OXYGEN TRANSPORT

Modes of O_2 transport

1. Dissolved in plasma (2%)
2. In combination with Hb in the red cell (98%)

1) In Physically Dissolved Form

- only about 2% of O_2 transport.

Henry's Law :- The amt of gas that dissolves in a liquid at a given temp is proportional to the partial pressure of the gas.

Dissolved O_2 = O_2 solubility × partial pressure.

- At PaO_2 of 95 mm Hg, the dissolved O_2 is 0.3 ml/dl.
- In a normal healthy adult, 0.3 ml of O_2 is transported in dissolved form in 100 ml of blood.
- cardiac output = 5 L/min, the O_2 transported in dissolved form at rest is about 15 ml/min.

2) In combination with Hb

- More than 98% of O_2
- Due to the binding affinity of Hb for O_2
- Hb binds with O_2 to form oxyhaemoglobin (HbO_2) & that doesn't bind with ~~Hb~~ O_2 is called deoxyhaemoglobin or reduced - Hb.

Oxyhemoglobin Formation

- Hb → made of 4 subunits → each subunit has a heme part & a polypeptide part
  ↳ 4 polypeptides together ↓ globin
- Each heme grp contains one atom of iron (Fe^{2+}) to which Oxygen binds
- Each iron atom can bind 1 O_2 molecule.
- A single Hb molecule can bind 4 O_2 molecules.
- Hb binds with O_2 ~~when~~ only when the iron is in ferrous (Fe^{2+}) state.

Fe^{2+} iron in Hb gets oxidised to ferric (Fe^{3+}) iron to form methemoglobin

- Methaemoglobin cannot bind to O_2.
- However, the enzyme methaemoglobin reductase is present in red cell that reduces the methemoglobin to Hb. Therefore, normally only abt 1.5% of the total Hb is methaemoglobin.
- Deficiency of metHb reductase → as genetic defect. - decreases O_2 carrying capacity.
  - O_2 binds rapidly & reversibly to Hb to form HbO_2 (oxyhaemoglobin)

R & T states of Hb

During the formation of HbO_2, heme remains in the ferrous state ∴ this process is oxygenation & not oxidation.

- As there are 4 subunits ⇒ HbO_8 is rapidly formed.

1. When O_2 is not bound to Hb → deoxyHb → The 4 subunits are tightly bound with each other. This configuration → Tense or T state.
   - affinity for of Hb for O_2 is less.

2. When, 1st O_2 molecule binds with Hb, the 4 subunits enter into Relaxed or R state that exposes more - binding sites.
   ∴ in R configuration → affinity for O_2 is increased 200 - 500 times

3. When PO_2 is less → Hb molecules in T state → low affinity for O_2
4. When PO_2 is ↑ → Hb molecules in R state → ↑ " " .

∴ The quantity of oxyhaemoglobin formation is a function of the partial pressure of O_2 in the blood.

In pulmonary capillaries pO_2 ↑ → formation of oxyHb
In tissue capillaries pO_2 ↓ → formation of deoxyHb
→ helps in unloaded O_2 from Hb for cell utilization

O_2 carrying capacity of Hb

- Each gm of Hb ~~[illegible]~~ binds with 1.34 ml of oxygen.
- The max amt of oxygen that can be carried by Hb is called oxygen carrying capacity.

1. In a healthy individual, the O_2-carrying c of arterial blood is about 20ml of O_2 per 100 ml of blood.
   (when Hb conc is of 15g%, 1.34mL × 15 g = 20.1 mL O_2/dL blood)

2. Oxygen content of Hb (HbO_2 content) is the amt of O_2 actually bound to Hb.

Oxygen capacity of Hb (HbO_2 capacity) is the amt of O_2 that can potentially bind with Hb.

3. % saturation of Hb with O_2 (SO_2)

$$SO_2 = \frac{HbO_2 \text{ content}}{HbO_2 \text{ capacity}} \times 100$$

- Normally in arterial blood, the % saturation of Hb with oxygen is about 98%.

Oxygen - Hb Dissociation Curve

- Oxy Hb D.C explains the relationship b/w partial pressure of O_2 and oxygen saturation of Hb.
- It is an S-shaped curve → with pO_2 range 0 → 100 mm of Hg.
- The sigmoid shape of curve results from Hb affinity for O_2 at various levels.
- As PO_2 ↑, Hb sat progressively ↑.
- that is not linear with ↑ of PO_2.

2 major phases :-

1) Steep Phase

- Steep slope b/w pO_2 of 10 mm Hg & 60 mm of Hg
- Combinatⁿ of Hb with O_2 ↑ rapidly as PO_2 ↑ from 0 → 60 mm of Hg.
- O_2 saturation of Hb is about 90% at PO_2 60 mm of Hg.

Significance

- Oxygen saturation of Hb is very ↑.
- Less ↑ in PO_2 leads to greater % sat of Hb ∴ facilitates oxygen loading.
- If it changes in reverse direction → causes unloading of O_2 in the tissues.
- A small ↓ in PO_2 in the tissue results in unloading of large amts of O_2 to the tissues

- Steep phase allows large quantities of O_2 to be released from Hb in the tissue capillaries where lower capillary PO_2 prevails.
- Achieved by shifting the curve to R. (increased H^+ / ↑ CO_2)

2) Plateau Phase

- Begins around 60 mm Hg and flattens at 70 mm Hg
- The ↑ in PO_2 above 60 produces only a small ↑ in O_2 binding
- Oxygen sat & content remain appreciably constant over a wide alteration of PO_2

Significance

1) In ↑ altitude or pulm. diseases, in which moderate hypoxia occurs (↓ in PO_2 from 95 mm Hg → 60) total amt of O_2 carried by Hb decreases only by 5-10%, since Hb sat at 60 mm Hg is abt 90%

- Safety factor → even a significant ↓ lung function allows normal sat of Hb.

2) O_2 sat & content remains fairly constant in spite of fluctuations in alveolar PO_2.

- Oxygen content cannot be raised appreciably by hyperventilation or by breathing 100% O_2 because Hb is already completely saturated with O_2 at PO_2 of 100 mm of Hg → only for normal people at sea level.
- If a person has low alveolar PO_2, due to lung disease or ascension to high altitude, hyperventilation or breathing 100% O_2 ↑ Hb sat with O_2 as they have more deoxyHb.

The P_{50}

- Level of PO_2 at which 50% of Hb is saturated with O_2.
- assesses binding affinity of Hb for O_2.
- If P_{50} is ↑ → signifies ↓ in affinity of Hb for O_2
  seen in right shift
- If P_{50} is ↓ → ↑ in affinity of Hb for O_2
  seen in left shift.

Factors Affecting Hb - binding Affinity with O_2:

① Temperature
② arterial PCO_2
③ arterial pH
④ 2,3-DPG

- ↑ in PCO_2, ↓ in pH, ↑ in temp → shift the curve to right
- The effect of CO_2 and H^+ ions on the affinity of Hb for O_2 is known as Bohr effect.
- A rightward shift enhances the unloading of O_2 for a given PO_2 in the tissues.
- A leftward shift increases the affinity for Hb for oxygen, thereby lowering the ability to release oxygen to the tissue.

1) Temperature

- ↑ in temp shifts the curve → right
- i.e. ↑ temp decreases the affinity of Hb for oxygen. helps in release of O_2 in metabolically active tissues in which temp is more.

2) pH

- Christian Bohr of Neils Bohr demonstrated that respiratory acidosis shifts Oxy-Hb curve to right.
- Since, then the decrease in affinity due to acidosis is known as Bohr effect.
- ↓ in pH → curve to right & vice versa
- When blood passes through capillaries, CO_2 enters the RBC that ↓ the intracellular pH and shifts the curve to R.
- Under normal physiological conditions, binding of about 0.7 mole of H^+ causes Hb to release 1 mole of O_2.
- Thus, when blood passes through tissue capillaries, the acidic environment facilitates release of O_2 from Hb into the tissues.

3) CO_2

- During cellular metabolism, CO_2 is released into circulation

that ↑ generation of H^+ and ↓ pH. → shifts the curve to R.

- CO_2 combines with unprotonated amino groups on Hb to form

carbamino groups. ↓ in oxygen affinity.

4) 2,3-DPG