## BEATING OF THE HEART

### Myogenic Stimulation of the Heart

All vertebrates' hearts are myogenic, that is the heart beat is initiated from within the heart muscle itself rather than by a nervous impulse from outside it. This is demonstrated when a heart is removed from mammal and placed in a well-oxygenated salt solution at 37$^{o}$C, it continues to beat rhythmically for a considerable time without stimulus from nervous system or hormones.

The initial stimulus for the contraction of the heart originates in a group of cardiac muscle fibres (cells) located in wall of the right atrium **Sino-atrial node** (SAN).

**Note**: The SAN also consists of few nerve endings from the autonomic nervous system. The SAN can initiate the heart beat on its own but the rate at which it beats can be varied by stimulation from the autonomic nervous system.

During atrial diastole, the cells of the SAN slowly become depolarized creating an action potential. A wave of excitation similar to a nerve impulse passes across the muscle fibres of the heart as the action potential spreads from the SAN. This causes the muscle fibre to contract. The SAN is known as the pace mar because each wave of excitation starts here and acts as the stimulus for the next wave of excitation.

Once the contraction has begun, it spreads through the wall of the atria through a network of cardiac muscle fibres causing both atria to contract simultaneously.

When the wave reaches the junction between the atria and ventricles, it excites another similar group of cardiac muscle fibres called the **atrio-ventricular node** (AVN). The AVN is connected to a bundle of specialised muscle fibres the **atrio-ventricular bundle** (AV bundle) which provides the only route for the transmission of the wave of excitation from the atria to ventricles. There is a delay in the conduction from SAN to AVN, therefore atria systole is completed before ventricular systole begins. The AV bundle is connected to a strand of cardiac muscle fibres called **bundle of His**, which give rise to fine branches known as **a purkinje (purkyne) tissue/fibres.** Purkinje tissue runs down the interventricular septum and fans over the walls of the ventricle where it breaks into a sheet-like reticulum just beneath the endothelium lining.

Impulses are conducted rapidly along the purkinje tissue and spread out from there to all parts of the ventricles stimulating both ventricles to contract simultaneously. The wave of ventricular contraction begins at the bottom of the heart and spreads upwards squeezing blood out of the ventricles towards the arteries which pass vertically upwards the heart.

Thus, the pace maker sends out rhymical waves of electrical excitation which are transmitted first over atria and then via the AVN and Purkinje tissue, to ventricles.
Therefore:

- The rhymical initiation of the excitatory waves is independent of the nervous control
- The amount of blood pumped into the arteries is the same amount of blood as received from the veins independent of nervous control

*Position of the SAN and AVN and the bundle of His showing the spread of excitation that accompanies contraction (FA pg 172 fig 11.13; make a drawing)*

## REGULATION OF THE HEART RATE

The basic rate of the heart is controlled by activity of the SAN but there is need to adjust the rate of heart in order to meet demands of the changing blood system. This is achieved by control systems which include:

1. Nervous control
2. Chemical (hormonal) control

**Cardiac output** is the amount of blood flowing from the heart over a given period of time e.g. per minute. It depends upon the volume of blood pumped out of the heart at each beat, the **stroke volume** and the **heart rate** (number of beats per minute)

*Cardiac output =stroke volume x heart rate*

It is the cardiac output which is the important variable in supplying blood to the body. One way of controlling cardiac output is to control the heart rate.

### Nervous control of the heart rate (innervation of the heart)

The nervous control of the heart is located in the hind brain known as the **Medulla Oblongata**. The Medulla has two regions affecting the heart rate i.e.

1. The cardiac inhibitory centre-which reduces the heart rate and
2. The cardiac accelerator centre-which stimulates the heart rate

The cardio-inhibitory centre is linked by two parasympathetic fibres/nerves called the **vagus nerve** to SAN, AVN and the bundle of His. Impulses passing along the Vagus nerve reduce the heart rate.

The cardio-accelerator centre is linked by the sympathetic nervous system to SAN. Stimulation by these nerves results in an increase in the heart rate. It is coordinated activity of the inhibitory and accelerator centres in the Medulla that controls the heart rate.

Sensory nerve fibres from **stretch receptors** within the walls of the artic arch, the carotid sinuses and vena cava run to cardiac inhibitory centre in the medulla. Impulses from the aorta and carotids decrease heart rate, while those from vena cava stimulate accelerator centre which increase the heart rate. The stimulation of the stretch receptors and the number of nerve impulses transmitted to the centres in the medulla depends on blood volume passing any of the above vessels. The greater the volume, the more the stimulation e.g. during conditions of intense activity of the body muscles. (if aorta and carotids have high blood volume, stimulation occurs leading to reduction in heart rate; if vena cava has high blood volume stimulation occurs leading to increased heart rate)

*(Make a drawing BS page 475 fig.14.24)*

**Hormonal control of heart rate**

A number of hormones affect the heart rate either directly or indirectly

1. **Adrenaline hormone** secreted by the medulla of the adrenal gland is the most important. Also, adrenal medulla secretes noradrenaline in smaller amount which has a similar effect as adrenaline. Both stimulate the heart, although adrenaline is more effective. Cardiac output and blood pressure are increased by increasing the heart rate.
2. **Thyroxine**, produced by the thyroid gland raises basal metabolic rate which leads to greater metabolic activity with greater demand for oxygen and production of more heat. As a result, vasodilation followed by increased blood flow occurs leading to increased cardiac output.

**Other factors controlling heart rate**

Which of these centres stimulate the heart depends on other factors which include the following

- **PH.** High $P^H$ decreases the heart rate while low pH (e.g. high $CO_2$ levels as is the case during exercise) accelerates the heart rate.
- **Temperature**. Low temperature decreases the heart rate, while high temperatures accelerate the heart rate.
- **Mineral ions**. The rate is affected directly or indirectly.
- **Sex.** The heat rate is high in females than in males because of the smaller heart.
- **Exercise.** Cardiac output increase during exercise because of increased heart rate and force of contraction
- **Altitude**. Heart rate is higher at at high altitude because of the reduced partial pressure of oxygen which stimulates the secretion of adrenaline increasing the heart rate, while lower at low altitude due to high oxygen partial pressure.
- **Emotional conditions**. Anxiety, apprehension and excitement increases CO through the release of certain chemicals (e.g. catecholamine) which increases heart rate and force of contraction
- **After meal.** During the first hour after taking meals, CO increases.
- **Diurnal variation.** CO is low in early morning and increases in the day time. It depends upon the basal conditions of the individual.
- **Age**. In children, cardiac output is less because of the less blood volume.
- **State of the health**. Fever, anaemia and hyperthyroidism increase the CO. Fever is due to increased oxidative processes, anaemis due to hypoxia (lack of oxygen) and hyperthyroidism due to increased basal metabolic rate.

**Note:** The amount of blood pumped out by the right ventricle goes to lungs. But blood pumped out by the left ventricle is distributed to different parts of the body. Fraction of the CO distributed to a particular region or organ depends upon the metabolic activities of that region or organ.

Cardiac output is maintained/determined by four factors:

1. Venous return-Amount of blood which is returned to the heart from different parts of the body
2. Force of contraction

3. Heart rate and
4. Peripheral resistance

**Effect of Carbon dioxide on the heart rate**

Under conditions of strenuous exercise, the $CO_2$ concentration of the blood increases as a result of greater respiratory rate. The $P^H$ of the blood is therefore lowered. Receptors in a swelling of the carotid artery called *carotid body* detect this change and send nerve impulse to the cardio-accelerator centre which increases the heartbeat, thereby increasing the rate at which $CO_2$ is delivered to the lungs for removal. A fall in $CO_2$ level (rise in PH) of the blood causes the carotid receptors to stimulate the cardio-inhibitory centre, thus reducing the heartbeat.

**Effect of exercise on the heart and circulatory system (cardiovascular system)**

**(a) Short term effect**

During exercise, the muscle needs an increased blood supply so that oxygen and glucose can be provided for aerobic respiration and waste $CO_2$ and heat can be removed. Blood flow to the muscles increases and this is achieved in a number of ways:

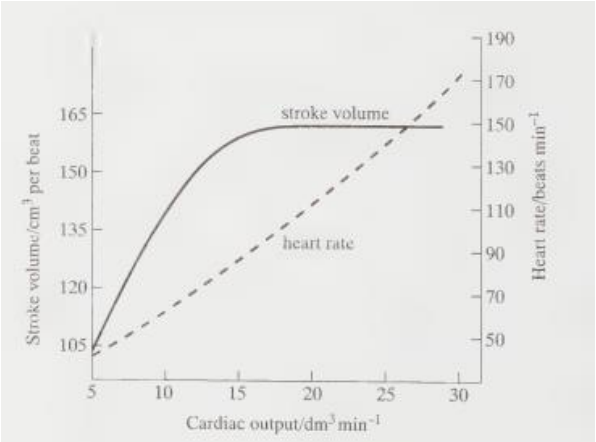
- Increasing the output of blood from the left ventricle of the heart from the resting condition. This is brought about by an increased rate of contraction (heart rate) and more complete emptying of the ventricles (stroke volume) =Cardiac output. It results in a rise in pressure of about 30% in arteries. Heart rate can triple and stroke volume can double in response to maximal exercise.
- Vasodilation of blood vessels (veins) due to increased blood pressure (due to adrenaline and sympathetic nervous system).
- Vasodilation of heart's own blood vessels and in the lungs

  **Note:** In a trained athlete increased heart rate, stroke volume and vasodilation of blood vessels can result in a 25-fold increase in blood flow through the muscles about half of which is due to vasodilation and half due to increased blood pressure,

  **How is the increased CO brought about?**

  In anticipation of exercise, and during its early phase, the sympathetic nervous system and adrenaline stimulate an increased heart rate. However, during a period of prolonged exercise, the rate is maintained by further nervous and hormonal factors e.g., dilation of veins in the muscles increases venous return to the heart, which increase results in increased cardiac output.
- Vasodilation of arterioles occurs in tissues which are less in need of oxygen particularly the gut, liver, kidneys and spleen
- Effect of a rising $CO_2$ concentration due to exercise (ref. to previous section)
- Eventually vasodilation of the skin blood vessels occurs in response to build-up of heat. The rising temperature of the blood is detected by the hypothalamus in the brain and this sends nerve impulses to the medulla which in turn will bring about vasodilation of arterioles in the skin. Capillary loops in the skin then open up allowing loss of heat through the skin.

*A graph showing the effect of exercise on a marathon runner and how cardiac output is increased from 5 to 30 $dm^3$/min (BS pg 476 fig. 14.25)*




**(a) Long term effects**

The heart like all muscles, gets stronger with exercise. Long term training therefore results in a stronger heart and higher cardiac output. (as seen above, a 40% increase in cardiac output is typical in marathon runner compared with untrained person)

The *chambers of the heart get stronger* and *the mass of the muscle increase by 40%* or more. All aspects of function improve, from *an increase in blood vessels to greater numbers* and *size of mitochondria in the muscle fibres.* Aerobic (endurance) exercise is necessary for those improvements, rather than short-burst anaerobic activity.

**Maintenance and control and blood pressure**

Blood pressure depends on several factors:

1. Heart rate
2. Stroke volume
3. Resistance to blood flow by the blood vessels (peripheral resistance)
4. Strength of the heart beat

Note: Control of cardiac output (heart rate and stroke volume) has been discussed (refer to previous sections)

- Resistance to blood flow is altered by contraction (vasoconstriction) or relaxation (vasodilation) of the smooth muscle in the blood vessel walls especially those of arteriole.
- Peripheral resistance is increased by vasoconstriction and decreased by vasodilation. Increased resistance leads to increased pressure whereas a decrease leads to a fall in blood pressure.
- Vasoconstriction and vasodilation are controlled by a **vasomotor centre** in the medulla Oblongata of the hind brain. From this centre, nerves run to the smooth muscles of arteriole throughout the body.
- Pressure receptors known as **baroreceptors** in the carotid artery detect blood pressure changes and relay impulses to the vasomotor centre.

- If blood pressure falls, the vasomotor centre sends impulses along sympathetic nerves to the arterioles. The muscles in the arterioles contract causing vasoconstriction and a consequent rise in blood pressure.
- A rise in blood pressure causes the vasomotor centre to send impulses/message via the parasympathetic system to the arteriole causing them to dilate and so reduce blood pressure.
- A rise in blood $CO_2$ concentration also causes a rise in blood pressure. High $CO_2$ concentration is detected by chemoreceptors in the carotid bodies which transmits impulses to the vasomotor centre. This sends impulses to blood vessels causing vasoconstriction hence increase in blood pressure. This increases the speed with which blood is delivered to the lungs and so helps to remove the $CO_2$ more quickly.
- Hormones like adrenaline also raise blood pressure.
- Other factors that affect blood pressure include: Age, Sex, state of health, emotional stress e.g. excitement, pain and annoyance e.t.c. (be able to give a brief explanation)

**Measuring of blood pressure**

Blood pressure is measured in mmHg. Because blood pressure changes from systole to diastole, it is usually recorded as two numbers:

The first number is the pressure during systole (systole pressure)

The second one is the pressure during diastole (diastolic pressure)

The blood pressure of a normal healthy adult at rest is $\frac{120 \quad Systole}{80 \quad diastole}$

Blood pressure is measured using a device called sphygmomanometer

**Heart diseases**

**Coronary heart disease**-Affects the pair of blood vessels- the coronary arteries- which serve the heart muscle itself.

There are three ways in which blood flow in these arteries may be impeded

1. **Coronary thrombosis**: A blood clot which becomes lodged in coronary vessel
2. **Atherosclerosis**: narrowing of the arteries due to thickening of the arterial wall caused by fat, fibrous tissue and salt being deposited on it. This is sometimes called hardening of the arteries
3. **Spasm:** repeated contraction of the muscle in the coronary artery wall
   A combined effect of the above can result into heart attach leading to death.

**Causes of heart diseases**

- Smoking-both thrombosis and atherosclerosis
- Raised level of fat especially cholesterol-atherosclerosis
- High level of salt in the diet
- High level of glucose in the diet (diabetes)
- Stress increases risk of heart diseases
- Age-older people are at a high risk than young ones
- Sex-males more at risk than females

**NB:** Exercise can reduce the risk of coronary heart disease

# BLOOD

Blood is a fluid connective tissue contained within a closed system of tubes (arteries, veins and capillaries) through which it is circulated by the pumping action of the heart. Blood is an unusual connective tissue in that specialized cells are surrounded by a fluid matrix (plasma) that is not secreted by blood cells themselves.

Blood constitutes about 10% of the body weight.

There are two major components of blood i.e.

(i) Plasma (make up about 55% by volume)

(ii) Blood cells (make up about 45% by volume)

**Blood plasma**

Constitutes 90% of water and 10% of a variety of substances.

Components of blood plasma and their function

1. **Water**
   - ❖ Is the major constituent of blood and lymph, and forms about 90%
   - ❖ Provides cells of the body with water (hydration of body cell)
   - ❖ Transports many dissolved materials around the body (medium of transport of many dissolved materials)
   - ❖ Regulation of water content helps to regulate blood volume and pressure.
2. **Plasma protein (7-9%)**

(i) Serum albumen -very abundant and produced by the liver

Function:

- ❖ Bind to and transport calcium
- ❖ Contribute to the solute potential of the blood.

(ii) Serum globulin-a globulin produced by the liver

- ❖ Bind and transport the hormone thyroxine, lipids and fat soluble vitamins (ADEK)

B-globulin-produced by liver

- ❖ Bind and transport ions, cholesterol and fat soluble vitamins.

γ-globulin-produced by lymphocytes

- ❖ Important in immune responses

(iii) Prothrombin-produced by the liver

- ❖ Involved in blood clotting.

(iv) Fibrinogen-produced by the liver

- ❖ Take part in blood clotting.

(v) Enzymes

- ❖ Take part in metabolic activities.

3. **Mineral ions**

These include; $Na^{+}$, $K^{+}$, $Ca^{2+}$, $Cl^{-}$, $HCO^{3-}$, $H_2PO_4^{2-}$, $PO_4^{3-}$, $SO_4^{2-}$

Function:

- ❖ All collectively help to regulate solute potential in blood and some regulate PH levels in blood.
- ❖ They also have a variety of other functions e.g. calcium ions may act as a clotting factor.

4. **Components that occur in varying concentrations**

- ✓ Products of digestion e.g. fatty acids, glycerol and amino acids being transported from small intestine to the liver.
- ✓ Excretory products being transported from the liver to the kidney
- ✓ Hormones e.g. insulin, sex hormones, growth hormones being transported from ductless glands to their target organs.
- ✓ Vitamins

**Note:**
The composition of plasma is carefully regulated by the body and most components are maintained at a constant concentration. The functions of plasma can be summarized as:

- ❖ Transport nutrients to the cells.
- ❖ Remove excretory products from the cells.
- ❖ Distribute hormones from the endocrine glands to the target organs.
- ❖ Distribute heat energy from warm parts of the body to the cooler parts.

These functions contribute to the homeostasis of the body.

- ❖ Plasma also protects the body from pathogens by forming clots at wound sites and distributing antibodies.

**Cellular components of blood**

(a) Red blood cells (erythrocytes)

- ➢ They are small sized cells and numerous, approx.. $5\times10^6$ per cubic millimeters
- ➢ Have no nucleus when mature.
- ➢ Appear circular biconcave discs.
- ➢ The cell membrane is very thin.
- ➢ The thin flexible membrane is packed or filled with red pigment, the haemoglobin which is a complex.
- ➢ The red blood cells have a limited life span of about 120 days
- ➢ The red blood cells contain carbon anhydrase which play a role in CO2 transport.
- ➢ Make up of about half the volume of the blood.

  The major function of the RBC is to carry oxygen from the raspatory organ to the tissues and their structure is modified accordingly.

  *Assignment: Write down the adaptations of red blood cells to their functions*

**Note:**
Red blood cells are produced in the bone marrow tissue called haemopoietic tissue of short bones like ribs, skull, vertebral column, sternum, pelvic e.t.c.
In infants, all bones have haemopoietic tissue and manufacture RBCs.
In adults, each RBC has a relatively short lifespan e.g. about 4 months due to lack of the nucleus to control repair process. After the RBC is broken down into amino acids, then iron of the haem group is extracted and stored in the live as ferritin (the iron containing protein), it may be reused later in the liver in the production of other RBCs or used as a component of cytochrome.
The remainder of the haem is broken down into two bile pigments i.e. bilirubin (red) and biliverdin (green). These are later excreted as bile into the gut.

The rate of destruction and replacement of the RBCs is partly determined by the amount of oxygen in the atmosphere. If the quantity of oxygen to be carried in blood is low, the marrow is stimulated to produce more RBCs than the liver destroys. This is one of the ways in which we acclimatize to lower oxygen levels at high altitudes and is made use of by athletes in high altitude training. When oxygen content of the blood is high, the situation is reversed.
Structure (*Make drawings*)
Surface view (disc shape) lateral view (biconcave shape)

**(b) White blood cells (leucocytes)**

These cells are larger than the RBCs and are present in much smaller numbers.
All have nucleus.
Although they the nucleus, their life span in the blood stream is normally only few days.
All are capable of a crawling movement (amoeboid movement) which allows them to squeeze through pores in capillary wall to reach the tissues and sites of infection.
Most of them are made from the bone marrow.
Role: they play an important role in body defense mechanisms.

**Types of white blood cells**

There are two main groups of WBCs as seen from the light microscope depending on whether they show granules in their cytoplasm or not.

1. **Granulocytes** (polymorphonuclear leucocytes)

- Have granular cytoplasm and lobed nucleus.
- They can engulf bacteria.
- They are made in the bone marrow but their stem cells are different from those that make RBCs.
- They are divided into neutrophils, eosinophils and basophils.

**(i) Neutrophils (phagocytes)**

These make up about 70% of the total number of WBCs, being the most numerous.
They commonly squeeze through the capillary walls and wander through the intercellular spaces to engulf and digest disease-causing bacteria.
Structure (*make a drawing*):

**(ii) Eosinophils**

They form 1.5% of the total number of WBCs but their number increases in people with allergic conditions such as asthma, or hay fever.
They are produced by the bone marrow.
They possess cytoplasmic granules which stain red when applied to the dye eosin.
They possess anti-histamine properties.

Their number in the blood stream is controlled by hormones produced by the adrenal cortex in response to stress of various kinds.
Function
Involved in allergic responses and inti-histamine properties.
Structure:

**(iii) Basophils**

These represent 0.5% of WBCs
They are produced by bone marrow
The granules of these cells stain basic dyes (e.g. methylene blue)
Structure:

**Function**

- Produce histamine and heparin. Heparin is anti-clotting protein and histamine is a chemical found in damaged tissues involved in inflammation
- Inflammation stimulates repair of damaged tissues. Therefore, their number may increase during allergic conditions to produce histamines.

**2. Agranulocytes (mononuclear leucocytes)**

They have non-granular cytoplasm and have either an oval or bean-shaped nucleus. They constitute about 28% of the WBCs. There two main types i.e.

**(i) Monocytes (constitutes 4% of WBCs)**

- Produced in the bone marrow.
- Have bean-shaped nucleus.
- Become macrophages when they enter tissues

**Structure:**

**Function**

- Macrophages are phagocytic and engulf bacteria and other particles.
- Also play a role in immune system by producing certain antigens

Together with neutrophils, they form a system of phagocytes throughout the body which act as the first line of defense against infection

**(ii) Lymphocytes**

They are produced in the thymus gland and lymphoid tissues from cells which originate in the bone (stem cells). The cells are rounded and possess only a small quantity of cytoplasm but with a prominent nucleus.
They are also found in lymph and body tissues.
Structure:

There are two types of lymphocytes i.e. **T-lymphocytes** (T-cells) and **B-lymphocytes** (B-cells).

**Function:**

They are involved in immune reactions such as anti-body reactions, graft rejection and in killing tumor cells.

**(c) Platelets**

Irregularly shaped, membrane-bound cell fragments formed from the cytoplasm of large cells, usually lacking nuclei and are smaller than RBCs

Have a life span of 5-9 days before being destroyed by spleen and liver.

Structure:

**Function:**

They are responsible for starting the process of blood clotting mechanisms.

**General functions of mammalian blood**

The functions of blood can be categorized into three:

1. Transport functions
2. Regulatory functions
3. Protective functions

**Transport functions**

1. Transport of respiratory gases; oxygen from lungs to tissues and carbon dioxide from the heart to the lungs.
2. Hormones are transported from glands to where they are needed (target organs).
3. Transport of excretory products from tissues to excretory organs e.g. urea from the liver to kidney. Other excretory organs include lungs, skin.
4. Transport of product of digestion like amino acids and glucose that transported from the alimentary canal to the liver and general circulation.
5. Fatty acids and glycerol are transported from the alimentary canal to lymphatic system and general circulation.
6. Transport of mineral ions/salts e.g. calcium ions from intestines to bones/teeth, iodine from intestine to thyroid gland, iron from intestine/liver to bone marrow.
7. Transport of water to all tissues.
8. Growth, development and coordination by transport of hormones.

Note: Apart from respiratory gases ($O_2$ & $CO_2$) which occur in RBCs, the transport of other materials occurs in blood plasma.

**Regulatory functions**

- Osmotic pressure of blood tissue is determined by plasma concentration of sodium ions and plasma proteins. This regulates water movement between blood and tissues.
- Body temperature regulation by distribution of heat between the organs that produce excess heat and all other tissues of the body e.g. metabolic heat from the liver and muscles to all other parts of the body.
- Maintenance of a constant PH carried out by the blood buffer system e.g. $HCO_3^-$ and $PO_4^{3-}$ ion via the maintenance and circulation of plasma proteins.

**Protective functions**

- White blood cells provide defense by phagocytosis and immune responses such as antibody-antigen reactions

- Blood clotting which involves platelets, calcium ion prevents blood loss and entry of pathogens

## Transport of oxygen

Oxygen is transported from lungs to tissues by a blood pigment called **haemoglobin** present in the RBCs.

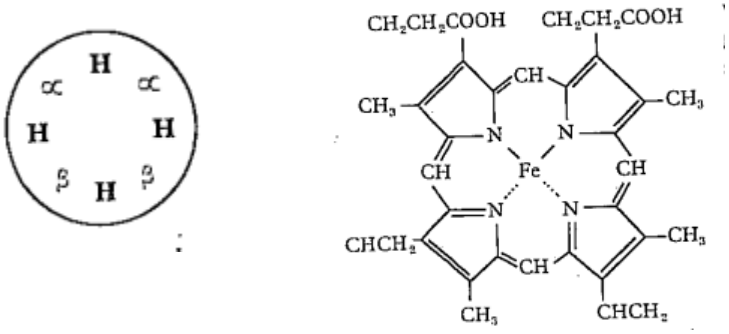
### Structure of haemoglobin

Haemoglobin is a compact molecule made up of four interlocking subunits. Each subunit is made up of a polypeptide chain which is a globin attached to a haem group. The haem group comprises a porphyrin ring containing an atom of iron (II) at the centre. The haem group in the haemoglobin is responsible for its red colour and is the site of oxygen transport. An iron atom combines with a molecule of oxygen but without oxidation of the iron of the iron (II). The oxygen molecule just fits into pockets of haemoglobin called binding sites. Up to four oxygen may be carried by each haemoglobin molecule.

The reaction between haemoglobin and oxygen to form oxy-haemoglobin is…

**Note:** two of the four globins of haemoglobin are known as α-globin and the other two are β-globins.

*Drawing of haemoglobin and haem group (ref. FA pg 164 fig. 11.2)*




### Carried of oxygen

Oxygen diffuses from the lungs into RBC and combines with haemoglobin to form oxy-haemoglobin where it is transported. Each of the four-iron containing haem group in haemoglobin can combine with oxygen. Therefore, up to a maximum of four oxygen molecules can be carried by each haemoglobin molecule. The reaction between oxygen and haemoglobin to form oxy-haemoglobin is reversible.

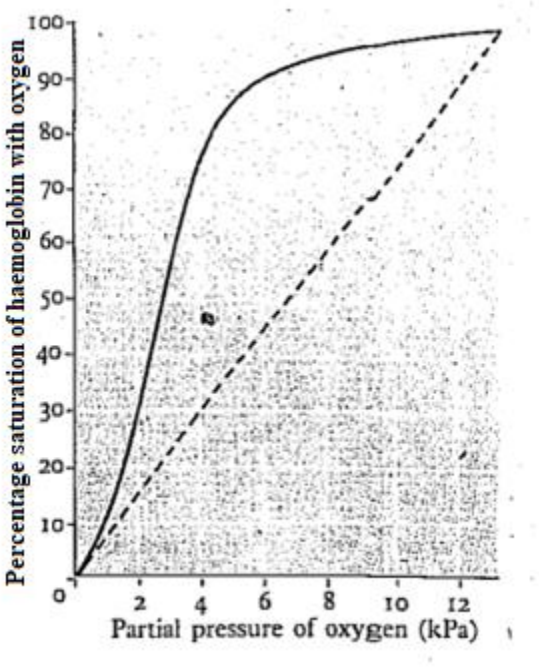
Haemoglobin combines with oxygen where it is at a higher concentration like in the lungs. When the oxygen concentration is low as in the capillaries of metabolically active tissues, the bonds holding oxygen to haemoglobin becomes unstable and oxygen is released which diffuses into the surrounding cells to be used in aerobic respiration.

**Note:** Release of oxygen from the haemoglobin is called **dissociation.** The amount of oxygen that combines with haemoglobin is determined by the **oxygen partial pressure** (partial pressure is used instead of concentration when referring to gases). The more the oxygen in air, the greater the partial pressure. Oxygen partial pressure also called **oxygen tension.**

## Oxygen dissociation curves

These show the relationship between the percentage saturation of haemoglobin with oxygen and the partial pressure of oxygen (oxygen tension).
Oxygen dissociation curve is obtained by plotting the percentage saturation of haemoglobin with oxygen against the partial pressure of oxygen. It illustrates the affinity of haemoglobin for oxygen at different partial pressures.

**Oxygen dissociation curve for an adult human haemoglobin**




The following should be noted from the above dissociation curve:
A sigmoid (S-shaped curve) is obtained which indicates that haemoglobin becomes fully saturated at relatively lower partial pressure of oxygen hence indicating the high affinity of haemoglobin for oxygen. The flat part indicates the loading of oxygen in the lungs where haemoglobin becomes 95% saturated (never 100% at normal conditions). The oxy-haemoglobin is then taken to respiring tissues.
The steeper part of the curve corresponds to the oxygen partial pressures found in the tissues. Oxygen dissociation curve facilitates unloading in the tissues. This is because over this part of the curve, if the partial pressure of oxygen falls as a result of the tissues utilizing oxygen, the haemoglobin responds by giving up oxygen faster which is made available to tissues (i.e. a drop in oxygen partial pressure causes a large fall in percentage saturation of blood).

In summary haemoglobin has a high affinity for oxygen where oxygen tension is high (in lungs) but a low affinity for oxygen where oxygen tension is low (as in respiring tissues). This property makes haemoglobin an efficient respiratory pigment.

**Why oxygen dissociation curve is S-shaped?**

At low oxygen partial pressures, the percentage saturation of haemoglobin with oxygen increases gradually. This is because the haemoglobin binds the first oxygen molecule with difficulty since the polypeptide chains are tightly bound together making it difficult for an oxygen molecule to gain access to the iron atoms. The steep part of the curve is because as one molecule of oxygen becomes bound to one haem group, it distorts the polypeptide chains exposing the other haem groups. The binding of each successive oxygen molecule to a subunit of the haemoglobin molecule therefore causes a conformational change in the protein that makes the remaining subunits much more likely to bind oxygen. As a result, the subsequent three molecules of oxygen are taken up more progressively quickly. The haemoglobin therefore takes up oxygen more readily and easily when it already has one or more oxygen molecules and releases oxygen readily if it has released one or more oxygen molecules. At very high partial pressure of oxygen, the haemoglobin molecules become saturated and the curve levels off.

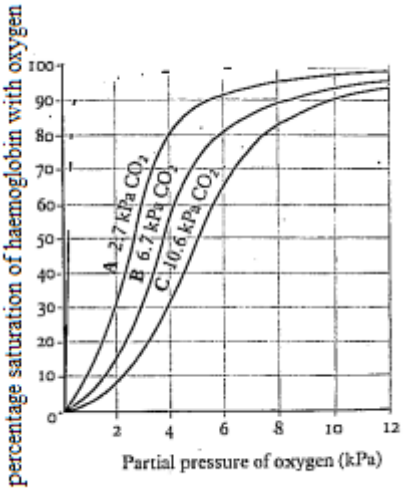
**Factors affecting oxygen dissociation curves**

The are some differences in the oxygen dissociation curves at different conditions. Before explaining the significance of these differences, it should be noted:

(i) The more the oxygen dissociation curve is shifted to the right, the less readily it picks up oxygen (low oxygen affinity) but the more easily it releases it.

(ii) The more the dissociation curve of a particular pigment is displaced to the left, the readily it picks up oxygen i.e. has a higher affinity for oxygen but the less readily it releases it

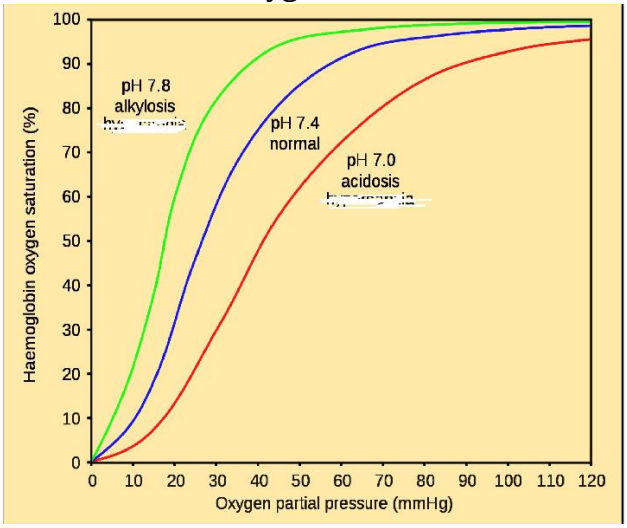
**Effects of carbon dioxide oxygen dissociation curve**




Increasing the partial pressure of carbon dioxide shifts the oxygen dissociation curve to the right. This is called the **Bohr effect** (after the man who first discovered it). Therefore, carbon dioxide makes the haemoglobin slow at taking up oxygen but more efficient at releasing it. The **physiological significance** of this is that carbon dioxide is a product of respiration and oxygen is required for this process. The release of oxygen therefore by haemoglobin is favoured in tissues where it is most needed for respiration since the partial pressures of carbon dioxide tends to be higher due to continuous release from the respiring tissues; and in the lungs where the partial pressure of carbon dioxide tends to be low owing to its continued escape to the atmosphere, uptake of oxygen is favoured.

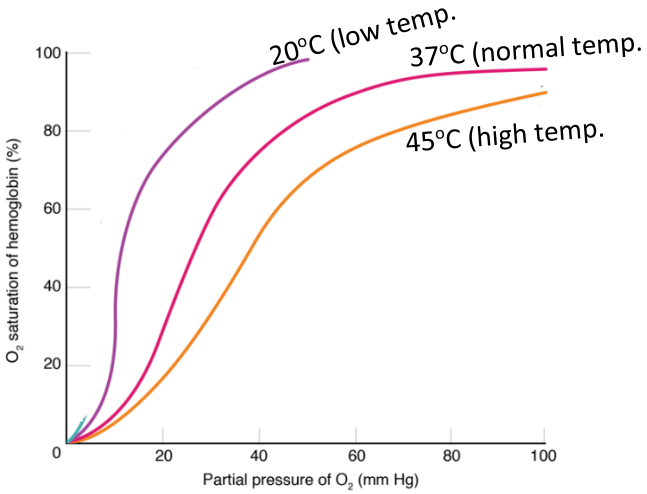
**Note:** Carbon dioxide has this effect because when it dissolves in tissue fluid, it forms a weak, carbonic acid which dissociates to form $H^+$ ions. The hydrogen ions released combines with haemoglobin to form haemoglobinic acid and makes it less able to carry oxygen.

**Effects of PH on oxygen dissociation curve**



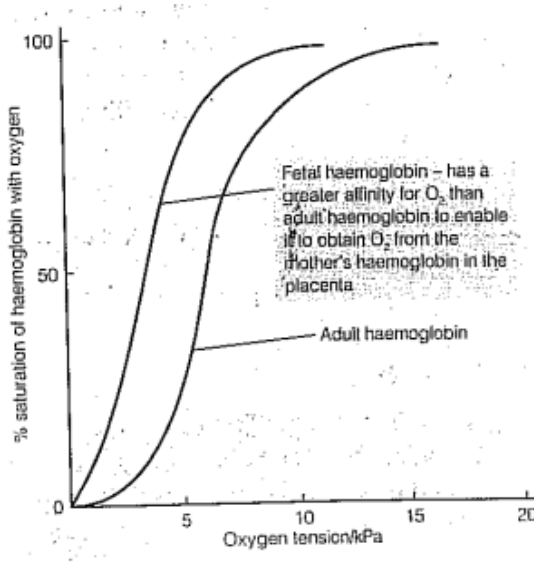

As the PH decreases (more acidity), the oxygen dissociation curve shifts down wards and to the right (Explain why). This implies that decrease in PH has the effect of reducing haemoglobin from taking up oxygen but more efficiently at releasing it. In tissues where oxygen is needed have low PH, this stimulates increased dissociation of oxy-haemoglobin to release oxygen and less uptake of oxygen by haemoglobin.

**Effects of temperature on oxygen dissociation curve**



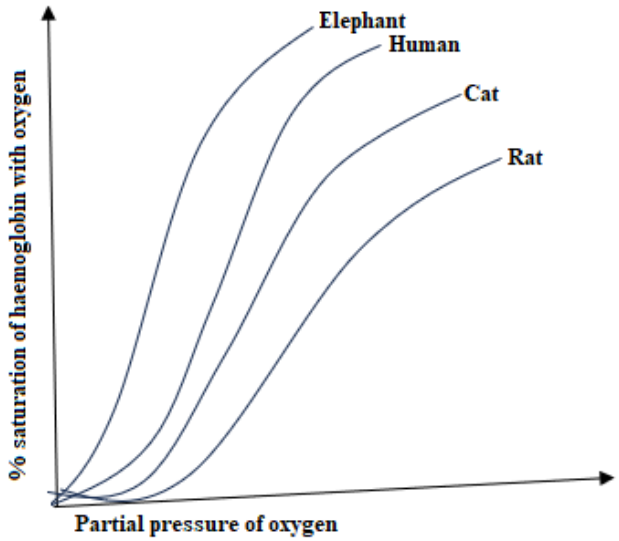

Increase in temperature shifts the oxygen dissociation curve to the right (why?). Increases metabolic activity increases the temperature in a part of the body system. This produces a reduction in the affinity of haemoglobin for oxygen and an increased dissociation of oxy-haemoglobin shifting the dissociation curve to the right. This is physiologically advantageous as more oxygen is released to active regions.

**Comparison of oxygen dissociation curves of adults and foetal haemoglobin**



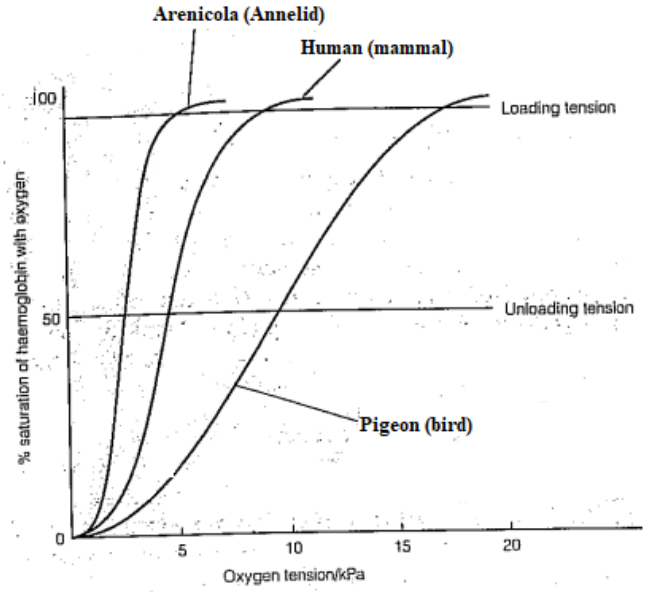

The haemoglobin of the foetus (foetal haemoglobin) has an oxygen dissociation curve shifted to the left of that of the adult haemoglobin. This means that its blood has a higher affinity for oxygen than the maternal blood. This has to be so as the foetus must obtain all of its oxygen from the mother's blood and the placenta. So, at any given partial pressure of oxygen, the foetal blood will take up oxygen from the maternal blood and will always be more saturated with oxygen than the maternal blood.

**Comparisons of oxygen dissociation curves of haemoglobin of mammals of different sizes**




The smaller the organism, the more its dissociation curve is shifted to the right. Smaller organisms have a large surface area to volume ratio and therefore lose heat to the surrounding more quickly. They have a higher metabolic rate to generate enough heat for maintenance of a constant body temperature. Therefore, their haemoglobin has a lower affinity for oxygen but easily releases it to the tissues to be used for increased metabolism to produce heat as compared to larger organisms like elephants which have smaller surface area to volume ratio, less heat is lost to the surrounding and hence having low metabolic rate.

**Oxygen dissociations curves for organisms living in different environments**




The Arenicola has oxygen dissociation curve displaced to the left of human. This means that it has a higher affinity for oxygen but less readily releases it. Arenicola lives in muddy water-logged humus where oxygen partial pressure is very low and has a low metabolic rate. The loading tension of the haemoglobin of Arenicola is at or about the partial pressure of oxygen in sea water, however this animal is able to retain the oxygen available and deliver it to the respiring cells.

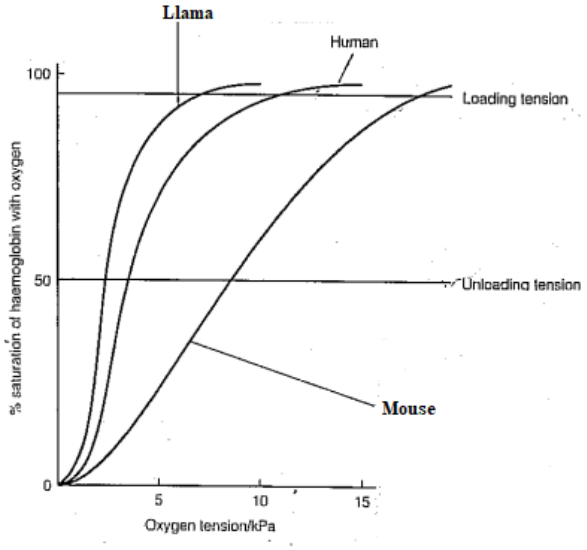
In comparison, pigeon has oxygen dissociation curve to right of that of the human. This means it has a low affinity for oxygen but readily releases it. The pigeon has high loading tension and high unloading tension. Pigeons have access to the 21% oxygen in air and have additional advantage of continuous ventilation of their lungs hence having high loading tension. Birds (pigeons) have a very high metabolic rate which requires more oxygen to be delivered to the respiring tissues. Therefore, pigeons have high unloading tension to ensure that oxygen is readily availed to the respiring tissues.

**Note:**

Loading tension-this is the oxygen partial pressure or oxygen tension at which 95% of haemoglobin is oxygenated.

Unloading tension-this is the oxygen partial pressure at which 50% of the haemoglobin release its oxygen.

**Question:**
The figure below shows oxygen dissociation curve for llama, human and mouse.




Explain why the curve of

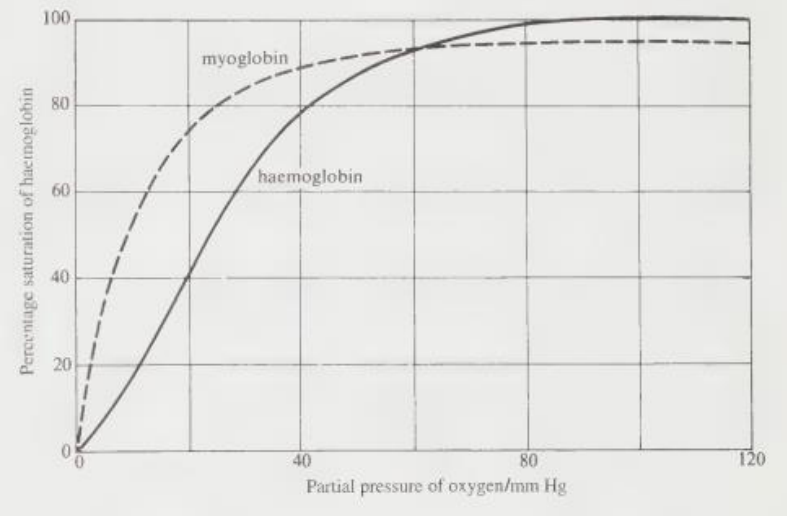
(i) llama is to the left of that of the human

(ii) the mouse is to the right of the that of the human

**Myoglobin**

Myoglobin is a red pigment with only one polypeptide chain and one haem group. It has a higher affinity for oxygen than haemoglobin and its oxygen dissociation curve is to the left of that of the haemoglobin.

*Comparison of haemoglobin and myoglobin oxygen dissociation curves*




Myoglobin remains fully saturated with oxygen at partial pressures below that required for haemoglobin to give up its oxygen. In this, it acts as a store for oxygen in resting muscles and only releases the oxygen when supplies of haemoglobin have been exhausted as in severe muscle exertion. When the exercise stops, the myoglobin store is replenished from the haemoglobin in blood.

Myoglobin is abundant in active animals which are liable to suffer oxygen shortages e.g. in diving mammals and the flight muscles of birds but less active ones like poultry (non-flying) lack myoglobin since they are relatively inactive and no need of oxygen storing pigment. This is why their breast meat appear white.

**Note:** The polypeptide chain of myoglobin is very similar to one of the polypeptide chains of haemoglobin.

**Carbon monoxide and haemoglobin**

Haemoglobin has a higher affinity for carbon monoxide than oxygen. Haemoglobin combines with the available carbon monoxide in preference to oxygen to form a relatively stable compound called carboxy-haemoglobin. This prevents oxygen from combining with haemoglobin making its transport impossible in the body. This makes carbon monoxide powerful respiring poison.

**Effect of altitude on the oxygen carrying capacity of blood**

**Living at high altitude**

At high altitude, there is reduced oxygen partial pressure which makes the loading of haemoglobin more difficult. This results into a lowered saturation of haemoglobin with oxygen. Humans inhabiting these places have become acclimatized in the following ways.

(i) Adjustment of blood PH; the reduced loading of haemoglobin leads to deeper breathing to compensate for lack of oxygen in blood which leads to excessive removal of carbon dioxide raising the blood PH. In acclimatized individuals, the hydrogen carbonate ions are removed by the kidneys restoring pH to norm.

(ii) More oxygen is absorbed by the lungs-this is as a result of improved capillary network in the lungs and deeper breathing.

(iii) Improved transport of oxygen to the tissues-this is as a result of increased red blood cells and haemoglobin concentration in red blood cells.

(iv) Increased affinity of haemoglobin for oxygen e.g. the loading tension of llama is much lower than that of low land. Therefore, it has a higher affinity for oxygen.

(v) Increased myoglobin levels in the muscles-these have a high affinity for oxygen and this facilitates the exchange of oxygen between blood and tissues.

**Diving mammals**

These are air breathing mammals which can endure long periods where there is limited oxygen supply i.e. seals, whales and dolphins.

**Adaptations of circulatory system in diving mammals**

(i) The blood makes greater portion of the body

(ii) There is increased concentration of red blood cells; maximising oxygen carriage capacity

(iii) There is high concentration of haemoglobin in the red blood cells.

(iv) During diving, heart beat is slowed down automatically with blood pressure maintained by constriction of arteries.

(v) Blood is distributed to vital organs during the dive by constriction of the veins that drain the less important organs like the kidney.

(vi) There is a high concentration of myoglobin in muscles, an additional oxygen store.

(vii) There is increased tolerance to high concentration of lactic acid in the muscle tissue due to reduced sensitivity to low PH.

**Transport of carbon dioxide**

Carbon dioxide is carried in blood in three different ways;

1. **In solution**-a very small quantity of about 5% of carbon dioxide is carried in solution in blood plasma.
2. **Combined with haemoglobin**-about (15-20) % of carbon dioxide combines with the amino groups of each polypeptide chain of haemoglobin to form carbamino-haemoglobin compound.

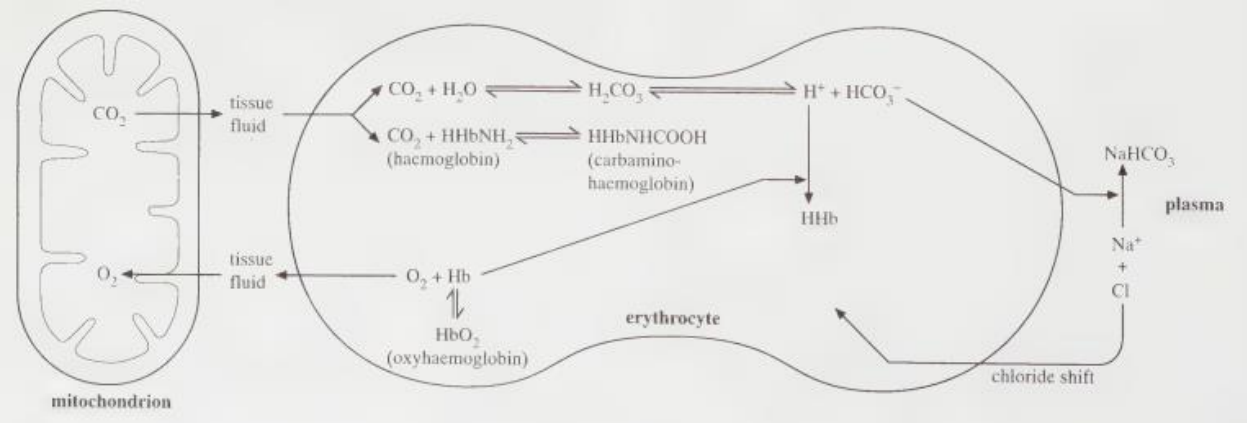
   **Note:** The amount of carbon dioxide that is able to combine with haemoglobin depends on the amount of oxygen carried by the haemoglobin. The less the oxygen carried by haemoglobin molecule, the more carbon dioxide that can be carried this way.
3. **As hydrogen carbonate ions (85%)-**The majority of carbon dioxide (about 85%) is transported in this form. Carbon dioxide produced by tissue respiration diffuse into the blood stream and enters red blood cells where it combines with water to form carbonic acid. This process is catalysed by an enzyme called **carbonic anhydrase.** Some of the carbonic acid dissociates into hydrogen ions and hydrogen carbonate ions

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

   The hydrogen ions combine with haemoglobin which loses its oxygen to form **haemoglobinic acid.** By accepting the hydrogen ions, the haemoglobin acts as a buffer enabling large quantities of carbonic acid to be transferred to the lungs without affecting blood PH.

   The hydrogen carbonate ions diffuse out of the red blood cells into plasma along the concentration gradient and combines with sodium ions from the dissociation of sodium chloride in the plasma to form **sodium hydrogen carbonate**. The sodium hydrogen carbonate is transferred to the respiratory surface (alveoli in the lungs) in plasma where the process is reversed releasing carbon dioxide which diffuses out of the body. The red blood cells become more positively charged due to loss of negatively charged hydrogen carbonate. This is balanced by chloride ions diffusing into the red blood cells from the plasma as a result of the dissociation of sodium chloride. This phenomenon is called **chloride shift.**

   (*Illustration BS 482 fig. 14.33; check also FA pg 166 fig. 11.6; UB pg 419)*




**Note:** $O_2$ released when $H^+$ ions combine with haemoglobin diffuses out of the red blood cell, through capillary wall and tissue fluid into respiring tissue cell.