HEMATOLOGY

&LYMPH SYSTEM

Biochemistry slides

Number: 2a

Doctor: Dr.nayef

iron above the plane of heme –
0.6 Å by sterric hindrance

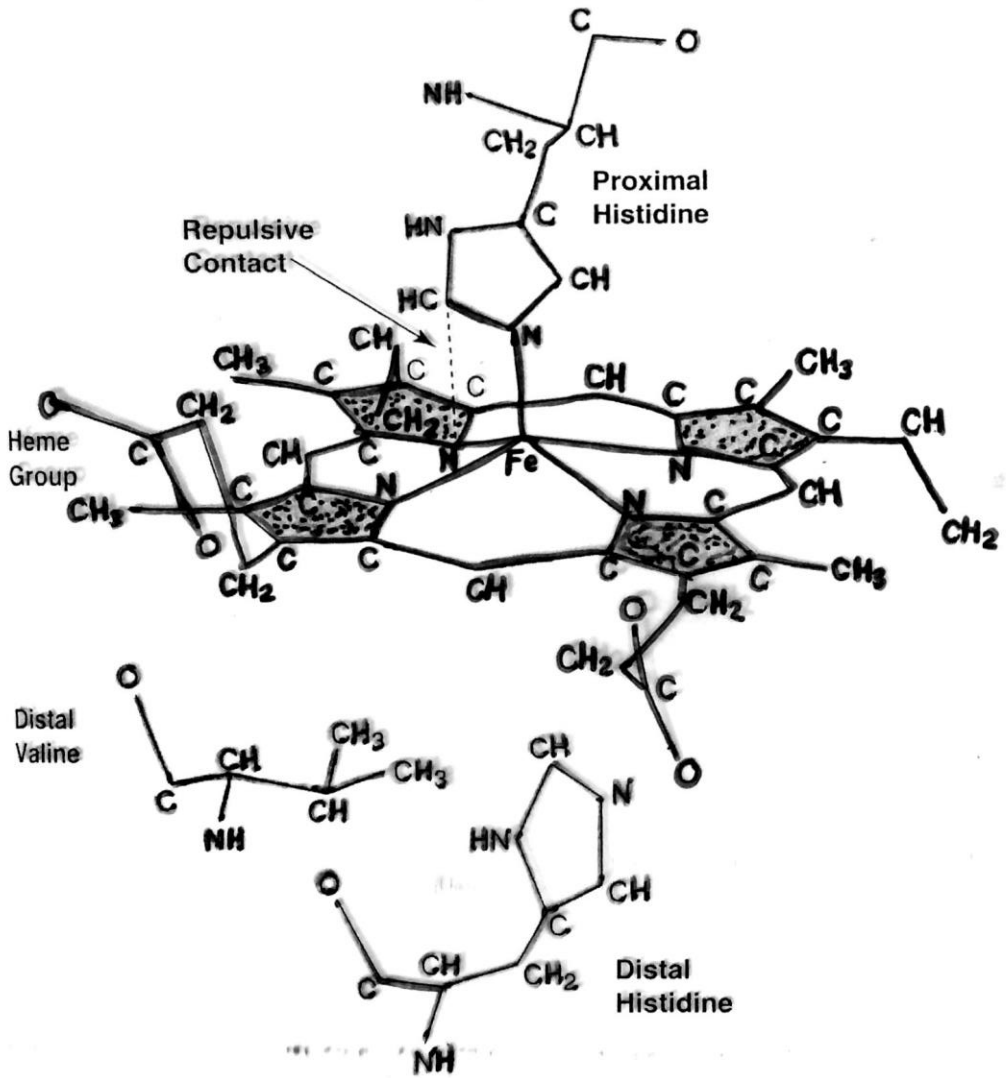
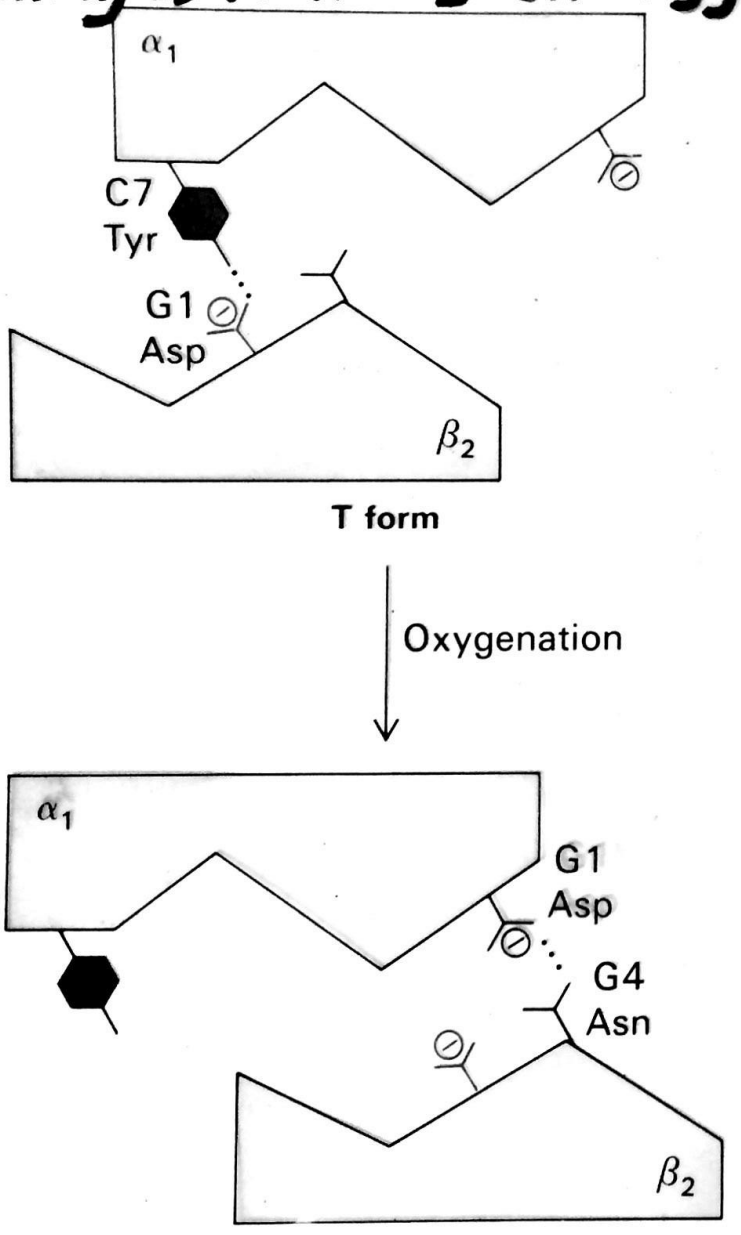
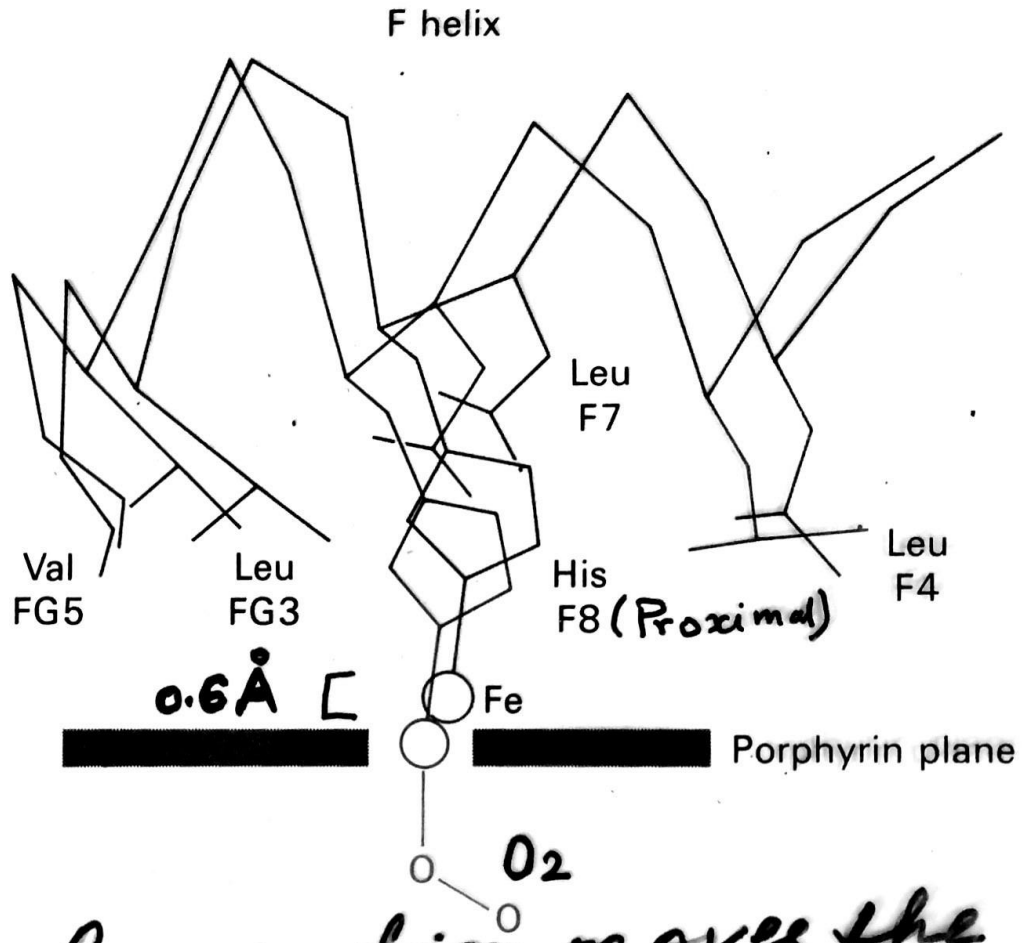


FIGURE 9.25

Steric hindrance between proximal histidine and porphyrin in deoxyhemoglobin.

- Quaternary structure of Hb changes markedly on Oxygenation





- Oxygenation moves the iron atom into the plane of porphyrine

Figure 7-30, page 62; Figure 7-32, page 163

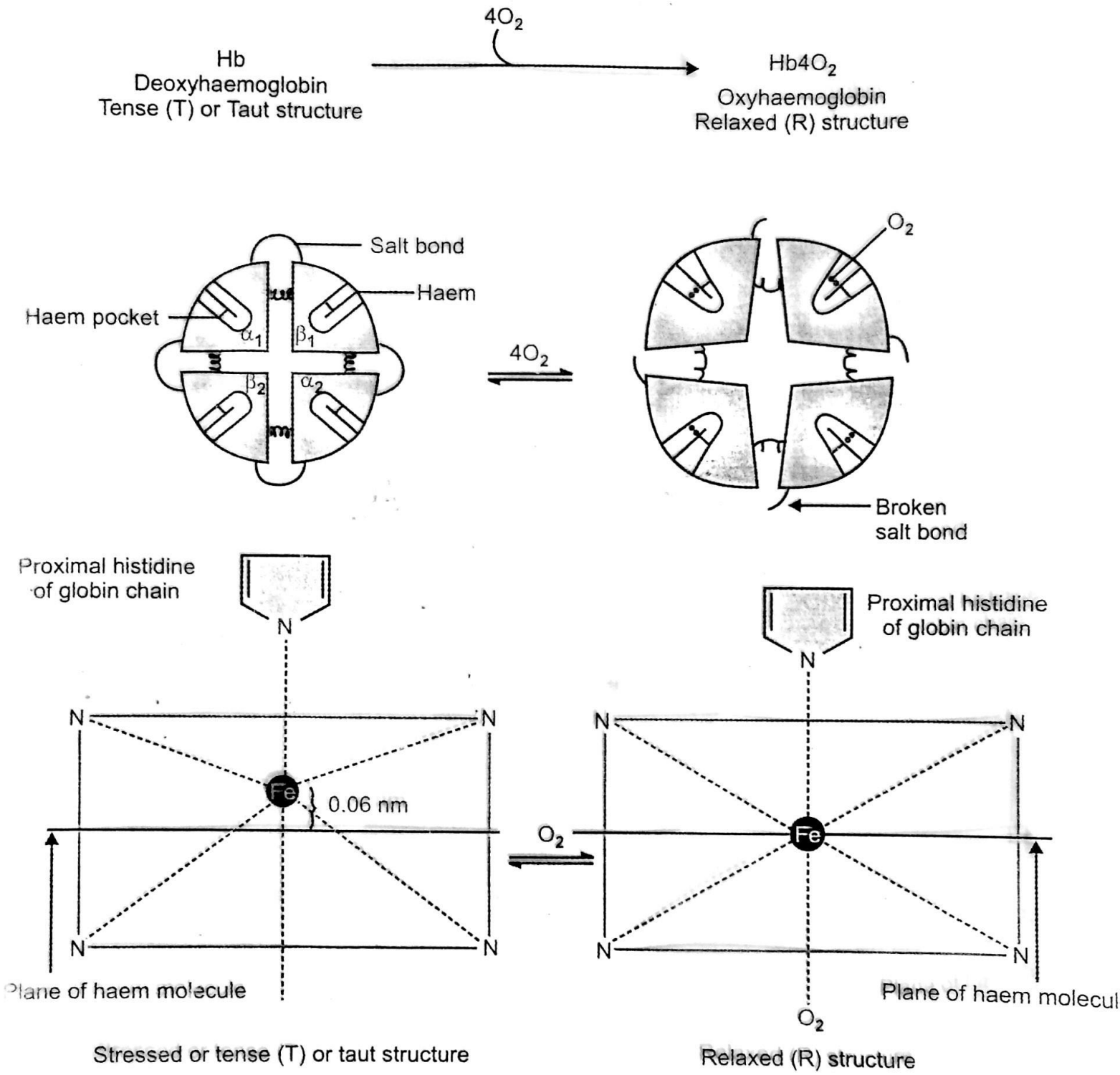


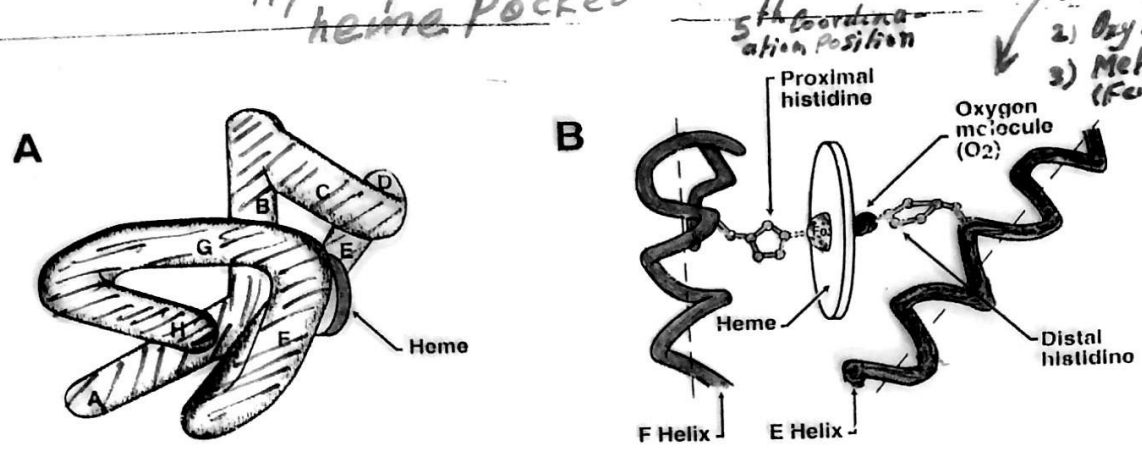
Figure 8.5: Schematic representation of changes during oxygenation of deoxy haemoglobin

Binding of O_2 Is Reversible

$$O_2 + Fe^{2+} \longleftrightarrow Fe - O_2 \xrightarrow{X} Fe^{3+} + O_2^-$$

Hydrophobic heme Pocket

6th position
1) Deoxy Hb: Empty
2) Oxy Hb: O_2
3) Met Hb (Ferri-Hb) H_2O



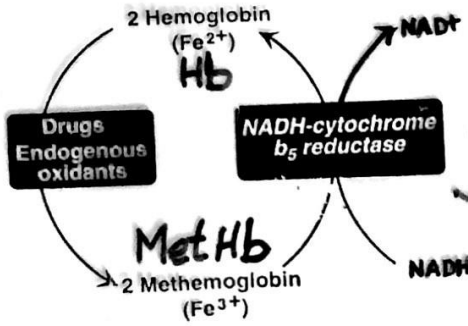
→ Formation of Methemoglobin:-

$$Fe^{2+} \longrightarrow Fe^{3+} \text{ in Hb or Mb}$$

Causes

1- Drugs & chemicals
2- Endogenous production of H_2O_2 & free radicals
3- Inherited defect in α- or β-chain → HbM

→ Reduction of Methemoglobin:-



NADH-Cyt b5 reductase
Activity is half of adults in newborns. More susceptible to HbM producing drugs

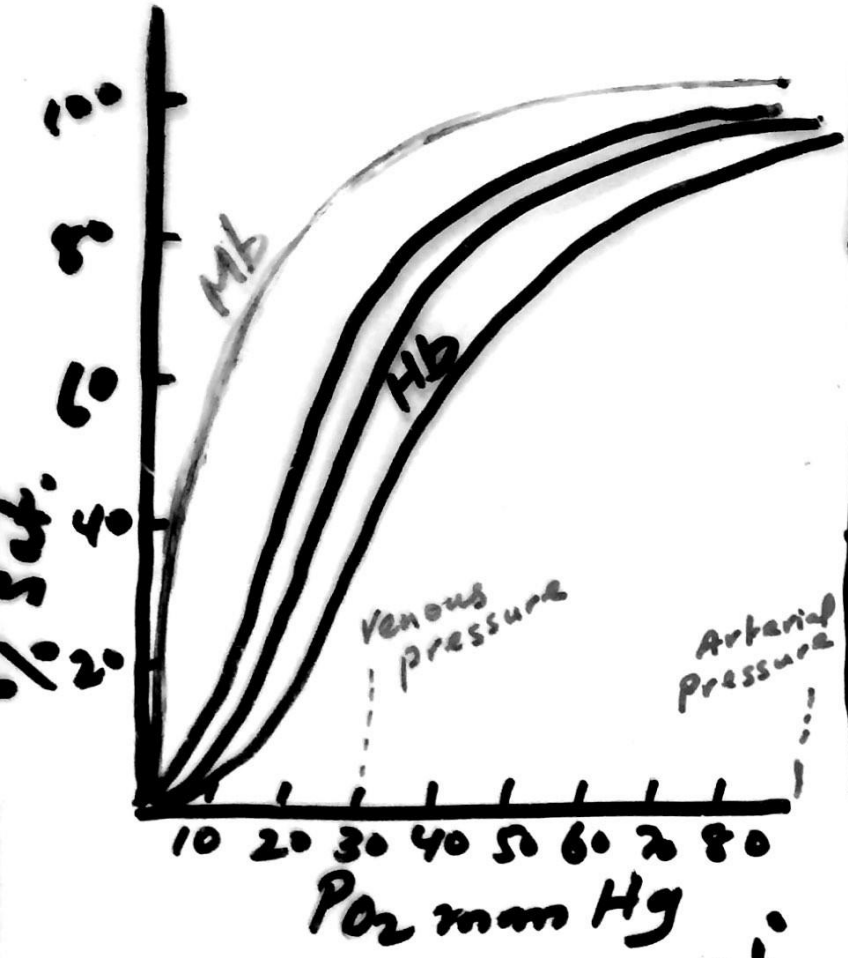
→ Role of Methemoglobin in Cyanide Poisning:-

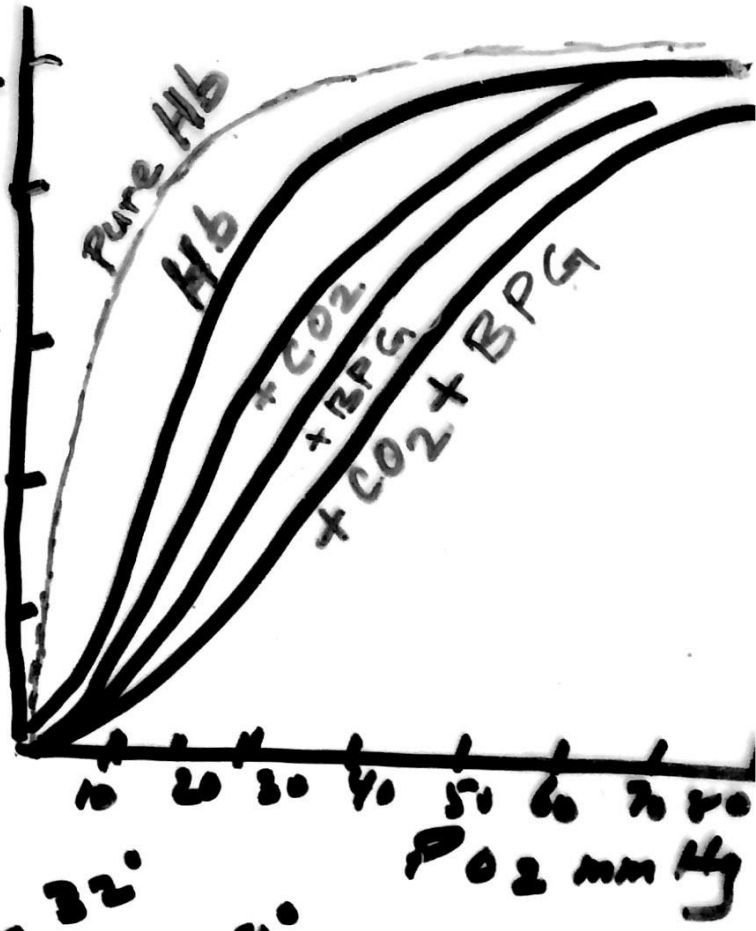
Treatment with Hb-M producing drugs to form some HbM to bind CN^- and protects complex IV of respiratory chains from poisning.

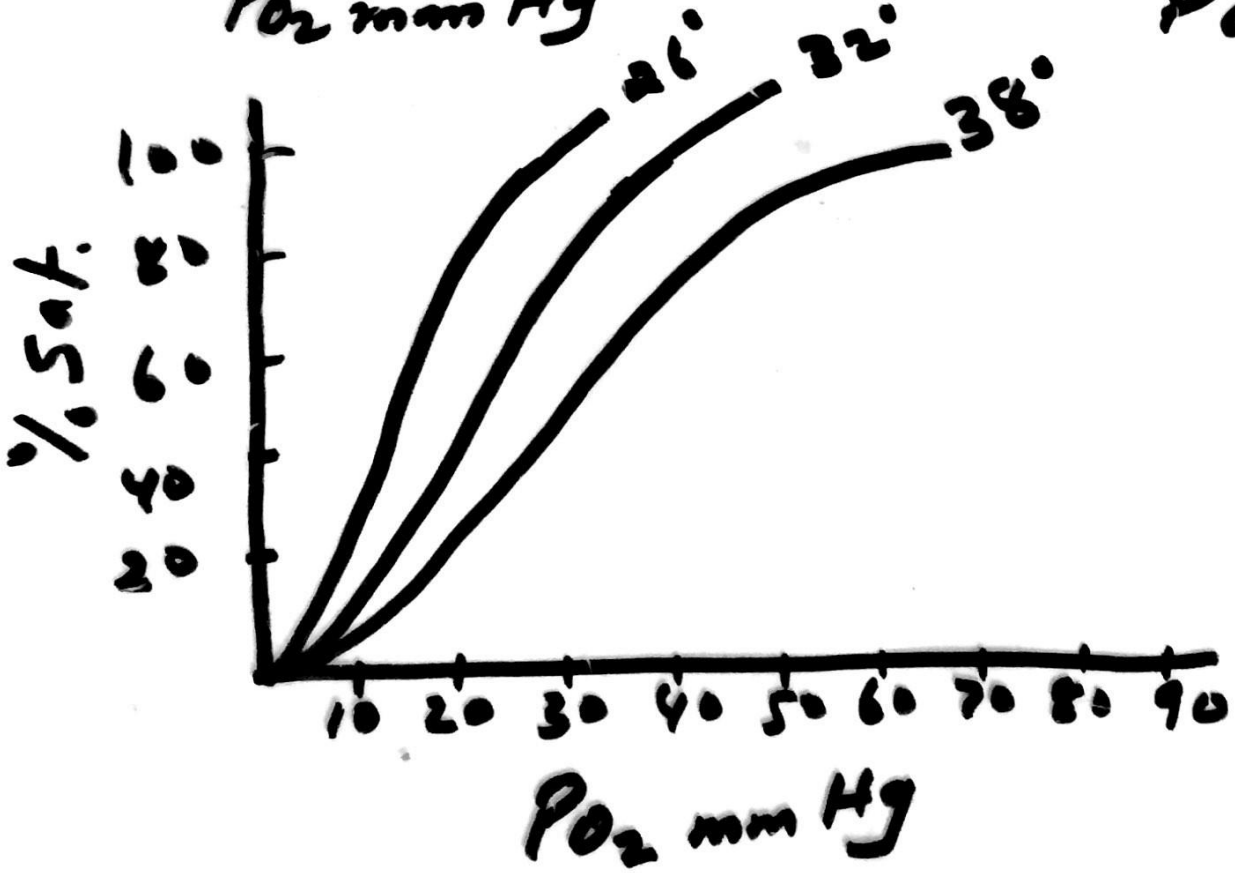
• Treatment of Methemoglobinemia:-

- With methylene blue or Ascorbate (less effective)
- Not effective in G6PD-deficiency

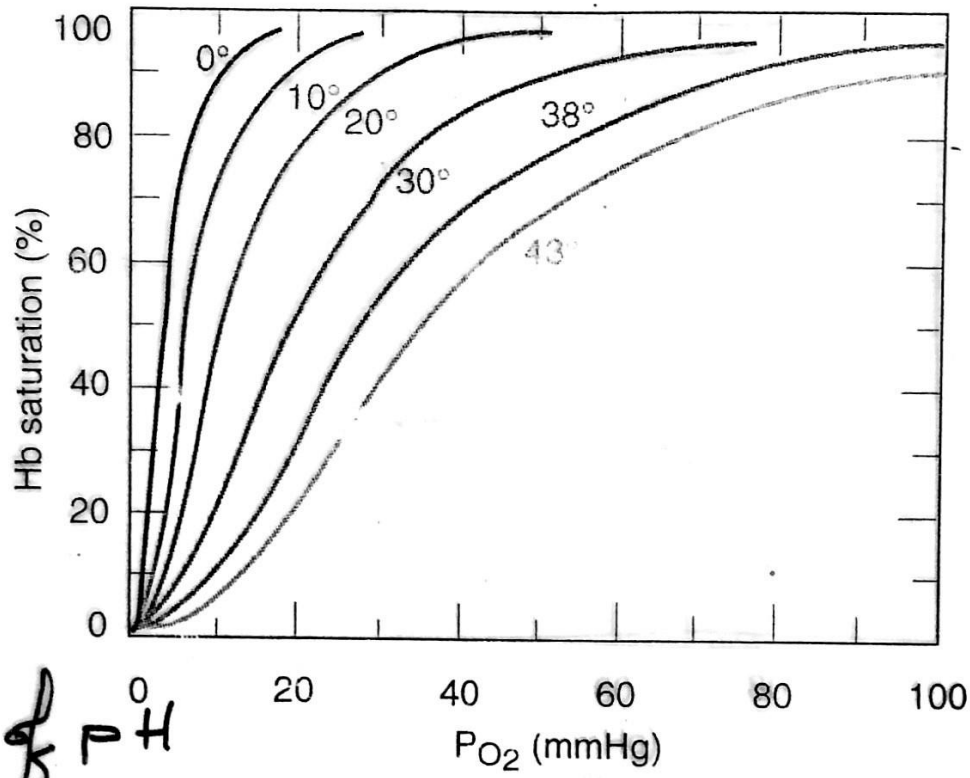
(because Methyle blue requires NADPH from G6PD)


100
80
60
40
20
% Sat.
Mb
Hb
Venous pressure
Arterial pressure
10 20 30 40 50 60 70 80
PO2 mm Hg

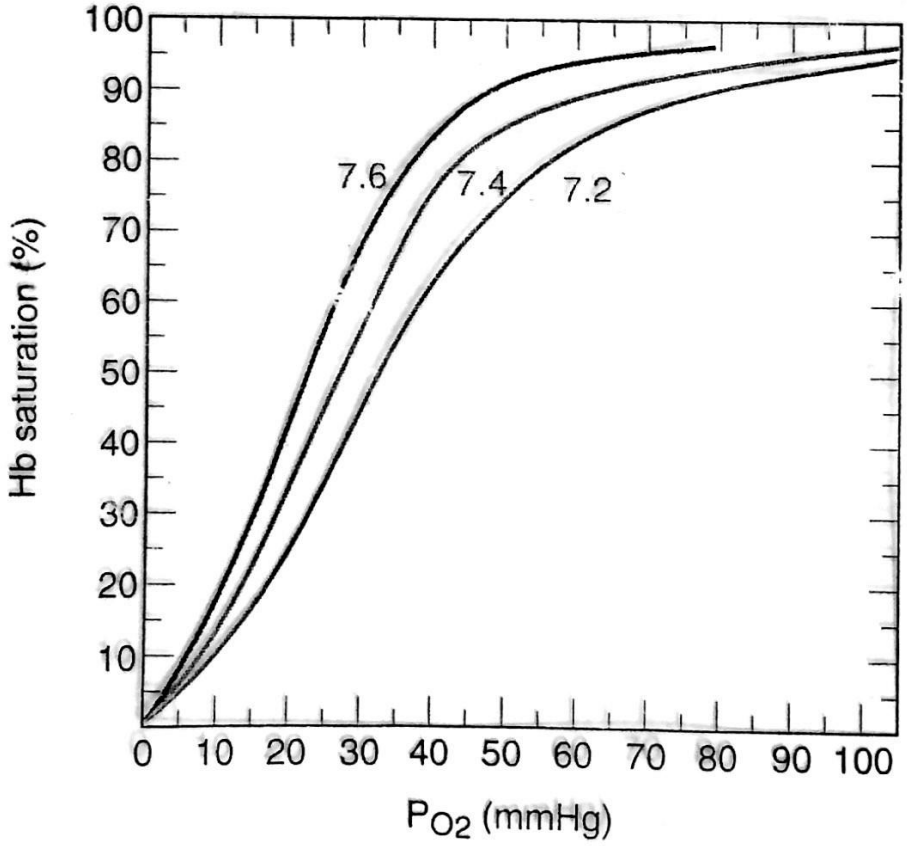

Pure Hb
Hb
+CO2
+BPG
+CO2 + BPG
10 20 30 40 50 60 70 80
PO2 mm Hg


26°
32°
38°
100
80
60
40
20
% Sat.
10 20 30 40 50 60 70 80 90
PO2 mm Hg

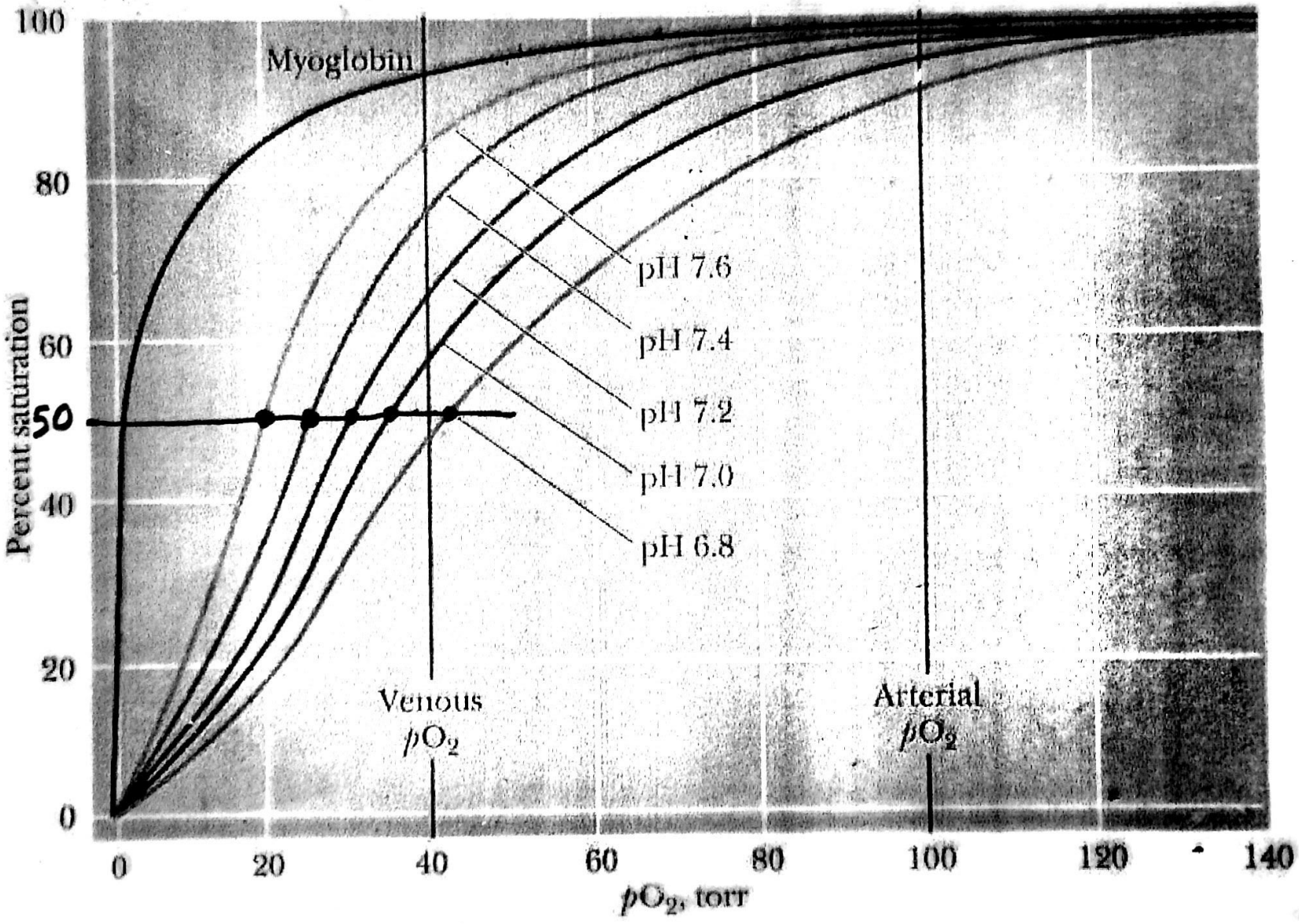
Effect of Temp.



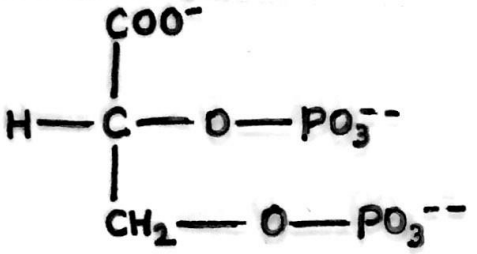
Effect of pH



The oxygen saturation curves for myoglobin and for hemoglobin at five different pH values: 7.6, 7.4, 7.2, 7.0, and 6.8.

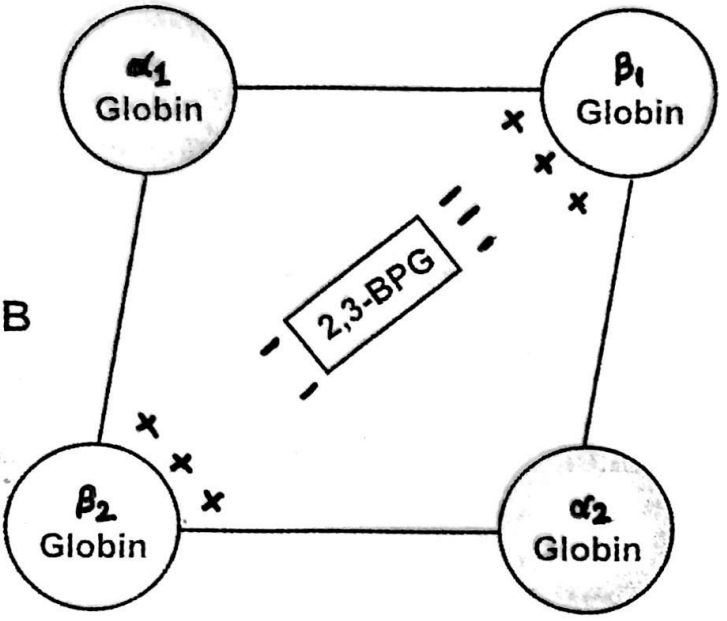


A

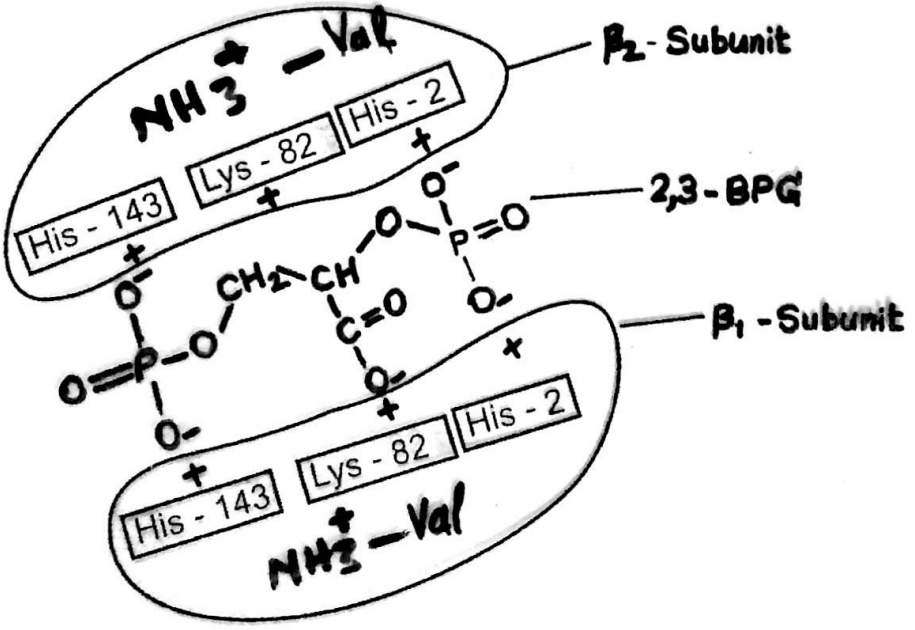


2, 3-Bisphosphoglycerate
(2,3-BPG)

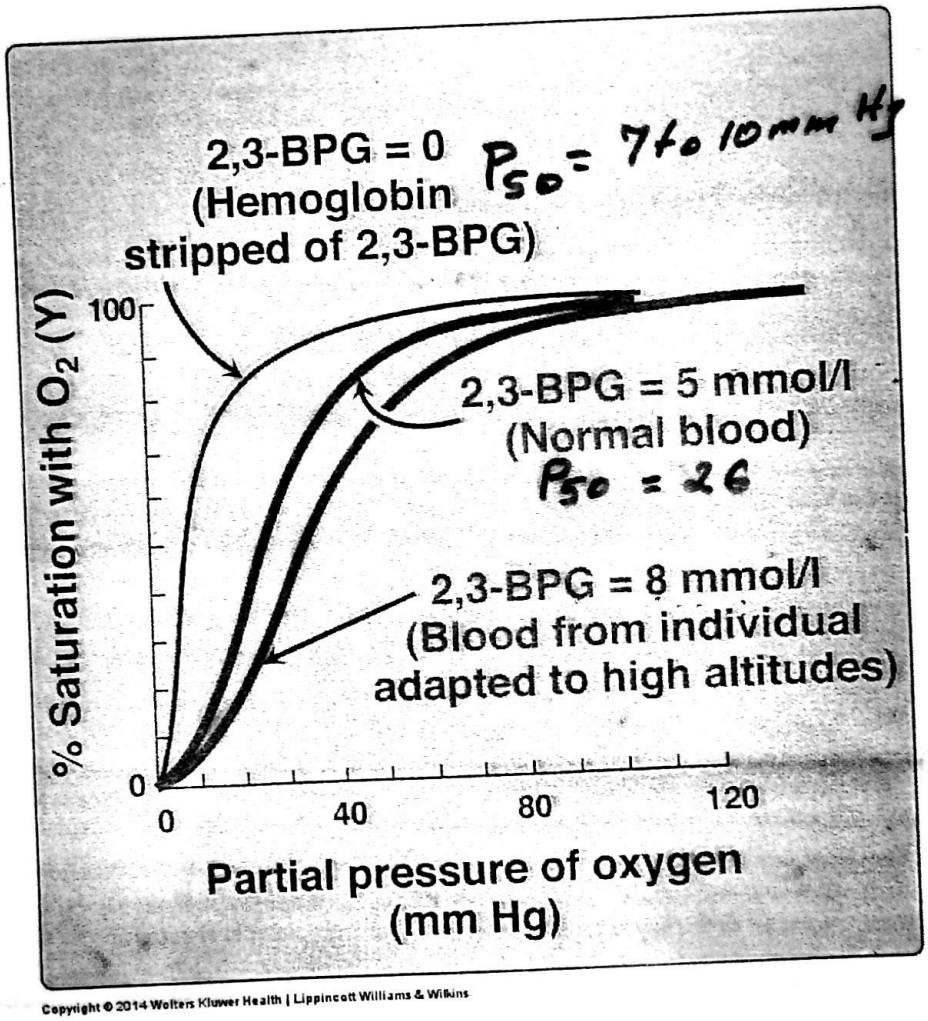
B



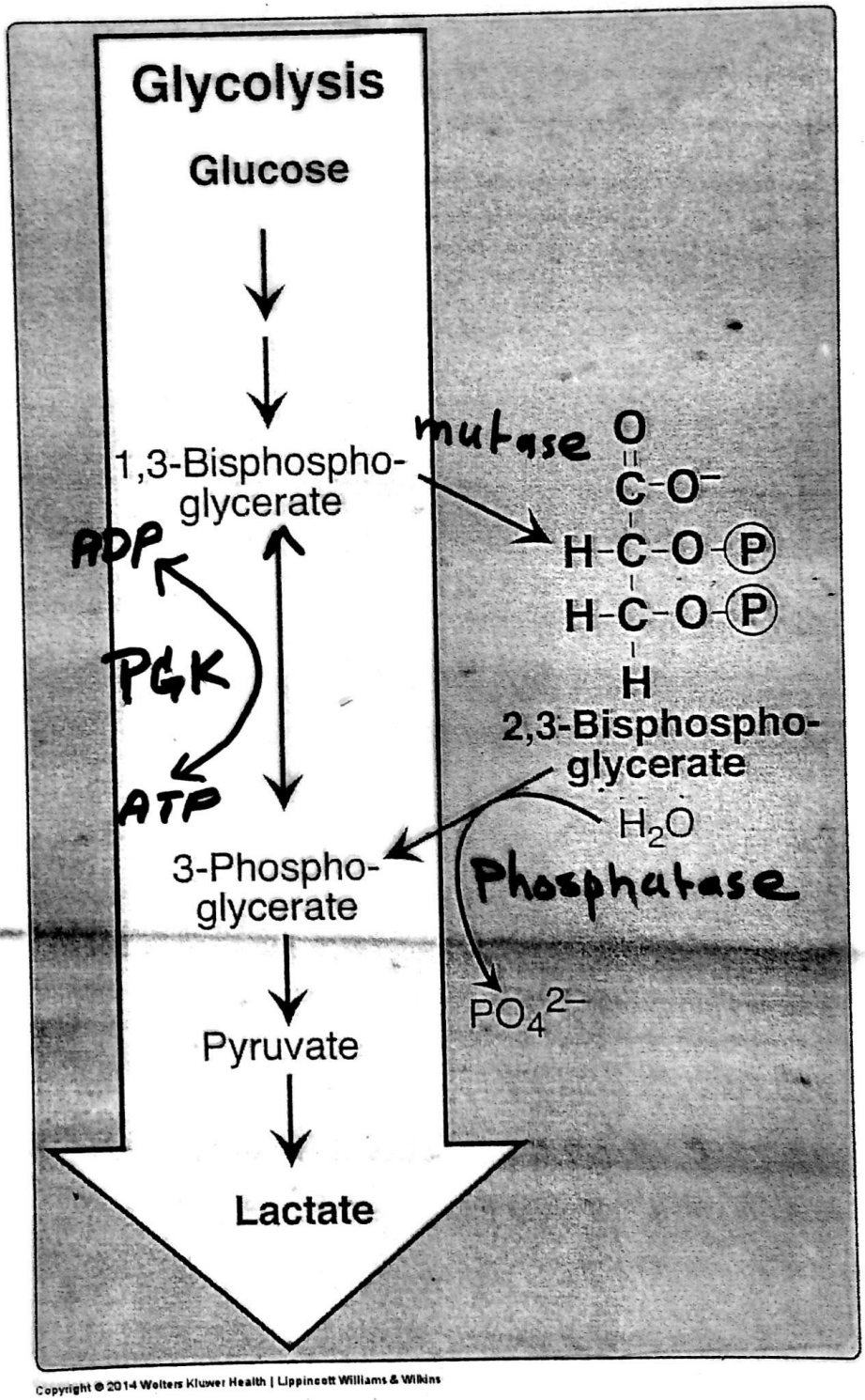
Figures 8.9A and B: (A) Structure of 2,3-BPG, (B) Schematic representation of binding of 2,3-BPG to the haemoglobin



Effect of 2,3-BPG on the Oxygen affinity of hemoglobin



Synthesis of 2,3-BPG



BPG decreases O_2 affinity by cross-linking deoxyHb

2,3-bisphosphoglycerate (BPG) interacts with 3 positively charged groups on each β-subunit

$HbA = \alpha_2^A \beta_2^A$

$HbF = \alpha_2 \gamma_2$

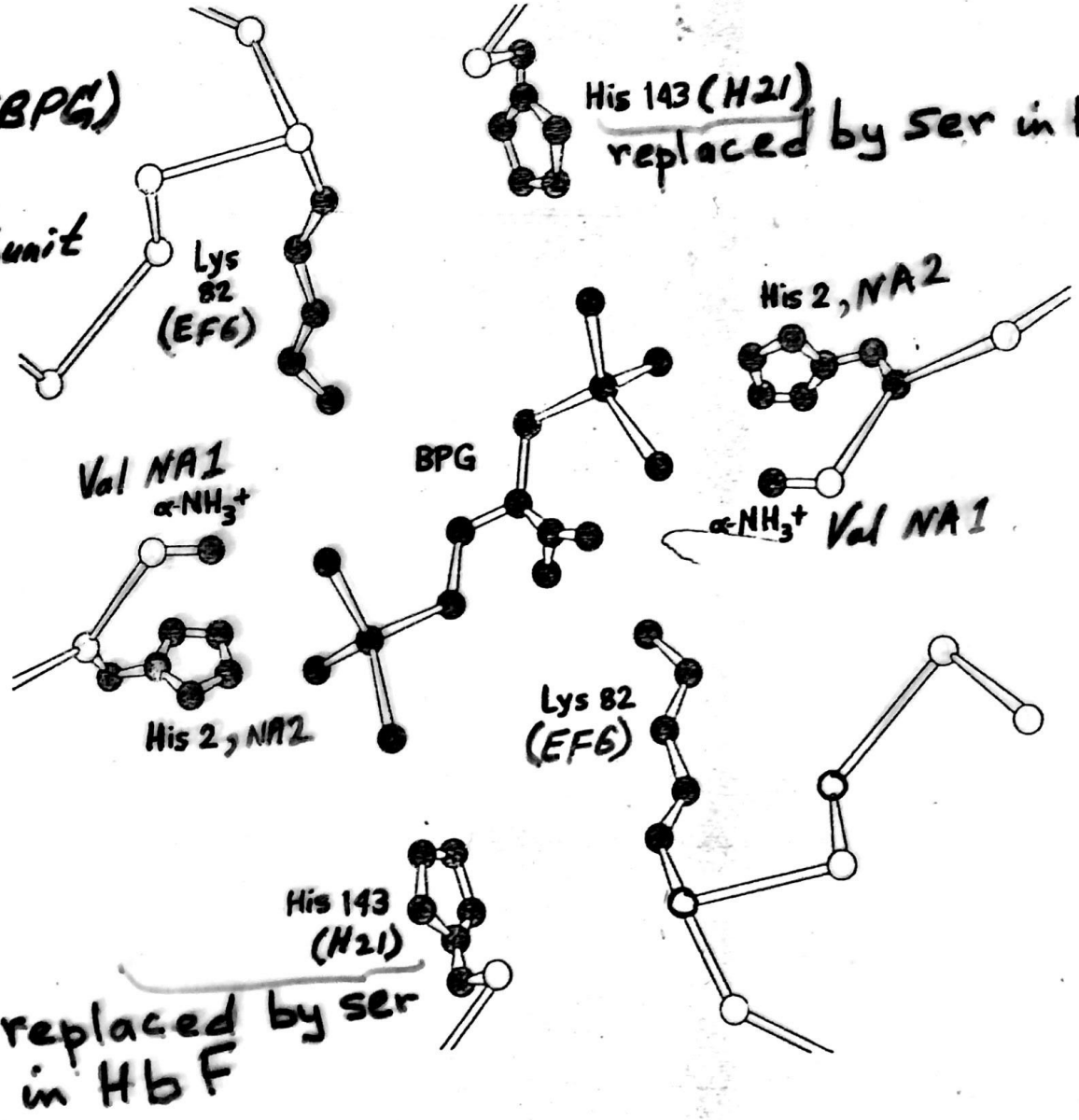
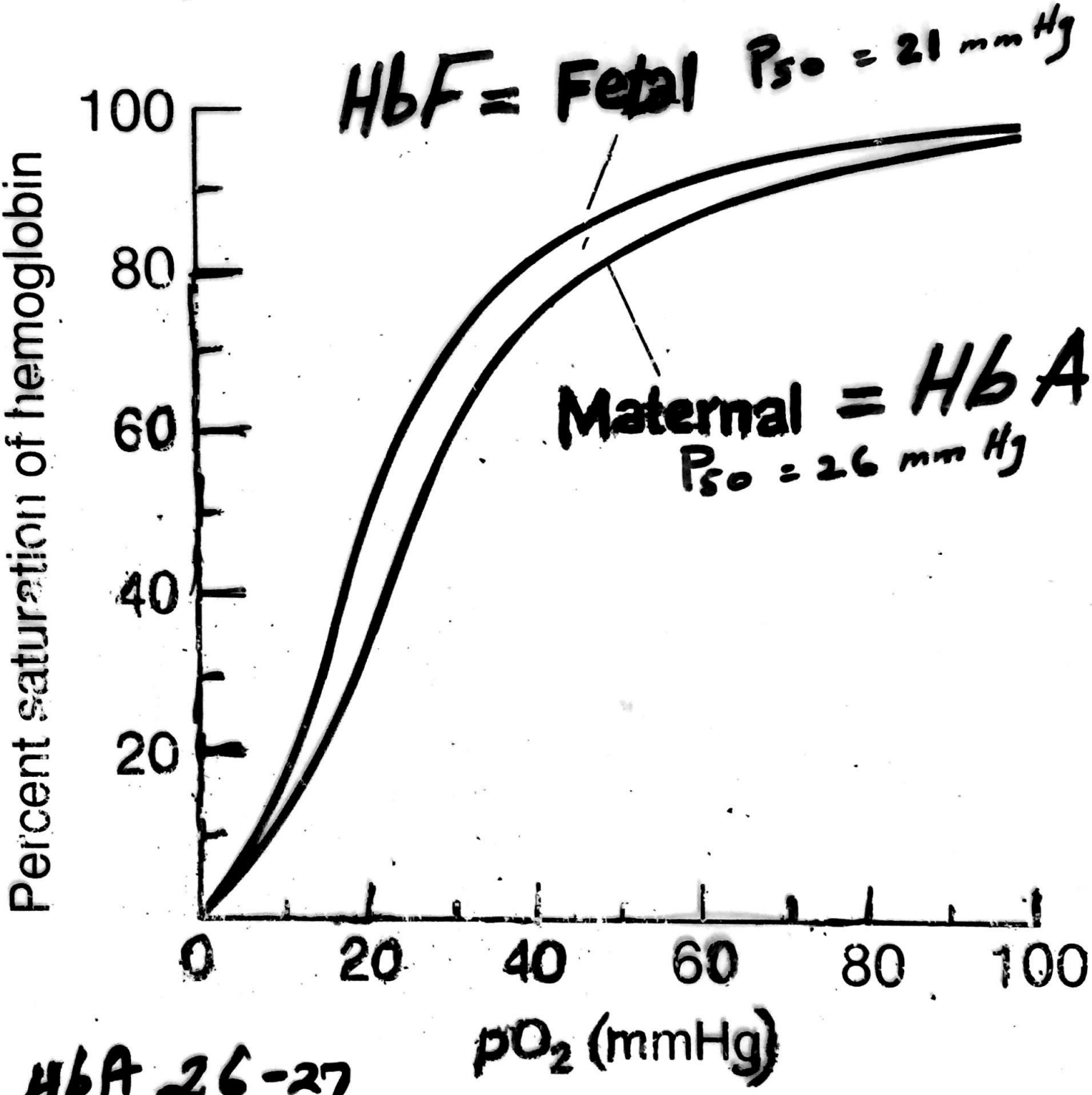


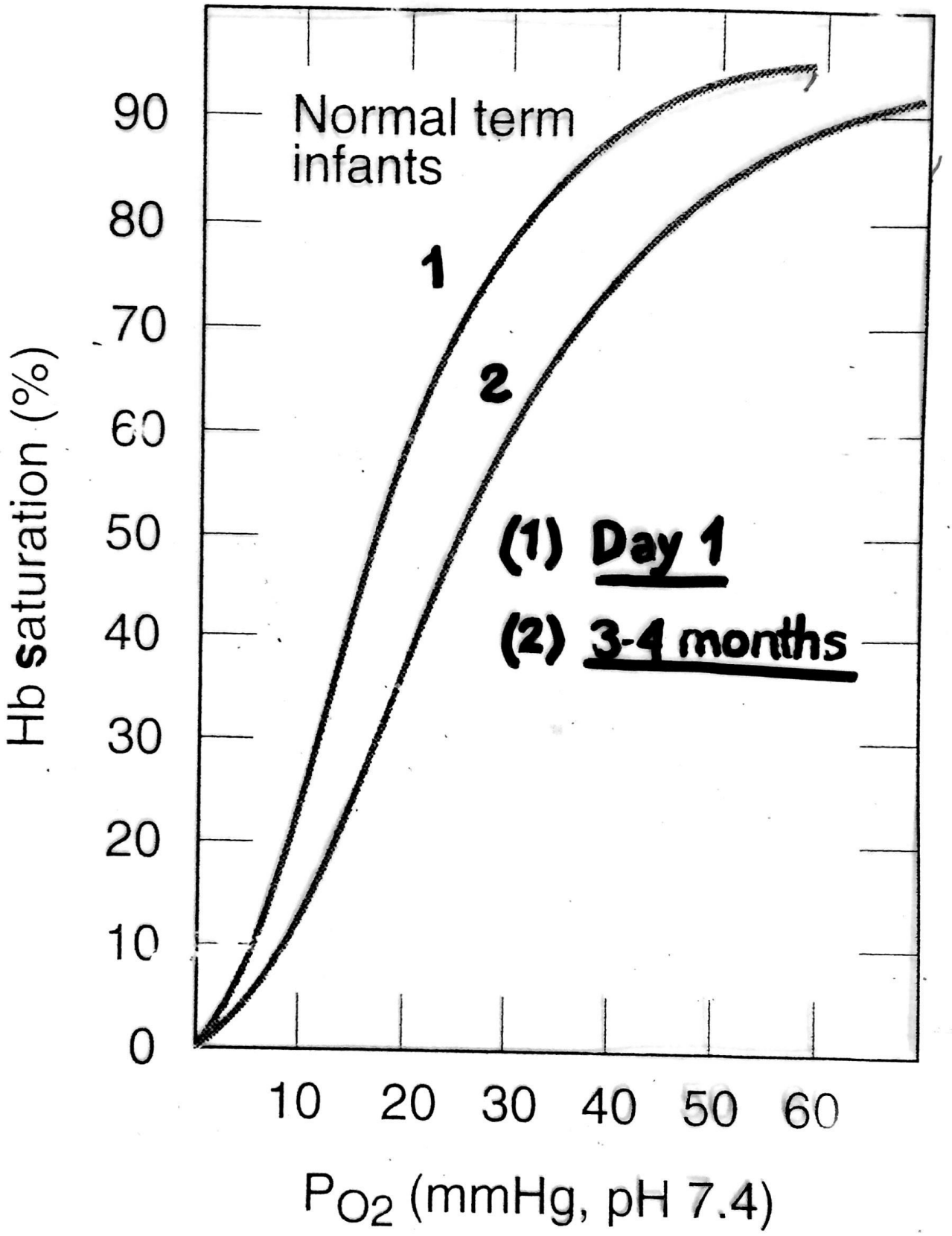
Figure 7-34
Mode of binding of BPG to human deoxyhemoglobin. BPG interacts with three positively charged groups on each β chain. [After A. Arnone. *Nature* 237(1972):148.]

Fetal Hemoglobin has a Higher Affinity for Oxygen than Adult Hemoglobin



HbA 26-27
HbF 20 mm Hg

Oxygen-hemoglobin Dissociation Curve; Comparison of Fetal and Maternal Hemoglobin


Normal term infants
1
2
(1) Day 1
(2) 3-4 months
Hb saturation (%)
90
80
70
60
50
40
30
20
10
0
10
20
30
40
50
60
P_{O_2} (mmHg, pH 7.4)