Hematology

- Histology
- **Biochemistry**
- Pathology
- Pharmacology
- Physiology
- Microbiology

- Handout
- **Slide** 6
- Sheet

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- lecture number :
- Done BY :

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Derivatives of Hemoglobin

- Normal Derivatives
  - Oxy Hb
  - Deoxy Hb
  - Carbamino Hb
- Abnormal Derivatives
  - Met Hb
  - Sulpha Hb
  - Carboxy Hb (HbCO)

Met Hb

normal level < 1%

Types

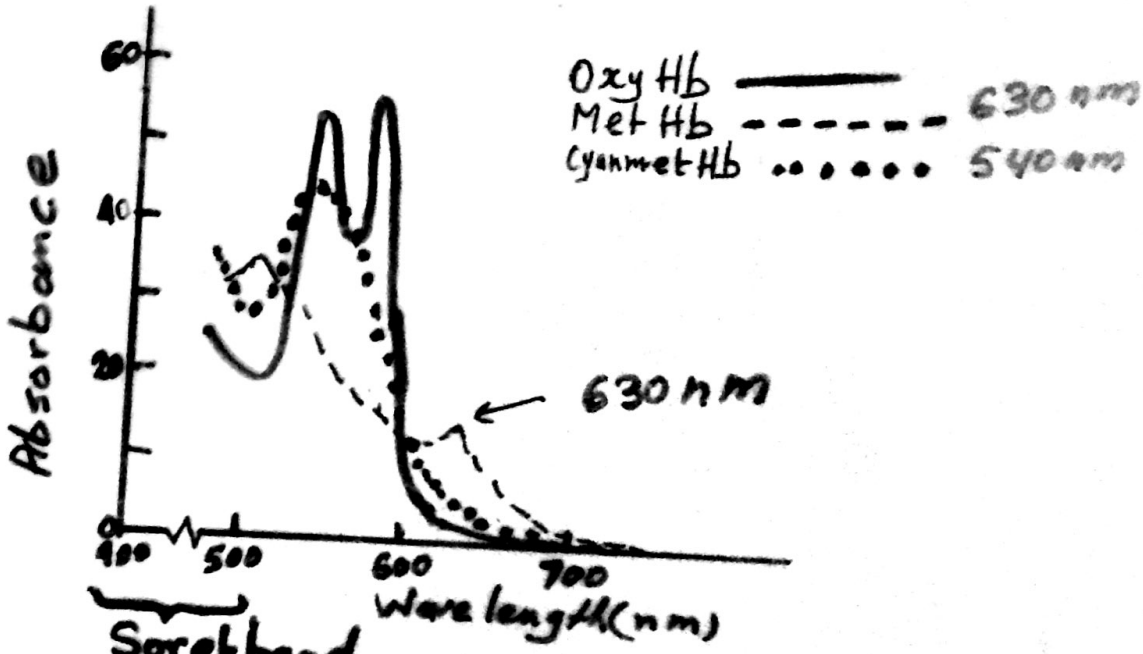
1. Inherited
2. Acquired
   - Certain drugs
   - chemicals
   - ox. agents in food

Inherited Methemoglobinemia :-

- Deficient MtHb reductase
  NADH-Cytb5 reductase
- Hemoglobinopathies HbM
  replacement of proximal His by tyr → HbM

Symptoms
Cyanosis :- bluish discoloration of the skin and mucous membrane

Diagnostic test
Spectroscopic analysis at 630nm



Soret band
400-440
Peak 10-times for all hemeproteins

Treatment :- Reducing Agents → Methylene blue, Ascorbic acid

$$2O_2^{\cdot -} \xrightarrow[+2H^+]{SOD} H_2O_2 + O_2$$

Removal of oxidants

$$H_2O_2 \xrightarrow{\text{Catalase}} H_2O + 1/2O_2$$

$$H_2O_2 \xrightarrow{\text{Glutathione peroxidase}} 2H_2O$$

2GSH — Reduced glutathione

2-G-S-S-G — Oxidised glutathione

A

Glutathione reductase

$NADP^+$ — $NADPH + H^+$

Reduction of Fe

$HbFe^{2+}$ normal — NAD^+

Oxidants (certain drugs) → e.g. phenacetin, sulphonamides

Chemicals: e.g. aniline, excess nitrite

Ox. agents in diet

Methaemoglobin reductase cytochrome b_5

B

$HbFe^{3+}$ Methaemoglobin — $NADH + H^+$

Figures 8.17A and B: Erythrocyte mechanisms for detoxification of methaemoglobin

Sulphahemoglobin

produced by the same substances that cause MetHb, but in presence of sulphur containing compd. e.g H_2S

- SulphaHb + MetHb often present together
- Can not act as O_2 carrier
- Can not be reversed back

CarboxyHb

Affinity 210 > than for O_2

1% of CO in inspired air — fatal in mins.

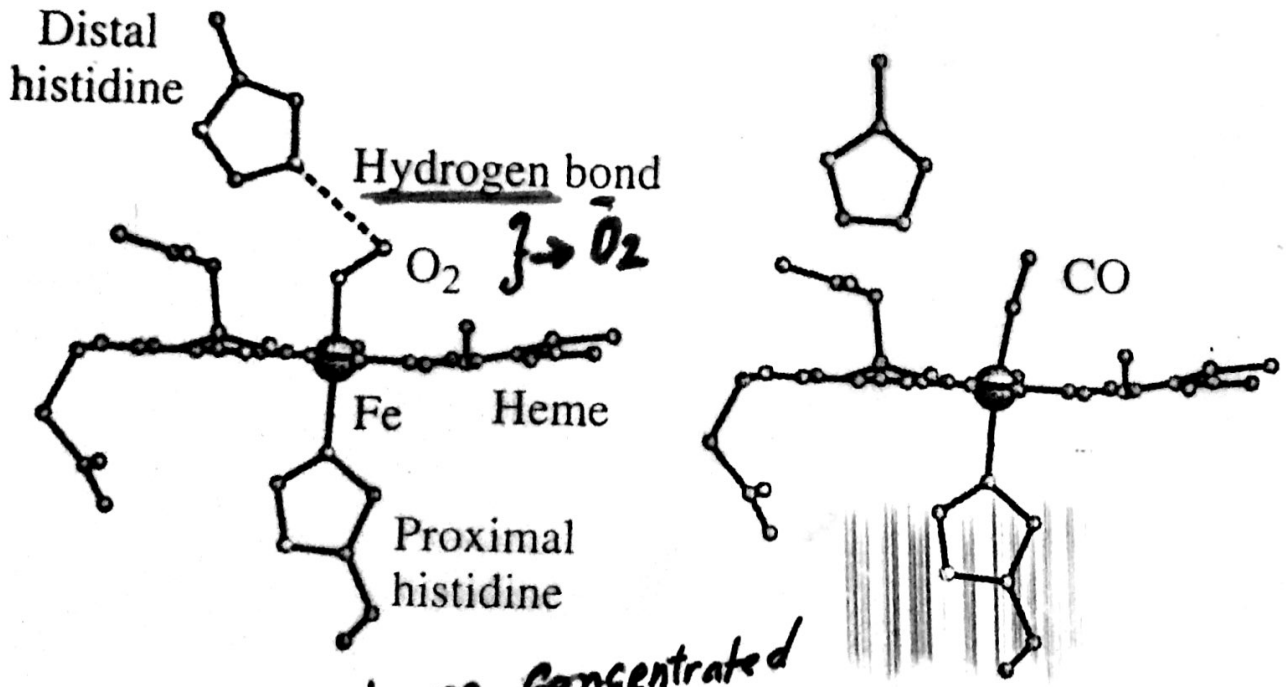
1% of CO Hb in non-smoker

10% or more CO Hb in smokers

>40% COHb → unconsciousness and fatal

O_2 & CO binding to Hb & Mb

In free heme CO binds 20,000 > O_2
in Mb " " 25 times > O_2
in Hb " " 200 " " "

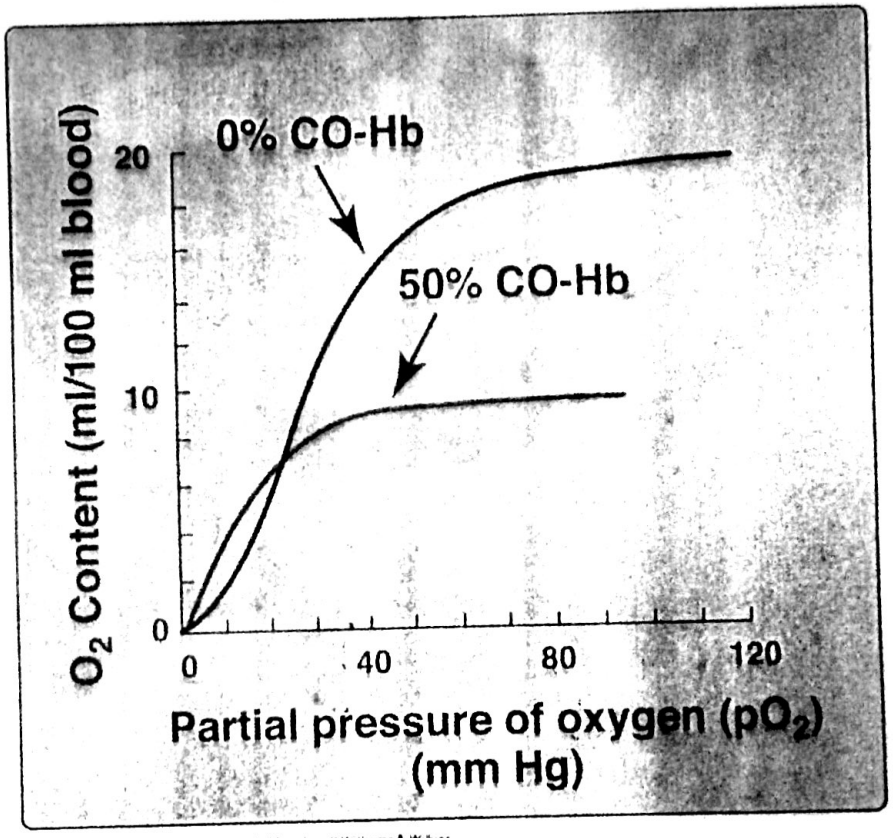


$\bar{O}_2$, negative charge concentrated on terminal oxygen bound to distal His. H-bond of O_2 with distal His further stabilize oxygen
Replacement of distal His by non-polar atom decreases affinity of modified heme by 100-fold

Binding of CO

CO binds tightly but reversibly to Hb
CO binding shifts Hb to the R state – remaining sites bind O_2 with high affinity

Binding of NO

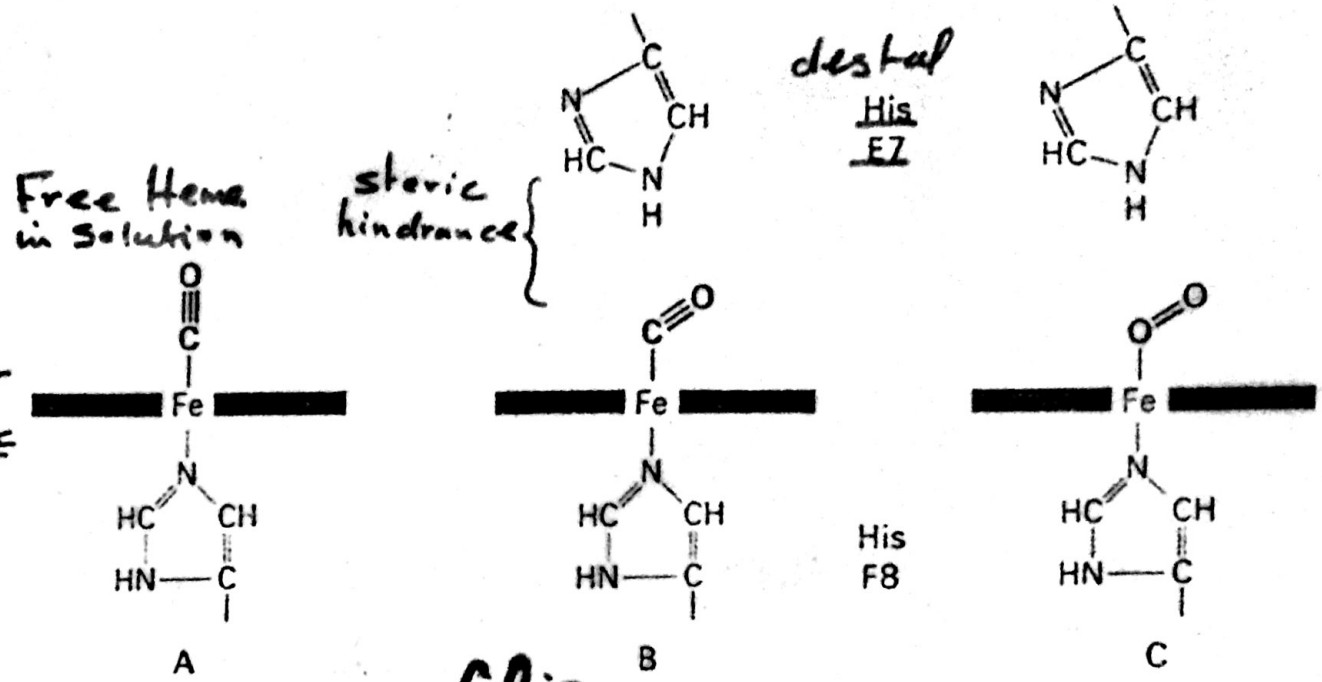


CO binding is diminished by distal His

- The function of prosthetic group is modulated by its polypeptide environment
  - Hb + presence of distal His
  - Cyt. C
  - Catalase

Figure 7-13
Structural basis of the diminished affinity of myoglobin and hemoglobin for carbon monoxide: (A) linear mode of binding of CO to isolated iron porphyrins; (B) bent mode of binding of CO to myoglobin and hemoglobin, in which the distal histidine (E7) prevents CO from binding linearly and so the affinity for CO is markedly reduced; (C) bent mode of binding of O_2 in myoglobin and hemoglobin. Isolated iron porphyrins also bind O_2 in a bent mode.

NOT TRUE



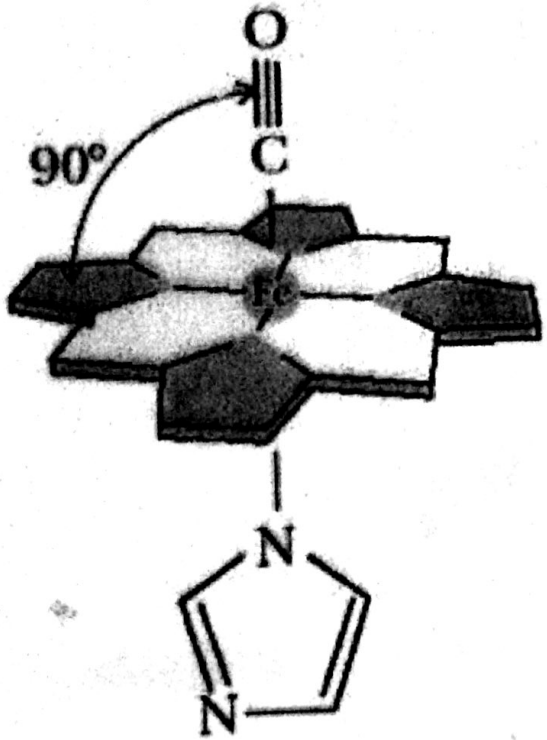
CO affinity is 25000 times > O_2 for free heme in solution

CO:- 200 times more affinity than O_2 for Hb
425 times more than Mb

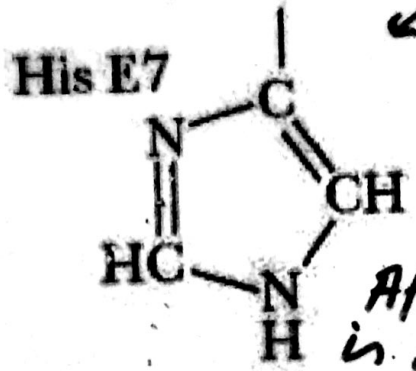
CO and O_2 binding

Distal His

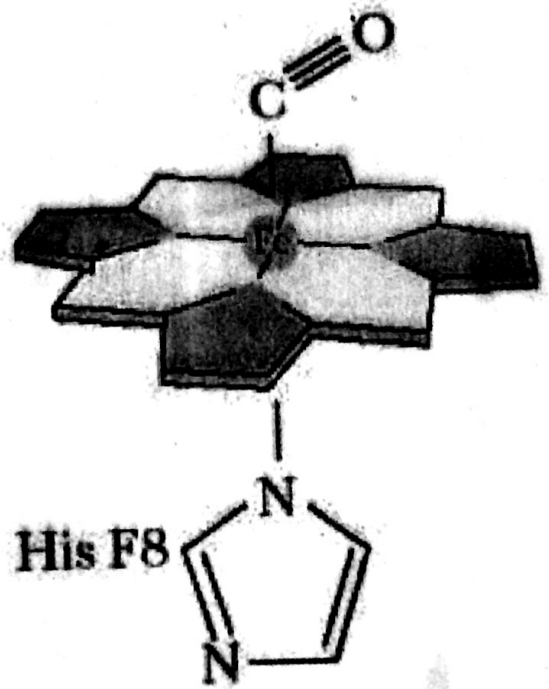
Affinity for CO is 25,000 more than O_2



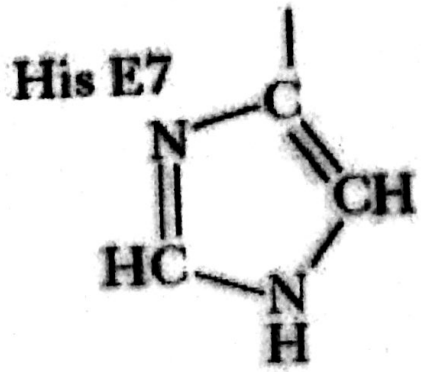
(a) Free heme with imidazole

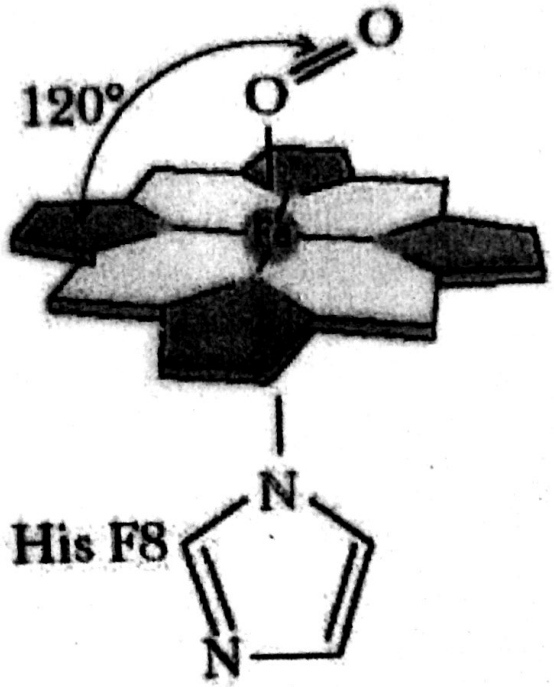


Affinity is 250 times more than O_2



(b) Mb:CO complex





(c) Oxymyoglobin