A sarcomere is the region from one Z line to the next Z line. Many sarcomeres are present in a myofibril, resulting in the striation pattern characteristic of skeletal

muscle.

Myofibrils are composed of smaller structures called myofilaments. There are two main types of filaments: thick filaments and thin filaments; each has different compositions and locations. Thick filaments occur only in the A band of a myofibril. Thin filaments attach to a protein in the Z disc called alpha-actinin and occur across the entire length of the I band and partway into the A band. The region at which thick and thin filaments overlap has a dense appearance, as there is little space between the filaments. Thin filaments do not extend all the way into the A bands, leaving a central region of the A band that only contains thick filaments. This central region of the A band looks slightly lighter than the rest of the A band and is called the H zone. The middle of the H zone has a vertical line called the M line, at which accessory proteins hold together thick filaments. Both the Z disc and the M line hold myofilaments in place to maintain the structural arrangement and layering of the myofibril. Myofibrils are connected to each other by intermediate, or desmin, filaments that attach to the Z disc.

Thick and thin filaments are themselves composed of proteins. Thick filaments are composed of the protein myosin. The tail of a myosin molecule connects with other myosin molecules to form the central region of a thick filament near the M line, whereas the heads align on either side of the thick filament where the thin filaments overlap. The primary component of thin filaments is the actin protein. Two other components of the thin filament are tropomyosin and troponin. Actin has binding sites for myosin attachment. Strands of tropomyosin block the binding sites and prevent actin–myosin interactions when the muscles are at rest. Troponin consists of three globular subunits. One subunit binds to tropomyosin, one subunit binds to actin, and one subunit binds Ca^{2+} ions.

Link to Learning

View this animation showing the organization of muscle fibers.

Bone

By the end of this section, you will be able to:

- Classify the different types of bones in the skeleton
- Explain the role of the different cell types in bone
- Explain how bone forms during development

Bone, or osseous tissue, is a connective tissue that constitutes the endoskeleton. It contains specialized cells and a matrix of mineral salts and collagen fibers.

The mineral salts primarily include hydroxyapatite, a mineral formed from calcium phosphate. Calcification is the process of deposition of mineral salts on the collagen fiber matrix that crystallizes and hardens the tissue. The process of calcification only occurs in the presence of collagen fibers.

The bones of the human skeleton are classified by their shape: long bones, short bones, flat bones, sutural bones, sesamoid bones, and irregular bones ([link]).

Shown are different types of bones: flat, irregular, long, short, and sesamoid.

Long bones are longer than they are wide and have a shaft and two ends. The diaphysis, or central shaft, contains bone marrow in a marrow cavity. The rounded ends, the epiphyses, are covered with articular cartilage and are filled with red bone marrow, which produces blood cells ([link]). Most of the limb bones are long bones—for example, the femur, tibia, ulna, and radius. Exceptions to this include the patella and the bones of the wrist and ankle.

The long bone is covered by articular cartilage at either end and contains bone marrow (shown in yellow in this illustration) in the marrow

cavity.

Short bones, or cuboidal bones, are bones that are the same width and length, giving them a cube-like shape. For example, the bones of the wrist (carpals) and ankle (tarsals) are short bones ([link]).

Flat bones are thin and relatively broad bones that are found where extensive protection of organs is required or where broad surfaces of muscle attachment are required. Examples of flat bones are the sternum (breast bone), ribs, scapulae (shoulder blades), and the roof of the skull ([link]).

Irregular bones are bones with complex shapes. These bones may have short, flat, notched, or ridged surfaces. Examples of irregular bones are the vertebrae, hip bones, and several skull bones.

Sesamoid bones are small, flat bones and are shaped similarly to a sesame seed. The patellae are sesamoid bones ([link]). Sesamoid bones develop inside tendons and may be found near joints at the knees, hands, and feet.

The patella of the knee is an example of a sesamoid

bone.

Sutural bones are small, flat, irregularly shaped bones. They may be found between the flat bones of the skull. They vary in number, shape, size, and position.

Bone Tissue

Bones are considered organs because they contain various types of tissue, such as blood, connective tissue, nerves, and bone tissue. Osteocytes, the living cells of bone tissue, form the mineral matrix of bones. There are two types of bone tissue: compact and spongy.

Compact Bone Tissue

Compact bone (or cortical bone) forms the hard external layer of all bones and surrounds the medullary cavity, or bone marrow. It provides protection and strength to bones. Compact bone tissue consists of units called osteons or Haversian systems. Osteons are cylindrical structures that contain a mineral matrix and living osteocytes connected by canaliculi, which transport blood. They are aligned parallel to the long axis of the bone. Each osteon consists of lamellae, which are layers of compact matrix that surround a central canal called the Haversian canal. The Haversian canal (osteonic canal) contains the bone's blood vessels and nerve fibers ([link]). Osteons in compact bone tissue are aligned in the same direction along lines of stress and help the bone resist bending or fracturing. Therefore, compact bone tissue is prominent in areas of bone at which stresses are applied in only a few directions.

Art Connection
Compact bone tissue consists of osteons that are aligned parallel to the long axis of the bone, and the Haversian canal that contains the bone's blood vessels and nerve fibers. The inner layer of bones consists of spongy bone tissue. The small dark ovals in the osteon represent

the living osteocytes. (credit: modification of work by NCI, NIH)

Which of the following statements about bone tissue is false?

a. Compact bone tissue is made of cylindrical osteons that are aligned such that they travel the length of the bone.
b. Haversian canals contain blood vessels only.
c. Haversian canals contain blood vessels and nerve fibers.
d. Spongy tissue is found on the interior of the bone, and compact bone tissue is found on the exterior.

Spongy Bone Tissue

Whereas compact bone tissue forms the outer layer of all bones, spongy bone or cancellous bone forms the inner layer of all bones. Spongy bone tissue does not contain osteons that constitute compact bone tissue. Instead, it consists of trabeculae, which are lamellae that are arranged as rods or plates. Red bone marrow is found between the trabuculae. Blood vessels within this tissue deliver nutrients to osteocytes and remove waste. The red bone marrow of the femur and the interior of other large bones, such as the ileum, forms blood cells.

Spongy bone reduces the density of bone and allows the ends of long bones to compress as the result of stresses applied to the bone. Spongy bone is prominent in areas of bones that are not heavily stressed or where stresses arrive from many directions. The epiphyses of bones, such as the neck of the femur, are subject to stress from many directions. Imagine laying a heavy framed picture flat on the floor. You could hold up one side of the picture with a toothpick if the toothpick was perpendicular to the floor and the picture. Now drill a hole and stick the toothpick into the wall to hang up the picture. In this case, the function of the toothpick is to transmit the downward pressure of the picture to the wall. The force on the picture is straight down to the floor, but the force on the toothpick is both the picture wire pulling down and the bottom of the hole in the wall pushing up. The toothpick will break off right at the wall.

The neck of the femur is horizontal like the toothpick in the wall. The weight of the body pushes it down near the joint, but the vertical diaphysis of the femur pushes it up at the other

end. The neck of the femur must be strong enough to transfer the downward force of the body weight horizontally to the vertical shaft of the femur ([link]).

Trabeculae in spongy bone are arranged such that one side of the bone bears tension and the other withstands compression.

Link to Learning

View micrographs of musculoskeletal tissues as you review the anatomy.

Cell Types in Bones

Bone consists of four types of cells: osteoblasts, osteoclasts, osteocytes, and osteoprogenitor cells. Osteoblasts are bone cells that are responsible for bone formation. Osteoblasts synthesize and secrete the organic part and inorganic part of the extracellular matrix of bone tissue, and collagen fibers. Osteoblasts become trapped in these secretions and differentiate into less active osteocytes. Osteoclasts are large bone cells with up to 50 nuclei. They remove bone structure by releasing lysosomal enzymes and acids that dissolve the bony matrix. These minerals, released from bones into the blood, help regulate calcium concentrations in body fluids. Bone may also be resorbed for remodeling, if the applied stresses have changed. Osteocytes are mature bone cells and are the main cells in bony connective tissue; these cells cannot divide. Osteocytes maintain normal bone structure by recycling the mineral salts in the bony matrix. Osteoprogenitor cells are squamous stem cells that divide to produce daughter cells that differentiate into osteoblasts. Osteoprogenitor cells are important in the repair of fractures.

Development of Bone

Ossification, or osteogenesis, is the process of bone formation by osteoblasts. Ossification is distinct from the process of calcification; whereas calcification takes place during the

ossification of bones, it can also occur in other tissues. Ossification begins approximately six weeks after fertilization in an embryo. Before this time, the embryonic skeleton consists entirely of fibrous membranes and hyaline cartilage. The development of bone from fibrous membranes is called intramembranous ossification; development from hyaline cartilage is called endochondral ossification. Bone growth continues until approximately age 25. Bones can grow in thickness throughout life, but after age 25, ossification functions primarily in bone remodeling and repair.

Intramembranous Ossification

Intramembranous ossification is the process of bone development from fibrous membranes. It is involved in the formation of the flat bones of the skull, the mandible, and the clavicles. Ossification begins as mesenchymal cells form a template of the future bone. They then differentiate into osteoblasts at the ossification center. Osteoblasts secrete the extracellular matrix and deposit calcium, which hardens the matrix. The non-mineralized portion of the bone or osteoid continues to form around blood vessels, forming spongy bone. Connective tissue in the matrix differentiates into red bone marrow in the fetus. The spongy bone is remodeled into a thin layer of compact bone on the surface of the spongy bone.

Endochondral Ossification

Endochondral ossification is the process of bone development from hyaline cartilage. All of the bones of the body, except for the flat bones of the skull, mandible, and clavicles, are formed through endochondral ossification.

In long bones, chondrocytes form a template of the hyaline cartilage diaphysis. Responding to complex developmental signals, the matrix begins to calcify. This calcification prevents diffusion of nutrients into the matrix, resulting in chondrocytes dying and the opening up of cavities in the diaphysis cartilage. Blood vessels invade the cavities, and osteoblasts and osteoclasts modify the calcified cartilage matrix into spongy bone. Osteoclasts then break down some of the spongy bone to create a marrow, or medullary, cavity in the center of the diaphysis. Dense, irregular connective tissue forms a sheath (periosteum) around the bones. The periosteum assists in attaching the bone to surrounding tissues, tendons, and ligaments. The bone continues to grow and elongate as the cartilage cells at the epiphyses divide.

In the last stage of prenatal bone development, the centers of the epiphyses begin to calcify. Secondary ossification centers form in the epiphyses as blood vessels and osteoblasts enter these areas and convert hyaline cartilage into spongy bone. Until adolescence, hyaline cartilage persists at the epiphyseal plate (growth plate), which is the region between the diaphysis and epiphysis that is responsible for the lengthwise growth of long bones ([link]).

Endochondral ossification is the process of bone development from hyaline cartilage. The periosteum is the connective tissue on the outside of bone that acts as the interface between bone, blood vessels, tendons, and

ligaments.

Growth of Bone

Long bones continue to lengthen, potentially until adolescence, through the addition of bone tissue at the epiphyseal plate. They also increase in width through appositional growth.

Lengthening of Long Bones

Chondrocytes on the epiphyseal side of the epiphyseal plate divide; one cell remains undifferentiated near the epiphysis, and one cell moves toward the diaphysis. The cells, which are pushed from the epiphysis, mature and are destroyed by calcification. This process replaces cartilage with bone on the diaphyseal side of the plate, resulting in a lengthening of the bone.

Long bones stop growing at around the age of 18 in females and the age of 21 in males in a process called epiphyseal plate closure. During this process, cartilage cells stop dividing and all of the cartilage is replaced by bone. The epiphyseal plate fades, leaving a structure called the epiphyseal line or epiphyseal remnant, and the epiphysis and diaphysis fuse.

Thickening of Long Bones

Appositional growth is the increase in the diameter of bones by the addition of bony tissue at the surface of bones. Osteoblasts at the bone surface secrete bone matrix, and osteoclasts on the inner surface break down bone. The osteoblasts differentiate into osteocytes. A balance between these two processes allows the bone to thicken without becoming too heavy.

Bone Remodeling and Repair

Bone renewal continues after birth into adulthood. Bone remodeling is the replacement of old bone tissue by new bone tissue. It involves the processes of bone deposition by osteoblasts and bone resorption by osteoclasts. Normal bone growth requires vitamins D, C, and A, plus minerals such as calcium, phosphorous, and magnesium. Hormones such as parathyroid hormone, growth hormone, and calcitonin are also required for proper bone growth and maintenance.

Bone turnover rates are quite high, with five to seven percent of bone mass being recycled every week. Differences in turnover rate exist in different areas of the skeleton and in different areas of a bone. For example, the bone in the head of the femur may be fully replaced every six months, whereas the bone along the shaft is altered much more slowly.

Bone remodeling allows bones to adapt to stresses by becoming thicker and stronger when subjected to stress. Bones that are not subject to normal stress, for example when a limb is in a cast, will begin to lose mass. A fractured or broken bone undergoes repair through four stages:

1. Blood vessels in the broken bone tear and hemorrhage, resulting in the formation of clotted blood, or a hematoma, at the site of the break. The severed blood vessels at the broken ends of the bone are sealed by the clotting process, and bone cells that are deprived of nutrients begin to die.
2. Within days of the fracture, capillaries grow into the hematoma, and phagocytic cells begin to clear away the dead cells. Though fragments of the blood clot may remain, fibroblasts and osteoblasts enter the area and begin to reform bone. Fibroblasts produce collagen fibers that connect the broken bone ends, and osteoblasts start to form spongy bone. The repair tissue between the broken bone ends is called the fibrocartilaginous callus, as it is composed of both hyaline and fibrocartilage ([link]). Some bone spicules may also appear at this point.
3. The fibrocartilaginous callus is converted into a bony callus of spongy bone. It takes about two months for the broken bone ends to be firmly joined together after the fracture. This is similar to the endochondral formation of bone, as cartilage becomes ossified; osteoblasts, osteoclasts, and bone matrix are present.
4. The bony callus is then remodelled by osteoclasts and osteoblasts, with excess material on the exterior of the bone and within the medullary cavity being removed. Compact bone is added to create bone tissue that is similar to the original, unbroken bone. This remodeling can take many months, and the bone may remain uneven for years.

After this bone is set, a callus will knit the two ends together. (credit: Bill Rhodes)

Scientific Method Connection

Decalcification of Bones **Question:** What effect does the removal of calcium and collagen have on bone structure?

Background: Conduct a literature search on the role of calcium and collagen in maintaining bone structure. Conduct a literature search on diseases in which bone structure is compromised.

Hypothesis: Develop a hypothesis that states predictions of the flexibility, strength, and mass of bones that have had the calcium and collagen components removed. Develop a hypothesis regarding the attempt to add calcium back to decalcified bones.

Test the hypothesis: Test the prediction by removing calcium from chicken bones by placing them in a jar of vinegar for seven days. Test the hypothesis regarding adding calcium back to decalcified bone by placing the decalcified chicken bones into a jar of water with calcium supplements added. Test the prediction by denaturing the collagen from the bones by baking them at 250°C for three hours.

Analyze the data: Create a table showing the changes in bone flexibility, strength, and mass in the three different environments.

Report the results: Under which conditions was the bone most flexible? Under which conditions was the bone the strongest?

Draw a conclusion: Did the results support or refute the hypothesis? How do the results observed in this experiment correspond to diseases that destroy bone tissue?

Section Summary

Bone, or osseous tissue, is connective tissue that includes specialized cells, mineral salts, and collagen fibers. The human skeleton can be divided into long bones, short bones, flat bones, and irregular bones. Compact bone tissue is composed of osteons and forms the external layer of all bones. Spongy bone tissue is composed of trabeculae and forms the inner part of all bones. Four types of cells compose bony tissue: osteocytes, osteoclasts, osteoprogenitor cells, and osteoblasts. Ossification is the process of bone formation by osteoblasts. Intramembranous ossification is the process of bone development from fibrous membranes. Endochondral ossification is the process of bone development from hyaline cartilage. Long bones lengthen as chondrocytes divide and secrete hyaline cartilage. Osteoblasts replace

cartilage with bone. Appositional growth is the increase in the diameter of bones by the addition of bone tissue at the surface of bones. Bone remodeling involves the processes of bone deposition by osteoblasts and bone resorption by osteoclasts. Bone repair occurs in four stages and can take several months.

Art Exercise

[link] Which of the following statements about bone tissue is false?

a. Compact bone tissue is made of cylindrical osteons that are aligned such that they travel the length of the bone.
b. Haversian canals contain blood vessels only.
c. Haversian canals contain blood vessels and nerve fibers.
d. Spongy tissue is found on the interior of the bone, and compact bone tissue is found on the exterior.

[link]B

Review Questions

The Haversian canal:

a. is arranged as rods or plates
b. contains the bone's blood vessels and nerve fibers
c. is responsible for the lengthwise growth of long bones
d. synthesizes and secretes matrix

B

The epiphyseal plate:

a. is arranged as rods or plates
b. contains the bone's blood vessels and nerve fibers
c. is responsible for the lengthwise growth of long bones
d. synthesizes and secretes bone matrix

C

The cells responsible for bone resorption are _____.

a. osteoclasts
b. osteoblasts
c. fibroblasts
d. osteocytes

A

Compact bone is composed of _____.

a. trabeculae

b. compacted collagen
c. osteons
d. calcium phosphate only

C

Free Response

What are the major differences between spongy bone and compact bone?

Compact bone tissue forms the hard external layer of all bones and consists of osteons. Compact bone tissue is prominent in areas of bone at which stresses are applied in only a few directions. Spongy bone tissue forms the inner layer of all bones and consists of trabeculae. Spongy bone is prominent in areas of bones that are not heavily stressed or at which stresses arrive from many directions.

What are the roles of osteoblasts, osteocytes, and osteoclasts?

Osteocytes function in the exchange of nutrients and wastes with the blood. They also maintain normal bone structure by recycling the mineral salts in the bony matrix. Osteoclasts remove bone tissue by releasing lysosomal enzymes and acids that dissolve the bony matrix. Osteoblasts are bone cells that are responsible for bone formation.

Glossary

appositional growth
: increase in the diameter of bones by the addition of bone tissue at the surface of bones

bone
: (also, osseous tissue) connective tissue that constitutes the endoskeleton

bone remodeling
: replacement of old bone tissue by new bone tissue

calcification
: process of deposition of mineral salts in the collagen fiber matrix that crystallizes and hardens the tissue

compact bone
: forms the hard external layer of all bones

diaphysis
: central shaft of bone, contains bone marrow in a marrow cavity

endochondral ossification
: process of bone development from hyaline cartilage

epiphyseal plate
: region between the diaphysis and epiphysis that is responsible for the lengthwise growth of long bones

epiphysis
: rounded end of bone, covered with articular cartilage and filled with red bone marrow, which produces blood cells

flat bone
: thin and relatively broad bone found where extensive protection of organs is required or where broad surfaces of muscle attachment are required

Haversian canal
: contains the bone’s blood vessels and nerve fibers

intramembranous ossification
: process of bone development from fibrous membranes

irregular bone
: bone with complex shapes; examples include vertebrae and hip bones

lamella
: layer of compact tissue that surrounds a central canal called the Haversian canal

long bone
: bone that is longer than wide, and has a shaft and two ends

osteoblast
: bone cell responsible for bone formation

osteoclast
: large bone cells with up to 50 nuclei, responsible for bone remodeling

osteocyte
: mature bone cells and the main cell in bone tissue

osseous tissue
: connective tissue that constitutes the endoskeleton

ossification
: (also, osteogenesis) process of bone formation by osteoblasts

osteon
: cylindrical structure aligned parallel to the long axis of the bone

resorption
: process by which osteoclasts release minerals stored in bones

sesamoid bone
: small, flat bone shaped like a sesame seed; develops inside tendons

short bone
: bone that has the same width and length, giving it a cube-like shape

spongy bone tissue
: forms the inner layer of all bones

suture bone
: small, flat, irregularly shaped bone that forms between the flat bones of the cranium

trabeculae
: lamellae that are arranged as rods or plates

Introduction

class="introduction" class="summary" title="Sections Summary" class="art-exercise" title="Art Connections" class="multiple-choice" title="Multiple Choice" class="free-response" title="Free Response"Lungs, which appear as nearly transparent tissue surrounding the heart in this X-ray of a dog (left), are the central organs of the respiratory system. The left lung is smaller than the right lung to accommodate space for the heart. A dog’s nose (right)

has a slit on the side of each nostril. When tracking a scent, the slits open, blocking the front of the nostrils. This allows the dog to exhale though the now-open area on the side of the nostrils without losing the scent that is being followed. (credit a: modification of work by Geoff Stearns; credit b: modification of work by Cory
Zanker)

Breathing is an involuntary event. How often a breath is taken and how much air is inhaled or exhaled are tightly regulated by the respiratory center in the brain. Humans, when they aren't exerting themselves, breathe approximately 15 times per minute on average. Canines, like the dog in [link], have a respiratory rate of about 15–30 breaths per minute. With every inhalation, air fills the lungs, and with every exhalation, air rushes back out. That air is doing more than just inflating and deflating the lungs in the chest cavity. The air contains oxygen that crosses the lung tissue, enters the bloodstream, and travels to organs and tissues. Oxygen (O_2) enters the cells where it is used for metabolic reactions that produce ATP, a high-energy compound. At the same time, these reactions release carbon dioxide (CO_2)

as a by-product. CO_2 is toxic and must be eliminated. Carbon dioxide exits the cells, enters the bloodstream, travels back to the lungs, and is expired out of the body during exhalation.

Systems of Gas Exchange
By the end of this section, you will be able to:

- Describe the passage of air from the outside environment to the lungs
- Explain how the lungs are protected from particulate matter

The primary function of the respiratory system is to deliver oxygen to the cells of the body's tissues and remove carbon dioxide, a cell waste product. The main structures of the human respiratory system are the nasal cavity, the trachea, and lungs.

All aerobic organisms require oxygen to carry out their metabolic functions. Along the evolutionary tree, different organisms have devised different means of obtaining oxygen from the surrounding atmosphere. The environment in which the animal lives greatly determines how an animal respires. The complexity of the respiratory system is correlated with the size of the organism. As animal size increases, diffusion distances increase and the ratio of surface area to volume drops. In unicellular organisms, diffusion across the cell membrane is sufficient for supplying oxygen to the cell ([link]). Diffusion is a slow, passive transport process. In order for diffusion to be a feasible means of providing oxygen to the cell, the rate of oxygen uptake must match the rate of diffusion across the membrane. In other words, if the cell were very large or thick, diffusion would not be able to provide oxygen quickly enough to the inside of the cell. Therefore, dependence on diffusion as a means of obtaining oxygen and removing carbon dioxide remains feasible only for small organisms or those with highly-flattened bodies, such as many flatworms (Platyhelminthes). Larger organisms had to evolve specialized respiratory tissues, such as gills, lungs, and respiratory passages accompanied by complex circulatory systems, to transport oxygen throughout their entire body.

The cell of the unicellular algae *Ventricaria ventricosa* is one of the largest known, reaching one to five centimeters in diameter. Like all single-celled organisms, *V. ventricosa* exchanges gases across the cell membrane.

Direct Diffusion

For small multicellular organisms, diffusion across the outer membrane is sufficient to meet their oxygen needs. Gas exchange by direct diffusion across surface membranes is efficient for organisms less than 1 mm in diameter. In simple organisms, such as cnidarians and flatworms, every cell in the body is close to the external environment. Their cells are kept moist and gases diffuse quickly via direct diffusion. Flatworms are small, literally flat worms, which ‘breathe’ through diffusion across the outer membrane ([link]). The flat shape of these organisms increases the surface area for diffusion, ensuring that each cell within the body is close to the outer membrane surface and has access to oxygen. If the flatworm had a cylindrical body, then the cells in the center would not be able to get oxygen.

This flatworm’s process of respiration works by diffusion across the outer membrane. (credit: Stephen Childs)

Skin and Gills

Earthworms and amphibians use their skin (integument) as a respiratory organ. A dense network of capillaries lies just below the skin and facilitates gas exchange between the external environment and the circulatory system. The respiratory surface must be kept moist in order for the gases to dissolve and diffuse across cell membranes.

Organisms that live in water need to obtain oxygen from the water. Oxygen dissolves in water but at a lower concentration than in the atmosphere. The atmosphere has roughly 21 percent oxygen. In water, the oxygen concentration is much smaller than that. Fish and many other aquatic organisms have evolved gills to take up the dissolved oxygen from water ([link]). Gills are thin tissue filaments that are highly branched and folded. When water passes over the gills, the dissolved oxygen in water rapidly diffuses across the gills into the bloodstream. The circulatory system can then carry the oxygenated blood to the other parts of the body. In animals that contain coelomic fluid instead of blood, oxygen diffuses across the gill surfaces into the coelomic fluid. Gills are found in mollusks, annelids, and crustaceans.

This common carp, like many other aquatic organisms, has gills that allow it to obtain oxygen from water. (credit: "Guitardude012"/Wikimedia

Commons)

The folded surfaces of the gills provide a large surface area to ensure that the fish gets sufficient oxygen. Diffusion is a process in which material travels from regions of high concentration to low concentration until equilibrium is reached. In this case, blood with a low concentration of oxygen molecules circulates through the gills. The concentration of oxygen molecules in water is higher than the concentration of oxygen molecules in gills. As a result, oxygen molecules diffuse from water (high concentration) to blood (low concentration), as shown in [link]. Similarly, carbon dioxide molecules in the blood diffuse from the blood (high concentration) to water (low concentration).

As water flows over the gills, oxygen is transferred to blood via the veins. (credit "fish": modification of work by Duane Raver,

NOAA)

Tracheal Systems

Insect respiration is independent of its circulatory system; therefore, the blood does not play a direct role in oxygen transport. Insects have a highly specialized type of respiratory system called the tracheal system, which consists of a network of small tubes that carries oxygen to the entire body. The tracheal system is the most direct and efficient respiratory system in active animals. The tubes in the tracheal system are made of a polymeric material called chitin.

Insect bodies have openings, called spiracles, along the thorax and abdomen. These openings connect to the tubular network, allowing oxygen to pass into the body ([link]) and regulating the diffusion of CO_2 and water vapor. Air enters and leaves the tracheal system through the spiracles. Some insects can ventilate the tracheal system with body movements.

Insects perform respiration via a tracheal

system.

Mammalian Systems

In mammals, pulmonary ventilation occurs via inhalation (breathing). During inhalation, air enters the body through the nasal cavity located just inside the nose ([link]). As air passes through the nasal cavity, the air is warmed to body temperature and humidified. The respiratory tract is coated with mucus to seal the tissues from direct contact with air. Mucus is high in water. As air crosses these surfaces of the mucous membranes, it picks up water. These processes help equilibrate the air to the body conditions, reducing any damage that cold, dry air can cause. Particulate matter that is floating in the air is removed in the nasal passages via mucus and cilia. The processes of warming, humidifying, and removing particles are important protective mechanisms that prevent damage to the trachea and lungs. Thus, inhalation serves several purposes in addition to bringing oxygen into the respiratory system.

Art Connection

Air enters the respiratory system through the nasal cavity and pharynx, and then passes through the trachea and into the bronchi, which bring air into the lungs. (credit: modification of work by NCI)

Which of the following statements about the mammalian respiratory system is false?

a. When we breathe in, air travels from the pharynx to the trachea.
b. The bronchioles branch into bronchi.
c. Alveolar ducts connect to alveolar sacs.
d. Gas exchange between the lung and blood takes place in the alveolus.

From the nasal cavity, air passes through the pharynx (throat) and the larynx (voice box), as it makes its way to the trachea ([link]). The main function of the trachea is to funnel the inhaled air to the lungs and the exhaled air back out of the body. The human trachea is a cylinder about 10 to 12 cm long and 2 cm in diameter that sits in front of the esophagus and extends from the larynx into the chest cavity where it divides into the two primary bronchi at the midthorax. It is made of incomplete rings of hyaline cartilage and smooth muscle ([link]). The trachea is lined with mucus-producing goblet cells and ciliated epithelia. The cilia propel foreign particles trapped in the mucus toward the pharynx. The cartilage provides strength and support to the trachea to keep the passage open. The smooth muscle can contract, decreasing the trachea's diameter, which causes expired air to rush upwards from the lungs at a great force. The forced exhalation helps expel mucus when we cough. Smooth muscle can contract or relax, depending on stimuli from the external environment or the body's nervous system.

The trachea and bronchi are made of incomplete rings of cartilage. (credit: modification of

work by Gray's Anatomy)

Lungs: Bronchi and Alveoli

The end of the trachea bifurcates (divides) to the right and left lungs. The lungs are not identical. The right lung is larger and contains three lobes, whereas the smaller left lung contains two lobes ([link]). The muscular diaphragm, which facilitates breathing, is inferior to (below) the lungs and marks the end of the thoracic cavity.

The trachea bifurcates into the right and left bronchi in the lungs. The right lung is made of three lobes and is larger. To accommodate the heart, the left lung is smaller and has only two

lobes.

In the lungs, air is diverted into smaller and smaller passages, or bronchi. Air enters the lungs through the two primary (main) bronchi (singular: bronchus). Each bronchus divides into secondary bronchi, then into tertiary bronchi, which in turn divide, creating smaller and smaller diameter bronchioles as they split and spread through the lung. Like the trachea, the

bronchi are made of cartilage and smooth muscle. At the bronchioles, the cartilage is replaced with elastic fibers. Bronchi are innervated by nerves of both the parasympathetic and sympathetic nervous systems that control muscle contraction (parasympathetic) or relaxation (sympathetic) in the bronchi and bronchioles, depending on the nervous system's cues. In humans, bronchioles with a diameter smaller than 0.5 mm are the respiratory bronchioles. They lack cartilage and therefore rely on inhaled air to support their shape. As the passageways decrease in diameter, the relative amount of smooth muscle increases.

The terminal bronchioles subdivide into microscopic branches called respiratory bronchioles. The respiratory bronchioles subdivide into several alveolar ducts. Numerous alveoli and alveolar sacs surround the alveolar ducts. The alveolar sacs resemble bunches of grapes tethered to the end of the bronchioles ([link]). In the acinar region, the alveolar ducts are attached to the end of each bronchiole. At the end of each duct are approximately 100 alveolar sacs, each containing 20 to 30 alveoli that are 200 to 300 microns in diameter. Gas exchange occurs only in alveoli. Alveoli are made of thin-walled parenchymal cells, typically one-cell thick, that look like tiny bubbles within the sacs. Alveoli are in direct contact with capillaries (one-cell thick) of the circulatory system. Such intimate contact ensures that oxygen will diffuse from alveoli into the blood and be distributed to the cells of the body. In addition, the carbon dioxide that was produced by cells as a waste product will diffuse from the blood into alveoli to be exhaled. The anatomical arrangement of capillaries and alveoli emphasizes the structural and functional relationship of the respiratory and circulatory systems. Because there are so many alveoli (~300 million per lung) within each alveolar sac and so many sacs at the end of each alveolar duct, the lungs have a sponge-like consistency. This organization produces a very large surface area that is available for gas exchange. The surface area of alveoli in the lungs is approximately 75 m^2. This large surface area, combined with the thin-walled nature of the alveolar parenchymal cells, allows gases to easily diffuse across the cells.

Terminal bronchioles are connected by respiratory bronchioles to alveolar ducts and alveolar sacs. Each alveolar sac contains 20 to 30 spherical alveoli and has the appearance of a bunch of grapes. Air flows into the atrium of the alveolar sac, then circulates into alveoli where gas exchange occurs with the capillaries. Mucous glands secrete mucous into the airways, keeping them moist and flexible. (credit: modification of work by Mariana Ruiz

Villareal)

Link to Learning

Watch the following video to review the respiratory system.

Gas Exchange across Respiratory Surfaces

By the end of this section, you will be able to:

- Name and describe lung volumes and capacities
- Understand how gas pressure influences how gases move into and out of the body

The structure of the lung maximizes its surface area to increase gas diffusion. Because of the enormous number of alveoli (approximately 300 million in each human lung), the surface area of the lung is very large (75 m^2). Having such a large surface area increases the amount of gas that can diffuse into and out of the lungs.

Basic Principles of Gas Exchange

Gas exchange during respiration occurs primarily through diffusion. Diffusion is a process in which transport is driven by a concentration gradient. Gas molecules move from a region of high concentration to a region of low concentration. Blood that is low in oxygen concentration and high in carbon dioxide concentration undergoes gas exchange with air in the lungs. The air in the lungs has a higher concentration of oxygen than that of oxygen-depleted blood and a lower concentration of carbon dioxide. This concentration gradient allows for gas exchange during respiration.

Partial pressure is a measure of the concentration of the individual components in a mixture of gases. The total pressure exerted by the mixture is the sum of the partial pressures of the components in the mixture. The rate of diffusion of a gas is proportional to its partial pressure within the total gas mixture. This concept is discussed further in detail below.

Lung Volumes and Capacities

Different animals have different lung capacities based on their activities. Cheetahs have evolved a much higher lung capacity than humans; it helps provide oxygen to all the muscles in the body and allows them to run very fast. Elephants also have a high lung capacity. In this case, it is not because they run fast but because they have a large body and must be able to take up oxygen in accordance with their body size.

Human lung size is determined by genetics, sex, and height. At maximal capacity, an average lung can hold almost six liters of air, but lungs do not usually operate at maximal capacity. Air in the lungs is measured in terms of lung volumes and lung capacities ([link] and [link]). Volume measures the amount of air for one function (such as inhalation or exhalation). Capacity is any two or more volumes (for example, how much can be inhaled from the end of a maximal exhalation).

Human lung volumes and capacities are shown. The total lung capacity of the adult male is six liters. Tidal volume is the volume of air inhaled in a single, normal breath. Inspiratory capacity is the amount of air taken in during a deep breath, and residual volume is the amount of air left in the lungs after forceful

respiration.

Lung Volumes and Capacities (Avg Adult Male)

Volume/Capacity	Definition	Volume (liters)	Equations
Tidal volume (TV)	Amount of air inhaled during a normal breath	0.5	-
Expiratory reserve volume (ERV)	Amount of air that can be exhaled after a normal exhalation	1.2	-
Inspiratory reserve volume (IRV)	Amount of air that can be further inhaled after a normal inhalation	3.1	-
Residual volume (RV)	Air left in the lungs after a forced exhalation	1.2	-
Vital capacity (VC)	Maximum amount of air that can be moved in or out of the lungs in a single respiratory cycle	4.8	ERV+TV+IRV
Inspiratory capacity (IC)	Volume of air that can be inhaled in addition to a normal exhalation	3.6	TV+IRV
Functional residual	Volume of air remaining after a	2.4	ERV+RV

Lung Volumes and Capacities (Avg Adult Male)

Volume/Capacity	Definition	Volume (liters)	Equations
capacity (FRC)	normal exhalation		
Total lung capacity (TLC)	Total volume of air in the lungs after a maximal inspiration	6.0	RV+ERV+TV+IRV
Forced expiratory volume (FEV1)	How much air can be forced out of the lungs over a specific time period, usually one second	~4.1 to 5.5	-

The volume in the lung can be divided into four units: tidal volume, expiratory reserve volume, inspiratory reserve volume, and residual volume. Tidal volume (TV) measures the amount of air that is inspired and expired during a normal breath. On average, this volume is around one-half liter, which is a little less than the capacity of a 20-ounce drink bottle.
The expiratory reserve volume (ERV) is the additional amount of air that can be exhaled after a normal exhalation. It is the reserve amount that can be exhaled beyond what is normal. Conversely, the inspiratory reserve volume (IRV) is the additional amount of air that can be inhaled after a normal inhalation. The residual volume (RV) is the amount of air that is left after expiratory reserve volume is exhaled. The lungs are never completely empty: There is always some air left in the lungs after a maximal exhalation. If this residual volume did not exist and the lungs emptied completely, the lung tissues would stick together and the energy necessary to re-inflate the lung could be too great to overcome. Therefore, there is always some air remaining in the lungs. Residual volume is also important for preventing large fluctuations in respiratory gases (O_2 and CO_2). The residual volume is the only lung volume that cannot be measured directly because it is impossible to completely empty the lung of air. This volume can only be calculated rather than measured.

Capacities are measurements of two or more volumes. The vital capacity (VC) measures the maximum amount of air that can be inhaled or exhaled during a respiratory cycle. It is the sum of the expiratory reserve volume, tidal volume, and inspiratory reserve volume.
The inspiratory capacity (IC) is the amount of air that can be inhaled after the end of a normal expiration. It is, therefore, the sum of the tidal volume and inspiratory reserve volume.
The functional residual capacity (FRC) includes the expiratory reserve volume and the residual volume. The FRC measures the amount of additional air that can be exhaled after a normal exhalation. Lastly, the total lung capacity (TLC) is a measurement of the total amount of air that the lung can hold. It is the sum of the residual volume, expiratory reserve volume, tidal volume, and inspiratory reserve volume.

Lung volumes are measured by a technique called spirometry. An important measurement taken during spirometry is the forced expiratory volume (FEV), which measures how much air can be forced out of the lung over a specific period, usually one second (FEV1). In addition, the forced vital capacity (FVC), which is the total amount of air that can be forcibly exhaled, is measured. The ratio of these values (FEV1/FVC ratio) is used to diagnose lung diseases including asthma, emphysema, and fibrosis. If the FEV1/FVC ratio is high, the lungs are not compliant (meaning they are stiff and unable to bend properly), and the patient most likely has lung fibrosis. Patients exhale most of the lung volume very quickly. Conversely, when the FEV1/FVC ratio is low, there is resistance in the lung that is characteristic of asthma. In this instance, it is hard for the patient to get the air out of his or her lungs, and it

takes a long time to reach the maximal exhalation volume. In either case, breathing is difficult and complications arise.

Career Connection

Respiratory Therapist Respiratory therapists or respiratory practitioners evaluate and treat patients with lung and cardiovascular diseases. They work as part of a medical team to develop treatment plans for patients. Respiratory therapists may treat premature babies with underdeveloped lungs, patients with chronic conditions such as asthma, or older patients suffering from lung disease such as emphysema and chronic obstructive pulmonary disease (COPD). They may operate advanced equipment such as compressed gas delivery systems, ventilators, blood gas analyzers, and resuscitators. Specialized programs to become a respiratory therapist generally lead to a bachelor's degree with a respiratory therapist specialty. Because of a growing aging population, career opportunities as a respiratory therapist are expected to remain strong.

Gas Pressure and Respiration

The respiratory process can be better understood by examining the properties of gases. Gases move freely, but gas particles are constantly hitting the walls of their vessel, thereby producing gas pressure.

Air is a mixture of gases, primarily nitrogen (N_2; 78.6 percent), oxygen (O_2; 20.9 percent), water vapor (H_2O; 0.5 percent), and carbon dioxide (CO_2; 0.04 percent). Each gas component of that mixture exerts a pressure. The pressure for an individual gas in the mixture is the partial pressure of that gas. Approximately 21 percent of atmospheric gas is oxygen. Carbon dioxide, however, is found in relatively small amounts, 0.04 percent. The partial pressure for oxygen is much greater than that of carbon dioxide. The partial pressure of any gas can be calculated by:

$P = (P\ atm) \times$ (percent content in mixture).

P_{atm}, the atmospheric pressure, is the sum of all of the partial pressures of the atmospheric gases added together,

$P\ atm = P\ N\ 2 + P\ O\ 2 + P\ H\ 2\ O + P\ CO\ 2 = 760$ mm Hg

× (percent content in mixture).

The pressure of the atmosphere at sea level is 760 mm Hg. Therefore, the partial pressure of oxygen is:

$P\ O\ 2 = (760$ mm Hg) $(0.21) = 160$ mm Hg

and for carbon dioxide:

$P\ CO\ 2 = (760$ mm Hg) $(0.0004) = 0.3$ mm Hg.

At high altitudes, P_{atm} decreases but concentration does not change; the partial pressure decrease is due to the reduction in P_{atm}.

When the air mixture reaches the lung, it has been humidified. The pressure of the water vapor in the lung does not change the pressure of the air, but it must be included in the partial pressure equation. For this calculation, the water pressure (47 mm Hg) is subtracted from the atmospheric pressure:

760 mm Hg − 47 mm Hg = 713 mm Hg

and the partial pressure of oxygen is:

(760 mm Hg − 47 mm Hg) × 0.21 = 150 mm Hg.

These pressures determine the gas exchange, or the flow of gas, in the system. Oxygen and carbon dioxide will flow according to their pressure gradient from high to low. Therefore, understanding the partial pressure of each gas will aid in understanding how gases move in the respiratory system.

Gas Exchange across the Alveoli

In the body, oxygen is used by cells of the body's tissues and carbon dioxide is produced as a waste product. The ratio of carbon dioxide production to oxygen consumption is the respiratory quotient (RQ). RQ varies between 0.7 and 1.0. If just glucose were used to fuel the body, the RQ would equal one. One mole of carbon dioxide would be produced for every mole of oxygen consumed. Glucose, however, is not the only fuel for the body. Protein and fat are also used as fuels for the body. Because of this, less carbon dioxide is produced than oxygen is consumed and the RQ is, on average, about 0.7 for fat and about 0.8 for protein.

The RQ is used to calculate the partial pressure of oxygen in the alveolar spaces within the lung, the alveolar P O 2 Above, the partial pressure of oxygen in the lungs was calculated to be 150 mm Hg. However, lungs never fully deflate with an exhalation; therefore, the inspired air mixes with this residual air and lowers the partial pressure of oxygen within the alveoli. This means that there is a lower concentration of oxygen in the lungs than is found in the air outside the body. Knowing the RQ, the partial pressure of oxygen in the alveoli can be calculated:

alveolar P O 2 = inspired P O 2 − (alveolar P O 2 RQ)

With an RQ of 0.8 and a P CO 2 in the alveoli of 40 mm Hg, the alveolar P O 2 is equal to:

alveolar P O 2 = 150 mm Hg − (40 mm Hg 0.8) = mm Hg.

Notice that this pressure is less than the external air. Therefore, the oxygen will flow from the inspired air in the lung (P O 2 = 150 mm Hg) into the bloodstream (P O 2 = 100 mm Hg) ([link]).

In the lungs, oxygen diffuses out of the alveoli and into the capillaries surrounding the alveoli. Oxygen (about 98 percent) binds reversibly to the respiratory pigment hemoglobin found in red blood cells (RBCs). RBCs carry oxygen to the tissues where oxygen dissociates from the hemoglobin and diffuses into the cells of the tissues. More specifically, alveolar P O 2 is higher in the alveoli (P ALVO 2 = 100 mm Hg) than blood P O 2 (40 mm

Hg) in the capillaries. Because this pressure gradient exists, oxygen diffuses down its pressure gradient, moving out of the alveoli and entering the blood of the capillaries where O_2 binds to hemoglobin. At the same time, alveolar P CO 2 is lower P ALVO 2 = 40 mm Hg than blood P CO 2 = (45 mm Hg). CO_2 diffuses down its pressure gradient, moving out of the capillaries and entering the alveoli.

Oxygen and carbon dioxide move independently of each other; they diffuse down their own pressure gradients. As blood leaves the lungs through the pulmonary veins,
the venous P O 2= 100 mm Hg, whereas the venous P CO 2 = 40 mm Hg. As blood enters the systemic capillaries, the blood will lose oxygen and gain carbon dioxide because of the pressure difference of the tissues and blood. In systemic capillaries, P O 2= 100 mm Hg, but in the tissue cells, P O 2= 40 mm Hg. This pressure gradient drives the diffusion of oxygen out of the capillaries and into the tissue cells. At the same time, blood P CO 2= 40 mm Hg and systemic tissue P CO 2= 45 mm Hg. The pressure gradient drives CO_2 out of tissue cells and into the capillaries. The blood returning to the lungs through the pulmonary arteries has a venous P O 2= 40 mm Hg and a P CO 2= 45 mm Hg. The blood enters the lung capillaries where the process of exchanging gases between the capillaries and alveoli begins again ([link]).

Art Connection
The partial pressures of oxygen and carbon dioxide change as blood moves through the

body.

Which of the following statements is false?

a. In the tissues, P_{O_2} drops as blood passes from the arteries to the veins, while P_{CO_2} increases.
b. Blood travels from the lungs to the heart to body tissues, then back to the heart, then the lungs.
c. Blood travels from the lungs to the heart to body tissues, then back to the lungs, then the heart.
d. P_{O_2} is higher in air than in the lungs.

In short, the change in partial pressure from the alveoli to the capillaries drives the oxygen into the tissues and the carbon dioxide into the blood from the tissues. The blood is then transported to the lungs where differences in pressure in the alveoli result in the movement of carbon dioxide out of the blood into the lungs, and oxygen into the blood.

Link to Learning

Watch this video to learn how to carry out spirometry.

Breathing
By the end of this section, you will be able to:

- Describe how the structures of the lungs and thoracic cavity control the mechanics of breathing
- Explain the importance of compliance and resistance in the lungs
- Discuss problems that may arise due to a V/Q mismatch

Mammalian lungs are located in the thoracic cavity where they are surrounded and protected by the rib cage, intercostal muscles, and bound by the chest wall. The bottom of the lungs is contained by the diaphragm, a skeletal muscle that facilitates breathing. Breathing requires the coordination of the lungs, the chest wall, and most importantly, the diaphragm.

Types of Breathing

Amphibians have evolved multiple ways of breathing. Young amphibians, like tadpoles, use gills to breathe, and they don't leave the water. Some amphibians retain gills for life. As the tadpole grows, the gills disappear and lungs grow. These lungs are primitive and not as evolved as mammalian lungs. Adult amphibians are lacking or have a reduced diaphragm, so breathing via lungs is forced. The other means of breathing for amphibians is diffusion across the skin. To aid this diffusion, amphibian skin must remain moist.

Birds face a unique challenge with respect to breathing: They fly. Flying consumes a great amount of energy; therefore, birds require a lot of oxygen to aid their metabolic processes.

Birds have evolved a respiratory system that supplies them with the oxygen needed to enable flying. Similar to mammals, birds have lungs, which are organs specialized for gas exchange. Oxygenated air, taken in during inhalation, diffuses across the surface of the lungs into the bloodstream, and carbon dioxide diffuses from the blood into the lungs and expelled during exhalation. The details of breathing between birds and mammals differ substantially.

In addition to lungs, birds have air sacs inside their body. Air flows in one direction from the posterior air sacs to the lungs and out of the anterior air sacs. The flow of air is in the opposite direction from blood flow, and gas exchange takes place much more efficiently. This type of breathing enables birds to obtain the requisite oxygen, even at higher altitudes where the oxygen concentration is low. This directionality of airflow requires two cycles of air intake and exhalation to completely get the air out of the lungs.

Evolution Connection

Avian Respiration Birds have evolved a respiratory system that enables them to fly. Flying is a high-energy process and requires a lot of oxygen. Furthermore, many birds fly in high altitudes where the concentration of oxygen in low. How did birds evolve a respiratory system that is so unique?

Decades of research by paleontologists have shown that birds evolved from therapods, meat-eating dinosaurs ([link]). In fact, fossil evidence shows that meat-eating dinosaurs that lived more than 100 million years ago had a similar flow-through respiratory system with lungs and air sacs. *Archaeopteryx* and *Xiaotingia*, for example, were flying dinosaurs and are believed to be early precursors of birds.

(a) Birds have a flow-through respiratory system in which air flows unidirectionally from the posterior sacs into the lungs, then into the anterior air sacs. The air sacs connect to openings in hollow bones. (b) Dinosaurs, from which birds descended, have similar hollow bones and are believed to have had a similar respiratory system. (credit b: modification of work by Zina

Deretsky, National Science

Foundation)

Most of us consider that dinosaurs are extinct. However, modern birds are descendants of avian dinosaurs. The respiratory system of modern birds has been evolving for hundreds of millions of years.

All mammals have lungs that are the main organs for breathing. Lung capacity has evolved to support the animal's activities. During inhalation, the lungs expand with air, and oxygen diffuses across the lung's surface and enters the bloodstream. During exhalation, the lungs expel air and lung volume decreases. In the next few sections, the process of human breathing will be explained.

The Mechanics of Human Breathing

Boyle's Law is the gas law that states that in a closed space, pressure and volume are inversely related. As volume decreases, pressure increases and vice versa ([link]). The relationship between gas pressure and volume helps to explain the mechanics of breathing.

This graph shows data from Boyle's original 1662 experiment, which shows that pressure and volume are inversely related. No units are given as Boyle used arbitrary units in his experiments.

There is always a slightly negative pressure within the thoracic cavity, which aids in keeping the airways of the lungs open. During inhalation, volume increases as a result of contraction of the diaphragm, and pressure decreases (according to Boyle's Law). This decrease of pressure in the thoracic cavity relative to the environment makes the cavity less than the atmosphere ([link]**a**). Because of this drop in pressure, air rushes into the respiratory passages. To increase the volume of the lungs, the chest wall expands. This results from the contraction of the intercostal muscles, the muscles that are connected to the rib cage. Lung volume expands because the diaphragm contracts and the intercostals muscles contract, thus expanding the thoracic cavity. This increase in the volume of the thoracic cavity lowers pressure compared to the atmosphere, so air rushes into the lungs, thus increasing its volume. The resulting increase in volume is largely attributed to an increase in alveolar space, because the bronchioles and bronchi are stiff structures that do not change in size.

The lungs, chest wall, and diaphragm are all involved in respiration, both (a) inhalation and (b) expiration. (credit: modification of work by Mariana Ruiz Villareal)

The chest wall expands out and away from the lungs. The lungs are elastic; therefore, when air fills the lungs, the elastic recoil within the tissues of the lung exerts pressure back toward the interior of the lungs. These outward and inward forces compete to inflate and deflate the lung with every breath. Upon exhalation, the lungs recoil to force the air out of the lungs, and the intercostal muscles relax, returning the chest wall back to its original position ([link]**b**). The diaphragm also relaxes and moves higher into the thoracic cavity. This increases the pressure within the thoracic cavity relative to the environment, and air rushes out of the lungs. The movement of air out of the lungs is a passive event. No muscles are contracting to expel the air.

Each lung is surrounded by an invaginated sac. The layer of tissue that covers the lung and dips into spaces is called the visceral pleura. A second layer of parietal pleura lines the interior of the thorax ([link]). The space between these layers, the intrapleural space, contains a small amount of fluid that protects the tissue and reduces the friction generated from rubbing the tissue layers together as the lungs contract and relax. Pleurisy results when these layers of tissue become inflamed; it is painful because the inflammation increases the pressure within the thoracic cavity and reduces the volume of the lung.

A tissue layer called pleura surrounds the lung and interior of the thoracic cavity. (credit:

modification of work by NCI)
Link to Learning

View how Boyle's Law is related to breathing and watch a video on Boyle's Law.

Transport of Gases in Human Bodily Fluids
By the end of this section, you will be able to:

- Describe how oxygen is bound to hemoglobin and transported to body tissues
- Explain how carbon dioxide is transported from body tissues to the lungs

Once the oxygen diffuses across the alveoli, it enters the bloodstream and is transported to the tissues where it is unloaded, and carbon dioxide diffuses out of the blood and into the alveoli to be expelled from the body. Although gas exchange is a continuous process, the oxygen and carbon dioxide are transported by different mechanisms.

Transport of Oxygen in the Blood

Although oxygen dissolves in blood, only a small amount of oxygen is transported this way. Only 1.5 percent of oxygen in the blood is dissolved directly into the blood itself. Most oxygen—98.5 percent—is bound to a protein called hemoglobin and carried to the tissues.

Hemoglobin

Hemoglobin, or Hb, is a protein molecule found in red blood cells (erythrocytes) made of four subunits: two alpha subunits and two beta subunits ([link]). Each subunit surrounds a central heme group that contains iron and binds one oxygen molecule, allowing each hemoglobin molecule to bind four oxygen molecules. Molecules with more oxygen bound to the heme groups are brighter red. As a result, oxygenated arterial blood where the Hb is carrying four oxygen molecules is bright red, while venous blood that is deoxygenated is darker red.

The protein inside (a) red blood cells that carries oxygen to cells and carbon dioxide to the lungs is (b) hemoglobin. Hemoglobin is made up of four symmetrical subunits and four heme groups. Iron associated with the heme binds oxygen. It is the iron in hemoglobin that gives blood its red color.

It is easier to bind a second and third oxygen molecule to Hb than the first molecule. This is because the hemoglobin molecule changes its shape, or conformation, as oxygen binds. The fourth oxygen is then more difficult to bind. The binding of oxygen to hemoglobin can be plotted as a function of the partial pressure of oxygen in the blood (x-axis) versus the relative Hb-oxygen saturation (y-axis). The resulting graph—an oxygen dissociation curve—is sigmoidal, or S-shaped ([link]). As the partial pressure of oxygen increases, the hemoglobin becomes increasingly saturated with oxygen.

Art Connection

The oxygen dissociation curve demonstrates that, as the partial pressure of oxygen increases, more oxygen binds hemoglobin. However, the affinity of hemoglobin for oxygen may shift to the left or the right depending on environmental conditions.

The kidneys are responsible for removing excess H+ ions from the blood. If the kidneys fail, what would happen to blood pH and to hemoglobin affinity for oxygen?

Factors That Affect Oxygen Binding

The oxygen-carrying capacity of hemoglobin determines how much oxygen is carried in the blood. In addition to P O 2, other environmental factors and diseases can affect oxygen carrying capacity and delivery.

Carbon dioxide levels, blood pH, and body temperature affect oxygen-carrying capacity ([link]). When carbon dioxide is in the blood, it reacts with water to form bicarbonate (HCO_3^-) and hydrogen ions (H^+). As the level of carbon dioxide in the blood increases, more H^+ is produced and the pH decreases. This increase in carbon dioxide and subsequent decrease in pH reduce the affinity of hemoglobin for oxygen. The oxygen dissociates from the Hb molecule, shifting the oxygen dissociation curve to the right.

Therefore, more oxygen is needed to reach the same hemoglobin saturation level as when the pH was higher. A similar shift in the curve also results from an increase in body temperature. Increased temperature, such as from increased activity of skeletal muscle, causes the affinity of hemoglobin for oxygen to be reduced.

Diseases like sickle cell anemia and thalassemia decrease the blood's ability to deliver oxygen to tissues and its oxygen-carrying capacity. In sickle cell anemia, the shape of the red blood cell is crescent-shaped, elongated, and stiffened, reducing its ability to deliver oxygen ([link]). In this form, red blood cells cannot pass through the capillaries. This is painful when it occurs. Thalassemia is a rare genetic disease caused by a defect in either the alpha or the beta subunit of Hb. Patients with thalassemia produce a high number of red blood cells, but these cells have lower-than-normal levels of hemoglobin. Therefore, the oxygen-carrying capacity is diminished.

Individuals with sickle cell anemia have crescent-shaped red blood cells. (credit: modification of work by Ed Uthman; scale-bar data from Matt Russell)

Transport of Carbon Dioxide in the Blood

Carbon dioxide molecules are transported in the blood from body tissues to the lungs by one of three methods: dissolution directly into the blood, binding to hemoglobin, or carried as a bicarbonate ion. Several properties of carbon dioxide in the blood affect its transport. First, carbon dioxide is more soluble in blood than oxygen. About 5 to 7 percent of all carbon dioxide is dissolved in the plasma. Second, carbon dioxide can bind to plasma proteins or can enter red blood cells and bind to hemoglobin. This form transports about 10 percent of the carbon dioxide. When carbon dioxide binds to hemoglobin, a molecule called carbaminohemoglobin is formed. Binding of carbon dioxide to hemoglobin is reversible. Therefore, when it reaches the lungs, the carbon dioxide can freely dissociate from the hemoglobin and be expelled from the body.

Third, the majority of carbon dioxide molecules (85 percent) are carried as part of the bicarbonate buffer system. In this system, carbon dioxide diffuses into the red blood cells. Carbonic anhydrase (CA) within the red blood cells quickly converts the carbon dioxide into carbonic acid (H_2CO_3). Carbonic acid is an unstable intermediate molecule that immediately dissociates into bicarbonate ions (HCO_3^-) and hydrogen (H^+) ions. Since carbon dioxide is quickly converted into bicarbonate ions, this reaction allows for the continued uptake of carbon dioxide into the blood down its concentration gradient. It also results in the production of H^+ ions. If too much H^+ is produced, it can alter blood pH. However, hemoglobin binds to the free H^+ ions and thus limits shifts in pH. The newly synthesized bicarbonate ion is transported out of the red blood cell into the liquid component of the blood in exchange for a chloride ion (Cl^-); this is called the chloride shift. When the blood reaches the lungs, the bicarbonate ion is transported back into the red blood cell in exchange for the chloride ion. The H^+ ion dissociates from the hemoglobin and binds to the bicarbonate ion. This produces the carbonic acid intermediate, which is converted back into carbon dioxide through the enzymatic action of CA. The carbon dioxide produced is expelled through the lungs during exhalation.

$$CO_2 + H_2O \leftrightarrow H_2CO_3 \text{ (carbonic acid)} \leftrightarrow HCO_3^- + H^+ \text{ (bicarbonate)}$$

The benefit of the bicarbonate buffer system is that carbon dioxide is “soaked up” into the blood with little change to the pH of the system. This is important because it takes only a small change in the overall pH of the body for severe injury or death to result. The presence of this bicarbonate buffer system also allows for people to travel and live at high altitudes: When the partial pressure of oxygen and carbon dioxide change at high altitudes, the bicarbonate buffer system adjusts to regulate carbon dioxide while maintaining the correct pH in the body.

Carbon Monoxide Poisoning

While carbon dioxide can readily associate and dissociate from hemoglobin, other molecules such as carbon monoxide (CO) cannot. Carbon monoxide has a greater affinity for hemoglobin than oxygen. Therefore, when carbon monoxide is present, it binds to hemoglobin preferentially over oxygen. As a result, oxygen cannot bind to hemoglobin, so very little oxygen is transported through the body ([link]). Carbon monoxide is a colorless, odorless gas and is therefore difficult to detect. It is produced by gas-powered vehicles and tools. Carbon monoxide can cause headaches, confusion, and nausea; long-term exposure can cause brain damage or death. Administering 100 percent (pure) oxygen is the usual treatment for carbon monoxide poisoning. Administration of pure oxygen speeds up the separation of carbon monoxide from hemoglobin.

As percent CO increases, the oxygen saturation of hemoglobin

decreases.

Section Summary

Hemoglobin is a protein found in red blood cells that is comprised of two alpha and two beta subunits that surround an iron-containing heme group. Oxygen readily binds this heme group. The ability of oxygen to bind increases as more oxygen molecules are bound to heme. Disease states and altered conditions in the body can affect the binding ability of oxygen, and increase or decrease its ability to dissociate from hemoglobin.

Carbon dioxide can be transported through the blood via three methods. It is dissolved directly in the blood, bound to plasma proteins or hemoglobin, or converted into bicarbonate. The majority of carbon dioxide is transported as part of the bicarbonate system. Carbon dioxide diffuses into red blood cells. Inside, carbonic anhydrase converts carbon dioxide into carbonic acid (H_2CO_3), which is subsequently hydrolyzed into bicarbonate ($HCO\ 3^-$) and H^+. The H^+ ion binds to hemoglobin in red blood cells, and bicarbonate is transported out of the red blood cells in exchange for a chloride ion. This is called the chloride shift. Bicarbonate leaves the red blood cells and enters the blood plasma. In the lungs, bicarbonate is transported back into the red blood cells in exchange for chloride. The H^+ dissociates from hemoglobin and combines with bicarbonate to form carbonic acid with the help of carbonic anhydrase, which further catalyzes the reaction to convert carbonic acid back into carbon dioxide and water. The carbon dioxide is then expelled from the lungs.

Art Connections

[link] The kidneys are responsible for removing excess H+ ions from the blood. If the kidneys fail, what would happen to blood pH and to hemoglobin affinity for oxygen?

[link] The blood pH will drop and hemoglobin affinity for oxygen will decrease.

Review Questions

Which of the following will NOT facilitate the transfer of oxygen to tissues?

a. decreased body temperature
b. decreased pH of the blood
c. increased carbon dioxide
d. increased exercise

A

The majority of carbon dioxide in the blood is transported by _____.

a. binding to hemoglobin
b. dissolution in the blood
c. conversion to bicarbonate
d. binding to plasma proteins

C

The majority of oxygen in the blood is transported by _____.

a. dissolution in the blood
b. being carried as bicarbonate ions
c. binding to blood plasma
d. binding to hemoglobin

D

Free Response

What would happen if no carbonic anhydrase were present in red blood cells?

Without carbonic anhydrase, carbon dioxide would not be hydrolyzed into carbonic acid or bicarbonate. Therefore, very little carbon dioxide (only 15 percent) would be transported in the blood away from the tissues.

How does the administration of 100 percent oxygen save a patient from carbon monoxide poisoning? Why wouldn't giving carbon dioxide work?

Carbon monoxide has a higher affinity for hemoglobin than oxygen. This means that carbon monoxide will preferentially bind to hemoglobin over oxygen. Administration of 100 percent oxygen is an effective therapy because at that concentration, oxygen will displace the carbon monoxide from the hemoglobin.

Glossary

bicarbonate buffer system
: system in the blood that absorbs carbon dioxide and regulates pH levels

bicarbonate (HCO_3^-) ion
: ion created when carbonic acid dissociates into H^+ and (HCO_3^-)

carbaminohemoglobin
: molecule that forms when carbon dioxide binds to hemoglobin

carbonic anhydrase (CA)
: enzyme that catalyzes carbon dioxide and water into carbonic acid

chloride shift
: chloride shift exchange of chloride for bicarbonate into or out of the red blood cell

heme group
: centralized iron-containing group that is surrounded by the alpha and beta subunits of hemoglobin

hemoglobin
: molecule in red blood cells that can bind oxygen, carbon dioxide, and carbon monoxide

oxygen-carrying capacity
: amount of oxygen that can be transported in the blood

oxygen dissociation curve
: curve depicting the affinity of oxygen for hemoglobin

sickle cell anemia
: genetic disorder that affects the shape of red blood cells, and their ability to transport oxygen and move through capillaries

thalassemia
: rare genetic disorder that results in mutation of the alpha or beta subunits of hemoglobin, creating smaller red blood cells with less hemoglobin

Introduction

class="introduction" class="summary" title="Sections Summary" class="art-exercise" title="Art Connections" class="multiple-choice" title="Multiple Choice" class="free-response" title="Free Response"Just as highway systems transport people and goods through a complex network, the circulatory system transports nutrients, gases, and wastes throughout the animal body. (credit: modification of work by Andrey

Belenko)

Most animals are complex multicellular organisms that require a mechanism for transporting nutrients throughout their bodies and removing waste products. The circulatory system has evolved over time from simple diffusion through cells in the early evolution of animals to a complex network of blood vessels that reach all parts of the human body. This extensive network supplies the cells, tissues, and organs with oxygen and nutrients, and removes carbon dioxide and waste, which are byproducts of respiration.

At the core of the human circulatory system is the heart. The size of a clenched fist, the human heart is protected beneath the rib cage. Made of specialized and unique cardiac muscle, it pumps blood throughout the body and to the heart itself. Heart contractions are driven by intrinsic electrical impulses that the brain and endocrine hormones help to regulate. Understanding the heart’s basic anatomy and

function is important to understanding the body's circulatory and respiratory systems.

Gas exchange is one essential function of the circulatory system. A circulatory system is not needed in organisms with no specialized respiratory organs because oxygen and carbon dioxide diffuse directly between their body tissues and the external environment. However, in organisms that possess lungs and gills, oxygen must be transported from these specialized respiratory organs to the body tissues via a circulatory system. Therefore, circulatory systems have had to evolve to accommodate the great diversity of body sizes and body types present among animals.

Overview of the Circulatory System
By the end of this section, you will be able to:

- Describe an open and closed circulatory system
- Describe interstitial fluid and hemolymph
- Compare and contrast the organization and evolution of the vertebrate circulatory system.

In all animals, except a few simple types, the circulatory system is used to transport nutrients and gases through the body. Simple diffusion allows some water, nutrient, waste, and gas exchange into primitive animals that are only a few cell layers thick; however, bulk flow is the only method by which the entire body of larger more complex organisms is accessed.

Circulatory System Architecture

The circulatory system is effectively a network of cylindrical vessels: the arteries, veins, and capillaries that emanate from a pump, the heart. In all vertebrate organisms, as well as some invertebrates, this is a closed-loop system, in which the blood is not free in a cavity. In a closed circulatory system, blood is contained inside blood vessels and circulates unidirectionally from the heart around the systemic circulatory route, then returns to the heart again, as illustrated in [link]**a**. As opposed to a closed system, arthropods—including insects, crustaceans, and most mollusks—have an open circulatory system, as illustrated in [link]**b**. In an open circulatory system, the blood is not enclosed in the blood vessels but is pumped into a cavity called a hemocoel and is called hemolymph because the blood mixes with the interstitial fluid. As the heart beats and the animal moves, the hemolymph circulates around the organs within the body cavity and then reenters the hearts through openings called ostia. This movement allows for gas and nutrient exchange. An open circulatory system does not use as much energy as a closed system to operate or to maintain; however, there is a trade-off with the amount of blood that can be moved to metabolically active organs and tissues that require high levels of oxygen. In fact, one reason that insects with wing spans of up to two feet wide (70 cm) are not around today is probably because they were outcompeted by the arrival of birds 150 million years ago. Birds, having a closed circulatory system, are thought to have moved more agilely, allowing them to get food faster and possibly to prey on the insects.

In (a) closed circulatory systems, the heart pumps blood through vessels that are separate from the interstitial fluid of the body. Most vertebrates and some invertebrates, like this annelid earthworm, have a closed circulatory system. In (b) open circulatory systems, a fluid called hemolymph is pumped through a blood vessel that empties into the body cavity. Hemolymph returns to the blood vessel through openings called ostia. Arthropods like this bee and most mollusks have open circulatory
systems.

Circulatory System Variation in Animals

The circulatory system varies from simple systems in invertebrates to more complex systems in vertebrates. The simplest animals, such as the sponges (Porifera) and rotifers (Rotifera), do not need a circulatory system because diffusion allows adequate exchange of water, nutrients, and waste, as well as dissolved gases, as shown in [link]**a**. Organisms that are more complex but still only have two layers of cells in their body plan, such as jellies (Cnidaria) and comb jellies (Ctenophora) also use diffusion through their epidermis and internally through the gastrovascular compartment. Both their internal and external tissues are bathed in an aqueous environment and exchange fluids by diffusion on both sides, as illustrated in [link]**b**. Exchange of fluids is assisted by the pulsing of the jellyfish body.

Simple animals consisting of a single cell layer such as the (a) sponge or only a few cell layers such as the (b) jellyfish do not have a circulatory system. Instead, gases, nutrients, and wastes are exchanged by
diffusion.

For more complex organisms, diffusion is not efficient for cycling gases, nutrients, and waste effectively through the body; therefore, more complex circulatory systems evolved. Most arthropods and many mollusks have open circulatory systems. In an open system, an elongated beating heart pushes the hemolymph through the body and muscle contractions help to move fluids. The larger more complex crustaceans, including lobsters, have developed arterial-like vessels to push blood through their bodies, and the most active mollusks, such as squids, have evolved a closed circulatory system and are able to move rapidly to catch prey. Closed circulatory systems are a characteristic of vertebrates; however, there are significant differences in the structure of the heart and the circulation of blood between the different vertebrate groups due to adaptation during evolution and associated differences in anatomy. [link] illustrates the basic circulatory systems of some vertebrates: fish, amphibians, reptiles, and mammals.

(a) Fish have the simplest circulatory systems of the vertebrates: blood flows unidirectionally from the two-chambered heart through the gills and then the rest of the body. (b) Amphibians have two circulatory routes: one for oxygenation of the blood through the lungs and skin, and the other to take oxygen to the rest of the body. The blood is pumped from a three-chambered heart with two atria and a single ventricle. (c) Reptiles also have two circulatory routes; however, blood is only oxygenated through the lungs. The heart is three chambered, but the ventricles are partially separated so some mixing of oxygenated and deoxygenated blood occurs except in crocodilians and birds. (d) Mammals and birds have the most efficient heart with four chambers that completely separate the oxygenated and deoxygenated blood; it pumps only oxygenated blood through the body and deoxygenated blood to the lungs.

As illustrated in [link]**a** Fish have a single circuit for blood flow and a two-chambered heart that has only a single atrium and a single ventricle. The atrium collects blood that has returned from the body and the ventricle pumps the blood to the gills where gas exchange occurs and the blood is re-oxygenated; this is called gill circulation. The blood then continues through the rest of the body before arriving back at the atrium; this is called systemic circulation. This unidirectional flow of blood produces a gradient of oxygenated to deoxygenated blood around the fish's systemic circuit. The result is a limit in the amount of

oxygen that can reach some of the organs and tissues of the body, reducing the overall metabolic capacity of fish.

In amphibians, reptiles, birds, and mammals, blood flow is directed in two circuits: one through the lungs and back to the heart, which is called pulmonary circulation, and the other throughout the rest of the body and its organs including the brain (systemic circulation). In amphibians, gas exchange also occurs through the skin during pulmonary circulation and is referred to as pulmocutaneous circulation.

As shown in [link]**b**, amphibians have a three-chambered heart that has two atria and one ventricle rather than the two-chambered heart of fish. The two atria (superior heart chambers) receive blood from the two different circuits (the lungs and the systems), and then there is some mixing of the blood in the heart's ventricle (inferior heart chamber), which reduces the efficiency of oxygenation. The advantage to this arrangement is that high pressure in the vessels pushes blood to the lungs and body. The mixing is mitigated by a ridge within the ventricle that diverts oxygen-rich blood through the systemic circulatory system and deoxygenated blood to the pulmocutaneous circuit. For this reason, amphibians are often described as having double circulation.

Most reptiles also have a three-chambered heart similar to the amphibian heart that directs blood to the pulmonary and systemic circuits, as shown in [link]**c**. The ventricle is divided more effectively by a partial septum, which results in less mixing of oxygenated and deoxygenated blood. Some reptiles (alligators and crocodiles) are the most primitive animals to exhibit a four-chambered heart. Crocodilians have a unique circulatory mechanism where the heart shunts blood from the lungs toward the stomach and other organs during long periods of submergence, for instance, while the animal waits for prey or stays underwater waiting for prey to rot. One adaptation includes two main arteries that leave the same part of the heart: one takes blood to the lungs and the other provides an alternate route to the stomach and other parts of the body. Two other adaptations include a hole in the heart between the two ventricles, called the foramen of Panizza, which allows blood to move from one side of the heart to the other, and specialized connective tissue that slows the blood flow to the lungs. Together these adaptations have made crocodiles and alligators one of the most evolutionarily successful animal groups on earth.

In mammals and birds, the heart is also divided into four chambers: two atria and two ventricles, as illustrated in [link]**d**. The oxygenated blood is separated from the deoxygenated blood, which improves the efficiency of double circulation and is probably required for the warm-blooded lifestyle of mammals and birds. The four-chambered heart of birds and mammals evolved independently from a three-chambered heart. The independent evolution of the same or a similar biological trait is referred to as convergent evolution.

Section Summary

In most animals, the circulatory system is used to transport blood through the body. Some primitive animals use diffusion for the exchange of water, nutrients, and gases. However, complex organisms use the circulatory system to carry gases, nutrients, and waste through the body. Circulatory systems may be open (mixed with the interstitial fluid) or closed (separated from the interstitial fluid). Closed circulatory systems are a characteristic of vertebrates; however, there are significant differences in the structure of the heart and the circulation of blood between the different vertebrate groups due to adaptions during evolution and

associated differences in anatomy. Fish have a two-chambered heart with unidirectional circulation. Amphibians have a three-chambered heart, which has some mixing of the blood, and they have double circulation. Most non-avian reptiles have a three-chambered heart, but have little mixing of the blood; they have double circulation. Mammals and birds have a four-chambered heart with no mixing of the blood and double circulation.

Review Questions

Why are open circulatory systems advantageous to some animals?

a. They use less metabolic energy.
b. They help the animal move faster.
c. They do not need a heart.
d. They help large insects develop.

A

Some animals use diffusion instead of a circulatory system. Examples include:

a. birds and jellyfish
b. flatworms and arthropods
c. mollusks and jellyfish
d. None of the above

D

Blood flow that is directed through the lungs and back to the heart is called _____.

a. unidirectional circulation
b. gill circulation
c. pulmonary circulation
d. pulmocutaneous circulation

C

Free Response

Describe a closed circulatory system.

A closed circulatory system is a closed-loop system, in which blood is not free in a cavity. Blood is separate from the bodily interstitial fluid and contained within blood vessels. In this type of system, blood circulates unidirectionally from the heart around the systemic circulatory route, and then returns to the heart.

Describe systemic circulation.

Systemic circulation flows through the systems of the body. The blood flows away from the heart to the brain, liver, kidneys, stomach, and other organs, the limbs, and the muscles of the body; it then returns to the heart.

Glossary

atrium
: (plural: atria) chamber of the heart that receives blood from the veins and sends blood to the ventricles

closed circulatory system
: system in which the blood is separated from the bodily interstitial fluid and contained in blood vessels

double circulation
: flow of blood in two circuits: the pulmonary circuit through the lungs and the systemic circuit through the organs and body

gill circulation
: circulatory system that is specific to animals with gills for gas exchange; the blood flows through the gills for oxygenation

hemocoel
: cavity into which blood is pumped in an open circulatory system

hemolymph
: mixture of blood and interstitial fluid that is found in insects and other arthropods as well as most mollusks

interstitial fluid
: fluid between cells

open circulatory system
: system in which the blood is mixed with interstitial fluid and directly covers the organs

ostium
: (plural: ostia) holes between blood vessels that allow the movement of hemolymph through the body of insects, arthropods, and mollusks with open circulatory systems

pulmocutaneous circulation
: circulatory system in amphibians; the flow of blood to the lungs and the moist skin for gas exchange

pulmonary circulation
: flow of blood away from the heart through the lungs where oxygenation occurs and then returns to the heart again

systemic circulation
: flow of blood away from the heart to the brain, liver, kidneys, stomach, and other organs, the limbs, and the muscles of the body, and then the return of this blood to the heart

unidirectional circulation
: flow of blood in a single circuit; occurs in fish where the blood flows through the gills, then past the organs and the rest of the body, before returning to the heart

ventricle
: (heart) large inferior chamber of the heart that pumps blood into arteries

By the end of this section, you will be able to:

- List the basic components of the blood
- Compare red and white blood cells
- Describe blood plasma and serum

Hemoglobin is responsible for distributing oxygen, and to a lesser extent, carbon dioxide, throughout the circulatory systems of humans, vertebrates, and many invertebrates. The blood is more than the proteins, though. Blood is actually a term used to describe the liquid that moves through the vessels and includes plasma (the liquid portion, which contains water, proteins, salts, lipids, and glucose) and the cells (red and white cells) and cell fragments called platelets. Blood plasma is actually the dominant component of blood and contains the water, proteins, electrolytes, lipids, and glucose. The cells are responsible for carrying the gases (red cells) and immune the response (white). The platelets are responsible for blood clotting. Interstitial fluid that surrounds cells is separate from the blood, but in hemolymph, they are combined. In humans, cellular components make up approximately 45 percent of the blood and the liquid plasma 55 percent. Blood is 20 percent of a person's extracellular fluid and eight percent of weight.

The Role of Blood in the Body

Blood, like the human blood illustrated in [link] is important for regulation of the body's systems and homeostasis. Blood helps maintain homeostasis by stabilizing pH, temperature, osmotic pressure, and by eliminating excess heat. Blood supports growth by distributing nutrients and hormones, and by removing waste. Blood plays a protective role by transporting clotting factors and platelets to prevent blood loss and transporting the disease-fighting agents or white blood cells to sites of infection.

The cells and cellular components of human blood are shown. Red blood cells deliver oxygen to the cells and remove carbon dioxide. White blood cells—including neutrophils, monocytes, lymphocytes, eosinophils, and basophils—are involved in the immune response.

Platelets form clots that prevent blood loss after injury.

Red Blood Cells

Red blood cells, or erythrocytes (erythro- = “red”; -cyte = “cell”), are specialized cells that circulate through the body delivering oxygen to cells; they are formed from stem cells in the bone marrow. In mammals, red blood cells are small biconcave cells that at maturity do not contain a nucleus or mitochondria and are only 7–8 μm in size. In birds and non-avian reptiles, a nucleus is still maintained in red blood cells.

The red coloring of blood comes from the iron-containing protein hemoglobin, illustrated in [link]**a**. The principal job of this protein is to carry oxygen, but it also transports carbon dioxide as well. Hemoglobin is packed into red blood cells at a rate of about 250 million molecules of hemoglobin per cell. Each hemoglobin molecule binds four oxygen molecules so that each red blood cell carries one billion molecules of oxygen. There are approximately 25 trillion red blood cells in the five liters of blood in the human body, which could carry up to 25 sextillion (25×10^{21}) molecules of oxygen in the body at any time. In mammals, the lack of organelles in erythrocytes leaves more room for the hemoglobin molecules, and the lack of mitochondria also prevents use of the oxygen for metabolic respiration. Only mammals have anucleated red blood cells, and some mammals (camels, for instance) even

have nucleated red blood cells. The advantage of nucleated red blood cells is that these cells can undergo mitosis. Anucleated red blood cells metabolize anaerobically (without oxygen), making use of a primitive metabolic pathway to produce ATP and increase the efficiency of oxygen transport.

Not all organisms use hemoglobin as the method of oxygen transport. Invertebrates that utilize hemolymph rather than blood use different pigments to bind to the oxygen. These pigments use copper or iron to the oxygen. Invertebrates have a variety of other respiratory pigments. Hemocyanin, a blue-green, copper-containing protein, illustrated in [link]**b** is found in mollusks, crustaceans, and some of the arthropods. Chlorocruorin, a green-colored, iron-containing pigment is found in four families of polychaete tubeworms. Hemerythrin, a red, iron-containing protein is found in some polychaete worms and annelids and is illustrated in [link]**c**. Despite the name, hemerythrin does not contain a heme group and its oxygen-carrying capacity is poor compared to hemoglobin.

In most vertebrates, (a) hemoglobin delivers oxygen to the body and removes some carbon dioxide. Hemoglobin is composed of four protein subunits, two alpha chains and two beta chains, and a heme group that has iron associated with it. The iron reversibly associates with oxygen, and in so doing is oxidized from Fe^{2+} to Fe^{3+}. In most mollusks and some arthropods, (b) hemocyanin delivers oxygen. Unlike hemoglobin, hemolymph is not carried in blood cells, but floats free in the hemolymph. Copper instead of iron binds the oxygen, giving the hemolymph a blue-green color. In annelids, such as the earthworm, and some other invertebrates, (c) hemerythrin carries oxygen. Like hemoglobin, hemerythrin is carried in blood cells and has iron associated with it, but despite its name, hemerythrin does not contain

heme.

The small size and large surface area of red blood cells allows for rapid diffusion of oxygen and carbon dioxide across the plasma membrane. In the lungs, carbon dioxide is released and oxygen is taken in by the blood. In the tissues, oxygen is released from the blood and carbon dioxide is bound for transport back to the lungs. Studies have found that hemoglobin also binds nitrous oxide (NO). NO is a vasodilator that relaxes the blood vessels and capillaries and may help with gas exchange and the passage of red blood cells through narrow vessels. Nitroglycerin, a heart medication for angina and heart attacks, is converted to NO to help relax the blood vessels and increase oxygen flow through the body.

A characteristic of red blood cells is their glycolipid and glycoprotein coating; these are lipids and proteins that have carbohydrate molecules attached. In humans, the surface glycoproteins and glycolipids on red blood cells vary between individuals, producing the different blood types, such as A, B, and O. Red blood cells have an average life span of 120 days, at which time they are broken down and recycled in the liver and spleen by phagocytic macrophages, a type of white blood cell.

White Blood Cells

White blood cells, also called leukocytes (leuko = white), make up approximately one percent by volume of the cells in blood. The role of white blood cells is very different than that of red blood cells: they are primarily involved in the immune response to identify and target pathogens, such as invading bacteria, viruses, and other foreign organisms. White blood cells are formed continually; some only live for hours or days, but some live for years.

The morphology of white blood cells differs significantly from red blood cells. They have nuclei and do not contain hemoglobin. The different types of white blood cells are identified by their microscopic appearance after histologic staining, and each has a different specialized function. The two main groups, both illustrated in [link] are the granulocytes, which include the neutrophils, eosinophils, and basophils, and the agranulocytes, which include the monocytes and lymphocytes.

(a) Granulocytes—including neutrophils, eosinophils and basophils—are characterized by a lobed nucleus and granular inclusions in the cytoplasm. Granulocytes are typically first-responders during injury or infection. (b) Agranulocytes include lymphocytes and monocytes. Lymphocytes, including B and T cells, are responsible for adaptive immune response. Monocytes differentiate into macrophages and dendritic cells, which in turn respond to infection or

injury.

Granulocytes contain granules in their cytoplasm; the agranulocytes are so named because of the lack of granules in their cytoplasm. Some leukocytes become macrophages that either stay at the same site or move through the blood stream and gather at sites of infection or inflammation where they are attracted by chemical signals from foreign particles and damaged cells. Lymphocytes are the primary cells of the immune system and include B cells, T cells, and natural killer cells. B cells destroy bacteria and inactivate their toxins. They also produce antibodies. T cells attack viruses, fungi, some bacteria, transplanted cells, and cancer cells. T cells attack viruses by releasing toxins that kill the viruses. Natural killer cells attack a variety of infectious microbes and certain tumor cells.

One reason that HIV poses significant management challenges is because the virus directly targets T cells by gaining entry through a receptor. Once inside the cell, HIV then multiplies using the T cell's own genetic machinery. After the HIV virus replicates, it is transmitted directly from the infected T cell to macrophages. The presence of HIV can remain unrecognized for an extensive period of time before full disease symptoms develop.

Platelets and Coagulation Factors

Blood must clot to heal wounds and prevent excess blood loss. Small cell fragments called platelets (thrombocytes) are attracted to the wound site where they adhere by extending many projections and releasing their contents. These contents activate other platelets and also interact with other coagulation factors, which convert fibrinogen, a water-soluble protein present in blood serum into fibrin (a non-water soluble protein), causing the blood to clot. Many of the clotting factors require vitamin K to work, and vitamin K deficiency can lead to problems with blood clotting. Many platelets converge and stick together at the wound site forming a platelet plug (also called a fibrin clot), as illustrated in [link]**b**. The plug or clot lasts for a number of days and stops the loss of blood. Platelets are formed from the disintegration of larger cells called megakaryocytes, like that shown in [link]**a**. For each megakaryocyte, 2000–3000 platelets are formed with 150,000 to 400,000 platelets present in each cubic millimeter of blood. Each platelet is disc shaped and 2–4 μm in diameter. They contain many small vesicles but do not contain a nucleus.

(a) Platelets are formed from large cells called megakaryocytes. The megakaryocyte breaks up into thousands of fragments that become platelets. (b) Platelets are required for clotting of the blood. The platelets collect at a wound site in conjunction with other clotting factors, such as fibrinogen, to form a fibrin clot that prevents blood loss and allows the wound to heal.

Plasma and Serum

The liquid component of blood is called plasma, and it is separated by spinning or centrifuging the blood at high rotations (3000 rpm or higher). The blood cells and platelets are separated by centrifugal forces to the bottom of a specimen tube. The upper liquid layer, the plasma, consists of 90 percent water along with various substances required for maintaining the body's pH, osmotic load, and for protecting the body. The plasma also contains the coagulation factors and antibodies.

The plasma component of blood without the coagulation factors is called the serum. Serum is similar to interstitial fluid in which the correct composition of key ions acting as electrolytes is essential for normal functioning of muscles and nerves. Other components in the serum include proteins that assist with maintaining pH and osmotic balance while giving viscosity to the blood. The serum also contains antibodies, specialized proteins that are important for defense against viruses and bacteria. Lipids, including cholesterol, are also transported in the serum, along with various other substances including nutrients, hormones, metabolic waste, plus external substances, such as, drugs, viruses, and bacteria.

Human serum albumin is the most abundant protein in human blood plasma and is synthesized in the liver. Albumin, which constitutes about half of the blood serum protein, transports hormones and fatty acids, buffers pH, and maintains osmotic pressures. Immunoglobin is a protein antibody produced in the mucosal lining and plays an important role in antibody mediated immunity.

Evolution Connection

Blood Types Related to Proteins on the Surface of the Red Blood Cells Red blood cells are coated in antigens made of glycolipids and glycoproteins. The composition of these molecules is determined by genetics, which have evolved over time. In humans, the different surface antigens are grouped into 24 different blood groups with more than 100 different antigens on each red blood cell. The two most well known blood groups are the ABO, shown in [link], and Rh systems. The surface antigens in the ABO blood group are glycolipids, called antigen A and antigen B. People with blood type A have antigen A, those with blood type B have antigen B, those with blood type AB have both antigens, and people with blood type O have neither antigen. Antibodies called agglutinougens are found in the blood plasma and react with the A or B antigens, if the two are mixed. When type A and type B blood are combined, agglutination (clumping) of the blood occurs because of antibodies in the plasma that bind with the opposing antigen; this causes clots that coagulate in the kidney causing kidney failure. Type O blood has neither A or B antigens, and therefore, type O blood can be given to all blood types. Type O negative blood is the universal donor. Type AB positive blood is the universal acceptor because it has both A and B antigen. The ABO blood groups were discovered in 1900 and 1901 by Karl Landsteiner at the University of Vienna.

The Rh blood group was first discovered in Rhesus monkeys. Most people have the Rh antigen (Rh+) and do not have anti-Rh antibodies in their blood. The few people who do not have the Rh antigen and are Rh– can develop anti-Rh antibodies if exposed to Rh+ blood. This can happen after a blood transfusion or after an Rh– woman has an Rh+ baby. The first exposure does not usually cause a reaction; however, at the second exposure, enough antibodies have built up in the blood to produce a reaction that causes agglutination and breakdown of red blood cells. An injection can prevent this reaction.

Human red blood cells may have either type A or B glycoproteins on their surface, both glycoproteins combined (AB), or neither (O). The glycoproteins serve as antigens and can elicit an immune response in a person who receives a transfusion containing unfamiliar antigens. Type O blood, which has no A or B antigens, does not elicit an immune response when injected into a person of any blood type. Thus, O is considered the universal donor. Persons with type AB blood can accept blood from any blood type, and type AB is considered the universal acceptor.

Link to Learning

Play a blood typing game on the Nobel Prize website to solidify your understanding of blood types.

Section Summary

Specific components of the blood include red blood cells, white blood cells, platelets, and the plasma, which contains coagulation factors and serum. Blood is important for regulation of the body's pH, temperature, osmotic pressure, the circulation of nutrients and removal of waste, the distribution of hormones from endocrine glands, and the elimination of excess heat; it also contains components for blood clotting. Red blood cells are specialized cells that contain hemoglobin and circulate through the body delivering oxygen to cells. White blood cells are involved in the immune response to identify and target invading bacteria, viruses, and other foreign organisms; they also recycle waste components, such as old red blood cells. Platelets and blood clotting factors cause the change of the soluble protein fibrinogen to the insoluble protein fibrin at a wound site forming a plug. Plasma consists of 90 percent water along with various substances, such as coagulation factors and antibodies. The serum is the plasma component of the blood without the coagulation factors.

Review Questions

White blood cells:

a. can be classified as granulocytes or agranulocytes
b. defend the body against bacteria and viruses
c. are also called leucocytes
d. All of the above

D

Platelet plug formation occurs at which point?

a. when large megakaryocytes break up into thousands of smaller fragments
b. when platelets are dispersed through the blood stream
c. when platelets are attracted to a site of blood vessel damage
d. none of the above

C

In humans, the plasma comprises what percentage of the blood?

a. 45 percent
b. 55 percent
c. 25 percent
d. 90 percent

B

The red blood cells of birds differ from mammalian red blood cells because:

a. they are white and have nuclei
b. they do not have nuclei
c. they have nuclei
d. they fight disease

C

Free Response

Describe the cause of different blood type groups.

Red blood cells are coated with proteins called antigens made of glycolipids and glycoproteins. When type A and type B blood are mixed, the blood agglutinates because of antibodies in the plasma that bind with the opposing antigen. Type O blood has no antigens. The Rh blood group has either the Rh antigen (Rh+) or no Rh antigen (Rh–).

List some of the functions of blood in the body.

Blood is important for regulation of the body's pH, temperature, and osmotic pressure, the circulation of nutrients and removal of wastes, the distribution of hormones from endocrine glands, the elimination of excess heat; it also contains components for the clotting of blood to prevent blood loss. Blood also transports clotting factors and disease-fighting agents.

How does the lymphatic system work with blood flow?

Lymph capillaries take fluid from the blood to the lymph nodes. The lymph nodes filter the lymph by percolation through connective tissue filled with white blood cells. The white blood cells remove infectious agents, such as bacteria and viruses, to clean the lymph before it returns to the bloodstream.

Glossary

plasma
: liquid component of blood that is left after the cells are removed

platelet
: (also, thrombocyte) small cellular fragment that collects at wounds, cross-reacts with clotting factors, and forms a plug to prevent blood loss

red blood cell
: small (7–8 μm) biconcave cell without mitochondria (and in mammals without nuclei) that is packed with hemoglobin, giving the cell its red color; transports oxygen through the body

serum
: plasma without the coagulation factors

white blood cell
: large (30 μm) cell with nuclei of which there are many types with different roles including the protection of the body from viruses and bacteria, and cleaning up dead cells and other waste

Mammalian Heart and Blood Vessels

By the end of this section, you will be able to:

- Describe the structure of the heart and explain how cardiac muscle is different from other muscles
- Describe the cardiac cycle

- Explain the structure of arteries, veins, and capillaries, and how blood flows through the body

The heart is a complex muscle that pumps blood through the three divisions of the circulatory system: the coronary (vessels that serve the heart), pulmonary (heart and lungs), and systemic (systems of the body), as shown in [link]. Coronary circulation intrinsic to the heart takes blood directly from the main artery (aorta) coming from the heart. For pulmonary and systemic circulation, the heart has to pump blood to the lungs or the rest of the body, respectively. In vertebrates, the lungs are relatively close to the heart in the thoracic cavity. The shorter distance to pump means that the muscle wall on the right side of the heart is not as thick as the left side which must have enough pressure to pump blood all the way to your big toe.

Art Connection
The mammalian circulatory system is divided into three circuits: the systemic circuit, the pulmonary circuit, and the coronary circuit. Blood is pumped from veins of the systemic circuit into the right atrium of the heart, then into the right ventricle. Blood then enters the pulmonary circuit, and is oxygenated by the lungs. From the pulmonary circuit, blood re-enters the heart through the left atrium. From the left ventricle, blood re-enters the systemic circuit through the aorta and is distributed to the rest of the body. The coronary circuit, which provides blood to the heart, is not shown.

Which of the following statements about the circulatory system is false?

a. Blood in the pulmonary vein is deoxygenated.
b. Blood in the inferior vena cava is deoxygenated.
c. Blood in the pulmonary artery is deoxygenated.
d. Blood in the aorta is oxygenated.

Structure of the Heart

The heart muscle is asymmetrical as a result of the distance blood must travel in the pulmonary and systemic circuits. Since the right side of the heart sends blood to the pulmonary circuit it is smaller than the left side which must send blood out to the whole body in the systemic circuit, as shown in [link]. In humans, the heart is about the size of a clenched fist; it is divided into four chambers: two atria and two ventricles. There is one atrium and one ventricle on the right side and one atrium and one ventricle on the left side. The atria are the chambers that receive blood, and the ventricles are the chambers that pump blood. The right atrium receives deoxygenated blood from the superior vena cava, which drains blood from the jugular vein that comes from the brain and from the veins that come from the arms, as well as from the inferior vena cava which drains blood from the veins that come from the lower organs and the legs. In addition, the right atrium receives blood from the coronary sinus which drains deoxygenated blood from the heart itself. This deoxygenated blood then passes to the right ventricle through the atrioventricular valve or the tricuspid valve, a flap of connective tissue that opens in only one direction to prevent the backflow of blood. The valve separating the chambers on the left side of the heart valve is called the biscuspid or mitral valve. After it is filled, the right ventricle pumps the blood through the pulmonary arteries, by-passing the semilunar valve (or pulmonic valve) to the lungs for re-oxygenation. After blood passes through the pulmonary arteries, the right semilunar valves close preventing the blood from flowing backwards into the right ventricle. The left atrium then receives the oxygen-rich blood from the lungs via the pulmonary veins. This blood passes through the bicuspid valve or mitral valve (the atrioventricular valve on the left side of the heart) to the left ventricle where the blood is pumped out through aorta, the major artery of the body, taking oxygenated blood to the organs and muscles of the body. Once blood is pumped out of the left ventricle and into the aorta, the aortic semilunar valve (or aortic valve) closes preventing blood from flowing backward into the left ventricle. This pattern of pumping is referred to as double circulation and is found in all mammals.

Art Connection
(a) The heart is primarily made of a thick muscle layer, called the myocardium, surrounded by membranes. One-way valves separate the four chambers. (b) Blood vessels of the

coronary system, including the coronary arteries and veins, keep the heart musculature

oxygenated.

Which of the following statements about the heart is false?

a. The mitral valve separates the left ventricle from the left atrium.
b. Blood travels through the bicuspid valve to the left atrium.
c. Both the aortic and the pulmonary valves are semilunar valves.
d. The mitral valve is an atrioventricular valve.

The heart is composed of three layers; the epicardium, the myocardium, and the endocardium, illustrated in [link]. The inner wall of the heart has a lining called the endocardium. The myocardium consists of the heart muscle cells that make up the middle layer and the bulk of the heart wall. The outer layer of cells is called the epicardium, of which the second layer is a membranous layered structure called the pericardium that surrounds and protects the heart; it allows enough room for vigorous pumping but also keeps the heart in place to reduce friction between the heart and other structures.

The heart has its own blood vessels that supply the heart muscle with blood. The coronary arteries branch from the aorta and surround the outer surface of the heart like a crown. They diverge into capillaries where the heart muscle is supplied with oxygen before converging again into the coronary veins to take the deoxygenated blood back to the right atrium where the blood will be re-oxygenated through the pulmonary circuit. The heart muscle will die

without a steady supply of blood. Atherosclerosis is the blockage of an artery by the buildup of fatty plaques. Because of the size (narrow) of the coronary arteries and their function in serving the heart itself, atherosclerosis can be deadly in these arteries. The slowdown of blood flow and subsequent oxygen deprivation that results from atherosclerosis causes severe pain, known as angina, and complete blockage of the arteries will cause myocardial infarction: the death of cardiac muscle tissue, commonly known as a heart attack.

The Cardiac Cycle

The main purpose of the heart is to pump blood through the body; it does so in a repeating sequence called the cardiac cycle. The cardiac cycle is the coordination of the filling and emptying of the heart of blood by electrical signals that cause the heart muscles to contract and relax. The human heart beats over 100,000 times per day. In each cardiac cycle, the heart contracts (systole), pushing out the blood and pumping it through the body; this is followed by a relaxation phase (diastole), where the heart fills with blood, as illustrated in [link]. The atria contract at the same time, forcing blood through the atrioventricular valves into the ventricles. Closing of the atrioventricular valves produces a monosyllabic “lup” sound. Following a brief delay, the ventricles contract at the same time forcing blood through the semilunar valves into the aorta and the artery transporting blood to the lungs (via the pulmonary artery). Closing of the semilunar valves produces a monosyllabic “dup” sound.

During (a) cardiac diastole, the heart muscle is relaxed and blood flows into the heart. During (b) atrial systole, the atria contract, pushing blood into the ventricles. During (c) atrial diastole, the ventricles contract, forcing blood out of the

heart.

The pumping of the heart is a function of the cardiac muscle cells, or cardiomyocytes, that make up the heart muscle. Cardiomyocytes, shown in [link], are distinctive muscle cells that are striated like skeletal muscle but pump rhythmically and involuntarily like smooth muscle; they are connected by intercalated disks exclusive to cardiac muscle. They are self-stimulated for a period of time and isolated cardiomyocytes will beat if given the correct balance of nutrients and electrolytes.

Cardiomyocytes are striated muscle cells found in cardiac tissue. (credit: modification of work by Dr. S. Girod, Anton Becker; scale-bar data from Matt

Russell)

The autonomous beating of cardiac muscle cells is regulated by the heart's internal pacemaker that uses electrical signals to time the beating of the heart. The electrical signals and mechanical actions, illustrated in [link], are intimately intertwined. The internal pacemaker starts at the sinoatrial (SA) node, which is located near the wall of the right atrium. Electrical charges spontaneously pulse from the SA node causing the two atria to contract in unison. The pulse reaches a second node, called the atrioventricular (AV) node, between the right atrium and right ventricle where it pauses for approximately 0.1 second before spreading to the walls of the ventricles. From the AV node, the electrical impulse enters the bundle of His, then to the left and right bundle branches extending through the interventricular septum. Finally, the Purkinje fibers conduct the impulse from the apex of the heart up the ventricular myocardium, and then the ventricles contract. This pause allows the atria to empty completely into the ventricles before the ventricles pump out the blood. The electrical impulses in the heart produce electrical currents that flow through the body and can be measured on the skin using electrodes. This information can be observed as an electrocardiogram (ECG)—a recording of the electrical impulses of the cardiac muscle.

The beating of the heart is regulated by an electrical impulse that causes the characteristic reading of an ECG. The signal is initiated at the sinoatrial valve. The signal then (a) spreads to the atria, causing them to contract. The signal is (b) delayed at the atrioventricular node before it is passed on to the (c) heart apex. The delay allows the atria to relax before the (d) ventricles contract. The final part of the ECG cycle prepares the heart for the next

beat.

Link to Learning

Visit this site and select the dropdown “Your Heart’s Electrical System” to see the heart’s “pacemaker” in action.

Arteries, Veins, and Capillaries

The blood from the heart is carried through the body by a complex network of blood vessels ([link]). Arteries take blood away from the heart. The main artery is the aorta that branches into major arteries that take blood to different limbs and organs. These major arteries include the carotid artery that takes blood to the brain, the brachial arteries that take blood to the

arms, and the thoracic artery that takes blood to the thorax and then into the hepatic, renal, and gastric arteries for the liver, kidney, and stomach, respectively. The iliac artery takes blood to the lower limbs. The major arteries diverge into minor arteries, and then smaller vessels called arterioles, to reach more deeply into the muscles and organs of the body.

The major human arteries and veins are shown. (credit: modification of work by Mariana Ruiz Villareal)

Arterioles diverge into capillary beds. Capillary beds contain a large number (10 to 100) of capillaries that branch among the cells and tissues of the body. Capillaries are narrow-diameter tubes that can fit red blood cells through in single file and are the sites for the exchange of nutrients, waste, and oxygen with tissues at the cellular level. Fluid also crosses into the interstitial space from the capillaries. The capillaries converge again into venules that connect to minor veins that finally connect to major veins that take blood high in carbon dioxide back to the heart. Veins are blood vessels that bring blood back to the heart. The major veins drain blood from the same organs and limbs that the major arteries supply. Fluid is also brought back to the heart via the lymphatic system.

The structure of the different types of blood vessels reflects their function or layers. There are three distinct layers, or tunics, that form the walls of blood vessels ([link]). The first tunic is a smooth, inner lining of endothelial cells that are in contact with the red blood cells. The endothelial tunic is continuous with the endocardium of the heart. In capillaries, this single layer of cells is the location of diffusion of oxygen and carbon dioxide between the endothelial cells and red blood cells, as well as the exchange site via endocytosis and exocytosis. The movement of materials at the site of capillaries is regulated by vasoconstriction, narrowing of the blood vessels, and vasodilation, widening of the blood vessels; this is important in the overall regulation of blood pressure.

Veins and arteries both have two further tunics that surround the endothelium: the middle tunic is composed of smooth muscle and the outermost layer is connective tissue (collagen and elastic fibers). The elastic connective tissue stretches and supports the blood vessels, and the smooth muscle layer helps regulate blood flow by altering vascular resistance through vasoconstriction and vasodilation. The arteries have thicker smooth muscle and connective tissue than the veins to accommodate the higher pressure and speed of freshly pumped blood. The veins are thinner walled as the pressure and rate of flow are much lower. In addition,

veins are structurally different than arteries in that veins have valves to prevent the backflow of blood. Because veins have to work against gravity to get blood back to the heart, contraction of skeletal muscle assists with the flow of blood back to the heart.

Arteries and veins consist of three layers: an outer tunica externa, a middle tunica media, and an inner tunica intima. Capillaries consist of a single layer of epithelial cells, the tunica intima. (credit: modification of work by NCI,

NIH)

Section Summary

The heart muscle pumps blood through three divisions of the circulatory system: coronary, pulmonary, and systemic. There is one atrium and one ventricle on the right side and one atrium and one ventricle on the left side. The pumping of the heart is a function of cardiomyocytes, distinctive muscle cells that are striated like skeletal muscle but pump rhythmically and involuntarily like smooth muscle. The internal pacemaker starts at the sinoatrial node, which is located near the wall of the right atrium. Electrical charges pulse from the SA node causing the two atria to contract in unison; then the pulse reaches the atrioventricular node between the right atrium and right ventricle. A pause in the electric signal allows the atria to empty completely into the ventricles before the ventricles pump out the blood. The blood from the heart is carried through the body by a complex network of blood vessels; arteries take blood away from the heart, and veins bring blood back to the heart.

Art Connections

[link] Which of the following statements about the circulatory system is false?

a. Blood in the pulmonary vein is deoxygenated.
b. Blood in the inferior vena cava is deoxygenated.
c. Blood in the pulmonary artery is deoxygenated.
d. Blood in the aorta is oxygenated.

[link] C

[link] Which of the following statements about the heart is false?

a. The mitral valve separates the left ventricle from the left atrium.
b. Blood travels through the bicuspid valve to the left atrium.
c. Both the aortic and the pulmonary valves are semilunar valves.
d. The mitral valve is an atrioventricular valve.

[link] B

Review Questions

The heart's internal pacemaker beats by:

a. an internal implant that sends an electrical impulse through the heart
b. the excitation of cardiac muscle cells at the sinoatrial node followed by the atrioventricular node
c. the excitation of cardiac muscle cells at the atrioventricular node followed by the sinoatrial node
d. the action of the sinus

B

During the systolic phase of the cardiac cycle, the heart is _____.

a. contracting
b. relaxing
c. contracting and relaxing
d. filling with blood

A

Cardiomyocytes are similar to skeletal muscle because:

a. they beat involuntarily
b. they are used for weight lifting
c. they pulse rhythmically
d. they are striated

D

How do arteries differ from veins?

a. Arteries have thicker smooth muscle layers to accommodate the changes in pressure from the heart.
b. Arteries carry blood.
c. Arteries have thinner smooth muscle layers and valves and move blood by the action of skeletal muscle.
d. Arteries are thin walled and are used for gas exchange.

A

Free Response

Describe the cardiac cycle.

The heart receives an electrical signal from the sinoatrial node triggering the cardiac muscle cells in the atria to contract. The signal pauses at the atrioventricular node before spreading to the walls of the ventricles so the blood is pumped through the body. This is the systolic phase. The heart then relaxes in the diastole and fills again with blood.

What happens in capillaries?

The capillaries basically exchange materials with their surroundings. Their walls are very thin and are made of one or two layers of cells, where gases, nutrients, and waste are diffused. They are distributed as beds, complex networks that link arteries as well as veins.

Glossary

angina
: pain caused by partial blockage of the coronary arteries by the buildup of plaque and lack of oxygen to the heart muscle

aorta
: major artery of the body that takes blood away from the heart

arteriole
: small vessel that connects an artery to a capillary bed

artery
: blood vessel that takes blood away from the heart

atherosclerosis
: buildup of fatty plaques in the coronary arteries in the heart

atrioventricular valve
: one-way membranous flap of connective tissue between the atrium and the ventricle in the right side of the heart; also known as tricuspid valve

bicuspid valve
: (also, mitral valve; left atrioventricular valve) one-way membranous flap between the atrium and the ventricle in the left side of the heart

capillary
: smallest blood vessel that allows the passage of individual blood cells and the site of diffusion of oxygen and nutrient exchange

capillary bed

large number of capillaries that converge to take blood to a particular organ or tissue

cardiac cycle
: filling and emptying the heart of blood by electrical signals that cause the heart muscles to contract and relax

cardiomyocyte
: specialized heart muscle cell that is striated but contracts involuntarily like smooth muscle

coronary artery
: vessel that supplies the heart tissue with blood

coronary vein
: vessel that takes blood away from the heart tissue back to the chambers in the heart

diastole
: relaxation phase of the cardiac cycle when the heart is relaxed and the ventricles are filling with blood

electrocardiogram (ECG)
: recording of the electrical impulses of the cardiac muscle

endocardium
: innermost layer of tissue in the heart

epicardium
: outermost tissue layer of the heart

inferior vena cava
: drains blood from the veins that come from the lower organs and the legs

myocardial infarction
: (also, heart attack) complete blockage of the coronary arteries and death of the cardiac muscle tissue

myocardium
: heart muscle cells that make up the middle layer and the bulk of the heart wall

pericardium
: membrane layer protecting the heart; also part of the epicardium

semilunar valve
: membranous flap of connective tissue between the aorta and a ventricle of the heart (the aortic or pulmonary semilunar valves)

sinoatrial (SA) node
: the heart’s internal pacemaker; located near the wall of the right atrium

superior vena cava
: drains blood from the jugular vein that comes from the brain and from the veins that come from the arms

systole
: contraction phase of cardiac cycle when the ventricles are pumping blood into the arteries

tricuspid valve

one-way membranous flap of connective tissue between the atrium and the ventricle in the right side of the heart; also known as atrioventricular valve

vasoconstriction
: narrowing of a blood vessel

vasodilation
: widening of a blood vessel

vein
: blood vessel that brings blood back to the heart

vena cava
: major vein of the body returning blood from the upper and lower parts of the body; see the superior vena cava and inferior vena cava

venule
: blood vessel that connects a capillary bed to a vein

Blood Flow and Blood Pressure Regulation

By the end of this section, you will be able to:

- Describe the system of blood flow through the body
- Describe how blood pressure is regulated

Blood pressure (BP) is the pressure exerted by blood on the walls of a blood vessel that helps to push blood through the body. Systolic blood pressure measures the amount of pressure that blood exerts on vessels while the heart is beating. The optimal systolic blood pressure is 120 mmHg. Diastolic blood pressure measures the pressure in the vessels between heartbeats. The optimal diastolic blood pressure is 80 mmHg. Many factors can affect blood pressure, such as hormones, stress, exercise, eating, sitting, and standing. Blood flow through the body is regulated by the size of blood vessels, by the action of smooth muscle, by one-way valves, and by the fluid pressure of the blood itself.

How Blood Flows Through the Body

Blood is pushed through the body by the action of the pumping heart. With each rhythmic pump, blood is pushed under high pressure and velocity away from the heart, initially along the main artery, the aorta. In the aorta, the blood travels at 30 cm/sec. As blood moves into the arteries, arterioles, and ultimately to the capillary beds, the rate of movement slows dramatically to about 0.026 cm/sec, one-thousand times slower than the rate of movement in the aorta. While the diameter of each individual arteriole and capillary is far narrower than the diameter of the aorta, and according to the law of continuity, fluid should travel faster through a narrower diameter tube, the rate is actually slower due to the overall diameter of all the combined capillaries being far greater than the diameter of the individual aorta.

The slow rate of travel through the capillary beds, which reach almost every cell in the body, assists with gas and nutrient exchange and also promotes the diffusion of fluid into the interstitial space. After the blood has passed through the capillary beds to the venules, veins, and finally to the main venae cavae, the rate of flow increases again but is still much slower than the initial rate in the aorta. Blood primarily moves in the veins by the rhythmic movement of smooth muscle in the vessel wall and by the action of the skeletal muscle as the

body moves. Because most veins must move blood against the pull of gravity, blood is prevented from flowing backward in the veins by one-way valves. Because skeletal muscle contraction aids in venous blood flow, it is important to get up and move frequently after long periods of sitting so that blood will not pool in the extremities.

Blood flow through the capillary beds is regulated depending on the body's needs and is directed by nerve and hormone signals. For example, after a large meal, most of the blood is diverted to the stomach by vasodilation of vessels of the digestive system and vasoconstriction of other vessels. During exercise, blood is diverted to the skeletal muscles through vasodilation while blood to the digestive system would be lessened through vasoconstriction. The blood entering some capillary beds is controlled by small muscles, called precapillary sphincters, illustrated in [link]. If the sphincters are open, the blood will flow into the associated branches of the capillary blood. If all of the sphincters are closed, then the blood will flow directly from the arteriole to the venule through the thoroughfare channel (see [link]). These muscles allow the body to precisely control when capillary beds receive blood flow. At any given moment only about 5-10% of our capillary beds actually have blood flowing through them.

Art Connection
(a) Precapillary sphincters are rings of smooth muscle that regulate the flow of blood through capillaries; they help control the location of blood flow to where it is needed. (b) Valves in

the veins prevent blood from moving backward. (credit a: modification of work by

NCI)

Varicose veins are veins that become enlarged because the valves no longer close properly, allowing blood to flow backward. Varicose veins are often most prominent on the legs. Why do you think this is the case?

Link to Learning

See the circulatory system’s blood flow.

Introduction

class="introduction" class="summary" title="Sections Summary" class="art-exercise" title="Art Connections" class="multiple-choice" title="Multiple Choice" class="free-

response" title="Free Response"Just as humans recycle what we can and dump the remains into landfills, our bodies use and recycle what they can and excrete the remaining waste products. Our bodies' complex systems have developed ways to treat waste and maintain a balanced internal environment. (credit: modification of work by Redwin Law)

The daily intake recommendation for human water consumption is eight to ten glasses of water. In order to achieve a healthy balance, the human body should excrete the eight to ten glasses of water every day. This occurs via the processes of urination, defecation, sweating and, to a small extent, respiration. The organs and tissues of the human body are soaked in fluids that are maintained at constant temperature, pH, and solute concentration, all crucial elements of homeostasis. The solutes in body fluids are mainly mineral salts and sugars, and osmotic regulation is the process by which the mineral salts and water are kept in balance. Osmotic homeostasis is maintained despite the influence of external factors like temperature, diet, and weather conditions.

Osmoregulation and Osmotic Balance
By the end of this section, you will be able to:

- Define osmosis and explain its role within molecules
- Explain why osmoregulation and osmotic balance are important body functions
- Describe active transport mechanisms
- Explain osmolarity and the way in which it is measured
- Describe osmoregulators or osmoconformers and how these tools allow animals to adapt to different environments

Osmosis is the diffusion of water across a membrane in response to osmotic pressure caused by an imbalance of molecules on either side of the membrane. Osmoregulation is the process of maintenance of salt and water balance (osmotic balance) across membranes within the body's fluids, which are composed of water, plus electrolytes and non-electrolytes. An electrolyte is a solute that dissociates into ions when dissolved in water. A non-electrolyte, in contrast, doesn't dissociate into ions during water dissolution. Both electrolytes and non-electrolytes contribute to the osmotic balance. The body's fluids include blood plasma, the cytosol within cells, and interstitial fluid, the fluid that exists in the spaces between cells and tissues of the body. The membranes of the body (such as the pleural, serous, and cell membranes) are semi-permeable membranes. Semi-permeable membranes are permeable (or permissive) to certain types of solutes and water. Solutions on two sides of a semi-permeable membrane tend to equalize in solute concentration by movement of solutes and/or water across the membrane. As seen in [link], a cell placed in water tends to swell due to gain of water from the hypotonic or "low salt" environment. A cell placed in a solution with higher salt concentration, on the other hand, tends to make the membrane shrivel up due to loss of water into the hypertonic or "high salt" environment. Isotonic cells have an equal concentration of solutes inside and outside the cell; this equalizes the osmotic pressure on either side of the cell membrane which is a semi-permeable membrane.

Cells placed in a hypertonic environment tend to shrink due to loss of water. In a hypotonic environment, cells tend to swell due to intake of water. The blood maintains an isotonic

environment so that cells neither shrink nor swell. (credit: Mariana Ruiz Villareal)

The body does not exist in isolation. There is a constant input of water and electrolytes into the system. While osmoregulation is achieved across membranes within the body, excess electrolytes and wastes are transported to the kidneys and excreted, helping to maintain osmotic balance.

Need for Osmoregulation

Biological systems constantly interact and exchange water and nutrients with the environment by way of consumption of food and water and through excretion in the form of sweat, urine, and feces. Without a mechanism to regulate osmotic pressure, or when a disease damages this mechanism, there is a tendency to accumulate toxic waste and water, which can have dire consequences.

Mammalian systems have evolved to regulate not only the overall osmotic pressure across membranes, but also specific concentrations of important electrolytes in the three major fluid compartments: blood plasma, extracellular fluid, and intracellular fluid. Since osmotic pressure is regulated by the movement of water across membranes, the volume of the fluid compartments can also change temporarily. Because blood plasma is one of the fluid components, osmotic pressures have a direct bearing on blood pressure.

Transport of Electrolytes across Cell Membranes

Electrolytes, such as sodium chloride, ionize in water, meaning that they dissociate into their component ions. In water, sodium chloride (NaCl), dissociates into the sodium ion (Na^+) and the chloride ion (Cl^-). The most important ions, whose concentrations are very closely regulated in body fluids, are the cations sodium (Na^+), potassium (K^+), calcium (Ca^{+2}),

magnesium (Mg^{+2}), and the anions chloride (Cl^{-}), carbonate (CO_3^{-2}), bicarbonate (HCO_3^{-}), and phosphate(PO_3^{-}). Electrolytes are lost from the body during urination and perspiration. For this reason, athletes are encouraged to replace electrolytes and fluids during periods of increased activity and perspiration.

Osmotic pressure is influenced by the concentration of solutes in a solution. It is directly proportional to the number of solute atoms or molecules and not dependent on the size of the solute molecules. Because electrolytes dissociate into their component ions, they, in essence, add more solute particles into the solution and have a greater effect on osmotic pressure, per mass than compounds that do not dissociate in water, such as glucose.

Water can pass through membranes by passive diffusion. If electrolyte ions could passively diffuse across membranes, it would be impossible to maintain specific concentrations of ions in each fluid compartment therefore they require special mechanisms to cross the semi-permeable membranes in the body. This movement can be accomplished by facilitated diffusion and active transport. Facilitated diffusion requires protein-based channels for moving the solute. Active transport requires energy in the form of ATP conversion, carrier proteins, or pumps in order to move ions against the concentration gradient.

Concept of Osmolality and Milliequivalent

In order to calculate osmotic pressure, it is necessary to understand how solute concentrations are measured. The unit for measuring solutes is the mole. One mole is defined as the gram molecular weight of the solute. For example, the molecular weight of sodium chloride is 58.44. Thus, one mole of sodium chloride weighs 58.44 grams. The molarity of a solution is the number of moles of solute per liter of solution. The molality of a solution is the number of moles of solute per kilogram of solvent. If the solvent is water, one kilogram of water is equal to one liter of water. While molarity and molality are used to express the concentration of solutions, electrolyte concentrations are usually expressed in terms of milliequivalents per liter (mEq/L): the mEq/L is equal to the ion concentration (in millimoles) multiplied by the number of electrical charges on the ion. The unit of milliequivalent takes into consideration the ions present in the solution (since electrolytes form ions in aqueous solutions) and the charge on the ions.

Thus, for ions that have a charge of one, one milliequivalent is equal to one millimole. For ions that have a charge of two (like calcium), one milliequivalent is equal to 0.5 millimoles. Another unit for the expression of electrolyte concentration is the milliosmole (mOsm), which is the number of milliequivalents of solute per kilogram of solvent. Body fluids are usually maintained within the range of 280 to 300 mOsm.

Osmoregulators and Osmoconformers

Persons lost at sea without any fresh water to drink are at risk of severe dehydration because the human body cannot adapt to drinking seawater, which is hypertonic in comparison to body fluids. Organisms such as goldfish that can tolerate only a relatively narrow range of salinity are referred to as stenohaline. About 90 percent of all bony fish are restricted to either freshwater or seawater. They are incapable of osmotic regulation in the opposite environment. It is possible, however, for a few fishes like salmon to spend part of their life in fresh water and part in sea water. Organisms like the salmon and molly that can tolerate a relatively wide range of salinity are referred to as euryhaline organisms. This is possible

because some fish have evolved osmoregulatory mechanisms to survive in all kinds of aquatic environments. When they live in fresh water, their bodies tend to take up water because the environment is relatively hypotonic, as illustrated in [link]**a**. In such hypotonic environments, these fish do not drink much water. Instead, they pass a lot of very dilute urine, and they achieve electrolyte balance by active transport of salts through the gills. When they move to a hypertonic marine environment, these fish start drinking sea water; they excrete the excess salts through their gills and their urine, as illustrated in [link]**b**. Most marine invertebrates, on the other hand, may be isotonic with sea water (osmoconformers). Their body fluid concentrations conform to changes in seawater concentration. Cartilaginous fishes' salt composition of the blood is similar to bony fishes; however, the blood of sharks contains the organic compounds urea and trimethylamine oxide (TMAO). This does not mean that their electrolyte composition is similar to that of sea water. They achieve isotonicity with the sea by storing large concentrations of urea. These animals that secrete urea are called ureotelic animals. TMAO stabilizes proteins in the presence of high urea levels, preventing the disruption of peptide bonds that would occur in other animals exposed to similar levels of urea. Sharks are cartilaginous fish with a rectal gland to secrete salt and assist in osmoregulation.

Fish are osmoregulators, but must use different mechanisms to survive in (a) freshwater or (b) saltwater environments. (credit: modification of work by Duane Raver,

NOAA)

Career Connection

Dialysis TechnicianDialysis is a medical process of removing wastes and excess water from the blood by diffusion and ultrafiltration. When kidney function fails, dialysis must be done to artificially rid the body of wastes. This is a vital process to keep patients alive. In some cases, the patients undergo artificial dialysis until they are eligible for a kidney transplant. In others who are not candidates for kidney transplants, dialysis is a life-long necessity.

Dialysis technicians typically work in hospitals and clinics. While some roles in this field include equipment development and maintenance, most dialysis technicians work in direct patient care. Their on-the-job duties, which typically occur under the direct supervision of a registered nurse, focus on providing dialysis treatments. This can include reviewing patient history and current condition, assessing and responding to patient needs before and during treatment, and monitoring the dialysis process. Treatment may include taking and reporting a patient's vital signs and preparing solutions and equipment to ensure accurate and sterile procedures.

Section Summary

Solute concentrations across a semi-permeable membranes influence the movement of water and solutes across the membrane. It is the number of solute molecules and not the molecular size that is important in osmosis. Osmoregulation and osmotic balance are important bodily functions, resulting in water and salt balance. Not all solutes can pass through a semi-permeable membrane. Osmosis is the movement of water across the membrane. Osmosis occurs to equalize the number of solute molecules across a semi-permeable membrane by the movement of water to the side of higher solute concentration. Facilitated diffusion utilizes protein channels to move solute molecules from areas of higher to lower concentration while active transport mechanisms are required to move solutes against concentration gradients. Osmolarity is measured in units of milliequivalents or milliosmoles, both of which take into consideration the number of solute particles and the charge on them. Fish that live in fresh water or saltwater adapt by being osmoregulators or osmoconformers.

Review Questions

When a dehydrated human patient needs to be given fluids intravenously, he or she is given:

a. water, which is hypotonic with respect to body fluids
b. saline at a concentration that is isotonic with respect to body fluids
c. glucose because it is a non-electrolyte
d. blood

B

The sodium ion is at the highest concentration in:

a. intracellular fluid
b. extracellular fluid
c. blood plasma
d. none of the above

B

Cells in a hypertonic solution tend to:

a. shrink due to water loss
b. swell due to water gain
c. stay the same size due to water moving into and out of the cell at the same rate
d. none of the above

A

Free Response

Why is excretion important in order to achieve osmotic balance?

Excretion allows an organism to rid itself of waste molecules that could be toxic if allowed to accumulate. It also allows the organism to keep the amount of water and dissolved solutes in balance.

Why do electrolyte ions move across membranes by active transport?

Electrolyte ions often require special mechanisms to cross the semi-permeable membranes in the body. Active transport is the movement against a concentration gradient.

Glossary

electrolyte
: solute that breaks down into ions when dissolved in water

molality
: number of moles of solute per kilogram of solvent

molarity
: number of moles of solute per liter of solution

mole
: gram equivalent of the molecular weight of a substance

non-electrolyte
: solute that does not break down into ions when dissolved in water

osmoconformer
: organism that changes its tonicity based on its environment

osmoregulation
: mechanism by which water and solute concentrations are maintained at desired levels

osmoregulator
: organism that maintains its tonicity irrespective of its environment

osmotic balance
: balance of the amount of water and salt input and output to and from a biological system without disturbing the desired osmotic pressure and solute concentration in every compartment

osmotic pressure
: pressure exerted on a membrane to equalize solute concentration on either side

semi-permeable membrane
: membrane that allows only certain solutes to pass through

The Kidneys and Osmoregulatory Organs

By the end of this section, you will be able to:

- Explain how the kidneys serve as the main osmoregulatory organs in mammalian systems
- Describe the structure of the kidneys and the functions of the parts of the kidney
- Describe how the nephron is the functional unit of the kidney and explain how it actively filters blood and generates urine
- Detail the three steps in the formation of urine: glomerular filtration, tubular reabsorption, and tubular secretion

Although the kidneys are the major osmoregulatory organ, the skin and lungs also play a role in the process. Water and electrolytes are lost through sweat glands in the skin, which helps moisturize and cool the skin surface, while the lungs expel a small amount of water in the form of mucous secretions and via evaporation of water vapor.

Kidneys: The Main Osmoregulatory Organ

The kidneys, illustrated in [link], are a pair of bean-shaped structures that are located just below and posterior to the liver in the peritoneal cavity. The adrenal glands sit on top of each kidney and are also called the suprarenal glands. Kidneys filter blood and purify it. All the blood in the human body is filtered many times a day by the kidneys; these organs use up almost 25 percent of the oxygen absorbed through the lungs to perform this function. Oxygen allows the kidney cells to efficiently manufacture chemical energy in the form of ATP through aerobic respiration. The filtrate coming out of the kidneys is called urine.

Kidneys filter the blood, producing urine that is stored in the bladder prior to elimination through the urethra. (credit: modification of work by

NCI)

Kidney Structure

Externally, the kidneys are surrounded by three layers, illustrated in [link]. The outermost layer is a tough connective tissue layer called the renal fascia. The second layer is called the perirenal fat capsule, which helps anchor the kidneys in place. The third and innermost layer is the renal capsule. Internally, the kidney has three regions—an outer cortex, a medulla in the middle, and the renal pelvis in the region called the hilum of the kidney. The hilum is the concave part of the bean-shape where blood vessels and nerves enter and exit the kidney; it is also the point of exit for the ureters. The renal cortex is granular due to the presence of nephrons—the functional unit of the kidney. The medulla consists of multiple pyramidal tissue masses, called the renal pyramids. In between the pyramids are spaces called renal columns through which the blood vessels pass. The tips of the pyramids, called renal papillae, point toward the renal pelvis. There are, on average, eight renal pyramids in each kidney. The renal pyramids along with the adjoining cortical region are called the lobes of the kidney. The renal pelvis leads to the ureter on the outside of the kidney. On the inside of the kidney, the renal pelvis branches out into two or three extensions called the major calyces, which further branch into the minor calyces. The ureters are urine-bearing tubes that exit the kidney and empty into the urinary bladder.

Art Connection

The internal structure of the kidney is shown. (credit: modification of work by

NCI)

Which of the following statements about the kidney is false?

a. The renal pelvis drains into the ureter.
b. The renal pyramids are in the medulla.
c. The cortex covers the capsule.
d. Nephrons are in the renal cortex.

Because the kidney filters blood, its network of blood vessels is an important component of its structure and function. The arteries, veins, and nerves that supply the kidney enter and exit at the renal hilum. Renal blood supply starts with the branching of the aorta into the renal arteries (which are each named based on the region of the kidney they pass through) and ends with the exiting of the renal veins to join the inferior vena cava. The renal arteries split into several segmental arteries upon entering the kidneys. Each segmental artery splits further into several interlobar arteries and enters the renal columns, which supply the renal lobes. The interlobar arteries split at the junction of the renal cortex and medulla to form the arcuate arteries. The arcuate “bow shaped” arteries form arcs along the base of the medullary pyramids. Cortical radiate arteries, as the name suggests, radiate out from the arcuate arteries. The cortical radiate arteries branch into numerous afferent arterioles, and then enter the capillaries supplying the nephrons. Veins trace the path of the arteries and have similar names, except there are no segmental veins.

As mentioned previously, the functional unit of the kidney is the nephron, illustrated in [link]. Each kidney is made up of over one million nephrons that dot the renal cortex, giving it a granular appearance when sectioned sagittally. There are two types of nephrons—cortical nephrons (85 percent), which are deep in the renal cortex, and juxtamedullary nephrons (15

percent), which lie in the renal cortex close to the renal medulla. A nephron consists of three parts—a renal corpuscle, a renal tubule, and the associated capillary network, which originates from the cortical radiate arteries.

Art Connection
The nephron is the functional unit of the kidney. The glomerulus and convoluted tubules are located in the kidney cortex, while collecting ducts are located in the pyramids of the medulla. (credit: modification of work by

NIDDK)

Which of the following statements about the nephron is false?

a. The collecting duct empties into the distal convoluted tubule.
b. The Bowman’s capsule surrounds the glomerulus.
c. The loop of Henle is between the proximal and distal convoluted tubules.
d. The loop of Henle empties into the distal convoluted tubule.

Renal Corpuscle

The renal corpuscle, located in the renal cortex, is made up of a network of capillaries known as the glomerulus and the capsule, a cup-shaped chamber that surrounds it, called the glomerular or Bowman's capsule.

Renal Tubule

The renal tubule is a long and convoluted structure that emerges from the glomerulus and can be divided into three parts based on function. The first part is called the proximal convoluted tubule (PCT) due to its proximity to the glomerulus; it stays in the renal cortex. The second part is called the loop of Henle, or nephritic loop, because it forms a loop (with descending and ascending limbs) that goes through the renal medulla. The third part of the renal tubule is called the distal convoluted tubule (DCT) and this part is also restricted to the renal cortex. The DCT, which is the last part of the nephron, connects and empties its contents into collecting ducts that line the medullary pyramids. The collecting ducts amass contents from multiple nephrons and fuse together as they enter the papillae of the renal medulla.

Capillary Network within the Nephron

The capillary network that originates from the renal arteries supplies the nephron with blood that needs to be filtered. The branch that enters the glomerulus is called the afferent arteriole. The branch that exits the glomerulus is called the efferent arteriole. Within the glomerulus, the network of capillaries is called the glomerular capillary bed. Once the efferent arteriole exits the glomerulus, it forms the peritubular capillary network, which surrounds and interacts with parts of the renal tubule. In cortical nephrons, the peritubular capillary network surrounds the PCT and DCT. In juxtamedullary nephrons, the peritubular capillary network forms a network around the loop of Henle and is called the vasa recta.

Link to Learning

Go to this website to see another coronal section of the kidney and to explore an animation of the workings of nephrons.

Kidney Function and Physiology

Kidneys filter blood in a three-step process. First, the nephrons filter blood that runs through the capillary network in the glomerulus. Almost all solutes, except for proteins, are filtered out into the glomerulus by a process called glomerular filtration. Second, the filtrate is collected in the renal tubules. Most of the solutes get reabsorbed in the PCT by a process called tubular reabsorption. In the loop of Henle, the filtrate continues to exchange solutes and water with the renal medulla and the peritubular capillary network. Water is also reabsorbed during this step. Then, additional solutes and wastes are secreted into the kidney tubules during tubular secretion, which is, in essence, the opposite process to tubular reabsorption. The collecting ducts collect filtrate coming from the nephrons and fuse in the medullary papillae. From here, the papillae deliver the filtrate, now called urine, into the minor calyces that eventually connect to the ureters through the renal pelvis. This entire process is illustrated in [link].

Each part of the nephron performs a different function in filtering waste and maintaining homeostatic balance. (1) The glomerulus forces small solutes out of the blood by pressure. (2) The proximal convoluted tubule reabsorbs ions, water, and nutrients from the filtrate into the interstitial fluid, and actively transports toxins and drugs from the interstitial fluid into the filtrate. The proximal convoluted tubule also adjusts blood pH by selectively secreting ammonia (NH_3) into the filtrate, where it reacts with H^+ to form NH_4^+. The more acidic the filtrate, the more ammonia is secreted. (3) The descending loop of Henle is lined with cells containing aquaporins that allow water to pass from the filtrate into the interstitial fluid. (4) In the thin part of the ascending loop of Henle, Na^+ and Cl^- ions diffuse into the interstitial fluid. In the thick part, these same ions are actively transported into the interstitial fluid. Because salt but not water is lost, the filtrate becomes more dilute as it travels up the limb. (5) In the distal convoluted tubule, K^+ and H^+ ions are selectively secreted into the filtrate, while Na^+, Cl^-, and HCO_3^- ions are reabsorbed to maintain pH and electrolyte balance in the blood. (6) The collecting duct reabsorbs solutes and water from the filtrate, forming dilute urine. (credit: modification of work by NIDDK)

Glomerular Filtration

Glomerular filtration filters out most of the solutes due to high blood pressure and specialized membranes in the afferent arteriole. The blood pressure in the glomerulus is maintained independent of factors that affect systemic blood pressure. The “leaky” connections between the endothelial cells of the glomerular capillary network allow solutes to pass through easily. All solutes in the glomerular capillaries, except for macromolecules like proteins, pass through by passive diffusion. There is no energy requirement at this stage of the filtration process. Glomerular filtration rate (GFR) is the volume of glomerular filtrate formed per minute by the kidneys. GFR is regulated by multiple mechanisms and is an important indicator of kidney function.

Link to Learning

To learn more about the vascular system of kidneys, click through this review and the steps of blood flow.

Tubular Reabsorption and Secretion

Tubular reabsorption occurs in the PCT part of the renal tubule. Almost all nutrients are reabsorbed, and this occurs either by passive or active transport. Reabsorption of water and some key electrolytes are regulated and can be influenced by hormones. Sodium (Na^+) is the most abundant ion and most of it is reabsorbed by active transport and then transported to the peritubular capillaries. Because Na^+ is actively transported out of the tubule, water follows it to even out the osmotic pressure. Water is also independently reabsorbed into the peritubular capillaries due to the presence of aquaporins, or water channels, in the PCT. This occurs due to the low blood pressure and high osmotic pressure in the peritubular capillaries. However, every solute has a transport maximum and the excess is not reabsorbed.

In the loop of Henle, the permeability of the membrane changes. The descending limb is permeable to water, not solutes; the opposite is true for the ascending limb. Additionally, the loop of Henle invades the renal medulla, which is naturally high in salt concentration and tends to absorb water from the renal tubule and concentrate the filtrate. The osmotic gradient increases as it moves deeper into the medulla. Because two sides of the loop of Henle perform opposing functions, as illustrated in [link], it acts as a countercurrent multiplier. The vasa recta around it acts as the countercurrent exchanger.

Art Connection
The loop of Henle acts as a countercurrent multiplier that uses energy to create concentration gradients. The descending limb is water permeable. Water flows from the filtrate to the interstitial fluid, so osmolality inside the limb increases as it descends into the renal medulla. At the bottom, the osmolality is higher inside the loop than in the interstitial fluid. Thus, as filtrate enters the ascending limb, Na^+ and Cl^- ions exit through ion channels present in the cell membrane. Further up, Na^+ is actively transported out of the filtrate and Cl^- follows.

Osmolarity is given in units of milliosmoles per liter

(mOsm/L).

Loop diuretics are drugs sometimes used to treat hypertension. These drugs inhibit the reabsorption of Na^+ and Cl^- ions by the ascending limb of the loop of Henle. A side effect is that they increase urination. Why do you think this is the case?

By the time the filtrate reaches the DCT, most of the urine and solutes have been reabsorbed. If the body requires additional water, all of it can be reabsorbed at this point. Further reabsorption is controlled by hormones, which will be discussed in a later section. Excretion of wastes occurs due to lack of reabsorption combined with tubular secretion. Undesirable products like metabolic wastes, urea, uric acid, and certain drugs, are excreted by tubular secretion. Most of the tubular secretion happens in the DCT, but some occurs in the early part of the collecting duct. Kidneys also maintain an acid-base balance by secreting excess H^+ ions.

Although parts of the renal tubules are named proximal and distal, in a cross-section of the kidney, the tubules are placed close together and in contact with each other and the glomerulus. This allows for exchange of chemical messengers between the different cell types. For example, the DCT ascending limb of the loop of Henle has masses of cells called macula densa, which are in contact with cells of the afferent arterioles called juxtaglomerular cells. Together, the macula densa and juxtaglomerular cells form the juxtaglomerular complex (JGC). The JGC is an endocrine structure that secretes the enzyme renin and the hormone erythropoietin. When hormones trigger the macula densa cells in the DCT due to variations in blood volume, blood pressure, or electrolyte balance, these cells can immediately communicate the problem to the capillaries in the afferent and efferent arterioles, which can constrict or relax to change the glomerular filtration rate of the kidneys.

Career Connection

NephrologistA nephrologist studies and deals with diseases of the kidneys—both those that cause kidney failure (such as diabetes) and the conditions that are produced by kidney disease (such as hypertension). Blood pressure, blood volume, and changes in electrolyte balance come under the purview of a nephrologist.

Nephrologists usually work with other physicians who refer patients to them or consult with them about specific diagnoses and treatment plans. Patients are usually referred to a nephrologist for symptoms such as blood or protein in the urine, very high blood pressure, kidney stones, or renal failure.

Nephrology is a subspecialty of internal medicine. To become a nephrologist, medical school is followed by additional training to become certified in internal medicine. An additional two or more years is spent specifically studying kidney disorders and their accompanying effects on the body.

Section Summary

The kidneys are the main osmoregulatory organs in mammalian systems; they function to filter blood and maintain the osmolarity of body fluids at 300 mOsm. They are surrounded by three layers and are made up internally of three distinct regions—the cortex, medulla, and pelvis.

The blood vessels that transport blood into and out of the kidneys arise from and merge with the aorta and inferior vena cava, respectively. The renal arteries branch out from the aorta and enter the kidney where they further divide into segmental, interlobar, arcuate, and cortical radiate arteries.

The nephron is the functional unit of the kidney, which actively filters blood and generates urine. The nephron is made up of the renal corpuscle and renal tubule. Cortical nephrons are found in the renal cortex, while juxtamedullary nephrons are found in the renal cortex close to the renal medulla. The nephron filters and exchanges water and solutes with two sets of blood vessels and the tissue fluid in the kidneys.

There are three steps in the formation of urine: glomerular filtration, which occurs in the glomerulus; tubular reabsorption, which occurs in the renal tubules; and tubular secretion, which also occurs in the renal tubules.

Art Connections

[link] Which of the following statements about the kidney is false?

a. The renal pelvis drains into the ureter.
b. The renal pyramids are in the medulla.
c. The cortex covers the capsule.
d. Nephrons are in the renal cortex.

[link] C

[link] Which of the following statements about the nephron is false?

a. The collecting duct empties into the distal convoluted tubule.
b. The Bowman’s capsule surrounds the glomerulus.
c. The loop of Henle is between the proximal and distal convoluted tubules.
d. The loop of Henle empties into the distal convoluted tubule.

[link] A

[link] Loop diuretics are drugs sometimes used to treat hypertension. These drugs inhibit the reabsorption of Na^+ and Cl^- ions by the ascending limb of the loop of Henle. A side effect is that they increase urination. Why do you think this is the case?

[link] Loop diuretics decrease the excretion of salt into the renal medulla, thereby reducing its osmolality. As a result, less water is excreted into the medulla by the descending limb, and more water is excreted as urine.

Review Questions

The macula densa is/are:

a. present in the renal medulla.
b. dense tissue present in the outer layer of the kidney.
c. cells present in the DCT and collecting tubules.
d. present in blood capillaries.

C

The osmolarity of body fluids is maintained at _____.

a. 100 mOsm
b. 300 mOsm
c. 1000 mOsm
d. it is not constantly maintained

B

The gland located at the top of the kidney is the _____ gland.

a. adrenal
b. pituitary
c. thyroid
d. thymus

A

Free Response

Why are the loop of Henle and vasa recta important for the formation of concentrated urine?

The loop of Henle is part of the renal tubule that loops into the renal medulla. In the loop of Henle, the filtrate exchanges solutes and water with the renal medulla and the vasa recta (the peritubular capillary network). The vasa recta acts as the countercurrent exchanger. The kidneys maintain the osmolality of the rest of the body at a constant 300 mOsm by concentrating the filtrate as it passes through the loop of Henle.

Describe the structure of the kidney.

Externally, the kidneys are surrounded by three layers. The outermost layer is a tough connective tissue layer called the renal fascia. The second layer is called the perirenal fat capsule, which helps anchor the kidneys in place. The third and innermost layer is the renal capsule. Internally, the kidney has three regions—an outer cortex, a medulla in the middle, and the renal pelvis in the region called the hilum of the kidney, which is the concave part of the "bean" shape.

Glossary

afferent arteriole
: arteriole that branches from the cortical radiate artery and enters the glomerulus

arcuate artery
: artery that branches from the interlobar artery and arches over the base of the renal pyramids

ascending limb
: part of the loop of Henle that ascends from the renal medulla to the renal cortex

Bowman's capsule
: structure that encloses the glomerulus

calyx
: structure that connects the renal pelvis to the renal medulla

cortex (animal)
: outer layer of an organ like the kidney or adrenal gland

cortical nephron
: nephron that lies in the renal cortex

cortical radiate artery
: artery that radiates from the arcuate arteries into the renal cortex

countercurrent exchanger
: peritubular capillary network that allows exchange of solutes and water from the renal tubules

countercurrent multiplier
: osmotic gradient in the renal medulla that is responsible for concentration of urine

descending limb
: part of the loop of Henle that descends from the renal cortex into the renal medulla

distal convoluted tubule (DCT)
: part of the renal tubule that is the most distant from the glomerulus

efferent arteriole
: arteriole that exits from the glomerulus

glomerular filtration
: filtration of blood in the glomerular capillary network into the glomerulus

glomerular filtration rate (GFR)
: amount of filtrate formed by the glomerulus per minute

glomerulus (renal)
: part of the renal corpuscle that contains the capillary network

hilum
: region in the renal pelvis where blood vessels, nerves, and ureters bunch before entering or exiting the kidney

inferior vena cava
: one of the main veins in the human body

interlobar artery
: artery that branches from the segmental artery and travels in between the renal lobes

juxtaglomerular cell
: cell in the afferent and efferent arterioles that responds to stimuli from the macula densa

juxtamedullary nephron
: nephron that lies in the cortex but close to the renal medulla

kidney
: organ that performs excretory and osmoregulatory functions

lobes of the kidney
: renal pyramid along with the adjoining cortical region

loop of Henle
: part of the renal tubule that loops into the renal medulla

macula densa
: group of cells that senses changes in sodium ion concentration; present in parts of the renal tubule and collecting ducts

medulla
: middle layer of an organ like the kidney or adrenal gland

nephron
: functional unit of the kidney

perirenal fat capsule
: fat layer that suspends the kidneys

peritubular capillary network
: capillary network that surrounds the renal tubule after the efferent artery exits the glomerulus

proximal convoluted tubule (PCT)
: part of the renal tubule that lies close to the glomerulus

renal artery
: branch of the artery that enters the kidney

renal capsule
: layer that encapsulates the kidneys

renal column
: area of the kidney through which the interlobar arteries travel in the process of supplying blood to the renal lobes

renal corpuscle
: glomerulus and the Bowman's capsule together

renal fascia
: connective tissue that supports the kidneys

renal pelvis
: region in the kidney where the calyces join the ureters

renal pyramid
: conical structure in the renal medulla

renal tubule
: tubule of the nephron that arises from the glomerulus

renal vein
: branch of a vein that exits the kidney and joins the inferior vena cava

segmental artery
: artery that branches from the renal artery

transport maximum
: maximum amount of solute that can be transported out of the renal tubules during reabsorption

tubular reabsorption
: reclamation of water and solutes that got filtered out in the glomerulus

tubular secretion
: process of secretion of wastes that do not get reabsorbed

ureter
: urine-bearing tube coming out of the kidney; carries urine to the bladder

urinary bladder
: structure that the ureters empty the urine into; stores urine

urine
: filtrate produced by kidneys that gets excreted out of the body

vasa recta
: peritubular network that surrounds the loop of Henle of the juxtamedullary nephrons

Excretion Systems

By the end of this section, you will be able to:

- Explain how vacuoles, present in microorganisms, work to excrete waste
- Describe the way in which flame cells and nephridia in worms perform excretory functions and maintain osmotic balance
- Explain how insects use Malpighian tubules to excrete wastes and maintain osmotic balance

Microorganisms and invertebrate animals use more primitive and simple mechanisms to get rid of their metabolic wastes than the mammalian system of kidney and urinary function. Three excretory systems evolved in organisms before complex kidneys: vacuoles, flame cells, and Malpighian tubules.

Contractile Vacuoles in Microorganisms

The most fundamental feature of life is the presence of a cell. In other words, a cell is the simplest functional unit of a life. Bacteria are unicellular, prokaryotic organisms that have some of the least complex life processes in place; however, prokaryotes such as bacteria do not contain membrane-bound vacuoles. The cells of microorganisms like bacteria, protozoa, and fungi are bound by cell membranes and use them to interact with the environment. Some cells, including some leucocytes in humans, are able to engulf food by endocytosis—the formation of vesicles by involution of the cell membrane within the cells. The same vesicles are able to interact and exchange metabolites with the intracellular environment. In some unicellular eukaryotic organisms such as the amoeba, shown in [link], cellular wastes and excess water are excreted by exocytosis, when the contractile vacuoles merge with the cell membrane and expel wastes into the environment. Contractile vacuoles (CV) should not be confused with vacuoles, which store food or water.

Some unicellular organisms, such as the amoeba, ingest food by endocytosis. The food vesicle fuses with a lysosome, which digests the food. Waste is excreted by exocytosis.

Flame Cells of Planaria and Nephridia of Worms

As multi-cellular systems evolved to have organ systems that divided the metabolic needs of the body, individual organs evolved to perform the excretory function. Planaria are flatworms that live in fresh water. Their excretory system consists of two tubules connected to a highly branched duct system. The cells in the tubules are called flame cells (or protonephridia) because they have a cluster of cilia that looks like a flickering flame when viewed under the microscope, as illustrated in [link]**a**. The cilia propel waste matter down the tubules and out of the body through excretory pores that open on the body surface; cilia also draw water from the interstitial fluid, allowing for filtration. Any valuable metabolites are recovered by reabsorption. Flame cells are found in flatworms, including parasitic tapeworms and free-living planaria. They also maintain the organism’s osmotic balance.

In the excretory system of the (a) planaria, cilia of flame cells propel waste through a tubule formed by a tube cell. Tubules are connected into branched structures that lead to pores located all along the sides of the body. The filtrate is secreted through these pores. In (b)

annelids such as earthworms, nephridia filter fluid from the coelom, or body cavity. Beating cilia at the opening of the nephridium draw water from the coelom into a tubule. As the filtrate passes down the tubules, nutrients and other solutes are reabsorbed by capillaries. Filtered fluid containing nitrogenous and other wastes is stored in a bladder and then secreted through a pore in the side of the body.

Earthworms (annelids) have slightly more evolved excretory structures called nephridia, illustrated in [link]**b**. A pair of nephridia is present on each segment of the earthworm. They are similar to flame cells in that they have a tubule with cilia. Excretion occurs through a pore called the nephridiopore. They are more evolved than the flame cells in that they have a system for tubular reabsorption by a capillary network before excretion.

Malpighian Tubules of Insects

Malpighian tubules are found lining the gut of some species of arthropods, such as the bee illustrated in [link]. They are usually found in pairs and the number of tubules varies with the species of insect. Malpighian tubules are convoluted, which increases their surface area, and they are lined with microvilli for reabsorption and maintenance of osmotic balance. Malpighian tubules work cooperatively with specialized glands in the wall of the rectum. Body fluids are not filtered as in the case of nephridia; urine is produced by tubular secretion mechanisms by the cells lining the Malpighian tubules that are bathed in hemolymph (a

mixture of blood and interstitial fluid that is found in insects and other arthropods as well as most mollusks). Metabolic wastes like uric acid freely diffuse into the tubules. There are exchange pumps lining the tubules, which actively transport H^+ ions into the cell and K^+ or Na^+ ions out; water passively follows to form urine. The secretion of ions alters the osmotic pressure which draws water, electrolytes, and nitrogenous waste (uric acid) into the tubules. Water and electrolytes are reabsorbed when these organisms are faced with low-water environments, and uric acid is excreted as a thick paste or powder. Not dissolving wastes in water helps these organisms to conserve water; this is especially important for life in dry environments.

Malpighian tubules of insects and other terrestrial arthropods remove nitrogenous wastes and other solutes from the hemolymph. Na^+ and/or K^+ ions are actively transported into the lumen of the tubules. Water then enters the tubules via osmosis, forming urine. The urine passes through the intestine, and into the rectum. There, nutrients diffuse back into the hemolymph. Na^+ and/or K^+ ions are pumped into the hemolymph, and water follows. The concentrated waste is then
excreted.

Link to Learning

See a dissected cockroach, including a close-up look at its Malpighian tubules, in this video.

Section Summary

Many systems have evolved for excreting wastes that are simpler than the kidney and urinary systems of vertebrate animals. The simplest system is that of contractile vacuoles present in microorganisms. Flame cells and nephridia in worms perform excretory functions and maintain osmotic balance. Some insects have evolved Malpighian tubules to excrete wastes and maintain osmotic balance.

Review Questions

Active transport of K^+ in Malpighian tubules ensures that:

a. water follows K^+ to make urine
b. osmotic balance is maintained between waste matter and bodily fluids
c. both a and b
d. neither a nor b

C

Contractile vacuoles in microorganisms:

a. exclusively perform an excretory function
b. can perform many functions, one of which is excretion of metabolic wastes
c. originate from the cell membrane
d. both b and c

D

Flame cells are primitive excretory organs found in _____.

a. arthropods
b. annelids
c. mammals
d. flatworms

D

Free Response

Why might specialized organs have evolved for excretion of wastes?

The removal of wastes, which could otherwise be toxic to an organism, is extremely important for survival. Having organs that specialize in this process and that operate separately from other organs provides a measure of safety for the organism.

Explain two different excretory systems other than the kidneys.

(1) Microorganisms engulf food by endocytosis—the formation of vacuoles by involution of the cell membrane within the cells. The same vacuoles interact and exchange metabolites with the intracellular environment. Cellular wastes are excreted by exocytosis when the vacuoles merge with the cell membrane and excrete wastes into the environment. (2) Flatworms have an excretory system that consists of two tubules. The cells in the tubules are called flame cells; they have a cluster of cilia that propel waste matter down the tubules and out of the body. (3) Annelids have nephridia which have a tubule with cilia. Excretion occurs through a pore called the nephridiopore. Annelids have a system for tubular reabsorption by a capillary network before excretion. (4) Malpighian tubules are found in some species of arthropods. They are usually found in pairs, and the number of tubules varies with the species of insect. Malpighian tubules are convoluted, which increases their surface area, and they are lined with microvilli for reabsorption and maintenance of osmotic balance. Metabolic wastes like uric acid freely diffuse into the tubules. Potassium ion pumps line the tubules, which actively transport out K^+ ions, and water follows to form urine. Water and electrolytes are reabsorbed when these organisms are faced with low-water environments, and uric acid is excreted as a thick paste or powder. By not dissolving wastes in water, these organisms conserve water.

Glossary

flame cell
: (also, protonephridia) excretory cell found in flatworms

Malpighian tubule
: excretory tubules found in arthropods

microvilli
: cellular processes that increase the surface area of cells

nephridia
: excretory structures found in annelids

nephridiopore
: pore found at the end of nephridia

Nitrogenous Wastes

By the end of this section, you will be able to:

- Compare and contrast the way in which aquatic animals and terrestrial animals can eliminate toxic ammonia from their systems
- Compare the major byproduct of ammonia metabolism in vertebrate animals to that of birds, insects, and reptiles

Of the four major macromolecules in biological systems, both proteins and nucleic acids contain nitrogen. During the catabolism, or breakdown, of nitrogen-containing macromolecules, carbon, hydrogen, and oxygen are extracted and

stored in the form of carbohydrates and fats. Excess nitrogen is excreted from the body. Nitrogenous wastes tend to form toxic ammonia, which raises the pH of body fluids. The formation of ammonia itself requires energy in the form of ATP and large quantities of water to dilute it out of a biological system. Animals that live in aquatic environments tend to release ammonia into the water. Animals that excrete ammonia are said to be ammonotelic. Terrestrial organisms have evolved other mechanisms to excrete nitrogenous wastes. The animals must detoxify ammonia by converting it into a relatively nontoxic form such as urea or uric acid. Mammals, including humans, produce urea, whereas reptiles and many terrestrial invertebrates produce uric acid. Animals that secrete urea as the primary nitrogenous waste material are called ureotelic animals.

Nitrogenous Waste in Terrestrial Animals: The Urea Cycle

The urea cycle is the primary mechanism by which mammals convert ammonia to urea. Urea is made in the liver and excreted in urine. The overall chemical reaction by which ammonia is converted to urea is 2 NH_3 (ammonia) + CO_2 + 3 ATP + H_2O → $H_2N\text{-}CO\text{-}NH_2$ (urea) + 2 ADP + 4 P_i + AMP.

The urea cycle utilizes five intermediate steps, catalyzed by five different enzymes, to convert ammonia to urea, as shown in [link]. The amino acid L-ornithine gets converted into different intermediates before being regenerated at the end of the urea cycle. Hence, the urea cycle is also referred to as the ornithine cycle. The enzyme ornithine transcarbamylase catalyzes a key step in the urea cycle and its deficiency can lead to accumulation of toxic levels of ammonia in the body. The first two reactions occur in the mitochondria and the last three reactions occur in the cytosol. Urea concentration in the blood, called blood urea nitrogen or BUN, is used as an indicator of kidney function.

The urea cycle converts ammonia to

urea.
Evolution Connection

Excretion of Nitrogenous WasteThe theory of evolution proposes that life started in an aquatic environment. It is not surprising to see that biochemical pathways like the urea cycle evolved to adapt to a changing environment when terrestrial life forms evolved. Arid conditions probably led to the evolution of the uric acid pathway as a means of conserving water.

Nitrogenous Waste in Birds and Reptiles: Uric Acid

Birds, reptiles, and most terrestrial arthropods convert toxic ammonia to uric acid or the closely related compound guanine (guano) instead of urea. Mammals also form some uric acid during breakdown of nucleic acids. Uric acid is a compound similar to purines found in nucleic acids. It is water insoluble and tends to form a white paste or powder; it is excreted by birds, insects, and reptiles. Conversion of ammonia to uric acid requires more energy and is much more complex than conversion of ammonia to urea [link].

Nitrogenous waste is excreted in different forms by different species. These include (a) ammonia, (b) urea, and (c) uric acid. (credit a: modification of work by Eric Engbretson,

USFWS; credit b: modification of work by B. "Moose" Peterson, USFWS; credit c: modification of work by Dave Menke,
USFWS)

Everyday Connection

GoutMammals use uric acid crystals as an antioxidant in their cells. However, too much uric acid tends to form kidney stones and may also cause a painful condition called gout, where uric acid crystals accumulate in the joints, as illustrated in [link]. Food choices that reduce the amount of nitrogenous bases in the diet help reduce the risk of gout. For example, tea, coffee, and chocolate have purine-like compounds, called xanthines, and should be avoided by people with gout and kidney stones.

Gout causes the inflammation visible in this person’s left big toe joint. (credit:

"Gonzosft"/Wikimedia Commons)

Section Summary

Ammonia is the waste produced by metabolism of nitrogen-containing compounds like proteins and nucleic acids. While aquatic animals can easily excrete ammonia into their watery surroundings, terrestrial animals have evolved special mechanisms to eliminate the toxic ammonia from their systems. Urea is the major byproduct of ammonia metabolism in vertebrate animals. Uric acid is the major byproduct of ammonia metabolism in birds, terrestrial arthropods, and reptiles.

Review Questions

BUN is _____.

a. blood urea nitrogen
b. blood uric acid nitrogen
c. an indicator of blood volume
d. an indicator of blood pressure

A

Human beings accumulate _____ before excreting nitrogenous waste.

a. nitrogen
b. ammonia
c. urea
d. uric acid

C

Free Response

In terms of evolution, why might the urea cycle have evolved in organisms?

It is believed that the urea cycle evolved to adapt to a changing environment when terrestrial life forms evolved. Arid conditions probably led to the evolution of the uric acid pathway as a means of conserving water.

Compare and contrast the formation of urea and uric acid.

The urea cycle is the primary mechanism by which mammals convert ammonia to urea. Urea is made in the liver and excreted in urine. The urea cycle utilizes five intermediate steps, catalyzed by five different enzymes, to convert ammonia to urea. Birds, reptiles, and insects, on the other hand, convert toxic ammonia to uric acid instead of urea. Conversion of ammonia to uric acid requires more energy and is much more complex than conversion of ammonia to urea.

Glossary

ammonia
: compound made of one nitrogen atom and three hydrogen atoms

ammonotelic
: describes an animal that excretes ammonia as the primary waste material

antioxidant
: agent that prevents cell destruction by reactive oxygen species

blood urea nitrogen (BUN)
: estimate of urea in the blood and an indicator of kidney function

urea cycle
: pathway by which ammonia is converted to urea

ureotelic
: describes animals that secrete urea as the primary nitrogenous waste material

uric acid
: byproduct of ammonia metabolism in birds, insects, and reptiles

Introduction

class="introduction" class="summary" title="Sections Summary" class="art-exercise" title="Art Connections" class="multiple-choice" title="Multiple Choice" class="free-response" title="Free Response"In this compound light micrograph purple-stained neutrophil (upper left) and eosinophil (lower right) are white blood cells that float among red blood cells in this blood smear. Neutrophils provide an early, rapid, and nonspecific defense against invading pathogens. Eosinophils play a variety of roles in the immune response. Red blood cells are about 7–8 µm in diameter, and a neutrophil is about 10–12µm. (credit: modification of work by Dr. David

Csaba)

The environment consists of numerous pathogens, which are agents, usually microorganisms, that cause diseases in their hosts. A host is the organism that is invaded and often harmed by a pathogen. Pathogens include bacteria, protists, fungi and other infectious organisms. We are constantly exposed to pathogens in food and water, on surfaces, and in the air. Mammalian immune systems evolved for protection from such pathogens; they are composed of an extremely diverse array of specialized cells and soluble molecules that coordinate a rapid and flexible defense system capable of providing protection from a majority of these disease agents.

Components of the immune system constantly search the body for signs of pathogens. When pathogens are found, immune factors are mobilized to the site of an infection. The immune factors identify the nature of the pathogen, strengthen the corresponding cells and molecules to combat it efficiently, and then halt the

immune response after the infection is cleared to avoid unnecessary host cell damage. The immune system can remember pathogens to which it has been exposed to create a more efficient response upon re-exposure. This memory can last several decades. Features of the immune system, such as pathogen identification, specific response, amplification, retreat, and remembrance are essential for survival against pathogens. The immune response can be classified as either innate or active. The innate immune response is always present and attempts to defend against all pathogens rather than focusing on specific ones. Conversely, the adaptive immune response stores information about past infections and mounts pathogen-specific defenses.

Glossary

pathogen

: an agent, usually a microorganism, that causes disease in the organisms that they invade

host

: an organism that is invaded by a pathogen or parasite

Innate Immune Response
By the end of this section, you will be able to:

- Describe physical and chemical immune barriers
- Explain immediate and induced innate immune responses
- Discuss natural killer cells
- Describe major histocompatibility class I molecules
- Summarize how the proteins in a complement system function to destroy extracellular pathogens

The immune system comprises both innate and adaptive immune responses. Innate immunity occurs naturally because of genetic factors or physiology; it is not induced by infection or vaccination but works to reduce the workload for the adaptive immune response. Both the innate and adaptive levels of the immune response involve secreted proteins, receptor-mediated signaling, and intricate cell-to-cell communication. The innate immune system developed early in animal evolution, roughly a billion years ago, as an essential response to infection. Innate immunity has a limited number of specific targets: any pathogenic threat triggers a consistent sequence of events that can identify the type of pathogen and either clear the infection independently or mobilize a highly specialized adaptive immune response. For example, tears and mucus secretions contain microbicidal factors.

Physical and Chemical Barriers

Before any immune factors are triggered, the skin functions as a continuous, impassable barrier to potentially infectious pathogens. Pathogens are killed or inactivated on the skin by desiccation (drying out) and by the skin's acidity. In addition, beneficial microorganisms that coexist on the skin compete with invading pathogens, preventing infection. Regions of the body that are not protected by skin (such as the eyes and mucus membranes) have alternative methods of defense, such as tears and mucus secretions that trap and rinse away pathogens, and cilia in the nasal passages and respiratory tract that push the mucus with the pathogens out of the body. Throughout the body are other defenses, such as the low pH of the stomach (which inhibits the growth of pathogens), blood proteins that bind and disrupt bacterial cell membranes, and the process of urination (which flushes pathogens from the urinary tract).

Despite these barriers, pathogens may enter the body through skin abrasions or punctures, or by collecting on mucosal surfaces in large numbers that overcome the mucus or cilia. Some pathogens have evolved specific mechanisms that allow them to overcome physical and chemical barriers. When pathogens do enter the body, the innate immune system responds with inflammation, pathogen engulfment, and secretion of immune factors and proteins.

Pathogen Recognition

An infection may be intracellular or extracellular, depending on the pathogen. All viruses infect cells and replicate within those cells (intracellularly), whereas bacteria and other parasites may replicate intracellularly or extracellularly, depending on the species. The innate immune system must respond accordingly: by identifying the extracellular pathogen and/or by identifying host cells that have already been infected. When a pathogen enters the body, cells in the blood and lymph detect the specific pathogen-associated molecular patterns (PAMPs) on the pathogen's surface. PAMPs are carbohydrate, polypeptide, and nucleic acid "signatures" that are expressed by viruses, bacteria, and parasites but which differ from molecules on host cells. The immune system has specific cells, described in [link] and shown in [link], with receptors that recognize these PAMPs. A macrophage is a large phagocytic cell that engulfs foreign particles and pathogens. Macrophages recognize PAMPs via complementary pattern recognition receptors (PRRs). PRRs are molecules on macrophages and dendritic cells which are in contact with the external environment. A monocyte is a type of white blood cell that circulates in the blood and lymph and differentiates into macrophages after it moves into infected tissue. Dendritic cells bind molecular signatures of pathogens and promote pathogen engulfment and destruction. Toll-like receptors (TLRs) are a type of PRR that recognizes molecules that are shared by pathogens but distinguishable from host molecules). TLRs are present in invertebrates as well as vertebrates, and appear to be one of the most ancient components of the immune system. TLRs have also been identified in the mammalian nervous system.

The characteristics and location of cells involved in the innate immune system are described. (credit: modification of work by
NIH)

Cells of the blood include (1) monocytes, (2) lymphocytes, (3) neutrophils, (4) red blood cells, and (5) platelets. Note the very similar morphologies of the leukocytes (1, 2, 3). (credit: modification of work by Bruce Wetzel, Harry Schaefer, NCI; scale-bar data from Matt

Russell)

Cytokine Release Effect

The binding of PRRs with PAMPs triggers the release of cytokines, which signal that a pathogen is present and needs to be destroyed along with any infected cells. A cytokine is a chemical messenger that regulates cell differentiation (form and function), proliferation (production), and gene expression to affect immune responses. At least 40 types of cytokines exist in humans that differ in terms of the cell type that produces them, the cell type that responds to them, and the changes they produce. One type cytokine, interferon, is illustrated in [link].

One subclass of cytokines is the interleukin (IL), so named because they mediate interactions between leukocytes (white blood cells). Interleukins are involved in bridging the innate and adaptive immune responses. In addition to being released from cells after PAMP recognition, cytokines are released by the infected cells which bind to nearby uninfected cells and induce those cells to release cytokines, which results in a cytokine burst.

A second class of early-acting cytokines is interferons, which are released by infected cells as a warning to nearby uninfected cells. One of the functions of an interferon is to inhibit viral replication. They also have other important functions, such as tumor surveillance. Interferons work by signaling neighboring uninfected cells to destroy RNA and reduce protein synthesis, signaling neighboring infected cells to undergo apoptosis (programmed cell death), and activating immune cells.

In response to interferons, uninfected cells alter their gene expression, which increases the cells' resistance to infection. One effect of interferon-induced gene expression is a sharply reduced cellular protein synthesis. Virally infected cells produce more viruses by synthesizing large quantities of viral proteins. Thus, by reducing protein synthesis, a cell becomes resistant to viral infection.

Interferons are cytokines that are released by a cell infected with a virus. Response of neighboring cells to interferon helps stem the

infection.

Phagocytosis and Inflammation

The first cytokines to be produced are pro-inflammatory; that is, they encourage inflammation, the localized redness, swelling, heat, and pain that result from the movement of leukocytes and fluid through increasingly permeable capillaries to a site of infection. The population of leukocytes that arrives at an infection site depends on the nature of the infecting pathogen. Both macrophages and dendritic cells engulf pathogens and cellular debris through phagocytosis. A neutrophil is also a phagocytic leukocyte that engulfs and digests pathogens. Neutrophils, shown in [link], are the most abundant leukocytes of the immune system. Neutrophils have a nucleus with two to five lobes, and they contain organelles, called lysosomes, that digest engulfed pathogens. An eosinophil is a leukocyte that works with other eosinophils to surround a parasite; it is involved in the allergic response and in protection against helminthes (parasitic worms).

Neutrophils and eosinophils are particularly important leukocytes that engulf large pathogens, such as bacteria and fungi. A mast cell is a leukocyte that produces inflammatory molecules, such as histamine, in response to large pathogens. A basophil is a leukocyte that, like a neutrophil, releases chemicals to stimulate the inflammatory response as illustrated in [link]. Basophils are also involved in allergy and hypersensitivity responses and induce specific types of inflammatory responses. Eosinophils and basophils produce additional inflammatory mediators to recruit more leukocytes. A hypersensitive immune response to harmless antigens, such as in pollen, often involves the release of histamine by basophils and mast cells.

In response to a cut, mast cells secrete histamines that cause nearby capillaries to dilate. Neutrophils and monocytes leave the capillaries. Monocytes mature into macrophages. Neutrophils, dendritic cells and macrophages release chemicals to stimulate the inflammatory response. Neutrophils and macrophages also consume invading bacteria by

phagocytosis.

Cytokines also send feedback to cells of the nervous system to bring about the overall symptoms of feeling sick, which include lethargy, muscle pain, and nausea. These effects may have evolved because the symptoms encourage the individual to rest and prevent them from spreading the infection to others. Cytokines also increase the core body temperature, causing a fever, which causes the liver to withhold iron from the blood. Without iron, certain pathogens, such as some bacteria, are unable to replicate; this is called nutritional immunity.

Link to Learning

Watch this 23-second stop-motion video showing a neutrophil that searches for and engulfs fungus spores during an elapsed time of about 79 minutes.

Natural Killer Cells

Lymphocytes are leukocytes that are histologically identifiable by their large, darkly staining nuclei; they are small cells with very little cytoplasm, as shown in [link]. Infected cells are identified and destroyed by natural killer (NK) cells, lymphocytes that can kill cells infected with viruses or tumor cells (abnormal cells that uncontrollably divide and invade other tissue). T cells and B cells of the adaptive immune system also are classified as lymphocytes. T cells are lymphocytes that mature in the thymus gland, and B cells are lymphocytes that mature in the bone marrow. NK cells identify intracellular infections, especially from viruses, by the altered expression of major histocompatibility class (MHC) I molecules on the surface of infected cells. MHC I molecules are proteins on the surfaces of all nucleated cells, thus they are scarce on red blood cells and platelets which are non-nucleated. The function of MHC I molecules is to display fragments of proteins from the infectious agents within the cell to T-cells; healthy cells will be ignored, while "non-self" or foreign proteins will be attacked by the immune system. MHC II molecules are found mainly on cells containing antigens ("non-self proteins") and on lymphocytes. MHC II molecules interact with helper T-cells to trigger the appropriate immune response, which may include the inflammatory response.

Lymphocytes, such as NK cells, are characterized by their large nuclei that actively absorb Wright stain and therefore appear dark colored under a

microscope.

An infected cell (or a tumor cell) is usually incapable of synthesizing and displaying MHC I molecules appropriately. The metabolic resources of cells infected by some viruses produce proteins that interfere with MHC I processing and/or trafficking to the cell surface. The

reduced MHC I on host cells varies from virus to virus and results from active inhibitors being produced by the viruses. This process can deplete host MHC I molecules on the cell surface, which NK cells detect as “unhealthy” or “abnormal” while searching for cellular MHC I molecules. Similarly, the dramatically altered gene expression of tumor cells leads to expression of extremely deformed or absent MHC I molecules that also signal “unhealthy” or “abnormal.”

NK cells are always active; an interaction with normal, intact MHC I molecules on a healthy cell disables the killing sequence, and the NK cell moves on. After the NK cell detects an infected or tumor cell, its cytoplasm secretes granules comprised of perforin, a destructive protein that creates a pore in the target cell. Granzymes are released along with the perforin in the immunological synapse. A granzyme is a protease that digests cellular proteins and induces the target cell to undergo programmed cell death, or apoptosis. Phagocytic cells then digest the cell debris left behind. NK cells are constantly patrolling the body and are an effective mechanism for controlling potential infections and preventing cancer progression.

Complement

An array of approximately 20 types of soluble proteins, called a complement system, functions to destroy extracellular pathogens. Cells of the liver and macrophages synthesize complement proteins continuously; these proteins are abundant in the blood serum and are capable of responding immediately to infecting microorganisms. The complement system is so named because it is complementary to the antibody response of the adaptive immune system. Complement proteins bind to the surfaces of microorganisms and are particularly attracted to pathogens that are already bound by antibodies. Binding of complement proteins occurs in a specific and highly regulated sequence, with each successive protein being activated by cleavage and/or structural changes induced upon binding of the preceding protein(s). After the first few complement proteins bind, a cascade of sequential binding events follows in which the pathogen rapidly becomes coated in complement proteins.

Complement proteins perform several functions. The proteins serve as a marker to indicate the presence of a pathogen to phagocytic cells, such as macrophages and B cells, and enhance engulfment; this process is called opsonization. Certain complement proteins can combine to form attack complexes that open pores in microbial cell membranes. These structures destroy pathogens by causing their contents to leak, as illustrated in [link].

The classic pathway for the complement cascade involves the attachment of several initial complement proteins to an antibody-bound pathogen followed by rapid activation and binding of many more complement proteins and the creation of destructive pores in the microbial cell envelope and cell wall. The alternate pathway does not involve antibody activation. Rather, C3 convertase spontaneously breaks down C3. Endogenous regulatory proteins prevent the complement complex from binding to host cells. Pathogens lacking these

regulatory proteins are lysed. (credit: modification of work by

NIH)

Section Summary

The innate immune system serves as a first responder to pathogenic threats that bypass natural physical and chemical barriers of the body. Using a combination of cellular and molecular attacks, the innate immune system identifies the nature of a pathogen and responds with inflammation, phagocytosis, cytokine release, destruction by NK cells, and/or a complement system. When innate mechanisms are insufficient to clear an infection, the adaptive immune response is informed and mobilized.

Review Questions

Which of the following is a barrier against pathogens provided by the skin?

a. high pH
b. mucus
c. tears
d. desiccation

D

Although interferons have several effects, they are particularly useful against infections with which type of pathogen?

a. bacteria
b. viruses
c. fungi
d. helminths

B

Which organelle do phagocytes use to digest engulfed particles?

a. lysosome
b. nucleus
c. endoplasmic reticulum
d. mitochondria

A

Which innate immune system component uses MHC I molecules directly in its defense strategy?

a. macrophages
b. neutrophils
c. NK cells
d. interferon

C

Free Response

Different MHC I molecules between donor and recipient cells can lead to rejection of a transplanted organ or tissue. Suggest a reason for this.

If the MHC I molecules expressed on donor cells differ from the MHC I molecules expressed on recipient cells, NK cells may identify the donor cells as “non-self” and produce perforin and granzymes to induce the donor cells to undergo apoptosis, which would destroy the transplanted organ.

If a series of genetic mutations prevented some, but not all, of the complement proteins from binding antibodies or pathogens, would the entire complement system be compromised?

The entire complement system would probably be affected even when only a few members were mutated such that they could no longer bind. Because the complement involves the binding of activated proteins in a specific sequence, when one or more proteins in the sequence are absent, the subsequent proteins would be incapable of binding to elicit the complement’s pathogen-destructive effects.

Glossary

basophil
: leukocyte that releases chemicals usually involved in the inflammatory response

B cell
: lymphocyte that matures in the bone marrow and differentiates into antibody-secreting plasma cells

complement system
: array of approximately 20 soluble proteins of the innate immune system that enhance phagocytosis, bore holes in pathogens, and recruit lymphocytes; enhances the adaptive response when antibodies are produced

cytokine
: chemical messenger that regulates cell differentiation, proliferation, gene expression, and cell trafficking to effect immune responses

eosinophil
: leukocyte that responds to parasites and is involved in the allergic response

granzyme
: protease that enters target cells through perforin and induces apoptosis in the target cells; used by NK cells and killer T cells

inflammation
: localized redness, swelling, heat, and pain that results from the movement of leukocytes and fluid through opened capillaries to a site of infection

innate immunity
: immunity that occurs naturally because of genetic factors or physiology, and is not induced by infection or vaccination

interferon
: cytokine that inhibits viral replication and modulates the immune response

lymphocyte
: leukocyte that is histologically identifiable by its large nuclei; it is a small cell with very little cytoplasm

macrophage
: large phagocytic cell that engulfs foreign particles and pathogens

major histocompatibility class (MHC) I/II molecule
: protein found on the surface of all nucleated cells (I) or specifically on antigen-presenting cells (II) that signals to immune cells whether the cell is healthy/normal or is infected/cancerous; it provides the appropriate template into which antigens can be loaded for recognition by lymphocytes

mast cell
: leukocyte that produces inflammatory molecules, such as histamine, in response to large pathogens and allergens

monocyte
: type of white blood cell that circulates in the blood and lymph and differentiates into macrophages after it moves into infected tissue

natural killer (NK) cell

lymphocyte that can kill cells infected with viruses or tumor cells

neutrophil

phagocytic leukocyte that engulfs and digests pathogens

opsonization

process that enhances phagocytosis using proteins to indicate the presence of a pathogen to phagocytic cells

pathogen-associated molecular pattern (PAMP)

carbohydrate, polypeptide, and nucleic acid "signature" that is expressed by viruses, bacteria, and parasites but differs from molecules on host cells

pattern recognition receptor (PRR)

molecule on macrophages and dendritic cells that binds molecular signatures of pathogens and promotes pathogen engulfment and destruction

perforin

destructive protein that creates a pore in the target cell; used by NK cells and killer T cells

T cell

lymphocyte that matures in the thymus gland; one of the main cells involved in the adaptive immune system

Adaptive Immune Response

By the end of this section, you will be able to:

- Explain adaptive immunity
- Compare and contrast adaptive and innate immunity
- Describe cell-mediated immune response and humoral immune response
- Describe immune tolerance

The adaptive, or acquired, immune response takes days or even weeks to become established—much longer than the innate response; however, adaptive immunity is more specific to pathogens and has memory. Adaptive immunity is an immunity that occurs after exposure to an antigen either from a pathogen or a vaccination. This part of the immune system is activated when the innate immune response is insufficient to control an infection. In fact, without information from the innate immune system, the adaptive response could not be mobilized. There are two types of adaptive responses: the cell-mediated immune response, which is carried out by T cells, and the humoral immune response, which is controlled by activated B cells and antibodies. Activated T cells and B cells that are specific to molecular structures on the pathogen proliferate and attack the invading pathogen. Their attack can kill pathogens directly or secrete antibodies that enhance the phagocytosis of pathogens and disrupt the infection. Adaptive immunity also involves a memory to provide the host with long-term protection from reinfection with the same type of pathogen; on re-exposure, this memory will facilitate an efficient and quick response.

Antigen-presenting Cells

Unlike NK cells of the innate immune system, B cells (B lymphocytes) are a type of white blood cell that gives rise to antibodies, whereas T cells (T lymphocytes) are a type of white blood cell that plays an important role in the immune response. T cells are a key component in the cell-mediated response—the specific immune response that utilizes T cells to neutralize cells that have been infected with viruses and certain bacteria. There are three types of T cells: cytotoxic, helper, and suppressor T cells. Cytotoxic T cells destroy virus-infected cells in the cell-mediated immune response, and helper T cells play a part in activating both the antibody and the cell-mediated immune responses. Suppressor T cells deactivate T cells and B cells when needed, and thus prevent the immune response from becoming too intense.

An antigen is a foreign or "non-self" macromolecule that reacts with cells of the immune system. Not all antigens will provoke a response. For instance, individuals produce innumerable "self" antigens and are constantly exposed to harmless foreign antigens, such as food proteins, pollen, or dust components. The suppression of immune responses to harmless macromolecules is highly regulated and typically prevents processes that could be damaging to the host, known as tolerance.

The innate immune system contains cells that detect potentially harmful antigens, and then inform the adaptive immune response about the presence of these antigens. An antigen-presenting cell (APC) is an immune cell that detects, engulfs, and informs the adaptive immune response about an infection. When a pathogen is detected, these APCs will phagocytose the pathogen and digest it to form many different fragments of the antigen. Antigen fragments will then be transported to the surface of the APC, where they will serve as an indicator to other immune cells. Dendritic cells are immune cells that process antigen material; they are present in the skin (Langerhans cells) and the lining of the nose, lungs, stomach, and intestines. Sometimes a dendritic cell presents on the surface of other cells to induce an immune response, thus functioning as an antigen-presenting cell. Macrophages also function as APCs. Before activation and differentiation, B cells can also function as APCs.

After phagocytosis by APCs, the phagocytic vesicle fuses with an intracellular lysosome forming phagolysosome. Within the phagolysosome, the components are broken down into fragments; the fragments are then loaded onto MHC class I or MHC class II molecules and are transported to the cell surface for antigen presentation, as illustrated in [link]. Note that T lymphocytes cannot properly respond to the antigen unless it is processed and embedded in an MHC II molecule. APCs express MHC on their surfaces, and when combined with a foreign antigen, these complexes signal a "non-self" invader. Once the fragment of antigen is embedded in the MHC II molecule, the immune cell can respond. Helper T- cells are one of the main lymphocytes that respond to antigen-presenting cells. Recall that all other nucleated cells of the body expressed MHC I molecules, which signal "healthy" or "normal."

An APC, such as a macrophage, engulfs and digests a foreign bacterium. An antigen from the bacterium is presented on the cell surface in conjunction with an MHC II molecule Lymphocytes of the adaptive immune response interact with antigen-embedded MHC II

molecules to mature into functional immune

cells.
Link to Learning

This animation from Rockefeller University shows how dendritic cells act as sentinels in the body's immune system.

T and B Lymphocytes

Lymphocytes in human circulating blood are approximately 80 to 90 percent T cells, shown in [link], and 10 to 20 percent B cells. Recall that the T cells are involved in the cell-mediated immune response, whereas B cells are part of the humoral immune response.

T cells encompass a heterogeneous population of cells with extremely diverse functions. Some T cells respond to APCs of the innate immune system, and indirectly induce immune responses by releasing cytokines. Other T cells stimulate B cells to prepare their own response. Another population of T cells detects APC signals and directly kills the infected cells. Other T cells are involved in suppressing inappropriate immune reactions to harmless or “self” antigens.

This scanning electron micrograph shows a T lymphocyte, which is responsible for the cell-mediated immune response. T cells are able to recognize antigens. (credit: modification of

work by NCI; scale-bar data from Matt Russell)

T and B cells exhibit a common theme of recognition/binding of specific antigens via a complementary receptor, followed by activation and self-amplification/maturation to specifically bind to the particular antigen of the infecting pathogen. T and B lymphocytes are also similar in that each cell only expresses one type of antigen receptor. Any individual may possess a population of T and B cells that together express a near limitless variety of antigen receptors that are capable of recognizing virtually any infecting pathogen. T and B cells are activated when they recognize small components of antigens, called epitopes, presented by APCs, illustrated in [link]. Note that recognition occurs at a specific epitope rather than on the entire antigen; for this reason, epitopes are known as “antigenic determinants.” In the absence of information from APCs, T and B cells remain inactive, or naïve, and are unable to prepare an immune response. The requirement for information from the APCs of innate immunity to trigger B cell or T cell activation illustrates the essential nature of the innate immune response to the functioning of the entire immune system.

An antigen is a macromolecule that reacts with components of the immune system. A given antigen may contain several motifs that are recognized by immune cells. Each motif is an epitope. In this figure, the entire structure is an antigen, and the orange, salmon and green components projecting from it represent potential

epitopes.

Naïve T cells can express one of two different molecules, CD4 or CD8, on their surface, as shown in [link], and are accordingly classified as $CD4^+$ or $CD8^+$ cells. These molecules are important because they regulate how a T cell will interact with and respond to an APC. Naïve $CD4^+$ cells bind APCs via their antigen-embedded MHC II molecules and are stimulated to become helper T (T_H) lymphocytes, cells that go on to stimulate B cells (or cytotoxic T cells) directly or secrete cytokines to inform more and various target cells about the pathogenic threat. In contrast, $CD8^+$ cells engage antigen-embedded MHC I molecules on APCs and are stimulated to become cytotoxic T lymphocytes (CTLs), which directly kill infected cells by apoptosis and emit cytokines to amplify the immune response. The two populations of T cells have different mechanisms of immune protection, but both bind MHC molecules via their antigen receptors called T cell receptors (TCRs). The CD4 or CD8 surface molecules differentiate whether the TCR will engage an MHC II or an MHC I molecule. Because they assist in binding specificity, the CD4 and CD8 molecules are described as coreceptors.

Art Connection
Naïve $CD4^+$ T cells engage MHC II molecules on antigen-presenting cells (APCs) and become activated. Clones of the activated helper T cell, in turn, activate B cells and $CD8^+$ T cells, which become cytotoxic T cells. Cytotoxic T cells kill infected

cells.

Which of the following statements about T cells is false?

a. Helper T cells release cytokines while cytotoxic T cells kill the infected cell.
b. Helper T cells are $CD4^+$, while cytotoxic T cells are $CD8^+$.
c. MHC II is a receptor found on most body cells, while MHC I is a receptor found on immune cells only.
d. The T cell receptor is found on both $CD4^+$ and $CD8^+$ T cells.

Consider the innumerable possible antigens that an individual will be exposed to during a lifetime. The mammalian adaptive immune system is adept in responding appropriately to each antigen. Mammals have an enormous diversity of T cell populations, resulting from the diversity of TCRs. Each TCR consists of two polypeptide chains that span the T cell membrane, as illustrated in [link]; the chains are linked by a disulfide bridge. Each polypeptide chain is comprised of a constant domain and a variable domain: a domain, in this sense, is a specific region of a protein that may be regulatory or structural. The intracellular domain is involved in intracellular signaling. A single T cell will express thousands of identical copies of one specific TCR variant on its cell surface. The specificity of the adaptive immune system occurs because it synthesizes millions of different T cell populations, each expressing a TCR that differs in its variable domain. This TCR diversity is achieved by the mutation and recombination of genes that encode these receptors in stem cell precursors of T cells. The binding between an antigen-displaying MHC molecule and a complementary TCR "match" indicates that the adaptive immune system needs to activate and produce that specific T cell because its structure is appropriate to recognize and destroy the invading pathogen.

A T cell receptor spans the membrane and projects variable binding regions into the extracellular space to bind processed antigens via MHC molecules on

APCs.

Helper T Lymphocytes

The T_H lymphocytes function indirectly to identify potential pathogens for other cells of the immune system. These cells are important for extracellular infections, such as those caused by certain bacteria, helminths, and protozoa. T_H lymphocytes recognize specific antigens displayed in the MHC II complexes of APCs. There are two major populations of T_H cells:

T_H1 and T_H2. T_H1 cells secrete cytokines to enhance the activities of macrophages and other T cells. T_H1 cells activate the action of cyotoxic T cells, as well as macrophages. T_H2 cells stimulate naïve B cells to destroy foreign invaders via antibody secretion. Whether a T_H1 or a T_H2 immune response develops depends on the specific types of cytokines secreted by cells of the innate immune system, which in turn depends on the nature of the invading pathogen.

The T_H1-mediated response involves macrophages and is associated with inflammation. Recall the frontline defenses of macrophages involved in the innate immune response. Some intracellular bacteria, such as *Mycobacterium tuberculosis*, have evolved to multiply in macrophages after they have been engulfed. These pathogens evade attempts by macrophages to destroy and digest the pathogen. When *M. tuberculosis* infection occurs, macrophages can stimulate naïve T cells to become T_H1 cells. These stimulated T cells secrete specific cytokines that send feedback to the macrophage to stimulate its digestive capabilities and allow it to destroy the colonizing *M. tuberculosis*. In the same manner, T_H1-activated macrophages also become better suited to ingest and kill tumor cells. In summary; T_H1 responses are directed toward intracellular invaders while T_H2 responses are aimed at those that are extracellular.

B Lymphocytes

When stimulated by the T_H2 pathway, naïve B cells differentiate into antibody-secreting plasma cells. A plasma cell is an immune cell that secrets antibodies; these cells arise from B cells that were stimulated by antigens. Similar to T cells, naïve B cells initially are coated in thousands of B cell receptors (BCRs), which are membrane-bound forms of Ig (immunoglobulin, or an antibody). The B cell receptor has two heavy chains and two light chains connected by disulfide linkages. Each chain has a constant and a variable region; the latter is involved in antigen binding. Two other membrane proteins, Ig alpha and Ig beta, are involved in signaling. The receptors of any particular B cell, as shown in [link] are all the same, but the hundreds of millions of different B cells in an individual have distinct recognition domains that contribute to extensive diversity in the types of molecular structures to which they can bind. In this state, B cells function as APCs. They bind and engulf foreign antigens via their BCRs and then display processed antigens in the context of MHC II molecules to T_H2 cells. When a T_H2 cell detects that a B cell is bound to a relevant antigen, it secretes specific cytokines that induce the B cell to proliferate rapidly, which makes thousands of identical (clonal) copies of it, and then it synthesizes and secretes antibodies with the same antigen recognition pattern as the BCRs. The activation of B cells corresponding to one specific BCR variant and the dramatic proliferation of that variant is known as clonal selection. This phenomenon drastically, but briefly, changes the proportions of BCR variants expressed by the immune system, and shifts the balance toward BCRs specific to the infecting pathogen.

B cell receptors are embedded in the membranes of B cells and bind a variety of antigens through their variable regions. The signal transduction region transfers the signal into the cell.

T and B cells differ in one fundamental way: whereas T cells bind antigens that have been digested and embedded in MHC molecules by APCs, B cells function as APCs that bind intact antigens that have not been processed. Although T and B cells both react with molecules that are termed “antigens,” these lymphocytes actually respond to very different types of molecules. B cells must be able to bind intact antigens because they secrete antibodies that must recognize the pathogen directly, rather than digested remnants of the pathogen. Bacterial carbohydrate and lipid molecules can activate B cells independently from the T cells.

Cytotoxic T Lymphocytes

CTLs, a subclass of T cells, function to clear infections directly. The cell-mediated part of the adaptive immune system consists of CTLs that attack and destroy infected cells. CTLs are particularly important in protecting against viral infections; this is because viruses replicate within cells where they are shielded from extracellular contact with circulating antibodies. When APCs phagocytize pathogens and present MHC I-embedded antigens to naïve $CD8^+$ T cells that express complementary TCRs, the $CD8^+$ T cells become activated to proliferate according to clonal selection. These resulting CTLs then identify non-APCs displaying the same MHC I-embedded antigens (for example, viral proteins)—for example, the CTLs identify infected host cells.

Intracellularly, infected cells typically die after the infecting pathogen replicates to a sufficient concentration and lyses the cell, as many viruses do. CTLs attempt to identify and destroy infected cells before the pathogen can replicate and escape, thereby halting the progression of intracellular infections. CTLs also support NK lymphocytes to destroy early cancers. Cytokines secreted by the T_H1 response that stimulates macrophages also stimulate CTLs and enhance their ability to identify and destroy infected cells and tumors.

CTLs sense MHC I-embedded antigens by directly interacting with infected cells via their TCRs. Binding of TCRs with antigens activates CTLs to release perforin and granzyme, degradative enzymes that will induce apoptosis of the infected cell. Recall that this is a similar destruction mechanism to that used by NK cells. In this process, the CTL does not become infected and is not harmed by the secretion of perforin and granzymes. In fact, the functions of NK cells and CTLs are complementary and maximize the removal of infected cells, as illustrated in [link]. If the NK cell cannot identify the "missing self" pattern of down-regulated MHC I molecules, then the CTL can identify it by the complex of MHC I with foreign antigens, which signals "altered self." Similarly, if the CTL cannot detect antigen-embedded MHC I because the receptors are depleted from the cell surface, NK cells will destroy the cell instead. CTLs also emit cytokines, such as interferons, that alter surface protein expression in other infected cells, such that the infected cells can be easily identified and destroyed. Moreover, these interferons can also prevent virally infected cells from releasing virus particles.

Art Connection
Natural killer (NK) cells recognize the MHC I receptor on healthy cells. If MHC I is absent, the cell is lysed.

Based on what you know about MHC receptors, why do you think an organ transplanted from an incompatible donor to a recipient will be rejected?

Plasma cells and CTLs are collectively called effector cells: they represent differentiated versions of their naïve counterparts, and they are involved in bringing about the immune defense of killing pathogens and infected host cells.

Mucosal Surfaces and Immune Tolerance

The innate and adaptive immune responses discussed thus far comprise the systemic immune system (affecting the whole body), which is distinct from the mucosal immune system. Mucosal immunity is formed by mucosa-associated lymphoid tissue, which functions independently of the systemic immune system, and which has its own innate and adaptive components. Mucosa-associated lymphoid tissue (MALT), illustrated in [link], is a collection of lymphatic tissue that combines with epithelial tissue lining the mucosa throughout the body. This tissue functions as the immune barrier and response in areas of the body with direct contact to the external environment. The systemic and mucosal immune systems use many of the same cell types. Foreign particles that make their way to MALT are taken up by absorptive epithelial cells called M cells and delivered to APCs located directly below the mucosal tissue. M cells function in the transport described, and are located in the Peyer's patch, a lymphoid nodule. APCs of the mucosal immune system are primarily dendritic cells, with B cells and macrophages having minor roles. Processed antigens displayed on APCs are detected by T cells in the MALT and at various mucosal induction sites, such as the tonsils, adenoids, appendix, or the mesenteric lymph nodes of the intestine. Activated T cells then migrate through the lymphatic system and into the circulatory system to mucosal sites of infection.

The topology and function of intestinal MALT is shown. Pathogens are taken up by M cells in the intestinal epithelium and excreted into a pocket formed by the inner surface of the cell. The pocket contains antigen-presenting cells such as dendritic cells, which engulf the antigens, then present them with MHC II molecules on the cell surface. The dendritic cells migrate to an underlying tissue called a Peyer's patch. Antigen-presenting cells, T cells, and B cells aggregate within the Peyer's patch, forming organized lymphoid follicles. There, some T cells and B cells are activated. Other antigen-loaded dendritic cells migrate through the lymphatic system where they activate B cells, T cells, and plasma cells in the lymph nodes. The activated cells then return to MALT tissue effector sites. IgA and other antibodies

are secreted into the intestinal

lumen.

MALT is a crucial component of a functional immune system because mucosal surfaces, such as the nasal passages, are the first tissues onto which inhaled or ingested pathogens are deposited. The mucosal tissue includes the mouth, pharynx, and esophagus, and the gastrointestinal, respiratory, and urogenital tracts.

The immune system has to be regulated to prevent wasteful, unnecessary responses to harmless substances, and more importantly so that it does not attack “self.” The acquired ability to prevent an unnecessary or harmful immune response to a detected foreign substance known not to cause disease is described as immune tolerance. Immune tolerance is crucial for maintaining mucosal homeostasis given the tremendous number of foreign substances (such as food proteins) that APCs of the oral cavity, pharynx, and gastrointestinal mucosa encounter. Immune tolerance is brought about by specialized APCs in the liver, lymph nodes, small intestine, and lung that present harmless antigens to an exceptionally diverse population of regulatory T (T_{reg}) cells, specialized lymphocytes that suppress local inflammation and inhibit the secretion of stimulatory immune factors. The combined result of T_{reg} cells is to prevent immunologic activation and inflammation in undesired tissue compartments and to allow the immune system to focus on pathogens instead. In addition to promoting immune tolerance of harmless antigens, other subsets of T_{reg} cells are involved in the prevention of

the autoimmune response, which is an inappropriate immune response to host cells or self-antigens. Another T_{reg} class suppresses immune responses to harmful pathogens after the infection has cleared to minimize host cell damage induced by inflammation and cell lysis.

Immunological Memory

The adaptive immune system possesses a memory component that allows for an efficient and dramatic response upon reinvasion of the same pathogen. Memory is handled by the adaptive immune system with little reliance on cues from the innate response. During the adaptive immune response to a pathogen that has not been encountered before, called a primary response, plasma cells secreting antibodies and differentiated T cells increase, then plateau over time. As B and T cells mature into effector cells, a subset of the naïve populations differentiates into B and T memory cells with the same antigen specificities, as illustrated in [link].

A memory cell is an antigen-specific B or T lymphocyte that does not differentiate into effector cells during the primary immune response, but that can immediately become effector cells upon re-exposure to the same pathogen. During the primary immune response, memory cells do not respond to antigens and do not contribute to host defenses. As the infection is cleared and pathogenic stimuli subside, the effectors are no longer needed, and they undergo apoptosis. In contrast, the memory cells persist in the circulation.

Art Connection
After initially binding an antigen to the B cell receptor (BCR), a B cell internalizes the antigen and presents it on MHC II. A helper T cell recognizes the MHC II–antigen complex and activates the B cell. As a result, memory B cells and plasma cells are

made.

The Rh antigen is found on Rh-positive red blood cells. An Rh-negative female can usually carry an Rh-positive fetus to term without difficulty. However, if she has a second Rh-positive fetus, her body may launch an immune attack that causes hemolytic disease of the newborn. Why do you think hemolytic disease is only a problem during the second or subsequent pregnancies?

If the pathogen is never encountered again during the individual's lifetime, B and T memory cells will circulate for a few years or even several decades and will gradually die off, having never functioned as effector cells. However, if the host is re-exposed to the same pathogen type, circulating memory cells will immediately differentiate into plasma cells and CTLs without input from APCs or T_H cells. One reason the adaptive immune response is delayed is because it takes time for naïve B and T cells with the appropriate antigen specificities to be identified and activated. Upon reinfection, this step is skipped, and the result is a more rapid production of immune defenses. Memory B cells that differentiate into plasma cells output tens to hundreds-fold greater antibody amounts than were secreted during the primary response, as the graph in [link] illustrates. This rapid and dramatic antibody response may stop the infection before it can even become established, and the individual may not realize they had been exposed.

In the primary response to infection, antibodies are secreted first from plasma cells. Upon re-exposure to the same pathogen, memory cells differentiate into antibody-secreting plasma cells that output a greater amount of antibody for a longer period of

time.

Vaccination is based on the knowledge that exposure to noninfectious antigens, derived from known pathogens, generates a mild primary immune response. The immune response to vaccination may not be perceived by the host as illness but still confers immune memory. When exposed to the corresponding pathogen to which an individual was vaccinated, the reaction is similar to a secondary exposure. Because each reinfection generates more memory cells and increased resistance to the pathogen, and because some memory cells die, certain vaccine courses involve one or more booster vaccinations to mimic repeat exposures: for instance, tetanus boosters are necessary every ten years because the memory cells only live that long.

Mucosal Immune Memory

A subset of T and B cells of the mucosal immune system differentiates into memory cells just as in the systemic immune system. Upon reinvasion of the same pathogen type, a pronounced immune response occurs at the mucosal site where the original pathogen deposited, but a collective defense is also organized within interconnected or adjacent mucosal tissue. For instance, the immune memory of an infection in the oral cavity would also elicit a response in the pharynx if the oral cavity was exposed to the same pathogen.

Career Connection

VaccinologistVaccination (or immunization) involves the delivery, usually by injection as shown in [link], of noninfectious antigen(s) derived from known pathogens. Other components, called adjuvants, are delivered in parallel to help stimulate the immune response. Immunological memory is the reason vaccines work. Ideally, the effect of vaccination is to elicit immunological memory, and thus resistance to specific pathogens without the individual having to experience an infection.

Vaccines are often delivered by injection into the arm. (credit: U.S. Navy Photographer's Mate Airman Apprentice Christopher D.

Blachly)

Vaccinologists are involved in the process of vaccine development from the initial idea to the availability of the completed vaccine. This process can take decades, can cost millions of dollars, and can involve many obstacles along the way. For instance, injected vaccines stimulate the systemic immune system, eliciting humoral and cell-mediated immunity, but have little effect on the mucosal response, which presents a challenge because many pathogens are deposited and replicate in mucosal compartments, and the injection does not provide the most efficient immune memory for these disease agents. For this reason, vaccinologists are actively involved in developing new vaccines that are applied via intranasal, aerosol, oral, or transcutaneous (absorbed through the skin) delivery methods. Importantly, mucosal-administered vaccines elicit both mucosal and systemic immunity and produce the same level of disease resistance as injected vaccines.

The polio vaccine can be administered orally. (credit: modification of work by UNICEF Sverige)

Currently, a version of intranasal influenza vaccine is available, and the polio and typhoid vaccines can be administered orally, as shown in [link]. Similarly, the measles and rubella vaccines are being adapted to aerosol delivery using inhalation devices. Eventually, transgenic plants may be engineered to produce vaccine antigens that can be eaten to confer disease resistance. Other vaccines may be adapted to rectal or vaginal application to elicit immune responses in rectal, genitourinary, or reproductive mucosa. Finally, vaccine antigens may be adapted to transdermal application in which the skin is lightly scraped and microneedles are used to pierce the outermost layer. In addition to mobilizing the mucosal immune response, this new generation of vaccines may end the anxiety associated with injections and, in turn, improve patient participation.

Primary Centers of the Immune System

Although the immune system is characterized by circulating cells throughout the body, the regulation, maturation, and intercommunication of immune factors occur at specific sites. The blood circulates immune cells, proteins, and other factors through the body. Approximately 0.1 percent of all cells in the blood are leukocytes, which encompass monocytes (the precursor of macrophages) and lymphocytes. The majority of cells in the blood are erythrocytes (red blood cells). Lymph is a watery fluid that bathes tissues and organs with protective white blood cells and does not contain erythrocytes. Cells of the immune system can travel between the distinct lymphatic and blood circulatory systems, which are separated by interstitial space, by a process called extravasation (passing through to surrounding tissue).

The cells of the immune system originate from hematopoietic stem cells in the bone marrow. Cytokines stimulate these stem cells to differentiate into immune cells. B cell maturation occurs in the bone marrow, whereas naïve T cells transit from the bone marrow to the thymus for maturation. In the thymus, immature T cells that express TCRs complementary to self-antigens are destroyed. This process helps prevent autoimmune responses.

On maturation, T and B lymphocytes circulate to various destinations. Lymph nodes scattered throughout the body, as illustrated in [link], house large populations of T and B cells, dendritic cells, and macrophages. Lymph gathers antigens as it drains from tissues. These antigens then are filtered through lymph nodes before the lymph is returned to circulation. APCs in the lymph nodes capture and process antigens and inform nearby lymphocytes about potential pathogens.

(a) Lymphatic vessels carry a clear fluid called lymph throughout the body. The liquid enters (b) lymph nodes through afferent vessels. Lymph nodes are filled with lymphocytes that purge infecting cells. The lymph then exits through efferent vessels. (credit: modification of

work by NIH, NCI)

The spleen houses B and T cells, macrophages, dendritic cells, and NK cells. The spleen, shown in [link], is the site where APCs that have trapped foreign particles in the blood can communicate with lymphocytes. Antibodies are synthesized and secreted by activated plasma cells in the spleen, and the spleen filters foreign substances and antibody-complexed pathogens from the blood. Functionally, the spleen is to the blood as lymph nodes are to the lymph.

The spleen is similar to a lymph node but is much larger and filters blood instead of lymph. Blood enters the spleen through arteries and exits through veins. The spleen contains two types of tissue: red pulp and white pulp. Red pulp consists of cavities that store blood. Within the red pulp, damaged red blood cells are removed and replaced by new ones. White pulp is

rich in lymphocytes that remove antigen-coated bacteria from the blood. (credit: modification of work by NCI)

Section Summary

The adaptive immune response is a slower-acting, longer-lasting, and more specific response than the innate response. However, the adaptive response requires information from the innate immune system to function. APCs display antigens via MHC molecules to complementary naïve T cells. In response, the T cells differentiate and proliferate, becoming T_H cells or CTLs. T_H cells stimulate B cells that have engulfed and presented pathogen-derived antigens. B cells differentiate into plasma cells that secrete antibodies, whereas CTLs induce apoptosis in intracellularly infected or cancerous cells. Memory cells persist after a primary exposure to a pathogen. If re-exposure occurs, memory cells differentiate into effector cells without input from the innate immune system. The mucosal immune system is largely independent from the systemic immune system but functions in a parallel fashion to protect the extensive mucosal surfaces of the body.

Art Connections

[link] Which of the following statements about T cells is false?

a. Helper T cells release cytokines while cytotoxic T cells kill the infected cell.
b. Helper T cells are CD4+, while cytotoxic T cells are $CD8^+$.
c. MHC II is a receptor found on most body cells, while MHC I is a receptor found on immune cells only.
d. The T cell receptor is found on both $CD4^+$ and $CD8^+$ T cells.

[link] C

[link] Based on what you know about MHC receptors, why do you think an organ transplanted from an incompatible donor to a recipient will be rejected?

[link] MHC receptors differ from person to person. Thus, MHC receptors on an incompatible donor are considered “non-self” and are rejected by the immune system.

[link] The Rh antigen is found on Rh-positive red blood cells. An Rh-negative female can usually carry an Rh-positive fetus to term without difficulty. However, if she has a second Rh-positive fetus, her body may launch an immune attack that causes hemolytic disease of the newborn. Why do you think hemolytic disease is only a problem during the second or subsequent pregnancies?

[link] If the blood of the mother and fetus mixes, memory cells that recognize the Rh antigen can form late in the first pregnancy. During subsequent pregnancies, these memory cells launch an immune attack on the fetal blood cells. Injection of anti-Rh antibody during the first pregnancy prevents the immune response from occurring.

Review Questions

Which of the following is both a phagocyte and an antigen-presenting cell?

a. NK cell
b. eosinophil
c. neutrophil
d. macrophage

D

Which immune cells bind MHC molecules on APCs via CD8 coreceptors on their cell surfaces?

a. T_H cells
b. CTLs
c. mast cells
d. basophils

B

What “self” pattern is identified by NK cells?

a. altered self
b. missing self
c. normal self
d. non-self

B

The acquired ability to prevent an unnecessary or destructive immune reaction to a harmless foreign particle, such as a food protein, is called _____.

a. the T_H2 response
b. allergy
c. immune tolerance

d. autoimmunity

C

A memory B cell can differentiate upon re-exposure to a pathogen of which cell type?

a. CTL
b. naïve B cell
c. memory T cell
d. plasma cell

D

Foreign particles circulating in the blood are filtered by the _____.

a. spleen
b. lymph nodes
c. MALT
d. lymph

A

Free Response

Explain the difference between an epitope and an antigen.

An antigen is a molecule that reacts with some component of the immune response (antibody, B cell receptor, T cell receptor). An epitope is the region on the antigen through which binding with the immune component actually occurs.

What is a naïve B or T cell?

A naïve T or B cell is one that has not been activated by binding to the appropriate epitope. Naïve T and B cells cannot produce responses.

How does the T_H1 response differ from the T_H2 response?

The T_H1 response involves the secretion of cytokines to stimulate macrophages and CTLs and improve their destruction of intracellular pathogens and tumor cells. It is associated with inflammation. The T_H2 response is involved in the stimulation of B cells into plasma cells that synthesize and secrete antibodies.

In mammalian adaptive immune systems, T cell receptors are extraordinarily diverse. What function of the immune system results from this diversity, and how is this diversity achieved?

The diversity of TCRs allows the immune system to have millions of different T cells, and thereby to be specific in distinguishing antigens. This diversity arises from mutation and recombination in the genes that encode the variable regions of TCRs.

How do B and T cells differ with respect to antigens that they bind?

T cells bind antigens that have been digested and embedded in MHC molecules by APCs. In contrast, B cells function themselves as APCs to bind intact, unprocessed antigens.

Why is the immune response after reinfection much faster than the adaptive immune response after the initial infection?

Upon reinfection, the memory cells will immediately differentiate into plasma cells and CTLs without input from APCs or T_H cells. In contrast, the adaptive immune response to the initial infection requires time for naïve B and T cells with the appropriate antigen specificities to be identified and activated.

Glossary

adaptive immunity
: immunity that has memory and occurs after exposure to an antigen either from a pathogen or a vaccination

antigen
: foreign or "non-self" protein that triggers the immune response

antigen-presenting cell (APC)
: immune cell that detects, engulfs, and informs the adaptive immune response about an infection by presenting the processed antigen on the cell surface

autoimmune response
: inappropriate immune response to host cells or self-antigens

cell-mediated immune response
: adaptive immune response that is carried out by T cells

clonal selection
: activation of B cells corresponding to one specific BCR variant and the dramatic proliferation of that variant

cytotoxic T lymphocyte (CTL)
: adaptive immune cell that directly kills infected cells via perforin and granzymes, and releases cytokines to enhance the immune response

dendritic cell
: immune cell that processes antigen material and presents it on the surface of other cells to induce an immune response

effector cell
: lymphocyte that has differentiated, such as a B cell, plasma cell, or cytotoxic T lymphocyte

epitope
: small component of an antigen that is specifically recognized by antibodies, B cells, and T cells; the antigenic determinant

helper T lymphocyte (T_H)
: cell of the adaptive immune system that binds APCs via MHC II molecules and stimulates B cells or secretes cytokines to initiate the immune response

humoral immune response

adaptive immune response that is controlled by activated B cells and antibodies

immune tolerance
: acquired ability to prevent an unnecessary or harmful immune response to a detected foreign body known not to cause disease or to self-antigens

lymph
: watery fluid that bathes tissues and organs with protective white blood cells and does not contain erythrocytes

mucosa-associated lymphoid tissue (MALT)
: collection of lymphatic tissue that combines with epithelial tissue lining the mucosa throughout the body

memory cell
: antigen-specific B or T lymphocyte that does not differentiate into effector cells during the primary immune response but that can immediately become an effector cell upon re-exposure to the same pathogen

plasma cell
: immune cell that secrets antibodies; these cells arise from B cells that were stimulated by antigens

regulatory T (T_{reg}) cell
: specialized lymphocyte that suppresses local inflammation and inhibits the secretion of cytokines, antibodies, and other stimulatory immune factors; involved in immune tolerance

Antibodies

By the end of this section, you will be able to:

- Explain cross-reactivity
- Describe the structure and function of antibodies
- Discuss antibody production

An antibody, also known as an immunoglobulin (Ig), is a protein that is produced by plasma cells after stimulation by an antigen. Antibodies are the functional basis of humoral immunity. Antibodies occur in the blood, in gastric and mucus secretions, and in breast milk. Antibodies in these bodily fluids can bind pathogens and mark them for destruction by phagocytes before they can infect cells.

Antibody Structure

An antibody molecule is comprised of four polypeptides: two identical heavy chains (large peptide units) that are partially bound to each other in a “Y” formation, which are flanked by two identical light chains (small peptide units), as illustrated in [link]. Bonds between the cysteine amino acids in the antibody molecule attach the polypeptides to each other. The areas where the antigen is recognized on the antibody are variable domains and the antibody base is composed of constant domains.

In germ-line B cells, the variable region of the light chain gene has 40 variable (V) and five joining (J) segments. An enzyme called DNA recombinase randomly excises most of these

segments out of the gene, and splices one V segment to one J segment. During RNA processing, all but one V and J segment are spliced out. Recombination and splicing may result in over 10^6 possible VJ combinations. As a result, each differentiated B cell in the human body typically has a unique variable chain. The constant domain, which does not bind antibody, is the same for all antibodies.

(a) As a germ-line B cell matures, an enzyme called DNA recombinase randomly excises V and J segments from the light chain gene. Splicing at the mRNA level results in further gene rearrangement. As a result, (b) each antibody has a unique variable region capable of binding a different

antigen.

Similar to TCRs and BCRs, antibody diversity is produced by the mutation and recombination of approximately 300 different gene segments encoding the light and heavy chain variable domains in precursor cells that are destined to become B cells. The variable domains from the heavy and light chains interact to form the binding site through which an antibody can bind a specific epitope on an antigen. The numbers of repeated constant domains in Ig classes are the same for all antibodies corresponding to a specific class. Antibodies are structurally similar to the extracellular component of the BCRs, and B cell maturation to plasma cells can be visualized in simple terms as the cell acquires the ability to secrete the extracellular portion of its BCR in large quantities.

Antibody Classes

Antibodies can be divided into five classes—IgM, IgG, IgA, IgD, IgE—based on their physiochemical, structural, and immunological properties. IgGs, which make up about 80 percent of all antibodies, have heavy chains that consist of one variable domain and three identical constant domains. IgA and IgD also have three constant domains per heavy chain, whereas IgM and IgE each have four constant domains per heavy chain. The variable domain determines binding specificity and the constant domain of the heavy chain determines the immunological mechanism of action of the corresponding antibody class. It is possible for two antibodies to have the same binding specificities but be in different classes and, therefore, to be involved in different functions.

After an adaptive defense is produced against a pathogen, typically plasma cells first secrete IgM into the blood. BCRs on naïve B cells are of the IgM class and occasionally IgD class. IgM molecules make up approximately ten percent of all antibodies. Prior to antibody secretion, plasma cells assemble IgM molecules into pentamers (five individual antibodies) linked by a joining (J) chain, as shown in [link]. The pentamer arrangement means that these macromolecules can bind ten identical antigens. However, IgM molecules released early in the adaptive immune response do not bind to antigens as stably as IgGs, which are one of the possible types of antibodies secreted in large quantities upon re-exposure to the same pathogen. [link] summarizes the properties of immunoglobulins and illustrates their basic structures.

Immunoglobulins have different functions, but all are composed of light and heavy chains that form a Y-shaped

structure.

IgAs populate the saliva, tears, breast milk, and mucus secretions of the gastrointestinal, respiratory, and genitourinary tracts. Collectively, these bodily fluids coat and protect the extensive mucosa (4000 square feet in humans). The total number of IgA molecules in these bodily secretions is greater than the number of IgG molecules in the blood serum. A small amount of IgA is also secreted into the serum in monomeric form. Conversely, some IgM is secreted into bodily fluids of the mucosa. Similar to IgM, IgA molecules are secreted as polymeric structures linked with a J chain. However, IgAs are secreted mostly as dimeric molecules, not pentamers.

IgE is present in the serum in small quantities and is best characterized in its role as an allergy mediator. IgD is also present in small quantities. Similar to IgM, BCRs of the IgD class are found on the surface of naïve B cells. This class supports antigen recognition and maturation of B cells to plasma cells.

Antibody Functions

Differentiated plasma cells are crucial players in the humoral response, and the antibodies they secrete are particularly significant against extracellular pathogens and toxins. Antibodies circulate freely and act independently of plasma cells. Antibodies can be transferred from one individual to another to temporarily protect against infectious disease. For instance, a person who has recently produced a successful immune response against a particular disease agent can donate blood to a nonimmune recipient and confer temporary immunity through antibodies in the donor's blood serum. This phenomenon is called passive immunity; it also occurs naturally during breastfeeding, which makes breastfed infants highly resistant to infections during the first few months of life.

Antibodies coat extracellular pathogens and neutralize them, as illustrated in [link], by blocking key sites on the pathogen that enhance their infectivity (such as receptors that "dock" pathogens on host cells). Antibody neutralization can prevent pathogens from entering and infecting host cells, as opposed to the CTL-mediated approach of killing cells that are already infected to prevent progression of an established infection. The neutralized antibody-coated pathogens can then be filtered by the spleen and eliminated in urine or feces.

Antibodies may inhibit infection by (a) preventing the antigen from binding its target, (b) tagging a pathogen for destruction by macrophages or neutrophils, or (c) activating the complement cascade.

Antibodies also mark pathogens for destruction by phagocytic cells, such as macrophages or neutrophils, because phagocytic cells are highly attracted to macromolecules complexed with antibodies. Phagocytic enhancement by antibodies is called opsonization. In a process called complement fixation, IgM and IgG in serum bind to antigens and provide docking sites onto which sequential complement proteins can bind. The combination of antibodies and complement enhances opsonization even further and promotes rapid clearing of pathogens.

Affinity, Avidity, and Cross Reactivity

Not all antibodies bind with the same strength, specificity, and stability. In fact, antibodies exhibit different affinities (attraction) depending on the molecular complementarity between antigen and antibody molecules, as illustrated in [link]. An antibody with a higher affinity for

a particular antigen would bind more strongly and stably, and thus would be expected to present a more challenging defense against the pathogen corresponding to the specific antigen.

(a) Affinity refers to the strength of single interaction between antigen and antibody, while avidity refers to the strength of all interactions combined. (b) An antibody may cross react with different epitopes.

The term avidity describes binding by antibody classes that are secreted as joined, multivalent structures (such as IgM and IgA). Although avidity measures the strength of binding, just as affinity does, the avidity is not simply the sum of the affinities of the antibodies in a multimeric structure. The avidity depends on the number of identical binding sites on the antigen being detected, as well as other physical and chemical factors. Typically, multimeric antibodies, such as pentameric IgM, are classified as having lower affinity than monomeric antibodies, but high avidity. Essentially, the fact that multimeric antibodies can bind many antigens simultaneously balances their slightly lower binding strength for each antibody/antigen interaction.

Antibodies secreted after binding to one epitope on an antigen may exhibit cross reactivity for the same or similar epitopes on different antigens. Because an epitope corresponds to such a small region (the surface area of about four to six amino acids), it is possible for different macromolecules to exhibit the same molecular identities and orientations over short regions. Cross reactivity describes when an antibody binds not to the antigen that elicited its synthesis and secretion, but to a different antigen.

Cross reactivity can be beneficial if an individual develops immunity to several related pathogens despite having only been exposed to or vaccinated against one of them. For instance, antibody cross reactivity may occur against the similar surface structures of various Gram-negative bacteria. Conversely, antibodies raised against pathogenic molecular components that resemble self molecules may incorrectly mark host cells for destruction and cause autoimmune damage. Patients who develop systemic lupus erythematosus (SLE) commonly exhibit antibodies that react with their own DNA. These antibodies may have been initially raised against the nucleic acid of microorganisms but later cross-reacted with self-antigens. This phenomenon is also called molecular mimicry.

Antibodies of the Mucosal Immune System

Antibodies synthesized by the mucosal immune system include IgA and IgM. Activated B cells differentiate into mucosal plasma cells that synthesize and secrete dimeric IgA, and to a lesser extent, pentameric IgM. Secreted IgA is abundant in tears, saliva, breast milk, and in secretions of the gastrointestinal and respiratory tracts. Antibody secretion results in a local humoral response at epithelial surfaces and prevents infection of the mucosa by binding and neutralizing pathogens.

Section Summary

Antibodies (immunoglobulins) are the molecules secreted from plasma cells that mediate the humoral immune response. There are five antibody classes; an antibody's class determines its mechanism of action and production site but does not control its binding specificity. Antibodies bind antigens via variable domains and can either neutralize pathogens or mark them for phagocytosis or activate the complement cascade.

Review Questions

The structure of an antibody is similar to the extracellular component of which receptor?

a. MHC I
b. MHC II
c. BCR
d. none of the above

C

The first antibody class to appear in the serum in response to a newly encountered pathogen is _____.

a. IgM
b. IgA
c. IgG
d. IgE

A

What is the most abundant antibody class detected in the serum upon reexposure to a pathogen or in reaction to a vaccine?

a. IgM
b. IgA
c. IgG
d. IgE

C

Breastfed infants typically are resistant to disease because of _____.

a. active immunity
b. passive immunity
c. immune tolerance
d. immune memory

B

Free Response

What are the benefits and costs of antibody cross reactivity?

Cross reactivity of antibodies can be beneficial when it allows an individual's immune system to respond to an array of similar pathogens after being exposed to just one of them. A potential cost of cross reactivity is an antibody response to parts of the body (self) in addition to the appropriate antigen.

Glossary

affinity
: attraction of molecular complementarity between antigen and antibody molecules

antibody
: protein that is produced by plasma cells after stimulation by an antigen; also known as an immunoglobulin

avidity
: total binding strength of a multivalent antibody with antigen

cross reactivity
: binding of an antibody to an epitope corresponding to an antigen that is different from the one the antibody was raised against

passive immunity
: transfer of antibodies from one individual to another to provide temporary protection against pathogens

Hormonal Control of Osmoregulatory Functions
By the end of this section, you will be able to:

- Explain how hormonal cues help the kidneys synchronize the osmotic needs of the body
- Describe how hormones like epinephrine, norepinephrine, renin-angiotensin, aldosterone, anti-diuretic hormone, and atrial natriuretic peptide help regulate waste elimination, maintain correct osmolarity, and perform other osmoregulatory functions

While the kidneys operate to maintain osmotic balance and blood pressure in the body, they also act in concert with hormones. Hormones are small molecules that act as messengers within the body. Hormones are typically secreted from one cell and travel in the bloodstream to affect a target cell in another portion of the body.

Different regions of the nephron bear specialized cells that have receptors to respond to chemical messengers and hormones. [link] summarizes the hormones that control the osmoregulatory functions.

Hormones That Affect Osmoregulation

Hormone	Where produced	Function
Epinephrine and Norepinephrine	Adrenal medulla	Can decrease kidney function temporarily by vasoconstriction
Renin	Kidney nephrons	Increases blood pressure by acting on angiotensinogen
Angiotensin	Liver	Angiotensin II affects multiple processes and increases blood pressure
Aldosterone	Adrenal cortex	Prevents loss of sodium and water
Anti-diuretic hormone (vasopressin)	Hypothalamus (stored in the posterior pituitary)	Prevents water loss
Atrial natriuretic peptide	Heart atrium	Decreases blood pressure by acting as a vasodilator and increasing glomerular filtration rate; decreases sodium reabsorption in kidneys

Epinephrine and Norepinephrine

Epinephrine and norepinephrine are released by the adrenal medulla and nervous system respectively. They are the flight/fight hormones that are released when the body is under extreme stress. During stress, much of the body's energy is used to combat imminent danger. Kidney function is halted temporarily by epinephrine and norepinephrine. These hormones function by acting directly on the smooth muscles of blood vessels to constrict them. Once the afferent arterioles are constricted, blood flow into the nephrons stops. These hormones go one step further and trigger the renin-angiotensin-aldosterone system.

Renin-Angiotensin-Aldosterone

The renin-angiotensin-aldosterone system, illustrated in [link] proceeds through several steps to produce angiotensin II, which acts to stabilize blood pressure and volume. Renin (secreted by a part of the juxtaglomerular complex) is produced by the granular cells of the afferent and efferent arterioles. Thus, the kidneys control blood pressure and volume directly. Renin acts on angiotensinogen, which is made in the liver and converts it to angiotensin I. Angiotensin converting enzyme (ACE) converts angiotensin I to angiotensin II. Angiotensin II raises blood pressure by constricting blood vessels. It also triggers the release of the mineralocorticoid aldosterone from the adrenal cortex, which in turn stimulates the renal tubules to reabsorb more sodium. Angiotensin II also triggers the release of anti-diuretic hormone (ADH) from the hypothalamus, leading to water retention in the kidneys. It acts directly on the nephrons and decreases glomerular filtration rate. Medically, blood pressure can be controlled by drugs that inhibit ACE (called ACE inhibitors).

The renin-angiotensin-aldosterone system increases blood pressure and volume. The hormone ANP has antagonistic effects. (credit: modification of work by Mikael

Häggström)

Mineralocorticoids

Mineralocorticoids are hormones synthesized by the adrenal cortex that affect osmotic balance. Aldosterone is a mineralocorticoid that regulates sodium levels in the blood. Almost all of the sodium in the blood is reclaimed by the renal tubules under the influence of aldosterone. Because sodium is always reabsorbed by active transport and water follows sodium to maintain osmotic balance, aldosterone manages not only sodium levels but also the water levels in body fluids. In contrast, the aldosterone also stimulates potassium secretion concurrently with sodium reabsorption. In contrast, absence of aldosterone means that no sodium gets reabsorbed in the renal tubules and all of it gets excreted in the urine. In addition, the daily dietary potassium load is not secreted and the retention of K^+ can cause a dangerous increase in plasma K^+ concentration. Patients who have Addison's disease have a failing adrenal cortex and cannot produce aldosterone. They lose sodium in their urine constantly, and if the supply is not replenished, the consequences can be fatal.

Antidiurectic Hormone

As previously discussed, antidiuretic hormone or ADH (also called vasopressin), as the name suggests, helps the body conserve water when body fluid volume, especially that of blood, is low. It is formed by the hypothalamus and is stored and released from the posterior pituitary. It acts by inserting aquaporins in the collecting ducts and promotes reabsorption of water. ADH also acts as a vasoconstrictor and increases blood pressure during hemorrhaging.

Atrial Natriuretic Peptide Hormone

The atrial natriuretic peptide (ANP) lowers blood pressure by acting as a vasodilator. It is released by cells in the atrium of the heart in response to high blood pressure and in patients with sleep apnea. ANP affects salt release, and because water passively follows salt to maintain osmotic balance, it also has a diuretic effect. ANP also prevents sodium reabsorption by the renal tubules, decreasing water reabsorption (thus acting as a diuretic) and lowering blood pressure. Its actions suppress the actions of aldosterone, ADH, and renin.

Section Summary

Hormonal cues help the kidneys synchronize the osmotic needs of the body. Hormones like epinephrine, norepinephrine, renin-angiotensin, aldosterone, anti-diuretic hormone, and atrial natriuretic peptide help regulate the needs of the body as well as the communication between the different organ systems.

Review Questions

Renin is made by _____.

a. granular cells of the juxtaglomerular apparatus
b. the kidneys
c. the nephrons
d. All of the above.

A

Patients with Addison's disease _____.

a. retain water
b. retain salts
c. lose salts and water
d. have too much aldosterone

C

Which hormone elicits the “fight or flight” response?

a. epinephrine
b. mineralcorticoids
c. anti-diuretic hormone
d. thyroxine

A

Free Response

Describe how hormones regulate blood pressure, blood volume, and kidney function.

Hormones are small molecules that act as messengers within the body. Different regions of the nephron bear specialized cells, which have receptors to respond to chemical messengers and hormones. The hormones carry messages to the kidney. These hormonal cues help the kidneys synchronize the osmotic needs of the body. Hormones like epinephrine, norepinephrine, renin-angiotensin, aldosterone, anti-diuretic hormone, and atrial natriuretic peptide help regulate the needs of the body as well as the communication between the different organ systems.

How does the renin-angiotensin-aldosterone mechanism function? Why is it controlled by the kidneys?

The renin-angiotensin-aldosterone system acts through several steps to produce angiotensin II, which acts to stabilize blood pressure and volume. Thus, the kidneys control blood pressure and volume directly. Renin acts on angiotensinogen, which is made in the liver and converts it to angiotensin I. ACE (angiotensin converting enzyme) converts angiotensin I to angiotensin II. Angiotensin II raises blood pressure by constricting blood vessels. It triggers the release of aldosterone from the adrenal cortex, which in turn stimulates the renal tubules to reabsorb more sodium. Angiotensin II also triggers the release of anti-diuretic hormone from the hypothalamus, which leads to water retention. It acts directly on the nephrons and decreases GFR.

Glossary

angiotensin converting enzyme (ACE)
: enzyme that converts angiotensin I to angiotensin II

angiotensin I
: product in the renin-angiotensin-aldosterone pathway

angiotensin II
: molecule that affects different organs to increase blood pressure

anti-diuretic hormone (ADH)
: hormone that prevents the loss of water

renin-angiotensin-aldosterone
: biochemical pathway that activates angiotensin II, which increases blood pressure

vasodilator
: compound that increases the diameter of blood vessels

vasopressin
: another name for anti-diuretic hormone

Disruptions in the Immune System

By the end of this section, you will be able to:

- Describe hypersensitivity
- Define autoimmunity

A functioning immune system is essential for survival, but even the sophisticated cellular and molecular defenses of the mammalian immune response can be defeated by pathogens at virtually every step. In the competition between immune protection and pathogen evasion, pathogens have the advantage of more rapid evolution because of their shorter generation time and other characteristics. For instance, *Streptococcus pneumoniae* (bacterium that cause pneumonia and meningitis) surrounds itself with a capsule that inhibits phagocytes from engulfing it and displaying antigens to the adaptive immune system. *Staphylococcus aureus* (bacterium that can cause skin infections, abscesses, and meningitis) synthesizes a toxin called leukocidin that kills phagocytes after they engulf the bacterium. Other pathogens can also hinder the adaptive immune system. HIV infects T_H cells via their CD4 surface molecules, gradually depleting the number of T_H cells in the body; this inhibits the adaptive immune system's capacity to generate sufficient responses to infection or tumors. As a result, HIV-infected individuals often suffer from infections that would not cause illness in people with healthy immune systems but which can cause devastating illness to immune-compromised individuals. Maladaptive responses of immune cells and molecules themselves can also disrupt the proper functioning of the entire system, leading to host cell damage that could become fatal.

Immunodeficiency

Failures, insufficiencies, or delays at any level of the immune response can allow pathogens or tumor cells to gain a foothold and replicate or proliferate to high enough levels that the immune system becomes overwhelmed. Immunodeficiency is the failure, insufficiency, or delay in the response of the immune system, which may be acquired or inherited. Immunodeficiency can be acquired as a result of infection with certain pathogens (such as HIV), chemical exposure (including certain medical treatments), malnutrition, or possibly by extreme stress. For instance, radiation exposure can destroy populations of lymphocytes and elevate an individual's susceptibility to infections and cancer. Dozens of genetic disorders result in immunodeficiencies, including Severe Combined Immunodeficiency (SCID), Bare lymphocyte syndrome, and MHC II deficiencies. Rarely, primary immunodeficiencies that are present from birth may occur. Neutropenia is one form in which the immune system produces a below-average number of neutrophils, the body's most abundant phagocytes. As a result, bacterial infections may go unrestricted in the blood, causing serious complications.

Hypersensitivities

Maladaptive immune responses toward harmless foreign substances or self antigens that occur after tissue sensitization are termed hypersensitivities. The types of hypersensitivities include immediate, delayed, and autoimmunity. A large proportion of the population is affected by one or more types of hypersensitivity.

Allergies

The immune reaction that results from immediate hypersensitivities in which an antibody-mediated immune response occurs within minutes of exposure to a harmless antigen is called an allergy. In the United States, 20 percent of the population exhibits symptoms of allergy or asthma, whereas 55 percent test positive against one or more allergens. Upon initial exposure to a potential allergen, an allergic individual synthesizes antibodies of the IgE class via the typical process of APCs presenting processed antigen to T_H cells that stimulate B cells to produce IgE. This class of antibodies also mediates the immune response to parasitic worms. The constant domain of the IgE molecules interact with mast cells embedded in connective tissues. This process primes, or sensitizes, the tissue. Upon subsequent exposure to the same allergen, IgE molecules on mast cells bind the antigen via their variable domains and stimulate the mast cell to release the modified amino acids histamine and serotonin; these chemical mediators then recruit eosinophils which mediate allergic responses. [link] shows an example of an allergic response to ragweed pollen. The effects of an allergic reaction range from mild symptoms like sneezing and itchy, watery eyes to more severe or even life-threatening reactions involving intensely itchy welts or hives, airway contraction with severe respiratory distress, and plummeting blood pressure. This extreme reaction is known as anaphylactic shock. If not treated with epinephrine to counter the blood pressure and breathing effects, this condition can be fatal.

On first exposure to an allergen, an IgE antibody is synthesized by plasma cells in response to a harmless antigen. The IgE molecules bind to mast cells, and on secondary exposure, the mast cells release histamines and other modulators that affect the symptoms of allergy.

(credit: modification of work by NIH)

Delayed hypersensitivity is a cell-mediated immune response that takes approximately one to two days after secondary exposure for a maximal reaction to be observed. This type of hypersensitivity involves the T_H1 cytokine-mediated inflammatory response and may manifest as local tissue lesions or contact dermatitis (rash or skin irritation). Delayed hypersensitivity occurs in some individuals in response to contact with certain types of jewelry or cosmetics. Delayed hypersensitivity facilitates the immune response to poison ivy and is also the reason why the skin test for tuberculosis results in a small region of inflammation on individuals who were previously exposed to *Mycobacterium tuberculosis*. That is also why cortisone is used to treat such responses: it will inhibit cytokine production.

Autoimmunity

Autoimmunity is a type of hypersensitivity to self antigens that affects approximately five percent of the population. Most types of autoimmunity involve the humoral immune response. Antibodies that inappropriately mark self components as foreign are termed autoantibodies. In patients with the autoimmune disease myasthenia gravis, muscle cell receptors that induce contraction in response to acetylcholine are targeted by antibodies. The result is muscle weakness that may include marked difficultly with fine and/or gross motor functions. In systemic lupus erythematosus, a diffuse autoantibody response to the individual's own DNA and proteins results in various systemic diseases. As illustrated in [link], systemic lupus erythematosus may affect the heart, joints, lungs, skin, kidneys, central nervous system, or other tissues, causing tissue damage via antibody binding, complement recruitment, lysis, and inflammation.

Systemic lupus erythematosus is characterized by autoimmunity to the individual's own DNA and/or proteins, which leads to varied dysfunction of the organs. (credit: modification of work by Mikael Häggström)

Autoimmunity can develop with time, and its causes may be rooted in molecular mimicry. Antibodies and TCRs may bind self antigens that are structurally similar to pathogen antigens, which the immune receptors first raised. As an example, infection with *Streptococcus pyogenes* (bacterium that causes strep throat) may generate antibodies or T cells that react with heart muscle, which has a similar structure to the surface of *S. pyogenes*. These antibodies can damage heart muscle with autoimmune attacks, leading to rheumatic fever. Insulin-dependent (Type 1) diabetes mellitus arises from a destructive inflammatory T_H1 response against insulin-producing cells of the pancreas. Patients with this autoimmunity must be injected with insulin that originates from other sources.

Section Summary

Immune disruptions may involve insufficient immune responses or inappropriate immune targets. Immunodeficiency increases an individual's susceptibility to infections and cancers. Hypersensitivities are misdirected responses either to harmless foreign particles, as in the

case of allergies, or to host factors, as in the case of autoimmunity. Reactions to self components may be the result of molecular mimicry.

Review Questions

Allergy to pollen is classified as:

a. an autoimmune reaction
b. immunodeficiency
c. delayed hypersensitivity
d. immediate hypersensitivity

D

A potential cause of acquired autoimmunity is _____.

a. tissue hypersensitivity
b. molecular mimicry
c. histamine release
d. radiation exposure

B

Autoantibodies are probably involved in:

a. reactions to poison ivy
b. pollen allergies
c. systemic lupus erythematosus
d. HIV/AIDS

C

Which of the following diseases is not due to autoimmunity?

a. rheumatic fever
b. systemic lupus erythematosus
c. diabetes mellitus
d. HIV/AIDS

D

Glossary

allergy
: immune reaction that results from immediate hypersensitivities in which an antibody-mediated immune response occurs within minutes of exposure to a harmless antigen

autoantibody

antibody that incorrectly marks “self” components as foreign and stimulates the immune response

autoimmunity
: type of hypersensitivity to self antigens

hypersensitivities
: spectrum of maladaptive immune responses toward harmless foreign particles or self antigens; occurs after tissue sensitization and includes immediate-type (allergy), delayed-type, and autoimmunity

immunodeficiency
: failure, insufficiency, or delay at any level of the immune system, which may be acquired or inherited

Reproduction Methods

By the end of this section, you will be able to:

- Describe advantages and disadvantages of asexual and sexual reproduction
- Discuss asexual reproduction methods
- Discuss sexual reproduction methods

Animals produce offspring through asexual and/or sexual reproduction. Both methods have advantages and disadvantages. Asexual reproduction produces offspring that are genetically identical to the parent because the offspring are all clones of the original parent. A single individual can produce offspring asexually and large numbers of offspring can be produced quickly. In a stable or predictable environment, asexual reproduction is an effective means of reproduction because all the offspring will be adapted to that environment. In an unstable or unpredictable environment asexually-reproducing species may be at a disadvantage because all the offspring are genetically identical and may not have the genetic variation to survive in new or different conditions. On the other hand, the rapid rates of asexual reproduction may allow for a speedy response to environmental changes if individuals have mutations. An additional advantage of asexual reproduction is that colonization of new habitats may be easier when an individual does not need to find a mate to reproduce.

During sexual reproduction the genetic material of two individuals is combined to produce genetically diverse offspring that differ from their parents. The genetic diversity of sexually produced offspring is thought to give species a better chance of surviving in an unpredictable or changing environment. Species that reproduce sexually must maintain two different types of individuals, males and females, which can limit the ability to colonize new habitats as both sexes must be present.

Asexual Reproduction

Asexual reproduction occurs in prokaryotic microorganisms (bacteria) and in some eukaryotic single-celled and multi-celled organisms. There are a number of ways that animals reproduce asexually.

Fission

Fission, also called binary fission, occurs in prokaryotic microorganisms and in some invertebrate, multi-celled organisms. After a period of growth, an organism splits into two separate organisms. Some unicellular eukaryotic organisms undergo binary fission by mitosis. In other organisms, part of the individual separates and forms a second individual. This process occurs, for example, in many asteroid echinoderms through splitting of the central disk. Some sea anemones and some coral polyps ([link]) also reproduce through fission.

Coral polyps reproduce asexually by fission. (credit: G. P. Schmahl, NOAA FGBNMS Manager)

Budding

Budding is a form of asexual reproduction that results from the outgrowth of a part of a cell or body region leading to a separation from the original organism into two individuals. Budding occurs commonly in some invertebrate animals such as corals and hydras. In hydras, a bud forms that develops into an adult and breaks away from the main body, as illustrated in [link], whereas in coral budding, the bud does not detach and multiplies as part of a new colony.

Hydra reproduce asexually through

budding.
Link to Learning

Watch a video of a hydra budding.

Fertilization

By the end of this section, you will be able to:

- Discuss internal and external methods of fertilization
- Describe the methods used by animals for development of offspring during gestation
- Describe the anatomical adaptions that occurred in animals to facilitate reproduction

Sexual reproduction starts with the combination of a sperm and an egg in a process called fertilization. This can occur either inside (internal fertilization) or outside (external fertilization) the body of the female. Humans provide an example of the former whereas seahorse reproduction is an example of the latter.

External Fertilization

External fertilization usually occurs in aquatic environments where both eggs and sperm are released into the water. After the sperm reaches the egg, fertilization takes place. Most external fertilization happens during the process of spawning where one or several females release their eggs and the male(s) release sperm in the same area, at the same time. The release of the reproductive material may be triggered by water temperature or the length of daylight. Nearly all fish spawn, as do crustaceans (such as crabs and shrimp), mollusks (such as oysters), squid, and echinoderms (such as sea urchins and sea cucumbers). [link] shows salmon spawning in a shallow stream. Frogs, like those shown in [link], corals, squid, and octopuses also spawn.

Salmon reproduce through spawning. (credit: Dan Bennett)

During sexual reproduction in toads, the male grasps the female from behind and externally fertilizes the eggs as they are deposited. (credit: "OakleyOriginals"/Flickr)

Pairs of fish that are not broadcast spawners may exhibit courtship behavior. This allows the female to select a particular male. The trigger for egg and sperm release (spawning) causes the egg and sperm to be placed in a small area, enhancing the possibility of fertilization.

External fertilization in an aquatic environment protects the eggs from drying out. Broadcast spawning can result in a greater mixture of the genes within a group, leading to higher genetic diversity and a greater chance of species survival in a hostile environment. For sessile aquatic organisms like sponges, broadcast spawning is the only mechanism for fertilization and colonization of new environments. The presence of the fertilized eggs and developing young in the water provides opportunities for predation resulting in a loss of offspring. Therefore, millions of eggs must be produced by individuals, and the offspring produced through this method must mature rapidly. The survival rate of eggs produced through broadcast spawning is low.

Internal Fertilization

Internal fertilization occurs most often in land-based animals, although some aquatic animals also use this method. There are three ways that offspring are produced following internal fertilization. In oviparity, fertilized eggs are laid outside the female's body and develop there, receiving nourishment from the yolk that is a part of the egg. This occurs in most bony fish, many reptiles, some cartilaginous fish, most amphibians, two mammals, and all birds. Reptiles and insects produce leathery eggs, while birds and turtles produce eggs with high concentrations of calcium carbonate in the shell, making them hard. Chicken eggs are an example of this second type.

In ovoviparity, fertilized eggs are retained in the female, but the embryo obtains its nourishment from the egg's yolk and the young are fully developed when they are hatched. This occurs in some bony fish (like the guppy *Lebistes reticulatus*), some sharks, some lizards, some snakes (such as the garter snake *Thamnophis sirtalis*), some vipers, and some invertebrate animals (like the Madagascar hissing cockroach *Gromphadorhina portentosa*).

In viviparity the young develop within the female, receiving nourishment from the mother's blood through a placenta. The offspring develops in the female and is born alive. This occurs in most mammals, some cartilaginous fish, and a few reptiles.

Internal fertilization has the advantage of protecting the fertilized egg from dehydration on land. The embryo is isolated within the female, which limits predation on the young. Internal fertilization enhances the fertilization of eggs by a specific male. Fewer offspring are produced through this method, but their survival rate is higher than that for external fertilization.

The Evolution of Reproduction

Once multicellular organisms evolved and developed specialized cells, some also developed tissues and organs with specialized functions. An early development in reproduction occurred in the Annelids. These organisms produce sperm and eggs from undifferentiated cells in their coelom and store them in that cavity. When the coelom becomes filled, the cells are released through an excretory opening or by the body splitting open. Reproductive organs evolved with the development of gonads that produce sperm and eggs. These cells went through

meiosis, an adaption of mitosis, which reduced the number of chromosomes in each reproductive cell by half, while increasing the number of cells through cell division.

Complete reproductive systems were developed in insects, with separate sexes. Sperm are made in testes and then travel through coiled tubes to the epididymis for storage. Eggs mature in the ovary. When they are released from the ovary, they travel to the uterine tubes for fertilization. Some insects have a specialized sac, called a spermatheca, which stores sperm for later use, sometimes up to a year. Fertilization can be timed with environmental or food conditions that are optimal for offspring survival.

Vertebrates have similar structures, with a few differences. Non-mammals, such as birds and reptiles, have a common body opening, called a cloaca, for the digestive, excretory and reproductive systems. Coupling between birds usually involves positioning the cloaca openings opposite each other for transfer of sperm. Mammals have separate openings for the systems in the female and a uterus for support of developing offspring. The uterus has two chambers in species that produce large numbers of offspring at a time, while species that produce one offspring, such as primates, have a single uterus.

Sperm transfer from the male to the female during reproduction ranges from releasing the sperm into the watery environment for external fertilization, to the joining of cloaca in birds, to the development of a penis for direct delivery into the female's vagina in mammals.

Section Summary

Sexual reproduction starts with the combination of a sperm and an egg in a process called fertilization. This can occur either outside the bodies or inside the female. Both methods have advantages and disadvantages. Once fertilized, the eggs can develop inside the female or outside. If the egg develops outside the body, it usually has a protective covering over it. Animal anatomy evolved various ways to fertilize, hold, or expel the egg. The method of fertilization varies among animals. Some species release the egg and sperm into the environment, some species retain the egg and receive the sperm into the female body and then expel the developing embryo covered with shell, while still other species retain the developing offspring through the gestation period.

Review Questions

External fertilization occurs in which type of environment?

a. aquatic
b. forested
c. savanna
d. steppe

A

Which term applies to egg development within the female with nourishment derived from a yolk?

a. oviparity
b. viviparity

c. ovoviparity
d. ovovoparity

C

Which term applies to egg development outside the female with nourishment derived from a yolk?

a. oviparity
b. viviparity
c. ovoviparity
d. ovovoparity

A

Free Response

What are the advantages and disadvantages of external and internal forms of fertilization?

External fertilization can create large numbers of offspring without requiring specialized delivery or reproductive support organs. Offspring develop and mature quickly compared to internally fertilizing species. A disadvantage is that the offspring are out in the environment and predation can account for large loss of offspring. The embryos are susceptible to changes in the environment, which further depletes their numbers. Internally fertilizing species control their environment and protect their offspring from predators but must have specialized organs to complete these tasks and usually produce fewer embryos.

Why would paired external fertilization be preferable to group spawning?

Paired external fertilization allows the female to select the male for mating. It also has a greater chance of fertilization taking place, whereas spawning just puts a large number of sperm and eggs together and random interactions result in the fertilization.

Glossary

cloaca
: common body opening for the digestive, excretory, and reproductive systems found in non-mammals, such as birds

external fertilization
: fertilization of egg by sperm outside animal body, often during spawning

internal fertilization
: fertilization of egg by sperm inside the body of the female

oviparity
: process by which fertilized eggs are laid outside the female's body and develop there, receiving nourishment from the yolk that is a part of the egg

ovoviparity

process by which fertilized eggs are retained within the female; the embryo obtains its nourishment from the egg's yolk and the young are fully developed when they are hatched

spermatheca
: specialized sac that stores sperm for later use

viviparity
: process in which the young develop within the female, receiving nourishment from the mother's blood through a placenta

Human Reproductive Anatomy and Gametogenesis

By the end of this section, you will be able to:

- Describe human male and female reproductive anatomies
- Discuss the human sexual response
- Describe spermatogenesis and oogenesis and discuss their differences and similarities

As animals became more complex, specific organs and organ systems developed to support specific functions for the organism. The reproductive structures that evolved in land animals allow males and females to mate, fertilize internally, and support the growth and development of offspring.

Human Reproductive Anatomy

The reproductive tissues of male and female humans develop similarly *in utero* until a low level of the hormone testosterone is released from male gonads. Testosterone causes the undeveloped tissues to differentiate into male sexual organs. When testosterone is absent, the tissues develop into female sexual tissues. Primitive gonads become testes or ovaries. Tissues that produce a penis in males produce a clitoris in females. The tissue that will become the scrotum in a male becomes the labia in a female; that is, they are homologous structures.

Male Reproductive Anatomy

In the male reproductive system, the scrotum houses the testicles or testes (singular: testis), including providing passage for blood vessels, nerves, and muscles related to testicular function. The testes are a pair of male reproductive organs that produce sperm and some reproductive hormones. Each testis is approximately 2.5 by 3.8 cm (1.5 by 1 in) in size and divided into wedge-shaped lobules by connective tissue called septa. Coiled in each wedge are seminiferous tubules that produce sperm.

Sperm are immobile at body temperature; therefore, the scrotum and penis are external to the body, as illustrated in [link] so that a proper temperature is maintained for motility. In land mammals, the pair of testes must be suspended outside the body at about 2° C lower than body temperature to produce viable sperm. Infertility can occur in land mammals when the testes do not descend through the abdominal cavity during fetal development.

Art Connection

The reproductive structures of the human male are

shown.

Which of the following statements about the male reproductive system is false?

a. The vas deferens carries sperm from the testes to the penis.
b. Sperm mature in seminiferous tubules in the testes.
c. Both the prostate and the bulbourethral glands produce components of the semen.
d. The prostate gland is located in the testes.

Sperm mature in seminiferous tubules that are coiled inside the testes, as illustrated in [link]. The walls of the seminiferous tubules are made up of the developing sperm cells, with the least developed sperm at the periphery of the tubule and the fully developed sperm in the lumen. The sperm cells are mixed with “nursemaid” cells called Sertoli cells which protect the germ cells and promote their development. Other cells mixed in the wall of the tubules are the interstitial cells of Leydig. These cells produce high levels of testosterone once the male reaches adolescence.

When the sperm have developed flagella and are nearly mature, they leave the testicles and enter the epididymis, shown in [link]. This structure resembles a comma and lies along the top and posterior portion of the testes; it is the site of sperm maturation. The sperm leave the epididymis and enter the vas deferens (or ductus deferens), which carries the sperm, behind the bladder, and forms the ejaculatory duct with the duct from the seminal vesicles. During a vasectomy, a section of the vas deferens is removed, preventing sperm from being passed out of the body during ejaculation and preventing fertilization.

Semen is a mixture of sperm and spermatic duct secretions (about 10 percent of the total) and fluids from accessory glands that contribute most of the semen’s volume. Sperm are haploid cells, consisting of a flagellum as a tail, a neck that contains the cell’s energy-producing mitochondria, and a head that contains the genetic material. [link] shows a micrograph of human sperm as well as a diagram of the parts of the sperm. An acrosome is found at the top of the head of the sperm. This structure contains lysosomal enzymes that can digest the protective coverings that surround the egg to help the sperm penetrate and fertilize the egg. An ejaculate will contain from two to five milliliters of fluid with from 50–120 million sperm per milliliter.

Human sperm, visualized using scanning electron microscopy, have a flagellum, neck, and head. (credit b: modification of work by Mariana Ruiz Villareal; scale-bar data from Matt Russell)

The bulk of the semen comes from the accessory glands associated with the male reproductive system. These are the seminal vesicles, the prostate gland, and the bulbourethral gland, all of which are illustrated in [link]. The seminal vesicles are a pair of glands that lie along the posterior border of the urinary bladder. The glands make a solution that is thick, yellowish, and alkaline. As sperm are only motile in an alkaline environment, a basic pH is important to reverse the acidity of the vaginal environment. The solution also contains mucus, fructose (a sperm mitochondrial nutrient), a coagulating enzyme, ascorbic acid, and local-acting hormones called prostaglandins. The seminal vesicle glands account for 60 percent of the bulk of semen.

The penis, illustrated in [link], is an organ that drains urine from the renal bladder and functions as a copulatory organ during intercourse. The penis contains three tubes of erectile tissue running through the length of the organ. These consist of a pair of tubes on the dorsal side, called the corpus cavernosum, and a single tube of tissue on the ventral side, called the corpus spongiosum. This tissue will become engorged with blood, becoming erect and hard,

in preparation for intercourse. The organ is inserted into the vagina culminating with an ejaculation. During intercourse, the smooth muscle sphincters at the opening to the renal bladder close and prevent urine from entering the penis. An orgasm is a two-stage process: first, glands and accessory organs connected to the testes contract, then semen (containing sperm) is expelled through the urethra during ejaculation. After intercourse, the blood drains from the erectile tissue and the penis becomes flaccid.

The walnut-shaped prostate gland surrounds the urethra, the connection to the urinary bladder. It has a series of short ducts that directly connect to the urethra. The gland is a mixture of smooth muscle and glandular tissue. The muscle provides much of the force needed for ejaculation to occur. The glandular tissue makes a thin, milky fluid that contains citrate (a nutrient), enzymes, and prostate specific antigen (PSA). PSA is a proteolytic enzyme that helps to liquefy the ejaculate several minutes after release from the male. Prostate gland secretions account for about 30 percent of the bulk of semen.

The bulbourethral gland, or Cowper's gland, releases its secretion prior to the release of the bulk of the semen. It neutralizes any acid residue in the urethra left over from urine. This usually accounts for a couple of drops of fluid in the total ejaculate and may contain a few sperm. Withdrawal of the penis from the vagina before ejaculation to prevent pregnancy may not work if sperm are present in the bulbourethral gland secretions. The location and functions of the male reproductive organs are summarized in [link].

Male Reproductive Anatomy

Organ	Location	Function
Scrotum	External	Carry and support testes
Penis	External	Deliver urine, copulating organ
Testes	Internal	Produce sperm and male hormones
Seminal Vesicles	Internal	Contribute to semen production
Prostate Gland	Internal	Contribute to semen production
Bulbourethral Glands	Internal	Clean urethra at ejaculation

Female Reproductive Anatomy

A number of reproductive structures are exterior to the female's body. These include the breasts and the vulva, which consists of the mons pubis, clitoris, labia majora, labia minora, and the vestibular glands, all illustrated in [link]. The location and functions of the female reproductive organs are summarized in [link]. The vulva is an area associated with the vestibule which includes the structures found in the inguinal (groin) area of women. The mons pubis is a round, fatty area that overlies the pubic symphysis. The clitoris is a structure with erectile tissue that contains a large number of sensory nerves and serves as a source of stimulation during intercourse. The labia majora are a pair of elongated folds of tissue that run posterior from the mons pubis and enclose the other components of the vulva. The labia majora derive from the same tissue that produces the scrotum in a male. The labia minora are thin folds of tissue centrally located within the labia majora. These labia protect the openings to the vagina and urethra. The mons pubis and the anterior portion of the labia majora become covered with hair during adolescence; the labia minora is hairless. The greater vestibular glands are found at the sides of the vaginal opening and provide lubrication during intercourse.

The reproductive structures of the human female are shown. (credit a: modification of work by Gray's Anatomy; credit b: modification of work by
CDC)

Female Reproductive Anatomy

Organ	Location	Function
Clitoris	External	Sensory organ
Mons pubis	External	Fatty area overlying pubic bone
Labia majora	External	Covers labia minora
Labia minora	External	Covers vestibule
Greater vestibular glands	External	Secrete mucus; lubricate vagina
Breast	External	Produce and deliver milk
Ovaries	Internal	Carry and develop eggs
Oviducts (Fallopian tubes)	Internal	Transport egg to uterus
Uterus	Internal	Support developing embryo

Female Reproductive Anatomy

Organ	Location	Function
Vagina	Internal	Common tube for intercourse, birth canal, passing menstrual flow

The breasts consist of mammary glands and fat. The size of the breast is determined by the amount of fat deposited behind the gland. Each gland consists of 15 to 25 lobes that have ducts that empty at the nipple and that supply the nursing child with nutrient- and antibody-rich milk to aid development and protect the child.

Internal female reproductive structures include ovaries, oviducts, the uterus, and the vagina, shown in [link]. The pair of ovaries is held in place in the abdominal cavity by a system of ligaments. Ovaries consist of a medulla and cortex: the medulla contains nerves and blood vessels to supply the cortex with nutrients and remove waste. The outer layers of cells of the cortex are the functional parts of the ovaries. The cortex is made up of follicular cells that surround eggs that develop during fetal development *in utero*. During the menstrual period, a batch of follicular cells develops and prepares the eggs for release. At ovulation, one follicle ruptures and one egg is released, as illustrated in [link]**a**.

Oocytes develop in (a) follicles, located in the ovary. At the beginning of the menstrual cycle, the follicle matures. At ovulation, the follicle ruptures, releasing the egg. The follicle becomes a corpus luteum, which eventually degenerates. The (b) follicle in this light micrograph has an oocyte at its center. (credit a: modification of work by NIH; scale-bar data from Matt

Russell)

The oviducts, or fallopian tubes, extend from the uterus in the lower abdominal cavity to the ovaries, but they are not in contact with the ovaries. The lateral ends of the oviducts flare out into a trumpet-like structure and have a fringe of finger-like projections called fimbriae, illustrated in [link]**b**. When an egg is released at ovulation, the fimbrae help the non-motile egg enter into the tube and passage to the uterus. The walls of the oviducts are ciliated and are made up mostly of smooth muscle. The cilia beat toward the middle, and the smooth muscle contracts in the same direction, moving the egg toward the uterus. Fertilization usually takes place within the oviducts and the developing embryo is moved toward the uterus for development. It usually takes the egg or embryo a week to travel through the oviduct. Sterilization in women is called a tubal ligation; it is analogous to a vasectomy in males in that the oviducts are severed and sealed.

The uterus is a structure about the size of a woman's fist. This is lined with an endometrium rich in blood vessels and mucus glands. The uterus supports the developing embryo and fetus during gestation. The thickest portion of the wall of the uterus is made of smooth muscle. Contractions of the smooth muscle in the uterus aid in passing the baby through the vagina during labor. A portion of the lining of the uterus sloughs off during each menstrual period,

and then builds up again in preparation for an implantation. Part of the uterus, called the cervix, protrudes into the top of the vagina. The cervix functions as the birth canal.

The vagina is a muscular tube that serves several purposes. It allows menstrual flow to leave the body. It is the receptacle for the penis during intercourse and the vessel for the delivery of offspring. It is lined by stratified squamous epithelial cells to protect the underlying tissue.

Sexual Response during Intercourse

The sexual response in humans is both psychological and physiological. Both sexes experience sexual arousal through psychological and physical stimulation. There are four phases of the sexual response. During phase one, called excitement, vasodilation leads to vasocongestion in erectile tissues in both men and women. The nipples, clitoris, labia, and penis engorge with blood and become enlarged. Vaginal secretions are released to lubricate the vagina to facilitate intercourse. During the second phase, called the plateau, stimulation continues, the outer third of the vaginal wall enlarges with blood, and breathing and heart rate increase.

During phase three, or orgasm, rhythmic, involuntary contractions of muscles occur in both sexes. In the male, the reproductive accessory glands and tubules constrict placing semen in the urethra, then the urethra contracts expelling the semen through the penis. In women, the uterus and vaginal muscles contract in waves that may last slightly less than a second each. During phase four, or resolution, the processes described in the first three phases reverse themselves and return to their normal state. Men experience a refractory period in which they cannot maintain an erection or ejaculate for a period of time ranging from minutes to hours.

Gametogenesis (Spermatogenesis and Oogenesis)

Gametogenesis, the production of sperm and eggs, takes place through the process of meiosis. During meiosis, two cell divisions separate the paired chromosomes in the nucleus and then separate the chromatids that were made during an earlier stage of the cell's life cycle. Meiosis produces haploid cells with half of each pair of chromosomes normally found in diploid cells. The production of sperm is called spermatogenesis and the production of eggs is called oogenesis.

Spermatogenesis

During spermatogenesis, four sperm result from each primary

spermatocyte.

Spermatogenesis, illustrated in [link], occurs in the wall of the seminiferous tubules ([link]), with stem cells at the periphery of the tube and the spermatozoa at the lumen of the tube. Immediately under the capsule of the tubule are diploid, undifferentiated cells. These stem cells, called spermatogonia (singular: spermatagonium), go through mitosis with one offspring going on to differentiate into a sperm cell and the other giving rise to the next generation of sperm.

Meiosis starts with a cell called a primary spermatocyte. At the end of the first meiotic division, a haploid cell is produced called a secondary spermatocyte. This cell is haploid and must go through another meiotic cell division. The cell produced at the end of meiosis is called a spermatid and when it reaches the lumen of the tubule and grows a flagellum, it is called a sperm cell. Four sperm result from each primary spermatocyte that goes through meiosis.

Stem cells are deposited during gestation and are present at birth through the beginning of adolescence, but in an inactive state. During adolescence, gonadotropic hormones from the anterior pituitary cause the activation of these cells and the production of viable sperm. This continues into old age.

Link to Learning

Visit this site to see the process of spermatogenesis.

Oogenesis

Oogenesis, illustrated in [link], occurs in the outermost layers of the ovaries. As with sperm production, oogenesis starts with a germ cell, called an oogonium (plural: oogonia), but this cell undergoes mitosis to increase in number, eventually resulting in up to about one to two million cells in the embryo.

The process of oogenesis occurs in the ovary's outermost layer.

The cell starting meiosis is called a primary oocyte, as shown in [link]. This cell will start the first meiotic division and be arrested in its progress in the first prophase stage. At the time of birth, all future eggs are in the prophase stage. At adolescence, anterior pituitary hormones cause the development of a number of follicles in an ovary. This results in the primary oocyte finishing the first meiotic division. The cell divides unequally, with most of the cellular material and organelles going to one cell, called a secondary oocyte, and only one set of chromosomes and a small amount of cytoplasm going to the other cell. This second cell is called a polar body and usually dies. A secondary meiotic arrest occurs, this time at the metaphase II stage. At ovulation, this secondary oocyte will be released and travel toward the uterus through the oviduct. If the secondary oocyte is fertilized, the cell continues through the meiosis II, producing a second polar body and a fertilized egg containing all 46 chromosomes of a human being, half of them coming from the sperm.

Egg production begins before birth, is arrested during meiosis until puberty, and then individual cells continue through at each menstrual cycle. One egg is produced from each meiotic process, with the extra chromosomes and chromatids going into polar bodies that degenerate and are reabsorbed by the body.

Section Summary

As animals became more complex, specific organs and organ systems developed to support specific functions for the organism. The reproductive structures that evolved in land animals allow males and females to mate, fertilize internally, and support the growth and development of offspring. Processes developed to produce reproductive cells that had exactly half the number of chromosomes of each parent so that new combinations would have the

appropriate amount of genetic material. Gametogenesis, the production of sperm (spermatogenesis) and eggs (oogenesis), takes place through the process of meiosis.

[link] Which of the following statements about the male reproductive system is false?

a. The vas deferens carries sperm from the testes to the penis.
b. Sperm mature in seminiferous tubules in the testes.
c. Both the prostate and the bulbourethral glands produce components of the semen.
d. The prostate gland is located in the testes.

[link] D

Review Questions

Sperm are produced in the _____.

a. scrotum
b. seminal vesicles
c. seminiferous tubules
d. prostate gland

C

Most of the bulk of semen is made by the _____.

a. scrotum
b. seminal vesicles
c. seminiferous tubules
d. prostate gland

C

Which of the following cells in spermatogenesis is diploid?

a. primary spermatocyte
b. secondary spermatocyte
c. spermatid
d. sperm

A

Which female organ has the same embryonic origin as the penis?

a. clitoris
b. labia majora
c. greater vestibular glands
d. vagina

A

Which female organ has an endometrial lining that will support a developing baby?

a. labia minora
b. breast
c. ovaries
d. uterus

D

How many eggs are produced as a result of one meiotic series of cell divisions?

a. one
b. two
c. three
d. four

A

Free Response

Describe the phases of the human sexual response.

In phase one (excitement), vasodilation leads to vasocongestion and enlargement of erectile tissues. Vaginal secretions are released to lubricate the vagina during intercourse. In phase two (plateau), stimulation continues, the outer third of the vaginal wall enlarges with blood, and breathing and heart rate increase. In phase three (orgasm), rhythmic, involuntary contractions of muscles occur. In the male, reproductive accessory glands and tubules constrict, depositing semen in the urethra; then, the urethra contracts, expelling the semen through the penis. In women, the uterus and vaginal muscles contract in waves that may last slightly less than a second each. In phase four (resolution), the processes listed in the first three phases reverse themselves and return to their normal state. Men experience a refractory period in which they cannot maintain an erection or ejaculate for a period of time ranging from minutes to hours. Women do not experience a refractory period.

Compare spermatogenesis and oogenesis as to timing of the processes and the number and type of cells finally produced.

Stem cells are laid down in the male during gestation and lie dormant until adolescence. Stem cells in the female increase to one to two million and enter the first meiotic division and are arrested in prophase. At adolescence, spermatogenesis begins and continues until death, producing the maximum number of sperm with each meiotic division. Oogenesis continues again at adolescence in batches of oogonia with each menstrual cycle. These oogonia finish the first meiotic division, producing a primary oocyte with most of the cytoplasm and its contents, and a second cell called a polar body containing 23 chromosomes. The second meiotic division results in a secondary oocyte and a second oocyte. At ovulation, a mature haploid egg is released. If this egg is fertilized, it finishes the second meiotic division, including the chromosomes donated by the sperm in the finished cell. This is a diploid, fertilized egg.

Glossary

bulbourethral gland
: secretion that cleanses the urethra prior to ejaculation

clitoris
: sensory structure in females; stimulated during sexual arousal

labia majora
: large folds of tissue covering the inguinal area

labia minora
: smaller folds of tissue within the labia majora

oogenesis
: process of producing haploid eggs

oviduct
: (also, fallopian tube) muscular tube connecting the uterus with the ovary area

penis
: male reproductive structure for urine elimination and copulation

prostate gland
: structure that is a mixture of smooth muscle and glandular material and that contributes to semen

scrotum
: sac containing testes; exterior to the body

semen
: fluid mixture of sperm and supporting materials

seminal vesicle
: secretory accessory gland in males; contributes to semen

seminiferous tubule
: site of sperm production in testes

spermatogenesis
: process of producing haploid sperm

testes
: pair of reproductive organs in males

uterus
: environment for developing embryo and fetus

vagina
: muscular tube for the passage of menstrual flow, copulation, and birth of offspring

Hormonal Control of Human Reproduction

By the end of this chapter, you will be able to:

- Describe the roles of male and female reproductive hormones
- Discuss the interplay of the ovarian and menstrual cycles
- Describe the process of menopause

The human male and female reproductive cycles are controlled by the interaction of hormones from the hypothalamus and anterior pituitary with hormones from reproductive tissues and organs. In both sexes, the hypothalamus monitors and

causes the release of hormones from the pituitary gland. When the reproductive hormone is required, the hypothalamus sends a gonadotropin-releasing hormone (GnRH) to the anterior pituitary. This causes the release of follicle stimulating hormone (FSH) and luteinizing hormone (LH) from the anterior pituitary into the blood. Note that the body must reach puberty in order for the adrenals to release the hormones that must be present for GnRH to be produced. Although FSH and LH are named after their functions in female reproduction, they are produced in both sexes and play important roles in controlling reproduction. Other hormones have specific functions in the male and female reproductive systems.

Male Hormones

At the onset of puberty, the hypothalamus causes the release of FSH and LH into the male system for the first time. FSH enters the testes and stimulates the Sertoli cells to begin facilitating spermatogenesis using negative feedback, as illustrated in [link]. LH also enters the testes and stimulates the interstitial cells of Leydig to make and release testosterone into the testes and the blood.

Testosterone, the hormone responsible for the secondary sexual characteristics that develop in the male during adolescence, stimulates spermatogenesis. These secondary sex characteristics include a deepening of the voice, the growth of facial, axillary, and pubic hair, and the beginnings of the sex drive.

Hormones control sperm production in a negative feedback system.

A negative feedback system occurs in the male with rising levels of testosterone acting on the hypothalamus and anterior pituitary to inhibit the release of GnRH, FSH, and LH. The Sertoli cells produce the hormone inhibin, which is released into the blood when the sperm count is too high. This inhibits the release of GnRH and FSH, which will cause spermatogenesis to slow down. If the sperm count reaches 20 million/ml, the Sertoli cells cease the release of inhibin, and the sperm count increases.

Female Hormones

The control of reproduction in females is more complex. As with the male, the anterior pituitary hormones cause the release of the hormones FSH and LH. In addition, estrogens and progesterone are released from the developing follicles. Estrogen is the reproductive hormone in females that assists in endometrial regrowth, ovulation, and calcium absorption; it is also responsible for the secondary sexual characteristics of females. These include breast development, flaring of the hips, and a shorter period necessary for bone

maturation. Progesterone assists in endometrial re-growth and inhibition of FSH and LH release.

In females, FSH stimulates development of egg cells, called ova, which develop in structures called follicles. Follicle cells produce the hormone inhibin, which inhibits FSH production. LH also plays a role in the development of ova, induction of ovulation, and stimulation of estradiol and progesterone production by the ovaries. Estradiol and progesterone are steroid hormones that prepare the body for pregnancy. Estradiol produces secondary sex characteristics in females, while both estradiol and progesterone regulate the menstrual cycle.

The Ovarian Cycle and the Menstrual Cycle

The ovarian cycle governs the preparation of endocrine tissues and release of eggs, while the menstrual cycle governs the preparation and maintenance of the uterine lining. These cycles occur concurrently and are coordinated over a 22–32 day cycle, with an average length of 28 days.

The first half of the ovarian cycle is the follicular phase shown in [link]. Slowly rising levels of FSH and LH cause the growth of follicles on the surface of the ovary. This process prepares the egg for ovulation. As the follicles grow, they begin releasing estrogens and a low level of progesterone. Progesterone maintains the endometrium to help ensure pregnancy. The trip through the fallopian tube takes about seven days. At this stage of development, called the morula, there are 30-60 cells. If pregnancy implantation does not occur, the lining is sloughed off. After about five days, estrogen levels rise and the menstrual cycle enters the proliferative phase. The endometrium begins to regrow, replacing the blood vessels and glands that deteriorated during the end of the last cycle.

Art Connection
The ovarian and menstrual cycles of female reproduction are regulated by hormones produced by the hypothalamus, pituitary, and

ovaries.

Which of the following statements about hormone regulation of the female reproductive cycle is false?

a. LH and FSH are produced in the pituitary, and estradiol and progesterone are produced in the ovaries.
b. Estradiol and progesterone secreted from the corpus luteum cause the endometrium to thicken.
c. Both progesterone and estradiol are produced by the follicles.
d. Secretion of GnRH by the hypothalamus is inhibited by low levels of estradiol but stimulated by high levels of estradiol.

Just prior to the middle of the cycle (approximately day 14), the high level of estrogen causes FSH and especially LH to rise rapidly, then fall. The spike in LH causes ovulation: the most mature follicle, like that shown in [link], ruptures and releases its egg. The follicles that did not rupture degenerate and their eggs are lost. The level of estrogen decreases when the extra follicles degenerate.

This mature egg follicle may rupture and release an egg. (credit: scale-bar data from Matt Russell)

Following ovulation, the ovarian cycle enters its luteal phase, illustrated in [link] and the menstrual cycle enters its secretory phase, both of which run from about day 15 to 28. The luteal and secretory phases refer to changes in the ruptured follicle. The cells in the follicle undergo physical changes and produce a structure called a corpus luteum. The corpus luteum produces estrogen and progesterone. The progesterone facilitates the regrowth of the uterine lining and inhibits the release of further FSH and LH. The uterus is being prepared to accept a fertilized egg, should it occur during this cycle. The inhibition of FSH and LH prevents any further eggs and follicles from developing, while the progesterone is elevated. The level of estrogen produced by the corpus luteum increases to a steady level for the next few days.

If no fertilized egg is implanted into the uterus, the corpus luteum degenerates and the levels of estrogen and progesterone decrease. The endometrium begins to degenerate as the progesterone levels drop, initiating the next menstrual cycle. The decrease in progesterone also allows the hypothalamus to send GnRH to the anterior pituitary, releasing FSH and LH and starting the cycles again. [link] visually compares the ovarian and uterine cycles as well as the commensurate hormone levels.

Art Connection

Rising and falling hormone levels result in progression of the ovarian and menstrual cycles. (credit: modification of work by Mikael

Häggström)

Which of the following statements about the menstrual cycle is false?

a. Progesterone levels rise during the luteal phase of the ovarian cycle and the secretory phase of the uterine cycle.
b. Menstruation occurs just after LH and FSH levels peak.
c. Menstruation occurs after progesterone levels drop.
d. Estrogen levels rise before ovulation, while progesterone levels rise after.

Menopause

As women approach their mid-40s to mid-50s, their ovaries begin to lose their sensitivity to FSH and LH. Menstrual periods become less frequent and finally cease; this is menopause. There are still eggs and potential follicles on the ovaries, but without the stimulation of FSH and LH, they will not produce a viable egg to be released. The outcome of this is the inability to have children.

The side effects of menopause include hot flashes, heavy sweating (especially at night), headaches, some hair loss, muscle pain, vaginal dryness, insomnia, depression, weight gain, and mood swings. Estrogen is involved in calcium metabolism and, without it, blood levels of calcium decrease. To replenish the blood, calcium is lost from bone which may decrease the bone density and lead to osteoporosis. Supplementation of estrogen in the form of hormone replacement therapy (HRT) can prevent bone loss, but the therapy can have negative side effects. While HRT is thought to give some protection from colon cancer, osteoporosis, heart disease, macular degeneration, and possibly depression, its negative side effects include increased risk of: stroke or heart attack, blood clots, breast cancer, ovarian cancer, endometrial cancer, gall bladder disease, and possibly dementia.

Career Connection

Reproductive Endocrinologist A reproductive endocrinologist is a physician who treats a variety of hormonal disorders related to reproduction and infertility in both men and women. The disorders include menstrual problems, infertility, pregnancy loss, sexual dysfunction, and menopause. Doctors may use fertility drugs, surgery, or assisted reproductive techniques (ART) in their therapy. ART involves the use of procedures to manipulate the egg or sperm to facilitate reproduction, such as *in vitro* fertilization.

Reproductive endocrinologists undergo extensive medical training, first in a four-year residency in obstetrics and gynecology, then in a three-year fellowship in reproductive endocrinology. To be board certified in this area, the physician must pass written and oral exams in both areas.

Section Summary

The male and female reproductive cycles are controlled by hormones released from the hypothalamus and anterior pituitary as well as hormones from reproductive tissues and organs. The hypothalamus monitors the need for the FSH and LH hormones made and released from the anterior pituitary. FSH and LH affect reproductive structures to cause the formation of sperm and the preparation of eggs for release and possible fertilization. In the male, FSH and LH stimulate Sertoli cells and interstitial cells of Leydig in the testes to facilitate sperm production. The Leydig cells produce testosterone, which also is responsible for the secondary sexual characteristics of males. In females, FSH and LH cause estrogen and progesterone to be produced. They regulate the female reproductive system which is divided into the ovarian cycle and the menstrual cycle. Menopause occurs when the ovaries lose their sensitivity to FSH and LH and the female reproductive cycles slow to a stop.

Art Connections

[link] Which of the following statements about hormone regulation of the female reproductive cycle is false?

a. LH and FSH are produced in the pituitary, and estradiol and progesterone are produced in the ovaries.
b. Estradiol and progesterone secreted from the corpus luteum cause the endometrium to thicken.
c. Both progesterone and estradiol are produced by the follicles.
d. Secretion of GnRH by the hypothalamus is inhibited by low levels of estradiol but stimulated by high levels of estradiol.

[link] C

[link] Which of the following statements about the menstrual cycle is false?

a. Progesterone levels rise during the luteal phase of the ovarian cycle and the secretory phase of the uterine cycle.
b. Menstruation occurs just after LH and FSH levels peak.
c. Menstruation occurs after progesterone levels drop.
d. Estrogen levels rise before ovulation, while progesterone levels rise after.

[link] B

Review Questions

Which hormone causes Leydig cells to make testosterone?

a. FSH
b. LH
c. inhibin
d. estrogen

A

Which hormone causes FSH and LH to be released?

a. testosterone
b. estrogen
c. GnRH
d. progesterone

C

Which hormone signals ovulation?

a. FSH
b. LH
c. inhibin
d. estrogen

B

Which hormone causes the re-growth of the endometrial lining of the uterus?

a. testosterone
b. estrogen
c. GnRH
d. progesterone

D

Free Response

If male reproductive pathways are not cyclical, how are they controlled?

Negative feedback in the male system is supplied through two hormones: inhibin and testosterone. Inhibin is produced by Sertoli cells when the sperm count exceeds set limits. The hormone inhibits GnRH and FSH, decreasing the activity of the Sertoli cells. Increased levels of testosterone affect the release of both GnRH and LH, decreasing the activity of the Leydig cells, resulting in decreased testosterone and sperm production.

Describe the events in the ovarian cycle leading up to ovulation.

Low levels of progesterone allow the hypothalamus to send GnRH to the anterior pituitary and cause the release of FSH and LH. FSH stimulates follicles on the ovary to grow and prepare the eggs for ovulation. As the follicles increase in size, they begin to release estrogen and a low level of progesterone into the blood. The level of estrogen rises to a peak, causing a spike in the concentration of LH. This causes the most mature follicle to rupture and ovulation occurs.

Glossary

estrogen
: reproductive hormone in females that assists in endometrial regrowth, ovulation, and calcium absorption

follicle stimulating hormone (FSH)
: reproductive hormone that causes sperm production in men and follicle development in women

gonadotropin-releasing hormone (GnRH)
: hormone from the hypothalamus that causes the release of FSH and LH from the anterior pituitary

inhibin
: hormone made by Sertoli cells; provides negative feedback to hypothalamus in control of FSH and GnRH release

interstitial cell of Leydig
: cell in seminiferous tubules that makes testosterone

luteinizing hormone (LH)
: reproductive hormone in both men and women, causes testosterone production in men and ovulation and lactation in women

menopause
: loss of reproductive capacity in women due to decreased sensitivity of the ovaries to FSH and LH

menstrual cycle
: cycle of the degradation and re-growth of the endometrium

ovarian cycle
: cycle of preparation of egg for ovulation and the conversion of the follicle to the corpus luteum

ovulation
: release of the egg by the most mature follicle

progesterone
: reproductive hormone in women; assists in endometrial re-growth and inhibition of FSH and LH release

Sertoli cell
: cell in seminiferous tubules that assists developing sperm and makes inhibin

testosterone
: reproductive hormone in men that assists in sperm production and promoting secondary sexual characteristics

Fertilization and Early Embryonic Development
By the end of this section, you will be able to:

- Discuss how fertilization occurs
- Explain how the embryo forms from the zygote
- Discuss the role of cleavage and gastrulation in animal development

The process in which an organism develops from a single-celled zygote to a multi-cellular organism is complex and well-regulated. The early stages of embryonic development are also crucial for ensuring the fitness of the organism.

Fertilization

Fertilization, pictured in [link]**a** is the process in which gametes (an egg and sperm) fuse to form a zygote. The egg and sperm each contain one set of chromosomes. To ensure that the offspring has only one complete diploid set of chromosomes, only one sperm must fuse with one egg. In mammals, the egg is protected by a layer of extracellular matrix consisting mainly of glycoproteins called the zona pellucida. When a sperm binds to the zona pellucida, a series of biochemical events, called the acrosomal reactions, take place. In placental mammals, the acrosome contains digestive enzymes that initiate the degradation of the glycoprotein matrix protecting the egg and allowing the sperm plasma membrane to fuse with the egg plasma membrane, as illustrated in [link]**b**. The fusion of these two membranes creates an opening through which the sperm nucleus is transferred into the ovum. The nuclear membranes of the egg and sperm break down and the two haploid genomes condense to form a diploid genome.

(a) Fertilization is the process in which sperm and egg fuse to form a zygote. (b) Acrosomal reactions help the sperm degrade the glycoprotein matrix protecting the egg and allow the sperm to transfer its nucleus. (credit: (b) modification of work by Mariana Ruiz Villareal;

scale-bar data from Matt

Russell)

To ensure that no more than one sperm fertilizes the egg, once the acrosomal reactions take place at one location of the egg membrane, the egg releases proteins in other locations to prevent other sperm from fusing with the egg. If this mechanism fails, multiple sperm can fuse with the egg, resulting in polyspermy. The resulting embryo is not genetically viable and dies within a few days.

Cleavage and Blastula Stage

The development of multi-cellular organisms begins from a single-celled zygote, which undergoes rapid cell division to form the blastula. The rapid, multiple rounds of cell division are termed cleavage. Cleavage is illustrated in ([link]**a**). After the cleavage has produced over 100 cells, the embryo is called a blastula. The blastula is usually a spherical layer of cells (the blastoderm) surrounding a fluid-filled or yolk-filled cavity (the blastocoel). Mammals at this stage form a structure called the blastocyst, characterized by an inner cell mass that is distinct from the surrounding blastula, shown in [link]**b**. During cleavage, the cells divide without an increase in mass; that is, one large single-celled zygote divides into multiple smaller cells. Each cell within the blastula is called a blastomere.

(a) During cleavage, the zygote rapidly divides into multiple cells without increasing in size. (b) The cells rearrange themselves to form a hollow ball with a fluid-filled or yolk-filled cavity called the blastula. (credit a: modification of work by Gray's Anatomy; credit b:

modification of work by Pearson Scott Foresman, donated to the Wikimedia

Foundation)

Cleavage can take place in two ways: holoblastic (total) cleavage or meroblastic (partial) cleavage. The type of cleavage depends on the amount of yolk in the eggs. In placental mammals (including humans) where nourishment is provided by the mother's body, the eggs have a very small amount of yolk and undergo holoblastic cleavage. Other species, such as birds, with a lot of yolk in the egg to nourish the embryo during development, undergo meroblastic cleavage.

In mammals, the blastula forms the blastocyst in the next stage of development. Here the cells in the blastula arrange themselves in two layers: the inner cell mass, and an outer layer called the trophoblast. The inner cell mass is also known as the embryoblast and this mass of cells will go on to form the embryo. At this stage of development, illustrated in [link] the inner cell mass consists of embryonic stem cells that will differentiate into the different cell types needed by the organism. The trophoblast will contribute to the placenta and nourish the embryo.

The rearrangement of the cells in the mammalian blastula to two layers—the inner cell mass and the trophoblast—results in the formation of the

blastocyst.

Link to Learning

Visit the Virtual Human Embryo project at the Endowment for Human Development site to step through an interactive that shows the stages of embryo development, including micrographs and rotating 3-D images.

Gastrulation

The typical blastula is a ball of cells. The next stage in embryonic development is the formation of the body plan. The cells in the blastula rearrange themselves spatially to form three layers of cells. This process is called gastrulation. During gastrulation, the blastula folds upon itself to form the three layers of cells. Each of these layers is called a germ layer and each germ layer differentiates into different organ systems.

The three germs layers, shown in [link], are the endoderm, the ectoderm, and the mesoderm. The ectoderm gives rise to the nervous system and the epidermis. The mesoderm gives rise to the muscle cells and connective tissue in the body. The endoderm gives rise to columnar cells found in the digestive system and many internal organs.

The three germ layers give rise to different cell types in the animal body. (credit: modification of work by NIH,

NCBI)

Everyday Connection

Are Designer Babies in Our Future?

This logo from the Second International Eugenics Conference in New York City in September of 1921 shows how eugenics attempted to merge several fields of study with the

goal of producing a genetically superior human

race.

If you could prevent your child from getting a devastating genetic disease, would you do it? Would you select the sex of your child or select for their attractiveness, strength, or intelligence? How far would you go to maximize the possibility of resistance to disease? The genetic engineering of a human child, the production of "designer babies" with desirable phenotypic characteristics, was once a topic restricted to science fiction. This is the case no longer: science fiction is now overlapping into science fact. Many phenotypic choices for offspring are already available, with many more likely to be possible in the not too distant future. Which traits should be selected and how they should be selected are topics of much debate within the worldwide medical community. The ethical and moral line is not always clear or agreed upon, and some fear that modern reproductive technologies could lead to a new form of eugenics.

Eugenics is the use of information and technology from a variety of sources to improve the genetic makeup of the human race. The goal of creating genetically superior humans was quite prevalent (although controversial) in several countries during the early 20th century, but fell into disrepute when Nazi Germany developed an extensive eugenics program in the 1930's and 40's. As part of their program, the Nazis forcibly sterilized hundreds of thousands of the so-called "unfit" and killed tens of thousands of institutionally disabled people as part of a systematic program to develop a genetically superior race of Germans known as Aryans. Ever since, eugenic ideas have not been as publicly expressed, but there are still those who promote them.

Efforts have been made in the past to control traits in human children using donated sperm from men with desired traits. In fact, eugenicist Robert Klark Graham established a sperm bank in 1980 that included samples exclusively from donors with high IQs. The "genius" sperm bank failed to capture the public's imagination and the operation closed in 1999.

In more recent times, the procedure known as prenatal genetic diagnosis (PGD) has been developed. PGD involves the screening of human embryos as part of the process of *in*

vitro fertilization, during which embryos are conceived and grown outside the mother's body for some period of time before they are implanted. The term PGD usually refers to both the diagnosis, selection, and the implantation of the selected embryos.

In the least controversial use of PGD, embryos are tested for the presence of alleles which cause genetic diseases such as sickle cell disease, muscular dystrophy, and hemophilia, in which a single disease-causing allele or pair of alleles has been identified. By excluding embryos containing these alleles from implantation into the mother, the disease is prevented, and the unused embryos are either donated to science or discarded. There are relatively few in the worldwide medical community that question the ethics of this type of procedure, which allows individuals scared to have children because of the alleles they carry to do so successfully. The major limitation to this procedure is its expense. Not usually covered by medical insurance and thus out of reach financially for most couples, only a very small percentage of all live births use such complicated methodologies. Yet, even in cases like these where the ethical issues may seem to be clear-cut, not everyone agrees with the morality of these types of procedures. For example, to those who take the position that human life begins at conception, the discarding of unused embryos, a necessary result of PGD, is unacceptable under any circumstances.

A murkier ethical situation is found in the selection of a child's sex, which is easily performed by PGD. Currently, countries such as Great Britain have banned the selection of a child's sex for reasons other than preventing sex-linked diseases. Other countries allow the procedure for "family balancing", based on the desire of some parents to have at least one child of each sex. Still others, including the United States, have taken a scattershot approach to regulating these practices, essentially leaving it to the individual practicing physician to decide which practices are acceptable and which are not.

Even murkier are rare instances of disabled parents, such as those with deafness or dwarfism, who select embryos via PGD to ensure that they share their disability. These parents usually cite many positive aspects of their disabilities and associated culture as reasons for their choice, which they see as their moral right. To others, to purposely cause a disability in a child violates the basic medical principle of *Primum non nocere*, "first, do no harm." This procedure, although not illegal in most countries, demonstrates the complexity of ethical issues associated with choosing genetic traits in offspring.

Where could this process lead? Will this technology become more affordable and how should it be used? With the ability of technology to progress rapidly and unpredictably, a lack of definitive guidelines for the use of reproductive technologies before they arise might make it difficult for legislators to keep pace once they are in fact realized, assuming the process needs any government regulation at all. Other bioethicists argue that we should only deal with technologies that exist now, and not in some uncertain future. They argue that these types of procedures will always be expensive and rare, so the fears of eugenics and "master" races are unfounded and overstated. The debate continues.

Section Summary

The early stages of embryonic development begin with fertilization. The process of fertilization is tightly controlled to ensure that only one sperm fuses with one egg. After fertilization, the zygote undergoes cleavage to form the blastula. The blastula, which in some species is a hollow ball of cells, undergoes a process called gastrulation, in which the three

germ layers form. The ectoderm gives rise to the nervous system and the epidermal skin cells, the mesoderm gives rise to the muscle cells and connective tissue in the body, and the endoderm gives rise to columnar cells and internal organs.

Review Questions

Which of the following is false?

a. The endoderm, mesoderm, ectoderm are germ layers.
b. The trophoblast is a germ layer.
c. The inner cell mass is a source of embryonic stem cells.
d. The blastula is often a hollow ball of cells.

B

During cleavage, the mass of cells:

a. increases
b. decreases
c. doubles with every cell division
d. does not change significantly

D

Free Response

What do you think would happen if multiple sperm fused with one egg?

Multiple sperm can fuse with the egg, resulting in polyspermy. The resulting embryo is not genetically viable and dies within a few days.

Why do mammalian eggs have a small concentration of yolk, while bird and reptile eggs have a large concentration of yolk?

Mammalian eggs do not need a lot of yolk because the developing fetus obtains nutrients from the mother. Other species, in which the fetus develops outside of the mother's body, such as occurs with birds, require a lot of yolk in the egg to nourish the embryo during development.

Glossary

acrosomal reaction
: series of biochemical reactions that the sperm uses to break through the zona pellucida

blastocyst
: structure formed when cells in the mammalian blastula separate into an inner and outer layer

gastrulation

process in which the blastula folds over itself to form the three germ layers

holoblastic

complete cleavage; takes place in cells with a small amount of yolk

inner cell mass

inner layer of cells in the blastocyst

meroblastic

partial cleavage; takes place in cells with a large amount of yolk

polyspermy

condition in which one egg is fertilized by multiple sperm

trophoblast

outer layer of cells in the blastocyst

zona pellucida

protective layer of glycoproteins on the mammalian egg

Human Pregnancy and Birth

By the end of this section, you will be able to:

- Explain fetal development during the three trimesters of gestation
- Describe labor and delivery
- Compare the efficacy and duration of various types of contraception
- Discuss causes of infertility and the therapeutic options available

Pregnancy begins with the fertilization of an egg and continues through to the birth of the individual. The length of time of gestation varies among animals, but is very similar among the great apes: human gestation is 266 days, while chimpanzee gestation is 237 days, a gorilla's is 257 days, and orangutan gestation is 260 days long. The fox has a 57-day gestation. Dogs and cats have similar gestations averaging 60 days. The longest gestation for a land mammal is an African elephant at 640 days. The longest gestations among marine mammals are the beluga and sperm whales at 460 days.

Human Gestation

Twenty-four hours before fertilization, the egg has finished meiosis and becomes a mature oocyte. When fertilized (at conception) the egg becomes known as a zygote. The zygote travels through the oviduct to the uterus ([link]). The developing embryo must implant into the wall of the uterus within seven days, or it will deteriorate and die. The outer layers of the zygote (blastocyst) grow into the endometrium by digesting the endometrial cells, and wound healing of the endometrium closes up the blastocyst into the tissue. Another layer of the blastocyst, the chorion, begins releasing a hormone called human beta chorionic gonadotropin (β-HCG) which makes its way to the corpus luteum and keeps that structure active. This ensures adequate levels of progesterone that will maintain the endometrium of the uterus for the support of the developing embryo. Pregnancy tests determine the level of β-HCG in urine or serum. If the hormone is present, the test is positive.

In humans, fertilization occurs soon after the oocyte leaves the ovary. Implantation occurs eight or nine days later.(credit: Ed

Uthman)

The gestation period is divided into three equal periods or trimesters. During the first two to four weeks of the first trimester, nutrition and waste are handled by the endometrial lining through diffusion. As the trimester progresses, the outer layer of the embryo begins to merge with the endometrium, and the placenta forms. This organ takes over the nutrient and waste requirements of the embryo and fetus, with the mother's blood passing nutrients to the placenta and removing waste from it. Chemicals from the fetus, such as bilirubin, are processed by the mother's liver for elimination. Some of the mother's immunoglobulins will pass through the placenta, providing passive immunity against some potential infections.

Internal organs and body structures begin to develop during the first trimester. By five weeks, limb buds, eyes, the heart, and liver have been basically formed. By eight weeks, the term fetus applies, and the body is essentially formed, as shown in [link]. The individual is about five centimeters (two inches) in length and many of the organs, such as the lungs and liver, are not yet functioning. Exposure to any toxins is especially dangerous during the first trimester, as all of the body's organs and structures are going through initial development. Anything that affects that development can have a severe effect on the fetus' survival.

Fetal development is shown at nine weeks gestation. (credit: Ed

Uthman)

During the second trimester, the fetus grows to about 30 cm (12 inches), as shown in [link]. It becomes active and the mother usually feels the first movements. All organs and structures continue to develop. The placenta has taken over the functions of nutrition and waste and the production of estrogen and progesterone from the corpus luteum, which has degenerated. The placenta will continue functioning up through the delivery of the baby.

This fetus is just entering the second trimester, when the placenta takes over more of the functions performed as the baby develops. (credit: National Museum of Health and

Medicine)

During the third trimester, the fetus grows to 3 to 4 kg (6 ½ -8 ½ lbs.) and about 50 cm (19-20 inches) long, as illustrated in [link]. This is the period of the most rapid growth during the pregnancy. Organ development continues to birth (and some systems, such as the nervous system and liver, continue to develop after birth). The mother will be at her most uncomfortable during this trimester. She may urinate frequently due to pressure on the bladder from the fetus. There may also be intestinal blockage and circulatory problems, especially in her legs. Clots may form in her legs due to pressure from the fetus on returning veins as they enter the abdominal cavity.

There is rapid fetal growth during the third trimester. (credit: modification of work by Gray's Anatomy)

Link to Learning

Visit this site to see the stages of human fetal development.

Labor and Birth

Labor is the physical efforts of expulsion of the fetus and the placenta from the uterus during birth (parturition). Toward the end of the third trimester, estrogen causes receptors on the uterine wall to develop and bind the hormone oxytocin. At this time, the baby reorients, facing forward and down with the back or crown of the head engaging the cervix (uterine opening). This causes the cervix to stretch and nerve impulses are sent to the hypothalamus, which signals for the release of oxytocin from the posterior pituitary. The oxytocin causes the smooth muscle in the uterine wall to contract. At the same time, the placenta releases prostaglandins into the uterus, increasing the contractions. A positive feedback relay occurs between the uterus, hypothalamus, and the posterior pituitary to assure an adequate supply of oxytocin. As more smooth muscle cells are recruited, the contractions increase in intensity and force.

There are three stages to labor. During stage one, the cervix thins and dilates. This is necessary for the baby and placenta to be expelled during birth. The cervix will eventually dilate to about 10 cm. During stage two, the baby is expelled from the uterus. The uterus contracts and the mother pushes as she compresses her abdominal muscles to aid the delivery. The last stage is the passage of the placenta after the baby has been born and the organ has completely disengaged from the uterine wall. If labor should stop before stage two is reached, synthetic oxytocin, known as Pitocin, can be administered to restart and maintain labor.

An alternative to labor and delivery is the surgical delivery of the baby through a procedure called a Caesarian section. This is major abdominal surgery and can lead to post-surgical complications for the mother, but in some cases it may be the only way to safely deliver the baby.

The mother's mammary glands go through changes during the third trimester to prepare for lactation and breastfeeding. When the baby begins suckling at the breast, signals are sent to the hypothalamus causing the release of prolactin from the anterior pituitary. Prolactin causes the mammary glands to produce milk. Oxytocin is also released, promoting the release of the milk. The milk contains nutrients for the baby's development and growth as well as immunoglobulins to protect the child from bacterial and viral infections.

Contraception and Birth Control

The prevention of a pregnancy comes under the terms contraception or birth control. Strictly speaking, contraception refers to preventing the sperm and egg from joining. Both terms are, however, frequently used interchangeably.

Contraceptive Methods

Method	Examples	Failure Rate in Typical Use Over 12 Months
Barrier	male condom, female condom, sponge, cervical cap, diaphragm, spermicides	15 to 24%
Hormonal	oral, patch, vaginal ring	8%
	injection	3%
	implant	less than 1%
Other	natural family planning	12 to 25%
	withdrawal	27%
	sterilization	less than 1%

[link] lists common methods of contraception. The failure rates listed are not the ideal rates that could be realized, but the typical rates that occur. A failure rate is the number of pregnancies resulting from the method's use over a twelve-month period. Barrier methods, such as condoms, cervical caps, and diaphragms, block sperm from entering the uterus, preventing fertilization. Spermicides are chemicals that are placed in the vagina that kill sperm. Sponges, which are saturated with spermicides, are placed in the vagina at the cervical opening. Combinations of spermicidal chemicals and barrier methods achieve lower failure rates than do the methods when used separately.

Nearly a quarter of the couples using barrier methods, natural family planning, or withdrawal can expect a failure of the method. Natural family planning is based on the monitoring of the menstrual cycle and having intercourse only during times when the egg is not available. A woman's body temperature may rise a degree Celsius at ovulation and the cervical mucus may increase in volume and become more pliable. These changes give a general indication of when intercourse is more or less likely to result in fertilization. Withdrawal involves the removal of the penis from the vagina during intercourse, before ejaculation occurs. This is a risky method with a high failure rate due to the possible presence of sperm in the bulbourethral gland's secretion, which may enter the vagina prior to removing the penis.

Hormonal methods use synthetic progesterone (sometimes in combination with estrogen), to inhibit the hypothalamus from releasing FSH or LH, and thus prevent an egg from being available for fertilization. The method of administering the hormone affects failure rate. The most reliable method, with a failure rate of less than 1 percent, is the implantation of the hormone under the skin. The same rate can be achieved through the sterilization procedures of vasectomy in the man or of tubal ligation in the woman, or by using an intrauterine device (IUD). IUDs are inserted into the uterus and establish an inflammatory condition that prevents fertilized eggs from implanting into the uterine wall.

Compliance with the contraceptive method is a strong contributor to the success or failure rate of any particular method. The only method that is completely effective at preventing conception is abstinence. The choice of contraceptive method depends on the goals of the woman or couple. Tubal ligation and vasectomy are considered permanent prevention, while other methods are reversible and provide short-term contraception.

Termination of an existing pregnancy can be spontaneous or voluntary. Spontaneous termination is a miscarriage and usually occurs very early in the pregnancy, usually within the first few weeks. This occurs when the fetus cannot develop properly and the gestation is naturally terminated. Voluntary termination of a pregnancy is an abortion. Laws regulating abortion vary between states and tend to view fetal viability as the criteria for allowing or preventing the procedure.

Infertility

Infertility is the inability to conceive a child or carry a child to birth. About 75 percent of causes of infertility can be identified; these include diseases, such as sexually transmitted diseases that can cause scarring of the reproductive tubes in either men or women, or developmental problems frequently related to abnormal hormone levels in one of the individuals. Inadequate nutrition, especially starvation, can delay menstruation. Stress can also lead to infertility. Short-term stress can affect hormone levels, while long-term stress can delay puberty and cause less frequent menstrual cycles. Other factors that affect fertility include toxins (such as cadmium), tobacco smoking, marijuana use, gonadal injuries, and aging.

If infertility is identified, several assisted reproductive technologies (ART) are available to aid conception. A common type of ART is *in vitro* fertilization (IVF) where an egg and sperm are combined outside the body and then placed in the uterus. Eggs are obtained from the woman after extensive hormonal treatments that prepare mature eggs for fertilization and prepare the uterus for implantation of the fertilized egg. Sperm are obtained from the man and they are combined with the eggs and supported through several cell divisions to ensure viability of the zygotes. When the embryos have reached the eight-cell stage, one or more is implanted into the woman's uterus. If fertilization is not accomplished by simple IVF, a procedure that injects the sperm into an egg can be used. This is called intracytoplasmic sperm injection (ICSI) and is shown in [link]. IVF procedures produce a surplus of fertilized eggs and embryos that can be frozen and stored for future use. The procedures can also result in multiple births.

A sperm is inserted into an egg for fertilization during intracytoplasmic sperm injection (ICSI). (credit: scale-bar data from Matt

Russell)

Section Summary

Human pregnancy begins with fertilization of an egg and proceeds through the three trimesters of gestation. The labor process has three stages (contractions, delivery of the fetus, expulsion of the placenta), each propelled by hormones. The first trimester lays down the basic structures of the body, including the limb buds, heart, eyes, and the liver. The second trimester continues the development of all of the organs and systems. The third trimester exhibits the greatest growth of the fetus and culminates in labor and delivery. Prevention of a pregnancy can be accomplished through a variety of methods including barriers, hormones, or other means. Assisted reproductive technologies may help individuals who have infertility problems.

Review Questions

Nutrient and waste requirements for the developing fetus are handled during the first few weeks by:

a. the placenta
b. diffusion through the endometrium
c. the chorion
d. the blastocyst

B

Progesterone is made during the third trimester by the:

a. placenta
b. endometrial lining
c. chorion

d. corpus luteum

A

Which contraceptive method is 100 percent effective at preventing pregnancy?

a. condom
b. oral hormonal methods
c. sterilization
d. abstinence

D

Which type of short term contraceptive method is generally more effective than others?

a. barrier
b. hormonal
c. natural family planning
d. withdrawal

B

Which hormone is primarily responsible for the contractions during labor?

a. oxytocin
b. estrogen
c. β-HCG
d. progesterone

A

Major organs begin to develop during which part of human gestation?

a. fertilization
b. first trimester
c. second trimester
d. third trimester

B

Free Response

Describe the major developments during each trimester of human gestation.

The first trimester lays down the basic structures of the body, including the limb buds, heart, eyes, and the liver. The second trimester continues the development of all of the organs and systems established during the first trimester. The placenta takes over the production of estrogen and high levels of progesterone and handles the nutrient and waste requirements of the fetus. The third trimester exhibits the greatest growth of the fetus, culminating in labor and delivery.

Describe the stages of labor.

Stage one of labor results in the thinning of the cervix and the dilation of the cervical opening. Stage two delivers the baby, and stage three delivers the placenta.

Glossary

contraception
: (also, birth control) various means used to prevent pregnancy

gestation
: length of time for fetal development to birth

human beta chorionic gonadotropin (β-HCG)
: hormone produced by the chorion of the zygote that helps to maintain the corpus luteum and elevated levels of progesterone

infertility
: inability to conceive, carry, and deliver children

morning sickness
: condition in the mother during the first trimester; includes feelings of nausea

placenta
: organ that supports the diffusion of nutrients and waste between the mother's and fetus' blood

Organogenesis and Vertebrate Formation

By the end of this section, you will be able to:

- Describe the process of organogenesis
- Identify the anatomical axes formed in vertebrates

Gastrulation leads to the formation of the three germ layers that give rise, during further development, to the different organs in the animal body. This process is called organogenesis. Organogenesis is characterized by rapid and precise movements of the cells within the embryo.

Organogenesis

Organs form from the germ layers through the process of differentiation. During differentiation, the embryonic stem cells express specific sets of genes which will determine their ultimate cell type. For example, some cells in the ectoderm will express the genes specific to skin cells. As a result, these cells will differentiate into epidermal cells. The process of differentiation is regulated by cellular signaling cascades.

Scientists study organogenesis extensively in the lab in fruit flies (*Drosophila*) and the nematode *Caenorhabditis elegans*. *Drosophila* have segments along their bodies, and the patterning associated with the segment formation has allowed scientists to study which genes play important roles in organogenesis along the length of the embryo at different time points. The nematode *C.elegans* has roughly 1000 somatic cells and scientists have studied the fate of each of these cells during their development in the nematode life cycle. There is little

variation in patterns of cell lineage between individuals, unlike in mammals where cell development from the embryo is dependent on cellular cues.

In vertebrates, one of the primary steps during organogenesis is the formation of the neural system. The ectoderm forms epithelial cells and tissues, and neuronal tissues. During the formation of the neural system, special signaling molecules called growth factors signal some cells at the edge of the ectoderm to become epidermis cells. The remaining cells in the center form the neural plate. If the signaling by growth factors were disrupted, then the entire ectoderm would differentiate into neural tissue.

The neural plate undergoes a series of cell movements where it rolls up and forms a tube called the neural tube, as illustrated in [link]. In further development, the neural tube will give rise to the brain and the spinal cord.

The central region of the ectoderm forms the neural tube, which gives rise to the brain and the spinal cord.

The mesoderm that lies on either side of the vertebrate neural tube will develop into the various connective tissues of the animal body. A spatial pattern of gene expression reorganizes the mesoderm into groups of cells called somites with spaces between them. The somites, illustrated in [link] will further develop into the ribs, lungs, and segmental (spine) muscle. The mesoderm also forms a structure called the notochord, which is rod-shaped and forms the central axis of the animal body.

In this five-week old human embryo, somites are segments along the length of the body.

(credit: modification of work by Ed Uthman)

Vertebrate Axis Formation

Even as the germ layers form, the ball of cells still retains its spherical shape. However, animal bodies have lateral-medial (left-right), dorsal-ventral (back-belly), and anterior-posterior (head-feet) axes, illustrated in [link].

Animal bodies have three axes for symmetry. (credit: modification of work by NOAA)

How are these established? In one of the most seminal experiments ever to be carried out in developmental biology, Spemann and Mangold took dorsal cells from one embryo and transplanted them into the belly region of another embryo. They found that the transplanted embryo now had two notochords: one at the dorsal site from the original cells and another at the transplanted site. This suggested that the dorsal cells were genetically programmed to form the notochord and define the axis. Since then, researchers have identified many genes that are responsible for axis formation. Mutations in these genes leads to the loss of symmetry required for organism development.

Animal bodies have externally visible symmetry. However, the internal organs are not symmetric. For example, the heart is on the left side and the liver on the right. The formation of the central left-right axis is an important process during development. This internal asymmetry is established very early during development and involves many genes. Research is still ongoing to fully understand the developmental implications of these genes.

Section Summary

Organogenesis is the formation of organs from the germ layers. Each germ layer gives rise to specific tissue types. The first stage is the formation of the neural system in the ectoderm. The mesoderm gives rise to somites and the notochord. Formation of vertebrate axis is another important developmental stage.

Review Questions

Which of the following gives rise to the skin cells?

a. ectoderm
b. endoderm
c. mesoderm
d. none of the above

A

The ribs form from the _____.

a. notochord
b. neural plate
c. neural tube
d. somites

D

Free Response

Explain how the different germ layers give rise to different tissue types.

Organs form from the germ layers through the process of differentiation. During differentiation, the embryonic stem cells express a specific set of genes that will determine their ultimate fate as a cell type. For example, some cells in the ectoderm will express the genes specific to skin cells. As a result, these cells will differentiate into epidermal cells. The process of differentiation is regulated by cellular signaling cascades.

Explain the role of axis formation in development.

Animal bodies have lateral-medial (left-right), dorsal-ventral (back-belly), and anterior-posterior (head-feet) axes. The dorsal cells are genetically programmed to form the notochord and define the axis. There are many genes responsible for axis formation. Mutations in these genes lead to the loss of symmetry required for organism development.

Glossary

neural tube
: tube-like structure that forms from the ectoderm and gives rise to the brain and spinal cord

organogenesis
: process of organ formation

somite
: group of cells separated by small spaces that form from the mesoderm and give rise to connective tissue

Introduction

class="introduction" class="summary" title="Sections Summary" class="art-exercise" title="Art Connections" class="multiple-choice" title="Multiple Choice" class="free-response" title="Free Response"Female seahorses produce eggs for reproduction that are then fertilized by the male. Unlike almost all other animals, the male seahorse then gestates the young until birth. (credit: modification of work by "cliff1066"/Flickr)

Animal reproduction is necessary for the survival of a species. In the animal kingdom, there are innumerable ways that species reproduce. Asexual reproduction produces genetically identical organisms (clones), whereas in sexual reproduction, the genetic material of two individuals combines to produce offspring that are genetically different from their parents. During sexual reproduction the male

gamete (sperm) may be placed inside the female's body for internal fertilization, or the sperm and eggs may be released into the environment for external fertilization. Seahorses, like the one shown in [link], provide an example of the latter. Following a mating dance, the female lays eggs in the male seahorse's abdominal brood pouch where they are fertilized. The eggs hatch and the offspring develop in the pouch for several weeks.

Introduction

class="introduction" class="summary" title="Sections Summary" class="art-exercise" title="Art Connections" class="multiple-choice" title="Multiple Choice" class="free-response" title="Free Response"The (a) deer tick carries the bacterium that produces Lyme disease in humans, often evident in (b) a symptomatic bull's eye rash. The (c) white-footed mouse is one well-known host to deer ticks carrying the Lyme disease bacterium. (credit a: modification of work by Scott Bauer, USDA ARS; credit b: modification of work by James Gathany, CDC; credit c: modification of work by Rob
Ireton)

Why study ecology? Perhaps you are interested in learning about the natural world and how living things have adapted to the physical conditions of their environment. Or, perhaps you're a future physician seeking to understand the connection between human health and ecology.

Humans are a part of the ecological landscape, and human health is one important part of human interaction with our physical and living environment. Lyme disease, for instance, serves as one modern-day example of the connection between our health and the natural world ([link]). More formally known as Lyme borreliosis, Lyme disease is a bacterial infection that can be transmitted to humans when they are bitten by the deer tick (*Ixodes scapularis*), which is the primary vector for this disease. However, not all deer ticks carry the bacteria that will cause Lyme disease in humans, and *I. scapularis* can have other hosts besides deer. In fact, it turns out that the probability of infection depends on the type of host upon which the tick develops: a higher proportion of ticks that live on white-footed mice carry the bacterium than do ticks that live on deer. Knowledge about the environments and population densities in which the host species is abundant would help a physician or an epidemiologist better understand how Lyme disease is transmitted and how its incidence could be reduced.

The Scope of Ecology

By the end of this section, you will be able to:

- Define ecology and the four levels of ecological research
- Describe examples of the ways in which ecology requires the integration of different scientific disciplines
- Distinguish between abiotic and biotic components of the environment
- Recognize the relationship between abiotic and biotic components of the environment

Ecology is the study of the interactions of living organisms with their environment. One core goal of ecology is to understand the distribution and abundance of living things in the physical environment. Attainment of this goal requires the integration of scientific disciplines inside and outside of biology, such as biochemistry, physiology, evolution, biodiversity, molecular biology, geology, and climatology. Some ecological research also applies aspects of chemistry and physics, and it frequently uses mathematical models.

Link to Learning

Climate change can alter where organisms live, which can sometimes directly affect human health. Watch the PBS video "Feeling the Effects of Climate Change" in which researchers discover a pathogenic organism living far outside of its normal range.

Levels of Ecological Study

When a discipline such as biology is studied, it is often helpful to subdivide it into smaller, related areas. For instance, cell biologists interested in cell signaling need to understand the chemistry of the signal molecules (which are usually proteins) as well as the result of cell signaling. Ecologists interested in the factors that influence the survival of an endangered species might use mathematical models to predict how current conservation efforts affect endangered organisms. To produce a sound set of management options, a conservation biologist needs to collect accurate data, including current population size, factors affecting reproduction (like physiology and behavior), habitat requirements (such as plants and soils), and potential human influences on the endangered population and its habitat (which might be derived through studies in sociology and urban ecology). Within the discipline of ecology, researchers work at four specific levels, sometimes discretely and sometimes with overlap: organism, population, community, and ecosystem ([link]).

Ecologists study within several biological levels of organization. (credit "organisms": modification of work by "Crystl"/Flickr; credit "ecosystems": modification of work by Tom Carlisle, US Fish and Wildlife Service Headquarters; credit "biosphere":

NASA)

Organismal Ecology

Researchers studying ecology at the organismal level are interested in the adaptations that enable individuals to live in specific habitats. These adaptations can be morphological, physiological, and behavioral. For instance, the Karner blue butterfly (*Lycaeides melissa samuelis*) ([link]) is considered a specialist because the females preferentially oviposit (that is, lay eggs) on wild lupine. This preferential adaptation means that the Karner blue butterfly is highly dependent on the presence of wild lupine plants for its continued survival.

The Karner blue butterfly (*Lycaeides melissa samuelis*) is a rare butterfly that lives only in open areas with few trees or shrubs, such as pine barrens and oak savannas. It can only lay its eggs on lupine plants. (credit: modification of work by J & K Hollingsworth, USFWS)

After hatching, the larval caterpillars emerge and spend four to six weeks feeding solely on wild lupine ([link]). The caterpillars pupate (undergo metamorphosis) and emerge as butterflies after about four weeks. The adult butterflies feed on the nectar of flowers of wild lupine and other plant species. A researcher interested in studying Karner blue butterflies at the organismal level might, in addition to asking questions about egg laying, ask questions about the butterflies' preferred temperature (a physiological question) or the behavior of the caterpillars when they are at different larval stages (a behavioral question).

The wild lupine (*Lupinus perennis*) is the host plant for the Karner blue butterfly.

Population Ecology

A population is a group of interbreeding organisms that are members of the same species living in the same area at the same time. (Organisms that are all members of the same species are called conspecifics.) A population is identified, in part, by where it lives, and its area of population may have natural or artificial boundaries: natural boundaries might be rivers, mountains, or deserts, while examples of artificial boundaries include mowed grass, manmade structures, or roads. The study of population ecology focuses on the number of individuals in an area and how and why population size changes over time. Population ecologists are particularly interested in counting the Karner blue butterfly, for example,

because it is classified as federally endangered. However, the distribution and density of this species is highly influenced by the distribution and abundance of wild lupine. Researchers might ask questions about the factors leading to the decline of wild lupine and how these affect Karner blue butterflies. For example, ecologists know that wild lupine thrives in open areas where trees and shrubs are largely absent. In natural settings, intermittent wildfires regularly remove trees and shrubs, helping to maintain the open areas that wild lupine requires. Mathematical models can be used to understand how wildfire suppression by humans has led to the decline of this important plant for the Karner blue butterfly.

Community Ecology

A biological community consists of the different species within an area, typically a three-dimensional space, and the interactions within and among these species. Community ecologists are interested in the processes driving these interactions and their consequences. Questions about conspecific interactions often focus on competition among members of the same species for a limited resource. Ecologists also study interactions among various species; members of different species are called heterospecifics. Examples of heterospecific interactions include predation, parasitism, herbivory, competition, and pollination. These interactions can have regulating effects on population sizes and can impact ecological and evolutionary processes affecting diversity.

For example, Karner blue butterfly larvae form mutualistic relationships with ants. Mutualism is a form of a long-term relationship that has coevolved between two species and from which each species benefits. For mutualism to exist between individual organisms, each species must receive some benefit from the other as a consequence of the relationship. Researchers have shown that there is an increase in the probability of survival when Karner blue butterfly larvae (caterpillars) are tended by ants. This might be because the larvae spend less time in each life stage when tended by ants, which provides an advantage for the larvae. Meanwhile, the Karner blue butterfly larvae secrete a carbohydrate-rich substance that is an important energy source for the ants. Both the Karner blue larvae and the ants benefit from their interaction.

Ecosystem Ecology

Ecosystem ecology is an extension of organismal, population, and community ecology. The ecosystem is composed of all the biotic components (living things) in an area along with the abiotic components (non-living things) of that area. Some of the abiotic components include air, water, and soil. Ecosystem biologists ask questions about how nutrients and energy are stored and how they move among organisms and the surrounding atmosphere, soil, and water.

The Karner blue butterflies and the wild lupine live in an oak-pine barren habitat. This habitat is characterized by natural disturbance and nutrient-poor soils that are low in nitrogen. The availability of nutrients is an important factor in the distribution of the plants that live in this habitat. Researchers interested in ecosystem ecology could ask questions about the importance of limited resources and the movement of resources, such as nutrients, though the biotic and abiotic portions of the ecosystem.

Career Connection

Ecologist A career in ecology contributes to many facets of human society. Understanding ecological issues can help society meet the basic human needs of food, shelter, and health care. Ecologists can conduct their research in the laboratory and outside in natural environments ([link]). These natural environments can be as close to home as the stream running through your campus or as far away as the hydrothermal vents at the bottom of the Pacific Ocean. Ecologists manage natural resources such as white-tailed deer populations (*Odocoileus virginianus*) for hunting or aspen (*Populus* spp.) timber stands for paper production. Ecologists also work as educators who teach children and adults at various institutions including universities, high schools, museums, and nature centers. Ecologists may also work in advisory positions assisting local, state, and federal policymakers to develop laws that are ecologically sound, or they may develop those policies and legislation themselves. To become an ecologist requires an undergraduate degree, usually in a natural science. The undergraduate degree is often followed by specialized training or an advanced degree, depending on the area of ecology selected. Ecologists should also have a broad background in the physical sciences, as well as a sound foundation in mathematics and statistics.

This landscape ecologist is releasing a black-footed ferret into its native habitat as part of a study. (credit: USFWS Mountain Prairie Region,

NPS)
Link to Learning

Visit this site to see Stephen Wing, a marine ecologist from the University of Otago, discuss the role of an ecologist and the types of issues ecologists explore.

Section Summary

Ecology is the study of the interactions of living things with their environment. Ecologists ask questions across four levels of biological organization—organismal, population,

community, and ecosystem. At the organismal level, ecologists study individual organisms and how they interact with their environments. At the population and community levels, ecologists explore, respectively, how a population of organisms changes over time and the ways in which that population interacts with other species in the community. Ecologists studying an ecosystem examine the living species (the biotic components) of the ecosystem as well as the nonliving portions (the abiotic components), such as air, water, and soil, of the environment.

Review Questions

Which of the following is a biotic factor?

a. wind
b. disease-causing microbe
c. temperature
d. soil particle size

B

The study of nutrient cycling though the environment is an example of which of the following?

a. organismal ecology
b. population ecology
c. community ecology
d. ecosystem ecology

D

Free Response

Ecologists often collaborate with other researchers interested in ecological questions. Describe the levels of ecology that would be easier for collaboration because of the similarities of questions asked. What levels of ecology might be more difficult for collaboration?

Ecologists working in organismal or population ecology might ask similar questions about how the biotic and abiotic conditions affect particular organisms and, thus, might find collaboration to be mutually beneficial. Levels of ecology such as community ecology or ecosystem ecology might pose greater challenges for collaboration because these areas are very broad and may include many different environmental components.

The population is an important unit in ecology as well as other biological sciences. How is a population defined, and what are the strengths and weaknesses of this definition? Are there some species that at certain times or places are not in populations?

It is beneficial to consider a population to be all of the individuals living in the same area at the same time because it allows the ecologist to identify and study all of the abiotic and biotic factors that may affect the members of the population. However, this definition of a population could be considered a drawback if it prohibits the ecologist from studying a

population’s individuals that may be transitory, but still influential. Some species with members that have a wide geographic range might not be considered to be a population, but could still have many of the qualities of a population.

Glossary

abiotic
: nonliving components of the environment

biotic
: living components of the environment

conspecifics
: individuals that are members of the same species

ecology
: study of interaction between living things and their environment

heterospecifics
: individuals that are members of different species

Introduction

class="introduction" class="summary" title="Sections Summary" class="art-exercise" title="Art Connections" class="multiple-choice" title="Multiple Choice" class="free-response" title="Free Response"Asian carp jump out of the water in response to electrofishing. The Asian carp in the inset photograph were harvested from the Little Calumet River in Illinois in May, 2010, using rotenone, a toxin often used as an insecticide, in an effort to learn more about the population of the species. (credit main image: modification of work by USGS; credit inset: modification of work by Lt. David French,

USCG)

Imagine sailing down a river in a small motorboat on a weekend afternoon; the water is smooth and you are enjoying the warm sunshine and cool breeze when suddenly you are hit in the head by a 20-pound silver carp. This is a risk now on many rivers and canal systems in Illinois and Missouri because of the presence of Asian carp.

This fish—actually a group of species including the silver, black, grass, and big head carp—has been farmed and eaten in China for over 1000 years. It is one of the most important aquaculture food resources

Population Demography
By the end of this section, you will be able to:

- Describe how ecologists measure population size and density
- Describe three different patterns of population distribution
- Use life tables to calculate mortality rates
- Describe the three types of survivorship curves and relate them to specific populations

Populations are dynamic entities. Populations consist all of the species living within a specific area, and populations fluctuate based on a number of factors: seasonal and yearly changes in the environment, natural disasters such as forest fires and volcanic eruptions, and competition for resources between and within species. The statistical study of population dynamics, demography, uses a series of mathematical tools to investigate how populations respond to changes in their biotic and abiotic environments. Many of these tools were originally designed to study human populations. For example, life tables, which detail the life expectancy of individuals within a population, were initially developed by life insurance companies to set insurance rates. In fact, while the term "demographics" is commonly used when discussing humans, all living populations can be studied using this approach.

Population Size and Density

The study of any population usually begins by determining how many individuals of a particular species exist, and how closely associated they are with each other. Within a particular habitat, a population can be characterized by its population size (*N*), the total number of individuals, and its population density, the number of individuals within a specific area or volume. Population size and density are the two main characteristics used to describe and understand populations. For example, populations with more individuals may be more stable than smaller populations based on their genetic variability, and thus their potential to adapt to the environment. Alternatively, a member of a population with low population density (more spread out in the habitat), might have more difficulty finding a mate to reproduce compared to a population of higher density. As is shown in [link], smaller organisms tend to be more densely distributed than larger organisms.

Art Connection

Australian mammals show a typical inverse relationship between population density and body size.

As this graph shows, population density typically decreases with increasing body size. Why do you think this is the case?

Population Research Methods

The most accurate way to determine population size is to simply count all of the individuals within the habitat. However, this method is often not logistically or economically feasible, especially when studying large habitats. Thus, scientists usually study populations by sampling a representative portion of each habitat and using this data to make inferences about the habitat as a whole. A variety of methods can be used to sample populations to determine their size and density. For immobile organisms such as plants, or for very small and slow-moving organisms, a quadrat may be used ([link]). A quadrat is a way of marking off square areas within a habitat, either by staking out an area with sticks and string, or by the use of a wood, plastic, or metal square placed on the ground. After setting the quadrats, researchers then count the number of individuals that lie within their boundaries. Multiple quadrat samples are performed throughout the habitat at several random locations. All of this data can then be used to estimate the population size and population density within the entire habitat. The number and size of quadrat samples depends on the type of organisms under study and other factors, including the density of the organism. For example, if sampling daffodils, a 1 m^2 quadrat might be used whereas with giant redwoods, which are larger and live much further apart from each other, a larger quadrat of 100 m^2 might be employed. This ensures that enough individuals of the species are counted to get an accurate sample that correlates with the habitat, including areas not sampled.

A scientist uses a quadrat to measure population size and density. (credit: NPS Sonoran Desert Network)

For mobile organisms, such as mammals, birds, or fish, a technique called mark and recapture is often used. This method involves marking a sample of captured animals in some way (such as tags, bands, paint, or other body markings), and then releasing them back into the environment to allow them to mix with the rest of the population; later, a new sample is collected, including some individuals that are marked (recaptures) and some individuals that are unmarked ([link]).

Mark and recapture is used to measure the population size of mobile animals such as (a) bighorn sheep, (b) the California condor, and (c) salmon. (credit a: modification of work by Neal Herbert, NPS; credit b: modification of work by Pacific Southwest Region USFWS;

credit c: modification of work by Ingrid

Taylar)

Using the ratio of marked and unmarked individuals, scientists determine how many individuals are in the sample. From this, calculations are used to estimate the total population size. This method assumes that the larger the population, the lower the percentage of tagged organisms that will be recaptured since they will have mixed with more untagged individuals. For example, if 80 deer are captured, tagged, and released into the forest, and later 100 deer are captured and 20 of them are already marked, we can determine the population size (*N*) using the following equation:

(number marked first catch x total number of second catch) number marked second catch = N

Using our example, the population size would be estimated at 400.

(80 x 100) 20 = 400

Therefore, there are an estimated 400 total individuals in the original population.

There are some limitations to the mark and recapture method. Some animals from the first catch may learn to avoid capture in the second round, thus inflating population estimates. Alternatively, animals may preferentially be retrapped (especially if a food reward is offered), resulting in an underestimate of population size. Also, some species may be harmed by the

marking technique, reducing their survival. A variety of other techniques have been developed, including the electronic tracking of animals tagged with radio transmitters and the use of data from commercial fishing and trapping operations to estimate the size and health of populations and communities.

Species Distribution

In addition to measuring simple density, further information about a population can be obtained by looking at the distribution of the individuals. Species dispersion patterns (or distribution patterns) show the spatial relationship between members of a population within a habitat at a particular point in time. In other words, they show whether members of the species live close together or far apart, and what patterns are evident when they are spaced apart.

Individuals in a population can be more or less equally spaced apart, dispersed randomly with no predictable pattern, or clustered in groups. These are known as uniform, random, and clumped dispersion patterns, respectively ([link]). Uniform dispersion is observed in plants that secrete substances inhibiting the growth of nearby individuals (such as the release of toxic chemicals by the sage plant *Salvia leucophylla*, a phenomenon called allelopathy) and in animals like the penguin that maintain a defined territory. An example of random dispersion occurs with dandelion and other plants that have wind-dispersed seeds that germinate wherever they happen to fall in a favorable environment. A clumped dispersion may be seen in plants that drop their seeds straight to the ground, such as oak trees, or animals that live in groups (schools of fish or herds of elephants). Clumped dispersions may also be a function of habitat heterogeneity. Thus, the dispersion of the individuals within a population provides more information about how they interact with each other than does a simple density measurement. Just as lower density species might have more difficulty finding a mate, solitary species with a random distribution might have a similar difficulty when compared to social species clumped together in groups.

Species may have uniform, random, or clumped distribution. Territorial birds such as penguins tend to have uniform distribution. Plants such as dandelions with wind-dispersed seeds tend to be randomly distributed. Animals such as elephants that travel in groups exhibit clumped distribution. (credit a: modification of work by Ben Tubby; credit b: modification of

work by Rosendahl; credit c: modification of work by Rebecca

Wood)

Demography

While population size and density describe a population at one particular point in time, scientists must use demography to study the dynamics of a population. Demography is the statistical study of population changes over time: birth rates, death rates, and life expectancies. Each of these measures, especially birth rates, may be affected by the population characteristics described above. For example, a large population size results in a higher birth rate because more potentially reproductive individuals are present. In contrast, a large population size can also result in a higher death rate because of competition, disease, and the accumulation of waste. Similarly, a higher population density or a clumped dispersion pattern results in more potential reproductive encounters between individuals, which can increase birth rate. Lastly, a female-biased sex ratio (the ratio of males to females) or age structure (the proportion of population members at specific age ranges) composed of many individuals of reproductive age can increase birth rates.

In addition, the demographic characteristics of a population can influence how the population grows or declines over time. If birth and death rates are equal, the population remains stable. However, the population size will increase if birth rates exceed death rates; the population

will decrease if birth rates are less than death rates. Life expectancy is another important factor; the length of time individuals remain in the population impacts local resources, reproduction, and the overall health of the population. These demographic characteristics are often displayed in the form of a life table.

Life Tables

Life tables provide important information about the life history of an organism. Life tables divide the population into age groups and often sexes, and show how long a member of that group is likely to live. They are modeled after actuarial tables used by the insurance industry for estimating human life expectancy. Life tables may include the probability of individuals dying before their next birthday (i.e., their mortality rate), the percentage of surviving individuals dying at a particular age interval, and their life expectancy at each interval. An example of a life table is shown in [link] from a study of Dall mountain sheep, a species native to northwestern North America. Notice that the population is divided into age intervals (column A). The mortality rate (per 1000), shown in column D, is based on the number of individuals dying during the age interval (column B) divided by the number of individuals surviving at the beginning of the interval (Column C), multiplied by 1000.

mortality rate = number of individuals dying / number of individuals surviving x 1000

For example, between ages three and four, 12 individuals die out of the 776 that were remaining from the original 1000 sheep. This number is then multiplied by 1000 to get the mortality rate per thousand.

mortality rate = 12 / 776 x 1000 ≈ 15.5

As can be seen from the mortality rate data (column D), a high death rate occurred when the sheep were between 6 and 12 months old, and then increased even more from 8 to 12 years old, after which there were few survivors. The data indicate that if a sheep in this population were to survive to age one, it could be expected to live another 7.7 years on average, as shown by the life expectancy numbers in column E.

This life table of *Ovis dalli* shows the number of deaths, number of survivors, mortality rate, and life expectancy at each age interval for the Dall mountain sheep.

Life Table of Dall Mountain Sheep[1]

Age interval (years)	Number dying in age interval out of 1000 born	Number surviving at beginning of age interval out of 1000 born	Mortality rate per 1000 alive at beginning of age interval	Life expectancy or mean lifetime remaining to those attaining age interval
0-0.5	54	1000	54.0	7.06
0.5-1	145	946	153.3	--
1-2	12	801	15.0	7.7
2-3	13	789	16.5	6.8
3-4	12	776	15.5	5.9
4-5	30	764	39.3	5.0
5-6	46	734	62.7	4.2
6-7	48	688	69.8	3.4

This life table of *Ovis dalli* shows the number of deaths, number of survivors, mortality rate, and life expectancy at each age interval for the Dall mountain sheep.

Life Table of Dall Mountain Sheep[1]

Age interval (years)	Number dying in age interval out of 1000 born	Number surviving at beginning of age interval out of 1000 born	Mortality rate per 1000 alive at beginning of age interval	Life expectancy or mean lifetime remaining to those attaining age interval
7-8	69	640	107.8	2.6
8-9	132	571	231.2	1.9
9-10	187	439	426.0	1.3
10-11	156	252	619.0	0.9
11-12	90	96	937.5	0.6
12-13	3	6	500.0	1.2
13-14	3	3	1000	0.7

Survivorship Curves

Another tool used by population ecologists is a survivorship curve, which is a graph of the number of individuals surviving at each age interval plotted versus time (usually with data compiled from a life table). These curves allow us to compare the life histories of different populations ([link]). Humans and most primates exhibit a Type I survivorship curve because a high percentage of offspring survive their early and middle years—death occurs predominantly in older individuals. These types of species usually have small numbers of offspring at one time, and they give a high amount of parental care to them to ensure their survival. Birds are an example of an intermediate or Type II survivorship curve because birds die more or less equally at each age interval. These organisms also may have relatively few offspring and provide significant parental care. Trees, marine invertebrates, and most fishes exhibit a Type III survivorship curve because very few of these organisms survive their younger years; however, those that make it to an old age are more likely to survive for a relatively long period of time. Organisms in this category usually have a very large number of offspring, but once they are born, little parental care is provided. Thus these offspring are “on their own” and vulnerable to predation, but their sheer numbers assure the survival of enough individuals to perpetuate the species.

Survivorship curves show the distribution of individuals in a population according to age. Humans and most mammals have a Type I survivorship curve because death primarily occurs in the older years. Birds have a Type II survivorship curve, as death at any age is equally probable. Trees have a Type III survivorship curve because very few survive the younger

years, but after a certain age, individuals are much more likely to

survive.

Section Summary

Populations are individuals of a species that live in a particular habitat. Ecologists measure characteristics of populations: size, density, dispersion pattern, age structure, and sex ratio. Life tables are useful to calculate life expectancies of individual population members. Survivorship curves show the number of individuals surviving at each age interval plotted versus time.

Art Connections

[link] As this graph shows, population density typically decreases with increasing body size. Why do you think this is the case?

[link] Smaller animals require less food and other resources, so the environment can support more of them.

Review Questions

Which of the following methods will tell an ecologist about both the size and density of a population?

a. mark and recapture
b. mark and release
c. quadrat
d. life table

C

Which of the following is best at showing the life expectancy of an individual within a population?

a. quadrat

b. mark and recapture
c. survivorship curve
d. life table

D

Humans have which type of survivorship curve?

a. Type I
b. Type II
c. Type III
d. Type IV

A

Free Response

Describe how a researcher would determine the size of a penguin population in Antarctica using the mark and release method.

The researcher would mark a certain number of penguins with a tag, release them back into the population, and, at a later time, recapture penguins to see what percentage of the recaptured penguins was tagged. This percentage would allow an estimation of the size of the penguin population.

Footnotes

- 1 Data Adapted from Edward S. Deevey, Jr., "Life Tables for Natural Populations of Animals," *The Quarterly Review of Biology* 22, no. 4 (December 1947): 283-314.

Glossary

demography
: statistical study of changes in populations over time

life table
: table showing the life expectancy of a population member based on its age

mark and recapture
: technique used to determine population size in mobile organisms

mortality rate
: proportion of population surviving to the beginning of an age interval that die during the age interval

population density
: number of population members divided by the area or volume being measured

population size (*N*)
: number of population members in a habitat at the same time

quadrat
: square made of various materials used to determine population size and density in slow moving or stationary organisms

species dispersion pattern
: (also, species distribution pattern) spatial location of individuals of a given species within a habitat at a particular point in time

survivorship curve
: graph of the number of surviving population members versus the relative age of the member

Behavioral Biology: Proximate and Ultimate Causes of Behavior

By the end of this section, you will be able to:

- Compare innate and learned behavior
- Discuss how movement and migration behaviors are a result of natural selection
- Discuss the different ways members of a population communicate with each other
- Give examples of how species use energy for mating displays and other courtship behaviors
- Differentiate between various mating systems
- Describe different ways that species learn

Behavior is the change in activity of an organism in response to a stimulus. Behavioral biology is the study of the biological and evolutionary bases for such changes. The idea that behaviors evolved as a result of the pressures of natural selection is not new. Animal behavior has been studied for decades, by biologists in the science of ethology, by psychologists in the science of comparative psychology, and by scientists of many disciplines in the study of neurobiology. Although there is overlap between these disciplines, scientists in these behavioral fields take different approaches. Comparative psychology is an extension of work done in human and behavioral psychology. Ethology is an extension of genetics, evolution, anatomy, physiology, and other biological disciplines. Still, one cannot study behavioral biology without touching on both comparative psychology and ethology.

One goal of behavioral biology is to dissect out the innate behaviors, which have a strong genetic component and are largely independent of environmental influences, from the learned behaviors, which result from environmental conditioning. Innate behavior, or instinct, is important because there is no risk of an incorrect behavior being learned. They are “hard wired” into the system. On the other hand, learned behaviors, although riskier, are flexible, dynamic, and can be altered according to changes in the environment.

Innate Behaviors: Movement and Migration

Innate or instinctual behaviors rely on response to stimuli. The simplest example of this is a reflex action, an involuntary and rapid response to stimulus. To test the “knee-jerk” reflex, a doctor taps the patellar tendon below the kneecap with a rubber hammer. The stimulation of the nerves there leads to the reflex of extending the leg at the knee. This is similar to the reaction of someone who touches a hot stove and instinctually pulls his or her hand away. Even humans, with our great capacity to learn, still exhibit a variety of innate behaviors.

Kinesis and Taxis

Another activity or movement of innate behavior is kinesis, or the undirected movement in response to a stimulus. Orthokinesis is the increased or decreased speed of movement of an organism in response to a stimulus. Woodlice, for example, increase their speed of movement when exposed to high or low temperatures. This movement, although random, increases the probability that the insect spends less time in the unfavorable environment. Another example is klinokinesis, an increase in turning behaviors. It is exhibited by bacteria such as *E. coli* which, in association with orthokinesis, helps the organisms randomly find a more hospitable environment.

A similar, but more directed version of kinesis is taxis: the directed movement towards or away from a stimulus. This movement can be in response to light (phototaxis), chemical signals (chemotaxis), or gravity (geotaxis) and can be directed toward (positive) or away (negative) from the source of the stimulus. An example of a positive chemotaxis is exhibited by the unicellular protozoan *Tetrahymena thermophila*. This organism swims using its cilia, at times moving in a straight line, and at other times making turns. The attracting chemotactic agent alters the frequency of turning as the organism moves directly toward the source, following the increasing concentration gradient.

Fixed Action Patterns

A fixed action pattern is a series of movements elicited by a stimulus such that even when the stimulus is removed, the pattern goes on to completion. An example of such a behavior occurs in the three-spined stickleback, a small freshwater fish ([link]). Males of this species develop a red belly during breeding season and show instinctual aggressiveness to other males during this time. In laboratory experiments, researchers exposed such fish to objects that in no way resemble a fish in their shape, but which were painted red on their lower halves. The male sticklebacks responded aggressively to the objects just as if they were real male sticklebacks.

Male three-spined stickleback fish exhibit a fixed action pattern. During mating season, the males, which develop a bright red belly, react strongly to red-bottomed objects that in no way resemble fish.

Migration

Migration is the long-range seasonal movement of animals. It is an evolved, adapted response to variation in resource availability, and it is a common phenomenon found in all major groups of animals. Birds fly south for the winter to get to warmer climates with sufficient food, and salmon migrate to their spawning grounds. The popular 2005 documentary *March of the Penguins* followed the 62-mile migration of emperor penguins through Antarctica to bring food back to their breeding site and to their young. Wildebeests ([link]) migrate over 1800 miles each year in search of new grasslands.

Wildebeests migrate in a clockwise fashion over 1800 miles each year in search of rain-ripened grass. (credit: Eric Inafuku)

Although migration is thought of as innate behavior, only some migrating species always migrate (obligate migration). Animals that exhibit facultative migration can choose to migrate or not. Additionally, in some animals, only a portion of the population migrates, whereas the rest does not migrate (incomplete migration). For example, owls that live in the tundra may migrate in years when their food source, small rodents, is relatively scarce, but not migrate during the years when rodents are plentiful.

Foraging

Foraging is the act of searching for and exploiting food resources. Feeding behaviors that maximize energy gain and minimize energy expenditure are called optimal foraging behaviors, and these are favored by natural section. The painted stork, for example, uses its long beak to search the bottom of a freshwater marshland for crabs and other food ([link]).

The painted stork uses its long beak to forage. (credit: J.M. Garg)

Innate Behaviors: Living in Groups

Not all animals live in groups, but even those that live relatively solitary lives, with the exception of those that can reproduce asexually, must mate. Mating usually involves one animal signaling another so as to communicate the desire to mate. There are several types of energy-intensive behaviors or displays associated with mating, called mating rituals. Other behaviors found in populations that live in groups are described in terms of which animal benefits from the behavior. In selfish behavior, only the animal in question benefits; in altruistic behavior, one animal's actions benefit another animal; cooperative behavior describes when both animals benefit. All of these behaviors involve some sort of communication between population members.

Communication within a Species

Animals communicate with each other using stimuli known as signals. An example of this is seen in the three-spined stickleback, where the visual signal of a red region in the lower half of a fish signals males to become aggressive and signals females to mate. Other signals are chemical (pheromones), aural (sound), visual (courtship and aggressive displays), or tactile (touch). These types of communication may be instinctual or learned or a combination of both. These are not the same as the communication we associate with language, which has been observed only in humans and perhaps in some species of primates and cetaceans.

A pheromone is a secreted chemical signal used to obtain a response from another individual of the same species. The purpose of pheromones is to elicit a specific behavior from the receiving individual. Pheromones are especially common among social insects, but they are

used by many species to attract the opposite sex, to sound alarms, to mark food trails, and to elicit other, more complex behaviors. Even humans are thought to respond to certain pheromones called axillary steroids. These chemicals influence human perception of other people, and in one study were responsible for a group of women synchronizing their menstrual cycles. The role of pheromones in human-to-human communication is still somewhat controversial and continues to be researched.

Songs are an example of an aural signal, one that needs to be heard by the recipient. Perhaps the best known of these are songs of birds, which identify the species and are used to attract mates. Other well-known songs are those of whales, which are of such low frequency that they can travel long distances underwater. Dolphins communicate with each other using a wide variety of vocalizations. Male crickets make chirping sounds using a specialized organ to attract a mate, repel other males, and to announce a successful mating.

Courtship displays are a series of ritualized visual behaviors (signals) designed to attract and convince a member of the opposite sex to mate. These displays are ubiquitous in the animal kingdom. Often these displays involve a series of steps, including an initial display by one member followed by a response from the other. If at any point, the display is performed incorrectly or a proper response is not given, the mating ritual is abandoned and the mating attempt will be unsuccessful. The mating display of the common stork is shown in [link].

Aggressive displays are also common in the animal kingdom. An example is when a dog bares its teeth when it wants another dog to back down. Presumably, these displays communicate not only the willingness of the animal to fight, but also its fighting ability. Although these displays do signal aggression on the part of the sender, it is thought that these displays are actually a mechanism to reduce the amount of actual fighting that occurs between members of the same species: they allow individuals to assess the fighting ability of their opponent and thus decide whether it is "worth the fight." The testing of certain hypotheses using game theory has led to the conclusion that some of these displays may overstate an animal's actual fighting ability and are used to "bluff" the opponent. This type of interaction, even if "dishonest," would be favored by natural selection if it is successful more times than not.

This stork's courtship display is designed to attract potential mates. (credit: Linda

"jinterwas"/Flickr)

Distraction displays are seen in birds and some fish. They are designed to attract a predator away from the nest that contains their young. This is an example of an altruistic behavior: it benefits the young more than the individual performing the display, which is putting itself at risk by doing so.

Many animals, especially primates, communicate with other members in the group through touch. Activities such as grooming, touching the shoulder or root of the tail, embracing, lip contact, and greeting ceremonies have all been observed in the Indian langur, an Old World monkey. Similar behaviors are found in other primates, especially in the great apes.

Link to Learning

The killdeer bird distracts predators from its eggs by faking a broken wing display in this video taken in Boise, Idaho.

Life Histories and Natural Selection
By the end of this section, you will be able to:

- Describe how life history patterns are influenced by natural selection
- Explain different life history patterns and how different reproductive strategies affect species' survival

A species' life history describes the series of events over its lifetime, such as how resources are allocated for growth, maintenance, and reproduction. Life history traits affect the life table of an organism. A species' life history is genetically determined and shaped by the environment and natural selection.

Life History Patterns and Energy Budgets

Energy is required by all living organisms for their growth, maintenance, and reproduction; at the same time, energy is often a major limiting factor in determining an organism's survival. Plants, for example, acquire energy from the sun via photosynthesis, but must expend this energy to grow, maintain health, and produce energy-rich seeds to produce the next generation. Animals have the additional burden of using some of their energy reserves to acquire food. Furthermore, some animals must expend energy caring for their offspring. Thus, all species have an energy budget: they must balance energy intake with their use of energy for metabolism, reproduction, parental care, and energy storage (such as bears building up body fat for winter hibernation).

Parental Care and Fecundity

Fecundity is the potential reproductive capacity of an individual within a population. In other words, fecundity describes how many offspring could ideally be produced if an individual has as many offspring as possible, repeating the reproductive cycle as soon as possible after the birth of the offspring. In animals, fecundity is inversely related to the amount of parental care given to an individual offspring. Species, such as many marine invertebrates, that produce many offspring usually provide little if any care for the offspring (they would not have the energy or the ability to do so anyway). Most of their energy budget is used to produce many tiny offspring. Animals with this strategy are often self-sufficient at a very early age. This is because of the energy tradeoff these organisms have made to maximize their evolutionary fitness. Because their energy is used for producing offspring instead of parental care, it makes sense that these offspring have some ability to be able to move within their environment and find food and perhaps shelter. Even with these abilities, their small size makes them extremely vulnerable to predation, so the production of many offspring allows enough of them to survive to maintain the species.

Animal species that have few offspring during a reproductive event usually give extensive parental care, devoting much of their energy budget to these activities, sometimes at the expense of their own health. This is the case with many mammals, such as humans, kangaroos, and pandas. The offspring of these species are relatively helpless at birth and need to develop before they achieve self-sufficiency.

Plants with low fecundity produce few energy-rich seeds (such as coconuts and chestnuts) with each having a good chance to germinate into a new organism; plants with high fecundity usually have many small, energy-poor seeds (like orchids) that have a relatively poor chance of surviving. Although it may seem that coconuts and chestnuts have a better chance of surviving, the energy tradeoff of the orchid is also very effective. It is a matter of where the energy is used, for large numbers of seeds or for fewer seeds with more energy.

Early versus Late Reproduction

The timing of reproduction in a life history also affects species survival. Organisms that reproduce at an early age have a greater chance of producing offspring, but this is usually at the expense of their growth and the maintenance of their health. Conversely, organisms that start reproducing later in life often have greater fecundity or are better able to provide parental care, but they risk that they will not survive to reproductive age. Examples of this can be seen in fishes. Small fish like guppies use their energy to reproduce rapidly, but never attain the size that would give them defense against some predators. Larger fish, like the bluegill or shark, use their energy to attain a large size, but do so with the risk that they will die before they can reproduce or at least reproduce to their maximum. These different energy strategies and tradeoffs are key to understanding the evolution of each species as it maximizes its fitness and fills its niche. In terms of energy budgeting, some species “blow it all” and use up most of their energy reserves to reproduce early before they die. Other species delay having reproduction to become stronger, more experienced individuals and to make sure that they are strong enough to provide parental care if necessary.

Single versus Multiple Reproductive Events

Some life history traits, such as fecundity, timing of reproduction, and parental care, can be grouped together into general strategies that are used by multiple species. Semelparity occurs when a species reproduces only once during its lifetime and then dies. Such species use most

of their resource budget during a single reproductive event, sacrificing their health to the point that they do not survive. Examples of semelparity are bamboo, which flowers once and then dies, and the Chinook salmon ([link]**a**), which uses most of its energy reserves to migrate from the ocean to its freshwater nesting area, where it reproduces and then dies. Scientists have posited alternate explanations for the evolutionary advantage of the Chinook's post-reproduction death: a programmed suicide caused by a massive release of corticosteroid hormones, presumably so the parents can become food for the offspring, or simple exhaustion caused by the energy demands of reproduction; these are still being debated.

Iteroparity describes species that reproduce repeatedly during their lives. Some animals are able to mate only once per year, but survive multiple mating seasons. The pronghorn antelope is an example of an animal that goes into a seasonal estrus cycle ("heat"): a hormonally induced physiological condition preparing the body for successful mating ([link]**b**). Females of these species mate only during the estrus phase of the cycle. A different pattern is observed in primates, including humans and chimpanzees, which may attempt reproduction at any time during their reproductive years, even though their menstrual cycles make pregnancy likely only a few days per month during ovulation ([link]**c**).

The (a) Chinook salmon mates once and dies. The (b) pronghorn antelope mates during specific times of the year during its reproductive life. Primates, such as humans and (c) chimpanzees, may mate on any day, independent of ovulation. (credit a: modification of work by Roger Tabor, USFWS; credit b: modification of work by Mark Gocke, USDA; credit c:

modification of work by "Shiny Things"/Flickr)

Link to Learning

Play this interactive PBS evolution-based mating game to learn more about reproductive strategies.

Evolution Connection

Energy Budgets, Reproductive Costs, and Sexual Selection in *Drosophila* Research into how animals allocate their energy resources for growth, maintenance, and reproduction has used a variety of experimental animal models. Some of this work has been done using the common fruit fly, *Drosophila melanogaster*. Studies have shown that not only does reproduction have a cost as far as how long male fruit flies live, but also fruit flies that have already mated several times have limited sperm remaining for reproduction. Fruit flies maximize their last chances at reproduction by selecting optimal mates.

In a 1981 study, male fruit flies were placed in enclosures with either virgin or inseminated females. The males that mated with virgin females had shorter life spans than those in contact with the same number of inseminated females with which they were unable to mate. This effect occurred regardless of how large (indicative of their age) the males were. Thus, males that did not mate lived longer, allowing them more opportunities to find mates in the future.

More recent studies, performed in 2006, show how males select the female with which they will mate and how this is affected by previous matings ([link]).[1] Males were allowed to select between smaller and larger females. Findings showed that larger females had greater fecundity, producing twice as many offspring per mating as the smaller females did. Males that had previously mated, and thus had lower supplies of sperm, were termed "resource-depleted," while males that had not mated were termed "non-resource-depleted." The study showed that although non-resource-depleted males preferentially mated with larger females, this selection of partners was more pronounced in the resource-depleted males. Thus, males with depleted sperm supplies, which were limited in the number of times that they could mate before they replenished their sperm supply, selected larger, more fecund females, thus maximizing their chances for offspring. This study was one of the first to show that the physiological state of the male affected its mating behavior in a way that clearly maximizes its use of limited reproductive resources.

Male fruit flies that had previously mated (sperm-depleted) picked larger, more fecund females more often than those that had not mated (non-sperm-depleted). This change in

behavior causes an increase in the efficiency of a limited reproductive resource:

sperm.

These studies demonstrate two ways in which the energy budget is a factor in reproduction. First, energy expended on mating may reduce an animal's lifespan, but by this time they have already reproduced, so in the context of natural selection this early death is not of much evolutionary importance. Second, when resources such as sperm (and the energy needed to replenish it) are low, an organism's behavior can change to give them the best chance of passing their genes on to the next generation. These changes in behavior, so important to evolution, are studied in a discipline known as behavioral biology, or ethology, at the interface between population biology and psychology.

Section Summary

All species have evolved a pattern of living, called a life history strategy, in which they partition energy for growth, maintenance, and reproduction. These patterns evolve through natural selection; they allow species to adapt to their environment to obtain the resources they need to successfully reproduce. There is an inverse relationship between fecundity and parental care. A species may reproduce early in life to ensure surviving to a reproductive age or reproduce later in life to become larger and healthier and better able to give parental care. A species may reproduce once (semelparity) or many times (iteroparity) in its life.

Review Questions

Which of the following is associated with long-term parental care?

a. few offspring
b. many offspring
c. semelparity
d. fecundity

A

Which of the following is associated with multiple reproductive episodes during a species' lifetime?

a. semiparity
b. iteroparity
c. semelparity
d. fecundity

B

Which of the following is associated with the reproductive potential of a species?

a. few offspring
b. many offspring
c. semelparity
d. fecundity

D

Free Response

Why is long-term parental care not associated with having many offspring during a reproductive episode?

Parental care is not feasible for organisms having many offspring because they do not have the energy available to take care of offspring. Most of their energy budget is used in the formation of seeds or offspring, so there is little left for parental care. Also, the sheer number of offspring would make individual parental care impossible.

Footnotes

- 1 Adapted from Phillip G. Byrne and William R. Rice, "Evidence for adaptive male mate choice in the fruit fly *Drosophila melanogaster*," Proc Biol Sci. 273, no. 1589 (2006): 917-922, doi: 10.1098/rspb.2005.3372.

Glossary

energy budget
: allocation of energy resources for body maintenance, reproduction, and parental care

fecundity
: potential reproductive capacity of an individual

iteroparity
: life history strategy characterized by multiple reproductive events during the lifetime of a species

life history

inherited pattern of resource allocation under the influence of natural selection and other evolutionary forces

semelparity

life history strategy characterized by a single reproductive event followed by death

Introduction

class="introduction" class="summary" title="Sections Summary" class="art-exercise" title="Art Connections" class="multiple-choice" title="Multiple Choice" class="free-response" title="Free Response"Lake Victoria in Africa, shown in this satellite image, was the site of one of the most extraordinary evolutionary findings on the planet, as well as a casualty of devastating biodiversity loss. (credit: modification of work by Rishabh Tatiraju, using NASA World Wind

software)

In the 1980s, biologists working in Lake Victoria in Africa discovered one of the most extraordinary products of evolution on the planet. Located in the Great Rift Valley, Lake Victoria is a large lake about 68,900 km^2 in area (larger than Lake Huron, the second largest of North America's Great Lakes). Biologists were studying species of a family of fish called cichlids. They found that as they sampled for fish in different locations of the lake, they never stopped finding new species, and they identified nearly 500 evolved types of cichlids. But while

studying these variations, they quickly discovered that the invasive Nile Perch was destroying the lake's cichlid population, bringing hundreds of cichlid species to extinction with devastating rapidity.

The Biodiversity Crisis

By the end of this section, you will be able to:

- Define biodiversity
- Describe biodiversity as the equilibrium of naturally fluctuating rates of extinction and speciation
- Identify historical causes of high extinction rates in Earth's history

Traditionally, ecologists have measured biodiversity, a general term for the variety present in the biosphere, by taking into account both the number of species and their commonness. Biodiversity can be estimated at a number of levels of organization of living things. These estimation indexes, which came from information theory, are most useful as a first step in quantifying biodiversity between and within ecosystems; they are less useful when the main concern among conservation biologists is simply the loss of biodiversity. However, biologists recognize that measures of biodiversity, in terms of species diversity, may help focus efforts to preserve the biologically or technologically important elements of biodiversity.

The Lake Victoria cichlids provide an example through which we can begin to understand biodiversity. The biologists studying cichlids in the 1980s discovered hundreds of cichlid species representing a variety of specializations to particular habitat types and specific feeding strategies: eating plankton floating in the water, scraping and then eating algae from rocks, eating insect larvae from the bottom, and eating the eggs of other species of cichlid. The cichlids of Lake Victoria are the product of an adaptive radiation. An adaptive radiation is a rapid (less than three million years in the case of the Lake Victoria cichlids) branching through speciation of a phylogenetic tree into many closely related species; typically, the species "radiate" into different habitats and niches. The Galápagos finches are an example of a modest adaptive radiation with 15 species. The cichlids of Lake Victoria are an example of a spectacular adaptive radiation that includes about 500 species.

At the time biologists were making this discovery, some species began to quickly disappear. A culprit in these declines was a species of large fish that was introduced to Lake Victoria by fisheries to feed the people living around the lake. The Nile perch was introduced in 1963, but lay low until the 1980s when its populations began to surge. The Nile perch population grew by consuming cichlids, driving species after species to the point of extinction (the disappearance of a species). In fact, there were several factors that played a role in the extinction of perhaps 200 cichlid species in Lake Victoria: the Nile perch, declining lake

water quality due to agriculture and land clearing on the shores of Lake Victoria, and increased fishing pressure. Scientists had not even catalogued all of the species present—so many were lost that were never named. The diversity is now a shadow of what it once was.

The cichlids of Lake Victoria are a thumbnail sketch of contemporary rapid species loss that occurs all over Earth and is caused by human activity. Extinction is a natural process of macroevolution that occurs at the rate of about one out of 1 million species becoming extinct per year. The fossil record reveals that there have been five periods of mass extinction in history with much higher rates of species loss, and the rate of species loss today is comparable to those periods of mass extinction. However, there is a major difference between the previous mass extinctions and the current extinction we are experiencing: human activity. Specifically, three human activities have a major impact: destruction of habitat, introduction of exotic species, and over-harvesting. Predictions of species loss within the next century, a tiny amount of time on geological timescales, range from 10 percent to 50 percent. Extinctions on this scale have only happened five other times in the history of the planet, and they have been caused by cataclysmic events that changed the course of the history of life in each instance. Earth is now in one of those times.

Types of Biodiversity

Scientists generally accept that the term biodiversity describes the number and kinds of species in a location or on the planet. Species can be difficult to define, but most biologists still feel comfortable with the concept and are able to identify and count eukaryotic species in most contexts. Biologists have also identified alternate measures of biodiversity, some of which are important for planning how to preserve biodiversity.

Genetic diversity is one of those alternate concepts. Genetic diversity or variation is the raw material for adaptation in a species. A species' future potential for adaptation depends on the genetic diversity held in the genomes of the individuals in populations that make up the species. The same is true for higher taxonomic categories. A genus with very different types of species will have more genetic diversity than a genus with species that look alike and have similar ecologies. If there were a choice between one of these genera of species being preserved, the one with the greatest potential for subsequent evolution is the most genetically diverse one. It would be ideal not to have to make such choices, but increasingly this may be the norm.

Many genes code for proteins, which in turn carry out the metabolic processes that keep organisms alive and reproducing. Genetic diversity can be measured as chemical diversity in that different species produce a variety of chemicals in their cells, both the proteins as well as the products and byproducts of metabolism. This chemical diversity has potential benefit for humans as a source of pharmaceuticals, so it provides one way to measure diversity that is important to human health and welfare.

Humans have generated diversity in domestic animals, plants, and fungi. This diversity is also suffering losses because of migration, market forces, and increasing globalism in agriculture, especially in heavily populated regions such as China, India, and Japan. The human population directly depends on this diversity as a stable food source, and its decline is troubling biologists and agricultural scientists.

It is also useful to define ecosystem diversity, meaning the number of different ecosystems on the planet or in a given geographic area ([link]). Whole ecosystems can disappear even if some of the species might survive by adapting to other ecosystems. The loss of an ecosystem means the loss of interactions between species, the loss of unique features of coadaptation, and the loss of biological productivity that an ecosystem is able to create. An example of a largely extinct ecosystem in North America is the prairie ecosystem. Prairies once spanned central North America from the boreal forest in northern Canada down into Mexico. They are now all but gone, replaced by crop fields, pasture lands, and suburban sprawl. Many of the species survive, but the hugely productive ecosystem that was responsible for creating the most productive agricultural soils is now gone. As a consequence, soils are disappearing or must be maintained at greater expense.

The variety of ecosystems on Earth—from (a) coral reef to (b) prairie—enables a great diversity of species to exist. (credit a: modification of work by Jim Maragos, USFWS; credit b: modification of work by Jim Minnerath,

USFWS)

Current Species Diversity

Despite considerable effort, knowledge of the species that inhabit the planet is limited. A recent estimate suggests that the eukaryote species for which science has names, about 1.5 million species, account for less than 20 percent of the total number of eukaryote species present on the planet (8.7 million species, by one estimate). Estimates of numbers of prokaryotic species are largely guesses, but biologists agree that science has only begun to catalog their diversity. Even with what is known, there is no central repository of names or samples of the described species; therefore, there is no way to be sure that the 1.5 million descriptions is an accurate number. It is a best guess based on the opinions of experts in

different taxonomic groups. Given that Earth is losing species at an accelerating pace, science is very much in the place it was with the Lake Victoria cichlids: knowing little about what is being lost. [link] presents recent estimates of biodiversity in different groups.

Estimates of the Numbers of Described and Predicted Species by Taxonomic Group

	Mora et al. 2011[1]		Chapman 2009[2]		Groombridge & Jenkins 2002[3]	
	Described	Predicted	Described	Predicted	Described	Predicted
Animalia	1,124,516	9,920,000	1,424,153	6,836,330	1,225,500	10,820,000
Chromista	17,892	34,900	25,044	200,500	—	—
Fungi	44,368	616,320	98,998	1,500,000	72,000	1,500,000
Plantae	224,244	314,600	310,129	390,800	270,000	320,000
Protozoa	16,236	72,800	28,871	1,000,000	80,000	600,000
Prokaryotes	—	—	10,307	1,000,000	10,175	—
Total	1,438,769	10,960,000	1,897,502	10,897,630	1,657,675	13,240,000

There are various initiatives to catalog described species in accessible ways, and the internet is facilitating that effort. Nevertheless, it has been pointed out that at the current rate of species description, which according to the State of Observed Species Report is 17,000 to 20,000 new species per year, it will take close to 500 years to finish describing life on this planet.[4] Over time, the task becomes both increasingly impossible and increasingly easier as extinction removes species from the planet.

Naming and counting species may seem an unimportant pursuit given the other needs of humanity, but it is not simply an accounting. Describing species is a complex process by which biologists determine an organism's unique characteristics and whether or not that organism belongs to any other described species. It allows biologists to find and recognize the species after the initial discovery, and allows them to follow up on questions about its biology. In addition, the unique characteristics of each species make it potentially valuable to humans or other species on which humans depend. Understanding these characteristics is the value of finding and naming species.

Patterns of Biodiversity

Biodiversity is not evenly distributed on Earth. Lake Victoria contained almost 500 species of cichlids alone, ignoring the other fish families present in the lake. All of these species were found only in Lake Victoria; therefore, the 500 species of cichlids were endemic. Endemic species are found in only one location. Endemics with highly restricted distributions are particularly vulnerable to extinction. Higher taxonomic levels, such as genera and families, can also be endemic. Lake Huron contains about 79 species of fish, all of which are found in many other lakes in North America. What accounts for the difference in fish diversity in these two lakes? Lake Victoria is a tropical lake, while Lake Huron is a temperate lake. Lake Huron in its present form is only about 7,000 years old, while Lake Victoria in its present form is about 15,000 years old. Biogeographers have suggested these two factors, latitude and age, are two of several hypotheses to explain biodiversity patterns on the planet.

Career Connection

BiogeographerBiogeography is the study of the distribution of the world's species—both in the past and in the present. The work of biogeographers is critical to understanding our physical environment, how the environment affects species, and how environmental changes impact the distribution of a species; it has also been critical to developing evolutionary theory. Biogeographers need to understand both biology and ecology. They also need to be well-versed in evolutionary studies, soil science, and climatology.

There are three main fields of study under the heading of biogeography: ecological biogeography, historical biogeography (called paleobiogeography), and conservation biogeography. Ecological biogeography studies the current factors affecting the distribution of plants and animals. Historical biogeography, as the name implies, studies the past distribution of species. Conservation biogeography, on the other hand, is focused on the protection and restoration of species based upon known historical and current ecological information. Each of these fields considers both zoogeography and phytogeography—the past and present distribution of animals and plants.

One of the oldest observed patterns in ecology is that species biodiversity in almost every taxonomic group increases as latitude declines. In other words, biodiversity increases closer to the equator ([link]).

This map illustrates the number of amphibian species across the globe and shows the trend toward higher biodiversity at lower latitudes. A similar pattern is observed for most

taxonomic

groups.

It is not yet clear why biodiversity increases closer to the equator, but hypotheses include the greater age of the ecosystems in the tropics versus temperate regions that were largely devoid of life or drastically impoverished during the last glaciation. The idea is that greater age provides more time for speciation. Another possible explanation is the increased energy the tropics receive from the sun versus the decreased energy that temperate and polar regions receive. It is not entirely clear how greater energy input could translate into more species. The complexity of tropical ecosystems may promote speciation by increasing the heterogeneity, or number of ecological niches, in the tropics relative to higher latitudes. The greater heterogeneity provides more opportunities for coevolution, specialization, and perhaps greater selection pressures leading to population differentiation. However, this hypothesis suffers from some circularity—ecosystems with more species encourage speciation, but how did they get more species to begin with? The tropics have been perceived as being more stable than temperate regions, which have a pronounced climate and day-length seasonality. The tropics have their own forms of seasonality, such as rainfall, but they are generally assumed to be more stable environments and this stability might promote speciation.

Regardless of the mechanisms, it is certainly true that all levels of biodiversity are greatest in the tropics. Additionally, the rate of endemism is highest, and there are more biodiversity

hotspots. However, this richness of diversity also means that knowledge of species is lowest, and there is a high potential for biodiversity loss.

Conservation of Biodiversity

In 1988, British environmentalist Norman Myers developed a conservation concept to identify areas rich in species and at significant risk for species loss: biodiversity hotspots. Biodiversity hotspots are geographical areas that contain high numbers of endemic species. The purpose of the concept was to identify important locations on the planet for conservation efforts, a kind of conservation triage. By protecting hotspots, governments are able to protect a larger number of species. The original criteria for a hotspot included the presence of 1500 or more endemic plant species and 70 percent of the area disturbed by human activity. There are now 34 biodiversity hotspots ([link]) containing large numbers of endemic species, which include half of Earth's endemic plants.

Conservation International has identified 34 biodiversity hotspots, which cover only 2.3 percent of the Earth's surface but have endemic to them 42 percent of the terrestrial vertebrate species and 50 percent of the world's

plants.

Biodiversity Change through Geological Time

The number of species on the planet, or in any geographical area, is the result of an equilibrium of two evolutionary processes that are ongoing: speciation and extinction. Both are natural “birth” and “death” processes of macroevolution. When speciation rates begin to outstrip extinction rates, the number of species will increase; likewise, the number of species will decrease when extinction rates begin to overtake speciation rates. Throughout Earth’s history, these two processes have fluctuated—sometimes leading to dramatic changes in the number of species on Earth as reflected in the fossil record ([link]).

Percent extinction occurrences as reflected in the fossil record have fluctuated throughout Earth’s history. Sudden and dramatic losses of biodiversity, called mass extinctions, have occurred five times.

Paleontologists have identified five strata in the fossil record that appear to show sudden and dramatic (greater than half of all extant species disappearing from the fossil record) losses in biodiversity. These are called mass extinctions. There are many lesser, yet still dramatic, extinction events, but the five mass extinctions have attracted the most research. An argument can be made that the five mass extinctions are only the five most extreme events in a continuous series of large extinction events throughout the Phanerozoic (since 542 million years ago). In most cases, the hypothesized causes are still controversial; however, the most recent event seems clear.

The Five Mass Extinctions

The fossil record of the mass extinctions was the basis for defining periods of geological history, so they typically occur at the transition point between geological periods. The transition in fossils from one period to another reflects the dramatic loss of species and the gradual origin of new species. These transitions can be seen in the rock strata. [link] provides data on the five mass extinctions.

This table shows the names and dates for the five mass extinctions in Earth's history.

Mass Extinctions

Geological Period	Mass Extinction Name	Time (millions of years ago)
Ordovician–Silurian	end-Ordovician O–S	450–440
Late Devonian	end-Devonian	375–360
Permian–Triassic	end-Permian	251
Triassic–Jurassic	end-Triassic	205
Cretaceous–Paleogene	end-Cretaceous K–Pg (K–T)	65.5

The Ordovician-Silurian extinction event is the first recorded mass extinction and the second largest. During this period, about 85 percent of marine species (few species lived outside the oceans) became extinct. The main hypothesis for its cause is a period of glaciation and then warming. The extinction event actually consists of two extinction events separated by about 1 million years. The first event was caused by cooling, and the second event was due to the subsequent warming. The climate changes affected temperatures and sea levels. Some researchers have suggested that a gamma-ray burst, caused by a nearby supernova, is a possible cause of the Ordovician-Silurian extinction. The gamma-ray burst would have stripped away the Earth's ozone layer causing intense ultraviolet radiation from the sun and may account for climate changes observed at the time. The hypothesis is speculative, but extraterrestrial influences on Earth's history are an active line of research. Recovery of biodiversity after the mass extinction took from 5 to 20 million years, depending on the location.

The late Devonian extinction may have occurred over a relatively long period of time. It appears to have affected marine species and not the plants or animals inhabiting terrestrial habitats. The causes of this extinction are poorly understood.

The end-Permian extinction was the largest in the history of life. Indeed, an argument could be made that Earth nearly became devoid of life during this extinction event. The planet looked very different before and after this event. Estimates are that 96 percent of all marine species and 70 percent of all terrestrial species were lost. It was at this time, for example, that the trilobites, a group that survived the Ordovician–Silurian extinction, became extinct. The causes for this mass extinction are not clear, but the leading suspect is extended and widespread volcanic activity that led to a runaway global-warming event. The oceans became largely anoxic, suffocating marine life. Terrestrial tetrapod diversity took 30 million years to recover after the end-Permian extinction. The Permian extinction dramatically altered Earth's biodiversity makeup and the course of evolution.

The causes of the Triassic–Jurassic extinction event are not clear and hypotheses of climate change, asteroid impact, and volcanic eruptions have been argued. The extinction event occurred just before the breakup of the supercontinent Pangaea, although recent scholarship suggests that the extinctions may have occurred more gradually throughout the Triassic.

The causes of the end-Cretaceous extinction event are the ones that are best understood. It was during this extinction event about 65 million years ago that the dinosaurs, the dominant vertebrate group for millions of years, disappeared from the planet (with the exception of a theropod clade that gave rise to birds). Indeed, every land animal that weighed more then 25 kg became extinct. The cause of this extinction is now understood to be the result of a cataclysmic impact of a large meteorite, or asteroid, off the coast of what is now the Yucatán Peninsula. This hypothesis, proposed first in 1980, was a radical explanation based on a sharp spike in the levels of iridium (which rains down from space in meteors at a fairly constant rate but is otherwise absent on Earth's surface) at the rock stratum that marks the boundary between the Cretaceous and Paleogene periods ([link]). This boundary marked the disappearance of the dinosaurs in fossils as well as many other taxa. The researchers who discovered the iridium spike interpreted it as a rapid influx of iridium from space to the atmosphere (in the form of a large asteroid) rather than a slowing in the deposition of sediments during that period. It was a radical explanation, but the report of an appropriately aged and sized impact crater in 1991 made the hypothesis more believable. Now an abundance of geological evidence supports the theory. Recovery times for biodiversity after the end-Cretaceous extinction are shorter, in geological time, than for the end-Permian extinction, on the order of 10 million years.

Art Connection
In 1980, Luis and Walter Alvarez, Frank Asaro, and Helen Michels discovered, across the world, a spike in the concentration of iridium within the sedimentary layer at the K–Pg boundary. These researchers hypothesized that this iridium spike was caused by an asteroid impact that resulted in the K–Pg mass extinction. In the photo, the iridium layer is the light band. (credit: USGS)

Scientists measured the relative abundance of fern spores above and below the K–Pg boundary in this rock sample. Which of the following statements most likely represents their findings?

a. An abundance of fern spores from several species was found below the K–Pg boundary, but none was found above.
b. An abundance of fern spores from several species was found above the K–Pg boundary, but none was found below.

c. An abundance of fern spores was found both above and below the K–Pg boundary, but only one species was found below the boundary, and many species were found above the boundary.
d. Many species of fern spores were found both above and below the boundary, but the total number of spores was greater below the boundary.

Link to Learning

Explore this interactive website about mass extinctions.

The Pleistocene Extinction

The Pleistocene Extinction is one of the lesser extinctions, and a recent one. It is well known that the North American, and to some degree Eurasian, megafauna, or large animals, disappeared toward the end of the last glaciation period. The extinction appears to have happened in a relatively restricted time period of 10,000–12,000 years ago. In North America, the losses were quite dramatic and included the woolly mammoths (last dated about 4,000 years ago in an isolated population), mastodon, giant beavers, giant ground sloths, saber-toothed cats, and the North American camel, just to name a few. The possibility that the rapid extinction of these large animals was caused by over-hunting was first suggested in the 1900s. Research into this hypothesis continues today. It seems likely that over-hunting caused many pre-written history extinctions in many regions of the world.

In general, the timing of the Pleistocene extinctions correlated with the arrival of humans and not with climate-change events, which is the main competing hypothesis for these extinctions. The extinctions began in Australia about 40,000 to 50,000 years ago, just after the arrival of humans in the area: a marsupial lion, a giant one-ton wombat, and several giant kangaroo species disappeared. In North America, the extinctions of almost all of the large mammals occurred 10,000–12,000 years ago. All that are left are the smaller mammals such as bears, elk, moose, and cougars. Finally, on many remote oceanic islands, the extinctions of many species occurred coincident with human arrivals. Not all of the islands had large animals, but when there were large animals, they were lost. Madagascar was colonized about 2,000 years ago and the large mammals that lived there became extinct. Eurasia and Africa do not show this pattern, but they also did not experience a recent arrival of humans. Humans arrived in Eurasia hundreds of thousands of years ago after the origin of the species in Africa. This topic remains an area of active research and hypothesizing. It seems clear that even if climate played a role, in most cases human hunting precipitated the extinctions.

Present-Time Extinctions

The sixth, or Holocene, mass extinction appears to have begun earlier than previously believed and has mostly to do with the activities of *Homo sapiens*. Since the beginning of the Holocene period, there are numerous recent extinctions of individual species that are

recorded in human writings. Most of these are coincident with the expansion of the European colonies since the 1500s.

One of the earlier and popularly known examples is the dodo bird. The dodo bird lived in the forests of Mauritius, an island in the Indian Ocean. The dodo bird became extinct around 1662. It was hunted for its meat by sailors and was easy prey because the dodo, which did not evolve with humans, would approach people without fear. Introduced pigs, rats, and dogs brought to the island by European ships also killed dodo young and eggs.

Steller's sea cow became extinct in 1768; it was related to the manatee and probably once lived along the northwest coast of North America. Steller's sea cow was first discovered by Europeans in 1741 and was hunted for meat and oil. The last sea cow was killed in 1768. That amounts to 27 years between the sea cow's first contact with Europeans and extinction of the species.

In 1914, the last living passenger pigeon died in a zoo in Cincinnati, Ohio. This species had once darkened the skies of North America during its migrations, but it was hunted and suffered from habitat loss through the clearing of forests for farmland. In 1918, the last living Carolina parakeet died in captivity. This species was once common in the eastern United States, but it suffered from habitat loss. The species was also hunted because it ate orchard fruit when its native foods were destroyed to make way for farmland. The Japanese sea lion, which inhabited a broad area around Japan and the coast of Korea, became extinct in the 1950s due to fishermen. The Caribbean monk seal was distributed throughout the Caribbean Sea but was driven to extinction via hunting by 1952.

These are only a few of the recorded extinctions in the past 500 years. The International Union for Conservation of Nature (IUCN) keeps a list of extinct and endangered species called the Red List. The list is not complete, but it describes 380 extinct species of vertebrates after 1500 AD, 86 of which were driven extinct by overhunting or overfishing.

Estimates of Present-Time Extinction Rates

Estimates of extinction rates are hampered by the fact that most extinctions are probably happening without observation. The extinction of a bird or mammal is likely to be noticed by humans, especially if it has been hunted or used in some other way. But there are many organisms that are of less interest to humans (not necessarily of less value) and many that are undescribed.

The background extinction rate is estimated to be about one per million species per year (E/MSY). For example, assuming there are about ten million species in existence, the expectation is that ten species would become extinct each year (each year represents ten million species per year).

One contemporary extinction rate estimate uses the extinctions in the written record since the year 1500. For birds alone this method yields an estimate of 26 E/MSY. However, this value may be underestimated for three reasons. First, many species would not have been described until much later in the time period, so their loss would have gone unnoticed. Second, the number of recently extinct species is increasing because extinct species now are being described from skeletal remains. And third, some species are probably already extinct even though conservationists are reluctant to name them as such. Taking these factors into account

raises the estimated extinction rate closer to 100 E/MSY. The predicted rate by the end of the century is 1500 E/MSY.

A second approach to estimating present-time extinction rates is to correlate species loss with habitat loss by measuring forest-area loss and understanding species-area relationships. The species-area relationship is the rate at which new species are seen when the area surveyed is increased. Studies have shown that the number of species present increases as the size of the island increases. This phenomenon has also been shown to hold true in other habitats as well. Turning this relationship around, if the habitat area is reduced, the number of species living there will also decline. Estimates of extinction rates based on habitat loss and species-area relationships have suggested that with about 90 percent habitat loss an expected 50 percent of species would become extinct. Species-area estimates have led to species extinction rate calculations of about 1000 E/MSY and higher. In general, actual observations do not show this amount of loss and suggestions have been made that there is a delay in extinction. Recent work has also called into question the applicability of the species-area relationship when estimating the loss of species. This work argues that the species-area relationship leads to an overestimate of extinction rates. A better relationship to use may be the endemics-area relationship. Using this method would bring estimates down to around 500 E/MSY in the coming century. Note that this value is still 500 times the background rate.

Studies have shown that the number of species present increases with the size of the habitat. (credit: modification of work by Adam B.

Smith)
Link to Learning

Check out this interactive exploration of endangered and extinct species, their ecosystems, and the causes of the endangerment or extinction.

Section Summary

Biodiversity exists at multiple levels of organization and is measured in different ways depending on the goals of those taking the measurements. These measurements include numbers of species, genetic diversity, chemical diversity, and ecosystem diversity. The number of described species is estimated to be 1.5 million with about 17,000 new species being described each year. Estimates for the total number of species on Earth vary but are on the order of 10 million. Biodiversity is negatively correlated with latitude for most taxa, meaning that biodiversity is higher in the tropics. The mechanism for this pattern is not known with certainty, but several plausible hypotheses have been advanced.

Five mass extinctions with losses of more than 50 percent of extant species are observable in the fossil record. Biodiversity recovery times after mass extinctions vary, but have been up to 30 million years. Recent extinctions are recorded in written history and are the basis for one method of estimating contemporary extinction rates. The other method uses measures of habitat loss and species-area relationships. Estimates of contemporary extinction rates vary, but some rates are as high as 500 times the background rate, as determined from the fossil record, and are predicted to rise.

Art Connections

[link] Scientists measured the relative abundance of fern spores above and below the K-Pg boundary in this rock sample. Which of the following statements most likely represents their findings?

a. An abundance of fern spores from several species was found below the K-Pg boundary, but none was found above.
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c. An abundance of fern spores was found both above and below the K-Pg boundary, but only one species was found below the boundary , and many species were found above the boundary.
d. Many species of fern spores were found both above and below the boundary, but the total number of spores was greater below the boundary.

[link] A. An abundance of fern spores from several species was found below the K-Pg boundary, but none was found above.

Review Questions

With an extinction rate of 100 E/MSY and an estimated 10 million species, how many extinctions are expected to occur in a century?

a. 100
b. 10, 000
c. 100, 000
d. 1, 000, 000

C

An adaptive radiation is_____.

a. a burst of speciation
b. a healthy level of UV radiation
c. a hypothesized cause of a mass extinction
d. evidence of an asteroid impact

A

The number of currently described species on the planet is about _____.

a. 17,000
b. 150,000
c. 1.5 million
d. 10 million

C

A mass extinction is defined as _____.

a. a loss of 95 percent of species
b. an asteroid impact
c. a boundary between geological periods
d. a loss of 50 percent of species

D

Free Response

Describe the evidence for the cause of the Cretaceous–Paleogene (K–Pg) mass extinction.

The hypothesized cause of the K–Pg extinction event is an asteroid impact. The first piece of evidence of the impact is a spike in iridium (an element that is rare on Earth, but common in meteors) in the geological layers that mark the K–Pg transition. The second piece of evidence is an impact crater off the Yucatán Peninsula that is the right size and age to have caused the extinction event.

Describe the two methods used to calculate contemporary extinction rates.

Extinction rates are calculated based on the recorded extinction of species in the past 500 years. Adjustments are made for unobserved extinctions and undiscovered species. The second method is a calculation based on the amount of habitat destruction and species-area curves.

Footnotes

- 1 Mora Camilo et al., “How Many Species Are There on Earth and in the Ocean?” *PLoS Biology* (2011), doi:10.1371/journal.pbio.1001127.

- 2 Arthur D. Chapman, *Numbers of Living Species in Australia and the World*, 2nd ed. (Canberra, AU: Australian Biological Resources Study, 2009). http://www.environment.gov.au/biodiversity/abrs/publications/other/species-numbers/2009/pubs/nlsaw-2nd-complete.pdf.
- 3 Brian Groombridge and Martin D. Jenkins. *World Atlas of Biodiversity: Earth's Living Resources in the 21st Century*. Berkeley: University of California Press, 2002.
- 4 International Institute for Species Exploration (IISE), *2011 State of Observed Species (SOS)*. Tempe, AZ: IISE, 2011. Accessed May, 20, 2012. http://species.asu.edu/SOS.

Glossary

adaptive radiation
: rapid branching through speciation of a phylogenetic tree into many closely related species

biodiversity
: variety of a biological system, typically conceived as the number of species, but also applying to genes, biochemistry, and ecosystems

biodiversity hotspot
: concept originated by Norman Myers to describe a geographical region with a large number of endemic species and a large percentage of degraded habitat

chemical diversity
: variety of metabolic compounds in an ecosystem

ecosystem diversity
: variety of ecosystems

endemic species
: species native to one place

extinction
: disappearance of a species from Earth; local extinction is the disappearance of a species from a region

extinction rate
: number of species becoming extinct over time, sometimes defined as extinctions per million species–years to make numbers manageable (E/MSY)

genetic diversity
: variety of genes in a species or other taxonomic group or ecosystem, the term can refer to allelic diversity or genome-wide diversity

heterogeneity
: number of ecological niches

megafauna
: large animals

species-area relationship

relationship between area surveyed and number of species encountered; typically measured by incrementally increasing the area of a survey and determining the cumulative numbers of species

The Importance of Biodiversity to Human Life

By the end of this section, you will be able to:

- Identify chemical diversity benefits to humans
- Identify biodiversity components that support human agriculture
- Describe ecosystem services

It may not be clear why biologists are concerned about biodiversity loss. When biodiversity loss is thought of as the extinction of the passenger pigeon, the dodo bird, and even the woolly mammoth, the loss may appear to be an emotional one. But is the loss practically important for the welfare of the human species? From the perspective of evolution and ecology, the loss of a particular individual species is unimportant (however, the loss of a keystone species can lead to ecological disaster). Extinction is a normal part of macroevolution. But the accelerated extinction rate means the loss of tens of thousands of species within our lifetimes, and it is likely to have dramatic effects on human welfare through the collapse of ecosystems and in added costs to maintain food production, clean air and water, and human health.

Agriculture began after early hunter-gatherer societies first settled in one place and heavily modified their immediate environment. This cultural transition has made it difficult for humans to recognize their dependence on undomesticated living things on the planet. Biologists recognize the human species is embedded in ecosystems and is dependent on them, just as every other species on the planet is dependent. Technology smoothes out the extremes of existence, but ultimately the human species cannot exist without its ecosystem.

Human Health

Contemporary societies that live close to the land often have a broad knowledge of the medicinal uses of plants growing in their area. Most plants produce secondary plant compounds, which are toxins used to protect the plant from insects and other animals that eat them, but some of which also work as medication. For centuries in Europe, older knowledge about the medical uses of plants was compiled in herbals—books that identified plants and their uses. Humans are not the only species to use plants for medicinal reasons: the great apes, orangutans, chimpanzees, bonobos, and gorillas have all been observed self-medicating with plants.

Modern pharmaceutical science also recognizes the importance of these plant compounds. Examples of significant medicines derived from plant compounds include aspirin, codeine, digoxin, atropine, and vincristine ([link]). Many medicines were once derived from plant extracts but are now synthesized. It is estimated that, at one time, 25 percent of modern drugs contained at least one plant extract. That number has probably decreased to about 10 percent as natural plant ingredients are replaced by synthetic versions. Antibiotics, which are

responsible for extraordinary improvements in health and lifespans in developed countries, are compounds largely derived from fungi and bacteria.

Catharanthus roseus, the Madagascar periwinkle, has various medicinal properties. Among other uses, it is a source of vincristine, a drug used in the treatment of lymphomas. (credit: Forest and Kim Starr)

In recent years, animal venoms and poisons have excited intense research for their medicinal potential. By 2007, the FDA had approved five drugs based on animal toxins to treat diseases such as hypertension, chronic pain, and diabetes. Another five drugs are undergoing clinical trials, and at least six drugs are being used in other countries. Other toxins under investigation come from mammals, snakes, lizards, various amphibians, fish, snails, octopuses, and scorpions.

Aside from representing billions of dollars in profits, these medicines improve people's lives. Pharmaceutical companies are actively looking for new compounds synthesized by living organisms that can function as medicine. It is estimated that 1/3 of pharmaceutical research and development is spent on natural compounds and that about 35 percent of new drugs brought to market between 1981 and 2002 were from natural compounds. The opportunities for new medications will be reduced in direct proportion to the disappearance of species.

Agricultural Diversity

Since the beginning of human agriculture more than 10,000 years ago, human groups have been breeding and selecting crop varieties. This crop diversity matched the cultural diversity of highly subdivided populations of humans. For example, potatoes were domesticated beginning around 7,000 years ago in the central Andes of Peru and Bolivia. The potatoes grown in that region belong to seven species and the number of varieties likely is in the thousands. Each variety has been bred to thrive at particular elevations and soil and climate conditions. The diversity is driven by the diverse demands of the topography, the limited movement of people, and the demands created by crop rotation for different varieties that will do well in different fields.

Potatoes are only one example of human-generated diversity. Every plant, animal, and fungus that has been cultivated by humans has been bred from original wild ancestor species into diverse varieties arising from the demands for food value, adaptation to growing conditions, and resistance to pests. The potato demonstrates a well-known example of the risks of low crop diversity: the tragic Irish potato famine when the single variety grown in Ireland became susceptible to a potato blight, wiping out the crop. The loss of the crop led to famine, death, and mass emigration. Resistance to disease is a chief benefit to maintaining crop biodiversity, and lack of diversity in contemporary crop species carries similar risks. Seed companies, which are the source of most crop varieties in developed countries, must continually breed new varieties to keep up with evolving pest organisms. These same seed companies, however, have participated in the decline of the number of varieties available as they focus on selling fewer varieties in more areas of the world.

The ability to create new crop varieties relies on the diversity of varieties available and the accessibility of wild forms related to the crop plant. These wild forms are often the source of new gene variants that can be bred with existing varieties to create varieties with new attributes. Loss of wild species related to a crop will mean the loss of potential in crop improvement. Maintaining the genetic diversity of wild species related to domesticated species ensures our continued food supply.

Since the 1920s, government agriculture departments have maintained seed banks of crop varieties as a way to maintain crop diversity. This system has flaws because, over time, seed banks are lost through accidents, and there is no way to replace them. In 2008, the Svalbard Global Seed Vault ([link]) began storing seeds from around the world as a backup system to the regional seed banks. If a regional seed bank stores varieties in Svalbard, losses can be replaced from Svalbard. The seed vault is located deep into the rock of an arctic island. Conditions within the vault are maintained at ideal temperature and humidity for seed survival, but the deep underground location of the vault in the arctic means that failure of the vault's systems will not compromise the climatic conditions inside the vault.

Art Connection
The Svalbard Global Seed Vault is a storage facility for seeds of Earth's diverse crops. (credit: Mari Tefre, Svalbard Global Seed

Vault)

The Svalbard Global Seed Vault is located on Spitsbergen island in Norway, which has an arctic climate. Why might an arctic climate be good for seed storage?

Crop success s is largely dependent on the quality of the soil. Although some agricultural soils are rendered sterile using controversial cultivation and chemical treatments, most contain a huge diversity of organisms that maintain nutrient cycles—breaking down organic matter into nutrient compounds that crops need for growth. These organisms also maintain soil texture that affects water and oxygen dynamics in the soil that are necessary for plant growth. If farmers had to maintain arable soil using alternate means, the cost of food would be much higher than it is now. These kinds of processes are called ecosystem services. They occur within ecosystems, such as soil ecosystems, as a result of the diverse metabolic activities of the organisms living there, but they provide benefits to human food production, drinking water availability, and breathable air.

Other key ecosystem services related to food production are plant pollination and crop pest control. Over 150 crops in the United States require pollination to produce. One estimate of the benefit of honeybee pollination within the United States is $1.6 billion per year; other pollinators contribute up to $6.7 billion more.

Many honeybee populations are managed by apiarists who rent out their hives' services to farmers. Honeybee populations in North America have been suffering large losses caused by a syndrome known as colony collapse disorder, whose cause is unclear. Other pollinators include a diverse array of other bee species and various insects and birds. Loss of these species would make growing crops requiring pollination impossible, increasing dependence on other crops.

Finally, humans compete for their food with crop pests, most of which are insects. Pesticides control these competitors; however, pesticides are costly and lose their effectiveness over time as pest populations adapt. They also lead to collateral damage by killing non-pest species and risking the health of consumers and agricultural workers. Ecologists believe that the bulk of the work in removing pests is actually done by predators and parasites of those pests, but the impact has not been well studied. A review found that in 74 percent of studies that looked for an effect of landscape complexity on natural enemies of pests, the greater the complexity, the greater the effect of pest-suppressing organisms. An experimental study found that introducing multiple enemies of pea aphids (an important alfalfa pest) increased the yield of alfalfa significantly. This study shows the importance of landscape diversity via the question of whether a diversity of pests is more effective at control than one single pest; the results showed this to be the case. Loss of diversity in pest enemies will inevitably make it more difficult and costly to grow food.

Wild Food Sources

In addition to growing crops and raising animals for food, humans obtain food resources from wild populations, primarily fish populations. For approximately 1 billion people, aquatic resources provide the main source of animal protein. But since 1990, global fish production has declined. Despite considerable effort, few fisheries on the planet are managed for sustainability.

Fishery extinctions rarely lead to complete extinction of the harvested species, but rather to a radical restructuring of the marine ecosystem in which a dominant species is so over-

harvested that it becomes a minor player, ecologically. In addition to humans losing the food source, these alterations affect many other species in ways that are difficult or impossible to predict. The collapse of fisheries has dramatic and long-lasting effects on local populations that work in the fishery. In addition, the loss of an inexpensive protein source to populations that cannot afford to replace it will increase the cost of living and limit societies in other ways. In general, the fish taken from fisheries have shifted to smaller species as larger species are fished to extinction. The ultimate outcome could clearly be the loss of aquatic systems as food sources.

Link to Learning

View a brief video discussing declining fish stocks.

Psychological and Moral Value

Finally, it has been argued that humans benefit psychologically from living in a biodiverse world. A chief proponent of this idea is entomologist E. O. Wilson. He argues that human evolutionary history has adapted us to live in a natural environment and that built environments generate stressors that affect human health and well-being. There is considerable research into the psychological regenerative benefits of natural landscapes that suggests the hypothesis may hold some truth. In addition, there is a moral argument that humans have a responsibility to inflict as little harm as possible on other species.

Section Summary

Humans use many compounds that were first discovered or derived from living organisms as medicines: secondary plant compounds, animal toxins, and antibiotics produced by bacteria and fungi. More medicines are expected to be discovered in nature. Loss of biodiversity will impact the number of pharmaceuticals available to humans.

Crop diversity is a requirement for food security, and it is being lost. The loss of wild relatives to crops also threatens breeders' abilities to create new varieties. Ecosystems provide ecosystem services that support human agriculture: pollination, nutrient cycling, pest control, and soil development and maintenance. Loss of biodiversity threatens these ecosystem services and risks making food production more expensive or impossible. Wild food sources are mainly aquatic, but few are being managed for sustainability. Fisheries' ability to provide protein to human populations is threatened when extinction occurs.

Biodiversity may provide important psychological benefits to humans. Additionally, there are moral arguments for the maintenance of biodiversity.

Art Connections

[link] The Svalbard Global Seed Vault is located on Spitsbergen island in Norway, which has an arctic climate. Why might an arctic climate be good for seed storage?

[link] The ground is permanently frozen so the seeds will keep even if the electricity fails.

Review Questions

A secondary plant compound might be used for which of the following?

a. a new crop variety
b. a new drug
c. a soil nutrient
d. a pest of a crop pest

B

Pollination is an example of _____.

a. a possible source of new drugs
b. chemical diversity
c. an ecosystem service
d. crop pest control

C

What is an ecosystem service that performs the same function as a pesticide?

a. pollination
b. secondary plant compounds
c. crop diversity
d. predators of pests

D

Free Response

Explain how biodiversity loss can impact crop diversity.

Crop plants are derived from wild plants, and genes from wild relatives are frequently brought into crop varieties by plant breeders to add valued characteristics to the crops. If the wild species are lost, then this genetic variation would no longer be available.

Describe two types of compounds from living things that are used as medications.

Secondary plant compounds are toxins produced by plants to kill predators trying to eat them; some of these compounds can be used as drugs. Animal toxins such as snake venom can also be used as drugs. (Alternate answer: antibiotics are compounds produced by bacteria and fungi which can be used to kill bacteria.)

Glossary

secondary plant compound
: compound produced as byproducts of plant metabolic processes that is usually toxic, but is sequestered by the plant to defend against herbivores

Threats to Biodiversity

By the end of this section, you will be able to:

- Identify significant threats to biodiversity
- Explain the effects of habitat loss, exotic species, and hunting on biodiversity
- Identify the early and predicted effects of climate change on biodiversity

The core threat to biodiversity on the planet, and therefore a threat to human welfare, is the combination of human population growth and resource exploitation. The human population requires resources to survive and grow, and those resources are being removed unsustainably from the environment. The three greatest proximate threats to biodiversity are habitat loss, overharvesting, and introduction of exotic species. The first two of these are a direct result of human population growth and resource use. The third results from increased mobility and trade. A fourth major cause of extinction, anthropogenic climate change, has not yet had a large impact, but it is predicted to become significant during this century. Global climate change is also a consequence of human population needs for energy and the use of fossil fuels to meet those needs ([link]). Environmental issues, such as toxic pollution, have specific targeted effects on species, but they are not generally seen as threats at the magnitude of the others.

Atmospheric carbon dioxide levels fluctuate in a cyclical manner. However, the burning of fossil fuels in recent history has caused a dramatic increase in the levels of carbon dioxide in the Earth's atmosphere, which have now reached levels never before seen in human history. Scientists predict that the addition of this "greenhouse gas" to the atmosphere is resulting in

climate change that will significantly impact biodiversity in the coming

century.

Habitat Loss

Humans rely on technology to modify their environment and replace certain functions that were once performed by the natural ecosystem. Other species cannot do this. Elimination of their ecosystem—whether it is a forest, a desert, a grassland, a freshwater estuarine, or a marine environment—will kill the individuals in the species. Remove the entire habitat within the range of a species and, unless they are one of the few species that do well in human-built environments, the species will become extinct. Human destruction of habitats accelerated in the latter half of the twentieth century. Consider the exceptional biodiversity of Sumatra: it is home to one species of orangutan, a species of critically endangered elephant, and the Sumatran tiger, but half of Sumatra's forest is now gone. The neighboring island of Borneo, home to the other species of orangutan, has lost a similar area of forest. Forest loss continues in protected areas of Borneo. The orangutan in Borneo is listed as endangered by the International Union for Conservation of Nature (IUCN), but it is simply the most visible of thousands of species that will not survive the disappearance of the forests of Borneo. The forests are removed for timber and to plant palm oil plantations ([link]). Palm oil is used in many products including food products, cosmetics, and biodiesel in Europe. A five-year estimate of global forest cover loss for the years 2000–2005 was 3.1 percent. In the humid tropics where forest loss is primarily from timber extraction, 272,000 km^2 was lost out of a global total of 11,564,000 km^2 (or 2.4 percent). In the tropics, these losses certainly also represent the extinction of species because of high levels of endemism.

(a) One species of orangutan, *Pongo pygmaeus*, is found only in the rainforests of Borneo, and the other species of orangutan (*Pongo abelii*) is found only in the rainforests of Sumatra. These animals are examples of the exceptional biodiversity of (c) the islands of Sumatra and

Borneo. Other species include the (b) Sumatran tiger (*Panthera tigris sumatrae*) and the (d) Sumatran elephant (*Elephas maximus sumatranus*), both critically endangered species. Rainforest habitat is being removed to make way for (e) oil palm plantations such as this one in Borneo's Sabah Province. (credit a: modification of work by Thorsten Bachner; credit b: modification of work by Dick Mudde; credit c: modification of work by U.S. CIA World Factbook; credit d: modification of work by "Nonprofit Organizations"/Flickr; credit e: modification of work by Dr. Lian Pin

Koh)
Everyday Connection

Preventing Habitat Destruction with Wise Wood ChoicesMost consumers do not imagine that the home improvement products they buy might be contributing to habitat loss and species extinctions. Yet the market for illegally harvested tropical timber is huge, and the wood products often find themselves in building supply stores in the United States. One estimate is that 10 percent of the imported timber stream in the United States, which is the world's largest consumer of wood products, is potentially illegally logged. In 2006, this amounted to $3.6 billion in wood products. Most of the illegal products are imported from countries that act as intermediaries and are not the originators of the wood.

How is it possible to determine if a wood product, such as flooring, was harvested sustainably or even legally? The Forest Stewardship Council (FSC) certifies sustainably harvested forest products, therefore, looking for their certification on flooring and other hardwood products is one way to ensure that the wood has not been taken illegally from a tropical forest. Certification applies to specific products, not to a producer; some producers' products may not have certification while other products are certified. While there are other industry-backed certifications other than the FSC, these are unreliable due to lack of independence from the industry. Another approach is to buy domestic wood species. While it would be great if there was a list of legal versus illegal wood products, it is not that simple. Logging and forest management laws vary from country to country; what is illegal in one country may

be legal in another. Where and how a product is harvested and whether the forest from which it comes is being maintained sustainably all factor into whether a wood product will be certified by the FSC. It is always a good idea to ask questions about where a wood product came from and how the supplier knows that it was harvested legally.

Habitat destruction can affect ecosystems other than forests. Rivers and streams are important ecosystems and are frequently modified through land development and from damming or water removal. Damming of rivers affects the water flow and access to all parts of a river. Differing flow regimes can reduce or eliminate populations that are adapted to these changes in flow patterns. For example, an estimated 91percent of river lengths in the United States have been developed: they have modifications like dams, to create energy or store water; levees, to prevent flooding; or dredging or rerouting, to create land that is more suitable for human development. Many fish species in the United States, especially rare species or species with restricted distributions, have seen declines caused by river damming and habitat loss. Research has confirmed that species of amphibians that must carry out parts of their life cycles in both aquatic and terrestrial habitats have a greater chance of suffering population declines and extinction because of the increased likelihood that one of their habitats or access between them will be lost.

Overharvesting

Overharvesting is a serious threat to many species, but particularly to aquatic species. There are many examples of regulated commercial fisheries monitored by fisheries scientists that have nevertheless collapsed. The western Atlantic cod fishery is the most spectacular recent collapse. While it was a hugely productive fishery for 400 years, the introduction of modern factory trawlers in the 1980s and the pressure on the fishery led to it becoming unsustainable. The causes of fishery collapse are both economic and political in nature. Most fisheries are managed as a common (shared) resource even when the fishing territory lies within a country's territorial waters. Common resources are subject to an economic pressure known as the tragedy of the commons in which essentially no fisher has a motivation to exercise restraint in harvesting a fishery when it is not owned by that fisher. The natural outcome of harvests of resources held in common is their overexploitation. While large fisheries are regulated to attempt to avoid this pressure, it still exists in the background. This overexploitation is exacerbated when access to the fishery is open and unregulated and when technology gives fishers the ability to overfish. In a few fisheries, the biological growth of the resource is less than the potential growth of the profits made from fishing if that time and money were invested elsewhere. In these cases—whales are an example—economic forces will always drive toward fishing the population to extinction.

Link to Learning

Explore a U.S. Fish & Wildlife Service interactive map of critical habitat for endangered and threatened species in the United States. To begin, select "Visit the online mapper."

For the most part, fishery extinction is not equivalent to biological extinction—the last fish of a species is rarely fished out of the ocean. At the same time, fishery extinction is still harmful to fish species and their ecosystems. There are some instances in which true extinction is a possibility. Whales have slow-growing populations and are at risk of complete extinction through hunting. There are some species of sharks with restricted distributions that are at risk of extinction. The groupers are another population of generally slow-growing fishes that, in the Caribbean, includes a number of species that are at risk of extinction from overfishing.

Coral reefs are extremely diverse marine ecosystems that face peril from several processes. Reefs are home to 1/3 of the world's marine fish species—about 4,000 species—despite making up only 1 percent of marine habitat. Most home marine aquaria are stocked with wild-caught organisms, not cultured organisms. Although no species is known to have been driven extinct by the pet trade in marine species, there are studies showing that populations of some species have declined in response to harvesting, indicating that the harvest is not sustainable at those levels. There are concerns about the effect of the pet trade on some terrestrial species such as turtles, amphibians, birds, plants, and even the orangutan.

Link to Learning

View a brief video discussing the role of marine ecosystems in supporting human welfare and the decline of ocean ecosystems.

Bush meat is the generic term used for wild animals killed for food. Hunting is practiced throughout the world, but hunting practices, particularly in equatorial Africa and parts of Asia, are believed to threaten several species with extinction. Traditionally, bush meat in Africa was hunted to feed families directly; however, recent commercialization of the practice now has bush meat available in grocery stores, which has increased harvest rates to the level of unsustainability. Additionally, human population growth has increased the need for protein foods that are not being met from agriculture. Species threatened by the bush meat trade are mostly mammals including many primates living in the Congo basin.

Exotic Species

Exotic species are species that have been intentionally or unintentionally introduced by humans into an ecosystem in which they did not evolve. Such introductions likely occur frequently as natural phenomena. For example, Kudzu (*Pueraria lobata*), which is native to Japan, was introduced in the United States in 1876. It was later planted for soil conservation. Problematically, it grows too well in the southeastern United States—up to a foot a day. It is now a pest species and covers over 7 million acres in the southeastern United States. If an introduced species is able to survive in its new habitat, that introduction is now reflected in the observed range of the species. Human transportation of people and goods, including the intentional transport of organisms for trade, has dramatically increased the introduction of

species into new ecosystems, sometimes at distances that are well beyond the capacity of the species to ever travel itself and outside the range of the species' natural predators.

Most exotic species introductions probably fail because of the low number of individuals introduced or poor adaptation to the ecosystem they enter. Some species, however, possess preadaptations that can make them especially successful in a new ecosystem. These exotic species often undergo dramatic population increases in their new habitat and reset the ecological conditions in the new environment, threatening the species that exist there. For this reason, exotic species are also called invasive species. Exotic species can threaten other species through competition for resources, predation, or disease.

Link to Learning

Explore an interactive global database of exotic or invasive species.

Lakes and islands are particularly vulnerable to extinction threats from introduced species. In Lake Victoria, as mentioned earlier, the intentional introduction of the Nile perch was largely responsible for the extinction of about 200 species of cichlids. The accidental introduction of the brown tree snake via aircraft ([link]) from the Solomon Islands to Guam in 1950 has led to the extinction of three species of birds and three to five species of reptiles endemic to the island. Several other species are still threatened. The brown tree snake is adept at exploiting human transportation as a means to migrate; one was even found on an aircraft arriving in Corpus Christi, Texas. Constant vigilance on the part of airport, military, and commercial aircraft personnel is required to prevent the snake from moving from Guam to other islands in the Pacific, especially Hawaii. Islands do not make up a large area of land on the globe, but they do contain a disproportionate number of endemic species because of their isolation from mainland ancestors.

The brown tree snake, *Boiga irregularis*, is an exotic species that has caused numerous extinctions on the island of Guam since its accidental introduction in 1950. (credit:

NPS)

It now appears that the global decline in amphibian species recognized in the 1990s is, in some part, caused by the fungus *Batrachochytrium dendrobatidis*, which causes the disease chytridiomycosis ([link]). There is evidence that the fungus is native to Africa and may have been spread throughout the world by transport of a commonly used laboratory and pet species: the African clawed toad (*Xenopus laevis*). It may well be that biologists themselves are responsible for spreading this disease worldwide. The North American bullfrog, *Rana catesbeiana*, which has also been widely introduced as a food animal but which easily escapes captivity, survives most infections of *Batrachochytrium dendrobatidis* and can act as a reservoir for the disease.

This Limosa Harlequin Frog (*Atelopus limosus*), an endangered species from Panama, died from a fungal disease called chytridiomycosis. The red lesions are symptomatic of the

disease. (credit: Brian Gratwicke)

Early evidence suggests that another fungal pathogen, *Geomyces destructans*, introduced from Europe is responsible for white-nose syndrome, which infects cave-hibernating bats in eastern North America and has spread from a point of origin in western New York State ([link]). The disease has decimated bat populations and threatens extinction of species already listed as endangered: the Indiana bat, *Myotis sodalis*, and potentially the Virginia big-eared bat, *Corynorhinus townsendii virginianus*. How the fungus was introduced is unclear, but one logical presumption would be that recreational cavers unintentionally brought the fungus on clothes or equipment from Europe.

This little brown bat in Greeley Mine, Vermont, March 26, 2009, was found to have white-nose syndrome. (credit: Marvin Moriarty,

USFWS)

Climate Change

Climate change, and specifically the anthropogenic (meaning, caused by humans) warming trend presently underway, is recognized as a major extinction threat, particularly when combined with other threats such as habitat loss. Scientists disagree about the likely magnitude of the effects, with extinction rate estimates ranging from 15 percent to 40 percent of species committed to extinction by 2050. Scientists do agree, however, that climate change will alter regional climates, including rainfall and snowfall patterns, making habitats less hospitable to the species living in them. The warming trend will shift colder climates toward the north and south poles, forcing species to move with their adapted climate norms while facing habitat gaps along the way. The shifting ranges will impose new competitive regimes on species as they find themselves in contact with other species not present in their historic range. One such unexpected species contact is between polar bears and grizzly bears. Previously, these two species had separate ranges. Now, their ranges are overlapping and there are documented cases of these two species mating and producing viable offspring. Changing climates also throw off species' delicate timing adaptations to seasonal food resources and breeding times. Many contemporary mismatches to shifts in resource availability and timing have already been documented.

Since 2008, grizzly bears (*Ursus arctos horribilis*) have been spotted farther north than their historic range, a possible consequence of climate change. As a result, grizzly bear habitat now overlaps polar bear (*Ursus maritimus*) habitat. The two kinds of bears, which are capable

of mating and producing viable offspring, are considered separate species as historically they lived in different habitats and never met. However, in 2006 a hunter shot a wild grizzly-polar bear hybrid known as a grolar bear, the first wild hybrid ever

found.

Range shifts are already being observed: for example, some European bird species ranges have moved 91 km northward. The same study suggested that the optimal shift based on warming trends was double that distance, suggesting that the populations are not moving quickly enough. Range shifts have also been observed in plants, butterflies, other insects, freshwater fishes, reptiles, and mammals.

Climate gradients will also move up mountains, eventually crowding species higher in altitude and eliminating the habitat for those species adapted to the highest elevations. Some climates will completely disappear. The rate of warming appears to be accelerated in the arctic, which is recognized as a serious threat to polar bear populations that require sea ice to hunt seals during the winter months: seals are the only source of protein available to polar bears. A trend to decreasing sea ice coverage has occurred since observations began in the mid-twentieth century. The rate of decline observed in recent years is far greater than previously predicted by climate models.

Finally, global warming will raise ocean levels due to melt water from glaciers and the greater volume of warmer water. Shorelines will be inundated, reducing island size, which will have an effect on some species, and a number of islands will disappear entirely. Additionally, the gradual melting and subsequent refreezing of the poles, glaciers, and higher elevation mountains—a cycle that has provided freshwater to environments for centuries—will also be jeopardized. This could result in an overabundance of salt water and a shortage of fresh water.

Section Summary

The core threats to biodiversity are human population growth and unsustainable resource use. To date, the most significant causes of extinctions are habitat loss, introduction of exotic species, and overharvesting. Climate change is predicted to be a significant cause of

extinctions in the coming century. Habitat loss occurs through deforestation, damming of rivers, and other activities. Overharvesting is a threat particularly to aquatic species, while the taking of bush meat in the humid tropics threatens many species in Asia, Africa, and the Americas. Exotic species have been the cause of a number of extinctions and are especially damaging to islands and lakes. Exotic species' introductions are increasing because of the increased mobility of human populations and growing global trade and transportation. Climate change is forcing range changes that may lead to extinction. It is also affecting adaptations to the timing of resource availability that negatively affects species in seasonal environments. The impacts of climate change are greatest in the arctic. Global warming will also raise sea levels, eliminating some islands and reducing the area of all others.

Art Connections

Converting a prairie to a farm field is an example of _____.

a. overharvesting
b. habitat loss
c. exotic species
d. climate change

B

Review Questions

Which two extinction risks may be a direct result of the pet trade?

a. climate change and exotic species introduction
b. habitat loss and overharvesting
c. overharvesting and exotic species introduction
d. habitat loss and climate change

C

Exotic species are especially threatening to what kind of ecosystem?

a. deserts
b. marine ecosystems
c. islands
d. tropical forests

C

Free Response

Describe the mechanisms by which human population growth and resource use causes increased extinction rates.

Human population growth leads to unsustainable resource use, which causes habitat destruction to build new human settlements, create agricultural fields, and so on. Larger

human populations have also led to unsustainable fishing and hunting of wild animal populations. Excessive use of fossil fuels also leads to global warming.

Explain what extinction threats a frog living on a mountainside in Costa Rica might face.

The frog is at risk from global warming shifting its preferred habitat up the mountain. In addition, it will be at risk from exotic species, either as a new predator or through the impact of transmitted diseases such as chytridiomycosis. It is also possible that habitat destruction will threaten the species.

Glossary

bush meat
: wild-caught animal used as food (typically mammals, birds, and reptiles); usually referring to hunting in the tropics of sub-Saharan Africa, Asia, and the Americas

chytridiomycosis
: disease of amphibians caused by the fungus *Batrachochytrium dendrobatidis;* thought to be a major cause of the global amphibian decline

exotic species
: (also, invasive species) species that has been introduced to an ecosystem in which it did not evolve

tragedy of the commons
: economic principle that resources held in common will inevitably be overexploited

white-nose syndrome
: disease of cave-hibernating bats in the eastern United States and Canada associated with the fungus *Geomyces destructans*

Preserving Biodiversity

By the end of this section, you will be able to:

- Identify new technologies for describing biodiversity
- Explain the legislative framework for conservation
- Describe principles and challenges of conservation preserve design
- Identify examples of the effects of habitat restoration
- Discuss the role of zoos in biodiversity conservation

Preserving biodiversity is an extraordinary challenge that must be met by greater understanding of biodiversity itself, changes in human behavior and beliefs, and various preservation strategies.

Measuring Biodiversity

The technology of molecular genetics and data processing and storage are maturing to the point where cataloguing the planet's species in an accessible way is close to feasible. DNA barcoding is one molecular genetic method, which takes advantage of rapid evolution in a

mitochondrial gene present in eukaryotes, excepting the plants, to identify species using the sequence of portions of the gene. Plants may be barcoded using a combination of chloroplast genes. Rapid mass sequencing machines make the molecular genetics portion of the work relatively inexpensive and quick. Computer resources store and make available the large volumes of data. Projects are currently underway to use DNA barcoding to catalog museum specimens, which have already been named and studied, as well as testing the method on less studied groups. As of mid 2012, close to 150,000 named species had been barcoded. Early studies suggest there are significant numbers of undescribed species that looked too much like sibling species to previously be recognized as different. These now can be identified with DNA barcoding.

Numerous computer databases now provide information about named species and a framework for adding new species. However, as already noted, at the present rate of description of new species, it will take close to 500 years before the complete catalog of life is known. Many, perhaps most, species on the planet do not have that much time.

There is also the problem of understanding which species known to science are threatened and to what degree they are threatened. This task is carried out by the non-profit IUCN which, as previously mentioned, maintains the Red List—an online listing of endangered species categorized by taxonomy, type of threat, and other criteria ([link]). The Red List is supported by scientific research. In 2011, the list contained 61,000 species, all with supporting documentation.

Art Connection
This chart shows the percentage of various animal species, by group, on the IUCN Red List as of 2007.

Which of the following statements is not supported by this graph?

a. There are more vulnerable fishes than critically endangered and endangered fishes combined.
b. There are more critically endangered amphibians than vulnerable, endangered and critically endangered reptiles combined.
c. Within each group, there are more critically endangered species than vulnerable species.
d. A greater percentage of bird species are critically endangered than mollusk species.

Changing Human Behavior

Legislation throughout the world has been enacted to protect species. The legislation includes international treaties as well as national and state laws. The Convention on International Trade in Endangered Species of Wild Fauna and Flora (CITES) treaty came into force in 1975. The treaty, and the national legislation that supports it, provides a legal framework for preventing approximately 33,000 listed species from being transported across nations' borders, thus protecting them from being caught or killed when international trade is involved. The treaty is limited in its reach because it only deals with international movement of organisms or their parts. It is also limited by various countries' ability or willingness to enforce the treaty and supporting legislation. The illegal trade in organisms and their parts is probably a market in the hundreds of millions of dollars. Illegal wildlife trade is monitored by another non-profit: Trade Records Analysis of Flora and Fauna in Commerce (TRAFFIC).

Within many countries there are laws that protect endangered species and regulate hunting and fishing. In the United States, the Endangered Species Act (ESA) was enacted in 1973. Species at risk are listed by the Act; the U.S. Fish & Wildlife Service is required by law to develop management plans that protect the listed species and bring them back to sustainable numbers. The Act, and others like it in other countries, is a useful tool, but it suffers because it is often difficult to get a species listed, or to get an effective management plan in place once it is listed. Additionally, species may be controversially taken off the list without necessarily having had a change in their situation. More fundamentally, the approach to protecting individual species rather than entire ecosystems is both inefficient and focuses efforts on a few highly visible and often charismatic species, perhaps at the expense of other species that go unprotected. At the same time, the Act has a critical habitat provision outlined in the recovery mechanism that may benefit species other than the one targeted for management.

The Migratory Bird Treaty Act (MBTA) is an agreement between the United States and Canada that was signed into law in 1918 in response to declines in North American bird species caused by hunting. The Act now lists over 800 protected species. It makes it illegal to disturb or kill the protected species or distribute their parts (much of the hunting of birds in the past was for their feathers).

The international response to global warming has been mixed. The Kyoto Protocol, an international agreement that came out of the United Nations Framework Convention on Climate Change that committed countries to reducing greenhouse gas emissions by 2012, was ratified by some countries, but spurned by others. Two important countries in terms of their potential impact that did not ratify the Kyoto Protocol were the United States and China. The United States rejected it as a result of a powerful fossil fuel industry and China because of a concern it would stifle the nation's growth. Some goals for reduction in greenhouse gasses were met and exceeded by individual countries, but worldwide, the effort to limit greenhouse gas production is not succeeding. The intended replacement for the Kyoto Protocol has not materialized because governments cannot agree on timelines and benchmarks. Meanwhile, climate scientists predict the resulting costs to human societies and biodiversity will be high.

As already mentioned, the private non-profit sector plays a large role in the conservation effort both in North America and around the world. The approaches range from species-specific organizations to the broadly focused IUCN and TRAFFIC. The Nature Conservancy takes a novel approach. It purchases land and protects it in an attempt to set up preserves for

ecosystems. Ultimately, human behavior will change when human values change. At present, the growing urbanization of the human population is a force that poses challenges to the valuing of biodiversity.

Conservation in Preserves

Establishment of wildlife and ecosystem preserves is one of the key tools in conservation efforts. A preserve is an area of land set aside with varying degrees of protection for the organisms that exist within the boundaries of the preserve. Preserves can be effective in the short term for protecting both species and ecosystems, but they face challenges that scientists are still exploring to strengthen their viability as long-term solutions.

How Much Area to Preserve?

Due to the way protected lands are allocated (they tend to contain less economically valuable resources rather than being set aside specifically for the species or ecosystems at risk) and the way biodiversity is distributed, determining a target percentage of land or marine habitat that should be protected to maintain biodiversity levels is challenging. The IUCN World Parks Congress estimated that 11.5 percent of Earth's land surface was covered by preserves of various kinds in 2003. This area is greater than previous goals; however, it only represents 9 out of 14 recognized major biomes. Research has shown that 12 percent of all species live only outside preserves; these percentages are much higher when only threatened species and high quality preserves are considered. For example, high quality preserves include only about 50 percent of threatened amphibian species. The conclusion must be that either the percentage of area protected must increase, or the percentage of high quality preserves must increase, or preserves must be targeted with greater attention to biodiversity protection. Researchers argue that more attention to the latter solution is required.

Preserve Design

There has been extensive research into optimal preserve designs for maintaining biodiversity. The fundamental principle behind much of the research has been the seminal theoretical work of Robert H. MacArthur and Edward O. Wilson published in 1967 on island biogeography.[1] This work sought to understand the factors affecting biodiversity on islands. The fundamental conclusion was that biodiversity on an island was a function of the origin of species through migration, speciation, and extinction on that island. Islands farther from a mainland are harder to get to, so migration is lower and the equilibrium number of species is lower. Within island populations, evidence suggests that the number of species gradually increases to a level similar to the numbers on the mainland from which the species is suspected to have migrated. In addition, smaller islands are harder to find, so their immigration rates for new species are lower. Smaller islands are also less geographically diverse so there are fewer niches to promote speciation. And finally, smaller islands support smaller populations, so the probability of extinction is higher.

As islands get larger, the number of species accelerates, although the effect of island area on species numbers is not a direct correlation. Conservation preserves can be seen as "islands" of habitat within "an ocean" of non-habitat. For a species to persist in a preserve, the preserve must be large enough. The critical size depends, in part, on the home range that is characteristic of the species. A preserve for wolves, which range hundreds of kilometers, must be much larger than a preserve for butterflies, which might range within ten kilometers

during its lifetime. But larger preserves have more core area of optimal habitat for individual species, they have more niches to support more species, and they attract more species because they can be found and reached more easily.

Preserves perform better when there are buffer zones around them of suboptimal habitat. The buffer allows organisms to exit the boundaries of the preserve without immediate negative consequences from predation or lack of resources. One large preserve is better than the same area of several smaller preserves because there is more core habitat unaffected by edges. For this same reason, preserves in the shape of a square or circle will be better than a preserve with many thin "arms." If preserves must be smaller, then providing wildlife corridors between them so that individuals and their genes can move between the preserves, for example along rivers and streams, will make the smaller preserves behave more like a large one. All of these factors are taken into consideration when planning the nature of a preserve before the land is set aside.

In addition to the physical, biological, and ecological specifications of a preserve, there are a variety of policy, legislative, and enforcement specifications related to uses of the preserve for functions other than protection of species. These can include anything from timber extraction, mineral extraction, regulated hunting, human habitation, and nondestructive human recreation. Many of these policy decisions are made based on political pressures rather than conservation considerations. In some cases, wildlife protection policies have been so strict that subsistence-living indigenous populations have been forced from ancestral lands that fell within a preserve. In other cases, even if a preserve is designed to protect wildlife, if the protections are not or cannot be enforced, the preserve status will have little meaning in the face of illegal poaching and timber extraction. This is a widespread problem with preserves in areas of the tropics.

Limitations on Preserves

Some of the limitations on preserves as conservation tools are evident from the discussion of preserve design. Political and economic pressures typically make preserves smaller, never larger, so setting aside areas that are large enough is difficult. If the area set aside is sufficiently large, there may not be sufficient area to create a buffer around the preserve. In this case, an area on the outer edges of the preserve inevitably becomes a riskier suboptimal habitat for the species in the preserve. Enforcement of protections is also a significant issue in countries without the resources or political will to prevent poaching and illegal resource extraction.

Climate change will create inevitable problems with the location of preserves. The species within them will migrate to higher latitudes as the habitat of the preserve becomes less favorable. Scientists are planning for the effects of global warming on future preserves and striving to predict the need for new preserves to accommodate anticipated changes to habitats; however, the end effectiveness is tenuous since these efforts are prediction based.

Finally, an argument can be made that conservation preserves reinforce the cultural perception that humans are separate from nature, can exist outside of it, and can only operate in ways that do damage to biodiversity. Creating preserves reduces the pressure on human activities outside the preserves to be sustainable and non-damaging to biodiversity. Ultimately, the political, economic, and human demographic pressures will degrade and

reduce the size of conservation preserves if the activities outside them are not altered to be less damaging to biodiversity.

Link to Learning

An interactive global data system of protected areas can be found at website. Review data about individual protected areas by location or study statistics on protected areas by country or region.

Habitat Restoration

Habitat restoration holds considerable promise as a mechanism for restoring and maintaining biodiversity. Of course once a species has become extinct, its restoration is impossible. However, restoration can improve the biodiversity of degraded ecosystems. Reintroducing wolves, a top predator, to Yellowstone National Park in 1995 led to dramatic changes in the ecosystem that increased biodiversity. The wolves ([link]) function to suppress elk and coyote populations and provide more abundant resources to the guild of carrion eaters. Reducing elk populations has allowed revegetation of riparian areas, which has increased the diversity of species in that habitat. Decreasing the coyote population has increased the populations of species that were previously suppressed by this predator. The number of species of carrion eaters has increased because of the predatory activities of the wolves. In this habitat, the wolf is a keystone species, meaning a species that is instrumental in maintaining diversity in an ecosystem. Removing a keystone species from an ecological community may cause a collapse in diversity. The results from the Yellowstone experiment suggest that restoring a keystone species can have the effect of restoring biodiversity in the community. Ecologists have argued for the identification of keystone species where possible and for focusing protection efforts on those species; likewise, it also makes sense to attempt to return them to their ecosystem if they have been removed.

(a) The Gibbon wolf pack in Yellowstone National Park, March 1, 2007, represents a keystone species. The reintroduction of wolves into Yellowstone National Park in 1995 led to a change in the grazing behavior of (b) elk. To avoid predation, the elk no longer grazed exposed stream and riverbeds, such as (c) the Lamar Riverbed in Yellowstone. This allowed willow and cottonwood seedlings to grow. The seedlings decreased erosion and provided shading to the creek, which improved fish habitat. A new colony of (d) beaver may also have benefited from the habitat change. (credit a: modification of work by Doug Smith, NPS;

credit c: modification of work by Jim Peaco, NPS; credit d: modification of work by “Shiny Things”/Flickr)

Other large-scale restoration experiments underway involve dam removal. In the United States, since the mid-1980s, many aging dams are being considered for removal rather than replacement because of shifting beliefs about the ecological value of free-flowing rivers and because many dams no longer provide the benefit and functions that they did when they were first built. The measured benefits of dam removal include restoration of naturally fluctuating water levels (the purpose of dams is frequently to reduce variation in river flows), which leads to increased fish diversity and improved water quality. In the Pacific Northwest, dam removal projects are expected to increase populations of salmon, which is considered a keystone species because it transports key nutrients to inland ecosystems during its annual spawning migrations. In other regions such as the Atlantic coast, dam removal has allowed the return of spawning anadromous fish species (species that are born in fresh water, live most of their lives in salt water, and return to fresh water to spawn). Some of the largest dam removal projects have yet to occur or have happened too recently for the consequences to be measured. The large-scale ecological experiments that these removal projects constitute will provide valuable data for other dam projects slated either for removal or construction.

The Role of Captive Breeding

Zoos have sought to play a role in conservation efforts both through captive breeding programs and education. The transformation of the missions of zoos from collection and exhibition facilities to organizations that are dedicated to conservation is ongoing. In general, it has been recognized that, except in some specific targeted cases, captive breeding programs for endangered species are inefficient and often prone to failure when the species are reintroduced to the wild. Zoo facilities are far too limited to contemplate captive breeding programs for the numbers of species that are now at risk. Education is another potential

positive impact of zoos on conservation efforts, particularly given the global trend to urbanization and the consequent reduction in contacts between people and wildlife. A number of studies have been performed to look at the effectiveness of zoos on people's attitudes and actions regarding conservation; at present, the results tend to be mixed.

Section Summary

New technological methods such as DNA barcoding and information processing and accessibility are facilitating the cataloging of the planet's biodiversity. There is also a legislative framework for biodiversity protection. International treaties such as CITES regulate the transportation of endangered species across international borders. Legislation within individual countries protecting species and agreements on global warming have had limited success; there is at present no international agreement on targets for greenhouse gas emissions. In the United States, the Endangered Species Act protects listed species but is hampered by procedural difficulties and a focus on individual species. The Migratory Bird Act is an agreement between Canada and the United States to protect migratory birds. The non-profit sector is also very active in conservation efforts in a variety of ways.

Conservation preserves are a major tool in biodiversity protection. Presently, 11percent of Earth's land surface is protected in some way. The science of island biogeography has informed the optimal design of preserves; however, preserves have limitations imposed by political and economic forces. In addition, climate change will limit the effectiveness of preserves in the future. A downside of preserves is that they may lessen the pressure on human societies to function more sustainably outside the preserves.

Habitat restoration has the potential to restore ecosystems to previous biodiversity levels before species become extinct. Examples of restoration include reintroduction of keystone species and removal of dams on rivers. Zoos have attempted to take a more active role in conservation and can have a limited role in captive breeding programs. Zoos also may have a useful role in education.

Art Connections

[link] Which of the following statements is not supported by this graph?

a. There are more vulnerable fishes than critically endangered and endangered fishes combined.
b. There are more critically endangered amphibians than vulnerable, endangered and critically endangered reptiles combined.
c. Within each group, there are more critically endangered species than vulnerable species.
d. A greater percentage of bird species are critically endangered than mollusk species.

[link] C

Review Questions

Certain parrot species cannot be brought to the United States to be sold as pets. What is the name of the legislation that makes this illegal?

a. Red List
b. Migratory Bird Act
c. CITES
d. Endangered Species Act (ESA)

C

What was the name of the first international agreement on climate change?

a. Red List
b. Montreal Protocol
c. International Union for the Conservation of Nature (IUCN)
d. Kyoto Protocol

D

About what percentage of land on the planet is set aside as a preserve of some type?

a. 1 percent
b. 6 percent
c. 11 percent
d. 15 percent

C

Free Response

Describe two considerations in conservation preserve design.

Larger preserves will contain more species. Preserves should have a buffer around them to protect species from edge effects. Preserves that are round or square are better than preserves with many thin arms.

Describe what happens to an ecosystem when a keystone species is removed.

When a keystone species is removed many species will disappear from the ecosystem.

Footnotes

- 1 Robert H. MacArthur and Edward O. Wilson, E. O., *The Theory of Island Biogeography* (Princeton, N.J.: Princeton University Press, 1967).

Glossary

DNA barcoding
: molecular genetic method for identifying a unique genetic sequence to associate with a species

Preface

Biology is designed for multi-semester biology courses for science majors. It is grounded on an evolutionary basis and includes exciting features that highlight careers in the biological sciences and everyday applications of the concepts at hand. To meet the needs of today's instructors and students, some content has been strategically condensed while maintaining the overall scope and coverage of traditional texts for this course. Instructors can customize the book, adapting it to the approach that works best in their classroom. Biology also includes an innovative art program that incorporates critical thinking and clicker questions to help students understand—and apply—key concepts.

Welcome to *Biology*, an OpenStax resource. This textbook was written to increase student access to high-quality learning materials, maintaining highest standards of academic rigor at little to no cost.

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Format

You can access this textbook for free in web view or PDF through openstax.org, and in low-cost print and iBooks editions.

About Biology

Biology is designed to cover the scope and sequence requirements of a typical two-semester biology course for science majors. The text provides comprehensive coverage of foundational research and core biology concepts through an evolutionary lens. *Biology* includes rich features that engage students in scientific inquiry, highlight careers in the biological sciences, and offer everyday applications. The book also includes clicker questions to help students understand—and apply—key concepts.

Coverage and Scope

In developing *Biology*, we listened to hundreds of General Biology instructors who readily provided feedback about their courses, students, challenges, and hopes for innovation. The expense of textbooks and related items did prove to be a barrier to learning. But more importantly, these teachers suggested improvements for the textbook, which would ultimately lead to more meaningful and memorable learning experiences for students.

The result is a book that addresses a core organizational reality of the course and its materials—the sheer breadth of the topical coverage. We provide a thorough treatment of biology's foundational concepts while condensing selected topics in response to the market's request for a textbook with a scope that is manageable for instructors and students alike. We also strive to make biology, as a discipline, interesting and accessible to students. In addition to a comprehensive coverage of core concepts and foundational research, we have incorporated features that draw learners into the discipline in meaningful ways.

The pedagogical choices, chapter arrangements, and learning objective fulfillment were developed and vetted with the feedback of another one hundred reviewers, who thoroughly read the material and offered detailed critical commentary.

- Unit 1: **The Chemistry of Life**. Our opening unit introduces students to the sciences, including the scientific method and the fundamental concepts of chemistry and physics that provide a framework within which learners comprehend biological processes.
- Unit 2: **The Cell**. Students will gain solid understanding of the structures, functions, and processes of the most basic unit of life: the cell.
- Unit 3: **Genetics**. Our comprehensive genetics unit takes learners from the earliest experiments that revealed the basis of genetics through the intricacies of DNA to current applications in the emerging studies of biotechnology and genomics.
- Unit 4: **Evolutionary Processes**. The core concepts of evolution are discussed in this unit with examples illustrating evolutionary processes. Additionally, the evolutionary basis of biology reappears throughout the textbook in general discussion and is

reinforced through special call-out features highlighting specific evolution-based topics.

- Unit 5: **Biological Diversity**. The diversity of life is explored with detailed study of various organisms and discussion of emerging phylogenetic relationships. This unit moves from viruses to living organisms like bacteria, discusses the organisms formerly grouped as protists, and devotes multiple chapters to plant and animal life.
- Unit 6: **Plant Structure and Function**. Our plant unit thoroughly covers the fundamental knowledge of plant life essential to an introductory biology course.
- Unit 7: **Animal Structure and Function**. An introduction to the form and function of the animal body is followed by chapters on specific body systems and processes. This unit touches on the biology of all organisms while maintaining an engaging focus on human anatomy and physiology that helps students connect to the topics.
- Unit 8: **Ecology**. Ecological concepts are broadly covered in this unit, with features highlighting localized, real-world issues of conservation and biodiversity.

Pedagogical Foundation and Features

Biology is grounded in a solid scientific base, with features that engage the students in scientific inquiry, including:

- **Evolution Connection** features uphold the importance of evolution to all biological study through discussions like "The Evolution of Metabolic Pathways" and "Algae and Evolutionary Paths to Photosynthesis."
- **Scientific Method Connection** call-outs walk students through actual or thought experiments that elucidate the steps of the scientific process as applied to the topic. Features include "Determining the Time Spent in Cell Cycle Stages" and "Testing the Hypothesis of Independent Assortment."
- **Career Connection** features present information on a variety of careers in the biological sciences, introducing students to the educational requirements and day-to-day work life of a variety of professions, such as microbiologist, ecologist, neurologist, and forensic scientist.
- **Everyday Connection** features tie biological concepts to emerging issues and discuss science in terms of everyday life. Topics include "Chesapeake Bay" and "Can Snail Venom Be Used as a Pharmacological Pain Killer?"

Art and Animations That Engage

Our art program takes a straightforward approach designed to help students learn the concepts of biology through simple, effective illustrations, photos, and micrographs. *Biology* also incorporates links to relevant animations and interactive exercises that help bring biology to life for students.

- **Art Connection** features call out core figures in each chapter for student study. Questions about key figures, including clicker questions that can be used in the classroom, engage students' critical thinking to ensure genuine understanding.
- **Link to Learning** features direct students to online interactive exercises and animations to add a fuller context to core content.

Additional Resources

Student and Instructor ResourcesWe've compiled additional resources for both students and instructors, including Getting Started Guides, an instructor solution manual, supplemental test items, and PowerPoint slides. Instructor resources require a verified instructor account, which can be requested on your openstax.org log-in. Take advantage of these resources to supplement your OpenStax book.

Partner ResourcesOpenStax Partners are our allies in the mission to make high-quality learning materials affordable and accessible to students and instructors everywhere. Their tools integrate seamlessly with our OpenStax titles at a low cost. To access the partner resources for your text, visit your book page on openstax.org.

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