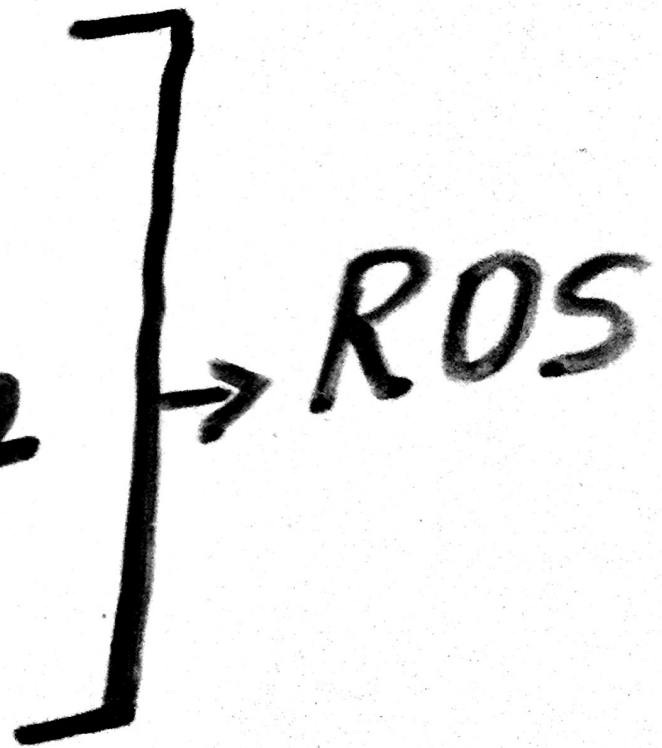
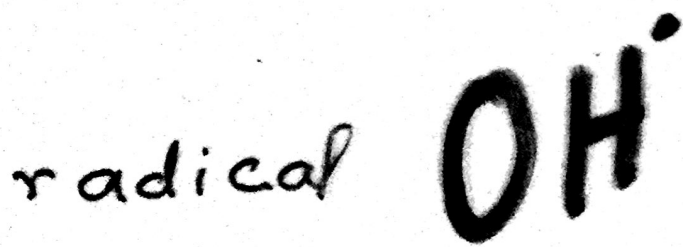
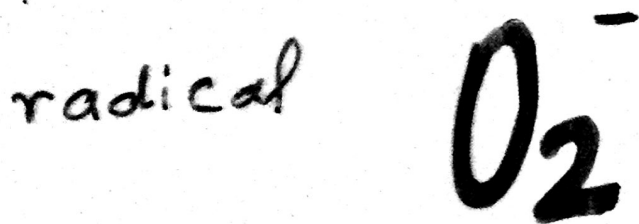
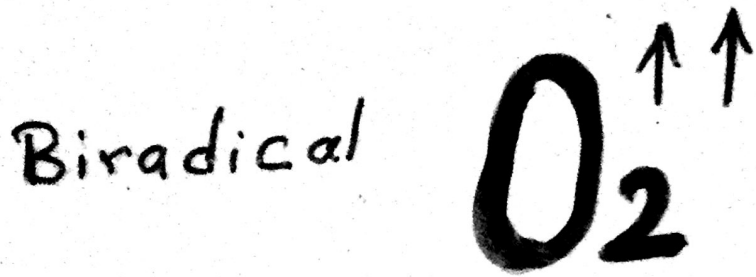
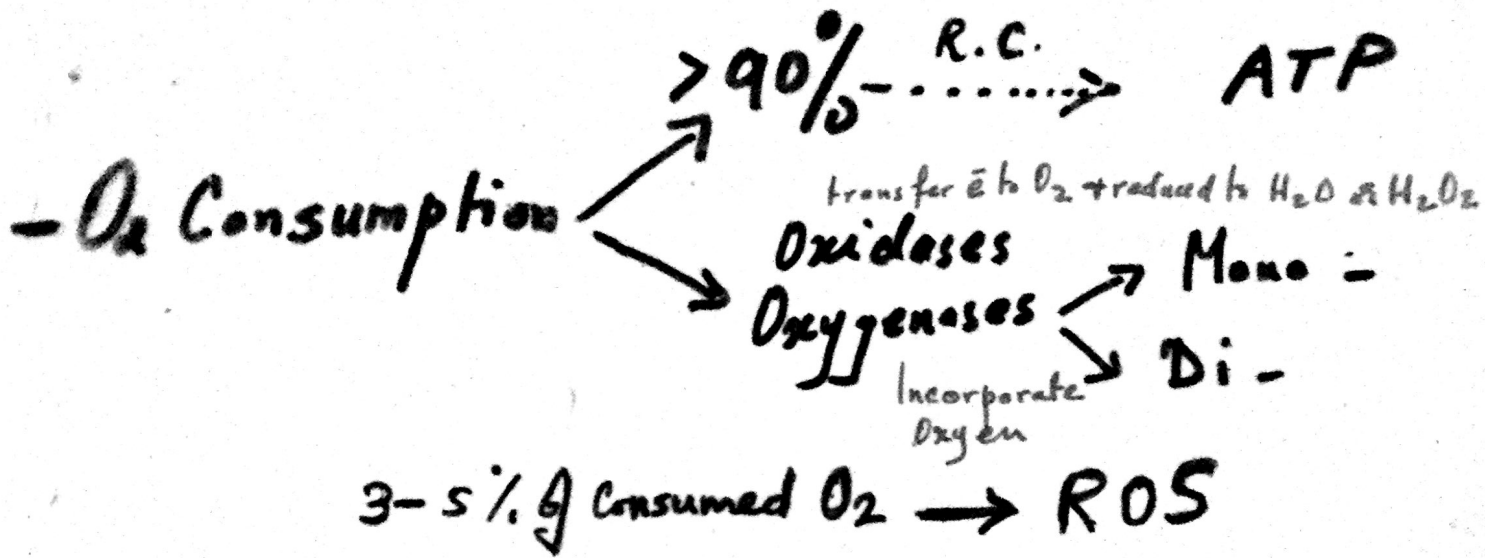


Oxygen Toxicity & Free Radical



O₂ Metabolism and Toxicity

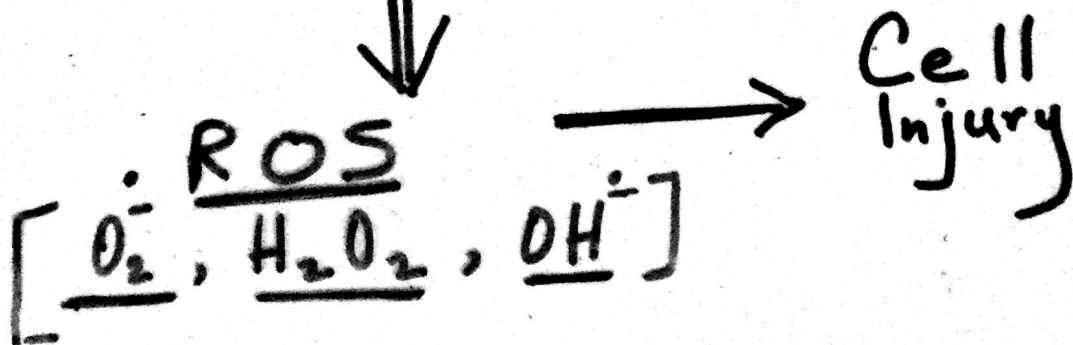
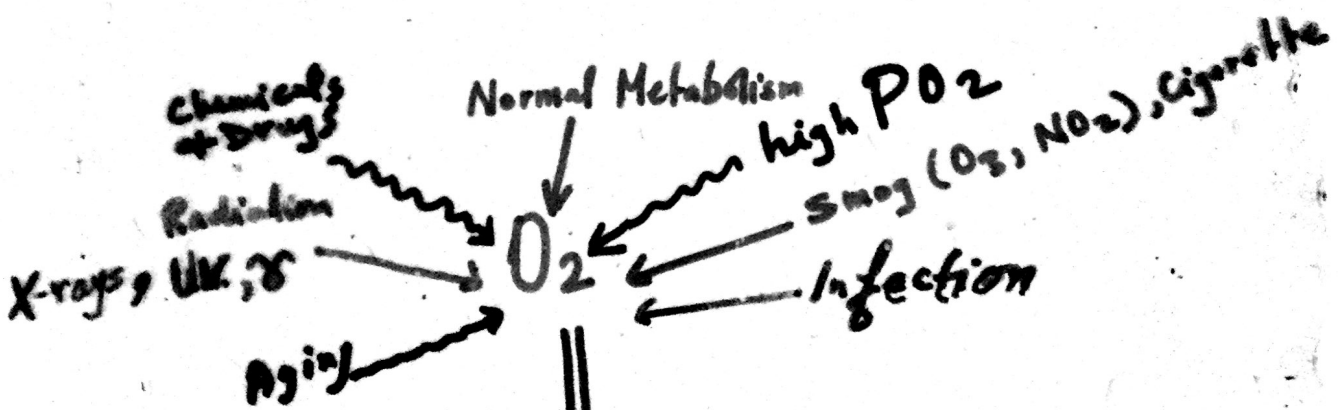


Reactive Oxygen Species (ROS) :-

Generated by

- normal Metabolism

- Environmental factors



Others → organic peroxides RCOO[•]
 hypochlorous acid HOCl
 •RNOS

- Some of the Diseases Associated with ROS injury:-

- Atherosclerosis
- Respiratory Disease (Emphysema / Bronchitis)
- Parkinson's Disease
- Cancer
- Diabetes
- Liver Damage
- motor neuron disease
- Aging

- ROS and Cellular Damage

- Causes of Diseases

- contribute to complication of many chronic diseases

• Proteins, lipids, Nucleic acids & Carbohydrates are affected

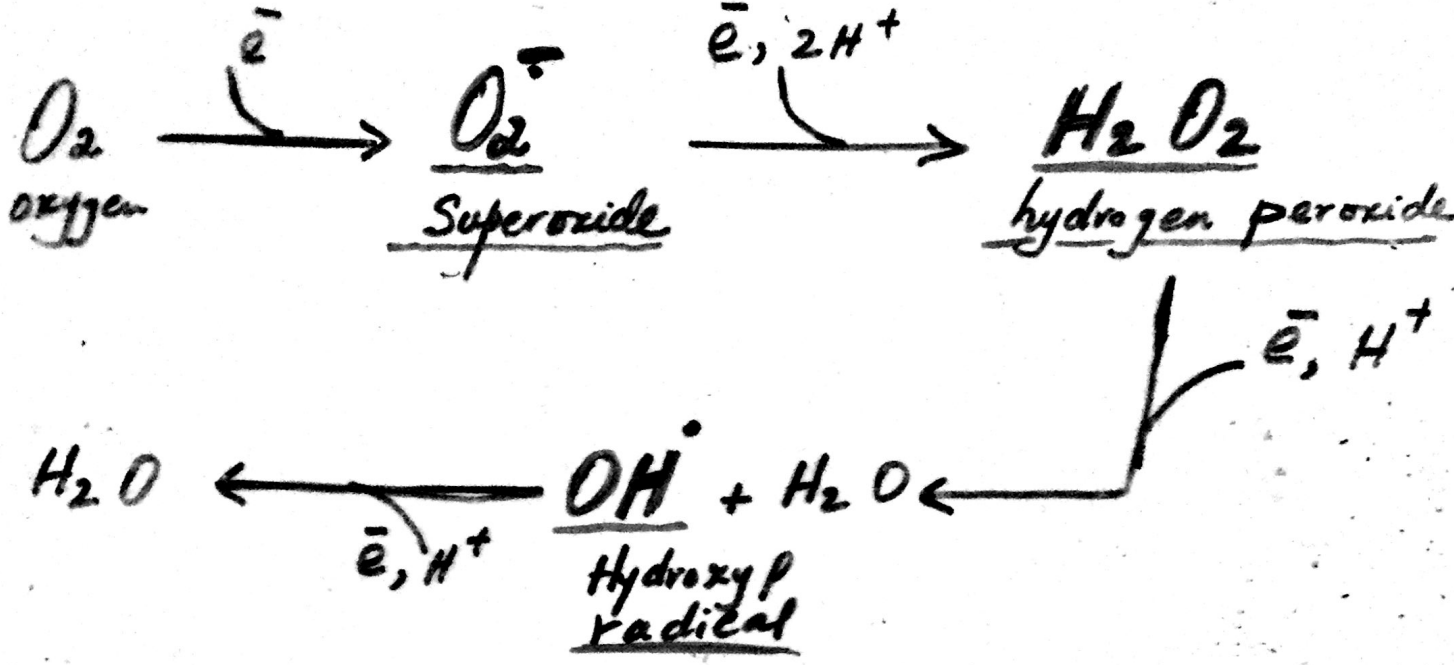
- Most susceptible amino acids
Pro, his, arg, Cys, Met.

Oxidation of a.a. → fragmentation of protein:
→ aggregation → proteolytic digestion

• Membrane lipids

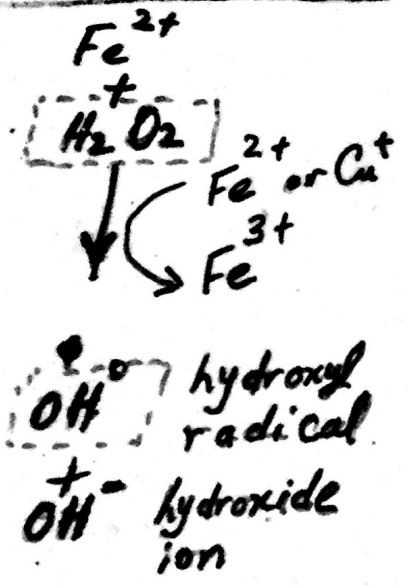
• DNA damage
e.g. strands break

One-Electron Reduction Steps of Oxygen (Generation of ROS)

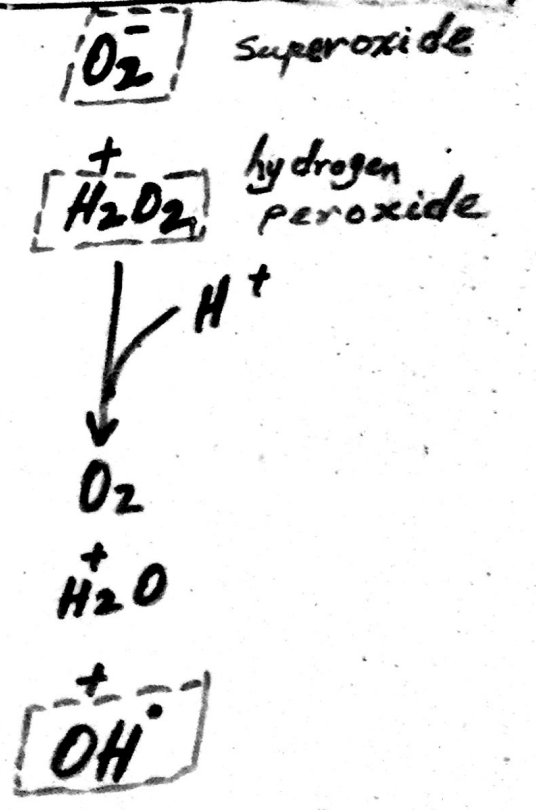


Generation of the hydroxyl radical OH^{\cdot}

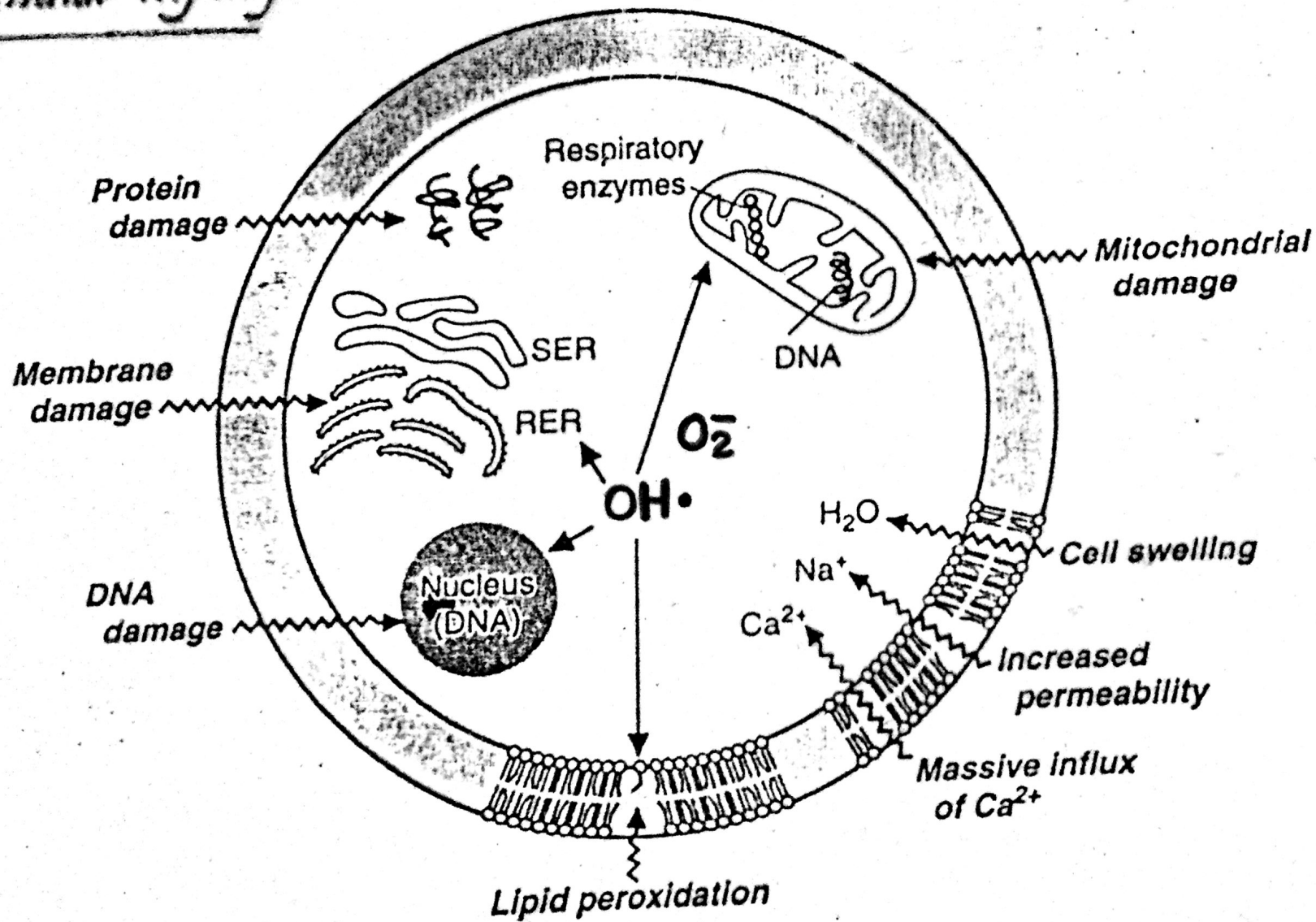
The Fenton Reaction



The Haber-Weiss Reaction



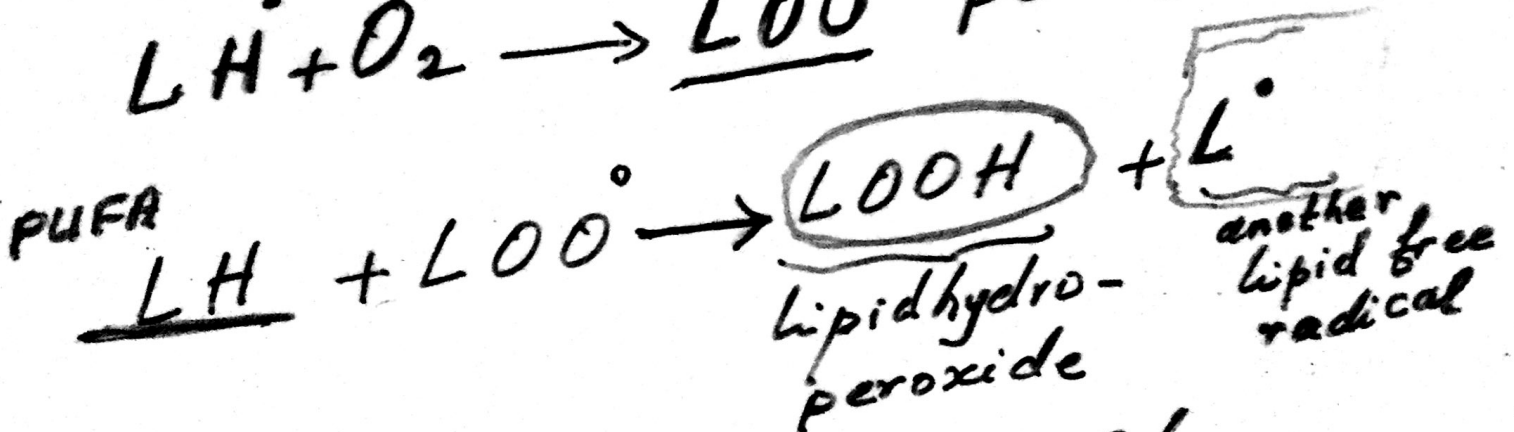
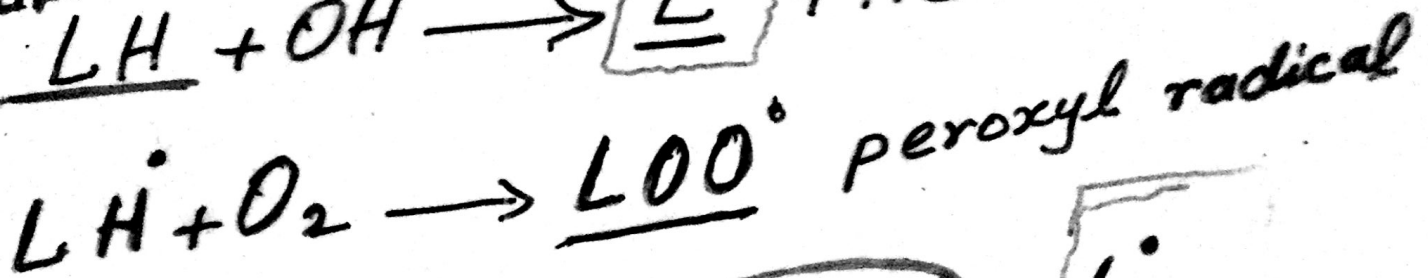
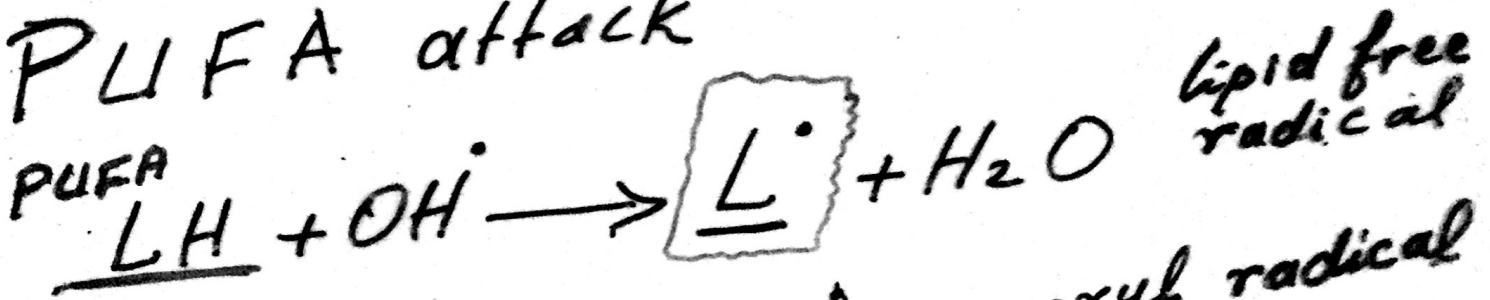
Free Radical-Mediated Cellular Injury



The Main Biological Targets of ROS ^{40.}

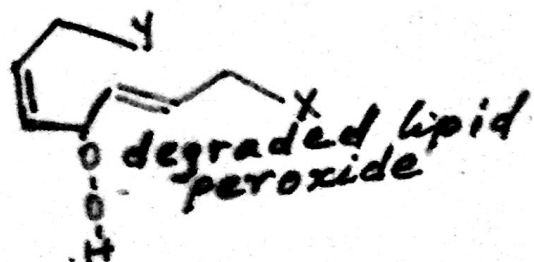
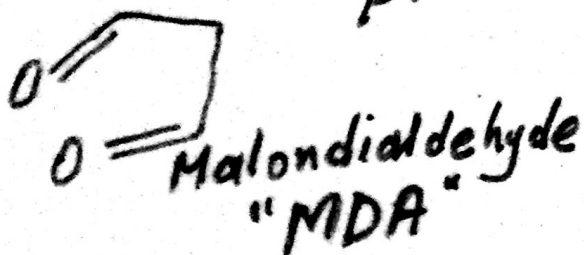
- PUFA: Polyunsaturated fatty acids.
- Proteins
- DNA

PUFA attack



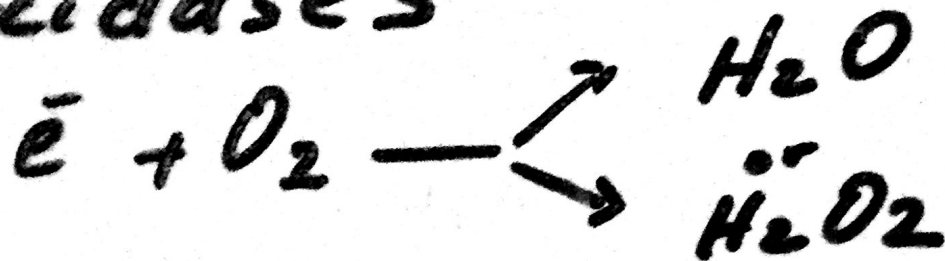
→ chain reaction is set via lipid radicals in producing lipid hydroperoxides

→ Degradation of peroxidized lipids → generating harmful products



SOURCES of ROS in the cell :- 5

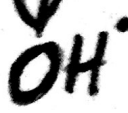
- Oxidases



most oxidases $\rightarrow H_2O_2$
(peroxidase)

Oxidases are confined to sites equipped with protective enzymes

Fenton reaction



- Oxygenases

• mono oxygenases
(hydroxylases)

• Dioxygenases

- \rightarrow Thromboxanes
- \rightarrow PG
- \rightarrow Leukotrienes

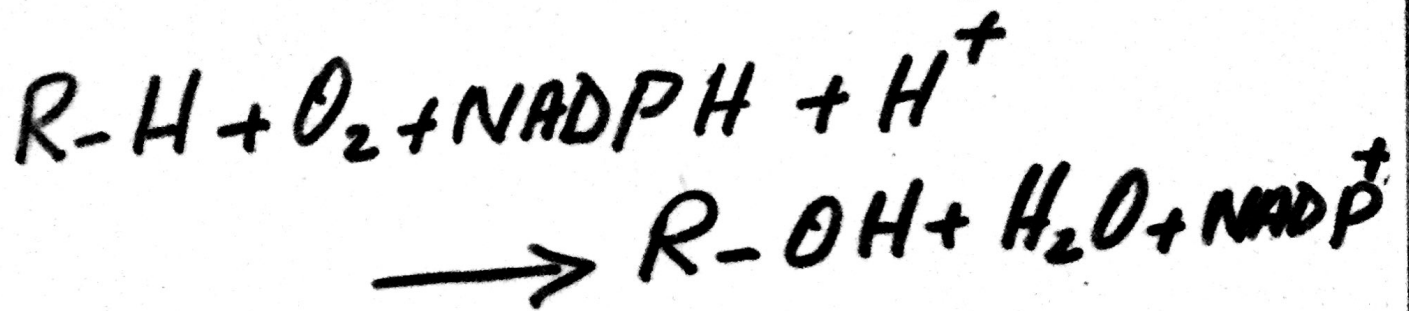
- Coenzyme Q in R.C.

- Respiratory Burst

during phagocytosis $\rightarrow O_2^\cdot, H_2O_2, OH^\cdot, NO, HOCl$

- Ionizing Radiation
 $\rightarrow OH^\cdot$

69
C. Cytochrome P450 Monooxygenase
(Mixed Function oxygenase)



R \nearrow steroid
 \rightarrow drug

\rightarrow other chemical

1. Mitochondrial System

Hydroxylation of steroids
in steroid hormone-producing tissues
synthesis of bile acids
synthesis of biologically active Vit D

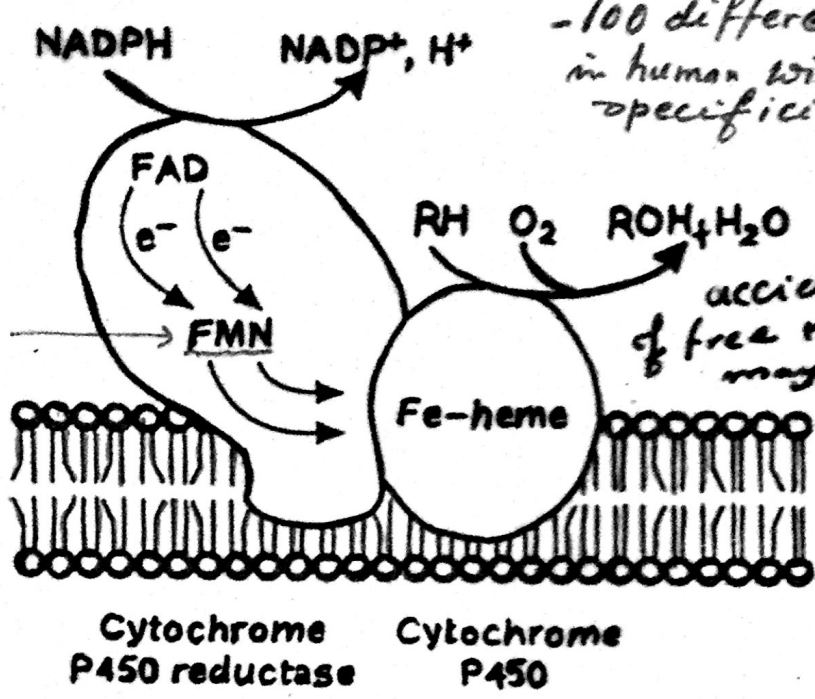
2. Microsomal System

Detoxification of foreign
compounds (xenobiotics)
Activation or inactivation of Drugs
solubilization

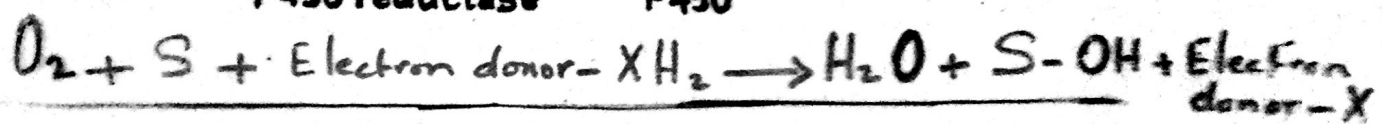
Cytochrome P450 enzymes:-
 Superfamily of structurally related monooxygenases

- 100 different iso enzymes in human with overlapping specificities.

Facilitate transfer of single e⁻ from NADPH to O₂



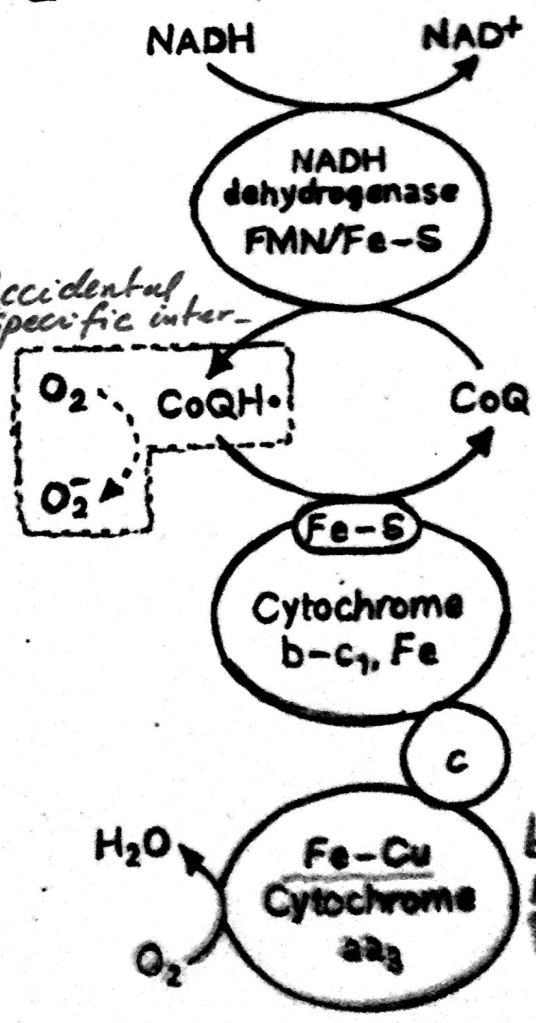
accidental release of free radical intermediates may occur



Generation of O₂⁻ by R.C.

Major source of O₂ free radicals

Accidental non-specific interaction



binuclear center prevents release of free O₂ radical