THE CIRCULATORY SYSTEM

Types of Circulatory Systems

Living things must be capable of transporting nutrients, wastes and gases to and from cells. Single-celled organisms use their cell surface as a point of exchange with the outside environment. Multicellular organisms have developed transport and circulatory systems to deliver oxygen and food to cells and remove carbon dioxide and metabolic wastes. Sponges are the simplest animals, yet even they have a transport system. Seawater is the medium of transport and is propelled in and out of the sponge by ciliary action. Simple animals, such as the hydra and planaria (shown in Figure 1), lack specialized organs such as hearts and blood vessels, instead using their skin as an exchange point for materials. This, however, limits the size an animal can attain. To become larger, they need specialized organs and organ systems.

![Figure 1. Structures that serve some of the functions of the circulatory system in animals that lack the system](image)

Multicellular animals do not have most of their cells in contact with the external environment and so have developed circulatory systems to transport nutrients, oxygen, carbon dioxide and metabolic wastes. Components of the circulatory system include
- blood: a connective tissue of liquid plasma and cells
- heart: a muscular pump to move the blood
- blood vessels: arteries, capillaries and veins that deliver blood to all tissues

There are several types of circulatory systems. The open circulatory system, examples of which are diagrammed in Figure 2, is common to molluscs and arthropods. Open circulatory systems (evolved in insects, mollusks and other invertebrates) pump blood into a hemocoel with the blood diffusing back to the circulatory system between cells. Blood is pumped by a heart into the body cavities, where tissues are surrounded by the blood. The resulting blood flow is sluggish.

Vertebrates, and a few invertebrates, have a closed circulatory system, shown in Figure 2. Closed circulatory systems (evolved in echinoderms and vertebrates) have the blood closed at all times within vessels of different size and wall thickness. In this type of system, blood is pumped by a heart through
Figure 2. Circulatory systems of an insect (right) and mollusc (left)

vessels, and does not normally fill body cavities. Blood flow is not sluggish. Hemoglobin causes vertebrate blood to turn red in the presence of oxygen; but more importantly hemoglobin molecules in blood cells transport oxygen. The human closed circulatory system is sometimes called the cardiovascular system. A secondary circulatory system, the lymphatic circulation, collects fluid and cells and returns them to the cardiovascular system.

Vertebrate Cardiovascular System

The vertebrate cardiovascular system includes a heart, which is a muscular pump that contracts to propel blood out to the body through arteries, and a series of blood vessels. The upper chamber of the heart, the atrium (pl. atria), is where the blood enters the heart. Passing through a valve, blood enters the lower chamber, the ventricle. Contraction of the ventricle forces blood from the heart through an artery. The heart muscle is composed of cardiac muscle cells.

Arteries are blood vessels that carry blood away from heart. Arterial walls are able to expand and contract. Arteries have three layers of thick walls. Smooth muscle fibers contract, another layer of connective tissue is quite elastic, allowing the arteries to carry blood under high pressure.

Figure 3. Structure of an artery
The aorta is the main artery leaving the heart. The pulmonary artery is the only artery that carries oxygen-poor blood. The pulmonary artery carries deoxygenated blood to the lungs. In the lungs, gas exchange occurs, carbon dioxide diffuses out, oxygen diffuses in. Arterioles are small arteries that connect larger arteries with capillaries. Small arterioles branch into collections of capillaries known as capillary beds, an example of one is shown in Figure 4.

![Figure 4. Structure and blood flow through a vein](image)

![Figure 5. Capillary with Red Blood Cell (TEM x32,830)](image)

Capillaries, shown in Figures 4 and 5, are thin-walled blood vessels in which gas exchange occurs. In the capillary, the wall is only one cell layer thick. Capillaries are concentrated into capillary beds. Some capillaries have small pores between the cells of the capillary wall, allowing materials to flow in and out of capillaries as well as the passage of white blood cells. Changes in blood pressure also occur in the various vessels of the circulatory system, as shown in Figure 6. Nutrients, wastes, and hormones are exchanged across the thin walls of capillaries. Capillaries are microscopic in size, although blushing is one manifestation of blood flow into capillaries. Control of blood flow into capillary beds is done by nerve-controlled sphincters.

![Figure 6. Changes in blood pressure, velocity, and the area of the arteries, capillaries, and veins of the circulatory system](image)

The circulatory system functions in the delivery of oxygen, nutrient molecules, and hormones and the
removal of carbon dioxide, ammonia and other metabolic wastes. Capillaries are the points of exchange between the blood and surrounding tissues. Materials cross in and out of the capillaries by passing through or between the cells that line the capillary, as shown in Figure 7.

The extensive network of capillaries in the human body is estimated at between 50,000 and 60,000 miles long. Thoroughfare channels allow blood to bypass a capillary bed. These channels can open and close by the action of muscles that control blood flow through the channels, as shown in Figure 8.

Blood leaving the capillary beds flows into a progressively larger series of venules that in turn join to form veins. Veins carry blood from capillaries to the heart. With the exception of the pulmonary veins, blood in veins is oxygen-poor. The pulmonary veins carry oxygenated blood from lungs back to the heart. Venules are smaller veins that gather blood from capillary beds into veins. Pressure in veins is low, so veins depend on nearby muscular contractions to move blood along. The veins have valves that prevent back-flow of blood, as shown in Figure 9.

![Figure 7. Capillary structure, and relationships of capillaries to arteries and veins](image7.png)

![Figure 8. Capillary beds and their feeder vessels](image8.png)
Figure 9. Structure of a vein (right) and the actions of muscles to propel blood through the veins (left)

Ventricular contraction propels blood into arteries under great pressure. Blood pressure is measured in mm of mercury; healthy young adults should have pressure of ventricular systole of 120mm, and 80 mm at ventricular diastole. Higher pressures (human 120/80 as compared to a 12/1 in lobsters) mean the volume of blood circulates faster (20 seconds in humans, 8 minutes in lobsters).

As blood gets farther from the heart, the pressure likewise decreases. Each contraction of the ventricles sends pressure through the arteries. Elasticity of lungs helps keep pulmonary pressures low. Systemic pressure is sensed by receptors in the arteries and atria. Nerve messages from these sensors communicate conditions to the medulla in the brain. Signals from the medulla regulate blood pressure.

**Vertebrate Vascular Systems**

Humans, birds, and mammals have a four-chambered heart that completely separates oxygen-rich and oxygen-depleted blood, as is shown in Figure 10. Fish have a two-chambered heart in which a single-loop circulatory pattern takes blood from the heart to the gills and then to the body. Amphibians have a three-chambered heart with two atria and one ventricle. A loop from the heart goes to the pulmonary capillary beds, where gas exchange occurs. Blood then is returned to the heart. Blood exiting the ventricle is diverted, some to the pulmonary circuit, some to systemic circuit. The disadvantage of the three-chambered heart is the mixing of oxygenated and deoxygenated blood. Some reptiles have partial separation of the ventricle. Other reptiles, plus, all birds and mammals, have a four-chambered heart, with complete separation of both systemic and pulmonary circuits.

**The Heart**

The heart, shown in Figure 11, is a muscular structure that contracts in a rhythmic pattern to pump blood. Hearts have a variety of forms: chambered hearts in mollusks and vertebrates, tubular hearts of arthropods, and aortic arches of annelids. Accessory hearts are used by insects to boost or supplement the main heart's actions. Fish, reptiles, and amphibians have lymph hearts that help pump lymph back into veins.

The basic vertebrate heart, such as occurs in fish, has two chambers. An auricle is the chamber of the heart where blood is received from the body. A ventricle pumps the blood it gets through a valve from the auricle out to the gills through an artery.
Figure 10. Circulatory systems of several vertebrates showing the progressive evolution of the four-chambered heart and pulmonary and systemic circulatory circuits.

Amphibians have a three-chambered heart: two atria emptying into a single common ventricle. Some species have a partial separation of the ventricle to reduce the mixing of oxygenated (coming back from the lungs) and deoxygenated blood (coming in from the body). Two sided or two chambered hearts permit pumping at higher pressures and the addition of the pulmonary loop permits blood to go to the lungs at lower pressure yet still go to the systemic loop at higher pressures.

Establishment of the four-chambered heart, along with the pulmonary and systemic circuits, completely separates oxygenated from deoxygenated blood. This allows higher the metabolic rates needed by warm-blooded birds and mammals.

The human heart, as seen in Figure 11, is a two-sided, four-chambered structure with muscular walls. An atrioventricular (AV) valve separates each auricle from ventricle. A semilunar (also known as arterial) valve separates each ventricle from its connecting artery.
Figure 11. The relationship of the heart and circulatory system to major visceral organs. Right: the structure of the heart

The heart beats or contracts approximately 70 times per minute. The human heart will undergo over 3 billion contraction cycles, as shown in Figure 12, during a normal lifetime. The cardiac cycle consists of two parts: systole (contraction of the heart muscle) and diastole (relaxation of the heart muscle). Atria contract while ventricles relax. The pulse is a wave of contraction transmitted along the arteries. Valves in the heart open and close during the cardiac cycle. Heart muscle contraction is due to the presence of nodal tissue in two regions of the heart. The SA node (sinoatrial node) initiates heartbeat. The AV node (atrioventricular node) causes ventricles to contract. The AV node is sometimes called the pacemaker since it keeps heartbeat regular. Heartbeat is also controlled by nerve messages originating from the autonomic nervous system.

Figure 12. The cardiac cycle
Blood flows through the heart from veins to atria to ventricles out by arteries. Heart valves limit flow to a single direction. One heartbeat, or cardiac cycle, includes atrial contraction and relaxation, ventricular contraction and relaxation, and a short pause. Normal cardiac cycles (at rest) take 0.8 seconds. Blood from the body flows into the vena cava, which empties into the right atrium. At the same time, oxygenated blood from the lungs flows from the pulmonary vein into the left atrium. The
muscles of both atria contract, forcing blood downward through each AV valve into each ventricle. Diastole is the filling of the ventricles with blood. Ventricular systole opens the SL valves, forcing blood out of the ventricles through the pulmonary artery or aorta. The sound of the heart contracting and the valves opening and closing produces a characteristic "lub-dub" sound. Lub is associated with closure of the AV valves, dub is the closing of the SL valves.

Human heartbeats originate from the sinoatrial node (SA node) near the right atrium. Modified muscle cells contract, sending a signal to other muscle cells in the heart to contract. The signal spreads to the atrioventricular node (AV node). Signals carried from the AV node, slightly delayed, through bundle of His fibers and Purkinje fibers cause the ventricles to contract simultaneously. Figure 13 illustrates several aspects of this.

![Heart Diagram](image)

Figure 13. The contraction of the heart and the action of the nerve nodes located on the heart

Heartbeats are coordinated contractions of heart cardiac cells, shown in an animate GIF image in Figure 14. When two or more of such cells are in proximity to each other their contractions synch up and they beat as one.

![GIF Image](image)

Figure 14. GIF image of a single human heart muscle cell beating

An electrocardiogram (ECG) measures changes in electrical potential across the heart, and can detect the contraction pulses that pass over the surface of the heart. There are three slow, negative changes, known as P, R, and T as shown in Figure 15. Positive deflections are the Q and S waves. The P wave represents the contraction impulse of the atria, the T wave the ventricular contraction. ECGs are useful in diagnosing heart abnormalities.
Cardiac muscle cells are serviced by a system of coronary arteries. During exercise the flow through these arteries is up to five times normal flow. Blocked flow in coronary arteries can result in death of heart muscle, leading to a heart attack.

Blockage of coronary arteries, shown in Figure 16, is usually the result of gradual buildup of lipids and cholesterol in the inner wall of the coronary artery. Occasional chest pain, angina pectoralis, can result during periods of stress or physical exertion. Angina indicates oxygen demands are greater than capacity to deliver it and that a heart attack may occur in the future. Heart muscle cells that die are not replaced since heart muscle cells do not divide. Heart disease and coronary artery disease are the leading causes of death in the United States.
Hypertension, high blood pressure (the silent killer), occurs when blood pressure is consistently above 140/90. Causes in most cases are unknown, although stress, obesity, high salt intake, and smoking can add to a genetic predisposition. Luckily, when diagnosed, the condition is usually treatable with medicines and diet/exercise.

The Vascular System

Two main routes for circulation are the pulmonary (to and from the lungs) and the systemic (to and from the body). Pulmonary arteries carry blood from the heart to the lungs. In the lungs gas exchange occurs. Pulmonary veins carry blood from lungs to heart. The aorta is the main artery of systemic circuit. The vena cavae are the main veins of the systemic circuit. Coronary arteries deliver oxygenated blood, food, etc. to the heart. Animals often have a portal system, which begins and ends in capillaries, such as between the digestive tract and the liver. Fish pump blood from the heart to their gills, where gas exchange occurs, and then on to the rest of the body. Mammals pump blood to the lungs for gas exchange, then back to the heart for pumping out to the systemic circulation. Blood flows in only one direction.

Blood

Plasma is the liquid component of the blood. Mammalian blood consists of a liquid (plasma) and a number of cellular and cell fragment components as shown in Figure 21. Plasma is about 60% of a volume of blood; cells and fragments are 40%. Plasma has 90% water and 10% dissolved materials including proteins, glucose, ions, hormones, and gases. It acts as a buffer, maintaining pH near 7.4. Plasma contains nutrients, wastes, salts, proteins, etc. Proteins in the blood aid in transport of large molecules such as cholesterol.

Red blood cells, also known as erythrocytes, are flattened, doubly concave cells about 7 µm in diameter that carry oxygen associated in the cell's hemoglobin. Mature erythrocytes lack a nucleus. They are small, 4 to 6 million cells per cubic millimeter of blood, and have 200 million hemoglobin molecules per cell. Humans have a total of 25 trillion red blood cells (about 1/3 of all the cells in the body). Red blood cells are continuously manufactured in red marrow of long bones, ribs, skull, and vertebrae. Life-span of an erythrocyte is only 120 days, after which they are destroyed in liver and spleen. Iron from hemoglobin is recovered and reused by red marrow. The liver degrades the heme units and secretes them as pigment in the bile, responsible for the color of feces. Each second two million red blood cells are produced to replace those thus taken out of circulation.

White blood cells, also known as leukocytes, are larger than erythrocytes, have a nucleus, and lack hemoglobin. They function in the cellular immune response. White blood cells (leukocytes) are less than 1% of the blood's volume. They are made from stem cells in bone marrow. There are five types of leukocytes, important components of the immune system. Neutrophils enter the tissue fluid by squeezing through capillary walls and phagocytozing foreign substances. Macrophages release white blood cell growth factors, causing a population increase for white blood cells. Lymphocytes fight infection. T-cells attack cells containing viruses. B-cells produce antibodies. Antigen-antibody complexes are phagocytized by a macrophage. White blood cells can squeeze through pores in the capillaries and fight infectious diseases in interstitial areas.
Platelets result from cell fragmentation and are involved with clotting, as is shown by Figures 17 and 18. Platelets are cell fragments that bud off megakaryocytes in bone marrow. They carry chemicals essential to blood clotting. Platelets survive for 10 days before being removed by the liver and spleen. There are 150,000 to 300,000 platelets in each milliliter of blood. Platelets stick and adhere to tears in blood vessels; they also release clotting factors. A hemophiliac's blood cannot clot. Providing correct proteins (clotting factors) has been a common method of treating hemophiliacs. It has also led to HIV transmission due to the use of transfusions and use of contaminated blood products.

Figure 17. Human Red Blood Cells, Platelets and T-lymphocyte (erythocytes = red; platelets = yellow; T-lymphocyte = light green) (SEM x 9,900)

Figure 18. The formation and actions of blood clots
The Lymphatic System

Water and plasma are forced from the capillaries into intracellular spaces. This interstitial fluid transports materials between cells. Most of this fluid is collected in the capillaries of a secondary circulatory system, the lymphatic system. Fluid in this system is known as lymph.

Lymph flows from small lymph capillaries into lymph vessels that are similar to veins in having valves that prevent backflow. Lymph vessels connect to lymph nodes, lymph organs, or to the cardiovascular system at the thoracic duct and right lymphatic duct.

Lymph nodes are small irregularly shaped masses through which lymph vessels flow. Clusters of nodes occur in the armpits, groin, and neck. Cells of the immune system line channels through the nodes and attack bacteria and viruses traveling in the lymph.
THE EXCRETORY SYSTEM

Cells produce water and carbon dioxide as by-products of metabolic breakdown of sugars, fats, and proteins. Chemical groups such as nitrogen, sulfur, and phosphorous must be stripped, from the large molecules to which they were formerly attached, as part of preparing them for energy conversion. The continuous production of metabolic wastes establishes a steep concentration gradient across the plasma membrane, causing wastes to diffuse out of cells and into the extracellular fluid. Single-celled organisms have most of their wastes diffuse out into the outside environment. Multicellular organisms, and animals in particular, must have a specialized organ system to concentrate and remove wastes from the interstitial fluid into the blood capillaries and eventually deposit that material at a collection point for removal entirely from the body.

Regulation of Extracellular Fluids

Excretory systems regulate the chemical composition of body fluids by removing metabolic wastes and retaining the proper amounts of water, salts, and nutrients. Components of this system in vertebrates include the kidneys, liver, lungs, and skin. Not all animals use the same routes or excrete their wastes the same way humans do. Excretion applies to metabolic waste products that cross a plasma membrane. Elimination is the removal of feces.

Nitrogen Wastes

Nitrogen wastes are by-products of protein metabolism. Amino groups are removed from amino acids prior to energy conversion. The NH₂ (amino group) combines with a hydrogen ion (proton) to form ammonia (NH₃). Ammonia is very toxic and usually is excreted directly by marine animals. Terrestrial animals usually need to conserve water. Ammonia is converted to urea, a compound the body can tolerate at higher concentrations than ammonia. Birds and insects secrete uric acid that they make through large energy expenditure but little water loss. Amphibians and mammals secrete urea that they form in their liver. Amino groups are turned into ammonia, which in turn is converted to urea, dumped into the blood and concentrated by the kidneys.

Water and Salt Balance

The excretory system is responsible for regulating water balance in various body fluids. Osmoregulation refers to the state aquatic animals are in: they are surrounded by freshwater and must constantly deal with the influx of water. Animals, such as crabs, have an internal salt concentration very similar to that of the surrounding ocean. Such animals are known as osmoconformers, as there is little water transport between the inside of the animal and the isotonic outside environment. Marine vertebrates, however, have internal concentrations of salt that are about one-third of the surrounding seawater. They are said to be osmoregulators. Osmoregulators face two problems: prevention of water loss from the body and prevention of salts diffusing into the body. Fish deal with this by passing water out of their tissues through their gills by osmosis and salt through their gills by active transport. Cartilaginous fish have a greater salt concentration than seawater, causing water to move into the shark by osmosis; this water is used for excretion. Freshwater fish must prevent water gain and salt loss. They do not drink water, and have their skin covered by a thin mucus. Water enters and leaves through the gills and the fish excretory system produces large amounts of dilute urine. Terrestrial animals use a variety of methods to reduce water loss: living in moist environments,
developing impermeable body coverings, production of more concentrated urine. Water loss can be considerable: a person in a 100 degree F temperature loses 1 liter of water per hour.

**Excretory System Functions**
- Collect water and filter body fluids.
- Remove and concentrate waste products from body fluids and return other substances to body fluids as necessary for **homeostasis**.
- Eliminate excretory products from the body.

**Invertebrate Excretory Organs**
Many invertebrates such as flatworms use a **nephridium** as their excretory organ. At the end of each blind tubule of the nephridium is a ciliated **flame cell**. As fluid passes down the tubule, solutes are reabsorbed and returned to the body fluids.

Excretory system of a flatworm

Excretory system of an earthworm
Vertebrates Have Paired Kidneys
ALL vertebrates have paired kidneys. Excretion is not the primary function of kidneys. Kidneys regulate body fluid levels as a primary duty, and remove wastes as a secondary one.

The Human Excretory System
The urinary system is made-up of the kidneys, ureters, bladder, and urethra. The nephron, an evolutionary modification of the nephridium, is the kidney's functional unit. Waste is filtered from the blood and collected as urine in each kidney. Urine leaves the kidneys by ureters, and collects in the bladder. The bladder can distend to store urine that eventually leaves through the urethra.
Proximal convoluted tubule
Peritubular capillaries
Loop of Henle (ascending limb)
Loop of Henle (descending limb)
Vasa recta capillaries
Bowman's capsule
Glomerulus
Afferent arteriole
Efferent arteriole
Distal convoluted tubule
Venules
Veins
Artery
Collecting duct

Microvilli
Epithelial cell
Mitochondria
Intercellular and subcellular spaces
Peritubular capillary

Lumen
Loop of Henle
Permeable to H₂O and small molecules

Lumen
Distal convoluted tubule
Transports Na⁺Cl⁻ out of tubular fluid
The Nephron

The nephron consists of a cup-shaped capsule containing capillaries and the glomerulus, and a long renal tube. Blood flows into the kidney through the renal artery, which branches into capillaries associated with the glomerulus. Arterial pressure causes water and solutes from the blood to filter into the capsule. Fluid flows through the proximal tubule, which include the loop of Henle, and then into the distal tubule. The distal tubule empties into a collecting duct. Fluids and solutes are returned to the capillaries that surround the nephron tubule.

Filtration of the blood in the fine structure of the kidneys

The nephron has three functions:

- Glomerular filtration of water and solutes from the blood.
- Tubular reabsorption of water and conserved molecules back into the blood.
- Tubular secretion of ions and other waste products from surrounding capillaries into the distal tubule.

Nephrons filter 125 ml of body fluid per minute; filtering the entire body fluid component 16 times each day. In a 24 hour period nephrons produce 180 liters of filtrate, of which 178.5 liters are reabsorbed. The remaining 1.5 liters forms urine.

Urine Production

- Filtration in the glomerulus and nephron capsule.
- Reabsorption in the proximal tubule.
- Tubular secretion in the Loop of Henle.
Components of The Nephron
- Glomerulus: mechanically filters blood
- Bowman's Capsule: mechanically filters blood
- Proximal Convoluted Tubule: Reabsorbs 75% of the water, salts, glucose, and amino acids
- Loop of Henle: Countercurrent exchange, which maintains the concentration gradient
- Distal Convoluted Tubule: Tubular secretion of H ions, potassium, and certain drugs.

Kidney Stones
In some cases, excess wastes crystallize as kidney stones. They grow and can become a painful irritant that may require surgery or ultrasound treatments. Some stones are small enough to be forced into the urethra, others are the size of huge, massive boulders (or so I am told).

Kidney Function
Kidneys perform a number of homeostatic functions:
- Maintain volume of extracellular fluid
- Maintain ionic balance in extracellular fluid
- Maintain pH and osmotic concentration of the extracellular fluid.
- Excrete toxic metabolic by-products such as urea, ammonia, and uric acid.

Hormone Control of Water and Salt
Water reabsorption is controlled by the antidiuretic hormone (ADH) in negative feedback. ADH is released from the pituitary gland in the brain. Dropping levels of fluid in the blood signal the hypothalamus to cause the pituitary to release ADH into the blood. ADH acts to increase water absorption in the kidneys. This puts more water back in the blood, increasing the concentration of the urine. When too much fluid is present in the blood, sensors in the heart signal the hypothalamus to cause a reduction of the amounts of ADH in the blood. This increases the amount of water absorbed by the kidneys, producing large quantities of a more dilute urine.
Aldosterone, a hormone secreted by the kidneys, regulates the transfer of sodium from the nephron to the blood. When sodium levels in the blood fall, aldosterone is released into the blood, causing more sodium to pass from the nephron to the blood. This causes water to flow into the blood by osmosis. Renin is released into the blood to control aldosterone.

Disruption of Kidney Function
Infection, environmental toxins such as mercury, and genetic disease can have devastating results by causing disruption of kidney function. Many kidney problems can be treated by dialysis, where a machine acts as a kidney. Kidney transplants are an alternative to dialysis.
THE RESPIRATORY SYSTEM

The Respiratory System and Gas Exchange
Cellular respiration involves the breakdown of organic molecules to produce ATP. A sufficient supply of oxygen is required for the aerobic respiratory machinery of Kreb's Cycle and the Electron Transport System to efficiently convert stored organic energy into energy trapped in ATP. Carbon dioxide is also generated by cellular metabolism and must be removed from the cell. There must be an exchange of gases: carbon dioxide leaving the cell, oxygen entering. Animals have organ systems involved in facilitating this exchange as well as the transport of gases to and from exchange areas.

Bodies and Respiration
Single-celled organisms exchange gases directly across their cell membrane. However, the slow diffusion rate of oxygen relative to carbon dioxide limits the size of single-celled organisms. Simple animals that lack specialized exchange surfaces have flattened, tubular, or thin shaped body plans, which are the most efficient for gas exchange. However, these simple animals are rather small in size.

Respiratory Surfaces
Large animals cannot maintain gas exchange by diffusion across their outer surface. They developed a variety of respiratory surfaces that all increase the surface area for exchange, thus allowing for larger bodies. A respiratory surface is covered with thin, moist epithelial cells that allow oxygen and carbon dioxide to exchange. Those gases can only cross cell membranes when they are dissolved in water or an aqueous solution, thus respiratory surfaces must be moist.

Methods of Respiration
Sponges and jellyfish lack specialized organs for gas exchange and take in gases directly from the surrounding water. Flatworms and annelids use their outer surfaces as gas exchange surfaces. Arthropods, annelids, and fish use gills; terrestrial vertebrates utilize internal lungs.

The Body Surface
Flatworms and annelids use their outer surfaces as gas exchange surfaces. Earthworms have a series of thin-walled blood vessels known as capillaries. Gas exchange occurs at capillaries located throughout the body as well as those in the respiratory surface. Amphibians use their skin as a respiratory surface. Frogs eliminate carbon dioxide 2.5 times as fast through their skin as they do through their lungs. Eels (a fish) obtain 60% of their oxygen through their skin. Humans exchange only 1% of their carbon dioxide through their skin. Constraints of water loss dictate that terrestrial animals must develop more efficient lungs.
**Gills**
Gills greatly increase the surface area for gas exchange. They occur in a variety of animal groups including arthropods (including some terrestrial crustaceans), annelids, fish, and amphibians. Gills typically are convoluted outgrowths containing blood vessels covered by a thin epithelial layer. Typically gills are organized into a series of plates and may be internal (as in crabs and fish) or external to the body (as in some amphibians). Gills are very efficient at removing oxygen from water: there is only 1/20 the amount of oxygen present in water as in the same volume of air. Water flows over gills in one direction while blood flows in the opposite direction through gill capillaries. This countercurrent flow maximizes oxygen transfer.

**Tracheal Systems**
Many terrestrial animals have their respiratory surfaces inside the body and connected to the outside by a series of tubes. Tracheae are these tubes that carry air directly to cells for gas exchange. Spiracles are openings at the body surface that lead to tracheae that branch into smaller tubes known as tracheoles. Body movements or contractions speed up the rate of diffusion of gases from tracheae into body cells. However, tracheae will not function well in animals whose body is longer than 5 cm.

**Lungs**
Lungs are ingrowths of the body wall and connect to the outside by as series of tubes and small openings. Lung breathing probably evolved about 400 million years ago. Lungs are not entirely the sole property of vertebrates, some terrestrial snails have a gas exchange structures similar to those in frogs.

**Respiratory System Principles**
- Movement of an oxygen-containing medium so it contacts a moist membrane overlying blood vessels.
- Diffusion of oxygen from the medium into the blood.
- Transport of oxygen to the tissues and cells of the body.
- Diffusion of oxygen from the blood into cells.
- Carbon dioxide follows a reverse path.

**The Human Respiratory System**
This system includes the lungs, pathways connecting them to the outside environment, and structures in the chest involved with moving air in and out of the lungs.

Air enters the body through the nose, is warmed, filtered, and passed through the nasal cavity. Air passes the pharynx (which has the epiglottis that prevents food from entering the trachea). The upper part of the trachea contains the larynx. The vocal cords are two
bands of tissue that extend across the opening of the larynx. After passing the larynx, the air moves into the bronchi that carry air in and out of the lungs.

Bronchi are reinforced to prevent their collapse and are lined with ciliated epithelium and mucus-producing cells. Bronchi branch into smaller and smaller tubes known as bronchioles. Bronchioles terminate in grape-like sac clusters known as alveoli. Alveoli are surrounded by a network of thin-walled capillaries. Only about 0.2 µm separate the alveoli from the capillaries due to the extremely thin walls of both structures.

The lungs are large, lobed, paired organs in the chest (also known as the thoracic cavity). Thin sheets of epithelium (pleura) separate the inside of the chest cavity from the outer surface of the lungs. The bottom of the thoracic cavity is formed by the diaphragm. Ventilation is the mechanics of breathing in and out. When you inhale, muscles in the chest wall contract, lifting the ribs and pulling them outward. The diaphragm at this time moves downward enlarging the chest cavity. Reduced air pressure in the lungs causes air to enter the lungs. Exhaling reverses these steps.

Diseases of the Respiratory System
The condition of the airways and the pressure difference between the lungs and atmosphere are important factors in the flow of air in and out of lungs. Many diseases affect the condition of the airways.

Asthma narrows the airways by causing an allergy-induced spasms of surrounding muscles or by clogging the airways with mucus.

Bronchitis is an inflammatory response that reduces airflow and is caused by long-term exposure to irritants such as cigarette smoke, air pollutants, or allergens.

Cystic fibrosis is a genetic defect that causes excessive mucus production that clogs the airways.

The Alveoli and Gas Exchange
Diffusion is the movement of materials from a higher to a lower concentration. The differences between oxygen and carbon dioxide concentrations are measured by partial pressures. The greater the difference in partial pressure the greater the rate of diffusion. Respiratory pigments increase the oxygen-carrying capacity of the blood. Humans have the red-colored pigment hemoglobin as their respiratory pigment. Hemoglobin increases the oxygen-carrying capacity of the blood between 65 and 70 times. Each red blood cell has about 250 million hemoglobin molecules, and each milliliter of blood contains $1.25 \times 10^{15}$ hemoglobin molecules. Oxygen concentration in cells is low (when leaving the lungs blood is 97% saturated with oxygen), so oxygen diffuses from the blood to the cells when it reaches the capillaries.

Carbon dioxide concentration in metabolically active cells is much greater than in
capillaries, so carbon dioxide diffuses from the cells into the capillaries. Water in the blood combines with carbon dioxide to form bicarbonate. This removes the carbon dioxide from the blood so diffusion of even more carbon dioxide from the cells into the capillaries continues yet still manages to "package" the carbon dioxide for eventual passage out of the body.

In the alveoli capillaries, bicarbonate combines with a hydrogen ion (proton) to form carbonic acid, which breaks down into carbon dioxide and water. The carbon dioxide then diffuses into the alveoli and out of the body with the next exhalation.

**Control of Respiration**
Muscular contraction and relaxation controls the rate of expansion and constriction of the lungs. These muscles are stimulated by nerves that carry messages from the part of the brain that controls breathing, the medulla. Two systems control breathing: an automatic response and a voluntary response. Both are involved in holding your breath. Although the automatic breathing regulation system allows you to breathe while you sleep, it sometimes malfunctions. Apnea involves stoppage of breathing for as long as 10 seconds, in some individuals as often as 300 times per night. This failure to respond to elevated blood levels of carbon dioxide may result from viral infections of the brain, tumors, or it may develop spontaneously. A malfunction of the breathing centers in newborns may result in SIDS (sudden infant death syndrome).

As altitude increases, atmospheric pressure decreases. Above 10,000 feet decreased oxygen pressures causes loading of oxygen into hemoglobin to drop off, leading to lowered oxygen levels in the blood. The result can be mountain sickness (nausea and loss of appetite). Mountain sickness does not result from oxygen starvation but rather from the loss of carbon dioxide due to increased breathing in order to obtain more oxygen.
THE DIGESTIVE SYSTEM
Animals, for the most part, ingest their food as large, complex molecules that must be broken down into smaller molecules (monomers) that can then be distributed throughout the body of every cell. This vital function is accomplished by a series of specialized organs that comprise the digestive system. Representative digestive systems are shown in Figure 1.

Digestive System
Single-celled organisms can directly take in nutrients from their outside environment. Multicellular animals, with most of their cells removed from contact directly with the outside environment, have developed specialized structures for obtaining and breaking down their food. Animals depend on two processes: feeding and digestion. Animals are **heterotrophs**, they must absorb nutrients or ingest food sources. **Ingestive eaters**, the majority of animals, use a mouth to ingest food. **Absorptive feeders**, such as tapeworms, live in a digestive system of another animal and absorb nutrients from that animal directly through their body wall. **Filter feeders**, such as oysters and mussels, collect small organisms and particles from the surrounding water. **Substrate feeders**, such as earthworms and termites, eat the material (dirt or wood) they burrow through. **Fluid feeders**, such as aphids, pierce the body of a plant or animal and withdraw fluids.

Plans and Locations
The digestive system uses mechanical and chemical methods to break food down into nutrient molecules that can be absorbed into the blood. Once in the blood, the food molecules are routed to every cell in the animal's body.
There are two types of animal body plans as well as two locations for digestion to occur. Sac-like plans are found in many invertebrates, who have a single opening for food intake
and the discharge of wastes. Vertebrates, the animal group humans belong to, use the more efficient **tube-within-a-tube plan** with food entering through one opening (the mouth) and wastes leaving through another (the anus).

Where the digestion of the food happens is also variable. Some animals use **intracellular digestion**, where food is taken into cells by **phagocytosis** with digestive enzymes being secreted into the phagocytic **vesicles**. This type of digestion occurs in sponges, coelenterates (corals, hydas and their relatives) and most protozoans. **Extracellular digestion** occurs in the lumen (or opening) of a digestive system, with the nutrient molecules being transferred to the blood or some other body fluid. This more advanced type of digestion occurs in chordates, annelids, and crustaceans.

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Food for the most part consists of various organic macromolecules such as starch, proteins, and fats. These molecules are polymers made of individual monomer units (as discussed in an earlier chapter). Breaking these large molecules into smaller components involves:

- **movement**: propels food through the digestive system
- **secretion**: release of digestive juices in response to a specific stimulus
- **digestion**: breakdown of food into molecular components small enough to cross the plasma membrane
- **absorption**: passage of the molecules into the body's interior and their passage throughout the body
- **elimination**: removal of undigested food and wastes

Three processes occur during what we loosely refer to as "digestion". Digestion proper, which is the mechanical and chemical breakdown of food into particles/molecules small enough to pass into the blood. Absorption is the passage of food monomers into the blood stream. Assimilation is the passage of the food molecules into body cells.

**Components of the Digestive System**

The human digestive system, is a coiled, muscular tube (6-9 meters long when fully extended) stretching from the mouth to the anus. Several specialized compartments occur along this length: mouth, pharynx, esophagus, stomach, small intestine, large intestine, and anus. Accessory digestive organs are connected to the main system by a series of ducts: salivary glands, parts of the pancreas, and the liver and gall bladder (**bilary system**).
The Mouth and Pharynx
Mechanical breakdown begins in the mouth by chewing (teeth) and actions of the tongue. Chemical breakdown of starch by production of salivary amylase from the salivary glands. This mixture of food and saliva is then pushed into the pharynx and esophagus. The esophagus is a muscular tube whose muscular contractions (peristalsis) propel food to the stomach.
In the mouth, teeth, jaws and the tongue begin the mechanical breakdown of food into smaller particles, as shown in Figure 3. Most vertebrates, except birds (who have lost their teeth to a hardened bill), have teeth for tearing, grinding and chewing food. The tongue manipulates food during chewing and swallowing; mammals have tastebuds clustered on
their tongues. Salivary glands secrete salivary amylase, an enzyme that begins the breakdown of starch into glucose. **Mucus** moistens food and lubricates the esophagus. Bicarbonate ions in saliva neutralize the acids in foods.

Swallowing moves food from the mouth through the pharynx into the esophagus and then to the stomach.

Step 1: A mass of chewed, moistened food, a bolus, is moved to the back of the mouth by the tongue. In the pharynx, the bolus triggers an involuntary swallowing reflex that prevents food from entering the lungs, and directs the bolus into the esophagus.

Step 2: Muscles in the esophagus propel the bolus by waves of involuntary muscular contractions (peristalsis) of smooth muscle lining the esophagus. Peristalsis is shown in Figure 4.

Step 3: The bolus passes through the gastroesophageal sphincter, into the stomach. Heartburn results from irritation of the esophagus by gastric juices that leak through this sphincter.

Figure 3. Structure of the throat and the mechanics of swallowing
The Stomach (or Churn, Churn, Churn)
During a meal, the stomach gradually fills to a capacity of 1 liter, from an empty capacity of 50-100 milliliters. At a price of discomfort, the stomach can distend to hold 2 liters or more.
Epithelial cells line inner surface of the stomach, as shown in Figure 5, and secrete about 2 liters of gastric juices per day. Gastric juice contains hydrochloric acid, pepsinogen, and mucus; ingredients important in digestion. Secretions are controlled by nervous (smells, thoughts, and caffeine) and endocrine signals. The stomach secretes hydrochloric acid and pepsin. Hydrochloric acid (HCl) lowers pH of the stomach so pepsin is activated. Pepsin is an enzyme that controls the hydrolysis of proteins into peptides. The stomach also mechanically churns the food. Chyme, the mix of acid and food in the stomach, leaves the stomach and enters the small intestine.
Hydrochloric acid does not directly function in digestion: it kills microorganisms, lowers the stomach pH to between 1.5 and 2.5; and activates pepsinogen. Pepsinogen is an enzyme that starts protein digestion. Pepsinogen is produced in cells that line the gastric pits. It is activated by cleaving off a portion of the molecule, producing the enzyme pepsin that splits off fragments of peptides from a protein molecule during digestion in the stomach.

Carbohydrate digestion, begun by salivary amylase in the mouth, continues in the bolus as it passes to the stomach. The bolus is broken down into acid chyme in the lower third of the stomach, allowing the stomach's acidity to inhibit further carbohydrate breakdown. Protein digestion by pepsin begins.

Alcohol and aspirin are absorbed through the stomach lining into the blood.

Epithelial cells secrete mucus that forms a protective barrier between the cells and the stomach acids. Pepsin is inactivated when it comes into contact with the mucus. Bicarbonate ions reduce acidity near the cells lining the stomach. **Tight junctions** link the epithelial stomach-lining cells together, further reducing or preventing stomach acids from passing.

**Ulcers**

Peptic ulcers result when these protective mechanisms fail. Bleeding ulcers result when tissue damage is so severe that bleeding occurs into the stomach. Perforated ulcers are life-threatening situations where a hole has formed in the stomach wall. At least 90% of all peptic ulcers are caused by *Helicobacter pylori*. Other factors, including stress and aspirin, can also produce ulcers.

**The Small Intestine**

The small intestine, shown in Figure 6, is where final digestion and absorption occur. The small intestine is a coiled tube over 3 meters long. Coils and folding plus villi give this 3m tube the surface area of a 500-600m long tube. Final digestion of proteins and carbohydrates must occur, and fats have not yet been digested. **Villi** have cells that produce intestinal enzymes which complete the digestion of peptides and sugars. The absorption process also occurs in the small intestine. Food has been broken down into particles small enough to pass into the small intestine. Sugars and amino acids go into the bloodstream via capillaries in each villus. Glycerol and fatty acids go into the lymphatic system. Absorption is an active transport, requiring cellular energy.
Food is mixed in the lower part of the stomach by peristaltic waves that also propel the acid-chyme mixture against the pyloric sphincter. Increased contractions of the stomach push the food through the sphincter and into the small intestine as the stomach empties over a 1 to 2 hour period. High fat diets significantly increase this time period. 

The small intestine is the major site for digestion and absorption of nutrients. The small intestine is up to 6 meters long and is 2-3 centimeters wide. The upper part, the duodenum, is the most active in digestion. Secretions from the liver and pancreas are used for digestion in the duodenum. Epithelial cells of the duodenum secrete a watery mucus. The pancreas secretes digestive enzymes and stomach acid-neutralizing bicarbonate. The liver produces bile, which is stored in the gall bladder before entering the bile duct into the duodenum. 

Digestion of carbohydrates, proteins, and fats continues in the small intestine. Starch and glycogen are broken down into maltose by small intestine enzymes. Proteases are enzymes
secreted by the pancreas that continue the breakdown of protein into small peptide fragments and amino acids.

Bile emulsifies fats, facilitating their breakdown into progressively smaller fat globules until they can be acted upon by lipases. Bile contains cholesterol, phospholipids, bilirubin, and a mix of salts. Fats are completely digested in the small intestine, unlike carbohydrates and proteins.

Most absorption occurs in the duodenum and jejunum (second third of the small intestine). The inner surface of the intestine has circular folds that more than triple the surface area for absorption. Villi covered with epithelial cells increase the surface area by another factor of 10. The epithelial cells are lined with microvilli that further increase the surface area; a 6 meter long tube has a surface area of 300 square meters.

Each villus has a surface that is adjacent to the inside of the small intestinal opening covered in microvilli that form on top of an epithelial cell known as a brush border. Each villus has a capillary network supplied by a small arteriole. Absorbed substances pass through the brush border into the capillary, usually by passive transport.

Maltose, sucrose, and lactose are the main carbohydrates present in the small intestine; they are absorbed by the microvilli. Starch is broken down into two-glucose units (maltose) elsewhere. Enzymes in the cells convert these disaccharides into monosaccharides that then leave the cell and enter the capillary. Lactose intolerance results from the genetic lack of the enzyme lactase produced by the intestinal cells.

Peptide fragments and amino acids cross the epithelial cell membranes by active transport. Inside the cell they are broken into amino acids that then enter the capillary. Gluten enteropathy is the inability to absorb gluten, a protein found in wheat.

Digested fats are not very soluble. Bile salts surround fats to form micelles, as shown in Figure 7, that can pass into the epithelial cells. The bile salts return to the lumen to repeat the process. Fat digestion is usually completed by the time the food reaches the ileum (lower third) of the small intestine. Bile salts are in turn absorbed in the ileum and are recycled by the liver and gall bladder. Fats pass from the epithelial cells to the small lymph vessel that also runs through the villus.
The Liver and Gall Bladder
The liver produces and sends bile to the small intestine via the hepatic duct, as illustrated in Figure 8. Bile contains bile salts, which emulsify fats, making them susceptible to enzymatic breakdown. In addition to digestive functions, the liver plays several other roles: 1) detoxification of blood; 2) synthesis of blood proteins; 3) destruction of old erythrocytes.
and conversion of **hemoglobin** into a component of bile; 4) production of bile; 5) storage of glucose as **glycogen**, and its release when blood sugar levels drop; and 6) production of urea from amino groups and ammonia.

Figure 8. The liver and associated organs and their connections to the digestive system
The gall bladder stores excess bile for release at a later time. We can live without our gall bladders, in fact many people have had theirs removed. The drawback, however, is a need to be aware of the amount of fats in the food they eat since the stored bile of the gall bladder is no longer available.

Glycogen is a polysaccharide made of chains of glucose molecules, as shown in Figure 9. In plants starch is the storage form of glucose, while animals use glycogen for the same purpose. Low glucose levels in the blood cause the release of hormones, such as glucagon, that travel to the liver and stimulate the breakdown of glycogen into glucose, which is then released into the blood(raising blood glucose levels). When no glucose or glycogen is available, amino acids are converted into glucose in the liver. The process of deamination removes the amino groups from amino acids. Urea is formed and passed through the blood to the kidney for export from the body. Conversely, the hormone insulin promotes the take-up of glucose into liver cells and its formation into glycogen.

Figure 9. Glycogen structure. Note the individual glucose molecules that are linked to form glycogen. Image from http://www.bio.brandeis.edu/classes/bio18/glycogen.gif.
Jaundice occurs when the characteristic yellow tint to the skin is caused by excess hemoglobin breakdown products in the blood, a sign that the liver is not properly functioning. Jaundice may occur when liver function has been impaired by obstruction of the bile duct and by damage caused by hepatitis.

Hepatitis A, B, and C are all viral diseases that can cause liver damage. Like any viral disease, the major treatment efforts focus on treatment of symptoms, not removal of the viral cause. Hepatitis A is usually mild malady indicated by a sudden fever, malaise, nausea, anorexia, and abdominal discomfort. Jaundice follows up for several days. The virus causing Hepatitis A is primarily transmitted by fecal contamination, although contaminated food and water also can promote transmission. A rare disease in the United States, hepatitis B is endemic in parts of Asia where hundreds of millions of individuals are possibly infected.

Hepatitis B may be transmitted by blood and blood products as well as sexual contact. The blood supply in developed countries has been screened for the virus that causes this disease for many years and transmission by blood transfusion is rare. The risk of HBV infection is high among promiscuous homosexual men although it is also transmitted heterosexually. Correct use of condoms is thought to reduce or eliminate the risk of transmission. Effective vaccines are available for the prevention of Hepatitis B infection. Some individuals with chronic hepatitis B may develop cirrhosis of the liver. Individuals with chronic hepatitis B are at an increased risk of developing primary liver cancer. Although this type of cancer is relatively rare in the United States, it is the leading cause of cancer death in the world, primarily because the virus causing it is endemic in eastern Asia.

Hepatitis C affects approximately 170 million people worldwide and 4 million in the United States. The virus is transmitted primarily by blood and blood products. Most infected individuals have either received blood transfusions prior to 1990 (when screening of the blood supply for the Hepatitis C virus began) or have used intravenous drugs. Sexual transmission can occur between monogamous couples (rare) but infection is far more common in those who are promiscuous. In rare cases, Hepatitis C causes acute disease and even liver failure. About twenty percent of individuals with Hepatitis C who develop cirrhosis of the liver will also develop severe liver disease. Cirrhosis caused by Hepatitis C is presently the leading cause of the need for liver transplants in the United States. Individuals with cirrhosis from Hepatitis C also bear increased chances of developing primary liver cancer. All current treatments for Hepatitis C employ of various preparations of the potent antiviral interferon alpha. However, not all patients who have the disease are good candidates for treatment, so infected individuals are urged to regularly consult their physician.

Cirrhosis of the liver commonly occurs in alcoholics, who place the liver in a stress situation due to the amount of alcohol to be broken down. Cirrhosis can cause the liver to become unable to perform its biochemical functions. Chemicals responsible for blood clotting are synthesized in the liver, as is albumin, the major protein in blood. The liver also makes or modifies bile components. Blood from the circulatory system passes through
the liver, so many of the body's metabolic functions occur primarily there including the metabolism of cholesterol and the conversion of proteins and fats into glucose. Cirrhosis is a disease resulting from damage to liver cells due to toxins, inflammation, and other causes. Liver cells regenerate in an abnormal pattern primarily forming nodules that are surrounded by fibrous tissue. Changes in the structure of the liver can decrease blood flow, leading to secondary complications. Cirrhosis has many causes, including alcoholic liver disease, severe forms of some viral hepatitis, congestive heart failure, parasitic infections (for example schistosomiasis), and long term exposure to toxins or drugs.

The Pancreas

The pancreas sends pancreatic juice, which neutralizes the chyme, to the small intestine through the pancreatic duct. In addition to this digestive function, the pancreas is the site of production of several hormones, such as glucagon and insulin. The pancreas contains exocrine cells that secrete digestive enzymes into the small intestine and clusters of endocrine cells (the pancreatic islets). The islets secrete the hormones insulin and glucagon, which regulate blood glucose levels.

After a meal, blood glucose levels rise, prompting the release of insulin, which causes cells to take up glucose, and liver and skeletal muscle cells to form the carbohydrate glycogen. As glucose levels in the blood fall, further insulin production is inhibited. Glucagon causes the breakdown of glycogen into glucose, which in turn is released into the blood to maintain glucose levels within a homeostatic range. Glucagon production is stimulated when blood glucose levels fall, and inhibited when they rise.

Diabetes results from inadequate levels of insulin. Type I diabetes is characterized by inadequate levels of insulin secretion, often due to a genetic cause. Type II usually develops in adults from both genetic and environmental causes. Loss of response of targets to insulin rather than lack of insulin causes this type of diabetes. Diabetes may cause impairment in the functioning of the eyes, circulatory system, nervous system, and failure of the kidneys. Diabetes is the second leading cause of blindness in the United States. Treatments might involve daily injections of insulin, oral medications such as metformin, monitoring of blood glucose levels, and a controlled diet. Type I diabetes may one day be cured by advances in gene therapy/stem cell research. On recently recognized condition is known as prediabetes, in which the body gradually loses its sensitivity to insulin, leading eventually to Type II diabetes. Or; medications, diet and behavior (in other words EXERCISE!!!) changes are thought to delay if not outright postpone the onset of diabetes if corrected soon enough.

The fifth leading cause of cancer death in the United States is from pancreatic cancer, which is nearly always fatal. Scientists estimate that 25,000 people may die from this disease each year. Standard treatments are ineffective, although some promising avenues may open with advances in genomics and molecular biology of cancer cells.

The Large Intestine
The large intestine is made up by the colon, cecum, appendix, and rectum. Material in the large intestine is mostly indigestible residue and liquid. Movements are due to involuntary contractions that shuffle contents back and forth and propulsive contractions that move material through the large intestine. The large intestine performs three basic functions in vertebrates: 1) recovery of water and electrolytes from digested food; 2) formation and storage of feces; and 3) microbial fermentation: The large intestine supports an amazing flora of microbes. Those microbes produce enzymes that can digest many of molecules indigestible by vertebrates.

Secretions in the large intestine are an alkaline mucus that protects epithelial tissues and neutralizes acids produced by bacterial metabolism. Water, salts, and vitamins are absorbed, the remaining contents in the lumen form feces (mostly cellulose, bacteria, bilirubin). Bacteria in the large intestine, such as *E. coli*, produce vitamins (including vitamin K) that are absorbed.

**Regulation of Appetite**

The hypothalamus in the brain has two centers controlling hunger. One is the appetite center, the other the satiety center. Gastrin, secretin, and cholecystokinin are hormones that regulate various stages of digestion. The presence of protein in the stomach stimulates secretion of gastrin, which in turn will cause increased stomach acid secretion and mobility of the digestive tract to move food. Food passing into the duodenum causes the production of secretin, which in turn promotes release of alkaline secretions from the pancreas, stops further passage of food into the intestine until the acid is neutralized. Cholecystokinin (CCK) is released from intestinal epithelium in response to fats, and causes the release of bile from the gall bladder and lipase (a fat digesting enzyme) from the pancreas.

**Nutrition**

Nutrition deals with the composition of food, its energy content, and slowly (or not at all) synthesized organic molecules. Chemotrophs are organisms (mostly bacteria) deriving their energy from inorganic chemical reactions. Phototrophs convert sunlight energy into sugar or other organic molecules. Heterotrophs eat to obtain energy from the breakdown of organic molecules in their food. Macronutrients are foods required on a large scale each day. These include carbohydrates, lipids, and amino acids. Water is essential, correct water balance is a must for proper functioning of the body.

About 60% of the diet should be carbohydrates, obtained from foods such as milk, meat, vegetables, grains and grain products. The diet should contain at least 100 grams of carbohydrate every day. Recently, however, new recommendations have been developed that suggest a lowering of the amount of carbohydrate. A more detailed presentation of this topic may be found at [http://health.discovery.com/diseasesandcond/encyclopedia/2935.html](http://health.discovery.com/diseasesandcond/encyclopedia/2935.html).
Proteins are polymers composed of amino acids. Proteins are found in meat, milk, poultry, fish, cereal grains and beans. They are needed for cellular growth and repair. Twenty amino acids are found in proteins, of which humans can make eleven. The remaining nine are the essential amino acids which must be supplied in the diet. Normally proteins are not used for energy, however during starvation (or a low-carb diet) muscle proteins are broken down for energy. Excess protein can be used for energy or converted to fats.

Lipids and fats generate the greatest energy yield, so a large number of plants and animals store excess food energy as fats. Lipids and fats are present in oils, meats, butter, and plants (such as avocado and peanuts). Some fatty acids, such as linoleic acid, are essential and must be included in the diet. When present in the intestine, lipids promote the uptake of vitamins A, D, E, and K.

Vitamins are organic molecules required for metabolic reactions. They usually cannot be made by the body and are needed in trace amounts. Vitamins may act as enzyme cofactors or coenzymes. Some vitamins are soluble in fats, some in water.

Minerals are trace elements required for normal metabolism, as components of cells and tissues, and for nerve conduction and muscle contraction. They can only be obtained from the diet. Iron (for hemoglobin), iodine (for thyroxin), calcium (for bones), and sodium (nerve message transmission) are examples of minerals.

There is a quantitative relationship between nutrients and health. Imbalances can cause disease. Many studies have concluded nutrition is a major factor in cardiovascular disease, hypertension, and cancer.