



Medical Committee
The University of Jordan



SLIDE



SHEET

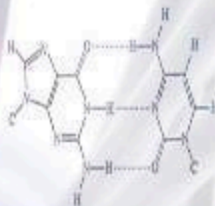


SLIDE : 10



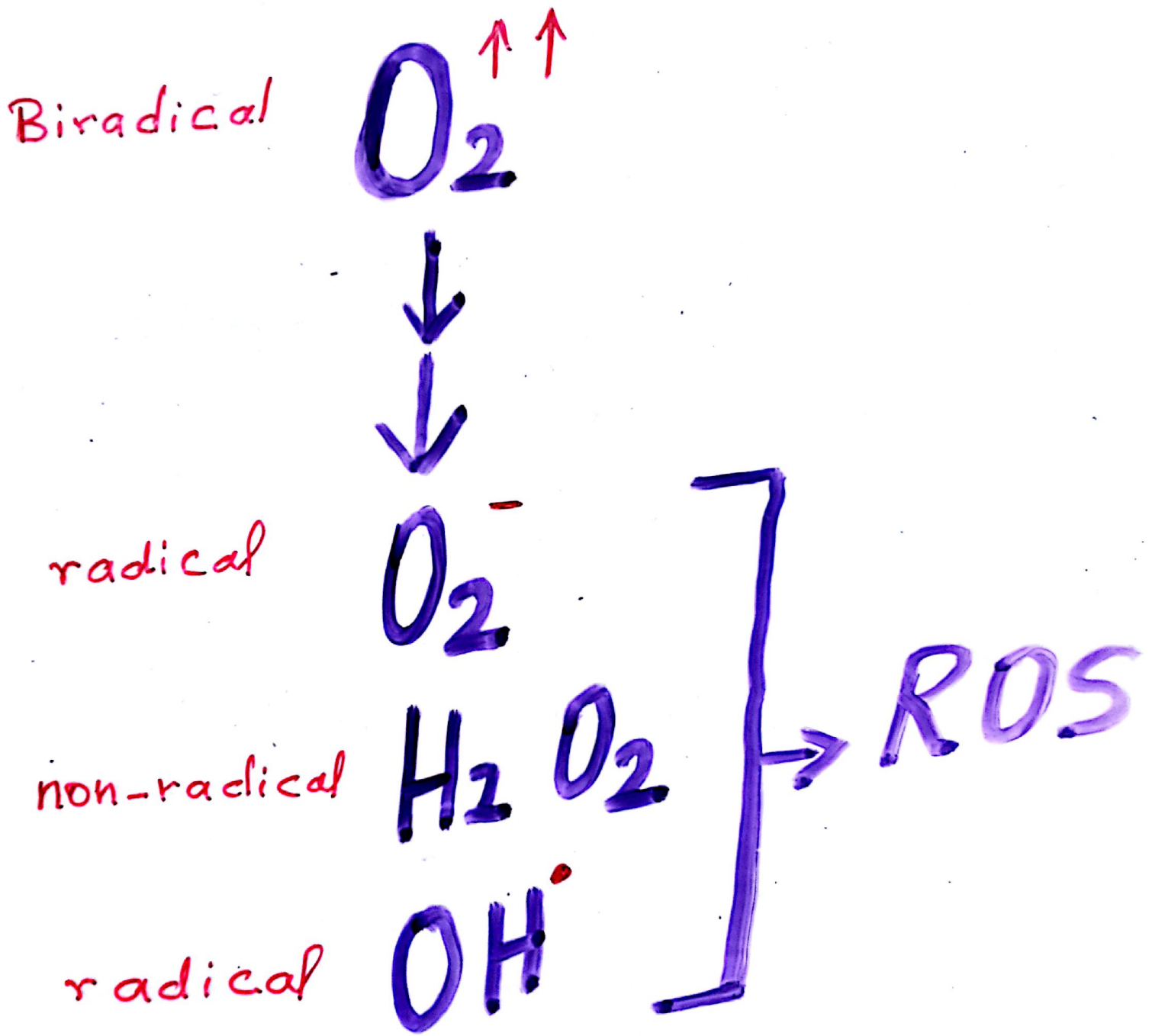
DR.NAME: Nayef Kradshah

Biochemistry

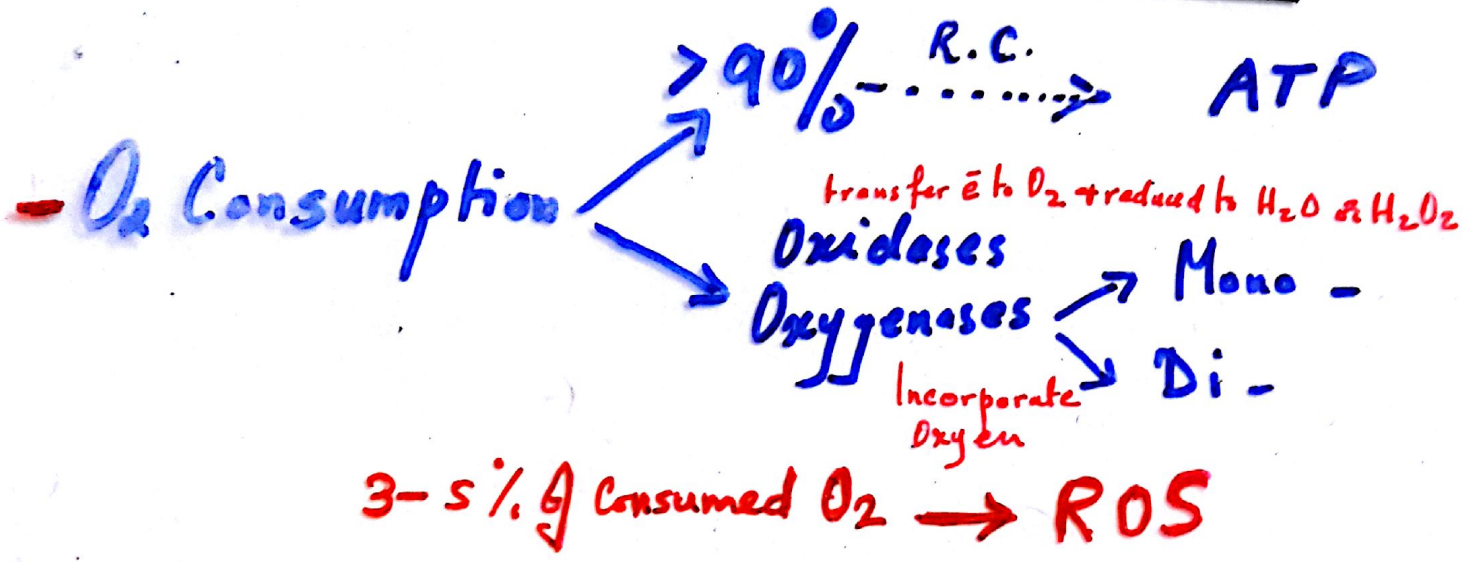


Majida Al-Foqaraa'

Oxygen Toxicity & Free Radical

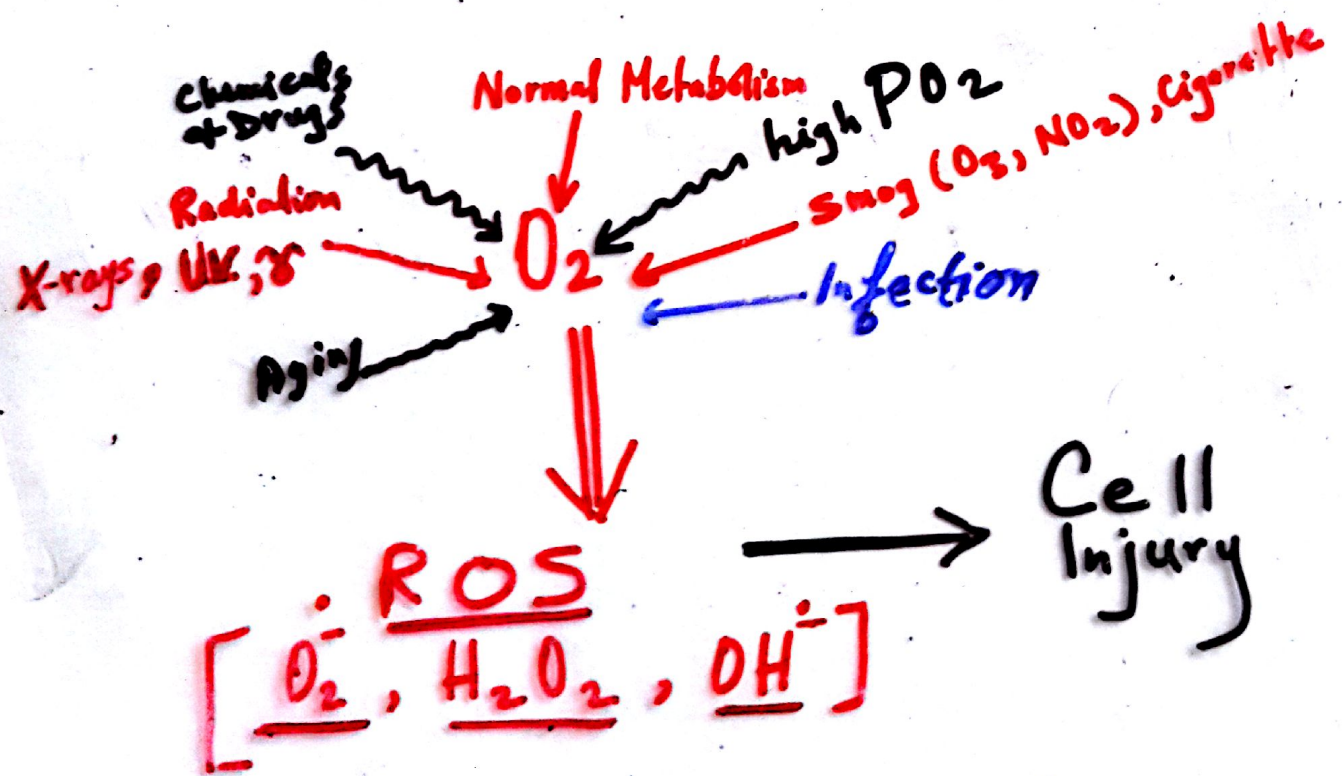


O₂ Metabolism and Toxicity



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

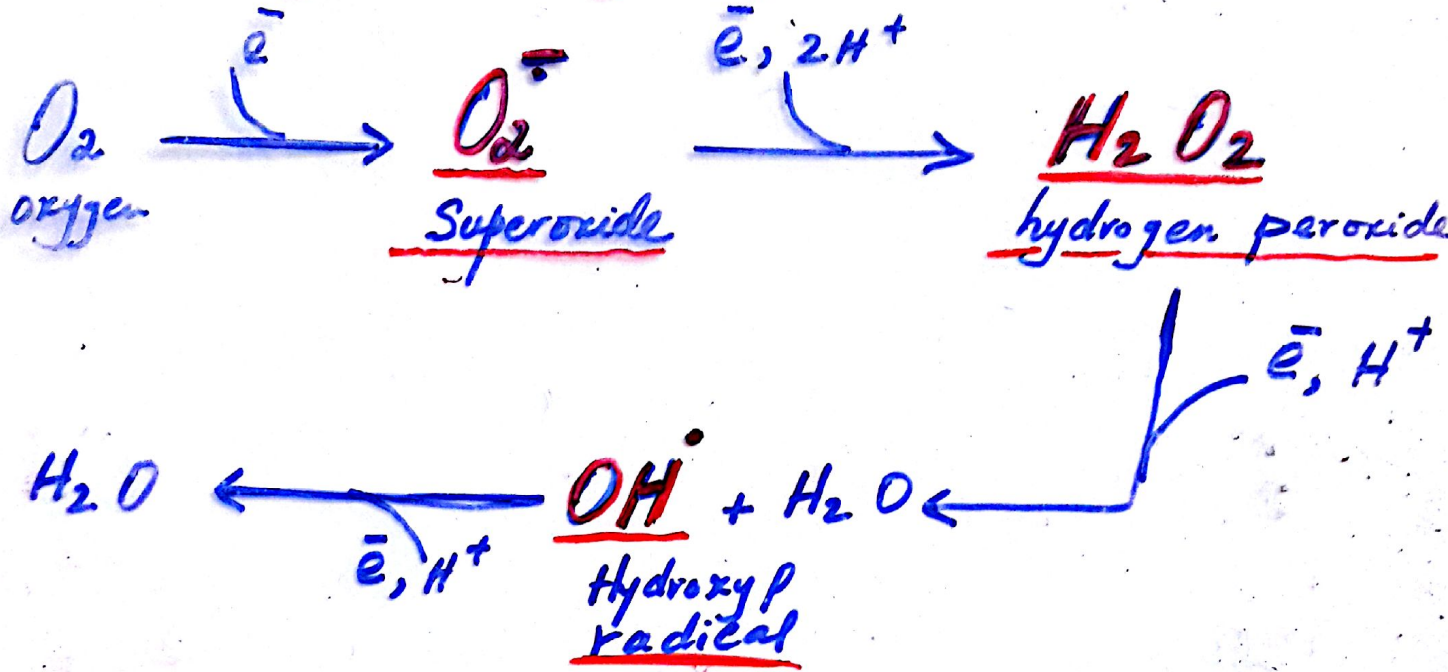
- Most susceptible amino acids
Pro, his, arg, Cys, Met.

oxⁿ of a.a. → fragmentation of proteins
→ aggregation → proteolytic digestion

- Membrane lipids

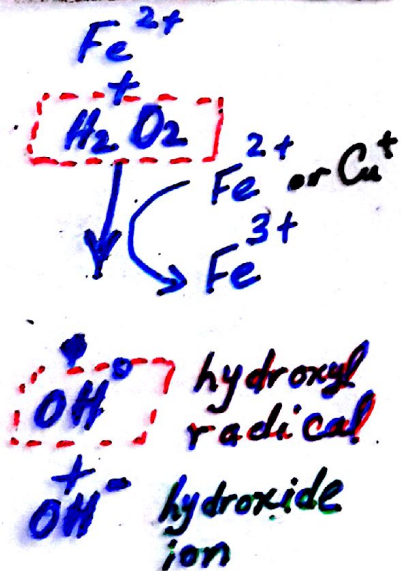
- DNA damage
e.g. strands break

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

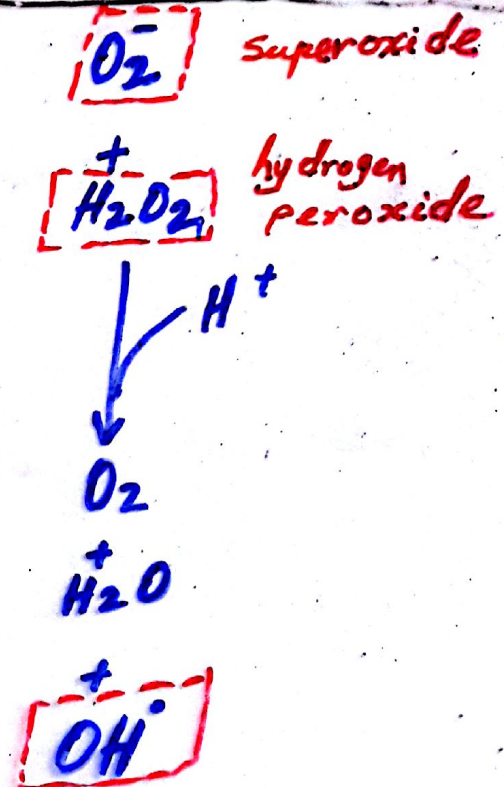


Generation of the hydroxyl radical OH^{\cdot}

The Fenton Reaction

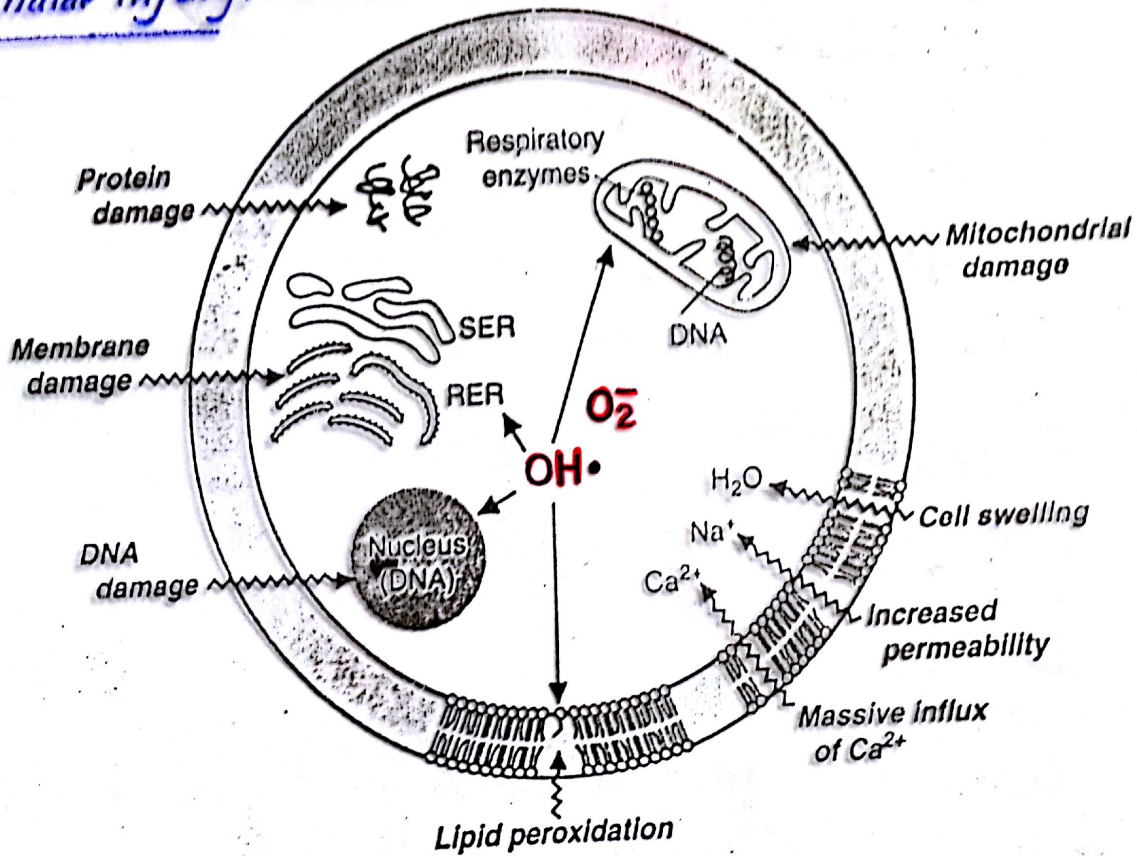


The Haber-Weiss Reaction



Free Radical-Mediated Cellular Injury.

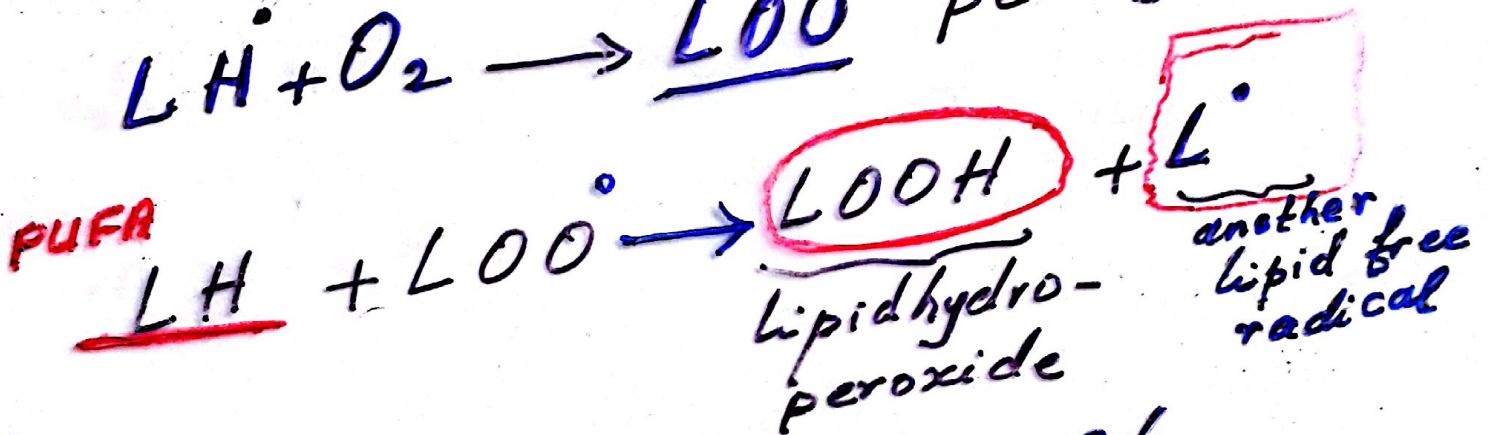
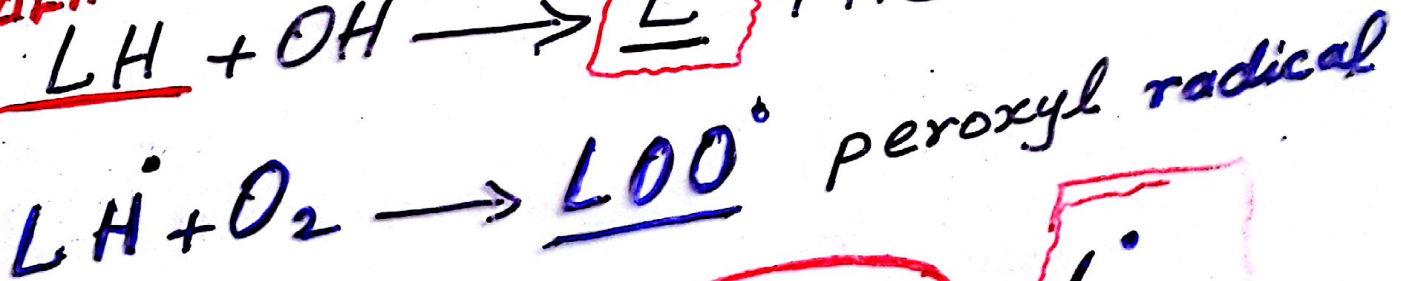
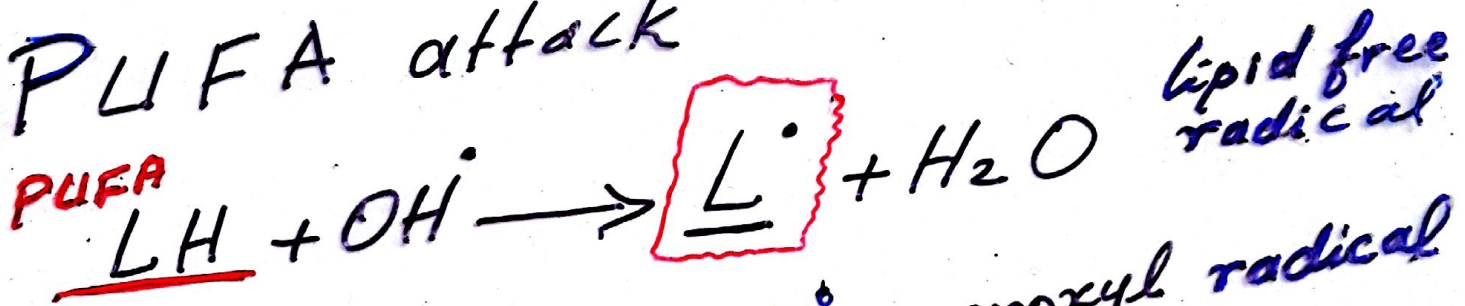
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The Main Biological Targets of ROS ^{4a}

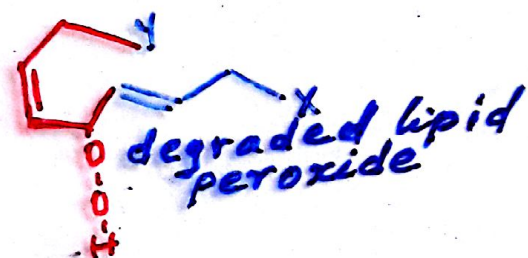
- PUFA: Poly unsaturated fatty acids.
- Proteins
- DNA

PUFA attack



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

→ Degradation of peroxidized lipids → generating harmful products



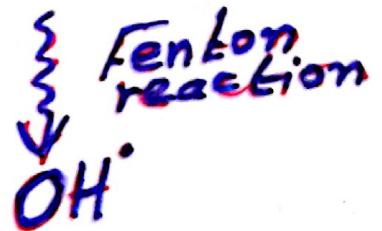
SOURCES of ROS in the cell :- 5

- Oxidases



most oxidases $\rightarrow H_2O_2$
(peroxidase)

Oxidases are confined to sites equipped with protective enzymes



- Oxygenases

• mono oxygenases
(hydroxylases)

• Dioxygenases

\rightarrow Thromboxanes
 \rightarrow PG
 \rightarrow Leukotrienes

- Coenzyme Q in R.C.

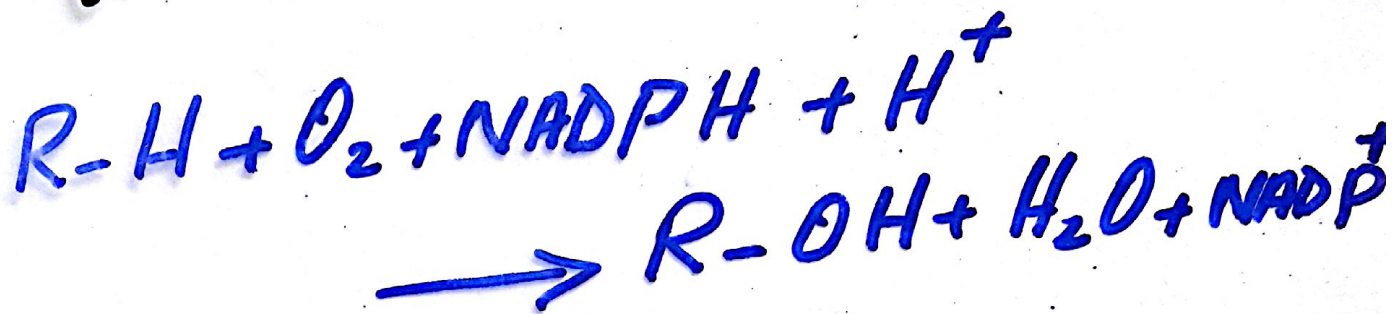
- Respiratory Burst

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

- Ionizing Radiation
 $\rightarrow OH^\bullet$

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C. Cytochrome P450 Monooxygenase (Mixed Function oxygenase)



R \nearrow steroid
R \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

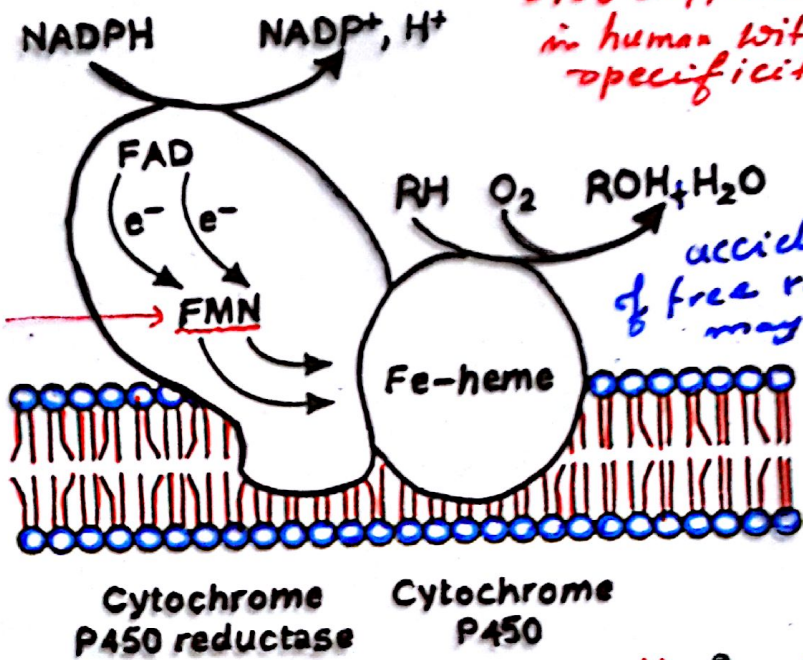
Cytochrome P450 enzymes :-

Superfamily of structurally related monooxygenases

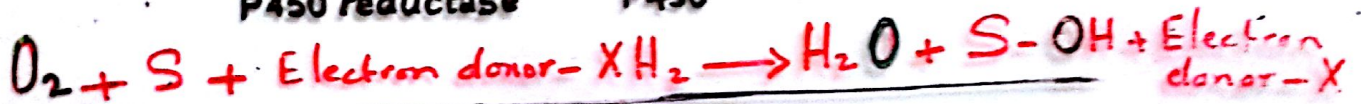
- 100 different iso enzymes in human with overlapping specificities.

Facilitate transfer of single e from NADPH to O₂

or Fe-S center



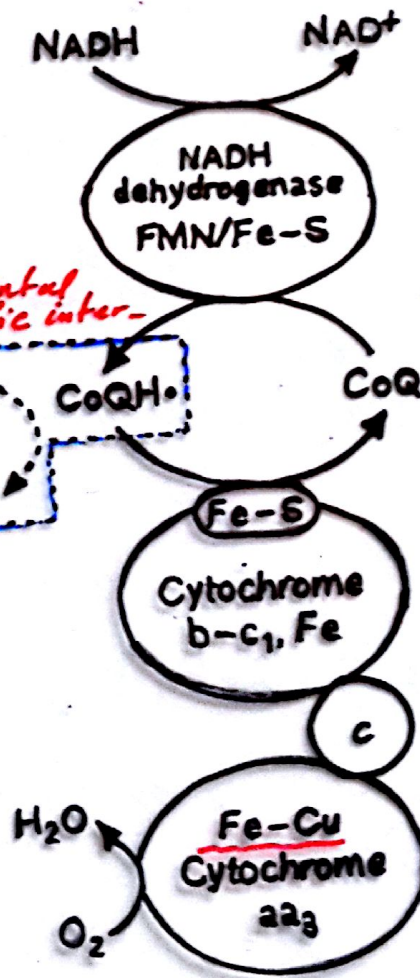
accidental release of free radical intermediates may occur



Generation of O₂⁻ by R.C.

Major source of O₂ free radicals

Accidental non-specific interaction



binuclear center prevents release of free O₂ radical

D. Phagocytosis by white blood cells

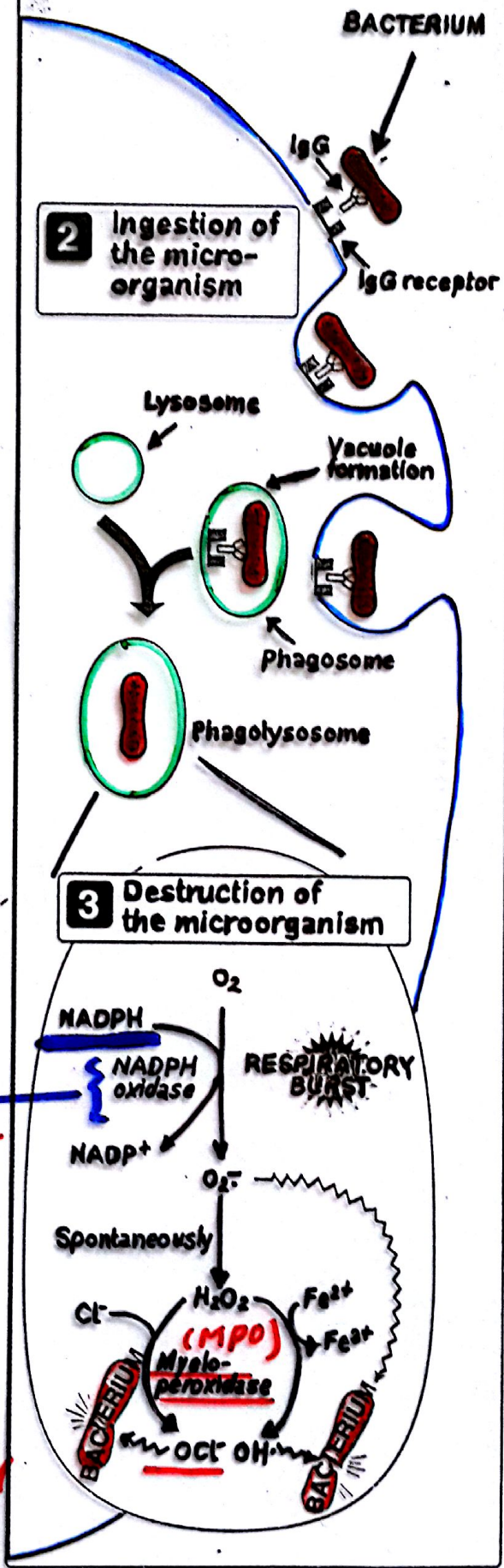
Uses NADPH

(7)

1 Attachment of the pathogen to a phagocytic cell

2 Ingestion of the micro-organism

3 Destruction of the microorganism



Deficiency

Chronic granulomatosis

MPO-lysosomal enz.

HOCl hypochlorous acid