Lecture 6
BLOOD GAS TRANSPORT of CO_2

OBJECTIVES:
1. CO_2 forms in blood.
2. Mechanism of CO_2 carriage.
3. Chloride shift phenomenon.
4. CO_2 dissociation curves, significance.

Carbon dioxide (CO_2) carriage by blood:

Normal arterial and venous CO_2 levels:

Parameter	CO_2 content	CO_2 tension
Arterial	**50 ml %**	**40 mmHg**
Venous	**55 ml %**	**46 mmHg**

Arterial blood CO_2 is present in the following forms:

1. Physical solution:
- It is about **5%** of the total CO_2 content (~ **2.5 ml %**).
- CO_2 in solution may dissolve in water to form carbonic acid which dissociates as follows:

$$CO_2 + H_2O \Longleftrightarrow H_2CO_3 \Longleftrightarrow H^+ + HCO_3^-$$

- The dissociation of carbonic acid (H_2CO_3) to $CO_2 + H_2O$ is **1000** times its dissociation to that to $H^+ + HCO_3$ (i.e. out of each 1000 molecules of H_2CO_3, 999 molecules are present as CO_2 and H_2O (i.e. physical solution), and **only** one molecule as **bicarbonate** (i.e. chemical combination) that can change the pH **very little**.

2. Chemical combination:
It forms about **95 %** of the total CO_2 content.

It is present in the following forms:

a) **Bicarbonates (89%):** e.g. sodium bicarbonate ($NaHCO_3$) in plasma and potassium bicarbonate ($KHCO_3$) in RBCs.

b) **Carbamino compounds (6%):** CO_2 combines with the NH_2 group of a protein to form Carbamino compounds. The **protein** may be plasma proteins (**2%**) in plasma or globin of haemoglobin (**4%**) inside the RBCs.

N.B.

- Reduced haemoglobin has **double** the affinity of oxyhemoglobin for CO_2.
- The ratio of CO_2 in physical solution **:** CO_2 in chemical combination is **5/95 = 1/20.**
- If this ratio changes, the blood pH will change.

Significance of arterial CO_2:

a) Stimulates the respiratory centre for **pacing**.

b) Bicarbonates form the blood **alkali reserve** that combats acidosis.

Tidal CO_2:

It the **difference** between **venous** and **arterial** CO_2 contents.

At **rest**, each 100 ml of arterial blood (CO_2 content = **50 ml** %) passing to the tissues are **loaded** with **5 ml** CO_2 to be venous blood (CO_2 content = **55 ml** %).

So, Tidal CO_2 = Venous CO_2 content - Arterial CO_2 content

Mechanism of tidal CO_2 carriage at tissues:

(i.e. The Chloride Shift Phenomenon):

The CO_2 tension at tissues is **46 mmHg**, while that of arterial blood supplying the tissues is **40 mmHg**, accordingly CO_2 passes from the tissue to the blood (i.e. down its pressure gradient) which changes into **venous blood**.

In the blood:

A. About 10 % of tidal CO_2 dissolves in plasma water (i.e. carried in physical solution) and raising the CO_2 tension **from 40** mmHg **to 46** mmHg in **venous blood**.

B. A small part of tidal CO_2 reacts with plasma water forming **carbonic acid,** which is rapidly **buffered** by the phosphate and protein buffers forming **weaker** acids than carbonic acid causing only **very minimal** change in blood **pH**.

C. The major part of CO_2 enters the **RBCs** where it is dealt with **as follows:**

1. CO_2 reacts with water in the presence of the enzyme carbonic anhydrase (CA) to form carbonic acid (i.e. the rate of the reaction is accelerated ~ **5000 times** the normal in presence of the enzyme).
2. The formed carbonic acid rapidly **dissociate** into hydrogen and bicarbonate ions (H^+ and HCO_3^-) → increased their levels of in RBCs.
3. **The increased** H^+ ions concentration in RBCs → **accelerates** the dissociation of O_2 from oxyhemoglobin (HbO_2) resulting in release and ↑ delivery of O_2 to the tissues (i.e. shift to the right). This called **(Bohr's effect).**
4. While, the free Hb **binds** with H^+ forming **reduced hemoglobin (i.e. HHb).**

5. **<u>In turn</u>**, most of bicarbonate ions (HCO_3^-) diffuse out of RBCs into the plasma along concentration gradient.
6. **<u>To keep the electric balance</u>**, <u>chloride</u> ions (Cl^-) present in plasma are **<u>shifted</u>** from plasma into the RBCs → increased Cl^- ions in RBCs → The osmotic pressure increases more in the RBCs → water **<u>shifts</u>** from plasma to RBCs → **<u>swelling</u>** of RBCs → increased HCT value of venous blood **<u>more</u>** than arterial blood.
7. **<u>Finally</u>**, the reduced Hb (i.e. HHb) formed in step (4) has more affinity to CO_2 than HbO_2. So, it <u>combines</u> with a small part of CO_2 forming carbamino-Hb.

<u>N.B.</u>

- The <u>diffusion</u> of HCO_3^- **<u>out</u>** and Cl^- **<u>into</u>** the RBCs occurs through a **<u>special</u>** bicarbonate-chloride **<u>exchanger</u>** protein <u>present</u> in the RBCs membrane.
- Haemoglobin by these steps buffers about **80%** of tidal CO_2.

<u>The Net Effects of Chloride Shift:</u>

- Bicarbonate **<u>increases</u>** in RBCs and plasma, but **<u>more</u>** in **RBCs**.
- Chloride ions **<u>decreased</u>** in plasma and **<u>increased</u>** in RBCs.
- Water **<u>diffuses</u>** from plasma to RBCs → **<u>swelling</u>** of RBCs.
- The pH is **<u>very little</u>** affected by a slight decrease in spite of the addition of 5 ml tidal CO_2.
- The pH of <u>arterial</u> blood is <u>about</u> 7.4, while that of <u>venous</u> blood is about 7.35.

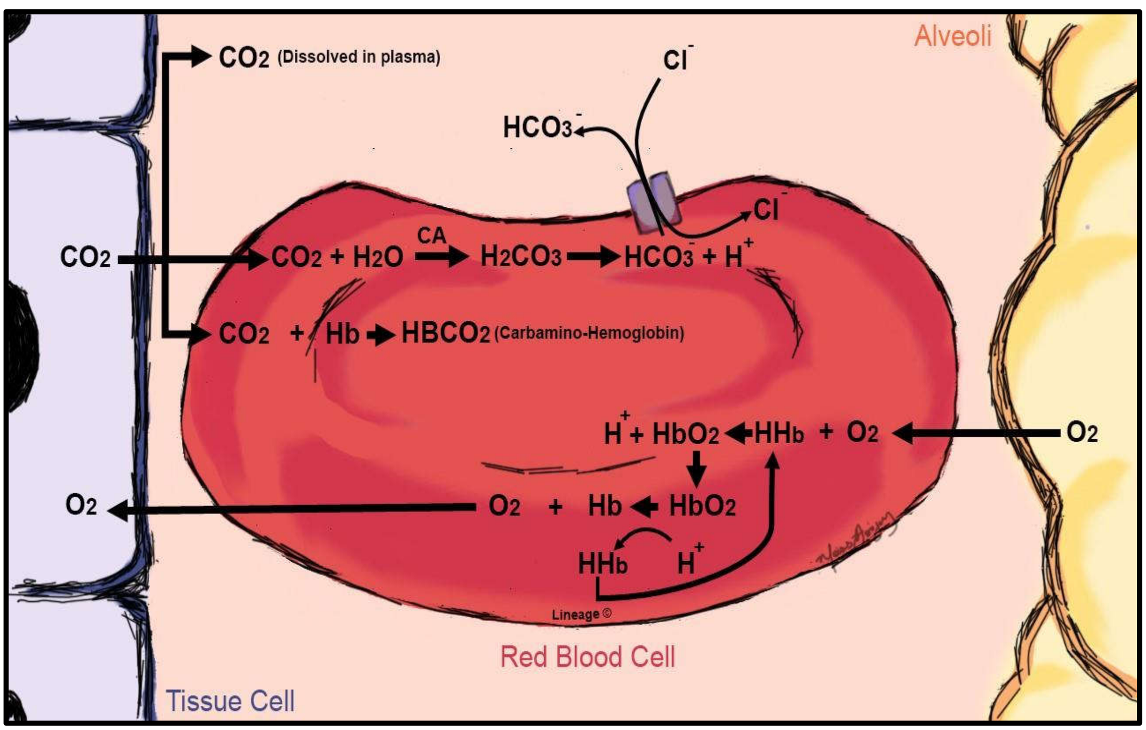

Figure: CO_2 carriage and chloride shift phenomenon (at tissues).

Mechanism of gas exchange at the lungs:
(i.e. Reverse chloride shift phenomenon)

1. As the tension in the alveolar air is **100 mmHg** and that of the venous blood reaching the lungs is **40 mmHg**. So, O_2 **diffuses** from the alveolar air to the blood.

2. As the CO_2 tension in venous blood reaching the lung is **46 mmHg** while, its tension in alveolar air is **40 mmHg**. So, CO_2 **diffuses** from blood to alveolar air.

3. CO_2 in **physical solution** in plasma is liberated **first** and diffuses to alveolar air → ↓ CO_2 tension → **reversal** of all the reactions that have occurred in plasma at the tissues → release of CO_2 chemically combined as bicarbonate and as carbamino compounds with plasma proteins and its diffusion to alveolar air **according to** pressure difference for CO_2.

4. Carbamino haemoglobin **inside** the RBCs releases its CO_2 and becomes reduced haemoglobin (HHb). The released CO_2 diffuses to alveolar air.

5. O_2 **enters** the RBCs and combines with HHb to form **HbO_2** and release of **H^+ ions**.

6. The **increased** H^+ ions (released from HHb) react with HCO_3^- present in RBCs forming carbonic acid which **dissociates** to $H_2O + CO_2$ (in the presence of CA enzyme) → CO_2 diffuse to the alveolar air (i.e. ↑ CO_2 removal).

7. Bicarbonate concentration is decreased in RBCs resulting in **diffusion** (i.e. re-entry) of HCO_3 from plasma **into** the RBCs down its concentration gradient **in exchange** with chloride ions **(i.e. reverse chloride shift).**

Net Results:

- Bicarbonate **decreases** in both plasma and RBCs, but the **decrease** is **more** in RBCs **due to** the presence of CA enzyme → more bicarbonate dissociation.
- Bicarbonate **diffuses** from plasma into RBCs **according** to concentration gradient **created** by the effect of the enzyme.
- $C1^-$ ions diffuse from the RBCs to plasma in **exchange** with bicarbonate (i.e. reversal of chloride shift).
- The osmotic concentration in RBCs **decreases** more than that of plasma → water **shift** from RBCs to plasma → ↓ volume of RBCs → ↓ **HCT** value in arterial blood.

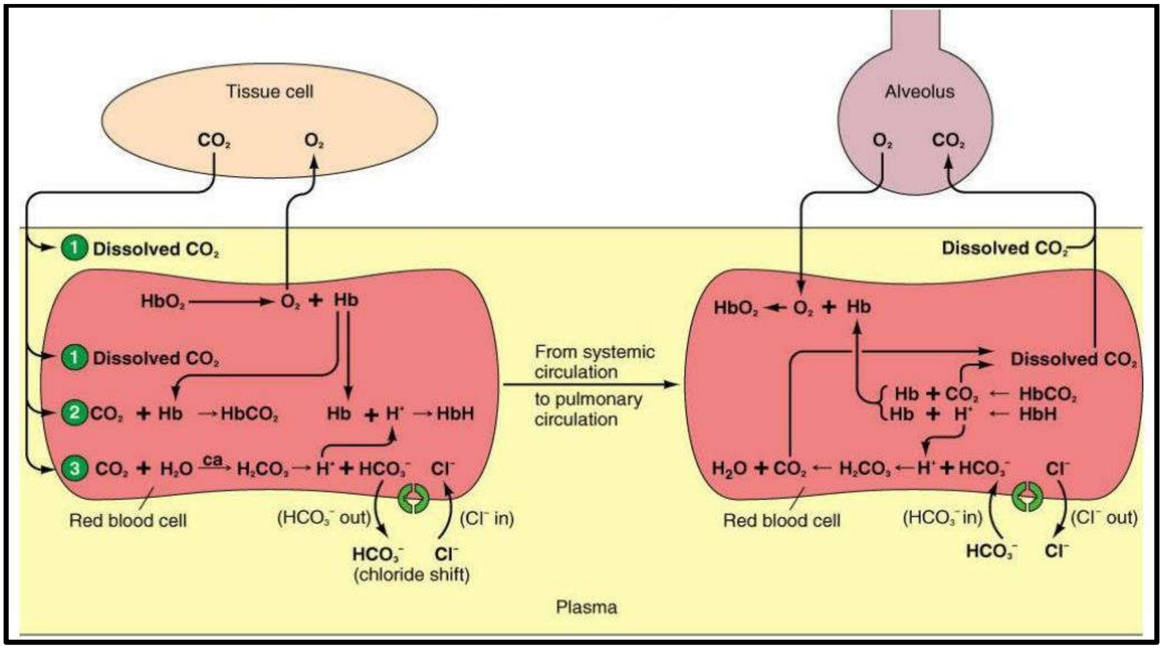

Figure: CO_2 transport in blood.

CO_2 Dissociation Curve(s):

They are obtained by drawing CO_2 content of blood samples **against** CO_2 tension.

Three curves are obtained:

1. **The curve of fully oxygenated blood: (i.e. PO_2 = 100 mmHg)**
   - It is obtained by using a tonometer containing enough oxygen to **fully** saturate haemoglobin.).
   - This curve represents the relation between CO_2 content and CO_2 tension when Hb is **fully** saturated.
   - **Point (A)** on the curve represents the condition of **arterial blood** where, CO_2 **content** equals **50** ml % and CO_2 **tension** = **40** mm Hg.
2. **The curve of 30% reduced blood resting venous blood: (i.e. PO_2 = 40 mmHg)**
   - Obtained by exposing the blood sample in the tonometer to oxygen which is **only** enough to saturate **70** % of the hemoglobin content.(i.e. Hb will be **30 %** reduced)
   - **Point (V)** on this curve represents the condition of the **resting venous blood** where CO_2 content = **55** ml % and CO_2 tension = **46** mm Hg.
3. **The curve of fully reduced blood: (i.e. PO_2 = 0 mmHg)**
   - It is obtained by using a tonometer containing **no** oxygen, and so, all Hb will be **fully reduced**.
   - This condition **never** occurs **normally** inside the body.
   - **Point (B)** on this curve represents the condition of the **fully reduced venous blood** where CO_2 content = **65** ml % and CO_2 tension = **60** mm Hg.

N.B.

Joining points A → V → B gives a **line** representing the **physiological CO_2 dissociation curve** inside the body.

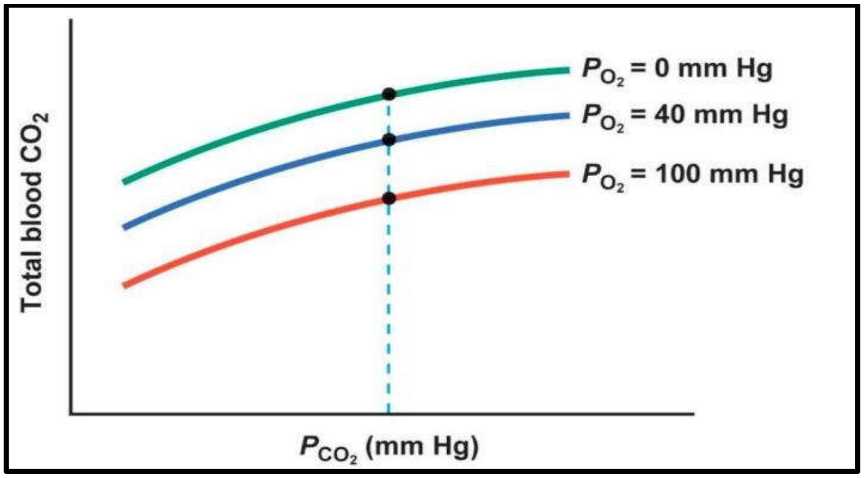

Figure: CO_2 dissociation curves.

Comments on CO_2 dissociation curves:

Reduced Hb (HHB) **carries more** CO_2 than **HbO_2** (at any given CO_2 tension).

(i.e. the oxygenation of hemoglobin promotes the dissociation of CO_2 from hemoglobin).

This is called the Haldane effect;

It describes the ability of hemoglobin to carry increased amounts of **carbon dioxide** (CO_2) in the deoxygenated state compared to the oxygenated state.

Significance:

- When HbO_2 gives its O_2 to the tissues and is **reduced** to Hb, its **capacity to carry** CO_2 from the tissues is **increased**.
- At the lung, **oxygenation** of Hb to HbO_2 **decreases** its capacity to **carry** **CO_2** which is released from venous blood to alveolar air (i.e. increased CO_2 removal).

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