U.P.e⁻ – Unpaired electron

## 1.4 FREE RADICAL INJURY

* Similar to Hypoxia, F.R. Can also injury.

Note: Incomplete oxidative phosphorylatn Can lead to prodn of F.Rs.

⊗ * F-R producn is a preceding event of Necrosis

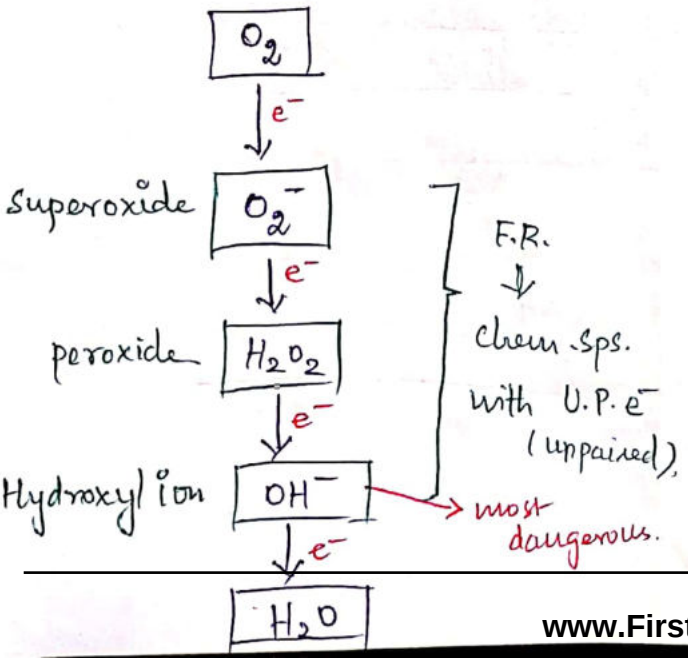
* FR can also cause apoptosis.

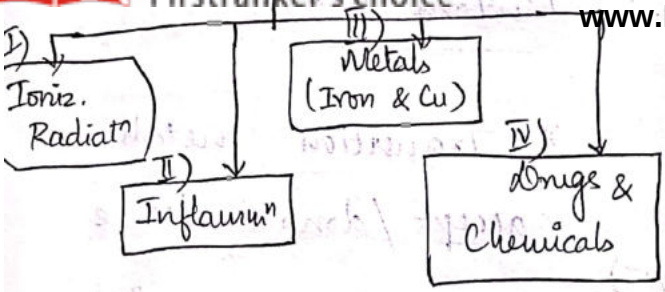
- Generatn (producn) of F.R.
  - physio
    - ⇩
    - during oxid. phosphorylatn.
  - patho.
    - (i) Radiatn (Ionizing).
    - (ii) Inflammn.
    - (iii) Metals ($Cu^{++}$ & $Fe^{++}$).
    - (iv) Drugs & chem.

How oxid. phosphorylatn leads to prodn of F.Rs. ?

* During oxid. phos. Cyt.C. Transfers ④e⁻ to $O_2$.

* $O_2$ after accepting 4e⁻ becomes $H_2O$.






## I) Ionizing Radiatn :

* F.R. produced → $OH^-$ (Hydroxyl ion).

**Mechanism:**

Radiation hits the water in the tissues. & $OH^-$ ions are produced.

$OH^-$ → most damaging FR.

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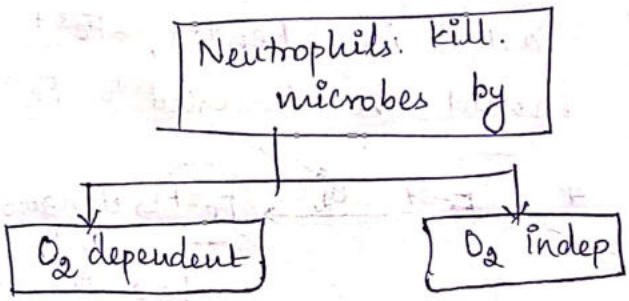
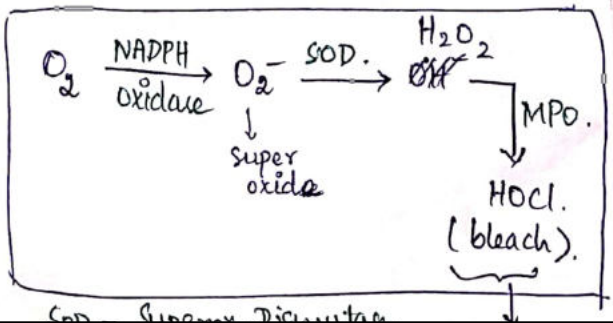
## II) Inflammation.




Rxn starts with oxidative burst.




SOD - Superox. Dismutase.
MPO - Myelo Peroxidase.

Metals such as Fe,

* Metals such as Cu & Fe can't remain free in blood.

* Free Fe can produce F.R by Fenton's Rxn. ($Fe^{++} + H_2O_2 \rightarrow OH^-$).

* $OH^-$ is produced

eg: Diseases in which Cu (or) & Fe build up.

(i) Hemochromatosis :

- $Fe^{++}$ accumulatn
- F.R. producn
- damage to Tissues (CIRRHOSIS).

(ii) Wilson's disease

- $Cu^{++}$ accumulatn
- F.R accumulatn
- damage to liver & lenticular system of Brain

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I/C - Intracellular

What's the reason behind Fenton's Rxn?

* Transition metals accept / donate free $e^-$ during I/C rxns & Catalyze fR formatn.

* Eg. for this is Fenton's rxn

$Fe^{2+} + H_2O_2$

$\downarrow$

$Fe^{3+} + OH^{\cdot} + OH^-$

* But luckily most of I/C Fe, is in $Fe^{3+}$ state. so in order to take part in Fenton, $Fe^{3+}$ should be Converted to $Fe^{2+}$

* $Fe^{3+} \xrightarrow{O_2^-} Fe^{2+}$ → dangerous

⇓

bcoz Now it can take part in Fenton's Rxn

Drugs & Chemicals

Acetaminophen $CCl_4$

* Acetaminophen
↓
goes to liver & detoxif. by Cyt. P-450.
↓
F.R. generated in the detox. process.

eg: Large dose of Acetaminophen taken by a pt. to commit suicide. (Necrosis of liver).

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F.R. damage.
↓
How?

- Peroxidatn of lipids.
- Oxidation
  - DNA ⇓ causes oncogenesis
  - proteins

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(i) Oxidn of A.A. side chains
(ii) formn of disulph. bonds.
(iii) Oxidn of protein backbone

③ Mech. of Elimination of F.R

~~* Incomplete~~

Antioxidants → gives $e^-$ so U.P.$e^-$ of F.R gets paired

Enzymes → (i) SOD (ii) Glutathione Peroxidase (iii) Catalase. (iv) Peroxi-redoxins.

Metal Carrier proteins → Prevention of F.R. produc$^n$. → Keeps the metal in bound state

Elimination of $ONOO^-$

$ONOO^-$ → Peroxi-redoxins. → $HNO_2$

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Oxygen $O_2$

Superoxide $O_2^-$

③ Enzymes

(i) S.O.D. "Superoxide" dismutase

Peroxide $H_2O_2$

(ii) CAT Catalase

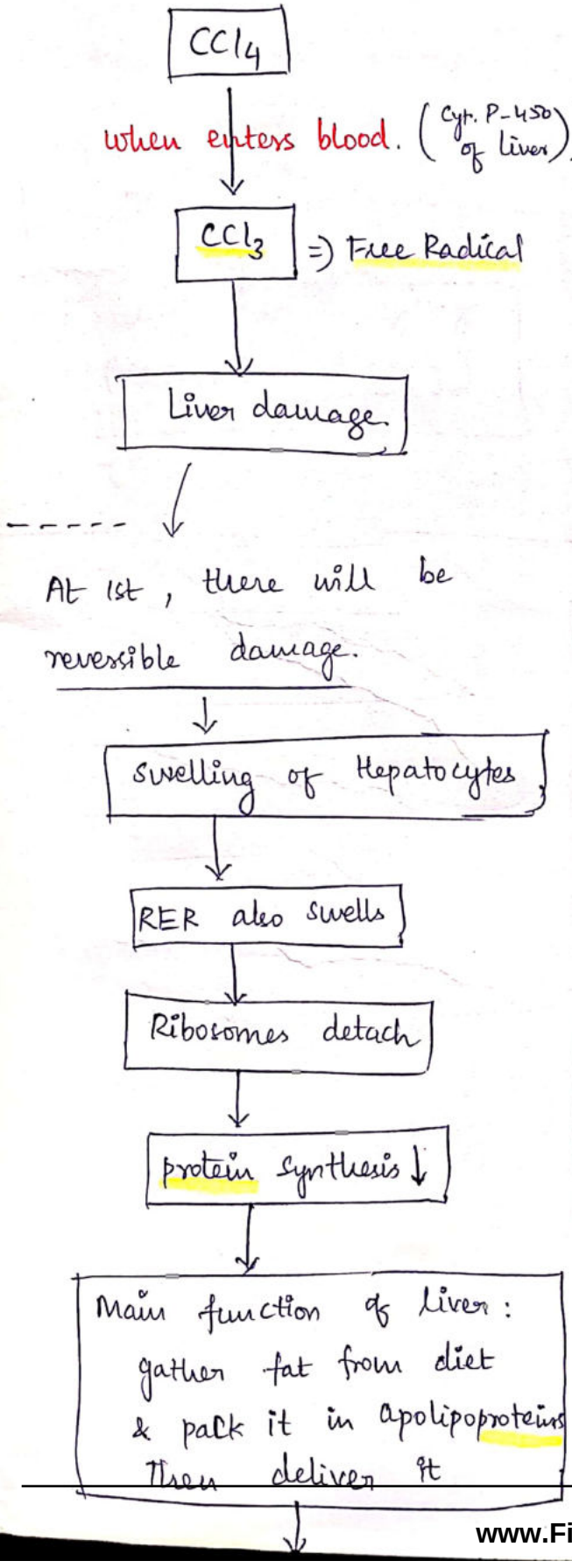
Hydroxyl ion $OH^-$

(iii) Glutathione Peroxidase. GP.

Water $H_2O$

(i) $CCl_4$ :

* produced from Dry cleaning industry.



Lack of Apolipoproteins
So Fat that Comes to liver
CAN'T get out

fatty change in liver

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(ii) Reperfusion Injury :

for eg: A pt. suffers a sudden MI., clot in his LCA (Left Coronary a.)

But he goes to Cathlab at the correct time & clot is relieved.

But already, the myocytes suffered Irrev. damage.
i) cardiac enzymes leaked.
ii) memb. damage

So when blood supply is restored, $O_2$ is & Inflamm. cells also restored.

Inflammatory cells produce F.R. are ~~to~~ High Og

↓

F.R can destroy healthy Cardiac myocytes (nearby).

↓

Now instead ~~of~~ expected ↓↓ in Cardiac enzymes, they ↑↑

↓

Which ~~intakes~~ indicate injury (Reperfusion injury)

—— X —— X ——