(juxta) the glomerulus. When the cells of the JG apparatus are stimulated by low blood pressure in the afferent arteriole or changes in solute content of the filtrate, they respond by releasing the enzyme **renin** into the blood. (Notice the different spelling of this enzyme from *rennin,* an enzyme secreted by stomach glands.) Renin catalyzes the series of reactions that produce angiotensin II, which in turn acts directly on the blood vessels to cause vasoconstriction (and an increase in peripheral resistance) and on the adrenal cortical cells to promote aldosterone release. As a result, blood volume and blood pressure increase (see Figure 15.10). The renin-angiotensin mechanism is extremely important for regulating blood pressure.

The pressure drop also excites baroreceptors in the larger blood vessels. These baroreceptors alert sympathetic nervous system centers of the brain to cause vasoconstriction (via release of epinephrine and norepinephrine), which increases the peripheral resistance (see Figure 15.10). However, this neural mechanism's major focus is blood pressure regulation, not water and electrolyte balance.

Homeostatic Imbalance

People with Addison's disease (hypoaldosteronism) have *polyuria* (excrete large volumes of urine) and lose tremendous amounts of salt and water to urine. As long as adequate amounts of salt and fluids are ingested, people with this condition can avoid problems, but they are constantly teetering on the brink of dehydration.

Maintaining Acid-Base Balance of Blood

For the cells of the body to function properly, blood pH must be maintained between 7.35 and 7.45, a very narrow range. Whenever the pH of arterial blood rises above 7.45, a person is said to have **alkalosis** (al″kah-lo′sis). A drop in arterial pH to below 7.35 results in **acidosis** (as″ĭ-do′sis). Because a pH of 7.0 is neutral, 7.35 is not acidic, chemically speaking; however, it represents a higher-than-optimal hydrogen ion concentration for the functioning of most body cells. Therefore, any arterial pH between 7.35 and 7.0 is called **physiological acidosis.**

Although small amounts of acidic substances enter the body in ingested foods, most hydrogen ions originate as by-products of cellular metabolism, which continuously adds substances to the blood that tend to disturb its **acid-base balance.** Many different acids are produced (for example, phosphoric acid, lactic acid, and many types of fatty acids). In addition, carbon dioxide, which is released during energy production, forms carbonic acid. Ammonia and other basic substances are also released to the blood as cells go about their usual "business." Although the chemical buffers in the blood can temporarily "tie up" excess acids and bases, and the lungs have the chief responsibility for eliminating carbon dioxide from the body, the kidneys assume most of the load for maintaining acid-base balance of the blood. Before describing how the kidneys function in acid-base balance, let's take a look at how each of our other two pH-controlling systems, blood buffers and the respiratory system, works.

Prove It Yourself

Demonstrate the Water-Retaining Power of Salt

The amount of water your body retains depends more on the amount of salt you consume than on how much water you drink. Here's how to demonstrate this.

On a normal day between meals, empty your bladder. Wait half an hour, and then urinate again. Measure the volume of urine you produced the second time. This is your baseline rate of urine production. Now quickly drink a quart of water and measure your urine output for four more consecutive half-hour periods. Subtract the baseline amount of urine from each time period to find out how much water you excreted in two hours.

Repeat the experiment on another day. This time dissolve 5 grams (approximately ¾ teaspoon) of salt in the water first. You should find that you excrete much less water during the next two hours than you did the first time.

People with certain health conditions, such as hypertension or congestive heart failure, may need to retain less water. Generally, they are advised to restrict their intake of salt, not water. Can you see why?

Blood Buffers

Chemical buffers are systems of one or two molecules that act to prevent dramatic changes in hydrogen ion (H^+) concentration when acids or bases are added. They do this by binding to hydrogen ions whenever the pH drops and by releasing hydrogen ions when the pH rises. Since the chemical buffers act within a fraction of a second, they are the first line of defense in resisting pH changes.

To better understand how a chemical buffer system works, let's review the definitions of strong and weak acids and bases. Recall that acids are proton (H^+) donors, and that the acidity of a solution reflects only the *free* hydrogen ions, not those still bound to anions. *Strong acids* dissociate completely and liberate all their H^+ in water. Consequently they can cause large changes in pH. By contrast, *weak acids* like carbonic acid dissociate only partially and so have a much slighter effect on a solution's pH (Figure 15.11). However, weak acids are very effective at preventing pH changes since they are forced to dissociate and release more H^+ when the pH rises over the desirable pH range. This feature allows them to play a very important role in the chemical buffer systems.

Also recall that bases are proton or hydrogen ion acceptors. *Strong bases* like hydroxides dissociate easily in water and quickly tie up H^+, but *weak bases* like bicarbonate ion (HCO_3^-) and ammonia (NH_3) are slower to accept H^+. However, as pH drops, the weak bases become "stronger" and begin to tie up more hydrogen ions. Thus, like weak acids, they are valuable members of the chemical buffer systems.

The three major chemical buffer systems of the body are the *bicarbonate, phosphate,* and *protein buffer systems,* each of which helps to maintain the pH in one or more of the fluid compartments. They all work together, and anything that causes a shift in H^+ concentration in one compartment also causes changes in the others. Thus, drifts in pH are resisted by the entire buffering system. Since all three systems operate in a similar way, examining just one, the bicarbonate buffer system, which is so important in preventing changes in blood pH, should be sufficient.

The **bicarbonate buffer system** is a mixture of *carbonic acid* (H_2CO_3) and its salt, *sodium bicarbonate* ($NaHCO_3$). Since carbonic acid is a weak acid, it does not dissociate much in neutral or acidic solutions. Thus, when a strong acid, such as hydrochloric acid (HCl) is added, most of the carbonic acid remains intact. However, the *bicarbonate ions* (HCO_3^-) of the salt act as bases to tie up the H^+ released by the stronger acid, forming more carbonic acid:

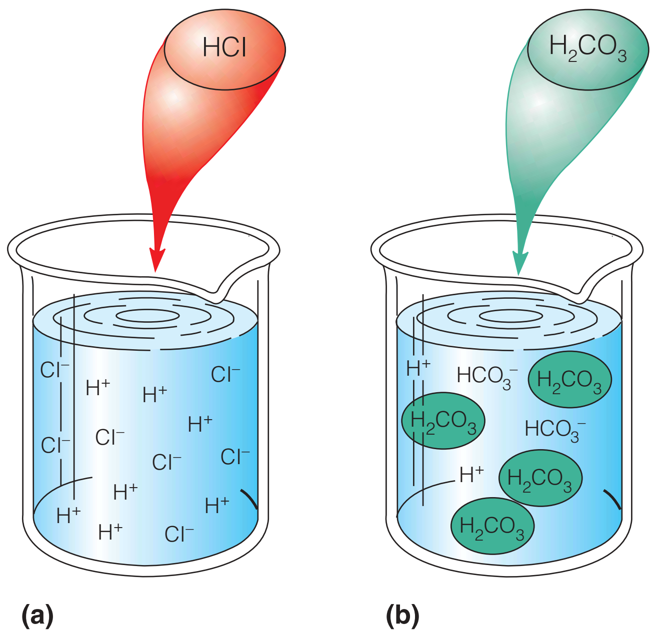

FIGURE 15.11 Dissociation of strong and weak acids. (a) When HCl, a strong acid, is added to water it dissociates completely into its ions (H^+ and Cl^-). **(b)** By contrast, dissociation of H_2CO_3, a weak acid, is very incomplete, and some molecules of H_2CO_3 remain undissociated (symbols shown in green ovals) in solution.

$$\underset{\text{strong acid}}{HCl} + \underset{\text{weak base}}{NaHCO_3} \longrightarrow \underset{\text{weak acid}}{H_2CO_3} + \underset{\text{salt}}{NaCl}$$

Because the strong acid is (effectively) changed to a weak one, it lowers the pH of the solution only very slightly.

Similarly, if a strong base like sodium hydroxide (NaOH) is added to a solution containing the bicarbonate buffer system, $NaHCO_3$ will not dissociate further under such alkaline conditions. However, carbonic acid will be forced to dissociate further by the presence of the strong base—liberating more H^+ to bind with the OH^- released by NaOH.

$$\underset{\text{strong base}}{NaOH} + \underset{\text{weak acid}}{H_2CO_3} \longrightarrow \underset{\text{weak base}}{NaHCO_3} + \underset{\text{water}}{H_2O}$$

The net result is replacement of a strong base by a weak one, so that the pH of the solution rises very little.

Respiratory System Controls

As described in Chapter 13, the respiratory system eliminates carbon dioxide from the blood while it "loads" oxygen into the blood. Remember that when carbon dioxide (CO_2) enters the blood from the tissue cells, most of it enters the red blood cells where it is converted to bicarbonate ion (HCO_3^-) for transport in the plasma as shown by the equation

$$\underset{\text{Carbon dioxide}}{CO_2} + \underset{\text{water}}{H_2O} \overset{\text{Carbonic anhydrase}}{\rightleftharpoons} \underset{\text{carbonic acid}}{H_2CO_3} \rightleftharpoons \underset{\text{hydrogen ion}}{H^+} + \underset{\text{bicarbonate ion}}{HCO_3^-}$$

The double-headed arrows reveal that an increase in carbon dioxide pushes the reaction to the right, producing more carbonic acid. Likewise, an increase in hydrogen ions pushes the equation to the left, producing more carbonic acid. In healthy people, carbon dioxide is expelled from the lungs at the same rate as it is formed in the tissues. Thus the H^+ released when carbon dioxide is loaded into the blood is not allowed to accumulate because it is tied up in water when CO_2 is unloaded in the lungs. So, under normal conditions, the hydrogen ions produced by carbon dioxide transport have essentially no effect on blood pH. However, when CO_2 accumulates in the blood (for example, during restricted breathing) or more H^+ is released to the blood by metabolic processes, the chemoreceptors in the respiratory control centers of the brain (or in peripheral blood vessels) are activated. As a result, breathing rate and depth increase, and the excess H^+ is "blown off" as more CO_2 is removed from the blood.

On the other hand, when blood pH begins to rise (alkalosis), the respiratory center is depressed. Consequently, the respiratory rate and depth fall, allowing carbon dioxide (hence, H^+) to accumulate in the blood. Again blood pH is restored to the normal range. Generally, these respiratory system corrections of blood pH (via regulation of CO_2 content of the blood) are accomplished within a minute or so.

Renal Mechanisms

Chemical buffers can tie up excess acids or bases temporarily, but they cannot eliminate them from the body. And while the lungs can dispose of carbonic acid by eliminating carbon dioxide, only the kidneys can rid the body of other acids generated during metabolism. Additionally, only the kidneys have the power to regulate blood levels of alkaline substances. Thus, although the kidneys act slowly and require hours or days to bring about changes in blood pH, they are the most potent of the mechanisms for regulating blood pH.

The most important means by which the kidneys maintain acid-base balance of the blood are by (1) excreting bicarbonate ions and (2) conserving (reabsorbing) or generating new bicarbonate ions. Look back again at the equation showing how the carbonic acid–bicarbonate buffer system operates. Notice that losing a HCO_3^- from the body has the same effect as gaining an H^+ because it pushes the equation to the right (that is, it leaves a free hydrogen ion). By the same token, reabsorbing or generating new HCO_3^- is the same as losing H^+ because it tends to combine with a hydrogen ion and pushes the equation to the left. Renal mechanisms undertake these adjustments: As blood pH rises, bicarbonate ions are excreted and hydrogen ions are retained by the tubule cells. Conversely, when blood pH falls, bicarbonate is reabsorbed and hydrogen ions are secreted. Urine pH varies from 4.5 to 8.0, which reflects the ability of the renal tubules to excrete basic or acid ions to maintain blood pH homeostasis.

Developmental Aspects of the Urinary System

When you trace the development of the kidneys in a young embryo, it almost seems as if they can't "make up their mind" about whether to come or go. The first tubule system forms and then begins to degenerate as a second, lower, set appears. The second set, in turn, degenerates as a third set makes its appearance. This third set develops into the functional kidneys, which are excreting urine by the third month of fetal life. It is important to remember that the fetal kidneys do not work nearly as hard as they will after birth, because exchanges with the mother's blood through the placenta allow her system to clear many of the undesirable substances from the fetal blood.

Homeostatic Imbalance

There are many congenital abnormalities of this system. Two of the most common are polycystic kidney and hypospadias.