

Renal System Physiology

OBJECTIVES

1. To define nephron, renal corpuscle, renal tubule, afferent arteriole, glomerular filtration, efferent arteriole, aldosterone, ADH, and reabsorption
2. To describe the components and functions of a nephron
3. To understand how arterial diameter affects nephron function
4. To understand how blood pressure affects nephron function
5. To explain the process of reabsorption
6. To explain the role of carriers in glucose reabsorption
7. To understand the actions of ADH and aldosterone on solute reabsorption and water uptake

The kidneys are excretory and regulatory organs. By excreting water and solutes, the kidneys are responsible for ridding the body of waste products and excess water. The kidneys regulate 1) plasma *osmolarity*, or the concentration of a solution expressed as osmoles of solute per liter of solvent; 2) plasma volume; 3) acid-base balance; 4) electrolyte balance; 5) excretion of metabolic wastes and foreign materials; and 6) the production and secretion of hormones that regulate osmolarity and electrolyte balance. All these activities are extremely important to maintaining homeostasis in the body.

The kidneys are located between the posterior abdominal wall and the abdominal peritoneum. Although many textbooks depict the kidneys directly across from each other, the right kidney is actually slightly lower than the left. Each human kidney contains approximately 1.2 million **nephrons**, the functional units of the kidney. Each nephron is composed of a **renal corpuscle** and a **renal tubule**. The renal corpuscle consists of a tuft of capillaries, called the *glomerulus*, which is enclosed by a fluid-filled capsule called *Bowman's capsule*. An **afferent arteriole** supplies blood to the glomerulus. As blood flows through the glomerular capillaries, protein-free plasma filters into the Bowman's capsule, a process called **glomerular filtration**. An **efferent arteriole** then drains the glomerulus of the remaining blood. The filtrate flows from Bowman's capsule to the start of the renal tubule, called the *proximal convoluted tubule*, then on to the *proximal straight tubule*, followed by the *loop of Henle*, a U-shaped hairpin loop. The filtrate then flows into the *distal convoluted tubule* before reaching the *connecting tubule* and the *collecting duct*, where urine collects. The distal tubule and collecting duct are composed of two cell types: *principal cells* and *intercalated cells*. Principal cells reabsorb Na^+ and water and secrete K^+ . Intercalated cells secrete either H^+ or HCO_3^- and are, therefore, very important in the regulation of the acid/base balance.

Glomerular Filtration

Let's take a closer look at what happens during glomerular filtration. Blood enters the glomerulus from the afferent arteriole. *Starling forces* (hydrostatic and osmotic pressure gradients) drive protein-free plasma from the blood across the walls of the glomerular capillaries and into the Bowman's capsule. The *glomerular filtration rate* is an index of kidney function. In humans, the filtration rate

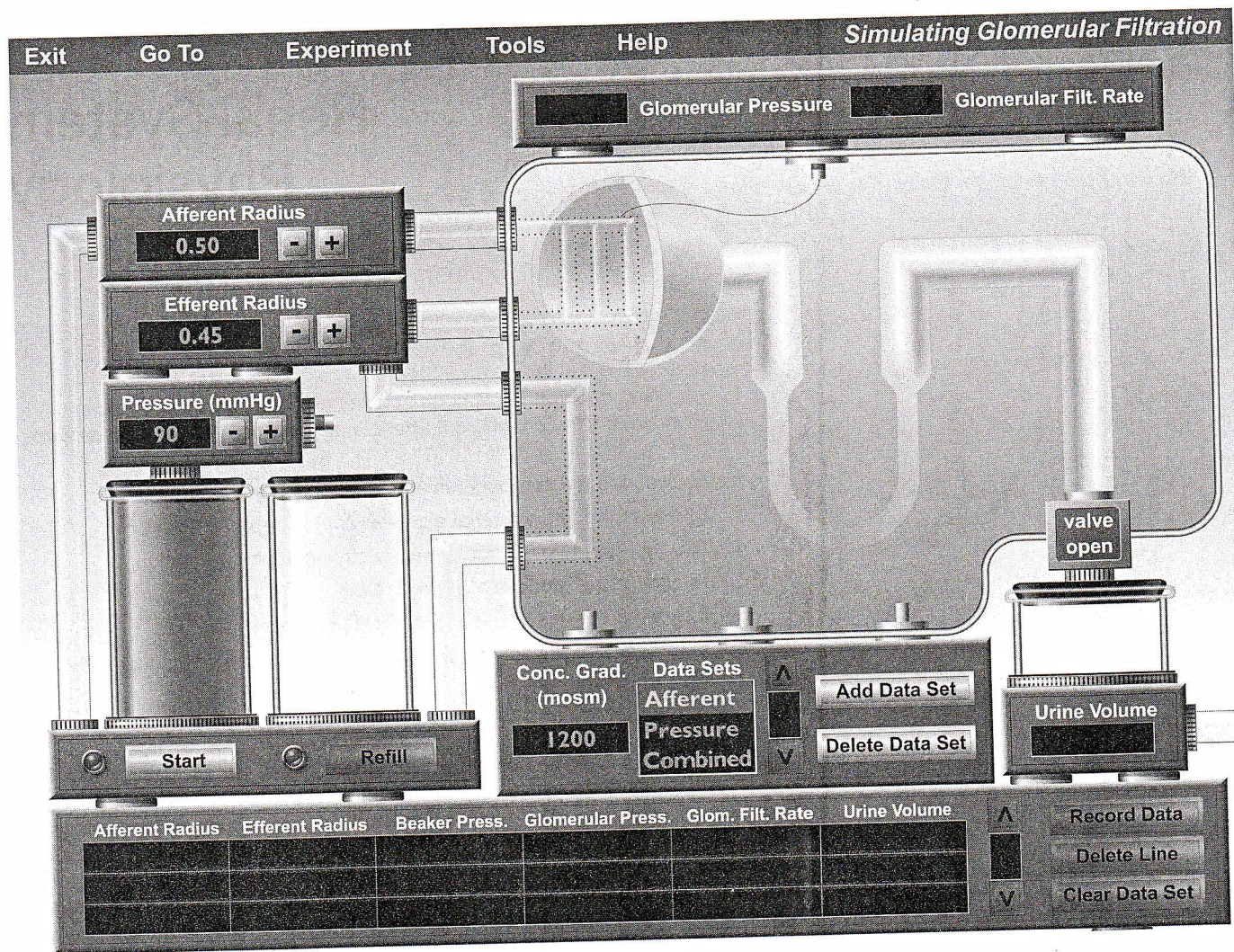


FIGURE 9.1 Opening screen of the Simulating Glomerular Filtration experiment.

ranges from 80 to 140 ml/min, so that in 24 hours as much as 180 liters of plasma is filtered by glomeruli. The filtrate formed is devoid of cellular debris and is essentially protein free. The concentration of salts and organic molecules are similar to that of blood. Normal urine output is 1–1.5 liters/24 hours. The difference is reabsorbed in the body. Normally, only about 20% of the blood that enters the nephron is filtered, due to the osmotic pressure of the blood (*oncotic pressure*) and the hydrostatic pressure from the fluids in Bowman's capsule. The glomerular filtration rate can be altered by changing afferent arteriole resistance, efferent arteriole pressure, or the size of the filtration surface, or by a process called renal autoregulation.

Once the filtrate is formed, the nephron must reabsorb materials that the body needs and excrete unneeded materials from the body. While as much as 180 liters are filtered each day, less than 1% of the filtered water, sodium chloride, and other solutes are excreted in the urine. More than 67% of this reabsorption takes place in the proximal convoluted tubule. The distal convoluted tubule and collecting duct reabsorb approximately 7% of the filtered NaCl, secrete a variable amount of K^+ and H^+ , and reabsorb a variable amount of water. It is in this distal part of the nephron that hormones act to

reabsorb water and electrolytes. **Aldosterone** regulates NaCl reabsorption (and thus NaCl excretion as well). **ADH** (anti-diuretic hormone) causes the permeability of the distal tubule and collecting duct to increase, promoting the uptake of water from the filtrate. ADH is considered the body's most important hormone for regulating water balance.

In the first three activities you will be concentrating on how arterial diameter and pressure affect glomerular filtration rate and urine volume. Follow the instructions for starting PhysioEx in the Getting Started section at the front of this manual. From the Main Menu, select **Renal System Physiology**. You will see the screen shown in Figure 9.1.

Click **Help** at the top of the screen and then select **Balloons On**. Now move your mouse around the simulated nephron in the yellow section of the screen. Labels will appear for the various parts of the nephron as you roll over them. Note in particular the glomerulus and the glomerulus capsule. Also note the "afferent tube" and "efferent tube" to the left of the glomerulus—these represent the afferent and efferent arterioles delivering and draining blood from the glomerulus. You may adjust the radius of either of these tubes by clicking the (+) and (-) buttons next to the respective tubes. You may also adjust the blood pressure of the source

beaker by clicking the (+) and (-) buttons next to the "Pressure (mmHg)" display.

Once you have identified all the equipment on screen, click **Help** again and select **Balloons Off** (you cannot proceed with the experiment unless the labels are turned off). At the bottom left of the screen are two beakers. The left beaker, which we call the "source beaker," represents the blood supply being delivered to the nephron. When the **Start** button is clicked, blood will flow from the source beaker to the afferent arteriole and then to the group of small tubes representing the glomerulus. As blood flows through the glomerulus, you will see *ultrafiltration* occur. (Ultrafiltration means filtration from the plasma of everything except proteins and cells.) Blood will then be drained from the glomerulus to the "drain beaker" next to the source beaker. At the end of the nephron tube, you will see the formation of urine in a small beaker at the lower right of the screen. To watch a test run of this process in action, click the **Start** button. At the end of the run, click **Refill** underneath the drain beaker before you begin the activities that follow.

ACTIVITY 1

Effect of Arteriole Diameter on Glomerular Filtration

In this activity you will investigate how the diameters of the afferent and efferent arterioles leading to and from the glomerulus can affect the glomerular filtration rate.

1. The afferent radius display should be set at 0.50 mm, and the efferent radius at 0.45 mm. If not, use the (+) or (-) buttons next to the afferent and efferent radius displays to adjust accordingly.
2. Be sure the left beaker is full. If not, click the **Refill** button.
3. The pressure gauge above the left beaker should read 90 mm Hg. If not, click the (+) or (-) buttons next to the pressure display to adjust accordingly.
4. Click the **Start** button. As the blood flows through the nephron, watch the displays for glomerular pressure and glomerular filtration rate at the top right of the screen, as well as the display for urine volume at the bottom right of the screen.
5. After the drain beaker has stopped filling with blood, click **Record Data**. This will be your baseline data for this activity.
6. Click the **Refill** button.
7. Increase the *afferent* radius by 0.05 mm and repeat steps 3–6, making sure to click **Record Data** at the end of each run. Keep all the other variables at their original settings. Continue repeating the activity until you have reached the maximum afferent radius of 0.60 mm.

Compare this data with your baseline data. How did increasing the afferent arteriole radius affect glomerular filtration rate?

8. Reduce the afferent arteriole radius to 0.30 mm, and click **Start**.

Under these conditions, does the fluid flow through the nephron?

What is the glomerular filtration rate?

How does it compare to your baseline data, and why?

9. Using the simulation, design and carry out an experiment for testing the effects of increasing or decreasing the *efferent* radius.

How did increasing the efferent radius affect glomerular filtration rate?

How did decreasing the efferent radius affect glomerular filtration rate?

Physiologically, what could be the cause of a change in afferent or efferent arteriole radius?

ACTIVITY 2

Effect of Pressure on Glomerular Filtration

Next you will investigate the effect of blood pressure on glomerular filtration rate.

1. Under the **Data Sets** display, highlight **Pressure**. This will allow you to save data in a new data set window. You can always retrieve your data from the previous activity by highlighting the **Afferent** data set.
2. Make sure that the source beaker is filled with blood, and that the drain beaker is empty. If not, click **Refill**.
3. Adjust the pressure gauge (on top of the source beaker) to 70 mm Hg. Set the afferent radius at 0.50 mm and the efferent radius at 0.45 mm.
4. Click the **Start** button. Watch the Glomerular Pressure and Glomerular Filtration Rate displays at the top right of the screen.

- When the run has finished, click the **Record Data** button. This is your baseline data.
- Increase the pressure by 5 mm Hg and repeat the experiment. Continue increasing the pressure by 5 mm and repeating the experiment until you have reached the maximum pressure of 100 mm Hg. Be sure to click **Record Data** and **Refill** after each experimental run.

As pressure increased, what happened to the pressure in the glomerulus?

What happened to the glomerular filtration rate?

Compare the urine volume in your baseline data with the urine volume as you increased the pressure.

How did the urine volume change?

How could increased urine volume be viewed as being beneficial to the body?

ACTIVITY 3

Combined Effects

In the first activity you looked at arteriole diameter and its role in glomerular filtration. Next you examined the effect of pressure on glomerular filtration. In the human body, both of these effects are occurring simultaneously. In this activity you will investigate the combined effects of arteriole diameter and pressure changes on glomerular filtration.

- Under the **Data Sets** window, highlight **Combined**. This will allow you to save data in a new data set window. You can always retrieve your data from previous activities by highlighting the **Afferent** data set or the **Pressure** data set.
- Set the pressure at 90 mm Hg, the afferent arteriole at 0.50 mm, and the efferent arteriole at 0.45 mm.
- Click the **Start** button and allow the run to complete. Then click **Record Data**. This is your baseline data.
- Click **Refill**.
- Lower the pressure to 80 mm Hg. Leave afferent arteriole at 0.50 and efferent arteriole at 0.45 mm.
- Click the **Start** button and allow the run to complete. Then click **Record Data**.
- Click **Refill**.

What happened to the glomerular filtration rate and urine volume after you reduced the pressure?

How could you adjust the afferent or efferent radius to compensate for the effect of the reduced pressure on glomerular filtration rate and urine volume? Use the simulation to determine your answer.

8. Next, click the square valve button (currently reading "valve open") above the collecting duct. The valve should now read "valve closed."

9. Click **Start**. At the end of the run, click **Record Data**. What changes are seen in nephron function when the valve is closed?

Why were these changes seen?

Is the kidney functional when the glomerular filtration rate is zero? Explain your answer.

What is the major "ingredient" that needs to be removed from the blood?

Studies on aging have demonstrated that some nephrons may fail as we get older. Will this be a problem regarding urine formation?

If blood pressure went down—for example, as the result of blood loss—what changes would the kidney need to make to maintain its normal filtration rate?

10. Click **Tools** → **Print Data** to print your data. █

MLC

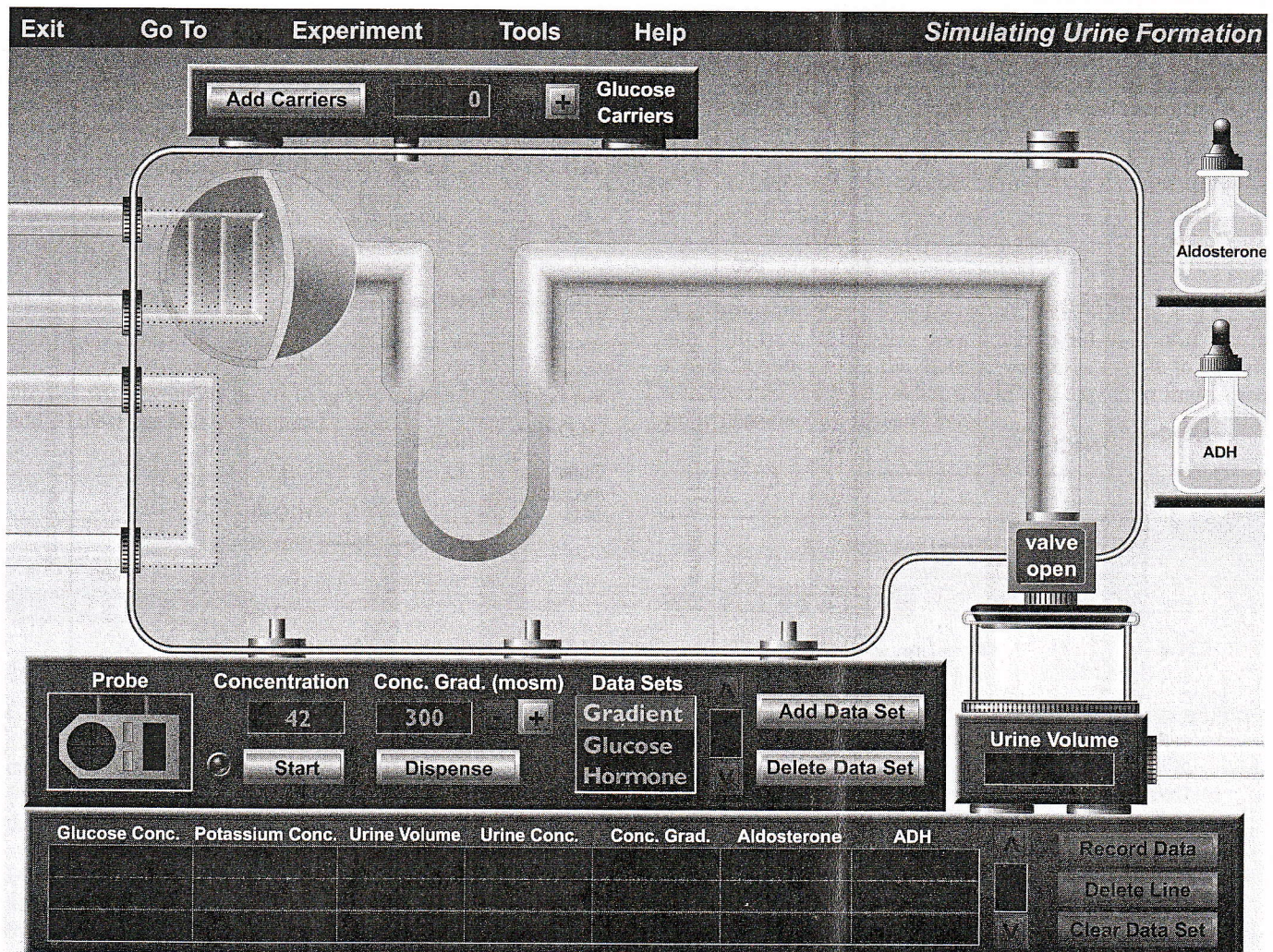


FIGURE 9.2 Urine Formation. (a) Opening screen of the Simulating Urine Formation experiment. Part (b) follows.

Simulating Urine Formation

Reabsorption is the movement of filtered solutes and water from the lumen of the renal tubules back into the plasma. Without reabsorption, we would excrete the solutes and water that our bodies need. In the next activity you will examine the process of passive reabsorption that occurs while filtrate travels through a nephron and urine is formed.

Click **Experiment** at the top of the screen and select **Simulating Urine Formation**. You will see the screen shown in Figure 9.2. The light yellow space surrounding the dark yellow nephron represents *interstitial space* between the nephron and *peritubular capillaries* that branch out from the efferent arteriole. The movement of solutes and water from the renal tubules to the interstitial space is dependent on the *concentration gradient*—that is, the difference between the concentration of solutes in the tubules and the concentration of solutes in the interstitial space. Notice the display for **Conc. Grad. (mosm)** near the bottom of the screen. By clicking the (+) and (–) buttons next to this display and then

clicking **Dispense**, you can adjust the solute concentration of the interstitial space. When you click **Start**, filtrate will begin flowing through the nephron, and solute and water will move from the tubules to the interstitial space to the peritubular capillaries, completing the process of reabsorption. Note that the capillaries are not shown on screen.

Note also the two dropper bottles at the right side of the screen, which contain the hormones aldosterone and ADH (antidiuretic hormone). For the first activity you will be dealing with ADH only, which increases the water permeability of the distal convoluted tube and the collecting duct of the nephron (Figure 9.2b and c). Near the bottom left of the screen you will notice a **Probe**. When the probe turns red, you can click and drag it over various parts of the nephron and over the beaker to measure the solute concentration present. Finally, notice the equipment at the very top of the screen for adding glucose carriers. We will explain this equipment in Activity 5, when you will be studying the reabsorption of glucose.

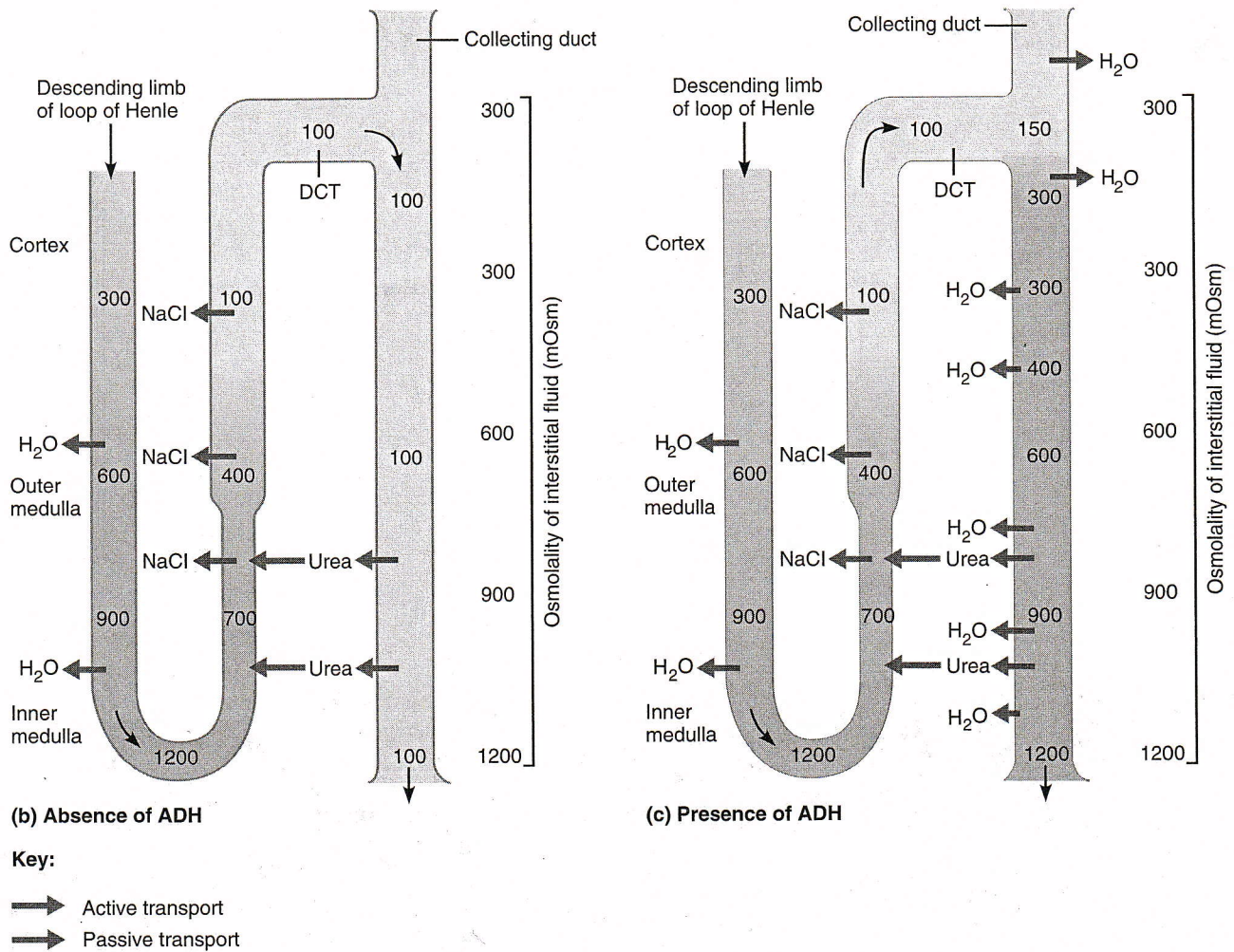


FIGURE 9.2 (continued) Urine Formation (b) Mechanisms for forming dilute urine (c) and concentrated urine.

ACTIVITY 4

Effect of Solute Gradient on Urine Concentration

1. Make sure **Gradient** is highlighted within the **Data Sets** window.
2. Click and drag the dropper top from the bottle of ADH and release it on top of the gray cap directly above the right side of the nephron. The cap will open, and ADH will be dropped onto the collecting duct. The cap will then close.
3. The **Conc. Grad. (mosm)** window should read 300. If not, adjust the (+) or (-) buttons accordingly.
4. Click **Dispense** to apply the 300 mosm concentration to the interstitial fluid. It is important to note that this is also the typical value of solute concentration in the blood.
5. Click **Start** and allow the blood to flow through the system. Watch the **Probe** at the bottom left of the screen. When

it turns red, click and drag it over to the urine collecting beaker to measure the urine solute concentration. The value will appear in the **Concentration** window next to the probe's original location.

6. At the end of the run, click **Record Data**.
7. Increase the concentration gradient by 300 mosm (i.e., set it at 600 mosm) and repeat the experiment. Remember to add ADH to the collecting duct before clicking **Start**. Continue increasing the gradient by 300 mosm and repeating the experiment until you reach 1200 mosm, the normal value for interstitial solute concentration in the kidney. Be sure to click **Record Data** after each run.

How did the urine solute concentration change as the concentration gradient of the interstitial fluid increased?

What happened to the urine volume as the concentration gradient increased? Why?

By increasing the concentration gradient, what are you doing to the urine that is formed?

Predict what would happen to urine volume if you did not add ADH to the collecting duct.

ACTIVITY 5

Reabsorption of Glucose

Glucose is not very large, and as such it is easily filtered out of the plasma into Bowman's capsule as part of the filtrate. To ensure that glucose is reabsorbed into the body so that it can form the starting material of metabolism, glucose carriers are present in the nephron. There is a finite number of carriers per cell, so if too much glucose is taken in, not all of it will be reabsorbed into the body. Glucose is absorbed by *secondary active transport*, the "push" of which comes from the gradient created by the transport of sodium. The carriers that transport these molecules across the membrane are proteins embedded in the cell membrane. In this activity you will examine the effect of glucose carriers on glucose reabsorption.

1. Highlight **Glucose** within the **Data Sets** window.
2. Set the **Conc. Grad. (mosm)** to 1200 and click **Dispense**. Recall that 1200 is the normal value for solute concentration in the kidney.
3. Click **Start**.
4. Click **Record Data** at the end of the run. This run will serve as a "control" run, with no glucose carriers present. Note that no ADH has been added, either—your focus will be on the absence or presence of glucose carriers.
5. At the top of the screen, click the (+) button until the **Glucose Carriers** window reads 100. Then click **Add Carriers**.
6. Click **Start**.
7. At the end of the run, click **Record Data**.
8. Continue to increase the number of glucose carriers by 100 at a time and repeat the experiment until you have reached the maximum number of carriers, 500. Be sure to dispense the concentration gradient before beginning each run, and to click **Record Data** after each run.

What happens to the glucose concentration as you add glucose carriers to the system?

At what point does the glucose concentration in the urine become zero?

A person with type I diabetes cannot make insulin, and a person with type II diabetes does not respond to insulin that is made. In either case, the diabetic person is unable to absorb glucose into the body. What would you expect to find in the urine of a diabetic person? Why?

ACTIVITY 6

Effect of Hormones on Reabsorption

By now you should understand how filtration occurs and how it is controlled. You should understand passive solute movement and the role of glucose carriers on glucose reabsorption. Next you will examine the actions of hormones on the nephron, most of which occur in the collecting duct.

Antidiuretic hormone (ADH) is influenced by the *osmolality* (the concentration of a solution expressed in osmoles of solute particles per kilogram of solvent) of body fluids as well as the volume and pressure of the cardiovascular system. A 1% change in body osmolality will cause this hormone to be secreted. The primary action of this hormone is to increase the permeability of the distal tubule and the collecting duct to water so that more water is taken up into the body. ADH binds to receptors in the principal cells to cause this reaction by opening *aquaporins*, or water channels in the apical membrane. Without water uptake, the body would quickly dehydrate. The kidney tightly regulates the amount of water excreted under normal conditions to maintain water balance in the body. Water intake must precisely match water loss from the body. If water intake is down, or if there has been a fluid loss from the body, the kidneys work to conserve water by making the urine very *hyperosmotic* (having a relatively high solute concentration) to the blood. If there has been a large intake of fluid, the urine is more *hypo-osmotic*. In the normal individual, urine osmolarity varies from 50 to 1200 milliosmoles/kg water. The osmolality of the body must be maintained within very narrow limits.

Aldosterone is an adrenal cortical hormone under the control of the body's *renin-angiotensin system*. A decrease in blood pressure is detected by cells in the afferent arteriole and triggers the release of renin. Renin acts as a proteolytic enzyme, causing angiotensinogen to be converted into angiotensin I. Endothelial cells have an enzyme, called the *converting enzyme*, which converts angiotensin I into angiotensin II. Angiotensin II works on the adrenal cortex to

induce it to secrete aldosterone. Aldosterone acts on the collecting duct of the kidney to promote the uptake of sodium from filtrate *into* the body and the release of potassium *from* the body. Coupled with the addition of ADH, this electrolyte shift also causes more water to be reabsorbed into the blood, resulting in increased blood pressure.

1. Highlight **Hormone** within the **Data Sets** window.
2. Set the number of **Glucose Carriers** to zero and click **Dispense** to ensure that no carriers from the previous activity remain in action.
3. Set the **Conc. Grad. (mosm)** to 1200 and click **Dispense**.
4. Click **Start**. At the end of the run, click **Record Data**. This is your "control" run and baseline data.

Baseline Urine Volume = _____

5. Click and drag the dropper top from the bottle of aldosterone and release it on top of the gray cap directly above the right side of the nephron. The cap will close, and aldosterone will be dropped onto the collecting duct.
6. Click **Start**. At the end of the run, click **Record Data**.

Urine volume with aldosterone present = _____

7. Click and drag the dropper top from the bottle of ADH and release it on top of the gray cap directly above the right side of the nephron. The cap will close, and ADH will be dropped onto the collecting duct.
8. Click **Start**. At the end of the run, click **Record Data**.
9. For your fourth run, dispense both ADH and aldosterone onto the collecting duct. You should see a yellow outline appear around the collecting duct.
10. Click **Start**. At the end of the run, click **Record Data**.
11. Click **Tools** → **Print Data** to print your data.

Which hormone has the greater effect on urine volume? Why?

How does the addition of aldosterone affect the concentration of potassium in the urine?

How does the addition of ADH affect the concentration of potassium in the urine? How does this compare to the effect of adding aldosterone, with respect to potassium concentration in the urine?

How does the addition of both hormones affect 1) urine concentration, 2) urine volume, and 3) potassium concentration?

If ADH were not used, how would the urine concentration vary? Explain your answer.

Histology Review Supplement

For a review of renal tissue, go to **Exercise H: Histology Atlas & Review** on the **PhysioEx™** website to print out the **Renal Tissue Review** worksheet.

MCM