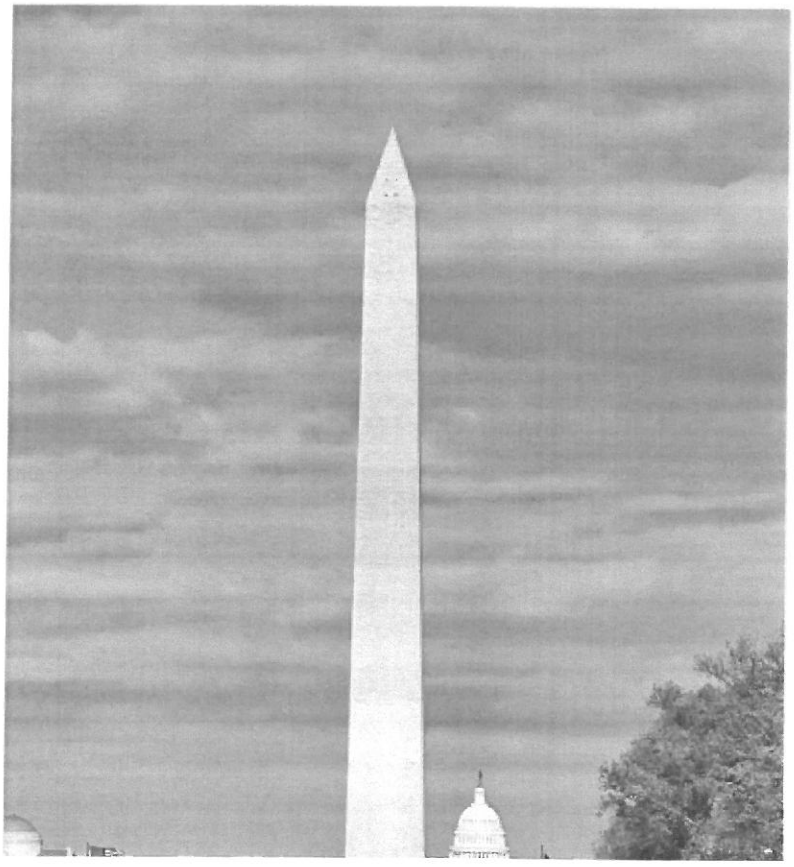
10.1 The Integrated Human

Imagine you are visiting Washington, DC, the capital of the United States of America. You've ridden a subway into a huge underground station and have come up onto the Mall — a vast grassy area, America's "front yard" surrounded by many monuments and museums. The most prominent structure on the Mall is the towering Washington Monument (See Figure 10.1). As you walk toward it, it just gets larger and larger! Rather than taking the elevator to the top, you decide to climb its 896 steps. By the 150th step, a tiny hint of boredom begins to set in. You begin to wonder—just a fleeting thought—if this whole climb is just a matter of your muscles driving mindlessly forward. This thought is born of a secret inner inclination of yours that life should be simple, but the biology text you've been reading argues that it is complex. Hmm. Is it really? How complex could this "just climbing stairs" be? Let's dissect that question a bit.

Figure 10.1

The Washington Monument.

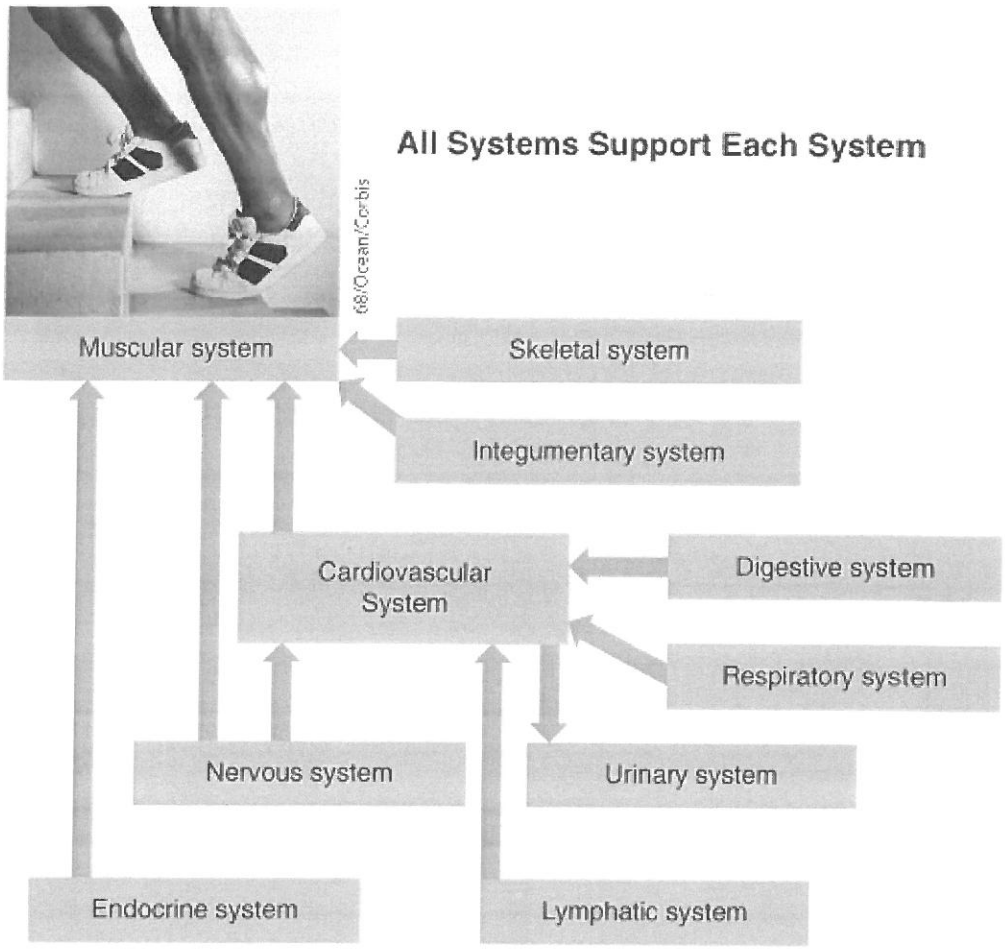


Rudy Sulgan/Terra/Corbis

Actually, several systems in your body ramp up to get you from the bottom to the top of the Monument (see Figure 10.2). Yes, your **muscular system** (a collection of organs (muscles) that facilitate movement of the body and movement within the body.) does the work, but muscles need something on which to pull. That something is provided by the **skeletal system** (a collection of organs (bones) that gives support and form to the body and that assists the muscular system during movement.) . As your muscles start using up the oxygen and nutrients they had when you started, your heart rate (within your **cardiovascular system** (a collection of organs that facilitate the movement of cells and soluble materials to and from all parts of the body.)) and breathing rate (in your **respiratory system** (a collection of organs that enables critical gaseous reactants and products to be added to and removed from blood.)) both increase. You start to sweat (from your **integumentary system** (a collection of organs (largely skin) that insulates the organism while protecting it from desiccation and invasion by foreign pathogens.)) to remove the heat your muscles are generating. In addition, part of your **nervous system** (a collection of organs composed of neurons that coordinates the activities of the organism while transmitting signals from one location to another.) (the sympathetic part) responds to the physical stress you are putting on your body by calling for hormones from the **endocrine system** (a collection of organs (glands) that secrete hormones into the bloodstream; the hormones in turn control many aspects of the body's form and function.) . The wastes being produced by the muscles' metabolism will be removed by the **urinary system** (a collection of organs that filters the blood, creating, collecting, and storing the resulting urine for excretion.) . On the way up, you grab the rail for support and then rub your eye to remove the sweat forming on your face. Now, your immune response, produced by the **lymphatic system** (a collection of organs that facilitates the surveillance of tissue fluids and their movement back to the bloodstream.) , will be stimulated to prevent you from getting sick due to viruses that were on the rail. Once you get to the top, you pull out a snack and activate your **digestive system** (a collection of organs that facilitates the intake and mechanical and enzymatic degradation of foods, followed by absorption of nutrients and elimination of wastes.) . All the systems in your body have worked together to get you to this point. Haven't we seen this sort of cooperation somewhere before?

Figure 10.2

Life is Internally Integrated. Every system in the body serves and is served by every other system. The level of integration is staggering.



"Life is Internally Integrated"

68/Ocean/Corbis

In Chapter 5 we peered into a cell and saw that its organelles worked together, sometimes through each other to perform tasks that supported the common welfare—the good of the entire cell. Then our study of development in Chapter 9 showed us that cells divide, differentiate, and begin to communicate and cooperate with each other to generate an entire multicellular organism. Here, however, the principle that the parts of a life-form support and function with and through each other is visible on a grander, macroscopic scale—the level of the entire organism. These cooperative activities are so dramatically displayed in your own body that we've decided to devote this entire chapter to a principle of life that embodies this concept: **Life Is Internally Integrated** (one of 12 principles of life on which this book is based.) . Entire multivolume works are devoted to an exploration of this principle. Our suspicion is that the integration between body systems is far more complex than research has yet revealed.

Let's return to our vertical hike inside the Washington Monument and look at each of these body systems in detail. Since the muscles appear to be doing all the work, let's start with them.

In Other Words

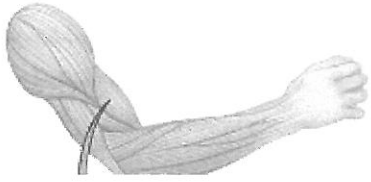
1. Climbing stairs requires the obvious activity of the muscular system, but it involves the cooperation of a variety of other systems as well.
2. The skeletal system provides leverage for the muscular system to get you up the stairs.
3. The cardiovascular system services your muscles with nutrients and oxygen, while removing carbon dioxide and other molecular wastes from them.
4. The respiratory system supplies oxygen and removes carbon dioxide from the body as a whole; the digestive system supplies the nutrients to be brought to the muscle tissues.
5. The kidneys remove cellular waste to the urinary system for excretion.
6. The immune response protects you from potential pathogens encountered in your environment.
7. Such cooperation between systems of organs in the body mirrors the cooperativity of organelles within a living cell.

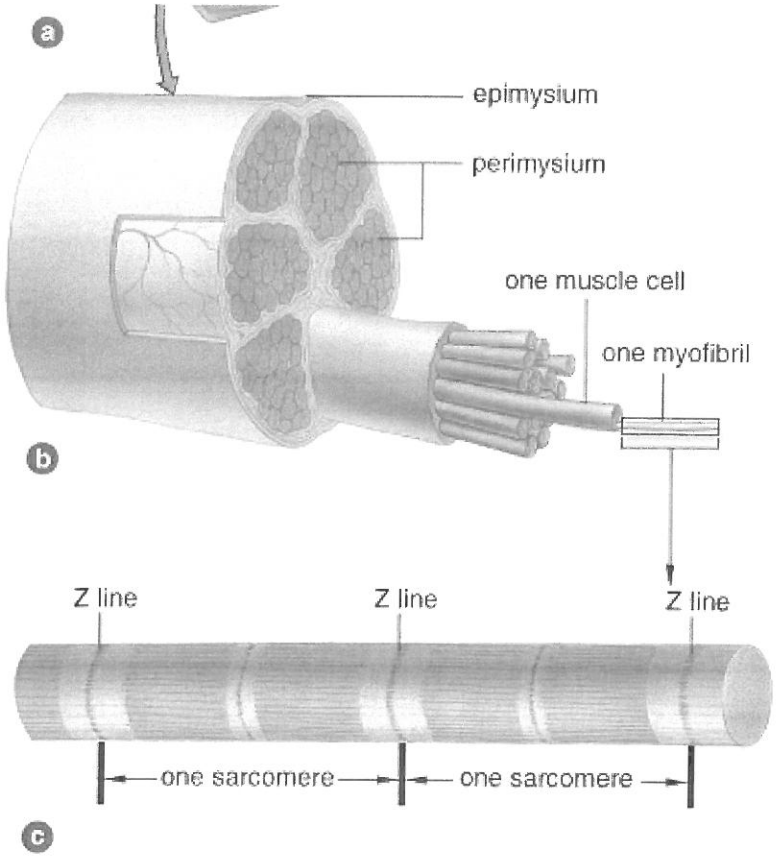
Muscle Structural Organization

The whole muscle is surrounded by a sheath of **connective tissue** (generally fibrous collections of cells throughout the body that add support and structure to the organs they are within; collagen fibers comprise 25% of the body's connective tissues.) called the **epimysium** (a sheet or layer of connective tissue that envelopes an entire muscle.) (see Figure 10.3a). A muscle is made up of bundles of muscle fibers called **fascicles** (a bundle of skeletal muscle fibers surrounded by a perimysium.) . Each fascicle is covered by **perimysium** (a layer of fibrous connective tissue that envelopes a fascicle or bundle of skeletal muscle fibers.) (more connective tissue). Each fascicle contains many **muscle fibers (individual muscle cells)** (elongated, cylindrical, multinucleated cells packed with contractile fibrils of actin and myosin proteins.) , each of which is covered by still more connective tissue called **endomysium** (a sheath of connective tissue that surrounds and carries capillaries and nerves to individual muscle fibers/cells.) . Within a fiber are contractile units called **sarcomeres** (the structural and functional unit within a muscle cell; intertwined protein fibrils of actin and myosin that pull against each other in the contraction process.) . When activated by the nervous system, sarcomeres shorten. They are microscopic in size, so each one shortens only a fraction of a micrometer; however, if hundreds of these are lined up end to end in a cell and if they all shorten, the entire muscle cell can shorten quite a bit! Bundle many of these cells into fascicles, bundle the fascicles into a muscle, and shorten many of them at once, and a lot of tension and force can be developed—enough to propel your whole body up the Washington Monument steps!

Figure 10.3

Levels of Organization in a Muscle. **(a)** Arrangement of muscles (organs) in the human forelimb. **(b)** a cross-section through a single muscle showing a bundle of muscle cells—a fasicle—drawn out. Within this tissue level of organization, single, elongated muscle cells are shown. **(c)** Within a muscle cell are elongated myofibrils (supra-molecular structures) that represent a linear array of sarcomere units (see text). Each sarcomere is bound to the next one by a complex of strong structural proteins called a "Z line". Contraction occurs within the structure of the sarcomere.





In Other Words

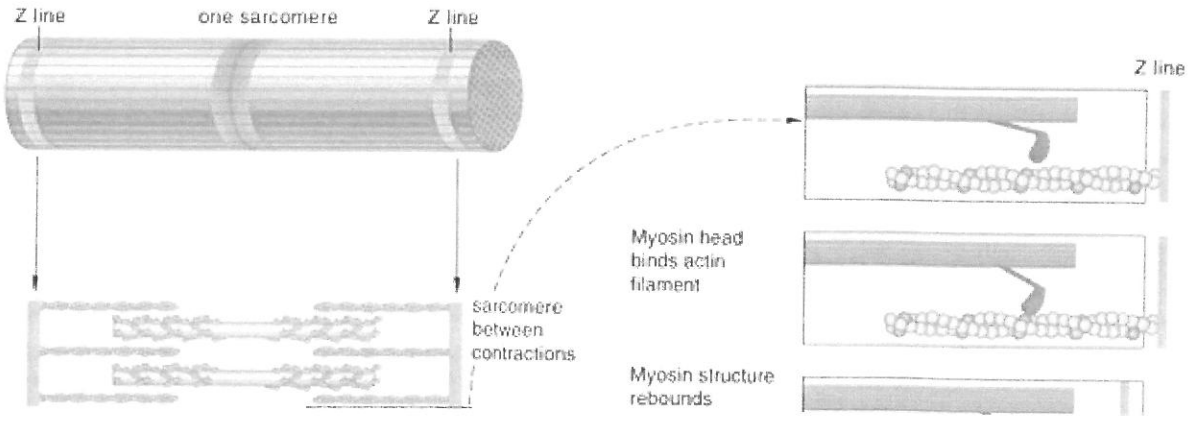
1. A typical skeletal muscle is composed of many bundles or fascicles, each of which is in turn composed of many individual cells called *muscle fibers*.

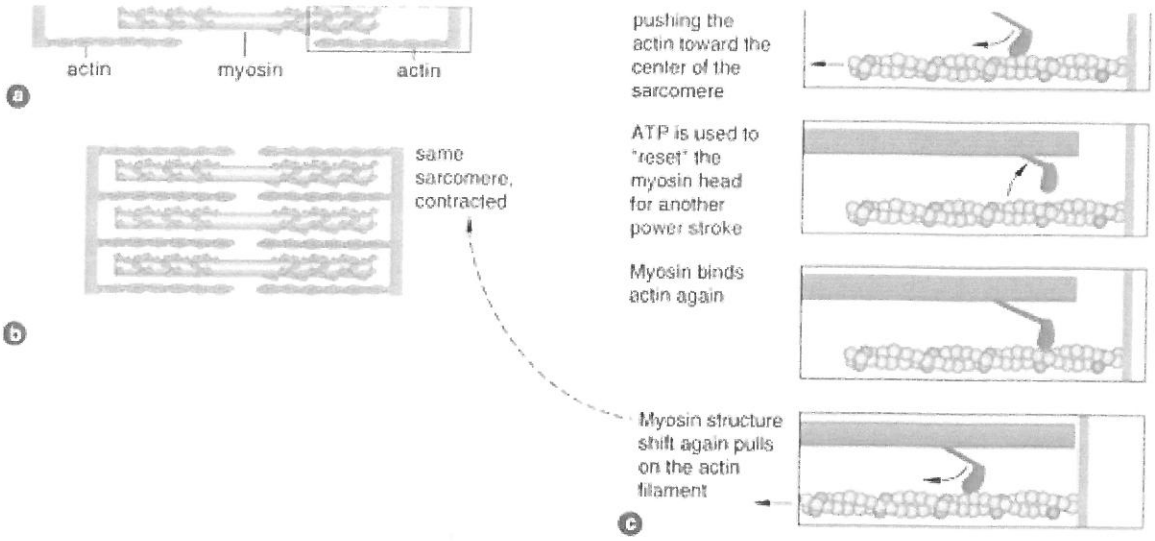
Muscle Contraction

At the most basic level, muscle shortening is produced by many **myofilaments** (a protein strand within a muscle cell; composed of myosin, actin, or elastic proteins.) sliding past each other. To understand how sliding filaments lead to contraction, we first need to understand the structure of the contractile unit, or sarcomere (see Figure 10.4). Each sarcomere has two types of filaments: thick **myosin** (a class of proteins that uses ATP energy and a flexible head domain for movement along a protein strand of actin.) filaments that are anchored together across the center of the sarcomere and thinner **actin** (a monomeric protein that makes up the structure of filaments—the scaffolding against which myosin proteins carry out linear movement by successive binding events between myosin head domains and the filament's own scaffolding.) filaments anchored to each other and to the sarcomere ends (see Figure 10.2d). During muscle contraction, protein heads on the myosin filaments attach to the actin filaments and pull on them (see Figure 10.4). This slides the actin filaments toward the middle of the myosin filaments, shortening the entire sarcomere. As mentioned earlier, one sarcomere shortens just a fraction of a micrometer, but many sarcomeres lined up end to end and all shortening at the same time can lead to an amount of muscular shortening that is many millimeters in length.

Figure 10.4

Internal Structure of the Sarcomere. **(a)** Actin and myosin fibers are interspersed within the sarcomere. Extensions of myosin protein called "heads" have binding sites on actin polymers to either side. **(b)** Successive binding and releasing of myosin heads causes them to crawl along the actin fibers resulting in a contracted state. **(c)** Each myosin head goes through succesive power strokes as it pulls on the actin fiber it binds to.





In Other Words

1. Each muscle fiber contains a long series of functional contractile units called *sarcomeres*; these in turn contain interwoven filaments of actin and myosin proteins.
2. The binding of protein extensions of myosin filaments to actin filaments and the subsequent pulling on these filaments is what enables sarcomeres and the muscles they comprise to contract.

Control of Contraction: Ions, Gradients, and Membrane Potentials

What tells the muscle when to contract and how strongly to do so? Here is a primary example of how two different systems in the body are integrated with each other: The nervous system controls the activities of the muscular system. The muscular system cooperates with still other body systems to nutritionally support the nervous system. The nervous system's control of the muscular system is mediated by **ion gradients** (a spatial variation from one point to another in the concentration of ions in solution, often over a short distance across a membrane.) and **membrane potentials** (the difference of voltage (or potential energy) between the inside and the outside of a cell.) . All cells in your body have a **resting membrane potential** (the relatively stable electrical charge difference across a cell membrane in an excitable cell not presently transmitting a signal; contrasts with action potential.) . This is the difference in the electrical charge from one side of the cell membrane to the other. This difference is called a *potential* because it represents a source of energy that can *potentially* do work. To see how this potential is formed, we first need to understand gradients. Examine the bowls in Figure 10.5. In the first bowl, there are more red dots in the left-hand portion of the bowl than in the right because that's where the dye (red dots) is being added. In other words, a gradient has been set up. Ordinary thermal energy allows the dots to move. In order for the red dots to reach equilibrium, some of them would have to move from the left to the right, so there would be an equal distribution of dots all through the bowl. (If thermal energy throws the dots around in random directions, a net dot movement from left to right will occur naturally.) Ions that are in different concentrations on either side of a cell's outer membrane are like the red dots. They tend to move toward an equilibrium distribution on either side of a membrane. There are actually two gradients of ions that cause them to move toward equilibrium: a concentration gradient and an electrical gradient. Like the red dots, ions will move back and forth so as to end up in equal numbers (concentrations) on either side of the plasma membrane. If there is a larger number of ions on the outside of the cell, there will be a net movement down the concentration gradient from the outside to the inside until their concentrations become equal on both sides. This occurs passively; no cellular energy input is required. To move them against the concentration gradient would require energy because they naturally tend to go to equilibrium.

Figure 10.5

Diffusion. The red dye molecules exhibit a gradient in the middle bowl: a higher concentration near where they were introduced, a lower concentration further away. Ordinary thermal energy will distribute them evenly within the bowl.

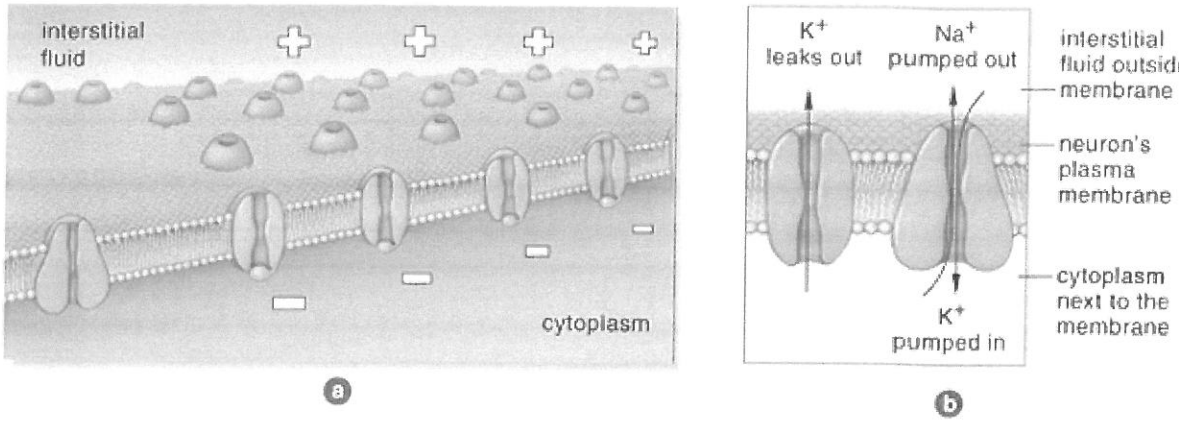
The other type of gradient is an **electrical gradient** (a spatial variation from one point to another in the concentration of charged substances in solution, often over a short distance across a membrane.) . Recall that ions are atoms that have lost or gained an electron(s). Because of this, they have a charge (either positive or negative). If there are more positive ions on the outside of the cell, then some of them will be *repelled* toward the inside of the membrane while any negative charges will be *attracted* toward the outside of the membrane until the ionic charge distribution is equal on both sides.

If more positive ions accumulate on the outside of the cell membrane and more negative ones are on the inside of the cell membrane, the inside of the membrane gains a net negative charge compared to the outside (see Figure 10.6a). This is the case in our cells. Each cell membrane contains special proteins called *sodium-potassium ATPase pumps,* or **Na-K-ATPase pumps** (a transmembrane protein complex using ATP energy to move sodium and potassium ions against their concentration gradients; the result is a membrane potential from the inside of the cell to the outside.) (see Figure 10.6b). These pumps use energy from ATP to push ions "uphill" against their concentration gradients. For each cycle of the pump, three sodium ions (Na^+) are pumped outside the cell and two potassium ions (K^+) into the cell, resulting in more positive ions outside the cell than in it.

Figure 10.6

Cell Membrane at Resting Potential. **(a)** Due to differential pumping of 3 sodium ions out for every 2 potassium ions in, there's a slight charge differential across the cell membrane. **(b)** The sodium-potassium pump on the right requires ATP to drive

sodium out and potassium in. If the gate (channel) on the left opens, it can relieve the gradient created by the pump by allowing any positive ions in.



In the cell membrane, along with these pumps, there are also **ion channels** (a protein complex within a cell membrane that allows ions to flow down their electrical/ chemical gradient across the membrane, influencing the membrane potential.) —gates—that allow ions to pass from one side of the membrane to the other. They allow potassium ions to leave the cell again, returning down their chemical/electrical gradient. The overall result is a slightly higher concentration of positive (Na^+) ions outside. The muscle cell's measured (resting) membrane potential is normally $-95\,\mathrm{mV}$, with the inside somewhat more negative than the outside.

In Other Words

1. The nervous system uses changes in electrical potential differences across cell membranes to communicate the need for contraction to muscle cells.
2. Electrical charge differences across a membrane (electrical potential) are chemical and electrical gradients that are established by pumping ions from where they are in lower concentration to where they are already in higher concentration.
3. Pumping of ions is accomplished by the Na-K-ATPase protein complex found in the membranes of neurons and muscle cells.
4. The membrane potential is achieved by pumping Na^+ ions out of the cell, pumping K^+ ions into the cell, and allowing a fraction of these K^+ ions to leak out of the cell through K^+ -specific ion channels.

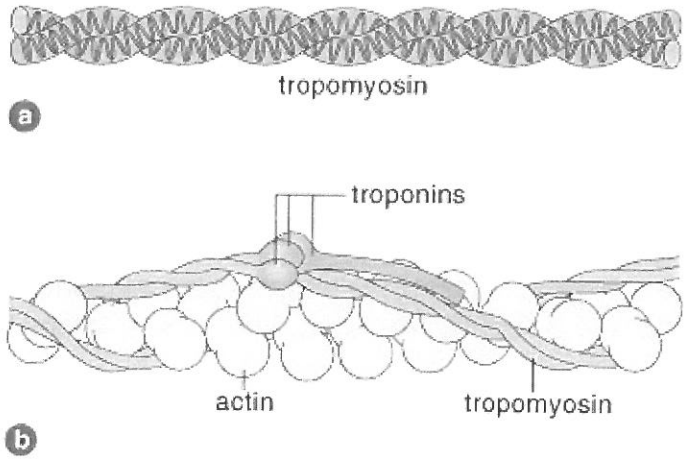
5. The result is a continuous membrane potential that is slightly more negative to the inside of the membrane; momentary change in this potential will initiate the signal for the muscle cell to contract.

Control of Contraction: The Nervous System

When they are at rest, the myosin fibers in the sarcomeres of the muscle cell cannot bind to the actin fibers. The binding sites on the actin fibers are covered with a protein called **tropomyosin** (a long protein-containing fiber that binds to actin filaments within the sarcomere; helps control actin-myosin binding and therefore muscle contraction.) that must shift its position in order for actin and myosin fibers to interact, thereby causing sarcomere contraction (see Figure 10.7). How does this shift take place?

Figure 10.7

Regulation of Sarcomere Contraction. Strands of the tropomyosin protein **(a)** are wound around the actin strands **(b)** in a sarcomere such that their troponin proteins conceal the sites where myosin heads bind. Increased calcium levels shift the troponin proteins laterally exposing the head binding sites allowing the sarcomere to contract.

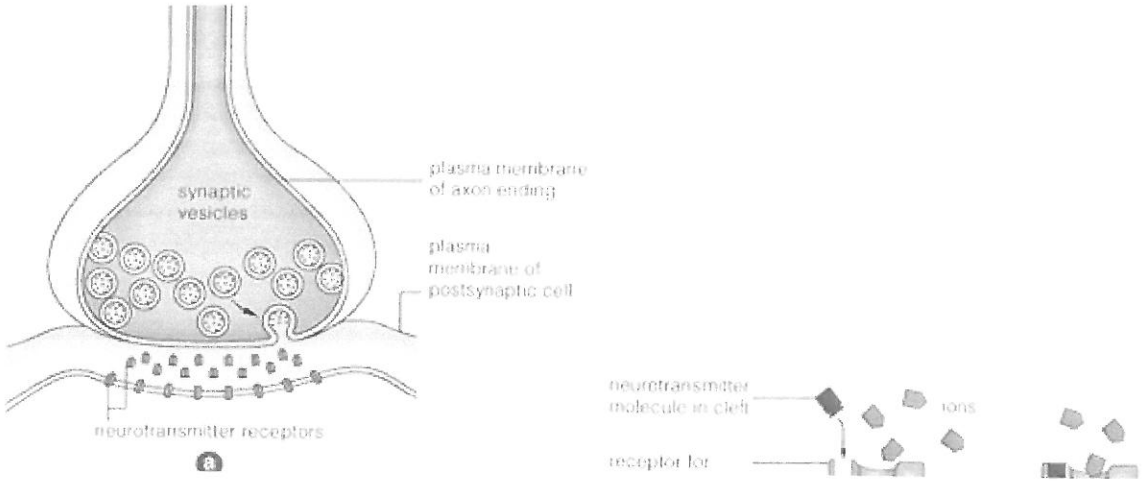


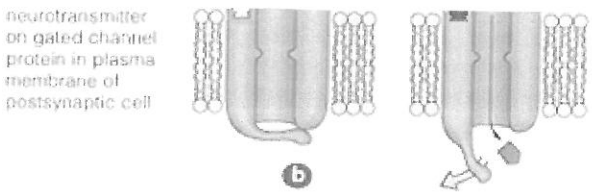
When the central nervous system (CNS) determines that a muscle needs to move, it sends a signal down a nerve cell to the place the cellmeets the muscle fiber, a narrow space or gap about 0.02 micrometers across called a **synapse** (a narrow gap or space between two excitable cells; a signal reaching the end of the first cell must become chemical in nature to cross the space and initiate a signal in the other cell.) (see Figure 10.8). The nerve cell signal arriving at this synapse is actually an electrical signal. When it reaches the synapse, it causes calcium channels in the membrane to open and calcium (which is at a higher level outside the cell than inside) rushes down its concentration gradient into the synaptic terminal of the nerve cell. That rush of calcium causes vesicles to open up into the synaptic

gap. The content of these vesicles is a chemical **neurotransmitter** (a chemical substance that by rapid diffusion carries a signal across a synaptic cleft to the membrane of an excitable cell, where it may initiate a new action potential.) substance called **acetylcholine** (a neurotransmitter chemical that is secreted into a synapse by the transmitting cell and that initiates a new signal in the receiving cell.) . The acetylcholine quickly crosses the narrow space in the synapse to the muscle cell surface. Located on the muscle cell membrane are receptor proteins that have a special binding site for acetylcholine. These receptors are actually ion channels! When acetylcholine binds to the receptors, they open, allowing sodium ions $\left(\mathrm{Na}^{+}\right)$ to rush into the muscle cell. This ionic movement changes the membrane potential of the muscle cell, which is its way of initiating a new electrical signal. This new signal spreads along the muscle cell and is called an **action potential** (a momentary steep electrical charge difference across a membrane; the physical basis for a nerve impulse.) . The signal is nothing more than a temporary, positive shift in the membrane potential across the membrane as positive charges enter the cell. This spreading action potential causes the calcium storage tanks (vesicles) in the muscle cell to release their calcium ions $\left(\mathrm{Ca}^{2+}\right)$. Along the tropomyosin fibers are proteins called **troponins** (a protein along the tropomyosin fiber that specifically locks onto actin at the site at which myosin heads would otherwise bind; involved in control of muscle contraction.) . When calcium ions bind to troponins s, they shift the tropomyosin fibers, exposing the myosin-binding sites on the actin (see Figure 10.7). With tropomyosin removed from the binding sites, the myosin heads can bind to the actin and pull on it. Muscle contraction is in this way enabled.

Figure 10.8

The Synapse. The nervous impulse travels down a nerve cell's axon till it reaches an end bulb **(a)** which lies very close to the membrane of the muscle cell. The impulse causes the release of neurotransmitter substances (like acetylcholine) from vessicles in the end bulb. **(b)** Binding of acetylcholine opens ion channels starting an action potential (impulse) in the membrane of the muscle cell.





Of course, for the pulling action to occur, the myosin must have ATP to do the mechanical work of pulling. ATP production will require the activity of still other body systems, as we will see. Therefore both calcium and ATP are required for controlled contraction of the sarcomere.

In Other Words

1. The calcium mediates a shift in the physical relationship between actin and tropomyosin proteins such that myosin-actin pulling can occur.
2. Electrical signals—action potentials—initiating skeletal muscle contraction originate in the nervous system and become chemical in nature when they cross the synaptic space between a neuron (in the nervous system) and a muscle cell (in the muscular system).
3. A neurotransmitting chemical such as acetylcholine diffuses across the synaptic space to start the action potential in the membrane of the muscle cell.
4. When the action potential causes calcium release within the muscle cell, the calcium binds to proteins called *troponins* along the tropomyosin filaments. This calcium binding is what causes the tropomyosin configuration to alter, allowing myosin-actin pulling.
5. Both calcium release and ATP energy release are required for a muscle to contract.

Contraction of Cardiac and Smooth Muscle

We've just seen how skeletal muscle works. **Skeletal muscle** (striated muscle generally attached to bones by tendons; under voluntary control of the peripheral nervous system.) is considered voluntary muscle as we can choose whether or not to contract it. We also have two other types of muscle in our bodies: **cardiac muscle** (striated muscle that comprises the walls of the heart; generally involuntary in its control.) and **smooth muscle** (nonstriated muscle under involuntary control; forms much of the structure of the digestive and vascular systems.) , both of which carry out involuntary contractions. The nervous and endocrine systems control these muscles without our conscious thought or voluntary desire. Cardiac muscle will be discussed in Section 10.3. Smooth muscle forms part of the digestive, urinary, respiratory, reproductive, and circulatory systems (see Table 10.1). Smooth muscle is similar to skeletal muscle in that contraction in both is generated by nervous stimulation involving an action potential, calcium signaling, and ATP energy. However, the calcium in smooth muscle binds to a different component—**calmodulin** (a protein whose action is controlled by calcium ion influx; controls contraction of smooth muscle.) instead of troponin—to uncover myosin-actin binding sites on their respective filaments. Smooth muscle serves many critical organismal functions (see Table 10.1); it helps keep our blood pressure regulated and our digestive processes effective. Each system of our body, though complex, is integrated with all of the others demonstrating a frighteningly high level of competence in design.

Table 10.1

Role of Smooth Muscle in Body Systems

System	Functions
circulatory	(in walls of arteries) maintenance of blood pressure
lymphatic	maintenance of lymph vessel structure; movement of lymph fluid

System	Functions
excretory	contraction of the urinary bladder during voiding of urine
reproductive	(female) contraction of uterus; (male) propulsion of sperm
digestive	peristaltic waves moving food through the intestines
respiratory	function not yet understood
integumentary	pilo-erection (added insulation at low temperatures)
sensory	alteration in size of the iris of the eye

In Other Words

1. On the basis of control and structural differences, muscles are classified into three categories: skeletal muscle, smooth muscle, and cardiac muscle.
2. In smooth muscle, a distinct controlling component, calmodulin, determines the level of myosin-actin pulling instead of the tropomyosin used in skeletal muscle.

10.3 The Cardiovascular System

As you continue climbing the stairs of the Washington Monument, your muscles are using a lot of oxygen and other nutrients while producing metabolic wastes and giving off carbon dioxide. This would be a problem—you would quickly run out of needed substances and have a toxic buildup of wastes—if you did not have a way of replacing nutrients and removing wastes. Thankfully, you do! A brilliant Designer gave you a cardiovascular system! This system consists of blood that carries the nutrients and wastes, vessels for the blood to flow through, and a heart to pump the blood through the vessels! Let's examine each of these components of the cardiovascular system in more detail.

In Other Words

1. The cardiovascular system supplies its own tissues and all other organ systems of the body with nutrients, oxygen, and hormonal signals. It removes waste products from these systems as well.

Chapter 10: The Internally Integrated Human Animal: 10.3 The Cardiovascular System
Book Title: Life by Design
Printed By: Shawanda Brown (srbrown9@liberty.edu)
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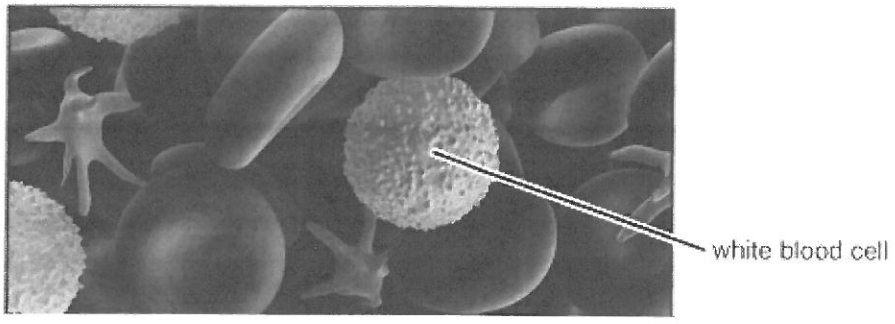
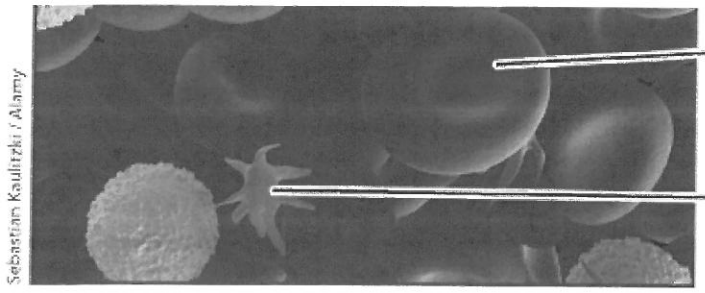
Blood: A Medium of Exchange

Did you know that blood is a tissue? It is a fluid type of connective tissue that functions to carry nutrients, oxygen, wastes, and hormones throughout the body while helping your **immune system** (a collection of organs that surveys blood and tissue fluids, detects and labels foreign particles or cells, and works to degrade and destroy those particles or cells.) and forming clots to prevent excessive bleeding. Blood is made up of **plasma** (the fluid component of blood that includes those factors that cause clotting of blood; it contains nutrients, hormones, and molecule wastes and is a vehicle for movement of the cellular components of blood.) and formed elements that are cells or parts of cells (see Figure 10.9). In the plasma (which is mostly water) are proteins, hormones, nutrients and wastes, oxygen and carbon dioxide. Each of the formed elements in the blood has a specific function: red blood cells **(erythrocytes)** (red blood cell whose hemoglobin-laden cytoplasm is a reservoir for oxygen being carried from the lungs to the body's tissues.) carry oxygen through the blood to supply tissues with it. White blood cells **(leukocytes)** (white blood cells that, as part of the body's immune system, help detect and destroy foreign cells and particles such as viruses.) help us fight infection (see Section 10.4). **Platelets** (fragment of a megakaryocyte cell that floats in the circulatory system helping to clot blood at sites of trauma and secreting growth hormone.) are actually small fragments of cells that help form clots to prevent you from bleeding to death when blood vessels are traumatically opened.

Figure 10.9

The Composition of Blood. At the top is an electron micrograph of the cellular parts of blood. The sample in the centrifuge tube results from putting whole blood in a tube, separating it from attachment to the tube wall, and simply waiting. Clotting factors pull the formed elements together into the bottom of the tube leaving clear plasma behind. Since the clotting factors are employed in the bottom of the tube, the plasma above (without these factors) is called serum.





Sebastian Kaulitzki / Alamy

Components	Relative Amounts
Plasma Portion (*50%–60% of total volume*):	
1. Water	91%–92% of plasma volume
2. Plasma proteins (albumin, globulins, fibrinogen, etc.)	7%–8%
3. Ions, sugars, lipids, amino acids, hormones, vitamins, dissolved gases	1%–2%
Cellular Portion (*40%–50% of total volume*):	
1. Red blood cells	4,800,000–5,400,000 per microliter
2. White blood cells:	
Neutrophils	3,000–6,750
Lymphocytes	1,000–2,700
Monocytes (macrophages)	150–720
Eosinophils	100–360
Basophils	25–90
3. Platelets	250,000–300,000

Sebastian Kaulitzki / Alamy

In Other Words

1. Blood, composed of plasma fluid, cells, and cellular fragments, is a tissue that carries nutrients, oxygen, wastes, and hormones throughout the body.
2. Erythrocytes are cells designed to carry oxygen to the tissues while leukocytes are cells designed to detect and respond to infectious agents.

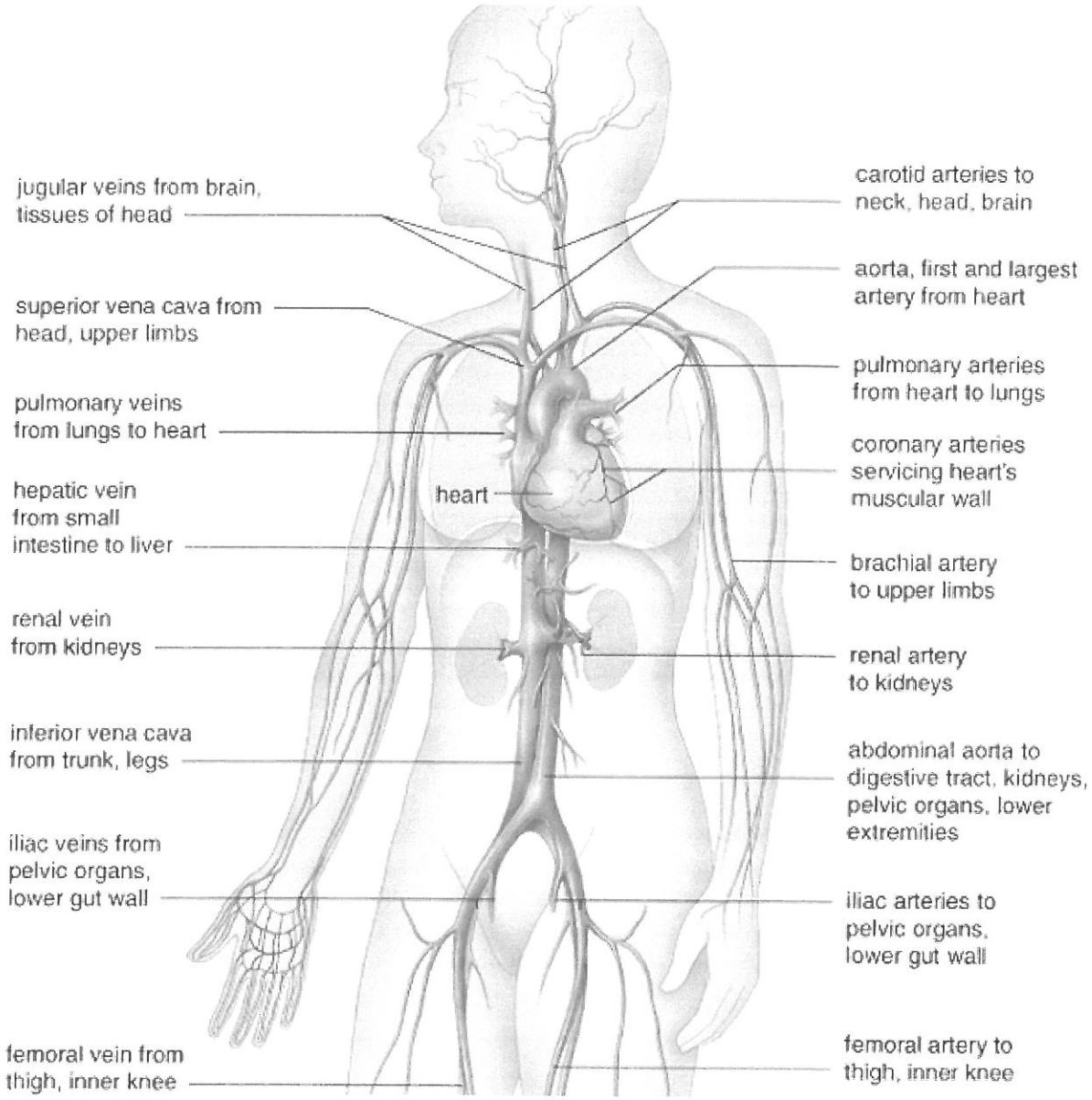
Blood Vessels: The Body's Avenue of Life

Blood is distributed throughout the body by a system of tubes or blood vessels—**veins** (a blood vessel that conducts blood away from the lung or tissues and toward the heart.) , **arteries** (a blood vessel that conducts blood toward the lung or tissues and away from the heart.) , and **capillaries** (small blood vessels extending between arteries and veins; blood flow is slowed within these vessels and nutrient, waste, and gas exchange occurs between them and the surrounding tissues.) . Arteries carry blood away from the heart and to the body's tissues. They are muscular tubes that can change their diameter based on the body's needs at a given time. While you are climbing the stairs of the Monument, the arteries supplying your skeletal muscles will **dilate** (to enlarge or expand.) (or open), allowing more blood—more oxygen and nutrients—to reach the muscles while carrying away more wastes and more carbon dioxide. At the same time, blood vessels supplying the gut/digestive system will **constrict** (to narrow or shrink.) (or narrow), as your body has less need to supply them with blood while you are climbing the stairs. Once you reach the top of the Monument and grab a snack while enjoying the view, however, the blood flow will change. Your muscles, now at rest, will not need as much blood, so the arteries supplying them will constrict while the arteries supplying the digestive system will dilate; this allows the digestive organs to process the snack you are eating.

How do arteries deliver these nutrients to your tissues? They branch into progressively smaller arteries that eventually lead to capillaries (see Figures 9.2, 10.10). These very small, very thin vessels are where the exchange between blood and tissues takes place. Oxygen and nutrients go through the walls of the blood vessels into the tissues, whereas carbon dioxide and waste leave the tissues and enter the blood to be carried away. After leaving the capillaries, blood—now having higher carbon dioxide levels and lower oxygen levels—runs through progressively larger veins until the largest veins head back to the heart, where blood is then pumped to the lungs to get rid of the excess carbon dioxide and pick up more oxygen (the pulmonary circuit). The metabolic wastes will be filtered out of the blood by the kidneys and leave the body as part of the urine.

Figure 10.10

The Human Cardiovascular System. Capillaries are too small and numerous to be represented here. They would connect the extremities of the red and blue vessels together. Notice where main arteries lead to in the body and how they are named.



In Other Words

1. Generally speaking, arteries carry blood away from the heart toward the lungs and body systems; veins carry blood back from these extremities.
2. Capillaries are tiny vessels within the tissues themselves that connect arteries to veins; they are sites where gas and nutrient exchange take place.
3. The diameter of arteries is flexible—blood flow can be regulated such that at any given time, tissues most needing it can receive a larger share of blood.
4. Blood also flows through the kidneys, where potentially toxic waste products are removed and targeted for excretion from the body in urine.

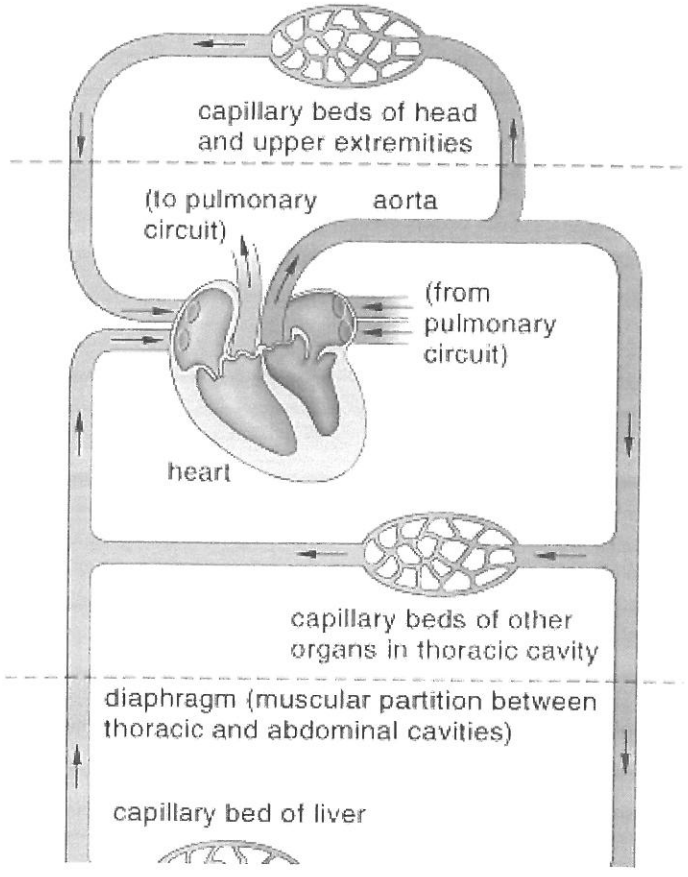
Chapter 10: The Internally Integrated Human Animal Blood Vessels: The Body's Avenue of Life
Book Title: Life by Design
Printed By: Shawanda Brown (srbrown9@liberty.edu)

The Heart: The Dynamo of Human Life

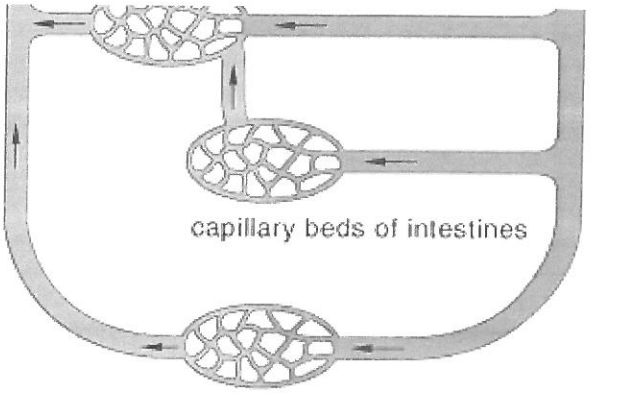
The heart is the engine that keeps your body heading toward the top of the Monument. It is actually two pumps in one! There are two circulatory systems in your body: the **pulmonary circulation** (those blood vessels that carry deoxygenated blood from the heart to the lungs and reoxygenated blood from the lungs to the heart.) and the **systemic circulation** (those blood vessels that carry blood from the heart to the tissues (other than the lungs) and from those tissues back to the heart.) (see Figure 10.11). Blood from the body enters the right side of the heart and is then pumped out of the right side into the lungs, where gas exchange occurs. The blood then returns to the left side of heart via the veins of the pulmonary circuit, and from there it's pumped to the rest of the body over the systemic circuit.

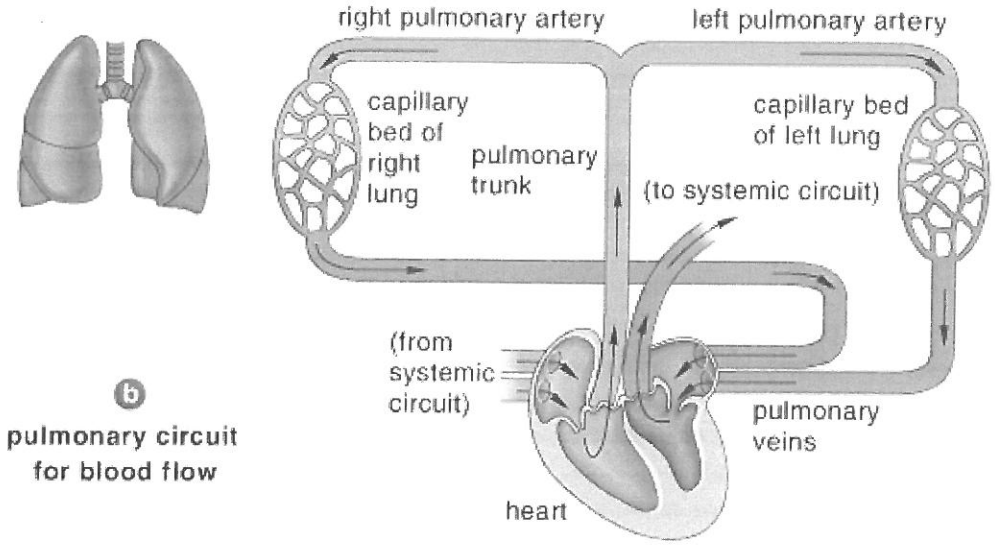
Figure 10.11

The Human Circulatory System is Two Systems! **(a)** The systemic circuit. **(b)** The pulmonary circuit.



a
systemic circuit for blood flow



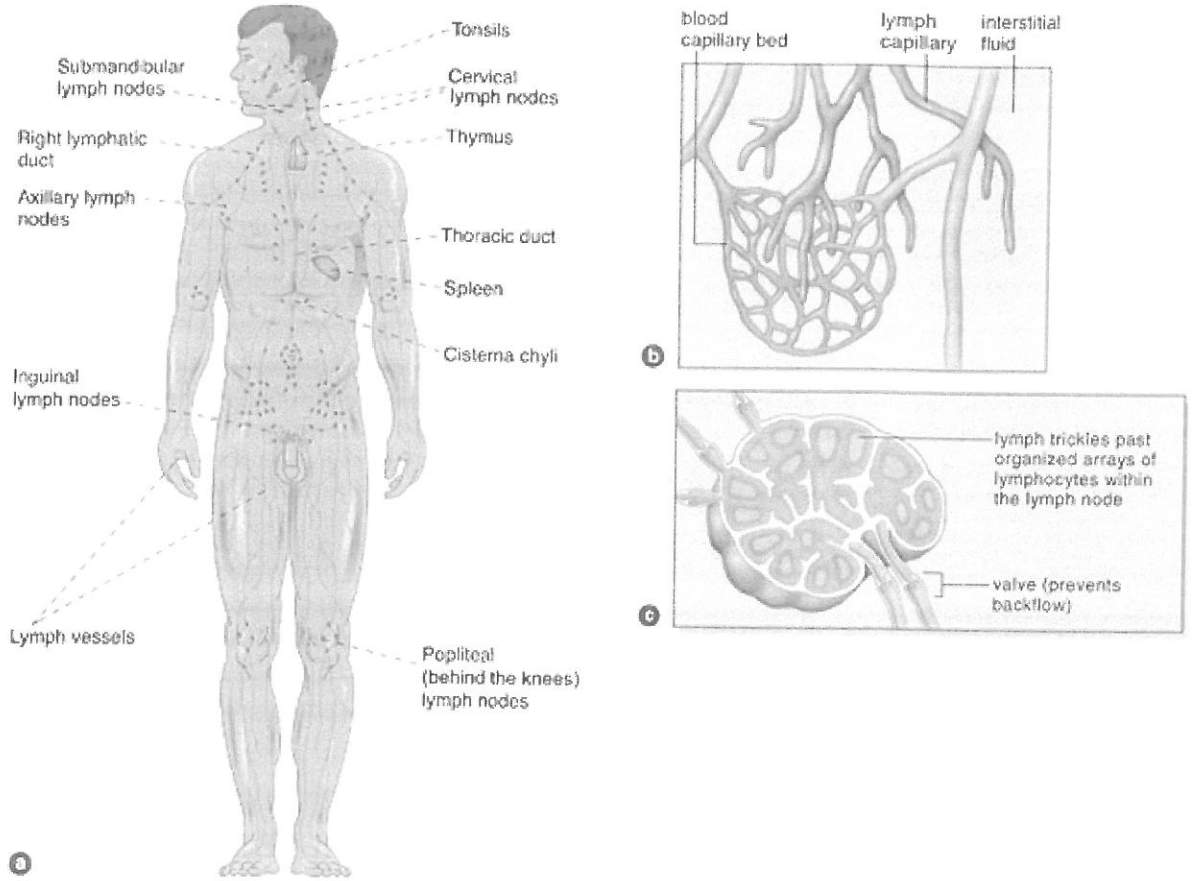


b **pulmonary circuit for blood flow**

What happens within the systemic circuit as the blood arrives at the tissues? There is a steady movement of plasma into the tissues. The residual fluid in the tissues (**interstitial fluid)** (that aqueous solution of biomolecules that exists between cells within tissues; it becomes lymph when transported in lymph capillaries back toward the heart.) is collected by tiny ducts of the lymphatic system, where it is called lymph, and returned to the major veins carrying blood to the heart (see Figure 10.12a,b). There it reenters the circulatory system. Hormones control this balance so as to maintain a fairly constant blood volume. On its way back to the heart, lymph is filtered by lima bean–sized **lymph nodes** (organ of the lymphatic system in which antigen-lymphocyte encounters occur; sites of tissue fluid filtration and surveillance.) distributed throughout the body (see Figure 10.12c). In these nodes, an immune response can be triggered if a foreign pathogen is detected (see Section 10.4).

Figure 10.12

The Lymphatic System. **(a)** Lymph vessels drain circulating interstitial fluid from all parts of the body back through ducts to the systemic circulatory system near the heart. Many more lymph nodes exist than those represented here. **(b)** Lymph capillaries are close to circulatory system capillaries so that fluid can efficiently percolate through the tissues and then into the lymphatic system. **(c)** A cross section through a lymph node that lies along the network of lymph ducts.



Most of the mass of the heart itself is made of cardiac muscle. It is similar to skeletal muscle except that cardiac muscle cells are connected by **gap junctions** (small connections between animal cells that allow direct contact between the cytoplasms of those cells; in cardiac muscle, sites of rapid propagation of impulses calling for muscle contraction.) , which unite the cells electrically, allowing the whole heart to contract together. This means an action potential in the heart will cause the heart as a whole to contract, squeezing blood out of both sides of the heart and into both the pulmonary and systemic circuits.

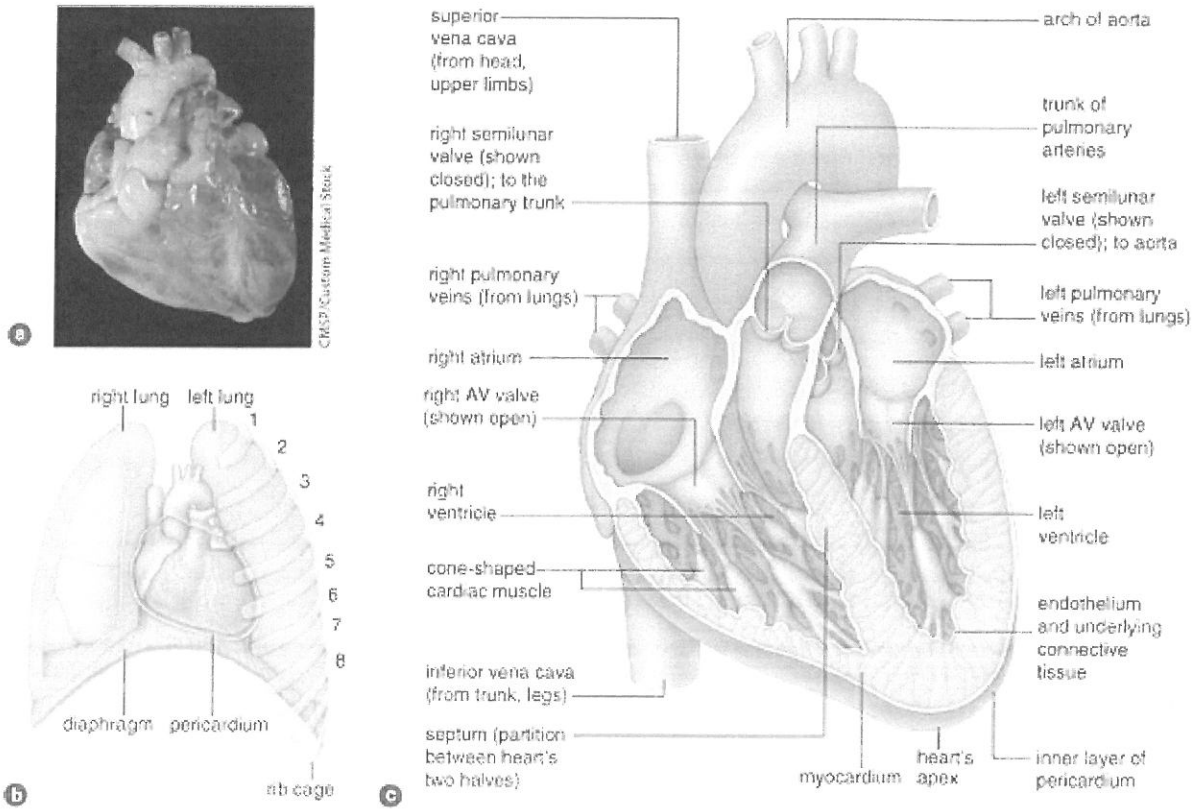
Blood enters the heart through the two **atria** (one of two chambers in the mammalian heart that receives blood from either the lungs or the tissues.) (see Figure 10.13). Blood from the systemic circuit empties into the right atrium and then goes to the right **ventricle** (one of two highly muscular chambers in the mammalian heart that pumps blood to either the lungs or the tissues.) from which it is pumped into the pulmonary circuit to the lungs. Blood from the

lungs enters the left atrium of the heart, goes to the left ventricle, and then is pumped to the systemic circuit to supply oxygen and nutrients to the rest of the body.

Between the atria and ventricles and between the ventricles and the outside of the heart are **valves** (folds of tissue within the major arteries that allow blood to pass during ventricular contraction but that then seat against each other to prevent backflow of blood during ventricular relaxation.) (see Figure 10.13). The closing of these valves is what produces the sounds of the heartbeat. These valves prevent the backflow of blood so that it has to go in one direction through the circulatory system. Imagine trying to design a heart valve using only mutations in a system with no valves. The blood must flow freely in the direction away from the heart and not at all in the opposite direction. The tissue composition and structure of valves is brilliantly crafted to achieve this purpose.

Figure 10.13

The Human Heart. **(a)** Your heart is about the size of your fist. **(b)** It's position within the thoracic cavity. **(c)** A section through the major heart chambers. The major vessels flowing into and out of the heart are here named.



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When the powerful left ventricle conracts, pressure in the arteries increases temporarily. Blood pressure is literally the pressure the blood puts on the blood vessel walls. You can feel that sudden increase in pressure—or **pulse** (the sudden dilation of arterial vessels

caused by ventricular contraction within the heart.) —in some superficial arteries (such as on the wrist or neck). When the heart contracts, the pulse pressure is at its highest value; we call that the **systolic pressure** (the outward pressure of blood on arterial walls under the full force of a ventricular contraction.) —the higher number of your blood pressure reading. When the heart relaxes, pressure drops a bit and that is the **diastolic pressure** (the outward pressure of blood on arterial walls during the period of ventricular relaxation between contractions.) —the lower number of your blood pressure reading.

Your heart rate is controlled by the **parasympathetic** and **sympathetic** nervous systems (see Section 10.8). Climbing stairs is a form of physical stress on the body. As you begin, the sympathetic nervous system, which is activated under stressful conditions, will increase your heart rate to ensure adequate oxygen delivery to your skeletal muscles. So here are six body systems immediately involved in obvious cooperation to convey you up the Monument stairs. The muscular system moves you there. The nervous system informs its activity. The cardiovascular system conveys the resources for climbing. The digestive and respiratory systems supply the resources, and the excretory and respiratory systems remove the waste products of the activity. No one system of the body can function without the others!

In Other Words

1. The heart is a dynamic organ that pushes blood toward the tissues in general and the lungs in particular.
2. It is a double pump; the larger chamber, the left ventricle, pumps blood to the tissues of the body for nutrient distribution.
3. In a separate system—the pulmonary circulation—the right ventricle pumps deoxygenated blood returning from the tissues to the lungs for dumping of carbon dioxide and resupply of oxygen.
4. Blood plasma that has crossed through capillaries and out into the tissues is called *interstitial fluid*.
5. Interstitial fluid gradually finds its way back to the blood from the tissues through lymph ducts, which converge and empty into the major veins returning to the heart, where it is reunited with the blood plasma.
6. On its journey through the lymphatic system, the lymph passes through lymph nodes, where it is assayed for the presence of any foreign objects that may be pathogenic.

7. Cardiac muscle has a unique arrangement of gap junction connections so that millions of individual cardiac cells can contract in synchrony, which gives rise to the heartbeat.

8. The human heart has four chambers. Two atria receive blood returning from major veins. Two ventricles pump blood out to major arteries.

9. Blood flow through the entire cardiovascular system is unidirectional because valves between the atria and the ventricles and between the ventricles and major arteries prevent its backflow.

10. When the ventricles contract, the pressure of the blood in the arterial system is at its highest value, termed systolic pressure; between these contractions, it reaches its lowest arterial pressure, termed diastolic pressure.

11. The rate at which your heart beats is modulated by two opposing branches of the nervous system: the sympathetic and parasympathetic systems. The parasympathetic branch controls the heart under normal circumstances, while the sympathetic branch increases the heart rate in times of stress.

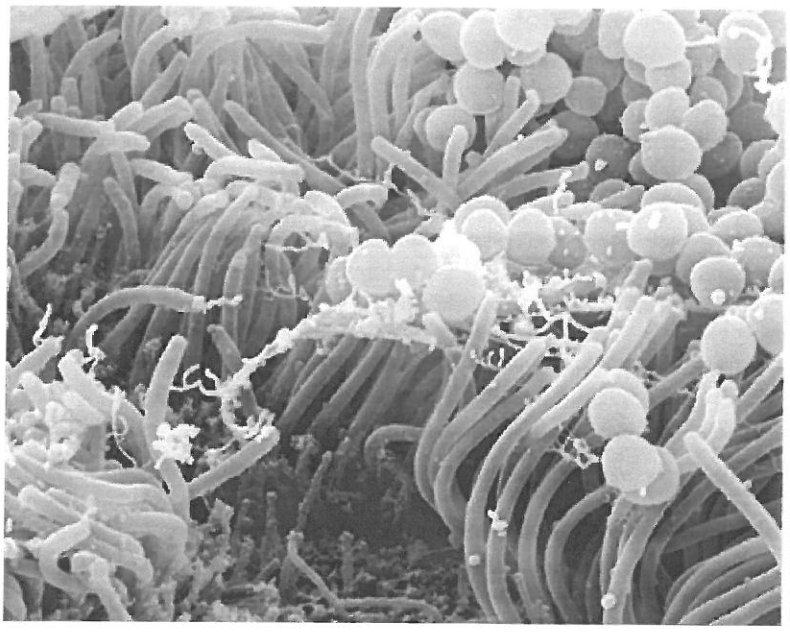
12. The various systems of the body are meticulously and substantially interconnected with each other so as to deliver the life-giving flow of blood to those various systems.

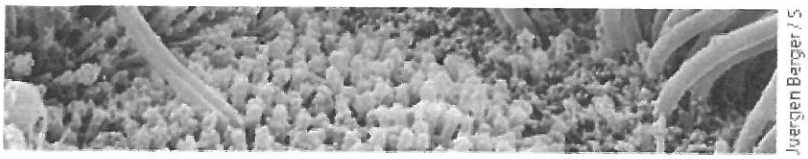
10.4 Basic Concepts of Immunity

While you climb the stairs of the Monument, you need some external support, so you grab the handrail. What you do not think about is that hundreds of other people h ave touched that rail in the last hour, perhaps thousands since this morning! Those peoples' hands had germs on them—the ones they normally carry around, plus some **pathogens** (any microorganism, viral, bacterial, or eukaryotic, that by its presence or growth in host tissues causes or contributes to a disease state.) too! Many handrail users have respiratory infections. One or two harbor HIV viruses and don't know it yet. Thankfully, most human pathogens die quickly with exposure to air. For example, HIV in the low concentrations found on a handrail would be inactivated within a few minutes' time. However, some microbes, like the bacterium *Staphylococcus aureus,* are quite resistant to dry environments and can live for a long time within the pitted surface of the rail inside the Monument (see Figure 10.14). Thankfully, your body has several lines of defense to protect you from these germs (see Table 10.2).

Figure 10.14

Staphylococcus aureus. This opportunistic pathogen is shown here entrained in mucous secretions of nasal epithelial cells. It's on its way to the stomach where acids will recycle it's biomolecules for absorption and use to make "our" biomolecules instead.





Juergen Berger / Science Source

Table 10.2

Three Lines of Defense in the Human Immune System

BARRIERS AT BODY SURFACES (*nonspecific* targets)

Intact skin; mucous membranes at other body surfaces

Infection-fighting chemicals in tears, saliva, etc.

Normally harmless bacterial inhabitants of skin and other body surfaces that can outcompete pathogenic visitors

Flushing effect of tears, saliva, urination, and diarrhea

NONSPECIFIC RESPONSES (*nonspecific* targets)

Inflammation:

1. Fast-acting white blood cells (neutrophils, eosinophils, and basophils)
2. Macrophages (also take part in immune responses)

Organs with pathogen-killing functions (such as lymph nodes)

Some cytotoxic cells (e.g., NK cells) with a range of targets

IMMUNE RESPONSES (*specific* targets only)

T cells and B cells; macrophages interact with them Communication signals and chemical weapons (e.g., antibodies)

In Other Words

1. Our body's surfaces are constantly being exposed to a variety of foreign substances and pathogens.

Chapter 10: The Internally Integrated Human Animal: 10.4 Basic Concepts of Immunity
Book Title: Life by Design
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Your First Line of Defense

The first line of defense is our integumentary system that provides a surface barrier. Your skin and mucous membranes form this barrier and prevent most things from the external environment from getting inside our bodies. Many pathogenic bacteria and viruses attach themselves to the surface of an epidermal skin cell that is already dead and will be sloughed off the next time you clap your hands or wash them. You just heard a climber, two flights up inside the Monument cough violently, spilling untold numbers of her respiratory microbes into the air. But as you inhale these microbes, they get entrained in the mucous secretions in your bronchial passages and slowly the **cilia** (organelles; projections from a cell's surface that oscillate in a whip-like fashion to generate movement of medium past a cell or movement of the cell within the medium.) on the cells lining your **bronchi** (elongated, tube-like organs in the respiratory system that conduct air from the tracheal passage down into the lungs.) carry those microbes and their mucus vehicle to your pharynx, where you swallow them (see Figure 10.14). The next stop—your acid-laden stomach—is death to the vast majority of such microbes.

In Other Words

1. The most widespread and pervasive first line of defense against pathogens is the epidermal surface of our integumentary system.
2. We constantly slough off dead skin cells to which potential pathogens have witlessly attached themselves.
3. Pathogens that enter our respiratory, digestive, or genital tracts become entrained in mucous secretions; these secretions are removed by the movement of cilia on our cell surfaces.

Chapter 10: The Internally Integrated Human Animal Your First Line of Defense
Book Title: Life by Design
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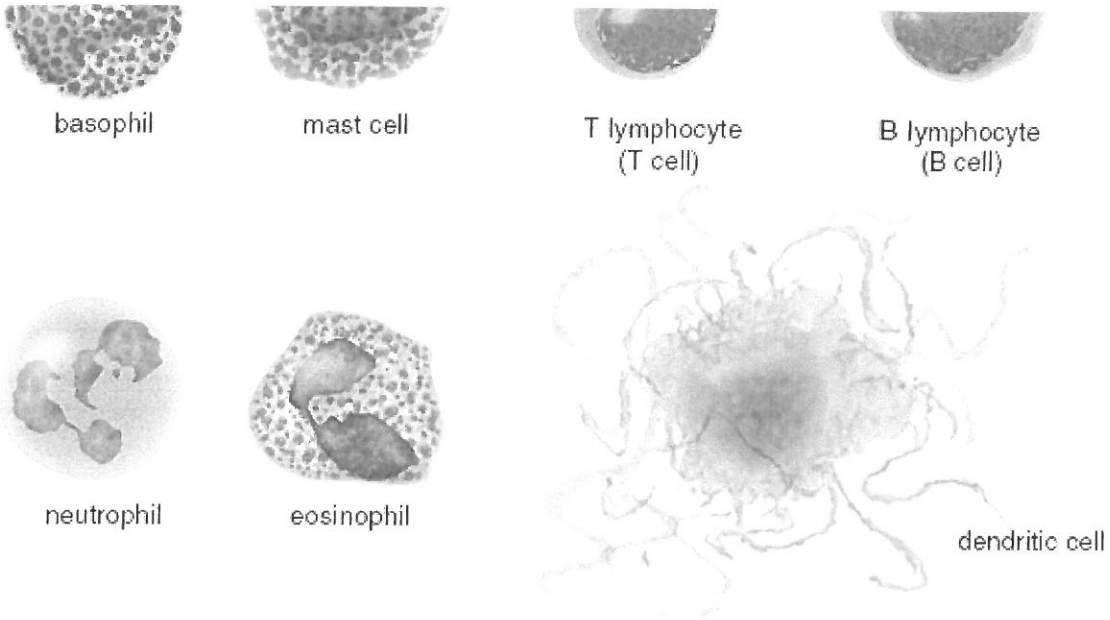
Your Second Line of Defense

A few germs manage to get past your surface barriers via cuts, surgery, or perhaps smoking-induced defects in your respiratory ciliary "escalator." These microbes, now in your interstitial fluids or bloodstream, cause you to mobilize a second line of defense (see Table 10.2). This line includes **natural killer cells** (a type of lymphocyte within the innate branch of the immune system that attacks tumor cells and virally infected cells using generalized markers on the surfaces of these cells.) that attach to your viral-infected cells or tumor cells and cause them to die. You also have a complete lineup of different types of white blood cells—leukocytes—each of which boasts a different strategy for doing warfare against foreign invaders (see Figure 10.15). These include the widespread **neutrophils** (a leukocyte within the innate branch of the immune system that patrols the bloodstream for foreign cells or objects; has phagocytic activity.) in the blood and **macrophages** (a large, wandering cell that engulfs and degrades foreign particles and cells in the tissues of vertebrates; functions in both the innate and adaptive immune responses.) in the tissues. Both of these ingest and digest foreign cells and particles. **Eosinophils** (a leukocyte within the innate branch of the immune system that recognizes and attacks multicelled parasites.) are leukocytes that attack invading parasites. **Basophils** (a leukocyte within the innate branch of the immune system that functions within the bloodstream by participating in various aspects of the inflammation response; releases histamines.) in the bloodstream and **mast cells** (a leukocyte within the innate branch of the immune system that functions within the body's tissues by participating in various aspects of the inflammation response; releases histamines.) in the tissues release **histamine** (an organic nitrogen-containing compound released by basophils and mast cells; triggers the inflammation response by increasing permeability of capillary walls to cells and signals involved in inflammation.) to support the inflammation process. So in both the bloodstream and the tissues, you have this second line of defense that detects and destroys foreign cells or inanimate particles that threaten your well-being. How does this second line of defense do its job?

Figure 10.15

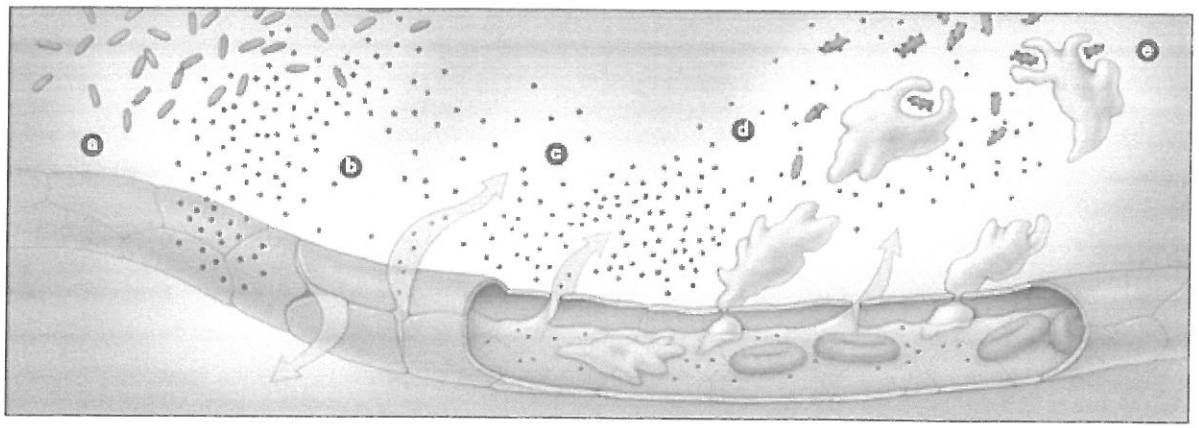
Cells of the Human Immune System. Nuclei are stained purple, cytoplasms are light blue in most cases. The large granules in eosinophils, basophils and mast cells are actually vesicles full of destructive enzymes, toxins, or signalling molecules.



One result of activating this second line of defense is the process of **inflammation** (a chemically complex process in the tissues that results in pain, redness, swelling and localized fever; facilitates response to invading microorganisms.) (see Figure 10.16a). In an area of the body where an infection is beginning, chemical signals from various leukocytes cause local capillaries to become dilated and more leaky. Increased release of fluid and cells into this area of tissue causes the redness, swelling, heat, and pain associated with inflammation. If the area is a joint, it may become immobilized or have reduced mobility due to the swelling. All of these symptoms of inflammation, although uncomfortable for us, are designed to promote healing by recognition and destruction of foreign bodies. Dilated, leaky capillaries allow tissue fluids to wash bacteria or viruses into the nearest lymph node, where they can be more completely recognized and responded to. Phagocytic leukocytes also leak into the area to engulf and degrade pathogens (see Figure 10.16b). Meanwhile, immobilization of an injured joint prevents further damage while it heals.

Figure 10.16

Inflammation in Response to Infection.



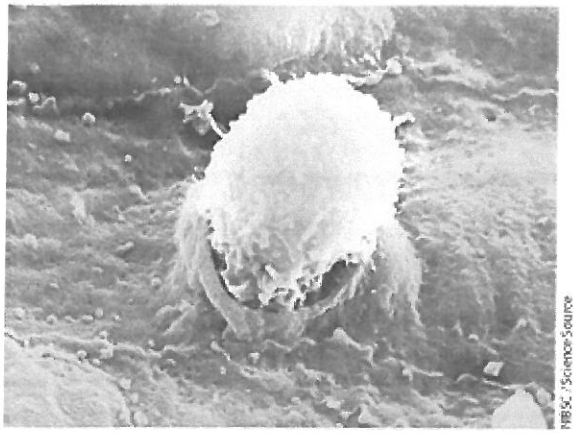
a Bacteria (purple) have invaded the tissues and are enzymatically degrading host cells as a nutrient source.

b Histamines (red) are released by mast cells in surrounding tissues causing local dilation of capillaries generating warmth and redness.

c The capillaries also become leaky and defensive proteins and signaling substance along with

d neutrophils leave the capillary and head out into the tissues.

e Phagocytosis of antibody-coated bacteria begins amidst tissue swelling and some pain.



f An electron micrograph of a neutrophil escaping a capillary to seek out a pathogen in nearby tissue.

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Another common result of the innate immune response is local or whole body temperature elevation. A fever is designed to help fight off foreign invaders. Again, although uncomfortable for us, the fever is actually a good thing as long as it does not get so high that it causes brain damage. The increase in body temperature helps the immune system components work better while inhibiting the growth of foreign invaders. For example, when your temperature is elevated, your own body's cells sequester iron. Iron is an important cofactor that many bacteria need for growth. So under feverish conditions, bacterial growth is slowed!

In Other Words

1. Pathogens that breach our primary defenses gain entry to our internal tissues, where they encounter an array of defensive cells designed to engulf or destroy them.
2. Natural killer cells attach to tumor cells or virus-infected cells and use toxic chemicals to kill them.
3. Neutrophils and macrophages engulf foreign cells and particles and then enzymatically degrade them. Eosinophils respond to multicellular parasites in a similar way.
4. Basophil and mast cells chemically support the inflammation process that helps get immune cells out of the circulatory system and into effective contact with pathogenic cells in the tissues.

5. Fever, an elevation of body temperature caused by microbial invasion, alters our physiology such that our defensive cells have functional and nutritional advantages over the invading microorganisms.

Your Third Line of Defense

The first and second lines of defense are part of our **innate immunity** (those generalized aspects of the immune response that are not pathogen-specific; they require no previous exposure to the pathogen.) . They attack anything foreign in a nonspecific manner. Sly pathogens or rapidly multiplying agents that overwhelm that second line of defense trigger a third line of defense: **adaptive immunity** (those pathogen-specific aspects of the immune response that involve antibodies and cells directed against the particular sort of pathogen that has bypassed initial, more generalized host defenses.) . The adaptive immune system develops an attack that is unique for each type of foreign substance or cell or virus we are presented with (see Table 10.3). It adapts to the needs of the moment.

Table 10.3

Characteristics of the Adaptive Immune Response

1. Requires exposure to foreign agent; non-innate
2. Is specific for the particular foreign agent
3. Is transferable from one host to another
4. Is remembered when foreign agent returns a second time.

In order for our immune system to protect us from anything foreign, the body must be able to distinguish between cells and substances that are our own (or "self") and ones that are *not* our own (or "non-self"). This is done by sensing the shapes of exterior molecules on cell or viral surfaces. All human cells, foreign cells, and viruses have a variety of proteins and carbohydrate groups on their surfaces that enable them to interact effectively with their environments. We have a class of defensive cells called **lymphocytes** (a class of leukocytes that form the third line of defense against pathogens; B lymphocytes make antibodies; T lymphocytes generate signal substances or kill self cells infected with pathogens.) that are designed in such a way that, as thousands of them mature, each one

has a uniquely shaped surface receptor protein that recognizes the shape of surface molecules on other cells. As they mature, those that would recognize and prepare to attack our own cell's surfaces are carefully destroyed. In addition, all of our body's cells have a particular class of molecules on them that signal to our immune system that they are "self." So the lymphocytes that survive maturation thus leave our cells alone (unless you have an autoimmune disorder). This maturation process then leaves us with an ever-changing population of lymphocytes well prepared to see and react to a wide variety of different foreign (bacterial, viral, parasitic) invaders. Any foreign object our lymphocytes react to is called an **antigen** (any foreign molecule or cell that generates an adaptive immune response.) because it is going to generate an antiforeign immune response.

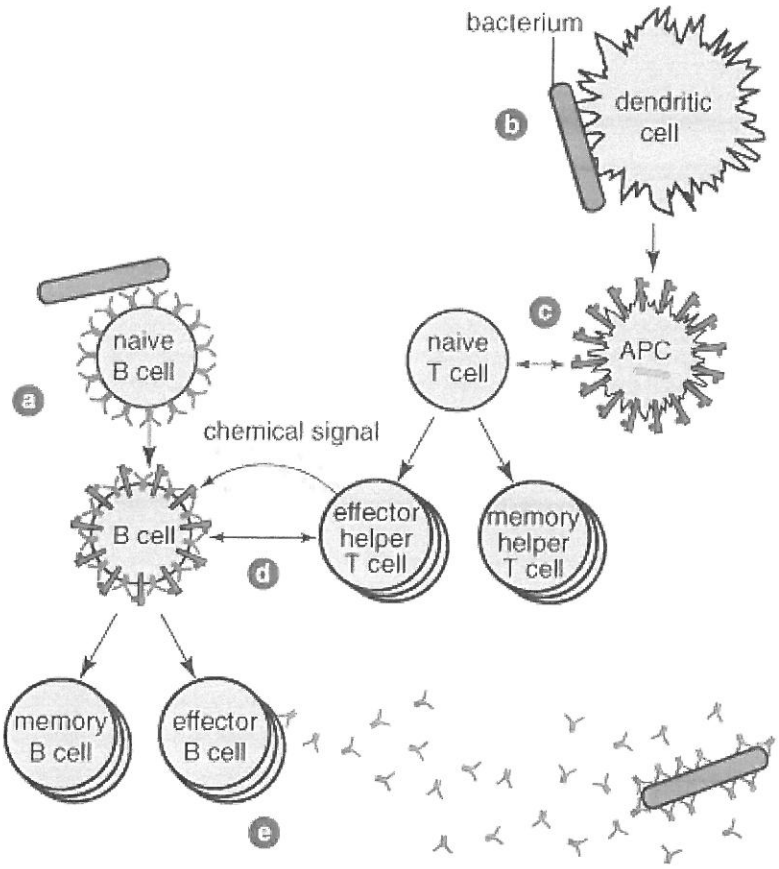
Our lymphocytes thus recognize cells both because they are foreign and because they are not "self." This third line of defense will then specifically tag foreign cells and particles with a signal that attracts immune cells such as macrophages and neutrophils that will either engulf or kill the foreign invaders (see Figure 10.15).

Virtually all interstitial fluid circulates through the lymphatic system on its way back to the heart. The lymph nodes stationed carefully along this system are perfect areas for surveillance of what is currently in our tissues (see Figure 10.12). This is where the third line of defense does its "detective work." Immune cells congregate in the lymph nodes, monitoring the lymph searching for anything foreign. If something foreign is detected, the cells can mount an immune response specifically against that foreign object. If the foreign object enters the bloodstream instead of the tissues, the blood eventually flows through an immune system organ called the **spleen** (organ of the lymphatic system in which antigen-lymphocyte encounters occur; sites of blood filtration and surveillance.) . Lymphocyte detective work takes place there as well! Do lymphocytes have eyes and brains? How does this happen?

The cells in the lymph nodes and spleen need no eyes and brains; rather, they are well designed. Two groups of defensive cells—the macrophages and the **dendritic cells** (part of mammalian immune system; engulfs foreign particles and cells, degrades them, and presents parts of the foreign entity on its surface for detection and binding by pathogen-specific lymphocytes of the adaptive immune system.) —also have surface receptor molecules that can distinguish self surfaces from non-self surfaces on the basis of surface shape (see Figures 10.15, 10.17b). This is all based on the same sort of molecular fit that enables an enzyme to distinguish its own substrate from other substrates. When a macrophage's receptors bump into a cell with only self surface markers, they ignore it. But when foreign-shaped surfaces are present (as in bacteria, viruses, or cells infected with these microbes), these foreign entities are engulfed, partially degraded and their foreign parts are "presented" to the lymphocytes standing sentinel in the lymph node (see Figure 10.17c)! The macrophage is now an *APC,* or *antigen-presenting cell.*

Figure 10.17

"Pathogen Wars Part I." An antibody-mediated adaptive immune response that occurs in lymph nodes or the spleen. See text for details.



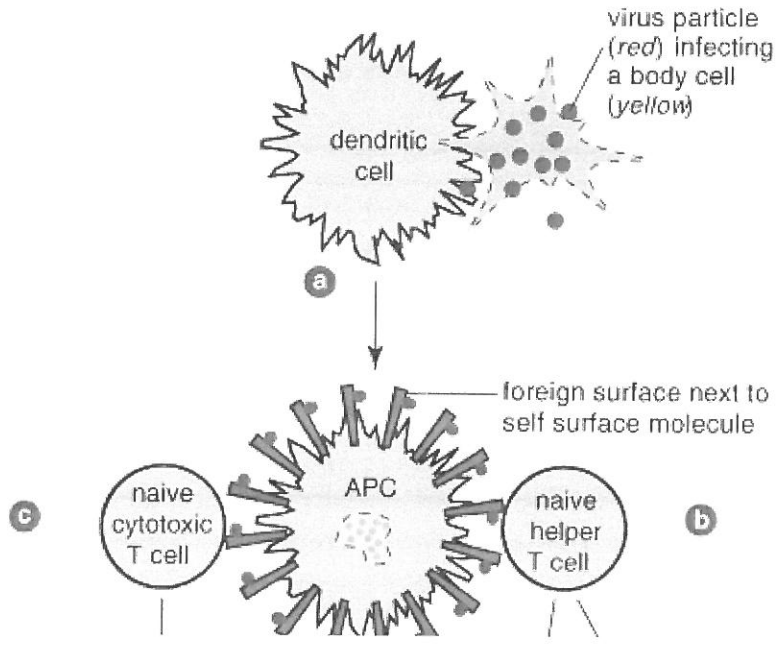
Among the lymphocytes that cruise around within the node, some did their maturation in the thymus gland and are called **T lymphocytes** (any lymphocyte that matures to competence in the thymus gland; several classes exist of which helpers and killers are most prominent.) , or *T cells*. Others that will serve a different role, matured in the bone marrow and are called **B lymphocytes** (a type of lymphocyte that detects foreign molecular surfaces on molecules or cells and generates soluble antibodies that will bind to those surfaces labeling them as foreign.) , or *B cells*. Now, among many thousands of B and T lymphocytes, a few happen to have surface receptor shapes specific to the foreign surfaces of the pathogen (see Figure 10.17a, c). The T cells sense these foreign molecular surfaces as displayed on the antigen-presenting cells. The B cells recognize those same foreign surfaces directly on the foreign cell itself. One group of T cells called **helper T cells** (a type of lymphocyte that detects foreign molecular surfaces on molecules or cells and assists specific B or T lymphocytes to divide and become numerous for defense against the foreign entities.) responds to foreign surfaces by dividing many times to form a population of cells that start putting out a "hey, there's something foreign here!" chemical signal (see Figure 10.17d). The B cells receive this signal: it releases them to undergo many divisions to become a much larger population

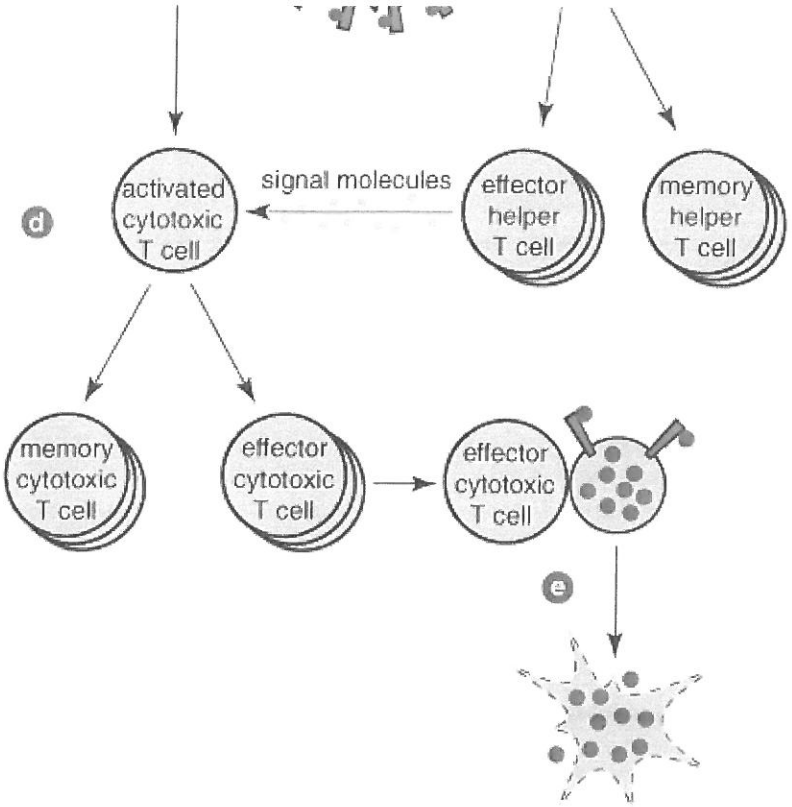
of effector B cells. This new population begins to produce soluble **antibody** (a soluble multimeric protein produced by descendants of B cells; it recognizes and binds to a specific antigenic (foreign) surface, molecule, or cell.) molecules, proteins with shapes identical in structure to the receptor proteins on the progenitor cells that first saw the foreign surfaces (see Figure 10.17e). These antibodies will now begin to bind to and tag this sort of foreign cell surface wherever it might be they are found in the body. Anything in your body that gets coated with antibodies is destined for destruction—macrophages see to that! So here is a critically important branch of your third line of defense: an antibody-mediated response. It finds pathogens, uses surface-specific antibodies to tag the pathogen, and then it destroys the coated pathogen.

If a pathogen that's "at large" in your tissues gets promptly recognized, coated with antibodies and destroyed, then what's the safest place for that pathogen to set up shop and grow in your body? Probably that would be somewhere inside your own cells. The immune system has been trained to ignore your own cells, correct? In fact, some of the most successful human pathogens like viruses and the eukaryotic malarial parasite *Plasmodium falciparum* take just that approach. It's a tricky strategy, however. They can't get very far growing in just one body cell. So they need to hop from cell to cell and that often means putting some kind of marker or protein on the surface of your cells to assist in leaving one cell and entering the next one. And that marker is foreign! So a whole branch of your third line of defense has been designed for the fallen world of *intracellular* pathogens. It's called the *cell-mediated immune response,* and it's pictured in Figure 10.18.

Figure 10.18

"Pathogen Wars Part II". A cell-mediated adaptive immune response that occurs in lymph nodes or the spleen. See text for details.





The cell-mediated response begins in essentially the same way as the antibody-mediated response. In a lymph node, dendritic cells or macrophages feel a non-self surface and promptly engulf the sample. Soon, foreign surface molecules are presented on the surface of the cell (see Figure 10.18a). Two classes of T lymphocytes begin feeling the presented antigen in case their surface receptors are specific for it (see Figure 10.18b, c). Again, helper T cells with receptors specific for the foreign surface begin to divide to form a population. Another class of T cells, **cytotoxic T lymphocytes** (a lymphocyte that matures in the thymus gland and recognizes and destroys host (self) cells that are infected by an intracellular parasite (i.e., a virus or bacterium).) (killer T cells), whose receptors are specific to the foreignness, also become activated. The green rectangles in the diagram indicate that these T cells are seeing antigens (red circles) presented right next to other surface molecules that define the cell as "self". This recognition will be critical to their later roles. The stimulated helper T cell population again puts out signal molecules. These induce any local activated cytotoxic T cells to begin to proliferate in response (see Figure 10.18d). These T cells now begin a recognition process throughout your body. Any time they find one of your body's cells that has surface foreignness right next to *normal self markers,* they secrete horribly toxic chemicals that punch large holes in the surface of these (infected) body cells and they soon die (see Figure 10.18e). In this way any of your body's cells that have "joined the other side" and are harboring or making pathogenic cells will be terminated by the cell-mediated portion of your third line of defense. Yes, a fallen world is jam-packed with pathogens that would sneak their foreignness past your sensory system's eyes. But whether

they attempt either an intercellular or intracellular attack, your elegant immune system is designed to discover them, label them, and destroy them.

In Other Words

1. The immune response has a third line of defense that is specific for any given pathogen that invades our tissues.
2. The third line of defense requires our immune system to distinguish between self cells or molecules and foreign or "non-self" cells or molecules.
3. Lymphocytes are the principle type of leukocyte involved in the third line of defense.
4. As lymphocytes mature in the thymus gland or bone marrow, those with receptors that would recognize and destroy self surfaces are eliminated leaving only those that seek out foreign surfaces.
5. Encounters between lymphocytes and foreign agents occur in lymph nodes that drain and filter our tissues and in the spleen that monitors foreignness in the bloodstream.
6. Dendritic cells and macrophages engulf non-self cells, degrade their structures, and present parts of their foreign molecules on their surfaces for T lymphocytes to detect.
7. When helper T lymphocytes are stimulated to divide in response to a foreign antigen, the resulting population functions by chemically signaling other classes of lymphocytes to divide in response to a foreign antigen they have detected.
8. When B lymphocytes are stimulated to divide in response to a foreign antigen, the resulting population functions by secreting antibodies that bind specifically to antigenic sites on the kind of foreign cell or molecule that stimulated B cell division in the first place.
9. Many pathogens avoid initial contact with host lymphocytes by quickly invading host cells and thus multiplying within a cell whose membrane surfaces are seen as self by the immune system.

10. When cytotoxic T lymphocytes are stimulated to divide in response to a foreign antigen, the resulting population functions by chemically attacking self cells whose surfaces also exhibit the foreign antigen that stimulated cytotoxic T cell division in the first place.

11. T cells differ from B cells in how they see antigen. B cells sense antigen on the surface of foreign cells. T cells sense it on the surfaces of your own infected cells because the antigen is right next to self surface marker proteins.

Preparing Your Immune System: The Preemptive Strike

Once exposed to something foreign, our adaptive immune system keeps a population of **memory lymphocytes** (a class of B or T cell that does not differentiate immediately into antibody secretion or killing activity; it divides to form a population of cells specific for an antigen just encountered and waits for a second encounter to differentiate.) around that remember—and have receptors specific for—that nasty foreign object (see Figures 10.17, 10.18d). If we are ever re-infected with that same foreign entity, we can respond faster to the threat the second time! This wonderful immunologic memory is the basis for the valuable process called **vaccination** (administering a preparation of killed microorganisms, living attenuated organisms, or parts of virulent organisms to produce or artificially increase immunity to a particular disease agent.) . When you receive a vaccine, you are receiving a dead or severely weakened form of the pathogen that would otherwise make you sick. Sometimes, the vaccine contains only certain molecular surface portions of the pathogen. Since these vaccine components are either:

(1) dead pathogens,

(2) weakened pathogens, or

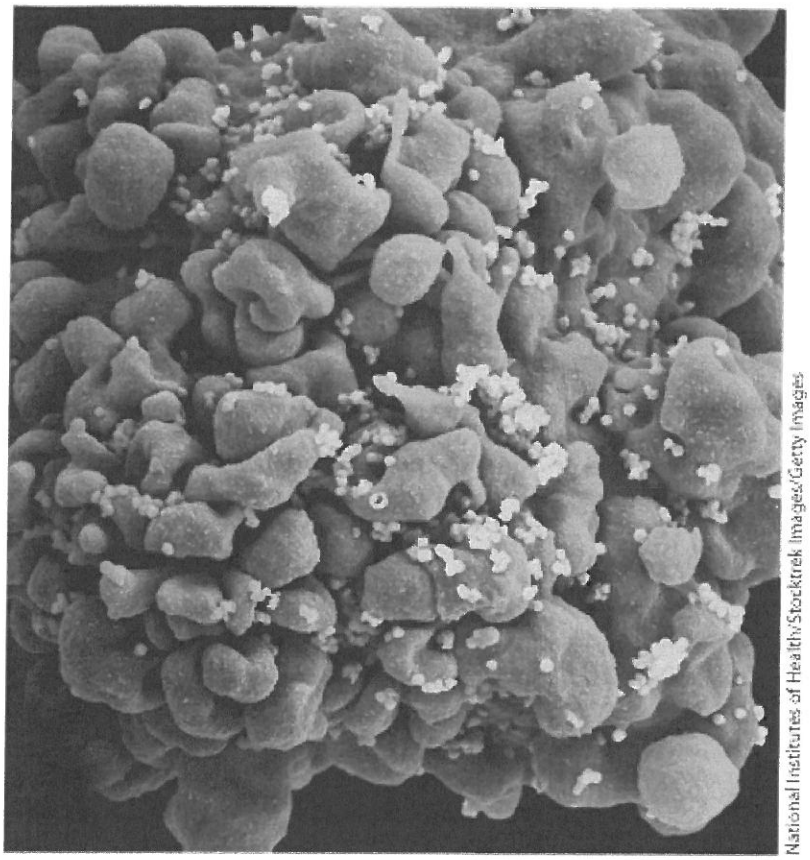
(3) only portions of the pathogen surface, they can't infect you.

But their presence in your tissues allows your immune defenses to recognize that something foreign is present and to mount an immune response. That is why you sometimes feel a bit sick after being vaccinated. Later on, if you are exposed to a virulent form of that pathogen, your body already has immunologic memory built up and can mount an immune response much faster and more effectively than if you had not been vaccinated against that foreign invader.

Unfortunately, people with **HIV virus** (a noncellular pathogenic molecular machine composed of proteins and an RNA genome; causes human immunodeficiency or AIDS (acquired immune deficiency syndrome).) infections do not respond well to vaccination. The virus invades and destroys their helper T lymphocytes (see Figure 10.19). Review the role of helper T cells in Figure 10.17 and 10.18. When helper T cell populations are depleted, your immune response isn't able to mount either a strong B cell or a strong killer T cell response to the vaccine. The HIV-positive individual just doesn't have much of a third-line of defense against pathogens anymore.

Figure 10.19

HIV Invasion. This color-modified scanning electron micrograph shows a helper T lymphocyte with a collection of HIV virus particles (yellow) adsorbed to its surfaces. The viruses may hide inside this cell in a dormant state for several years, or they may begin to destroy the cell if it becomes sensitized to some foreign antigen.



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So as you are climbing stairs and touching handrails, your skin—your first line of defense—will prevent most germs from entering your body. If you have an open cut on your hand or forget to wash or sanitize your hands before grabbing that snack and eating, a second line of defense will turn on. Any pathogen resourceful enough to evade your macrophages or natural killer cells will generate a specific third-line attack by means of your adaptive immune system. If this third line of defense gets involved, you may get sick while it is revving up, but you will generally conquer the pathogen and get better in a few days. Isn't it magnificent that we are able to defend ourselves against organisms our sensory systems are totally incapable of detecting?

In Other Words

1. Whenever B or T cell populations expand by cell division, one subpopulation of cells becomes a set of memory cells instead of secreting antibodies or attacking infected cells.
2. These memory cell populations can more quickly expand and attack a pathogen the second time it invades the host's tissues.
3. Vaccination generates these memory populations by using harmless vaccines to force B and T cells to respond to foreign antigen. When the real virulent pathogen arrives, the memory populations are present to attack it.