Exchange and transport of respiratory gases

Dr Suman Ahuja

Associate professor

Department of Kriya sharir

PROGRAMME OUTCOMES

- PO1- Demonstrate comprehensive knowledge and application of the Trisutra concept to explore root causes, identify clinical manifestations of disease to treat ailments and maintain healthy status.
- PO2- Demonstrate knowledge and skills in Ayurveda, acquired through integration of multidisciplinary perspectives and keen observation of clinical and practical experiences.

COURSE OUTCOMES

- CO1- Explain all basic principles & concepts of Kriya Sharir along with essentials of contemporary human physiology and biochemistry related to all organ systems.

- **Teaching learning methods-** lecture with power point presentation
  Domain- Cognitive/comprehension
  Must to know / desirable to know / Nice to know- Nice to know
  Millers pyramid- Knows how(applied knowledge)
  Bloom taxonomy- Understand

- Oxygen is essential for the cells. Carbon dioxide, which is produced as waste product in the cells must be expelled from the cells and body. Lungs serve to exchange these two gases with blood.

EXCHANGE OF RESPIRATORY GASES IN LUNGS

- In the lungs, exchange of respiratory gases takes place between the alveoli of lungs and the blood. Oxygen enters the blood from alveoli and carbon dioxide is expelled out of blood into alveoli. Exchange occurs through **bulk flow diffusion.**
- Exchange of gases between blood and alveoli takes place through respiratory membrane.

RESPIRATORY MEMBRANE

- It is formed by **epithelium of respiratory unit** and **endothelium of pulmonary capillary. Epithelium** of respiratory unit is a very thin layer. Since, the capillaries are in close contact with this membrane, alveolar air is in close proximity to capillary blood. This facilitates gaseous exchange between air and blood .
- Respiratory membrane is formed by different layers of structures belonging to the alveoli and capillaries.

Layers of Respiratory Membrane

- **Alveolar portion**

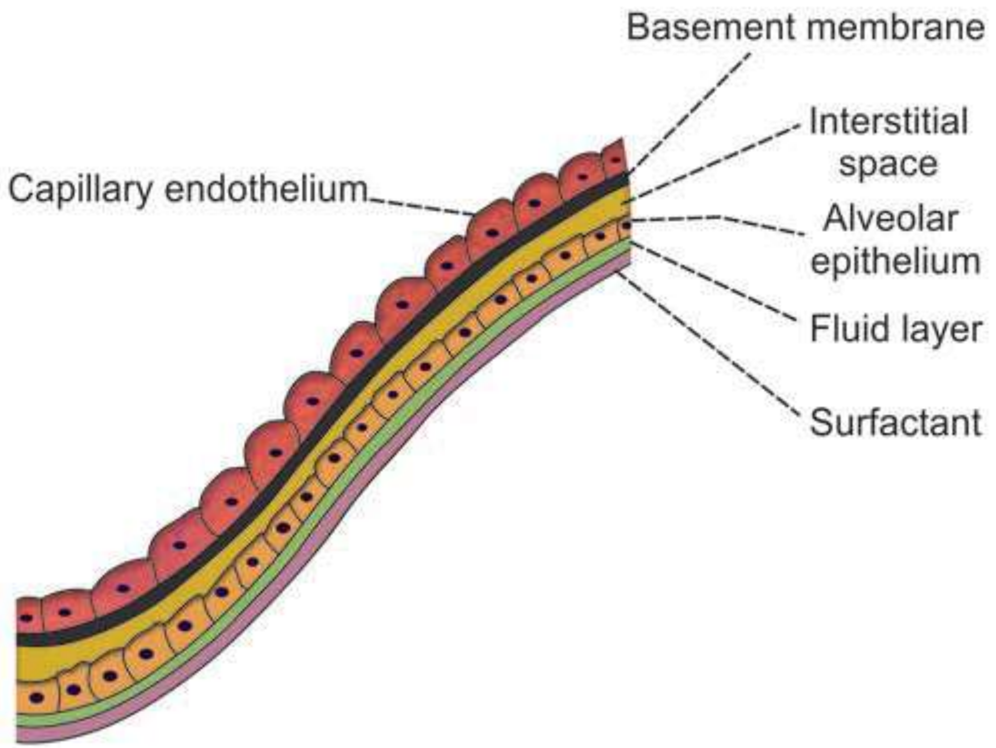
1. Monomolecular layer of surfactant, which spreads over the surface of alveoli
2. Thin fluid layer that lines the alveoli
3. Alveolar epithelial layer, which is composed of thin epithelial cells resting on a basement membrane

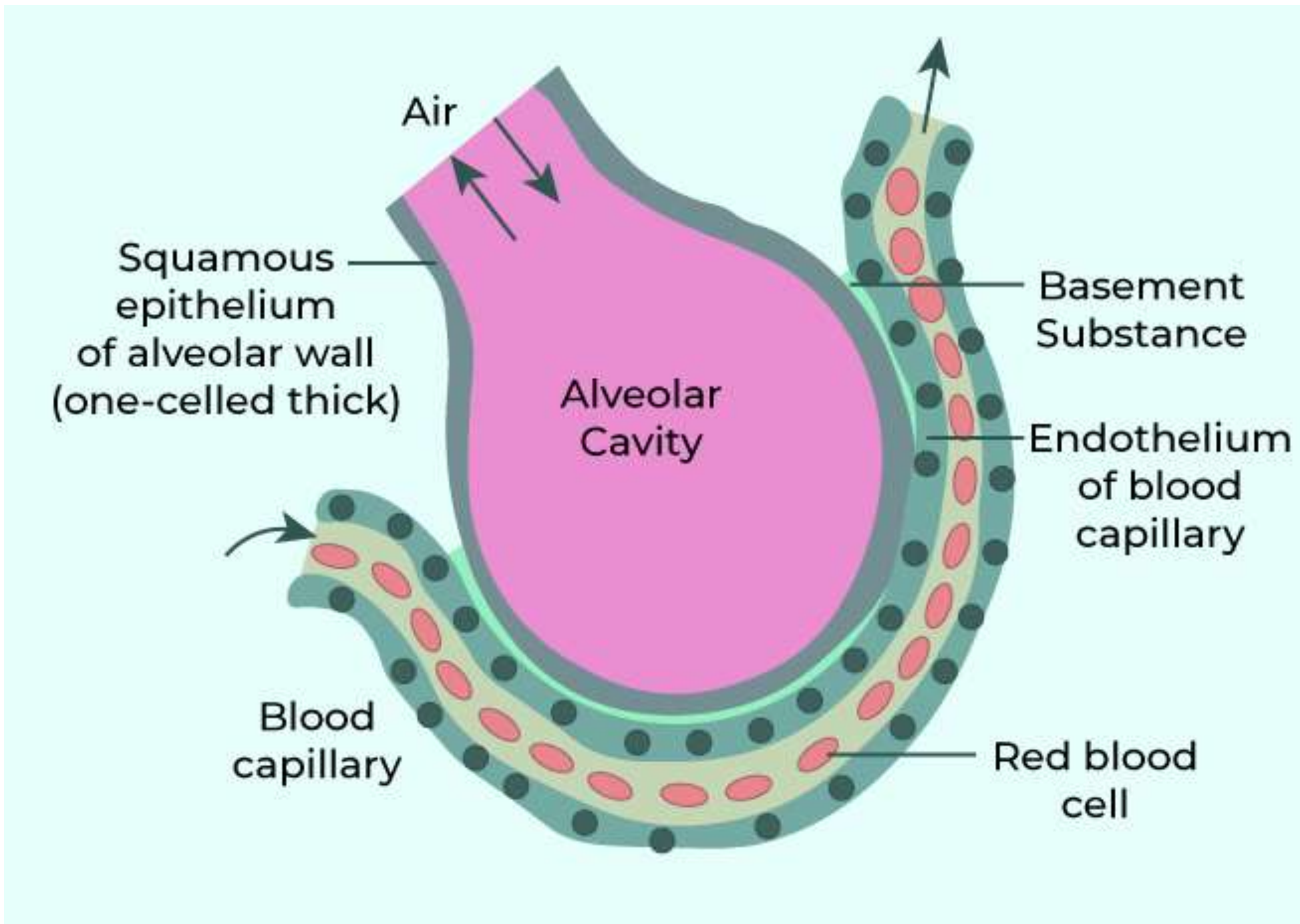
- **Between alveolar and capillary portions-** There is a interstitial space
- **Capillary portion**

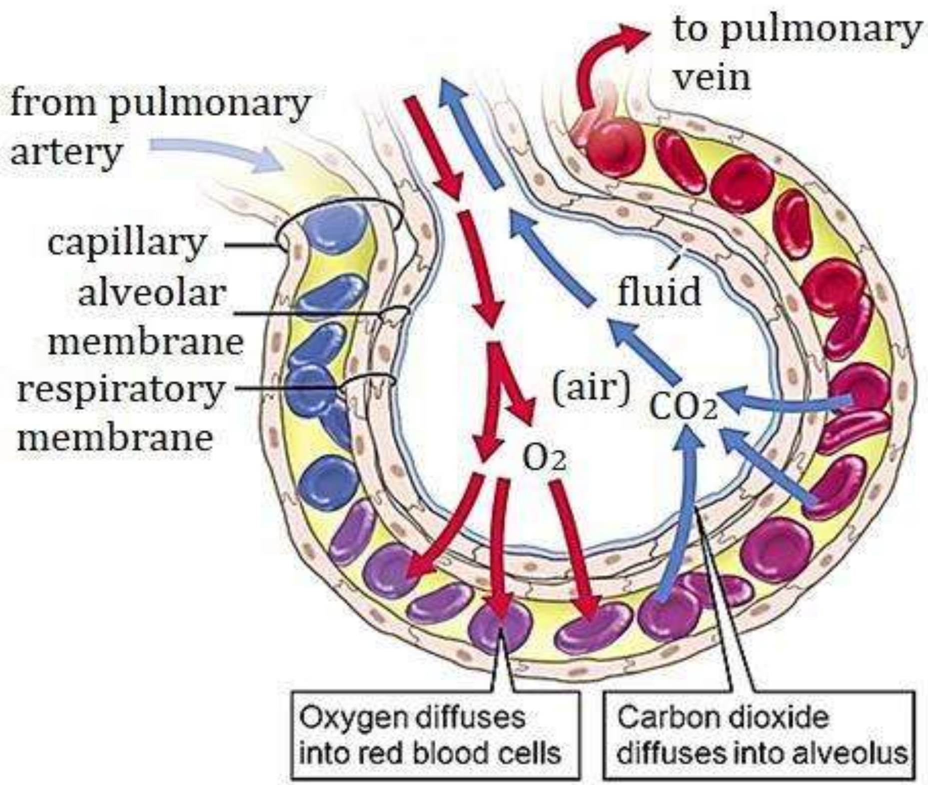
5. Basement membrane of capillary
6. Capillary endothelial cells

In spite of having many layers, respiratory membrane is very thin with an **average thickness of 0.5 μ**. Total surface area of the respiratory membrane in both the lungs is about **70 square meter.** Average diameter of pulmonary capillary is only 8 μ, which means that the RBCs with a diameter of 7.4 μ actually squeeze through the capillaries. Therefore, the membrane of RBCs is in close contact with capillary wall. This facilitates quick exchange of oxygen and carbon dioxide between the blood and alveoli.

Layers of resting membrane




Air
Squamous
epithelium
of alveolar wall
(one-celled thick)
Alveolar
Cavity
Basement
Substance
Endothelium
of blood
capillary
Blood
capillary
Red blood
cell



Respiratory Membrane

- **DIFFUSING CAPACITY**

It is defined as the volume of gas that diffuses through the respiratory membrane each minute for a pressure gradient of 1 mm Hg.

- **Diffusing Capacity for Oxygen and Carbon Dioxide**

Diffusing capacity for oxygen is **21mL/minute/1 mm Hg**. Diffusing capacity for carbon dioxide is **400 mL/minute/1mm Hg**. Thus, the diffusing capacity for carbon dioxide is about 20 times more than that of oxygen.

- **Factors Affecting Diffusing Capacity**

1. Pressure gradient

Diffusing capacity is **directly proportional to pressure** gradient. Pressure gradient is the difference between the partial pressure of a gas in alveoli and pulmonary capillary blood. It is the major factor, which affects the diffusing capacity.

2. Solubility of gas in fluid medium

Diffusing capacity is **directly proportional to solubility** of the gas. If the solubility of a gas is more in the fluid medium, a large number of molecules dissolve in it and diffuse easily.

3. Total surface area of respiratory membrane

Diffusing capacity is **directly proportional to surface area** of respiratory membrane. Surface area of respiratory membrane in each lung is about 70 sq m. If the total surface area of respiratory membrane decreases, the diffusing capacity for the gases is decreased. Diffusing capacity is decreased in emphysema in which many of the alveoli are collapsed because of heavy smoking or oxidant gases.

4. Molecular weight of the gas

Diffusing capacity is **inversely proportional to molecular** weight of the gas. If the molecular weight is more, the density is more and the rate of diffusion is less.

5. Thickness of respiratory membrane

Diffusion is **inversely proportional to the thickness** of respiratory membrane. More the thickness of respiratory membrane less is the diffusion. It is because the distance through which the diffusion takes place is long. In conditions like fibrosis and edema, the diffusion rate is reduced, because the thickness of respiratory membrane is increased.

- **DIFFUSION COEFFICIENT AND FICK LAW OF DIFFUSION**

Diffusion Coefficient

Diffusion coefficient is defined as a constant (a factor of proportionality), which is the measure of a substance diffusing through the concentration gradient. It is also known as **diffusion constant. It is related to size and** shape of the molecules of the substance.

- **Fick Law of Diffusion**

Diffusion is well described by Fick law of diffusion. According to this law, amount of a substance crossing a given area is directly proportional to the area available for diffusion, concentration gradient and a constant known as diffusion coefficient.

Thus,

Amount diffused = Area × Concentration gradient × Diffusion coefficient

Formula of Fick law:

$$J = -D \times A \times \frac{dc}{dx}$$

Where,

J = Amount of substance diffused

D = Diffusion coefficient

A = Area through which diffusion occurs

dc/dx = Concentration gradient.

Negative sign in the formula indicates that diffusion occurs from region of higher concentration to region of lower concentration. Diffusion coefficient reduces when the molecular size of diffusing substance is increased. It increases when the size is decreased, i.e. the smaller molecules diffuse rapidly than the larger ones.

- **DIFFUSION OF OXYGEN**

Diffusion of Oxygen from Atmospheric Air into Alveoli

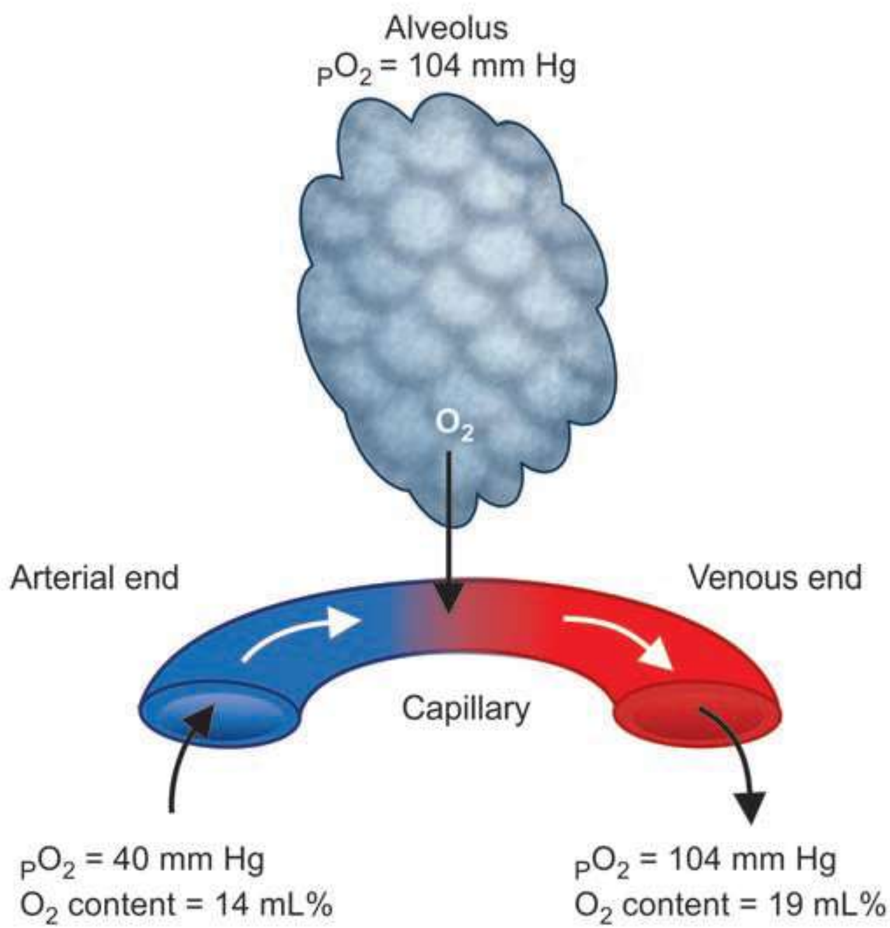
pO_2 in the atmospheric air is 159mm Hg and in the alveoli, it is 104mm Hg. Because of the pressure gradient of 55 mm Hg, O_2 easily enters from atmospheric air into the alveoli

Diffusion of Oxygen from Alveoli into Blood

When blood passes through pulmonary capillary, RBC is exposed to O_2 only for 0.75 second at rest and only for 0.25 second during severe exercise. So, diffusion of O_2 must be quicker and effective. Fortunately, this is possible because of pressure gradient.

- pO_2 in the pulmonary capillary is 40 mm Hg and in the alveoli, it is 104 mm Hg. Pressure gradient is 64 mm Hg. It facilitates the diffusion of O_2 from alveoli into the blood.

Diffusion of oxygen from alveolus to pulmonary capillary



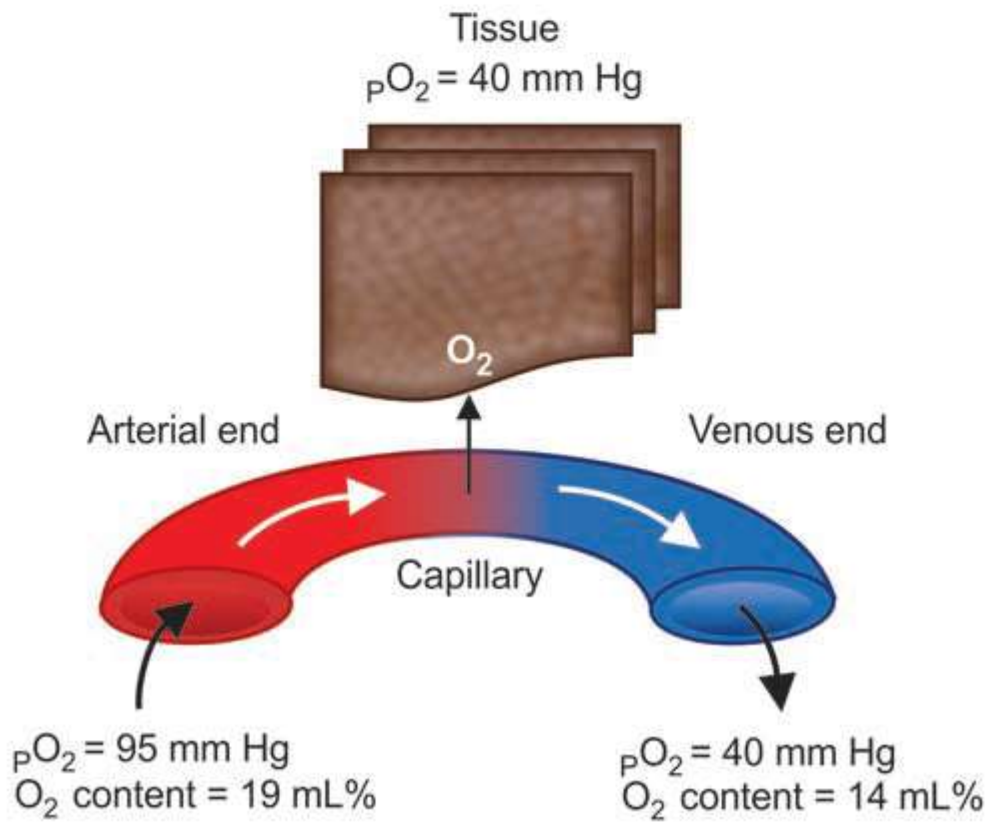
- **Diffusion of oxygen from blood into the tissues**

pO_2 in venous end of pulmonary capillary is 104 mm Hg. However, pO_2 in the arterial end of systemic capillary is only 95 mm Hg. It may be because of physiological shunt in lungs. Due to **venous admixture in the shunt**, 2% of blood reaches the heart without being oxygenated.

Average O_2tension in the tissues is 40 mm Hg because of continuous metabolic activity and constant utilization of O_2. Thus, a pressure gradient of about 55 mm Hg exists between capillary blood and the tissues so that O_2 can easily diffuse into the tissues.

O_2 content in arterial blood is 19 mL% and in the venous blood, it is 14 mL%. Thus, the diffusion of O_2 from blood to tissues is 5 mL/100 mL of blood.

Diffusion of oxygen from blood into the tissues



DIFFUSION OF CARBON DIOXIDE

- **Diffusion of carbon dioxide from tissues into the blood**

  Due to continuous metabolic activity, Co_2 is produced constantly in the cells of tissues. So, the pCo_2 in the cells is about 46 mm Hg while in arterial blood is 40 mm Hg. Pressure gradient of 6 mm Hg is responsible for the diffusion of Co_2 from tissues to the blood.

  Co_2 content in arterial blood is 48 mL%.And in the venous blood, it is 52 mL%. So, the diffusion of Co_2 from tissues to blood is 4 mL/100 mL of blood

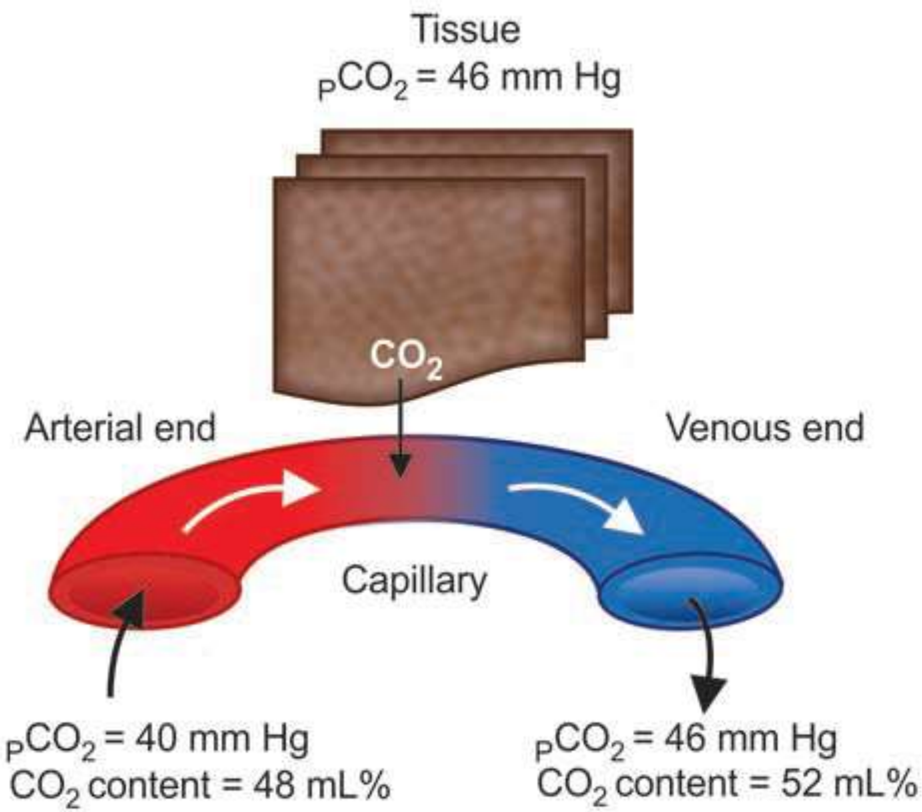
- **Diffusion of Carbon Dioxide from Blood into Alveoli**

  pCo_2in alveoli is 40 mm Hg whereas in the blood it is 46 mm Hg. Pressure gradient of 6 mm Hg is responsible for the diffusion of Co_2 from blood into the alveoli.

- **Diffusion of Carbon Dioxide from Alveoli into Atmospheric Air**

  In atmospheric air, pCo_2 is very insignificant and is only about 0.3 mm Hg whereas, in the alveoli, it is 40 mm Hg. So, Co_2 enters passes to atmosphere from alveoli easily.

Diffusion of carbon dioxide from tissues into the blood



Transport of respiratory Gases

Blood serves to transport the respiratory gases. Oxygen, which is essential for the cells is transported from alveoli of lungs to the cells. Carbon dioxide, which is the waste product in cells is transported from cells to lungs.

TRANSPORT OF OXYGEN

Oxygen is transported from alveoli to the tissue by blood in two forms:

1. As simple physical solution
2. In combination with hemoglobin.

In Arterial blood-

pO_2 - 95mmHg

O_2 content- 19ml%

pCo_2 - 40mmHg

Co_2 content- 48ml%

In venous blood-

pO_2 - 40mmHg

O_2 content- 14ml%

pCo_2 - 46mmHg

Co_2 content- 52ml%

AS SIMPLE SOLUTION

- In dissolved form, amount of O2 is 0.3ml per 100ml of blood per 100mmHg PO2.
- Amount of dissolved O2 increases in linearity with arterial blood pO2 i.e. greater the arterial pO2, more the amount in dissolved form.
- It forms only about 3% of total oxygen in blood, because of poor solubility of oxygen in water content of plasma. Still, transport of oxygen in this form becomes important during the conditions like muscular exercise to meet the excess demand of oxygen by the tissues.

IN COMBINATION WITH HEMOGLOBIN

- Oxygen combines with hemoglobin in blood and is transported as **oxyhemoglobin. Transport of oxygen** in this form is important because, maximum amount (97%) of oxygen is transported by this method.
- This type of combination of oxygen with hemoglobin has got some advantages. Oxygen can be readily released from hemoglobin when it is needed.

Oxygenation of Hemoglobin

- Oxygen combines with hemoglobin only as a physical combination. It is only **oxygenation and not oxidation.**
- This type of combination of oxygen with hemoglobin has got some advantages. Oxygen can be readily released from hemoglobin when it is needed.
- Hemoglobin accepts oxygen readily whenever the partial pressure of oxygen in the blood is more. Hemoglobin gives out oxygen whenever the partial pressure of oxygen in the blood is less.
- Each molecule of hemoglobin contains 4 atoms of iron. Iron of the hemoglobin is present in ferrous form. Each iron atom combines with one molecule of oxygen. After combination, iron remains in ferrous form only. That is why the combination of oxygen with hemoglobin is called oxygenation and not oxidation.

- **Oxygen Carrying Capacity of Hemoglobin**

  Oxygen carrying capacity of hemoglobin is the amount of oxygen transported by 1 gram of hemoglobin. It is 1.34 mL/g.

  Oxygen Carrying Capacity of Blood

- O_2 carrying capacity of blood refers to the amount of O_2 transported by blood.
- Normal Hb content in blood is 15 g%.Since O_2 carrying capacity of Hb is 1.34 mL/g, blood with 15 g% of Hb should carry 20.1 mL% of O_2, i.e. 20.1 mL of O_2 in 100 mL of blood. But, blood with 15 g% of Hb carries only 19 mL% of O_2, i.e. 19 mL of O_2 is carried by 100 mL of blood .
- O_2 carrying capacity of blood is only 19 mL% because the hemoglobin is not fully saturated with O_2. It is saturated only for about 95%.

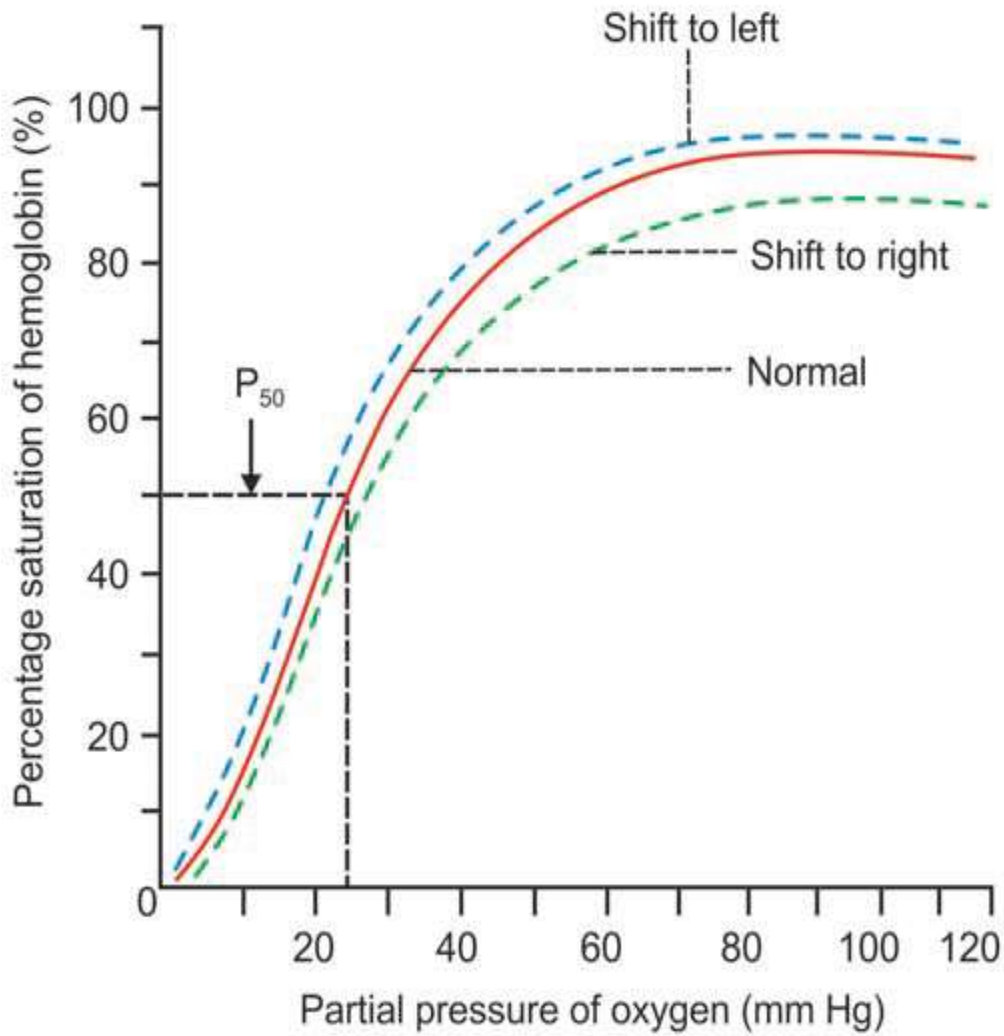
Saturation of Hemoglobin with Oxygen

Saturation is the state or condition when Hb is unable to hold or carry any more O_2. Saturation of Hb with O_2 depends upon pO_2. And it is explained by oxygen hemoglobin dissociation curve.

OXYGEN-HEMOGLOBIN DISSOCIATION CURVE

- Oxygen-hemoglobin dissociation curve is the curve that demonstrates the relationship between pO_2 and the percentage saturation of hemoglobin with O_2. It explains hemoglobin's affinity for O_2.
- Normally in the blood, hemoglobin is saturated with O_2 only up to 95%. Saturation of hemoglobin with O_2 depends upon the partial pO_2. When the partial pressure of oxygen is more, hemoglobin accepts oxygen and when the p O_2 is less, hemoglobin releases oxygen.

Normal Oxygen-hemoglobin Dissociation Curve


Shift to left
Shift to right
Normal
P50
Percentage saturation of hemoglobin (%)
100
80
60
40
20
0
20
40
60
80
100
120
Partial pressure of oxygen (mm Hg)

- Under normal conditions, oxygen-hemoglobin dissociation curve is ‘S’ shaped or **sigmoid shaped .**
- Lower part of the curve indicates dissociation of oxygen from hemoglobin. Upper part of the curve indicates the uptake of oxygen by hemoglobin depending upon partial pressure of oxygen.
- **P_{50}**

  P_{50} is the partial pressure of oxygen at which Hb saturation with oxygen is 50%. When the partial pressure of oxygen is 25 to 27 mm Hg, the hemoglobin is saturated to about 50%. That is, the blood contains 50% of oxygen.
- At 40 mm Hg of partial pressure of oxygen, the saturation is 75%. It becomes 95% when the pO_2 is 100 mm Hg.

- **Factors Affecting Oxygen-hemoglobin Dissociation Curve**

  Oxygen-hemoglobin dissociation curve is shifted to left or right by various factors:

1. Shift to left indicates acceptance **(association) of** oxygen by hemoglobin
2. Shift to right indicates **dissociation of oxygen from** hemoglobin.

1. Shift to right

Oxygen-hemoglobin dissociation curve is shifted to right in the following conditions:

i. Decrease in partial pressure of oxygen

ii. Increase in partial pressure of carbon dioxide (Bohr effect)

iii. Increase in hydrogen ion concentration and decrease in pH (acidity)

iv. Increased body temperature

- **v.** Excess of 2,3-diphosphoglycerate (DPG) in RBC.

  It is a byproduct of glycolysis . It combines with β-chains of deoxyhemoglobin. It competes with O2 for the binding sites on the hemoglobin molecule and therefore, at a given pO2 the percentage saturation of Hb with O2 will be reduced in the presence of 2,3 DPG.

  In conditions Like muscular exercise, in high attitude, anaemia and high body temperature, the DPG increases in RBC. So, the oxygen-hemoglobin dissociation curve shifts to right to a great extent.

- **Bohr Effect**

  Bohr effect is the effect by which presence of Co_2 decreases the affinity of hemoglobin for oxygen. Bohr effect was postulated by **Christian Bohr in 1904.**

- In the tissues, due to continuous metabolic activities, the pCo_2 is very high and the pO_2 is low.
- Due to this pressure gradient, Co_2 enters the blood and O_2 is released from the blood to the tissues. Presence of Co_2 decreases the affinity of hemoglobin for oxygen. It enhances further release of oxygen to the tissues and oxygen dissociation curve is shifted to right.
- All the factors, which shift the oxygen-dissociation curve to right enhance the Bohr effect.

2. Shift to left

Oxygen-hemoglobin dissociation curve is shifted to left in the following conditions:

i. In fetal blood because, fetal hemoglobin has got more affinity for oxygen than the adult hemoglobin

ii. Decrease in hydrogen ion concentration and increase in pH (alkalinity).

- **Carbon Dioxide Transport**
- Tissue Activity produces Co_2 which enters the blood due to:

1. Difference in pCo_2 between arterial blood and tissues.

   Arterial blood pCo_2-40 mm of Hg

   Tissue pCo2 – 46mm Hg

2. Co_2 has high diffusion coefficient, 20 times more than that of O_2 therefore even this smaller pressure gradient of Co_2 is sufficient for Co_2 transport
3. Decrease in O_2 content, shifts Co_2 dissociation curve to left causing further loading of Co_2 from the tissues to blood.

- **Carriage of CO_2 in the blood**
- CO_2 content of arterial blood is 48ml/dl and that of venous blood is 52ml/dl, Therefore, each 100ml of arterial blood which passes through tissues picks up 4ml of CO_2.
- As a rule CO_2 first get accommodated in plasma, when it becomes fully saturated, then it is accommodated in the RBC. Thus of 4ml 60% is transported in plasma and rest 40% in RBC
- CO_2 is carried in the plasma and RBC in 3 forms

1. in dissolved form(0.3ml/dl)
2. as carbamino compounds(0.7ml/dl)
3. as bicarbonate(3ml/dl)

- **In dissolved form(0.3ml)**

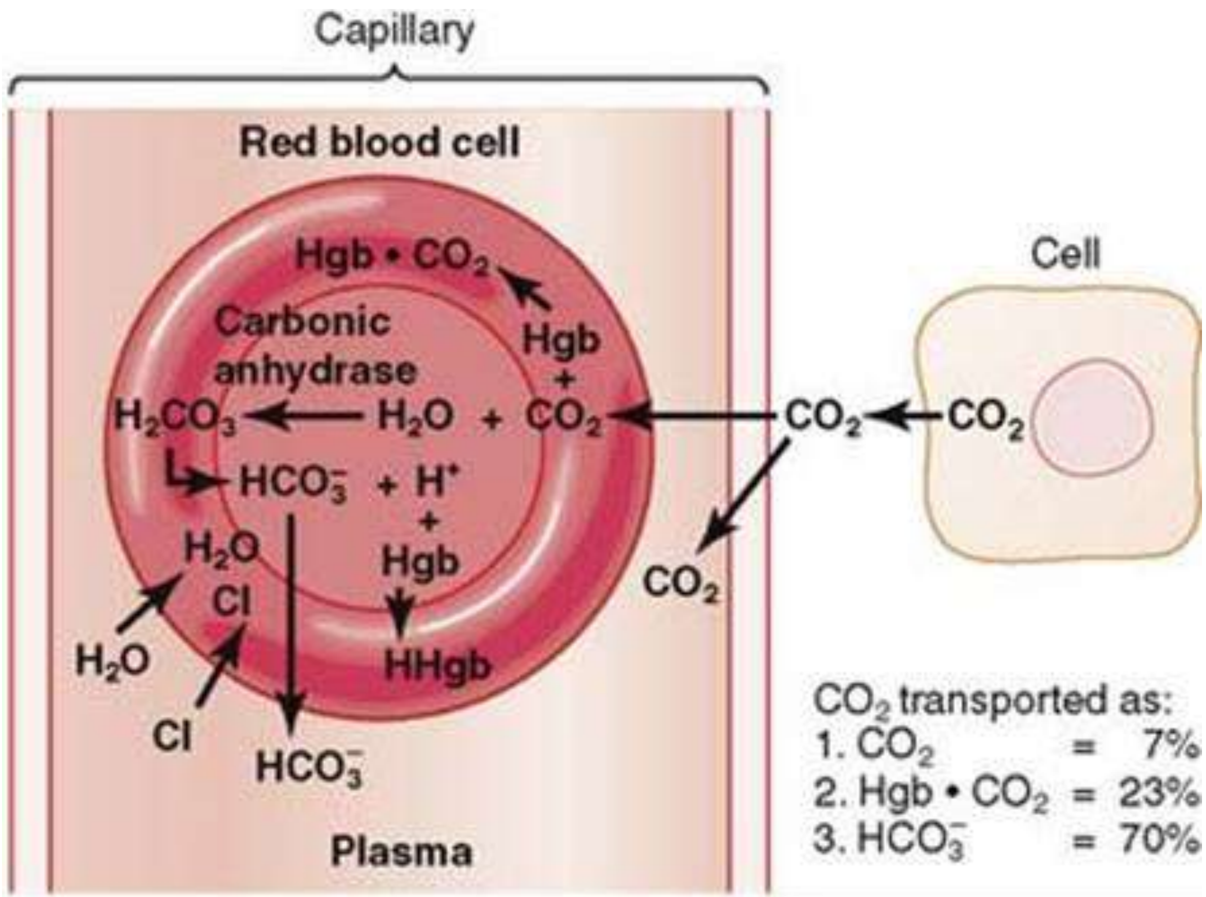
1. In plasma(0.2ml/dl)- CO_2 as it enters plasma, a part goes to solution as CO_2,remaining in small amounts with water to form carbonic acid(H_2Co_3,a slow reaction due to absence of carbonic anhydrase enzyme)
2. In RBC(0.1ml)- Here CO_2 gets rapidly hydrated to H_2Co_3 due to presence of CA enzyme in the RBC(rapid reaction)

As Carbamino Compounds (0.7ml/dl)

1. In plasma(0.1ml)- CO_2 combines with plasma proteins to form carbamino proteins(slow reaction)
2. In RBC (0.6ml)- CO_2 with amino group of Hb forms carbamino haemoglobin(fast reaction)

AS BICARBONATE (3ml/dl)

- From plasma, carbon dioxide enters the RBCs. In the RBCs, carbon dioxide combines with water to form carbonic acid. The reaction inside RBCs is very rapid because of the presence of carbonic anhydrase. This enzyme accelerates the reaction.
- Carbonic anhydrase is present only inside the RBCs and not in plasma. That is why carbonic acid formation is at least 200 to 300 times more in RBCs than in plasma.
- Carbonic acid is very unstable. Almost all carbonic acid (99.9%) formed in red blood corpuscles, dissociates into bicarbonate and hydrogen ions. Concentration of bicarbonate ions in the cell increases more and more.
- Due to high concentration, bicarbonate ions diffuse through the cell membrane into plasma.

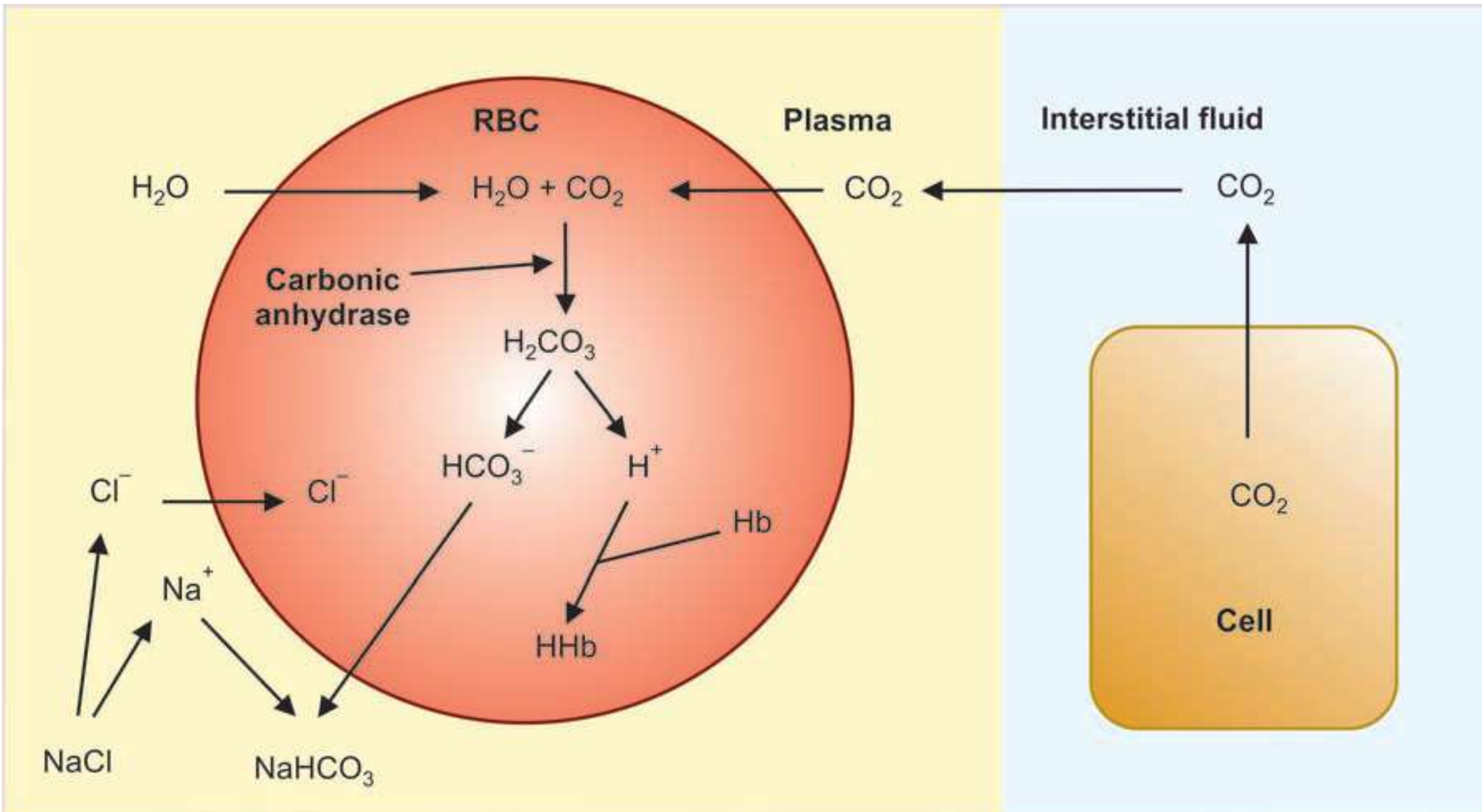

Capillary
Red blood cell
Hgb • CO_2
Carbonic anhydrase
Hgb
+
H_2CO_3
H_2O + CO_2
HCO_3^- + H^+
+
Hgb
HHgb
H_2O
Cl
H_2O
Cl
HCO_3^-
Plasma
Cell
CO_2
CO_2
CO_2
CO_2 transported as:
1. CO_2 = 7%
2. Hgb • CO_2 = 23%
3. HCO_3^- = 70%

- **Chloride Shift or Hamburger Phenomenon**

  It is the exchange of a chloride ion for a bicarbonate ion across RBC membrane. It was discovered by **Hartog Jakob Hamburger in 1892.**

  Chloride shift occurs when carbon dioxide enters the blood from tissues. In plasma, plenty of sodium chloride is present. It dissociates into sodium and chloride ions.

  When the negatively charged bicarbonate ions move out of RBC into the plasma, the negatively charged chloride ions move into the RBC in order to maintain the **electrolyte equilibrium (ionic balance).**
- Anion exchanger 1 (band 3 protein), which acts like antiport pump in RBC membrane is responsible for the exchange of bicarbonate ions and chloride ions. Bicarbonate ions combine with sodium ions in the plasma and form sodium bicarbonate. In this form, it is transported in the blood.
- Hydrogen ions dissociated from carbonic acid are buffered by hemoglobin inside the cell.


RBC
Plasma
Interstitial fluid
H_2O
$H_2O + CO_2$
CO_2
CO_2
Carbonic anhydrase
H_2CO_3
HCO_3^-
H^+
Cl^-
Cl^-
Hb
Na^+
HHb
CO_2
Cell
NaCl
$NaHCO_3$

- **Reverse Chloride Shift**

  Reverse chloride shift is the process by which chloride ions are moved back into plasma from RBC shift. It occurs in lungs.

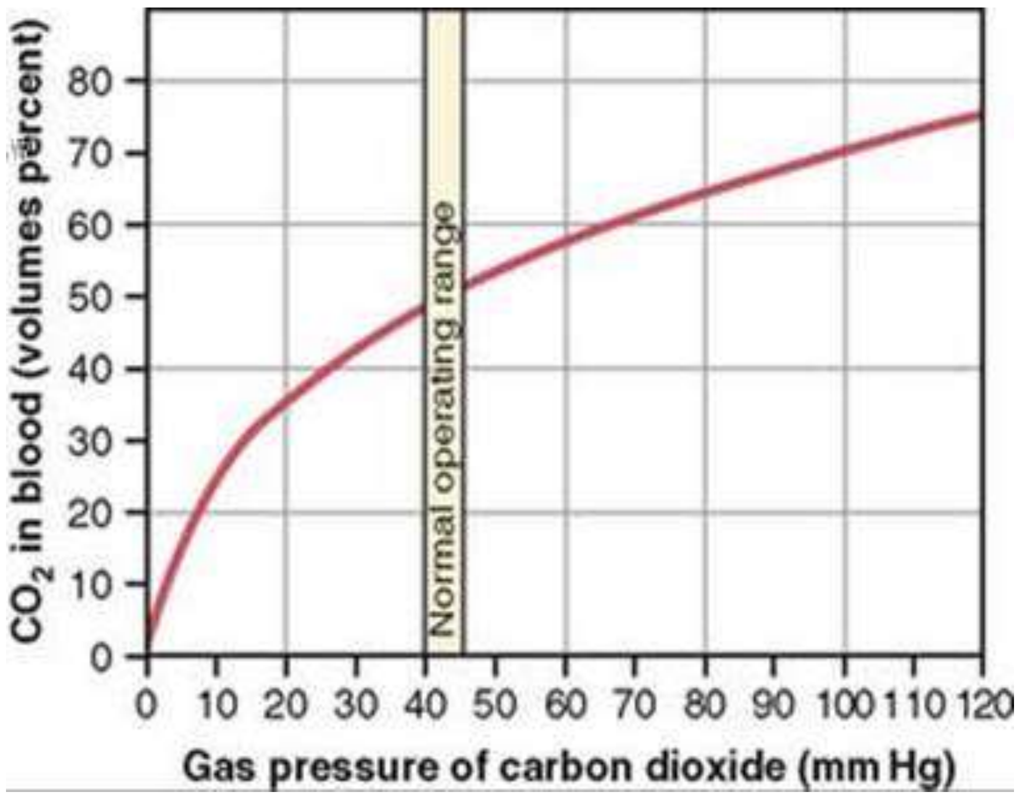
  It helps in elimination of carbon dioxide from the blood. Bicarbonate is converted back into carbon dioxide, which has to be expelled out. It takes place by the following mechanism:

  When blood reaches the alveoli, sodium bicarbonate in plasma dissociates into sodium and bicarbonate ions. Bicarbonate ion moves into the RBC.

  It makes chloride ion to move out of the RBC into the plasma, where it combines with sodium and forms sodium chloride. Bicarbonate ion inside the RBC combines with hydrogen ion forms carbonic acid, which dissociates into water and carbon dioxide. Carbon dioxide is then expelled out.

- **CARBON DIOXIDE DISSOCIATION CURVE**
- Carbon dioxide dissociation curve is the curve that demonstrates the relationship between the partial pressure of carbon dioxide and the quantity of carbon dioxide that combines with blood.
- **Normal Carbon Dioxide Dissociation Curve**

  Normal carbon dioxide dissociation curve shows that the carbon dioxide content in the blood is 48 mL% when the partial pressure of carbon dioxide is 40mm Hg and it is 52 mL% when the partial pressure of carbon dioxide is 48 mm Hg.



CO2 in blood (volumes percent)
80
70
60
50
40
30
20
10
0
Normal operating range
0 10 20 30 40 50 60 70 80 90 100 110 120
Gas pressure of carbon dioxide (mm Hg)

- **Haldane Effect**

  Haldane effect is the effect by which combination of oxygen with hemoglobin displaces carbon dioxide from hemoglobin.

- Excess of oxygen content in blood causes shift of the carbon dioxide dissociation curve to right.

Causes for Haldane effect

Due to the combination with oxygen, hemoglobin becomes strongly acidic. It causes displacement of carbon dioxide from hemoglobin in two ways:

1. Highly acidic hemoglobin has low tendency to combine with carbon dioxide. So, carbon dioxide is displaced from blood.
2. Because of the acidity, hydrogen ions are released in excess. Hydrogen ions bind with bicarbonate ions to form carbonic acid. Carbonic acid in turn dissociates into water and carbon dioxide. Carbon dioxide is released from blood into alveoli.

- Factors affecting CO_2 dissociation curve:

1. increase in body temp.- causes release of O_2 from blood, this shifts the curve to left i.e larger amount of CO_2 can be taken at a given pCO_2.
2. Decrease in pO2 shifts the curve to left, thereby helps in loading of CO_2

This shows deoxygenation of Hb carries more CO_2 at any level of pCO_2.

- **Carriage of CO2 in lungs**

Sequence of events in the lungs is as follows:

1. A part of CO2 from dissolved solution and carbamino compound breaks up to liberate CO2
2. Hb becomes oxygenated forming oxyhaemoglobin(acidic) which increases the acidity of the cell to mobilize chloride ion shift in reverse order.
3. Bicarbonate from plasma enters the cell and chloride ion comes out of the cell.
4. Within RBC H^+ ions joins with bicarbonate ion to form carbonic acid, which in turn broken up by the carbonic anhydrase enzyme into water and carbon dioxide. CO_2 diffuses out in the plasma and since there is nothing to fix it, it is liberated through the lungs along the pressure gradient

THANKS