MECHANISM OF CELL INJURY

① DECREASED PRODUCTION OF ATP :

↓

Required for all processes within the cell.

→ INJURY LIKE HYPOXIA, CHEMICALS (eg. Cyanide) CAN CAUSE ↓ed ATP PRODUCTION.

→ EFFECTS OF ↓ed ATP :
i) Failure of cell membrane Na^+ pump.
ii) ↑ed Anaerobic Glycolysis
iii) Failure of Ca^{2+} pump.
iv) Failure of Protein synthesis in Ribosomes.

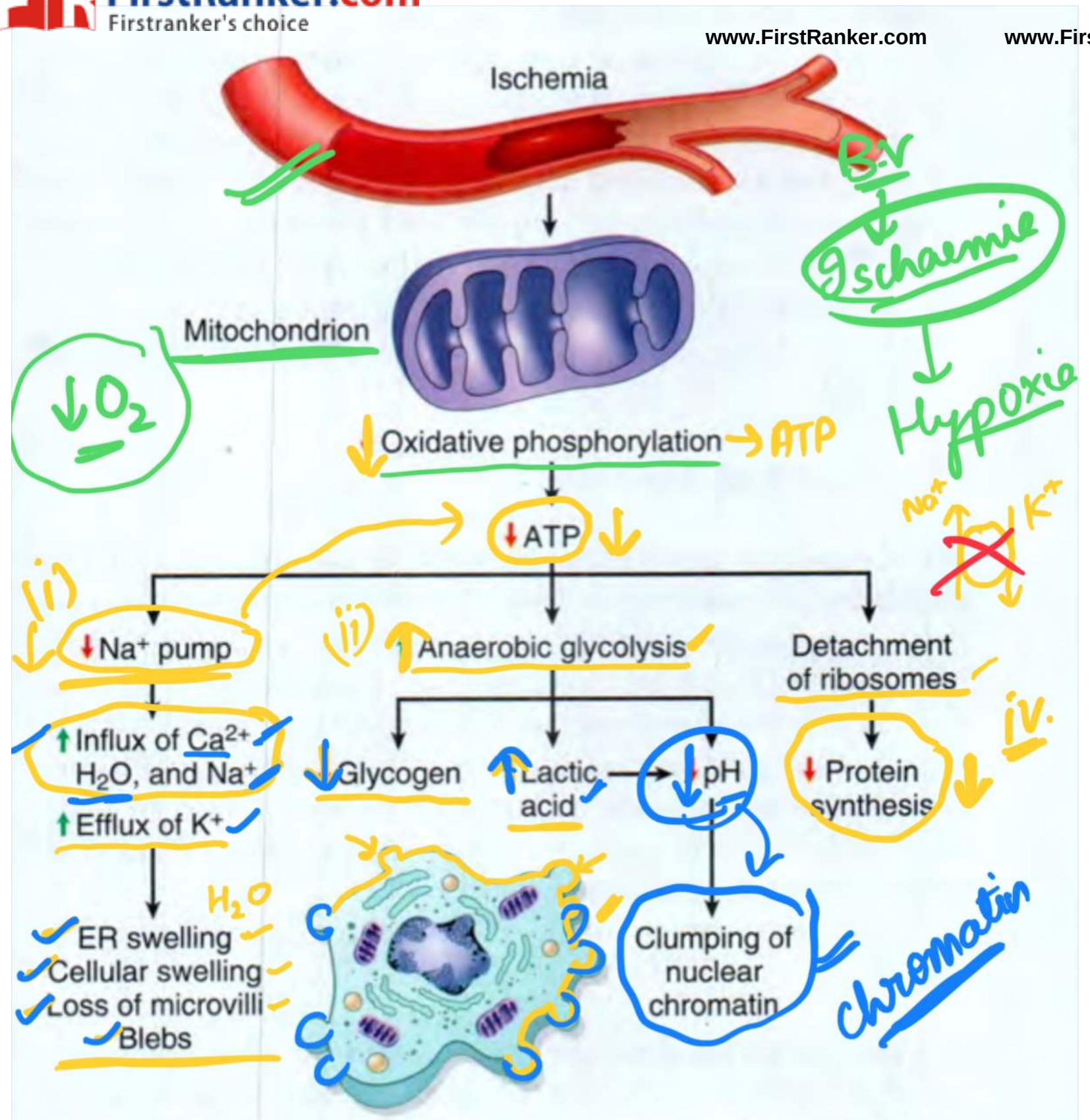

Figure 2-17 Functional and morphologic consequences of decreased intracellular adenosine triphosphate (ATP) during cell injury. The morphologic changes shown here are indicative of reversible cell injury. Further depletion of ATP results in cell death, typically by necrosis. ER, Endoplasmic

reticulum.

② MITOCHONDRIAL DAMAGE :

→ MITOCHONDRIA ARE SENSITIVE TO ALMOST ALL TYPES OF INJURIOUS STIMULI. (eg. Hypoxia, Toxins).

→ CONSEQUENCES :

i) Depletion of ATP.
ii) Formation of Reactive Oxygen Species [ROS].
iii) Formation of Mitochondrial Permeability Transition Pore.
iv) Leakage of Mitochondrial Proteins into cytoplasm.

③ INFLUX OF CALCIUM & LOSS OF CALCIUM HOMEOSTASIS:

→ NORMALLY, CONCENTRATION OF CYTOSOLIC CALCIUM IS LOW & MOST OF IT IS SEQUESTERED IN MITOCHONDRIA & ER.

→ ISCHAEMIA & CERTAIN TOXINS CAUSES ↑ IN CYTOSOLIC CALCIUM.

→ INITIALLY, IT IS DUE TO RELEASE FROM INTRACELLULAR STORES & LATER DUE TO INFLUX ACROSS CELL MEMBRANE.

④ ACCUMULATION OF OXYGEN DERIVED FREE RADICALS : → ROS.

(eg. H_2O_2 ; SUPEROXIDE ANION ; HYDROXYL IONS)

→ FREE RADICALS ARE UNSTABLE CHEMICAL COMPOUNDS WITH A SINGLE UNPAIRED e^- IN OUTER ORBIT.

→ NORMALLY, FREE RADICALS PRODUCED IN THE CELL ARE UNSTABLE & ARE RAPIDLY DESTROYED.

→ WHEN FREE RADICALS REACT WITH ANY MOLECULE THEY CONVERT THOSE MOLECULES INTO FREE RADICALS & INITIATE AUTOCATALYTIC REACTIONS.

→ EXCESS OF FREE RADICALS MAY BE EITHER DUE TO ↑ed PRODUCTION OR INEFFECTIVE DEGRADATION.

→ PATHOLOGIC EFFECTS OF FREE RADICALS :

i) LIPID PEROXIDATION IN MEMBRANES- causes extensive membrane

damage.

ii) CROSS LINKING & OXIDATIVE MODIFICATION OF PROTEINS - damages enzyme activity & causes abnormal folding of proteins.

iii) DAMAGE TO DNA.

* FREE RADICALS CAN ACTIVATE BOTH NECROSIS & APOPTOSIS.

CELL INJURY

REVERSIBLE	IRREVERSIBLE
• cell can return to	• cell cannot return

NORMAL to NORMAL.