

* MECHANISM OF CELL INJURY (PATHOGENESIS)

For Class- B.Pharmacy 2nd Semester
Subject- Pathophysiology (BP204T)

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Introduction

Injury to cells may have many causes. In such case oxygen plays a central role in the cell injury.

Mechanisms of cell injury include-

Hypoxic & Ischemic cell injury

- Cell membrane damage
- Mitochondrial damage
- Ribosome damage
- Nuclear damage

Free radicle mediation of cell injury

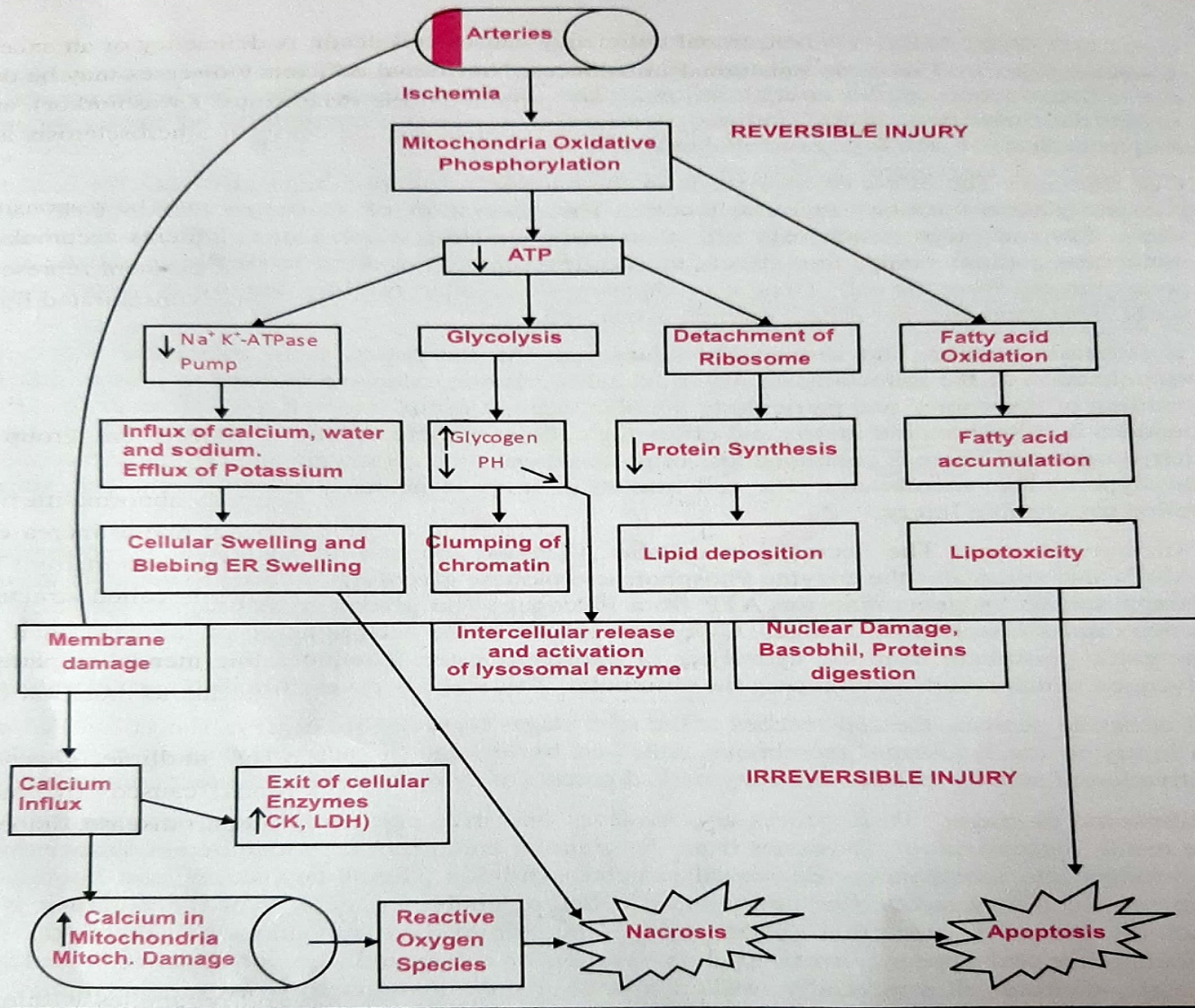
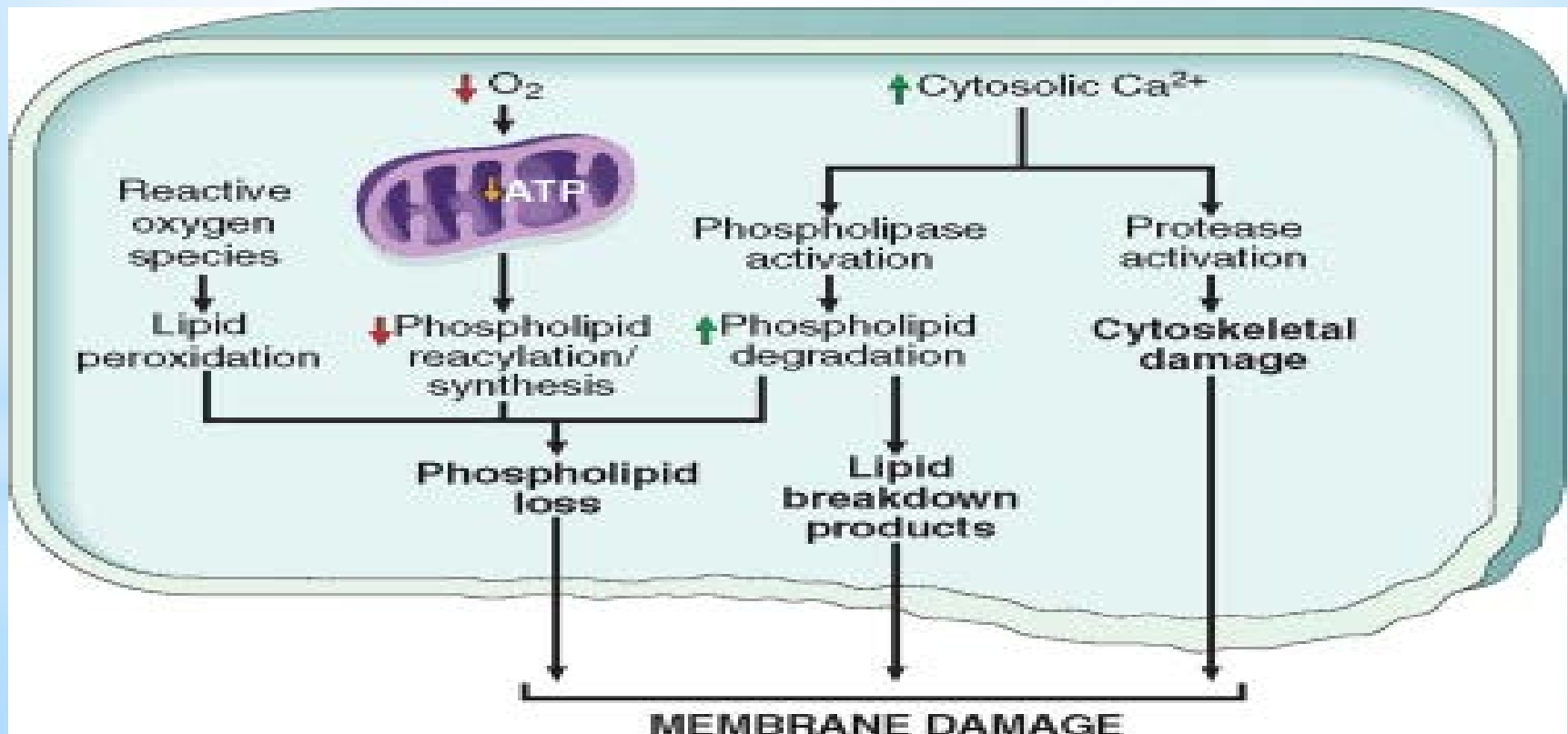


FIGURE 15-15 A detail diagram reversible and irreversible ischemic cell injury. The ATP levels have a key role, ischemia can cause direct membrane damage, mitochondrial damage, ribosome damage and nuclear damage

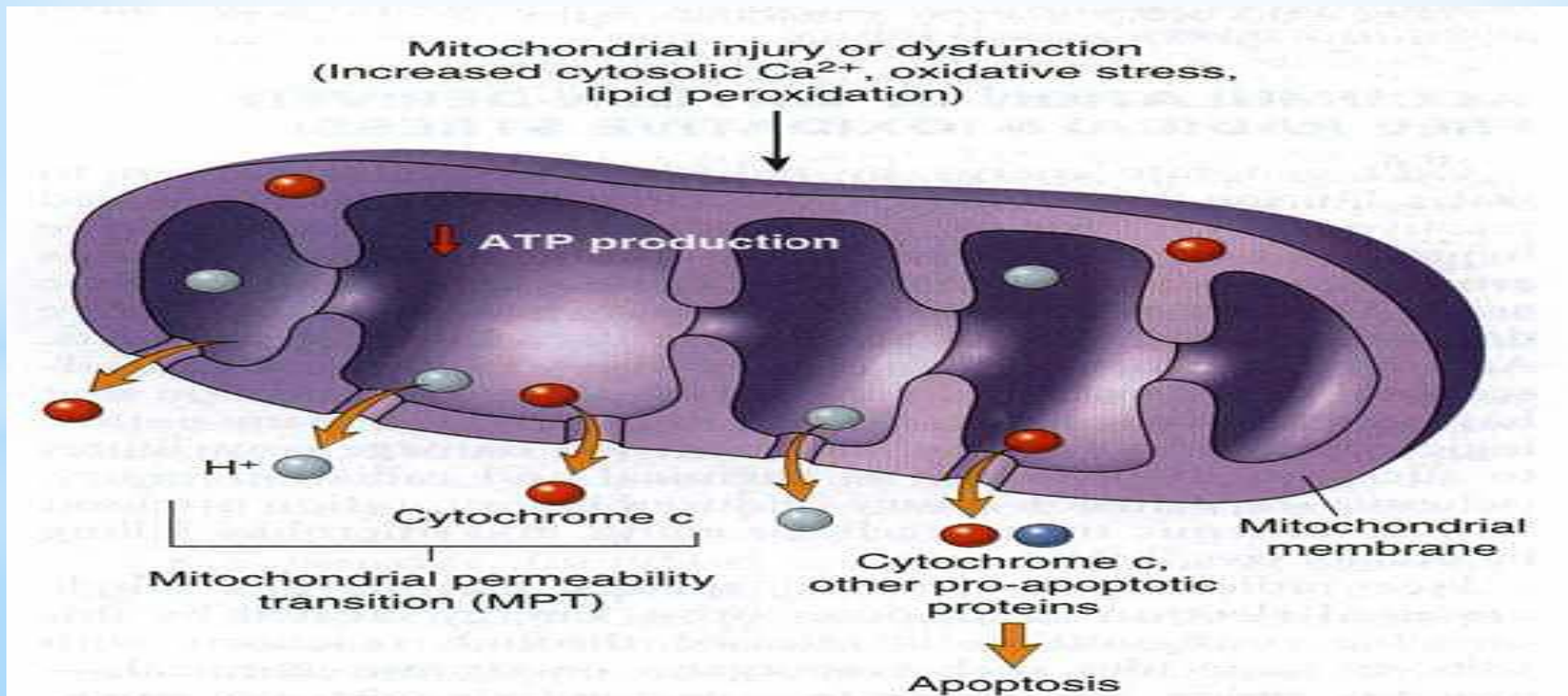
Cell membrane damage

- ❑ Physical agents such as heat or radiation can damage a cell by literally cooking or coagulating their contents.
- ❑ Impaired nutrient supply, such as lack of oxygen or glucose, or impaired production of adenosine triphosphate (ATP) may deprive the cell of essential materials needed to survive.



Mitochondrial damage

- ❑ Increases in cytosolic Calcium, coupled by an increase in inorganic phosphate and certain fatty acids.
- ❑ High inorganic phosphate and fatty acids alone cannot damage the mitochondria but coupled with high Ca^{2+} are extremely damaging to a cell. Note that high Calcium alone can still damage mitochondria.



Ribosome damage

- ❑ Leading to altered protein synthesis.
- ❑ If hypoxia continues, intracellular protein synthesis decreases due to damage to ribosomes and polysomes. Continue hypoxia causes cytoskeleton changes with loss of microvilli and formation of blebs on the surface of the cell. This swelling results in swelling at mitochondria and ER (endoplasmic reticulum).

Nuclear damage

- ❑ The decrease in cellular ATP and increase in adenosine monophosphate (AMP) also stimulates the enzyme phosphofructokinase glycolysis in order to maintain the cells energy source by generating the ATP from glycogen.
- ❑ This stage is reversible if oxygen is restored.

Free radicle mediation of cell injury

- ❑ Free radicals are chemical species that have a single unpaired electron in outer orbit. Free radicals initiate autocatalytic reaction.
- ❑ It is mainly occur in reperfusion of the ischemic cell. There are many more causes like chemical injury, cellular aging, hyperoxia, killing of exogenous biological agents, destruction of tumor cells, inflammatory damage, chemical injuries, ionization, arteriosclerosis.
- ❑ There are some radicals, like superoxide radicals, hydroxyl ions, peroxide ions, very destructive to cells which cause lipid peroxidation, oxidation of protein, DNA damage, cytoskeleton damage etc.