Bio Factsheet

Oxygen Dissociation Curves

This Factsheet summarises:
>   1. **The mechanisms of oxygen and carbon dioxide transport in blood**
>   2. **The interactions between the mechanisms of oxygen and carbon dioxide transport and blood pH control.**
>   3. **The effects of factors such as temperature, pH, birth, body size and disease on oxygen dissociation curves.**

Examination questions on this topic usually test recall and understanding by providing data for comment and analysis. A detailed knowledge of haemoglobin structure is not required.

Transport of Oxygen

The respiratory pigment **haemoglobin** enables the blood to carry enough oxygen for the body's needs. The solubility of oxygen in the water of the plasma is low and decreases even further as the temperature rises. Thus the quantity of oxygen that could be carried by the plasma alone is not enough. The extra carriage of oxygen depends on the fact that one molecule of haemoglobin can **onload** four molecules of oxygen, one on each of the four haem groups of the pigment.

Inhaled alveolar air has an oxygen tension around 14kPa (kilopascals) whereas the oxygen tension in the blood supplying the lungs is between 2.7 and 5.3kPa. (This range depends on the oxygen tension of the tissues the blood has just left; 5.3kPa is the tension for resting tissues which are using little oxygen and 2.7kPa is for active tissues which are using much oxygen). Thus, there is a diffusion gradient across the alveolar surface (e.g. 14kPa - 5.3kPa = 8.7kPa) and so oxygen will diffuse from the alveolar surface into the blood and into the red blood cells. Once inside the red blood cells the oxygen is **onloaded** onto the haemoglobin until it is about 96% saturated. It is now called **oxyhaemoglobin**. The equation for this association of oxygen with haemoglobin is:
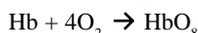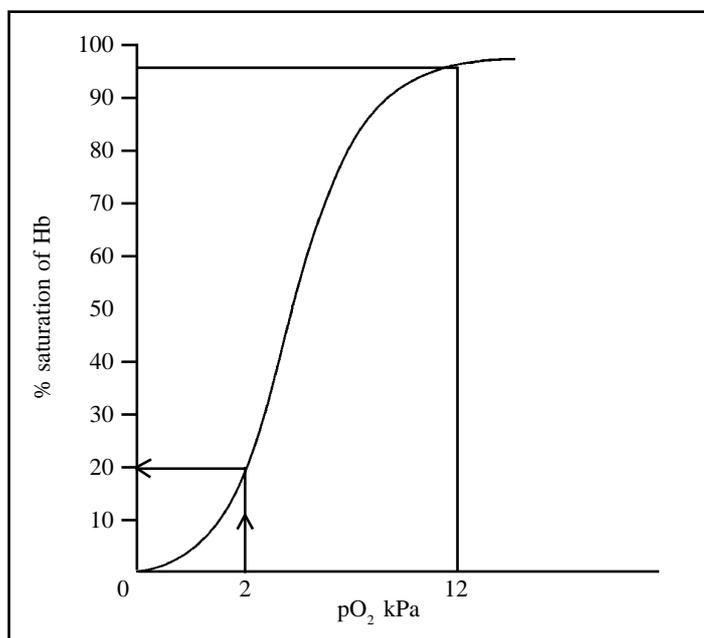
$$Hb + 4O_2 \rightarrow HbO_8$$

Fig 1. shows the percentage saturation of haemoglobin as it passes through areas of the body which have very different partial pressures of oxygen. At 2kPa of oxygen - i.e. at the very low partial pressures of oxygen which we would expect in actively respiring muscles, the percentage saturation of haemoglobin is very low (it is only 20% saturated; the other 76% has been released to the muscles through which the blood is flowing).

At 12kPa - i.e. at the very high partial pressures of oxygen found in the lungs - the haemoglobin is 96% saturated.

So, imagine a red blood cell in a capillary. As it passes through capillaries in the lungs, where the partial pressure of oxygen is very high (12-14kPa) it will **onload** oxygen i.e. pick up 8 oxygen atoms and become 96% saturated. The red blood cell then goes to the heart from where it is pumped out to the left leg of a marathon runner. The muscle is working hard i.e. respiring and using up a lot of oxygen. The partial pressure of oxygen in the muscle tissues is therefore very low (eg. 2kPa). As the red blood cell enters the capillaries within the muscle it finds itself in a region of very low partial pressures of oxygen and the haemoglobin therefore loses 76% of its oxygen. In other words, it releases 76% to the muscles and ends up only 20% saturated (see Fig 1). The muscle cells will use this oxygen to maintain aerobic respiration which thus provides a good supply of ATP so that it can carry on contracting and so that the athlete can carry on running (see Factsheet 12: Respiration).

Why is the oxygen dissociation curve (ODC) S shaped ?

Each haemoglobin molecule can combine with a total of 4 O_2 molecules (one O_2 molecule for each of the haem groups).

1. The first O_2 molecule combines relatively slowly with the first haem group. Thus, the first part of the ODC is not very steep. However, the binding of oxygen with the first haem group causes the shape of the whole haemoglobin molecule to change.

2. As a result of its altered shape, it is much easier for the second and third O_2 molecules to bind to their haem groups. Thus, the ODC becomes much steeper.

3. The curve flattens off because it then becomes harder for the fourth (i.e. the last) oxygen molecule to combine with the fourth haem group.

Exam Hint - Candidates frequently confuse oxygen pressure with blood pressure. Oxygen pressure, oxygen partial pressure and oxygen tension can be regarded as essentially the same thing - they are simply a measure of the concentration of oxygen in the blood.

Exam Hint - This is a favourite synoptic topic because it links molecular biology, biochemistry, physiology and adaptation.

**Fig 1. Oxygen dissociation curve for haemoglobin**

The effect of pH

The quantity of oxygen carried by haemoglobin depends on pH as well as on oxygen tension. In a more acidic environment oxygen dissociates from the haemoglobin more readily, whereas in a more alkaline environment association of oxygen with haemoglobin is favoured, forming more oxyhaemoglobin. This results in the **Bohr effect** which is illustrated in Figure 2.

For example, imagine the blood is flowing through capillaries where the surrounding tissues have an oxygen tension of 4 kPa:

At pH7.6 the Hb would be 74% saturated
But at pH 7.4 the Hb would be 59% saturated

In other words, as pH decreases (becomes more acidic) the haemoglobin has become less saturated - it has given some of its oxygen to the tissues.

At pH7.2 (even more acidic conditions) the haemoglobin is only 36% saturated i.e. it has released even more oxygen to the tissues. So as a general rule, as pH decreases (as conditions become more acidic) haemoglobin becomes less saturated and gives up more oxygen. Acidity can be defined as the concentration of hydrogen ions. Hydrogen ions can reduce haemoglobin by attaching to the same sites as oxygen atoms and thus they compete with oxygen for these sites. In an acidic environment the higher concentration of hydrogen ions displaces oxygen from haemoglobin and thus improves oxygen release into the tissues.

$$HbO_2 \quad + \quad H^+ \rightarrow HHb \quad + \quad O_2$$

oxyhaemoglobin   reduced haemoglobin
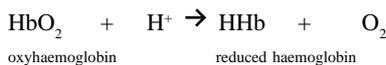
This is perfect because respiring tissues are acidic as a result of the carbon dioxide and/or lactic acid produced in respiration. Carbon dioxide dissolves to form carbonic acid and this stimulates the release of oxygen from haemoglobin, thus allowing the tissues to keep respiring aerobically.

The environment in the alveoli is less acidic (due to the lowering of carbon dioxide tension) and thus oxygen atoms predominate and tend to displace the hydrogen from the haemoglobin. This enhances the uptake of oxygen.

In this way the haemoglobin is acting as a **buffer**, limiting the range of blood pH between 7.2 and 7.6. This is an example of homeostasis, in this case keeping the blood pH within optimum range.

From Figure 2 it can be seen that: As pH decreases, the ODC moves to the right. This is called the **Bohr Effect**.

Figure 2. The effect of pH on the ODC (The Bohr Effect)
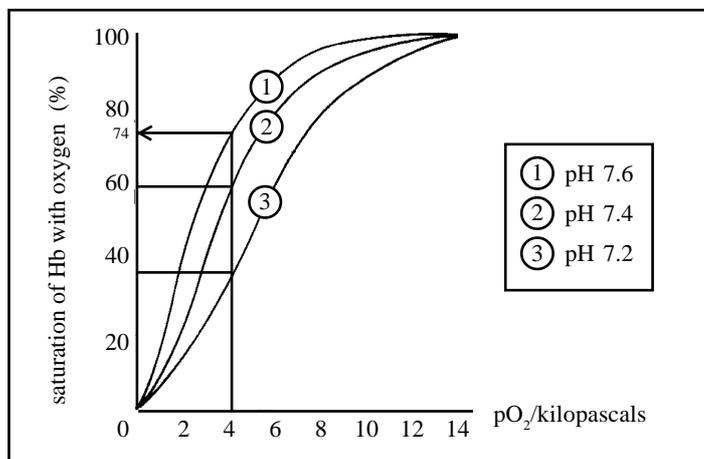
Transport of carbon dioxide

Carbon dioxide is released by respiring cells and diffuses into the blood plasma. About 5% of it dissolves directly and is carried in solution. The rest diffuses into the red blood cells where about 25% of it attaches onto the amino acid side chains of the protein globin in haemoglobin, forming **carbaminohaemoglobin**. (This is still able to carry oxygen or hydrogen on its haem groups.) The remaining 70% of the carbon dioxide enters red blood cells and is converted by the enzyme **carbonic anhydrase** to carbonic acid. This dissociates at once to form hydrogen ions and hydrogen carbonate ions.

$$CO_2 \; + H_2O \quad \rightarrow \quad H_2CO_3 \rightarrow \; H^+ + HCO_3^-$$

carbonic   carbonic
anhydrase   acid
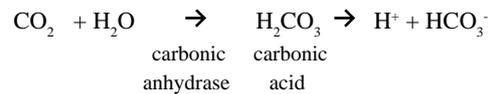
The hydrogen ions would decrease the pH of the blood if they remained free but they attach to the haem groups, displacing the oxygen into the tissues whilst limiting the pH change to pH 7.2. The hydrogencarbonate ions diffuse out of the red cells into the plasma, thus leaving a shortage of negative ions in the red cells. To compensate for this, chloride ions (Cl^-) move from the plasma into the red cells to restore the electrical balance. This is known as the **chloride shift**.

In the alveolar capillaries the equilibria of these reactions is altered. Carbaminohaemoglobin releases its carbon dioxide into the alveoli and the higher oxygen tension dislodges the hydrogen ions from the haem groups. Hydrogen ions react more easily with hydrogencarbonate ions than with chloride ions and so hydrogencarbonate ions diffuse back into the red cell from the plasma in exchange for chloride ions. Carbonic acid then reforms and at once dissociates under the influence of carbonic anhydrase to give water and carbon dioxide. This diffuses along the concentration gradient into the alveolar air and is expired. The blood pH rises no further than pH 7.6.

The effects of other factors on blood gas transport

1. Carbon monoxide tension. This gas is released from car exhausts and from inadequately ventilated gas fires. It competes with oxygen for the haem groups of haemoglobin with which it binds irreversibly, causing death. Haemoglobin in combination with carbon monoxide is called **carboxyhaemoglobin**.

2. Birth. Although a foetus has lungs, it does not use them until the moment of birth. Fetal haemoglobin takes oxygen from mother's haemoglobin across the placenta. Thus fetal haemoglobin must **onload** oxygen at the oxygen tension at which maternal haemoglobin is offloading it. Thus fetal haemoglobin has a greater affinity for oxygen than adult haemoglobin. This can be seen in Figure 3.

Fig 3. ODCs of maternal and fetal haemoglobin
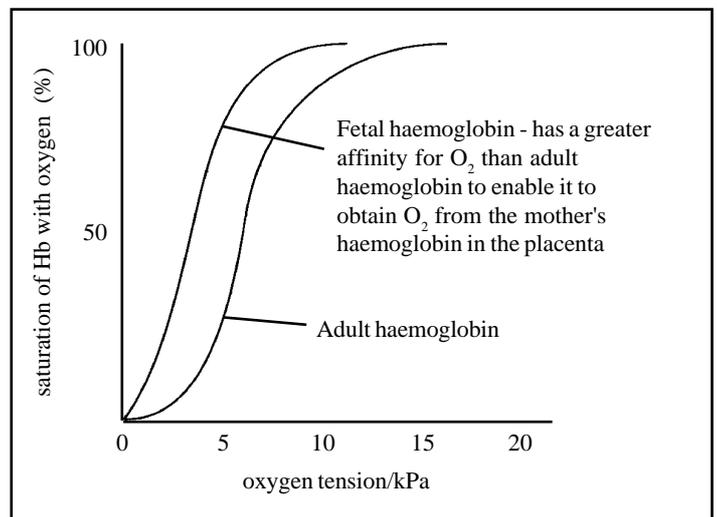
3. Temperature. As temperature increases, less oxygen combines with haemoglobin and the dissociation curve shifts to the right. This can be seen in Fig 4. In other words, as temperature rises, more oxygen is released from haemoglobin. Again, this is exactly what is needed. Heat energy is a product of metabolism. Active tissues such as contracting muscle fibres require large quantities of oxygen, and because of their activity release more acid and heat. These in turn stimulate the haemoglobin to release more oxygen.

Fig 4. The effect of temperature on the oxygen dissociation curves
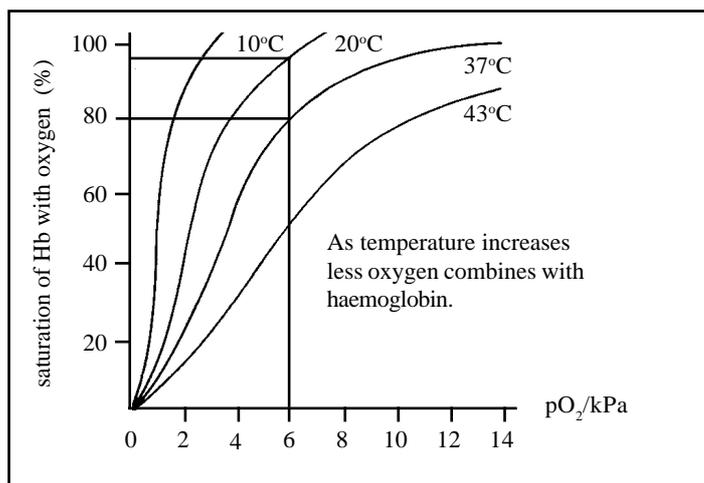
For example, in tissues which have $pO_2 = 6kPa$:

At 20°C the Hb would be 97% saturated

At 37°C the Hb would be 80% saturated

The difference - 17% - has been released to the respiring tissues. Clearly, the temperature of mammalian blood does not fluctuate between 20°C and 30°C but this does illustrate the general principle.

Fig 5. Oxygen dissociation curves for haemoglobin and myoglobin
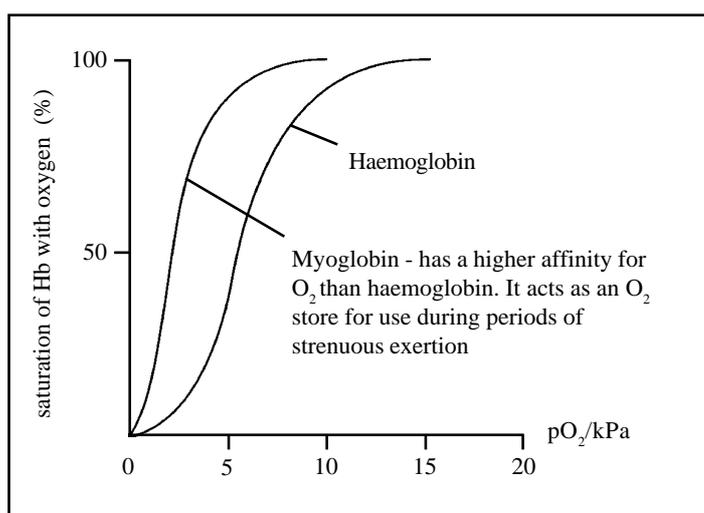
Skeletal muscle also contains its own respiratory pigment, **myoglobin**. This has similar structure and function to haemoglobin and will hold and store oxygen in the muscle until required. Its oxygen dissociation curve lies to the left of that for haemoglobin so that it can onload oxygen at tensions where haemoglobin is releasing it (Fig 5). Myoglobin will only release oxygen at very low partial pressures of oxygen - in other words, it acts as an **oxygen store**.

4. Disease. This may cause elevation in the body temperature and thus increase oxygen release to tissues (Fig 4). Anaemia will reduce the quantity of red blood cells and haemoglobin available to transport oxygen. Haemoglobin which is present in sickle cell anaemia has greatly reduced ability to transport oxygen.

5. Ecological factors. Animals which live in permanently reduced oxygen tensions tend to have haemoglobins which will pick up oxygen more readily at such tensions than normal haemoglobin. Thus, the dissociation curves of organisms such as mammalian parasites or mud dwelling worms usually lie to the **left** of the normal curve.

6. Body size. Small animals tend to have higher metabolic rates than large animals and thus their tissues require larger quantities of oxygen. Thus their dissociation curves will lie to the **left** of the normal curve, thus enhancing oxygen uptake and release. Their haemoglobins should however be equally effective at onloading oxygen.

Practice Questions

1. The graph shows the effect of different partial pressures of carbon dioxide on the oxygen dissociation curves.
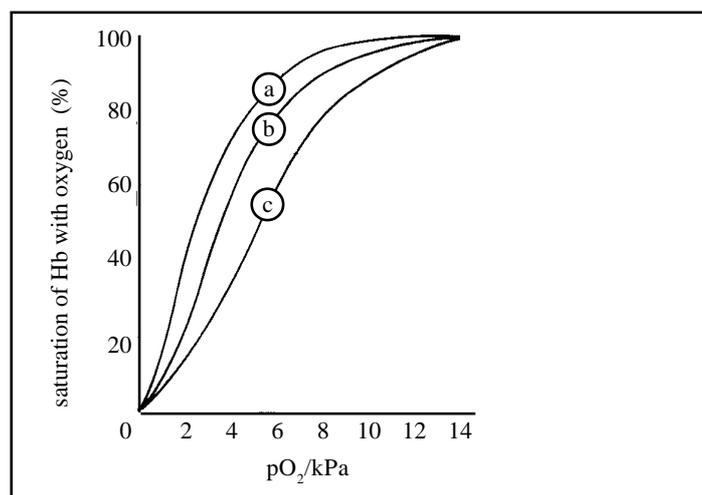
(a) Which of the curves a, b or c represents the greatest carbon dioxide concentration? (1 mark)

(b) What name is given to the effect shown in the graph? (1 mark)

(c) Explain how this enables respiring tissues to effectively obtain oxygen. (3 marks)

(d) State one other factor which has a similar effect on the oxygen dissociation curve. (1 mark)

Answers

1.

(a) c;

(b) Bohr effect;

(c) Respiring tissues release CO_2;

As CO_2 increases saturation of Hb decreases;

This provides respiring tissues with O_2;

Allowing aerobic respiration to continue; *(any three)*

(d) Temperature;