Cell Injury

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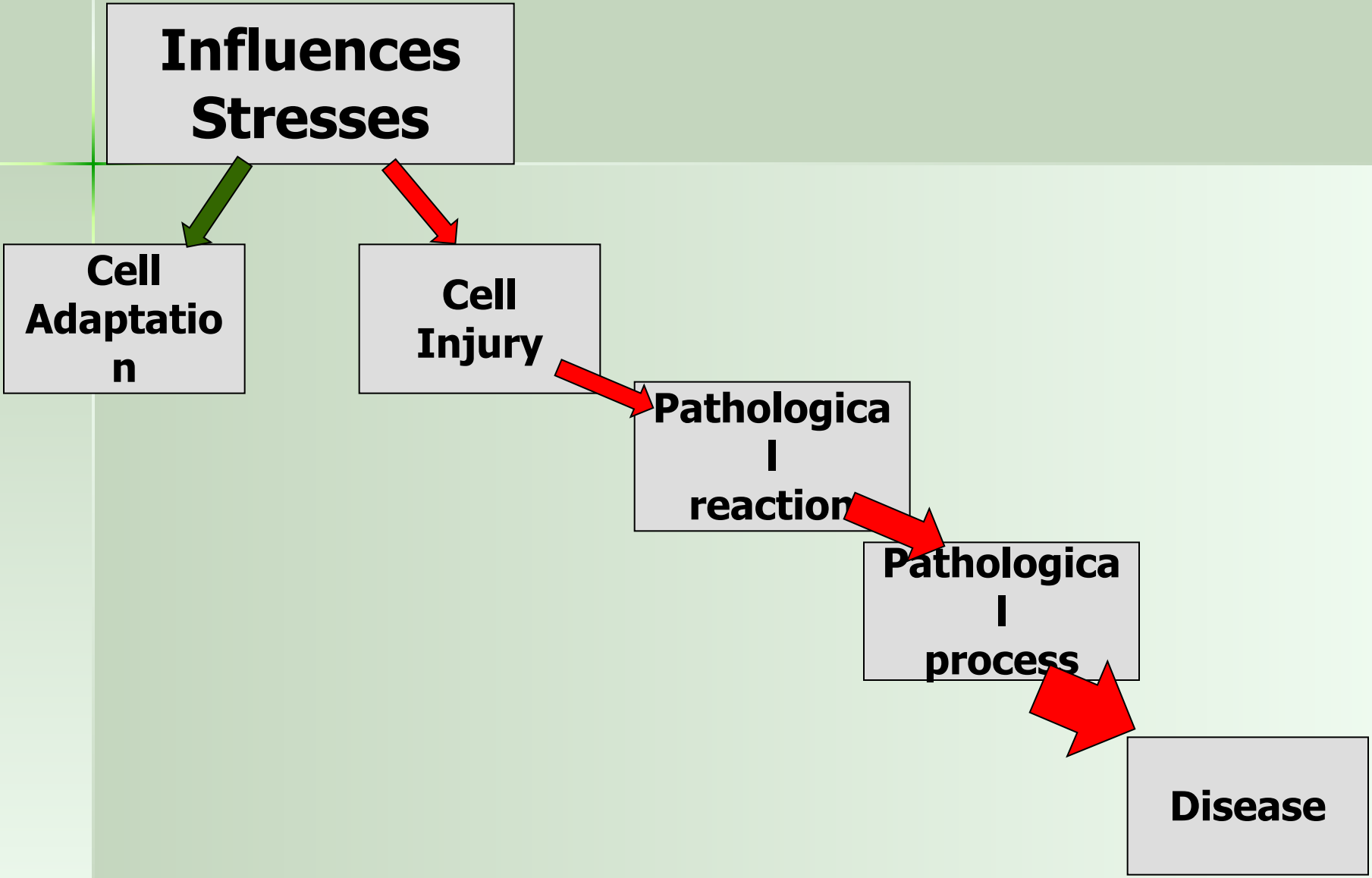
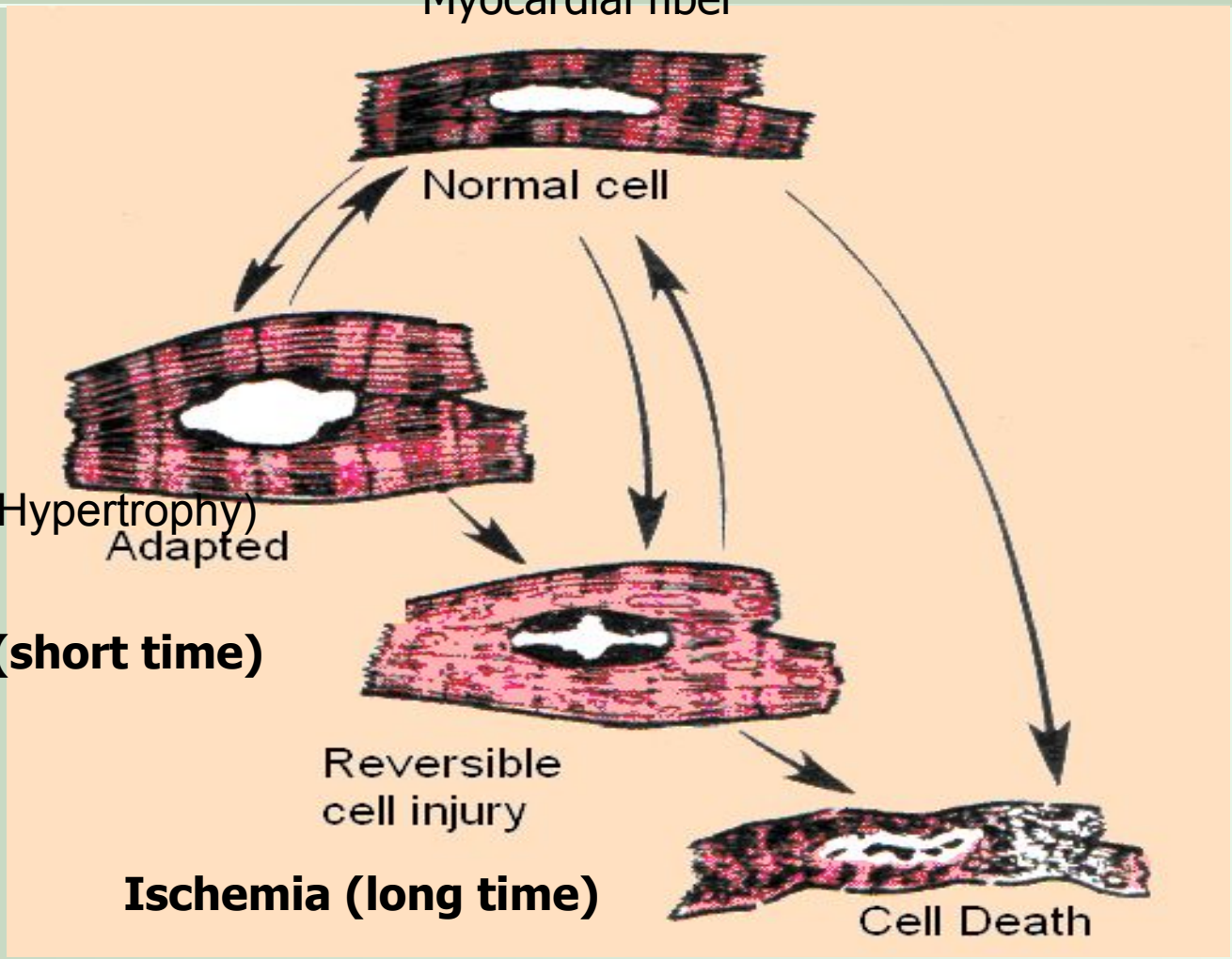
Conception of cell injury



The relationships among cell states



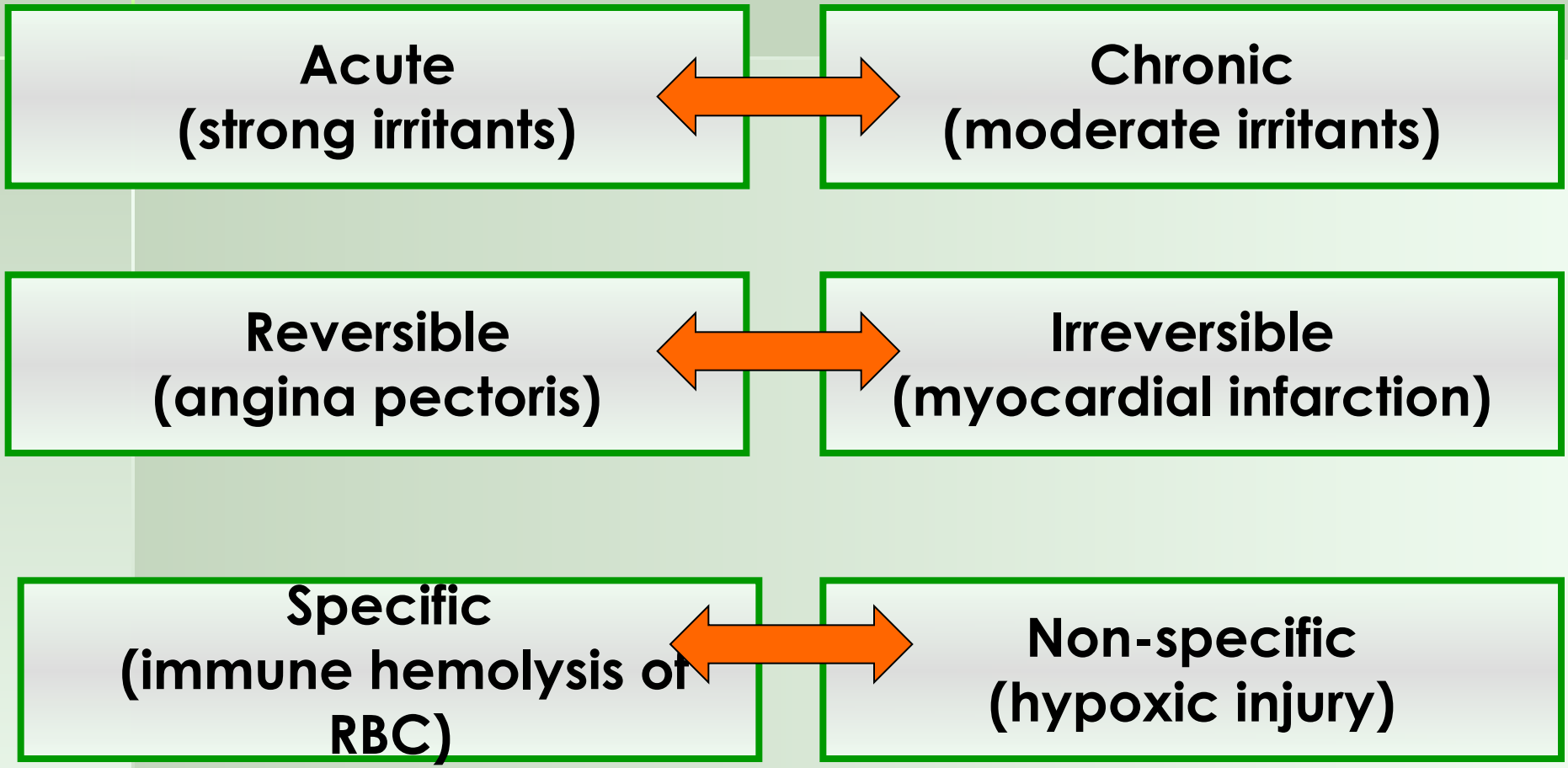
Injury From Physical Agents

- Causes:
  - Mechanical forces - trauma.
  - Extremes of temperature – burns, heat stroke, freezing, frostbites.
  - Electrical injuries - disruption of nervous and cardiac impulses.
  - Ionizing radiation - radiation sickness, mutations, tumors.
  - Ultraviolet radiation- sunburn, ageing, skin cancers.

Other causes of cell damage

- Chemicals – substances or their metabolites
- Hypoxia – as a result of ischemia, cardiac failure or Hb abnormalities
- Biological agents – from viruses to parasites
- Nutritional imbalances – excesses and deficiencies

Types of Cell Injury



Signs of Cell Injury

Morphological

- changes of shape and color
- swelling or shrinking
- the disturbance of contact between cells
- damage of cell membrane
- damage of cell organelles membranes
- intracellular accumulation of substances

Functional

- reduction of cell mobility
- disturbance of cell division
- change of cellular membrane permeability
- intracellular enzymes presence in blood
- appearance of new functions
- changes of biochemical processes in injured cells

General Principles of Cell Injury

Factors, which determine cell response

- Kind, severity, and duration of injury.
- Type of affected cell, its prior state of health.

Major sensitive cell components:

- integrity of cell membrane
- aerobic respiration
- protein synthesis
- genetic integrity

Major Processes of Cell Injury

- Decreased ATP production
- Injury by toxic oxygen radicals
- Disturbances of Ca regulation
- Mitochondrial injury

Example test

Chose the example of specific cell injury from listed below:

- myocardial ischemia
- intestinal epithelial injury due to bacterial toxins
- immune hemolysis of RBC
- liver cell injury due to chemicals
- skin damage due to mechanical trauma

Example test

Which factors determine the type of cell's response to injuring stimuli?

- kind of injuring factor
- injuring factor severity and time of duration
- prior state of the cell
- type of the affected cell
- all is correct

Example test

Patient was made blood biochemical test in order to confirm hepatitis. Increased level of alanine transaminase (ALT) and aspartate transaminase (AST) was found. It has been defined as a functional sign of hepatic cells injury. Which from the listed may be the reason of it?

- cell's membrane damage
- damage to plasma membrane sodium pump
- depletion of ATP store in the cell
- nonperoxidative mitochondrial injury
- disturbance of cells aerobic respiration

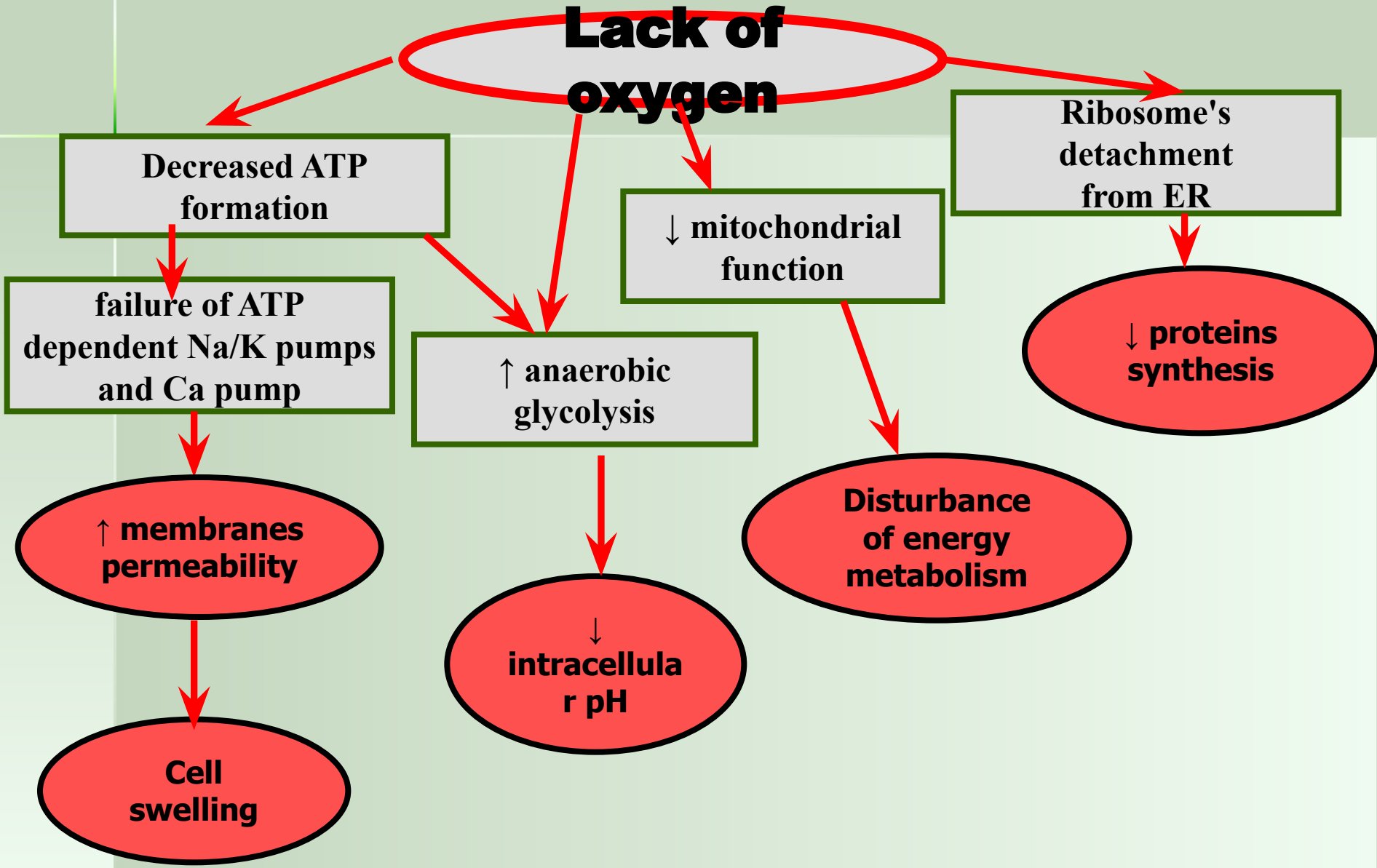
Major Types of Cell Injury

Hypoxia

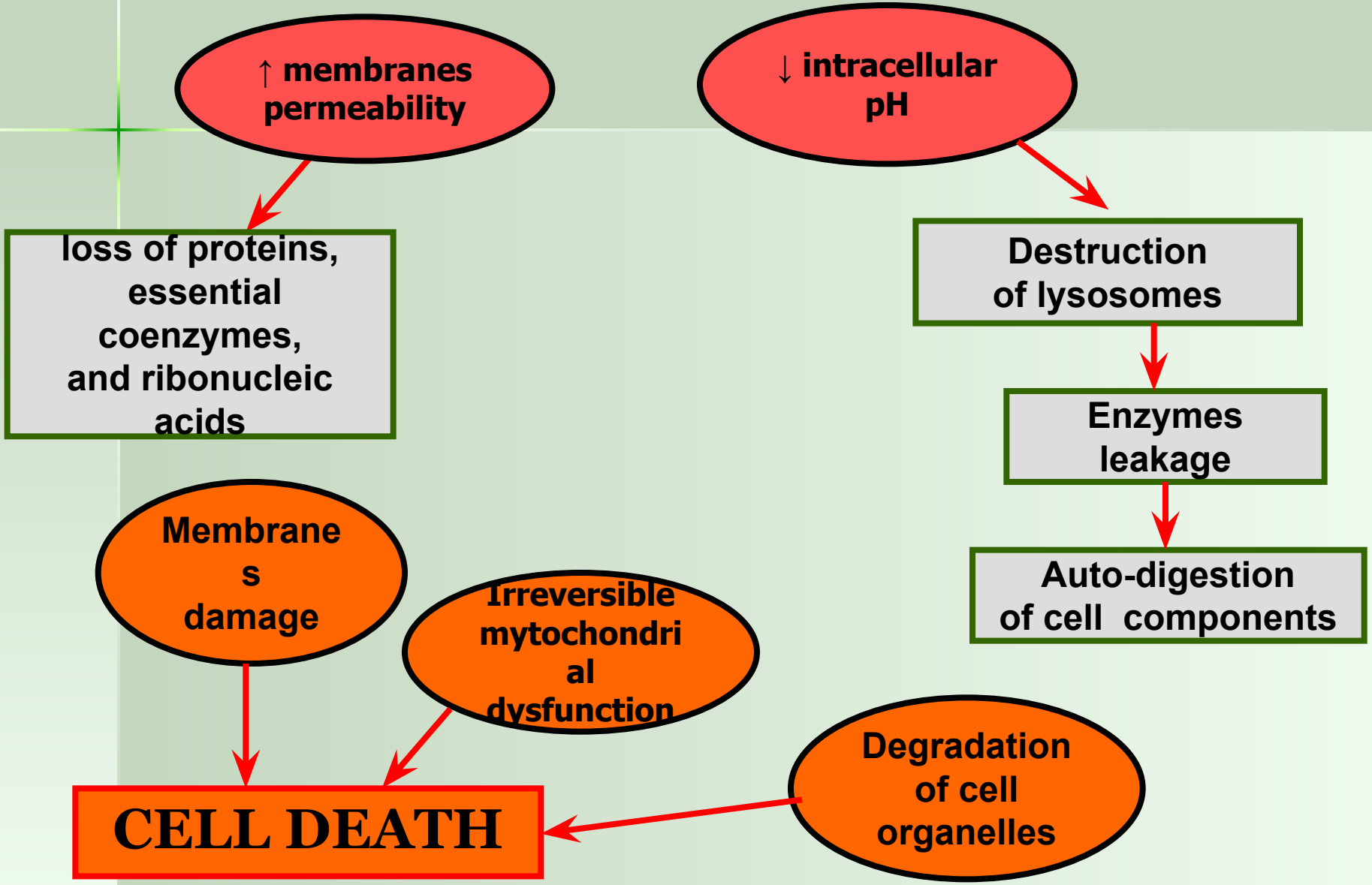
Free radicals

Chemicals

Reversible Hypoxic Injury

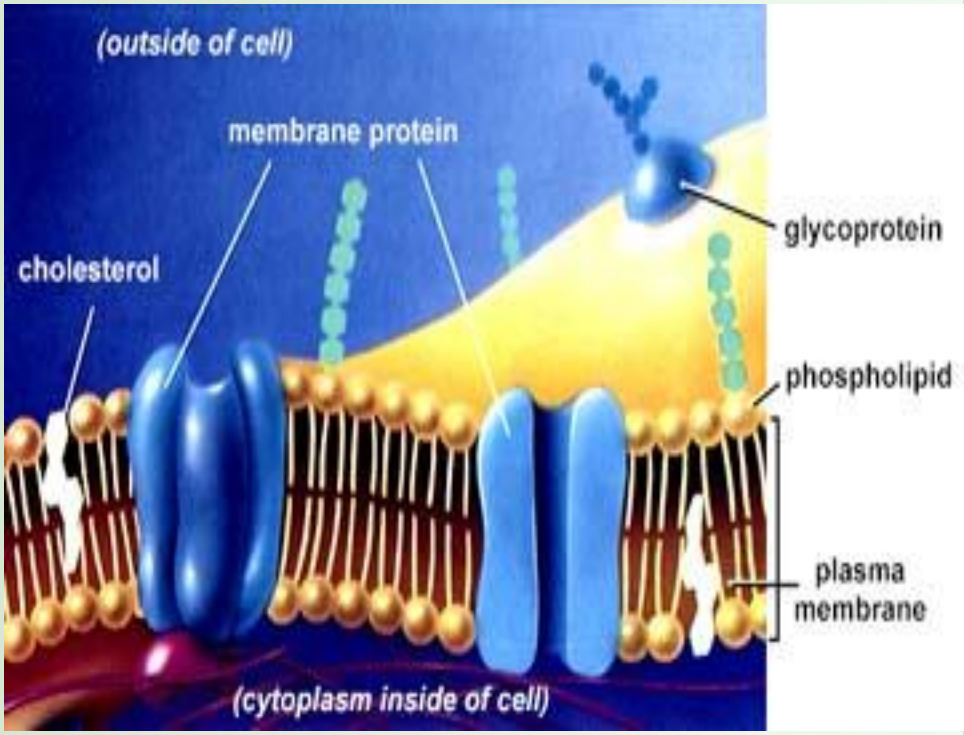


Irreversible Hypoxic Injury

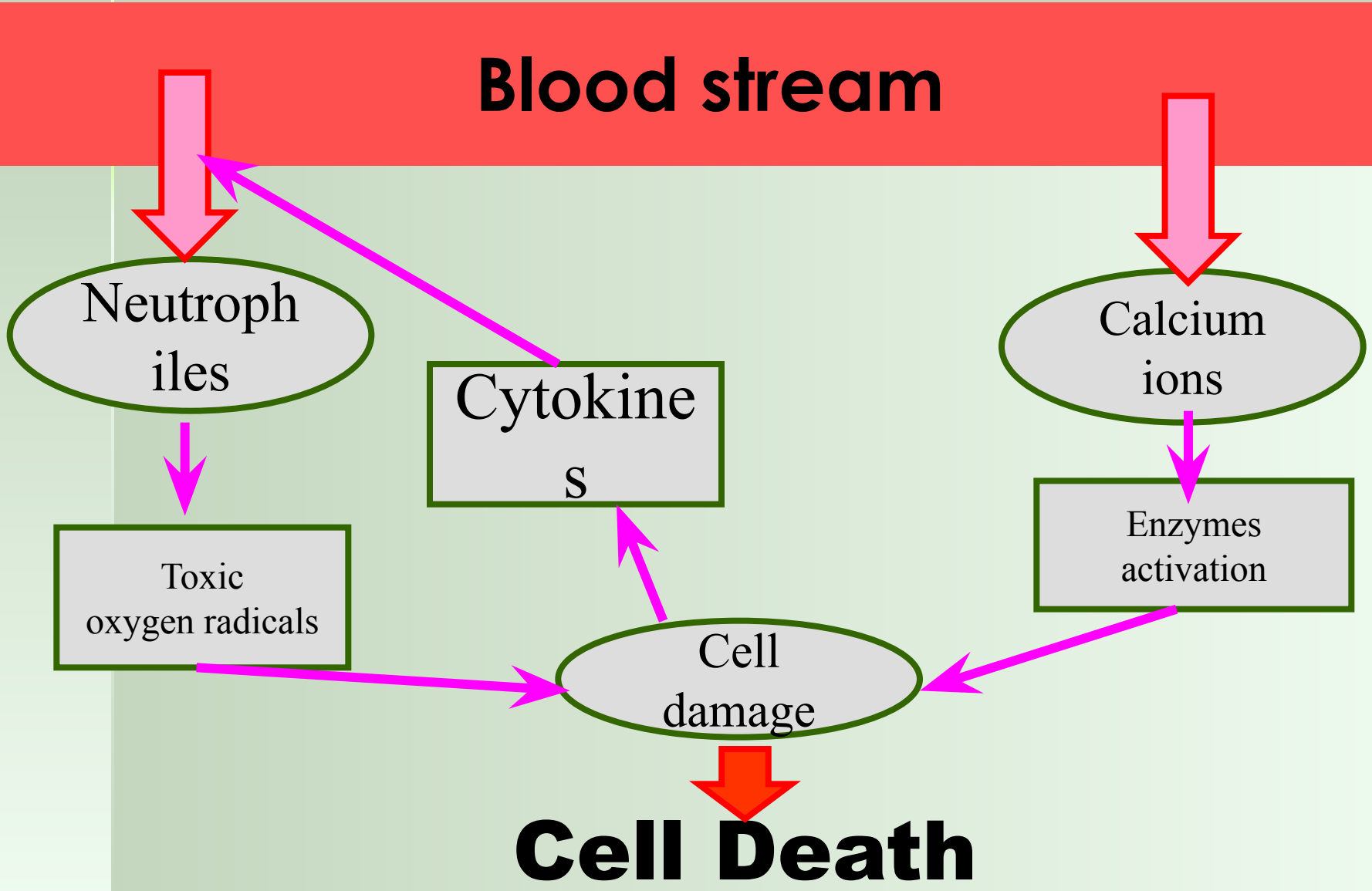


Mechanisms of membranes damage

- Progressive loss of membrane phospholipids
- Cytoskeletal abnormalities
- Toxic oxygen radicals
- Lipid breakdown products



Reperfusion injury



Example test

Disturbance of which process is primary observed in hypoxic injury:

- detachment of ribosomes from EPR
- reduction of intracellular pH
- oxidative phosphorilation by mitochondria
- sodium pump activity
- activation of glycolysis

Example test

Which factor directly causes the decrease of intracellular pH in the case of hypoxic injury?

- detachment of ribosomes from EPR
- decreased oxidative phosphorilation by mitochondria
- failure of sodium pump
- activation of anaerobic glycolysis
- increased membranes permeability

Example test

Which process is initiated by calcium in hypoxic cell injury?

- detachment of ribosomes from EPR
- disturbance of cells aerobic respiration
- disturbance of sodium pump
- activation of glycolysis
- activation of intracellular enzymes

Example test

Which process determines irreversibility of hypoxic injury?

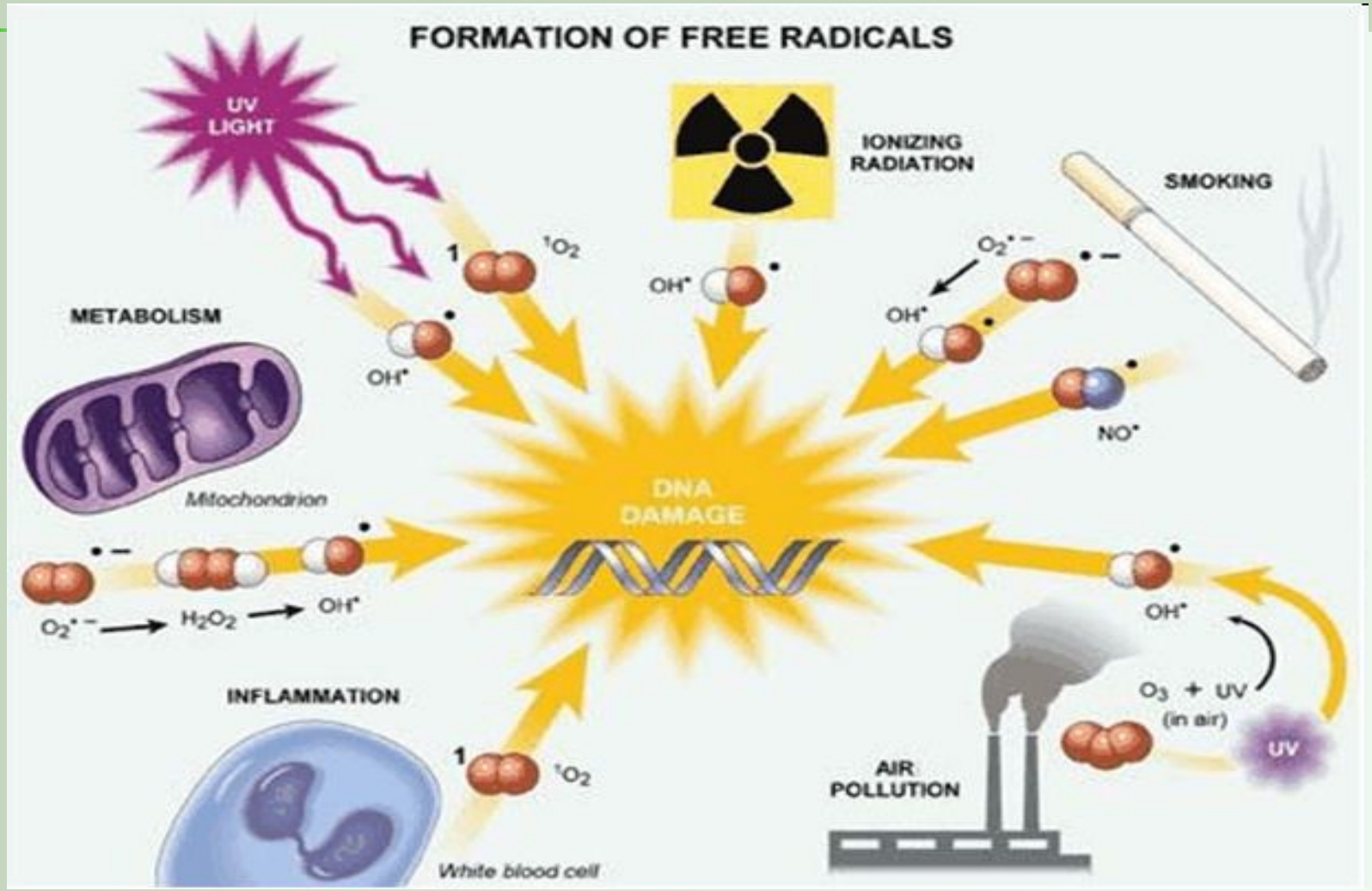
- inability to reverse mitochondrial dysfunction
- damage to plasma membrane sodium pump
- inability to re-start protein synthesis
- extremely low pH
- depletion of ATP store in the cell

Example test

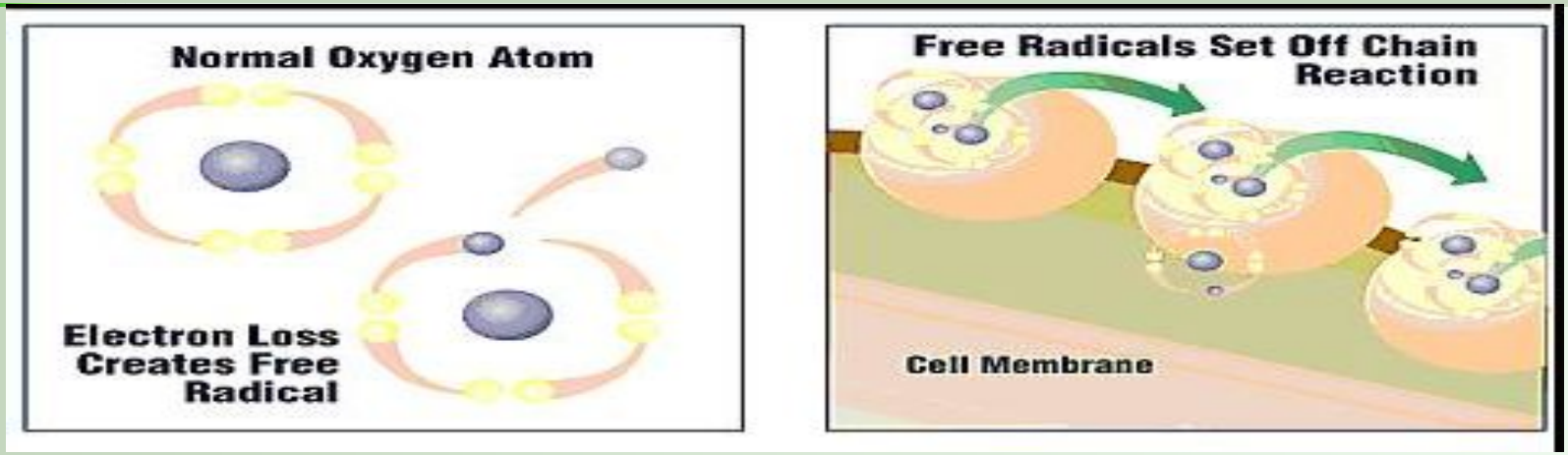
Which tissue cells are most sensitive to hypoxic injury?

- skeletal muscles
- smooth muscles
- myocardial cells
- brain cells
- liver cells

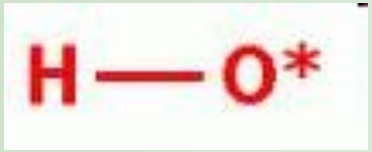
Sources of free radicals



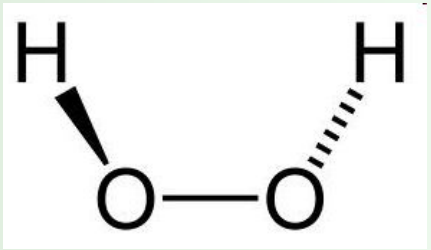
Reactive oxygen species



Superoxide O_2^-



Hydroxyl radical OH^-



Hydrogen peroxide

H_2O_2

The effects of free radicals

Positive: phagocytosis, energy production

Negative:

- Lipid peroxidation of membranes
- Nonperoxidative mitochondrial injury
- Lesions in DNA
- Oxidation of proteins

Antioxidative substances

Enzymatic antioxidants

- Thioredoxin system
- Glutathione system
- Superoxide dismutase
- Catalase

Non-enzymatic antioxidants

- Vitamins A, C, E
- Coenzyme Q10
- Selenium
- Zinc
- Carotenoids
- Bioflavonoids

Example test

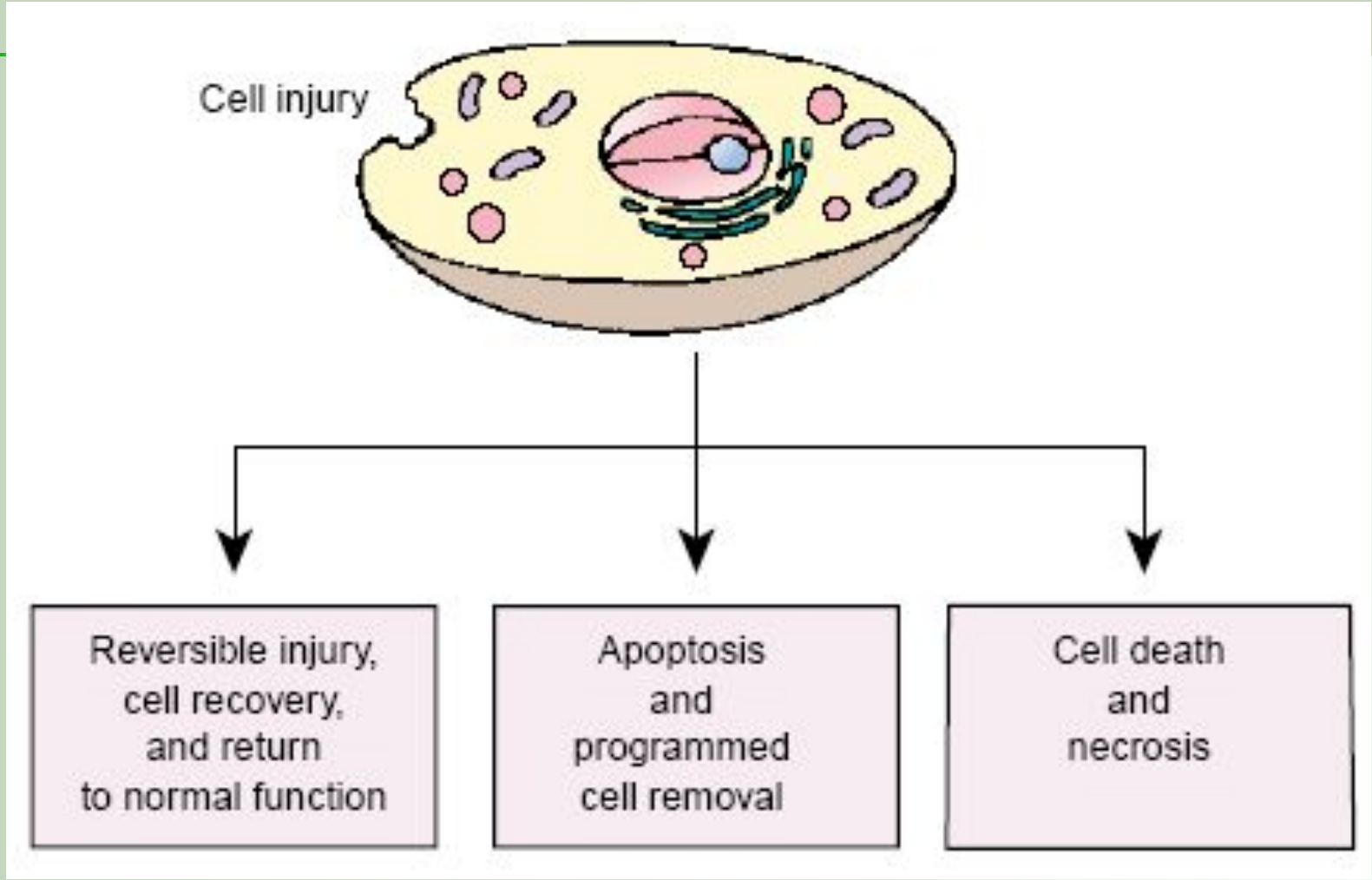
Choose the effect which IS NOT directly caused by free radicals:

- lipid peroxidation of membranes
- nonperoxidative mitochondrial injury
- disturbance of cells aerobic respiration
- DNA lesions
- cross-linking of proteins

Chemical injury mechanisms

- **Direct cytotoxic effect**
  - **mercury damages GIT and kidneys**
  - **cyanide breaks oxidative phosphorilation.**
- **Conversion to reactive toxic metabolites**
  - **free radicals**
  - **lipid peroxodation.**

Outcomes of cell injury



Cell death

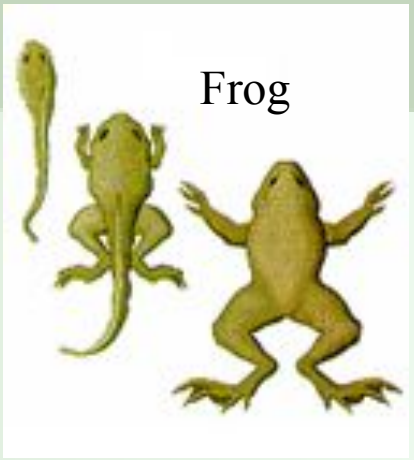
Necrosis - death of a cell due to external forces

Apoptosis - programmed cell death

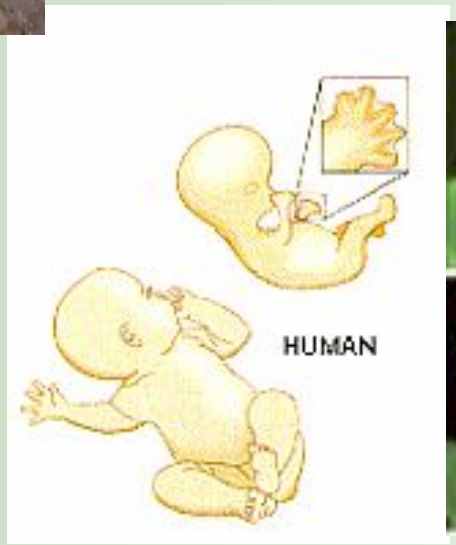
- gene-related
- energy dependent
- initiated by external and internal influences)

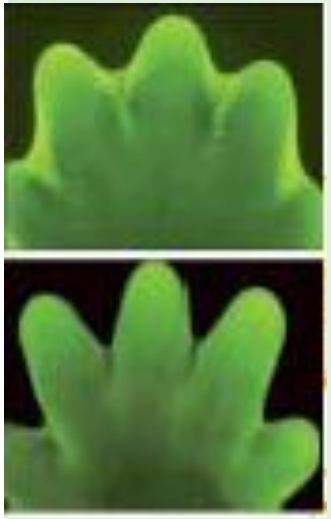
Physiological apoptosis

plants



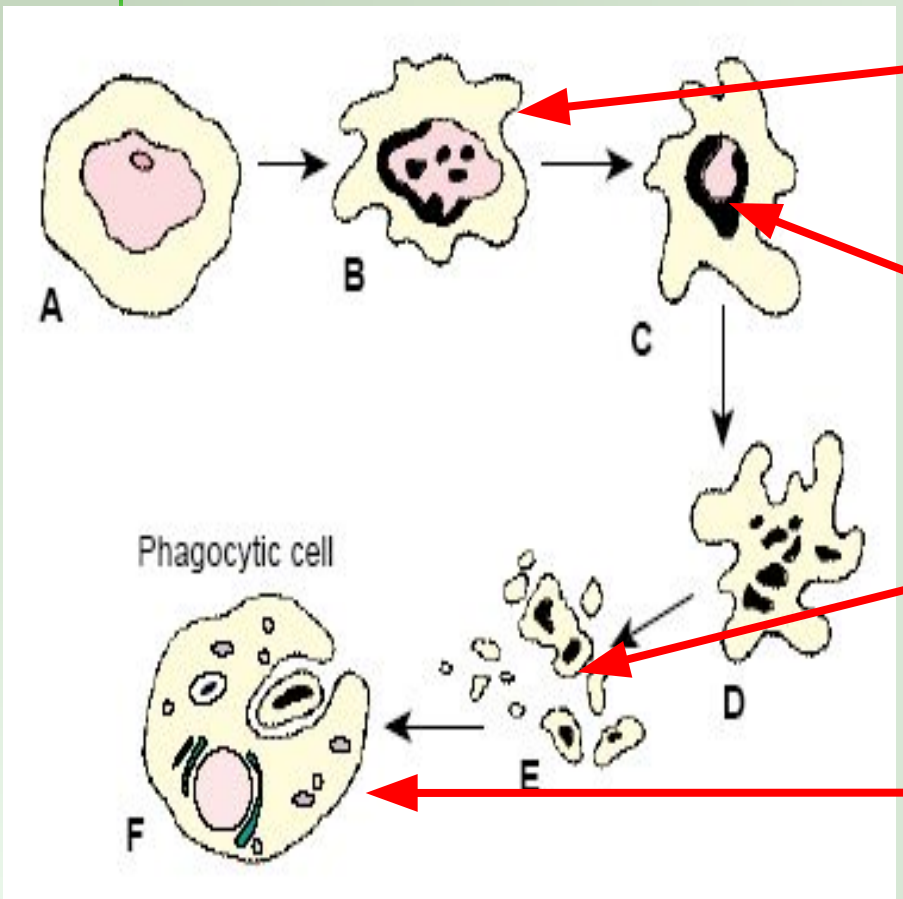
amphibia





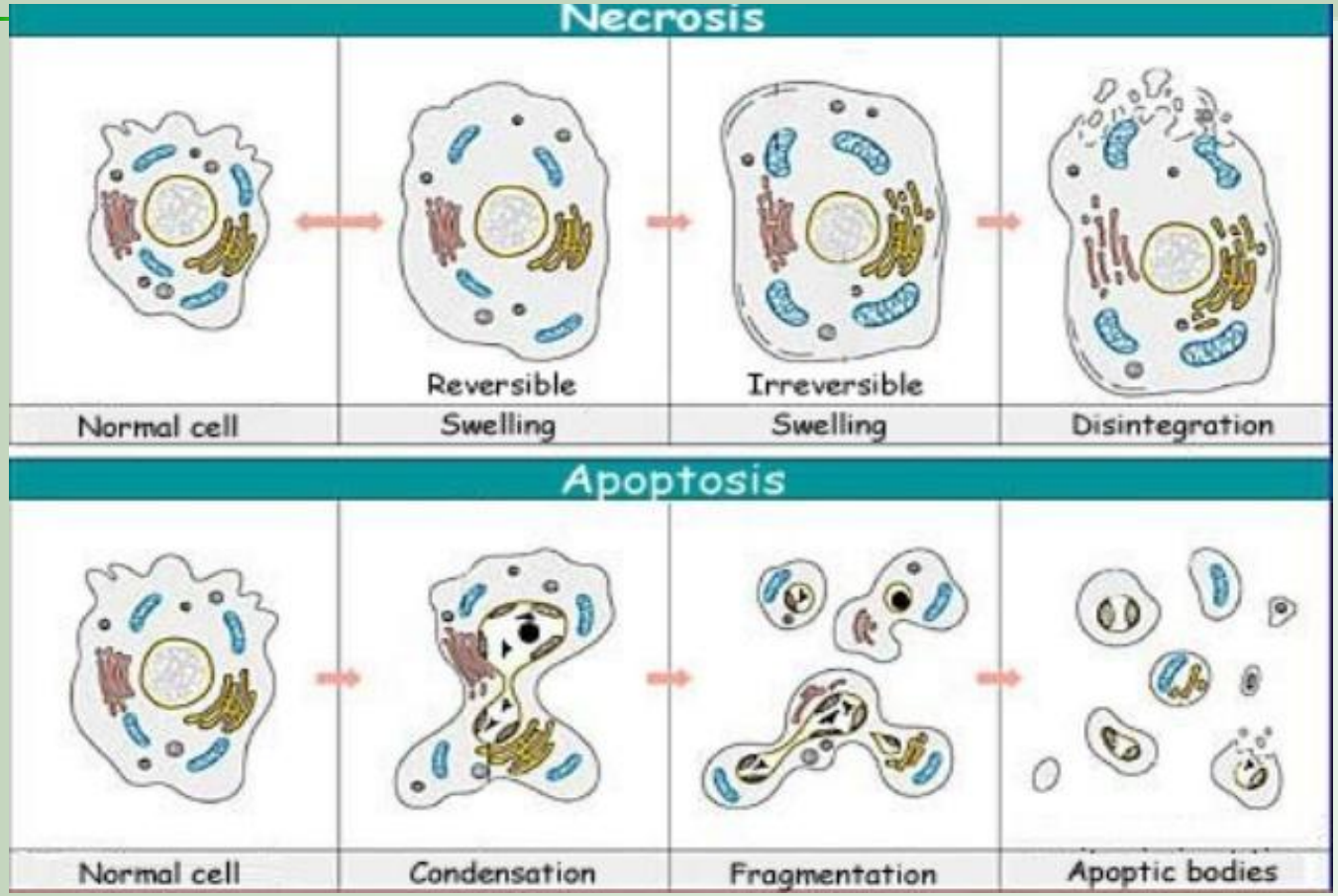
human

Morphological signs of apoptosis



- Shrinkage of the cell.
- Condensation of chromatin around the nucleus.
- Formation of apoptic bodies.
- Phagocytosis of apoptic bodies by macrophages.

Necrosis and apoptosis



Example test

Give the correct definition of apoptosis.

Apoptosis is…

- a process of virus infected cells killing
- a programmed cell death
- a death of the cell after injuring factor influence
- a cell's death as a result of enzymes action
- an irreversible cell injury

Example test

Which from the following is the most typical morphological sign of cell death by apoptosis?

- condensation of nucleus and cytoplasm
- presence of inflammatory reaction
- compensatory increase of DNA-synthesis
- swelling of mitochondrions
- increase of cell's size

Example test

Every day, blood cells in our body become senescent and die without producing signs of inflammation, and yet, massive injury or destruction of tissue, such as occurs with a heart attack, produces significant signs of inflammation. Why it happens?

- due to necrosis of heart muscle
- due to apoptosis of heart muscle
- due to atrophy of heart muscle
- due to swelling of heart muscle
- due to disturbances in calcium metabolism

Cell Adaptation to Injury

- compensation of energy metabolism disturbance
- protection of cells membranes
- compensation of water-ion disbalance
- repair of cell genome

Compensation of energy metabolism disturbance

- increased ATP formation, transport and effectiveness of ATP use
- increase of enzymes activity taking part in reduction-oxidation reactions
- decrease of cell's functional activity and protein synthesis

Protection of cells membranes

- activation of antioxidants action
- activation of cells buffer system
- activation of EPR enzymes
- activation of cellular structures reparation

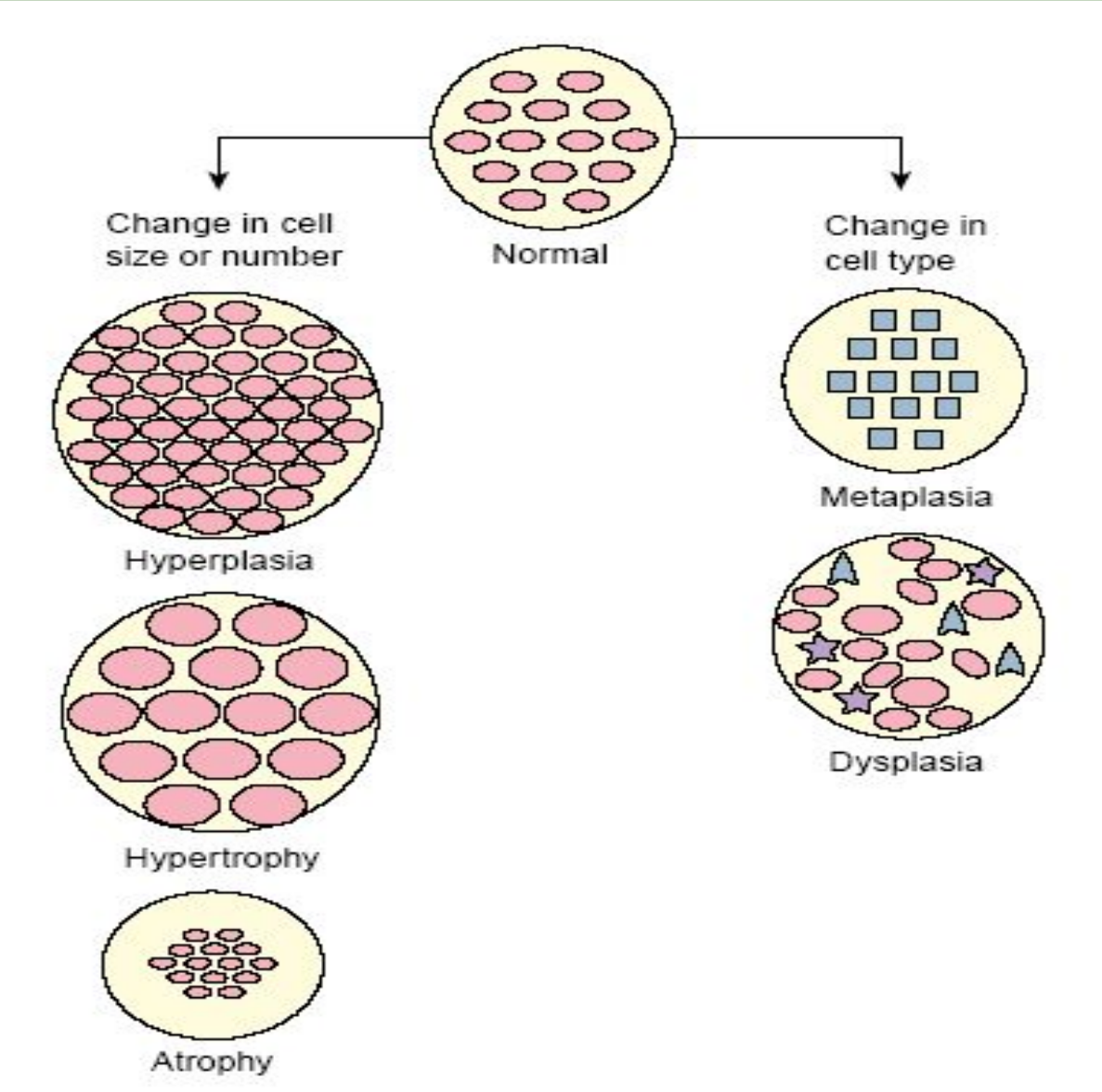
Compensation of water-ion disbalance

- activation of ion “pumps” energy supply
- increase of ion-transporting enzymes
- activation of cell’s buffer system

Mechanisms of cell genome repair

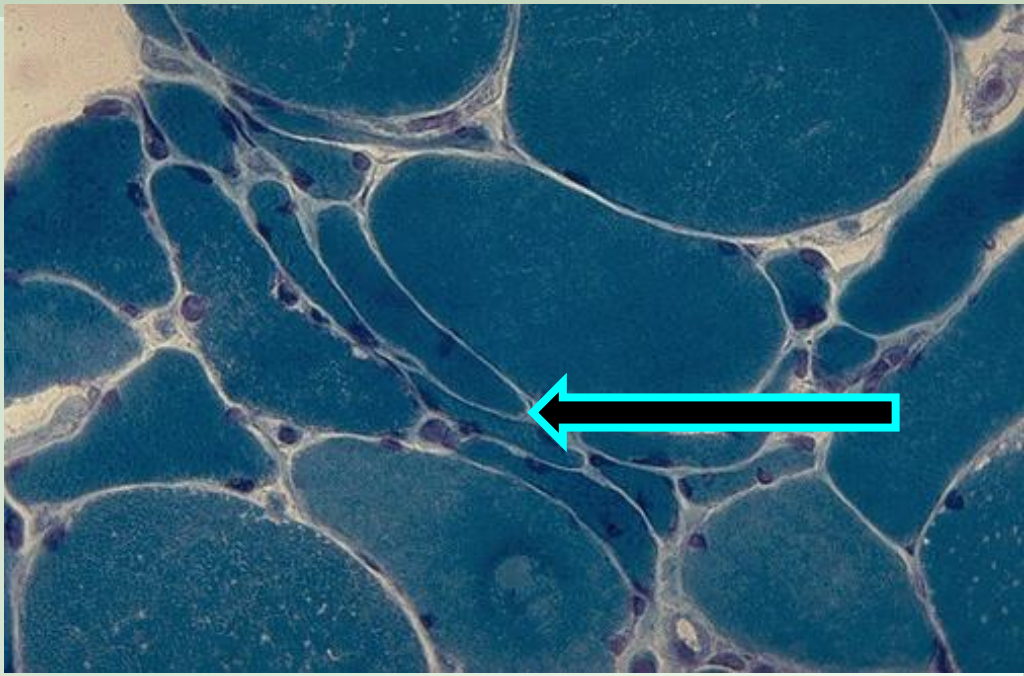
- revealing and elimination of damaged DNA fragment
- replacement of damaged DNA fragments
- elimination of DNA ruptures
- normalization of DNA transcription and translation

The types of cellular adaptations



Causes of atrophy

- decreased workload,
- loss of innervation,
- diminished blood supply,
- inadequate nutrition,
- loss of endocrine stimulation,
- aging.



Muscle fibers atrophy

Hypertrophy

increase in the size of cells

REASONS:

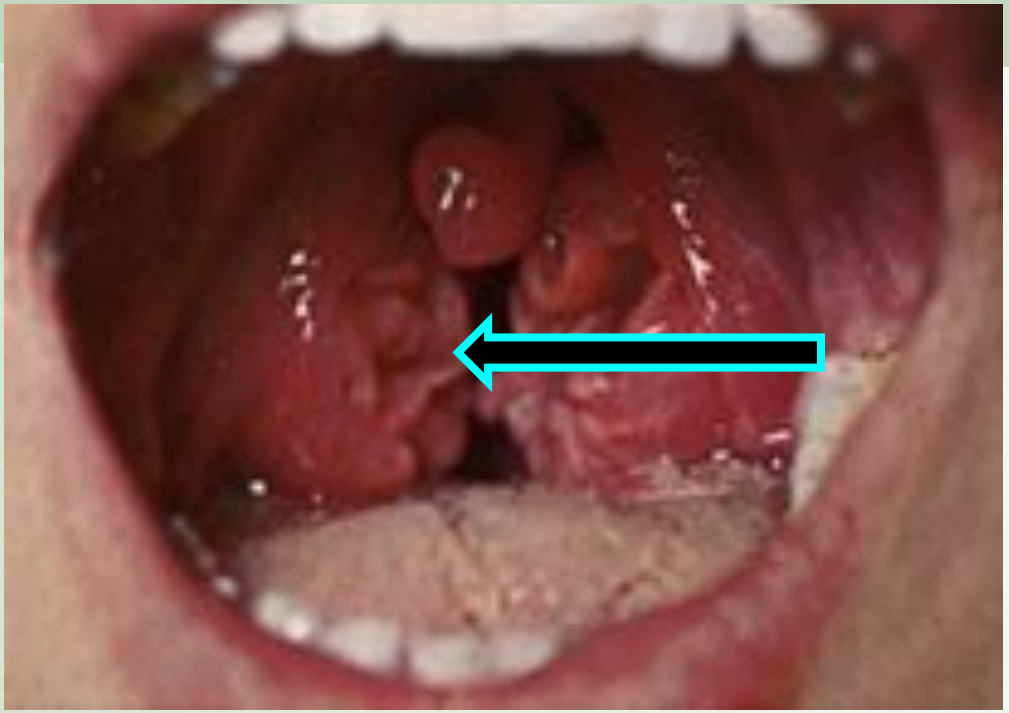
- increased functional demand
- specific hormonal stimulation
- occurs under both physiologic and pathologic conditions

Left ventricle hypertrophy in hypertonic patient

Hyperlasia

increase in the number of cells

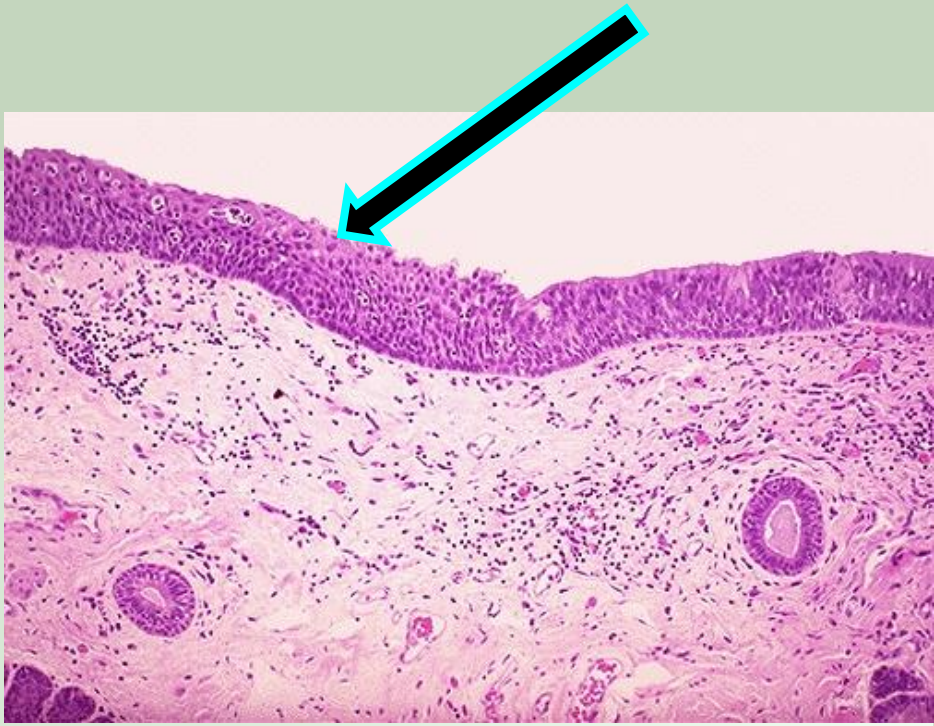
- It occurs in tissues where cells are capable of mitotic division.



Hyperplasia of tonsills

Metaplasia

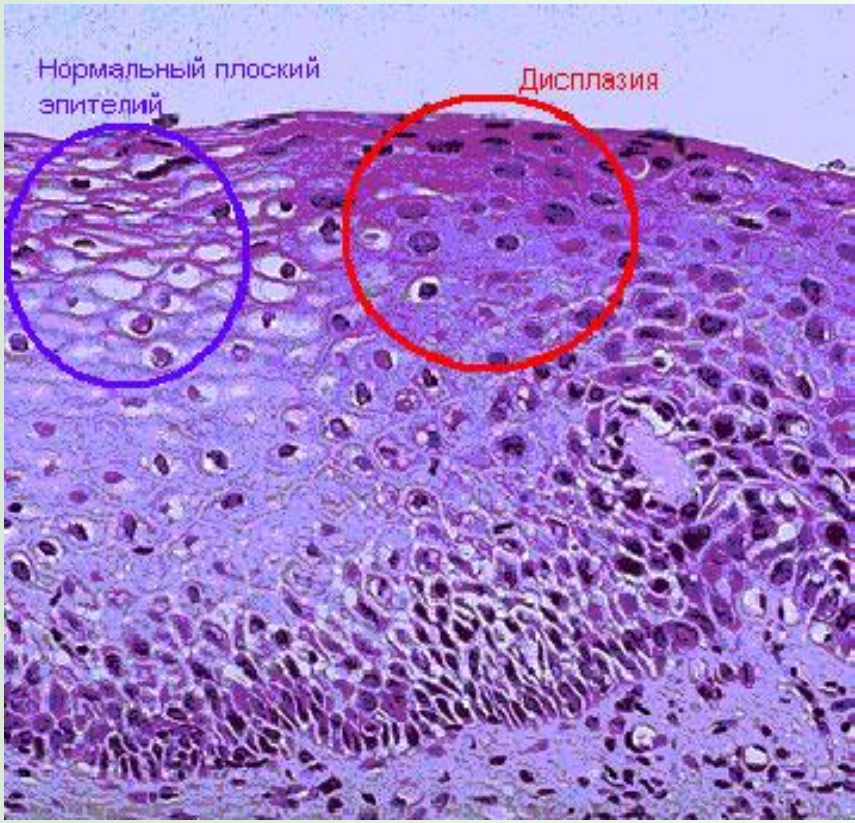
- one adult cell type (epithelial or mesenchymal) is replaced by another adult cell type



Squamous metaplasia in respiratory tract of the habitual cigarette smoker

Dysplasia

- Deranged cell growth of a specific tissue that results in cells that vary in size, shape, and organization.
- Causes:
  - chronic irritation
  - chronic inflammation
  - pre-cancer state



Example test

Cells may adapt to external and internal stimuli by undergoing changes in their size, number and type. What happens to other kidney when one is damaged? It undergoes…:

- hypertrophy
- atrophy
- hyperplasia
- metaplasia
- dysplasia

Example test

Cells may adapt to external and internal stimuli by undergoing changes in their size, number and type. What happens to muscles of extremities that have been encased in plaster casts? The muscles undergo…:

- hypertrophy
- atrophy
- hyperplasia
- metaplasia
- dysplasia

Example test

A 30-year-old man sustained a fracture of his leg 2 months ago. The leg had been encased in a cast, which was just removed. The patient is amazed at the degree to which the muscles in his leg have shrunk. Which is the reason of it?

- inadequate nutrition
- loss of innervation
- loss of endocrine stimulation
- decreased workload
- diminished blood supply