Transport of Respiratory Gases- O_2 Transport

All living animals require some energy to perform their activities & chief source of supply is the oxidation of food by O_2 inspired through breathing mechanism & taken into lungs. From lungs O_2 is transported to tissues & cells of the organism via blood for the oxidation of food stuffs.

The transport of O_2 & the direction of its transport is determined by its partial pressure in the lungs & tissues.

Some facts about O_2 in body-

1) Partial pressure of O_2- a) In alveolar air - 104 mmHg.

b) In arterial blood - 90-104 mmHg.

c) In venous blood - 40 mmHg.

d) In tissue - 40 mmHg.

2) Vol. of oxygen/100 cc of blood

In arterial blood - 0.29 ml in water.

- 19.4 ml in Hb.

In mixed venous blood - 0.12 ml in water

- 14.4 ml with Hb

Partial pressure & direction of flow-

The partial pressure of oxygen in alveolar air is about 104 mmHg as compared to that of 159 mmHg for the oxygen in the atmosphere. The partial pressure of oxygen in the blood of the alveolar capillaries is considerably lower being only about 40 mmHg. Accordingly the oxygen diffuses from the alveolar air into the blood. Oxygen therefore passes in the direction of pressure gradient ie from alveolar air to blood till Po_2 is brought up to 104 mmHg.

Carriage of Oxygen-

Oxygen is carried in the blood in the following forms

1) In simple physical solution

2) In Chemical compound

1) **In simple physical solution-** At the normal arterial PO_2 of 104 mmHg, approximately 0.29 ml of oxygen is dissolved in every 100 ml of water in the blood. When the PO_2 of the blood falls to 40 mmHg in the tissue capillaries, 0.12 ml of oxygen remains dissolved. In other words 0.17 ml of oxygen is transported to the tissues by each 100 ml of blood water. Therefore, the amount of oxygen transported to the tissue in the dissolved state is normally slight, only about 3% of the total blood as compared to 97% transported by hemoglobin.

2) **In chemical compounds-** In chemical compound O_2 is carried combined with Hb. The haeme group of hemoglobin participates in this combination. This may be represented as-

Haeme + O_2 = oxyhaemoglobin

Or Hb + O_2= HbO_2

The amount of O_2 which is taken up by a given amount of hemoglobin depends on the partial pressure of the oxygen.

Haemoglobin-

It is mainly synthesized from acetic acid & glycine. It is that acetic acid is changed into alpha ketoglutaric acid & then 2 molecules of this combines with one molecule of glycine to form a pyrole compound.

2 alpha ketoglutaric acid + glycine = HC – CH

C C

N

Pyrole-H

In turn 4 pyrole compound combines to form a protoporphyrin compound which combines only with iron. One of the protoporphyrine compound then combines with iron to form the haeme molecule. Finally 4 haeme molecule combines with one molecule of globin to form haemoglobin. Each haeme molecule is associated with a polypeptide chain. There are 4 polypeptide chains viz 2 alpha chains & 2 B chains. Thus the Hb can be symbolically represented by the formula a_2B_2

The polypeptide chains are so tightly coiled with the haeme molecule that the haeme portion lies at the corner of the tetrahedron.

4 Pyrole Protoporphyrine IX

Protoporphyrine + Iron Haeme

4 Haeme + globin Haemoglobin

Oxygenation of Haemoglobin- In the haemoglobin molecule the iron remains permanently in the ferrous form. Ordinarily when haeme is alone it can react with oxygen & the iron in it change to ferric state but the combination of haeme with a globin molecule stabilizes the whole Hb molecule so during oxygenation no change in valency takes place in iron atom.

The iron in the haeme molecule is in hexacovalent stage. 4 of the bonds linked with 4 pyrole rings of the porphyrin molecule, one bond attaches to the globin polypeptide chain & the sixth covalent bond which sticks out from the haeme molecule is the site for the attachment of O_2 molecule.

Since the haemoglobin molecule contains 4 haeme group hence it can combine with 4 oxygen molecule. The oxygenation of one of the 4 haeme enhances the oxygen binding capacity of the rest three haemes group in preference to the other haemoglobin molecule.

N O_2

N Fe N

Globin N

Fig- A subunit in oxidised state

The saturation of haemoglobin occurs as follows-

$Hb_4globin + O_2 = Hb_4O_2g$

$Hb_4O_2g + O_2 = Hb_4O_4g$

$Hb_4O_4g + O_2 = Hb_4O_6g$

$Hb_4O_6g + O_2 = Hb_4O_8g$ (because Hb reacts with 4 molecules of O_2)

The amount of oxygen carried depends upon the haemoglobin content of the RBC.

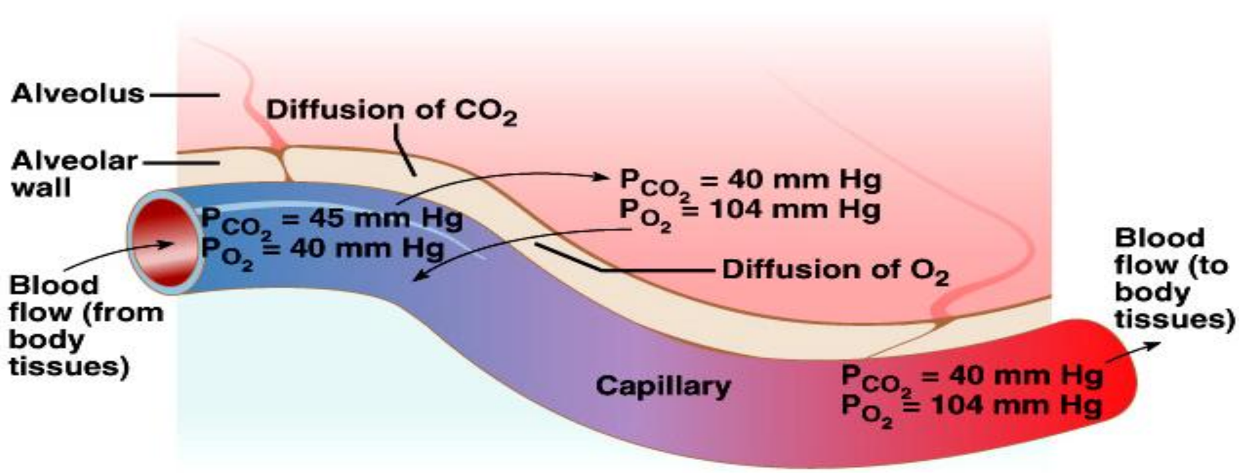
One mole (22,400ml) of O_2 combines with 16,700 gms of Hb, so 1 gm of Hb combines with 1.34 ml of O_2 (22,400/16,700). In normal healthy person the Hb is approximately 15 gms per 100 ml of blood. Thus on an avg. 15 gms of haemoglobin in 100 ml of blood will contain 20.0 ml (19.4 ml exactly as Hb of arterial blood at PO_2 104 mmHg is 98% saturated) of O_2.

Diffusion of oxygen in lungs-

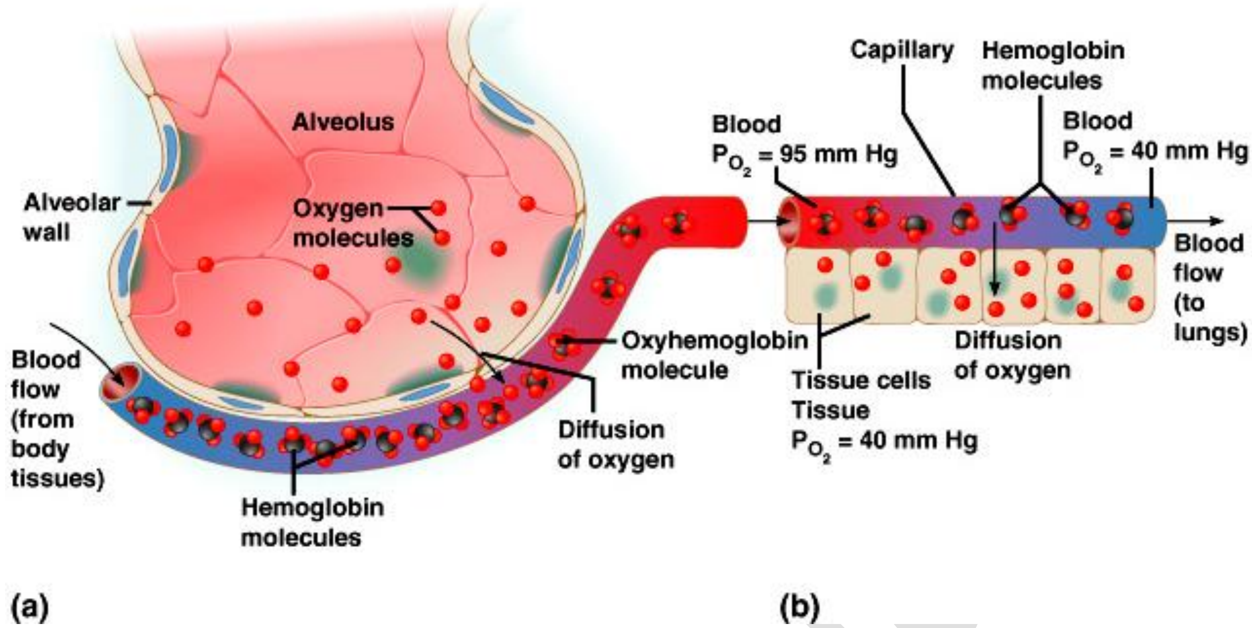
When the venous blood passes through the pulmonary capillaries into the lungs it has got the O_2 tension of about 40 mmHg. O_2 tension in the alveoli is about 104 mmHg hence O_2 diffuses from the alveoli into the venous blood due to pressure difference of 64 mmHg through the pulmonary capillary endothelium. O_2 tension rises & more HbO_2 is formed in the corpuscles. CO_2 tension & hydrogen ion concentration in the venous blood falls which favors the entry of oxygen in the blood capillaries.

Diffusion of O_2 in tissue-

The O_2 tension in arterial blood is about 104 mmHg (97% saturated with O_2) & of the tissue is less than 40 mmHg. The total quantity of O_2 bound with Hb in the normal arterial blood is approximately 19.4 ml & 0.29 ml in physical solution. As the oxygen tension in the tissue is much low the O_2 tension of the arterial blood falls to about 14.4 ml (75% saturated with O_2) ie about 5 ml of oxygen diffuse from the arterial blood to the tissue from each 100 ml of blood.



However during heavy exercise the PO_2 of tissue falls as low as 15 mmHg. At this pressure only 4.4 ml of O_2 bind with the Hb in each 100 ml of blood. Thus 15 ml of O_2 is transported by each 100 ml of blood in each cycle through the tissue.

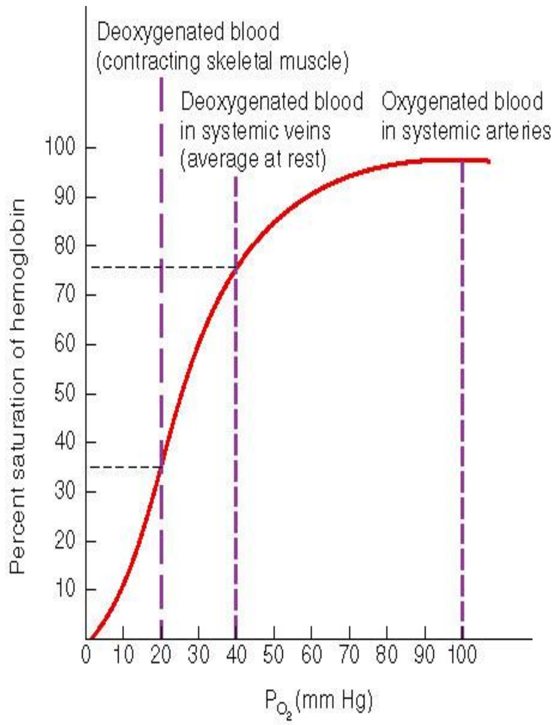


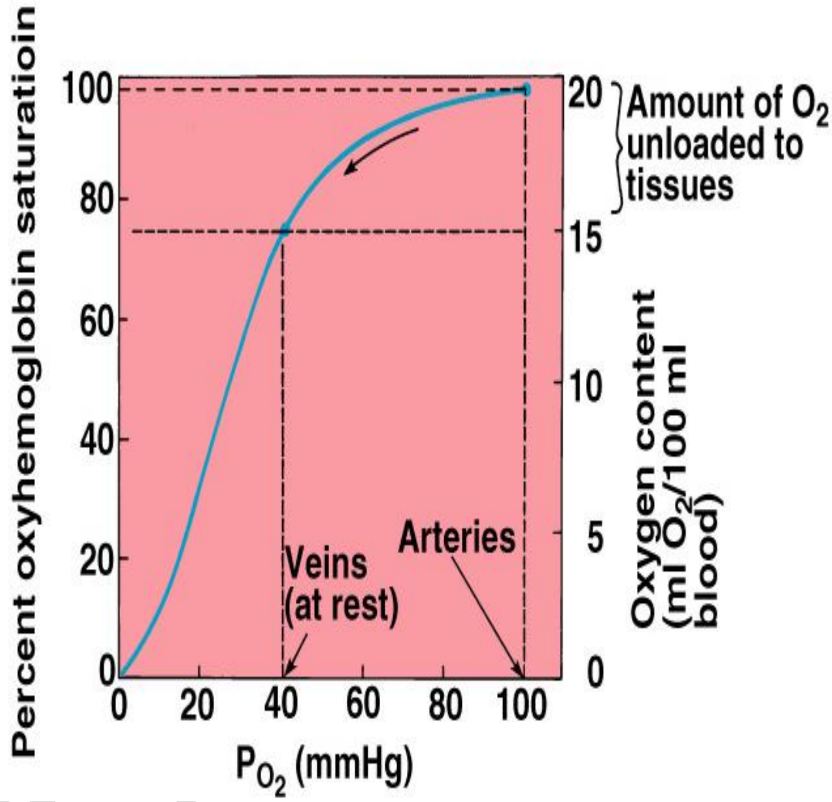
The rate at which hemoglobin binds or releases oxygen is regulated by several factors. These factors are- Po_2, temperature, blood pH, Pco_2, & the concentration of organic chemical called BPG in the blood. These factors interact to ensure adequate deliveries of oxygen to tissue cells.

Influence of Po_2 on hemoglobin saturation or Oxygen-hemoglobin dissociation curve-:

The degree of saturation of Hb with oxygen is shown in oxygen-hemoglobin dissociation curve. Po_2 is the most important factor that determines how much O_2 binds to hemoglobin- the higher the PO_2, the more O_2 combines with Hb. A hemoglobin saturation curve reveals the following important piece of information-

When Po_2 is high (Po_2=104 mmHg) hemoglobin binds with large amounts of oxygen & is almost 100% saturated & 100 ml of systemic arterial blood contains about 20 ml of oxygen. When Po_2 is low, hemoglobin is only partially saturated. In other words, the greater the Po_2, the more O_2 will bind to hemoglobin, until all the available hemoglobin molecules are saturated. Therefore, in pulmonary capillaries, where Po_2 is high, a lot of oxygen binds to hemoglobin. In tissue capillaries, where the Po_2 is lower, hemoglobin does not hold as much O_2, & the dissolved O_2 is unloaded via diffusion into tissue cells. Thus as arterial blood flows through the systemic capillaries about 5 ml of O_2/100 ml of blood is released & still Hb is 75% saturated with O_2 at 40 mm Hg in venous blood. The graph shows that only 25% of the available O_2 unloads from Hb & is used by tissue cells under resting condition.



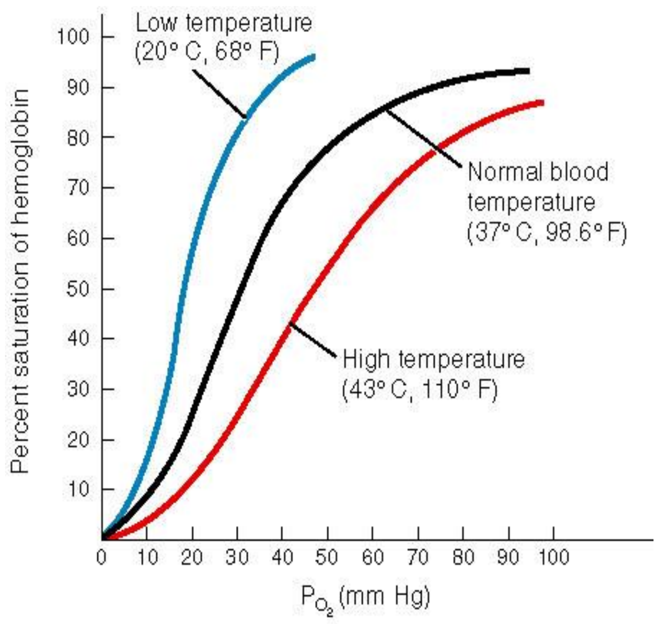


2) When the Po_2 is between 60 & 100 mmHg hemoglobin is 90% or more saturated with O_2. The adaptive value of this is that adequate oxygen loading & delivery to the tissues can occur when the Po_2 of inspired air is well below its usual levels. Thus, blood picks up nearly full load of oxygen from the lungs even when the Po_2 of alveolar air is as low as 60 mmHg. The Hb-Po_2 curve explains why people can still perform well at high altitudes or when they have certain cardiac & pulmonary diseases, even though Po_2 may drop as low as 60 mmHg.

3) Further the graph shows that the oxygen saturation of hemoglobin drops to 35% at 20 mmHg. Thus between 40 & 20 mmHg large amounts of O_2 are released from hemoglobin in response to only small decrease in Po_2. Hence if oxygen tension drops to very low levels in the tissues, as might occur during vigorous muscle activity, much more oxygen can dissociate from hemoglobin to be used by the tissue cells without requiring an increase in respiratory rate or cardiac output.

Influence of temperature in the affinity of hemoglobin for oxygen-

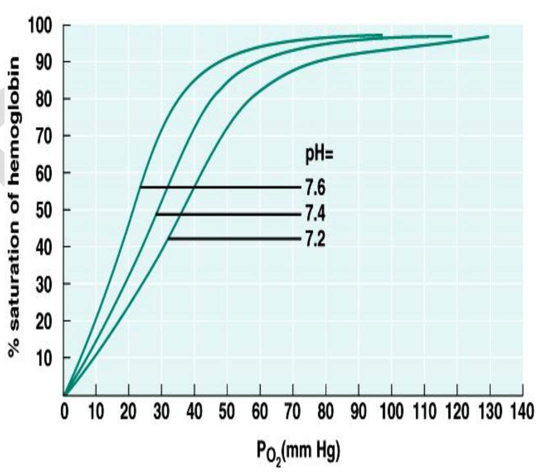
The rise in temperature shifts the curve to the right. Blood parts with its oxygen more readily at higher temperature. Conversely a fall in temperature shifts the curve to the left.



Influence of pH (acidity) in the affinity of hemoglobin for oxygen-

As acidity increases (pH decreases), the affinity of hemoglobin for O_2 decreases, & O_2 dissociates more readily from hemoglobin. Thus with the decrease in pH the entire oxygen-hemoglobin dissociation curve shifts to the right as hemoglobin imparts O_2. This is known as Bohr effect. Thus lowered pH drives off hemoglobin, making more O_2 available for tissue cells. By contrast, elevated pH increases the affinity of hemoglobin for oxygen & shifts the oxygen-

hemoglobin dissociation curve to the left.

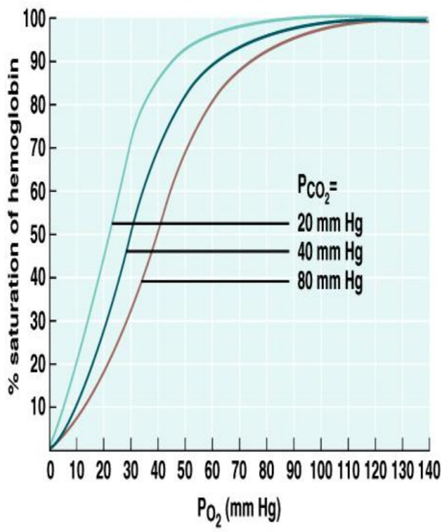


Oxyhemoglobin dissociation at 38°C

Influence of Carbon dioxide in the affinity of hemoglobin for oxygen-

Pco_2 & pH are related factors.

An increased Pco_2 produces a more acidic environment, which helps release O_2 from hemoglobin shifting the curve towards right. During exercise, lactic acid- a byproduct of anaerobic metabolism within muscles- also decreases blood pH. Decreased Pco_2 and elevated pH shifts the saturation curve to the left.



Oxyhemoglobin dissociation at 38°C

Influence of BPG in the affinity of hemoglobin for oxygen-

A substance found in RBC called 2,3-biphosphoglycerate (BPG) decreases the affinity of hemoglobin for oxygen & thus helps unload oxygen from hemoglobin. BPG is formed in red blood cells when they break down glucose to produce ATP in a process called glycolysis. When BPG combines with hemoglobin by binding to the terminal amino groups of the two beta globin chains, the hemoglobin binds oxygen less tightly at the heme group sites. The greater the level of BPG, the more oxygen is unloaded from hemoglobin.

Certain hormones, such as thyroxine, testosterone, growth hormones & Catecholamines increases RBC metabolic rate & BPG formation. As a result, these hormone enhance oxygen delivery to the tissues.