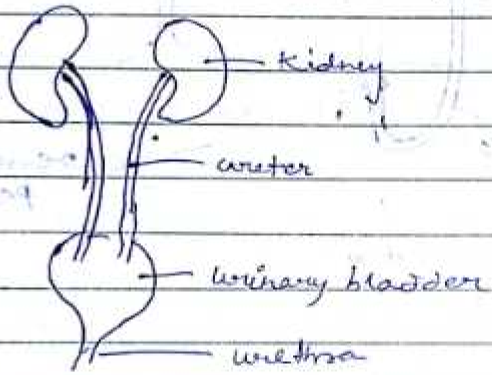
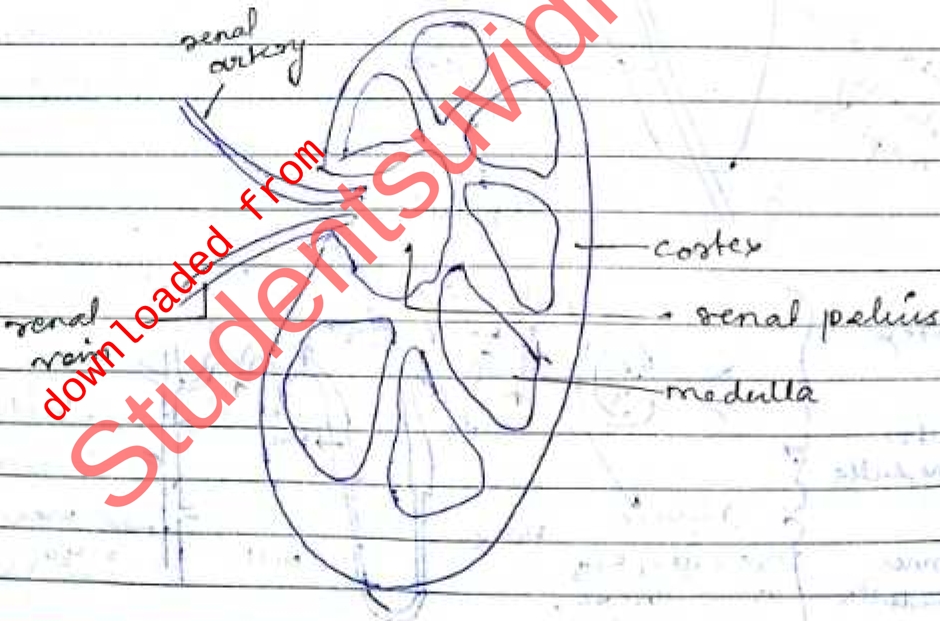
(11)

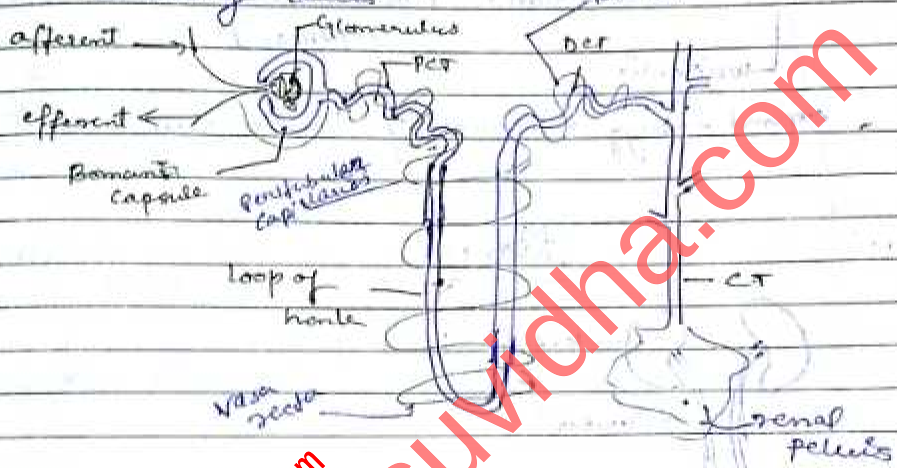
Kidney

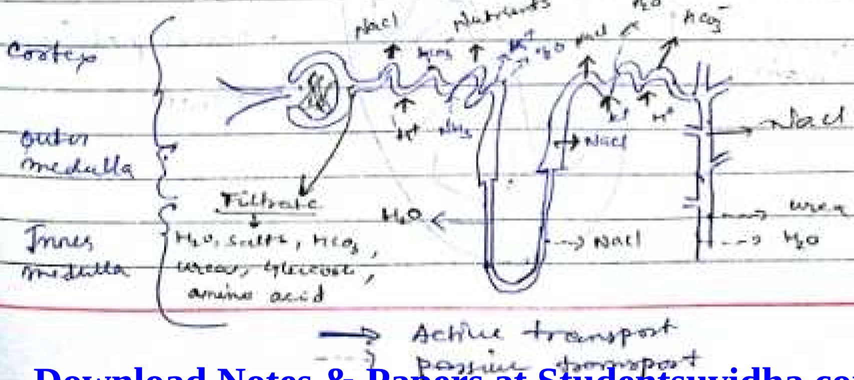

kidney
ureter
urinary bladder
urethra


renal artery
renal vein
cortex
renal pelvis
medulla

Nephron

- Bowman's capsule
- Glomerulus
- Proximal convoluted tubule
- Loop of Henle
- Distal convoluted tubule
- Collecting ducts





Gaseous exchange

The O_2 which once reach the alveoli must move across the alveoli membrane into pulmonary capillary from where it is transported by the blood to the tissue.

Respiratory quotient : It is a balance ratio of CO_2 produced to the O_2 consumed. It is approximately around 0.8

Dalton's law : In a mixture of gases the pressure exerted by each gas is independent of the pressure exerted by the other. Thus, the total pressure of mixture is simply the sum of individually pressure. The partial pressure of gas is directly proportional to concⁿ, the net diffusion of a gas will occur from a region where its partial pressure is high to a region where it is low.

Diffusion of gases and liquid :
When a liquid is exposed to air containing a particular gas, the molecules of gas will enter the liquid and dissolve in it.

Henry's law state that the amount of gas dissolved will be directly proportional to the partial pressure of gas with which the liquid is in equilibrium

Alveolar gas pressure : The alveolar gas pressure are around 105 mm Hg = PO_2 and PCO_2 = 40 mm Hg whereas the gas pressure in the air which is being inhaled has PO_2 = 160 mmHg and PCO_2 = 0.3 mm Hg.

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The factors that determine the alveolar PO_2 (partial pressure of O_2):

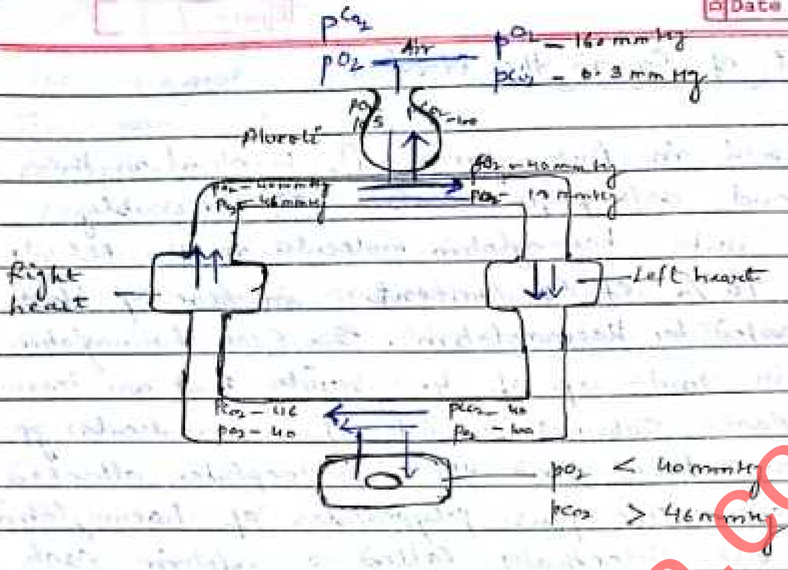
1. The pO_2 of atmospheric air.
2. The rate of alveolar ventilation.
3. The rate of total body O_2 consumption.

In case of pCO_2, the atmospheric pCO_2 have negligible effect.

Gas exchange between alveoli and blood:

The blood that enters the plumonary capillary has systemic venous blood pumped to the lung via plumonary artery. The blood that comes from the tissues have relatively high pCO_2 that is 46 mmHg and is relatively low pO_2 that is around 40 mmHg. The difference in the partial pressure of O_2 and CO_2 on the two sides of the alveolar capillary membrane results in the net diffusion of O_2 from the alveoli to the blood and of CO_2 from blood to alveoli. As this diffusion occur the capillary blood pO_2 rises and pCO_2 falls. The net diffusion of these gases stops when the capillary partial pressure becomes equal to that in alveoli.

	Venous blood	Arterial blood	Alveoli	Atmosphere
PO_2	40 mmHg	100 mmHg	105 mmHg	160 mmHg
pCO_2	46 mmHg	40 mmHg	40 mmHg	0.3 mmHg



The blood that leave the pulmonary capillary is return to the heart and it is pumped into systemic artery which have similar pO_2 and pCO_2 as that of alveolar air.

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Gas exchange between tissues and blood

As the systemic arterial blood enters the capillary throughout the body it is separated from interstitial fluid by only a thin capillary wall which is highly permeable to both O_2 and CO_2. The interstitial fluid in turn is separated from intra cellular fluid by the plasma membrane of the cell which are also quite permeable to O_2 and CO_2. The metabolic rxn occuring within the cell are constantly consuming the O_2 and producing the CO_2. Therefore the intracellular pO_2 is lower ~~than~~ and pCO_2 is higher than in blood. As a result, there is a net diffusion of O_2 from blood into the cells and a net diffusion of CO_2 from the cells into the blood. In this manner, as the blood flows through systemic capillaries its pO_2 ↓ses and its pCO_2 ↑ses.

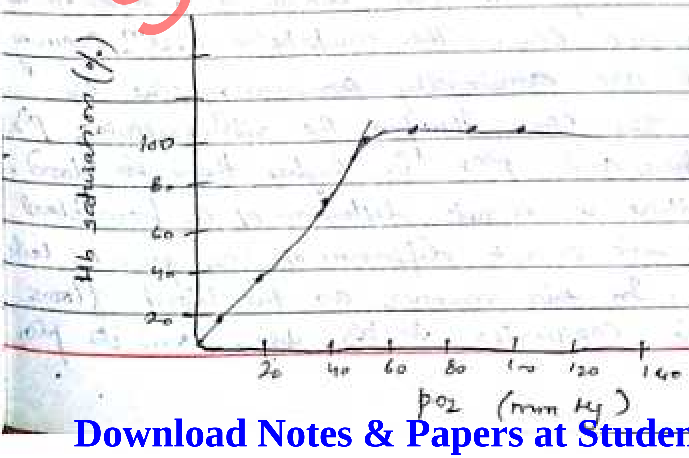
Transport of O_2 in the blood :

O_2 is present in two forms – (1) Dissolved in the plasma and extracellular water (2) reversibly combined with haemoglobin molecule in the RBCs. More than 98% of O_2 content in litre of blood is transported by Haemoglobin. Each haemoglobin molecule is made up of 4-subunits that are bound together. Each subunit consists of a molecule of known as haem and the polypeptide attached to the haem. The four polypeptides of haemoglobin molecule are collectively called as globin. Each of the four haem groups in a haemoglobin molecule contains 1 atom of iron to which the O_2 binds. Each iron atom can bind one molecule of O_2. i.e. single haemoglobin molecule can bind 4 molecules of O_2.

$$O_2 + Hb \rightleftharpoons HbO_2$$

Effect of pO_2 on haemoglobin saturation

The quantitative relationship b/w Haemoglobin and O_2 as determined experimentally is called O_2-haemoglobin dissociation curve.



The combination of O_2 with Hb is an e.g. of cooperativity. The globin unit of deoxyHb are tightly held by electrostatic bonds in a conformation with a relatively low affinity for O_2. The binding of O_2 to a Haem molecules break some of the bond b/w the globin units. This leads to a conformation change such that the remaining O_2 binding sites are more exposed. Thus, the binding of one O_2 molecule to deoxyHb ↑ses the affinity for the remaining sites on the same Hb molecule.

The shape of O_2 haemoglobin dissociation curve is extremely impt in understanding the O_2 exchange. The curve has a steep ~~slow~~ slope b/w 10 to 60 mmHg and a relatively flat portion b/w 70 to 100 mmHg. The extent to which the O_2 combined with Hb ↑ses very rapidly as the pO_2 ↑ses from 10 to 60 mmHg so that at pO_2 of 60 mmHg the 90% of total Hb is combined with O_2. ∴ the further ↑se in pO_2 produces only a small ↑se in O_2 binding. The importance of this plateau at higher pO_2 values is as follows. In many situations like high altitude or pulmonary disease they have moderate reduction in alveolar and arterial tube. Even if the pO_2 fell from the normal value of 100 to 60 mmHg the total quantity of O_2 carried by Hb would ↓se by only 10% ~~since~~ ∴ the Hb saturation is still close to 90% at pO_2 of 60 mmHg ∴ the plateau provides an excellent safety factor such that a significant limitations of lung function can still allow almost normal O_2 saturation of Hb. The steep portion of the curves from 60 to 20 mmHg is ideal for unloading O_2 in the tissues that is a small ↓se in pO_2 results in unloading of large amt of O_2

in the peripheral tissue. Small shifts in the position of curve due to various factors can significantly ↑se the O_2 unloading.

Factors affecting Haemoglobin affinity for the Oxygen

Although the pO_2 is the most impt factor that determines the % oxygen saturation of Hb. Several other factors influence the affinity with which Hb bind the O_2. These factors shift the entire curve either to the left or to the right accordingly. The changing affinity of the Hb for O_2 is another org of How the homeostatic mechanisms adjust the body activities to the cellular needs.

① Acidity or pH : As the acidity ↑ses the pH ↓ses. The affinity of Hb for O_2 ↓ses and the O_2 dissociates more readily from the Hb. The ↑sed acidity enhances the unloading of O_2 from Hb. The main acid produced by the metabolically active tissues are lactic acid and carbonic acid. When the pH ↓es, entire $Hb-O_2$ dissociation curve shifts to the right. At any given pO_2, Hb is less saturated with O_2. This change is termed as Bohr effect

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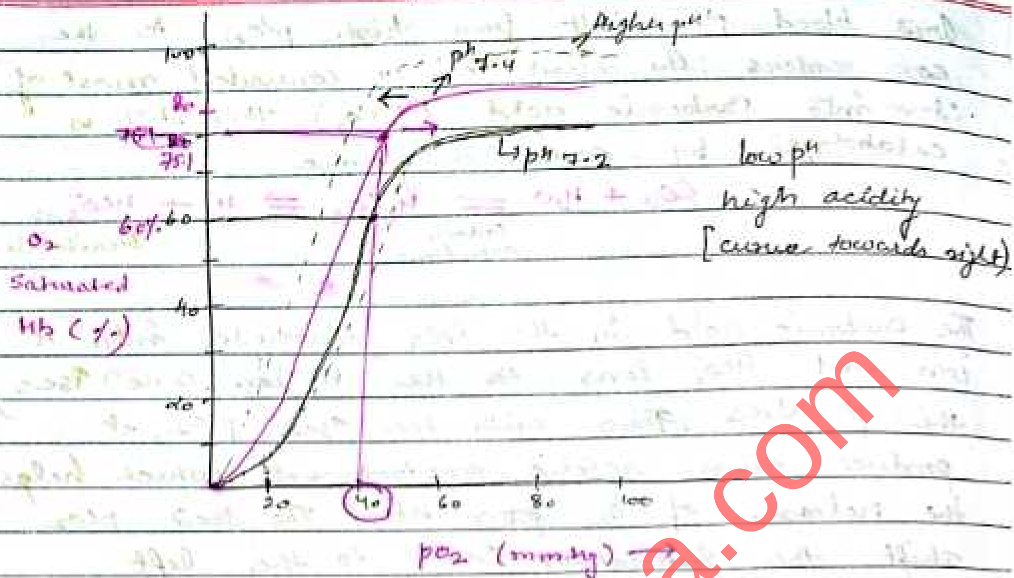
pH and Hb dissociation



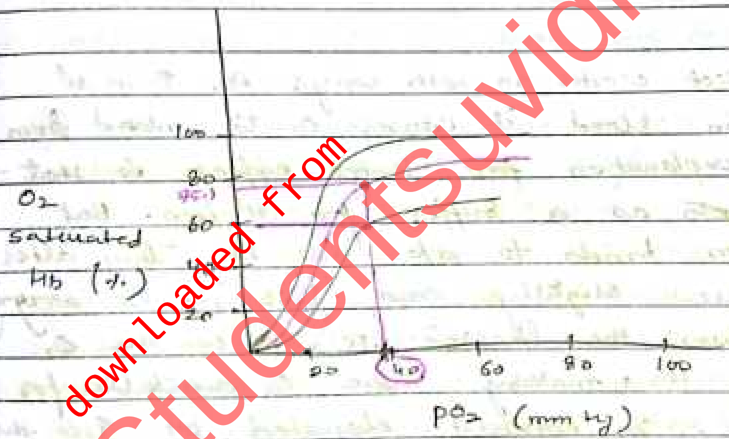
The Bohr effect works in both ways. An ↑ in H^+ ion concn in blood it causes O_2 to unload from Hb. The explanation for Bohr effect is that – Hb can act as a buffer for H^+ ion. But when H^+ ion binds to a/a in Hb they alter its structure slightly and ↓ses its O_2 carrying capacity. Thus, the lowered pH drives the O_2 off from Hb, making more O_2 available for tissue cell. In contrast elevated pH ↑ses the affinity of Hb for O_2 and shifts the O_2-Hb dissociation curve to the left.

(2) ~~Partial pressure of CO_2~~ P_{CO_2} – CO_2 can bind with Hb and this effect is similar to that of H^+ ions ie it is shifting the curve to the right. As the pCO_2 rises the Hb releases the O_2 more readily. The pCO_2 and pH are related factors (because they act on same way) becoz

low blood pH result from high pCO_2. As the CO_2 enters the blood it is converted most of it into carbonic acid (H_2CO_3) - This rxn is catalyzed by carbonic anhydrase.

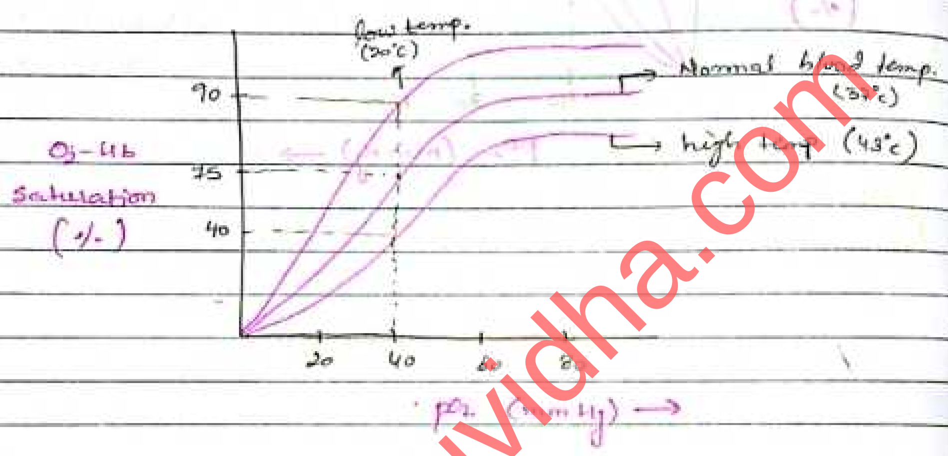
$$CO_2 + H_2O \underset{\text{Carbonic anhydrase}}{\rightleftharpoons} H_2CO_3 \rightleftharpoons H^+ + HCO_3^- \text{ (Bicarbonate)}$$

The carbonic acid in the RBCs dissociates into H^+ ions and HCO_3^- ions. As the H^+ ion conc^n ↑ses, the pH ↓ses. Thus with the ↑sed pCO_2, it produce more acidic environment which helps the release of O_2 from Hb. The ↓sed pCO_2 shift the saturation curve to the left.



③ Temp.

As the temp. ↑ses so does the amt of O_2 released from Hb. Heat is the byproduct of metabolic rxn of all the cells and the heat released by contracting the muscle fibres tends to raise the body temp. The metabolically active cells require more O_2 and liberates more acid and heat. The acid & the heat in turn promotes the release of O_2 from oxyHb. In contrast, during Hypothermia i.e low body temp. cellular metabolism slows down and the need for O_2 is reduced. ∴ more O_2 remains bound to the Hb i.e curve shifts to the left.



(4) BPG or DPG : BPG = 2,3 Bisphosphoglycerate
DPG = di-phosphoglycerate

They ↓ses the affinity of Hb for O_2 and helps to unload the O_2 from Hb. BPG is formed in RBC when the breakdown of glucose to produce the ATP in the process of glycolysis when the BPG combines with Hb by binding to the terminal amino-gp of two β globin chain in Hb, then the Hb binds the O_2 less tightly at the Haem gp. The greater the level of BPG, the more O_2 is unloaded from Hb. Certain hormone such as thyroxine, HGH, epinephrine etc ↑ses the formation of BPG. The levels of BPG are also higher in the people living in high altitude.

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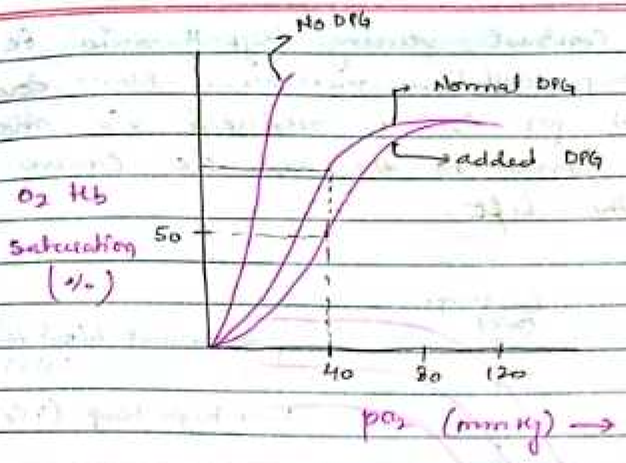
No DPG
Normal DPG
added DPG
O_2 Hb
Saturation
(%)
50
40
80
120
pO_2 (mm Hg) →

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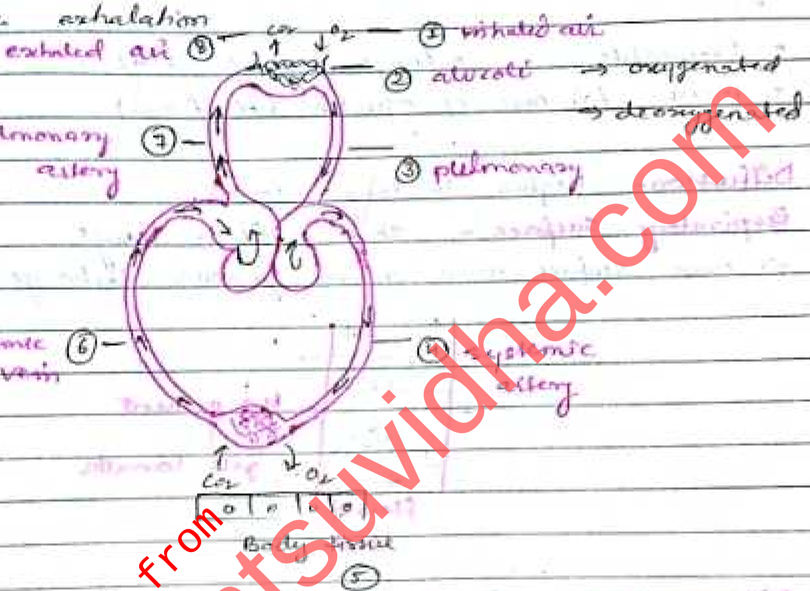
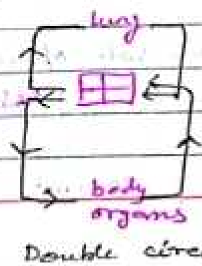
Vital capacity : It is tidal volume during max. inhalation and exhalation.
→ It is around 3.4 l

Residual volume - The air that remains after force exhalation





Haemoglobin has four peptides and carry haem as a cofactor.

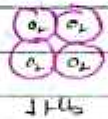
→ It can carry four O_2 molecule = 1 Hb

Hemocyanin – found in arthropods, molluscs to carry O_2 molecules.

$Hb \rightleftharpoons O_2$

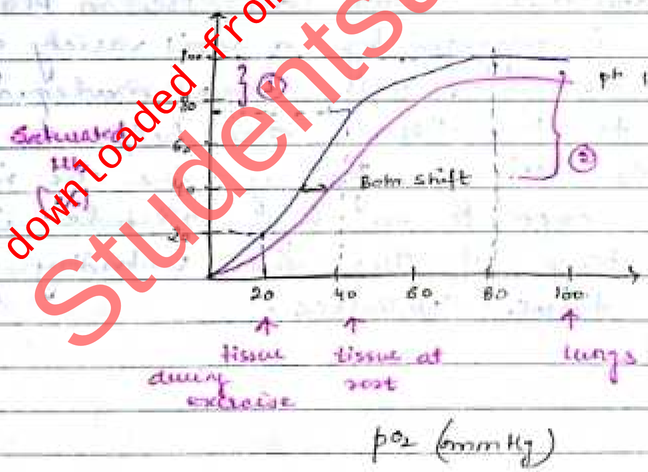
Cooperative binding

→ Binding and diffusion depends on pO_2 or dissociation constant.



→ If O_2 binds to 1 subunit there is conformational change in other 3 subunit and they become vulnerable & binds frequently to O_2.

* pO_2 and Hb dissociation curve at pH 7.4



1) O_2 unload to tissue at rest.
2) O_2 unload to tissue during exercise

The difference makes the blood to move in tissue from lungs.

Tissue at rest → Amt of O_2 dissociates from lungs is 30 %. (100 - 70 = 30)

pO_2 (100 - 40 = 60) makes diffusion to take place.

Tissue during Exercise - Amt of O_2 dissociate from lungs is 80 %. (100 - 20 = 80)

Erythrocyte contains large quantities of DPG which is present in only traces amounts in the other mammalian cells. DPG which is produced by erythrocytes during glycolysis reversibly binds with Hb, allosterically causing it to have lower affinity for O_2. The net result is that whenever DPG levels are ↑sed there is enhance unloading of O_2 from Hb as the blood flows through tissue capillaries. Such an ↑se in DPG concentration is triggered by a vast variety of conditions associated with inadequate O_2 supply to the tissue and helps to maintain O_2 delivery. for eg the ↑se in DPG during exposure to high altitude is important bcoz it ↑ses the unloading of O_2 in the tissue capillaries.

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Transport of CO_2 in blood :

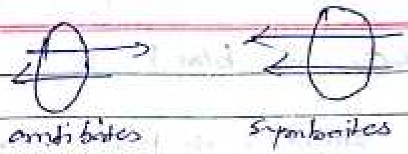
CO_2 is much more soluble in H_2O than the O_2 so more dissolved CO_2 is carried by the blood than the dissolved O_2. A small amount of blood transport the CO_2 around 10 %. In order to transport CO_2 produced in tissue to the lungs, it must be carried in other forms also. Around 30 % CO_2 molecules enters the blood and react reversibly with the amino group of Hb to form Carba-amino Hb

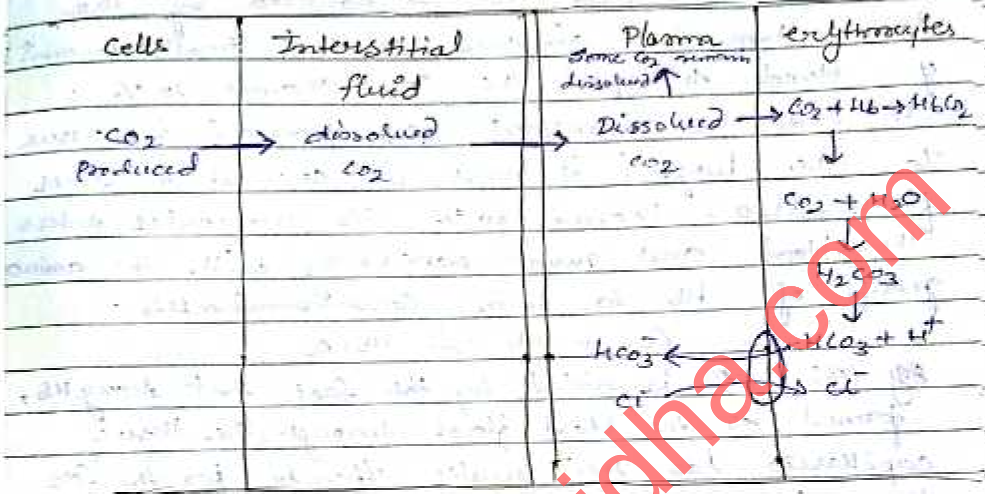
$$CO_2 + Hb \rightleftharpoons HbCO_2$$

By This rxn is aided by the fact that deoxy Hb, formed as the blood flows through the tissue capillaries has the greater affinity for the CO_2 than as the oxy Hb. The remaining 60 % of CO_2 enters the blood in the tissue is converted into bicarbonate (HCO_3)

$$CO_2 + H_2O \xrightleftharpoons{\text{Carbonic anhydrase}} \underset{\text{carbonic acid}}{H_2CO_3} \rightleftharpoons HCO_3^- + H^+$$

The first rxn is the rate limiting and is very slow unless it is catalysed by enzymes carbonic anhydrase. This enzyme is present in the erthrocyte but not in the plasma ∴ this rxn occurs mainly in the erthrocytes. The carbonic acid dissociates very rapidly into a bicarbonate ion (HCO_3^-) and a Hydrogen ion without any enzyme assistance. Once formed most of the bicarbonate moves out of the RBCs into the plasma via a transporter that exchanges one bicarbonate for one Cl^- ion. This is called chloride shift.





The blood pCO_2 is higher than the alveolar pCO_2 i.e. a net diffusion of CO_2 from the blood into alveoli occurs. This loss of CO_2 from the blood lowers the blood pCO_2 and drives the reaction to the left i.e. bicarbonates and H^+ ions combines to give H_2CO_3 (carbonic acid) which then dissociates into CO_2 and H_2O. $HbCO_2$ generates the Hb and free CO_2 thus, the CO_2 so generated diffuses into the alveoli.

Transport of H^+ ions between tissue and lung

The deoxy Hb have much greater affinity for the H^+ ion than does the oxy Hb i.e. it binds most of the H^+ ions.

$$Hb + H^+ \longrightarrow HbH$$

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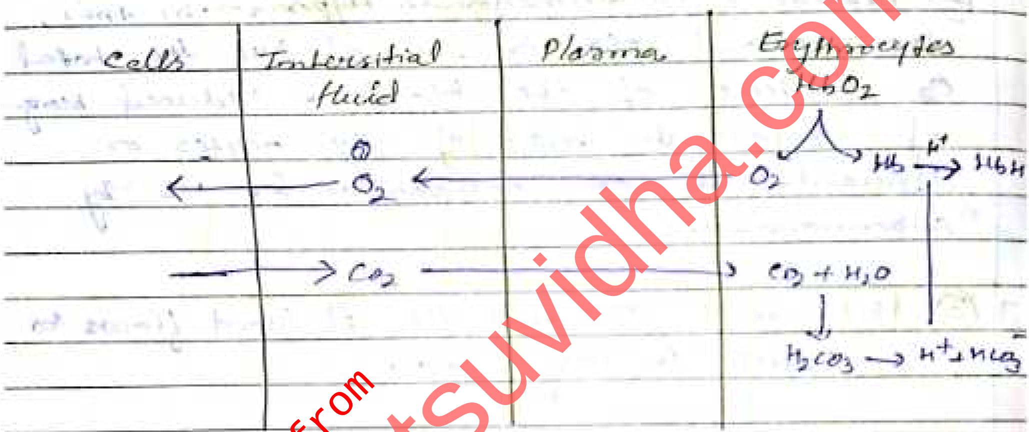
As the various blood passes through the lungs ; all the rxn. are reversed . The deoxyHb becomes converted into oxyHb in the process it releases the H^+ ions which are picked up in the tissues . The H^+ ions reacts with bicarbonate to give the carbonic acid which dissociates to form CO_2 and H_2O . The CO_2 diffuses into the alveoli to be expired.



If the person is hypoventillated or has a lung disease that prevents the normal elimination of CO_2 , the arterial pCO_2 rises as a result arterial H^+ ion concn also rises . The raised arterial H^+ ion concn due to CO_2 retention is termed as respiratory acidosis . Conversely hypo. hyperventillation would lower the arterial value of both pCO_2 and halogen ion concn producing respiratory alkalosis . The Hb also has ability to bind and transport nitric oxide as the blood passes through the lung . It carries it to peripheral tissues and releases it along with O_2 . Nitric oxide in the pulmonary vasodilator . The administration of nitric oxide by inhilation is a treatment for persistence pulmonary hypertension in the new born children.

Hypoxia : It is defined as the deficiency of O_2 at the tissue level. It is of 4 types - (1) Hypoxic hypoxia - In this the arterial ~~(2) anemic~~ pO_2 is reduced

(2) Anemic or carbonmonoxide Hypoxia - In this the arterial pO_2 is normal but the total O_2 Content of the blood is reduced bcoz of inadequate no.s of erythrocytes or deficient Hb or competition for Hb by carbonmonoxide

(3) Ischemic - In this the rate of blood flows to the tissue is very low.

(4) Histotoxic - In this the quantity of O_2 reaching the tissues is normal but the cell is unable to utilise the O_2 because of a toxic agent for e.g cyanide.