

## Cell Injury & Death

A closer look at reversible and NORMAL NORMAL irreversible CELL CELL injury Reversible Recovery injury Condensation 00 of chromatin Swelling of Membrane blebs Hydropic change endoplasmic reticulum and Vacuolar degeneration Myelin mitochondria figure Membrane blebs Cellular Chromatin fragmentation clumping Progressive injury Myelin Breakdown of Apoptotic **APOPTOSIS** Ribosome figures body plasma membrane, Loss organelles, and nucleus; leakage of contents Inflammation **NECROSIS** Phagocytosis Lysosome Phagocyte of apoptotic cells Rupture and fragments Amorphous densities in mitochondria Moth **Nuclear** Eaten condensation

<sup>\*</sup> 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

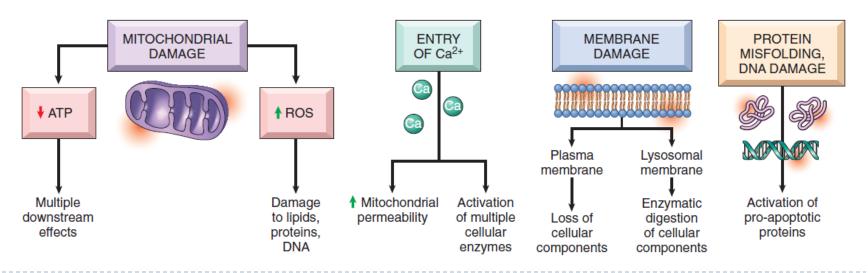
Aging



### Principles & mechanisms of cell injury

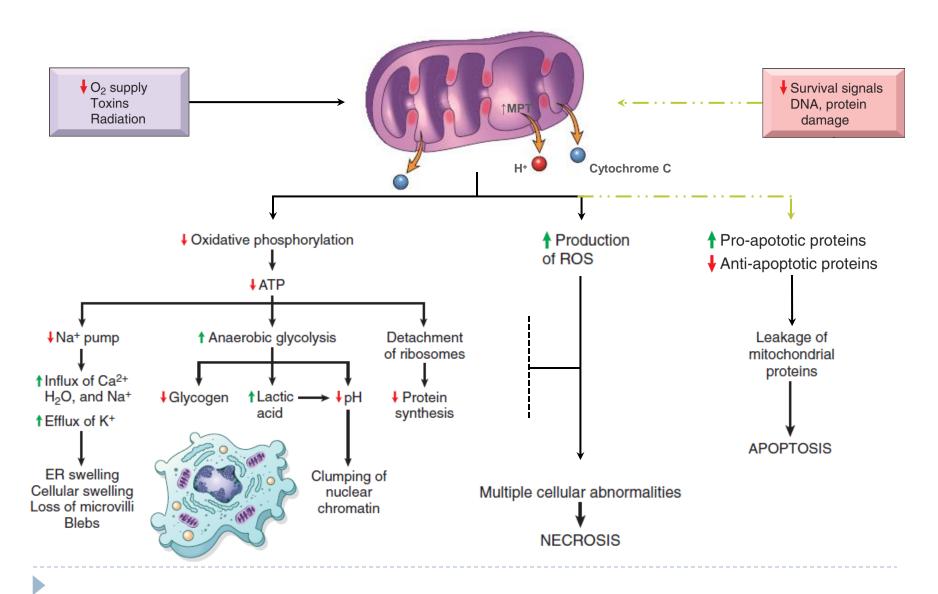
- Injury outcome depends on:
  - Injury
    - Type
    - Duration
    - Dose

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



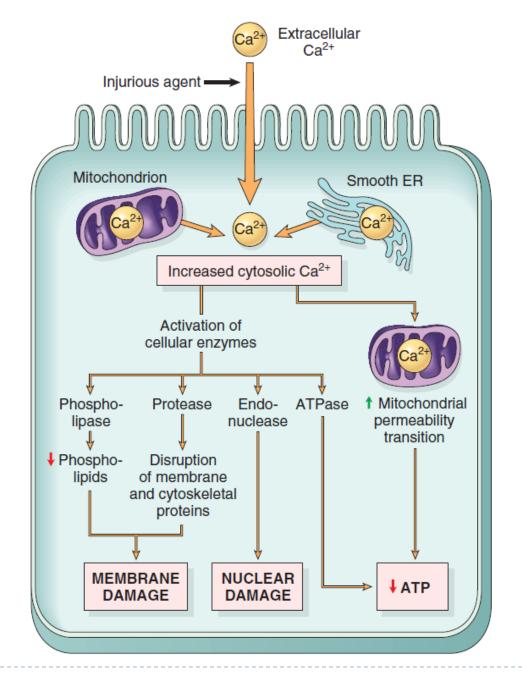


### Mitochondria



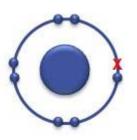
### Ca<sup>2+</sup> influx

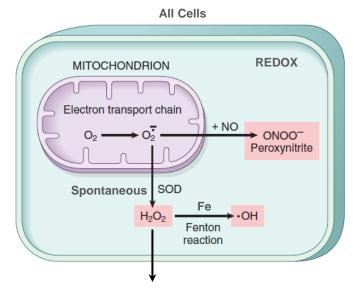
- ▶ 10,000x difference in conc.
- ATP dependent conc. Gradient
- ▶ Low EC Ca²+ delays cell death

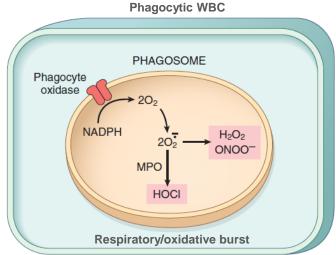


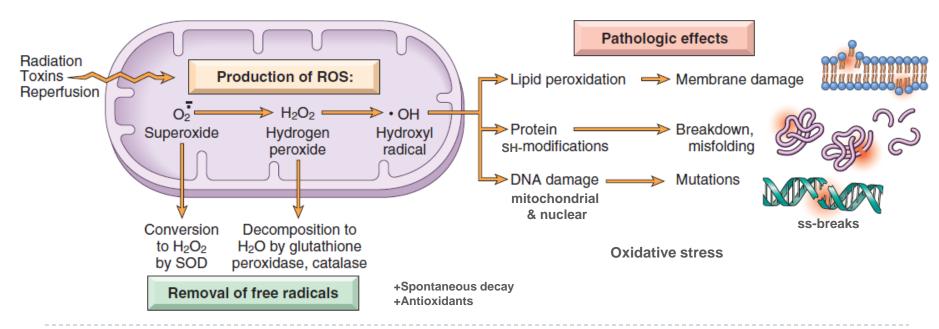


# Free radicals & ROS

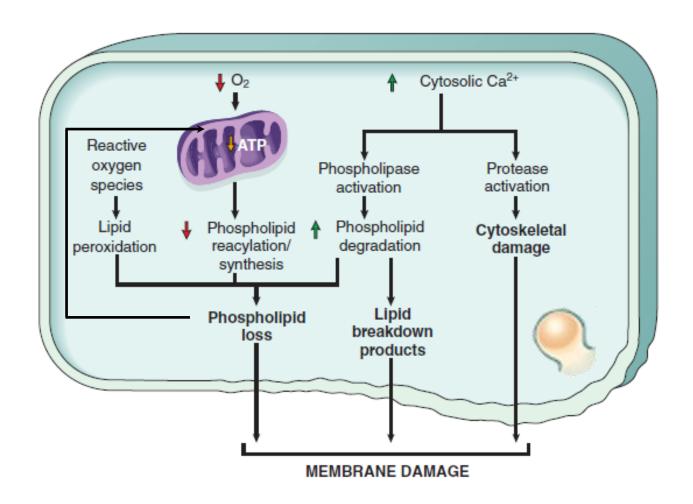






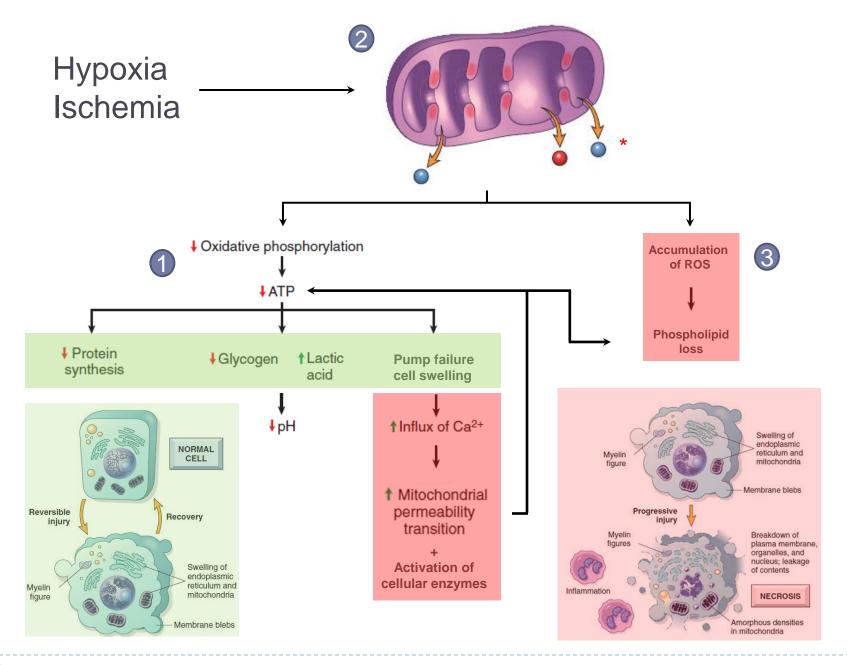


# Membrane damage



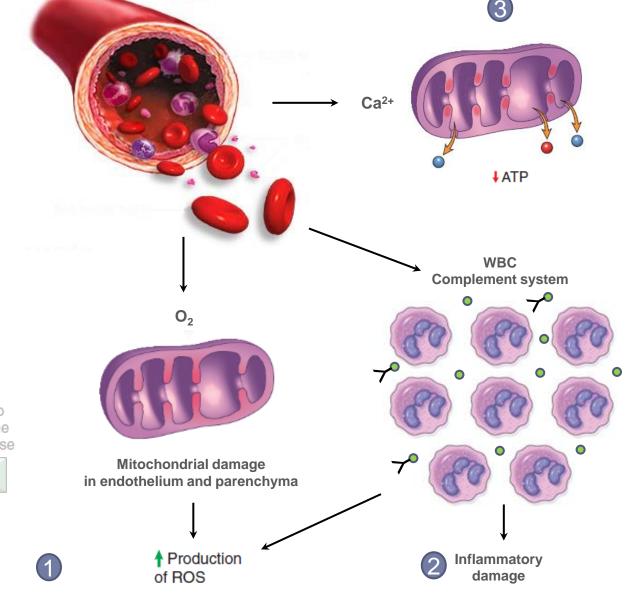


# Causes and Mechanisms of Cell injury in practice



<sup>\*</sup> Some apoptosis may also occur due to leakage of pro-apoptotic molecules

# Reperfusion Injury



↓ATP
Compromised enzymatic clearance

Conversion Decomposition to to H<sub>2</sub>O<sub>2</sub> H<sub>2</sub>O by glutathione peroxidase, catalase

Removal of free radicals

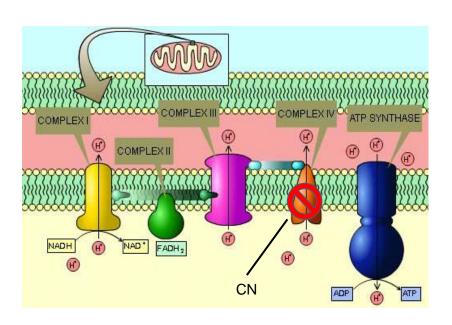
Accumulation of ROS



## Chemical (Toxic) Injury

### **Direct toxicity**

Cyanide

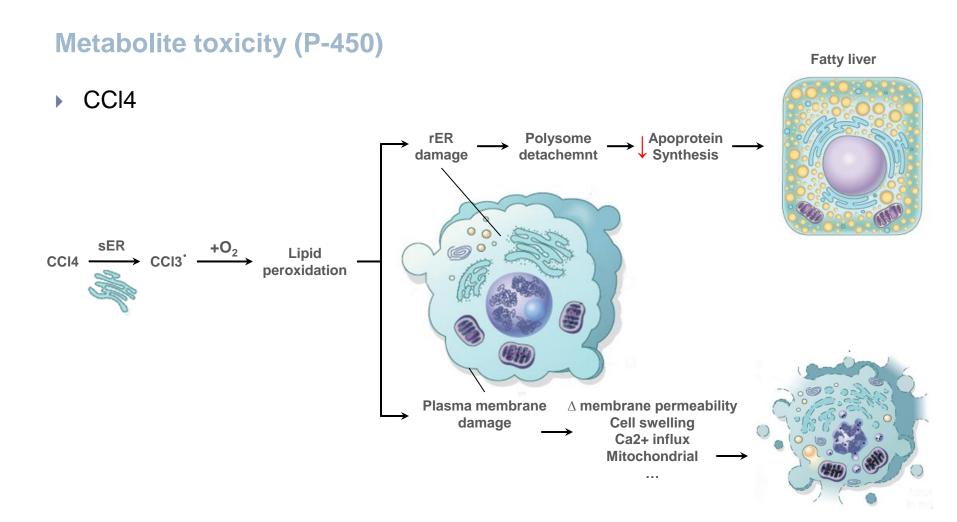


- Mercuric chloride (seafood)
  - SH-membrane proteins
  - ▶ ∆ membrane permeability

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



## Chemical (Toxic) Injury



## Chemical (Toxic) Injury

#### **Metabolite toxicity (P-450)**

