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Unit 3 a : Respiratory System

PROBLEM 1: Discuss the role of hemoglobin in the transport of oxygen and of carbon dioxide.

Solution: Hemoglobin is the pigment in red blood cells that is responsible for transporting nearly all the oxygen and some of the carbon dioxide in the body. In arterial blood, oxygen is present in two forms. It is either physically dissolved in the blood plasma or chemically bound to hemoglobin. Because oxygen is relatively insoluble in water, and blood plasma is comprised primarily of water, only 3 ml. of oxygen can be dissolved in 1 liter of plasma at normal oxygen pressure (100 mm Hg on average). Hence, approximately 2% of the oxygen in the blood is dissolved in the plasma; the rest is transported via hemoglobin. In the lungs, oxygen enters the capillaries, and diffuses into the red blood cells where it binds to hemoglobin. Four oxygen molecules are attached to four iron atoms in a single hemoglobin molecule (see Figure 32-6). The chemical reaction between oxygen and hemoglobin is usually written as:

$$O_2 + Hb \rightleftarrows HbO_2 \text{ (oxyhemoglobin)}$$

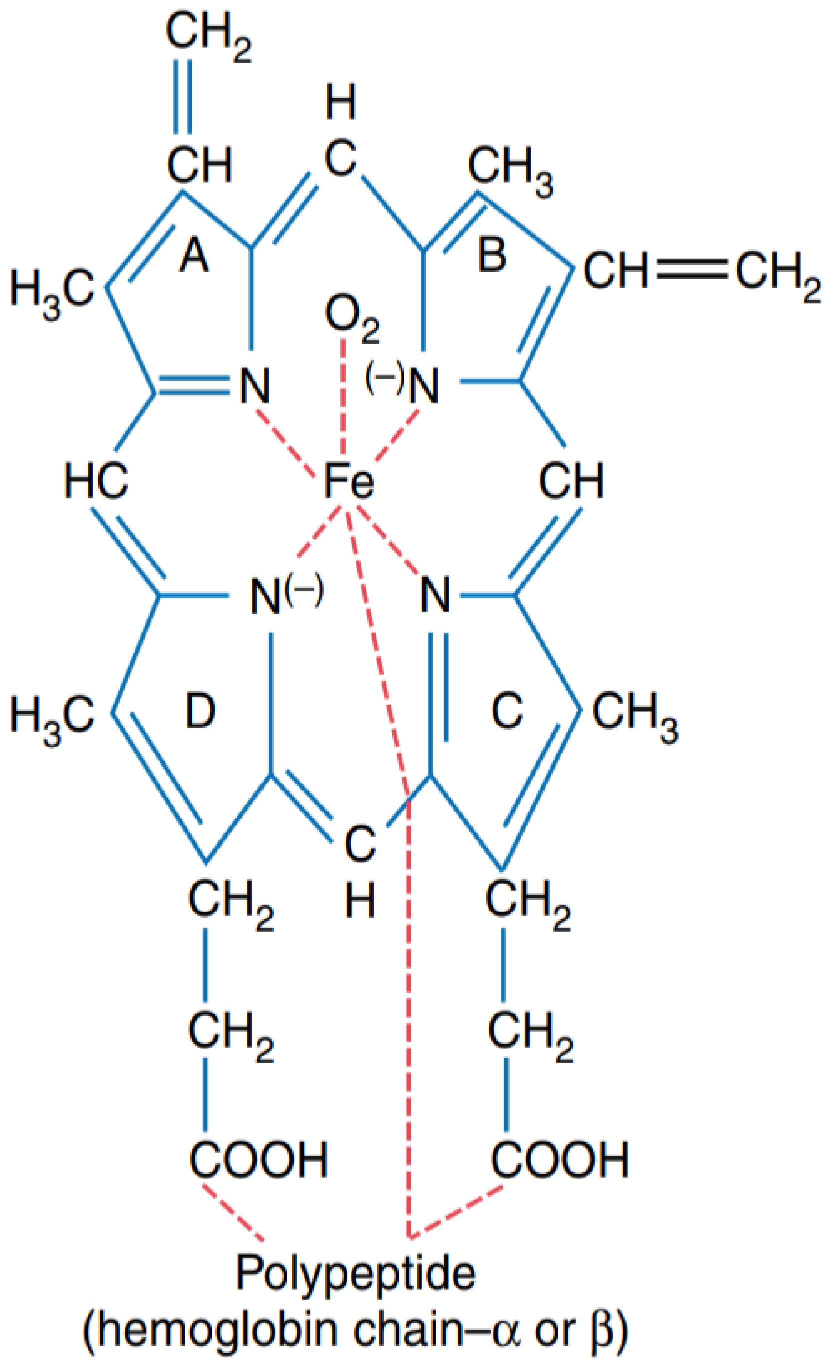

Figure 32-6 Basic structure of the hemoglobin molecule, showing one of the four heme chains that bind together to form the hemoglobin molecule.

The reaction goes to the right in the lungs and to the left in the body tissues. Hemoglobin combined with oxygen (HbO_2) is called oxyhemoglobin; when not combined (Hb), it is called reduced hemoglobin or deoxyhemoglobin. Because there is a finite number (four) of binding sites for oxygen on the hemoglobin molecule, there is a maximum amount of oxygen which can combine with hemoglobin. When hemoglobin exists as both Hb and HbO_2, it is said to be partially saturated. When it exists as only HbO_2, it is said to be fully saturated. The combination of oxygen with hemoglobin and its release from oxyhemoglobin are controlled by the concentration of oxygen present and, to a lesser extent, by the amount of carbon dioxide present. For example, the percentage of saturated hemoglobin undergoes little change between the lungs and the arteries, because the oxygen concentration in the lungs is very similar to that of the arteries. However, in the tissues, the concentration of oxygen is low, so by the law of mass action, the reaction will go to the left. As a result, oxygen will break off from the oxyhemoglobin to diffuse into the tissues.Carbon dioxide reacts with water to form carbonic acid, H_2CO_3, which then dissociates:

$CO_2 + H_2O \rightleftarrows H_2CO_3 \rightleftarrows H^+ + HCO_3^-$(Bicarbonate)

An increase in the concentration of CO_2 drives the reaction to the right, increasing the H^+ concentration and hence the acidity of the blood. The oxygen carrying capacity of hemoglobin decreases as the blood becomes more acidic. Thus, more O_2 is released to the tissues under conditions of increasing acidity. This shows that the combination of hemoglobin and oxygen is controlled, in part, by the amount of CO_2 present. This results in a very efficient transport system. In the lung capillaries, oxygen is taken up by the hemoglobin due to the effects of high oxygen tension and low CO_2 tension. The situation is reversed in the tissues. There, CO_2 pressure is high and oxygen pressure is low, so oxygen dissociates from oxyhemoglobin and diffuses into the tissues. It is important to realize that the principal factor that determines the mode of hemoglobin dissociation and rate of diffusion is the partial pressure (Pgas) of each particular gas. As is true for oxygen, the quantity of carbon dioxide that can physically dissolve in blood is quite small. Carbon dioxide can undergo the following reaction:

$$CO_2 + H_2O \rightleftarrows H_2CO_3 \text{ (carbonic acid)}$$

This reaction would go quite slowly if it were not catalyzed by the enzyme carbonic anhydrase. The quantities of both dissolved carbon dioxide and carbonic acid are directly proportional to the partial pressure of CO_2. In this case, as in the case with oxygen, we are only concerned with the pressure of the gas in question. This is because in a mixture of gases, each one acts independently of the others, and exerts the same pressure it would if it were present alone. The actual quantity of carbonic acid in the blood is small, because, as we saw previously, it dissociates into H^+ and HCO_3^- ions. These ions are quite soluble in the blood. Thus, the addition of carbon dioxide to blood plasma results ultimately in the production of hydrogen and bicarbonate ions. Carbon dioxide is transported primarily as bicarbonate ions to the lungs, where it is excreted as carbon dioxide. Carbon dioxide can also react with proteins, particularly hemoglobin, to form carbamino compounds.

$$CO_2 + Hb \rightleftharpoons HbCO_2 \text{ (carbamino hemoglobin)}$$

Carbon dioxide diffuses from the tissues into the blood. In the blood, some (8%) of the CO_2 stays dissolved, and some (25%) reacts with hemoglobin to form $HbCO_2$. The largest fraction (67%) is converted to H^+ and HCO_3^-. This occurs primarily within the red cells because they contain large quantities of carbonic anhydrase, whereas the plasma does not. This dissociation into H^+ and HCO_3^- explains why tissues and capillaries, where CO_2 concentration is high, have a hydrogen ion concentration higher than that of arterial blood. This also explains the increase in H^+ concentration as metabolic rate increases. The CO_2 itself passes from the tissues to the blood, and then to the lungs by diffusing from a region of high CO_2 tension to one of low CO_2 tension.

PROBLEM 2 : Where is the respiratory center and what are its functions? Describe briefly the neural control of breathing.

Solution: Breathing requires the coordinated contraction and relaxation of several muscles. This is achieved by the respiratory center, which is composed of special groups of cells in the medulla and pons of the brain. From this respiratory center, nerve impulses are rhythmically discharged to the intercostal (rib) muscles, resulting in their periodic contraction every 4 to 5 seconds. The breathing movements are automatic and occur without voluntary control under normal conditions. We can voluntarily hold our breath, but not indefinitely, since then the automatic center eventually takes over and forces us to exhale. By experimentation, neurons have been found in the medulla which propagate action potentials in perfect synchrony with inspiration. A smaller number of other neurons have been discovered which discharge synchronously with expiration. These two types of neurons are called inspiratory and expiratory neurons, respectively. These may also bebreferred to as inspiratory and expiratory centers. Electrical stimulation of the inspiratory neurons can produce a maximal inspiration. Conversely, electrical stimulation of the expiratory neurons shuts off inspiration abruptly, and produces contraction of the expiratory muscles. The question arises as to what induces firing of the medullary inspiratory neurons. It appears that these neurons have inherent autorhythmicity – the capacity for periodic self-excitation. However, synaptic input from other neurons plays an essential role in regulating the rhythmicity of these inspiratory neurons. There are three vital inputs to the medullary inspiratory neurons, which play a role in modulating respiratory rhythm. They are (1) direct intracranial connections between the medulla and the pons (2) reciprocal connections with the medullary expiratory neurons, and (3) afferent input from stretch receptors in the lung (see Figure 41-1). The connections between the inspiratory and expiratory centers are inhibitory in nature. Thus at the beginning of inspiration, when the inspiratory neurons are firing, the expiratory center is prevented from firing so that expiration is inhibited. When inspiration ceases, expiratory inhibition also stops, and expiration is able to occur which then, in turn, inhibits inspiration. These reciprocal connections serve to synchronize inspiration and expiration. As was previously mentioned, the medullary inspiratory center is connected to the pons. This area of the pons is often called the pneumotaxic center, and destruction of this center produces profound changes in respiration. The medullary neurons receive neural input from the pons, which exerts a tonic effect upon the inspiratory neurons. It is also likely that the pneumotaxic center serves as a central relay station for the respiratory inhibition initiated by the lung stretch receptors. As the lungs expand during inspiration, these receptors are stimulated, and impulses travel up the afferent nerves to the brainstem, where they aid in terminating inspiration To summarize, the medullary inspiratory neurons primarily control the cycle of ventilation. These inspiratory neurons innervate the inspiratory muscles. The spontaneous increase in the firing rate of these inspiratory neurons is a crucial factor for initiating ventilation. Due to the inhibitory impulses from medullary expiratory neurons and pulmonary stretch receptors which act through higher brain centers, these neurons will

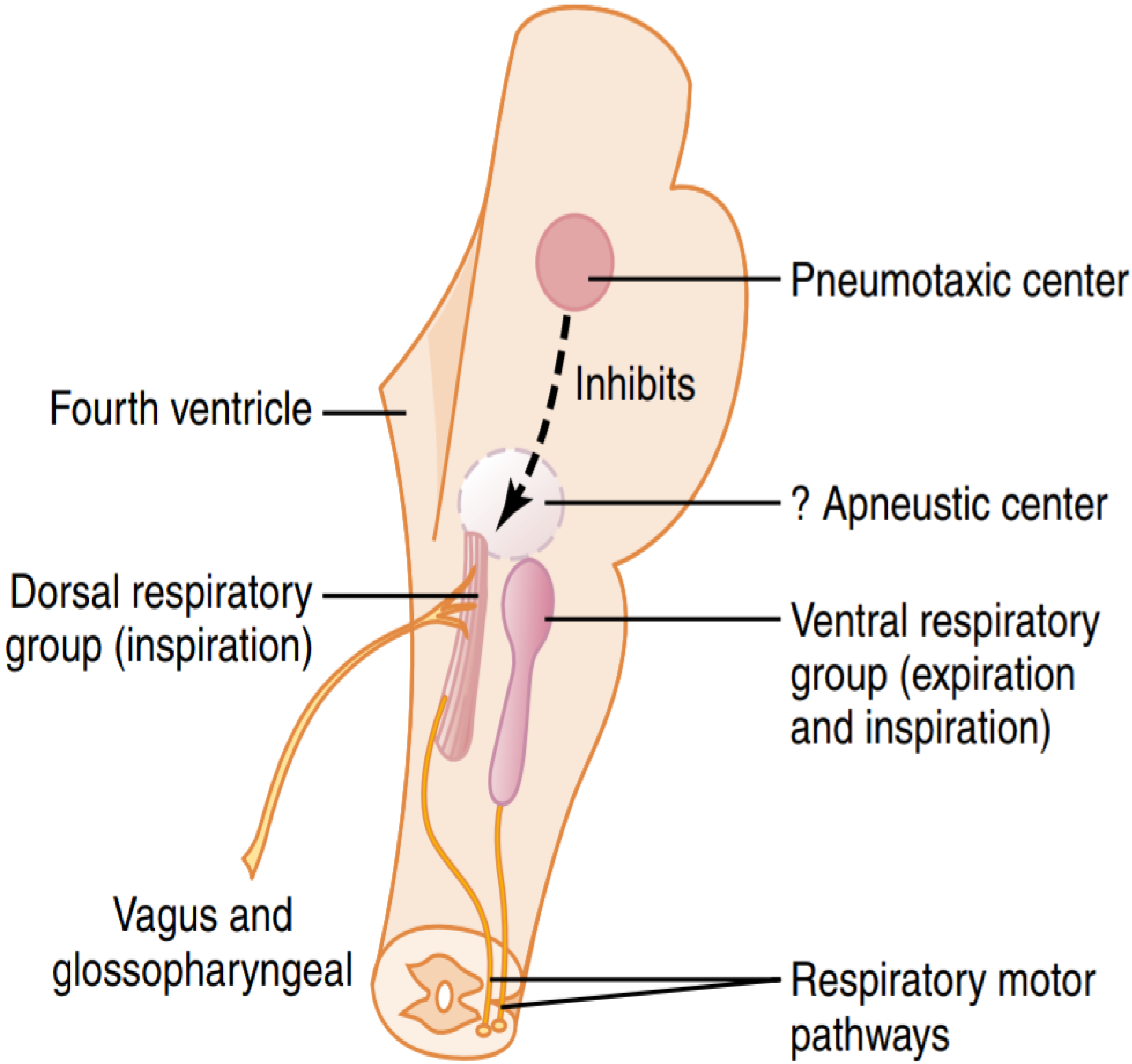

Figure 41-1 Organization of the respiratory center.

stop firing. The cessation of activity by the inspiratory neurons releases the inhibition on the expiratory neurons so that expiration can passively occur. Only in forced expiration are the expiratory muscles themselves used. This active expiratory movement is synchronized with the passive component of expiration. This is possible because of the reciprocal connections between the medullary inspiratory and expiratory centers.