

## Chapter 42

# Circulation and Gas Exchange

### *Lecture Outline*

#### Overview: Trading Places

- Every organism must exchange materials with its environment, and this exchange ultimately occurs at the cellular level.
  - The resources that animal cells need, such as nutrients and oxygen, move across the plasma membrane to the cytoplasm.
  - Metabolic wastes, such as carbon dioxide, move out of the cell.
- In unicellular organisms, exchanges occur directly with the external environment.
- Multicellular organisms have specialized systems for exchanging materials with the environment and for transporting system materials between sites of exchange and the rest of the body.
- For aquatic animals, structures such as gills present an expansive surface area to the outside environment.
- Oxygen dissolved in the surrounding water diffuses across the thin epithelium covering the gills and into a network of tiny blood vessels (capillaries).
- At the same time, carbon dioxide diffuses out into the water.
  - Diffusion is rapid due to the short distances involved.
- Pumping of the heart moves oxygen-rich blood from the gills to the other tissues of the body.
- There, further short-range exchange of gases, nutrients, and wastes occurs.

#### Concept 42.1 Circulatory systems enable exchange at a distance

- Diffusion alone is not adequate for transporting substances over long distances in animals—for example, for moving glucose from the digestive tract and oxygen from the lungs to the brain of a mammal.
- Diffusion is insufficient over distances of more than a few millimeters because the time it takes for a substance to diffuse from one place to another is proportional to the *square* of the distance.
  - For example, if it takes 1 second for a given quantity of glucose to diffuse 100  $\mu\text{m}$ , it will take 100 seconds for it to diffuse 1 mm and almost 3 hours to diffuse 1 cm.
- The relationship between distance and diffusion time places a major constraint on the body plan of animals.
- One solution is a body size and shape that bring many or all cells in direct contact with the environment.

- Such a body plan is found in invertebrates such as cnidarians and flatworms.
- All other animals have a circulatory system that brings fluid from the site of exchange to all the other cells of the body.

***Some invertebrates have a gastrovascular cavity for internal transport.***

- The body plan of hydras and other cnidarians makes a circulatory system unnecessary.
- Instead, a central gastrovascular cavity with a single opening serves both in digestion and in the distribution of substances throughout the body.
- The body wall is only two cells thick. The products of digestion in the gastrovascular cavity are directly available to the cells of the inner layer, and it is only a short distance to diffuse to the cells of the outer layer.
- The branches of the gastrovascular cavity extend even into the hydra's tentacles.
- Planarians and other flatworms also lack a circulatory system.
  - These animals have gastrovascular cavities that exchange materials with the environment through a single opening.
  - The flat shape of the body is particularly advantageous for exchange with the environment, optimizing exchange by diffusion by increasing the surface area and minimizing the distance.
- Circulatory systems have three basic components: a circulatory fluid, a set of interconnecting tubes, and a muscular pump (the **heart**).
- The heart powers circulation by using metabolic power to elevate the hydrostatic pressure of the circulatory fluid, which flows down a pressure gradient through a circuit of vessels back to the heart.
- By transporting fluid throughout the body, the circulatory system connects the aqueous environment of the body cells to the organs that exchange gases, absorb nutrients, and dispose of wastes.

***There are two types of circulatory systems: open and closed.***

- In arthropods and most molluscs, the circulatory fluid bathes organs directly in an **open circulatory system**.
  - There is no distinction between blood and *interstitial fluid*, collectively called **hemolymph**.
- One or more hearts pump the hemolymph into interconnected sinuses surrounding the organs, allowing exchange between the hemolymph and body cells.
  - When the heart contracts, it pumps hemolymph through vessels out into sinuses.
  - When the heart relaxes, it draws hemolymph into the circulatory system through pores, which are equipped with valves that close when the heart contracts.
  - Body movements that squeeze the sinuses help circulate the hemolymph.
- In a **closed circulatory system**, found in annelids, cephalopods, and vertebrates, blood is confined to vessels and is different from interstitial fluid.
  - One or more hearts pump blood into large vessels that branch into smaller ones that infiltrate the organs.
  - Materials are exchanged by diffusion between the blood and the interstitial fluid bathing the cells.

- The fact that open and closed circulatory systems are both widespread in the animal kingdom suggests that both systems offer advantages.
- What are the advantages of open circulatory systems?
  - Because fluids do not compress readily, open systems are efficient in animals in which a rigid body covering deflects circulating fluid back toward the heart.
  - The lower hydrostatic pressures associated with open circulatory systems make them less costly than closed circulatory systems.
    - In spiders, the hydrostatic pressure generated by the open circulatory system provides the force used to extend the legs.
- Why are closed circulatory systems advantageous?
  - Closed systems, with their higher blood pressure, are more effective at transporting circulatory fluids to meet the high metabolic demands of the tissues and cells of larger and more active animals.
    - Among the molluscs, only the large and active squid and octopuses have closed circulatory systems.

***Vertebrate phylogeny is reflected in adaptations of the cardiovascular system.***

- The closed circulatory system of humans and other vertebrates is often called the **cardiovascular system**.
- Blood circulates to and from the heart through a series of vessels.
  - The total length of blood vessels in an average adult human is twice Earth's circumference at the equator.
- Arteries, veins, and capillaries are the three main kinds of blood vessels.
- All **arteries** carry blood away from the heart toward organs. Within the organs, arteries branch into **arterioles** and then into capillaries.
  - **Capillaries** are microscopic vessels with thin, porous walls.
  - Networks called **capillary beds** infiltrate each tissue, passing within a few cell diameters of every cell in the body.
- Chemicals, including dissolved gases, are exchanged across the thin walls of the capillaries between the blood and the interstitial fluid.
- At their “downstream” end, capillaries converge into **venules** and venules converge into **veins**, which return blood to the heart.
- Arteries and veins are distinguished by the *direction* in which they carry blood, not by the oxygen content or other characteristics of the blood they carry.
- Arteries carry blood from the heart *toward* capillaries, and veins return blood to the heart *from* capillaries.
- An important exception is portal veins, which carry blood between pairs of capillary beds outside of the heart and lungs.
  - For example, the hepatic portal vein carries blood from capillary beds in the digestive system to capillary beds in the liver.
- The heart consists of one atrium or two **atria**, the chambers that receive blood returning to the heart, and one or two **ventricles**, the chambers that pump blood out of the heart.
- A fish heart has two main chambers, one atrium and one ventricle.

- In fish, the blood passes through the heart once in each complete circuit in an arrangement called **single circulation**.
  - Blood is pumped from the ventricle to the gills, where it picks up oxygen and disposes of carbon dioxide across the capillary walls.
  - The gill capillaries converge into a vessel that carries oxygenated blood to capillary beds in the other organs and back via veins to the atrium of the heart.
- In fish, blood must pass through two capillary beds, gill capillaries and systemic capillaries, before returning to the heart.
  - When blood flows through a capillary bed, blood pressure—the motive force for circulation—drops substantially.
  - Therefore, oxygen-rich blood leaving the gills flows to the systemic circulation under low pressure, although the process is aided by body movements during swimming.
  - This slowdown constrains the delivery of oxygen to body tissues and, hence, the maximum aerobic metabolic rate of fishes.
- The circulatory systems of amphibians, reptiles, and mammals have two distinct circuits, a system called **double circulation**.
- The pumps for the two circuits serve different tissues but are combined in a single organ, the heart.
- The right side of the heart delivers oxygen-poor blood to the capillary beds of the gas exchange tissues, where there is a net diffusion of oxygen into and carbon dioxide out of the blood.
  - This part of the circulation is called a **pulmonary circuit** if the capillary beds are all in the lungs and a **pulmocutaneous circuit** if the capillaries are in both the lungs and the skin.
- Oxygen-rich blood enters the second pump, the left side of the heart.
  - Contraction of the heart pumps this blood into the **systemic circuit**, which supplies the capillary beds in all body organs and tissues.
- Double circulation provides a vigorous flow of blood to the brain, muscles, and other organs because the blood is pumped a second time after it loses pressure in the capillary beds of the lung or skin.

### **Concept 42.2 Coordinated cycles of heart contraction drive double circulation in mammals**

- To trace the double circulation pattern of the mammalian cardiovascular system, we'll start with the pulmonary (lung) circuit, which carries blood from the heart to the lungs and back again.
- The right ventricle pumps blood to the lungs via the pulmonary arteries.
- As blood flows through capillary beds in the right and left lungs, it loads O<sub>2</sub> and unloads CO<sub>2</sub>.
- Oxygen-rich blood returns from the lungs via the pulmonary veins to the left atrium of the heart.
- Next, the oxygen-rich blood flows to the left ventricle, as the ventricle opens and the atrium contracts.
- The left ventricle pumps oxygen-rich blood out to the body tissues through the systemic circuit.

- Blood leaves the left ventricle via the aorta, which conveys blood to arteries leading throughout the body.
  - The first branches from the aorta are the coronary arteries, which supply blood to the heart muscle.
  - The next branches lead to capillary beds in the head and arms.
  - The aorta continues in a posterior direction, supplying oxygen-rich blood to arteries leading to arterioles and capillary beds in the abdominal organs and legs.
  - Within the capillaries, blood gives up much of its O<sub>2</sub> and picks up CO<sub>2</sub> produced by cellular respiration.
- Venous return to the right side of the heart begins as capillaries rejoin to form venules and then veins.
  - Oxygen-poor blood from the head, neck, and forelimbs is channeled into a large vein called the superior vena cava.
  - Another large vein called the inferior vena cava drains blood from the trunk and hind limbs.
  - The two venae cavae empty their blood into the right atrium, from which the oxygen-poor blood flows into the right ventricle.
- The mammalian heart is located beneath the breastbone (sternum) and consists of mostly cardiac muscle.
- The two atria have relatively thin walls and function as collection chambers for blood returning to the heart from the lungs or other body tissues.
- Most of the blood flows into the ventricles as they relax, with atrial contraction completing the transfer.
- The ventricles have thicker walls and contract much more strongly than the atria, especially the left ventricle, which pumps blood into the systemic circuit.
- A **cardiac cycle** is one complete sequence of pumping, as the heart contracts, and filling, as the heart relaxes and its chambers fill with blood.
  - The contraction phase is called **systole**, and the relaxation phase is called **diastole**.
- **Cardiac output** is the volume of blood pumped per minute, and it depends on two factors: the rate of contraction or **heart rate** (number of beats per second) and the **stroke volume**, the amount of blood pumped by the left ventricle in each contraction.
  - The average stroke volume for a human is about 70 mL.
  - A typical resting heart rate is about 72 beats per minute.
  - The typical resting cardiac output, about 5 L/min, is equivalent to the total volume of blood in the human body.
  - Cardiac output can increase about fivefold during heavy exercise.
- Four valves in the heart, each consisting of flaps of connective tissue, prevent backflow and keep blood moving in the correct direction.
  - Between each atrium and ventricle is an **atrioventricular (AV) valve**, which keeps blood from flowing back into the atria when the ventricles contract.
  - The AV valves are anchored by strong fibers that prevent them from turning inside out.
  - Two sets of **semilunar valves**, one between the left ventricle and the aorta and the other between the right ventricle and the pulmonary artery, prevent backflow from these vessels into the ventricles while they are relaxing.
- The heart sounds we can hear with a stethoscope are caused by the closing of the valves.

- The sound pattern is “lub-dup, lub-dup, lub-dup.”
- The first heart sound (“lub”) is created by the recoil of blood against the closed AV valves.
- The second sound (“dup”) is the recoil of blood against the shut semilunar valves.
- A defect in one or more of the valves causes a **heart murmur**, which may be detectable as a hissing sound when a stream of blood squirts backward through a valve.
  - Some people are born with heart murmurs.
  - Other murmurs are due to damage to the valves by infection.
  - Most heart murmurs do not reduce the efficiency of blood flow enough to warrant surgery.

***The heartbeat originates in the heart itself.***

- Because the timely delivery of oxygen to the body’s organs is critical for survival, several mechanisms have evolved to assure continuity and control of the heartbeat.
- Some cardiac muscle cells are autorhythmic, meaning they contract and relax without any signal from the nervous system.
- Each cardiac cell has its own intrinsic contraction rhythm.
- These cardiac cells are synchronized by the **sinoatrial (SA) node**, or *pacemaker*, which sets the rate and timing at which all cardiac muscle cells contract.
  - The SA node is located in the wall of the right atrium.
  - In contrast, the pacemakers of some arthropod hearts are located outside the heart.
  - The SA node generates electrical impulses much like those produced by nerve cells.
- Cardiac muscle cells are electrically coupled through gap junctions, allowing impulses from the SA node to spread rapidly within heart tissue.
  - The impulses also generate currents in body fluids that are conducted to the skin. These currents can be detected by an **electrocardiogram (ECG or EKG)**.
- Impulses from the SA node spread rapidly through the wall of the atria, making them contract in unison.
- The impulses from the SA node reach additional autorhythmic cells at the **atrioventricular (AV) node**, the relay point to the ventricle.
- The impulses are delayed for 0.1 second before spreading to the walls of the ventricle, allowing the atria to empty completely before the ventricles contract.
- Specialized muscle fibers called bundle branches and Purkinje fibers conduct the signals from the AV node throughout the ventricular walls.
- The ventricles are stimulated to contract from the apex toward the atria, driving blood into the large arteries.
- Although the SA node sets the tempo for the entire heart, it is influenced by a variety of physiological cues.
- Two portions of the nervous system, the sympathetic and parasympathetic divisions, affect the heart rate, with one division speeding up the pacemaker and the other set slowing it down.
  - Heart rate is a compromise regulated by the opposing actions of these two sets of nerves.
- The pacemaker is also influenced by hormones.
  - For example, epinephrine from the adrenal glands increases heart rate.
- A third type of input that affects the pacemaker is body temperature.

### **Concept 42.3 Patterns of blood pressure and flow reflect the structure and arrangement of blood vessels**

- Lining the lumen of all blood vessels, including capillaries, is an **endothelium**, a single layer of flattened cells that minimizes resistance to blood flow.
  - The smooth surface of the endothelium minimizes resistance to blood flow.
- Structural differences correlate with the different functions of capillaries, arteries, and veins.
- Capillaries have a diameter only slightly greater than that of a red blood cell.
- The very thin walls of capillaries consist of just endothelium and its basal lamina, thus enhancing exchange.
- Both arteries and veins have two layers of tissue surrounding the endothelium: an outer layer of connective tissue containing elastic fibers that allow the vessel to stretch and recoil, and a middle layer containing smooth muscle and more elastic fibers.
- Artery walls are three times as thick as the walls of veins.
- The thicker walls of arteries provide strength to accommodate blood pumped rapidly and at high pressure by the heart.
- The elasticity (elastic recoil) of artery walls helps maintain blood pressure even when the heart relaxes.
- Impulses from the nervous system and hormones circulating in the blood act on smooth muscle in arteries, controlling blood flow to different parts of the body.
- The thinner-walled veins convey blood back to the heart at low velocity and pressure.
  - Blood flows through the veins mainly because skeletal muscle contractions squeeze blood in veins.
  - Within larger veins, flaps of tissues act as one-way valves that allow blood to flow only toward the heart.

#### ***Physical laws governing the movement of fluids through pipes affect blood flow and blood pressure.***

- The observation that blood travels more than a thousand times faster in the aorta than in capillaries follows from the laws describing fluid movement through pipes.
- If a pipe's diameter changes over its length, a fluid will flow through narrower segments faster than it flows through wider segments because the volume of flow per second must be constant throughout the entire pipe.
- Each artery conveys blood to such an enormous number of capillaries that the *total* cross-sectional area is much greater in capillary beds than in any other part of the circulatory system.
  - Blood flows at speeds of about 0.1 cm/sec in the capillaries and 48 cm/sec in the aorta.
- The resulting slow flow rate and thin capillary walls promote the exchange of substances between the blood and interstitial fluid by providing time for exchange to occur.
- As blood leaves the capillary beds and passes to venules and veins, it speeds up again as a result of the reduction in *total* cross-sectional area.
- Blood, like all fluids, flows from areas of high pressure to areas of lower pressure.

- Blood pressure, the hydrostatic force that blood exerts against vessel walls, is much higher in arteries than in veins and is highest in arteries when the heart contracts during ventricular systole.
- The thick and elastic walls of arteries play a critical role in maintaining blood pressure and hence blood flow.
- In contrast, the blood encounters resistance as it passes through the tiny arterioles and capillaries. This resistance dissipates much of the pressure generated by the heart.
- Arteriole blood pressure is highest when the heart contracts during ventricular systole, producing **systolic pressure**.
- When you take your **pulse** by placing your fingers on your wrist, you can feel an artery bulge with each heartbeat.
  - The surge of pressure is partly due to the narrow openings of arterioles impeding the exit of blood from the arteries, the peripheral resistance.
  - Thus, when the heart contracts, blood enters the arteries faster than it can leave, and the vessels stretch from the pressure.
- The elastic walls of the arteries snap back during diastole, but the heart contracts again before enough blood has flowed into the arterioles to completely relieve pressure in the arteries.
- As a consequence of the elastic arteries working against peripheral resistance, there is substantial **diastolic pressure** even during diastole.
- Before blood has flowed from arteries into arterioles, the heart contracts again, maintaining arterial pressure.
  - As a result, blood flows into arterioles and capillaries continuously.
- Physical or emotional stress can trigger nervous and hormonal responses that cause smooth muscles in arteriole walls to contract, a process called **vasoconstriction**.
- Contraction of smooth muscles in the walls of arterioles constricts these vessels, increasing blood pressure upstream in the arteries.
- Researchers have identified a gas, nitric oxide (NO), as a major inducer of vasodilation and a peptide, endothelin, as the most potent inducer of vasoconstriction.
  - Both NO and endothelin are produced in blood vessels in response to cues from the nervous and endocrine systems.
  - Each molecule binds to a specific receptor, activating a signal transduction pathway that alters smooth muscle contraction and thus changes blood vessel diameter.
- Vasoconstriction and vasodilation may be coupled to changes in cardiac output that affect blood pressure.
- This coordination of regulatory mechanisms maintains adequate blood flow as the demands on the circulatory system change.
  - For example, during strenuous exercise, arterioles in the working muscles dilate, admitting a greater flow of oxygen-rich blood to the muscles and decreasing peripheral resistance.
  - At the same time, cardiac output increases, maintaining blood pressure and supporting the necessary increase in blood flow.
- The arterial blood pressure of a healthy human oscillates between about 120 mm Hg at systole and 70 mm Hg at diastole.
- In large land animals, blood pressure is also affected by gravity.

- When a person stands up, an extra 27 mm of Hg pressure is required to move blood from the heart to the brain.
- If blood flow to the brain is inadequate, fainting may result. Fainting places the head at the level of the heart, thus reducing the need for additional blood pressure.
- A giraffe requires a systolic pressure near the heart of over 250 mm Hg.
  - One-way valves and sinuses, as well as feedback mechanisms that reduce cardiac output, prevent this high pressure from damaging the giraffe's brain when it puts its head down.
- Long-necked dinosaurs would have required even higher systolic pressure—nearly 760 mm Hg—to pump blood to their brains when their heads were fully raised.
  - Such blood pressures seem unlikely; it is more likely that these dinosaurs fed close to the ground rather than raising their heads to feed on high foliage.
- By the time blood reaches the veins, its pressure is not affected much by the action of the heart.
  - The resistance of tiny arterioles and capillaries has dissipated the pressure generated by the pumping heart.
- Rhythmic contractions of smooth muscles in the walls of veins and venules account for some movement of blood.
- More importantly, the activity of skeletal muscles during exercise squeezes blood through the veins.
  - One-way valves built into veins ensure that blood flows toward the heart.
- In addition, inhalation changes the pressure in the thoracic (chest) cavity, causing the venae cavae and other large veins near the heart to expand and fill with blood.
- In rare cases, runners may risk heart failure if they stop vigorous exercise abruptly.
  - Venous return to the heart is reduced when leg muscle contraction stops.
  - If the heart continues to beat rapidly, it may have inadequate blood flow.
  - Strenuous exercise should be followed by moderate activity, a “cool-down” period.

***Transfer of substances between the blood and the interstitial fluid occurs across the thin walls of capillaries.***

- At any given time, only about 5–10% of the body's capillaries have blood flowing through them.
  - Capillaries in the brain, heart, kidneys, and liver are usually filled to capacity, but in many other sites, the blood supply varies over time as blood is diverted.
  - For example, after a meal, blood supply to the digestive tract increases.
  - During strenuous exercise, blood is diverted from the digestive tract and supplied to skeletal muscles.
- Two mechanisms, both dependent on smooth muscles controlled by nerve signals and hormones, regulate the distribution of blood in capillary beds.
- In one mechanism, contraction of the smooth muscle layer in the wall of an arteriole constricts the vessel, decreasing blood flow through it to a capillary bed.
  - When the muscle layer relaxes, the arteriole dilates, allowing blood to enter the capillaries.
- In the other mechanism, rings of smooth muscles, called precapillary sphincters because they are located at the entrance to capillary beds, control the flow of blood between arterioles and venules.

- Nerve impulses, hormones, and local chemicals regulate blood flow.
  - For example, release of histamine at a wound site causes smooth muscle relaxation.
  - This relaxation increases blood flow to bring disease-fighting white blood cells to the wound.
- The exchange of substances between the blood and the interstitial fluid that bathes the cells takes place across the thin endothelial walls of the capillaries.
- Some substances are carried across endothelial cells in vesicles that form by endocytosis on one side and then release their contents by exocytosis on the other side.
- Small molecules such as oxygen and carbon dioxide simply diffuse between the blood and the interstitial fluid across cells or through openings between adjoining cells.
- Transport through these openings allows bulk flow driven by blood pressure.
- Two opposing forces control the movement of fluid between the capillaries and the surrounding tissues.
  - Blood pressure within the capillary drives fluid, containing water and small solutes, out of the capillary.
  - Blood cells and most blood proteins are too large and remain in the capillaries.
- The dissolved proteins that remain in the blood are responsible for the blood's *osmotic pressure*, which opposes fluid movement out of the capillaries.
- On average, blood pressure is greater than the opposing forces, leading to a net loss of fluid from capillaries.
  - The net loss is generally greatest at the arterial end of these vessels, where blood pressure is highest.

***The lymphatic system returns fluid to the blood and aids in body defense.***

- Fluids and some blood proteins that leak from the capillaries into the interstitial fluid are returned to the blood via the **lymphatic system**.
- Fluid enters the lymphatic system by diffusing into tiny lymph capillaries intermingled among the capillaries of the cardiovascular system.
- Once inside the lymphatic system, the fluid is called **lymph**, with a composition similar to that of the interstitial fluid.
- The lymphatic system drains into the large veins of the circulatory system at the base of the neck.
- Lymph vessels, like veins, have valves that prevent the backflow of fluid toward the capillaries.
- Rhythmic contraction of the vessel walls helps draw fluid into lymphatic capillaries.
- Like veins, lymph vessels depend mainly on the movement of skeletal muscle to squeeze fluid toward the heart.
- Disruptions in the movement of lymph cause edema, a swelling due to fluid accumulation in tissues.
  - Certain parasitic worms can lodge in lymph vessels to produce elephantiasis, a condition characterized by extremely swollen limbs.
- Along lymph vessels are organs called **lymph nodes**.
- The lymph nodes filter the lymph and house cells that attack viruses and bacteria.

- Inside a lymph node is a honeycomb of connective tissue with spaces filled with white blood cells specialized for defense.
- When the body is fighting an infection, these cells multiply, and the lymph nodes become swollen.
- The lymphatic system also plays a role in harmful immune responses such as those causing asthma.

### **Concept 42.4 Blood components contribute to exchange, transport, defense, and disease**

- In invertebrates with open circulation, blood (hemolymph) is not different from interstitial fluid.
- In the closed circulatory systems of vertebrates, blood is a specialized connective tissue consisting of several kinds of cells suspended in a liquid matrix called **plasma**.
- Blood includes cellular elements (cells and cell fragments), which make up about 45% of the blood volume, and transparent, straw-colored plasma.
  - Blood plasma is about 90% water. Dissolved in the plasma are a variety of ions, sometimes referred to as blood electrolytes.
- Blood electrolytes are important in maintaining the osmotic balance of the blood and help buffer the blood at a pH of about 7.4.
- The proper functioning of muscles and nerves depends on the concentrations of key ions in the interstitial fluid, which reflects concentrations in the plasma.
- Plasma electrolytes must be kept within a narrow concentration range.

#### ***Blood's plasma proteins have many functions.***

- Collectively, blood's plasma proteins act as buffers against pH changes, help maintain osmotic balance, and contribute to the blood's viscosity.
- Some specific proteins transport otherwise insoluble lipids in the blood.
- Other proteins—the immunoglobulins, or antibodies—help combat viruses and other foreign agents that invade the body.
- A group of plasma proteins helps plug leaks when blood vessels are injured.
  - Blood plasma with such clotting factors removed is called *serum*.
- Plasma carries a wide variety of substances in transit from one part of the body to another, including nutrients, metabolic wastes, respiratory gases, and hormones.
  - Blood plasma and interstitial fluid are similar in composition, although plasma has a much higher protein concentration.
- Suspended in blood plasma are two classes of cells: red blood cells, which transport oxygen, and white blood cells, which function in defense.
- A third cellular element is **platelets**, fragments of cells that are involved in clotting.

#### ***Erythrocytes carry oxygen in the blood.***

- Red blood cells, or **erythrocytes**, are by far the most numerous blood cells.
  - Each microliter of blood contains 5 to 6 million red blood cells.
  - There are about 25 trillion red blood cells in the human body's 5 L of blood.

- The main function of red blood cells, oxygen transport, depends on rapid diffusion of oxygen across the red blood cell's plasma membranes.
  - Human erythrocytes are small biconcave disks, which present a large surface area.
- Mammalian erythrocytes lack nuclei, an unusual characteristic that leaves more space in the tiny cells for **hemoglobin**, the iron-containing protein that transports oxygen.
- Red blood cells also lack mitochondria and generate ATP exclusively by anaerobic metabolism.
- An erythrocyte contains about 250 million molecules of hemoglobin.
- Each hemoglobin molecule binds up to four molecules of O<sub>2</sub>, so one erythrocyte can transport a billion O<sub>2</sub> molecules.
- As erythrocytes pass through the capillary beds of lungs, gills, or other respiratory organs, oxygen diffuses into the erythrocytes and hemoglobin binds O<sub>2</sub>.
- In the systemic capillaries, hemoglobin unloads oxygen, which then diffuses into body cells.
- In **sickle-cell disease**, an abnormal form of hemoglobin (Hb<sup>S</sup>) polymerizes into aggregates.
  - Because the concentration of hemoglobin in erythrocytes is so high, these aggregates are large enough to distort the erythrocyte into an elongated, curved shape that resembles a sickle.
- Sickle-cell disease significantly impairs the function of the circulatory system.
  - Sickled cells often lodge in arterioles and capillaries, preventing delivery of O<sub>2</sub> and nutrients and removal of CO<sub>2</sub> and wastes.
  - Blood vessel blockage and resulting organ swelling often also result in severe pain.
  - In addition, sickled cells frequently rupture, reducing the number of red blood cells available for transporting O<sub>2</sub>.
  - The average life span of a sickled erythrocyte is only 20 days—one-sixth that of a normal erythrocyte.
  - The rate of erythrocyte loss outstrips the replacement capacity of the bone marrow.
- Short-term therapy includes replacement of erythrocytes by blood transfusion; long-term treatments are generally aimed at inhibiting aggregation of Hb<sup>S</sup>.

***Leukocytes fight infections.***

- There are five major types of white blood cells, or **leukocytes**. Their collective function is to fight infection.
- Some leukocytes are phagocytic, engulfing and digesting microbes and debris from dead body cells.
- Other leukocytes develop into specialized B cells and T cells, which produce immune responses against foreign substances.
- 1 μL of human blood normally has about 5,000 to 10,000 leukocytes, but their numbers increase temporarily when the body is fighting infection.
- Leukocytes spend most of their time outside the circulatory system, patrolling through interstitial fluid and the lymphatic system, fighting pathogens.

***Platelets serve structural and molecular functions in blood clotting.***

- Platelets are fragments of cells about 2 to 3 μm in diameter. They have no nuclei and originate as pinched-off cytoplasmic fragments of large cells in the bone marrow.
- Blood contains a self-sealing material that plugs leaks from cuts and scrapes.

- The clotting process begins when a blood vessel wall is damaged, exposing proteins that attract platelets and initiate coagulation of the liquid components of blood into a solid clot.
- The sealant circulates in an inactive form called *fibrinogen*.
- In response to a broken blood vessel, platelets release clotting factors that trigger reactions leading to the formation of *thrombin*, an enzyme that converts fibrinogen to *fibrin*.
- Fibrin aggregates into threads that form the framework of the clot.
- Thrombin also activates a factor that catalyzes the formation of more thrombin, driving clotting to completion through positive feedback.
- An inherited defect in any step of the clotting process causes hemophilia, a disease characterized by excessive bleeding from even minor cuts and bruises.
- Anticlotting factors in the blood normally prevent spontaneous clotting in the absence of injury.
  - Sometimes a clot called a **thrombus** forms within a blood vessel, blocking the flow of blood.

***Stem cells replace cellular elements.***

- Erythrocytes, leukocytes, and platelets all develop from a single population of cells, multipotent **stem cells** in the red marrow of bones, particularly the ribs, vertebrae, breastbone, and pelvis.
  - Multipotent means that these cells have the potential to differentiate into multiple types of blood cells, including myeloid and lymphoid cell lineages.
  - When a stem cell divides, one daughter cell remains a stem cell while the other becomes specialized.
- Erythrocytes usually circulate for about 120 days before being replaced.
  - The old cells are consumed by phagocytotic cells in the liver and spleen.
  - Many of the iron atoms derived from hemoglobin in old red blood cells are incorporated into new hemoglobin molecules.
- A negative-feedback mechanism, sensitive to the amount of oxygen reaching the tissues via the blood, controls erythrocyte production.
- If the tissues do not produce enough oxygen, the kidney synthesizes and secretes a hormone called **erythropoietin (EPO)**, which stimulates the production of erythrocytes.
- If the blood is delivering more oxygen than the tissues can use, the level of EPO is reduced, and erythrocyte production slows.
- Physicians use synthetic EPO to treat people who have anemia, a condition of low hemoglobin levels.
- Some athletes abuse EPO by injecting themselves with the drug to increase their erythrocyte levels.
  - This practice, known as blood doping, is banned by the International Olympic Committee and other sports federations.

***Cardiovascular diseases are the leading cause of death in the United States and xother developed nations.***

- More than half of the deaths in the United States are caused by cardiovascular diseases—diseases of the heart and blood vessels.
- Cholesterol travels in blood plasma mainly in the form of particles made up of thousands of cholesterol molecules or other lipids bound to protein.

- **Low-density lipoproteins (LDLs)** deliver cholesterol to cells for membrane production.
- **High-density lipoproteins (HDLs)** scavenge excess cholesterol for return to the liver.
  - Individuals with a high LDL/HDL ratio are at increased risk of heart disease.
- *Inflammation*, the body's reaction to injury, plays a central role in cardiovascular disease.
  - Tissue damage leads to recruitment of two types of circulating immune cells, macrophages and leukocytes.
  - Signals released by these cells trigger a flow of fluid out of blood vessels at the site of injury, resulting in the tissue-swelling characteristic of inflammation.
  - This swelling can significantly disrupt circulatory function.
- **Atherosclerosis** is hardening of the arteries caused by the accumulation of fatty deposits.
  - Healthy arteries have smooth inner linings that permit unimpeded blood flow.
  - Damage or infection can roughen the lining and lead to inflammation.
  - Leukocytes are attracted to the damaged lining and begin to take up lipids, including cholesterol.
  - A fatty deposit called a plaque develops in the inner wall of the arteries, causing the wall to become thick and stiff.
- As atherosclerosis progresses, coronary arteries become more and more clogged and the threat of heart attack or stroke becomes much greater.
- A **heart attack**, also called a *myocardial infarction*, is the damage or death of cardiac muscle tissue resulting from the blockage of one or more coronary arteries.
  - The coronary arteries are small in diameter and vulnerable to obstruction.
  - Such blockage can destroy cardiac muscle quickly because the beating heart cannot survive without oxygen.
  - Even if the heart stops breathing, the victim may survive if a heartbeat is restored by cardiopulmonary resuscitation (CPR) within a few minutes of the attack.
- A **stroke** is the death of nervous tissue in the brain due to a lack of oxygen.
  - Strokes usually result from rupture or blockage of arteries in the head.
  - The effects of a stroke and the individual's chance of survival depend on the extent and location of the damaged brain tissue.
- There may be warnings of the impending threat from atherosclerosis.
  - For example, if a coronary artery is partially blocked, a person may feel occasional chest pains, a condition known as angina pectoris.
  - Angina pectoris is a signal that part of the heart is not receiving enough blood, especially when the heart is laboring because of physical or emotional stress.

***The tendency to develop cardiovascular disease is inherited but also influenced by lifestyle.***

- Smoking and consumption of certain processed vegetable oils called trans fats increase the ratio of LDL to HDL, raising the risk of cardiovascular disease.
  - In contrast, exercise decreases the LDL/HDL ratio.
- Many individuals at high risk of cardiovascular disease are now treated with drugs called statins, which lower LDL levels and reduce the risk of heart attacks.
- Aspirin, which inhibits the inflammatory response, helps prevent the recurrence of heart attacks and stroke.

- C-reactive protein (CRP) is produced by the liver and found in the blood during episodes of acute inflammation.
  - Like high levels of LDL cholesterol, the presence of significant amounts of CRP in blood is a useful predictor of risk for cardiovascular disease.
- **Hypertension** (high blood pressure) is a proven contributor to heart attack and stroke.
  - According to one hypothesis, high blood pressure causes chronic damage to the endothelium that lines the arteries, promoting plaque formation.
  - A systolic pressure above 140 mm Hg or a diastolic pressure above 90 mm Hg is cause for concern.
  - Hypertension is simple to diagnose and can usually be controlled by diet, exercise, medication, or a combination of these.

### **Concept 42.5 Gas exchange occurs across specialized respiratory surfaces**

- **Gas exchange** is the uptake of molecular oxygen (O<sub>2</sub>) from the environment and the discharge of carbon dioxide (CO<sub>2</sub>) to the environment.
  - This process is different from the production of ATP in cellular respiration.
- **Partial pressure** is the pressure exerted by a particular gas in a mixture of gases.
  - At sea level, the atmosphere exerts a total pressure of 760 mm Hg.
  - Since the atmosphere is 21% O<sub>2</sub> by volume, the *partial pressure* of oxygen is  $0.21 \times 760$ , or about 160 mm Hg.
  - P<sub>CO<sub>2</sub></sub>, the partial pressure of CO<sub>2</sub>, is only 0.29 mm Hg.
- Partial pressure can also be calculated for a gas dissolved in liquid.
  - When water is exposed to air, equilibrium is reached in which the partial pressure of each gas in solution equals the partial pressure of that gas in the air.
  - However, the *concentrations* of the gas in air and in water may differ, based on the solubility of the gas in the two media.
- A gas always diffuses from a region of higher partial pressure to a region of lower partial pressure.
- The conditions for gas exchange vary depending on whether the source of oxygen, the respiratory medium, is air or water.
- Compared to water, air is much less dense and viscous. As a result, breathing in air is relatively easy.
- Gas exchange with water as the respiratory medium is much more demanding.
  - Dissolved oxygen levels in lakes, oceans, and other bodies of water vary considerably, but are always much lower than the levels in an equivalent volume of air.
  - The warmer and saltier the water, the less dissolved O<sub>2</sub> it can hold.
  - Water's lower O<sub>2</sub> content, greater density, and greater viscosity mean that aquatic animals must expend considerable energy to carry out gas exchange.

#### ***Most animals have specialized respiratory surfaces.***

- The part of an animal where gases are exchanged with the environment is the respiratory surface.

- Respiratory surfaces are always moist. Gases must dissolve in water before diffusing across respiratory surfaces.
- Movements of CO<sub>2</sub> and O<sub>2</sub> across the respiratory surface occur entirely by diffusion.
- The rate of diffusion is proportional to the surface area across which diffusion occurs, and inversely proportional to the square of the distance through which molecules must move.
  - Therefore, respiratory surfaces tend to be thin and have large areas, maximizing the rate of gas exchange.
- In some relatively simple animals, such as sponges, cnidarians, and flatworms, the plasma membrane of every cell in the body is close enough to the outside environment for gases to diffuse in and out.
  - In most animals, the bulk of the body lacks direct access to the respiratory medium.
- The respiratory surface in these animals is a thin, moist epithelium that constitutes a respiratory organ.
- Some animals, such as earthworms and some amphibians, use the skin as a respiratory organ.
  - Just below the moist skin is a dense net of capillaries.
  - Because the respiratory surface must be moist, however, the possible habitats of these animals are limited to water or damp places.
- For most animals, the general body surface is not sufficient to exchange gases for the entire body.
- The evolutionary solution is a respiratory organ that is extensively folded or branched, thus enlarging the surface area for gas exchange.
- Gills, tracheae, and lungs are the three most common respiratory organs.

***Gills are respiratory adaptations of most aquatic animals.***

- **Gills** are outfoldings of the body surface that are suspended in water.
  - The distribution of gills over the body can vary considerably.
  - The total surface area of gills is often much larger than the body surface.
- **Ventilation**, movement of the respiratory medium over the respiratory surface, maintains the partial pressure gradients of O<sub>2</sub> and CO<sub>2</sub> across the gill.
  - Gill-bearing animals move their gills through water or move water over their gills.
  - Crayfish and lobsters have paddle-like appendages that drive a current of water over their gills.
  - Octopuses and squids ventilate their gills by taking in and ejecting water, with the side benefit of locomotion by jet propulsion.
  - Fish gills are ventilated by a current of water that enters the mouth, passes through slits in the pharynx, flows over the gills, and exits the body.
- The arrangement of blood capillaries in fish gills and the flow of water over the gills allow **countercurrent exchange**, maximizing the efficiency of gas exchange.
  - Blood flows in the opposite direction to the water flowing over the gills.
  - As blood enters a gill capillary, it meets water that has already passed over the gill.
  - Although it has lost much of its dissolved oxygen, this water still has a higher P<sub>O<sub>2</sub></sub> than incoming blood, and oxygen is exchanged from water to blood.
  - As blood moves over the gill, its P<sub>O<sub>2</sub></sub> increases, but so does the P<sub>O<sub>2</sub></sub> of the water it encounters.

- A partial pressure gradient favors the diffusion of oxygen from water to blood along the length of the capillary.
- Countercurrent exchange mechanisms enable fishes to remove more than 80% of the oxygen dissolved in water.
- Gills are generally unsuited for an animal living on land.
  - An expansive surface of wet membrane exposed to air would lose too much water by evaporation.
  - In addition, the gills would collapse as their fine filaments, no longer supported by water, cling together, reducing the surface area for exchange.
- Most terrestrial animals have their respiratory surfaces within the body, opening to the atmosphere through narrow tubes.

***Tracheal systems and lungs are respiratory adaptations of terrestrial animals.***

- The **tracheal system** of insects is composed of air tubes that branch throughout the body.
- The largest tubes, called tracheae, open to the outside, and the finest branches extend to the surface of nearly every cell, where gas is exchanged by diffusion across the moist epithelium that lines the terminal ends.
- The open circulatory system does not participate in the transportation of oxygen and carbon dioxide.
- For a small insect, diffusion through the trachea brings in enough O<sub>2</sub> and removes enough CO<sub>2</sub> to support cellular respiration.
- Larger insects with higher energy demands ventilate their tracheal systems with rhythmic body movements that compress and expand the air tubes like bellows.
- An insect in flight has a very high metabolic rate, consuming 10 to 200 times more O<sub>2</sub> than it does at rest.
  - Alternating contraction and relaxation of flight muscles compress and expand the body, rapidly pumping air through the tracheal system.
  - The flight muscles are packed with mitochondria, and the tracheal tubes supply each with ample oxygen.
- Unlike branching tracheal systems, **lungs** are restricted to one location.
- Lungs are an infolding of the body surface, typically subdivided into numerous pockets.
- Because the respiratory surface of the lung is not in direct contact with all other parts of the body, the circulatory system transports gases between the lungs and the rest of the body.
- Lungs have evolved in animals with open circulatory systems, such as spiders and terrestrial snails, as well as vertebrates.
- Among the vertebrates, amphibians have relatively small lungs that do not provide a large surface area, and many lack lungs altogether.
  - Amphibians rely heavily on diffusion across other body surfaces, especially their moist skin, for gas exchange.
- In contrast, most reptiles (including all birds) and all mammals rely entirely on lungs for gas exchange.
  - Turtles may supplement lung breathing with gas exchange across moist epithelial surfaces in their mouth and anus.
  - Lungs and air breathing have evolved in a few fish species (lungfishes) as adaptations to living in oxygen-poor water or to spending time exposed to air.

- In mammals, a system of branching ducts conveys air to the lungs.
- Air enters through the nostrils and is then filtered by hairs, warmed and humidified, and sampled for odors as it flows through the nasal cavity.
- The nasal cavity leads to the pharynx, an intersection of the paths for air and food.
- When food is swallowed, the **larynx** moves upward and tips the epiglottis (the opening of the **trachea**, or windpipe) over the glottis.
- The rest of the time, the glottis is open, and air enters the upper part of the respiratory tract.
- From the larynx, air passes into the trachea, whose shape is maintained by rings of cartilage.
- The trachea forks into two **bronchi**, one leading into each lung.
- Cartilage reinforcing the walls of the larynx and the trachea keeps this part of the airway open.
- Within the larynx of most mammals, exhaled air rushes by a pair of elastic *vocal folds* (or *vocal cords*, in humans) producing sounds.
  - These sounds are high-pitched when the vocal cords are stretched tight and vibrate rapidly, and low-pitched when the cords are less tense and vibrate slowly.
- The trachea branches into two **bronchi**, one leading to each lung.
  - Within the lung, each bronchus branches repeatedly into finer and finer tubes, called **bronchioles**.
- The epithelium lining the major branches of the respiratory tree is covered by cilia and a thin film of mucus.
  - The mucus traps dust, pollen, and other particulate contaminants, and the beating cilia move the mucus upward to the pharynx, where it is swallowed.
  - This “mucus escalator” plays an important role in cleaning the respiratory system.
- At their tips, the tiniest bronchioles dead-end as a cluster of air sacs called **alveoli**.
- Gas exchange occurs across the thin epithelium of the lung’s millions of alveoli.
  - The alveoli have a total surface area of about 100 m<sup>2</sup> in humans, sufficient to carry out gas exchange for the whole body.
- Oxygen in the air entering the alveoli dissolves in the moist film and rapidly diffuses across the epithelium into a web of capillaries that surrounds each alveolus.
- Carbon dioxide diffuses in the opposite direction.
- White blood cells patrol the alveoli, engulfing foreign particles.
  - If too much particulate matter reaches the alveoli, these defenses can break down, leading to disease.
  - Cigarette smoke brings damaging particulates into the alveoli.
  - Coal miners exposed to large amounts of dust from rock may develop silicosis, a disabling, irreversible, and sometimes fatal lung disease.
- Specialized secretions called **surfactants** relieve the surface tension in the fluid that coats the surface of alveoli.
  - These secretions contain a mixture of phospholipids and proteins.
  - In their absence, the alveoli collapse, blocking the entry of air.
- Surfactants are formed in the lungs after 33 weeks of embryonic development.
  - Half of premature infants born before week 28 suffer *respiratory distress syndrome (RDS)* due partially to the lack of surfactants.

- Artificial surfactants are now used routinely to treat such preterm infants.

### **Concept 42.6 Breathing ventilates the lungs**

- The process of **breathing**, the alternate inhalation and exhalation of air, ventilates the lungs.
- A frog ventilates its lungs by **positive pressure breathing**.
  - During a breathing cycle, muscles lower the floor of the oral cavity, enlarging it and drawing in air through the nostrils.
  - With the nostrils and mouth closed, the floor of the oral cavity rises and air is forced down the trachea.
  - Elastic recoil of the lungs, together with compression of the muscular body wall, forces air back out of the lungs during exhalation.
  - For display purposes, male frogs may take in several gulps of air with releasing any.
- Ventilation is highly efficient in birds for two reasons.
  - When birds breathe, they pass air over the gas exchange surface in a single direction.
  - Incoming fresh air is not mixed with air that has already carried out gas exchange.
- Besides lungs, birds have eight or nine air sacs that do not function directly in gas exchange but act as bellows that keep air flowing through the lungs.
- Instead of alveoli, which are dead ends, the sites of gas exchange in bird lungs are tiny channels called *parabronchi*, through which air flows in one direction.
- In birds, the passage of air through the entire system—lungs and air sacs—requires two cycles of inhalation and exhalation.
- Mammals ventilate their lungs by **negative pressure breathing**.
  - Negative pressure breathing works like a suction pump, pulling air instead of pushing it into the lungs.
- Active expansion of the thoracic cavity by muscle contraction lowers the air pressure in the lungs below the pressure of the air outside the body.
  - These changes increase the lung volume, and as a result, the air pressure within the alveoli becomes lower than atmospheric pressure.
  - Because air flows from higher pressure to lower pressure, air rushes into the respiratory system.
- During exhalation, the muscles controlling the thoracic cavity relax, the volume of the cavity is reduced, and the increased air pressure within the alveoli forces air up the breathing tubes and out of the body through the nostrils.
- Inhalation is always active and requires work, whereas exhalation is usually passive.
- Lung volume increases as a result of the contraction of the rib muscles and the **diaphragm**, a sheet of skeletal muscle that forms the bottom wall of the chest cavity.
  - Contraction of the rib muscles expands the rib cage by pulling the ribs upward and the sternum outward.
  - At the same time, the diaphragm contracts and descends like a piston to increase the lung volume.
- Within the thoracic cavity, the lungs are enclosed by a double-walled pleural sac, with the inner layer of the sac adhering to the outside of the lungs and the outer layer adhering to the wall of the chest cavity.

- A thin space filled with fluid separates the two layers.
- Because of surface tension, the two layers behave like two plates of glass stuck together by the adhesion and cohesion of a film of water.
  - The layers can slide smoothly past each other, but they cannot be pulled apart easily.
  - As a result, the volumes of the thoracic cavity and the lungs change in unison.
- Actions of the rib muscles and diaphragm account for changes in lung volume during shallow breathing, when a mammal is at rest.
- During vigorous exercise, other muscles of the neck, back, and chest further increase ventilation volume by raising the rib cage even more.
- In some species, rhythmic movements during running cause visceral organs, including the stomach and liver, to slide forward and backward in the body cavity with each stride.
  - This piston-like pumping motion further increases ventilation volume.
- The volume of air an animal inhales and exhales with each breath is called the **tidal volume**.
  - The tidal volume averages about 500 mL in resting humans.
- The maximum tidal volume during forced breathing is the **vital capacity**, about 3.4 L and 4.8 L for college-age females and males, respectively.
- The lungs hold more air than the vital capacity, but some air, the **residual volume**, remains in the lungs because the alveoli do not completely collapse.
- Since the lungs do not completely empty with each breath, newly inhaled air is mixed with oxygen-depleted residual air.
  - Therefore, the maximum  $P_{O_2}$  in the alveoli is considerably less than in the atmosphere.
- In contrast, the system of ventilation in birds completely exchanges the air in the lungs with every two breaths.
  - As a result, the maximum  $P_{O_2}$  in the lungs is higher in birds than mammals.
- Partly because of this efficiency advantage, birds perform much better than mammals at high altitudes.
  - For example, while human mountaineers experience tremendous difficulty obtaining oxygen when climbing Earth's highest peaks, several species of birds easily fly over the same mountains during migration at altitudes of 9,000 m or higher.

***Control centers in the brain regulate the rate and depth of breathing.***

- Although we can voluntarily hold our breath or breathe faster and deeper, most of the time involuntary mechanisms regulate our breathing.
- This involuntary control ensures that gas exchange is coordinated with circulation and with metabolic demand.
- **Breathing control centers** are located in two brain regions: the medulla oblongata and the pons.
  - Control circuits in the medulla set the basic breathing rhythm, while neurons in the pons regulate its tempo.
- A negative-feedback mechanism via stretch receptors prevents our lungs from overexpanding by inhibiting the breathing center in the medulla.
- The medulla's control center uses the pH of the surrounding tissue to monitor  $CO_2$  level of the blood and regulate breathing activity appropriately.

- Blood CO<sub>2</sub> concentration is the main determinant of the pH of *cerebrospinal fluid* bathing the brain and spinal cord.
  - Carbon dioxide reacts with water to form carbonic acid, which dissociates into a bicarbonate ion and a hydrogen ion to lower the pH:  

$$\text{CO}_2 + \text{H}_2\text{O} \leftrightarrow \text{H}_2\text{CO}_3 \leftrightarrow \text{HCO}_3^- + \text{H}^+$$
- When the control center in the medulla registers a slight drop in pH, it increases the depth and rate of breathing, and the excess CO<sub>2</sub> is eliminated in exhaled air.
- Oxygen concentrations in the blood usually have little effect on the breathing control centers.
  - However, when the O<sub>2</sub> level is severely depressed—at high altitudes, for example—O<sub>2</sub> sensors in the aorta and carotid arteries in the neck send alarm signals to the breathing control centers, which respond by increasing breathing rate.
- The breathing center adjusts the rate and depth of breathing to meet the changing demands of the body.
  - However, breathing control is effective only if it is coordinated with control of the circulatory system, so that there is a good match between lung ventilation and the amount of blood flowing through alveolar capillaries.
  - For example, during exercise, increased cardiac output is matched to the increased breathing rate, which enhances O<sub>2</sub> uptake and CO<sub>2</sub> removal as blood flows through the lungs.

### **Concept 42.7 Adaptations for gas exchange include pigments that bind and transport gases**

- Blood flowing into the alveolar capillaries has a lower P<sub>O<sub>2</sub></sub> and a higher P<sub>CO<sub>2</sub></sub> than the air in the alveoli.
  - CO<sub>2</sub> diffuses down its partial pressure gradient from the blood to the air within the alveoli.
  - Oxygen in the alveolar air dissolves in the fluid that coats the epithelium and diffuses across the surface into the blood.
- By the time the blood leaves the lungs in the pulmonary veins, its P<sub>O<sub>2</sub></sub> has been raised and its P<sub>CO<sub>2</sub></sub> has been lowered.
- In the tissue capillaries, gradients of partial pressure favor the diffusion of O<sub>2</sub> out of the blood and CO<sub>2</sub> into the blood.
- Cellular respiration removes O<sub>2</sub> from and adds CO<sub>2</sub> to the interstitial fluid by diffusion.
- After the blood unloads O<sub>2</sub> and loads CO<sub>2</sub>, it is returned to the heart and pumped to the lungs again.
- The low solubility of O<sub>2</sub> in water (and blood) is a fundamental problem for animals that rely on circulatory systems for O<sub>2</sub> delivery.
  - For example, a person exercising consumes almost 2 L of O<sub>2</sub> per minute, but at normal body temperature and air pressure, only 4.5 mL of O<sub>2</sub> can dissolve in a liter of blood in the lungs.
  - If 80% of the dissolved O<sub>2</sub> were delivered to the tissues (an unrealistically high percentage), the heart would need to pump 555 L of blood per minute!
- In fact, most animals transport most of the O<sub>2</sub> bound to special proteins called **respiratory pigments**.

- Respiratory pigments, often contained within specialized cells, circulate with the blood or hemolymph.
- The presence of respiratory pigments increases the amount of oxygen that the blood can carry to about 200 mL of O<sub>2</sub> per liter of blood.
- For our exercising individual, the cardiac output would need to be a manageable 12.5 L of blood per minute to meet the oxygen demands of the systemic system.
- A diversity of respiratory pigments has evolved in various animal taxa to support their normal energy metabolism.
- The blue pigment *hemocyanin*, found in the hemolymph of arthropods and many molluscs, has copper as its oxygen-binding component, which colors the blood bluish.
- The respiratory pigment of almost all vertebrates is the protein hemoglobin, contained within erythrocytes.
  - Hemoglobin consists of four polypeptide subunits, each with a cofactor called a heme group that has an iron atom at its center.
  - Because iron actually binds the O<sub>2</sub>, each hemoglobin molecule can carry four molecules of O<sub>2</sub>.
- Like all respiratory pigments, hemoglobin binds oxygen reversibly, loading oxygen at the lungs or gills and unloading it in other parts of the body.
  - Loading and unloading depend on cooperation among the subunits of the hemoglobin molecule.
  - The binding of O<sub>2</sub> to one subunit induces the remaining subunits to change their shape slightly such that their affinity for oxygen increases.
  - When one subunit releases O<sub>2</sub>, the other three quickly follow suit as a shape change lowers their affinity for oxygen.
- Cooperative oxygen binding and release are evident in the **dissociation curve** for hemoglobin.
- Where the dissociation curve has a steep slope, even a slight change in P<sub>O<sub>2</sub></sub> causes hemoglobin to load or unload a substantial amount of O<sub>2</sub>.
  - This steep part corresponds to the range of P<sub>O<sub>2</sub></sub> found in body tissues.
  - Because of the effect of subunit cooperativity, a slight drop in P<sub>O<sub>2</sub></sub> causes a relatively large increase in the amount of oxygen the blood unloads.
- As in all proteins, hemoglobin's conformation is sensitive to a variety of factors.
  - For example, a drop in pH lowers the affinity of hemoglobin for O<sub>2</sub>, an effect called the **Bohr shift**.
- Because CO<sub>2</sub> reacts with water to form carbonic acid, an active tissue will lower the pH of its surroundings and induce hemoglobin to release more oxygen.
- In addition to transporting oxygen, hemoglobin helps transport CO<sub>2</sub> and assists in buffering blood pH.
  - About 7% of the CO<sub>2</sub> released by respiring cells is transported in solution.
  - Another 23% binds to amino groups of hemoglobin.
  - About 70% is transported as bicarbonate ions (HCO<sub>3</sub><sup>-</sup>).
- Carbon dioxide from respiring cells diffuses into the blood plasma and then into erythrocytes.
  - The CO<sub>2</sub> first reacts with water, assisted by the enzyme carbonic anhydrase, to form H<sub>2</sub>CO<sub>3</sub>, which then dissociates into a hydrogen ion (H<sup>+</sup>) and a bicarbonate ion (HCO<sub>3</sub><sup>-</sup>)

- Most of the  $H^+$  attaches to hemoglobin and other proteins, minimizing the change in blood pH.
- The  $HCO_3^-$  diffuses into the plasma.
- As blood flows through the lungs, the process is rapidly reversed as diffusion of  $CO_2$  out of the blood shifts the chemical equilibrium in favor of the conversion of  $HCO_3^-$  to  $CO_2$ .

***Diving mammals have respiratory adaptations.***

- When an air-breathing animal swims underwater, it lacks access to its normal respiratory medium.
  - Most humans can hold their breath for only 2 to 3 minutes and swim to depths of 20 m or so.
- The Weddell seal of Antarctica can plunge to depths of 200–500 m and remain there from 20 minutes to longer than an hour.
- Elephant seals can dive to 1,500 m and stay submerged for as long as 2 hours.
- Several adaptations have created physiological differences between the deep-diving seals and humans.
- One adaptation of these deep-diving seals is an ability to store large amounts of  $O_2$ .
  - Compared to a human, a seal can store about twice as much  $O_2$  per kilogram of body mass, mostly in the blood and muscles.
  - About 36% of the total  $O_2$  in humans is in our lungs, and 51% is in our blood.
  - In contrast, the Weddell seal holds only about 5% of its  $O_2$  in its small lungs, and it stockpiles 70% in the blood.
- The seal has about twice the volume of blood per kilogram of body weight as a human.
- Diving mammals also have a high concentration of an oxygen-storing protein called **myoglobin** in their muscles.
  - The Weddell seal can store about 25% of its  $O_2$  in muscle, compared with 13% in humans.
- Not only do diving vertebrates start a dive with a relatively large  $O_2$  stockpile, but they also have adaptations that conserve  $O_2$ .
  - They swim with little muscular effort and often use buoyancy changes to glide passively upward or downward.
  - Their heart rate and  $O_2$  consumption rate decrease during the dive, and most blood is routed to the brain, spinal cord, eyes, adrenal glands, and placenta (in pregnant seals).
  - Their blood supply to the muscles is restricted or even shut off.
  - During dives lasting longer than 20 minutes, a Weddell seal's muscles deplete the  $O_2$  stored in myoglobin and then derive ATP from fermentation instead of respiration.