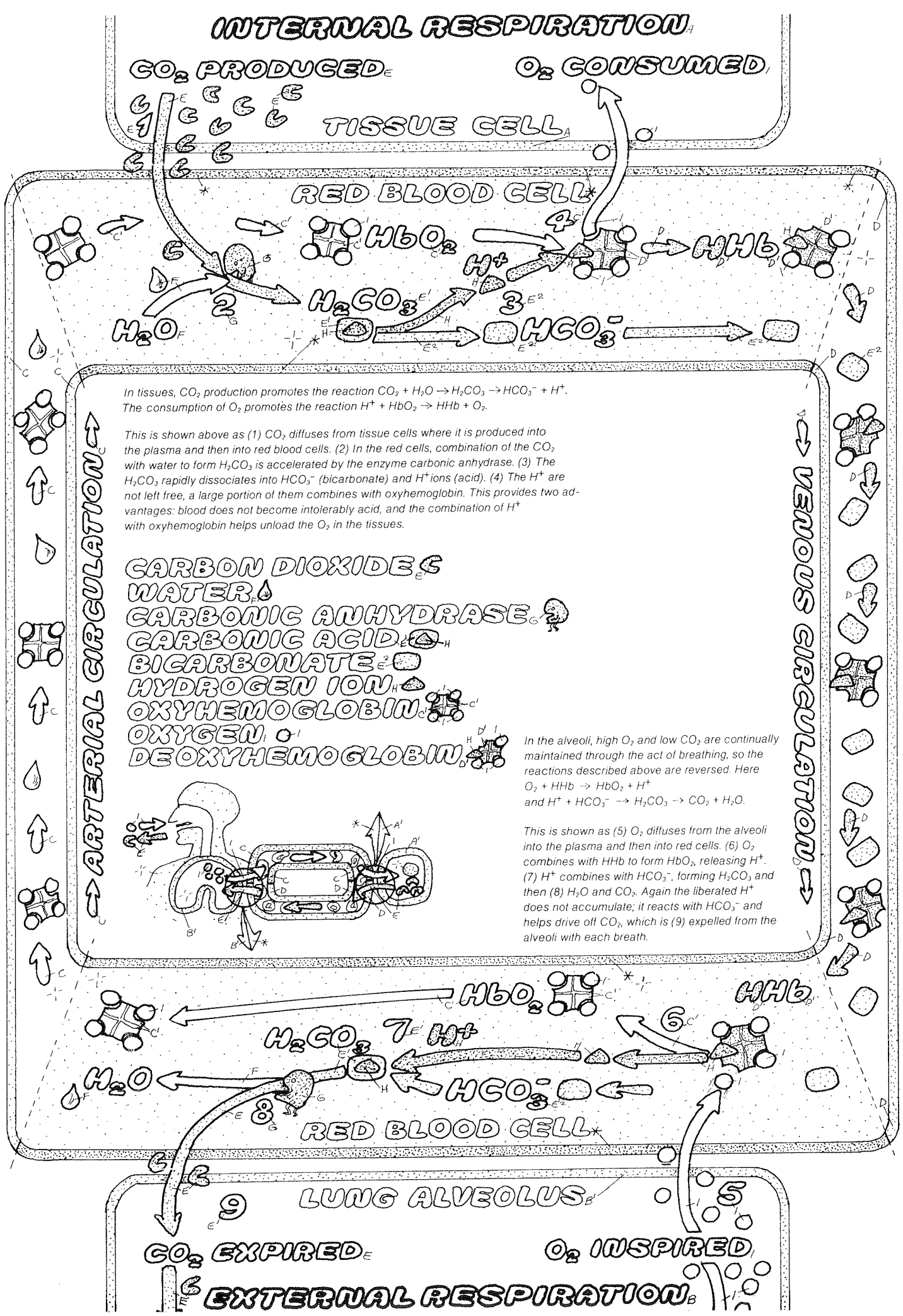


*In tissues, $CO_2$ production promotes the reaction $CO_2 + H_2O \rightarrow H_2CO_3 \rightarrow HCO_3^- + H^+$. The consumption of $O_2$ promotes the reaction $H^+ + HbO_2 \rightarrow HHb + O_2$.*

*This is shown above as (1) $CO_2$ diffuses from tissue cells where it is produced into the plasma and then into red blood cells. (2) In the red cells, combination of the $CO_2$ with water to form $H_2CO_3$ is accelerated by the enzyme carbonic anhydrase. (3) The $H_2CO_3$ rapidly dissociates into $HCO_3^-$ (bicarbonate) and $H^+$ ions (acid). (4) The $H^+$ are not left free, a large portion of them combines with oxyhemoglobin. This provides two advantages: blood does not become intolerably acid, and the combination of $H^+$ with oxyhemoglobin helps unload the $O_2$ in the tissues.*

*In the alveoli, high $O_2$ and low $CO_2$ are continually maintained through the act of breathing, so the reactions described above are reversed. Here $O_2 + HHb \rightarrow HbO_2 + H^+$ and $H^+ + HCO_3^- \rightarrow H_2CO_3 \rightarrow CO_2 + H_2O$.*

*This is shown as (5) $O_2$ diffuses from the alveoli into the plasma and then into red cells. (6) $O_2$ combines with HHb to form $HbO_2$, releasing $H^+$. (7) $H^+$ combines with $HCO_3^-$, forming $H_2CO_3$ and then (8) $H_2O$ and $CO_2$. Again the liberated $H^+$ does not accumulate; it reacts with $HCO_3^-$ and helps drive off $CO_2$, which is (9) expelled from the alveoli with each breath.*

# TRANSPORT OF $CO_2$, $H^+$, AND $O_2$

In plate 49, we saw how the subunit structure of Hb introduces into the molecule new properties that are not shared by the simpler single unit analog, myoglobin. In particular, increasing the concentrations of $CO_2$ and $H^+$ drives $O_2$ off the Hb molecule. The converse also holds: increasing the concentration of $O_2$ drives off both $CO_2$ and $H^+$. At first, this unusual sensitivity of Hb to its environment may seem undesirable in a molecule whose function is to stabilize the $PO_2$ in body fluids. However, the function of Hb goes beyond this; it not only transports $O_2$, it also transports both $CO_2$ and $H^+$. Further, Hb reacts with these three substances in a remarkable way so that just the "right" thing happens at the "right" time.

Like $O_2$, $CO_2$ transport is passive. $PCO_2$ is high in the tissues because it is produced there. It is low in the lung alveoli because it is swept out with each breath, and therefore it is also low in the arterial blood that enters tissue capillaries. $CO_2$ moves down its partial pressure gradient from tissue to capillary blood to lung alveoli (plate 48). Although blood holds a small amount of $CO_2$ (about 9%) in simple solution and another fraction (about 27%) in combination with Hb, the major portion (64%) reacts with water, forming *bicarbonate* ($HCO_3^-$) and *hydrogen ions* ($H^+$).

$$CO_2 + H_2O \rightleftharpoons H_2CO_3 \rightleftharpoons HCO_3^- + H^+$$

Because $PCO_2$ is high in the tissues, this reaction proceeds to the right, and $CO_2$ is carried as bicarbonate. However, there is a major problem with this reaction; it leads to the accumulation of $H^+$ ions. Not only are $H^+$ ions acid, but their accumulation will slow down and block the reaction of $CO_2$ with water, which severely limits the amounts of $CO_2$ that can be carried. The dilemma is resolved by substances in the blood that "soak up" or *buffer* excess $H^+$ ions. Hb is one of the most important of these buffers; its reaction with $H^+$ can be represented as follows:

$$H^+ + HbO_2^- \rightleftharpoons HHb + O_2$$

where the $HbO_2^-$ represents Hb with $O_2$ attached (*oxyhemoglobin*), and the (-) sign signifies one of the many (-) charges carried by the Hb molecule. Similarly, HHb represents Hb with an extra $H^+$ attached.

Notice that these reactions are both reversible (i.e., they can proceed from left to right or from right to left depending on the concentrations of reactants and products). At *equilibrium*, the reaction proceeds in both directions, but at equal rates so that no noticeable change takes place. However, when concentrations of substances on the right are decreased, the reaction gets "pulled" from left to right. Increasing concentrations on the left will "push" the reaction from left to right. Conversely, decreasing the concentrations of substances on the left, or increasing them on the right, moves the reaction from right to left.

In the tissues, the reactions involving Hb and bicarbonate are coupled because $H^+$ ions are a common participant in both. In the tissues:

$$CO_2 + H_2O \longrightarrow H_2CO_3 \longrightarrow HCO_3^- + H^+$$

$$H^+ + HbO_2^- \longrightarrow HHb + O_2$$

The first reaction proceeds in the indicated direction because (1) $CO_2$ is produced in tissues so its concentration is high, and (2) as soon as excess $H^+$ begins to accumulate, it is consumed by the second reaction. The second reaction proceeds in the indicated direction because (1) a steady supply of $H^+$ is liberated by the first reaction, (2) a steady supply of $HbO_2^-$ at high concentration is coming from the lungs, (3) HHb is continually swept away in the venous blood, and (4) $O_2$ is consumed by the tissues, so its concentration is low. Note that as soon as $H^+$ is produced, it is picked up by the Hb, so free $H^+$ does not accumulate to dangerous levels. In the process, the tissues receive an extra dividend: more $O_2$ is driven off the Hb than would be without the $H^+$ binding.

In the lungs, these same reactions occur, but now in reverse:

$$O_2 + HHb \longrightarrow HbO_2^- + H^+$$

$$H^+ + HCO_3^- \longrightarrow H_2CO_3 \longrightarrow H_2O + CO_2$$

The first reaction proceeds in the direction of the arrow because (1) $PO_2$ is high in the lungs, (2) there is a steady supply of HHb at high concentration coming from the tissues (via systemic venous blood), and (3) as soon as excess $H^+$ accumulates, it is consumed by the second reaction. The second reaction proceeds as shown because (1) there is a steady supply of $H^+$ liberated by the first reaction, (2) there is a steady supply of $HCO_3^-$ at high concentration coming from the tissues, and (3) breathing keeps $CO_2$ at a low level.

Thus, $H^+$ ions, which at first appeared to be a problem, actually play a very useful role: in the tissues they drive $O_2$ off of Hb, and in the lungs they help drive $CO_2$ off of $HCO_3^-$. They never accumulate in the free state because they are passed back and forth like a "hot potato" between Hb and $HCO_3^-$.

*CN: Use the same colors as on previous page for $O_2$ (I). Use red for C, blue for D, and light blue for F. Use a dark color for H.*
*1. Begin by coloring the tissue cell and the titles at the top of the page and the lung alveolus and titles at the bottom. Then color the red blood cell section. Color the two horizontal bands (where gas exchanges occur) gray, and color the vertical bands, of arterial (C) and venous (D) circulation.*
*2. Start with number 1 at the top (under $CO_2$ produced), and follow the numbered sequence. Continue down the right side, coloring all symbols. Then color all the processes of gas exchange in the lungs, beginning with number 5 in the lower right corner.*
*3. Color the overview diagram within the rectangle.*