

Renal System Physiology

OBJECTIVES

1. To define the following terms:
glomerulus, glomerular capsule, renal corpuscle, renal tubule, nephron, proximal convoluted tubule, loop of Henle, and distal convoluted tubule.
2. To describe the blood supply to each nephron.
3. To identify the regions of the nephron involved in glomerular filtration and tubular reabsorption.
4. To study the factors affecting glomerular filtration.
5. To explore the concept of carrier transport maximum.
6. To understand how the hormones aldosterone and ADH affect the function of the kidney.
7. To describe how the kidneys can produce urine that is four times more concentrated than the blood.

Metabolism produces wastes that must be eliminated from the body. This excretory function is the job of the renal system, most importantly the paired kidneys. Each kidney consists of about one million nephrons that carry out two crucial services, blood filtration and fluid processing.

Microscopic Structure and Function of the Kidney

Each of the million or so **nephrons** in each kidney is a microscopic tubule consisting of two major parts: a glomerulus and a renal tubule. The **glomerulus** is a tangled capillary knot that filters fluid from the blood into the lumen of the renal tubule. The function of the **renal tubule** is to process that fluid, also called the **filtrate**. The beginning of the renal tubule is an enlarged end called the **glomerular capsule**, which surrounds the glomerulus and serves to funnel the filtrate into the rest of the renal tubule. Collectively, the glomerulus and the glomerular capsule are called the **renal corpuscle**.

As the rest of the renal tubule extends from the glomerular capsule, it becomes twisted and convoluted, then dips sharply down to form a hairpin loop, and then coils again before entering a collecting duct. Starting at the glomerular capsule, the anatomical parts of the renal tubule are as follows: the **proximal convoluted tubule**, the **loop of Henle** (nephron loop), and the **distal convoluted tubule**.

Two arterioles supply each glomerulus: an afferent arteriole feeds the glomerular capillary bed and an efferent arteriole drains it. These arterioles are responsible for blood flow through the glomerulus. Constricting the afferent arteriole lowers the downstream pressure in the glomerulus, whereas constricting the efferent arteriole will increase the pressure in the glomerulus. In addition, the diameter of the efferent arteriole is smaller than the diameter of the afferent arteriole, restricting blood flow out of the glomerulus. Consequently, the pressure in the glomerulus forces fluid through the endothelium of the glomerulus into the lumen of the surrounding glomerular capsule. In essence, everything in the blood except the cells and proteins are filtered through the glomerular wall. From the capsule, the filtrate moves into the rest of the renal tubule for processing. The job of the tubule is to reabsorb all the beneficial substances from its lumen while allowing the wastes to travel down the tubule for elimination from the body.

The nephron performs three important functions to process the filtrate into urine: glomerular filtration, tubular reabsorption, and tubular secretion. **Glomerular filtration** is a passive process in which fluid passes from the lumen of the glomerular capillary into the glomerular capsule of the renal tubule. **Tubular reabsorption** moves most of the filtrate back into the blood, leaving principally salt water plus the wastes in the lumen of the tubule. Some of the desirable or needed solutes are actively reabsorbed, and others move passively from the lumen of the tubule into the interstitial spaces. **Tubular secretion** is essentially the reverse of tubular reabsorption and is a process by which the kidneys can rid the blood of additional unwanted substances such as creatinine and ammonia.

The reabsorbed solutes and water that move into the interstitial space between the nephrons need to be returned to the blood, or the kidneys will rapidly swell like balloons. The peritubular capillaries surrounding the renal tubule reclaim the reabsorbed substances and return them to general circulation. Peritubular capillaries arise from the efferent arteriole exiting the glomerulus and empty into the veins leaving the kidney.

Simulating Glomerular Filtration

This computerized simulation allows you to explore one function of a single simulated nephron, glomerular filtration. The concepts you will learn by studying a single nephron can then be applied to understand the function of the kidney as a whole.

Choose **Exercise 9: Renal System Physiology** from the drop-down menu and click **GO**. Then click **Simulating Glomerular Filtration**. The opening screen for the Simulating Glomerular Filtration experiment will appear in a few seconds (Figure 9.1). The main features on the screen when the program starts are a *simulated blood supply* at the left side of the screen, a *simulated nephron* within a supporting tank on the right side, and a *data control unit* at the bottom of the display.

The left beaker is the “blood” source representing the general circulation supplying the nephron. The “blood pressure” in the beaker is adjustable by clicking the (+) and (–) buttons on top of the beaker. A tube with an adjustable radius called the *afferent flow tube* connects the left beaker to the simulated glomerulus. Another adjustable tube called the *efferent flow*

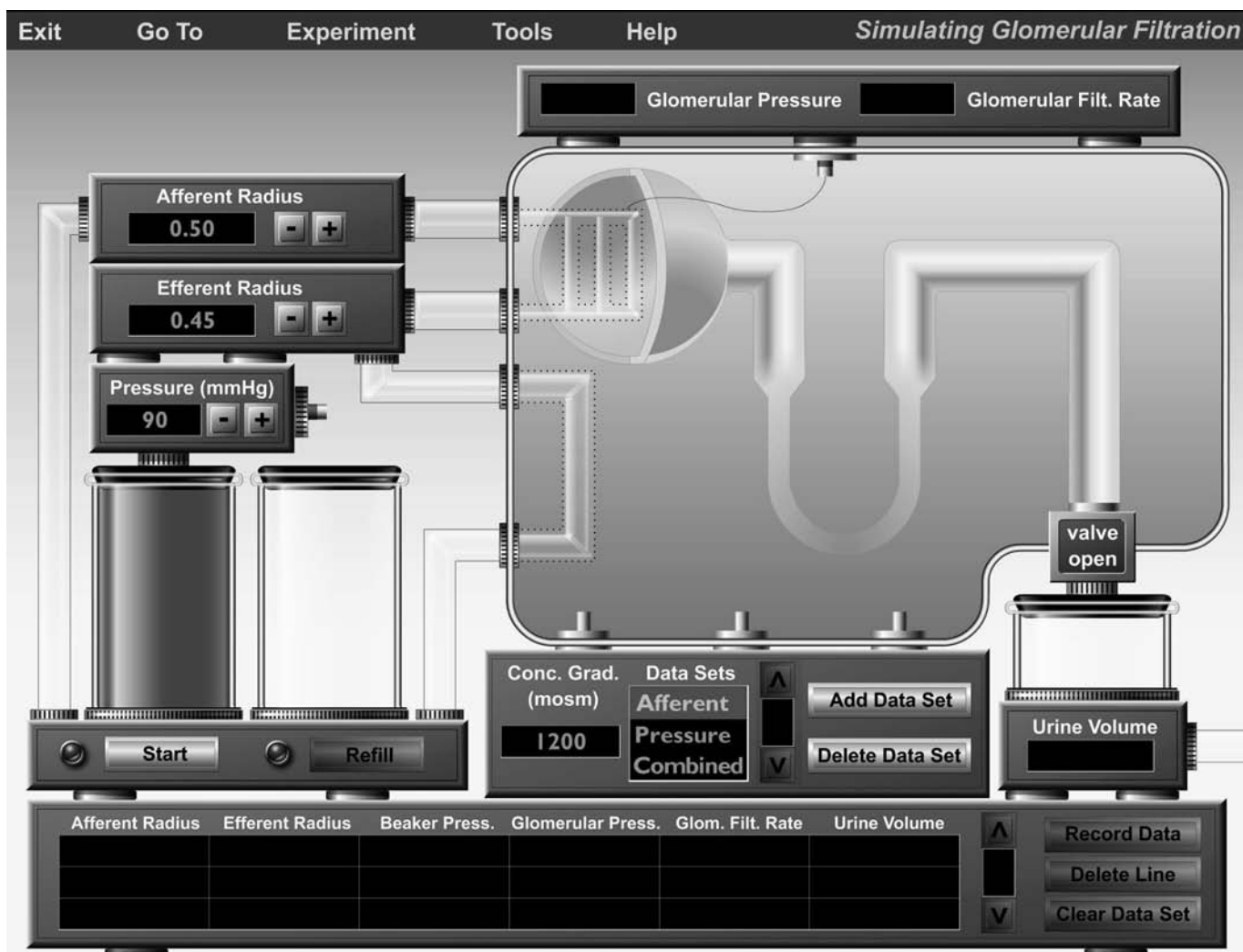


FIGURE 9.1 Opening screen of the Simulating Glomerular Filtration experiment.

tube drains the glomerulus. The afferent flow tube represents the afferent arteriole feeding the glomerulus of each nephron, and the efferent flow tube represents the efferent arteriole draining the glomerulus. The outflow of the nephron empties into a collecting duct, which in turn drains into another small beaker at the bottom right part of the screen. Clicking the valve at the end of the collecting duct (which currently reads **valve open**) stops the flow of fluid through the nephron and collecting duct.

The **Glomerular Pressure** window on top of the nephron tank displays the pressure within the glomerulus. The **Glomerular Filtr. Rate** window indicates the flow rate of the fluid moving from the lumen of the glomerulus into the lumen of the renal tubule.

The concentration gradient bathing the nephron is fixed at 1200 milliosmoles (mosm). Clicking **Start** begins the experiment. Clicking **Refill** resets the equipment to begin another run.

The equipment in the lower part of the screen is called the *data control unit*. This equipment records and displays data you accumulate during the experiments. The data set for the first experiment (Afferent) is highlighted in the **Data Sets** window. You can add or delete a data set by clicking the appropriate button to the right of the Data Sets window. When you click **Record Data**, your data is recorded in the computer's memory and is displayed in the data grid. Data displayed in the data grid include the afferent radius, efferent radius, beaker pressure, glomerular pressure, glomerular filtration rate, and urine volume. Clicking **Delete Line** allows you to discard data values for a single run, and clicking **Clear Data Set** erases the entire experiment to allow you to start over.

If you need help identifying any piece of equipment, choose **Balloons On/Off** from the **Help** menu and move the mouse pointer onto any piece of equipment visible on the computer's screen. As the pointer touches the object, a pop-up window appears identifying the equipment. To close the pop-up window, move the mouse pointer away from the equipment. Choose **Balloons On/Off** to turn off this Help feature.

ACTIVITY 1

Investigating the Effect of Flow Tube Radius on Glomerular Filtration

Your first experiment will examine the effects of flow tube radii and pressures on the rate of glomerular filtration. Click **Start** to see the on-screen action. Continue when you understand how the simulation operates. Click **Refill** to reset the experiment.

1. The **Afferent** line in the **Data Sets** window of the data control unit should be highlighted in bright blue. If it is not, choose it by clicking the **Afferent** line. The data control unit will now record filtration rate variations due to changing afferent flow tube radius.
2. If the data grid is not empty, click **Clear Data Set** to discard all previous data.
3. Adjust the afferent radius to 0.35 mm and the efferent radius to 0.40 mm by clicking the appropriate (+) or (–) buttons.
4. If the left beaker is not full, click **Refill**.
5. Keep the beaker pressure at 90 mm Hg during this part of the experiment.

6. Click **Start**, and watch the blood flow. Simultaneously, filtered fluid will be moving through the nephron and into the collecting duct. The Glomerular Filtration Rate window will display the fluid flow rate into the renal tubule when the left beaker has finished draining.

7. Now click **Record Data** to record the current experiment data in the data grid. Click **Refill** to replenish the left beaker and prepare the nephron for the next run.

8. Increase the afferent radius in 0.05-mm increments and repeat steps 6 and 7 until the maximum radius (0.60 mm) is achieved. Be sure to click **Record Data** after each trial. If you make an error and want to delete a single value, click the data line in the data grid and then click **Delete Line**.

What happens to the glomerular filtration rate as the afferent radius is increased?

What happens to the glomerular pressure as the afferent radius is increased?

Predict what effect increasing or decreasing the efferent radius will have on glomerular filtration rate. Use the simulation to check your prediction and record your results.

ACTIVITY 2

Studying the Effect of Pressure on Glomerular Filtration

Both the blood pressure supplying the glomerulus and the pressure in the renal tubule have a significant impact on the glomerular filtration rate. In this activity, the data control unit will record filtration rate variations due to changing pressure.

1. Click the **Pressure** line in the **Data Sets** window of the data control unit.
2. If the data grid is not empty, click **Clear Data Set** to discard all previous data.
3. If the left beaker is not full, click **Refill**.
4. Adjust the pressure in the left beaker to 70 mm Hg by clicking the appropriate (+) or (–) button.
5. During this part of the experiment, maintain the afferent flow tube radius at 0.55 mm and the efferent flow tube radius at 0.45 mm.
6. Click **Start**, and watch the blood flow. Filtrate will move through the nephron into the collecting duct. At the end of the run, the Glomerular Filtration Rate window will display the filtrate flow rate into the renal tubule.

7. Now click **Record Data** to record the current experiment data in the data grid. Click **Refill** to replenish the left beaker.
8. Increase the pressure in the left beaker in increments of 10 mm Hg and repeat steps 6 and 7 until the maximum pressure (100 mm Hg) is achieved. Be sure to click **Record Data** after each trial. If you make an error and want to delete a single value, click the data line in the data grid and then click **Delete Line**.

What happened to the glomerular filtration rate as the beaker pressure was increased?

What was the effect on glomerular pressure as beaker pressure increased?

ACTIVITY 3

Exploring Intrinsic Controls: Renal Autoregulation

So far, you have examined the effects of flow tube radius and pressure on glomerular filtration rate. In this experiment you will be altering both variables to explore the combined effects on glomerular filtration rate and to see how one can compensate for the other to maintain an adequate glomerular filtration rate.

1. Click **Combined** in the **Data Sets** window of the data control unit.
2. If the data grid is not empty, click **Clear Data Set** to discard all previous data.
3. If the left beaker is not full, click **Refill**.
4. Set the starting conditions at:
 - 100 mm Hg beaker pressure
 - 0.55 mm afferent radius
 - 0.45 mm efferent radius
5. Click **Start**.
6. Now click **Record Data** to record the current baseline data in the data grid.
7. Click **Refill**.
8. Set the starting conditions at:
 - 80 mm Hg beaker pressure
 - 0.55 mm afferent radius
 - 0.45 mm efferent radius
9. Record the glomerular filtration rate at a beaker pressure of 80 mm Hg: _____
10. If the left beaker is not full, click **Refill**.

11. Adjust the pressure in the left beaker to 85 mm Hg by clicking the appropriate (+) or (–) button.

12. Maintain the starting conditions for the afferent flow tube radius and the efferent flow tube radius.

13. Record the glomerular filtration rate at a beaker pressure of 85 mm Hg: _____

14. What variables other than beaker pressure could you change to return the glomerular filtration rate to “normal” (the value when beaker pressure is 80 mm Hg)? Circle the correct change in each set of parentheses: (increase / decrease) in the afferent radius, (increase / decrease) in the efferent radius.

15. Test your predictions. Hint: Try small changes of each variable one at a time.

16. List the value of each variable that results in a glomerular filtration rate approximately the same as its starting value when beaker pressure is 85 mm Hg.

Afferent radius _____ mm

Efferent radius _____ mm

17. Click **Tools** → **Print Data** to print your recorded data. ■

Simulating Urine Formation

This part of the computer simulation allows you to explore some aspects of urine formation by manipulating the interstitial solute concentration. Other activities include investigating the effects of aldosterone and ADH (antidiuretic hormone) and the role that glucose carrier proteins play in renal function.

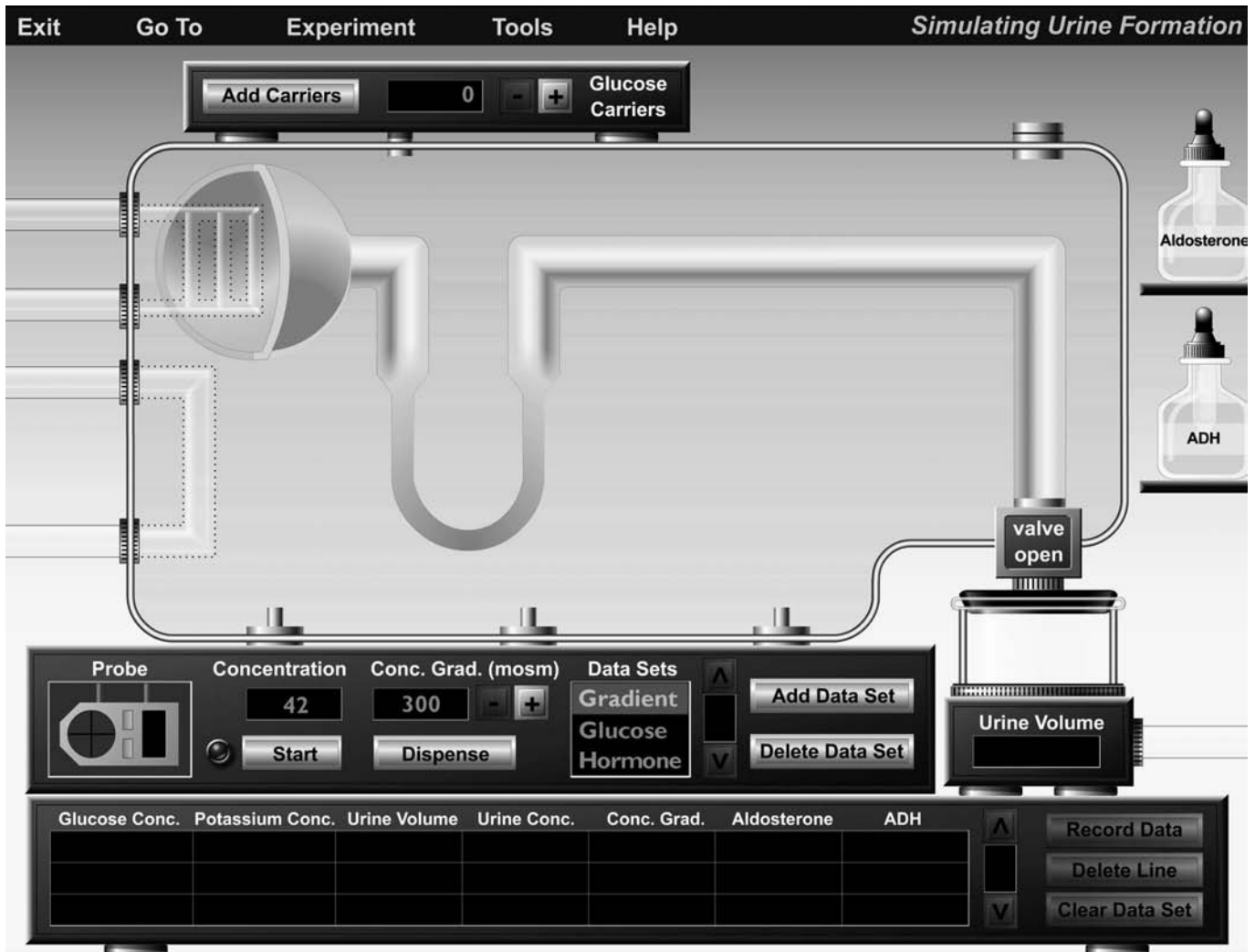
Choose **Simulating Urine Formation** from the **Experiment** menu. The opening screen will appear in a few seconds (Figure 9.2). The basic features on the screen when the program starts are similar to the glomerular filtration screen. Most of the vascular controls have been moved off-screen to the left because they will not be needed in this set of experiments. Additional equipment includes *supply shelves* at the right side of the screen, a *glucose carrier control* located at the top of the nephron tank, and a *concentration probe* at the bottom left part of the screen.

The maximum concentration of the interstitial gradient to be dispensed into the tank surrounding the nephron is adjusted by clicking the (+) and (–) buttons next to the Conc. Grad. window. Click **Dispense** to fill the tank through the jets at the bottom of the tank with the chosen solute gradient. Click **Start** to begin a run. While the experiment is running, the concentration probe can be clicked and dragged over the nephron to display the solute concentration within.

Hormone is dispensed by dragging a hormone dropper cap to the gray cap button in the nephron tank at the top of the collecting duct and then letting go of the mouse button.

The (+) and (–) buttons in the glucose carrier control are used to adjust the number of glucose carriers that will be inserted into the simulated proximal convoluted tubule when the **Add Carriers** button is clicked.

Data displayed in the data grid will depend on which experiment is being conducted. Clicking **Delete Line** allows you to discard data values for a single run, and clicking **Clear Data Set** erases the entire experiment to allow you to start over.



(a)

FIGURE 9.2 Urine formation. (a) Opening screen of the Simulating Urine Formation experiment.

ACTIVITY 4

Exploring the Role of the Solute Gradient on Maximum Urine Concentration Achievable

In the process of urine formation, solutes and water move from the lumen of the nephron into the interstitial spaces. The passive movement of solutes and water from the lumen of the renal tubule into the interstitial spaces relies in part on the total solute gradient surrounding the nephron. When the nephron is permeable to solutes or water, an equilibrium will be reached between the interstitial fluid and the contents of the nephron. Antidiuretic hormone (ADH) increases the water permeability of the distal convoluted tubule and the collecting duct, allowing water to flow to areas of higher solute concentration, usually from the lumen of the nephron into the surrounding interstitial area. You will explore the process of passive reabsorption in this experiment. While doing this part of the simulation, assume that when ADH is present the conditions favor the formation of the most concentrated urine possible. (Figure 9.2b and c).

1. **Gradient** in the **Data Sets** window of the data control unit should be highlighted in bright blue. If it is not, then click **Gradient**.
2. If the data grid is not empty, click **Clear Data Set** to discard all previous data.
3. Click and hold the mouse button on the **ADH** bottle cap and drag it to the gray cap at the top right side of the nephron tank. Release the mouse button to dispense ADH onto the collecting duct.
4. Adjust the maximum total solute concentration of the gradient (**Conc. Grad.**) to 300 mosm by clicking the appropriate (+) or (–) button. Because the blood solute concentration is also 300 mosm, there is no osmotic difference between the lumen of the nephron and the surrounding interstitial fluid.
5. Click **Dispense**.
6. Click **Start** to begin the experiment. Filtrate will move through the nephron and then drain into the beaker below the collecting duct.

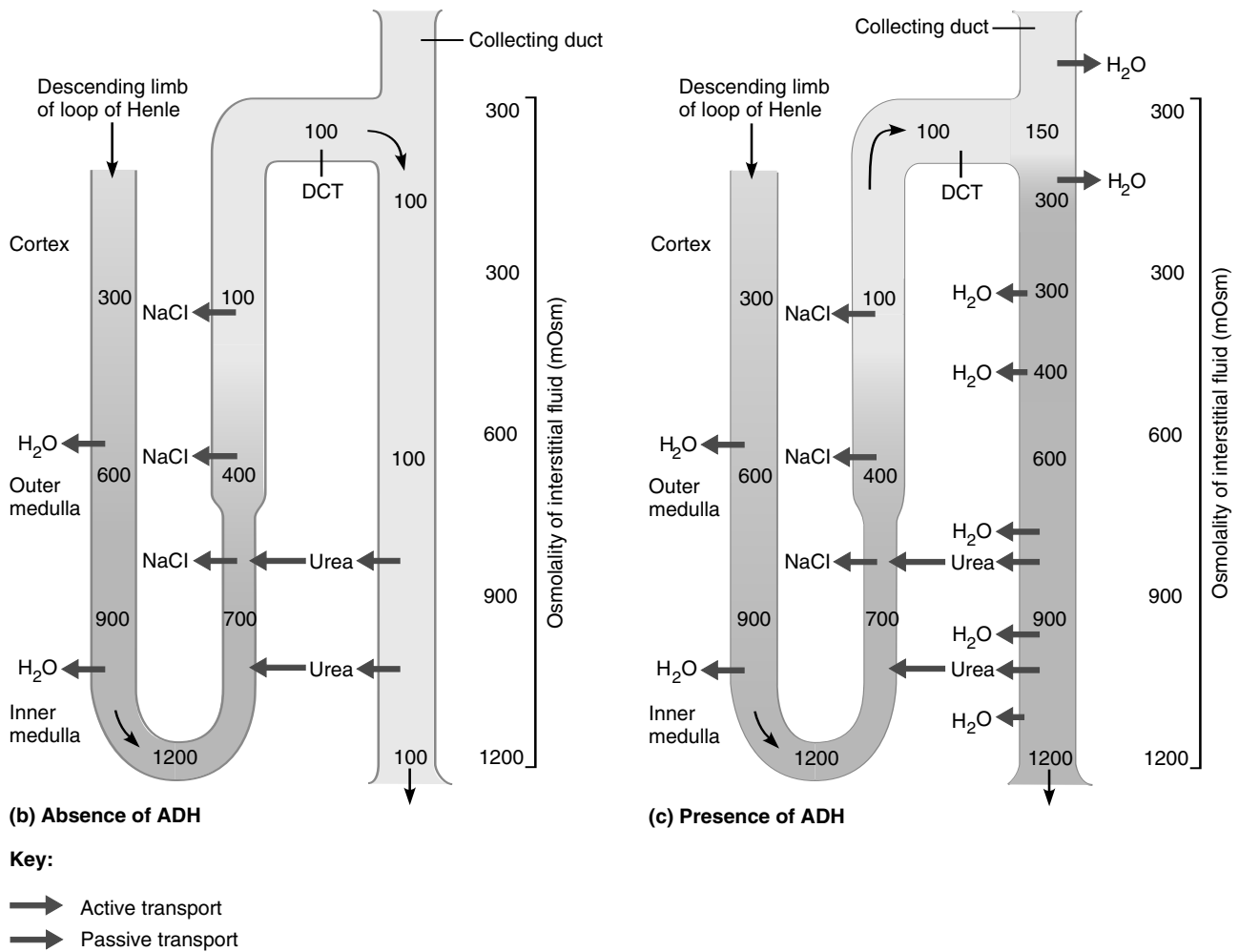


FIGURE 9.2 (continued) Urine formation. (b) Mechanisms for forming dilute urine (c) and concentrated urine.

- While the experiment is running, watch the **Probe**. When it turns red, click and hold the mouse on it, and drag it to the urine beaker. Observe the total solute concentration in the **Concentration** window.
- Now click **Record Data** to record the current experiment data in the data grid.
- Increase the maximum concentration of the gradient in 300-mosm increments, and repeat steps 3 through 8 until 1200 mosm is achieved. Be sure to click **Record Data** after each trial. If you make an error and want to delete a single value, click the data line in the data grid and then click **Delete Line**.

What happened to the urine concentration as the gradient concentration was increased?

What happened to the volume of urine?

What factor limits the maximum possible urine concentration?

Was equilibrium achieved?

ACTIVITY 5

Studying the Effect of Glucose Carrier Proteins on Glucose Reabsorption

Because carrier proteins are needed to move glucose from the lumen of the nephron into the interstitial spaces, there is a limit to the amount of glucose that can be reabsorbed. When all glucose carriers are bound with the glucose they are transporting, excess glucose is eliminated in urine. In this experiment, you will examine the effect of varying the

number of glucose transport proteins in the proximal convoluted tubule.

1. Click **Glucose** in the **Data Sets** window of the data control unit.
2. If the data grid is not empty, click **Clear Data Set** to discard all previous data.
3. Set the concentration gradient (**Conc. Grad.**) to 1200 mosm.
4. Click **Dispense**.
5. Adjust the number of glucose carriers to 100 (an arbitrary figure) by clicking the appropriate (+) or (–) button.
6. Click **Add Carriers**. This action inserts the specified number of glucose carrier proteins per unit area into the membrane of the proximal convoluted tubule.
7. Click **Start** to begin the run after the carriers have been added.
8. Click **Record Data** to record the current experimental data in the data grid. Glucose presence in the urine will be displayed in the data grid.
9. Now increase the number of glucose carrier proteins in the proximal convoluted tubule in increments of 100 glucose carriers, and repeat steps 6 through 8 until the maximum number of glucose carrier proteins (500) is achieved. Remember to click **Add Carriers** each time. Be sure to click **Record Data** after each trial. If you make an error and want to delete a single value, click the data line in the data grid and then click **Delete Line**.

What happened to the amount of glucose present in the urine as the number of glucose carriers was increased?

The amount of glucose present in normal urine is minimal because there are normally enough glucose carriers present to handle the “traffic.” Predict the consequence in the urine if there was more glucose than could be transported by the available number of glucose carrier proteins.

Explain why we would expect to find glucose in the urine of a diabetic person.

ACTIVITY 6

Testing the Effect of Hormones on Urine Formation

The concentration of the urine excreted by our kidneys changes depending on our immediate needs. For example, if

a person consumes a large quantity of water, the excess water will be eliminated, producing dilute urine. On the other hand, under conditions of dehydration, there is a clear benefit in being able to produce urine as concentrated as possible, thereby retaining precious water. Although the medullary gradient makes it possible to excrete concentrated urine, urine dilution or concentration is ultimately under hormonal control. In this experiment, you will investigate the effects of two different hormones on renal function, aldosterone produced by the adrenal gland and ADH manufactured by the hypothalamus and stored in the posterior pituitary gland. Aldosterone works to reabsorb sodium ions (and thereby water) at the expense of losing potassium ions; its site of action is the distal convoluted tubule. ADH makes the distal tubule and collecting duct more permeable to water, thereby allowing the body to reabsorb more water from the filtrate when it is present.

1. Click **Hormone** in the **Data Sets** window of the data control unit.
2. If the data grid is not empty, click **Clear Data Set** to discard all previous data.
3. During this part of the experiment, keep the concentration gradient at 1200 mosm.
4. Click **Dispense** to add the gradient, and then click **Start** to begin the experiment.
5. Now click **Record Data** to record the current experimental data in the data grid.

You will use this baseline data to compare with the conditions of the filtrate under the control of the two hormones.

Baseline urine volume _____

6. Keeping all experiment conditions the same as before, do the following:
 - Drag the **Aldosterone** dropper cap to the gray cap on the top right side of the nephron tank, and release the mouse to automatically dispense aldosterone into the tank surrounding the distal convoluted tubule and collecting duct.
 - Click **Start**, and allow the run to complete.
 - Click **Record Data**.

Urine volume with aldosterone present _____

In this run, how does the volume of urine differ from the previously measured baseline volume?

Explain the difference in the total amount of potassium in the urine between this run and the baseline run.

7. Drag the **ADH** bottle cap to the gray cap on the top right side of the nephron tank, and release it to dispense ADH.

- Click **Start**, and allow the run to complete.
- Click **Record Data**.

In this run, how does the volume of urine differ from the baseline measurement?

Is there a difference in the total amount of potassium in this run and the total amount of potassium in the baseline run? Explain your answer. (Hint: The urine volume with ADH present is about one-tenth the urine volume when it is not present.)

Are the effects of aldosterone and ADH similar or antagonistic? _____

Consider this situation: we want to reabsorb sodium ions but do not want to increase the volume of the blood by reabsorbing water from the filtrate. Assuming that aldosterone and ADH are both present, how would you adjust the hormones to accomplish the task?

8. Click **Tools** → **Print Data** to print your recorded data. ■

Histology Review Supplement

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