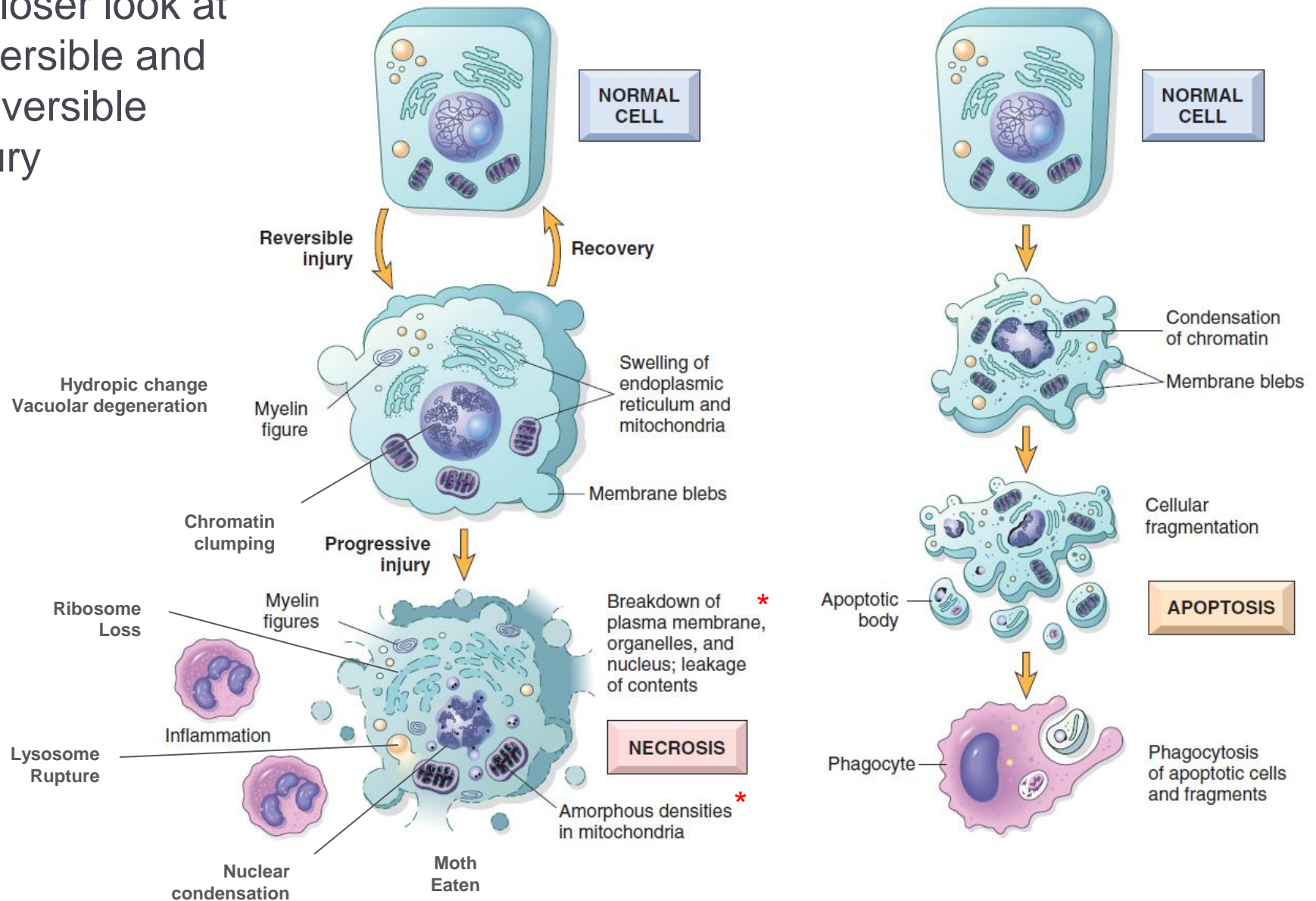


Cell Injury & Death

A closer look at reversible and irreversible injury



► * Irreversible membrane dysfunction & mitochondrial dysfunction ≈ Irreversible injury

Causes and Mechanisms of Cell injury

Causes of Cell Injury Quiz!

- ▶ Hypoxia and ischemia
- ▶ Immunological reactions
- ▶ “Chemical” agents
- ▶ Genetic defects
- ▶ “Physical” agents
- ▶ Nutritional defects
- ▶ Infections
- ▶ Aging



Principles & mechanisms of cell injury

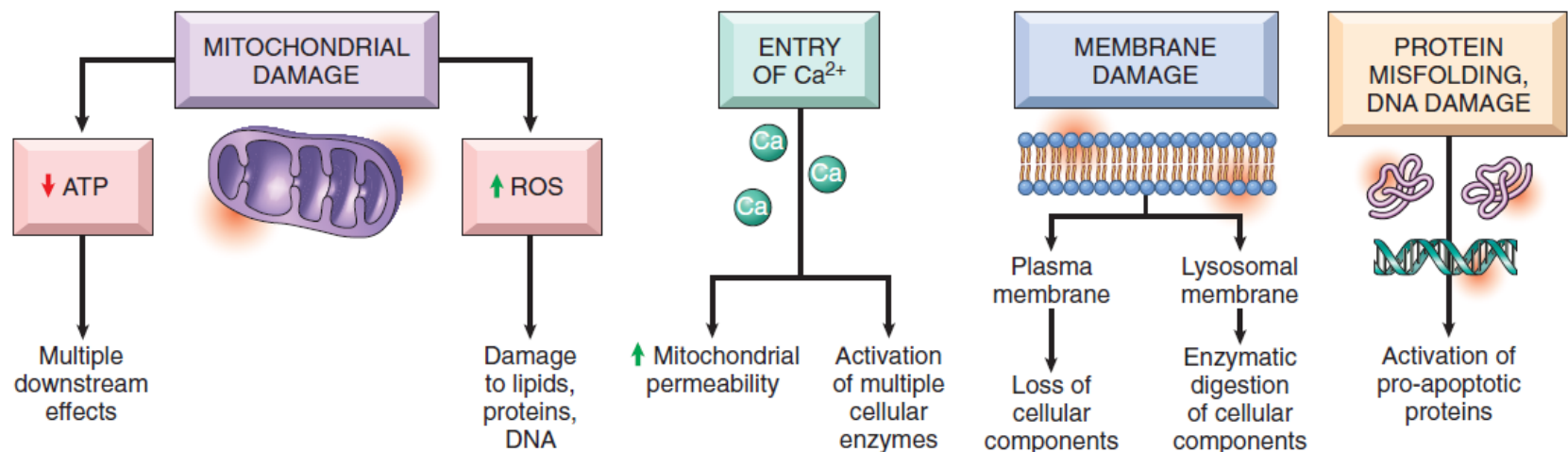
▶ Injury outcome depends on:

▶ Injury

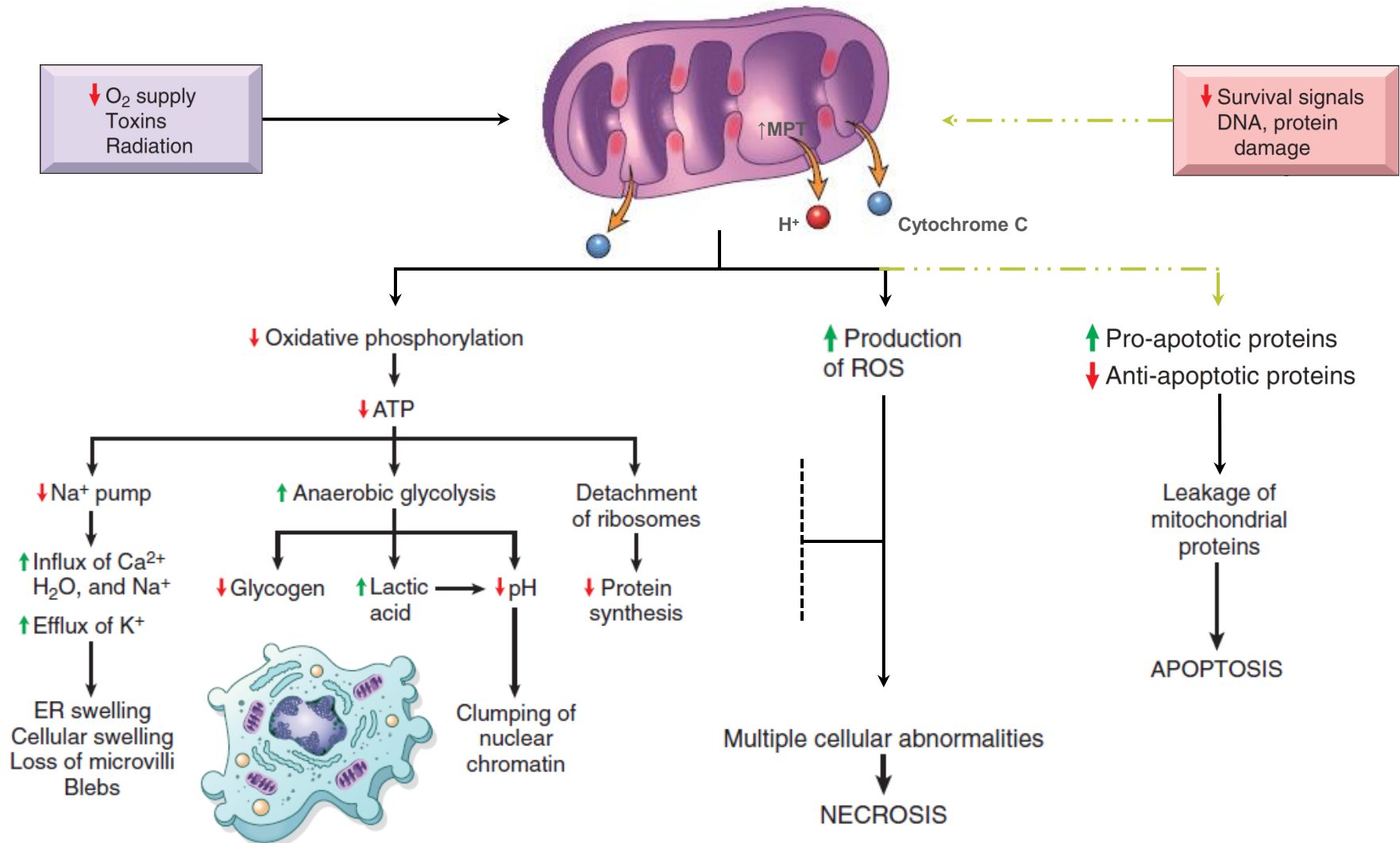
- ▶ Type
- ▶ Duration
- ▶ Dose

▶ Cell

- ▶ Type (including genetic makeup and polymorphisms)
- ▶ Adaptability (including basal state)

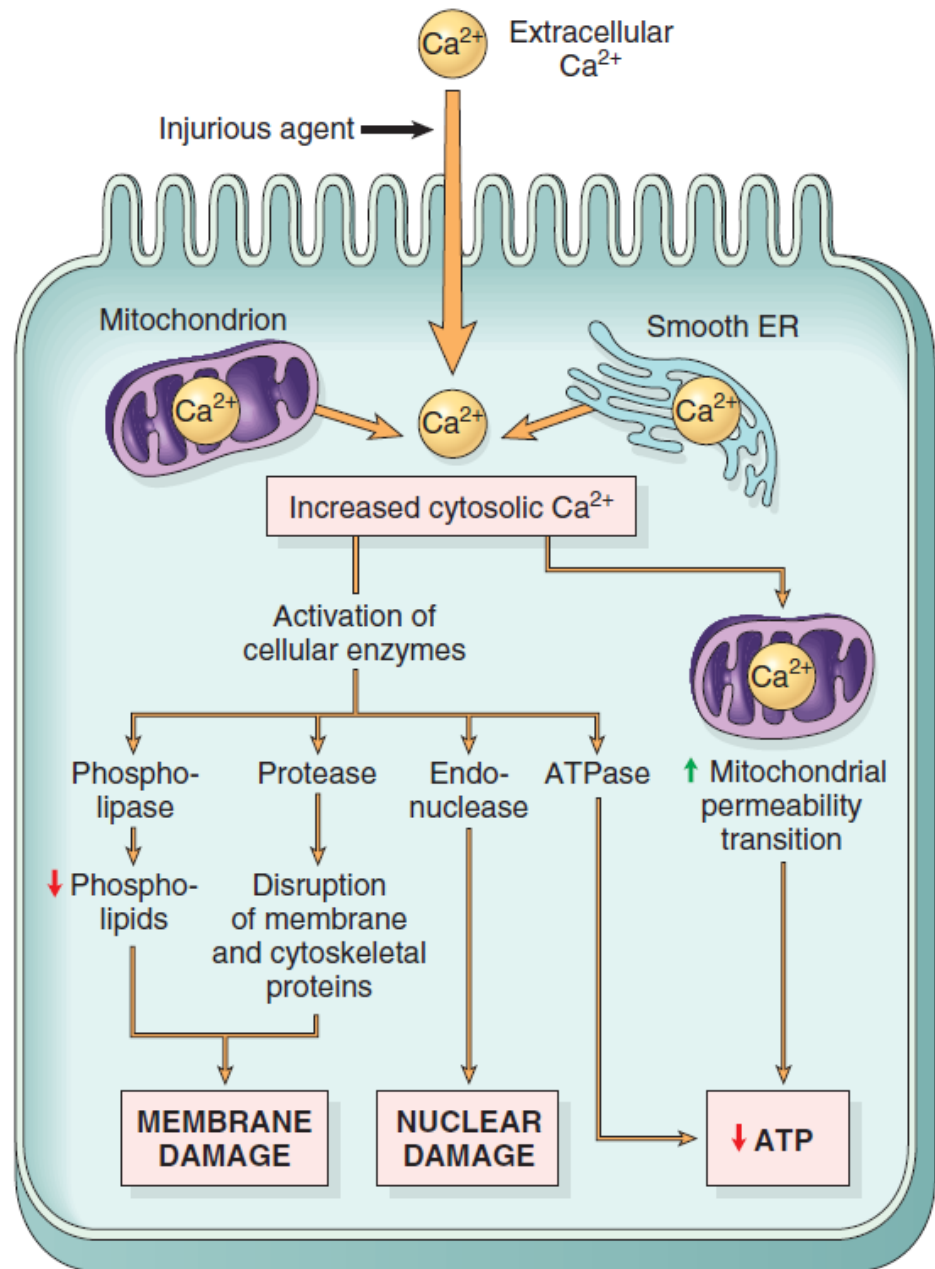


Mitochondria

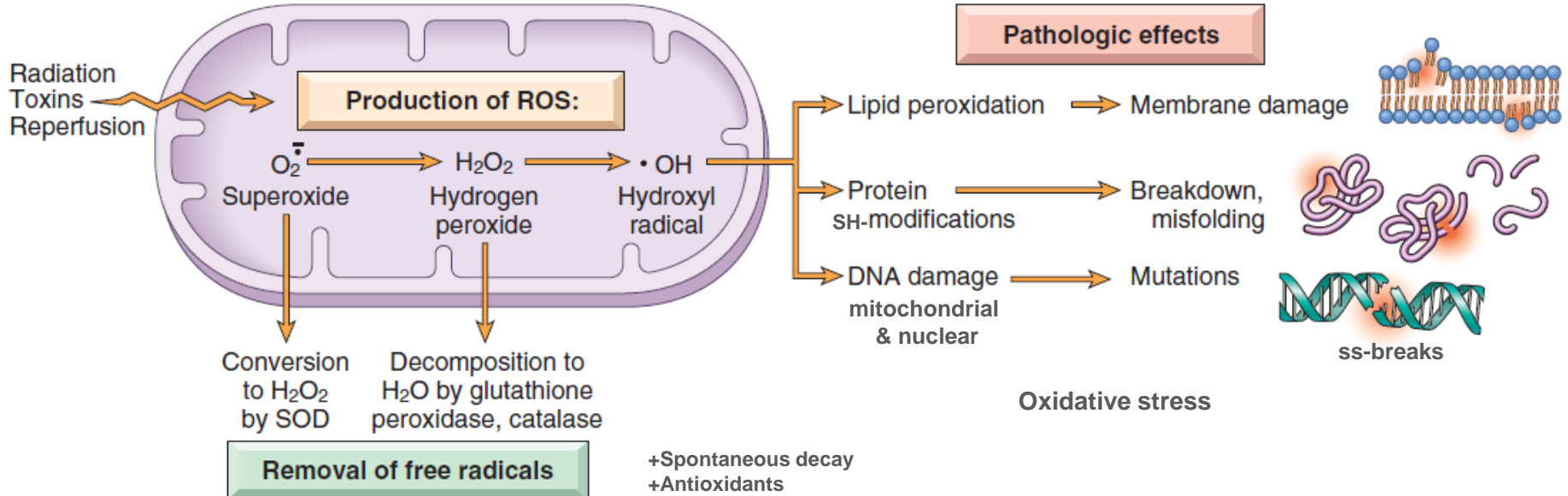
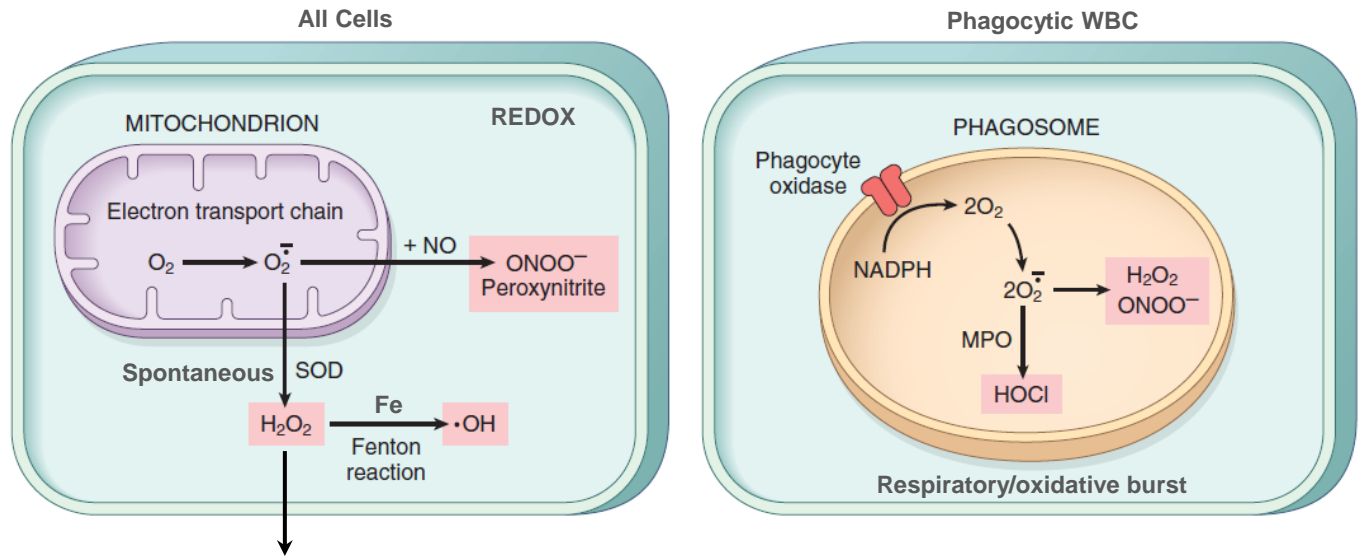
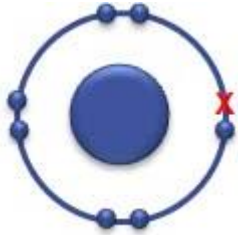


Ca²⁺ influx

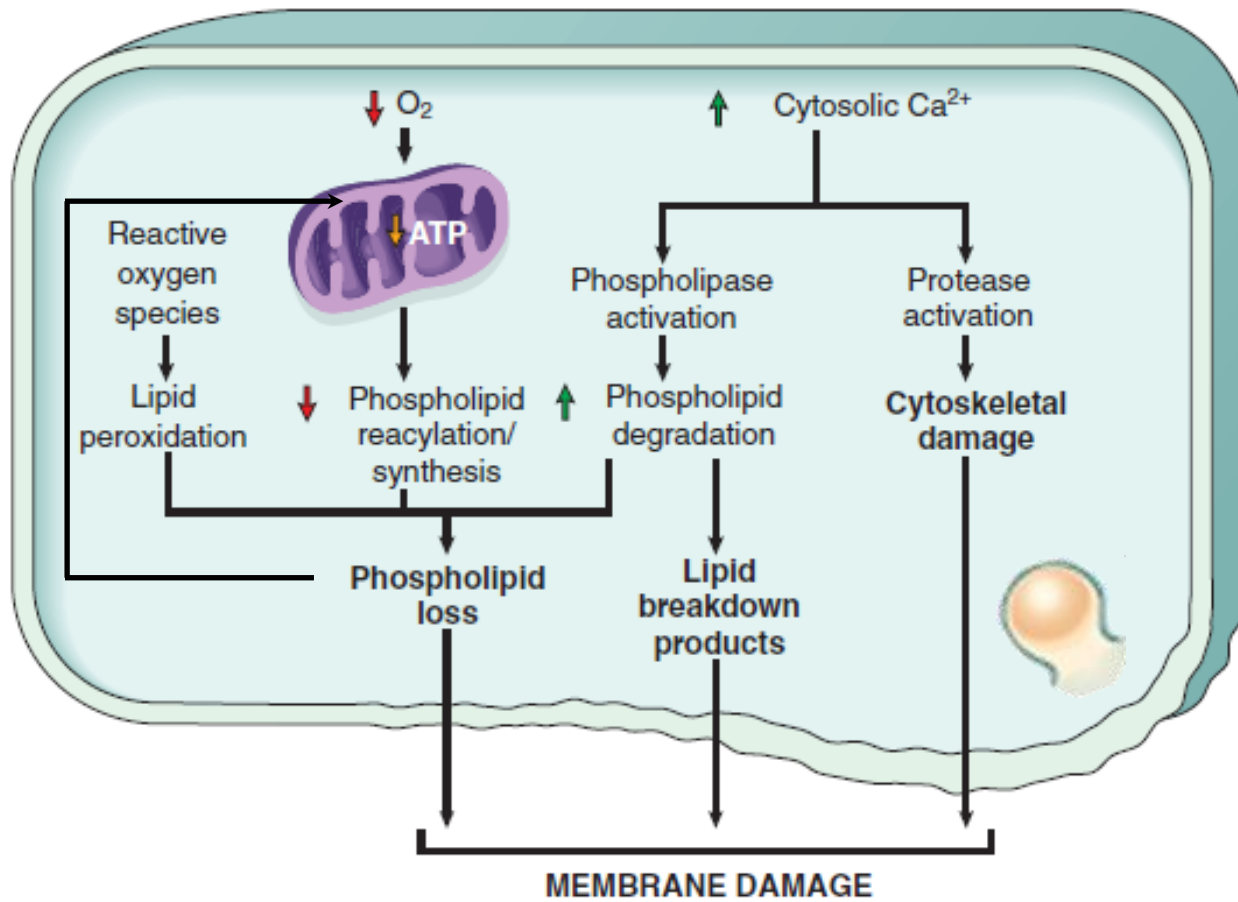
- ▶ 10,000x difference in conc.
- ▶ ATP dependent conc. Gradient
- ▶ Low EC Ca²⁺ delays cell death



Free radicals & ROS



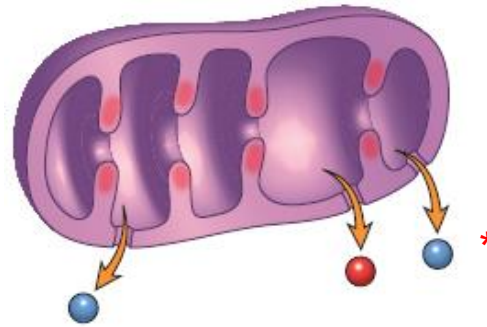
Membrane damage



Causes and Mechanisms of Cell injury in practice

Hypoxia Ischemia

2



1

↓ Oxidative phosphorylation

↓ ATP

↓ Protein
synthesis

↓ Glycogen

↑ Lactic
acid

Pump failure
cell swelling

↓ pH

↑ Influx of Ca^{2+}

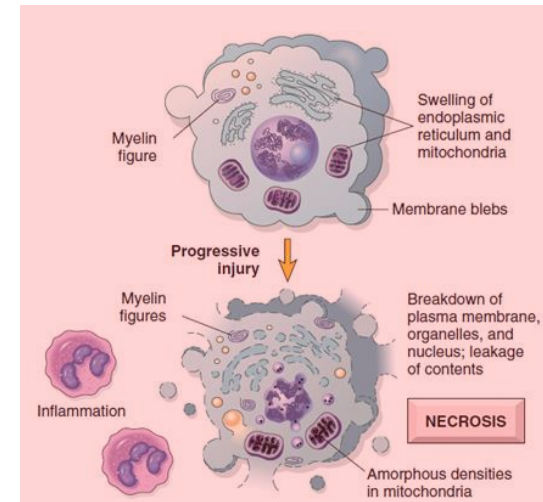
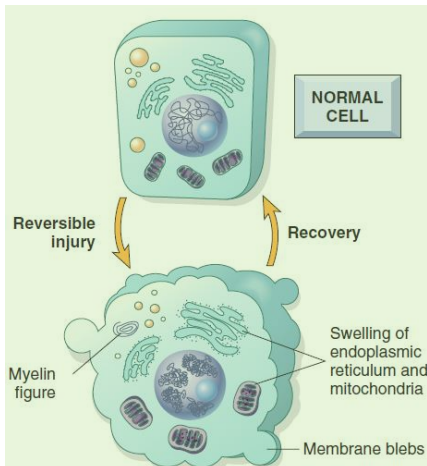
↑ Mitochondrial
permeability
transition

+
Activation of
cellular enzymes

Accumulation
of ROS

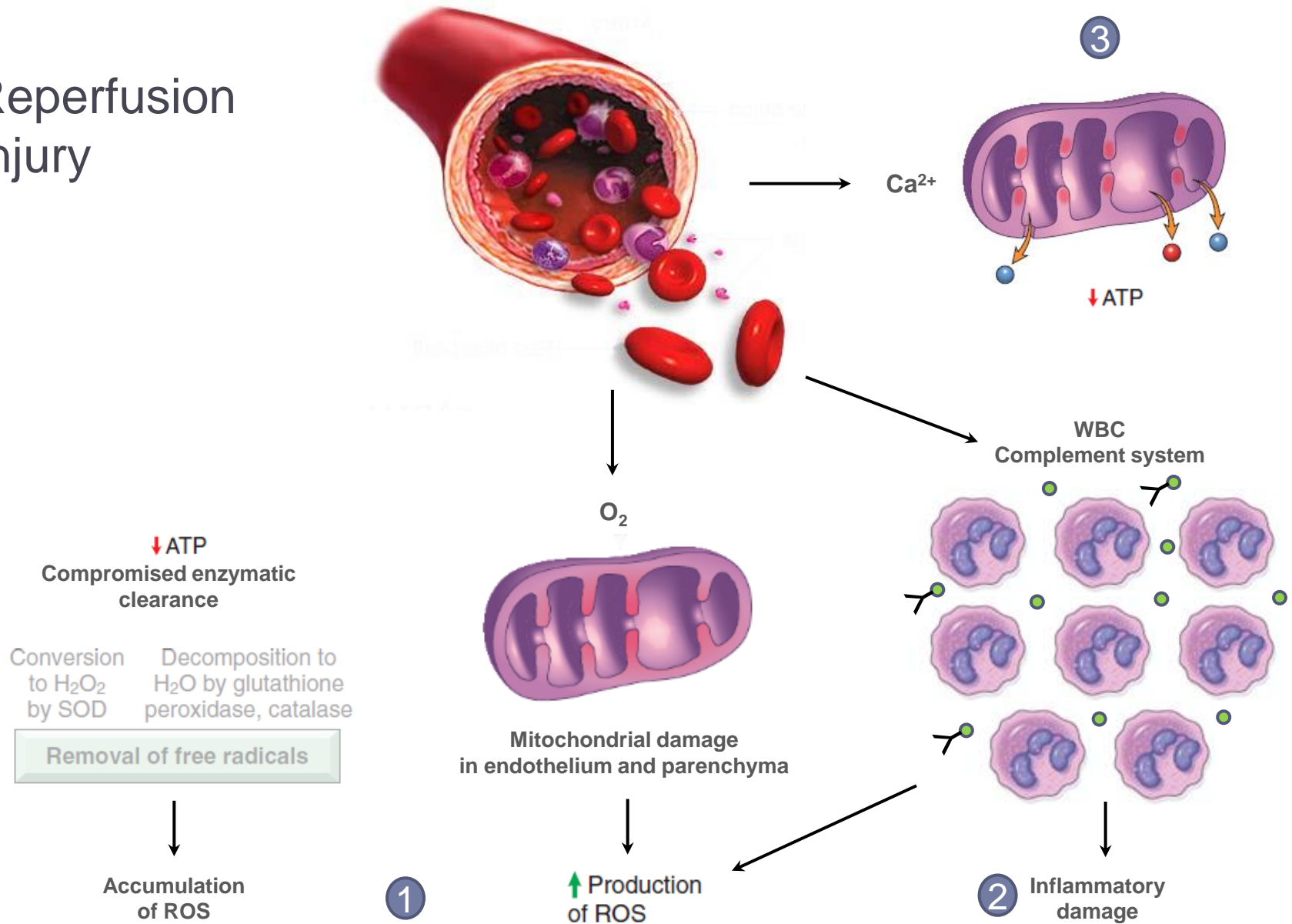
3

↓
Phospholipid
loss



* Some apoptosis may also occur due to leakage of pro-apoptotic molecules

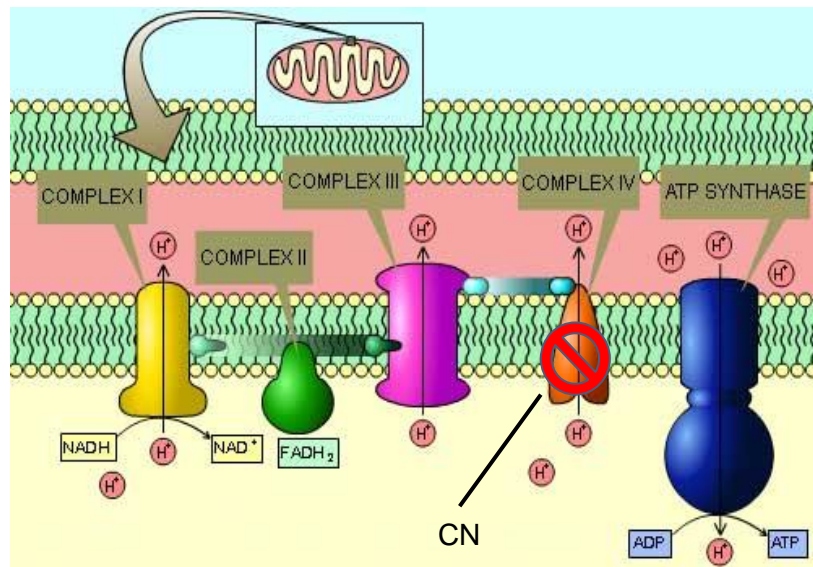
Reperfusion Injury



Chemical (Toxic) Injury

Direct toxicity

► Cyanide



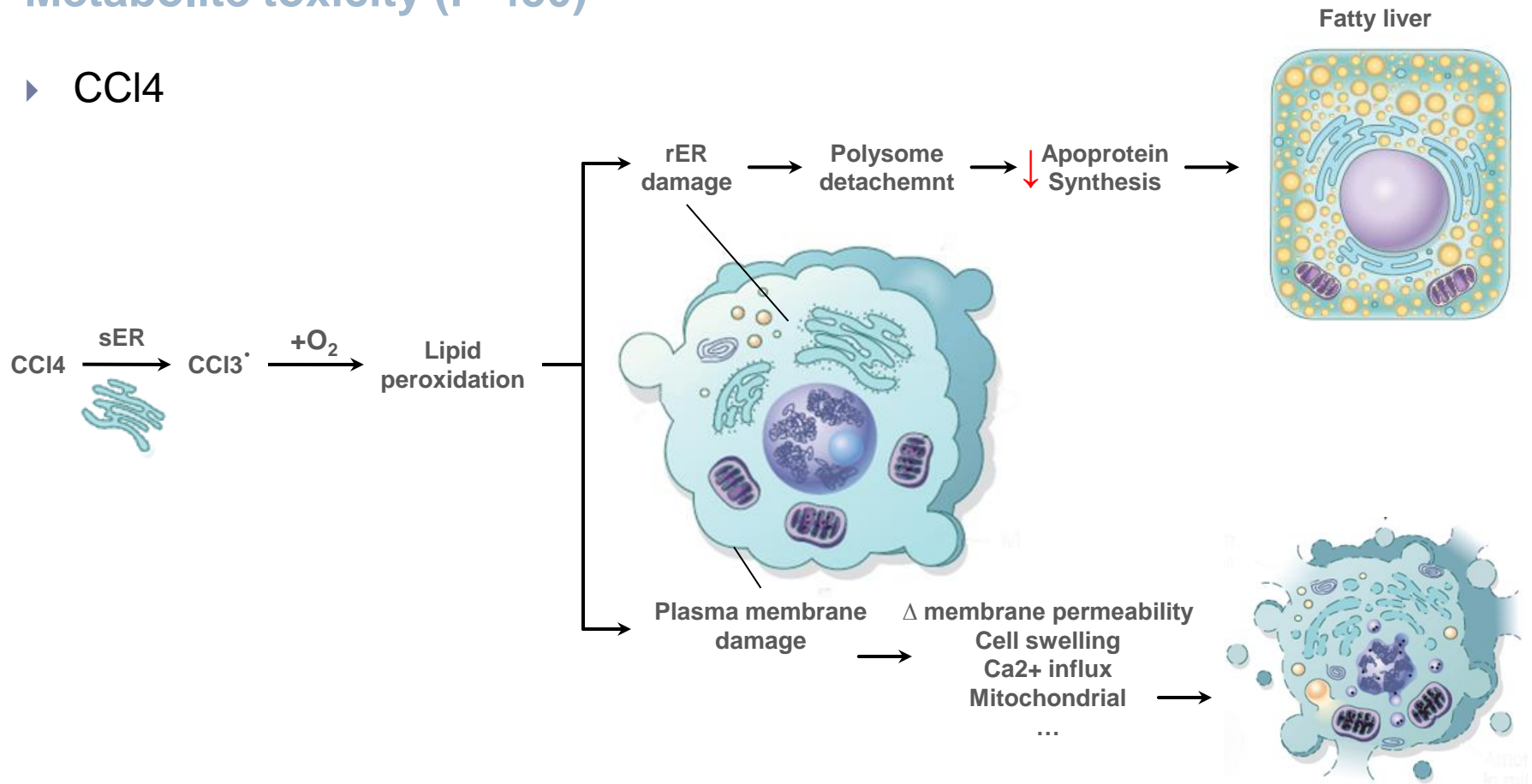
- Mercuric chloride (seafood)
 - SH-membrane proteins
 - Δ membrane permeability

The greatest damage is usually to the cells that use, absorb, excrete, or concentrate the chemicals.

Chemical (Toxic) Injury

Metabolite toxicity (P-450)

► CCl₄



Chemical (Toxic) Injury

Metabolite toxicity (P-450)

