



# HEMOGLOBIN – THE MAGNIFICENT

by *Bill Wojciechowski, MS, RRT*

During my childhood back in elementary school in Chicago, I recall watching a movie entitled, "Hemo – The Magnificent." This movie was presented by the Nationwide Bell System (well before its divestiture into the seven sisters). The teacher presented this 35-mm, reel-to-reel film to our sixth grade class. The movie was narrated by an elderly gentleman, and was filled with animation about the hemoglobin molecule. I do not know how many of you Focus readers saw, or even heard of this movie, but it made a huge impression on me about the hemoglobin molecule. That impression extends to the present, and is responsible for the title of this article.

Respiratory therapists focus daily on the oxygenation and acid-base status of their patients. The status of a patient's blood oxygenation and pH involves the hemoglobin molecule. Despite the prominence of hemoglobin in both of these physiologic processes, respiratory therapists often give cursory attention, if any, to the role of the hemoglobin molecule in these activities. Regarding oxygenation, respiratory therapists often devote their attention to the partial pressure of dissolved oxygen in the plasma, despite the fact that only about 1.5% of the oxygen transported in the blood is dissolved. Approximately, 250 ml of oxygen are consumed by the tissues of a resting adult per minute. To meet this oxygen demand, a mechanism more sophisticated than dissolving oxygen in plasma is required. To meet this challenge, the body is equipped with an exquisite transport method that centers on the hemoglobin molecule.

Concerning acid-base, the bicarbonate ion often steals the spotlight. Nonetheless, hemoglobin binds H<sup>+</sup> ions when oxygen is released to the tissues. Hemoglobin works to control the pH of the blood, especially during exercise, by binding many of the excess protons generated by metabolically active tissues.

### **Hemoglobin Structure**

Despite the presence of approximately 280 million hemoglobin molecules in a red blood cell, hemoglobin is a large protein molecule with a molecular weight of about 66,700 daltons. Hemoglobin contains a protein component known as globin, and a non-protein constituent called heme. The globin portion is comprised of two alpha and two beta polypeptide chains. These alpha and beta chains consist of 141 and 146 amino acids, respectively. Generally, protein molecules possess a low helix content. In other words, their polypeptide chains have few twists, turns, or coils. The globin polypeptide chains have a large helix content.

Each alpha and beta chain folds into eight helical sections. These eight helical segments fold and bend further to form a glob-

ular tertiary structure. The configuration of these four polypeptide chains is responsible for hemoglobin's globular or spherical appearance. Each of the four folded helix arrangements forms a pocket that accommodates the non-protein component of the hemoglobin molecule – heme.

Heme is a complex, non-protein, organic, ring-shaped molecule. The ring-shaped configuration develops because heme consists of four pyrrole groups connected by methylene bridges. The combination of four pyrroles connected via methylene bridges is termed a porphyrin ring. Porphyrin rings are abundant in nature, and have a proclivity for reacting with metals. For example, chlorophyll and vitamin B12 are porphyrins, which contain magnesium and cobalt, respectively. The porphyrin ring of heme normally reacts with iron in the ferrous state (Fe<sup>2+</sup>).

The Fe<sup>2+</sup> ion resides in the center of the porphyrin ring, and has the capacity to form six covalent bonds. Four of these bonds are formed with the nitrogen atoms of each of the four pyrroles comprising the porphyrin ring. The fifth covalent bond binds the porphyrin ring to the globin portion of the hemoglobin molecule. The sixth bond is available for the reversible reaction that occurs between heme and oxygen.

Embedded within each of the four polypeptide chains of globin is a heme molecule. Therefore, since each hemoglobin molecule contains four heme molecules, each hemoglobin molecule has the capacity to transport four molecules of oxygen.

### **Hemoglobin Function**

Hemoglobin is capable of carrying oxygen, carbon dioxide, and H<sup>+</sup> ions. Each of these substances combines with a different portion of the hemoglobin molecule.

### **Oxyhemoglobin**

Again, oxygen combines reversibly with heme. When hemoglobin binds with one oxygen molecule, it has the unique characteristic of developing an increased affinity for subsequent oxygen molecules at the remaining heme binding sites. So, when a second oxygen molecule reacts with another heme, the other two heme molecules have a more voracious attraction for oxygen. This property of hemoglobin is called cooperativity. The physiologic advantage of this cooperative binding is to enhance the loading of oxygen when mixed venous blood traverses ventilated alveoli.

Conversely, when oxygenated blood reaches the tissues, the release of one oxygen molecule from one heme, decreases the

## The Last Suction Regulator You Will Ever Buy



**Outperforms the Competition**

**Outlasts the Competition**

**A Solution for Every Clinical Need**

**Introducing the NEW Platinum Series Suction Regulators from Boehringer Laboratories, Inc.**

**12 Year Warranty**   **Self-Cleaning Technology**   **High Performance**

800-642-4945  
www.boehringerlabs.com  
Boehringer Laboratories, Inc.  
500 East Washington St. P.O. Box 870  
Norristown, PA 19404

**BOEHRINGER**

**CIRCLE READER ACTION CARD # 7**

affinity for subsequent oxygen molecules from the other heme components. The benefit in this situation is the augmentation of tissue oxygenation. This cooperative binding and releasing of oxygen is responsible for the sigmoid shape of the oxyhemoglobin dissociation curve. The oxymyoglobin dissociation curve, which reflects the noncooperative binding and releasing interaction between oxygen and myoglobin, has a hyperbolic shape.

Metabolizing tissues, such as contracting muscles, generate vast amounts of H<sup>+</sup> ions and carbon dioxide. Both of these species interact with hemoglobin enhancing its release of oxygen manifesting the Bohr effect, i.e., the effect of pH on oxygen-hemoglobin affinity. Hemoglobin's affinity for oxygen decreases as blood pH decreases from 7.40 in the lungs to around 7.34 in the tissues.

### Carbaminohemoglobin

When carbon dioxide reacts with hemoglobin to form carbaminohemoglobin, CO<sub>2</sub> does not affix to the heme molecule like oxygen does. Rather, it attaches to hemoglobin by combining with a terminal amine group on globin. The reaction between the terminal amine group and CO<sub>2</sub> is rapid and reversible. The unloading of oxygen from hemoglobin to the tissues increases hemoglobin's affinity for CO<sub>2</sub> – the Haldane effect. Interestingly, hemoglobin transports only 10% to 25% of the CO<sub>2</sub> excreted by the lungs. Therefore, hemoglobin is not the major vehicle for CO<sub>2</sub> transport. The bicarbonate ion in the plasma is because it carries 75% of metabolically produced CO<sub>2</sub>.

### Hemoglobin Buffer

The hemoglobin molecule also functions as an effective buffer by accepting free H<sup>+</sup> ions present in red blood cells after oxygen has been released to the tissues. The main source of H<sup>+</sup> ions in the red blood cells is the CO<sub>2</sub> + H<sub>2</sub>O reaction occurring in the presence of the catalyst carbonic anhydrase. The products of this reaction are bicarbonate ions and H<sup>+</sup> ions. The bicarbonate ions leave the erythrocytes, and enter the plasma in exchange for chloride ions, a process described as the chloride shift. The H<sup>+</sup> ions are effectively buffered by deoxyhemoglobin.

Because hemoglobin is a protein, it is able to function as a buffer. As the pH in the erythrocyte falls at the tissue level, the side chain of the amino acid histidine on the beta polypeptide chain (globin) accepts a free H<sup>+</sup> ion. The majority of the buffering ability of hemoglobin is accomplished via the imidazole group of the amino acid histidine, a component of the globin molecule. The imidazole group has a pK of approximately 7.00, giving it an effective buffering range of 6.00 to 8.00. The physiologic range of blood pH lies well within hemoglobin's effective buffering range.

Current research is beginning to elucidate the interplay among nitric oxide (NO), hemoglobin, oxygen, and erythrocytes concerning the dilatation of blood vessels and oxygen delivery. Heme has been found to render nitric oxide non-functional, but sulfur atoms among the amino acids in globin (S-nitrosothiol or SNO) have demonstrated a protective mechanism for NO. Evidence indicates that the SNO-hemoglobin complex enables NO delivery to the microvasculature upon the release of oxygen. Thus, a physiologic link between hemoglobin deoxygenation and microvasculature vasodilatation seem evident. After all these years, the title, "Hemo – The Magnificent" appears justified. Although in light of recent research, perhaps, a new movie with a more towering superlative is warranted.

*William Wojciechowski, MS, RRT is a veteran therapist/educator as well as Chairman and Associate Professor of the Department of Cardio-Respiratory Care at the University of South Alabama in Mobile, Alabama. He can be reached at wwjciec@usouthal.edu*



**Transtracheal Systems proudly announces its 20th anniversary as the world leader in SCOOP oxygen therapy. 1986-2006**

Scientifically validated in medical literature.

Thousands of satisfied patients, RT's, and physicians.

Cost effective, revenue enhancing program for hospital RT department.



CHEST Booth 102

Complete line of accessories to optimize the TTO2 experience.



On-site in-service available.

**What are you waiting for? Get the SCOOP!**

For more information call: 800-527-2667 ext. 202 or e-mail drscoop@tto2.com

**CIRCLE READER ACTION CARD # 8**