

Acid/Base Balance

OBJECTIVES

1. To define *pH* and identify the normal range of human blood pH levels.
2. To define *acid* and *base*, and explain what characterizes each of the following: *strong acid*, *weak acid*, *strong base*, *weak base*.
3. To explain how chemical and physiological buffering systems help regulate the body's pH levels.
4. To define the conditions of *acidosis* and *alkalosis*.
5. To explain the difference between *respiratory acidosis and alkalosis* and *metabolic acidosis and alkalosis*.
6. To understand the causes of respiratory acidosis and alkalosis.
7. To explain how the renal system compensates for respiratory acidosis and alkalosis.
8. To understand the causes of metabolic acidosis and alkalosis.
9. To explain how the respiratory system compensates for metabolic acidosis and alkalosis.

The term **pH** is used to denote the hydrogen ion concentration $[H^+]$ in body fluids. pH values are the reciprocal of $[H^+]$ and follow the formula

$$pH = \log(1/[H^+])$$

At a pH of 7.4, $[H^+]$ is about 40 nanomolars (nM) per liter. Because the relationship is reciprocal, $[H^+]$ is higher at *lower* pH values (indicating higher acid levels) and lower at *higher* pH values (indicating lower acid levels).

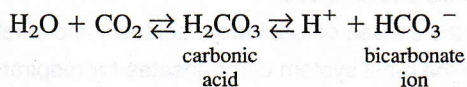
The pH of a body's fluids is also referred to as its **acid/base balance**. An **acid** is a substance that releases H^+ in solution (such as in body fluids). A **base**, often a hydroxyl ion (OH^-) or bicarbonate ion (HCO_3^-), is a substance that binds to H^+ . A *strong acid* is one that completely dissociates in solution, releasing all of its hydrogen ions and thus lowering the solution's pH level. A *weak acid* dissociates incompletely and does not release all of its hydrogen ions in solution. A *strong base* has a strong tendency to bind to H^+ , which has the effect of raising the pH value of the solution. A *weak base* binds less of the H^+ , having a lesser effect on solution pH.

The body's pH levels are very tightly regulated. Blood and tissue fluids normally have pH values between 7.35 and 7.45. Under pathological conditions, blood pH values as low as 6.9 or as high as 7.8 have been recorded; however, values higher or lower than these cannot sustain human life. The narrow range of 7.35–7.45 is remarkable when one considers the vast number of biochemical reactions that take place in the body. The human body normally produces a large amount of H^+ as the result of metabolic processes, ingested acids, and the products of fat, sugar, and amino acid metabolism. The regulation of a relatively constant internal pH environment is one of the major physiological functions of the body's organ systems.

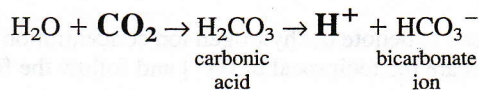
To maintain pH homeostasis, the body utilizes both *chemical* and *physiological* buffering systems. Chemical buffers are composed of a mixture of weak acids and weak bases. They help regulate body pH levels by binding H^+ and removing it from solution as its concentration begins to rise, or releasing H^+ into solution

as its concentration begins to fall. The body's three major chemical buffering systems are the *bicarbonate*, *phosphate*, and *protein buffer systems*. We will not focus on chemical buffering systems in this lab, but keep in mind that chemical buffers are the fastest form of compensation and can return pH to normal levels within a fraction of a second.

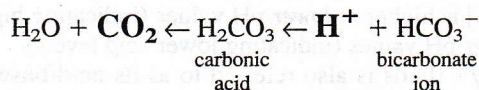
The body's two major physiological buffering systems are the renal and respiratory systems. The renal system is the slower of the two, taking hours to days to do its work. The respiratory system usually works within minutes, but cannot handle the amount of pH change that the renal system can. These physiological buffer systems help regulate body pH by controlling the output of acids, bases, or CO_2 from the body. For example, if there is too much acid in the body, the renal system may respond by excreting more H^+ from the body in urine. Similarly, if there is too much carbon dioxide in the blood, the respiratory system may respond by breathing faster to expel the excess carbon dioxide. Carbon dioxide levels have a direct effect on pH levels because the addition of carbon dioxide to the blood results in the generation of more H^+ . The following reaction shows what happens in the respiratory system when carbon dioxide combines with water in the blood:



This is a reversible reaction and is useful for remembering the relationships between CO_2 and H^+ . Note that as more CO_2 accumulates in the blood (which frequently is caused by reduced gas exchange in the lungs), the reaction moves to the right and more H^+ is produced, lowering the pH:



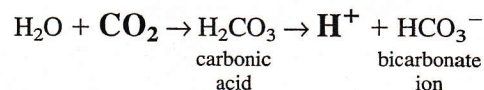
Conversely, as $[\text{H}^+]$ increases, more carbon dioxide will be present in the blood:



Disruptions of acid/base balance occur when the body's pH levels fall below or above the normal pH range of 7.35–7.45. When pH levels fall below 7.35, the body is said to be in a state of **acidosis**. When pH levels rise above 7.45, the body is said to be in a state of **alkalosis**. **Respiratory acidosis** and **respiratory alkalosis** are the result of the respiratory system accumulating too much or too little carbon dioxide in the blood. **Metabolic acidosis** and **metabolic alkalosis** refer to all other conditions of acidosis and alkalosis (i.e., those not caused by the respiratory system). The experiments in this lab will focus on these disruptions of acid/base balance, and on the physiological buffer systems (renal and respiratory) that compensate for such imbalances (Figure 10.1b and c).

Respiratory Acidosis and Alkalosis

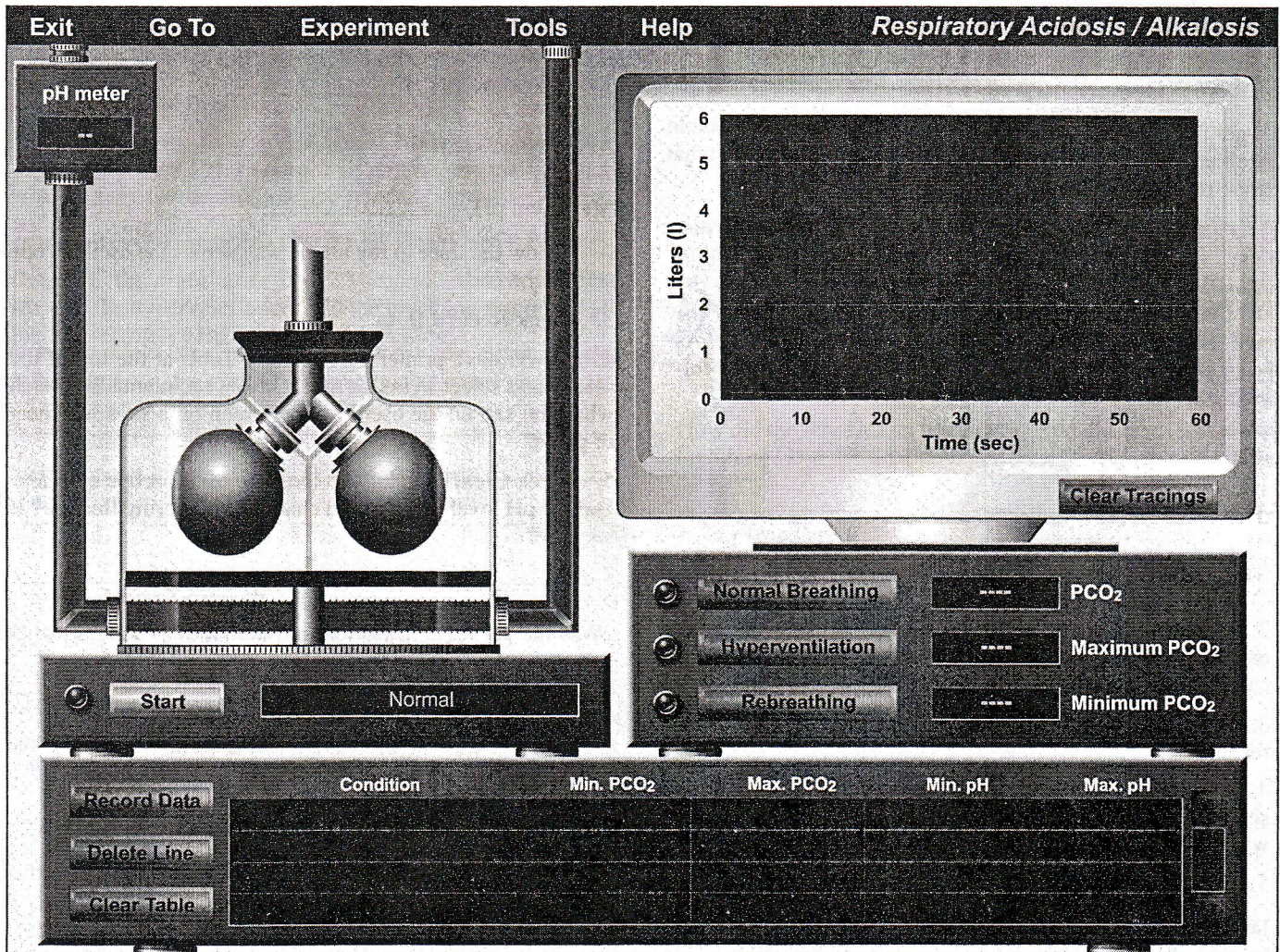
Respiratory acidosis is the result of impaired respiration, or *hypoventilation*, which leads to the accumulation of too much carbon dioxide in the blood. The causes of impaired respiration include airway obstruction, depression of the respiratory center in the brain stem, lung disease, and drug overdose. Recall that carbon dioxide acts as an acid by forming carbonic acid when it combines with water in the body's blood. The carbonic acid then forms hydrogen ions plus bicarbonate ions:



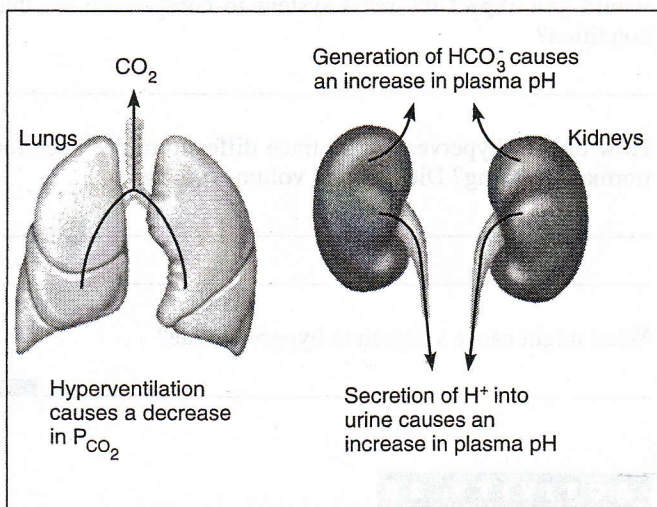
Because hypoventilation results in elevated carbon dioxide levels in the blood, the H^+ levels increase, and the pH value of the blood decreases.

Respiratory alkalosis is the condition of too little carbon dioxide in the blood. It is commonly the result of traveling to a high altitude (where the air contains less oxygen) or hyperventilation, which may be brought on by fever or anxiety. Hyperventilation removes more carbon dioxide from the blood, reducing the amount of H^+ in the blood and thus increasing the blood's pH level.

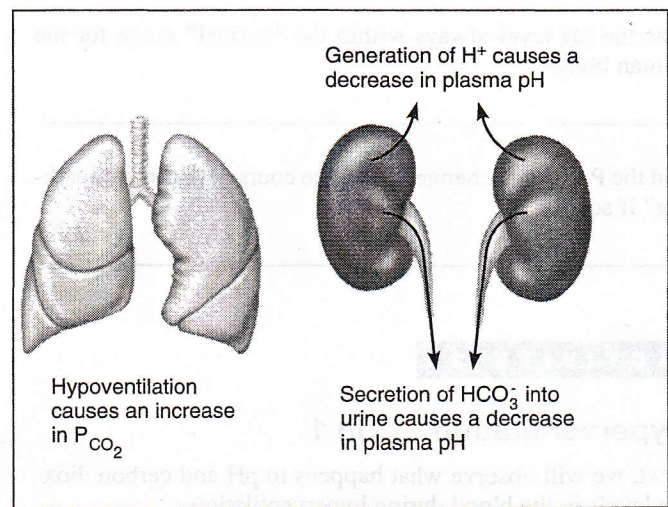
In this first set of activities, we focus on the causes of respiratory acidosis and alkalosis. Follow the instructions in the Getting Started section at the beginning of this lab manual. From the Main Menu, select **Acid/Base Balance**. You will see the opening screen for "Respiratory Acidosis/Alkalosis" (Figure 10.1). If you have already completed PhysioEx Exercise 7 on respiratory system mechanics, this screen should look familiar. At the left is a pair of simulated lungs, which look like balloons, connected by a tube that looks like an upside-down Y. Air flows in and out of this tube, which simulates the trachea and other air passageways into the lungs. Beneath the "lungs" is a black platform simulating the diaphragm. The long, U-shaped tube containing red fluid represents blood flowing through the lungs. At the top left of the U-shaped tube is a pH meter that will measure the pH level of the blood once the experiment is begun (experiments are begun by clicking the **Start** button at the left of the screen). To the right is an oscilloscope monitor, which will graphically display respiratory volumes. Note that respiratory volumes are measured in liters (l) along the Y-axis, and time in seconds is measured along the X-axis. Below the monitor are three buttons: **Normal Breathing**, **Hyperventilation**, and **Rebreathing**. Clicking any one of these buttons will induce the given pattern of breathing. Next to these buttons are three data displays for P_{CO_2} (partial pressure of carbon dioxide)—these will give us the levels of carbon dioxide in the blood over the course of an experimental run. At the very bottom of the screen is the data collection grid, where you may record and view your data after each activity.



(a)



(b) Respiratory and renal response to acidosis



(c) Respiratory and renal response to alkalosis

FIGURE 10.1 Maintaining acid-base balance. (a) Opening screen of the Respiratory Acidosis/Alkalosis experiment. (b) Compensatory mechanisms for acidosis. (c) Compensatory mechanisms for alkalosis.

ACTIVITY 1

Normal Breathing

To get familiarized with the equipment, as well as to obtain baseline data for this experiment, we will first observe what happens during normal breathing.

1. Click **Start**. Notice that the **Normal Breathing** button dims, indicating that the simulated lungs are “breathing” normally. Also notice the reading in the pH meter at the top left, the readings in the P_{CO_2} displays, and the shape of the trace that starts running across the oscilloscope screen. As the trace runs, record the readings for pH at each of the following times:

At 20 seconds, pH = _____

At 40 seconds, pH = _____

At 60 seconds, pH = _____

2. Allow the trace to run all the way to the right side of the oscilloscope screen. At this point, the run will automatically end.

3. Click **Record Data** at the bottom left to record your results.

4. If you have printer access, click **Tools** at the top of the screen and select **Print Graph**. Otherwise, manually sketch what you see on the oscilloscope screen.

5. Click **Clear Tracings** to clear the oscilloscope screen.

Did the pH level of the blood change at all during normal breathing? If so, how?

Was the pH level always within the “normal” range for the human body?

Did the P_{CO_2} level change during the course of normal breathing? If so, how?

ACTIVITY 2A

Hyperventilation—Run 1

Next, we will observe what happens to pH and carbon dioxide levels in the blood during hyperventilation.

1. Click **Start**. Allow the normal breathing trace to run for 10 seconds; then at the 10-second mark, click **Hyperventilation**. Watch the pH meter display, as well as the readings in the P_{CO_2} displays and the shape of the trace. As the trace runs, record the readings for pH at each of the following times:

At 20 seconds, pH = _____

At 40 seconds, pH = _____

At 60 seconds, pH = _____

Maximum pH = _____

2. Allow the trace to run all the way across the oscilloscope screen and end.

3. Click **Record Data**.

4. If you have printer access, click **Tools** at the top of the screen and select **Print Graph**. Otherwise, manually sketch what you see on the oscilloscope screen on a separate sheet of paper.

5. Click **Clear Tracings** to clear the oscilloscope screen. Did the pH level of the blood change at all during this run? If so, how?

Was the pH level always within the “normal” range for the human body? _____

If not, when was the pH value outside of the normal range, and what acid/base imbalance did this pH value indicate?

Did the P_{CO_2} level change during the course of this run? If so, how?

If you observed an acid/base imbalance during this run, how would you expect the renal system to compensate for this condition?

How did the hyperventilation trace differ from the trace for normal breathing? Did the tidal volumes change?

What might cause a person to hyperventilate?

ACTIVITY 2B

Hyperventilation—Run 2

This activity is a variation on Activity 2a.

1. Click **Start**. Allow the normal breathing trace to run for 10 seconds, then click **Hyperventilation** at the 10-second mark. Allow the hyperventilation trace to run for 10 seconds,

then click **Normal Breathing** at the 20-second mark. Allow the trace to finish its run across the oscilloscope screen. Observe the changes in the pH meter and the P_{CO_2} displays.

2. Click **Record Data**.
3. If you have printer access, click **Tools** at the top of the screen and select **Print Graph**. Otherwise, manually sketch what you see on the oscilloscope screen.
4. Click **Clear Tracings** to clear the oscilloscope screen.

Describe the trace after the 20-second mark when you stopped the hyperventilation. Did the breathing return to normal immediately? Explain your observation.

ACTIVITY 3

Rebreathing

Rebreathing is the action of breathing in air that was just expelled from the lungs. Breathing into a paper bag is an example of rebreathing. In this activity, we will observe what happens to pH and carbon dioxide levels in the blood during rebreathing.

1. Click **Start**. Allow the normal breathing trace to run for 10 seconds; then at the 10 second mark, click **Rebreathing**. Watch the pH meter display, as well as the readings in the P_{CO_2} displays and the shape of the trace. As the trace runs, record the readings for pH at each of the following times:

At 20 seconds, pH = _____

At 40 seconds, pH = _____

At 60 seconds, pH = _____

2. Allow the trace to run all the way across the oscilloscope screen and end.
3. Click **Record Data**.
4. If you have printer access, click **Tools** at the top of the screen and select **Print Graph**. Otherwise, manually sketch what you see on the oscilloscope screen.
5. Click **Clear Tracings** to clear the oscilloscope screen.

Did the pH level of the blood change at all during this run? If so, how?

Was the pH level always within the "normal" range for the human body? _____

If not, when was the pH value outside of the normal range, and what acid/base imbalance did this pH value indicate?

Did the P_{CO_2} level change during the course of this run? If so, how?

If you observed an acid/base imbalance during this run, how would you expect the renal system to compensate for this condition?

How did the rebreathing trace differ from the trace for normal breathing? Did the tidal volumes change?

Give examples of respiratory problems that would result in pH and P_{CO_2} patterns similar to what you observed during rebreathing.

6. To print out all of the recorded data from this activity, click **Tools** and then **Print Data**.

In the next set of activities, we will focus on the body's primary mechanism of compensating for respiratory acidosis or alkalosis: renal compensation.

Renal System Compensation

The kidneys play a major role in maintaining fluid and electrolyte balance in the body's internal environment. By regulating the amount of water lost in the urine, the kidneys defend the body against excessive hydration or dehydration. By regulating the excretion of individual ions, the kidneys maintain normal electrolyte patterns of body fluids. By regulating the acidity of urine and the rate of electrolyte excretion, the kidneys maintain plasma pH levels within normal limits. Renal compensation is the body's primary method of compensating for conditions of respiratory acidosis or respiratory alkalosis. (Although the renal system also compensates for metabolic acidosis or metabolic alkalosis, a more immediate mechanism for compensating for metabolic acid/base imbalances is the respiratory system, as we will see in a later experiment.)

The activities in this section examine how the renal system compensates for respiratory acidosis or alkalosis. The primary variable we will be working with is P_{CO_2} (the partial pressure of carbon dioxide in the blood). We will observe how increases and decreases in P_{CO_2} affect the levels of $[H^+]$ and $[HCO_3^-]$ (bicarbonate) that the kidneys excrete in urine.

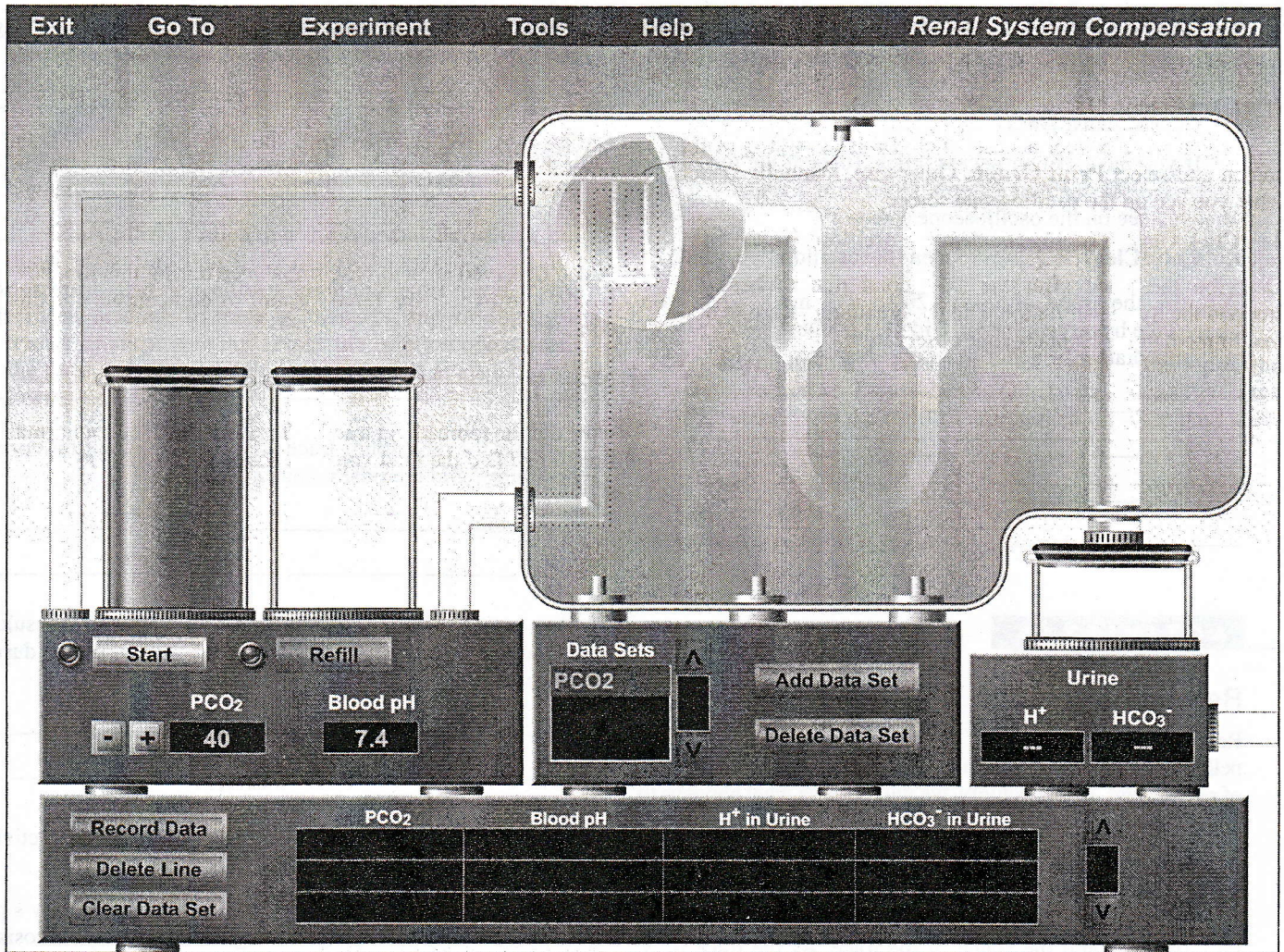


FIGURE 10.2 Opening screen of the Renal Compensation experiment.

Click on **Experiment** at the top of the screen and select **Renal System Compensation**. You will see the screen shown in Figure 10.2. If you completed Exercise 9 on renal physiology, this screen should look familiar. There are two beakers on the left side of the screen, one of which is filled with blood, simulating the body's blood supply to the kidneys. Notice that the P_{CO_2} level is currently set to 40, and that the corresponding pH value is 7.4—both “normal” values. By clicking **Start**, you will initiate the process of delivering blood to the simulated nephron at the right side of the screen. As blood flows through the glomerulus of the nephron, you will see the filtration from the plasma of everything except proteins and cells (note that the moving red dots in the animation do *not* include red blood cells). Blood will then drain from the glomerulus to the beaker at the right of the original beaker. At the end of the nephron tube, you will see the collection of urine in a small beaker. Keep in mind that although only one nephron is depicted here, there are actually over a million nephrons in each human kidney. Below the urine beaker are displays for H^+ and HCO_3^- , which will tell us the relative levels of these ions present in the urine.

ACTIVITY 4

Renal Response to Normal Acid/Base Balance

1. Increase or decrease P_{CO_2} by clicking the (–) or (+) buttons. (Notice that as P_{CO_2} changes, so does the blood pH level.)
2. Click **Start** and allow the run to finish.
3. At the end of the run, click **Record Data**.
At normal P_{CO_2} and pH levels, was the level of H^+ present in the urine normal? _____

What level of $[HCO_3^-]$ was present in the urine? _____

Why does the blood pH value change as P_{CO_2} changes?

How does the blood pH value change as P_{CO_2} changes?

- Click **Refill** to prepare for the next activity. ■

ACTIVITY 5

Renal Response to Respiratory Alkalosis

In this activity, we will simulate respiratory alkalosis by setting the P_{CO_2} to values lower than normal (thus, blood pH will be *higher* than normal). We will then observe the renal system's response to these conditions.

- Set P_{CO_2} to 35 by clicking the (-) button. Notice that the corresponding blood pH value is approximately 7.5.
- Click **Start**.
- At the end of the run, click **Record Data**.
- Click **Refill**.
- Repeat steps 1–4, setting P_{CO_2} to increasingly lower values (i.e., set P_{CO_2} to 30 and then 20, the lowest value allowed).

What level of $[H^+]$ was present in the urine at each of these P_{CO_2} /pH levels?

What level of $[HCO_3^-]$ was present in the urine at each of these P_{CO_2} /pH levels?

Recall that it may take hours or even days for the renal system to respond to disruptions in acid/base balance. Assuming that enough time has passed for the renal system to fully compensate for respiratory alkalosis, would you expect P_{CO_2} levels to increase or decrease? Would you expect blood pH levels to increase or decrease?

Recall your activities in the first experiment on respiratory acidosis and alkalosis. Which type of breathing resulted in P_{CO_2} levels closest to the ones we experimented with in this activity—normal breathing, hyperventilation, or rebreathing?

Explain why this type of breathing resulted in alkalosis.

ACTIVITY 6

Renal Response to Respiratory Acidosis

In this activity, we will simulate respiratory acidosis by setting the P_{CO_2} values higher than normal (thus, blood pH will be *lower* than normal). We will then observe the renal system's response to these conditions.

- Make sure the left beaker is filled with blood. If not, click **Refill**.
- Set P_{CO_2} to 60 by clicking the (+) button. Notice that the corresponding blood pH value is 7.3.
- Click **Start**.
- At the end of the run, click **Record Data**.
- Click **Refill**.
- Repeat steps 1–5, setting P_{CO_2} to increasingly higher values (i.e., set P_{CO_2} to 75 and then 90, the highest value allowed).

What level of $[H^+]$ was present in the urine at each of these P_{CO_2} /pH levels?

What level of $[HCO_3^-]$ was present in the urine at each of these P_{CO_2} /pH levels?

Recall that it may take hours or even days for the renal system to respond to disruptions in acid/base balance. Assuming that enough time has passed for the renal system to fully compensate for respiratory acidosis, would you expect P_{CO_2} levels to increase or decrease? Would you expect blood pH levels to increase or decrease?

Recall your activities in the first experiment on respiratory acidosis and alkalosis. Which type of breathing resulted in P_{CO_2} levels closest to the ones we experimented with in this activity—normal breathing, hyperventilation, or rebreathing?

Explain why this type of breathing resulted in acidosis.

- Before going on to the next activity, select **Tools** and then **Print Data** in order to save a hard copy of your data results. ■

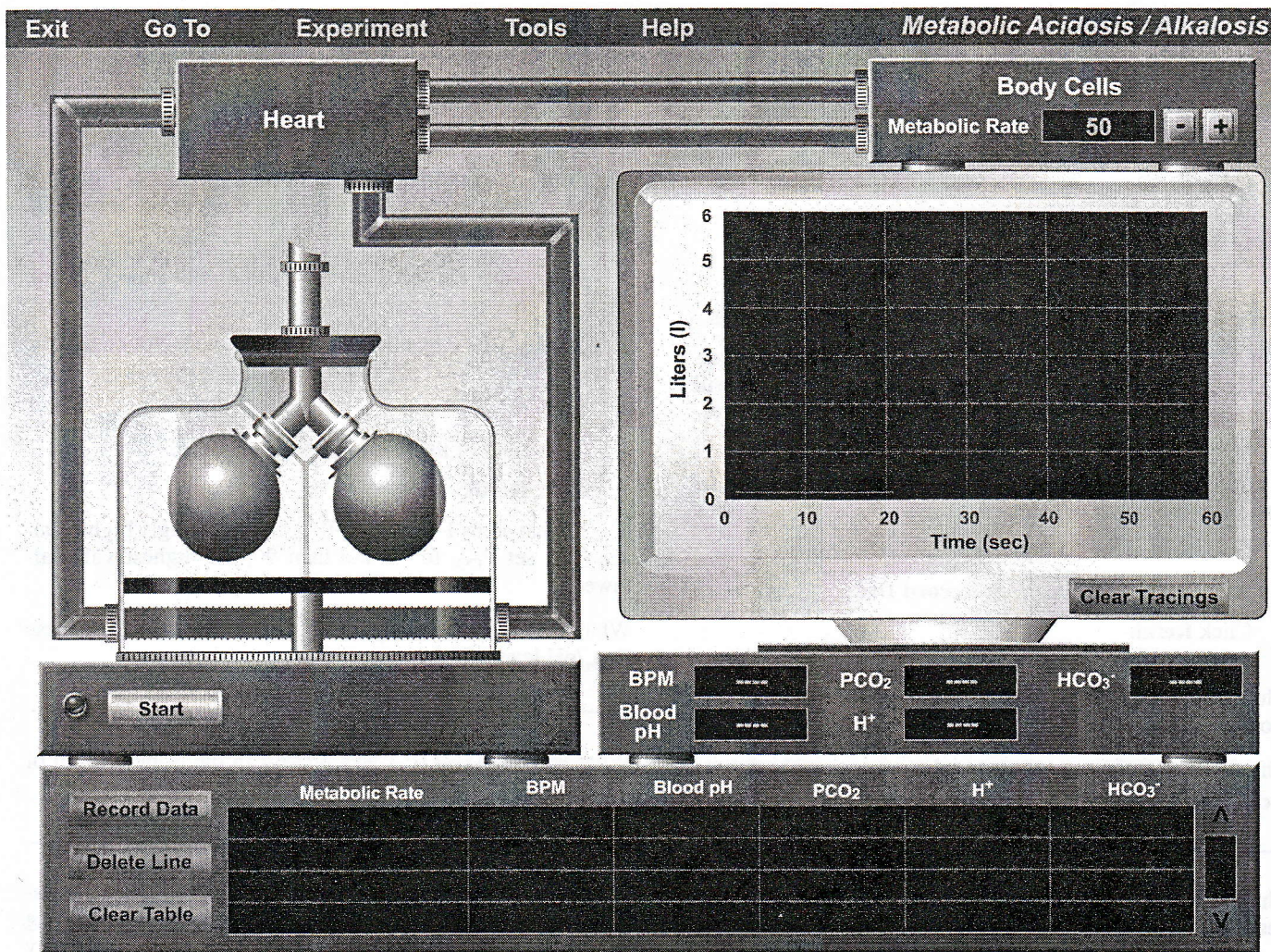


FIGURE 10.3 Opening screen of the Metabolic Acidosis/Alkalosis experiment.

Metabolic Acidosis and Alkalosis

Conditions of acidosis or alkalosis that do not have respiratory causes are termed *metabolic acidosis* or *metabolic alkalosis*.

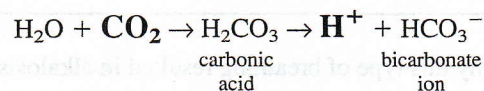
Metabolic acidosis is characterized by low plasma HCO_3^- and pH. The causes of metabolic acidosis include:

- *Ketoacidosis*, a buildup of keto acids that can result from diabetes mellitus
- *Salicylate poisoning*, a toxic condition resulting from ingestion of too much aspirin or oil of wintergreen (a substance often found in laboratories)
- The ingestion of too much alcohol, which metabolizes to acetic acid
- Diarrhea, which results in the loss of bicarbonate with the elimination of intestinal contents
- Strenuous exercise, which may cause a buildup of lactic acid from anaerobic muscle metabolism

Metabolic alkalosis is characterized by elevated plasma HCO_3^- and pH. The causes of metabolic alkalosis include:

- Alkali ingestion, such as antacids or bicarbonate
- Vomiting, which may result in the loss of too much H^+
- Constipation, which may result in reabsorption of elevated levels of HCO_3^-

Increases or decreases in the body's normal metabolic rate may also result in metabolic acidosis or alkalosis. Recall that carbon dioxide—a waste product of metabolism—mixes with water in plasma to form carbonic acid, which in turn forms H^+ :



Therefore, an increase in the normal rate of metabolism would result in more carbon dioxide being formed as a metabolic waste product, resulting in the formation of more H^+ —lowering plasma pH and potentially causing acidosis. Other

acids that are also normal metabolic waste products, such as ketone bodies and phosphoric, uric, and lactic acids, would likewise accumulate with an increase in metabolic rate. Conversely, a decrease in the normal rate of metabolism would result in less carbon dioxide being formed as a metabolic waste product, resulting in the formation of less H^+ —raising plasma pH and potentially causing alkalosis. Many factors can affect the rate of cell metabolism. For example, fever, stress, or the ingestion of food all cause the rate of cell metabolism to increase. Conversely, a fall in body temperature or a decrease in food intake causes the rate of cell metabolism to decrease.

The respiratory system compensates for metabolic acidosis or alkalosis by expelling or retaining carbon dioxide in the blood. During metabolic acidosis, respiration increases to expel carbon dioxide from the blood and decrease $[H^+]$ in order to raise the pH level. During metabolic alkalosis, respiration decreases to promote the accumulation of carbon dioxide in the blood, thus increasing $[H^+]$ and decreasing the pH level.

The renal system also compensates for metabolic acidosis and alkalosis by conserving or excreting bicarbonate ions. However, in this set of activities we will focus on respiratory compensation of metabolic acidosis and alkalosis.

To begin, click **Experiment** at the top of the screen and select **Metabolic Acidosis/Alkalosis**. The screen shown in Figure 10.3 will appear. This screen is similar to the screen from the first experiment; the main differences are the addition of a box representing the heart; tubes showing the double circulation of the heart; and a box representing the body's cells. The default "normal" metabolic rate has been set to 50 kcal/h—an arbitrary value, given that "normal" metabolic rates vary widely from individual to individual. The (+) and (−) buttons in the Body Cells box allow you to increase or decrease the body's metabolic rate. In the following activities, we will observe the respiratory response to acidosis or alkalosis brought on by increases or decreases in the body's metabolic rate.

ACTIVITY 7

Respiratory Response to Normal Metabolism

We will begin by observing respiratory activity at normal metabolic conditions. This data will serve as a baseline against which we will compare our data in Activities 8 and 9.

1. Make sure the Metabolic Rate is set to 50, which for the purposes of this experiment we will consider the "normal" value.
2. Click **Start** to begin the experiment. Notice the arrows showing the direction of blood flow. A graph displaying respiratory activity will appear on the oscilloscope screen.
3. After the graph has reached the end of the screen, the experiment will automatically stop. Note the data in the displays below the oscilloscope screen:
 - The **BPM** display gives you the *breaths-per-minute*—the rate at which respiration occurred.
 - Blood pH tells you the pH value of the blood.

- PCO_2 (shown as P_{CO_2} in the text) tells you the partial pressure of carbon dioxide in the blood.
- H^+ and HCO_3^- tell you the levels of each of these ions present.

4. Click **Record Data**.

5. Click **Tools** and then **Print Graph** in order to print your graph.

What is the respiratory rate (BPM)? _____

What is the blood pH? _____

Are the blood pH and P_{CO_2} values within normal ranges?

6. Click **Clear Tracings** before proceeding to the next activity. ■

ACTIVITY 8

Respiratory Response to Increased Metabolism

1. Increase the metabolic rate to 60.
2. Click **Start** to begin the experiment.
3. Allow the graph to reach the end of the oscilloscope screen. Note the data in the displays below the oscilloscope screen.
4. Click **Record Data**.
5. Click **Tools** and then **Print Graph** in order to print your graph.
6. Repeat steps 1–5 with the metabolic rate set at 70, and then 80.

As the body's metabolic rate increased:
How did respiration change with respect to BPM and tidal volume?

How did blood pH change?

How did P_{CO_2} change?

How did $[H^+]$ change?


How did $[HCO_3^-]$ change?

Explain why these changes took place as metabolic rate increased. Hint: Start with the formation of excess CO_2 waste and explain the changes.

Which metabolic rates caused pH levels to decrease to a condition of metabolic acidosis?

What were the pH values at each of these rates?

By the time the respiratory system fully compensated for acidosis, how would you expect the pH values to change?

7. Click **Clear Tracings** before proceeding to the next activity. 

ACTIVITY 9

Respiratory Response to Decreased Metabolism

1. Decrease the metabolic rate to 40.
2. Click **Start** to begin the experiment.
3. Allow the graph to reach the end of the oscilloscope screen. Note the data in the displays below the oscilloscope screen.
4. Click **Record Data**.
5. Click **Tools** and then **Print Graph** in order to print your graph.
6. Repeat steps 1–5 with the metabolic rate set at 30, and then 20.

As the body's metabolic rate decreased:

How did respiration change?

How did blood pH change?

How did P_{CO_2} change?

How did $[\text{H}^+]$ change?

How did $[\text{HCO}_3^-]$ change?

Explain why these changes took place as the metabolic rate decreased.

Which metabolic rates caused pH levels to increase to a condition of metabolic alkalosis?

What were the pH values at each of these rates?

By the time the respiratory system fully compensated for alkalosis, how would you expect the pH values to change?

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