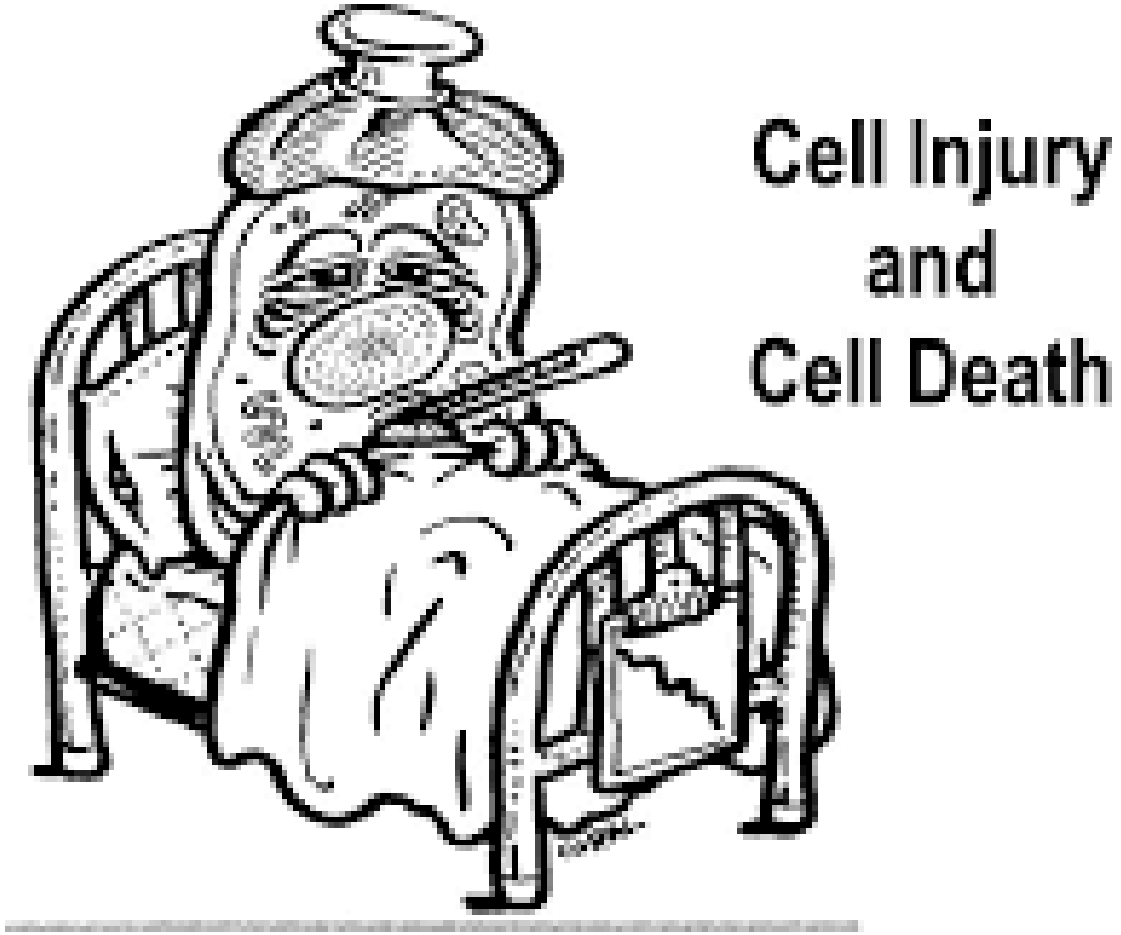
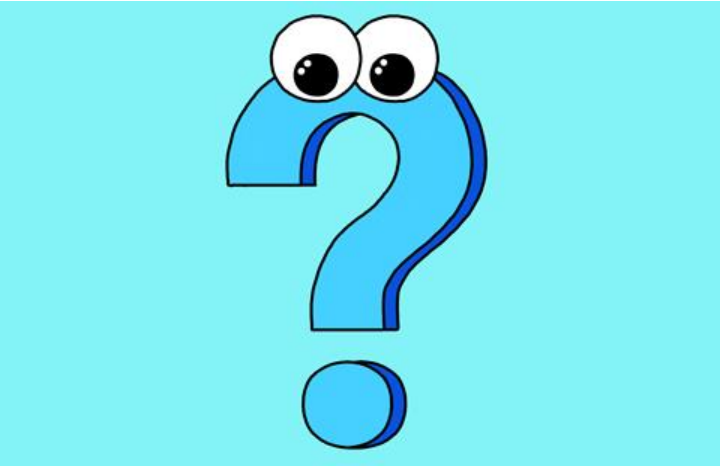
CELL INJURY AND CELL DEATH



durre.sameen@duhs.edu.pk

A Quick Recap



- Define with examples of:

- Hyperplasia;
- Metaplasia;
- Atrophy;
- Hypertrophy.

Objectives

At the end of the session student's should be able to:

- Name causes of cell injury
- Understand mechanisms underlying cell injury
- Describe the sequence of the ultra-structural and biochemical changes which occur in the cell in response to cell injury
- Distinguish between irreversible and reversible injury

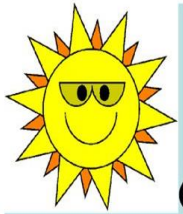
CAUSES

Mechanical trauma

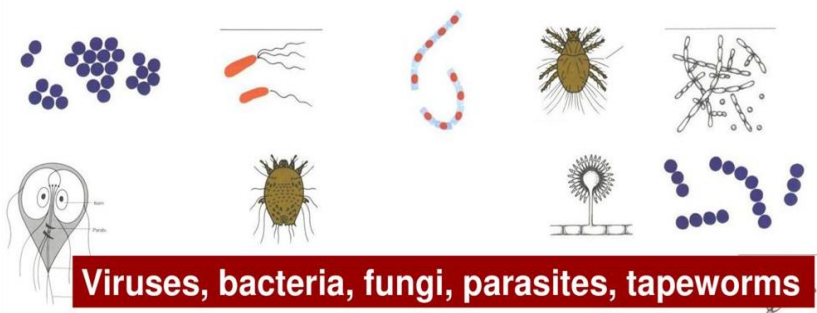
Thermal: heat or cold

Drugs & Poisons

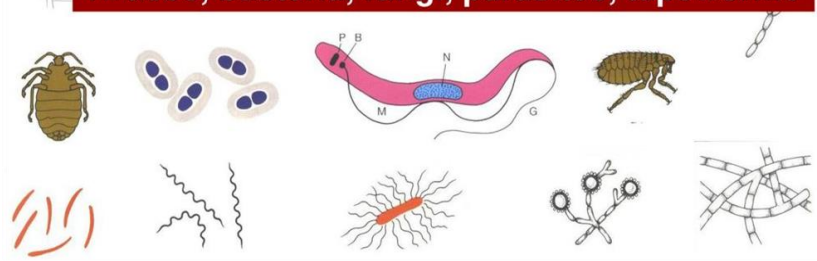
Electrical shock

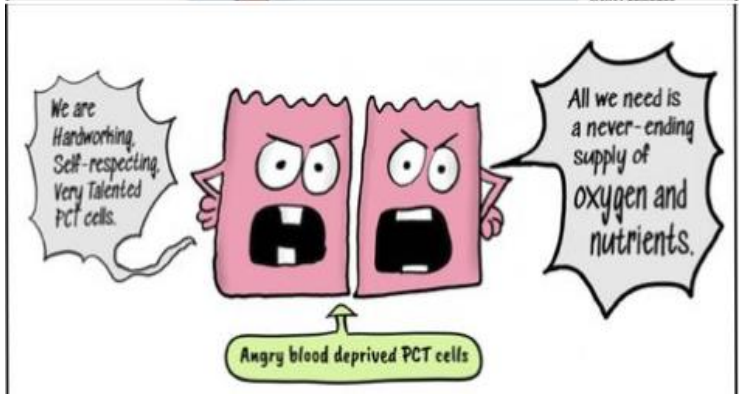


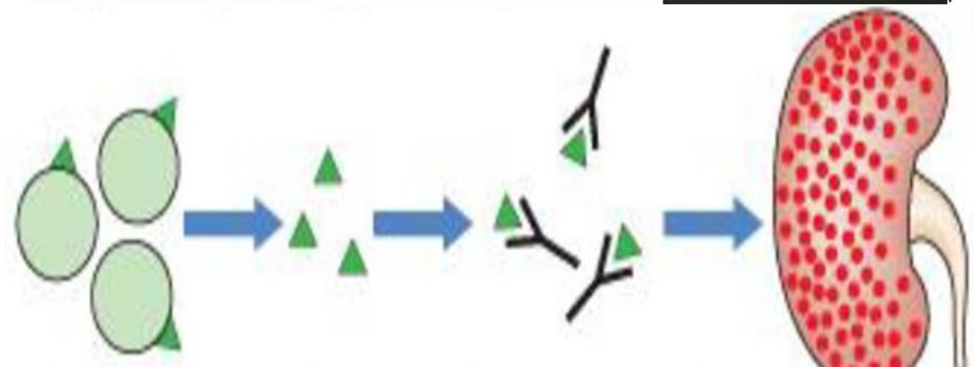
Radiation

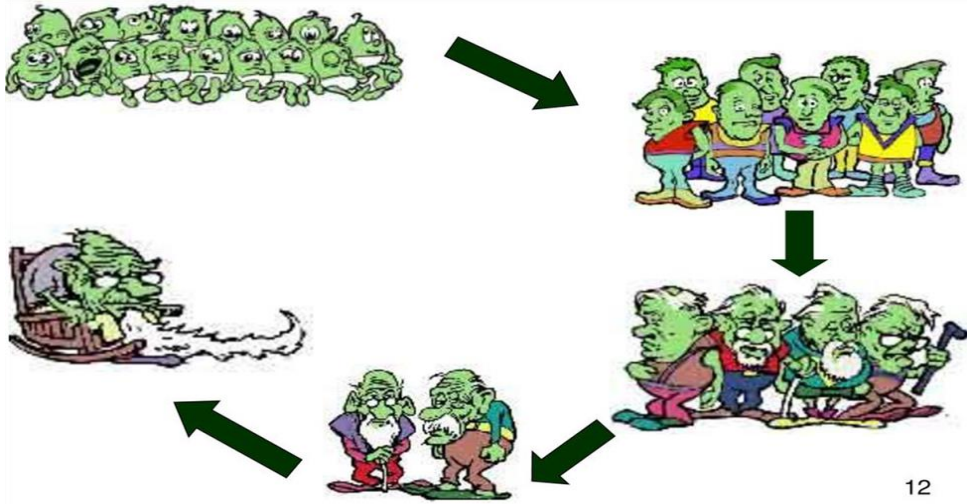


Viruses, bacteria, fungi, parasites, tapeworms





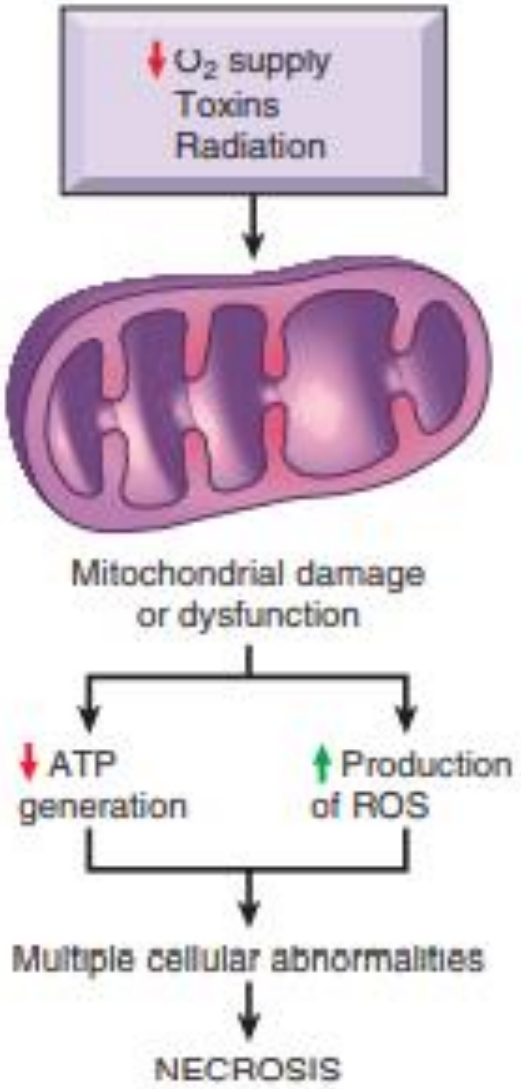


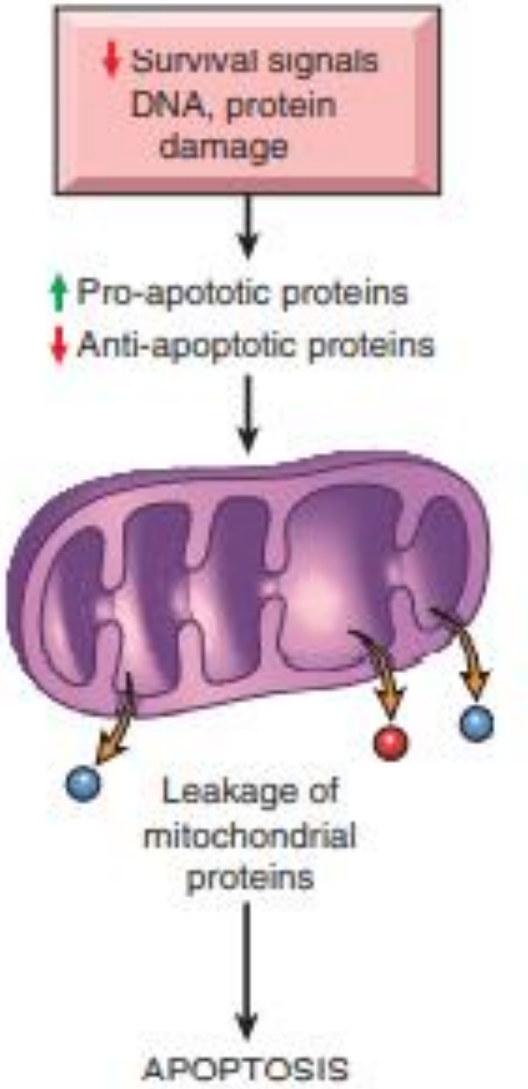


MECHANISMS OF CELL INJURY

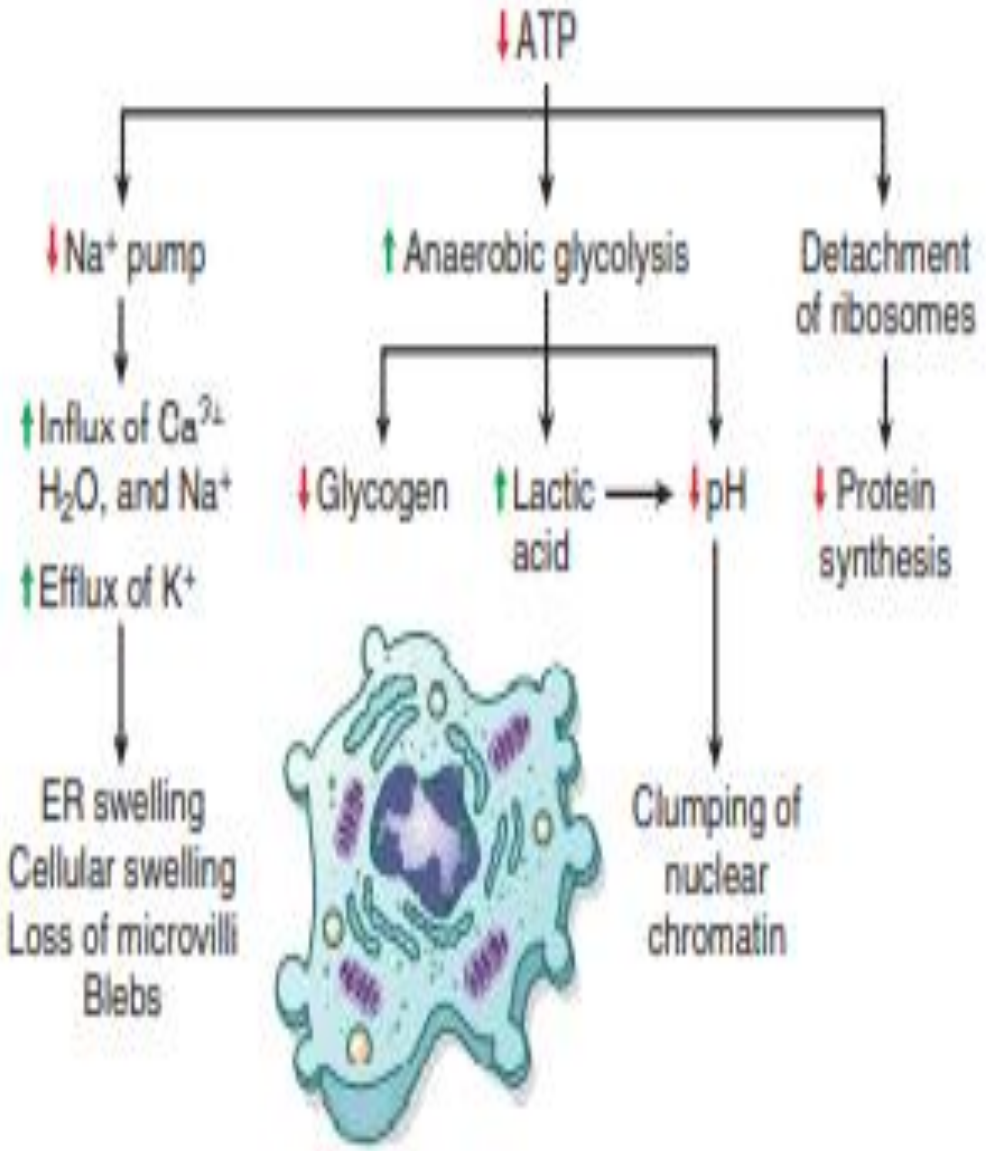
- The cellular response to injurious stimuli depends on the nature of the injury, its duration, and its severity
- The consequences of cell injury depend on the type, state, and adaptability of the injured cell
- Cell injury results from different biochemical mechanisms acting on several essential cellular components

MITOCHONDRIAL DAMAGE

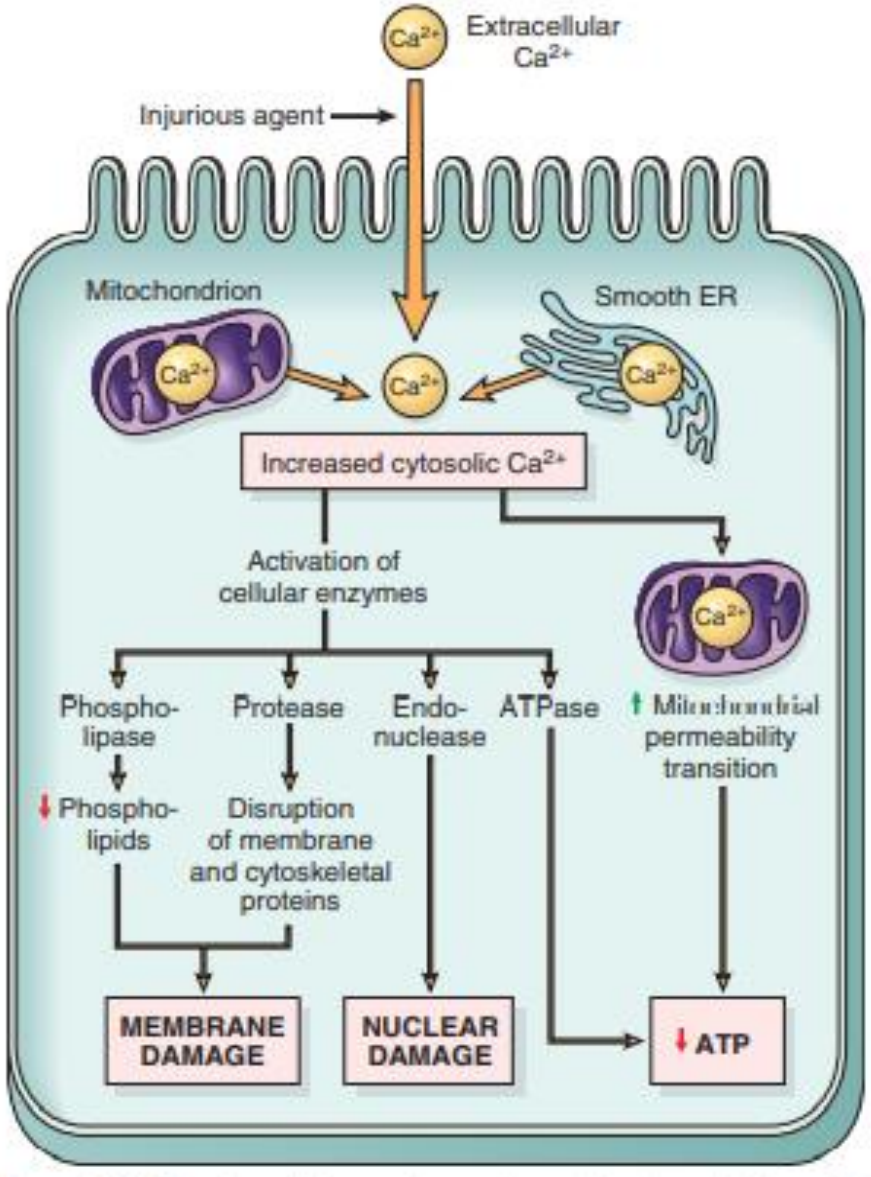




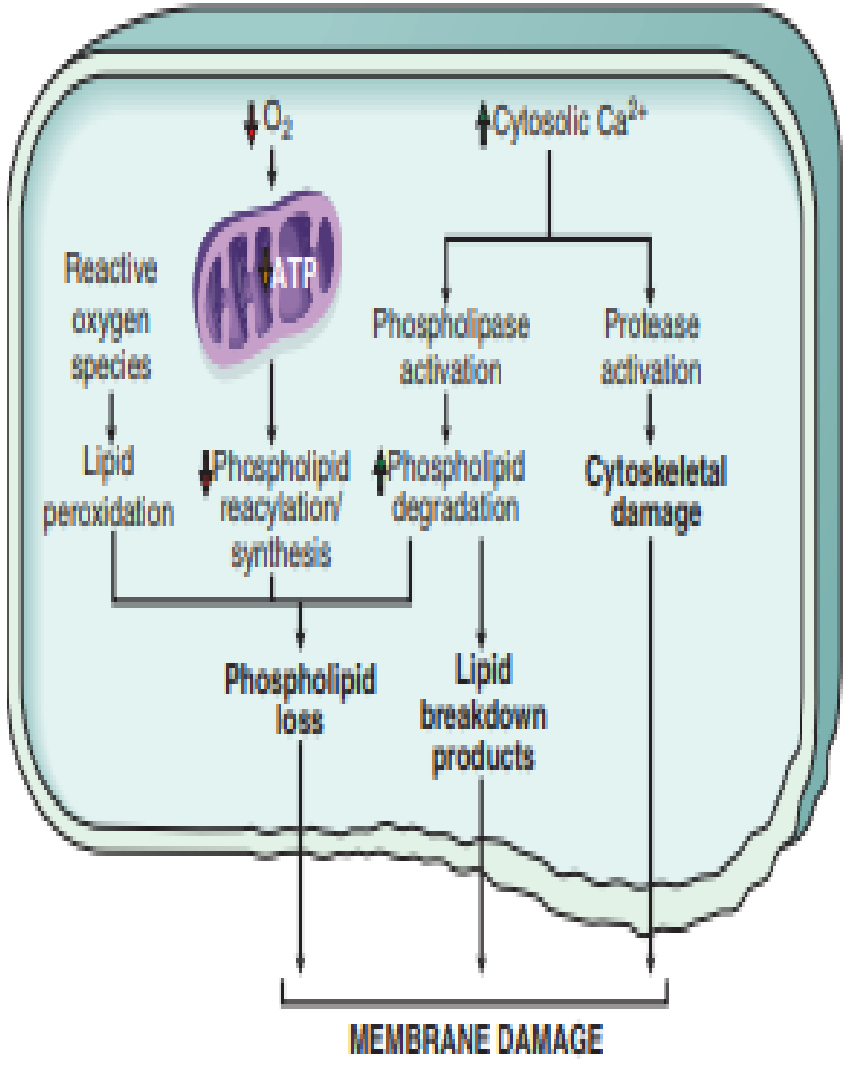
DEPLETION OF ATP



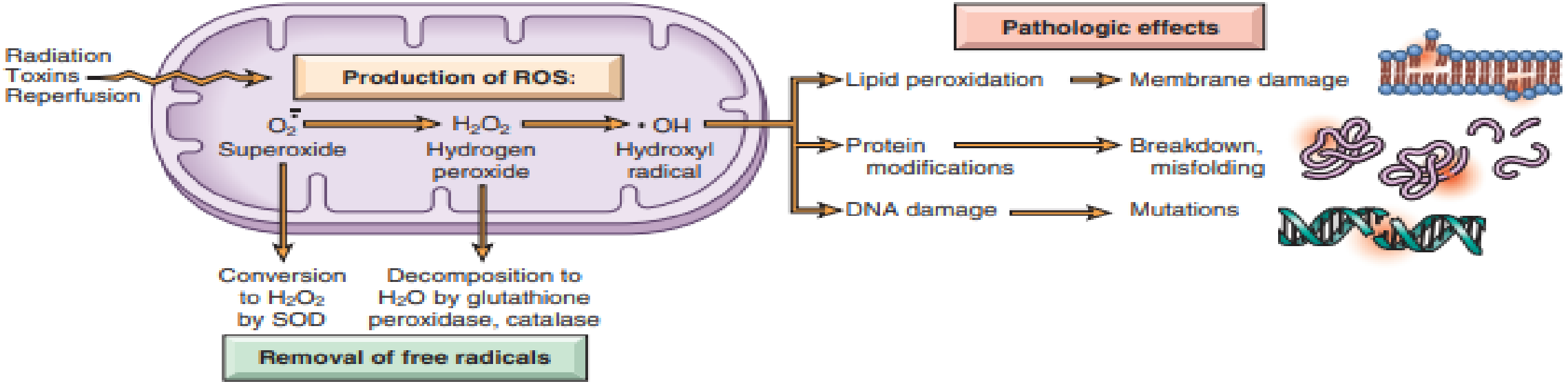
LOSS OF CALCIUM HOMEOSTASIS



DEFECTS IN MEMBRANE PERMEABILITY

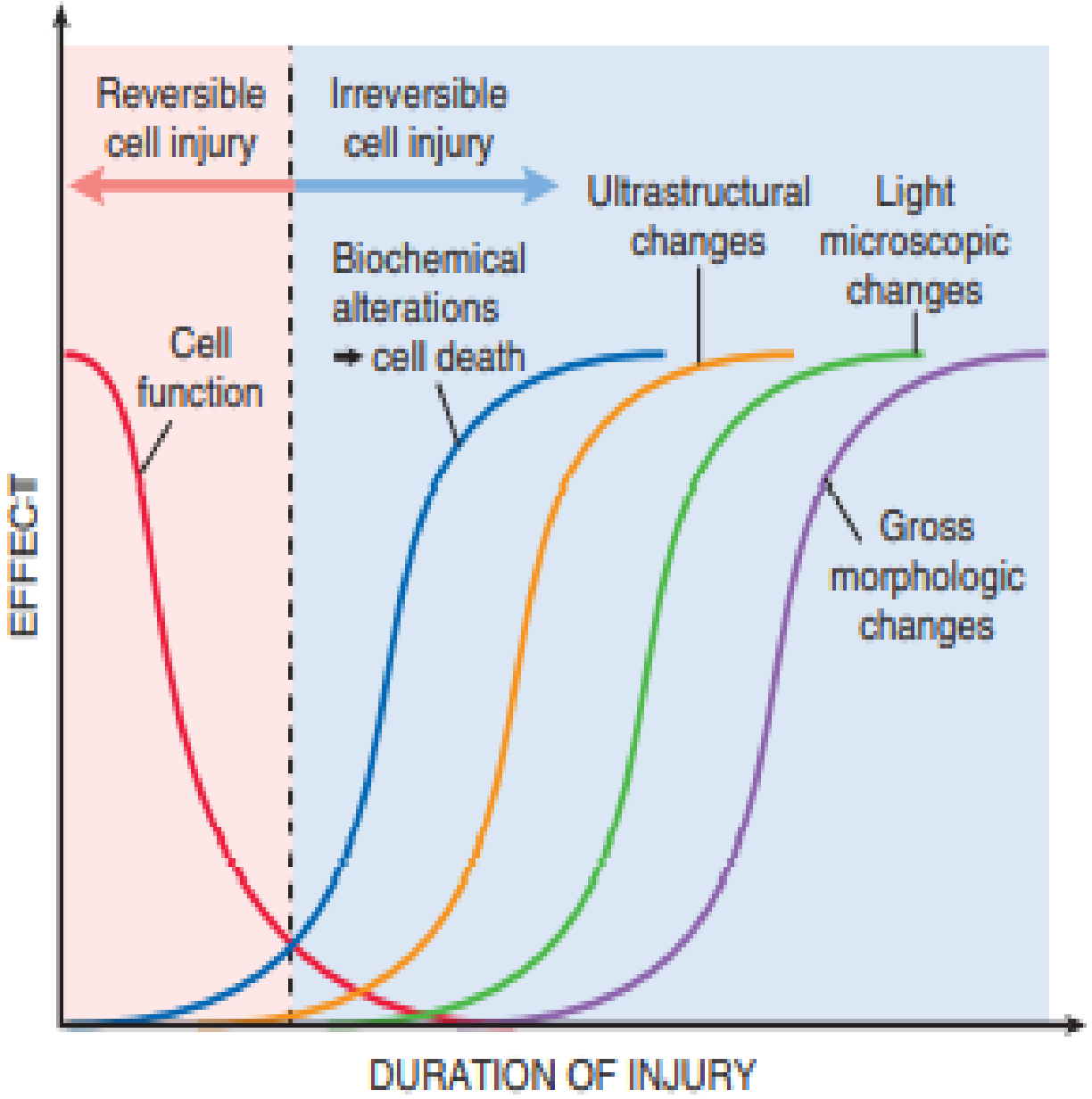


DAMAGE TO DNA AND PROTEINS



Accumulation of Oxygen-Derived Free Radicals (Oxidative Stress)

MORPHOLOGICAL ALTERATIONS



Two features of reversible cell injury can be recognized under the light microscope: cellular swelling and fatty change

Cellular swelling appears whenever cells are incapable of maintaining ionic and fluid homeostasis and is the result of failure of energy-dependent ion pumps in the plasma membrane.

Fatty change occurs in hypoxic injury and various forms of toxic or metabolic injury. It is manifested by the appearance of lipid vacuoles in the cytoplasm. It is seen mainly in cells involved in and dependent on fat metabolism, such as hepatocytes and myocardial cells

Difference Between Reversible and Irreversible cell injury

Pathologic changes that can be reversed when the stimulus is removed

- Cellular Swelling
- Swelling of endoplasmic reticulum and mitochondria
- Blebs formation
- Clumping of chromatin

Pathologic changes that are permanent and cause cell death

Severe mitochondrial vacuolization
Extensive damage to plasma membranes
Detachment of ribosomes from the granular endoplasmic reticulum (ER).
Injury to lysosomal bodies leads to leakage of lysosomal enzymes into the cytoplasm which causes cell lysis

Table 2-2 Features of Necrosis and Apoptosis

Feature	
Cell size	
Nucleus	
Plasma membrane	
Cellular contents	
Adjacent inflammation	
Physiologic or pathologic role	

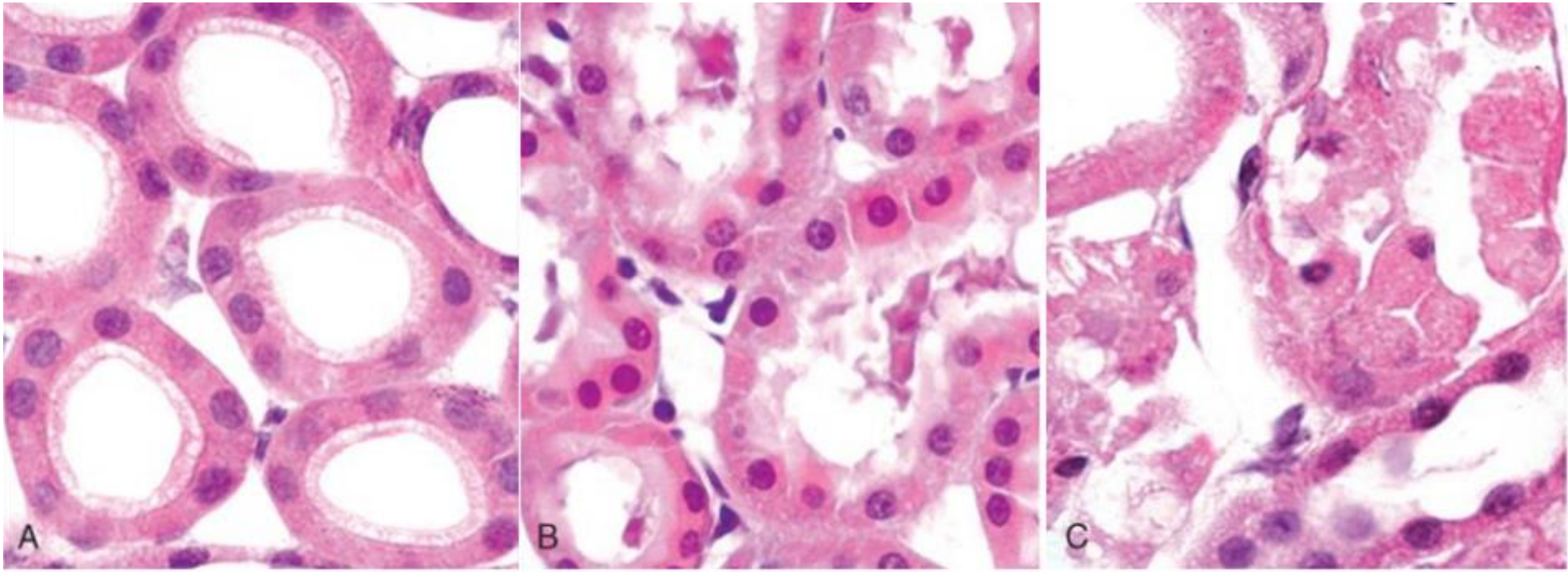
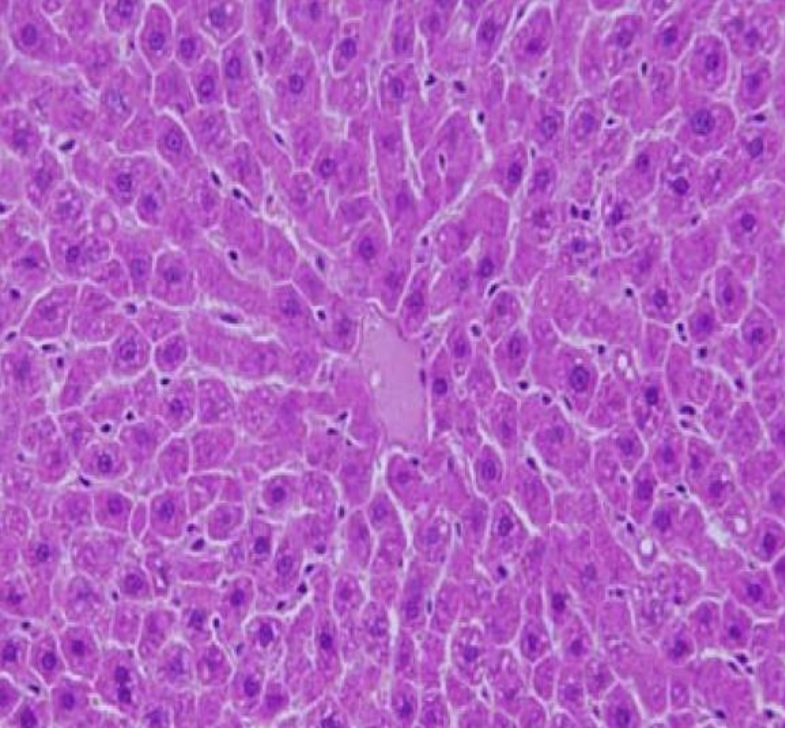
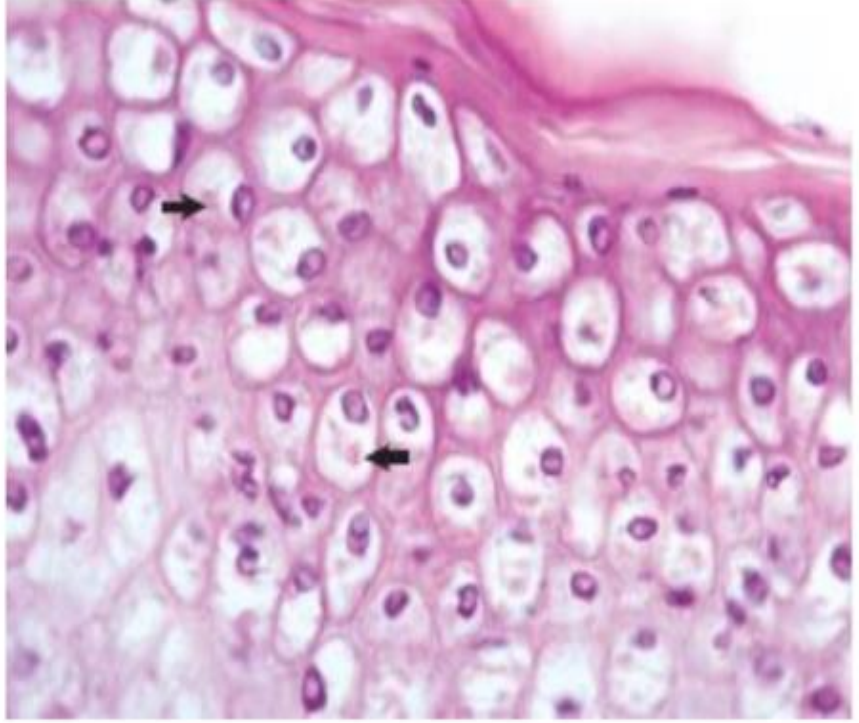
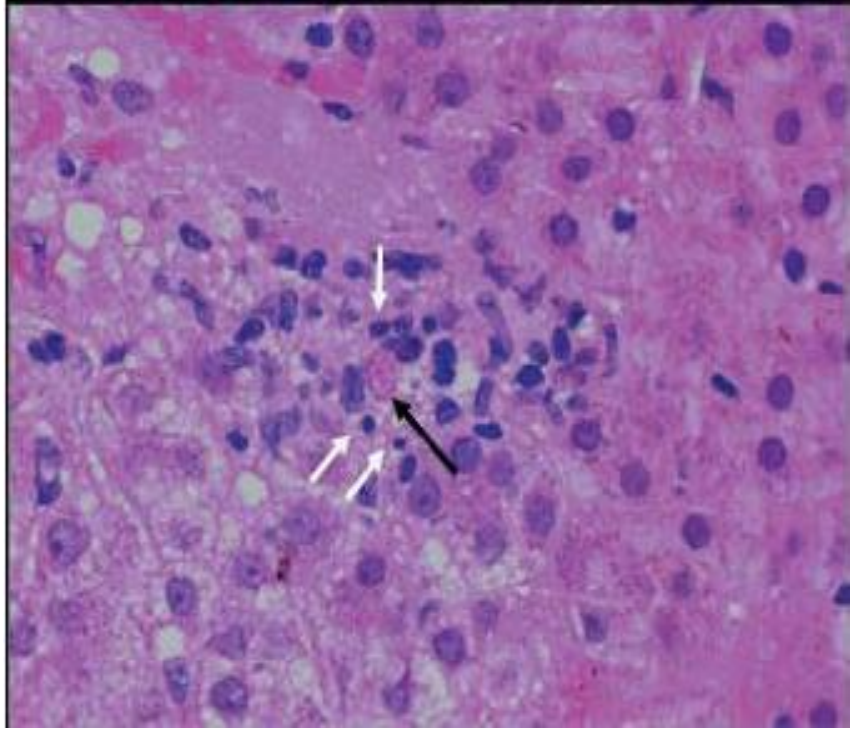
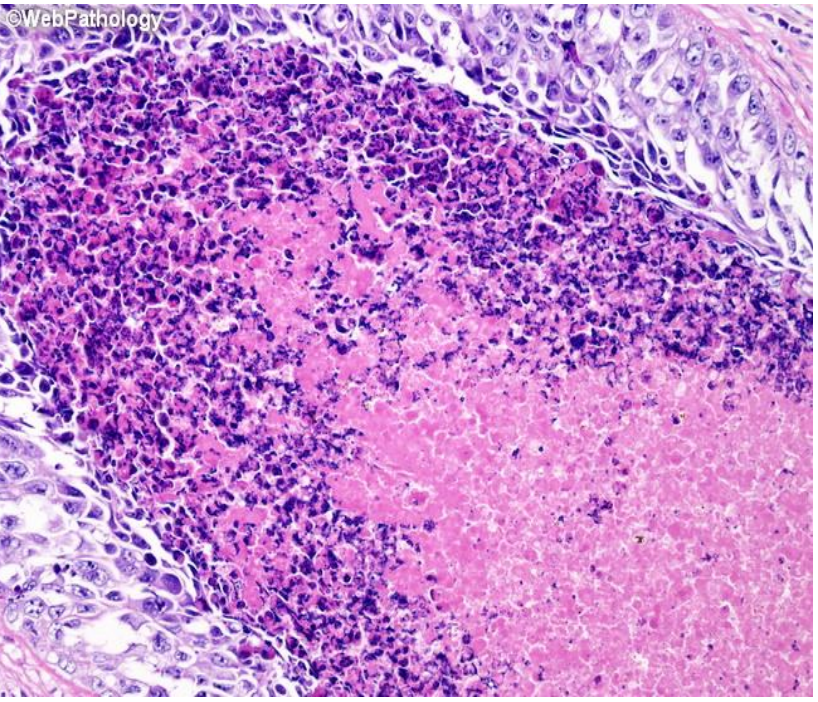


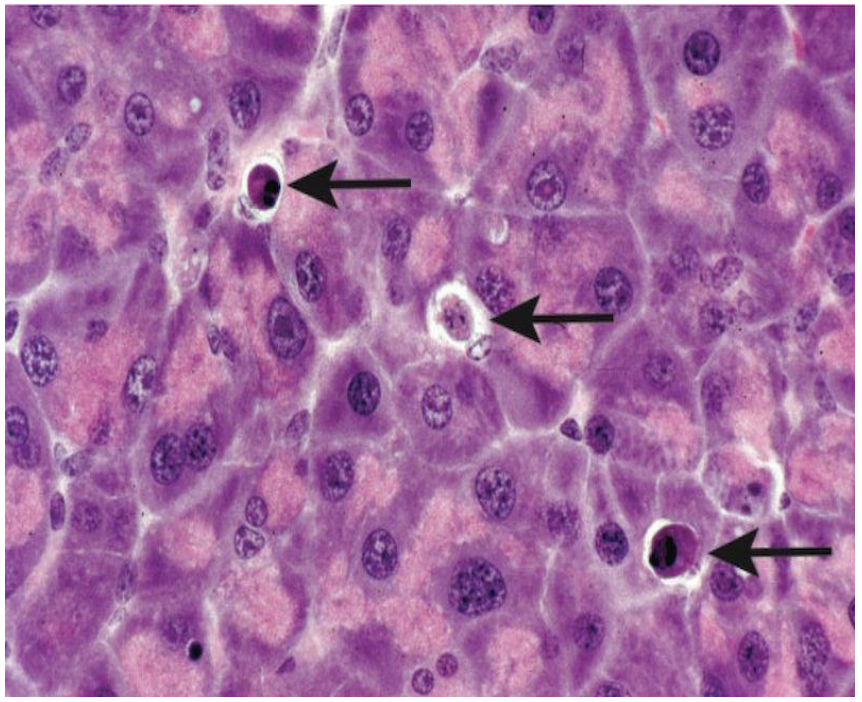
Figure 2-9A Morphologic changes in reversible cell injury and necrosis. **A,** Normal kidney tubules with viable epithelial cells. **B,** Early (reversible) ischemic injury showing surface blebs, increased eosinophilia of cytoplasm, and swelling of occasional cells. **C,** Necrosis (irreversible injury) of epithelial cells, with loss of nuclei, fragmentation of cells, and leakage of contents. The ultrastructural features of these stages of cell injury are shown in Fig. 2-10.

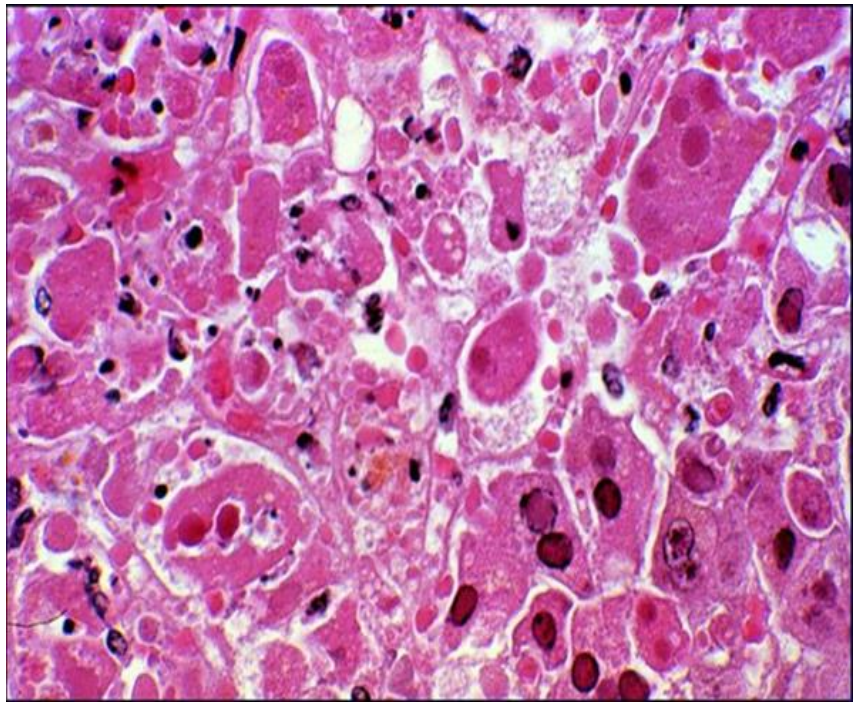







©WebPathology





A 55-year-old-man on irregular treatment for hypertension for the last 5 years presented with complaints of increasing breathlessness.

Upon examination, pulse was 90/min, Blood Pressure (BP) 160/110 mmHg and there was mild bilateral pedal edema.

Despite treatment over the next three months, BP was poorly controlled and one day while climbing stairs he had acute chest pain, collapsed and died.

This is an image of the heart on post-mortem examination

Identify the pathologic change. Which chamber of the heart is affected and why?

Long-term high blood pressure strains the left side of the heart, causing it to grow bigger

What is cause of the pathophysiologic change?

Response of the heart to increased workload, Cardiac hypertrophy is usually characterized by an increase in cardiomyocyte size and thickening of ventricular walls

What cellular changes occur in myocardial ischemia?

Myocardial ischemia leads to progressive cellular injury due to reduced oxygen and nutrient supply.

Reversible Cell Injury (within minutes to early hours)
Irreversible Cell Injury (after prolonged ischemia, ~20–40 minutes onward)

What are the possible outcomes of ischemic injury?

Reversible Injury with Recovery (if ischemia is brief and blood flow is restored in time)

- Cells regain function if ATP production resumes.
- Seen in transient ischemia (e.g., unstable angina).

- Cell Death (Necrosis or Apoptosis)
- Necrosis (Predominantly Coagulative Necrosis in MI)
  - Loss of nuclei, eosinophilic cytoplasm, and neutrophilic infiltration.
- Apoptosis (if mild, in periphery of infarct area).

In hypoxic cell injury, cell swelling occurs because of increased intracellular:

A.Lipid

B.Protein

C.Lipofuscin

D.Water

E.Glycogen

A patient is admitted with severe substernal chest pain for 4 hours. Lab tests reveal an increased level of serum creatine kinase. This is most likely due to:

A. Mitochondrial swelling

B. Nuclear lysis

C. Damage of plasma membranes

D. Increased endoplasmic reticulum

E. Increased Golgi activity

A pathologist notes cloudy swelling, hydropic change, and fatty change in a patient's liver with a history of alcohol abuse. These morphological changes are all examples of:

A. Early neoplastic change

B. Hyaline change

C. Patterns of cell death

D. Postmortem artifact

E. Reversible cell injury

What would be an example of hypertrophy?

A. Breast development at puberty

B. Enlargement of the uterus during pregnancy

C. Enlargement of the uterus during menstruation

D. A papillomavirus induced skin wart

E. Liver regeneration after partial hepatectomy

Examples of hyperplasia include

A. cardiac enlargement seen in hypertension

A. fatty liver

A. skeletal muscle enlargement with weightlifting

A. glandular epithelium of pubertal breasts

A. Liver Cirrhosis

Additional Read

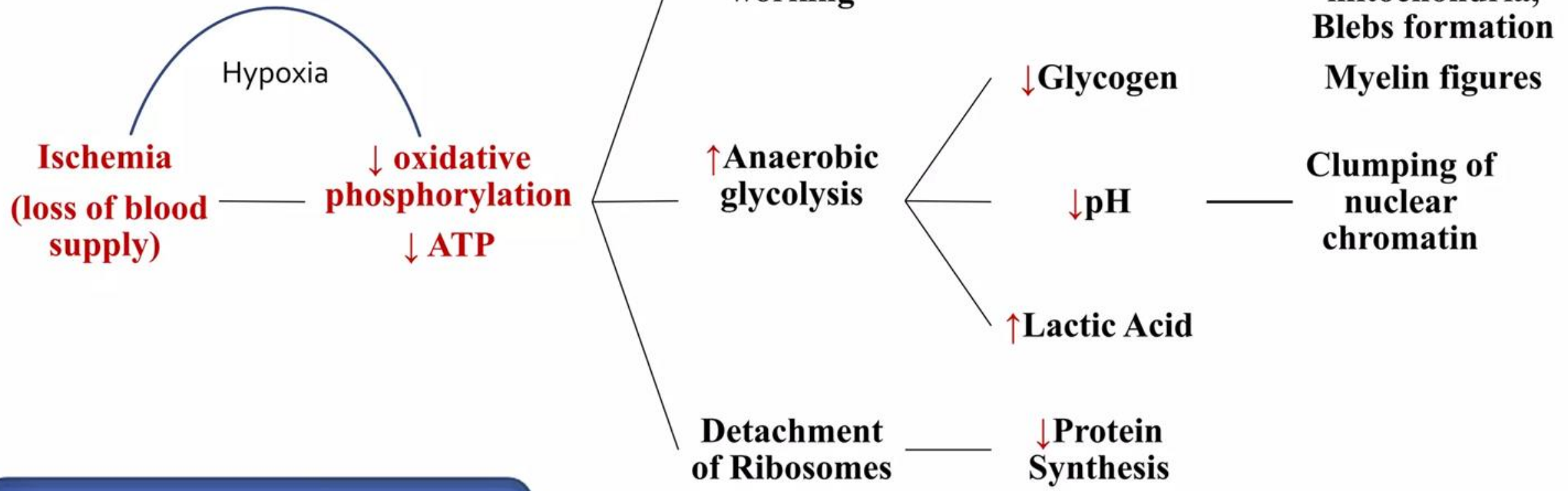
POINT OF NO RETURN????

1- The inability to reverse mitochondrial dysfunction (lack of oxidative phosphorylation and ATP generation) even after resolution of the original injury, and

2- Profound disturbances in membrane function

3- DNA damage

Mechanism Of Cell Injury



Mitochondria is the earliest organelle affected in cell injury