Cell Injury and Necrosis -1

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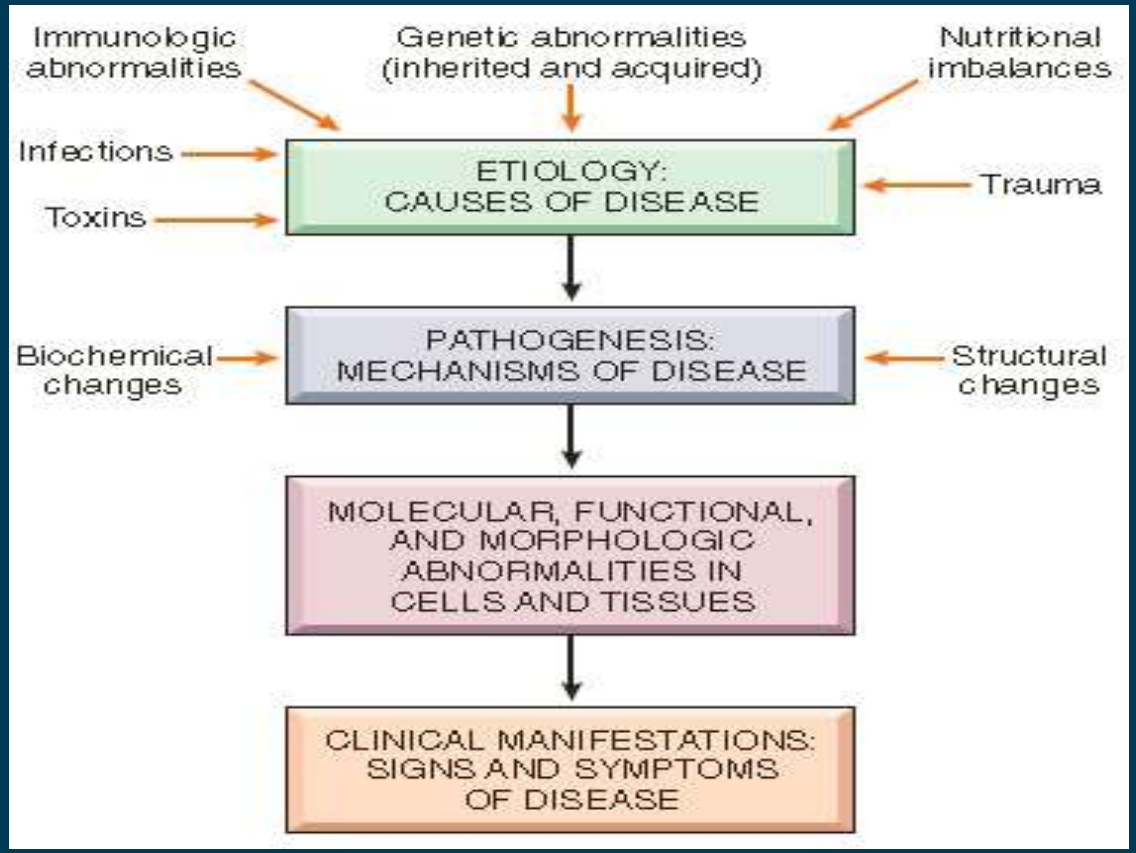
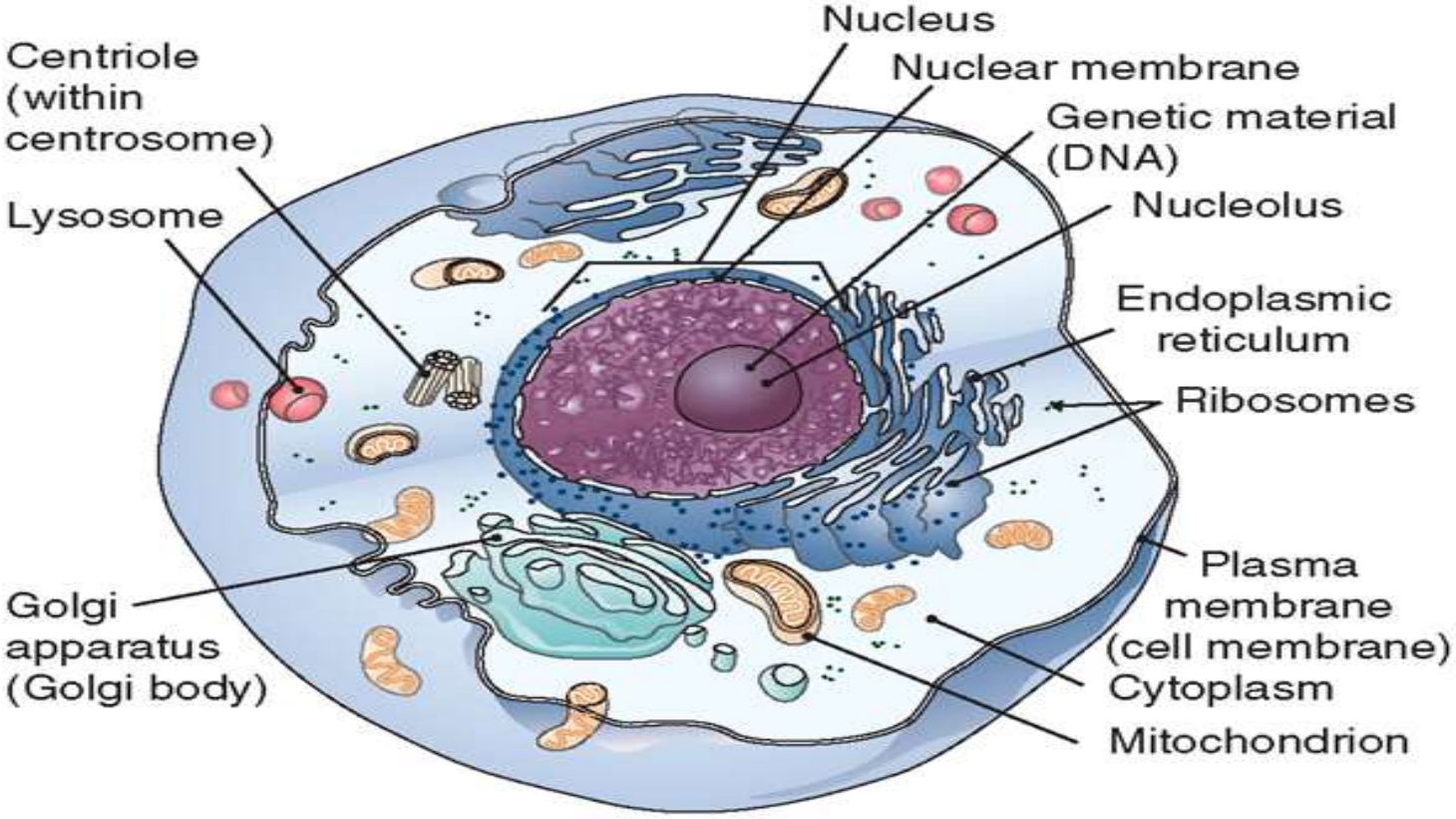
The evolution of disease

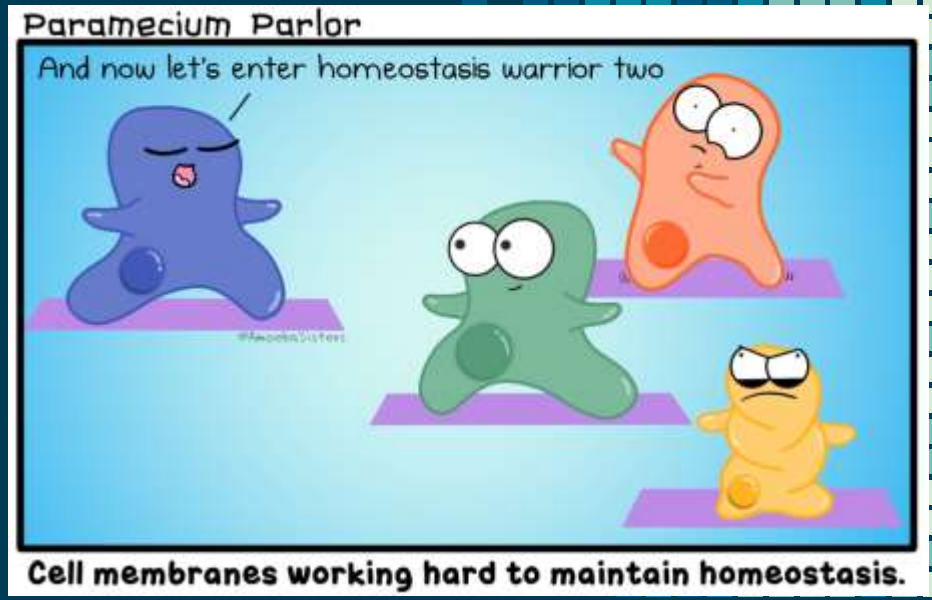


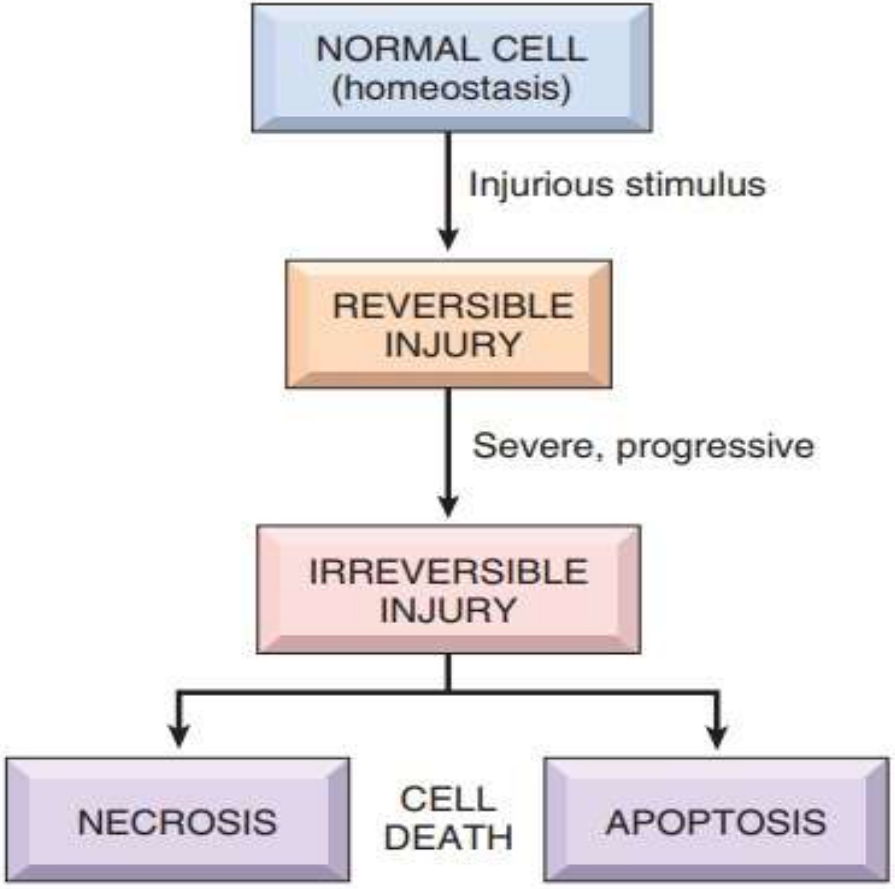
Normal cell


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

Homeostasis..

+ a state of 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

- Oxygen Deprivation (Hypoxia Vs ischemia)
- Toxins
- Infectious Agents
- Immunologic Reactions
- Genetic Abnormalities
- Nutritional Imbalances
- Physical Agents
- Aging

Hypoxia and ischemia..

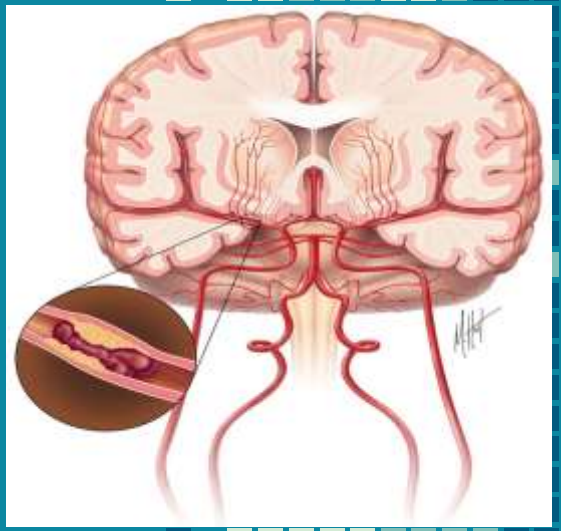
+ most common causes of injury.

+Hypoxia: Oxygen deficiency:

Ischemia, anemia, lung disease, CO

+Ischemia: reduce blood supply:

arterial obstruction



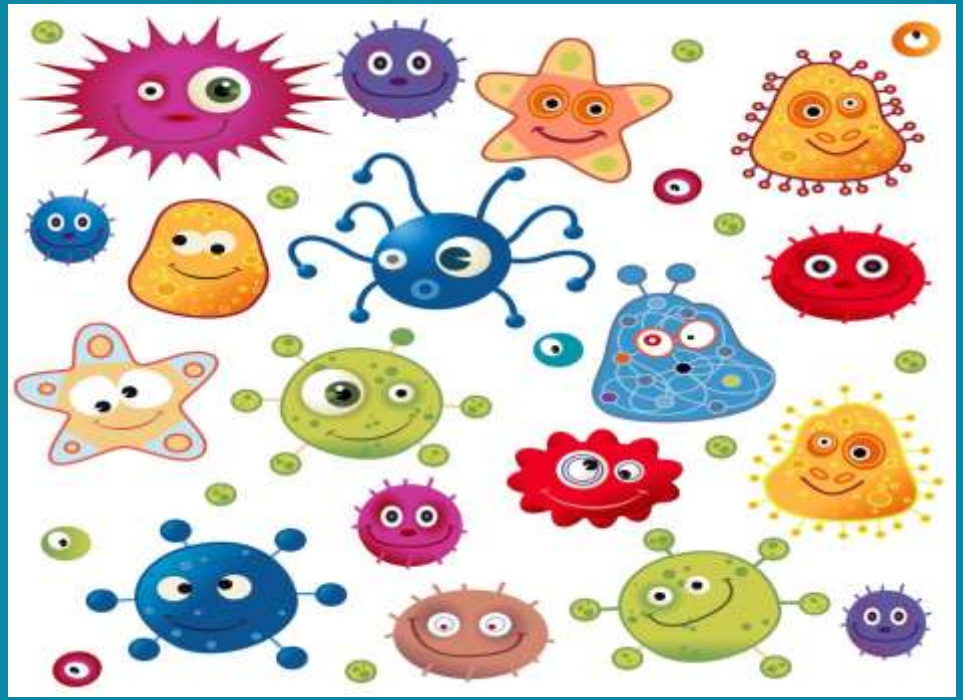
Toxins

+*air pollutant, CO, asbestos, cigarette smoke, ethanol & insecticides.*

+ *drugs: susceptible patients, excessively and inappropriately.*

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

“ *Infectious Agents*



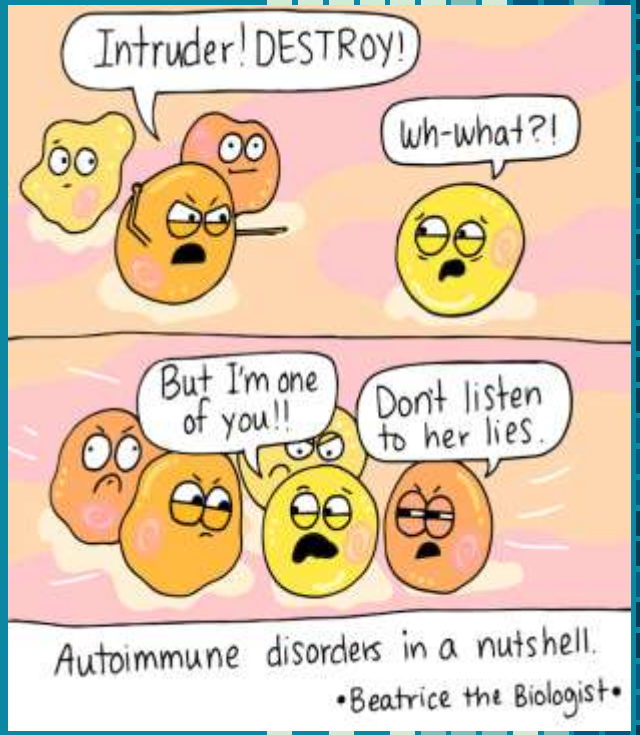
Immunologic Reactions

+ Autoimmune reactions

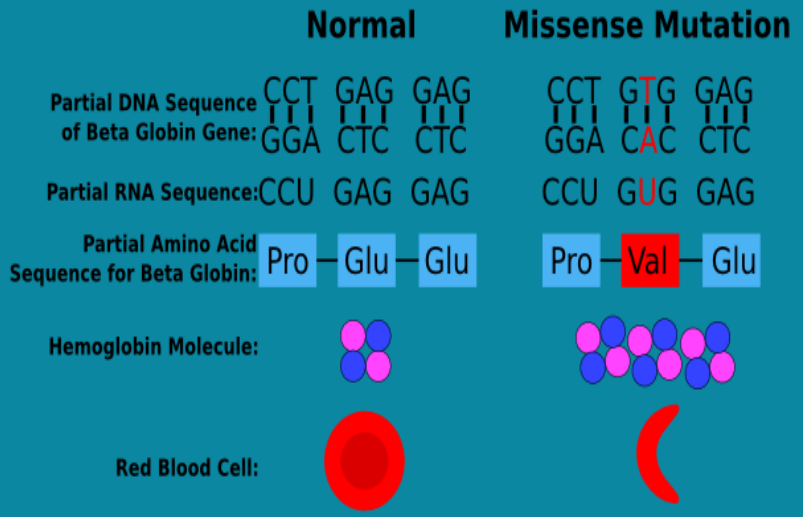
+ Allergic reactions: innocuous environmental substances.

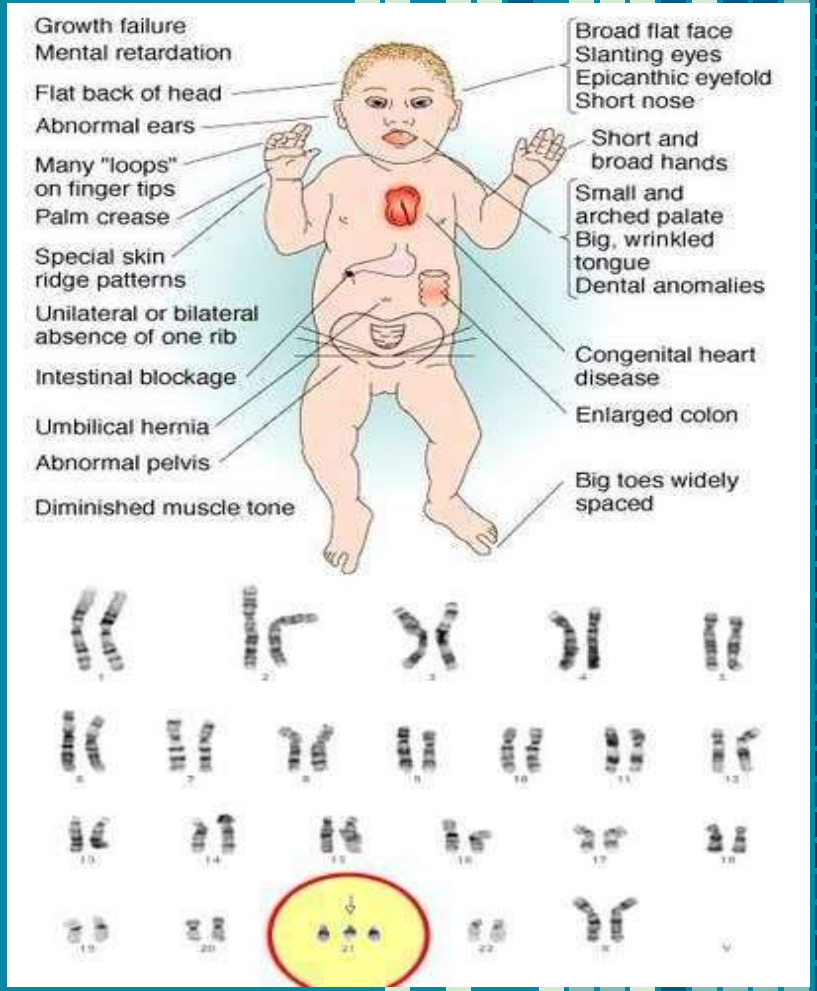
+excessive response to microbes

.. Inflammatory reaction that damage cells and tissue



“ Genetic abnormalities





Nutritional Imbalances

+ Protein-calorie insufficiency: countries in Poverty

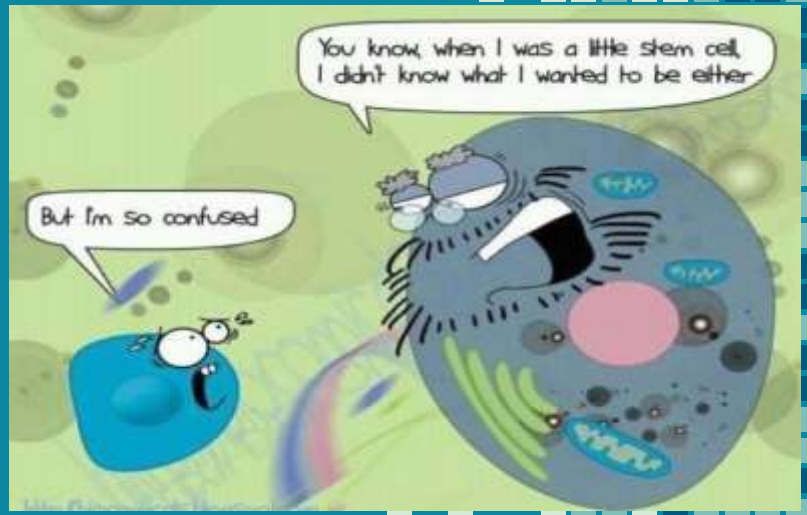
+ Specific vitamin deficiencies

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

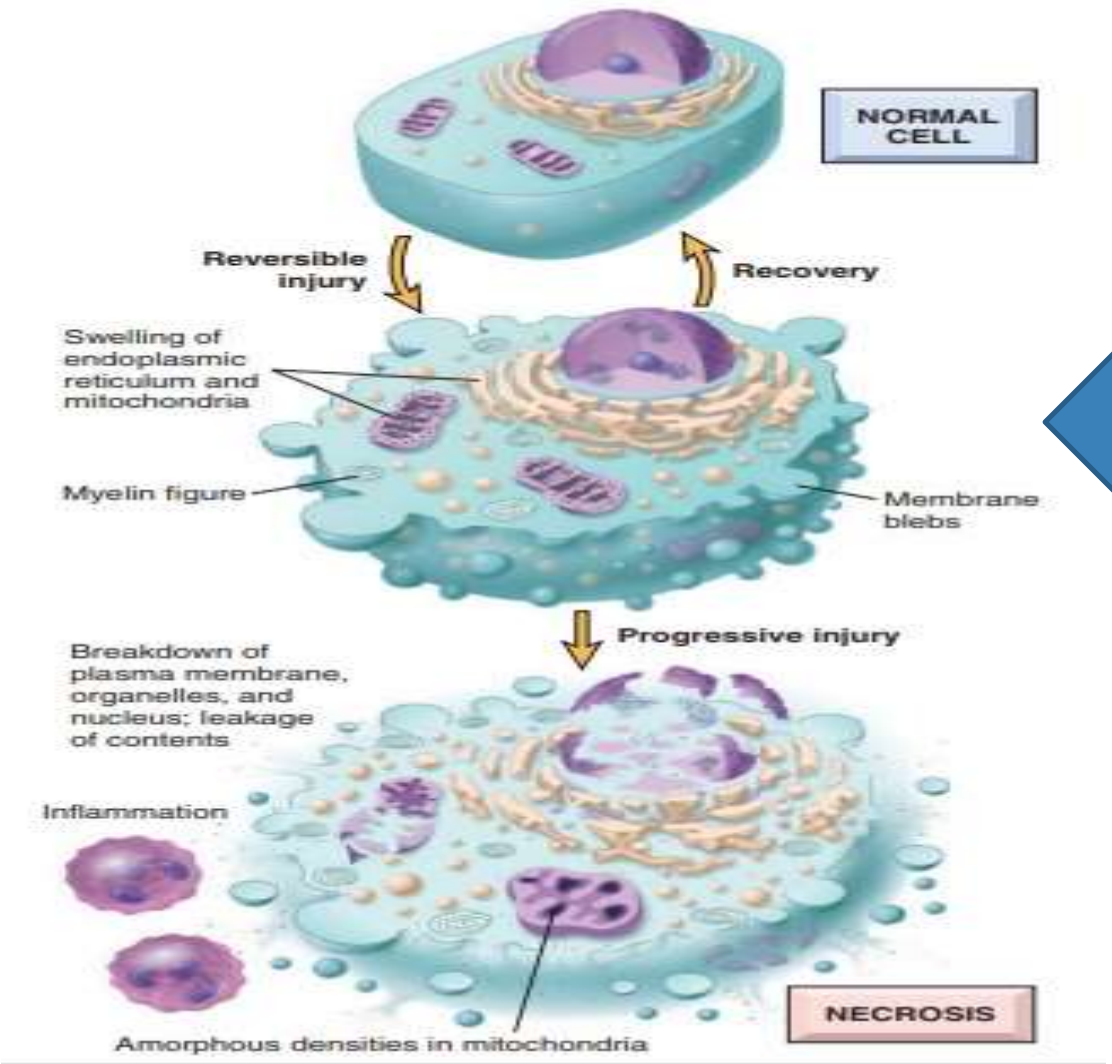
“ Physical Agents

Aging

+ diminished ability of cells to respond to stress eventually, the death of cells and of the organism.



SEQUENCE OF EVENTS IN CELL INJURY AND CELL DEATH..



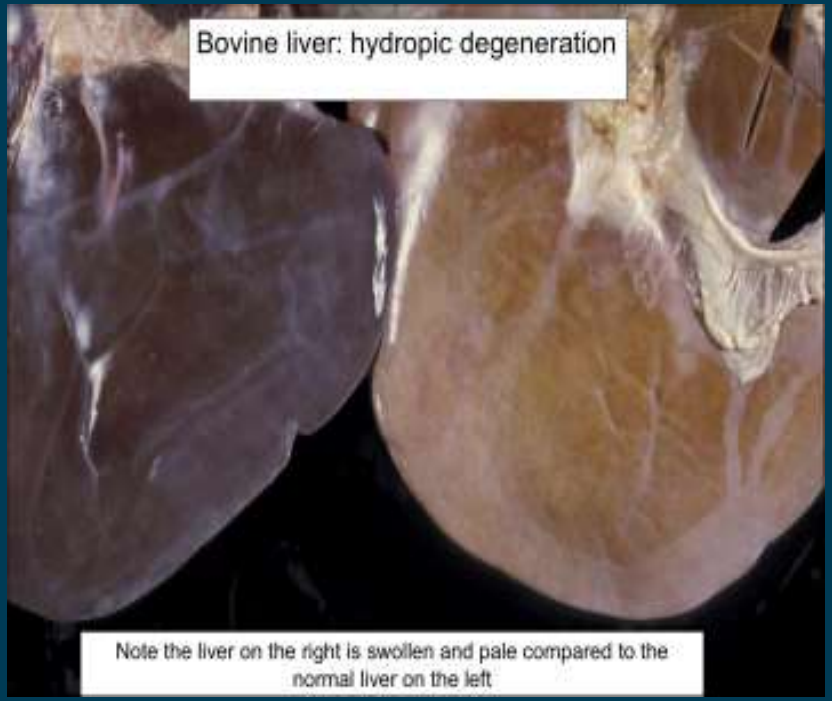
Reversible injury

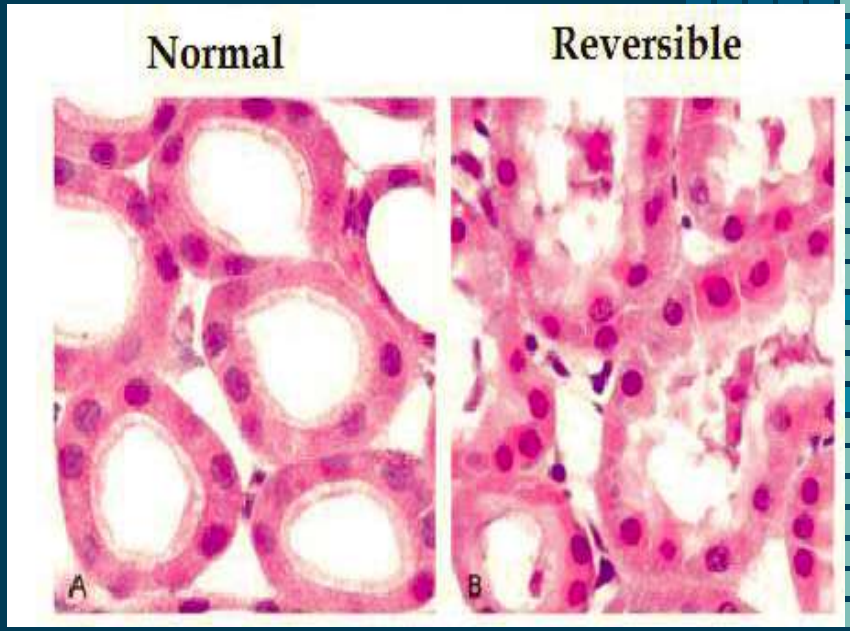
REVERSIBLE Cell injury

+ the stage of cell injury at which the deranged function and morphology of the injured cells can return to normal if the damaging stimulus is removed

Two main morphological abnormalities in reversible cell injury; 1. Cellular Swelling

- Results from failure of the sodium potassium pump (energy-dependent ion pumps) due to ATP depletion.
- It is reversible
- **Gross** > microscope
- Gross: pallor, ↑turgor, ↑weight.
- Microscopy: small clear vacuoles within the cytoplasm (hydropic change or vacuolar degeneration)
- The organelles within the cells are also swollen

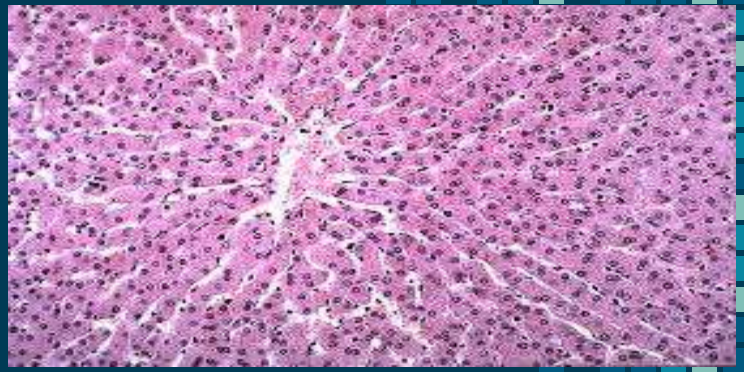

Bovine liver: hydropic degeneration
Note the liver on the right is swollen and pale compared to the normal liver on the left

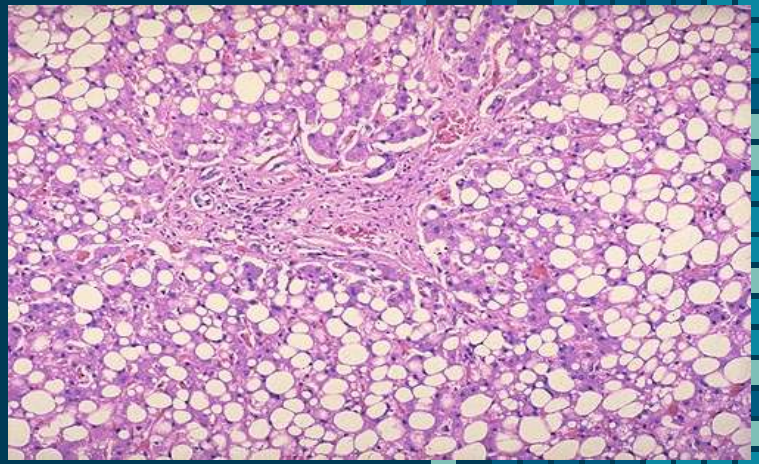

Normal
Reversible
A
B

Two main morphological abnormalities in reversible cell injury; 2. Fatty change

- Occurs mainly in hypoxic injury and in toxic and metabolic injury.
- 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.

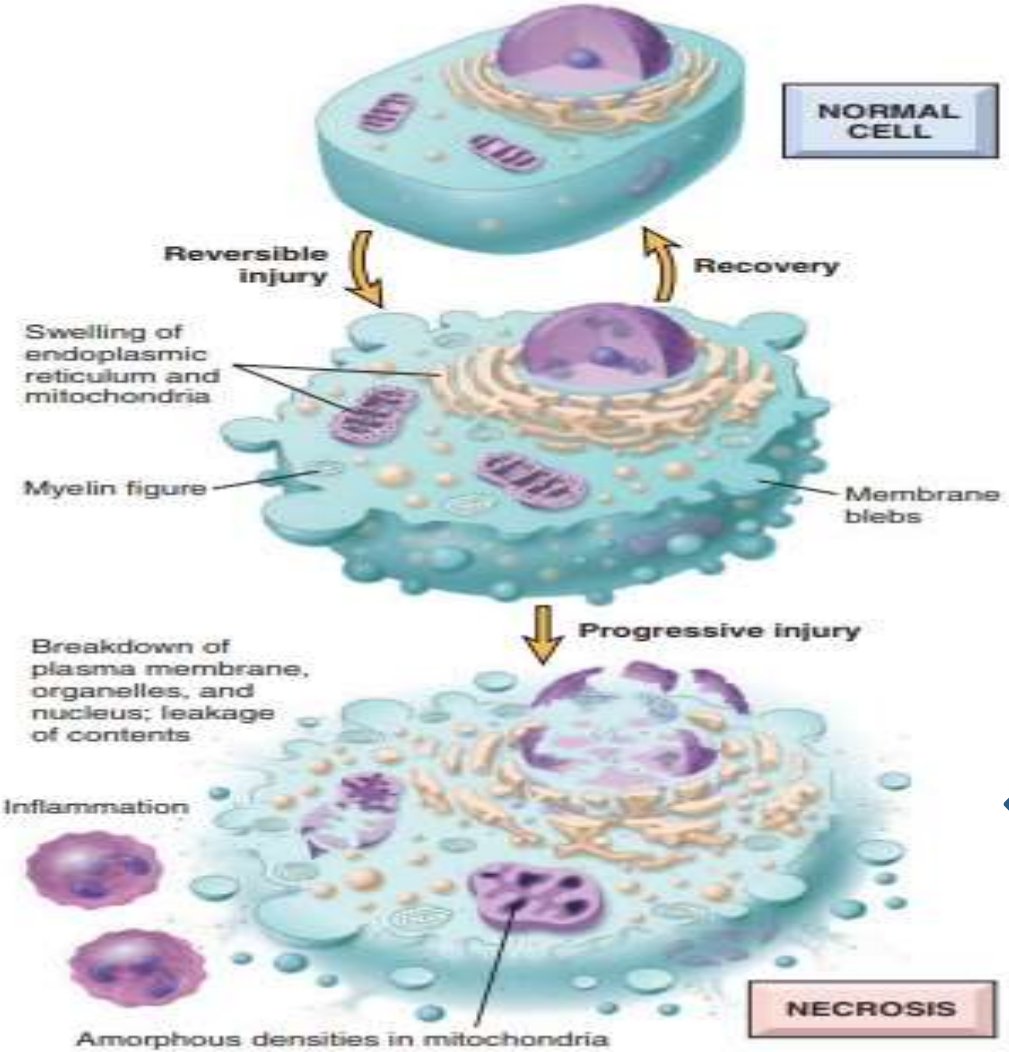

Healthy
Fatty
Cirrhosis





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.

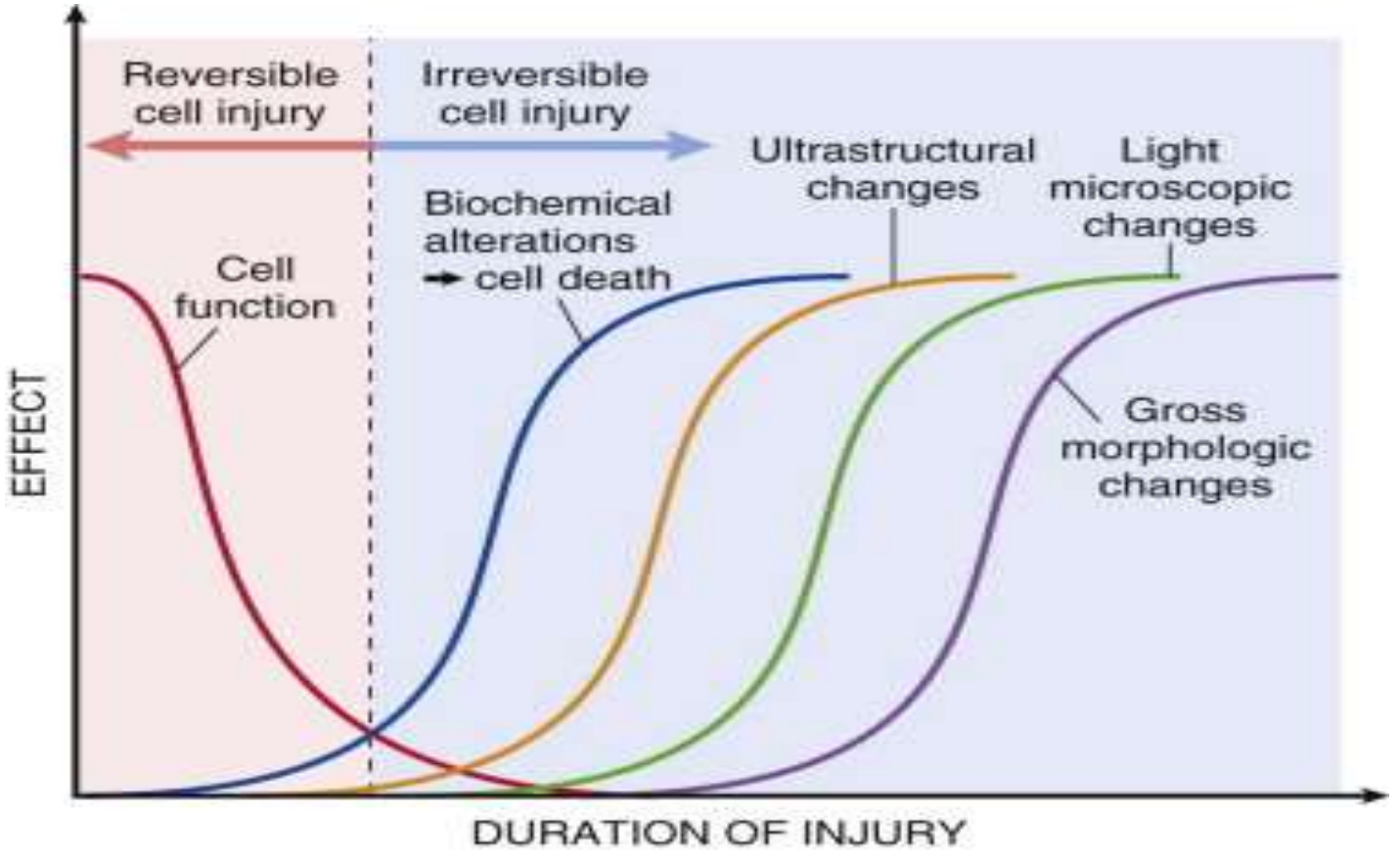
+ injured cells pass a nebulous “point of no return” and undergo cell death.

Irreversible injury: three phenomena

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***
- **and the *loss of DNA and chromatin structural integrity*.**

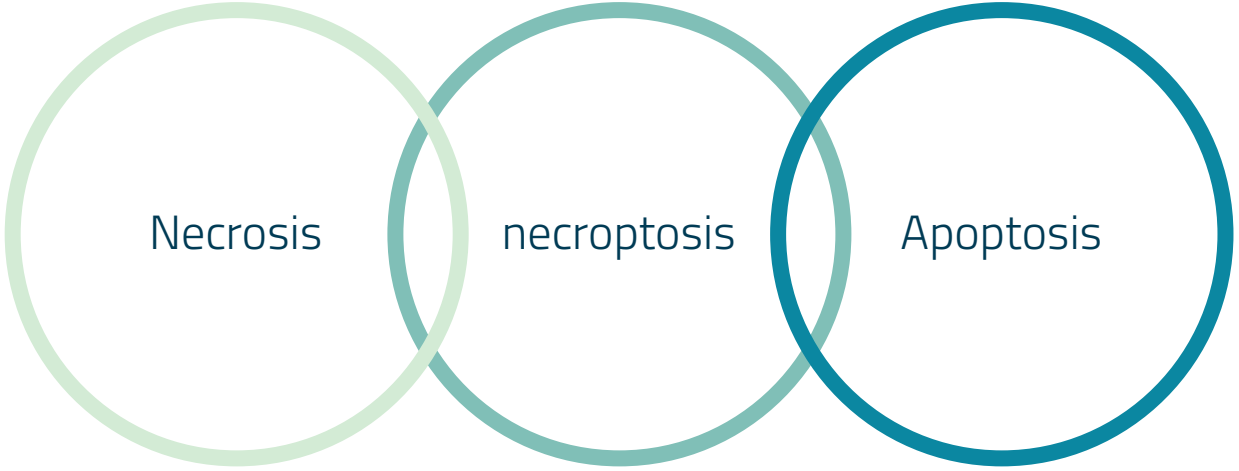
> Cellular function may be lost long before cell death occurs, and that the morphologic changes of cell injury (or death) lag far behind loss of function and viability


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?