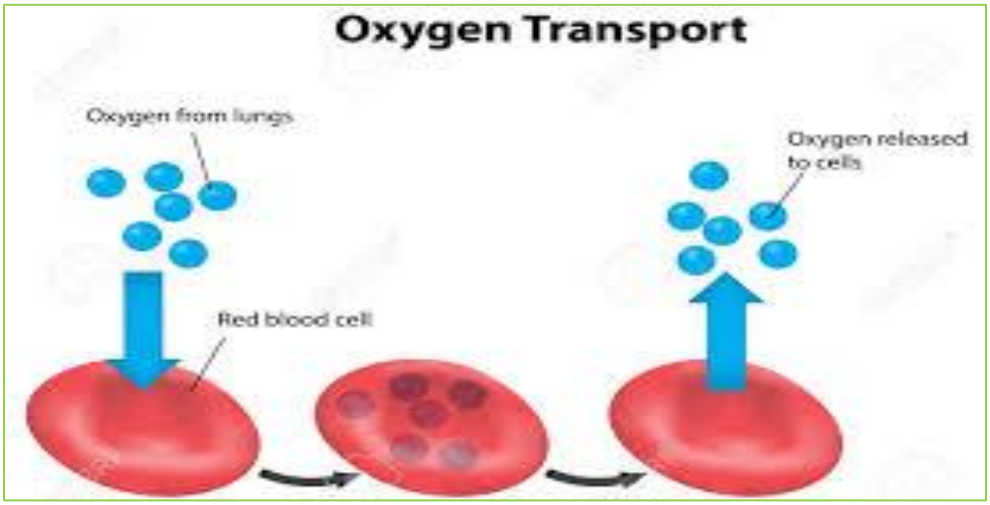

Lecture 12: Mechanism of Oxygen carriage in the blood

Code: RRS-209

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Learning Objective :

Knowledge:

- Know how the oxygen is carried by the blood.
- Define O_2 content, O_2 saturation, O_2 utilization.
- Describe the O_2 dissociation curve and the physiological significance of the curve.
- Know the causes of failure of oxygen transport and cyanosis.
- Explain myoglobin dissociation curve, fetal Hbg.

Intellectual:

- Explore the factors causes shifting of O_2 dissociation curve.
- Compare between types of hypoxia

O_2 Carriage by the blood

- Oxygen is transported in the blood from the alveolar capillaries of the lungs (where blood is loaded with O2) to the peripheral capillaries in the tissues.
- O_2 is transported in blood in two distinct ways:

1- Bounded to heamoglobin (Hb) **OR**

2- Dissolved in solution in ICF and ECF fluids

***O_2 in Physical solution*:**

- The amount of oxygen dissolved in the blood is proportional to its partial pressure (Henry's law).
- At 37°C, 3ml O_2 is dissolved in each liter of arterial blood per mmHg. So there is 3 ml / liter. In whole blood volume = 3X5= 15 ml.
- Resting O2 consumption is approximately (300L /min) So the physical form of O_2 can not support the body's O_2 requirement.
- However, dissolved O_2 determine the major pathway (direction of diffusion of O_2) for transport of O_2 across capillary walls to the cells.
- So an additional form of O_2 transport is needed. Heamoglobin provides this transport.

2- Chemical combination with Hb (98.5%)

- Hb contains 4 atoms of iron. Each atom combines with one molecule of O_2 = Hb_4O_8 (*there are only four ' hooks ' for O_2 per molecule*)
- ***O2 content*** : The amount of O_2 that can be bound to hemoglobin (mL/dL blood) in a liter of arterial blood.
- calculated as 1.34 mL O_2/dL blood × [Hemoglobin].
- As 1gm Hbg contains 1.34 ml O_2 and every 100 ml blood contain 15 gram of Hb.
- in arterial blood =1.34 X 15 =20.1ml O_2/100 ml blood Venous blood contains 15 ml/100 ml blood.
- So 1L of blood containing 150g Hb can transport 200 ml. *Compare this value with that of dissolved form*
- **O_2 saturation**: The percentage of total oxygen-binding sites on hemoglobin that are actually occupied by oxygen, also called the saturation of peripheral oxygen.
- **O_2 utilization**: Every 100 ml of arterial blood while passing in the tissues loses O_2 and changes to venous blood.
- Every 100 ml of arterial blood loses 5ml (20-15gm) = (50 ml / liter) to the tissues.

$$\text{Coefficient } O_2 \text{ Utilization} = \frac{\text{Arterial } O_2 \text{ content - venous } O_2 \text{ content X 100}}{\text{Arterial } O_2 \text{ content}}$$

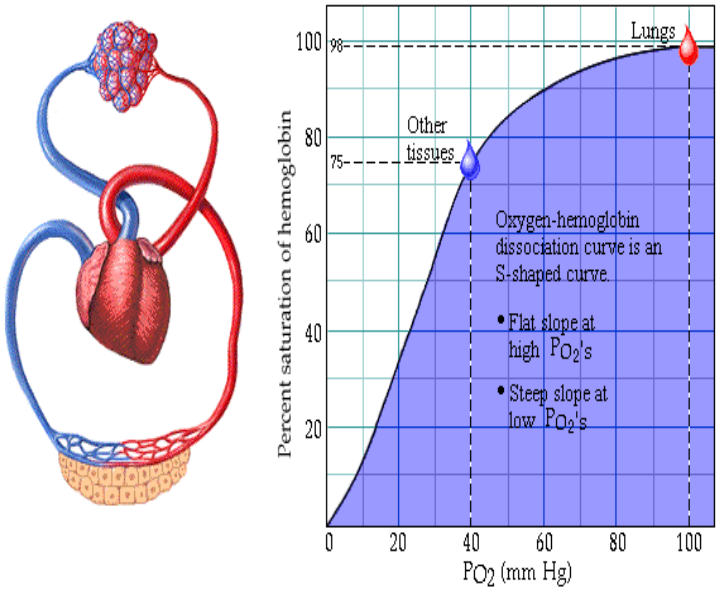
O_2 Dissociation Curve

- It's the relationship between the O_2 tension (PO_2) and % HbO_2 saturation. It describes how the oxygen saturation of hemoglobin varies with the Po2 in the blood
- The reaction between Hb and O_2 is both rapid and reversible.
- It's not linear but it's S (sigmoid) shaped curve. The curve has a steep slope between 10 and 60 mmHg *PO2* and a relatively flat portion (or plateau) between 60 and 100 mmHg *PO2.*

Causes of the sigmoid shape:

- The intermediates compounds (Hb_4O_4 & Hb_4O_6) are responsible for the S shaped. If these compounds aren't formed and Hb_4O_8 is formed directly the curve would be straight line.
- Binding of O_2 to Hb is cooperative such that the binding of each O_2 molecule to the Hb tetramer facilitates the binding of the next
- So, the combination of the 1st heam with O_2 ↑ the affinity of the 2nd heam for O_2 and oxygenation of the 2nd ↑ affinity of the 3rd heam for O_2 and so on.

- $Hb_4 + O_2 \rightarrow Hb_4O_2$
- $Hb_4O_2 + O_2 \rightarrow Hb_4O_4$
- $Hb_4O_4 + O_2 \rightarrow Hb_4O_6$
- $Hb_4O_6 + O_2 \rightarrow Hb_4O_8$



- The major function of Hb is to *load with* O2 at the lungs and *unload at the tissues. This function* is carried out at the flat (**loading region) part of the** curve and at the steep **unloading region.**

The physiological significance of the flat part (used at the lungs):

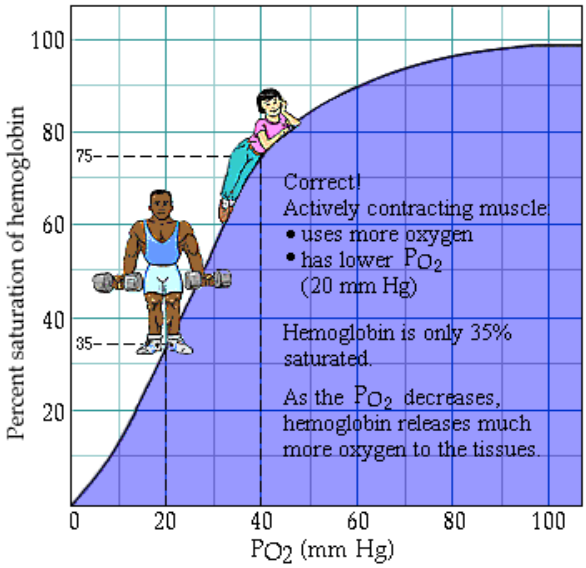
- At 100 mmHg O_2 tension, the Hb is 98 % saturated.
- At 80 mmHg O_2 tension, the Hb is 95 %saturated.
- At 60 mmHg.O_2 tension, the Hb is 90 % saturated.

From the curve you can observe

- ✓ Thus, despite the marked fall in alveolar Po_2 from 100 to 60 mm Hg, the Hbg saturation changed from (98%) to (90%) which is still within normal levels. *Thus the tissue Po_2 hardly changes*

The physiological significance of the flat part (used at the lungs):

- ***Note :*** Even a small fall in blood *Po_2 causes a* large unloading of O_2 .
- At O_2 tension = 40 mmHg, the Hb saturation is75 %. So, Hb saturation decreases by **20 %** (95% - 75 %).
- Significance: During muscular exercise, PO_2 is ranged from 15 -30 mmHg. The Hb saturation is 35% . So, Hb saturation decreases by **60%** (3 times the normal) (95-35%). Which means that there is more O_2 delivered to tissues as they need more amount of O_2 due to ↑ the activity of them.



***Factors affecting O_2 D curve**:*

Factors shifting to the right: It means the affinity of Hb to O_2 is decreased OR more release of O_2 from the Hb, caused by:

1-↑ temperature

2- ↑CO_2 concentration in the blood.

3- ↓ in PH of the blood = ↑ in H^+ conc.

4- ↑ in concentration Of 2'3 Diphosphoglycerate (DPG)

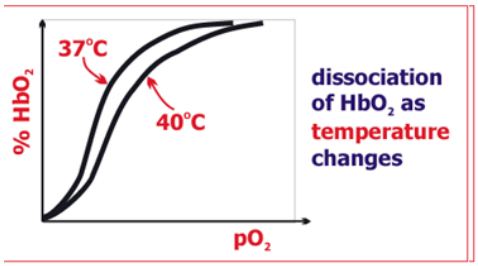
Shifting to the left : (The affinity to O_2 is increased) OR more bind of O_2

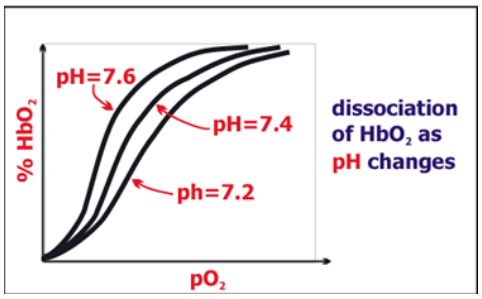
1-↓ temperature

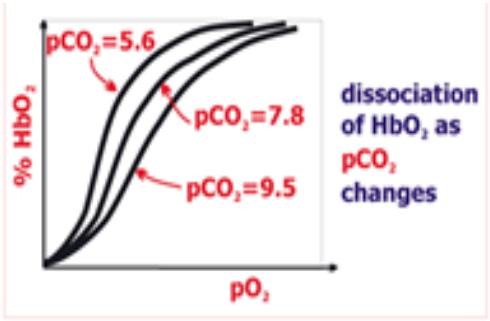
2- ↓ CO_2 conc. In the blood.

3- ↑ in PH of the blood = ↓ in H^+ conc.

4- ↓ in conc. Of 2'3 DPG.

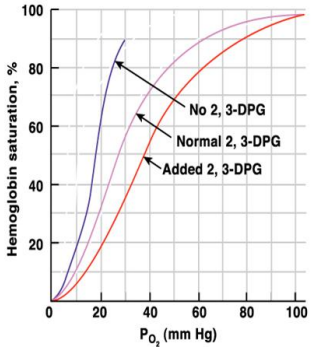






4- Effect of 2,3 Diphosphoglycerate (2,3 DPG)

- 2,3-DPG is produced by erythrocytes during glycolysis, binds to Hb and reduces its affinity for O_2. The production of 2, 3-DPG is raised during hypoxic conditions, the



Graph question: Blood stored in blood banks loses its normal content of 2, 3-DPG. Is this good or bad? Explain.

Significance of shift O2 D curve **:**

1-The Bohr Effect:

It is the ↑ of O2 delivery to the tissues when CO2 and H+ shift the curve to the right.

In the lungs:

- As the blood passes in the lungs, CO_2 diffuses (Why ?) from blood into the alveoli, this ↓the blood PCO_2 so ↓ H+ concentration.
- This leads to shift to left → More binding of O_2 to Hb so oxygenation of the blood occurs

In tissues:

- When blood reaches the tissues , the CO2 diffuse from the tissues to the blood , so PCO2↑ so shift the curve to the right which cause more release of O2 to the tissue.

2- In muscular exercise :

- There are high CO_2 amount released and acids are produced .In addition, temperature of the muscle rises from 2-3C. All these factors cause shift the O_2 hemoglobin dissociation curve to right which allows more release of O_2 to the muscle.

Variant types of HB

1-Fetal haemoglobin (HbF) has a raised affinity for O_2

- Compared with adult haemoglobin. This allows an increase in oxygen uptake in the placenta. Therefore, although fetal arterial *PO2 is lower than that in the* air-breathing newborn, fetal hemoglobin allows adequate oxygen supply to the developing organs.

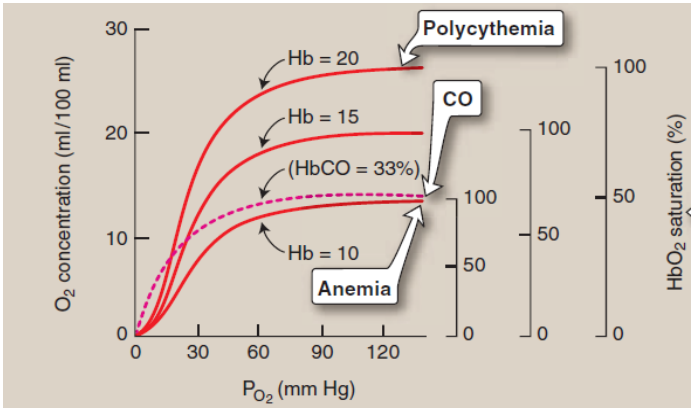
2- O2 D curve of myoglobin:

- Is a form of haemoglobin expressed in striated muscle fibers. It has a much higher affinity for O_2 than haemoglobin and does not demonstrate cooperativity in its binding of O_2
- It can combine with one molecule of O_2 . and does not demonstrate cooperativity in its binding of O_2
- The curve is rectangular hyperbola (remains horizontal till very low O_2 tension then suddenly descends vertically).
- ***So it acts as store of O_2*** to be used by muscle where O_2 tension becomes very low in tissues (as in severe exercise or hypoxic conditions), and also allows O_2 to be delivered to cells when muscle is contracted and perfusion reduced.

3- Carbon monoxide:

- It is a colorless, odorless gas that is a product of the incomplete combustion of fuel (e.g. gasoline).
- It is a common cause of sickness and death due to poisoning,
- It has extremely high affinity— 210 times that of oxygen—for the oxygen-binding sites in hemoglobin. For this reason, it reduces the amount of oxygen that combines with hemoglobin in pulmonary capillaries
- It also exerts a second deleterious effect as it ***shift the oxygen-hemoglobin dissociation curve to the left***, thus decreasing the unloading of oxygen from hemoglobin in the tissues.
- *Why Carbon monoxide is highly toxic gas?*
- 1-The affinity of Hbg to CO is 210 times its affinity for O_2 So, Once Hb combines with CO, it can not combine with O_2 . 2- The Hb CO shift the O dissociation curve of the remaining oxy Hbg to the left.
- The Hb CO breaks down very slowly.

Describe effects (Polycythemia, Anemia and CO on Hb concentration)



Hypoxia (Failure of O2 transport)

- The term for a lack of oxygen in the tissues is **hypoxia** . Lack of O 2 in arterial blood is termed **hypoxaemia** . Total absence of O 2 is **anoxia.**
- **Types of hypoxia :**

1- Hypoxic hypoxia
2- Anaemic hypoxia
3- Stagnant hypoxia
4- Histotoxic hypoxia

1- Hypoxic Hypoxia:

- In this type , there is ↓ PO2 of arterial blood, The Hbg saturation with O2 is decreased and there is ↓ PO2 of venous blood.
- When there is decrease in arterial PO2 which goes to the tissues, there will be decrease in average PO2 in capillary blood so the rate of O diffusion to the tissues is ↓ which causes symptoms of O2 lack.

Causes:

1- High altitude 2- Breathing low % of O2.

3- Shallow rapid breathing *(may results from pulmonary congestion)*because there is :

a- ↑ ratio of the volume of the DS to Tidal air.

b- Greater number of alveoli will not be distensible.

4- Depression of respiratory centers: as in morphine poisoning.

5-Diseases of the lung : may cause hypoxia but with different mechanisms:

a- By diffusion impairment : due to thickened pulmonary membrane as in pneumonia, pulmonary oedema

b- By decreasing surface area : emphysema.

c- Difficulty in breathing : Bronchial asthma in which there is increased resistance to air flow in the respiratory passages.

6- Shunting of venous blood.

2- Anaemic Hypoxia

- In this type; Normal Pa O2 ,normal % saturation of Hb.
- Arterial O2 content is ↓because of ↓ Hb amount which is capable of carrying O2.
- During passage of the blood in the tissues, a fewer number of RBCs. passes through the tissues and, so the O_2 tension decreased in the venous blood and then it decreased in the capillary blood leading to production of the hypoxic symptoms.

Causes:

1- All types of anemia. 2- Carbon monoxide (CO) poisoning.

3- Stagnant Hypoxia

In this type:

Normal Pa O_2, normal % saturation of Hbg.

Caused by decreased blood flow through the tissues ,May be :

1- Generalized (congestive heart failure) 2- Localized (Cold).

4- Histotoxic Hypoxia

- O_2 released from Hbg is transported to the cell by the cytochrome system.
- Histotoxic Hypoxia results from inactivation of metabolic enzymes which facilitate this transport.These enzymes are Cytochrome dehydrogenase and cytochrome oxidase
- *Cyanide can block the cytochrome oxidase & Alcohol block the cytochrome dehydrogenase.*

Cyanosis

- Means the blue discoloration of the skin and mucous membrane, due to excessive amounts of deoxygenated Hbg in skin vessels.
- Threshold of cyanosis:
- Appears when the arterial blood contains more than 5 grams deoxygenated Hbg in each deciliter of blood.
- Causes:

1-Alveolar hypoventilation:

2-Inadequate oxygenation: as in deficiency of O in atmosphere.

3- Diffusion impairment 4- Ventilation-perfusion mismatch

4- Right to left shunt. 5- Circulatory defect (generalized &localized)

6- Abnormal forms of Hb

Central cyanosis:

- Caused by reduced O2 saturation. Involves highly vascularized tissues such as lips and tongue and mucous membrane.

Peripheral cyanosis:

- Results from increased oxygen extraction from the peripheral blood resulting from sluggish movement of blood through capillary circulation.
- Affects distal extremities

Cyanosis occurs in moderate cold in exposed areas in normal individuals because there is arteriolar and venous constriction and there is slow blood flow in the capillaries & more oxygen is removed from Hg.

Cyanosis is not present in:

Sever cold: the drop in temperature causes shift to the left and the O2 uptake of the cold tissues is reduced.