* IMP Structure of Haemoglobin

Sourodeepa

M.W. — 64,028 dalton

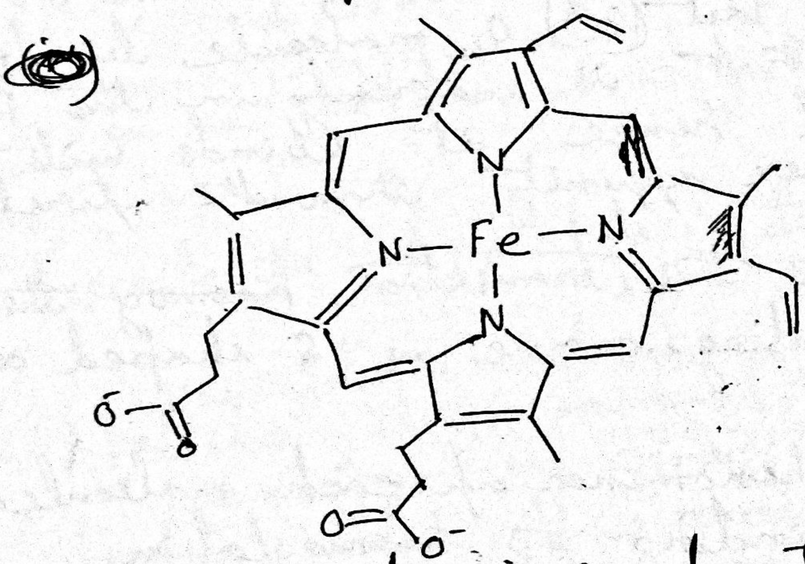
Haemoglobin molecule is consists of two parts — haem (non protein) and globin (protein). It is a tetrameric structure.

① Haem

(i) It is acyclic tetrapyrrole consisting of 4 molecules of pyrrole linked by α-methylene bridges.

(ii) The β-positions of haem are substituted by methyl(M) vinyl(V) and propionate(Pr) groups arranged in the order M, V, M, V, M, Pr, Pr, M.

(iii) One atom of Ferrous iron (Fe^{2+}) resides at the centre of the planer tetrapyrrole.



(iv) The pyrrole rings and methylene bridge carbons are co-planer and the iron atom resides almost the same plane.

The 5th and 6th co-ordination positions of Fe^{2+} are directed perpendicular to and directly above and below the plane of haem ring

Co-operative binding of Oxygen

Binding of O_2 to individual subunits of haemoglobin alters the affinity for O_2 in adjacent subunits. The first molecule of O_2 that interacts with deoxyhaemoglobin binds weakly because it binds to a subunit in the T state. Its binding leads to conformational changes that are communicated to adjacent subunits making it easier for additional molecules of O_2 to bind. The T → R transition occurs more readily in the second subunit once O_2 is bound to the first. The last (4th) O_2 molecule binds to a haem that is already in the R state and hence it binds with much higher affinity than the first molecule.

Due to this slow transition, ~~haemog~~ the oxygen binding curve is S-shaped or sigmoid. ~~sh~~

The phenomenon of each molecule of oxygen binding to haemoglobin independently and facilitating the next one to bind is called co-operative binding.

Paper — III
Gr — D
Puhan Chakraborty

HAEMOGLOBIN IN RELATION TO O_2 & CO_2 TRANSPORT

Q What is haemoglobin?

Haemoglobin is the red coloured respiratory pigment of all red blood and it is a conjugated chromoprotein containing of 4% haem (a Fe containing pigment) and 96% globin (a simple histone protein). Haem is the prosthetic gr. of haemoglobin.

Q What is the amount of Hb in Human male & female?

Although the concentration of Hb in our blood varies, its normal range in adult males per 100ml of blood is 14-18 gm and the same is 12-15 gm in adult females.

Q Describe the role of Hb in O_2 transport.

Haemoglobin is a red coloured respiratory pigment of all red blood. It is a conjugated chromoprotein containing 4% haem (a Fe containing pigment) and 96% globin (a simple histone protein). It is present in the RBC, but it remains in plasma of some invertebrates like (Earthworm). It is concerned with the transport of respiratory gases like O_2 and CO_2.
In each molecule of haemoglobin, there are four iron atoms in Fe^{2+} state. Each Fe^{2+} atom can bound to one molecule of O_2 (2 atoms of O). Thus one molecule of haemoglobin can combine with

four oxygen molecules. The formula of fully oxy haemoglobin (oxyhaemoglobin) is Hb_2O_8.

3) Role of Hb in O_2 transport

Before discussing the role of Hb in O_2 transport, we consider the O_2 tension amount in the vein, artery, tissues and in the respiratory organs.

Taking human as example the tension, amount of O_2 different sites are:

Tension of O_2 in different sites:

i) In venous blood – about 40 mm of Hg
ii) In arterial blood – " 90-100 " " "
iii) In tissue cells – " 40 " " "
iv) In lung alveoli – " 100 " " "

Amount of O_2 present in blood :–

(A) In venous blood → About 14-15 ml of O_2/100 ml of venous blood present in two states:

(i) In physical soln – 0.15 ml/100 ml of venous blood.
(ii) As oxyhaemoglobin – 13.85-14.85 ml / " "
Total = 14-15 ml O_2/100 ml of venous blood.

(B) In arterial blood :– ~~About 19-20ml of O₂/100ml O₂~~ About 19-20ml of O_2/ml 100ml of arterial blood & remains in the states as follows :–

i) In physical solution – 0.3 ml/100ml of art. blood.
ii) As chemical compound – 18.7-19.7 ml/ "

Total = 19-20 ml of O_2/100ml of arterial blood.

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Mechanism of O_2 transport

The transport of O_2 from respiratory organs to the body tissues, involves three steps as follows:

A. Diffusion of O_2 from respiratory organ to blood and its conversion into different forms.
B. Carriage of O_2 through blood to tissue sites.
C. Evolution of O_2 from blood and its diffusion into tissue cells.

A. Diffusion of O_2 from respiratory organ to blood and its conversion into different forms:

When the venous blood passes through the pulmonary capillaries in the ~~blood~~ lungs, it has got O_2 tension about 40mm Hg while the same in the alveoli is about 100mm Hg. This differential pressure causes diffusion of O_2 molecules from alveoli to blood through capillary endothelium. Simultaneously CO_2 is liberated from the venous blood to the lungs by diffusion. So the CO_2 tension and H^+ ion concentration fall in the blood of capillaries. These also favours the diffusion of O_2 into the capilcories. Entering into the bl... is carried in two forms:

1. 0.3 ml/100ml is carried as physical solution into blood and the rest amount is carried as oxyhaemoglobin compound.

2. <u>Oxyhaemoglobin formation</u> - About 19-20 ml of O_2 ... ml of arterial blood is carried in the ... of oxyhaemoglobin compound.

Hb4 combines with 4 molecules of O_2 ... wise and finally forms saturated oxyhaemoglobin (Hb_4O_8) -

$$Hb_4 + O_2 \rightleftharpoons Hb_4O_2$$
$$Hb_4O_2 + O_2 \rightleftharpoons Hb_4O_4$$
$$Hb_4O_4 + O_2 \rightleftharpoons Hb_4O_6$$
$$Hb_4O_6 + O_2 \rightleftharpoons Hb_4O_8$$

<u>Note</u> - The compound oxyhaemoglobin is loose and reversi... i.e. it is quickly formed in the respiratory organ (where O_2 tension is high) and equally qui... dissociates in the tissues (where O_2-tension is low...

B. Carriage of O_2 through blood circulation to tissue site

Oxyhaemoglobin is formed within the RBC and it is then carried through blood circulation to the tiss... sites. When the blood passes through tissue capilla... oxyhaemoglobin dissociates to liberate O_2 to supply the tissues.

C. Evalution of O_2 from blood and its diffusion into tis...

The tension of O_2 in arterial blood is about 90-100 of Hg and that in the tissues is 40mm of Hg. This

~~differential pressure causes the diffusion of O_2 into~~ differential tension and some other factors (like temp, CO_2 tension etc) causes the dissociation of oxyhaemoglobin in RBC.

$$Hb_4O_8 \rightleftharpoons Hb_4O_6 + O_2$$
$$Hb_4O_6 \rightleftharpoons Hb_4O_4 + O_2$$
$$Hb_4O_4 \rightleftharpoons Hb_4O_2 + O_2$$
$$Hb_4O_2 \rightleftharpoons Hb_4 + O_2$$

This O_2 is ~~liberated~~ diffused out through RBC membrane to plasma and then through capillary wall to the tissues. About 25-30% O_2 is liberated from arterial blood when the tissues are in a resting phase. After liberating O_2 Hb_4 becomes reduced and combines with CO_2 to form carbaminohaemoglobin to be carried through veins.

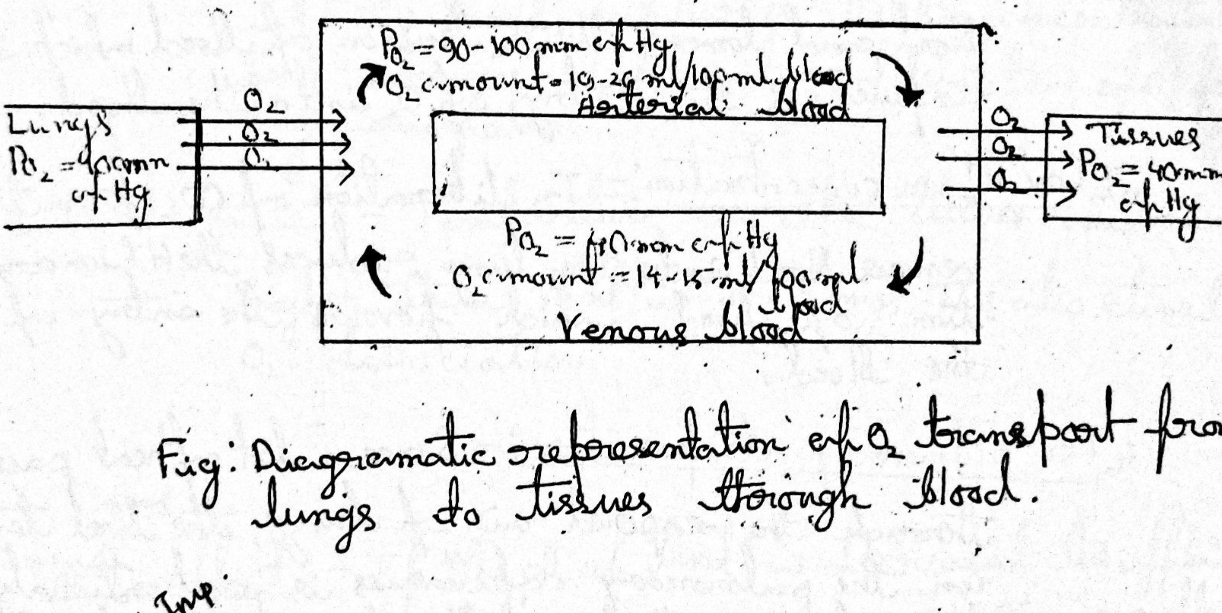

Fig: Diagramatic representation of O_2 transport from lungs to tissues through blood.

V. Imp.

Q. Mention the factors regulating the transport of O_2

or

Mention the factors regulating the O_2 diffusion from lung to blood and from blood to tissues.

The factors regulating the O_2 transport can be stated steps :

left shift.

A. Factors regulating the entry of O_2 from lungs to blood

1. O_2 pressure gradient :- The difference of O_2 tension in alveo air (100 mmHg) and venous blood (40 mmHg) of pulmonary arteriolar capillaries influences the diffusion of O_2 alveoli to the pulmonary venule capillaries.

2. Low CO_2 tension :- In the lungs, CO_2 is liberated from blood and lowers the CO_2 tension of blood which in t influences the entry of O_2 into the blood.

3. Low H^+ ion concentration :- In liberation of CO_2 from the venous blood into the lung reduces the H^+ ion concen -tion of blood which favours the entry of O_2 the blood.

4. Low pulmonary temperature :- Since, a lot of heat passes through the expired air of lungs, the blood temp in the pulmonary capillaries is proportionaly lowered then that in the tissues. The facilitat O_2 intake by blood.

right shift

Imp.

B. Factors regulating the evolutions of O_2 from blood of tissue capillaries (Dissociation of O_2) / factor

Oxygen leaves the blood stream and enters the tissues.

because of the condition prevailing in the tissues capillaries are exactly opposite to those present in the lungs. These are:

1. O_2 pressure gradient:- The difference of O_2 tension in the tissues (40mmHg) and arterial blood (90-100mmHg) causes dissociation of O_2 from oxyhaemoglobin and diffusion of O_2 to the tissues.

2. CO_2 tension:- CO_2 tension of blood in the arteriolar capillaries is lower than the tissues and CO_2 enters the blood raising its tension in blood. These favours dissociation of oxygen from oxyhaemoglobin.

3. H^+ ion concentration:- With the entry of CO_2 from tissues into the blood capillaries, the H^+ ion concentration of blood increases which induces dissociation of O_2 from oxyhaemoglobin.

4. Temperature:- Temperature in the tissues capillaries is higher than that in the lungs. This also stimulates O_2 dissociation.

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Bohr effect - If the pH of blood is decreased, the affinity of Hb towards O_2 is decreased. This is called Bohr effect.

2. What is oxygen-dissociation curve?
Write notes on oxygen dissociation curve.
or
Oxygen saturation curve oxyhaemoglobin disso. curve

About 95-96% of haemoglobin in blood is converted oxyhaemoglobin at an O_2 tension of 100mm Hg (O_2 tension in lung alveoli is about 100 mmHg) and Hb is said 95-96% saturated with O_2. Below this O_2 tension, degree of saturation varies with O_2 tension.

The relation between the partial pressure of O_2 and amount of oxyhaemoglobin formed on dissociation has been studied under various condition. The: when plotted in the graph, it gives a curve oxygen-dissociation curve.

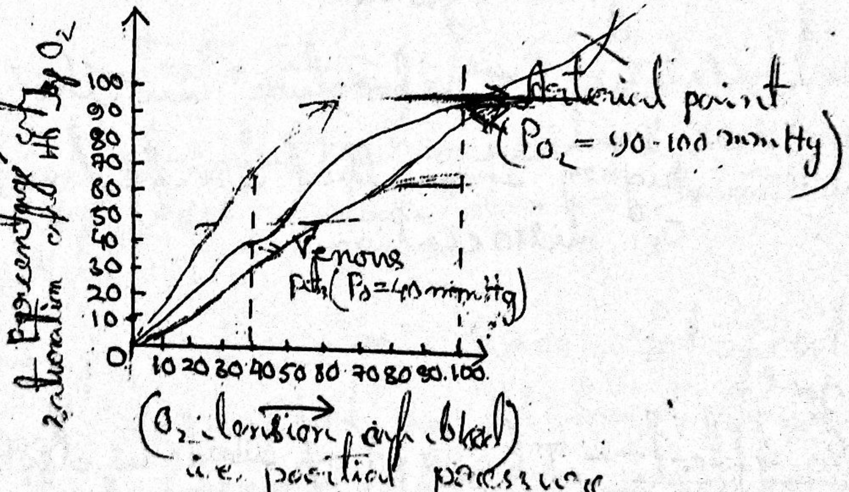

fig: O_2 disso. curve / O_2 saturation curve / HbO_8 disso. curve

The curve shows ~~that the middle~~ % of saturation of haemoglobin by O_2 (i.e. oxyhaemoglobin formation) against O_2 tension of blood at the CO_2 tension of 40 mm of Hg.

Leis imp (5)

Describe the role of Hb in CO_2 transport.

Due to metabolic activities of the cells, CO_2 is produced & enters the blood of the body & is carried to the respiratory organ from where it is got rid off from the body. The transport of CO_2 through the red blood occurs in two states — in physical solution and by formation of chemical compounds.

In the following description the transport of CO_2 w reference to the haemoglobin is discussed takin human being as an example. Before discussing the role of haemoglobin in CO_2 transport we should consider the CO_2 tension of blood, respiratory organ and tissues, and amount of CO_2 in venous & at arterial blood at various states.

<u>CO_2 tension at diff. sites</u>:

i) In the tissue cells — about 46 mm of Hg
ii) " " lung alveoli — " 35-40 " "
iii) " " venous blood — " 46 " "
iv) " " arterial " — " 35-40 " "

Amount of CO_2 present in blood

i) In venous blood — About 52 ml of CO_2/100 ml venous blood which remains in the following states:
   ⓐ In physical solution — 2.7 ml/100 ml blood
   ⓑ As bicarbonates — 45.7 " / "
   ⓒ As carbamino compounds — 3.7 " / "
   Total — 52.2 ml/100 ml blood

ii) In arterial blood — About 48 ml CO_2/100 ml arterial blood which remains in following states:
   ⓐ In physical solution — 2.4 ml/100 ml blood
   ⓑ As bicarbonates — 42.9 " / "

(c) As carbamino compounds – 3.0 ml / 100 ml blood
= 4.8 3 ml / 100 ml blood

lession

Mechanism of CO_2 transport by haemoglobin

A. Saturation of haemoglobin by CO_2 :– About 3.7 ml of ~~venous b~~ venous blood is carried as carbamino compounds of w 2.6 ml CO_2 / 100 ml venous blood is carried in RBC a carbamino haemoglobin (Hb.NH.COOH). The trace rest amount (about 1.1 ml / 100 ml) is carried in the pla as carbamino protein.

CO_2 enters the RBC & combines with globin por haemoglobin to form carbamino haemoglobin. In the p process the NH_2 radicles of the globin part of Hb comb with 2 moles of CO_2 (as free gas). It does not require the help of enzyme. It is a very rapid reacti

$$Hb.NH_2 + CO_2 \rightarrow Hb.NH.COOH \text{ (Carbamino haemoglobin)}$$

B. Carriage of CO_2 to the lungs :– Carbamino haemoglobin carried to the lung capillaries through the blood circulation.

C. Dissociation of CO_2 in the lungs :– The release of CO_2 fr the venous blood takes place in the lung capillaries with involves the reverse reaction to that occurred in the tissue sites.

The carbamino haemoglobin, as a rule undergoes dissociation to release CO_2 which differes through the capillary wall into the alveoli. From the alveoli the CO_2 is expired. The Hb after releasing CO_2 becomes combined with O_2 to form oxyhaemoglobin to be carried to the tissue sites.

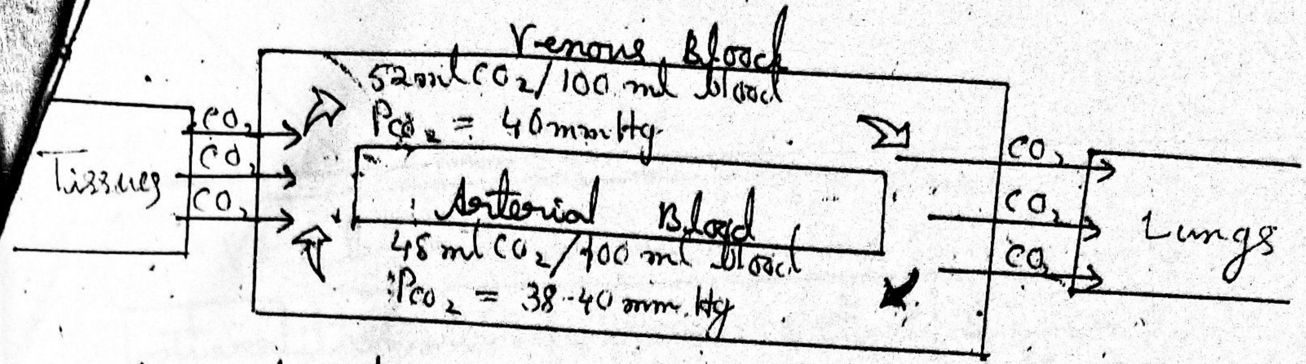

fig: Schematic representation of CO_2 transport from body tissues to the lungs.

1. What are the factors determining CO_2 transport?

A. Factors determining intake of CO_2 from tissue into blood

1) Pressure gradient - The difference of pressure of CO_2 in the tissues capillaries (40 mmHg) & the resting tissue cells (46 mm Hg) & makes diffusion of CO_2 from tissue to blood capillaries.

2) Reduction of haemoglobin - Oxyhaemoglobin is reduced in tissue capillaries, so that the based freed from the reduced haemoglobin is made available for fixing H_2CO_3.

3) Chloride shift - Cl^- shifting from plasma to RBC, more Na^+ ions are made available in the plasma for fixing HCO_3^-.

4) Carbamino compound formation - Carbamino compounds are formed very quickly by increased CO_2 tension and reduction of oxyhaemoglobin in the tissue capillaries.

B. Factors concerned with the liberation of CO_2 in lung.

1) Pressure gradient – The difference of CO_2 pressure in the venous blood (40mmHg) & lung alveoli (40mmHg) makes diffusion of CO_2 from blood to lung alveoli.

2) Oxygenation of haemoglobin – Oxygenation of haemoglobin in lung capillaries help to break the carbamino compound to release CO_2. Again oxyhaemoglobin being a stronger acid, takes ~~away~~ away K from $KHCO_3$ & liberate carbamino acid which in turn releases CO_2.

3) Reverse Cl^- shifting reaction – It helps in breaking bicarbonate to form HCO_3 from which CO_2 is realeased.

Q. What is CO_2 - dissociation curve ?

With a comparative study of the CO_2 contents of reduced blood, oxygenated blood, bicarbonate solution & water, under different pressure of CO_2, important facts have been known regarding the behaviour of CO_2 of blood under different physiological conditions.

The results when plotted on graph, it form the curves, called CO_2 - dissociation curves.

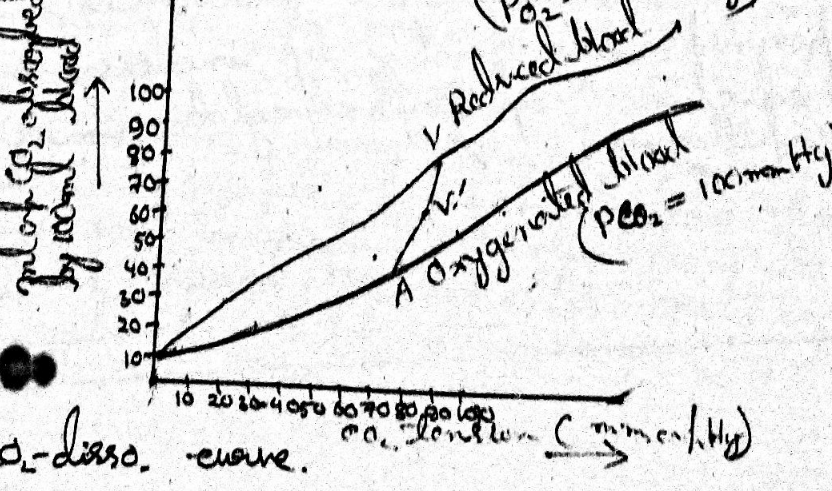

fig: CO_2-disso. curve.

∴ A = Arterial point where P_{O_2} = 40 mm of Hg
• V = Fully reduced ~~point~~ where P_{O_2} = 40 mm Hg
V' = Mixed venous point where P_{O_2} = 46 mm Hg

• Upper curve → CO_2 dissociation in reduced blood where O_2 tension is 0
• Lower curve → CO_2 dissociation in oxygenated blood where O_2 tension is 100 mm of Hg.

Q. Mention the findings from the CO_2-dissociation curve.

From the CO_2-disso. curve, the following facts are seen:

① In a vacuum, CO_2 content of blood is nil.

② At any given CO_2 tension, reduced blood takes up larger amount of CO_2 than oxygenated blood. So that in the body, reduction of blood in the tissue capillaries increase the degree of CO_2 uptake from the tissues.

③ Oxygenation of blood causes evolution of CO_2 from blood which occurs in the lungs.

④ As the CO_2 tension is increased, the ~~blood~~ total amount of CO_2 taken up by blood also rises. As the CO_2 tension falls, CO_2 content also diminishes.