Cell Injury and Necrosis -1

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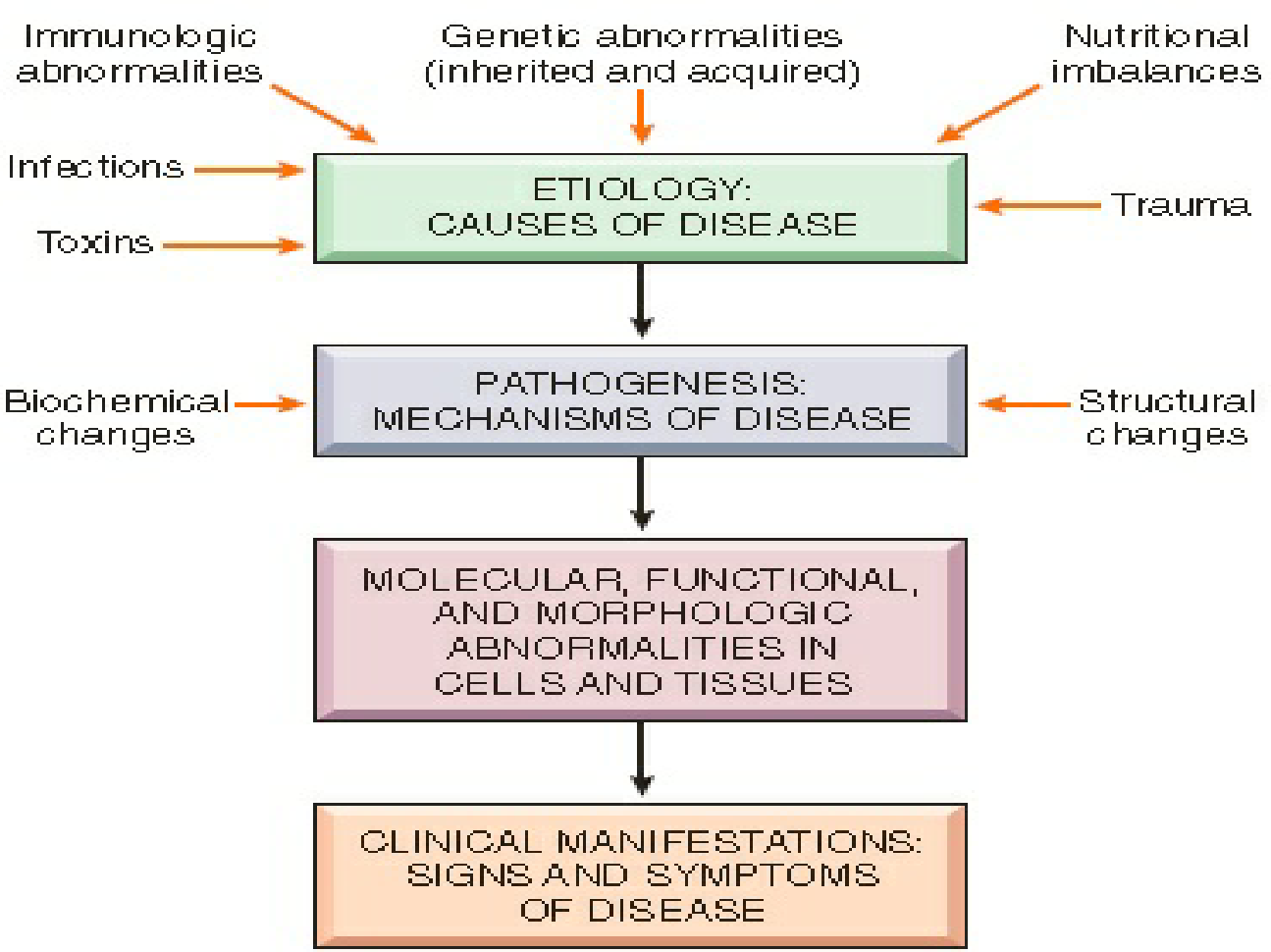
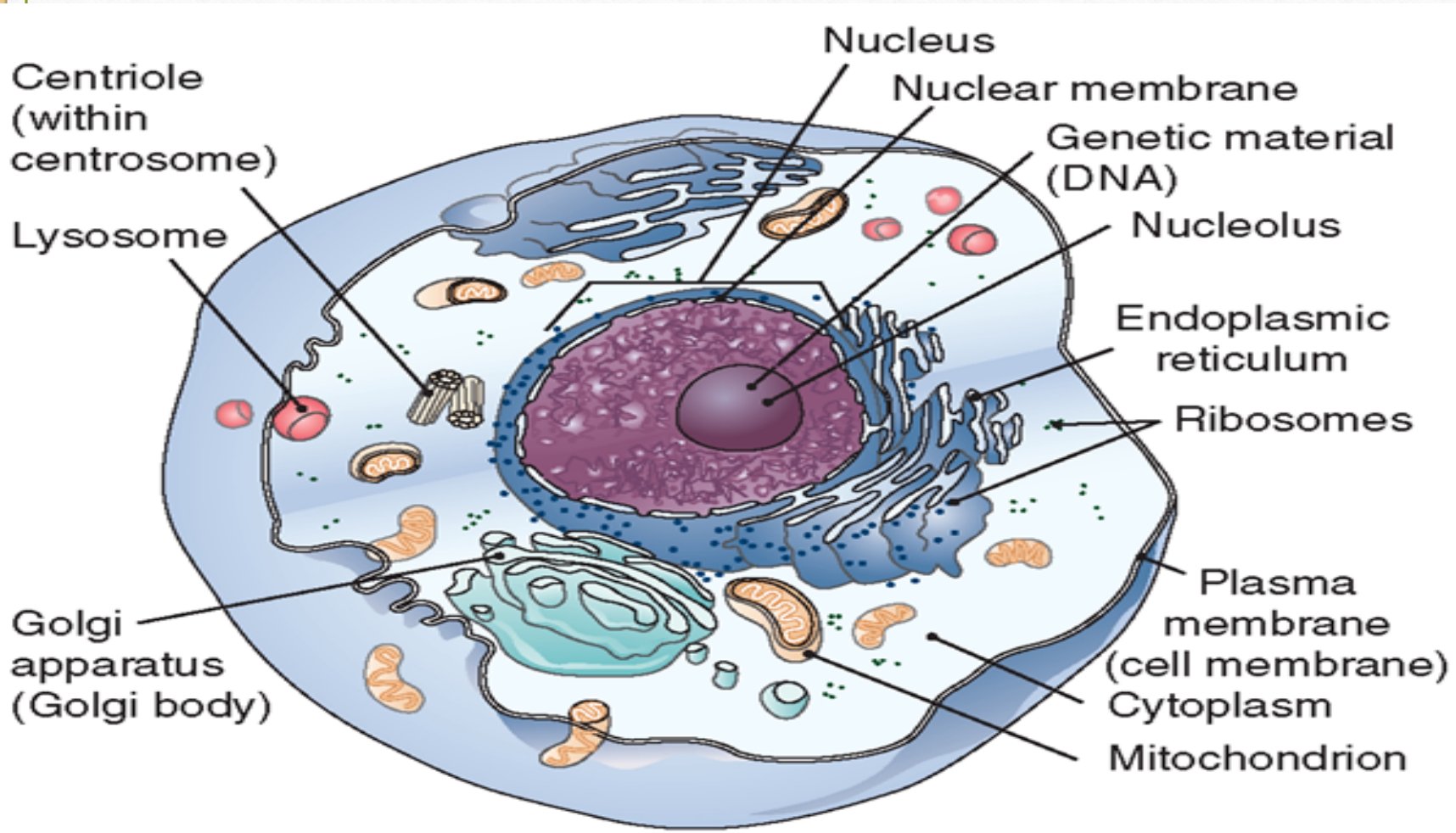

Immunologic abnormalities
Genetic abnormalities (inherited and acquired)
Nutritional imbalances
Infections
Toxins
ETIOLOGY: CAUSES OF DISEASE
Trauma
Biochemical changes
PATHOGENESIS: MECHANISMS OF DISEASE
Structural changes
MOLECULAR, FUNCTIONAL, AND MORPHOLOGIC ABNORMALITIES IN CELLS AND TISSUES
CLINICAL MANIFESTATIONS: SIGNS AND SYMPTOMS OF DISEASE

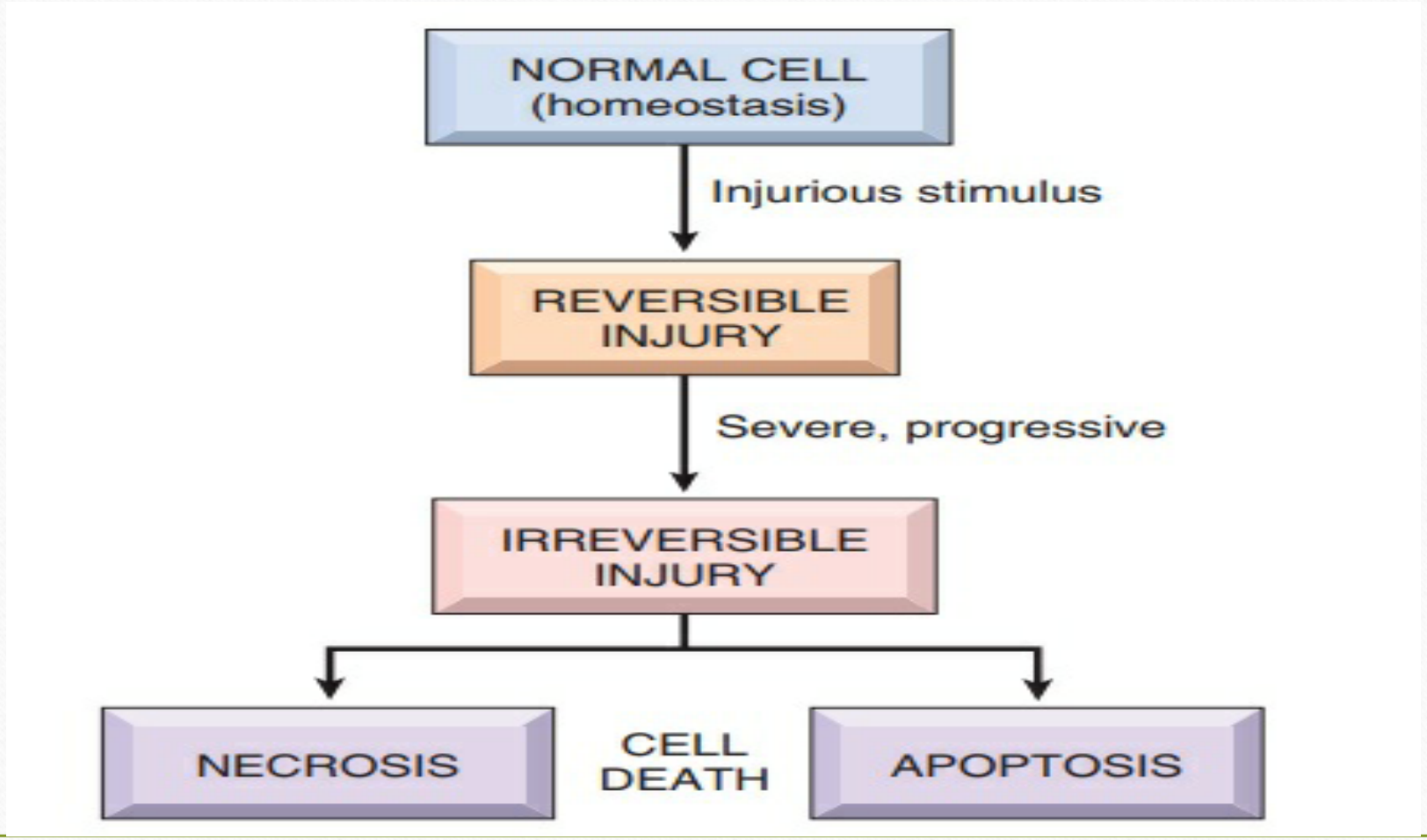
Normal cell


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

Homeostasis..

Normal cell is nevertheless able to handle physiologic demands, maintaining a healthy steady state called homeostasis.

Stages of the cellular response to stress and injurious stimuli.



Adaptations

Adaptations are reversible functional and structural responses to changes in physiologic states (e.g., pregnancy) and some pathologic stimuli, during which new but altered steady states are achieved, allowing the cell to survive and continue to function.

The adaptive response may consist of:

- an increase in the size (hypertrophy)
- functional activity of cells, an increase in cell number (hyperplasia)
  .
- a decrease in the size and metabolic activity of cells (atrophy).
- a change in the phenotype of cells (metaplasia).

If the stress is eliminated, the cell can return to its original state without having suffered any harmful consequences.

Causes of cell injury

- Hypoxia Vs ischemia
- Chemical Agents and Drugs
- Infectious Agents
- Immunologic Reactions
- Genetic Abnormalities
- Nutritional Imbalances
- Physical Agents

Hypoxia and ischemia..

+ most common causes of injury.

+Hypoxia: Oxygen deficiency:

Ischemia, anemia, lung disease, CO

+Ischemia: reduce blood supply: arterial obstruction

Chemical Agents and Drugs :

-The list of chemicals that may produce cell injury defies compilation.

-Simple chemicals such as glucose or salt in hypertonic concentrations may cause cell injury directly or by deranging electrolyte and fluid balance in cells. Even oxygen at high concentrations is toxic.

-Trace amounts of poisons, such as arsenic, cyanide, or mercury, may damage sufficient numbers of cells within minutes or hours to cause death.

- Other potentially injurious substances are our daily companions: environmental pollutants, insecticides, and herbicides; industrial and occupational hazards, such as carbon monoxide and asbestos; recreational drugs such as alcohol; and the ever increasing variety of therapeutic drugs, many of which have toxic side effects.

- ***Infectious Agents.***

- *These agents range from submicroscopic viruses to tapeworms several feet in length. In between are rickettsiae, bacteria, fungi, and higher forms of parasites.*

- ***Immunologic Reactions***
- *-The immune system serves an essential function in defense*
- *against infectious pathogens, but immune reactions may*
- *also cause cell injury.*
- *-Injurious reactions to endogenous self antigens or external agents, such as viruses and environmental substances.*

Nutritional shortages:

- Nutritional imbalances continue to be major causes of cell injury.

Anorexia nervosa

-Obesity.

-In addition to the problems of undernutrition and overnutrition.

Genetic Abnormalities

- *genetic aberrations as extreme as an extra chromosome, as in Down syndrome, or as subtle as a single base pair substitution leading to an amino acid substitution, as in sickle cell anemia.*
- *Genetic defects may cause cell injury because of deficient protein function, such as enzyme defects in inborn errors of metabolism, or accumulation of damaged DNA or misfolded proteins, both of which trigger cell death when they are beyond repair.*

Physical Agents

Physical agents capable of causing cell injury include mechanical trauma, extremes of temperature (burns and deep cold), sudden changes in atmospheric pressure, radiation, and electric shock.

The Progression of Cell Injury and Death

- If the limits of adaptive responses are exceeded or if cells are exposed to damaging insults, deprived of critical nutrients, or compromised by mutations that affect essential cellular functions, a sequence of events follows that is termed cell injury.

-Cell injury is reversible up to a point, but if the injurious stimulus is persistent or severe, the cell suffers irreversible injury and ultimately undergoes cell death.

- Adaptation, reversible injury, and cell death may be stages of progressive impairment following different types of insults.

REVERSIBLE Cell injury

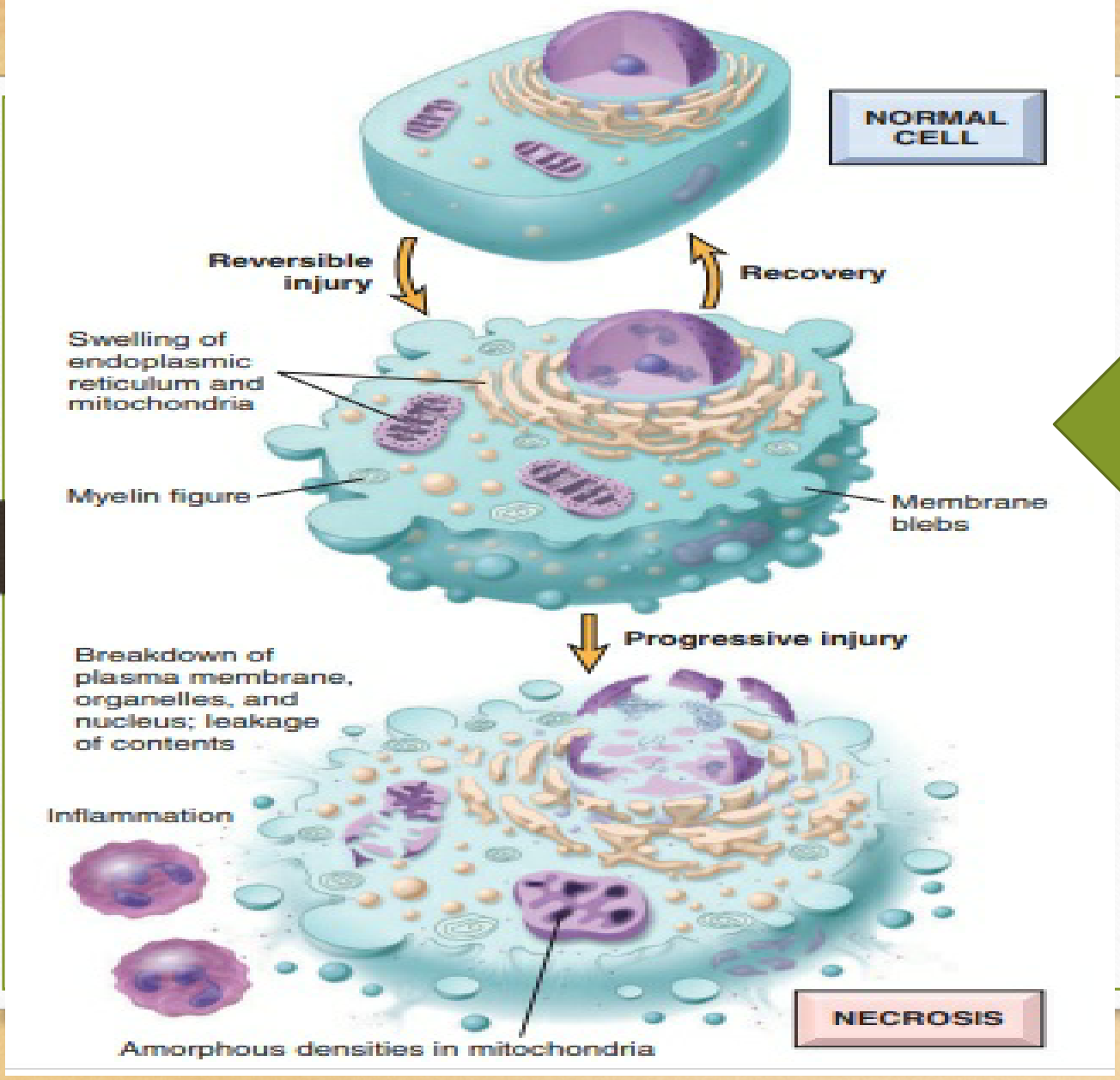
Reversible cell injury is characterized by functional and structural alterations in early stages or mild forms of injury, which are correctable if the damaging stimulus is removed.

Two features are consistently seen in reversibly injured cells.

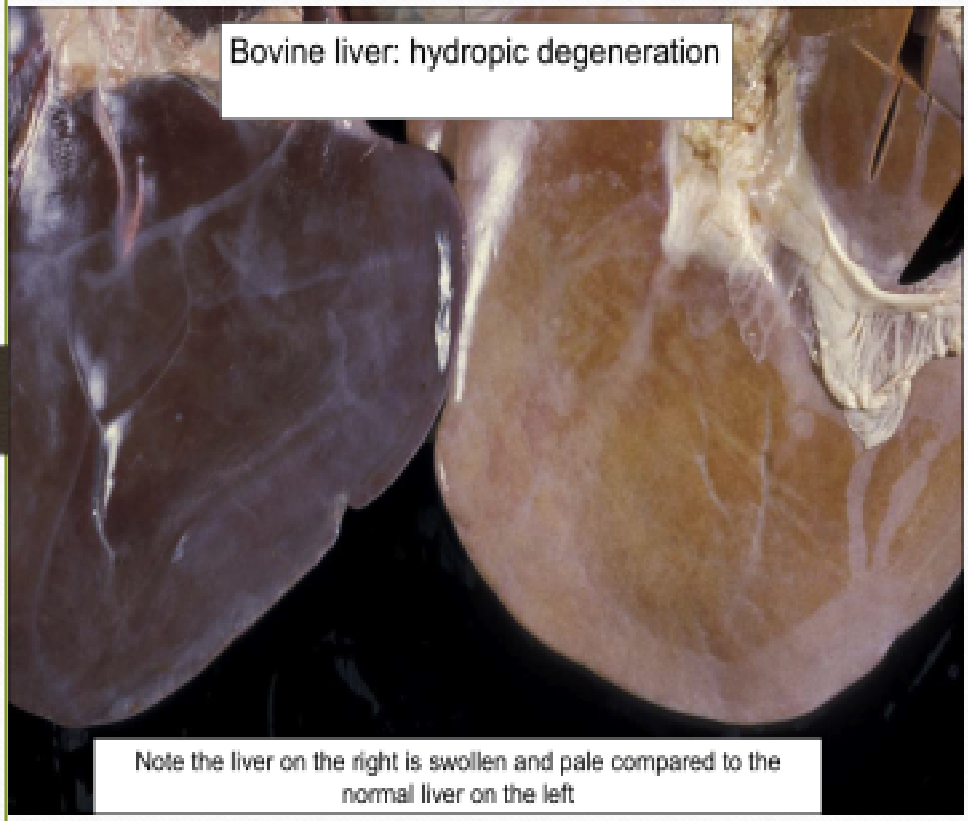
- Early alterations in reversible injury include generalized swelling of the cell
- Fatty change.

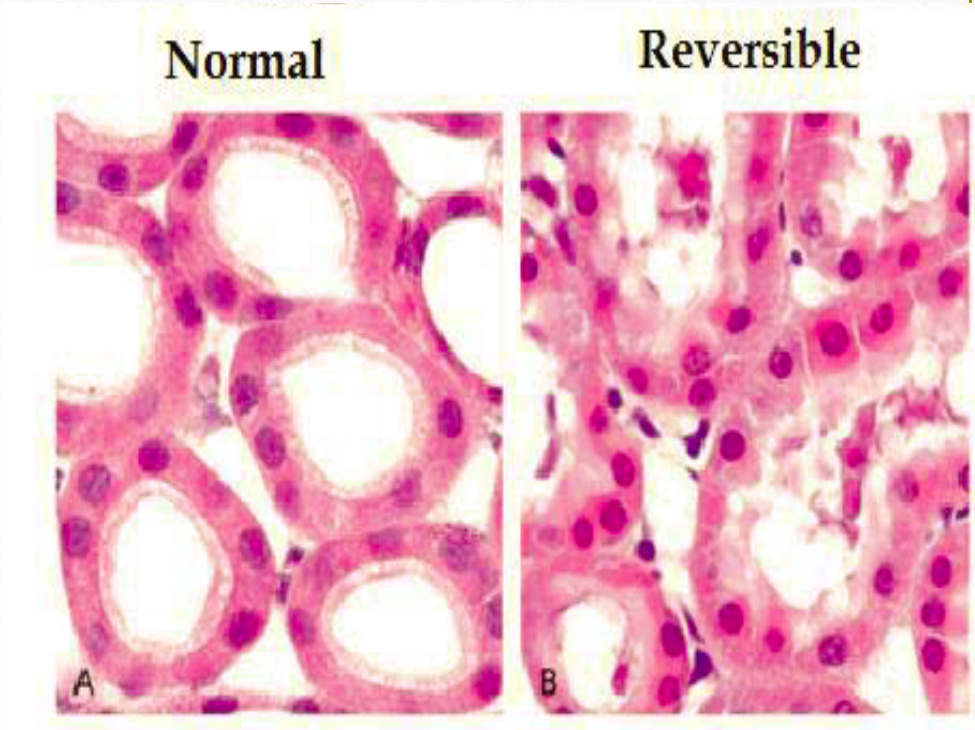
Two main morphological abnormalities in reversible cell injury; 1. Cellular Swelling

- 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.



Reversible injury

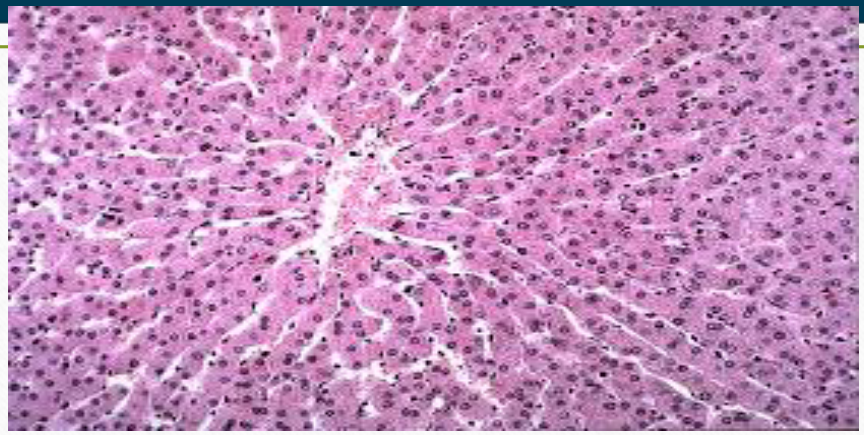

Bovine liver: hydropic degeneration
Note the liver on the right is swollen and pale compared to the normal liver on the left

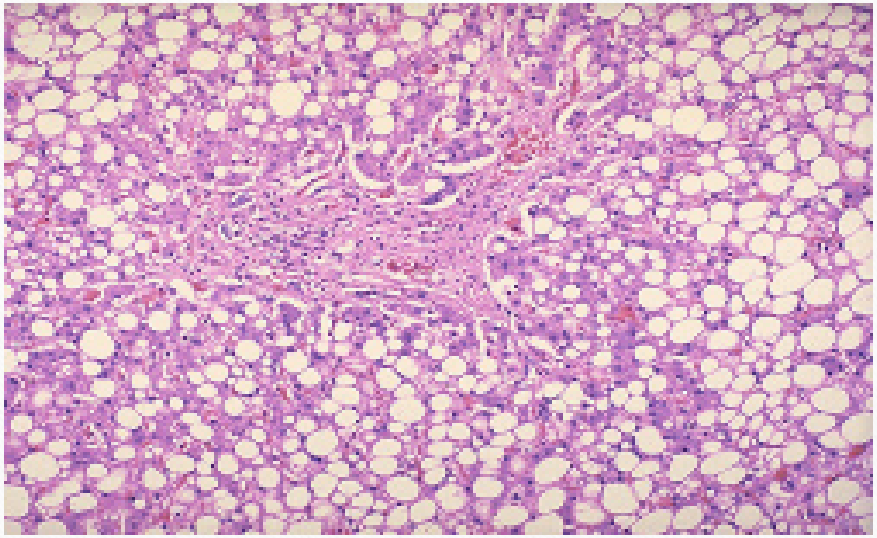

Normal
Reversible
A
B

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 Cell injury

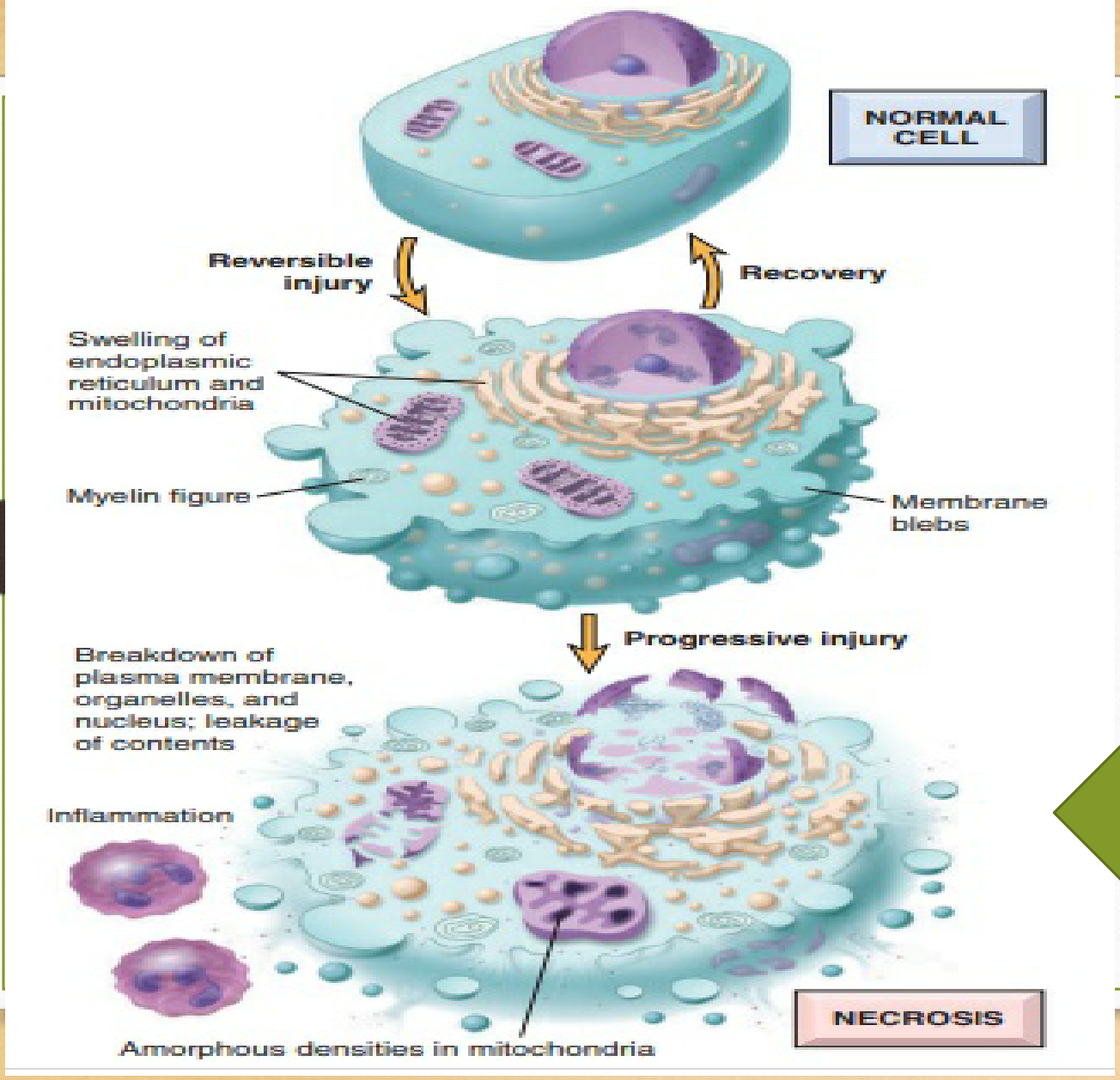
+ if the stress is severe, persistent, or rapid in onset.

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

Irreversible injury: three phenomena

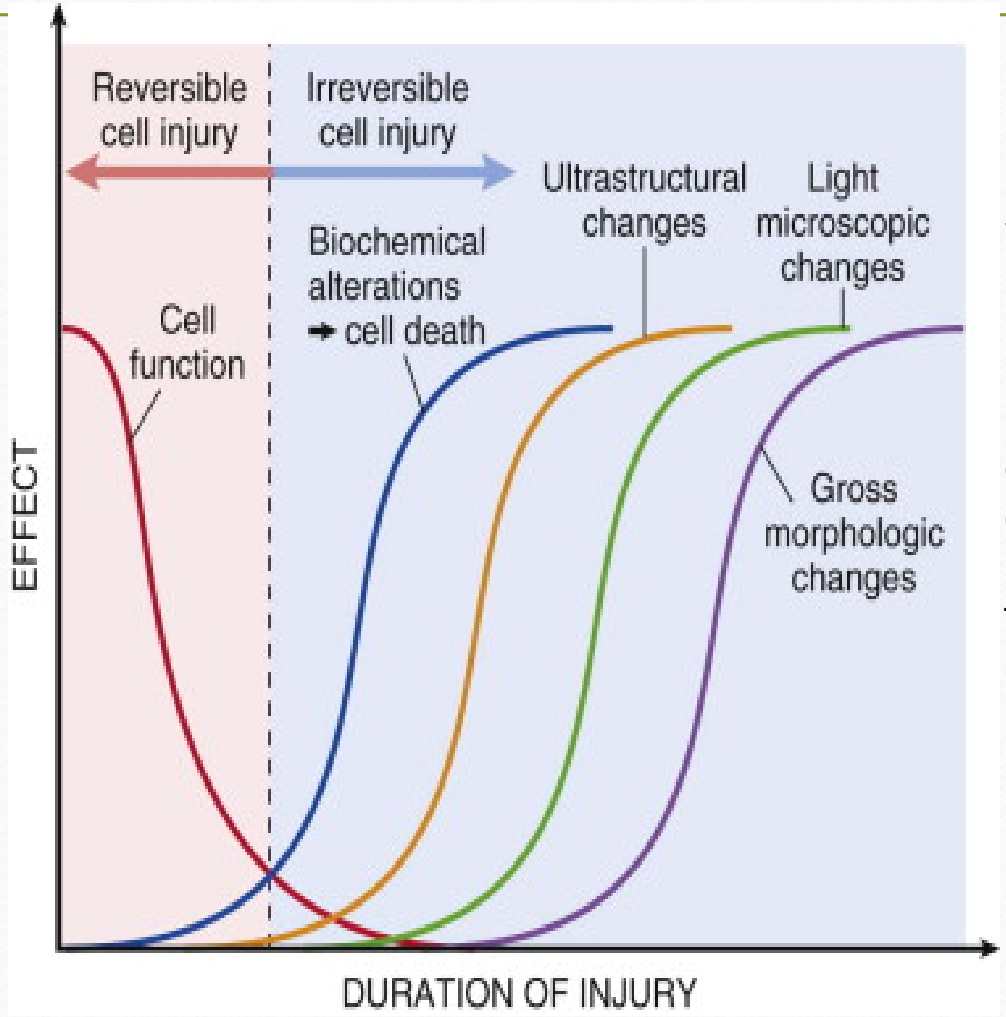
Although there are no definitive morphologic or biochemical correlates of irreversibility, it is consistently characterized by three phenomena:

- **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*.**



Irreversible injury

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



Sequential development of biochemical and morphologic changes in cell injury. Cells may become rapidly nonfunctional after the onset of injury, although they may still be viable, with potentially reversible damage; a longer duration of injury may lead to irreversible damage and cell death. Note that irreversible biochemical alterations may cause cell death, and typically this precedes ultrastructural, light microscopic, and grossly visible morphologic changes.

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