Gas transport in blood

The partial pressure of O_2 in atmosphere is about 160 mm Hg or 21.3 KPa. At this pressure it can oxidise many compounds of cells such as essential sulphahydril groups of enzymes. But in animal system, by the time the oxygen gets through the transport system of the body its partial pressure is reduced to a much less damaging 20 mm Hg (2.67 kPa) or less.

In case of CO_2, it is relatively more concentrated in body and becomes diluted in transit to atmosphere.

pCO_2 (tissues)	pCO_2 (Lungs)	pCO_2 (atmosphere)
46 mm Hg (6.13 kPa)	40 mm Hg (5.33 kPa)	0.2 mm Hg (0.03 kPa)

High concentration of CO_2 is useful for many components of physiologically important buffer system.

Transport of oxygen

At 38°C, 1 litre of plasma dissolves only 2.3 ml of oxygen. 1 litre of blood contains about 150 g of haemoglobin within RBCs. Each gram of Hb can combine with 1.34 ml of oxygen. Therefore 1 litre of blood can carry 200 ml of oxygen that is 87 times as much as that by plasma alone would carry.

The oxygen needs a carrier in blood to be transported in blood. The carrier should have moderate oxygen binding capacity (not very high and not very low).

The haemoglobin has got moderate oxygen binding capacity. If the carrier has very high oxygen binding capacity then the oxygen will not be released in the site of extra-pulmonary tissues. And on the other hand if the binding efficiency is very low than very less amount of oxygen will be bound to haemoglobin.

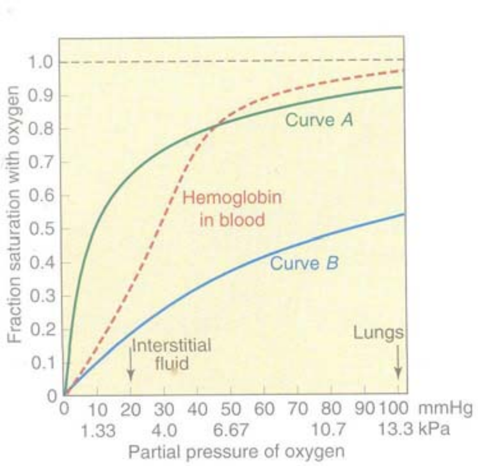
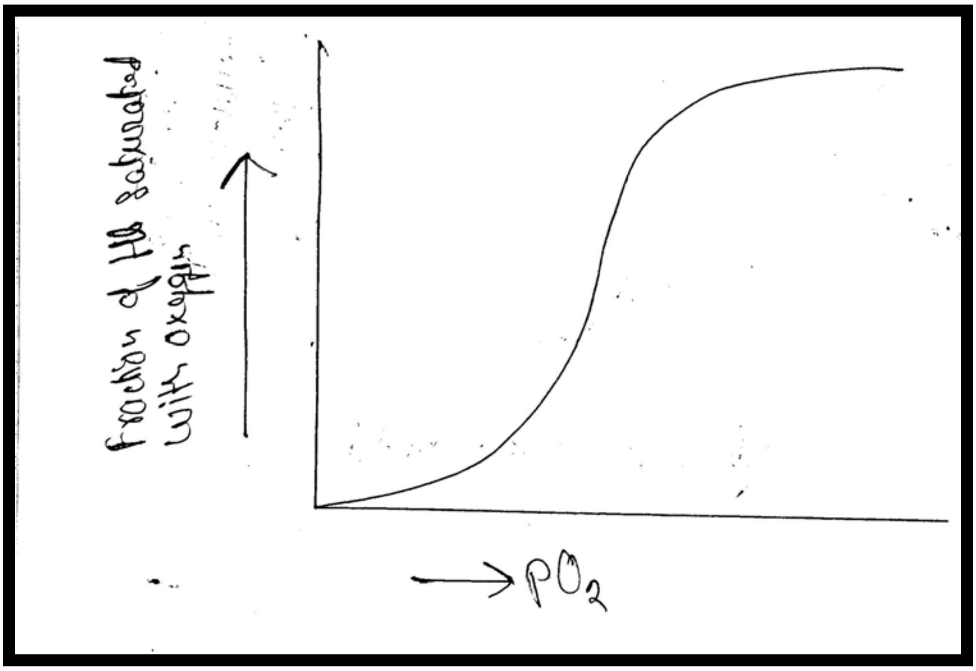


Fig: Oxygen dissociation curve. Here the curve is made between two hypothetical curves (A and B) and haemoglobin. The Oxygen carrier A is having high oxygen binding affinity and B has very low oxygen binding affinity. The curve A of carrier A is shifted towards left and curve B of carrier B is shifted towards right with respect to that of haemoglobin.

This curve indicates that when the oxygen binding affinity of an oxygen carrier increases, the oxygen dissociation curve shifts towards left and when the oxygen binding affinity of an oxygen carrier decreases, the oxygen dissociation curve shifts towards right.

Why does the oxygen dissociation curve of haemoglobin is sigmoid ?



The oxygen carrier Hb shows the sigmoid curve owing to cooperativity. The binding of one oxygen molecule to haemoglobin exhibit positive cooperativity. Binding of first oxygen to deoxy Hb facilitates the binding of oxygen to the other subunits in molecule. Conversely, the dissociation of one oxygen molecule from oxy-Hb would facilitate the dissociation of other three. Because of this cooperative nature, the oxygen saturation curve for Hb is sigmoid.

Effect of 2,3 bisphosphoglycerate (BPG) on Hb:

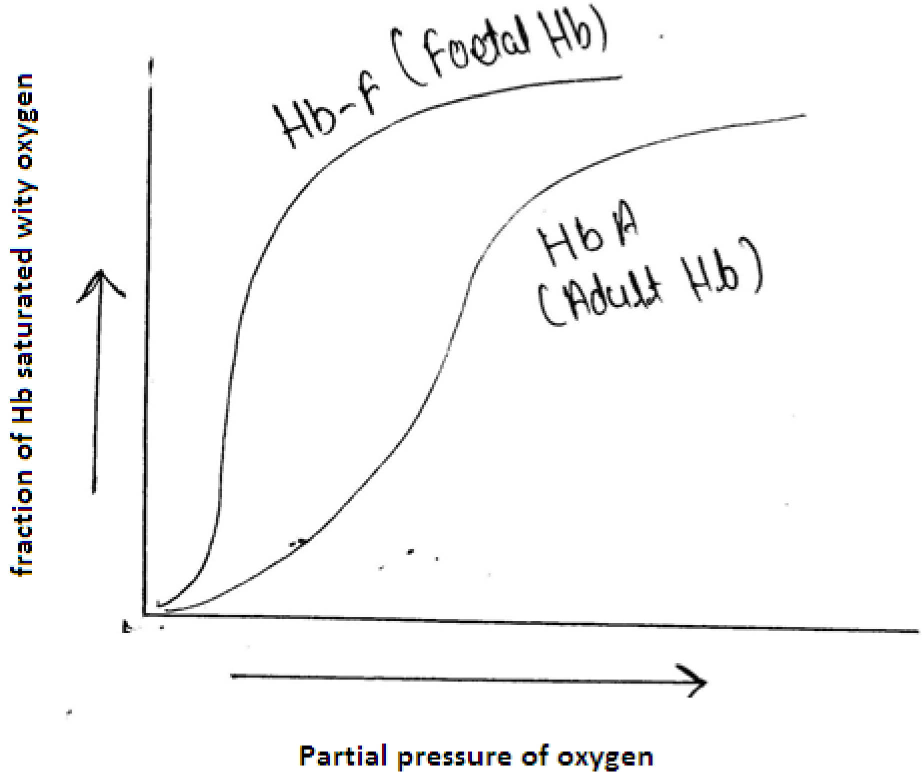
Hb exists in two states viz. T state and R state. The T-state contains pocket for BPG but no pocket for oxygen. On contrary, the R-state contains pocket for oxygen but no pocket for BPG. The BPG favours the transition of R state to T state. In order to bind the Hb, oxygen is required to be in high concentration. Oxygen in lungs is sufficiently high concentration to overcome T state induced by BPG.

Significance of BPG:

1. Efficient delivery of oxygen to extra pulmonary tissues where the oxygen concentration is less.
2. Concentration of BPG is high in tissue hypoxia such as anaemia, cardiopulmonary insufficiency and high altitude.

Haemoglobin F (Hb F) of foetus

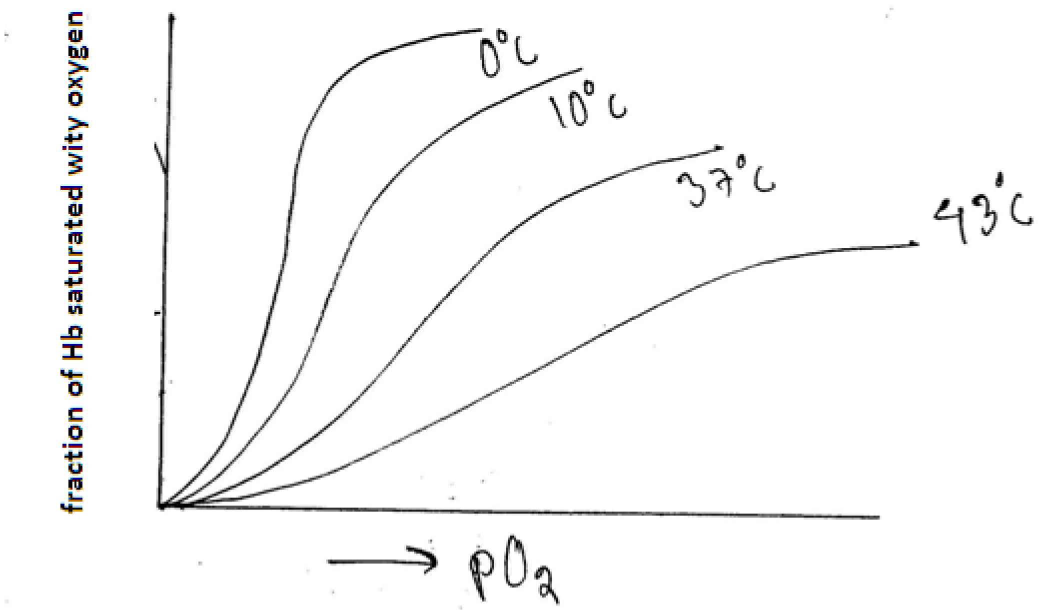
In foetus, the HbF plays major role in oxygen transport. The HbF binding efficiency of BPG is very less thus the HbF has high affinity for oxygen and the oxygen dissociation curve of in case of HbF is shifted to left (corresponding to curve A in the figure)



Factors affecting oxygen binding of Haemoglobin

1. <u>Temperature</u>: the oxygen binding to haemoglobin becomes tighter at low temperature leading to leftward shift of oxygen dissociation curve. The oxygen binding becomes weaker in high temperature causing rightward shift of oxygen dissociation curve. The temperature effect is physiologically useful. It makes the additional oxygen available to support high metabolic rates during fever and exercising muscle where the temperature use to be very high.

2. <u>pH</u>: low pH weakens haemoglobin's oxygen affinity and shifts the oxygen dissociation curve to the right, enhancing oxygen delivery. In high pH, the oxygen binding ability increases in haemoglobin shifting the oxygen dissociation curve to left.



- *During hypothermia due to low temperature, the oxygen binding becomes tighter in case of haemoglobin that may deleterious to tissues due to low efficiency of oxygen delivery to the tissues. But due to more amount of CO_2 produced by hypothermic tissues, the pH of the medium becomes low that again lowers the oxygen binding efficiency of haemoglobin thus compensating the negative effect of high temperature.*

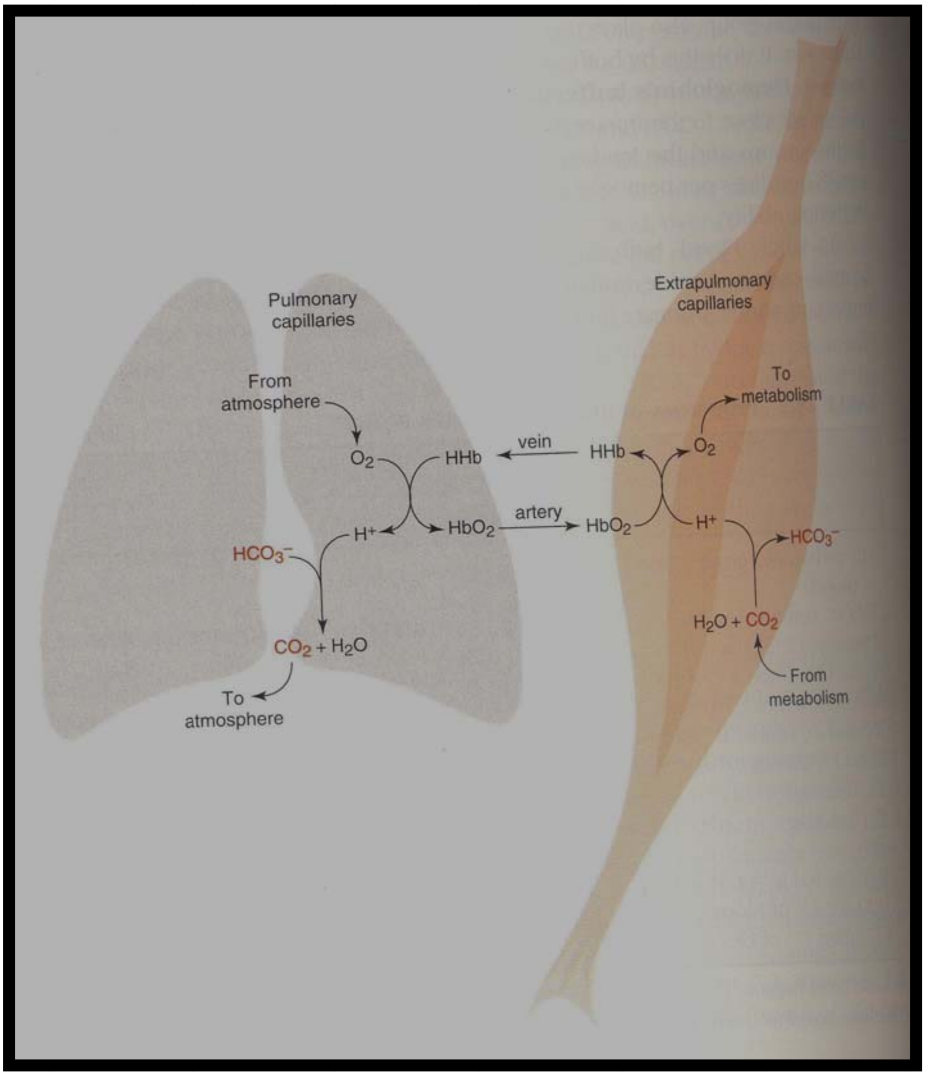


Fig. Schematic diagram of oxygen transport and isohydric carriage of CO_2 by haemoglobin.

Carbon dioxide transport in blood

The CO_2 is transported to lungs by blood that is subsequently released into atmosphere. The CO_2 is transported in three major forms:

1. Dissolved CO_2.
2. As HCO^-_3 (Formed by ionization of H_2CO_3 produced when the CO_2 reacts with H_2O).
3. Carbamino-haemoglobin.

The venous blood contain 10% more total CO_2 than arterial blood.

Bicarbonate formation

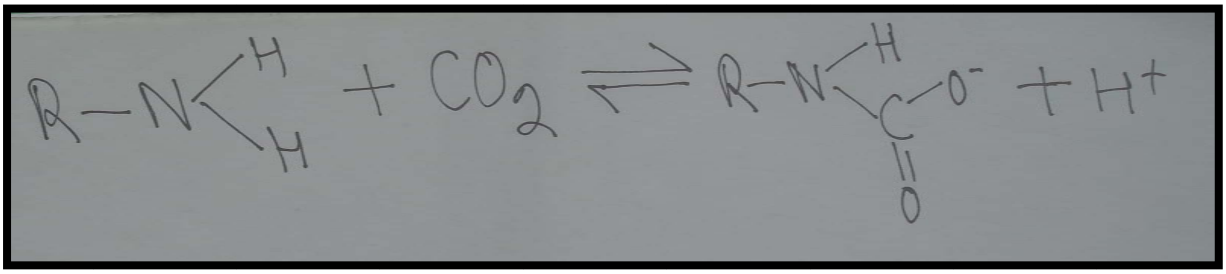
CO_2 diffuses freely into erythrocytes. And inside the erythrocytes the CO_2 is acted upon by **carbonic acid anhydrase**.

$$\boxed{CO_2 + H_2O \leftrightarrow H_2CO_3 \leftrightarrow H^+ + HCO^-_3}$$

The H^+ generated in this reaction lowers the pH of the medium. Negligible amount of CO_2 undergoes this reaction in plasma (non-enzymatically). Most of the HCO_3^- generated in RBCs diffuses out to plasma.

Carbamino haemoglobin formation

Unlike that of oxygen that binds to Hb in a special pocket in the globin protein, the CO_2 binds the globin protein though covalent linkage. The formation of carbaminoHb generates the H^+ ions (like HCO_3^-).



The two processes that regulate the H^+ derived from CO_2 transport

1. Buffering action of Hb: About 50% of buffering in blood is performed by Hb, 10 % by organic phosphates and rest by plasma proteins and other buffering systems.
2. Isohydric mechanism: when Hb becomes oxygenated, it becomes a strong acid and release H^+ that is called **Bohr's effect**. In capillaries, where the O_2 is released, the reverse of Bohr effect occurs.

$$\boxed{HbO_2 + H^+ \leftrightarrow H\text{-}Hb + O_2}$$

Simultaneously, when the CO_2 enters the capallaries and is hydrated:

$$\boxed{CO_2 + H_2O \leftrightarrow H^+ + HCO_3^-}$$

Addition of these two equations gives:

$$\mathbf{HbO_2 + CO_2 + H_2O \leftrightarrow H\text{-}Hb + O_2 + HCO_3^{-}}$$

In the reaction shown above it is evident that Hb takes up H^+ ions generated from CO_2.

The ability of haemoglobin to take up H^+ ions through the operation of Bohr's Effect is referred to as ***isohydric carriage of CO_2.***

Chloride bicarbonate shift (or simply Chloride shift)

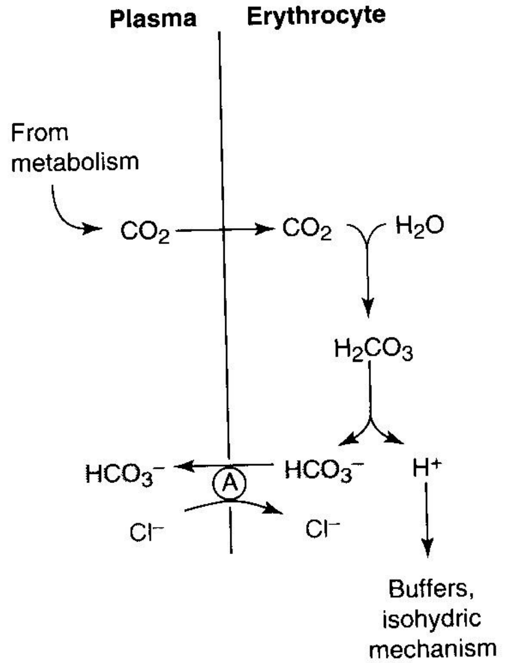
Elevated level of HCO_3^- concentration inside the RBC leads to its diffusion outside the cell to plasma. Now in order to maintain the electrical neutrality either of two things is required to be done.

1. A positively charged cation must accompany HCO_3^-.
2. Entry of other negatively charged anion inside the erythrocyte in exchange of HCO_3^-.

In case of first possibility, the positively charged cations such as Na^+, K^+ are under tight regulation through ion pumps. So, the Na^+ and K^+ cannot accompany HCO_3^-.

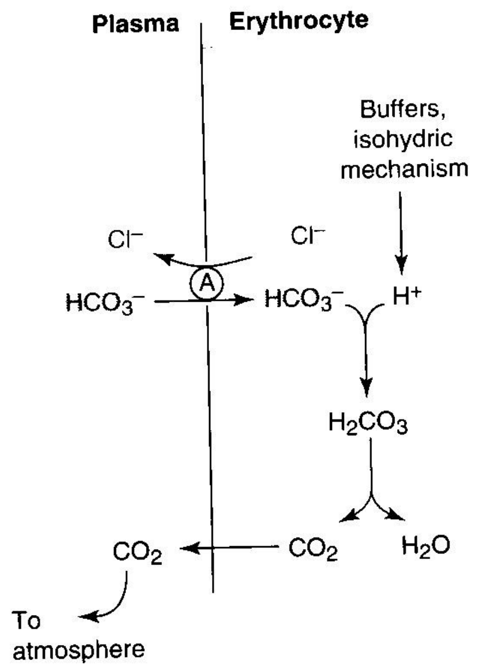
In case of second possibility, the exchange of HCO_3^- with Cl^- can be accomplished. This exchange of HCO_3^- with Cl^- is called ***Chloride bicarbonate shift***.

Extrapulmonary capillaries



(a) Bicarbonate efflux from and chloride influx into erythrocytes in extrapulmonary tissues.

Pulmonary capillaries



(b) Chloride efflux from and bicarbonate influx into erythrocytes in pulmonary tissues.