Exchanges of gases in lungs and tissues

- **Diffusion of gases across the Alveolar Membrane**
- **Diffusion of gases across the Tissue layer**
- **OXYGEN TRANSPORT**

Composition of Gases

- The composition of inspired air (given in table) is equal to that of atmosphere and contains water vapour at a concentration related to that environment (as temperature increases level of water vapour increases).
- The inspired air contains about 21% O_2.
- As the air passes through the respiratory airways it is warmed to body temperature and saturated with water vapour.
- Thus, the composition is altered to accommodate an additional amount of water vapour and still maintain the total pressure of atmosphere.
- The amount of water vapour added is dependent on the animals' body temperature.
- **In a dog, with a body temperature of 37.5 to 39.5°C, the water vapour pressure in respiratory passage is 47 mmHg. Therefore, the composition of lower respiratory tract air differs from inspired air.**

Compo sition air of

Gas	Inspired Air (dry) %	Expired Air (dry) %	Difference %	Alveolar Air (dry) %
O_2	20.93	16.29	**4.64**	14.0
CO_2	0.03	4.21	**4.18**	5.6
N_2	79.04	79.5	**0.46**	80.4

Fundamental Laws for transport and exchange of gases

- ***Boyle's Law*** Temperature -constant

  Pα1/V

- ***Charles' Law*** **Vα T**
- The volume of a given mass of a gas kept at **constant pressure** increases by 1/273 of its volume at 0℃ for each degree rise in temperature.
- ***Dalton's Law of Partial Pressure***
- Each gas in a mixture exerts a pressure according to its own concentration independently of the other gases present. The pressure of each constituent gas is referred to as its ***partial pressure*** **or tension**. Total pressure is the sum of partial pressure of all the gases present.

- ***Henry's Law of Solution of Gases***
- When temperature remains constant, the quantity of gas, which goes into solution in any given liquid, is proportional to the partial pressure of the gas.

- The ratio of volume of CO_2 / volume of O_2 is called ***respiratory quotient***, (R.Q).
- R.Q. varies with the kind of foodstuff oxidised;
- For carbohydrates, the R Q is 1, for lipids 0.7, and for protein 0.8.

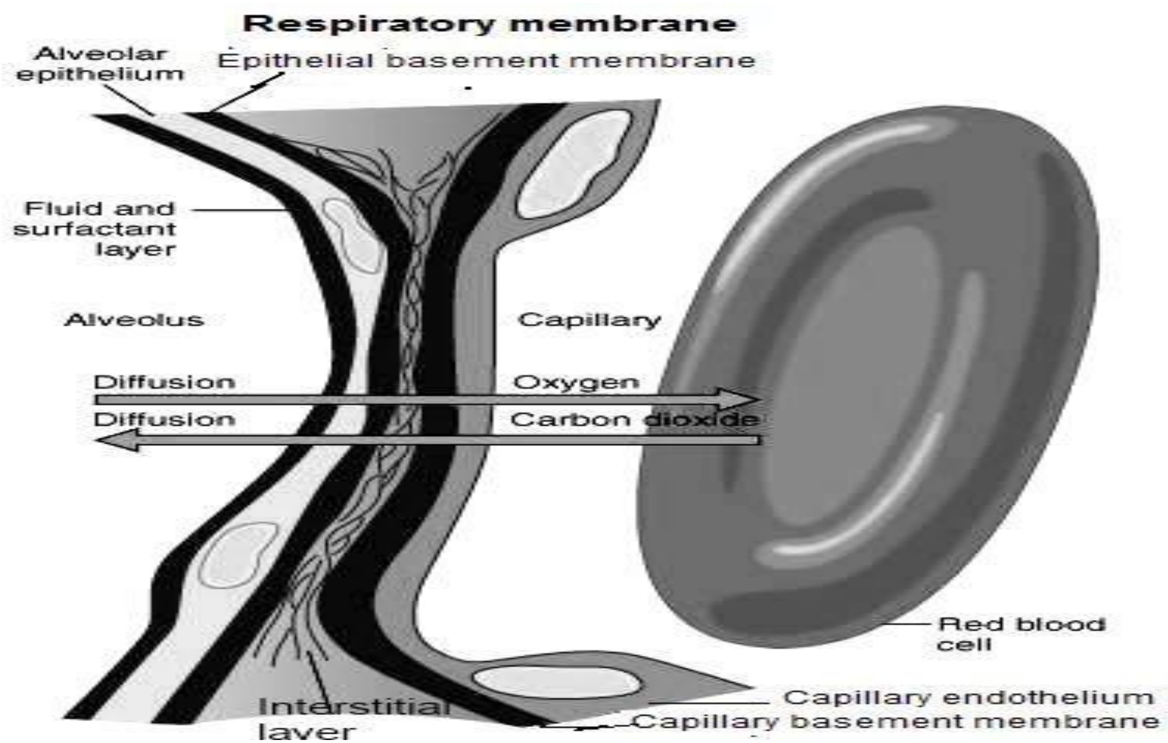
Partial pressures of gases

	Atmospheric air (dry)		Alveolar air (dry)	
	Composition %	Partial pressure (mmHg)	Composition %	Partial pressure (mmHg)
O_2	20.93	20.93x760/100=159.2	14	14 x713/100=100
CO_2	0.03	0.03 x760/100=0.23	5.6	5.6x713/100=40
N_2	79.04	79 x760/100=600	80	80 x713/100=570

Diffusion of gases across the Alveolar Membrane

- Diffusion is the passive movement of gases down a partial pressure (concentration) gradient.
- The alveolar air in the lungs is separated from the blood in capillaries by a thin layer of **1-2µm thick.**
- It is constituted by a layer of liquid and surfactant lining the alveoli, an epithelial layer, a basement membrane, an interstitum and a layer of capillary endothelium.
- Across this membrane, O_2 diffuse from alveolar air into the blood and CO_2 diffuse from the blood into the alveolar air.

- The rate of gaseous exchange at lungs depends on
  - Partial pressure gradient of the gases in the alveolar air and blood in lung capillaries
  - Physical properties of the gases
  - Surface area available for diffusion
  - Thickness of the air-blood barrier
  - Velocity of the blood


Respiratory membrane
Alveolar epithelium
Epithelial basement membrane
Fluid and surfactant layer
Alveolus
Capillary
Diffusion
Oxygen
Diffusion
Carbon dioxide
Red blood cell
Capillary endothelium
Capillary basement membrane
Interstitial layer

Partial pressures of gases

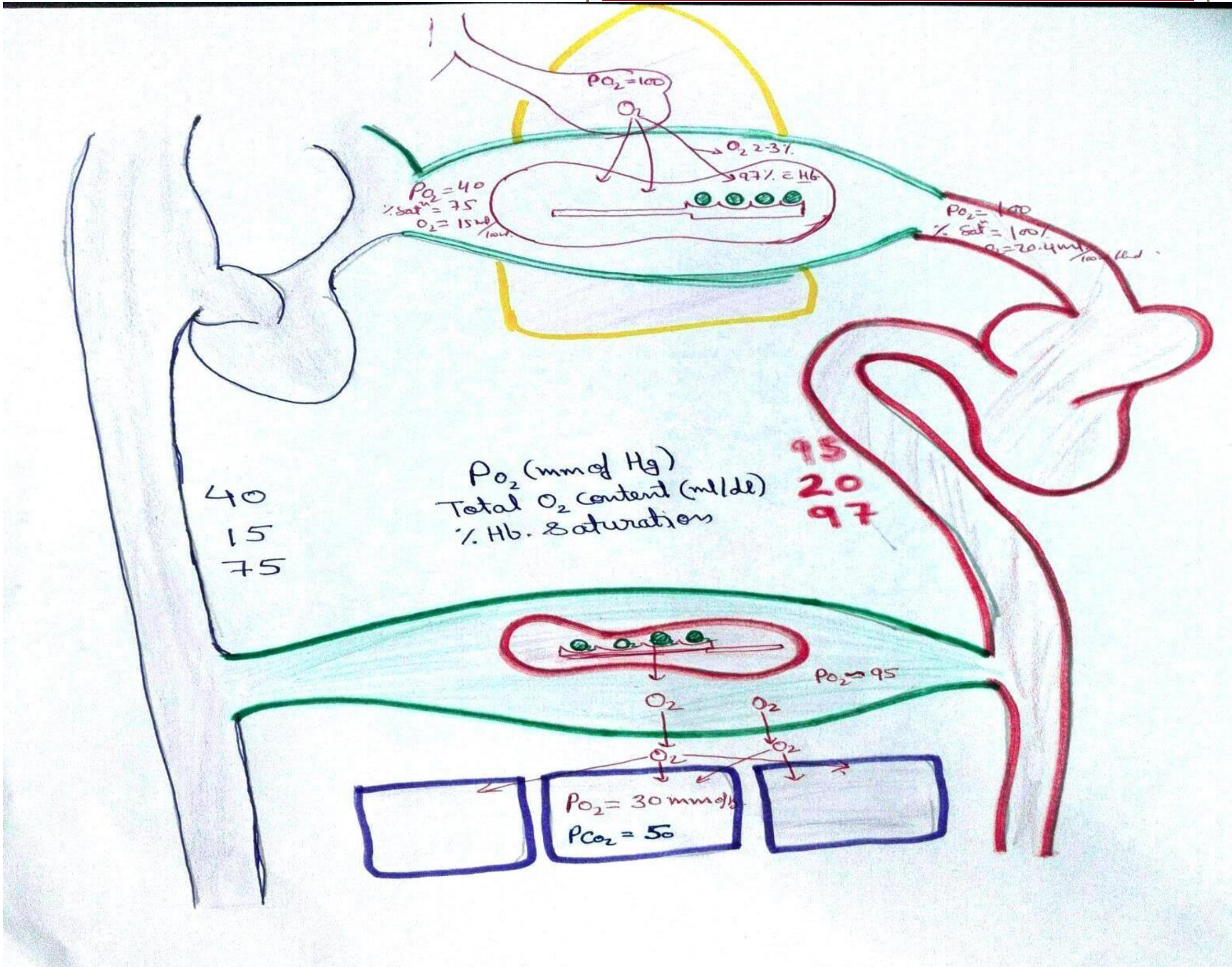
- Alveolar PO_2 averages about **100 mmHg**; the venous blood returning to lungs has a PO_2 of **40 mmHg**; this provides a driving force of 60 mmHg, resulting in rapid diffusion of O_2 into capillaries where it combines with haemoglobin.
- The Hb provides a sink for O_2 and maintains a gradient for O_2 diffusion.
- PCO_2 of venous blood in lungs is about **46 mmHg** and alveolar PCO_2 is **40 mmHg**; this provides a pressure difference of about 6 mmHg only. Despite this small driving force, the diffusion of CO_2 per minute equals that of O_2.
- **This is due to 22 times more solubility of CO_2 than O_2.**

Diffusion at the Tissue Level

- At the tissue level, the capillary blood has a **PO_2 of 85-100 mmHg** and **PCO_2 is 40 mmHg.**
- Tissue O_2 tension averages **30 mmHg** (can vary according to O_2 utilisation) and CO_2 tension is **50 mmHg** (varies according to metabolic activity).
- Because of partial pressure difference, O_2 diffuses into the tissues and CO_2 diffuses into blood.
- Tissues with high O_2 demand have more capillaries per gram, which provides more diffusing surface area.

OXYGEN TRANSPORT

- The amount of O_2 dissolved in plasma is directly proportional to **PO_2 and solubility coefficient**
- O_2 diffuses across all membranes relatively easily
- O_2 combines with haemoglobin and released from haemoglobin easily
- Oxygen is transported in blood in two forms:
- **O_2 as physically dissolved O_2**
- **O_2 in combination with haemoglobin**



PO_2=100
O_2
O_2 2-3%
97% $\bar{c}$ Hb
PO_2=40
% Sat^n = 75
O_2 = 15 ml/100 ml
PO_2=100
% Sat^n = 100%
PO_2 (mm of Hg)
Total O_2 content (ml/dl)
% Hb. Saturation
40
15
75
95
20
97
PO_2 = 95
O_2
O_2
O_2
O_2
PO_2 = 30 mm of Hg
PCO_2 = 50

As Physically Dissolved O_2

- In the process of O_2 transport from inspired air to tissues, the O_2 diffuses across the alveolar membrane and the lung capillary endothelium into the blood plasma where it is physically dissolved according to its solubility co-efficient and partial pressure.
- **0.003ml of O_2 is dissolved in 100ml plasma at a PO_2 of 1mmHg.**
- As the blood equilibrates with alveolar O_2, which is at a PO_2 of 100 mmHg, a quantity of 0.3ml O_2 dissolves in each 100ml blood.

Transport of O_2 with haemoglobin

- After entry into the blood plasma, most of the O_2 enters across the red cell membrane into the cell.
- The major portion of O_2 carried by blood is not in physical solution but is associated with haemoglobin molecule inside the red cells.
- The movement of O_2 in the respiratory circuit is effected under continual O_2 pressure gradient and haemoglobin serves as a reservoir charged with O_2.
- If 100 ml plasma is exposed to an atmosphere of 100mmHg partial pressure of O_2 and allowed to equilibrate, only 0.3 ml of O_2 is taken up.
- But if 100 ml blood is similarly allowed to equilibrate at an O_2 tension of 100mmHg, its final O_2 content will be 19-20 ml/100 ml.
- The extra uptake of O2 is contributed by the haemoglobin present within the erythrocytes.

- Each Hb molecule contains 4 haeme groups.

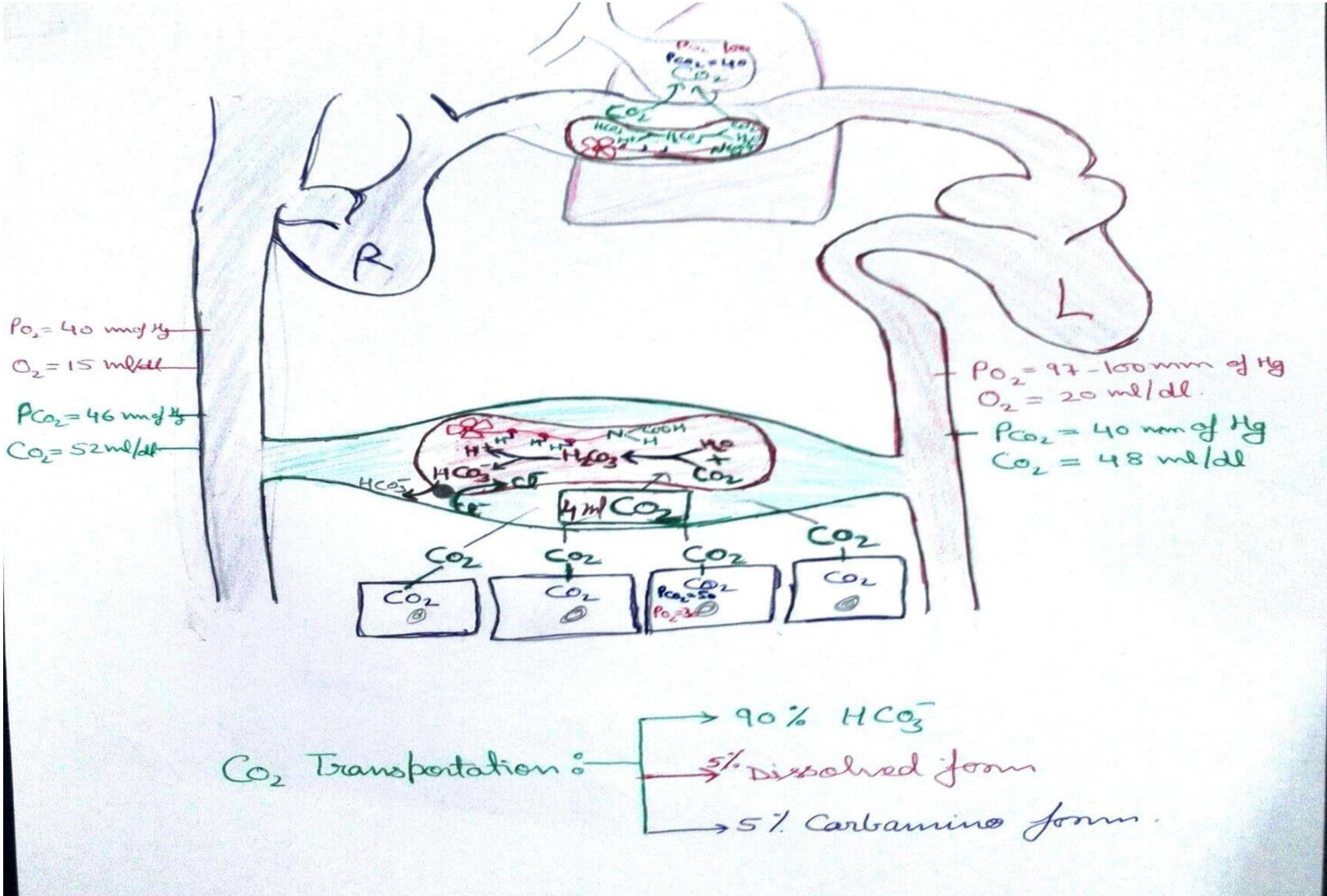
- Each haeme molecule contains one Fe^{2+} atom in a reduced state and each Fe^{2+} atom can bind with one molecule of O_2
- Hence, each Hb molecule is capable of combining with up to 4 molecules of O_2 depending on the relative concentration of Hb and O_2 in blood.

- The valency of the ferrous iron of haeme is not changed when it combines with O_2.
- **So, when reduced Hb combines with O_2 it has been oxygenated and not oxidised, and then it is called *Oxy –Haemoglobin.***
- Oxygen binding with Hb is a four step process; the O_2 affinity of a particular haeme is influenced by the oxygenation of other haemes in that haemoglobin molecule.
- These haeme-haeme interactions are responsible for the *sigmoid shape* of the oxyhaemoglobin curve.

- Greater the concentration of Hb in blood greater the amount of O_2 the blood can carry.
- When all the 4 atoms of Fe^{2+} in all the Hb molecules in the blood have attached with O_2, Hb is said to be 100% saturated and when only half of Hb is saturated with O_2, it is 50% saturation
- **When the blood is fully saturated with O_2, its O_2 content is called *O_2 carrying capacity.***

CARBON DIOXIDE TRANSPORT

- The CO_2 produced during metabolism is a waste product and has to be eliminated.
- The flow of CO_2 is effected under a continuous pressure gradient.
- Tissues (50 mm Hg)
- Venous blood (46 mm Hg)
- Alveolar air (40 mm Hg)


R
L
PO_2 = 40 mm of Hg
O_2 = 15 ml/dl
PCO_2 = 46 mm of Hg
CO_2 = 52 ml/dl
PO_2 = 97-100 mm of Hg
O_2 = 20 ml/dl.
PCO_2 = 40 mm of Hg
CO_2 = 48 ml/dl
4 ml CO_2
CO_2 Transportation :
90% HCO_3^-
5% Dissolved form
5% Carbamino form.

- ***As Physically Dissolved CO_2***
- ***Transport in Chemical Combination***
  - **By hydration reaction**
  - ***Transport as carbamino compounds***

- *The transport of CO_2 is effected in the following ways.*
- ***As Physically Dissolved CO_2***
- Compared with O_2, CO_2 is about **22 times more** soluble in blood plasma.
- In spite of this, only about 5 – 7 % of total CO_2 carried by blood is in a simple physical solution.
- Arterial blood (pCO_2 of 40mmHg) carries 2.5 ml and mixed venous blood (pCO_2 of 46mmHg) carries 2.9 ml of dissolved CO_2 in each 100ml blood i.e about 0.4ml CO_2 is transported from tissues to lungs by 100ml blood.
- The factors that determine this transport are the partial pressure of CO_2 (Henry's law) and temperature. Both plasma and cells can transport CO_2 in a physically dissolved state.

Transport in Chemical Combination

- **By hydration reaction**
- Most of the CO_2 within erythrocytes combine with water (*hydration*) and form carbonic acid which then dissociate to bicarbonate and hydrogen ions

$CO_2 + H_2O$ « H_2CO_3 « $H^+ + HCO_3$ (reaction 1)

- The erythrocytes contain an enzyme **carbonic anhydrase** which accelerates the hydration of CO_2 several hundred times.
- H_2CO_3 ionizes rapidly and H^+ and HCO_3 accumulate within the erythrocytes.
- Since the H^+ ions formed is buffered by haemoglobin and HCO_3 diffuses out, the reaction is accelerated to the right.
- HCO_3 ions accumulate and their concentration increases within the erythrocytes which diffuse out from erythrocytes into plasma due to concentration gradient.

- To maintain electrical neutrality, chloride ions diffuse from the plasma into erythrocytes along concentration gradient. This transfer of Cl ions is known as ***chloride shift* or *Hamburger shift*.**
- Deoxyhaemoglobin formed in capillaries due to unloading of O_2 to the tissues is a weaker acid than oxyhaemoglobin and hence it is a better buffer.
- Thus deoxyhaemoglobin easily combines with H^+ ions and facilitate the break down of H_2CO_3 by removing the H^+ ions.

- When venous blood reaches lungs, CO_2 in solution from plasma begins to diffuse toward the alveoli followed by movement of CO_2 in solution from erythrocytes. This favours dehydration of H_2CO_3 to produce CO_2 pushing the reaction (1) towards left.
- Simultaneously carbamino haemoglobin reaction (2) also shifts to left releasing CO_2 thus CO_2 is unloaded into alveoli.
- Reversing of these reactions is facilitated because haemoglobin is being oxygenated at lung capillaries which become more acidic and releases H^+ ions easily.
- These H^+ ions combine with HCO_3 to form H_2CO_3 which is dehydrated to H_2O and CO_2.
- The effect of O_2 on H^+ ion and CO_2 loading and unloading from haemoglobin is known as ***Haldane effect* or *C-D-H effect*.** i.e. oxygenation of hemoglobin reduces it's ability to bind with CO_2 Deoxygenation of the hemoglobin increases its ability to carry CO_2.

  This is a consequence of the fact that reduced (deoxygenated) hemoglobin is a better proton (H^+) acceptor than the oxygenated form.