32.1 What Are Some of the Important Body Fluids?

Single-cell organisms receive their nutrients directly from the environment and discard waste products directly into it. In multicellular organisms, the situation is not so simple. There, too, each cell needs nutrients and produces wastes, but most of the cells are not directly in contact with the environment. Body fluids serve as a medium for carrying nutrients to and waste products from the cells, as well as a means for carrying the chemical communicators (Chapter 24) that coordinate activities among cells.

The body fluids that are not inside the cells are collectively known as extracellular fluids. These fluids make up about one-fourth of a person’s body weight. The most abundant is interstitial fluid, which directly surrounds most cells and fills the spaces between them. It makes up about 17% of body weight. Another body fluid is blood plasma, which flows in the arteries and veins. It makes up about 5% of body weight. Other body

Key Questions

32.1 What Are Some of the Important Body Fluids?
32.2 What Are the Functions and Composition of Blood?
32.3 How Does Blood Serve as a Carrier of Oxygen?
32.4 How Does the Transport of Carbon Dioxide in the Blood Take Place?
32.5 What Role Do the Kidneys Play in Cleansing the Blood?
32.6 How Do the Kidneys Play a Role in the Body’s Buffers?
32.7 How Are Water and Salt Balance Maintained in the Blood and Kidneys?
32.8 What Are the Biochemistry and Physiology of Blood Pressure?
32.1 What Are Some of the Important Body Fluids?

fluids that occur in lesser amounts are urine, lymph, cerebrospinal fluid, the aqueous humor of the eye, and synovial fluid. All body fluids are aqueous solutions—water is the only solvent in the body.

The blood plasma circulates in the body and comes in contact with the other body fluids through the semipermeable membranes of the blood vessels (Figure 32.1). In this way, blood can exchange chemical compounds with other body fluids, such as lymph and interstitial fluid, and, through them, with the cells and organs of the body.

There is only a limited exchange between blood and cerebrospinal fluid on the one hand and between blood and the interstitial fluid of the brain on the other hand. The limited exchange between blood and interstitial fluid of the brain is referred to as the blood–brain barrier. This barrier is permeable to water, oxygen, carbon dioxide, glucose, alcohols, and most anesthetics, but only slightly permeable to electrolytes such as Na⁺, K⁺, and Cl⁻ ions. Many higher-molecular-weight compounds are also excluded.

The blood–brain barrier protects the cerebral tissue from detrimental substances in the blood and allows it to maintain a low K⁺ concentration, which is needed to generate the high electrical potential essential for neurotransmission. It is vital that the body maintain a proper balance of levels of salts, proteins, and all other components in the blood. Homeostasis is the process of maintaining the levels of nutrients in the blood, as well as the body's temperature.

Body fluids have special importance for the health care professions. Samples of body fluid can be taken with relative ease. The chemical analysis of blood plasma, blood serum, urine, and occasionally cerebrospinal fluid is of major importance in diagnosing disease.

**Chemical Connections 32A**

**Using the Blood–Brain Barrier to Eliminate Undesirable Side Effects of Drugs**

Many drugs have undesirable side effects. For example, many antihistamines, such as Dramamine and Benadryl (Section 24.5), cause drowsiness. These antihistamines are supposed to act on the peripheral H₁ histamine receptors to relieve seasickness, hay fever, or asthma. Because they penetrate the blood–brain barrier, they also act as antagonists to the H₁ receptors in the brain, causing sleepiness. One drug that also acts on the peripheral H₁ receptors, fexofenadine (sold under the trade name Allegra), cannot penetrate the blood–brain barrier. This antihistamine alleviates seasickness and asthma in the same way as the old antihistamines, but it does not cause drowsiness as a side effect.

**Chemical Connections 32A**

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**Test your knowledge with Problem 32.36.**

**Interstitial fluid** The fluid that surrounds the cells and fills the spaces between them

**Blood plasma** The noncellular portion of blood

**Blood–brain barrier** A barrier limiting the exchange of blood components between blood and the cerebrospinal and brain interstitial fluids to water, carbon dioxide, glucose, and other small molecules but excluding electrolytes and large molecules
32.2 What Are the Functions and Composition of Blood?

It has been known for centuries that “life’s blood” is essential to human life. Blood has many functions, including the following:

1. It carries $O_2$ from the lungs to the tissues.
2. It carries $CO_2$ from the tissues to the lungs.
3. It carries nutrients from the digestive system to the tissues.
4. It carries waste products from the tissues to the excretory organs.
5. With its buffer systems, it maintains the pH of the body (with the help of the kidneys).
6. It maintains a constant body temperature.
7. It carries hormones from the endocrine glands to wherever they are needed.
8. It transports infection-fighting blood cells (leukocytes) and antibodies.

Figure 32.1 shows some of these functions. The rest of this chapter describes how the blood carries out some of these functions.

Whole blood is a complicated mixture. It contains several types of cells (Figure 32.2) plus a liquid, noncellular portion called plasma, in which many substances are dissolved (Table 32.1). There are three main types of cellular elements of blood: erythrocytes, leukocytes, and platelets.

A. Erythrocytes

The most prevalent cells of blood are the red blood cells, which are called erythrocytes. There are about 5 million red blood cells in every cubic millimeter of blood, or roughly 100 million in every drop. Erythrocytes are very
32.2 What Are the Functions and Composition of Blood?

Erythrocytes are specialized cells. They have no nuclei and, hence, no DNA. Their main function is to carry oxygen to the cells and carbon dioxide away from the cells. Erythrocytes are formed in the bone marrow, and they stay in the bloodstream for about 120 days. Old erythrocytes are removed by the liver and spleen and destroyed. The constant formation and destruction of red blood cells maintain a steady number of erythrocytes in the body.

B. Leukocytes

Leukocytes (white blood cells) are relatively minor cellular components (minor in numbers, not in function). For each 1000 red blood cells, there are only one or two white blood cells. Most of the different leukocytes destroy invading bacteria or other foreign substances by devouring them (phagocytosis).

Like erythrocytes, leukocytes are manufactured in the bone marrow. Specialized white blood cells formed in the lymph nodes and in the spleen are called lymphocytes. They synthesize immunoglobulins (antibodies; see Section 31.4) and store them.

C. Platelets

When a blood vessel is cut or injured, the bleeding is controlled by a third type of cellular element: the platelets (also called thrombocytes). They are formed in the bone marrow and spleen and are more numerous than leukocytes but less numerous than erythrocytes.

D. Plasma

If all the cellular elements from whole blood are removed by centrifugation, the resulting liquid is the plasma. The cellular elements—mainly red blood cells, which settle at the bottom of the centrifuge tube—account for between 40 and 50% of the blood volume.

Blood plasma is 92% water. The dissolved solids in the plasma are mainly proteins (7%). The remaining 1% contains glucose, lipids, enzymes, vitamins,
Blood Clotting

When body tissues are damaged, the blood flow must be stopped or else enough of it will pour out to cause death. The mechanism used by the body to stem leaks in the blood vessels is clotting. This complicated process involves many factors. Here we mention only a few important steps.

When a blood vessel is injured, the first line of defense is the platelets, which circulate constantly in the blood. They rush to the site of injury, adhere to the collagen molecules in the capillary wall that are exposed by the cut, and form a gel-like plug. At the signal of thromboxane A\(_2\), more platelets enlarge the size of the clot (Section 21.12). This plug is porous, however, and a firmer gel (a clot) is needed to seal the site. A clot is a three-dimensional network of fibrin molecules that also contains platelets. The fibrin network is formed from the blood fibrinogen by the enzyme thrombin. Together with the embedded platelets, it constitutes the blood clot.

Why doesn’t the blood clot in the blood vessels under normal conditions (with no injury or disease)? The reason is that the enzyme that starts clot formation, thrombin, exists in the blood only in its inactive form, called prothrombin. Prothrombin itself is manufactured in the liver, and vitamin K is needed for its production. Even when prothrombin is in sufficient supply, a number of proteins are needed to change it to thrombin. These proteins are given the collective name thromboplastin. Any thromboplastic substance can activate prothrombin in the presence of Ca\(^{2+}\) ions. Thromboplastic substances exist in the platelets, in the plasma, and in the injured tissue itself.

Clotting is nature’s way of protecting us from loss of blood. However, we don’t want the blood to clot during blood transfusions because that would stop the flow. To prevent this problem, we add sodium citrate to the blood. Sodium citrate interacts with Ca\(^{2+}\) ions and removes them from the solution, so the thromboplastic substances cannot activate prothrombin and no clot forms.

A clot is not dangerous if it stays near the injury because, once the body repairs the tissue, the clot is digested and removed. However, a clot formed in one part of the body may break loose and travel to other parts, where it may lodge in an artery. This condition is called thrombosis. If the clot then blocks the oxygen and nutrient supply to the heart and brain, it can result in paralysis and death. After surgery, anticoagulant drugs are occasionally administered to prevent clot formation.

The most common anticoagulants are heparin and dicumarol. Heparin enhances the inhibition of thrombin by antithrombin (Section 20.6B), and dicumarol blocks the transport of vitamin K to the liver, preventing prothrombin formation.


**Test your knowledge with Problems 32.37–32.39.**

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**Serum** Blood plasma from which fibrinogen has been removed

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hormones, and waste products such as urea and CO\(_2\). Of the plasma proteins, 55% is albumin, 38.5% is globulin, and 6.5% is fibrinogen. If plasma is allowed to stand, it forms a clot, a gel-like substance. We can squeeze out a clear liquid from the clot, called serum. It contains all the components
of the plasma except the fibrinogen. This protein is involved in the complicated process of clot formation (Chemical Connections 32B).

As for the other plasma proteins, most of the globulins take part in immune reactions (Section 31.4) and the albumin provides proper osmotic pressure. If the albumin concentration drops (from malnutrition or from kidney disease, for example), the water from the blood oozes into the interstitial fluid and creates the swelling of tissues called edema.

32.3 How Does Blood Serve as a Carrier of Oxygen?

One of the most important functions of blood is to carry oxygen from the lungs to the tissues. This task is accomplished by hemoglobin molecules located inside the erythrocytes. As we saw in Section 22.11, hemoglobin is made up of two alpha and two beta protein chains, each attached to a molecule of heme.

The active sites are the hemes, and at the center of each heme is an iron(II) ion. The heme with its central Fe$^{2+}$ ion forms a plane. Because each hemoglobin molecule has four hemes, it can hold a total of four O$_2$ molecules. In reality, the ability of the hemoglobin molecule to hold O$_2$ depends on how much oxygen is in the environment. Consider Figure 32.3, which shows how the oxygen-carrying ability of hemoglobin depends on oxygen pressure. When oxygen enters the lungs, the pressure is high (100 mm Hg). At this pressure, all the Fe$^{2+}$ ions of the hemes bind oxygen molecules; they are fully saturated. By the time the blood reaches the muscles through the capillaries, the oxygen pressure in the muscle is only 20 mm Hg (Chemical Connections 32C). At this pressure, only 30% of the binding sites carry oxygen. Thus, 70% of the oxygen carried will be released to the tissues. The S shape of the binding (dissociation) curve (Figure 32.3) implies that the reaction is not a simple equilibrium reaction.

$$\text{HbO}_2 \rightleftharpoons \text{Hb} + \text{O}_2$$

In hemoglobin, each heme has a cooperative effect on the other hemes. This cooperative action allows hemoglobin to deliver twice as much oxygen to the tissues as it would if each heme acted independently. The reason for

This allosteric effect (Section 22.6) explains the S-shaped curve shown in Figure 32.3.
Chemical Connections 32C

Breathing and Dalton’s Law

A gas naturally flows from an area of higher pressure to one of lower pressure. This fact is responsible for respiration, though we must look not at the total pressure of air but only at the partial pressure of O\textsubscript{2} and CO\textsubscript{2} (see the discussion of Dalton’s law in Section 5.5). Respiration is the process by which blood carries O\textsubscript{2} from the lungs to tissues; collects the CO\textsubscript{2} manufactured by cells; and brings it to the lungs, where it is breathed out.

The air we breathe contains about 21% O\textsubscript{2} at a partial pressure of approximately 159 mm Hg. The partial pressure of O\textsubscript{2} in the alveoli (tiny air sacs) in the lungs is about 100 mm Hg. Because the partial pressure is higher in the inhaled air, O\textsubscript{2} flows to the alveoli. At this point, venous blood flows past the alveoli. The partial pressure of O\textsubscript{2} in the venous blood is only 40 mm Hg, so O\textsubscript{2} flows from the alveoli to the venous blood. This new supply of O\textsubscript{2} raises the partial pressure to about 100 mm Hg, and the blood becomes arterial blood and flows to the body tissues. There, the partial pressure of O\textsubscript{2} is 30 mm Hg or less (because the metabolic activity of the tissue cells has used up most of their oxygen to provide energy). Oxygen now flows from the arterial blood to the body tissues. The partial pressure of O\textsubscript{2} in the blood decreases (to about 40 mm Hg), and the blood becomes venous blood again and returns to the lungs for a fresh supply of O\textsubscript{2}. At each step of the cycle, O\textsubscript{2} flows from a region of higher partial pressure to one of lower partial pressure.

Meanwhile, CO\textsubscript{2} goes in the opposite direction for the same reason. The partial pressure of CO\textsubscript{2} as a result of metabolic activity is about 60 mm Hg in tissues. CO\textsubscript{2} flows from tissues to arterial blood, changing it to venous blood and reaching a CO\textsubscript{2} pressure of 46 mm Hg. The blood then flows to the lungs. The CO\textsubscript{2} pressure in the alveoli is 40 mm Hg, and so the CO\textsubscript{2} flows to the alveoli. Because the partial pressure of CO\textsubscript{2} in air is only 0.3 mm Hg, CO\textsubscript{2} flows from the alveoli and is exhaled.

Test your knowledge with Problem 32.40.

Lowering the pH decreases the oxygen-binding capacity of hemoglobin.

this is as follows: When a hemoglobin molecule is carrying no oxygen, the four globin units coil into a certain shape (Section 22.11). When the first oxygen molecule attaches to one of the heme subunits, it changes the shape not only of that subunit but also of a second subunit, making it easier for the second subunit to bind an oxygen. When the second heme binds, the shape changes once again, and the oxygen-binding ability of the two remaining subunits increases still more.
The oxygen-delivering capacity of hemoglobin is also affected by its environment. A slight change in the pH of the environment changes the oxygen-binding capacity, a phenomenon called the **Bohr effect**. An increase in CO₂ pressure also decreases the oxygen-binding capacity of hemoglobin. When a muscle contracts, H⁺ ions and CO₂ are produced. The newly produced CO₂ enhances the release of oxygen. At the same time, H⁺ ions lower the pH of the muscle. Thus, at the same pressure (20 mm Hg), more oxygen is released for an active muscle than for a muscle at rest.

### 32.4 How Does the Transport of Carbon Dioxide in the Blood Take Place?

What happens to the CO₂ and H⁺ produced in metabolically active cells? They bind to the hemoglobin of erythrocytes, and carbaminohemoglobin is formed. This is an equilibrium reaction.

\[ \text{Hb} - \text{NH}_2 + \text{CO}_2 \rightleftharpoons \text{Hb} - \text{NH} - \text{COO}^- + \text{H}^+ \]

**Carbaminohemoglobin**

The CO₂ is bound to the terminal α-NH₂ groups of the four polypeptide chains, so each hemoglobin can carry a maximum of four CO₂ molecules, one for each chain. How much CO₂ each hemoglobin actually carries depends on the pressure of CO₂. The higher the CO₂ pressure, the more carbaminohemoglobin formed.

Only 25% of the total CO₂ produced by the cells is transported to the lungs in the form of carbaminohemoglobin. Another 70% is converted in the red blood cells to carbonic acid by the enzyme carbonic anhydrase. A large part of this H₂CO₃ is carried as HCO₃⁻ and H⁺ associated with hemoglobin to the lungs, where it is converted back to CO₂ by carbonic anhydrase and released. The remaining 5% of the total CO₂ is carried in the plasma as dissolved gas.

<table>
<thead>
<tr>
<th><strong>Peripheral tissues</strong></th>
<th><strong>Blood</strong></th>
<th><strong>Lungs</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>2CO₂ + 2H₂O</td>
<td>2CO₂ + 2H₂O</td>
<td>2CO₂ + 2H₂O</td>
</tr>
<tr>
<td>Carbonic anhydrase</td>
<td>Carbonic anhydrase</td>
<td>Carbonic anhydrase</td>
</tr>
<tr>
<td>2H₂CO₃</td>
<td>2H₂CO₃</td>
<td>2H₂CO₃</td>
</tr>
<tr>
<td>2HCO₃⁻ + 2H⁺</td>
<td>2H⁺ + 2HCO₃⁻</td>
<td></td>
</tr>
<tr>
<td>Hb · 4O₂</td>
<td>Hb · 2H⁺</td>
<td></td>
</tr>
<tr>
<td>4O₂</td>
<td>4O₂</td>
<td></td>
</tr>
</tbody>
</table>

The reaction proceeds to the CO₂ production (top) because loss of CO₂ from the lungs causes this equilibrium to shift to replace it (Le Chatelier’s principle).

### 32.5 What Role Do the Kidneys Play in Cleansing the Blood?

We have seen that one of blood’s functions is to maintain the pH at 7.4 (Section 8.10). Another is to carry waste products away from the cells. CO₂, one of the principal waste products of respiration, is carried by the blood to the lungs and exhaled. The other waste products are filtered out by the kidneys and eliminated in the urine.
The kidney is a superfiltration machine. In the event of kidney failure, filtration can be done by hemodialysis (Figure 32.4). About 100 L of blood passes through a normal human kidney daily. Of this amount, only about 1.5 L of liquid is excreted as urine. Obviously, we do not have here just a simple filtration system in which small molecules are lost and large ones are retained. The kidneys also reabsorb from the urine those small molecules that are not waste products.

A. Kidney

The biological units inside the kidneys that perform these functions are called nephrons, and each kidney contains about a million of them. A nephron is made up of a filtration head called a Bowman's capsule connected to a tiny U-shaped tube called a tubule. The part of the tubule close to the Bowman's capsule is the proximal tubule, the U-shaped twist is called Henle's loop, and the part of the tubule farthest from the capsule is the distal tubule (Figure 32.5).

Blood vessels penetrate the kidney throughout. The arteries branch into capillaries, and one tiny capillary enters each Bowman's capsule. Inside the capsule, the capillary first branches into even smaller vessels, called glomeruli, and then leaves the capsule. The blood enters the glomeruli with every heartbeat, and the pressure forces the water, ions, and all small molecules (urea, sugars, salts, amino acids) through the walls of the glomeruli and the Bowman's capsule. These molecules and ions enter the proximal tubule. Blood cells and large molecules (proteins) are retained in the capillary and exit with the blood.

As shown in Figure 32.5, the tubules and Henle's loop are surrounded by blood vessels; these blood vessels reabsorb vital nutrients. Eighty percent of the water is reabsorbed in the proximal tubule. Almost all the glucose and amino acids are reabsorbed here. When excess sugar is present in the blood (diabetes; see Chemical Connections 24F), some of it passes into the urine. As a consequence, the measurement of glucose concentration in the urine is used in diagnosing diabetes.

By the time the glomerular filtrate reaches Henle's loop, the solids and most of the water have been reabsorbed. Only wastes (such as urea, creatinine, uric acid, ammonia, and some salts) pass into the collecting tubules that bring the urine to the ureter, from which it passes to the bladder, as shown in Figure 32.5(a).
32.5 What Role Do the Kidneys Play in Cleansing the Blood?

B. Urine

Normal urine contains about 4% dissolved waste products; the rest is water. Although the daily amount of urine varies greatly, it averages about 1.5 L per day. The pH varies from 5.5 to 7.5. The main solute is urea, the end product of protein metabolism (Section 28.8). Other nitrogenous waste products, such as creatine, creatinine, ammonia, and hippuric acid, are also present, albeit in much smaller amounts.

In addition, normal urine contains inorganic ions such as Na$^+$, Ca$^{2+}$, Mg$^{2+}$, Cl$^-$, PO$_4^{3-}$, SO$_4^{2-}$, and HCO$_3^-$.

Under certain pathological conditions, other substances can appear in the urine. This possibility makes urine analysis a highly important part of diagnostic medicine. We have already noted that the presence of glucose and ketone bodies is an indication of diabetes. Other abnormal constituents may include proteins, which can indicate kidney diseases such as nephritis.
32.6 How Do the Kidneys Play A Role in the Body’s Buffers?

Among the waste products sent into the blood by the tissues are H\(^+\) ions. They are neutralized by the HCO\(_3^-\) ions that are a part of the blood’s buffer system:

\[
H^+ + HCO_3^- \rightleftharpoons H_2CO_3
\]

When the blood reaches the lungs, as we saw in Section 32.4, H\(_2\)CO\(_3\) is decomposed by carbonic anhydrase and CO\(_2\) is exhaled. If the body had no mechanism for replacing HCO\(_3^-\), we would lose most of the bicarbonate buffer from the blood and the blood pH would eventually drop (acidosis). In reality, the lost HCO\(_3^-\) ions are continuously replaced by the kidneys—another principal kidney function. This replacement takes place in the distal tubules. The cells lining the walls of the distal tubules reabsorb the CO\(_2\) that was lost in the glomeruli. With the aid of carbonic anhydrase, carbonic acid forms quickly and then dissociates to HCO\(_3^-\) and H\(^+\) ions:

\[
CO_2 + H_2O \rightleftharpoons H_2CO_3 \rightleftharpoons H^+ + HCO_3^- 
\]

The H\(^+\) ions move from the cells into the urine in the tubule, where they are partially neutralized by a phosphate buffer. To compensate for the lost positive ions, Na\(^+\) ions from the tubule enter the cells. When this happens, Na\(^+\) and HCO\(_3^-\) ions move from the cells into the capillaries. In this way, the H\(^+\) ions picked up at the tissues and temporarily neutralized in the blood by HCO\(_3^-\) are finally pumped out into the urine. At the same time, the HCO\(_3^-\) ions lost in the lungs are regained by the blood in the distal tubules.

32.7 How Are Water and Salt Balance Maintained in the Blood and Kidneys?

In Section 32.5, we mentioned that there is a balance in the kidneys between filtration and reabsorption. This balance is under hormonal control. The reabsorption of water is promoted by vasopressin, a small peptide hormone manufactured in the pituitary gland (Figure 24.2). In the absence of this hormone, only the proximal tubules—not the distal tubules or the collecting tubules—reabsorb water. As a consequence, without vasopressin, too much water passes into the urine. In the presence of vasopressin, water is reabsorbed in these parts of the nephrons; thus, vasopressin causes the blood to retain more water and produces a more concentrated urine. The production of urine is called diuresis. Any agent that reduces the volume of urine is called an antidiuretic.

Usually, the vasopressin level in the body is sufficient to maintain the proper amount of water in tissues under various levels of water intake. However, when severe dehydration occurs (as a result of diarrhea, excessive sweating, or insufficient water intake), another hormone helps to maintain proper fluid level. This hormone, aldosterone (Section 21.10), controls the Na\(^+\) ion concentration in the blood. In the presence of aldosterone, the reabsorption of Na\(^+\) ions increases. When more Na\(^+\) ions enter the blood, more Cl\(^-\) ions follow (to maintain electroneutrality) as well as more water to solvate these ions. Thus, increased aldosterone production enables the body to retain more water. When the Na\(^+\) ion and water levels in the blood return to normal, aldosterone production stops.
Sex Hormones and Old Age

The same sex hormones that provide a healthy reproductive life in young people can and do cause problems in the aging body. For male fertility, the prostate gland and testis provide semen. The prostate gland is situated at the exit of the bladder, surrounding the ureter. Its growth is promoted by the conversion of the male sex hormone, testosterone, to 5-α dihydrotestosterone by the enzyme 5-α reductase. The majority of men over the age of 50 have enlarged prostate glands, a condition known as benign prostatic hyperplasia. In fact, this condition affects more than 90% of men older than age 70. The enlarged prostate gland constricts the ureter and causes a restricted flow of urine.

This symptom can be partially relieved by an oral drug called terazosin (trade name Hytrin). This drug was originally approved for treatment of high blood pressure, where its action results from its ability to block the α-1-adrenoreceptors, thereby reducing the constriction around peripheral blood vessels. In a similar way, it reduces constriction around the ureter (the duct that conveys urine from the kidney to the bladder), allowing an unrestricted flow of urine. Terazosin, if taken as the sole antihypertensive, antiprostate drug, has come under scrutiny lately, however. A study released in 2000 concluded that this drug may contribute to the occurrence of heart attacks.

A more accurate measure of prostate cancer is the percentage of free (not bound) PSA. When this level is higher than 15%, the likelihood of cancer diminishes with increasing percentage. When it is 9% or lower, the prostate cancer has probably already spread. The ultimate confirmation of cancer is microscopic examination of tissue taken by biopsy.

Estradiol and progesterone control sexual characteristics in the female body (Section 21.10). With the onset of menopause, smaller amounts of these and other sex hormones are secreted. This drop-off not only stops fertility but occasionally creates medical problems. The most serious complication is osteoporosis, which is the loss of bone tissue through absorption. It results in brittle and occasionally deformed bone structure. Estrogens (a general name for female sex hormones other than progesterone) in the proper amount can help to absorb calcium from the diet and thus prevent osteoporosis. The lack of enough female sex hormones can also result in atrophic vaginitis and atrophic urethritis.

A large number of postmenopausal women take pills that contain a synthetic progesterone analog and natural estrogens. However, continuous medication with these pills—for example, Premarin (mixed estrogens) and Provera (a progesterone analog)—is not without danger. A slight but statistically significant increase in cancer of the uterus has been reported in postmenopausal women who use such medication. A slight risk of heart problems was also noticed in women taking such drugs. A physician’s advice is needed in weighing the benefits against the risks.

Test your knowledge with Problems 32.41 and 32.42.

32.8 What Are the Biochemistry and Physiology of Blood Pressure?

Blood pressure is produced by the pumping action of the heart. The blood pressure at the arterial capillary end is about 32 mm Hg, a level higher than the osmotic pressure of the blood (18 mm Hg). The osmotic pressure of the blood is caused by the fact that more solutes are dissolved in the blood than in the interstitial fluid. At the capillary end, therefore, nutrient solutes flow from the capillaries into the interstitial fluid and from there into the cells (see Figure 32.1). By contrast, the blood pressure in the venous capillaries is about 12 mm Hg. This level is less than the osmotic pressure, so solutes (waste products) from the interstitial fluid flow into the capillaries.

The blood pressure is maintained by the total volume of blood, by the pumping of the heart, and by the muscles that surround the blood vessels and provide the proper resistance to blood flow (see Chemical Connections 5D). Blood pressure is controlled by several very complex systems—some that
Hypertension and Its Control

Nearly one third of the U.S. population has high blood pressure (hypertension). Epidemiological studies have shown that even mild hypertension (diastolic pressure between 90 and 104 mm Hg) brings the risk of cardiovascular disease. It can lead to heart attack, stroke, or kidney failure. Hypertension can be managed effectively with diet and drugs. As noted in the text, blood pressure is under the control of a complex system, so hypertension must be managed on more than one level. Recommended dietary practices are low Na$^+$ ion intake and abstention from caffeine and alcohol.

The most commonly used drugs for lowering blood pressure are diuretics. A number of synthetic organic compounds (mostly thiazides such as Diuril and Enduron) increase urine excretion. By doing so, they decrease the blood volume as well as the Na$^+$ ion concentration, thereby lowering blood pressure.

Other antihypertensive drugs affect the nerve control of blood pressure. Propranolol hydrochloride blocks the adrenoreceptor sites of beta-adrenergic neurotransmitters (Section 24.5). By doing so, it reduces the flow of nerve signals as well as the blood output of the heart; it affects the responses of baroreceptors and chemoreceptors in the central nervous system and the adrenergic receptors in the smooth muscles surrounding the blood vessels. Propranolol and other beta blockers (such as metoprolol) not only lower blood pressure, but also reduce the risk of myocardial infarction. Similar lowering of blood pressure is achieved by drugs that block calcium channels (for example, nifedipine/Adalat or diltiazem hydrochloride/Cardizem). For proper muscle contraction, calcium ions must pass through muscle cell membranes, an activity facilitated by calcium channels. If a drug blocks these channels, the heart muscles will contract less frequently, pumping less blood and reducing blood pressure.

Other drugs that reduce hypertension include the vasodilators that relax the vascular smooth muscles. However, many of these agents have side effects such as causing fast heartbeat (tachycardia) and promoting Na$^+$ and water retention. Some drugs on the market act on one specific site rather than on many sites as the blockers do, which obviously reduces the possible side effects. An example is an enzyme inhibitor that prevents the production of angiotensin. Captopril (Chemical Connections 15A) and Accupril are both ACE (angiotensin-converting enzyme) inhibitors that lower blood pressure only if the sole cause of hypertension is angiotensin production. Prostaglandins PGE and PGA (Section 21.12) lower the blood pressure and, when taken orally, have prolonged duration of action. Because hypertension is such a common problem, and it is manageable by drugs, there is great activity in drug research to come up with even more effective and safer antihypertension drugs.

Test your knowledge with Problems 32.43 and 32.44.

Baroreceptors A feedback mechanism in the neck that detects changes in the blood pressure and sends signals to the heart to counteract those changes by pumping harder or slower as the need arises.
to form carbaminohemoglobin, 70% is carried in the plasma as $\text{H}_2\text{CO}_3$, and 5% is carried as dissolved gas.

Section 32.5 What Role Do the Kidneys Play in Cleansing the Blood?
- Waste products are removed from the blood in the kidneys.
- The filtration units—nephrons—contain an entering blood vessel that branches out into fine vessels called glomeruli.
- Water and all the small molecules in the blood diffuse out of the glomeruli, enter the Bowman’s capsules of the nephrons, and from there go into the tubules. The blood cells and large molecules remain in the blood vessels.
- The water, inorganic salts, and organic nutrients are then reabsorbed into the blood vessels. The waste products plus water form the urine, which goes from the tubule into the ureter and finally into the bladder.

Section 32.6 How Do the Kidneys Play a Role in the Body’s Buffers?
- The kidneys not only filter out waste products, but also produce $\text{HCO}_3^-$ ions for buffering, replacing those lost through the lungs.

Section 32.7 How Are Water and Salt Balance Maintained in the Blood and Kidneys?
- The water and salt balance of the blood and urine are under hormonal control.
- Vasopressin helps to retain water, and aldosterone increases the $\text{Na}^+$ ion concentration in the blood by reabsorption.

Section 32.8 What Are the Biochemistry and Physiology of Blood Pressure?
- Blood pressure is controlled by a large number of factors.

Summary

(a) Is the blood plasma in contact with the other body fluids?
(b) If so, in what manner?

Section 32.1 What Are Some of the Important Body Fluids?
32.1 What is the blood–brain barrier?
32.2 What percentage of our body weight is blood plasma?

Section 32.2 What Are the Functions and Composition of Blood?
32.3 Which blood cell is the most abundant?
32.4 What is the function of erythrocytes?
32.5 Which blood cells are the largest?
32.7 Define:
(a) Interstitial fluid  (b) Plasma
(c) Serum  (d) Cellular elements

32.8 Where are the following manufactured?
(a) Erythrocytes  (b) Leukocytes
(c) Lymphocytes  (d) Platelets

32.9 How is plasma prepared from whole blood?
32.10 State the function of the following:
(a) Albumin  (b) Globulin
(c) Fibrinogen

32.11 Which blood plasma component protects against infections?
32.12 How is serum prepared from blood plasma?

Section 32.3 How Does Blood Serve as a Carrier of Oxygen?
32.13 How many molecules of O\(_2\) are bound to a hemoglobin molecule at full saturation?
32.14 A chemist analyzes contaminated air from an industrial accident and finds that the partial pressure of oxygen is only 38 mm Hg. How many O\(_2\) molecules, on average, will be transported by each hemoglobin molecule when someone breathes such air? (Consult Figure 32.3.)

32.15 Which inorganic ion is involved in the definition of percent saturation? Explain.
32.16 From Figure 32.3, predict the O\(_2\) pressure at which the hemoglobin molecule binds four, three, two, one, and zero O\(_2\) molecules to its heme.
32.17 Explain how the absorption of O\(_2\) on one binding site in the hemoglobin molecule increases the absorption capacity at other sites.
32.18 (a) What happens to the oxygen-carrying capacity of hemoglobin when the pH is lowered?
   (b) What is the name of this effect?

Section 32.4 How Does the Transport of Carbon Dioxide in the Blood Take Place?
32.19 (a) Where does CO\(_2\) bind to hemoglobin?
   (b) What is the name of the complex formed?
32.20 In carboxy-hemoglobin, the N-terminal ends of globin chains carry a carbamate group, R — NH — COO\(^-\). The anionic site can form a salt bridge with a cationic amino group on a side chain of the globin molecule and stabilize it. Draw the formula of the salt bridge.
32.21 If the plasma carries 70% of its carbon dioxide in the form of H\(_2\)CO\(_3\) and 5% in the form of dissolved CO\(_2\) gas, calculate the equilibrium constant of the reaction catalyzed by carbonic anhydrase:

\[
\text{H}_2\text{O} + \text{CO}_2 \rightleftharpoons \text{H}_2\text{CO}_3
\]

(Assume that the H\(_2\)O concentration is included in the equilibrium constant.)

32.22 How is the equilibrium reaction of carboxyhemoglobin formation influenced by the CO\(_2\) concentration of the surroundings? Apply Le Chatelier’s principle.

Section 32.5 What Role Do the Kidneys Play in Cleansing the Blood?
32.23 Where is most of the water reabsorbed in the kidney?
32.24 What nitrogenous waste products are eliminated in the urine?
32.25 Besides nitrogenous waste products, what other components are normal constituents of urine?

Section 32.6 How Do the Kidneys Play a Role in the Body’s Buffers?
32.26 What happens to the H\(^+\) ions sent into the blood as waste products made by the cells of the tissues?
32.27 The pH of blood is maintained at 7.4. What would be the pH of an active muscle cell relative to that of blood? What component and process generates this pH?

Section 32.7 How Are Water and Salt Balance Maintained in the Blood and Kidneys?
32.28 In which part of the kidneys does vasopressin change the permeability of membranes?
32.29 How does aldosterone production counteract the excessive sweating that usually accompanies a high fever?
32.30 Caffeine is a diuretic. What effect will drinking a lot of coffee have on the specific gravity of your urine?

Section 32.8 What Are the Biochemistry and Physiology of Blood Pressure?
32.31 What is the function of baroreceptors?
32.32 What would happen to the glucose in an arterial capillary if the blood pressure at the end of the capillary were 12 mm Hg rather than the normal 32 mm Hg?
32.33 Some drugs used as antihypertensive agents—for example, Captopril (Chemical Connections 32E)—inhibit the enzyme that activates angiotensinogen. What is the mode of action of such drugs in lowering blood pressure?
32.34 A number of drugs combating high blood pressure go under the name ACE (angiotensin-converting enzyme) inhibitors. A patient takes diuretics and ACE inhibitors. How do these drugs lower blood pressure?

Chemical Connections
32.36 (Chemical Connections 32A) What side effect of antihistamines is avoided by using the drug fexofenadine?
32.37 (Chemical Connections 32B) Which molecules help to anchor the platelets when a blood vessel is cut?
32.38 (Chemical Connections 32B) What are the functions of (a) thrombin, (b) vitamin K, and (c) thromboplastin in clot formation?

32.39 (Chemical Connections 32B) What is the first line of defense when a blood vessel is cut?

32.40 (Chemical Connections 32C) In circulating blood, where is the partial pressure of CO\(_2\) the highest? The lowest?

32.41 (Chemical Connections 32D) What are the symptoms of an enlarged prostate gland (benign prostatic hyperplasia)?

32.42 (Chemical Connections 32D) What causes osteoporosis in postmenopausal women?

32.43 (Chemical Connections 32E) How do calcium-channel blockers act in lowering blood pressure?

32.44 (Chemical Connections 32E) People with high blood pressure are advised to follow a low-sodium diet. How does such a diet lower blood pressure?

Additional Problems

32.45 Albumin makes up 55% of the protein content of plasma. Is the albumin concentration of the serum higher, lower, or the same as that of the plasma? Explain.

32.46 Which nitrogenous waste product of the body can be classified as an amino acid?

32.47 What happens to the oxygen-carrying ability of hemoglobin when acidosis occurs in the blood?

32.48 Does the heme of hemoglobin participate in CO\(_2\) transport as well as in O\(_2\) transport?

32.49 Is the blood–brain barrier permeable to insulin? Explain.

32.50 When kidneys fail, the body swells, which is a condition called edema. Why and where does the water accumulate?

32.51 Which hormone controls water retention in the body?

32.52 Describe the action of renin.

32.53 The oxygen dissociation curve of fetal hemoglobin is higher than that of adult hemoglobin. How does the fetus obtain its oxygen supply from the mother's blood when the two circulations meet?