Cell injury mechanisms

* **Ischemia and hypotoxia** → affect → **mitochondria**
  - ribosome disruption → ↓prot. synth
  - Na^+/K^+ pump defective → cell swell
  - ↓ATP / ↑ROS (reactive) → (Lipid peroxidation) membrane disruption → mito. permiability transition pores → ↓ATP, cytochrome c release → apoptosis
  - ↑ anaerobic respiration (in SK. muscles and Liver) → ↑LA. acid → ↓pH → protien denature (enzymatic disfunction)

* **Ischemia reperfusion** → (restoration blood supply after ischemia) affect → mithochondria metabolic → ↑ ROS [oxidative stress because of the high metabolic reactions making ROS more than cell capacity of antioxidant defence system]

* **ROS** → in all cell normally : in redox rxns when (O_2) reduced to (H_2O) (normal ammount unless ischemia reperfusion (oxidative stress))
  - aging, radiation → leukocytes (O_2^- superoxide → H_2O_2 Hydrogen peroxide (myeloperoxidase) → ClO^- hypochlorite (for killing microbes and cause inflamation)) / pathogen cause cell necrosis so leukocytes accumulate and cause inflamation

→ **ROS effects** → lipid peroxidation (membrane disruption) / protiens denaturation / DNA damage

antioxidant enzymes → O_2^- {SOD} (superoxide dismutase) / H_2O_2 {GSH} (Glutathion peroxidase & catalase) → absorbed via → Vit (E, A, C, β carotene)

* **Toxins** →
  - direct : ① HgCl (bind with (in cysteine and selenium)) → SH-group- of membrane protiens (denaturation) → ↓active transport (↑permiability) / ② chemotherapetic agents / ③ microorganism toxins
  - label : CCl_4 (in mitochondria) → Cytochrome 450 → in SER in Liver converted into free radical (harmfull effect in lipids (membranes of ER → protein synth → fatty liver / mitochondrial membrane → ↓ATP) protiens, DNA)

* **Misfolded protiens** → when increase → ↓prot-synth, ↑degradation, ↑chaperon synth.
  - failure → proapoptic sensor (ER$_{Ca}$) → caspase activation → apoptosis
  - diseases → protien deficiency (cystic fibrosis, α-1 antitrypsin) / Neurodegenerative (parkinson, Huntington, Alzheimer, prion, 2-diabetes)

* **DNA damage** → because (mutation, radiation, ROS, chem. agent) → p53 activate → stay in G1 or apoptosis
  - p53 mutation → mutation replication → neoplastic changes