4. **Alveolus.** Each bronchiole branch ends in a small sac called an **alveolus** (plural, **alveoli**). Each alveolus is densely surrounded by blood-carrying capillaries.
5. **Diffusion between alveolar chambers and blood.** Gas exchange occurs by diffusion across the moist, sac membranes of the alveoli. Oxygen diffuses into the moisture covering the membrane, through the alveolar wall, through the blood capillary wall, into the blood, and into red blood cells. Carbon dioxide diffuses in the opposite direction.
6. **Bulk flow of O_2.** The circulatory system transports O_2 throughout the body within red blood cells. Red blood cells contain hemoglobin, iron-containing proteins to which O_2 bonds.
7. **Diffusion between blood and cells.** Blood capillaries permeate the body. Oxygen diffuses out of the red blood cells, across blood capillary walls, into interstitial fluids (the fluids surrounding the cells), and across cell membranes. Carbon dioxide diffuses in the opposite direction.
8. **Bulk flow of CO_2.** Most CO_2 is transported as dissolved bicarbonate ions (HCO_3^-) in the plasma, the liquid portion of the blood. The formation of HCO_3^-, however, occurs in the red blood cells, where the formation of carbonic acid (H_2CO_3) is catalyzed by the enzyme **carbonic anhydrase,** as follows:

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

   Following their formation in the red blood cells, HCO_3^- ions diffuse back into the plasma. Some CO_2, however, does not become HCO_3^-; instead, it mixes directly with the plasma (as CO_2 gas) or binds with the amino groups of the hemoglobin molecules inside red blood cells.
9. **Bulk flow of air into and out of the lungs (mechanics of respiration).** Air is moved into and out of the lungs by changing their volume. The volume of the lungs is increased by the contraction of the **diaphragm** (a muscle under the lungs) and the **intercostal** muscles (muscles between the ribs). When the lung volume increases, the air pressure within the lungs decreases. This causes a pressure difference between the air in the lungs and the air outside the body. As a result, air rushes into the lungs by bulk flow. When the diaphragm and intercostal muscles relax, the volume of the lungs decreases, raising the pressure on the air, causing the air to rush out.
10. **Control of respiration.** Chemoreceptors in the carotid arteries (arteries that supply blood to the brain) monitor the pH of the blood. When a body is active, CO_2 production increases. When the CO_2 that enters the plasma is converted to HCO_3^- and H^+, the blood pH drops (becomes more acidic). In response, the chemoreceptors send nerve impulses to the diaphragm and intercostal muscles to increase respiratory rate. This results in a faster turnover in gas exchange, which, in turn, returns blood pH to normal. The regulation of the respiratory rate in this manner is an example of how homeostasis is maintained by negative feedback.

The Circulatory System

Large organisms require a transport system to distribute nutrients and oxygen and to remove wastes and CO_2 from cells distributed throughout the body. Two kinds of circulatory systems accomplish this internal transport.

1. **Open circulatory systems** pump blood into an internal cavity called a **hemocoel** (or cavities called **sinuses**), which bathe tissues with an oxygen- and nutrient-carrying fluid called **hemolymph.** The hemolymph returns to the pumping mechanism of the system, a **heart,** through holes called **ostia.** Open circulatory systems occur in insects and most mollusks.
2. In **closed circulatory systems,** the nutrient-, oxygen-, and waste-carrying fluid, **blood,** is *confined* to vessels. Closed circulatory systems are found among members of the phylum Annelida (earthworms, for example), certain mollusks (octopuses and squids), and vertebrates.

In the closed circulatory system of vertebrates, vessels moving *away* from the heart are called **arteries.** Arteries branch into smaller vessels, the **arterioles,** and then branch further into the smallest vessels, the **capillaries.** Gas and nutrient exchange occurs by diffusion across capillary walls into interstitial fluids and into surrounding cells. Wastes and excess interstitial fluids move in the opposite direction as they diffuse into the capillaries. The blood, now deoxygenated, remains in the capillaries and *returns* to the heart through **venules,** which merge to form larger **veins.** The heart then pumps the deoxygenated blood to the respiratory organ (gills or lungs) where arteries again branch into a capillary bed for gas exchange. The oxygenated blood then returns to the heart through veins. From here, the oxygenated blood is pumped, once again, throughout the body.