Bio Factsheet

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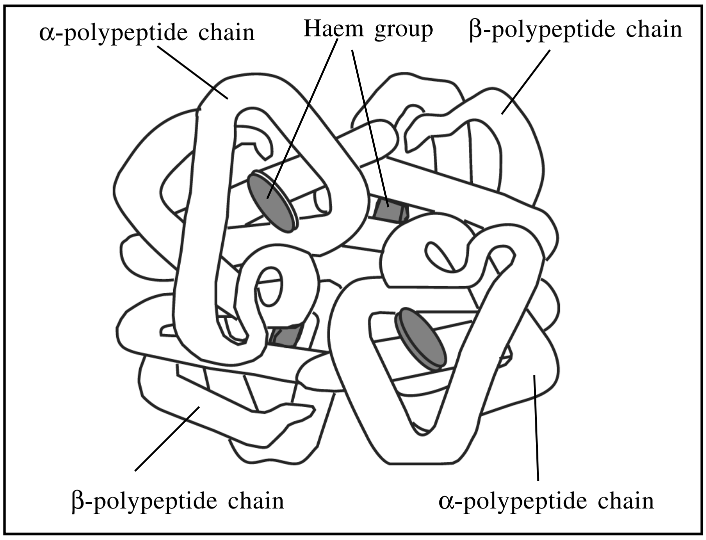
# Haemoglobin: Structure & Function

Haemoglobin is the oxygen – carrying pigment in red blood cells. It is a globular protein consisting of four tightly packed polypeptide chains.

There are two identical alpha chains and two identical beta chains (Fig 1).

**Fig 1. Molecule of human haemoglobin.**




- The hydrophobic parts of the chains point inwards towards the centre of the molecule and interactions between these hydrophobic parts help to maintain the 3-D shape
- The hydrophilic parts point outwards and help maintain haemoglobin's solubility
- Each polypeptide chain contains an iron-containing haem group
- Each haem group can bind with one oxygen molecule, so each molecule of haemoglobin can carry 4 oxygen molecules at a time.
- The aggregation of several (4) polypeptide chains gives haemoglobin a **quaternary structure**.

**Typical Exam Questions**

Q1. Use Fig 1 to explain why the haemoglobin molecule has a quaternary structure.

*Answer: It is made of several/ four polypeptides; Note it has nothing to do with the fourth dimension of protein structure*

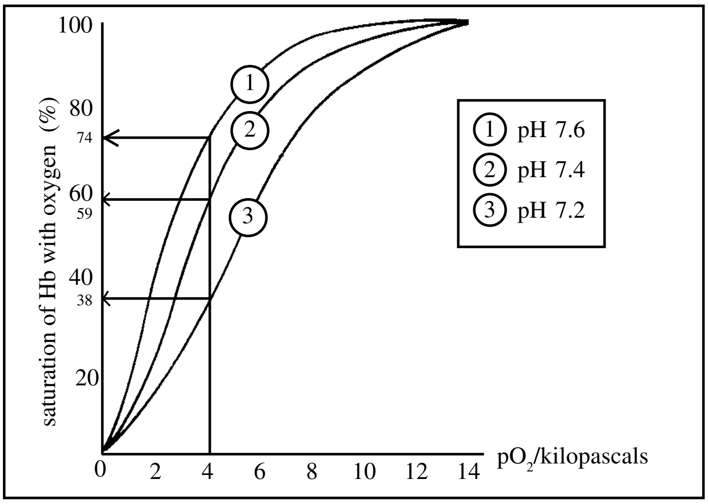
Q2. Why do all human haemoglobin molecules always have identical tertiary structure?

*Answer: Because they contain an identical sequence of amino acids and thus the bonds always occur in the same positions*

By far the most common exam question concerns how haemoglobin picks up oxygen in the lungs and offloads it at the respiring tissues. To get good marks, precision is vital. Here are the key facts to learn.

1. Oxygen diffuses across the alveoli into the haemoglobin in red cells
2. Haemoglobin has a high affinity for oxygen **in the high oxygen concentration that exist there**
   The point is that haemoglobin **doesn't have a high affinity no matter what the oxygen concentration is**! If it did, it would never let go of the oxygen!
3. Oxygen atoms combine with the haem groups of the haemoglobin. The addition of one oxygen molecule to the first haem group distorts the shape of the haemoglobin molecule, making it easier for the second oxygen molecule to combine with haem. This, in turn, makes it easier for the third oxygen molecule to combine with a third haem group. It then becomes a little harder for the fourth oxygen molecule to join the fourth haem group. This trend explains the sigmoid shape of the oxygen dissociation curve.
4. Oxyhaemoglobin is formed;
5. Haemoglobin unloads / has a low affinity for oxygen in areas eg the respiring tissues, where oxygen is in low concentration;
6. This is a consequence of its dissociation curve i.e. small changes in concentration gives large changes in saturation;
7. Respiration in tissues gives high $CO_2$ concentration, high temperature and high $H^+$ concentration
9. Under these conditions the dissociation curve shifts to the right (Fig 2)

**Fig 2. The effect of pH on the ODC (The Bohr Effect)**




At a $ppO_2$ of 4 kilopascals, how saturated is the haemoglobin at:
pH 7.6 ?…………………answer = 74%
pH 7.4 ?…………………answer = 59%
pH 7.2 ?…………………answer = 38%

You can see that the curve has moved to the right
As the tissues get more acidic, haemoglobin releases more oxygen (becomes less saturated). Increasing temperature and increasing $CO_2$ concentrations have just the same effect.

These are the conditions in the respiring tissues (high temperatures and $CO_2$ from respiration, high $H^+$ concentrations from dissociation of bicarbonate ions or production of lactic acid.

**Extract Chief Examiner's Report**

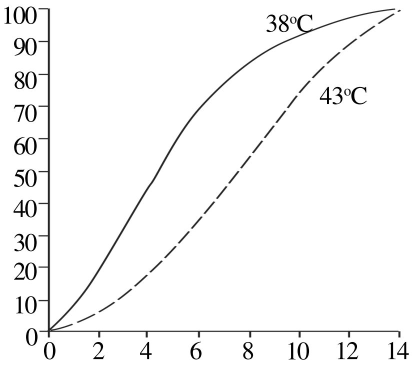
Many candidates had a poor understanding of the processes involved in the transport of oxygen by haemoglobin and the dissociation curve. It was often stated that haemoglobin has ' a high affinity for oxygen', but rarely was the answer qualified by explaining that it has a high affinity at higher partial pressures, while oxyhaemoglobin readily dissociates at lower ones. Only a small minority linked their explanation to the dissociation curve.

A significant minority confused haemoglobin with red cells, and referred to oxygen being transported in the 'dip' in the haemoglobin.

The commonest problem was the use of inappropriate terminology. For example, descriptions of the haemoglobin 'picking up' or 'dropping off' oxygen were frequent. When describing the formation of oxyhaemoglobin, candidates frequently made statements such as 'haemoglobin joins with 4 oxygen molecules'.

Fig 3 shows the oxygen dissociation curve of haemoglobin from a mammal at two different temperatures, 38 ºC and 43 ºC.

**Fig 3.**




You can see that, at any particular partial pressure of oxygen, haemoglobin is less saturated at 43 ºC than at 38 ºC. that is, if the temperature increases, the haemoglobin releases more of its oxygen.

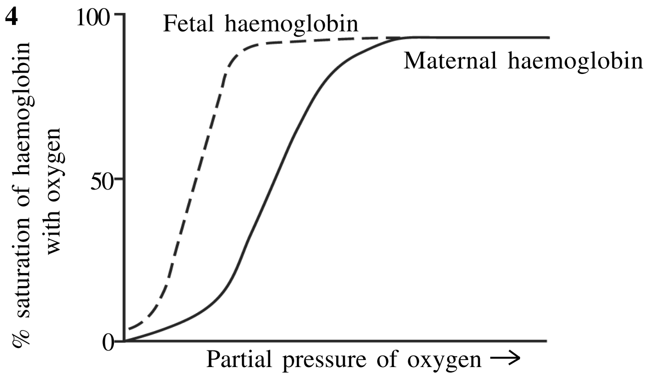
Blood that is fully (100%) saturated with oxygen carries 105 $cm^3$ of oxygen in 1 $dm^3$(litre) of blood. Imagine 1 $dm^3$ of blood that has become 90% saturated at 38 ºC. It now reaches a part of the body where intense respiration is occurring. Oxygen is being used up rapidly in respiration to release ATP. This metabolic activity has increased the temperature. The temperature is 43ºC and the partial pressure of oxygen is 4 kPa. At this temperature and pressure, haemoglobin will become 18% saturated (see Fig 3). The difference ( 90% -18% =72% and 72% of 105 = 75.6$cm^3$ will have been released to the respiring tissues.

### Mother and foetus

The foetus needs to get its oxygen from the mother's blood. Differences in maternal and foetal haemoglobin ensure that this happens.

Fig 4 shows the dissociation curves for fetal and maternal haemoglobin.

**Fig 4**




You can see that at low partial pressures of oxygen (as there are in the placenta), the foetal haemoglobin is much more saturated than the maternal haemoglobin. This is because fetal haemoglobin has a greater affinity for oxygen at low partial pressures of oxygen than adult haemoglobin.

At the low partial pressure of oxygen at the placenta the maternal oxyhaemoglobin dissociates and releases oxygen. The fetal circulation rapidly carries the oxygenated blood away. There is a higher partial pressure of oxygen in maternal blood than in fetal blood entering placenta and so the oxygen concentration gradient is maintained. It is the ability of the foetal haemoglobin to pick up oxygen at the partial pressures at which the maternal haemoglobin is dissociating that is crucial.

**Extract from Chief Examiner's report**

Many candidates explained that fetal haemoglobin has a high affinity for oxygen, but only the better candidates went on to explain that this means that fetal haemoglobin takes up oxygen when adult oxygen haemoglobin dissociates.

### Structure of foetal and maternal haemoglobin

Foetal red cells are nucleated and contain foetal haemoglobin, which is a conjugated protein with four haem prosthetic groups linked to two $\alpha$ and two $\gamma$ polypeptide chains. Thus their different affinities for oxygen have a structural basis. One difference between them is shown below.

Sequence of amino acids in part of adult haemoglobin
- Phe – Ala – Thr – Leu – Ser – Glu – Leu – His – Cys –

Sequence of amino acids in corresponding part of fetal haemoglobin
- Phe – Ala – Gln – Leu – Ser – Glu – Leu – His – Cys –

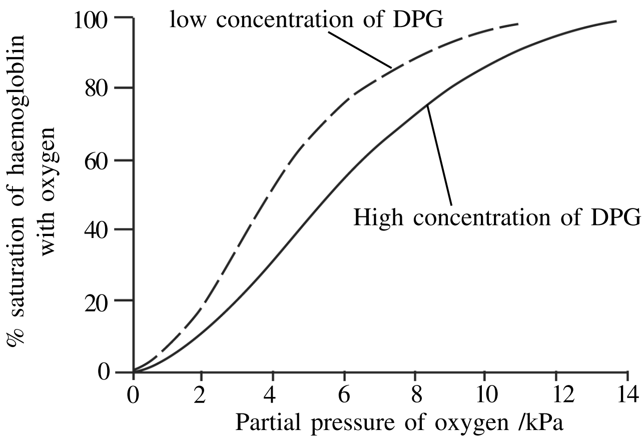
The difference in the sequence of amino acids results in different binding sites for oxygen and, in turn, different oxygen dissociation curves.

Another difference between the blood of the mother and the foetus is that foetal red cells are nucleated. As birth approaches, foetal haemoglobin genes are switched off, adult haemoglobin genes are
switched on and adult red cells containing adult haemoglobin are produced.

### Effect of altitude

Less oxygen is available at high altitudes. When humans live at high altitudes, the concentration of DPG (2,3-diphosphoglycerate, in their red blood cells increases. DPG is a substance which affects the dissociation curve. Fig 5 shows the effect of a high concentration of DPG on the dissociation

**Fig 5. Effect of DPG on dissociation curve**

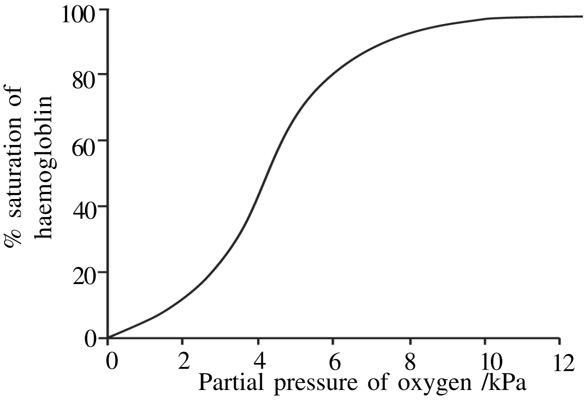



curve.

At low partial pressures of oxygen, eg 2kPa, the haemoglobin with high DPG in the red cells has released 7-8 % more oxygen than when there was a low DPG concentration. Once again the haemoglobin has releasedoxygen just when it is most needed.

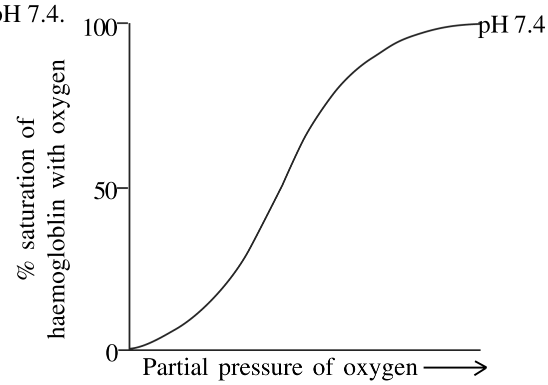
**Practice Questions**

1. The graph shows the dissociation curve for human oxyhaemoglobin.
Using the graph, explain how haemoglobin transports oxygen




from the lungs to respiring tissues. (5 marks)

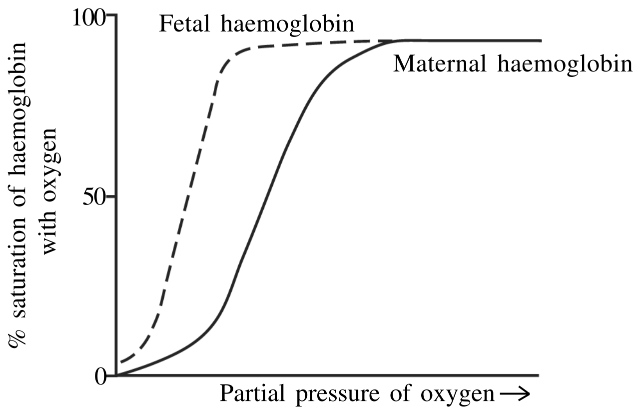
**2** The graph shows a dissociation curve for human haemoglobin at pH 7.4.




(a) (i) Sketch a curve on the graph to show the likely position of the dissociation curve at pH 7.2. *(1 mark)*
(ii) Suggest what might cause this change in pH (*3 marks*)

(iii) Explain how this change in pH affects the supply of oxygen by haemoglobin to respiring tissues. *(2 marks)*

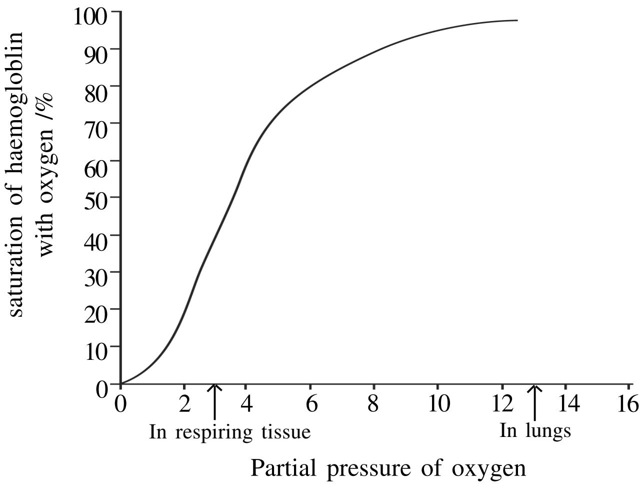
3. The graph shows the dissociation curves for fetal and maternal




haemoglobin
(a) Use the graph to explain how maternal haemoglobin can load oxygen in the lungs and unload oxygen in the placenta. (3 marks)

(b) How does fetal haemoglobin makes it possible for the fetus to obtain oxygen from the mother's blood ? (2 marks)

4. The graph shows the dissociation curve for adult human haemoglobin.




(a) Blood leaving the lungs is 98% saturated. 1 dm3 blood leaving the lungs carries 100 $cm^3$ oxygen. Use the graph to calculate the amount of oxygen that this volume of blood will unload to the respiring tissue. (2 marks)

(b) Outline the conditions in the tissues that stimulate oxyhaemoglobin to offload oxygen (3 marks)

**Answers**

1. Haemoglobin has high affinity for oxygen at high partial pressures in alveoli;
Becomes saturated;
Oxygen molecules bind to haem groups;
In tissues, oxygen partial pressure much lower;
Haemoglobin has low affinity in these conditions;
Oxygen offloaded;
Steep curve reflects large reduction in saturation for small drop in partial pressure;

2. (a) (i) curve to right of curve for pH 7.4; 1
(ii) aerobic respiration produces carbon dioxide;
carbon dioxide dissolves in blood;
forming acid;
increases hydrogen ion concentration;
(iii) more oxygen unloaded/given up / affinity decreased /reduced saturation;
oxyhaemoglobin dissociates at higher oxygen concentration/ partial pressure / more oxygen unloaded at the same $ppO_2$;

3 (a) High pp of oxygen in lungs, low pp in placenta;
High percentage of haemoglobin can bind / saturate with oxygen in lungs;
Low percentage of haemoglobin can bind / saturate with oxygen in placenta;
Dissociates in placenta;
(b) Fetal haemoglobin has a higher affinity for oxygen / eq.;
At low pps of oxygen;
Fetal haemoglobin can associate with oxygen at low partial pressures;
Maternal haemoglobin dissociates at low partial pressures

4. (a) Blood is 0.98 x = $100cm^3$ x = 100/0.98 = $102cm^3$;
Therefore 40% of $102cm^3$ = 40-41%;
(b) higher temperature;
greater $H^+$ concentration;

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