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**Hemoglobin and Structure**

Haemoglobin (also hemoglobin, or abbreviated Hb) is a [protein](https://teaching.ncl.ac.uk/bms/wiki/index.php/Proteins) which is used in red [blood](https://teaching.ncl.ac.uk/bms/wiki/index.php/Blood) cells to store and transport [oxygen](https://teaching.ncl.ac.uk/bms/wiki/index.php/Oxygen). It is found in many multi-cellular [organisms](https://teaching.ncl.ac.uk/bms/wiki/index.php/Organism) such as [mammals](https://teaching.ncl.ac.uk/bms/wiki/index.php/Mammals) where simple diffusion would be unable to supply adequate oxygen to tissue and cells**.**

\* **Hemoglobin** is a two-way respiratory carrier, transporting oxygen ( as oxyhemoglobin) from the lungs to the tissues and facilitating the return transport of carbone dioxide (as carbamino hemoglobin).

\*In the arterial circulation ,hemoglobin has a high affinity for oxygen and a low affinity for carbon dioxide, organic phosphates ,hydrogen and chloride ions.

\*Normal concentration of hemoglobin (male): 14-16 gm% and normal concentration of hemoglobin (female): 13 -15gm %.

\* Normal hemoglobin mean 97 %HbA+2% HbA2+1% HbF.

\*Glycated hemoglobin or HbA1C (α2 β2) is found ˃ 5% in diabtes mellitus patients .

\*It is composed of 4 globin chains and porphyrin ring with central iron.

\*Iron must be in ferrous state which can binds to oxygen and form oxyhemoglobin. Ferric state can't carry oxygen and its form methemoglobin.

\* hemoglobin comprises four subunits, each having one polypeptide chain and one heme group .Each subunit has a molecular weight of about 16,000 Daltons ,for a total molecular weight of the tetramer of about 64,000 Daltons .

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\*Hemoglobin, the red pigment in blood , consists of a protein component and the iron complex of a porphyrin derivative .

 **Hemoglobin = globin (protein ) + haemochromogen (F(II)complex).**

\*There are four heme group each attached to one globin chain .So, one Hb molecule can carry 4 oxygen molecules .

\*All hemoglobins carry the same prosthetic heme group iron protoporphyrin 1x(4 %) associated with globin ( 96 % ) made up of polypeptide chain of 141 ( alpha ) and (146 (beta ) amino acid residues .

\* The ferrous ion of the heme is linked to the imidazole N of two histidine residues of the polypeptide chain .

\* The porphyrin ring is wedged into its pocket by a phenylanine of its polypeptide chain .

 **Synthesis and levels in blood and in erythrocytes**

The two main components of hemoglobin synthesis are globin production and heme synthesis. Globin chain production occurs in the cytosol of erythrocytes and occurs by genetic transcription and translation. Many studies have shown that the presence of heme induces globin gene transcription. Genes for the alpha chain are on chromosome 16, and genes for the beta chain are on chromosome 11. Heme synthesis occurs in both the cytosol and the mitochondria of erythrocytes. It begins with glycine and succinyl coenzyme A and ends with the production of a protoporphyrin IX ring. The binding of the protoporphyrin to a Fe2+ ion forms the final heme molecule.

**During pregnancy**, the fetus primarily produces fetal hemoglobin (HbF). HbF comprises two gamma-globin subunits. HbF has a stronger oxygen affinity than HbA, allowing oxygen to flow from maternal to fetal circulation through the placenta. Production of HbF drops significantly after

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 birth, reaches low, near-adult levels by two years, and ultimately makes up 2 to 3% of hemoglobin in adults. HbA, the most common adult form of hemoglobin, comprises two alpha and two beta-globin subunits. Inversely to HbF, HbA production explodes after birth and ultimately makes up 95-98% of hemoglobin in adults. HbA2 is a less common adult form of hemoglobin. It comprises two alpha and two delta-globin subunits and makes up 1 to 3% of hemoglobin in adults.

**Molecular**

There are multiple steps involved in heme synthesis. Eight enzymes accomplish this process, four of which work in the mitochondria and four in the cytosol. **The process** **starts in the mitochondria**, where ALA (aminolevulinic acid) synthase links glycine and succinyl coenzyme A to form ALA.

 **Steps 2 through 5** occur in the cytosol. Next, ALA dehydratase takes two molecules of ALA and produces porphobilinogen (PBG).

**In the third step**, porphobilinogen deaminase takes four molecules of PBG and produces hydroxymethylbilane. Next, uroporphyrinogen III cosynthase takes hydroxymethylbilane and produces uroporphyrinogen III.

**In the fifth step,** uroporphyrinogen decarboxylase takes uroporphyrinogen III and produces coproporphyrinogen III.

**The final three steps of heme synthesis** occur in the mitochondria. Coproporphyrinogen III is then transformed to protoporphyrinogen IX by coproporphyrinogen oxidase.

**The seventh step** occurs when protoporphyrinogen oxidase converts protoporphyrinogen IX to protoporphyrin IX.

**The eighth and final step** of heme synthesis is the addition of Fe to protoporphyrin IX by ferrochelatase, producing a heme molecule.

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**Normal hemoglobin concentrations** are approximately 13.5 to 18.0 grams per deciliter in men and 11.5 to 16.0 grams per deciliter in women.

**An individual erythrocyte** may contain **about 300 million hemoglobin molecules**, and therefore can bind to and transport up to 1.2 billion oxygen molecules (see Figure 3b). In the lungs, hemoglobin picks up oxygen, which binds to the iron ions, forming oxyhemoglobin.

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