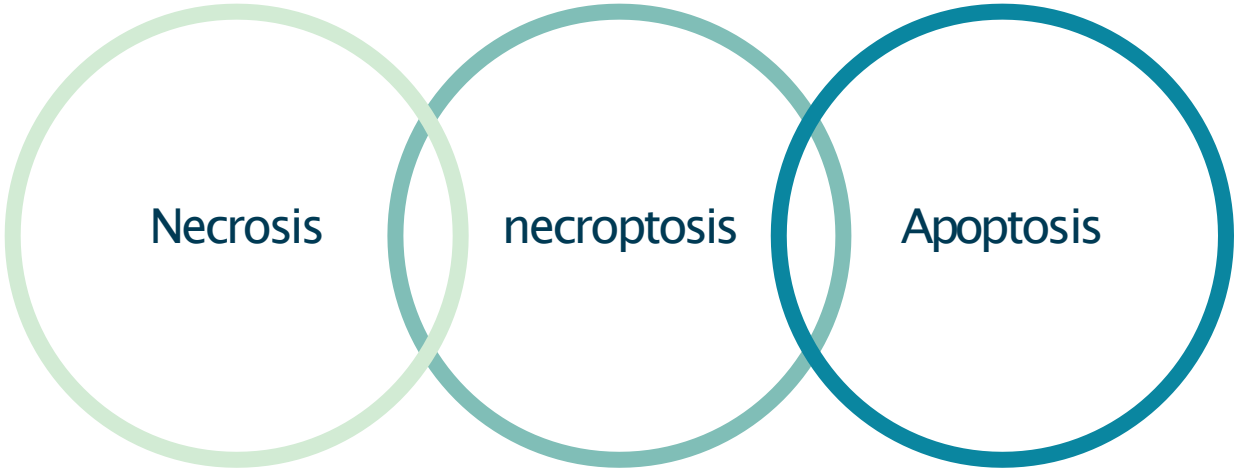
Cellular function may be lost long before cell death occurs, and that the morphologic changes of cell injury (or death) lag far behind loss of function and viability.


Reversible cell injury
Irreversible cell injury
Ultrastructural changes
Light microscopic changes
Biochemical alterations → cell death
Cell function
Gross morphologic changes
EFFECT
DURATION OF INJURY

Myocardial Infarction

- **1-2 minutes: non-contractile myocardial cells.**
- **Death: 20-30 minutes.**
- **Morphology EM: 2-3 hours**
- **Morphology LM: 6-12 hours**
- **Morphology Gross: 12-24 hours**

When cells are injured they die by different mechanisms, depending on the nature and severity of the insult.



THANKS!

Any questions?