# Hemoglobin and gas transport

Structure of hemoglobin

Approximately one third of the mass of a mammalian red blood cell is hemoglobin. Its major function is to carry oxygen from the lungs through the arteries to the tissues and help to carry carbon dioxide through the veins back to the lungs.

The hemoglobin molecule is made up of four polypeptide chains: two alpha chains of 141 amino acid residues each and two beta chains of 146 amino acid residues each. The alpha and beta chains have different sequences of amino acids. There are four binding sites for oxygen on the hemoglobin molecule, because each chain contains one heme group. In the alpha chain, the 87th residue is histidine F8 and in the beta chain the 92nd residue is histidine F8. A heme group is attached to each of the four histidines. The heme consists of an organic part and an iron atom. The iron atom in heme binds to the four nitrogens in the center of the protoporphyrin ring.

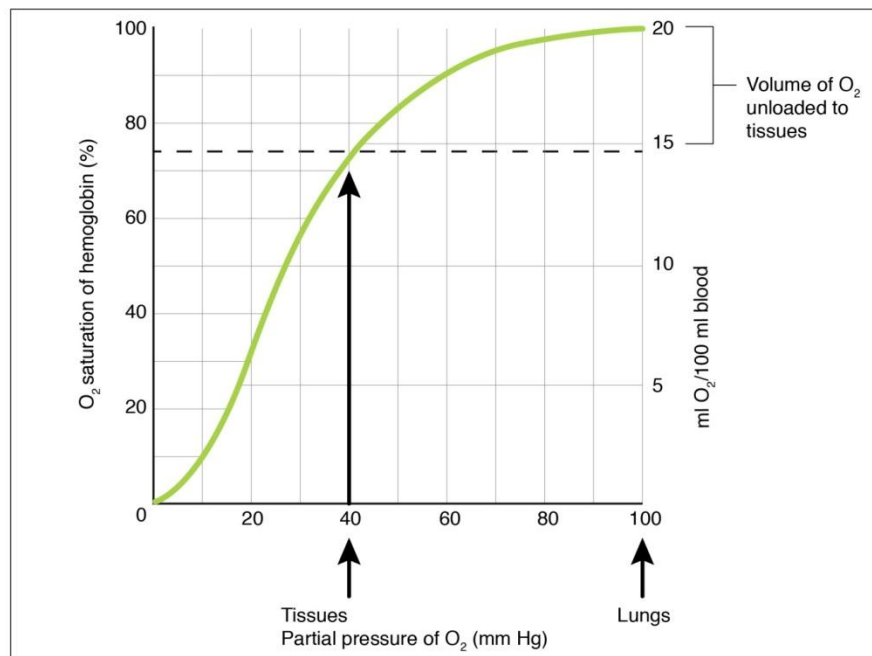**Heme**

Hemoglobin molecule
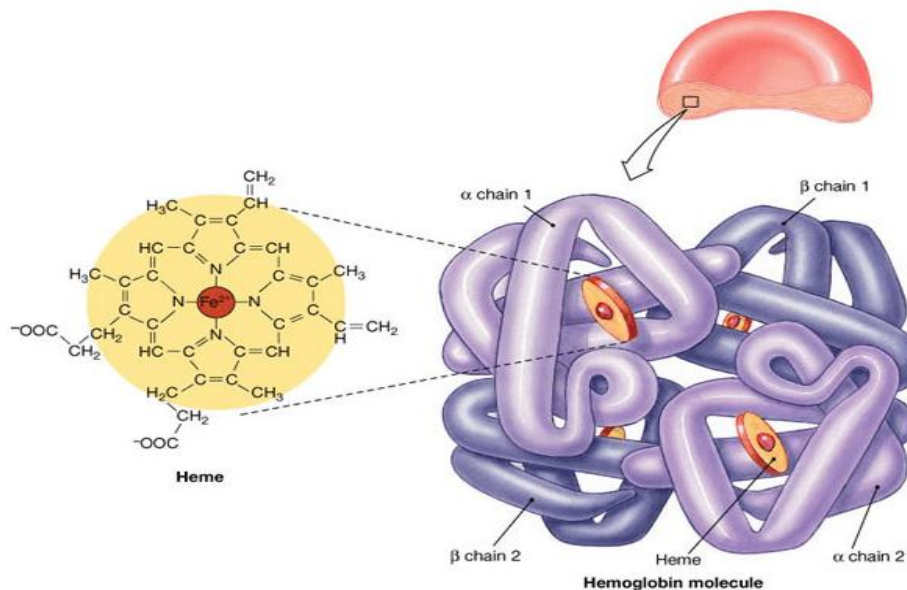
Oxygen Transport in the Blood

Even though oxygen is transported via the blood, you may recall that oxygen is not very soluble in liquids. A small amount of oxygen does dissolve in the blood and is transported in the bloodstream, but it is only about 1.5% of the total amount. The majority of oxygen molecules (98.5%) are carried from the lungs to the body's tissues by a specialized transport system, which relies on the erythrocyte—the red blood cell. Erythrocytes contain a hemoglobin, which serves to bind oxygen molecules to the erythrocyte. Heme is the portion of hemoglobin that contains iron, and it is heme that binds oxygen. One hemoglobin molecule contains iron-containing Heme molecules, and because of this, each hemoglobin molecule is capable of carrying up to four molecules of oxygen. As oxygen diffuses across the respiratory membrane from the alveolus to the capillary, it also diffuses into the red blood cell and is bound by hemoglobin. The following reversible chemical reaction describes the production of the final product, oxyhemoglobin (Hb–O2), which is formed when oxygen binds to hemoglobin. Oxyhemoglobin is a bright red-colored molecule that contributes to the bright red color of oxygenated blood.

Hemoglobin saturation of 100 percent means that every heme unit in all of the erythrocytes of the body is bound to oxygen. In a healthy individual with normal hemoglobin levels, hemoglobin saturation generally ranges from 95 percent to 99 percent. The binding of oxygen to the heme group of one subunit has the effect of increasing the affinity of a neighboring subunit (on the same molecule) for oxygen.

Oxygen Dissociation from Hemoglobin

Partial pressure is an important aspect of the binding of oxygen to and disassociation from heme. An oxygen–hemoglobin dissociation curve is a graph that describes the relationship of partial pressure to the binding of oxygen to heme and its subsequent dissociation from heme. Remember that gases travel from an area of higher partial pressure to an area of lower partial pressure. In addition, the affinity of an oxygen molecule for heme increases as more oxygen molecules are bound. Therefore, in the oxygen–hemoglobin saturation curve, as the partial pressure of oxygen increases, a proportionately greater number of oxygen molecules are bound by heme. Not surprisingly, the oxygen–hemoglobin saturation/dissociation curve also shows that the lower the partial pressure of oxygen, the fewer oxygen molecules are bound to heme. As a result, the partial pressure of oxygen plays a major role in determining the degree of binding of oxygen to heme at the site of the respiratory membrane, as well as the degree of dissociation of oxygen from heme at the site of body tissues.

(a) Partial pressure of oxygen and hemoglobin saturation

The mechanisms behind the oxygen–hemoglobin saturation/dissociation curve also serve as automatic control mechanisms that regulate how much oxygen is delivered to different tissues throughout the body. This is important because some tissues have a higher metabolic rate than others. Highly active tissues, such as muscle, rapidly use oxygen to produce ATP, lowering the partial pressure of oxygen in the tissue to about 20 mm Hg. The partial pressure of oxygen inside capillaries is about 100 mm Hg, so the difference between the two becomes quite high, about 80 mm Hg. As a result, a greater number of oxygen molecules dissociate from hemoglobin and enter the tissues. The reverse is true of tissues, such as adipose (body fat), which have lower metabolic rates. Because less oxygen is used by these cells, the partial pressure of oxygen within such tissues remains relatively high, resulting in fewer oxygen molecules

dissociating from hemoglobin and entering the tissue interstitial fluid. Although venous blood is said to be deoxygenated, some oxygen is still bound to hemoglobin in its red blood cells. This provides an oxygen reserve that can be used when tissues suddenly demand more oxygen.

Factors other than partial pressure also affect the oxygen–hemoglobin saturation/dissociation curve. For example, a higher temperature promotes hemoglobin and oxygen to dissociate faster, whereas a lower temperature inhibits dissociation.

Certain hormones, such as androgens, epinephrine, thyroid hormones, and growth hormone, can affect the oxygen–hemoglobin saturation/disassociation curve by stimulating the production of a compound called 2,3-bisphosphoglycerate (BPG) by erythrocytes. BPG is a byproduct of glycolysis. Because erythrocytes do not contain mitochondria, glycolysis is the sole method by which these cells produce ATP. BPG promotes the disassociation of oxygen from hemoglobin. Therefore, the greater the concentration of BPG, the more readily oxygen dissociates from hemoglobin.

The pH of the blood is another factor that influences the oxygen–hemoglobin saturation/dissociation curve. The Bohr effect is a phenomenon that arises from the relationship between pH and oxygen's affinity for hemoglobin: A lower, more acidic pH promotes oxygen dissociation from hemoglobin. In contrast, a higher, or more basic, pH inhibits oxygen dissociation from hemoglobin. The greater the amount of carbon dioxide in the blood, the more molecules that must be converted, which in turn generates hydrogen ions and thus lowers blood pH. Furthermore, blood pH may become more acidic when certain byproducts of cell metabolism, such as lactic acid, carbonic acid, and carbon dioxide, are released into the bloodstream.
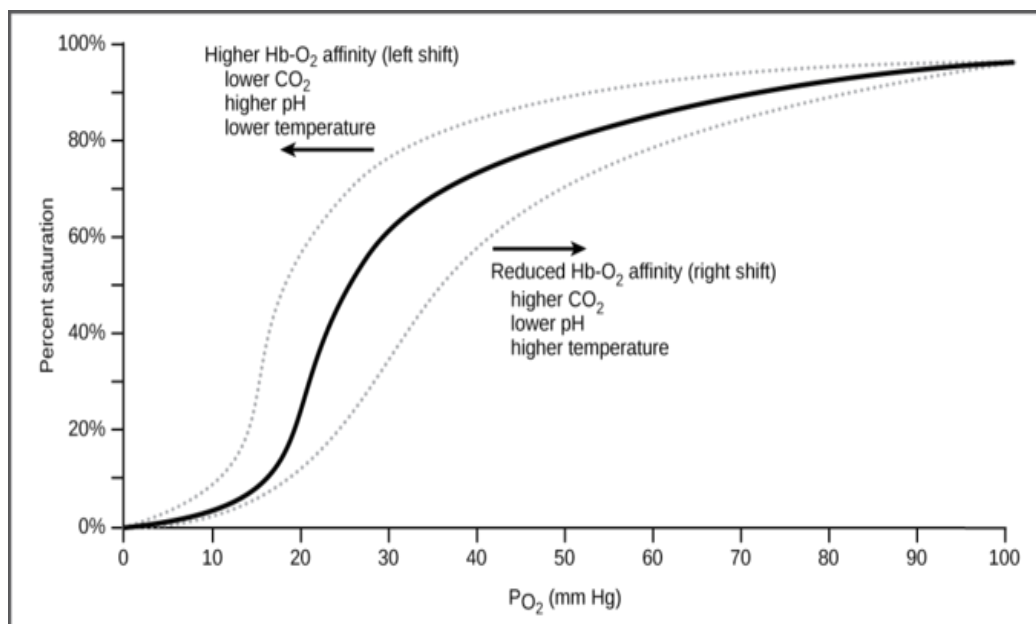
Myoglobin

Myoglobin, a protein found in the muscle cells of animals. It functions as an oxygen-storage unit, providing oxygen to the working muscles. Diving mammals such as seals and whales are able to remain

submerged for long periods because they have greater amounts of myoglobin in their muscles than other animals do.

There is a close chemical similarity between myoglobin and hemoglobin, the oxygen-binding protein of red blood cells. Both proteins contain a molecular constituent called heme, which enables them to combine reversibly with oxygen. The heme group, which contains iron, imparts a red-brown color to the proteins. In humans, myoglobin is only found in the bloodstream after muscle injury. It is an abnormal finding, and can be diagnostically relevant when found in blood.

Differences from hemoglobin

Like hemoglobin, myoglobin is a cytoplasmic protein that binds oxygen on a heme group. It harbors only one heme group, whereas hemoglobin has four. Although its heme group is identical to those in Hb, Mb has a higher affinity for oxygen than does hemoglobin. This difference is related to its different role: whereas hemoglobin transports oxygen, myoglobin's function is to store oxygen. Myoglobin found only in muscle tissues, while hemoglobin found in the blood. The globin chains in the myoglobin consists of 154 amino acid sequence, while hemoglobin consists of 141 and 146 amino acid sequence according to alpha and beta chains.

Disease

When muscle tissue is damaged, very large concentrations of myoglobin enters the kidneys. When this happens, myoglobin is then considered highly toxic and may contribute to acute renal failure. Muscle injury is commonly associated with the release of myoglobin, and is known to be the cause of heart attacks .
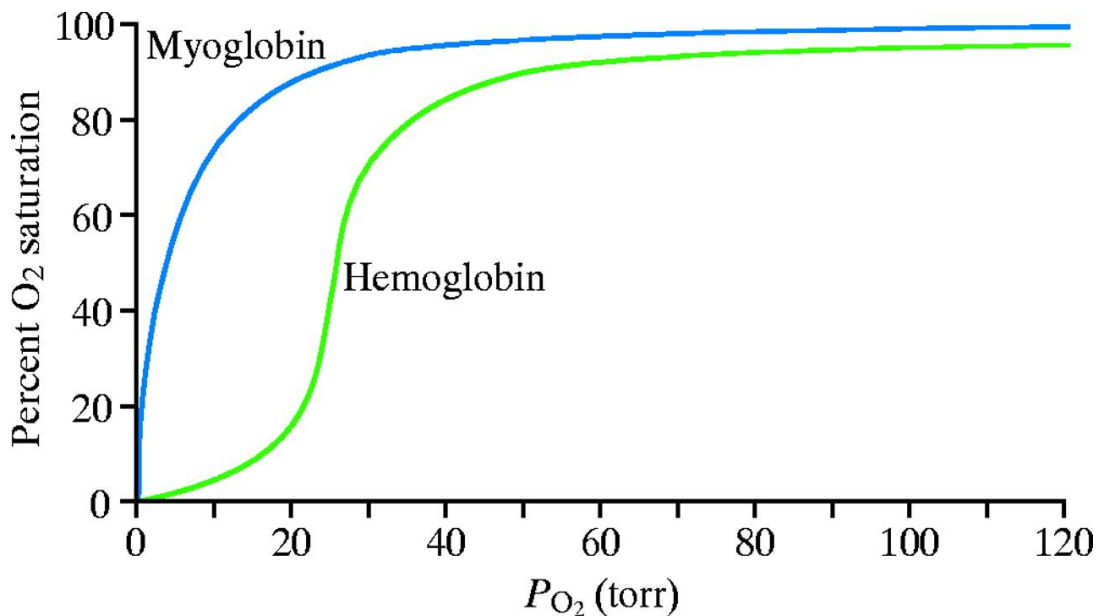
Carbon Dioxide Transport in the Blood

Carbon dioxide is transported by three major mechanisms. The first mechanism of carbon dioxide transport is by blood plasma, as some carbon dioxide molecules dissolve in the blood. The second

mechanism is transport in the form of bicarbonate (HCO3⁻), which also dissolves in plasma. The third mechanism of carbon dioxide transport is similar to the transport of oxygen by erythrocytes.
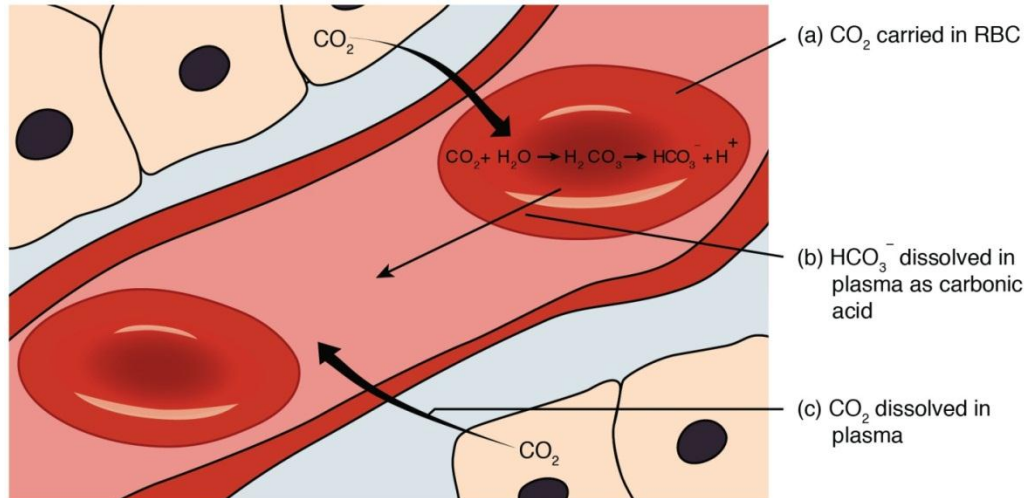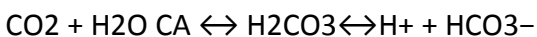

Carbon Dioxide Transport Carbon dioxide is transported by three different methods: (a) in erythrocytes; (b) after forming carbonic acid (H2CO3), which is dissolved in plasma; (c) and in plasma.

Dissolved Carbon Dioxide

Although carbon dioxide is not considered to be highly soluble in blood, a small fraction—about 7 to 10 percent—of the carbon dioxide that diffuses into the blood from the tissues dissolves in plasma. The dissolved carbon dioxide then travels in the bloodstream and when the blood reaches the pulmonary capillaries, the dissolved carbon dioxide diffuses across the respiratory membrane into the alveoli, where it is then exhaled during pulmonary ventilation.

Bicarbonate Buffer

A large fraction—about 70 percent—of the carbon dioxide molecules that diffuse into the blood is transported to the lungs as bicarbonate. Most bicarbonate is produced in erythrocytes after carbon dioxide diffuses into the capillaries, and subsequently into red blood cells. Carbonic anhydrase (CA) causes carbon dioxide and water to form carbonic acid (H2CO3), which dissociates into two ions: bicarbonate (HCO3−) and hydrogen (H+). The following formula depicts this reaction:

$$CO2 + H2O \; CA \leftrightarrow H2CO3 \leftrightarrow H+ + HCO3−$$

Carbaminohemoglobin

About 20 percent of carbon dioxide is bound by hemoglobin and is transported to the lungs. Carbon dioxide does not bind to iron as oxygen does; instead, carbon dioxide binds amino acid moieties on the globin portions of hemoglobin to form carbaminohemoglobin, which forms when hemoglobin and carbon dioxide bind. When hemoglobin is not transporting oxygen, it tends to have a bluish-purple tone to it, creating the darker maroon color typical of deoxygenated blood. The following formula depicts this reversible reaction:

$$CO2 + Hb \leftrightarrow HbCO2$$
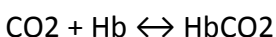
Similar to the transport of oxygen by heme, the binding and dissociation of carbon dioxide to and from hemoglobin is dependent on the partial pressure of carbon dioxide. Because carbon dioxide is released from the lungs, blood that leaves the lungs and reaches body tissues has a lower partial pressure of carbon dioxide than is found in the tissues. As a result, carbon dioxide leaves the tissues because of its higher partial pressure, enters the blood, and then moves into red blood cells, binding to hemoglobin. In contrast, in the pulmonary capillaries, the partial pressure of carbon dioxide is high compared to within the alveoli. As a result, carbon dioxide dissociates readily from hemoglobin and diffuses across the respiratory membrane into the air.

In addition to the partial pressure of carbon dioxide, the oxygen saturation of hemoglobin and the partial pressure of oxygen in the blood also influence the affinity of hemoglobin for carbon dioxide. The Haldane effect is a phenomenon that arises from the relationship between the partial pressure of oxygen and the affinity of hemoglobin for carbon dioxide. Hemoglobin that is saturated with oxygen does not readily bind carbon dioxide. However, when oxygen is not bound to heme and the partial pressure of oxygen is low, hemoglobin readily binds to carbon dioxide.

Once the oxygen diffuses across the alveoli, it enters the bloodstream and is transported to the tissues where it is unloaded, and carbon dioxide diffuses out of the blood and into the alveoli to be expelled from the body. Although gas exchange is a continuous process, the oxygen and carbon dioxide are transported by different mechanisms.

LE 22-9

Gas Exchange

External Respiration

Internal Respiration

Exhaled air   Inhaled air

Alveolar epithelial cells — Air spaces

CO_2 O_2

Alveolar capillaries of lung

CO_2-rich, O_2-poor blood

O_2-rich, CO_2-poor blood

Heart

Tissue capillaries

CO_2

O_2

CO_2 Interstitial fluid O_2

Tissue cells throughout body