EXAMINING THE EFFECTS OF SPACE FLIGHT ON THE FLUID REGULATING SYSTEMS OF THE BODY

FLUID-ELECTROLYTE REGULATION DURING SPACE FLIGHT

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Introduction

Have you ever wondered why you sometimes excrete great volumes of urine and sometimes none at all? Have you ever wondered why sometimes you feel so thirsty that you can hardly get enough to drink and other times you want no liquids at all? Have you ever wondered why every time you go to the movie theater and drink a large soda at the beginning of the movie, you almost always have to go to the bathroom during the middle of the movie (usually during the best part)? Did you know that if you were eating salty popcorn along with your large soda, you would not have to interrupt your movie to go to the bathroom? These conditions, and many more, relate to one of the body's most important functions - that of maintaining its **fluid and electrolyte balance.**

Earth Physiology

If you are a healthy young person weighing 120 pounds, one substance alone, out of the hundreds of compounds present in your body, weighs about 72 pounds, or 60% of your total body weight. This, the body's most abundant compound, is water. Water is tremendously important to the health of the body. In fact, **water is the syrup of life** and our bodies can go a much longer period of time without food than they can without water.

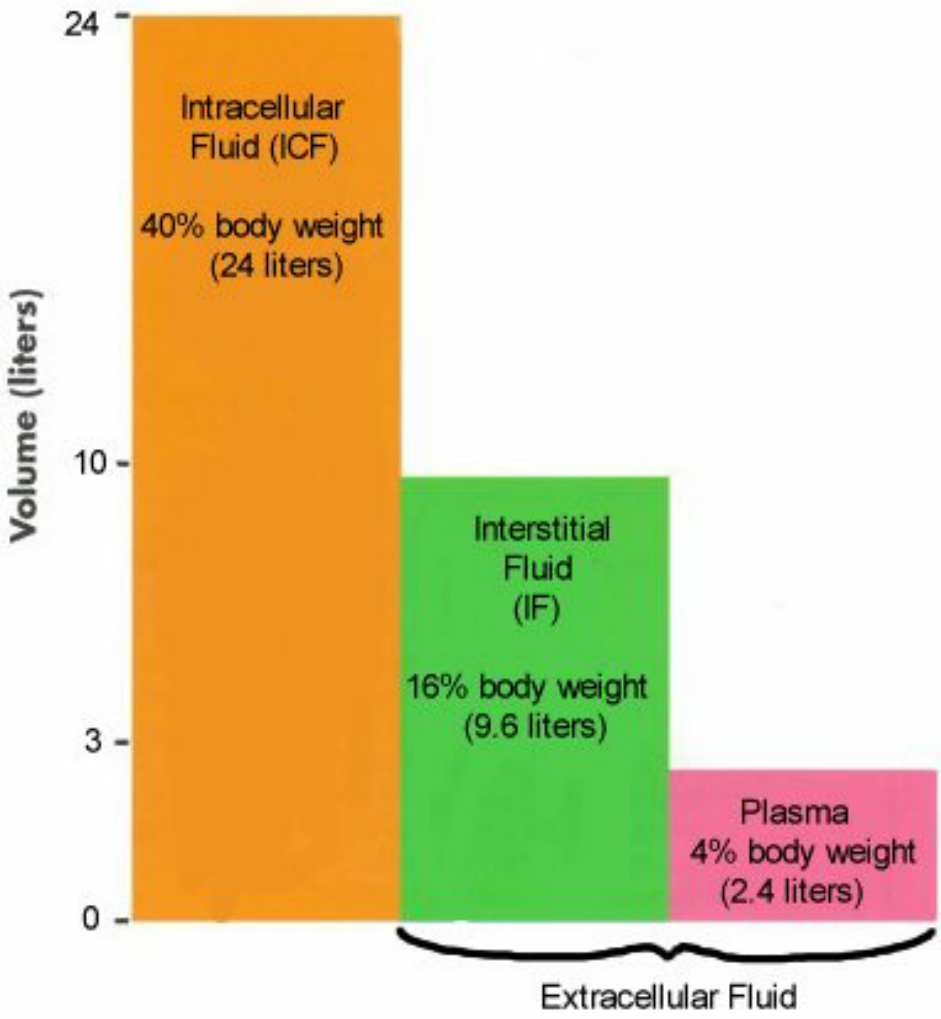
Inside the body, water is distributed into three physically distinct locations known as **fluid compartments**. Figure 1 illustrates the relative sizes of these fluid compartments. Note that the largest volume of water by far lies inside the cells and is called, appropriately, **intracellular fluid (ICF)** Note also that the water that is located outside of the cells - **extracellular fluid (ECF)** - is located in two compartments: in the microscopic spaces between cells, where it is coiled **interstitial fluid (IF)**; and in the blood vessels, where it is the principal constituent of plasma, the liquid part of blood. In summary, then:

A. Intracellular Fluid (ICF) = fluid in the cells
B. Extracellular Fluid (ECF) = fluid **outside** the cells consisting of:
    1. Interstitial Fluid (IF) = fluid **between** cells
    2. Plasma = fluid in the **blood vessels**

A normal body maintains **fluid balance**. The term "fluid balance" means that the volumes of ICF and ECF, and, therefore, the total volume of water in the body, all remain relatively constant. Under normal conditions, **homeostasis** (relative uniformity of the body's internal environment) of the total volume of water in the body is maintained or restored primarily by devices that adjust urine output to compensate for greater or less fluid intake (drinking), and secondarily, by mechanisms that adjust fluid intake to respond to the fluid needs of the body. **The body's chief mechanism, by far, for maintaining fluid balance is to adjust its fluid output so that, over time, average fluid output equals average fluid intake**. Everyone knows this by experience. The more liquid one drinks, the more urine one excretes. Conversely, the less the fluid intake, the less the urine volume output. This balance is maintained mainly through the **kidney** acting together with certain **hormones** in the body.

We will discuss the kidney and the formation of urine in a moment; however, let us discuss what **electrolytes** are. Electrolytes are chemical compounds that dissociate (or break up) in solution into separate positively or negatively charged particles, called **ions**. For example, table salt (NaCl) is an electrolyte that dissociates in water to form the ions sodium (Na^+) and chloride (Cl^-). Positively charged particles, such as Na^+, are called **cations**, and negatively charged particles, such as Cl^-, are called **anions**. A variety of anions and cations serve important nutrient or regulatory roles in the body. Important cations include sodium (Na^+), calcium (Ca^{++}), potassium (K^+), and magnesium (Mg^{++}). Important anions include chloride (Cl^-), bicarbonate (HCO_3^-), phosphate (PO_4^{-3}), and many proteins. Although blood plasma contains a number of important electrolytes, by far the most abundant one is sodium chloride (ordinary table salt, NaCl).

Figure 1. Names and relative proportions of the main body fluid compartments. Volumes given are for young adults weighing 720 pounds (54.5 Kg); 1 liter is approximately equivalent to 1 quart.



The concentrations of all the electrolytes and ions in the different fluid compartments are controlled very closely by the body, but our discussion will focus primarily on how Na^+ levels in the extracellular compartment profoundly affect the amount of urine that is excreted. (Remember, the more salted popcorn you eat at the movies, the less you have to go to the bathroom.) We will also look briefly at how K^+ levels affect the production of urine. Let's start with a description of our kidney, the site in our bodies where urine is produced.

THE KIDNEY

There are only two major sets of **paired organs** in the body, the kidneys and the lungs. It seems that in the original plans for the human body, the architect (whoever that may be in each of our minds) recognized the crucial nature of the kidney's and lung's assigned tasks and included an "extra" organ in each case to assure that the respiratory and excretory gateways of the body could operate with some kind of a back-up system. In a spacecraft, many of the main computer systems that are extremely crucial to the safe operation of the spacecraft have back-up systems that are included just in case the main system breaks down. These are what are known as redundant systems (redundant = serving as a duplicate for preventing failure of an entire system). Many systems that operate with redundancy utilize the back-up system **only** if the primary system breaks down. However, the body utilizes a different approach. Under normal conditions, the body will utilize both organs, but if one of the organs is damaged in some way, the other organ can take over the entire function and operate as if **both** organs were present. Many human beings are alive and thriving today, despite damage or actual removal of one lung or kidney, because the remaining organ fills the breach and continues to do the work of both. In this chapter, we will be focusing on the structure and fluid-regulating function of the **kidneys**.

We have already seen in the last chapter how the kidneys are a major participant in the regulation of red blood cell (RBC) production. Remember, they act as **sensors** to detect low levels of oxygen in the blood, then they release the hormone erythropoietin, which is the **effector** that travels to the bone marrow to stimulate RBC production. Remember further that this is a **negative feedback** loop. In this chapter we will examine how the kidneys play an essential role in the regulation of an appropriate fluid balance within the body. Again, through their release of hormones, the kidneys participate in this other negative feedback loop, which operates to regulate the amount of water in the body. With their multiple roles within the body, the kidneys are a very good example of how everything in the body is somehow connected or **integrated**. That is, on the one hand, the kidneys must pay close attention to the RBC volume in the body to ensure that oxygen levels are correct and, on the other hand, they must pay close attention to the amount of water in the body. The kidneys even perform **another** function that we will mention later. Let's first discuss the kidney's structure. At first sight, a kidney looks like a four-or-five-inch-long bean (Figure 2a)!

Figure 2.(a) The position of the kidneys in the body.

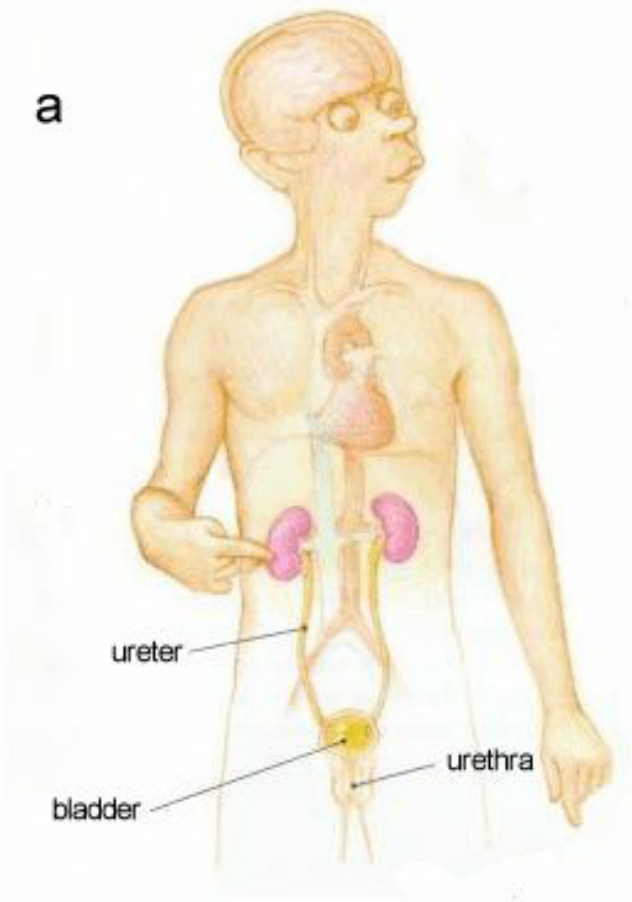


Figure 2. (b) The inside of the kidney has two main parts, the cortex and the medulla. The medulla is composed of medullary pyramids (so named because of their shape).

The outer skin of the kidney is called the **renal capsule** (renal refers to the kidney). If you were to slice through a kidney from side to side and open it like the pages of a book, you would see two main parts, a

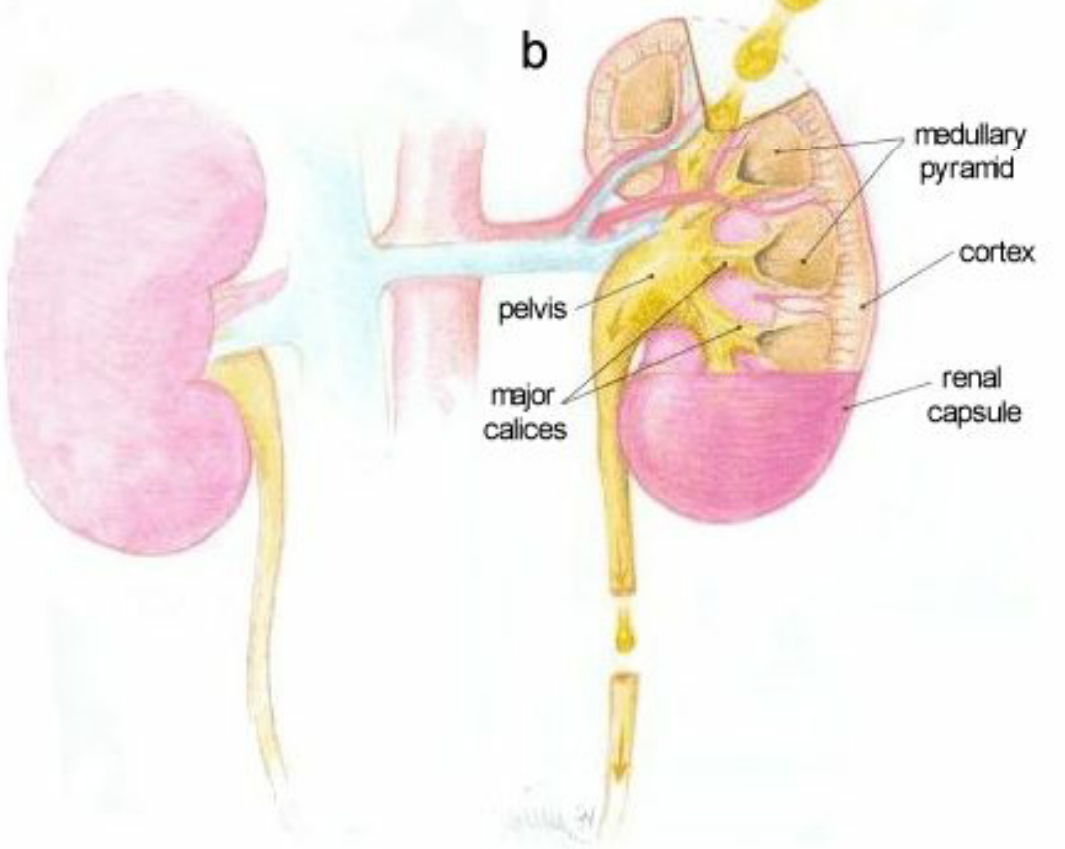
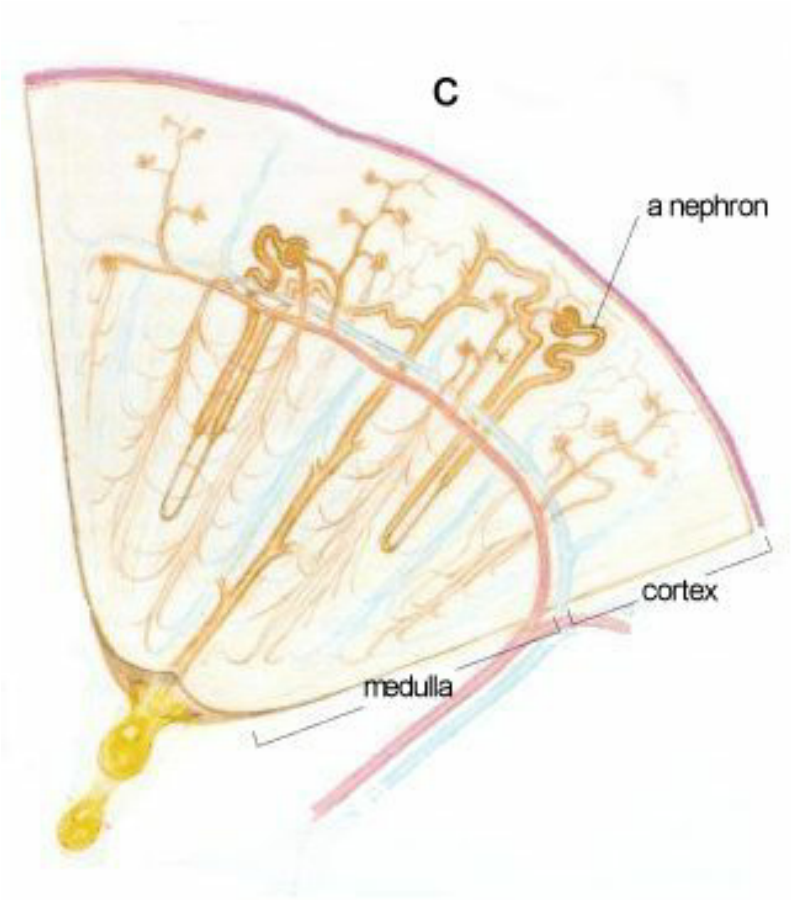


Figure 2. (c) Within the cortex and the medulla of each kidney are about a million nephrons responsible for the production of urine through the processes of filtration, reabsorption, and secretion.



central part and an outer, peripheral part (Figure 2b). The peripheral part consists of the **cortex** and the **medulla**, with the medulla consisting of **medullary pyramids**; the inner, central part consists of a group of tubes (the **calyx** and the **pelvis**) that lead out of each pyramid and into the **ureter** (the tube that drains urine into the bladder).

Within the cortex and the medullary pyramids are found millions of tiny structures called **nephrons** (Figure 2c). The nephrons are responsible for filtering out of the bloodstream an estimated 43 gallons of water a day- about twice the body's entire weight in fluid - through an intricate network of **tubules** (little tubes

The shape of a nephron is unique, unmistakable, and admirably suited to its function of producing urine (Figure 2c).It looks a little like a big "mouth" hooked to a really long and winding neck. The "mouth" is filled with what looks like a round lawbreaker that is so big that the "mouth" cannot close! In reality, the nephron is composed of two main parts: the **renal corpuscle** (the mouth and the jawbreaker) and the **renal tubule** (the long and winding neck). The "mouth" of the renal corpuscle is actually called **Bowman's capsule** and the " jawbreaker" is actually called the **glomerulus** from the Latin word for "small ball" (the plural form is glomeruli). The glomerulus is a network of blood capillaries that is surrounded, first, by a double membrane (the **glomerular capsular membrane**) and then is

surrounded by Bowman's capsule. The renal tubule (the long and winding neck) consists of the **proximal tubule** (the thick, winding part of the neck that extends just up to where it begins to make a U-turn); the **loop of Henle** (the thinner part of the neck that actually makes the U-turn); and the **distal tubule** (the last, thicker part of the neck that travels away from the U-turn, winds all around, and eventually leads into **collecting tubules**). Now that you are familiar with the structure of the kidney and, in particular, the nephron, let's see how the whole system works to produce urine so that waste products can be removed from the body.

THE FORMATION OF URINE

FIGURATION, REABSORPTION, AND SECRETION

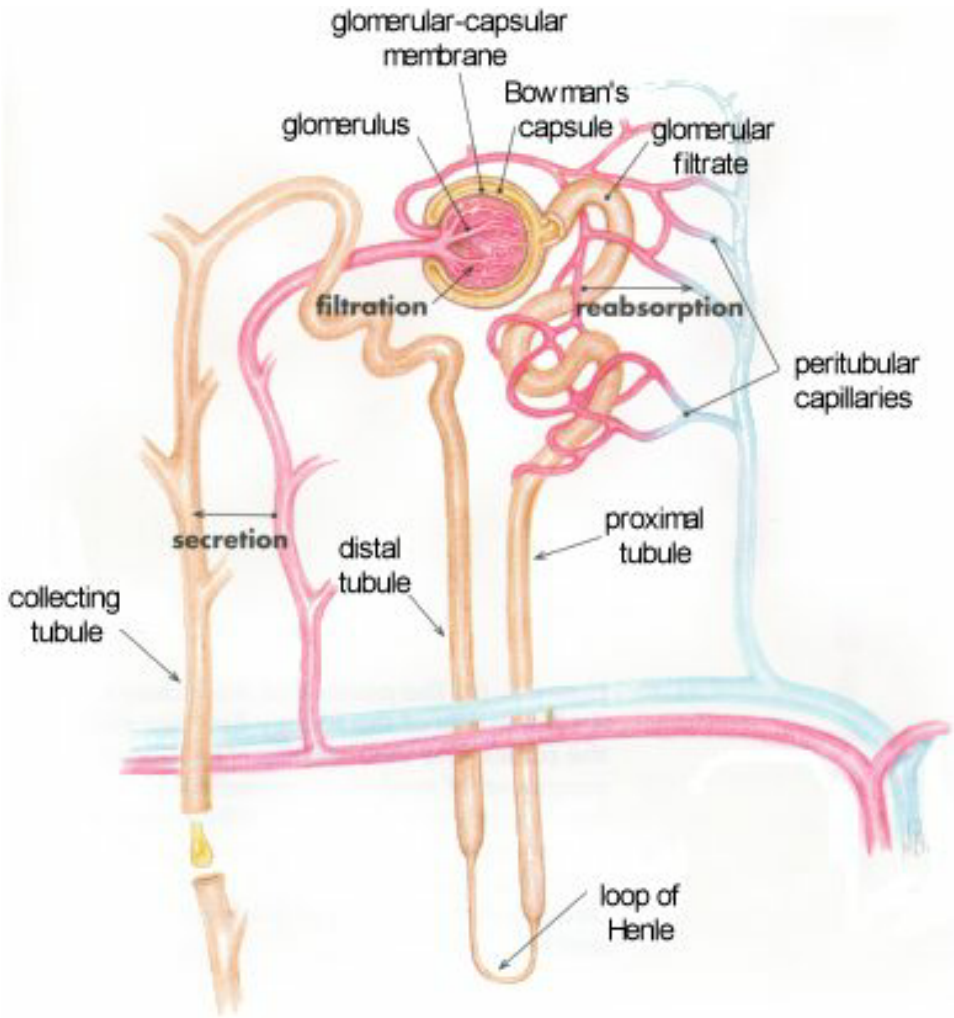
Every one of us depends on the process of urination for the removal of certain waste products in the body. The production of urine is vital to the health of the body. Most of us have probably never thought of urine as valuable, but we could not survive if we did not produce it and eliminate it. Urine is composed of water, certain electrolytes, and various waste products that are filtered out of the blood system. Remember, as the blood flows through the body, wastes resulting from the metabolism of foodstuffs in the body cells are deposited into the bloodstream, and this waste must be disposed of in some way. A major part of this "cleaning" of the blood takes place in the kidneys and, in particular, in the nephrons, where the blood is filtered to produce the urine. Both kidneys in the body carry out this essential blood cleansing function. Normally, about 20% of the total blood pumped by the heart each minute will enter the kidneys to undergo filtration. This is called the **filtration fraction**. The rest of the blood (about 80%) does not go through the filtering portion of the kidney, but flows through the rest of the body to service the various nutritional, respiratory, and other needs that are always present.

For the production of urine, the kidneys do not simply pick waste products out of the bloodstream and send them along for final disposal. The kidneys' 2 million or more nephrons (about a million in each kidney) form urine by three precisely regulated processes: filtration, reabsorption, and secretion.

Filtration

Urine formation begins with the process of **filtration**, which goes on continually in the renal corpuscles (Figure 3). As blood courses through the glomeruli, much of its fluid, containing both useful chemicals and dissolved waste materials, soaks out of the blood through the membranes (by osmosis and diffusion) where it is filtered and then flows into the Bowman's capsule. This process is called **glomerular filtration**. The water, waste products, salt, glucose, and other chemicals that have been filtered out of the blood are known collectively as glomerular filtrate. The glomerular filtrate consists primarily of water, excess salts (primarily Na^+ and K^+), glucose, and a waste product of the body called **urea**. Urea is formed in the body to eliminate the very toxic ammonia products that are formed in the liver from amino acids. Since humans cannot excrete ammonia, it is converted to the less dangerous urea and then filtered out of the blood. Urea is the most abundant of the waste products that must be excreted by the kidneys. The

Figure 3. Urine formation takes place in the nephron.



total rate of glomerular filtration (**glomerular filtration rate** or **GFR**) for the whole body (i.e., for all of the nephrons in both kidneys) is normally about 125 ml per minute. That is, about 125 ml of water and dissolved substances are filtered out of the blood per minute. The following calculations may help you visualize how enormous this volume is. The GFR per hour is:

125 ml/min X 60min/hr= 7500 ml/hr.

The GFR per day is:
7500 ml/hr X 24 hr/day = 180,000 ml/day or 180 liters/day.

Now, see if you can calculate how many **gallons of water** we are talking about. Here are some conversion factors for you to consider: 1 quart = 960 ml, 1 liter = 1000 ml, 4 quarts. = 1 gallon. Remember to cancel units and you will have no problem.

Now, what we have just calculated is the **amount of water** that is removed from the blood each day - about 180 liters per day. (Actually it also includes other chemicals, but the vast majority of this glomerular filtrate is water.) Imagine the size of a 2-liter bottle of soda pop. About 90 of those bottles equals 180 liters! Obviously no one ever excretes anywhere near 180 liters of urine per day! Why? Because almost all of the estimated 43 gallons of water (which is about the same as 180 liters - did you get the right answer?) that leaves the blood by glomerular filtration, the first process in urine formation, returns to the blood by the second process - reabsorption.

Reabsorption

Reabsorption, by definition, is the movement of substances out of the renal tubules back into the blood capillaries located around the tubules (called the **peritubular copillaries**). Substances reabsorbed are water, glucose and other nutrients, and sodium (Na^+) and other ions. Reabsorption begins in the proximal convoluted tubules and continues in the loop of Henle, distal convoluted tubules, and collecting tubules (Figure 3). Let's discuss for a moment the three main substances that are reabsorbed back into the bloodstream.

Large amounts of water - more than 178 liters per day - are reabsorbed back into the bloodstream from the proximal tubules because the physical forces acting on the water in these tubules actually push most of the water back into the blood capillaries. In other words, about 99% of the 180 liters of water that leave the blood each day by glomerular filtration returns to the blood from the proximal tubule through the process of **passive reabsorption**.

The nutrient glucose (blood sugar) is **entirely** reabsorbed back into the blood from the proximal tubules. In fact, it is **actively transported** out of the tubules and into the peritubular capillary blood. None of this valuable nutrient is wasted by being lost in the urine. However, even when the kidneys are operating at peak efficiency, the nephrons can reabsorb only so much sugar and water. Their limitations are dramatically illustrated in cases of diabetes mellitus, a disease which causes the amount of sugar in the blood to rise far above normal. As already mentioned, in ordinary cases all the glucose that seeps out through the glomeruli into the tubules is reabsorbed into the blood. But if too much is present, the tubules reach the limit of their ability to pass the sugar back into the bloodstream, and the tubules retain some of it. It is then carried along in the urine, often providing a doctor with her first clue that a patient has diabetes mellitus. The value of urine as a diagnostic aid has been known to the world of medicine since as far back as the time of Hippocrates. Since then, examination of the urine has become a regular procedure for physicians as well as scientists.

Sodium ions (Na^+) and other ions are only partially reabsorbed from the renal tubules back into the blood. For the most part, however, sodium ions are **actively transported** back into blood from the tubular fluid. The amount of sodium reabsorbed varies from time to time; it depends largely on how much salt we take in from the foods that we eat. (As stated earlier, sodium is a major component of table salt, known chemically as sodium chloride.) As a person increases the amount of salt taken into the body, that person's kidneys decrease the amount of sodium reabsorption back into the blood. That is, more sodium is retained in the tubules. Therefore, the amount of salt excreted in the urine increases. The process works the other way as well. The less the salt intake, the greater the amount of sodium reabsorbed back into the blood, and the amount of salt excreted in the urine decreases.

Secretion

Now, let's describe the third important process in the formation of urine. **Secretion** is the process by which substances move into the distal and collecting tubules from blood in the capillaries around these tubules (Figure 3). In this respect, secretion is reabsorption in reverse. Whereas reabsorption moves substances out of the tubules and into the blood, secretion moves substances out of the blood and into the tubules where they mix with the water and

other wastes and are converted into urine. These substances are secreted through either an **active transport** mechanism or as a result of **diffusion** across the membrane. Substances secreted are hydrogen ions (H+), potassium ions (K+), ammonia (NH3), and certain drugs. Kidney tubule secretion plays a crucial role in maintaining the body's acid-base balance, another example of an important body function that the kidney participates in.

Summary

In summary, three processes occurring in successive portions of the nephron accomplish the function of urine formation:

1. Filtration of water and dissolved substances out of the blood in the glomeruli and into Bowman's capsule;
2. Reabsorption of water and dissolved substances out of the kidney tubules back into the blood (note that this process prevents substances needed by the body from being lost in the urine);
3. Secretion of hydrogen ions (H^+), potassium ions (K^+), ammonia (NH_3), and certain drugs out of the blood and into the kidney tubules, where they are eventually eliminated in the urine.

Control of Urine Volume

Our urine is produced not only in order to eliminate many of the cellular waste products, but also to control both the amount and the composition of the extracellular fluid in the body. Controlling the amount of water and chemicals in the body is essential to life, and our body does so by producing various amounts of urine so that we can either excrete the "extra" water and chemicals (mainly sodium) or conserve the water and chemicals when they are in short supply. Therefore, the volume of urine that we excrete everyday is a reflection of how much extracellular fluid and sodium our bodies have to spare. **The kidney tubule regulation of the salt and water in our bodies is the most important factor in determining urine volume**. Too much water and salt in our bodies is dangerous and too little water and salt in our bodies is dangerous. Therefore, the level of water and salts excreted in urine - the urine volume - is adjusted to the needs of the body. As a general rule, however, and under optimum conditions, the body produces urine at a rate of about 1 ml/min.

Control of Urine Volume through Hormones

One of the mechanisms that the body uses to control such things is through the action of **hormones**, chemical messengers that travel through the blood system and act as regulators of many of the body's internal activities. Hormones are secreted by specialized **glands** in the body. By definition, a gland is any cell or organ that secretes some substance. But not all glands secrete hormones. Let's find out which ones do.

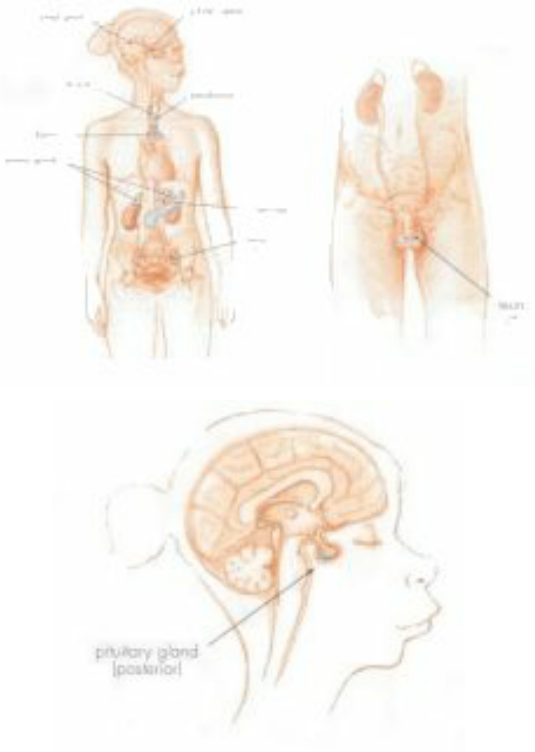
The body contains two types of glands, classified according to the way they secrete. One type is the **exocrine gland** (exo = outward), whose secretions move outward, usually by way of ducts, **to some body surface**, whether it be to the skin itself or, for example, the lining of the digestive or respiratory tract. Among the exocrines are the sweat and sebaceous glands, whose respective secretions of water and oil are evident on the skin; the mucus glands, whose mucus moistens the digestive and respiratory tract; the salivary glands, whose saliva softens food when it enters the mouth; and the mammary glands, which provide milk for the nursing infant.

The second type is the **endocrine gland** (endo = into), whose secretions move **into the bloodstream**. The endocrines are the great chemical regulators of bodily function. The substances which they secrete serve as chemical messengers and are called **hormones**, from the Greek hormon, meaning "arouse to activity." Compared with such organs as the heart or the lungs, the endocrines seem ridiculously small and unimpressive. They are bits of tissue tucked away in obscure corners of the body (Figure 4); all of them together weigh no more than about five ounces. But in the widespread control they exercise over the body, they act like giants. The key to their extraordinary power lies in the hormones they secrete - among the most powerful and remarkable substances in the body.

The two endocrine glands that are concerned with the regulation of fluid balance within the body are the **adrenal glands** and the **pituitary gland**. Let's first examine the pituitary gland, one of the tiniest endocrines of all. The pituitary hangs from the bottom of the brain by a little stalk just above the nasal passage (Figure 4b). It was originally and mistakenly believed that it discharged mucus into the nose, and therefore its name is derived from the Latin word for "nasal secretion." The pituitary is insignificant in appearance (about the size of an acorn) but it packs an extremely powerful punch. The pituitary is actually two glands in one - posterior and anterior (we will not discuss the anterior pituitary in this chapter). Of the two, the **posterior pituitary** manufactures no hormones of its own, but stores two that are initially secreted in a part of the brain known as the **hypothalamus**. These hormones are **oxytocin** (a hormone responsible for stimulating labor at the end of pregnancy), and **anti-diuretic hormone (ADH)**, which helps the body retain its fluids. Of the two hormones secreted by the posterior pituitary, our focus for this chapter will be on ADH.

Control of Urine Volume through ADH (anti-diuretic hormone)

Figure 4. (a) Endocrine glands regulate many vital body processes. The pineal gland seems to be involved with body "rhythms" associated with night and day; the thyroid helps control energy production; the parathyroid distributes calcium between blood and bone; the thymus produces T-cells, which are lymphocytes involved in immune responses. Adrenal glands regulate salt and water levels and secrete stimulants; cells in the pancreas control blood sugar. Sex glands govern reproduction and the development of secondary sexual characteristics. The pituitary controls some of the other endocrine glands. (b) The pituitary gland consists of two glands in one: the anterior and posterior pituitaries. (c) The adrenal gland also consists of two glands in one: the adrenal medulla and the adrenal cortex.

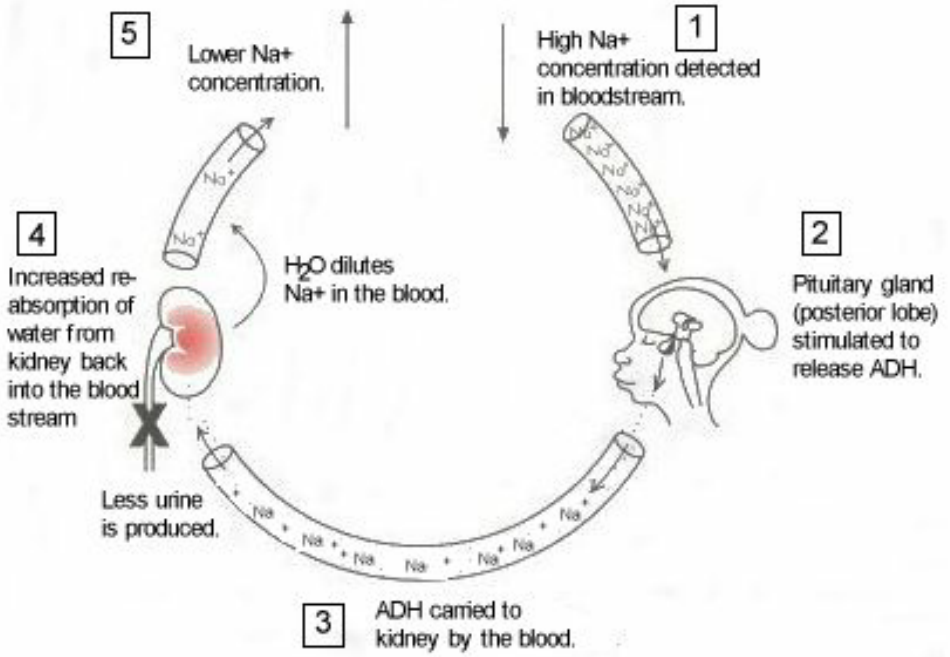


(Click on pictures for a better view.)

A **diuretic** is a substance that acts to **increase urine production**. Sometimes when a person is feeling "bloated" (which often occurs when a woman is about to begin menstruation), it usually means that she is retaining water. If the condition is extremely uncomfortable to the woman, a doctor may prescribe a diuretic to eliminate extra water and reduce the bloating. An anti-diuretic, on the other hand, is a chemical that inhibits urine formation. ADH produces its anti-diuretic effect by acting on the kidneys and causing them to reduce the amount of water they excrete. In this way, ADH is important in regulating the water concentration of body fluids, which ultimately helps to maintain an appropriate sodium concentration in the body. In fact, the sodium concentration in the extracellular fluid is the factor that either stimulates the pituitary to release ADH or to inhibit the release of ADH. This process operates as one of our "famous" negative feedback loops (Figure 5). Let's take a look at how this loop operates.

The release of ADH is regulated by the hypothalamus. Apparently certain sensors in this part of the brain are sensitive to changes in the salt concentration of body fluids, particularly the blood. If, for example, a person is sweating and losing large amounts of water, the sodium in the blood becomes more and more concentrated. The hypothalamus can sense this high concentration of sodium and it signals the posterior lobe of the pituitary to release ADH. The ADH is transmitted by the blood to the kidneys causing the kidney tubules to reabsorb more water into the blood stream to dilute the sodium. As a result of this effect, less urine is produced. This action conserves water in the body. The mechanism of action seems to be that **the presence of ADH makes distal and collecting tubules in the nephron more permeable to water**. That is, water is moved more easily through the tubule membrane back into the blood and less urine is produced. For this reason, ADH is described as the "water-retaining hormone." You might also think of it as the "urine-decreasing hormone."

Figure 5. The regulation of body water and sodium ion (Na+) concentration in the blood is controlled through the release of anti-diuretic hormone (ADH). This system operates using a negative feedback loop.



If, on the other hand, a person drinks an excess of water, the sodium in the body fluids, including the blood becomes more dilute and the release of ADH is inhibited. The lack of ADH causes the distal and collecting tubules to become practically impermeable to water, and little or no water is reabsorbed from them back into the blood. Consequently, the kidneys excrete more watery urine until the water concentration of the body fluids returns to normal.

You can probably relate this hormone activity to your own experience. If you have ever been urinating and notice that the urine is extremely yellow, this means that ADH is probably circulating in your body, causing less water to be excreted and more water to be reabsorbed into the bloodstream to stay in your body. Therefore, the urine becomes concentrated with urea and all of the other chemicals, causing it to turn yellow. On the other hand, if you notice your urine to be very watery, you can probably win a bet that says very little ADH is circulating in your body. With less ADH, your kidneys will reabsorb less water back into the bloodstream and more of it will be excreted in the urine.

Control of Urine Volume through Adrenal Glands

The phenomenon of **thirst** is equally important for regulating body water and sodium concentration as is the ADH system. Thirst is the primary regulator of **intake** of water and the ADH system is the primary regulator of **output** of water. Thirst is not stimulated through the release of a **specific** hormone but instead, it is stimulated by the hypothalamus in response to too much salt and is expressed through a **conscious desire for water**. The phenomenon of thirst is not only important, it is very interesting! A thirsty person receives relief from thirst immediately after drinking water, even before the water has been absorbed from the stomach into the blood system and the rest of the body. You might wonder what the value of this temporary relief from thirst could be, but there is good reason for its occurrence. After a person has drunk water, as long as one half to one hour may be required for all the water to be absorbed and distributed throughout the body. Were the thirst sensation not temporarily relieved after dringing water, the person would continue to drink more and more. When all this water should finally become absorbed, the body fluids would be far more diluted than normal - too much so. Whoever put the human body together really knew what they were doing!

Figure 6. A thirsty person drinks only as much water as his or her body needs even before his or her body begins to absorb and distribute that water.

So far we have discussed the role of the pituitary gland (through the release of ADH) and thirst in the regulation of body fluids. These are the **two primary mechanisms** that are responsible for making sure that there is an appropriate water and sodium level in the blood. The second set of glands that participate in the regulation of body fluids is the **adrenal glands**. The adrenals sit on top of each kidney like a cap and, although they usually vary somewhat in size and shape, they generally look like pyramids. Like the pituitary, each adrenal gland is really two glands in one (Figure 4c). The central portion is termed the **adrenal medulla**, and the outer part is the **adrenal cortex**. The two sections represent distinct glands that secrete different hormones.

The adrenal medulla secretes both epinephrine (more popularly referred to as adrenalin from the days when it was thought to be the only hormone made by the adrenals) and norepinephrine. Both play a part in helping the body respond to emergency situations. Our main interest in this chapter leads us to focus more on the adrenal cortex, which is responsible for the production of at least 30 hormones. (Don't worry! We will only be looking at one!) All of the hormones secreted by the adrenal cortex are **steroids**, after a Greek word meaning "solid," or "firm." (You may have heard of the steroids that musclebuilders use to become larger. Those are synthetic steroids whose use can be extremely dangerous.) Because they are manufactured by the adrenal cortex, they are called "adrenocorticosteroids."

There are three groups of adrenocorticosteroids, each secreted by cells in a different layer of the cortex:

1. Mineralocorticoids, which help to regulate the concentrations of extracellular electrolytes;
2. Glucocorticoids, which influence the metabolism of carbohydrates, proteins, and fats;
3. Sex hormones, which affect sexual characteristics.

Figure 7. Aldosterone secreted by the adrenal cortex causes the kidney to excrete potassium (K 1 and the kidney to reabsorb sodium back into the blood stream.

Of the thirty adrenocorticosteroids that exist, we will only be looking at the most important mineralocortocoid - **aldosterone**. This hormone acts mainly through the kidneys to maintain the homeostasis of sodium and potassium ions. More specifically, **aldosterone causes the kidneys to conserve sodium ions (Na^+) and to excrete potassium ions (K^+)**. At the same time, it promotes water conservation and reduces urine output.

The mechanism that controls the secretion of aldosterone is primarily responsive to the potassium ion (K^+) concentration in body fluids. This mechanism operates as a negative feedback loop (Figure 7) to detect high levels of K^+ and to release aldosterone so that the K^+ level can be reduced. Or, if the K^+ level is too low, less aldosterone will be released so that K^+ is allowed to accumulate. This is how it works when the body contains too much K^+:

1. as the K^+ concentration rises, sensors in the body detect this increase and signal the adrenal cortex to release more

aldosterone into the bloodstream;

2. the blood carries aldosterone to the kidneys which, in turn, stop reabsorbing the K^+ back into the bloodstream, causing more K^+ to be excreted in the urine.

Aldosterone secretion is also stimulated in response to changes in the sodium on (Na^+) concentration in the blood. In this case, if low levels of Na^+ are detected by the body, the adrenal cortex is stimulated to release aldosterone. The presence of aldosterone stimulates the tubules to reabsorb sodium salts back into the blood at a faster rate so that it can remain in the body. On the other hand, if high levels of Na^+ are detected by the body, the adrenal cortex holds back on the release of aldosterone to decrease reabsorption of the salt back into the blood, allowing more to be excreted. Finally, the presence of aldosterone tends to increase tubular water reaborption (that is, water tends to flow out of the kidney tubules back into the blood). Let's summarize briefly what conditions would cause the body to release more of the hormone aldosterone:

- If the K^+ levels in the bloodstream are detected as being **too high**, aldosterone will be released so that more K^+ is excreted in the urine;
- If the Na^+ levels in the bloodstream are detected by the body as being **too low**, aldosterone will be released so that less Na^+ is excreted in the urine; and
- If the water level in the blood is **too low** (meaning that the cellular portion of the blood is too concentrated), aldosterone will be released so that less water is excreted in the urine.

The term "salt- and water-retaining hormone," therefore, is a descriptive nickname for aldosterone. (Remember, ADH is also known as the "water- retaining hormone.") Based on what we've just learned, aldosterone can also be called the "potassium-eliminating hormone"!

Summary

Urine volume control is influenced by a combination of many factors, and the precise regulation of urine volume is important and essential for a variety of different reasons. Ultimately, the body's main requirement is to maintain a balance of fluids and a balance of many chemicals (especially sodium) that flow throughout the system. From previous chapters, you are well aware of the fact that fluid volumes are affected by space flight. Overall fluid volume is decreased in microgravity. It is important to find out how microgravity affects the regulatory systems that control the fluid volumes and electrolyte concentrations in our bodies.

Let's move on to our investigation into how space flight affects the kidneys and the fluid regulating systems of the body.

SPACE PHYSIOLOGY

We have seen that the volume of fluid in the body and the fluid pressures inside the veins and arteries are well-regulated by the various components of the **renal/endocrine system**. On Earth, gravity affects the **distribution** of fluids inside the body by pulling the various body fluids down towards the feet. Upon entry into space, the virtual absence of gravity causes these fluids to redistribute upwards towards the chest and the head. This perceived increase in fluid volume in the upper part of the body causes multiple physiologic changes in the kidneys and associated fluid-regulating hormones, in the cardiovascular system, and in the red blood system. We have already covered this "headward fluid shift" in detail, particularly in terms of the cardiovascular and erythropoeitic changes that take place. Now, we will discuss how your kidneys, working with certain hormones, adapt to space flight and regulate the levels of fluids and electrolytes in the body. In fact, it turns out that changes in the body's fluid volumes begin on the launch pad even before space flight.

Pretend you are an astronaut preparing for launch. You are strapped into your seat in the shuttle at least three hours before launch; you are wearing your **Launch and Entry Suit (LES)** with an attached helmet and visor. The LES is a pressurized space suit that provides pure oxygen for breathing in the event of a bailout at high altitude. In addition, the LES is a buoyant suit (it floats). You are also wearing a parachute. With all of these safety measures in place, you are still not protected from the fluid elimination function that your body will soon begin!

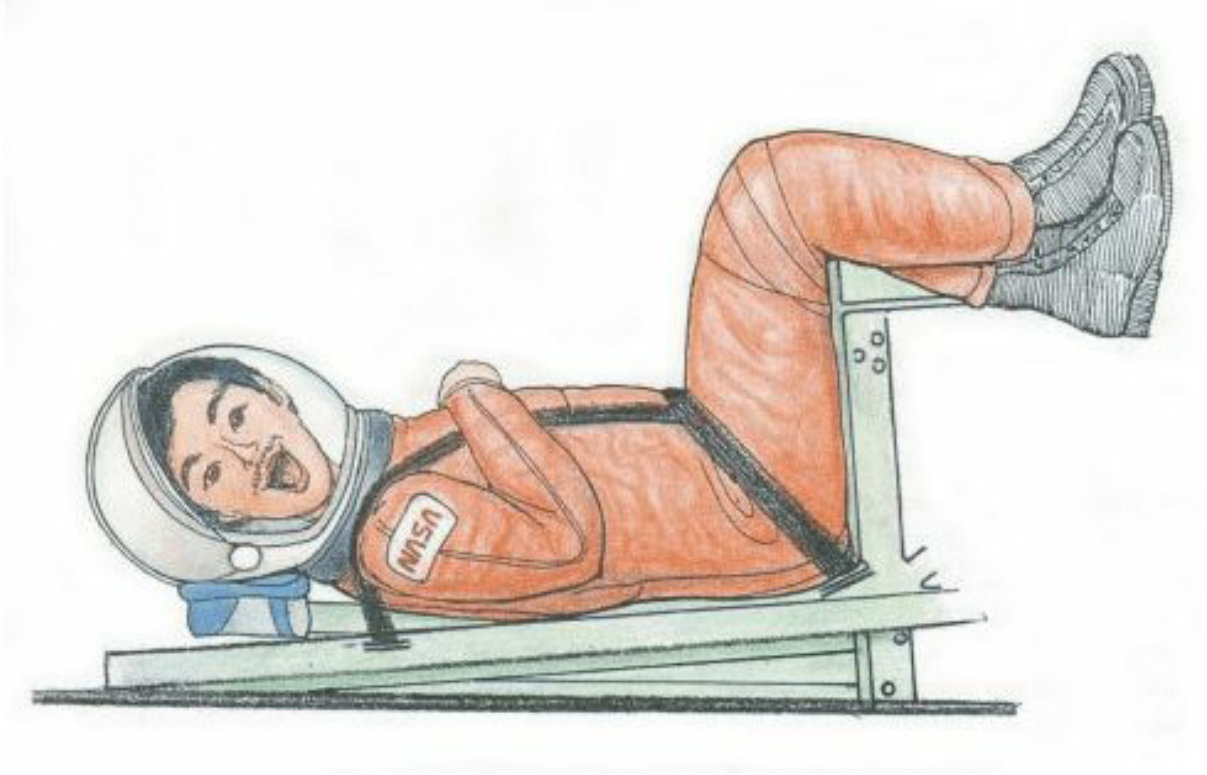


Figure 8. The launch position in the space shuttle.

As you are seated with your head back and your legs and feet inclined upward, the fluids in your body are already beginning to redistribute. While sitting in the launch position, your body begins to respond to the increased volume of fluid that it senses in the upper part of the body and it begins to tell you so. As part of this response, you feel as though you must go to the bathroom, but, of course, that is impossible given your situation. At this point, it is time to be thankful for the "diaper" that all astronauts must wear during launch. It is the finest and most absorbent diaper ever made! This is important, because you stand to lose up to about a liter of urine.

All astronauts wear these diapers and all astronauts experience the need to urinate during this early pre-launch phase. Even if the astronauts attempt to dehydrate themselves on the day prior to launch (which many of them do), the fact that the kidneys work very hard to maintain the production of about one milliter of urine per minute under normal Earthbound circumstances means that the astronaut's bodies will continue to produce at least a minimum

amount of urine. And the fact that the body is oriented in the head-down, legs-up launch position means that, as fluids are pulled upwards by gravity, the body will respond by attempting to eliminate what it detects as a "flood" of fluid in the chest, resulting in even more urine production. All of this results in the need to urinate. Besides, as you probably have experienced, during times when you are excited and nervous (which you can imagine the astronauts feel before launch), the need to urinate is exacerbated! Primarily, however, the "upward" fluid shift created by the astronaut's launch position is responsible for the size of the response that occurs.

Once you arrive in space, you will notice that, even though you continue to slowly eliminate more fluid, you do not feel thirsty. Scientists believe that the kidneys and endocrine glands ad just the fluid-regulating hormones to stimulate the excretion of salt and minerals that will help to diminish your desire to drink. Later in the mission, your kidneys and hormones establish new "space-normal" levels of salts, minerals, and hormones appropriate for the reduced fluid volume.

The renal/endocrine system works **in conjunction with** the cardiovascular system. Experiments that are carried out to study the heart and blood system are naturally linked to experiments that study thekidney's blood cleansing system and the release of fluid-regulatinghormones and salts. This makes sense and further underscores our need to look at the body as an **integrated system**. For the remainder of this chapter, we will examine a comprehensive space flight experiment that was designed by Dr. Carolyn Leach from the NASA Johnson Space Center in Houston, Texas, to investigate how the kidneys and the associated electrolyte and hormone balances in the body contribute to the adaptation of the body to space flight. This investigation measured:

- changes in kidney function, including glomerular filtration rate (GFR) and plasma flow through the kidney;
- changes in body fluid volumes, including plasma volume (PV), extracellular fluid volume (ECV), and total body water (TBW);
- hormone, electrolyte, and other chemical changes;
- body mass measurements and food and water intake.

Just as in all of our other chapters, we should consider some general statements - or hypotheses - about what is expected from the results of Dr. Leach's experiment. Dr. Leach's original hypotheses, which served as the foundation for the development of her space flight study are very complicated and incorporate her predictions for many more scientific measurement areas than we plan to look at. In addition, a large part of her experiment involved looking at **the connections among** more than two dozen variables that she measures. We will be looking at only five variables and will discuss only a very simplified subset of her very comprehensive experiment. For this reason, we will not be concerned with her original hypotheses, but will treat her experiment as if it involves only two "hypotheses":

Hypothesis 1

Adaptation of kidney and electrolyte fluid-regulating functions in microgravity occurs in two stages: an acute, rapid stage (hours to days) and an adaptive, longer-term stage (days to weeks).

Hypothesis 2

The overall renal/endocrine adaptation process in space is primarily a general response to a headward shift of body fluids.

Remember to keep these hypotheses in mind as we review some of the important measurement sets that were actually carried out during Dr. Leach's experiment in space. We will return to them at the conclusion of our examination of Dr. Leach's experiment.

Your Perspective

Before we begin to understand some of the actual experimental procedures that Dr. Leach and her team carried out, and before we present the results of those experiments, let's participate in a few activities that can help clarify certain important concepts and techniques related to her study. The first exercise is designed to provide you with practice in data interpretation. The data involved presents a comparison of measurements of certain components of both blood and urine. From this activity, you will understand the kinds of chemicals that: (1) are "**washed out**" of the blood and excreted by the kidneys, (2) that **remain** in the blood, or (3) that **return** to the blood from the kidney tubules through reabsorption. This activity will indicate which of these chemicals are important for the body to keep and which are important for the body to get rid of.

The second exercise will familiarize you with the particular technique used for the determination of glomerular filtration rate (GFR). This measurement of the **rate** at which the blood is filtered in the glomerulus is based on measuring how fast a certain chemical tracer is eliminated from the body. You will be participating in a **demonstration activity** known as a "serial dilution" that will serve as a **model** representation of how a tracer substance can be used to determine the elimination rate of the tracer, and thus, GFR. A model is often used in the scientific world to help demonstrate the principles of a particular technique without having to actually carry out the technique. For instance, you may have a model of some part of the human anatomy in your classroom. This model substitutes for the need to actually take a body apart to investigate some of the internal structures! The use of a model can also help you predict some kind of outcome in the real experiment that the model is representing. The value of a model in being able to predict outcomes, however, depends on how close the model actually comes to duplicating the real system. **Keep in mind that this is only a demonstration exercise**. There are some significant differences between the serial dilution technique and the technique that is used to measure GFR. By identifying those differences, your understanding of the GFR measurement technique will be enhanced.

The last exercise centers on the idea of developing a **concept map** to illustrate the relationships among the various responses of the body to microgravity. In particular, this exercise will tie together the cardiovascular, blood system, and renal/endocrine changes that occur due to the "upward" fluid shift that you are familiar with by now.

Let's begin our Student Investigations!

STUDENT INVESTIGATION 1

The Kidney and Homeostasis

Background

The cells of the human body are surrounded by liquid that is remarkably constant in its properties. The continued regulation of the many dissolved compounds and ions in this internal environment is one aspect of what is referred to as **homeostasis**.

As you learned at the beginning of this chapter, the kidneys are extremely important in maintaining homeostasis. They function rapidly and sensitively in regulating blood composition and maintaining optimum concentration of dissolved substances. About 1440 liters of blood flow through the kidneys of an average person in a single day (which is about 1 liter/min). Of this amount, about 180 liters are filtered through the glomeruli into the nephrons, but only about 2-3 liters of this filtrate are excreted as urine. The amount of urine produced varies, depending on the individual's health, activity, water and salt intake, temperature, and many other factors. The amount of many of the various constituents of urine varies, as well, depending on the concentration of those constituents in the blood and depending on the hormone activity as the blood enters the kidney.

As the blood is filtered in the kidney, the concentration of two of the main electrolytes, sodium (Na^+) and potassium (K^+), is regulated primarily by the hormone aldosterone. This control is of vital importance to the body because Na+ is important in the regulation of blood volume and pressure, and K+ is required to maintain proper function of cardiac and skeletal muscles. Whereas the first step in the control and regulation of all blood electrolytes involves filtration out of the blood, the majority of electrolytes are subsequently reabsorbed back into the blood from the proximal tubule. Because of aldosterone, the control of potassium (K^+) follows a different process. In the absence of aldosterone, all of the filtered K^+ is reabsorbed from the proximal tubule back into the blood. In the absence of aldosterone, therefore, no K^+ is excreted in the urine. In contrast, the presence of aldosterone stimulates the secretion of K^+ from the peritubular blood into the distal tubule. Thus, secretion is the only means by which K^+ can be eliminated in the urine. This information will be of importance in the interpretation of the data in Parts A and B that follow.

Part A-Blood vs. Urine

Procedure

The relationship between structure and function in the kidney is described in the beginning sections of this chapter. Review this relationship, review the above Background section, and review the data given in Table 1 to answer the discussion questions.

Questions

1. What does the data for water indicate?
2. Protein molecules are not normally found in the urine. Give some possible reasons for this.
3. The information for glucose is similar to that for protein. Can you explain this data?
4. Look at the sodium data. Based on these data, what may happen to the sodium content in the urine of a person who increased his or her intake of sodium chloride?
5. How does the data for potassium differ from that of sodium? How can you explain the fact that there is more potassium in the urine than what was originally filtered out of the blood?
6. How would you interpret the data given for urea?

Table 1. Comparison of materials present in the blood as it enters the kidney, and materials in the urine as it leaves the kidney

% in Blood as it enters Kidney		% in Urine as it Leaves Kidney	
Water	91.50	Water	96.00
Protein	7.00	Protein	0.00
Glucose	0.10	Glucose	0.00
Sodium	0.29	Sodium	0.29
Potassium	0.02	Potassium	0.24
Urea	0.03	Urea	2.70

Part B-Filtration Reabsorption, and Secretion

Procedure

Using a specialized test procedure called the **micropuncture method**, an experiment was done to study the six substances presented in Table 2. This procedure involves withdrawing samples of blood using a very fine pipette at four points within the kidney: where the blood enters the kidney, at a point within the kidney, where the blood exits the kidney, and in the urine collecting tubule. Study Table 2, which shows the data, collected using this technique. Use the data to answer the discussion questions.

Table 2. A comparison of substances that are found in fluid samples taken at four points within the kidney.*

	In blood entering kidney	Within kidney along tubule	In blood leaving kidney	In urine
Water	100	30	99	1
Protein	100	0	100	0
Glucose	100	20	100	0
Sodium	100	30	99	1
Potassium	100	23	88	12
Urea	100	50	10	90

Questions

1. For each of the substances listed in Table 2, state which of the following processes are involved in the movement of each substance: filtration, reabsorption, or secretion.
2. If you are in the movie theater and you were to eat some very salty popcorn and you did not drink a soda with it, which substance(s) would be affected? How would they be affected?
3. Explain the fact that 20% of glucose is filtered into the kidney but all of it is reabsorbed back into the blood.

STUDENT INVESTIGATION 2

Performing a Serial Dilution to Demonstrate the Principles Behind the Measurement of Glomerulor Filtration Rate

Background

The measurement of **glomerular filtration rate (GFR)** in space is one of the very important measurements to make in order to understand how the body responds to the "upward" fluid shift that occurs in space. In fact, it is one of the major components of Dr. Leach's space flight experiment. The technique that is used to measure GFR is known as the **plasma clearance method**. The term "plasma clearance" is somewhat self-explanatory; it is used to express the ability of the kidneys to clean, or "clear," the plasma of various substances. This technique is essentially the same as the "dilution method" that we discussed in the previous chapter because it involves the determination of how fast the body is able to eliminate a chemical tracer, or "marker" substance from the bloodstream. The **difference** between the "plasma clearance method" and the "dilution method" is that the tracer substance that is chosen for the plasma clearance method will be filtered out of the bloodstream and eliminated in the urine. The tracer that is chosen to carry out the dilution method is selected for its ability to stay in the bloodstream and not be eliminated by the kidneys.

Specifically, the plasma clearance method to measure GFR is based on a determination of how quickly a chemical tracer that is injected into the bloodstream of the astronauts is removed from the blood plasma by filtration in the glomeruli of the kidneys. Thus, the method involves determining **the rate of loss of the tracer**.

The tracer used in this technique must have the following properties:

1. It should be non-toxic to the human body;
2. It should be able to be measured accurately by chemical or physical means;
3. It should be freely and evenly diffusible throughout the **extracellular fluid (ECF) compartment**;
4. It should be removed from the blood **only by filtration in the kidneys**;
5. It **should not be reabsorbed into the blood** from the renal tubules or other parts of the urinary system;
6. It should be completely excluded from the **intracellular fluid (ICF) compartment**.

A chemical product known as **Inutest** fits all of these criteria and was used as a tracer for this part of Dr. Leach's experiment. We will discuss the actual steps that were used to measure GFR in space along with the results of this test when we begin our "Space Flight Investigation" section. But for now, we will participate in an exercise that is will help you understand how the concentration of the tracer substance changes as the body continues to eliminate it. We will carry out a **serial dilution** where each dilution will represent a distinct glomerular filtration that takes place to "clear" the blood of a substance. In reality, glomerular filtration is a continuous process and, thus, this demonstration only serves as a model of what happens in the body.

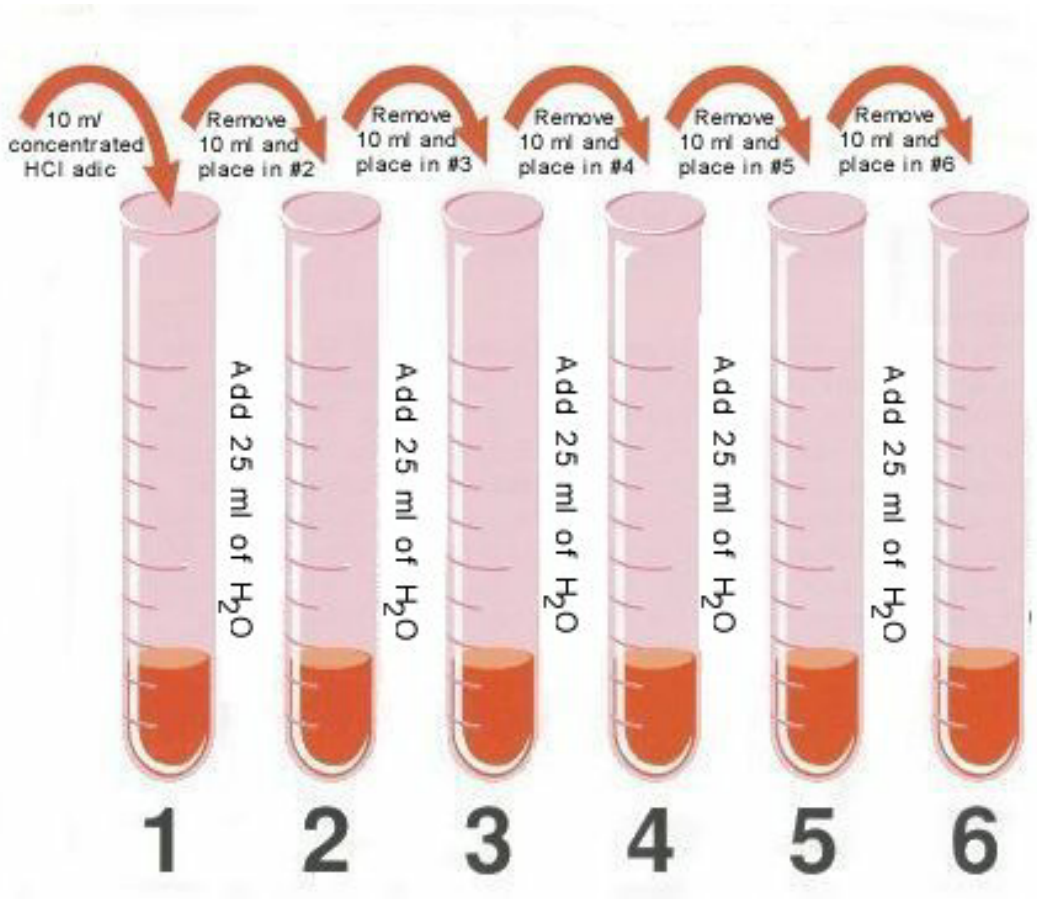


Figure 9. For this demonstration activity you are simulating, with each successive dilution, the kidney's "clearance" of a tracer out of the bloodstream. After the addition of methyl violet indicator, test tube # i win represent the initial concentration of the tracer that is injected into the bloodstream. Test tubes #2, #3, #4, #5, and #6 will represent the tracer concentration in the bloodstream after longer and longer periods of glomerular filtration.

First of all, you will be using a concentrated acid for this experiment. Therefore, **review the laboratory safety instructions with your teacher**. Above all, **use safety goggles** and be aware of the chemical wash facilities (at least the sink) in the event that you splash the acid onto your skin. Secondly, when mixing acid and water, always remember: **never add water to acid**. This will cause a violent and dangerous reaction. For this experiment, you will only add acid to water.

For this activity, you will be diluting acid/water solutions five different times. As an **analogy**, think of the water in each test tube as your blood supply and think of the concentrated hydrochloric acid (HCL) as the tracer substance that will be injected into your bloodstream. Each time you remove some of the solution from one of the test tubes, you should imagine this as the process of glomerular filtration where some of the tracer substance is being eliminated from the bloodstream. Finally, you will add a special **indicator substance** to each of the completed HCL/water solutions so that you are able to analyze the **relative differences** in HCL concentration of the six solutions. This will give you an idea of how different tracer concentrations determined from blood samples taken from the astronauts will indicate the rate at which the tracer is being eliminated from the system.

Remember, analogies can only serve as a partial representation of what is really happening. It is important to remember that for the actual determination of glomerular filtration rate, **the time between blood samples must be carefully recorded**. You will be asked to think about why and to respond to a question about this at the end of the experiment. You may want to discuss this with your experiment group.

Finally, since this is a demonstration experiment, there is no need to develop an hypothesis about the results that you expect. There are, however, a few **objectives** for you to keep in mind that will define what you are **supposed to**

learn from this activity. From your experiment, you should be able to:

1. perform a serial dilution;
2. understand that indicator molecules respond to a different tracer concentration;
3. realize that color indicators are an accurate method of measuring concentration differences; and, probably most important
4. translate how an analogy (in case, the serial dilution) is similar to and different from reality (in this case, a determination of GFR).

Now that you have the picture, let's begin the experiment.

Materials

Safety goggles
Concentrated HCL acid
Methyl violet indicator
Six test tubes
Graduated cylinders: 10 ml and 100 ml
Distilled water
Cork

Procedure

1. Label six test tubes 1, 2, 3, 4, 5, and 6.
2. Place 25 ml of distilled water into each test tube.
3. Measure 10 ml of concentrated HCL acid and add to test tube #1. Cork the top of the test tube and shake it.
4. Remove 10 ml from test tube #1 and add it to test tube #2. Cork and shake.
5. Remove 10 ml from test tube # 2 and add it to test tube # 3. Cork and shake.
6. Repeat procedure for test tubes #4, #5, and #6.
7. Remove 10 ml from test tube #6 and discard.
8. When complete, each test tube will contain 25 ml of fluid.
9. Place 2 to 3 drops of methyl violet indicator to each test tube.
10. Observe and record the final colors of each solution. It may be necessary to "rate" the colors numerically (for instance, between 1 and 12 to obtain values that reflect the relative color differences among the test tubes).

Questions

1. What is an indicator and how does it work?
2. What general term is used in place of "indicator" for the substance used in the plasma clearance technique described for the measurement of GFR? And what is the name of the chemical product used for this purpose?
3. How is the indicator used in this activity **similar to** and **different from** the chemical product used to measure GFR?
4. How would you design a test that is more similar to the actual measurement technique that is used to measure GFR? Hint: Time.

STUDENT INVESTIGATION 3

An Integrated Look at the cardiovascular Blood, and Renal/ Endocrine Responses to the Fluid shift Phenomena of Space Flight

Background

When one body system is affected by an external stimulus (for example, a change in environment), all the other body systems play an interactive role in helping to maintain a stable condition in the body. In other words, each body system helps the other in the face of a challenge until all of the responses cascade down towards a new adaptive state. In the case of space flight, the human body moves from an "Earth-normal" condition to a "space-normal" condition. When the astronaut returns home, the body systems must again work together to reestablish that "Earth-normal" condition. The human body is truly amazing.

Procedure

A concept map is a flow diagram that illustrates the cascading nature lone leading to others, which lead to others, which lead to others, etc.) of a related set of responses for a particular phenomenon. It illustrates how the various systems react in response to a **stimulus**. In this case, we are interested in illustrating the flow of events that occurs in the human body as a result of space flight (Figure 10). The stimulus, which causes the flow of events to begin, is, in our case, the removal of gravity. The **primary response** from which all other responses follow is, in our case, the increase in volume the of fluids in the upper body (the headward fluid shift). We chose this as our starting point because by now, you are well familiar with this human response to space flight.

What follows from the primary response are the **secondary responses** in Figure 10.

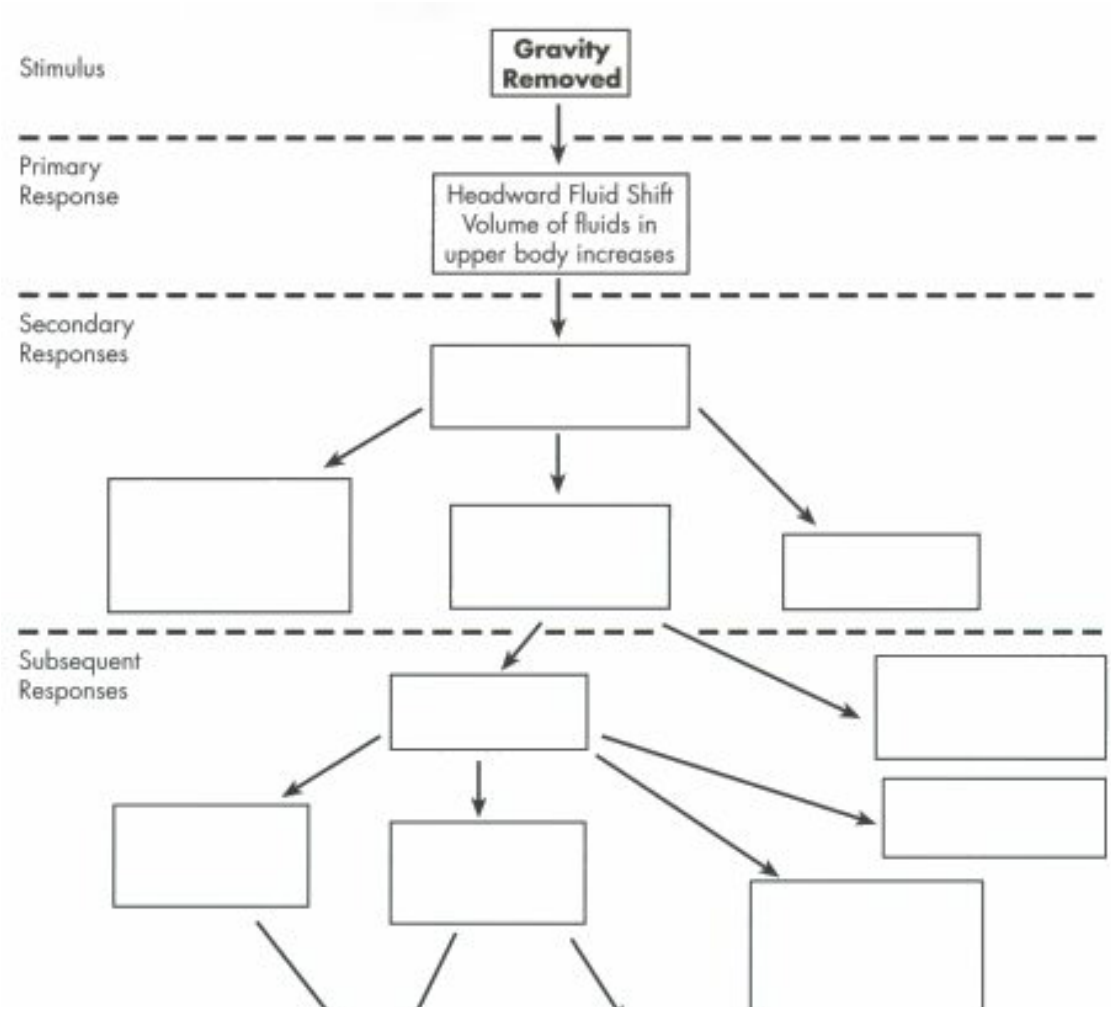


Figure 10. Concept map illustrating the inter-relationships of the various body responses to the removal of gravity.

Your teacher will provide each of you with a copy of Figure 10. You are instructed to fill in the blank compartments for both the secondary responses and the **subsequent responses** with the appropriate statements, which are provided for you. Be aware that the statements which we have provided to you will all be used and they are **not in order**.

The following is the list of the secondary responses and the subsequent responses for your use in filling out the compartments on the concept map provided to you by your teacher. Use your logic and experience that you have gained through your use of this manual to complete the map.

SECONDARY RESPONSES

A. Increase in CVP, BP, HR, CO
B. Kidney stimulated to increase urine output
C. Body senses a "flood" in upper body
D. Change in physical characteristics: Puffy Face-Bird Legs Syndrome

SUBSEQUENT RESPONSES

E. Increased destruction of RBCs
F. Decrease in RBC production
G. Stabilization of CVP, BP, HR,CO
H. Initial increase in RBC concentration
I. Decrease in plasma volume
J. Heart shrinks in size because of decrease in workload
K. Decrease in body mass because of fluid loss
L. Altered hormone and electrolyte balance

KEY

CVP - Central Venous Pressure
RBC - Red Blood Cell
BP - Blood Pressure
HR - Heart Rate
CO - Cardiac Output

THE SPACE FLIGHT INVESTIGATION

Just as a thermostat keeps a room at a set temperature, the kidneys and hormones, working together, keep the body in a stable condition with the right amount of fluids and electrolytes so that the body functions well. One of the main functions of the kidneys and hormones is to regulate blood volume, so it will come as no surprise to you that the kidneys and hormones must play a large part in the body's adaptation to space flight. In fact, the responses to microgravity of the renal/endocrine system must be closely related to the cardiovascular responses because both have a great deal to do with fluid volume. As we discussed earlier, going from Earth to space causes fluid to migrate toward the head. As a result, the cardiovascular system perceives an increase in blood volume, and the renal/endocrine system reacts by removing fluids and electrolytes. This is another example of the need for an **integrated approach to physiology** to understand what's happening in the body.

Before experiments were carried out in space, scientists did not know the **mechanisms** that cause changes in fluid and electrolyte balance during space flight. Did the kidney actually change the way it operates in space? Did hormones influence fluid retention or fluid elimination in space in the same way that they do on Earth? Are electrolyte concentrations maintained at the same levels in space as they are on Earth? These are only a few of the many complicated questions that Dr. Leach's study was designed to examine. But before we begin our discussion of some of her results, let's see how her study was designed to eliminate certain **confounding factors**, or factors that have interfered in the past with the scientific examination of fluid and other dynamics of the body in space.

On many space flight missions, astronauts have experienced space motion sickness, a malady similar in some respects to motion sickness on Earth, which can decrease their desire to eat or drink. You know how it feels if you have ever felt queasy and sick to your stomach; your normal diet of both solids and liquids is interrupted. Also, you may have heard from the doctor or your parents that when you actually get to the point of vomiting, you have become very dehydrated. These same things can happen early in a space flight: such space motion sickness can be a problem for the scientist who is interested in understanding **normal** fluid intake and output dynamics of space flight. A related problem can occur when the astronauts take certain medications to help reduce the effects of space motion sickness. Such medication introduces chemicals into the body that can alter the results of an experiment. It was fortunate that Dr. Leach's experimental results were obtained from astronauts who did not experience significant space motion sickness. Because the astronauts did not report sickness as being a problem, they did not have to use medication.

Another factor that should be understood in interpreting body fluid volumes and electrolyte levels is the dietary change that occurs in space. In order for scientific results to be accurately interpreted, essentially all nutrients and any other chemicals taken into the body from the food and beverages that the astronauts ingest must be well documented. Diet, and its effect on renal/endocrine function, can be monitored quite closely by the use of a **diet log**, which is similar to a diary that one keeps to record everything one eats and drinks. As an example, if you eat a lot of salty popcorn at the movies without drinking anything, your glomerular filtration rate (GFR) is likely to **decrease** so that water is preserved in your system to dilute the salt. You will probably not be interrupted during your movie to go to the bathroom! On the other hand, if you drink a large soda during the movie without eating something salty, the GFR is likely to **increase** in response to the need to eliminate an excess of fluid in the body. You know what this means! Of course, these examples are simplified. In reality, the effects of diet on GFR and other renal/endocrine functions are complicated and involve hormonal and other chemical interactions occurring at many levels.

Another factor that, in the past, has interfered with the study of fluid regulation in space is preflight self-imposed dehydration. This means that during the immediate preflight period, certain astronauts have been known to stop drinking fluids so that they do not have to urinate as often after all, you can imagine how uncomfortable a very wet diaper can be! (Remember from a previous section, it was mentioned that all astronauts wear a diaper because of the long wait on the launch pad before they finally take off.) Previous renal/endocrine results have probably been altered by this artificial attempt to influence fluid dynamics. In a well-designed scientific study of the body, only **natural** events should be taking place so that **natural** events can be measured. For Dr. Leach's study, the astronauts were instructed to hydrate themselves normally before the flight and during the flight. That is, they were told to hydrate themselves **ad libitum** (a Latin term for "in accordance with one's wishes"!. They were asked to drink freely if they became thirsty.

Finally, for the results that you are going to see, the postflight fluid intake level **was** artificially influenced, but for a very good reason. The astronauts were asked to **fluid load**, which means that they drank about two liters of **saline solution** just before reentering the Earth's atmosphere (Figure 11). Saline is a water and salt, combination; the salt is added so that the body will retain the water. This fluid loading approach seems to be in contradiction to the maintenance of "natural" effects that scientists normally want to measure. The difference here is that, while in space, the astronauts have established a "space-normal" fluid level in the body that is lower than their "Earth-normal" fluid level. These space-normal fluid levels, while fine for the space environment, create problems for the astronauts when they return to the clutches of gravity here on Earth). Astronauts experience **orthostatic intolerance** (the inability to maintain a standing posture), and they can become very weak for a period of time. We discussed this problem in the cardiovascular chapter. Therefore, fluid loading is considered a **countermeasure** (counter = reverse, measure = effort), which is an effort taken to counteract or reverse these unfavorable effects. Dr. Leach measured certain renal/endocrine parameters in astronauts that had not fluid loaded and in astronauts who had. Therefore, she was able to compare and determine how well this countermeasure works.

Figure 11. Astronauts "fluid load" before returning home after a mission. This ingestion of extra fluid is necessary to counteract some of the physiological effects of a sudden return to gravity.

Preflight, inflight, and postflight portions of Dr. Leach's experiment were all done on two space missions. We will review two measurement sets from one of those missions to compare certain aspects of renal/endocrine behavior before, during, and after space flight. For each measurement set, we will include information about **why the measurements are important**, the **equipment or technique used** to make the measurement, the **expected results**, and the **actual results**. These measurement sets were designed to measure changes in:

- glomerular filtration rate (GFR) and renal plasma flow (RPF); and
- hormone (ADH and aldosterone) and electrolyte levels (Na^+).

Once again, the results that you will see involve real experimental data. Let's get started!

I. Renal Function Measurements: Glomerular Filtration Rate (GFR) and Renal Plasma Flow (RPF)

Three of the biggest jobs that the kidneys have are: (1) to cleanse the blood, (2) to regulate and maintain an appropriate fluid and chemical balance in the body, and (3) to produce the urine. Each of these functions is closely related to the other two, not only because each involves the removal or addition of fluid and chemicals from the blood, but also because each of these functions takes place in the kidney's **nephrons**. The starting point in the nephron for each of these functions is the **glomerulus**. It is the "gateway" that the blood must pass through in order to be cleansed by the kidneys.

The **glomerular filtration rate (GFR)** and the **renal plasma flow (RPF)** are both **rate measurements** that help scientists and physicians characterize the status of renal function. When looked at together, they provide information about how fast the kidney can process the blood through its various structures and, therefore, can indicate how efficiently the kidneys operate. What about space flight? Does the renal system respond to the fluid shies that occur in microgravity by participating in the increased elimination of fluids? In particular, does GFR increase to eliminate the "flood" of fluids that the body detects in the "upper" part of the body? And is this flood reflected as an increase in RPF? Dr. Leach measured both of these variables in astronauts before, during, and after a space flight mission, and we will look at those results in a moment. First, let's see how GFR and RPF were measured.

GFR, remember, is the **rate** at which water and dissolved substances are filtered out of the blood and into the kidneys. Recall that as the blood flows through the glomerulus, the water and the various salts and other dissolved substances flow through the glomerular-capsular membrane and into Bowman's capsule. A "normal" GFR in an average adult who is at rest is about 125 ml/min. **This is not how much blood passes through the glomerulus each minute, but instead, it is how much filtrate is removed from the blood each minute.**

RPF is the **rate** at which plasma flows through the kidney. Of course, we learned in the last chapter that blood consists of about 55% plasma and about 45% cellular components (mostly RBCs). By estimating the rate of plasma flow through the kidneys, one can obtain an estimate of the rate of total blood flow through the kidneys. You might ask why the **plasma flow rate** is measured and not the **blood flow rate**. Well, the reason for this lies in the technique that is used to measure the plasma flow rate. We will discuss this in detail in a moment, but suffice it to say that the plasma flow rate is measured because it is only the plasma that carries the tracer substance. And it is the plasma that is filtered out of the glomerulus and into the nephron, not the blood cells. Therefore, the plasma delivers the tracer substance to the kidney, where it will be washed out of the system. It is the **rate of elimination of the tracer from the plasma** and into the urine that will provide the scientist with the information needed to **calculate** how fast the blood is flowing through the kidney. The normal rate of **plasma flow** through both kidneys of a 70 kg human on Earth is about 650 ml/min, and the normal rate of **blood flow** is about 1200 ml/min. Plasma makes up about 55% of the total blood volume and the plasma flow rate is about 55% of the total blood flow rate. This is no coincidence!

GFR and RPF are both measured using a technique known as the **plasma clearance method**. As stated earlier, this technique is based on a determination of how quickly a chemical tracer is removed from the blood plasma by the action of the kidneys. In other words, the plasma clearance is the **rate of elimination** of the tracer from the plasma. For the determination of both GFR and RPF, non-radioactive tracers are used. A product known as **Inutest** (a derivative of the polysaccharide inulin) is used as the tracer for the determination of GFR because it meets the criteria found in Table 3.

Table 3. Criteria used for the secretion of Inutest as a tracer for the determination of glomerular filtration rate.

1. It is nontoxic to the human body;
2. It can be measured accurately by chemical means;
3. It diffuses freely and evenly throughout **only** the extracellular fluid (ECF) compartment (remember, ECF= PV + ISF);
4. It stays completely out of the intracellular fluid (ICF) compartment ;
5. It is removed from the blood **only by filtration** out of the glomerulus and into Bowman's capsule; and
6. It is **not reabsorbed** into the blood from the renal tubules and it is **not secreted** from the blood into the renal tubules or any other part of the urinary system.

In summary, Inutest mixes evenly in the blood and is only removed by glomerular filtration. The glomerular filtrate, then, contains the same concentration of Inutest as does plasma, and as the filtrate flows down the kidney tubules, **all** the filtered Inutest continues on into the urine while 99% of the filtrate is returned to the blood. As time goes on, the concentration of Inutest in the plasma decreases at a rate that reflects how fast the nephron is able to filter the blood in the glomerulus. Therefore, **the plasma clearance per minute of Inutest is equal to the GFR**.

As an example (Figure 12), let us assume that it is found by chemical analysis that: (1) there is 0.1 gram of Inutest in each 100 ml of plasma, and (2) that 0.125 grams of Inutest passes into the urine per minute. By dividing 0.1 into 0. 125, one finds that 1.25 **100-milliliter** portions of glomerular filtrate must be formed each minute in order to deliver to the urine the analyzed quantity of Inutest. In other words, since plasma clearance of Inutest occurs at a rate of 0.125 grams per minute (measured from the urine), this means that 125 ml of glomerular filtrate is formed per minute.

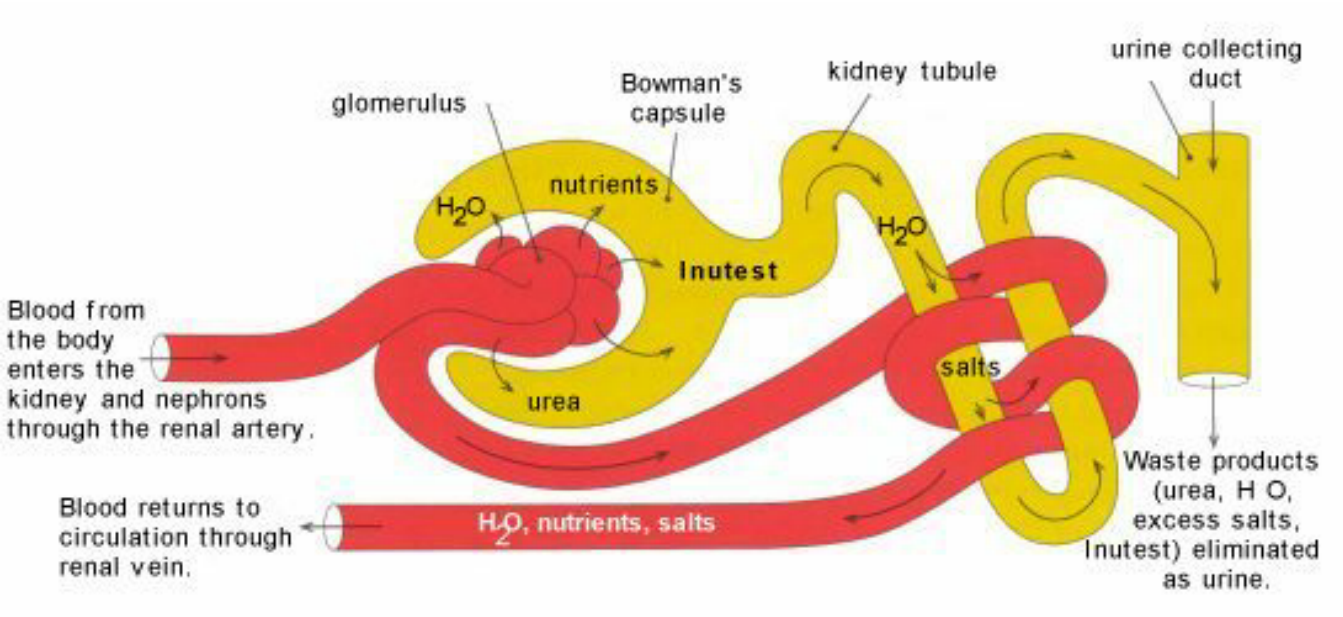


Figure 12. The plasma clearance rate of Inutest in the nephron is equal to the glomerular filtration rate (GFR).

1. Chemical analysis finds every 100 ml of plasma contains 0.1 g. of Inutest:

$$\left(\frac{100 \text{ ml plasma}}{0.1 \text{ g Inutest}}\right)$$

2. Chemical analysis finds 0.125 g of Inutest passes into the urine per minute

$$\left(\frac{0.125 \text{ g Inutest}}{\text{minute}}\right)$$

3. To calculate the glomerular filtration rate:

$$\frac{100 \text{ ml plasma}}{0.1 \cancel{\text{g Inutest}}} \times \frac{0.125 \cancel{\text{g Inutest}}}{\text{minute}} = \text{GFR} = \frac{125 \text{ ml plasma}}{\text{minute}}$$

On the other hand, a different chemical tracer called para-amino hippuric acid (PAM) is used to determine RPF. PAH is used because it meets the criteria found in Table 4.

Table 4. Criteria used for the selection of PAH as a tracer for the determination of renal plasma volume.

1. It is nontoxic to the human body
2. It can be measured accurately by chemical means;
3. It diffuses freely and evenly throughout **only** the extracellular fluid (ECF) compartment (remember, ECF = PV + ISF);
4. It stays completely out of the intracellular fluid (ICF) compartment;
5. It is removed from the blood into the blood from the renal tubules
6. It is into the blood from the renal tubules.

Both Inutest and PAH are filtered out of the glomerulus and into Bowman's capsule with perfect ease. However, PAH is **different** from Inutest in that most of the PAH remaining in the plasma after passing through the glomerulus is secreted out of the bloodstream and into the nephron's proximal tubule. Therefore, only about one-tenth (actually about 9%) of the original PAH remains in the plasma by the time the blood leaves the kidneys. As an example, let us assume that it is found by chemical analysis that: (1) 1.0 mg of PAH is present in each 100 ml of plasma and that, (2) **after five minutes**, 29.25 mg of PAH has passed into the urine (Figure 13). This means that 5.85 mg of PAH has passed into the urine per minute. Consequently, 585 ml of plasma is cleared of PAH each minute. Obviously, if this much plasma is cleared of PAH, **at least this much plasma must have passed through the kidneys** in this same period of time.

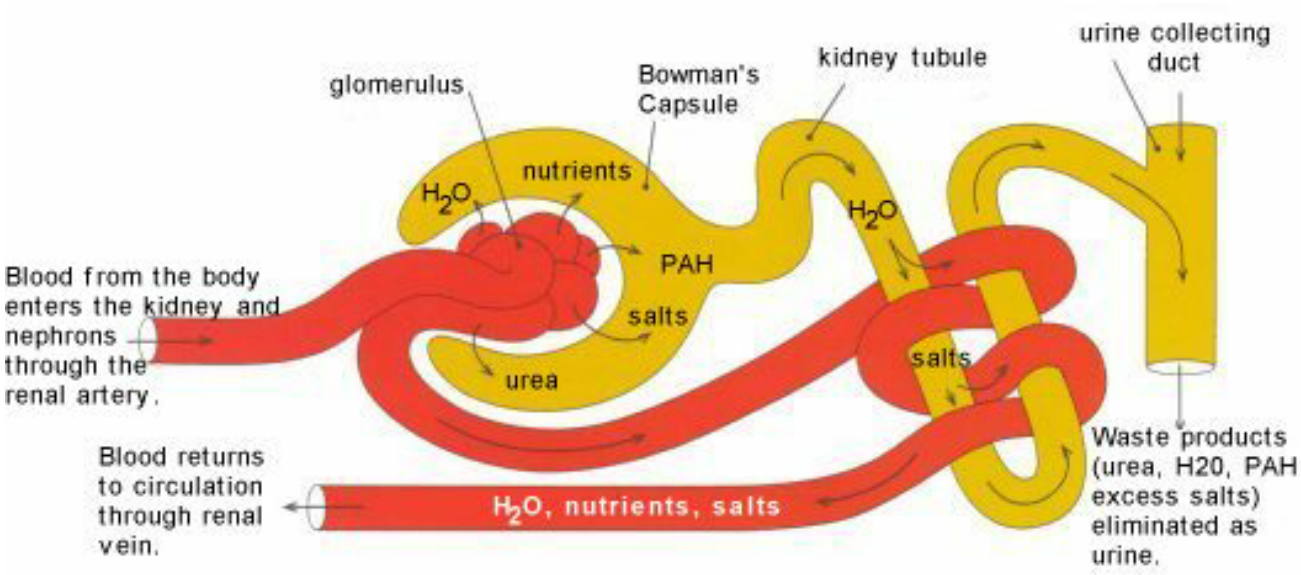


Figure 13: PAH is the tracer used for the determination of the renal plasma flow (RPF) rate.

Keep in mind, however, that the 585 ml of plasma just calculated would be only 91 % of the total amount of plasma flowing through the kidneys. In order to be still more accurate, you can correct this figure through a simple calculation to account for the other 9% of the PAH that is still in the blood when it leaves the kidney. Dividing 585 by 0.91 gives a total plasma flow per minute of approximately 650 ml.

Finally, you can calculate **total blood flow** through the kidney by taking into consideration the **hematocrit** (remember from the last chapter that a hematocrit is a measurement of the percentage of RBCs in the blood). If a person's hematocrit is 45%, this means that the plasma volume is 55%. We've already calculated plasma flow as 650 ml/min. Therefore, the total blood flow through both kidneys is determined by dividing the plasma flow by the proportion of plasma in the blood, or 650/. 55 = 1182 ml/min. What would be the total blood flow if a person had a hematocrit level of 42%?

For Dr. Leach's experiment, a variety of space flight equipment was utilized, including the **Blood Collection and Injection Kit**, the **Blood Sample Storage Kit**, the flight **Centrifuge** for the processing of blood, and the **Urine Monitoring System (UMS)**. Recall that the Blood Collection and Injection Kit and the Blood Sample Storage Kit contain all of the necessary materials and storage capability for the blood tests that must be done inflight.

The Urine Monitoring System (UMS) shown in Figure 14 provides for the collection, volume measurement, and sampling of urine in microgravity. Measurement of the total volume of urine "voided" by each astronaut is automatically made as the urine enters the system. Each urine sample is then collected and moved to a freezer where it is preserved at-20°C. An automatic water flush capability in the system is provided to reduce cross-contamination from sample to sample.

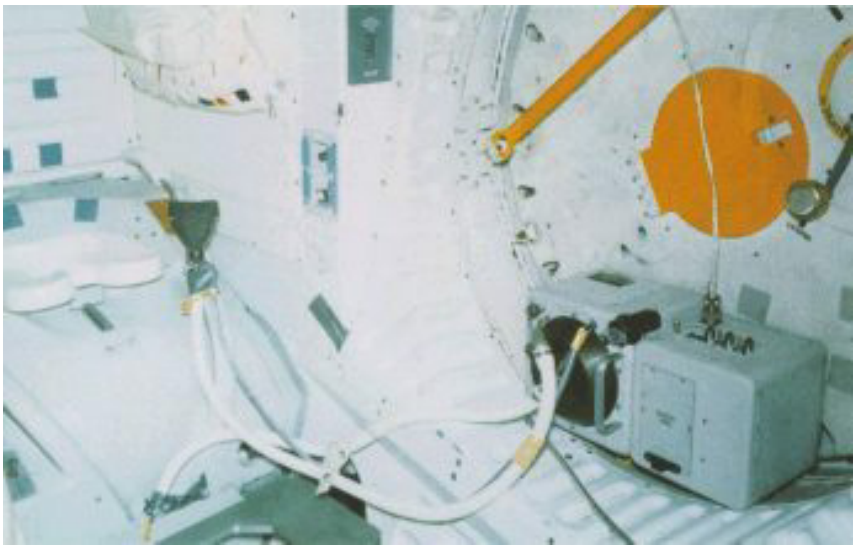


Figure 14. The Urine Monitoring System (UMS).

Using some of the equipment just mentioned, the determination of GFR and RPF was carried out before, during, and after the space flight. First, to establish baseline measurement values, a blood sample and several urine samples were taken from each astronaut before the injection of tracers. Following this, known quantities of Inutest and PAH were injected into a vein in the astronaut's forearm. The exact start and finish times for each injection were recorded. After sufficient time (about 90 minutes) had elapsed for the tracer to mix uniformly in the blood, blood samples were collected at about 15- 20 minute intervals and urine samples were collected whenever the astronaut's felt the need to urinate.

The amount of tracer injected and the actual times of blood sample and urine sample collection were carefully recorded since this was a determination of the elimination **rate** of the tracer. Following the collection of each sample and after the time was recorded, the blood samples were centrifuged and hematocrit levels were determined for each sample. Then, the blood cells were discarded and the plasma was frozen for later analysis. The volume of the urine samples was measured as they were collected and then the samples were frozen for later analysis.

The results of the GFR measurements are shown in Figure 15. This graph indicates the **percent change from preflight baseline measurements**. As you can see, GFR was elevated at all times inflight. Once the astronauts returned (R+0 is landing day), it looked like the GFR was **trying** to return quickly back to preflight levels. The subsequent increase after six days back from space is hard to interpret because of the huge variability in the measurements among the astronauts (indicated by the error bars). Remember, many other hormonal and chemical activities must be considered before any interpretation of the data will make sense.

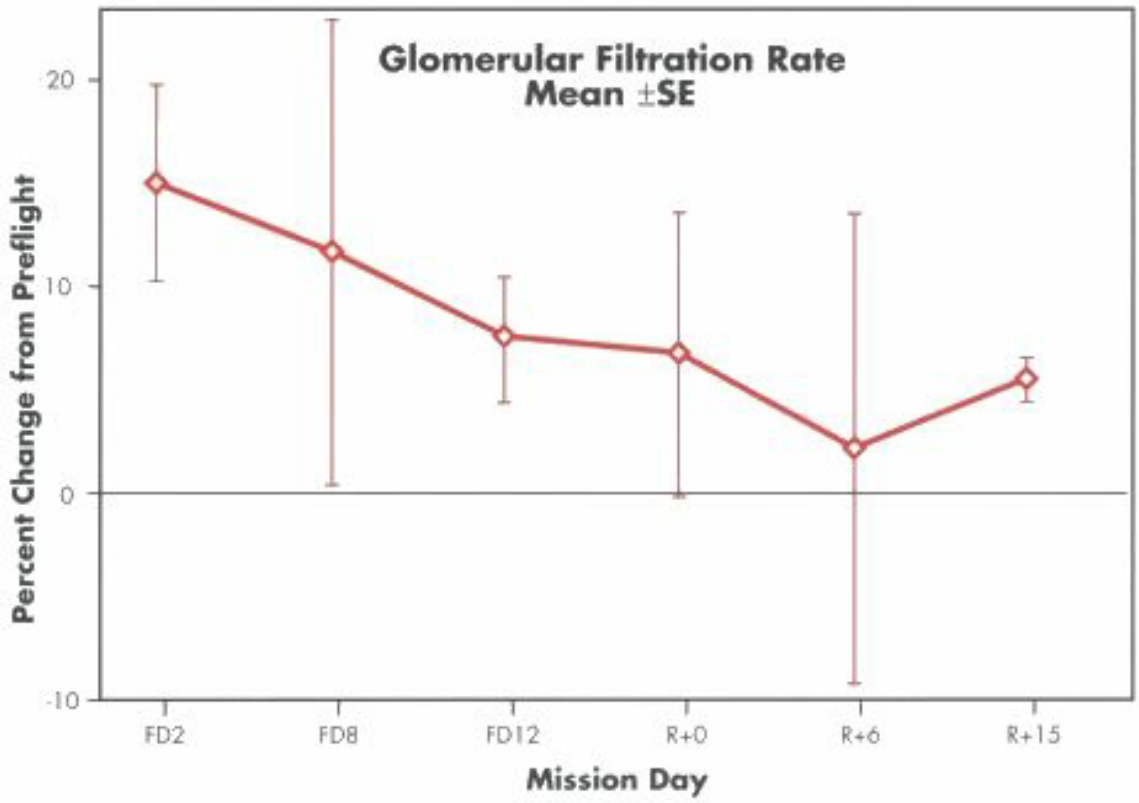


Figure 15. Inflight and postflight glomerular filtration rate data.

The results of the renal plasma flow (RPF) are shown in Figure 16. Again, the graph indicates **the percent change from preflight baseline measurements**. As you can see, RPF was also increased inflight. However, the pattern of increase for RPF was different from that of GFR. In particular, look at the data point in both Figure 15 and Figure 16 for flight day 8 (FD8). While GFR has already begun to decrease, RPF jumps to a much higher level. For which data point does this opposite effect happen again? One can probably conclude from this that, while certain hormones or other chemicals may affect both GFR and RPF, there are probably some different factors that influence each of them. This is very interesting and indicates the complexity of the renal/endocrine system.

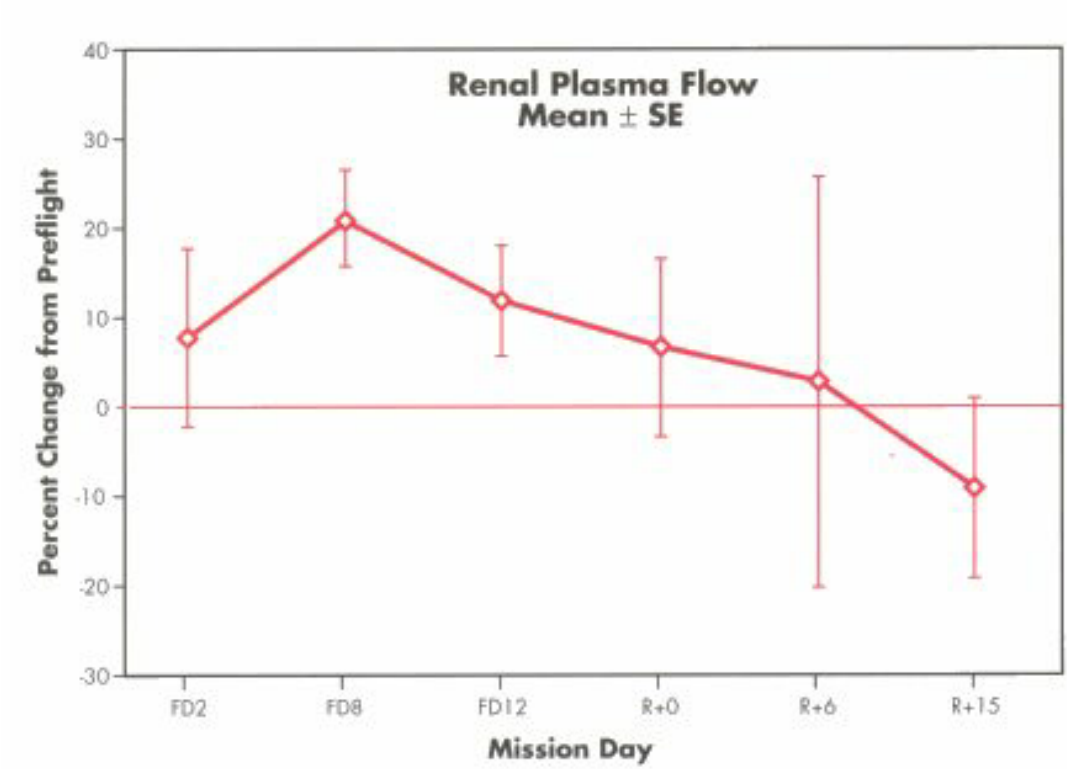


Figure 16. Inflight and postflight renal plasma flow data.

Finally, the GFR and RPF values can be used to calculate **filtration fraction** - that is, the fraction of the plasma that is filtered in the kidney each minute - from the following equation:

$$\textbf{Filtration Fraction} = \frac{\textbf{GFR}}{\textbf{RPF}}$$

Remember from an earlier section that the filtration fraction is normally about 20%, meaning that 20% of the blood that circulates around the body each minute is filtered in the kidney and about 80% of the blood continues to travel to other parts of the body to deliver O2 and other nutrients. It would be interesting to see if space flight affects this filtration fraction. As an exercise in graphical interpretation, you should determine filtration fraction based on your teacher's instructions. You have almost everything you need to accomplish this. You have the equation. And, although you don't have the specific values for GFR and RPF, you have percent changes of both variables shown in Figures 15 and 16.

If you assume that a normal value for GFR is about 125 ml/min and a normal value for RPF is about 650 ml/min, you can estimate, from the graph, an approximate value for both variables. Remember, **the values that you calculate are not real experimental data**. An exercise such as this is merely an example of what one can do through graphical interpretation. It is up to your teacher to instruct you how to calculate your approximations of GFR, RPF, and ultimately, filtration fraction. Let's move on to a discussion of the space flight changes in hormone and electrolyte levels.

II. Hormonal and Electrolyte Changes in Space

We have already discussed the negative feedback loops in the body that are responsible for controlling the release of anti-diuretic hormone (ADH) and aldosterone in response to sodium (Na^+) potassium (K^+), and water levels in the bloodstream. Table 5 is a summary of these important fluid and chemical regulatory mechanisms. Although we will not be looking at Dr. Leach's space flight data about potassium, we will look at sodium data, as well as ADH and aldosterone data to determine how space flight affects the way that ADH and aldosterone are released in response to Na+ levels. Does the negative feedback loop relating these three important chemicals operate in the same way in space as it does on Earth? Let's find out.

Dr. Leach and her colleagues measured a variety of chemical constituents in the blood and urine samples that were collected daily from the astronauts. In order to be able to understand and relate the measurements to each other, it's important to know essentially everything that was going into the astronaut's body (and for that matter, almost everything that was leaving the body). Therefore, to support Dr. Leach's experiment, daily diet and fluid intake logs were maintained by each of the astronauts. In fact, before the mission, the astronauts and the scientists planned for a diet that would meet all of the Recommended Daily Allowances (RDA) of the nutrients that our bodies need. (Most of you have heard of RDAs on some cereal commercial at one time or another!) Of course, each astronaut selects what they want from the meal developed for the shuttle. Each item on this list has been analyzed for its chemical and nutritional content. From these logs and from the blood and urine samples taken daily, Dr. Leach was able to determine: (1) the daily level of **sodium intake**, (2) the daily **plasma sodium level**, and (3) the **sodium level in the urine** that was excreted daily.

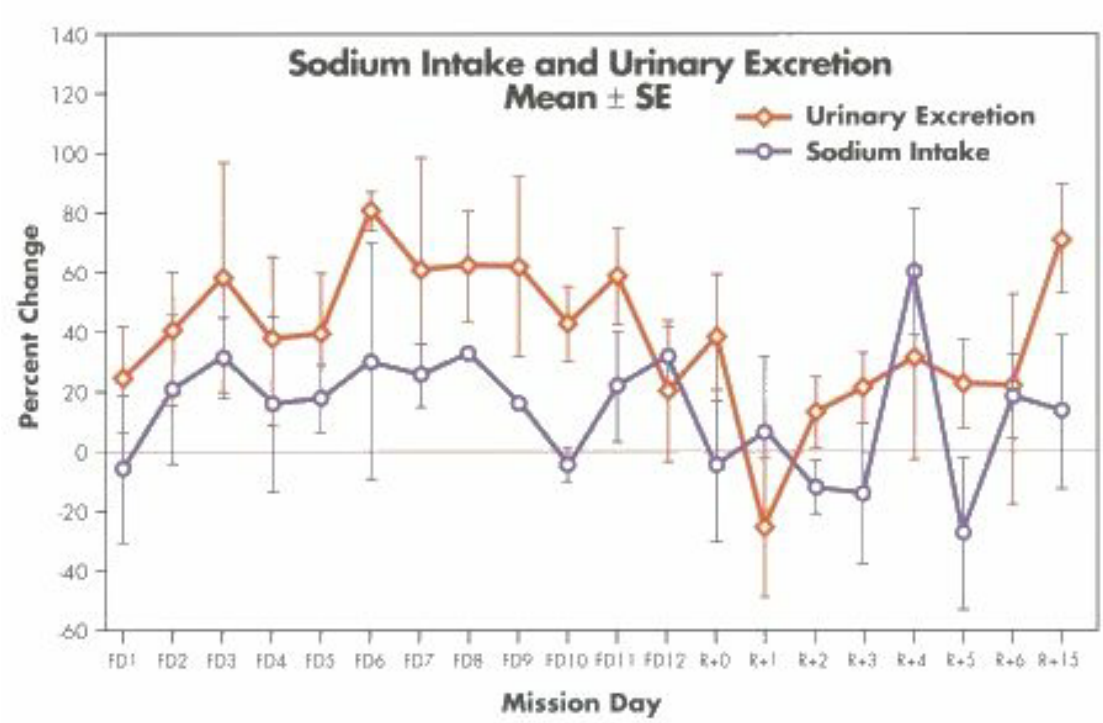


Figure 17. Inflight and postflight sodium intake and urinary excretion levels as a percentage of preflight levels.

The role of the kidney in sodium excretion is quite a delicate one. On Earth, the large amount of glomerular filtrate that is formed per day (180 liters) contains a total of about 26,000 milliequivalents (mEq) of salt. The average intake of sodium per day is only 150 mEq. Therefore, in order to maintain a tight equilibrium of sodium content in the body, the kidneys can be allowed to excrete only about 150 of the 26,000 mEq. Consequently, the principal role of the kidney tubules in sodium excretion is to reabsorb sodium back into the bloodstream, not to excrete it. Furthermore, it must reabsorb just exactly the right amount of sodium, about 99.3% of the total, and must adjust the final amount of sodium that flows into the urine hour by hour or day by day so that it will balance the daily intake of sodium. Thus, the two jobs that the kidney's tubular system must perform for sodium excretion are: (1) to reabsorb nearly all sodium back into the bloodstream, and (2) to adjust the remaining amount that is excreted very carefully so that an absolute balance can occur between sodium intake and sodium excretion. Is this balance maintained in space? Well, we are about to find out.

For Dr. Leach's experiment, sodium intake was measured to be about 140 mEq per day before flight. The results shown in Figure 17 reflect the percent change from that value for the inflight and postflight periods. Both sodium intake levels and the level of sodium excretion in the urine are shown and, as you can see, **sodium intake** increased during flight except on the first and tenth days. **Urinary excretion of sodium** was elevated by an even greater percentage, but until FD12, intake and excretion behaved in an almost parallel fashion. This indicates that intake and excretion remained essentially in balance. But what happened on FD12 and after landing (R+0 through R+15)? A complete explanation has yet to be developed for these "special" periods, but you can bet that the system was working to reestablish an "Earth-normal" condition after the space part of the mission was completed. Remember, too, that the astronauts fluid loaded on the last day inflight. Thus, some of the data beyond that point were influenced by this rapid ingestion of saline.

Table 5. A summary of hormone responses to sodium and potassium levels in the bloodstream.

What is detected in the bloodstream	Endocrine Response	Renal Response	Result
High concentration of Na^+ in the bloodstream	Posterior pituitary gland releases ADH	Kidneys increase reabsorbtion of water in to bloodstream to dilute Na^+.	Less urine is produced
High condentration of K^+ in the bloodstream	Adrenal cortex gland releases aldosterone	Kidneys stop reabsorbing and begin excreting K^+.	More K^+ excreted in the urine
Low concentration of Na^+ in the bloodstream	Adrenal cortex gland released aldosterone	Kidneys increase reabsorption of Na^+ back into bloodstream to preserve plasma Na^+.	Less Na^+ excreted in the urine

We have just been looking at the results of measurements made of levels of sodium intake and of **urinary** excretion of sodium. The urinary sodium data gave an indication of how much sodium was **not reabsorbed** from the kidneys back into the bloodstream. Now let's look at how well the sodium levels in the bloodstream were regulated by looking at the results of Dr. Leach's analysis of plasma sodium levels. From Figure 18, you can see that, although the **plasma sodium levels** were elevated compared to preflight values, their difference was never more than about 2%. The initial increase, shown on FD1, was a measurement made just 3.5 hours after launch; this increase may be due to the fact that the astronauts were eliminating fluid in response to the "flood" into the upper part of the body. The body may have been reabsorbing more sodium into the bloodstream to slow the elimination of fluids. For the remainder of the flight, plasma sodium was increased less than 1% from preflight values.

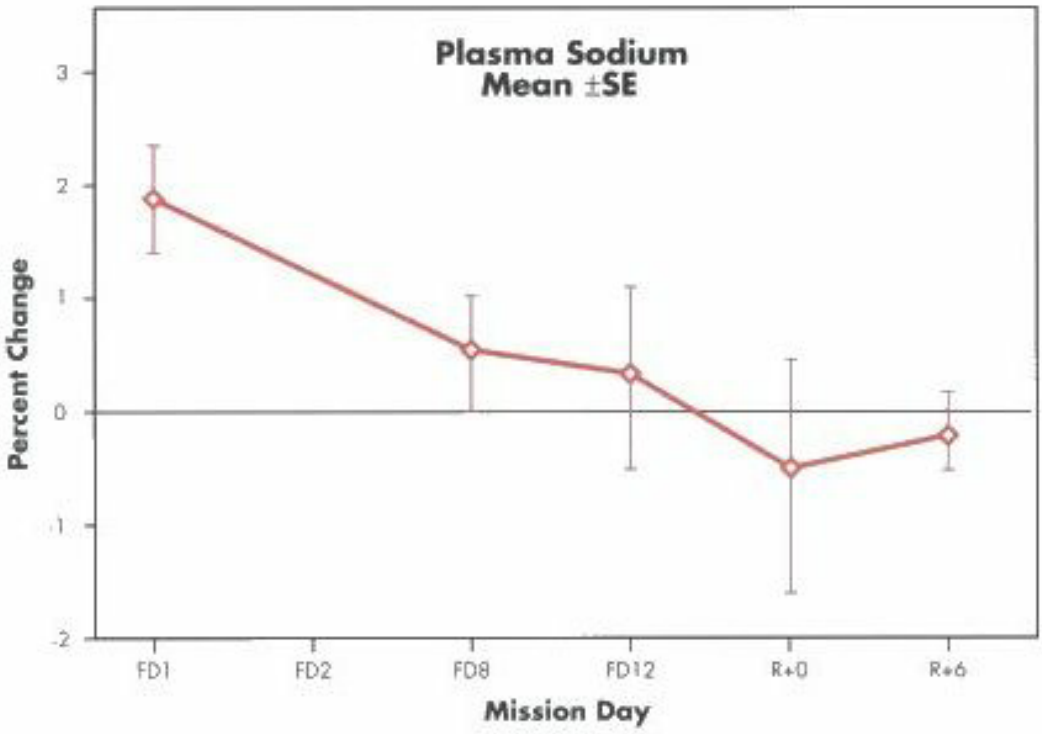


Figure 18. Inflight and postflight plasma sodium changes compared to preflight values.

Now, let's look at the results of Dr. Leach's measurement of ADH and aldosterone. Keep the sodium data in mind as we attempt to connect the inflight and postflight hormone levels with those of the sodium levels. The question is, can we predict how ADH and aldosterone levels will behave? Before we look at Dr. Leach's space flight data for ADH and aldosterone, let's first examine how hormones are measured.

As powerful and important as hormones are to the body, most hormones are present in the blood in incredibly tiny quantities, some in concentrations as low as one-millionth of a milligram (1 nanogram or 10 grams) per milliliter of blood. This is an amazingly small amount! Therefore, except in a few instances, it has been almost impossible to measure these concentrations by any of the usual chemical means. Fortunately, though, an extremely sensitive method, known as a **radioimmunoassay technique**, was developed in the late 1960s that revolutionized the measurement of hormones. Let's take this word apart to get a better idea of what is involved in the method. This is often helpful if you are faced with what seems to be a very complicated term. Don't let it scare you. Rip it apart and then put it back together so that it makes sense!

The first part, **radio-**, usually refers to radioactivity. The second part, **immuno-**, usually refers to something related to the immune system. In this case, it refers to the use of **antibodies** that are highly specific for the hormone of interest. And the third part, **-assay**, is defined in the dictionary as "to analyze for one or more specific components." So, let's see if we can put it all together. The radioimmunoassay technique is an analysis technique (assay) that uses antibodies (immuno) and radioactivity (radio). Actually, we are right! Let's talk about the radioimmunoassay approach to the measurement of hormones. In particular, let's see how ADH levels are measured.

First of all, a **synthetic antibody** (synthetic = artificially produced) is developed in the laboratory that is able to bind together with the ADH. The role of **natural** antibodies that circulate in our bloodstream is to "capture" and bind with viruses, bacteria, and other foreign cells in the body so that the cells cannot cause the damage that they otherwise would. It is the antibody's binding capability that is their strength. In the case of the radioimmunoassay technique, the **synthetic** antibodies are developed and used for their binding capability as part of the technique to measure hormone levels.

A plasma (or urine) sample from the astronaut that contains ADH is mixed with the antibodies. In addition, a known amount of **"standard" ADH** that has been tagged with radioactivity is added to the antibody mixture. The "standard" ADH is something that is prepared in the laboratory to serve as **a reference**, something that has already been measured and that can be used to compare the unknown quantity of natural ADH. The radioactive tag is added to the standard ADH so that it can be distinguished from the natural ADH that is coming from the astronaut's plasma. As the antibodies,

the standard radioactive ADH, and the astronaut's plasma are mixed, one main requirement must be met: **there must be too little antibody to bind completely to both the radioactive hormone and the natural hormone in the fluid to be assayed**. Therefore, the natural hormone in the plasma and the radioactive standard hormone compete for the binding sites on the antibody (Figure 19). The quality of each hormone that binds to the antibodies reflects the concentration of the hormones in the mixture.

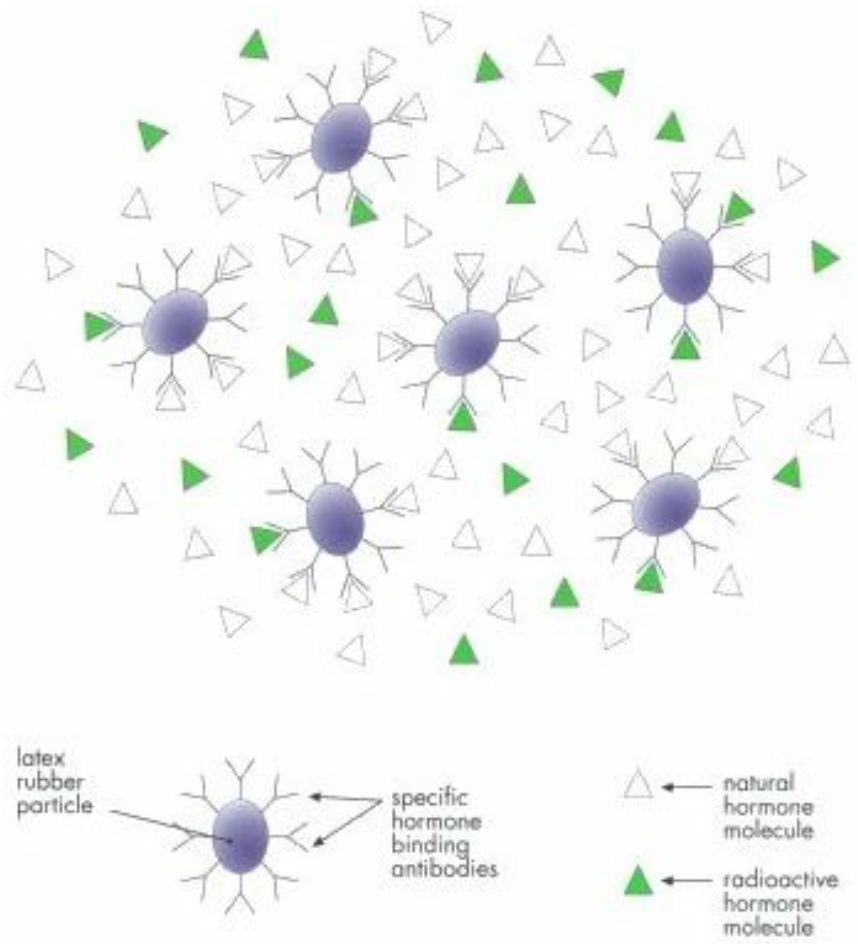


Figure 19. The radioimmunoassay technique to measure hormone levels in the body involves mixing natural hormones (from a blood sample) and radioactively prepared hormones together, and adding that mixture to a solution containing artificially produced antibodies. The two hormones compete for binding sites on the antibodies. The hormones attach to the antibodies in amounts that ore proportional to their concentration.

After binding has reached equilibrium, the antibody-hormone complex is separated from the remainder of the solution, and the quantity of radioactive hormone bound with antibody is measured by radioactive counting techniques. We have already discussed this technique in the previous chapter. If a **large amount of radioactive ADH** has bound with the antibody, then it is clear that there was only a **small amount of natural ADH** to compete with the radioactive hormone, and therefore the concentration of the natural ADH in the assayed fluid was small. Conversely, if only a small amount of radioactive ADH has bound, it is clear that there was a very large amount of natural ADH to compete for the binding sites. It is not enough, though, to say that a "small amount" or a "large amount" of natural ADH is present. The final step in the technique is to **quantify** (to determine the actual quantity of) the ADH level.

Quantifying the data is done by performing the radioimmunoassay technique on a known "standard" amount of untagged ADH at different concentration levels and plotting the data to establish a "standard curve" on a graph. By comparing the radioactive counts recorded from the original assay procedure with the standard curve, one can determine within an error of + 10 to 15% the concentration of ADH in the assayed fluid. Of course, other hormones besides ADH can be measured this way. In fact, as little as **one-trillionth of a gram** of hormone is often assayed in this way! Dr. Leach employed this technique not only for the measurement of ADH, but also for aldosterone. Let's look at the data.

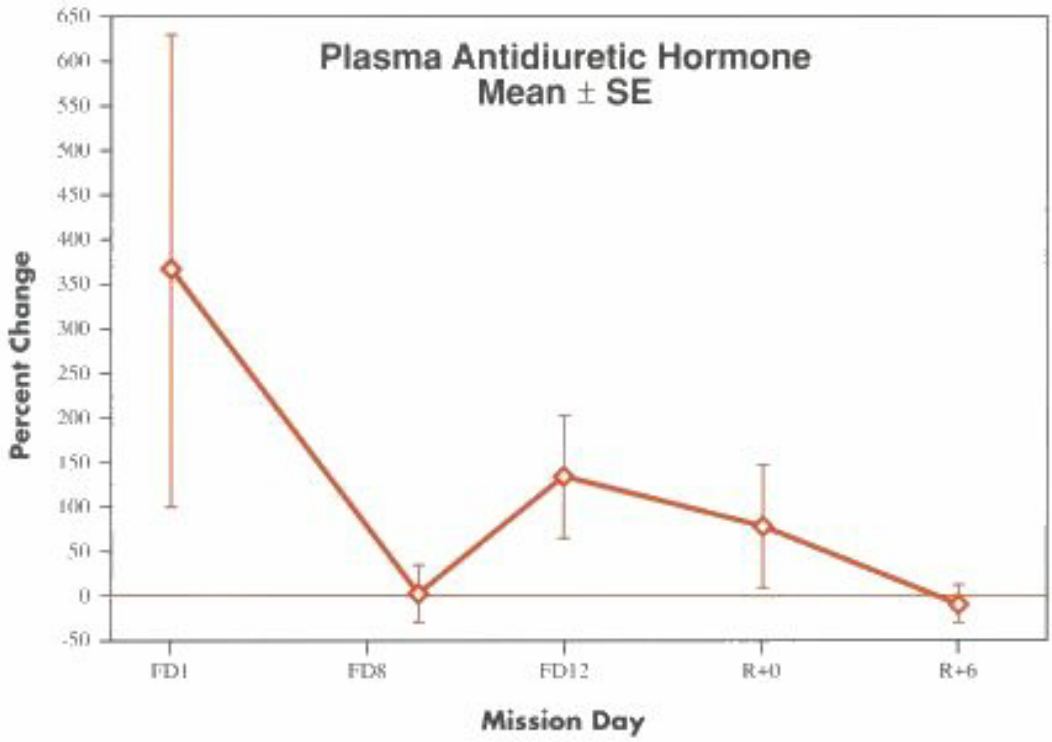


Figure 20. Inflight and postflight plasma ADH changes compared with preflight values.

Hormone assays were performed on samples obtained on the first day of the mission, just 3.5 hours after launch. This is the earliest time for which measurements of hormones have ever been made during space flight. From Figure 20, you can see that the effect of space flight on plasma ADH was highly variable on FD1 but that it averaged about a 360% increase on that day! Remember, ADH is released in the body in response to high levels of sodium. If you look back at Figure 18, the plasma sodium was at its highest inflight level on FD1. Therefore, there may be a connection here that indicates that, at least initially, the release of ADH corresponds to the increased sodium levels in the blood. Let's look next at the amount of ADH that was excreted in the urine.

Figure 21 shows the inflight and postflight urinary ADH levels as a percentage of preflight baseline values. These data show that the level of ADH that was being excreted in the urine was increased throughout most of the flight. And, in spite of the fluid loading that occurred on landing day, urinary ADH was increased. This may have been due, in part, to the fact that the astronauts drank a special solution containing extra salt on that day. The extra water and salt in the system may have contributed to the body's decreased need for and elimination of ADH. Again, so many factors are operating that it is very difficult to interpret this data without having all of the pieces of the puzzle.

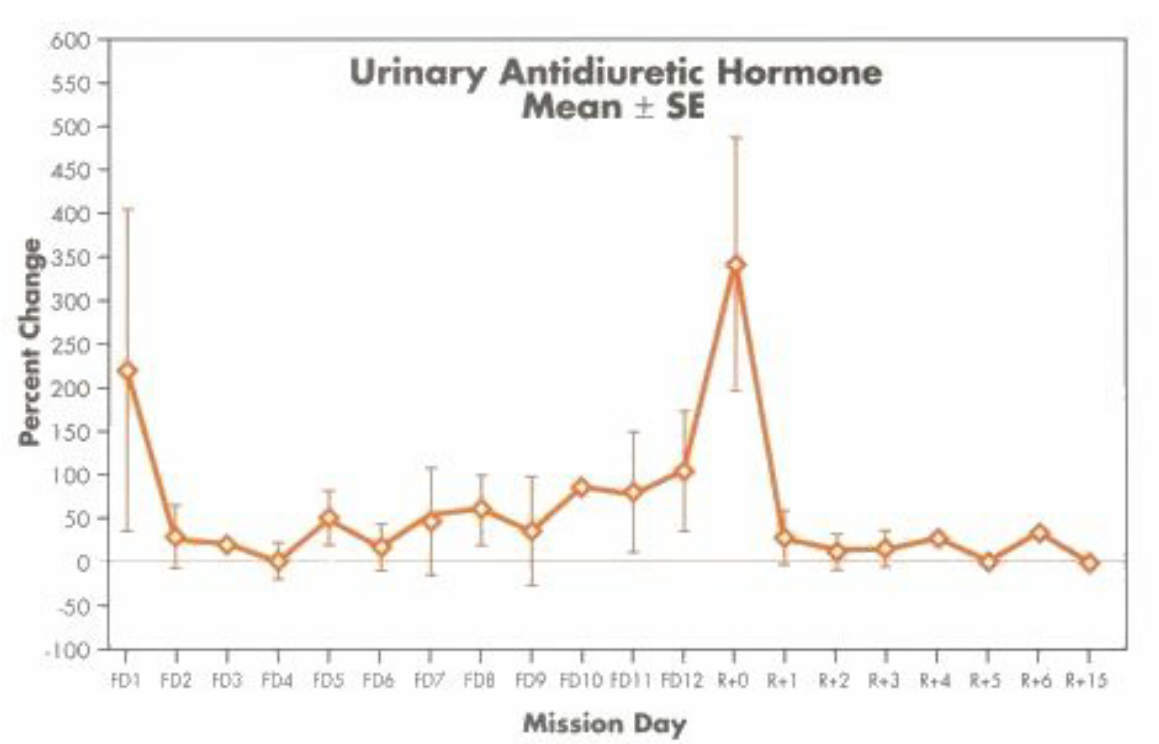


Figure 21. Inflight and post flight ADH changes compared with preflight values.

Finally, Figure 22 represents the inflight and postflight behavior of the aldosterone system. Once again, the data indicates the percent change from preflight baseline values for plasma aldosterone levels. Remember, in contrast to body's release of ADH in response to **high sodium levels in the bloodstream**, aldosterone is released in response to **low sodium levels in the bloodstream**. Therefore, we would predict an opposite response behavior for aldosterone compared to ADH. In fact, this is what we observe if we compare the general features of Figures 21 and 22. A few hours after launch, the plasma aldosterone was reduced by almost 60% but then it began a slow return to preflight values. On FD8, it was reduced less than 20% and on FD12, it was close to preflight levels. Upon landing, however, the aldosterone levels jumped above preflight baseline values. A major factor to remember regarding aldosterone behavior is that it is highly responsive to potassium levels in the bloodstream. To properly interpret this data would require potassium data and we have not reported this here. We do not have the space flight data for the behavior of potassium, so it is impossible to truly understand what is causing the changes in aldosterone levels in space.

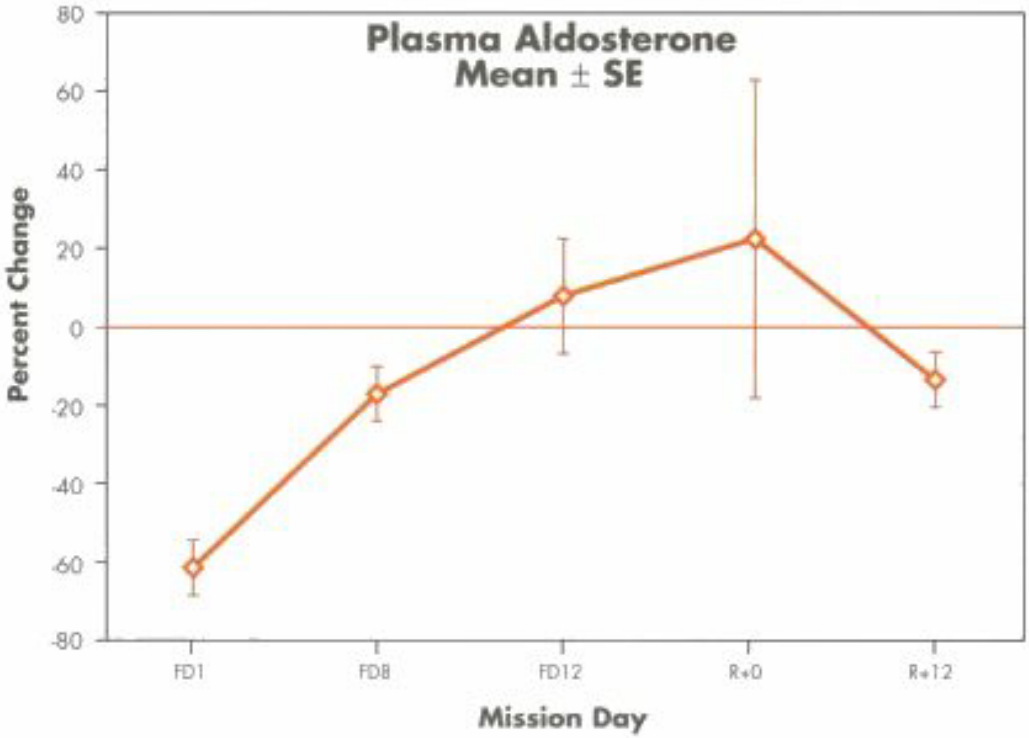


Figure 22 . Inflight and postflight plasma aldosterone changes compared to preflight values.

Conclusion

We have just completed our examination of Dr. Leach's space flight results. You have been presented with a great deal of information but you should realize by now that, what you have seen here is only a very small part of a very big picture.

Now is the time to take what you have learned, break it into pieces, and apply this knowledge in a "Speaking of Space" activity that should be even more fun than usual. You will be asked to break into small groups to answer a few questions about the data sets or graphs from Dr. Leach's experiments that we just reviewed.

Speaking of Space

For this chapter, instead of the usual "Speaking of Space" activity where members of your class have been involved in the development of a scientific presentation, you will be asked to break into seven groups to deliver a different kind of presentation. This activity will be somewhat less formal than what you've been asked to do in previous chapters, but it should be very interesting. Here is the new assignment.

For each of the seven graphs of space flight results presented in this chapter (Figures 15, 16, 17, 1 8, 20, 21, and 22) a small group will evaluate the data and the techniques that were used to collect the data in order to answer the following five questions:

1. What does the data in the graph represent?
2. What technique was used to obtain the data?
3. For the technique that was used to obtain the data, what are the different kinds of individual jobs that people had to do to make sure that all the steps were carried out? Which of these jobs seems to be the most fun? Why?
4. Name two other body systems besides the kidneys and endocrine glands that somehow contributed to the body's response that was measured in your data set.
5. Does the data in the graph support or refute the following hypotheses (which were presented earlier)? Explain.

Hypothesis 1

Adaptation of kidney and electrolyte fluid-regulating functions in microgravity occurs in two stages: an acute, rapid stage (hours to days) and an adaptive, longer-term stage (days to weeks).

Hypothesis 2

The overall renal/endocrine adaptation process in space is primarily a general response to a headward shift of body fluids.

Use visual aids to make your presentation more exciting. Your teacher will give you more details about your approach to each question. Whenever possible, let the audience ask questions and make comments. Most of all, have fun.

Good luck!

Review Questions

Earth Physiology

1. Describe the various fluid compartments in the body and how the fluid in each compartment is defined.

2. Identify the body's chief mechanism for maintaining fluid balance.

3. Briefly describe what electrolytes are and give a few examples.

4. Explain the major function of the kidney, then sketch or describe its basic functional unit.

5. Identify and describe the three regulatory processes that the nephrons perform in filtering the body's blood.

6. A. Name the chemical that is normally entirely reabsorbed back into the blood from the tubules.
   B. Identify the disease state that is associated with the tubules inability to reabsorb the chemical.
   C. Explain the diagnostic procedure used to identify this disease.

7. What is the most important factor that determines urine volume?

8. What are the two primary regulators of body water?

Space Physiology

1. Name the body changes in flight that were studied by Dr. Carolyn Leach in her space flight experiments. Select one and briefly describe the changes.

2.
    A. A. What measurement is made with the use of the "plasma clearance method"?
    B. Describe this measurement procedure.
    C. How is the kidney involved?

3. Anatomically, at what place in the kidney does the cleansing of blood begin?

4. Describe the mechanisms that operate for the kidneys to keep the sodium level in the body at equilibrium.

5. Name a tracer that is used in kidney function tests and identify at least 3 of the criteria that it must meet to be used as a tracer.

6. From the data that are presented in this chapter, determine which daily measurements of sodium were taken during flight, whether the results were elevated or decreased during the first twelve days of flight, and what this information might indicate?

CRITICAL THINKING

1. List the basic chemical components of plasma and identify a major function of each.
2.
    A. What daily measurements of sodium were taken during flight?
    B. Were the results elevated or decreased during the first twelve days of flight, and what might this data indicate as to what is occurring to the body's fluid regulation system ?
3.
    A. How is total blood flow through the kidney calculated?
    B. Calculate the plasma flow rate for a person with a hematocrit of 2%.

    Remember the hematocrit is the % RBC mass, so to find the plasma volume, you must subtract the hematocrit % from 100%. This will give you the plasma volume.

References

Certain parts of the text were excerpted and adapted from the following publications and other references: For the section describing Earth Physiology:

1. Fox SI (1987) **Human Physiology**, 2nd ed. William C Brown Publishers, Dubuque, lowa.
2. Guyton AC (1986). **Textbook of Medical Physiology**, 7th ed. WB Sounders Company, Philadelphia, PA.
3. Nourse AE (1964). **The Body**. Life Science Laboratory, Time Incorporated, New York.
4. Oram RF (1989) Biology: Living Systems. Merrill Publishing Company, Columbus, OH.

For the section describing the space flight results and as influence for numerous figures and tables:

1. Leach-Huntoon CS (1994) **Fluid-electrolyte Regulation During Space Flight**. Report to the SLS-2 Investigator Working Group meeting, Washington, DC.
2. Frequent personal communications with Daniel Inners, Krug Life Sciences, Houston, TX.

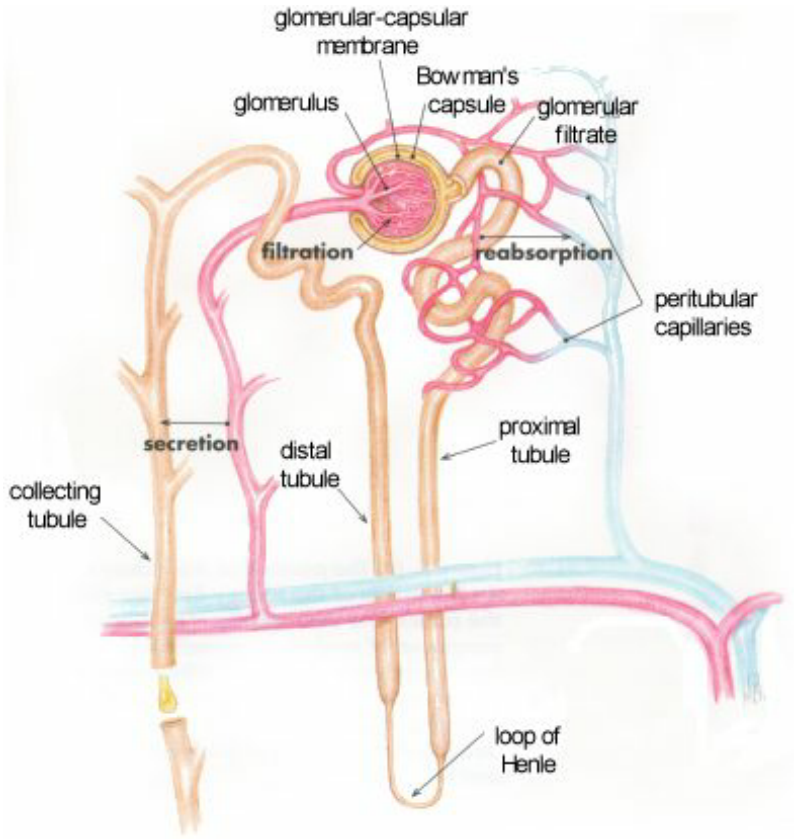


Figure 3. Urine formation takes place in the nephron. Filtration of the blood from the glomerulus occurs in Bowman's capsule. Reabsorption and secretion occur along the renal tubules where important chemicals and water are returned to and waste products are removed from the bloodstream. The resulting urine then travels through the collecting tubule and out of the body (via the ureters and the blatter).