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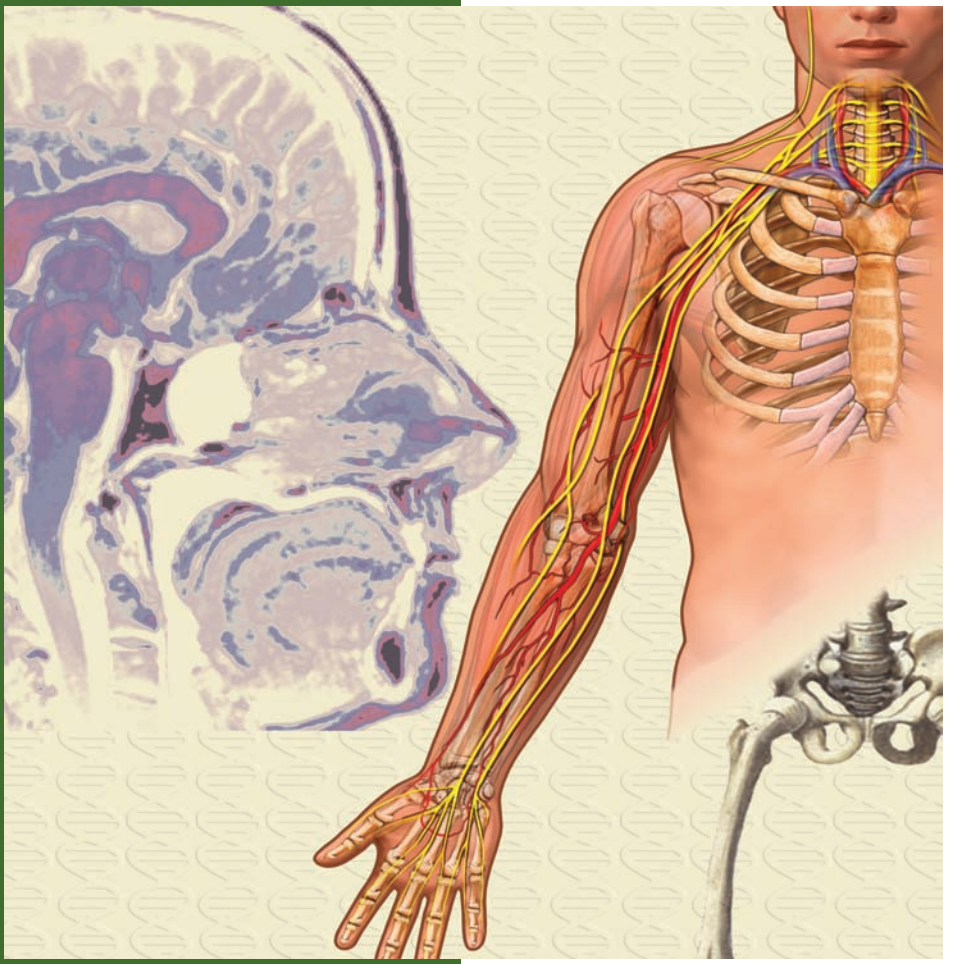
HUMAN ANATOMY:
THE BEAUTY OF FORM AND FUNCTION

COURSE GUIDE



Professor John K. Young

HOWARD UNIVERSITY
COLLEGE OF MEDICINE

Human Anatomy:
The Beauty of Form and Function

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Course Syllabus

Human Anatomy: The Beauty of Form and Function

Photo courtesy of John K. Young

About Your Professor

John K. Young

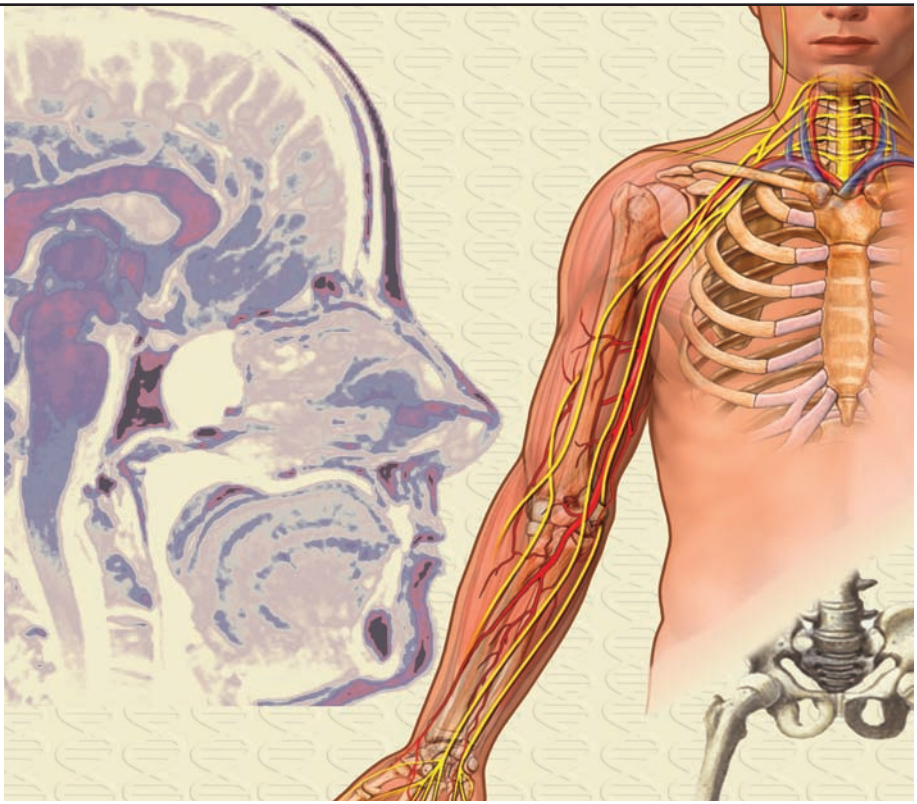
John K. Young is a professor of anatomy at Howard University, where he conducts research on the hypothalamus, the part of the brain that regulates eating, drinking, and sexual behavior.

In 1998, Professor Young won the Kaiser-Permanente Award for Excellence in Teaching. He is a member of the American Association of Anatomists, the Endocrine Society, and the Society for Neuroscience.

Professor Young has published more than forty articles in scientific journals and is the author of the books *Hormones: Molecular Messengers* and *Cells: Amazing Forms and Functions*. Professor Young also coauthored *Cell Biology/Histology Tutorial* with R.S. Hakim and *Integrated Histology* with Alvin Telser and Kate Baldwin.

You will get the most out of this course if you have the following book:

Marieb, Elaine N., Jon Mallatt, and Patricia Brady Wilhelm. *Human Anatomy*. 5th ed. New York: Benjamin Cummings, 2007.



Introduction

The structures that lie beneath our skin represent a remarkable and beautiful assortment of biological machines that are essential for our lives. Often, however, we take these structures for granted; it is only when we become ill that we wonder how the body functions and what has gone wrong. This lecture series provides a basic overview of the muscles, bones, brain, gut, kidneys, and other organ systems of the body; describes how they function; and relates how they can be restored to a normal function after an injury. Professor John K. Young has taught human anatomy for thirty years and has collected many fascinating and little-known stories about the body. In the following lectures, Professor Young shares the knowledge he has gained during his tenure as a teacher and leads his audience on a fascinating journey through the human body.

Lecture 1:
Introduction to Anatomy and the Axial Skeleton

The Suggested Reading for this lecture is Elaine N. Marieb, Jon Mallatt, and Patricia Brady Wilhelm's *Human Anatomy* (chapters 1 and 7).

Anatomical Terminology

Before beginning to describe the structure and function of the body, it is important to become familiar with a few descriptive terms that anatomists use. Without a knowledge of these terms, the names of muscles and bones become incomprehensible.

The face and belly of your body represent the *ventral* surface of a human, whereas the back represents the *dorsal* surface (remember the dorsal fin on the back of a shark?). The same terms apply to the different surfaces of the arms and legs and are more precise than front or back. The midline of your body is its *axis*, and is formed by the axial skeleton of the vertebral column. Organs far away from the midline (for example, your shoulders or your ears) are *lateral* to the midline. Structures closer to the midline than lateral organs (for example, your nipples or your cheekbones) are *medial* to the more lateral structures. Finally, features at the end of a bone (for example, your hand at the end of the arm) are *distal* (distant) structures, whereas features at the beginning of a bone (for example, your shoulder joint) are *proximal* (nearby) structures.

When you bend your arms or legs, this movement is called *flexion*; it is the opposite of straightening them out, or *extension*. If you extend (straighten) your arm and also move your hand away from your body, this movement is called *abduction*. If you move your hand back toward the midline, this is termed *adduction*. If you fall flat on your back, you are in a *supine* (rhymes with spine) position; if you roll over on your stomach, you are in a *prone* position.

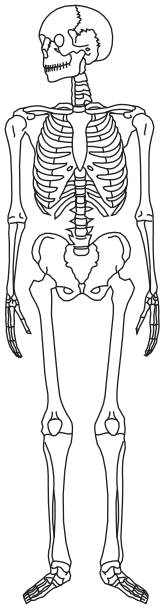


Fig. 1
The Human Skeleton

Axial Skeleton

Many animals make do without a skeleton of any kind. For example, earthworms, sea worms, and mollusks like octopuses have muscles and complex nervous systems, but have no rigid skeletal elements at all. This is because their bodies have no need to resist gravity. Humans, on the other hand, need to stand upright and walk in opposition to gravity, so our muscles need rigid structural elements to pull upon to produce movement.

The axial skeleton begins with the skull. The cranial part of the skull is composed of eight curved plates of bone that interlock with each other and enclose the brain. The

bone beneath your forehead is the frontal bone, while the bone at the back of the skull is the occipital bone. Left and right temporal bones are found beneath each ear, and above them are the right and left parietal bones. The bottom of the brain is supported by a single sphenoid bone, which extends flat plates from the midline that rather resemble the wings of a butterfly.

There are fourteen bones in the portion of the skull forming the face. One large bone is the jawbone, or mandible. Nine of them (nasal, lacrimal, palatine, vomer, and inferior nasal conchae) form the structure of the nasal cavity and have a complicated anatomy that can only be viewed by dissecting the skull apart. The remaining four bones are the right and left maxillary and zygomatic bones that form the cheeks and upper jaw. Your upper teeth are rooted into the maxilla, whereas the lower teeth insert into the mandible.

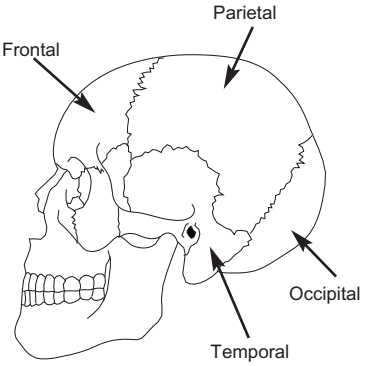


Fig. 2
The Human Skull

The vertebral column forms the next portion of the axial skeleton. The vertebral column is composed of individual vertebral bones that vary considerably in shape and function. All vertebrae have two main parts: a hollow, dorsal neural arch that encloses the spinal cord, and a sturdy, solid, ventral spool-shaped centrum. The weight of the body is supported by the vertebral centra, which are stacked up upon each other to form a flexible column. This column is flexible because pliable intravertebral discs form cushions between each vertebral bone.

Humans and most other mammals have seven bones in the neck (cervical vertebrae), twelve bones in the thorax (thoracic vertebrae), and five bones in the lower back (lumbar vertebrae). A good anatomist can easily distinguish which region of the body a vertebral bone comes from, because they have different structures to fulfill different tasks.

Cervical vertebrae are distinctive because they possess small holes on each side of the centrum. These holes are for the passage up the neck of vertebral arteries that supply blood to the brain. The also have prominent dorsal spinous processes; the largest one is on cervical vertebra number 7 (C7), which is responsible for the bump you can feel at the back of the neck. Thoracic vertebrae possess stout transverse processes that attach to and buttress the twelve

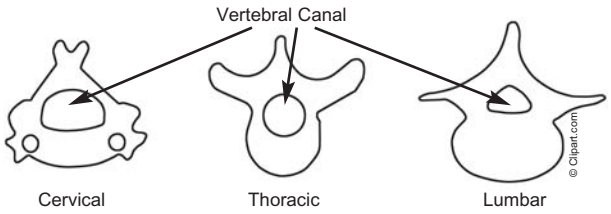


Fig. 3

Diagrams of the three types of vertebrae as seen from above, illustrating their anatomical differences.

ribs that join to the vertebral column. Ribs attach to the thoracic vertebrae, curve around to the ventral side of the body, and terminate upon the breastbone, or sternum. Lumbar vertebrae are larger and have larger centra, which are needed to support all the weight of the upper skeleton.

Why do these vertebrae develop these different features? More generally, how does the body come to be divided into all of these segments? Even the skull can be divided into three segments, the cranium, the maxilla, and the mandible. Segmentation in animals is very helpful for the process of evolution: instead of changing the entire body to adapt to new environments, a change in a single body segment can be helpful. We now know that the body segments are formed in the embryo under the influence of DNA-binding proteins called homeotic proteins. These are expressed in stripes along the body during embryogenesis and force the cells that they control to become structures appropriate for that segment. Experimental alterations in these homeotic proteins can produce missing ribs, or vertebrae, or abnormalities in fingers or toes.

Because joints between all the bones of the vertebral column are flexible, you can rotate your shoulders forwards and backwards a bit. Your head, however, can be rotated from side to side much more dramatically than your shoulders. What accounts for this unusual freedom of rotation of the skull?

The solution to this riddle is the peculiar anatomy of the first two cervical vertebrae. The first one is in direct contact with the skull and is called the atlas, after the Greek god who held the earth in his arms. This bone has a normal neural arch that encloses the spinal cord; however, the centrum for this bone is missing. So the spinal canal in this area is enclosed by a roof of bone and a floor formed only by a tough ligament that spans the middle of the atlas, which looks like a hollow circle divided in two by the ligament.

The second cervical vertebra (C2) is called the axis. It has a more normal appearance, except for an addition to its centrum. The upper face of the C2 centrum has a large spike, or dens, which projects upwards from it. This dens of the axis fits into the ventral opening of the atlas above it. When you turn your head, the atlas freely rotates around the dens, allowing this easy movement.

Where does the dens come from? It originates in the embryo as the centrum of the atlas (C1), which detaches from it and becomes fused to the centrum of the axis (C2), just beneath the atlas. This remarkable adaptation evolved long ago, when ancestral reptiles arose from amphibians. Fish and amphibians lack these special features and cannot rotate their heads as freely as mammals or reptiles.

One common problem with the vertebral column is scoliosis. In scoliosis, the spine, as seen from the dorsal surface, develops an s-shaped curve rather than forming a straight line from pelvis to neck.

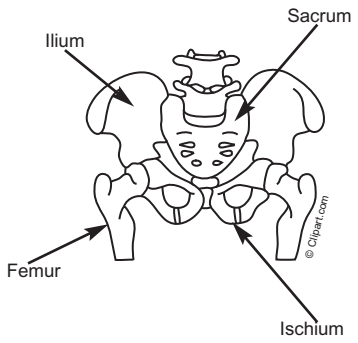


Fig. 4
The bones of the pelvis.

About 2 percent of the population will develop scoliosis, which may sometimes require surgery to straighten the spine. There is a tendency to inherit this condition. Recently, a gene (called CHD7) that affects the function of homeotic proteins has been found to contribute to the development of scoliosis.

The axial skeleton ends at the sacrum and pelvis. The sacrum is a triangle-shaped mass of bone that arises from the fusion of five sacral vertebrae. It is connected on each side by ligaments to fan-shaped bones of the pelvis called the iliac bones. This arrangement is ingenious, since a great load on the sacrum wedges it harder into the pelvis and causes the iliac bones to move closer together for a stronger load-transmitting mechanism. The iliac bones are joined to two other pelvic bones. The ischial bones on each side have downward-projecting, rounded processes called ischial tuberosities (these are what we sit on). More ventrally, the pubic bones of each side come together to form the front of the pelvic basin. The bones of the thighs insert into a cup-shaped cavity, the acetabulum, that transmits forces from the six pelvic bones to the two thigh bones.

Muscles of the Axial Skeleton

There are about 146 named skeletal muscles in the body (depending upon how you name and count them) and it is far beyond the scope of this course to name all of them. It is appropriate, however, to name the largest and most important of them and to convey a sense of how they operate.

There are two large muscles on each side of the skull that close the jaw. One of them, the temporalis, can be felt to contract at the temples when you clench your jaw. The other, called the masseter, arises from the cheekbone (zygomatic bone) and can be felt by putting your finger below and in front of your ear when you clench your jaw. Muscles that open the mouth are located beneath the chin, and additional muscles that adjust the position of the jawbone are located medially to it. A complicated network of eleven muscles that surround the eyes and mouth adjusts facial features during various types of activity.

Two prominent tendons can be felt arising from the top of the sternum and proceeding toward the back of the jaw. These belong to the sternocleidomastoid muscles, which flex the neck when you are nodding “yes.” (Push on your forehead with the flat of your palm and you will feel these muscles contract.)

The relatively superficial muscle of the back of the neck is called the splenius; this muscle helps to bend the neck backwards or rotate the head, and covers over deeper neck muscles that also adjust the position of the skull. Proceeding downwards from the splenius is a collection of back muscles called the erector spinae, which acts to arch the back; some portions of the erector spinae extend all the way down to the pelvis.

FOR GREATER UNDERSTANDING

Questions

The pelvic bones of the human female are wider than those of the male. What purpose does this serve?

Suggested Reading

Marieb, Elaine N., Jon Mallatt, and Patricia Brady Wilhelm. *Human Anatomy*. 5th ed. New York: Benjamin Cummings, 2007.

Other Books of Interest

Romer, Alfred S. *The Vertebrate Body*. New York: W.B. Saunders, 1970.

Articles of Interest

Berdnikovs, S., et al. "Pelvic Growth: Ontogeny of Size and Shape Sexual Dimorphism in Rat Pelves." *Journal of Morphology*. Vol. 268, pp. 12–22, 2007.

Gao, X., et al. "*CHD7* Gene Polymorphisms Are Associated with Susceptibility to Idiopathic Scoliosis." *American Journal of Human Genetics*. Vol. 80, pp. 957–961, 2007.

Tabin, C.J. "Why We Have (Only) Five Fingers Per Hand: Hox Genes and the Evolution of Paired Limbs." *Development*. Vol. 116, pp. 289–296, 1992.

Websites to Visit

The most useful website for people interested in biology is maintained by the National Institutes of Health in Washington, DC. *PubMed* contains links to all the scientific papers published on biology. When you type in the name of an author of a scientific paper and the year it was published, the website will find the paper and display a summary of it. This is useful for non-scientists as well as scientists. If you want to know more about the papers cited above, see this website. — www.pubmed.gov

Lecture 2:
Bones and Muscles of the Arms and Hands

The Suggested Reading for this lecture is Elaine N. Marieb, Jon Mallatt, and Patricia Brady Wilhelm's *Human Anatomy* (chapters 8 and 11).

Bones of the Upper Extremity

The first bone of the arm is held tightly against the back. This is the shoulder blade, or scapula. The scapula is a flat, triangle-shaped piece of bone that has a prominent spine on its surface; this spine is easily felt projecting away from your shoulder and down your back. Although the scapula seems to be part of the back, it is not directly connected by any joints to the axial skeleton. The scapula freely floats in a mass of muscles that anchor it to bones of the arm and ribs. Because of this, the position of the scapula can be widely adjusted to allow for free movements of the arm.

The lateral point of the scapular triangle possesses a socket called the glenoid fossa. The bone of the upper arm, the humerus, inserts a ball-shaped ending called the head of the humerus into this socket. This joint allows a wide range of movement of the arm back and forth and up and down relative to the body. The remainder of the humerus forms a relatively simple, strong cylinder until you reach its distal end at the elbow joint. Here, the surface of the end of the humerus becomes complicated.

If you hold the end of the humerus between your thumb and index finger and flex your arm repeatedly, you will feel a sharp point on the medial surface and a larger sharp point on the lateral surface. These are the medial and lateral epicondyles of the humerus, respectively. They are attachment points for strong ligaments, called collateral ligaments, that attach the humerus to the bones of the forearm. The dorsal surface (back) of the elbow has a large, sharp, moveable point known as the "funny bone," but known by anatomists as the olecranon of the ulna. A large nerve called the ulnar nerve wraps around this process; if you bang against it, the compression of the nerve causes a painful tingling to be perceived in the forearm.

This distal end of the humerus also must articulate with the two bones of the forearm: the radius and ulna. If you go to shake hands, the bone on the lower surface of your forearm is the ulna (ulna = "under"). The ulna forms a hinge-like joint with the humerus. The other bone, the radius, has a very peculiar joint with the humerus: the radius begins as a concave, circular plate that interacts with a ball-shaped process, the capitulum, which is found on the end of the humerus. When pulled by muscles, the radius twirls around on its own axis against this ball-shaped capitulum. This allows you to pronate and supinate your hand (flip it from palm side down to palm side up).

When you touch your wrist with your thumb and forefinger, you will feel a medial bump and a lateral bump. These bumps are the styloid processes of the ulna and radius, respectively. They are points of attachment for strong ligaments that hold your hand onto your forearm.

Each hand contains twenty-seven bones. Fourteen of these are bones of the fingers, or phalanges (the thumb has two phalangeal bones, the other fingers three). There is a sexual difference, or dimorphism, in the anatomy of the hand. Males tend to have an index finger that is shorter than the third (ring) finger, whereas females tend to have an index finger that is relatively longer. This seems due to effects of testosterone on bone development.

Five stronger metacarpal bones form the palm of the hand, and are connected to a mass of eight irregular bones called the carpal bones.

One final bony element of the upper appendicular skeleton is the collarbone, or clavicle. One end of each clavicle is attached to the midline breastbone, or sternum. The other end attaches via ligaments to a hook-shaped projection from the scapula. The clavicle acts like a strut and pushes the scapula away from the ribcage. This allows us to throw back and straighten our shoulders. The clavicle is the most frequently fractured bone in the body.

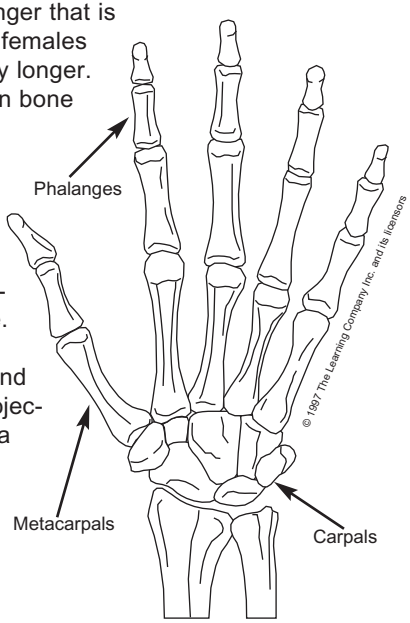


Fig. 5
The bones of the hand.

Major Muscles of the Upper Extremity

The muscles of the arm serve both to anchor the arm onto the body and, of course, to move the arm. The first muscles we need to describe are the ones that hold the scapula in place. The most superficial muscle that does this is called the trapezius, a triangle-shaped muscle that begins at the base of the neck, fans out to cover the spine of the scapula, and then attaches to all of the thoracic vertebrae. This muscle helps us to shrug our shoulders and, when twisted abnormally during sleep, can give us the sensation of a “crick” in our neck. The scapula is also anchored to the vertebral column on its most medial border by two muscles called the rhomboid muscles.

A major superficial muscle that covers the shoulder is the deltoid muscle, which inserts onto the humerus and helps abduct the arm. If you touch your fingertips to your shoulder, it will contract when you raise your arm.

A collection of four other deeper muscles is termed the “rotator cuff,” because these muscles and associated tendons surround the head of the humerus and prevent it from being dislocated. Two of these muscles arise from the dorsal surface of the scapula: the supraspinatus and infraspinatus. Another muscle arises from the underside, or ventral, surface of the scapula: the subscapularis. A fourth muscle, the teres minor, arises from the lateral border of the scapula. All of these muscles insert upon the humerus and stabilize it. Injury to portions of the rotator cuff can cause a dislocation of the shoulder, usually toward the weaker, anterior portion of the joint.

An arm muscle, the biceps brachii, forms a firm mound on the ventral surface of the arm when we flex the arm. This muscle gets its name from the fact that it originates from two places, or "heads" (from the Latin *bis* for two, *caput* for head, and *brachius* for arm). The two heads of the biceps arise from two different locations on the scapula and lead to a common tendon that is easily felt at the inner surface of the elbow. The tendon inserts onto the radius, and allows us to flex the arm and rotate the radius.

Located at the back of the arm is the major extensor of the arm, a muscle called the triceps brachii. This muscle has three heads rather than two, and originates from one spot on the scapula and two spots on the humerus itself. It is the major extensor of the arm and is put into action when we do push-ups.

Two large muscles that originate from the chest wall also insert onto the humerus. The ventral chest muscle is called the pectoralis, which originates from the sternum and ventral portions of the ribs; the dorsal muscle is called the latissimus dorsi, which originates from the vertebral column and dorsal ribs. Both are large, strong muscles that pull the humerus closer to the body (adduct it). These muscles are active when an athlete performs a maneuver like an iron cross on the rings.

The ventral surface of the forearm has eight muscles that help flex the arm or fingers. Some of the tendons of these muscles are easily felt at the wrist when the hand is held palm up. At the wrist, just below the thumb, you can palpate the strong tendon of a muscle called the flexor carpi radialis if you put your hand, palm upwards, underneath a table and try to flex or bend the hand upwards. Next to this tendon you can feel the pulsations of the radial artery that feeds blood to the hand. All of the muscles that flex the fingers have to pass into the hand underneath a strap of connective tissue called the flexor retinaculum. This covers the "carpal tunnel" that has the carpal bones as a floor. If the flexor muscles of the hand are used repetitively (as in typing), they may swell and press against nerves that enter the hand through the carpal tunnel. This results in the carpal tunnel syndrome.

The palm of the hand has nineteen muscles that originate on the metacarpal bones and insert via tendons onto the fingers. The fingers possess no muscles, so the finger bones are entirely surrounded by tendons that originate from the palm of the hand or the forearm.

On the dorsal surface (back) of the forearm, ten muscles are present that permit straightening (extension) of the fingers. Some of them have tendons that are particularly noticeable. For example, if you place your hand on a table palm down and fan your fingers and thumb, a large tendon can be seen occupying the middle of your thumb. This is the tendon of the extensor pollicis longus ("pollux" is the Latin for thumb). It forms one border of a triangular depression in your hand at the base of the thumb called the "anatomical snuff box." This derives its name from the eighteenth-century practice of putting a pinch of snuff on this spot so that it could be sniffed into the nose. Anatomical terms often originate long ago and persist longer than one would predict.

FOR GREATER UNDERSTANDING

Questions

In cats, the clavicle is smaller than that of humans and has lost its articulation with the scapula. Why would this be an advantage in cats and a disadvantage in humans?

Suggested Reading

Marieb, Elaine N., Jon Mallatt, and Patricia Brady Wilhelm. *Human Anatomy*. 5th ed. New York: Benjamin Cummings, 2007.

Articles of Interest

Jubel, A., et al. "Elastic Stable Intramedullary Nailing of Midclavicular Fractures in Athletes." *British Journal of Sports Medicine*. Vol. 37, pp. 480–484, 2003.

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Owens, B.D., et al. "The Incidence and Characteristics of Shoulder Instability at the United States Military Academy." *American Journal of Sports Medicine*. Vol. 35, pp. 1168–1173, 2007.

Lecture 3:
Bones and Muscles of the Legs and Feet

The Suggested Reading for this lecture is Elaine N. Marieb, Jon Mallatt, and Patricia Brady Wilhelm's *Human Anatomy* (chapters 8 and 11).

Bones of the Lower Extremity

A quick glance at the bones of the lower extremity shows that they are similar to those of the upper extremity: the thigh bone (femur) rather resembles the humerus, and the two lower leg bones (tibia and fibula) rather resemble the radius and ulna. Furthermore, the general structure of the feet resembles the structure of the hands. The major difference between the upper and lower limbs is that they bend (flex) in opposite directions. Why are the upper and lower limbs so similar in structure and yet different in function?

During embryogenesis, the limbs first form as flaps of cells that project from the sides of the embryo. At first, the upper and lower limbs are almost identical. The elbow of the arm is located on the lateral surface of the arm, so that when the limb bends, the palms of the hands are brought close to the body. Similarly, the kneecap region of the leg is on the lateral surface of the leg, so when it bends, the sole of the foot is brought closer to the body. Then, everything changes.

As the embryo develops, the right arm rotates clockwise around its own axis, so that the elbow is brought to the back of the arm from its position on the side of the arm. Thus, when the arm flexes, the palm of the hand is brought up toward the face, rather than toward the body. The right leg, in contrast, rotates around its own axis 90 degrees in a counterclockwise direction, bringing the kneecap region toward the front of the leg from its position on the side. This means the adult leg, when flexed, will move the sole of the foot downwards.

Why do these events happen? One clue is derived from the study of a DNA-binding protein called Pitx1. This protein is normally found only in cells of the hindlimb of mice and turns on the genes necessary for lower limb development. If it is introduced into the cells that normally form a forelimb (arm), the joints and structure of this forelimb are partially converted into structures normally found only in the hindlimb (for example, a knee-like joint instead of an elbow).

The main bone of the leg is the femur. The top of the femur is a ball-shaped structure called the head of the femur. The femoral head articulates into a cup-shaped depression on the pelvis called the acetabulum (Latin for "vinegar cup"). The femoral head joins to the rest of the femur via a cylindrical portion called the neck of the femur. This femoral neck is the most commonly fractured part of the femur, and usually accounts for the symptoms of a broken "hip." Also, arthritis can damage the smooth surface of the femoral head, making leg movements very painful. One solution for this problem is a total "hip" replacement, in which the femoral head and neck are removed and

replaced by artificial structures made of titanium that articulate with the acetabulum of the pelvis.

The female pelvis is broader and wider compared to the male pelvis, so that the two femurs diverge farther from the midline in females, making women more “knock-kneed” than men. This seems mainly due to effects of the female sex hormone, estrogen, upon pelvic shape.

Leg muscles do not attach to the femoral head or neck at all; this is why these structures can be readily removed and replaced with an artificial substitute. Many of the thigh muscles attach to the femur on large processes just below the neck called the greater and lesser trochanters.

The bulk of the femur resembles a strong cylinder with many attachment sites for muscles. Two ball-shaped surfaces, called the medial and lateral condyles, form the end of the femur and articulate with the flat ends of the tibia and fibula. The front of the knee joint is protected by a flat bone called the patella (kneecap) that is held in place by a strong patellar ligament. Other strong ligaments on either side of the patella anchor the femur to the tibia and fibula. Finally, just behind the patella are two additional strong ligaments that cross each other within the joint cavity. Because of this crossing pattern, these ligaments are called the anterior and posterior cruciate ligaments (from the Latin *crus* for cross). Tears that form in these ligaments during sports activity usually require surgery to repair them.

The two condyles of the femur do not directly contact the bony surfaces of the tibia and fibula and grind against them. Instead, the femur is supported by two soft pads of cartilage called the medial and lateral menisci. These can also develop tears, which must often be surgically corrected to allow knee movement.

The tibia and the more delicate fibula make up the lower portion of the leg. The tibia conducts all the weight into the foot. The fibula is not a weight-bearing bone, but does serve as a site of origin of a number of muscles. Each bone ends at the ankle; the medial bump that you can feel at the ankle is the medial malleolus of the tibia, whereas the bump on the outside (lateral portion) of the ankle that you can feel is the lateral malleolus of the fibula.

The structure of the foot is somewhat similar to that of the hand, but has had to be modified because of the substantial weight supported by the foot. The seven tarsal bones of the foot are quite different in appearance from the comparable carpal bones of the hand. Two very large carpal bones transmit weight to the ground. First, the tibia transfers force to a large tarsal bone

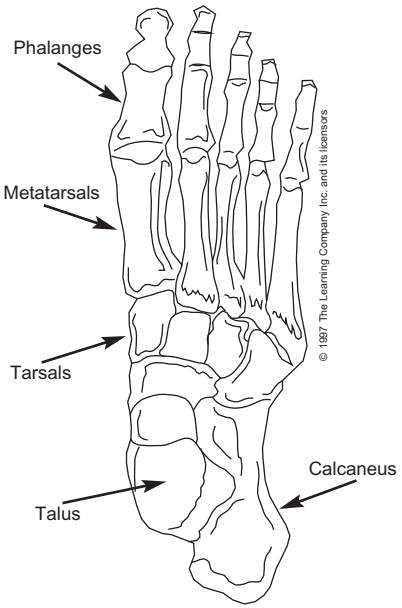

Fig. 6
The bones of the foot.

called the talus, which articulates with the tibia. The talus in turn transmits force to another large bone underneath it called the calcaneus. The calcaneus is what we term the heel bone. The remainder of the weight borne by the foot is distributed from the talus to other tarsal bones and thence to the metatarsals and phalanges of the foot.

Muscles of the Lower Extremity

There are thirty-six different muscles that move the bones of the lower extremity. We will not try to list them all here, but a few of them are particularly prominent and necessary for an understanding of how the leg functions.

Let's start by remembering that the back (dorsal) surface of the leg is analogous to the front (ventral) surface of the arm. The ventral surface of the arm is covered by a muscle called the biceps brachii. It should be no surprise, then, that a prominent muscle of the back of the thigh is called the biceps femoris. It arises from two spots, one on the ischial bone of the pelvis and the other on a long area of the femur, and inserts via a strong tendon onto the fibula. You can feel this tendon at the back of the knee at its lateral margin. At the medial margin of the back of the knee you can feel two strong tendons belonging to muscles called the semitendinosus and semimembranosus. All three of these muscles strongly flex the leg at the knee and are termed the hamstring muscles.

The arm is abducted away from the body by the deltoid muscle. The leg is abducted away from the body by an analogous muscle called the gluteus maximus that arises from the pelvis and inserts onto the femur. When you are seated, the ischial tuberosities of the pelvis come in contact with overlying muscle of the gluteus maximus.

The arm is extended by the triceps muscle. An analogous muscle called the quadriceps femoris, which has four heads instead of the three heads of the triceps, extends the lower leg. The quadriceps makes up most of the muscle mass that you can feel underneath the skin of the front of the thigh when you raise your foot off the ground at a sitting position.

Touch the fingertips of both your hands to your shinbone (tibia), just below the knee. Then, flex your foot upwards. You will feel the contractions of a major muscle called the tibialis anterior, located just lateral to the shinbone. This muscle sends a tendon that curves around the medial margin of the big toe and is anchored to the bottom of the foot at the bottom of the first metatarsal bone. This muscle flexes the foot. Another muscle located just lateral to the tibialis anterior is called the fibularis longus. This muscle sends another tendon that curves around the smooth surface of the lateral malleolus of the fibula, much as a rope passes beneath the wheel of a pulley. This tendon passes beneath the surface of the foot to insert onto the lateral surface of the first metatarsal. Together, the tendon of fibularis longus and the tendon of the tibialis anterior form kind of a "stirrup"-shaped structure that supports the bottom of the foot and helps form the springy arch at the bottom of the foot. Another structure that helps form the arch of the foot is a mass of tough connective tissue on the bottom of the foot called the plantar fascia, which tugs upon the lateral and medial margins of the foot. If this tissue becomes inflamed, a condition called plantar fasciitis, long-lasting foot pain, may result.

The back of the lower leg, or calf, has six muscles, but two of them are the most prominent. The most superficial muscle of the calf is called the gastrocnemius. Just beneath it is a flatter muscle called the soleus. Both muscles insert into the heel bone (calcaneus) via a common tendon called the Achilles tendon, which is the largest and strongest tendon in the body. Even this tendon, however, can be torn with the type of violent movements experienced during a basketball game. Repair of a ruptured Achilles tendon, which must be sewn back together to heal, involves a lengthy immobilization of the lower leg.

One thing we are taking for granted is something called bilateral symmetry, that is, the fact that both arms and both legs are roughly the same size. The limbs of an adult are three to four times larger than those of an infant, but generally they grow at such similar rates that right-left variations in limb length do not amount to much more than a 3 percent difference. This almost perfect symmetry of the skeleton is essential for a normal gait. What causes this perfect symmetry?

Presumably, factors that promote or inhibit growth must exert almost exactly the same influence in both the right and left limbs. However, these influences can be defeated in rare clinical conditions. In one peculiar case of a disease called Marfan syndrome, the left leg and arm grew more than an inch longer than the right leg and arm. Also, in a poorly understood disorder called Proteus syndrome, individual fingers or limbs can become greatly overgrown.

The foot itself has nineteen muscles that move the toes. Many of these lie beneath the tendons that you can feel on the front of your foot; these tendons are from muscles that originate farther up the leg.

FOR GREATER UNDERSTANDING

Questions

In humans, the right humerus is typically five millimeters longer than the left humerus. However, there are no significant differences between the average lengths of the right tibia as compared to the left tibia. What accounts for the asymmetry of the arm bones and not the leg bones?

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Lecture 4:
The Cardiovascular System

The Suggested Reading for this lecture is Elaine N. Marieb, Jon Mallatt, and Patricia Brady Wilhelm's *Human Anatomy* (chapters 18 and 19).

The Heart

Any discussion of the cardiovascular system must begin at the heart, which provides the force that moves blood throughout the body. In one sense, the heart can be regarded as just a complicated and very muscular version of a large blood vessel. And in fact, during early evolution, this is how the heart began, as a single tube, constricted in several places, that received blood at the posterior (caudal) end and pumped it out at the other (cranial) end. In certain animals today, like sharks, the heart retains much of this simple structure.

In humans and other mammals, the early development of the heart retraces this evolutionary history, so that the heart of the embryo does begin as a simple tube. Quite quickly, however, shelves of tissue called septa divide the simple tube into two paired tubes. Then each tube becomes divided into a thin-walled atrium that receives blood and a thicker, more muscular ventricle that does most of the pumping work. So the heart actually forms two pumps, acting simultaneously, that pump blood through two different regions of the circulatory system. The right side of the heart receives poorly oxygenated blood from the entire body and sends it to the lungs via the pulmonary arteries. The left side of the heart receives blood from the lungs and pumps it into a large vessel called the aorta, which distributes the oxygenated blood to all the arteries of the body. By definition, all vessels that leave the heart are termed arteries and all vessels that bring blood to the heart are veins.

The rate of the heartbeat varies between animals, depending upon the metabolic rate of the body. The heart of a cold-blooded codfish, for example, may beat only twenty times per minute, while human hearts beat about seventy times per minute and the hearts of rats beat 350 times per minute. It has been stated poetically that the lifespan of an animal can range from one year to one hundred years, but all of us seem to have the same number of heartbeats in our lives.

During development, the heart not only becomes divided into four separate chambers, but it also develops an S-shaped bend. This moves the atria and the veins that fill them from a position at the bottom (caudal region) of the heart to a position near the top of the heart (cranial portion), close to where the arteries emerge from the heart. This is very helpful, because when development is complete, all the vessels coming into and out of the heart come close together, so that the heart resembles a tomato hanging from a "vine" of vessels. This suspension of the heart from large vessels means the heart is free to twist and shake as it contracts without tearing any contacts with the rest of the body. The heart is surrounded on most of its surface only by fluid contained within a sac called the pericardial sac.

Heart muscle cells have the amazing ability to contract (beat) without any outside instructions from other cells, so that heart cells will continue to contract even when they are isolated from one another in a Petrie dish. In a living organism, however, the rate and force of heartbeats are regulated by a specialized patch of tissue located at the top of the right atrium. This is the so-called sinoatrial node, or pacemaker. Specialized muscle cells in this pacemaker initiate an electrical charge seventy times a minute. This surge of electricity is carried throughout all the other muscle cells of the atria, causing them to contract. This forces blood from the atria into the ventricles. Blood cannot flow back from the ventricles into the atria because of the presence of one-way valves between the atria and ventricles.

One potential problem for the heart is the presence of a mass of tissue called the fibrous cardiac skeleton that is interposed between the atria and the ventricles. This tissue, unlike muscle, does not conduct electricity. So how can an electrical impulse reach the ventricles and initiate contraction? The solution is the presence of another specialized patch of tissue at the junction of the atria and ventricles called the atrioventricular node. Cells in this node slow the electrical impulse briefly and then conduct it to the ventricles via a specialized pathway called the atrioventricular bundle (bundle of His).

Since each beat of the heart is associated with a flow of electricity across the heart, the electrical events of a heartbeat can be detected using electrodes pasted to the wall of the chest or to the hands and feet. This procedure is called an electrocardiogram (EKG). On an EKG, a stylus records changes in detected voltage as a series of waves drawn upon a moving paper. The electrical disturbance associated with atrial contraction is called the P wave, which precedes all other waves. Following the P wave is the so-called QRS complex of waves, which signals that the ventricles have contracted. Finally, the T wave signals that the ventricles have recovered a normal electrical charge after contracting.

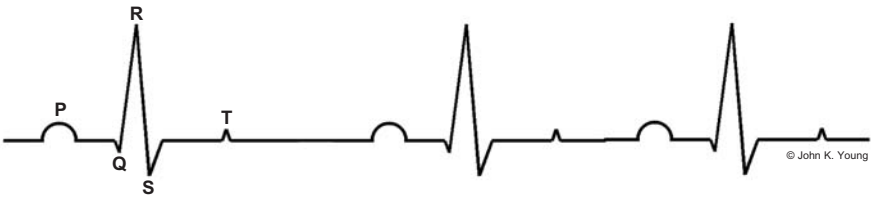

Fig. 7

Diagram of the electrical waves detected in an electrocardiogram (EKG).

The size and timing of each of these waves can be used by a physician to diagnose the health of the heart. For example, the interval between QRS waves is the time between heartbeats. If the QRS wave fails to appear between two successive P waves, this shows that the ventricles have failed to contract after the atria. This is diagnostic of a condition called atrioventricular block, in which electricity is not conducted properly through the atrioventricular bundle. One solution for this problem is the implantation of a battery-powered,

artificial pacemaker beneath the skin that shocks the ventricles seventy times a minute and forces them to contract.

The walls of the heart are so thick that cardiac muscle cannot rely upon the blood within the heart cavities as a source of oxygen and nutrition. Instead, many capillaries penetrate the heart muscle to nourish the heart. The sources of these capillaries are the so-called coronary arteries that branch directly off of the aorta as it leaves the heart. If coronary arteries become occluded, due to atherosclerosis, this can starve portions of the heart of nutrients and cause a heart attack. One common treatment now is an insertion of metal tubes, called stents, into the coronary arteries. This enlarges the arteries and keeps them open to resist blockage.

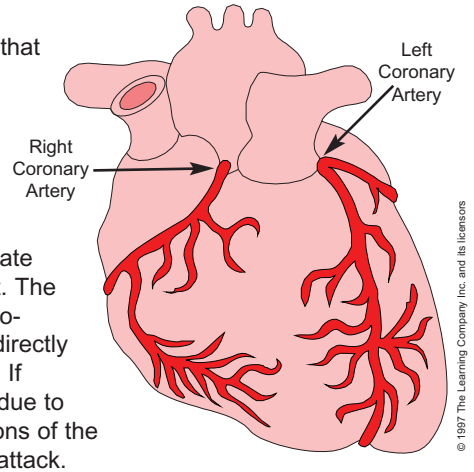

Fig. 8

The heart and coronary arteries.

Major Blood Vessels of the Body

All oxygenated blood leaves the heart via the aorta. The first branches of the aorta are the brachiocephalic artery, which supplies blood to the right arm and head by branching into the right common carotid and right subclavian arteries. The next branches of the aorta are the left common carotid artery, which supplies blood to the left side of the head, and the left subclavian (beneath the clavicle) artery. These large arteries that spring directly off the aorta tend to be encircled by many layers of a stretchy material called *elastin*. When the ventricles force blood into these larger arteries, they absorb the force of the pulse, expand, and then when the pulse diminishes, the elastin in their walls keeps pushing the blood forward. This minimizes the variations in blood pressure that would otherwise occur between heartbeats.

Each subclavian artery has many branches and changes its name as it traverses the arm. Three branches of the subclavian are most important: 1) the vertebral arteries, which find passages up to the brain that are formed by holes in the cervical vertebrae, 2) the radial artery, and 3) the ulnar artery.

As the aorta curves around the heart and descends into the thorax and abdomen, it gives off many branches that supply the thoracic wall, the

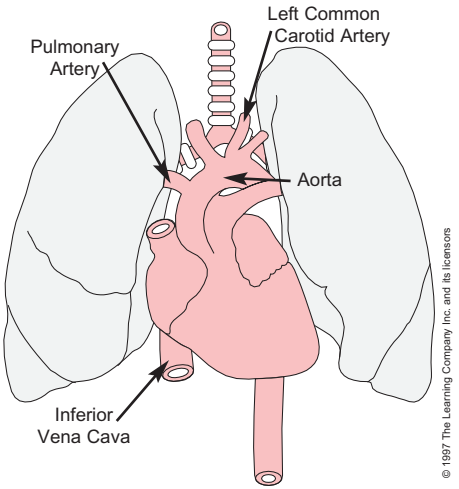

Fig. 9

The major vessels surrounding the heart.

spleen, the stomach, the kidneys, and the intestines. When the aorta reaches the pelvis, it splits into two common iliac arteries. The major branch of the iliac artery in the leg is called the femoral artery. The beginning of the femoral artery is not buried deep beneath the leg muscles, and is fairly easily palpated and accessible to surgeons. This allows it to be used for a number of procedures. For example, a catheter can be threaded all the way up the femoral artery until it reaches the base of the aorta as it leaves the heart. Then, special dyes can be injected into the aorta that can be detected as they fill the coronary arteries. This procedure can detect whether or not a coronary artery is constricted or blocked.

After passing through smaller and smaller arteries and arterioles, blood enters the tiniest vessels of the body, the capillaries. There are about one hundred billion capillaries in the body, having a total surface area of about one hundred square meters. Capillaries are the sites of nutrient and gas exchange between the cardiovascular system and the rest of the tissues.

Blood leaves the capillaries and is collected into venules and veins of increasing diameter for transport back to the heart. Many of the larger veins accompany arteries and are given the names of these arteries (for example, femoral vein). In the neck, the major veins draining blood from the head travel alongside the carotid arteries and are called jugular veins. All the veins of the body lead to two main veins, the superior vena cava (from the head and upper extremities) and the inferior vena cava, which collects blood from the thorax, abdomen, and lower extremities. These two large veins deliver blood to the right atrium, which sends this oxygen-depleted blood to the right ventricle and thence to the lungs, via the pulmonary arteries. Pulmonary veins send blood back to the left side of the heart, and the whole circuit of blood starts over.

FOR GREATER UNDERSTANDING

Questions

The walls of arteries are typically thicker and contain more smooth muscle than the walls of veins. What functional reason explains this?

Suggested Reading

Marieb, Elaine N., Jon Mallatt, and Patricia Brady Wilhelm. *Human Anatomy*. 5th ed. New York: Benjamin Cummings, 2007.

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Lecture 5:
Lymphatic Vessels and Organs of the Immune System

The Suggested Reading for this lecture is Elaine N. Marieb, Jon Mallatt, and Patricia Brady Wilhelm's *Human Anatomy* (chapter 20).

Lymph Vessels and Lymph Nodes

The capillaries that receive blood from arterioles are extremely small and thin walled. This is appropriate for their function of exchanging molecules with the cells of tissues surrounding them, but these features of capillaries may also pose some problems.

One problem is that most capillaries in the body are extremely leaky. Fluid and molecules easily pass through their thin walls into surrounding tissues. There are some exceptions to this rule. For example, the capillaries of the brain are unusually nonpermeable and don't permit the escape of many molecules into the brain. This arrangement, termed the blood-brain barrier, protects the brain from potentially toxic molecules within the bloodstream. However, capillaries in most of the rest of the body are much more leaky.

If escaped fluid and blood proteins were allowed to remain in tissues surrounding the capillaries, this material would accumulate and cause tremendous swelling of the limbs, called edema. To prevent this, specialized, thin-walled vessels called lymphatics penetrate into all the non-brain regions of the body and collect this fluid as *lymph*.

Fluid that seeps out of capillaries easily penetrates into lymphatic vessels by passing between the cells that line these vessels. Flaps of cell cytoplasm allow fluid to enter the vessel, but do not permit it to leave, so fluid accumulates. Contractions of muscles near the lymphatics push on them and propel the fluid into larger vessels that lead to the heart; lymph cannot flow backwards because of the presence of valves—flaps formed by cells—that point in one direction and which do not allow backflow of lymph. Thus, even though lymphatics lack an active pump like the heart that is directly connected to them, fluid is still forced toward the heart to return to the circulation.

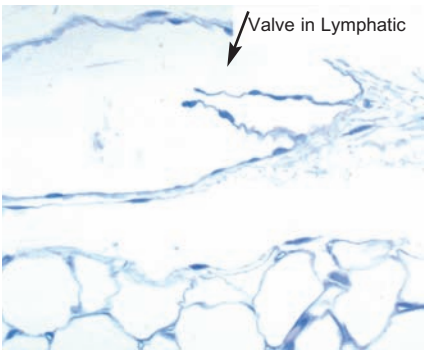

Fig. 10

Microscopic view of a lymphatic vessel containing a valve.

Because lymphatics are so permeable, bacteria or other pathogens that accumulate in infected areas could potentially spread throughout the body via the lymphatics. This is prevented by lymph nodes, small bean-shaped organs that form along lymph vessels. Lymph nodes function to survey lymph for pathogens and filter them out; they contain masses of cells called lymphocytes

that vigorously react to foreign materials, called antigens. Two types of lymphocytes are found in lymph nodes: B-lymphocytes, which migrate to lymph nodes from the bone marrow, and T-lymphocytes, which migrate to the nodes from the thymus gland. When B-lymphocytes in a lymph node detect a foreign antigen, they multiply at an enormous rate and form spherical masses of lymphocytes called nodules. Many of the cells born in these nodules then acquire the capacity to produce antibodies, proteins that bind foreign antigens and target them for destruction.

When lymph nodes become enlarged and swollen with these masses of lymphocytes, this is a sure sign that an infectious process is developing in the body. So when you see a physician for a sore throat, and he feels the base of your jaw to detect swollen "glands," he is actually palpating lymph nodes to see if they are enlarged.

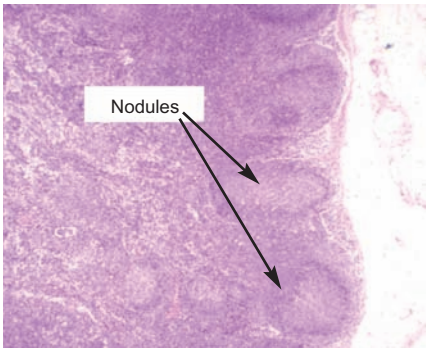

Fig. 11

View of a lymph node through the microscope. Thousands of B-lymphocytes accumulate in nodules.

Lymph nodes can be found in many portions of the body, but they are particularly prominent near large joints. Accumulations of lymph nodes can be found behind the knee (popliteal nodes), near the groin (inguinal nodes), in the armpit (axillary nodes), and in the neck (cervical nodes). In addition, clusters of nodes can be found in the abdomen around the aorta and in the thorax at the root of the lungs. These lymph nodes are interconnected by delicate lymphatic vessels. As these vessels ascend in the body, they grow larger and eventually connect to the two largest lymphatic vessels in the body. The first of these is called the thoracic duct, which lies alongside the vertebral column and which eventually connects to the left subclavian vein to return fluid to the cardiovascular system. A second large lymphatic duct is called the right lymphatic duct, which drains lymph from the right arm and neck only and delivers it into the right subclavian vein.

Certain diseases have a prominent effect upon lymph vessels and nodes. In *elephantiasis*, a parasitic worm blocks the lymphatics of the lower limbs and can cause enormous swelling of the limbs and testicles. This disease affects one hundred million people worldwide. Another disease, bubonic plague (the "black death" that decimated medieval Europe), is caused by a virulent bacterium. Axillary and inguinal lymph nodes respond to this infection by becoming very enlarged and swollen, symptoms that were termed "buboes" in medieval times. Finally, cancer cells that are shed from tumors can enter the lymphatic system and become trapped in lymph nodes, where they continue to multiply. This is why, when treating breast cancer, a physician will remove axillary nodes and examine them for signs that the breast cancer cells have spread to the nodes. Removal of the axillary nodes will frequently result in swelling (edema) of the arm on that side.

Spleen

The spleen is the largest lymphoid organ in the body. It is about the size of a fist and is found just dorsal and lateral to the stomach. It receives an abundant blood supply from a large artery, the splenic artery, which originates from a short, stout blood vessel called the celiac trunk that sprouts directly off of the descending aorta. While lymph nodes filter lymph, the function of the spleen is to filter the blood, remove aged red blood cells, and destroy pathogens that may be present in the blood.

When the spleen is removed and cut open, two types of tissue are visible by inspecting its cut surface. Irregular regions of white-appearing tissue form the so-called *white pulp*, which is composed of millions of white blood cells clustered around blood vessels. When the white pulp is stained and viewed through a microscope, it turns blue because the DNA in the nuclei of white blood cells stains blue. Adjoining regions of the spleen are filled with red blood cells and constitute the red pulp. These cells stain red because of their hemoglobin content and because they lack cell nuclei and DNA.

Arteries that penetrate past the capsule of the spleen, called central arteries, become surrounded by masses of T-lymphocytes. These lymphocytes form cylindrical masses called periarteriolar lymphoid sheathes (PALS). Lymph nodules mainly containing B-lymphocytes adhere to the PALS at intervals. These discrete accumulations of two different types of lymphocytes in two distinct portions of the white pulp seem to be due to the production of specific molecules, called CCL21 and CXCL13, that attract T- and B-lymphocytes to their correct locations. Both types of lymphocytes attack foreign invaders that are present in the bloodstream.

In the red pulp, red blood cells pour directly into the connective tissue from capillaries that have large openings at their ends. In order to get back into the venous circulation and leave the spleen, red blood cells have to push their way out of the connective tissue, between the cells that line veins, and into the circulation. Aged red blood cells are

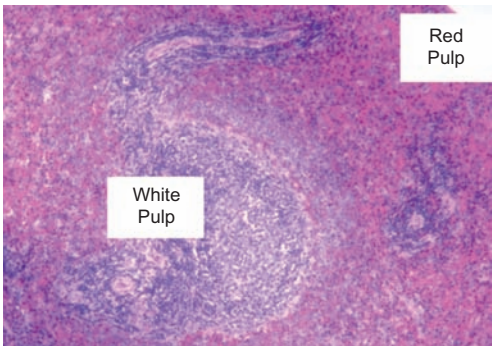

Fig. 12

View of the structure of the spleen. Lymphocytes are abundant in white pulp, and red blood cells are abundant in red pulp.

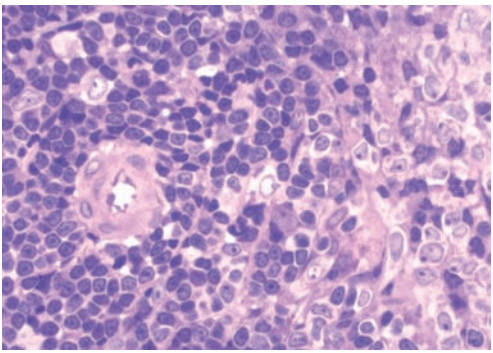

Fig. 13

View of hundreds of T-lymphocytes surrounding a central artery of the white pulp of the spleen.

detected by specialized cells of the spleen as they do this. If the red blood cell is too old and has acquired damage to its cell membrane, it is targeted for destruction by these specialized spleen cells.

The spleen sometimes can rupture after a person falls or collides with something, and can spill large amounts of blood into the abdominal cavity. In these cases, the spleen can be removed. The only major consequence of this is that older red blood cells are not removed from the blood as efficiently.

Thymus

In newborns, the thymus is a relatively large and prominent structure that lies just beneath the breastbone (sternum). It is an important site for the maturation of cells that become T-lymphocytes. These T-cells are released from the thymus in great numbers during the first twenty years of life, and are responsible for our ability to destroy foreign tissues that enter (or are grafted onto) the body. T-cells are particularly damaged by the human immunodeficiency virus (HIV) that causes AIDS. With age, the thymus becomes less and less active, so that by age forty only about 5 percent of the originally active portions of the thymus remain. However, since lymphocytes may live for decades, the T-cells produced years previously are still active in defense of the body.

Tonsils

The tonsils are defined as aggregations of lymphocytes that accumulate beneath the covering epithelium of the oral or nasal cavities. There is a single tonsil found in the back of the nasal cavity called the pharyngeal tonsil. At the back of the mouth, there are two palatine tonsils that lie on either side of the pendulous tissue (uvula) that is suspended from the palate. These are the tonsils that, for years, have been surgically removed on the premise that badly infected tonsils could promote more frequent throat infections. More recent studies suggest that this premise is untrue, and that tonsillectomies do not reliably improve health.

Finally, masses of lymphocytes that form beneath the posterior epithelium of the tongue form the lingual tonsil. All of these tonsils form a ring around the oral and nasal cavities and help fight pathogens that might be eaten or inhaled into the body.

FOR GREATER UNDERSTANDING

Questions

It is not uncommon to experience swollen feet after sitting in an airplane for a long flight or after standing quietly behind a cash register. However, prolonged walking does not provoke the same symptoms. Why not?

Suggested Reading

Marieb, Elaine N., Jon Mallatt, and Patricia Brady Wilhelm. *Human Anatomy*. 5th ed. New York: Benjamin Cummings, 2007.

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Lecture 6:
Spinal Cord and Brain

The Suggested Reading for this lecture is Elaine N. Marieb, Jon Mallatt, and Patricia Brady Wilhelm's *Human Anatomy* (chapters 12, 13, and 14).

The central nervous system (CNS) of the human originates in the embryo as a simple, hollow tube called the neural tube. As the CNS develops further, the portion of the neural tube that forms the spinal cord retains a rather simple organization. However, the more cranial portion of the neural tube develops large bulges, constrictions, and folds that transform it into the vastly more complicated brain.

Spinal Cord

The spinal cord is a cylindrical mass of nerve cells and nerve axons that extends from the base of the skull to about the level of the second lumbar vertebra (L2). Flexing the back tugs on the spinal cord so that it retreats a bit further up the spinal canal. The cord is surrounded by fluid called cerebrospinal fluid.

Bundles of axons called peripheral spinal nerves pass through openings between the vertebrae at regular intervals on both sides of the cord. In the thoracic region of the cord, these nerves are relatively small and have sparse structures to innervate, like the muscles of the chest wall. However, in the cervical and lumbar regions of the cord, nerves must innervate many targets like the muscles of the neck, arm, and leg. Spinal nerves in these regions are much thicker and intertwine to form networks called plexuses. In the armpit, the brachial plexus is formed by thick branches, or rami, from spinal nerves C5 through T1. These rami converge and diverge from each other to form eleven major nerves that provide sensory and motor innervation to the arm. Three of these nerves are the main ones: the radial, ulnar, and median nerves. The ulnar nerve enters the forearm by passing behind the medial epicondyle of the humerus. It is vulnerable to compression at this point ("funny bone" sensation), so that when you bang your elbow into something, you can feel burning, tingling sensations in the little finger and the medial one-half of the ring finger, which are innervated by the ulnar nerve. Most of the other fingers are innervated by the median nerve, with the exception of a portion of the thumb, which is innervated by the radial nerve.

A similar nerve plexus, called the lumbosacral plexus, innervates the leg. This also has many branches, but the major ones are the femoral nerve, which innervates the front (ventral portion) of the leg, and the sciatic nerve, which innervates the back (dorsal) portion of the leg. Excessive tension on the femoral nerve can cause pain and temporary paralysis of the quadriceps muscles of the leg; similarly, excessive tension on the sciatic nerve can cause painful symptoms called *sciatica*.

Portions of the lumbosacral plexus arise from openings in the sacrum, the bottom of the pelvis. However, the spinal cord does not extend past L2, so

where do these nerves come from? The answer is that, while the nerve cells of the spinal cord never are seen below L2, these cells do extend processes called axons that form bundles (nerves). These bundles form the so-called *cauda equina* ("tail of the horse" in Latin) that continue down through the spinal canal to form the lower nerves of the lumbosacral plexus. This anatomical arrangement of the lower CNS is helpful to physicians, because it makes it possible to insert a needle into the spinal canal between L4 and L5 to administer anesthetic or to sample cerebrospinal fluid.

Brain

The brain can be divided into seven major regions: the medulla oblongata, the pons, the cerebellum, the midbrain, the hypothalamus, the thalamus, and the cortex. Each of these regions has many subdivisions, and each region makes extensive connections with all the others. Nevertheless, some generalizations about the functions of each region can be made.

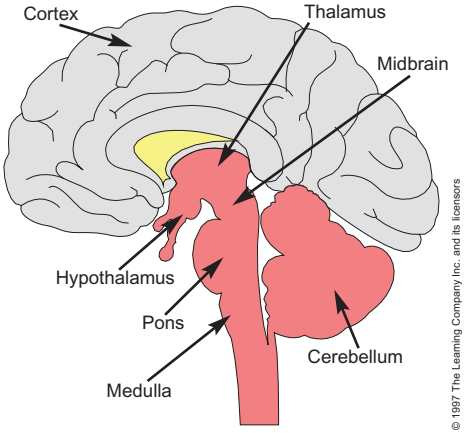

Fig. 14

View of the brain as sectioned in half, front to back (sagittal section).

The medulla provides repetitive, rhythmic impulses to specific portions of the body. For example, there is a collection of neurons in the medulla called the pre-Botzinger complex that continuously generates bursts of electrical impulses. These impulses are conveyed to the diaphragm and other muscles and are responsible for the regular movements of respiration. Similarly, areas for the control of heart rate and similar functions are present in the medulla.

The pons and cerebellum are brain regions that act in synchrony to regulate the movements of the limbs. Complex systems that provide constant information about the positions of the limbs in three-dimensional space operate in these regions. Damage to the cerebellum or pons results in poor coordination of limb movements.

The midbrain contains a portion of specialized nerve cells that regulate posture and muscle tone. Neurons in this area utilize a neurotransmitter called dopamine to communicate with other neurons. A metabolic by-product of dopamine is a brown pigment called neuromelanin, which accumulates in these neurons and causes this brain area to be named the *substantia nigra* (Latin for "black substance"). In most people, these neurons function well throughout life, but in a fraction of people over the age of fifty, these specific neurons begin to die. This results in a disorder called Parkinson's disease and symptoms of tremor and difficulty in walking. Parkinson's disease is relatively common and affects about five hundred thousand Americans. Treatment mainly consists of administering drugs that increase effects of dopamine in the brain, but these approaches only slow the progression of

the disease. Recent work suggests that these neurons die because they possess a special type of calcium channel in their cell membranes; more study of these channels may lead toward better treatments for this disease.

Fig. 15

Cross section through the midbrain, showing the dopaminergic neurons of the substantia nigra. These neurons (stained to demonstrate an enzyme of dopamine synthesis) become damaged in Parkinson's disease.

Cranial Nerves

The midbrain, pons, and medulla together constitute the so-called "brainstem" of the brain. In addition to the functions mentioned above, the brainstem is the main site of origin of cranial nerves. Cranial nerves erupt from the brain at regular intervals, much like spinal nerves erupt from the spinal cord, but cranial nerves mainly innervate structures of the head and neck.

There are twelve cranial nerves:

1 = olfactory
2 = optic
3 = oculomotor
4 = trochlear
5 = trigeminal
6 = abducens
7 = facial
8 = auditory
9 = glossopharyngeal
10 = vagus
11 = spinal accessory
12 = hypoglossal

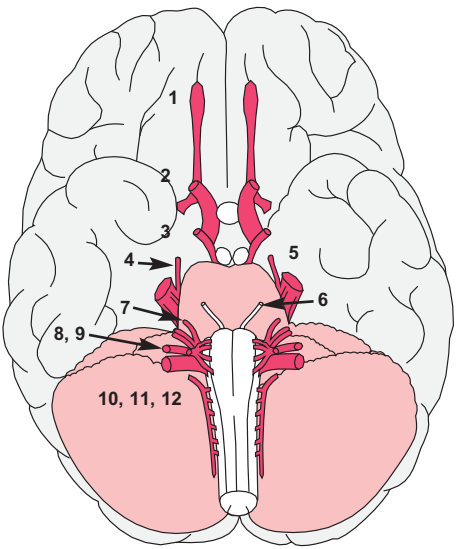

Fig. 16

View of the ventral surface (bottom) of the brain, showing the points of origin of the twelve cranial nerves.

Most of these nerves are confined to head and neck structures, except for the vagus ("wandering vagabond") nerve that travels down the neck to provide innervation to the respiratory and gastrointestinal tracts. Clusters of neurons called cranial nerve nuclei within the brainstem give rise to ten of the twelve cranial nerves.

Higher Brain Structures

Just above the brainstem is the hypothalamus, a brain region that has diverse functions. Nerve cells in the hypothalamus regulate body temperature, sexual behavior, appetite, drinking behavior, sleep, and the secretion of hormones from the pituitary gland. It has recently been found that specific nerve cells in the hypothalamus, which contain a neurotransmitter called orexin, mysteriously die in some individuals. This causes affected patients to develop a condition called narcolepsy, which causes them to fall asleep frequently in the daytime. Another cluster of nerve cells is larger in males than in females and may be responsible for modulating male sexual behavior.

The thalamus is the so-called "gateway" to the cortex, in that sensory and motor information going to and from the cortex must first pass through the thalamus. Auditory and visual information are relayed directly to specific thalamic nuclei as well as to the cortex. The thalamus also seems to be important for the perception of and reactions to painful stimuli.

The cortex, or covering, of the brain is much more elaborate and larger in humans than in most vertebrates, and is responsible for the more complicated patterns of thinking and emotion in humans relative to many other animals. The occipital region of the cortex is specialized for processing visual information, whereas other regions are required for recognition of sounds, of speech, or of faces. In humans, unlike in many other animals, the cortex has become so large that in order to fit within the cranial cavity, it is thrown into folds called gyri that are separated from one another by gaps called sulci. One large gyrus is called the pre-central gyrus, and is specialized for the production of movement by the body. Anterior to this is the so-called premotor cortex, where movements are "planned," but not initiated.

Curiously, the ability to produce and respond to language is localized mainly in the left cerebral cortex, whereas non-verbal abilities and the ability to respond to emotions are the products of activity in the right cerebral cortex.

In Alzheimer's disease, nerve cells in specific portions of the cortex (temporal lobe), connected to a subcortical structure called the hippocampus, are particularly affected. This condition leads first to a deterioration of memory and then to more general abilities such as dressing and walking. It affects as many as five million Americans. Many of the proteins and genes involved in the development of Alzheimer's disease have been identified, but dramatically effective treatments remain elusive.

FOR GREATER UNDERSTANDING

Questions

The brain floats suspended within the cranial cavity in a fluid called cerebrospinal fluid. If a person experiences a blow to the head, the brain bounces away from the point of injury and often crashes against the skull at a spot 180 degrees away from the area of impact. What cortical function might be impaired following a blow to the forehead?

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Lecture 7:
Eye and Ear

The Suggested Reading for this lecture is Elaine N. Marieb, Jon Mallatt, and Patricia Brady Wilhelm's *Human Anatomy* (chapter 16).

The Eye

The eye is basically a fluid-filled sphere composed mainly of a tough outer layer of connective tissue that is lined on the inside with a thinner vascular layer called the uvea, and, underlying the uvea, a layer rich in neurons called the retina. Most of the outer connective tissue of the eye (the sclera) is unremarkable, but the anterior-most connective tissue is unique in being *transparent* (the cornea). How does this amazing property come to be?

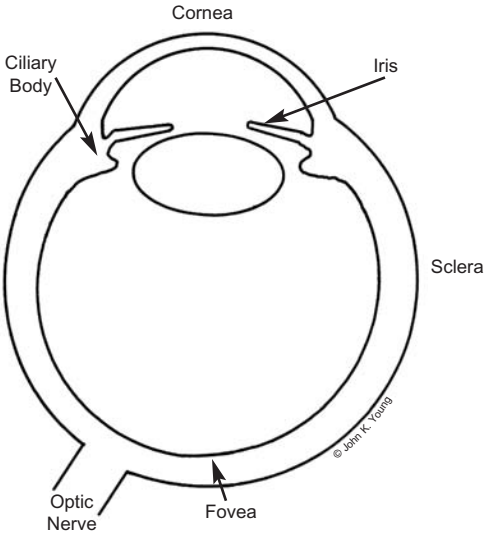

Fig. 17
Diagram of the eyeball.

One reason why the cornea is transparent is that it completely lacks blood vessels. This is because the connective tissue cells of the cornea secrete a protein called tenomodulin that prevents blood vessels from growing into it. Due to a lack of blood vessels, cells in the cornea are completely dependent upon a diffusion of nutrients and oxygen from the tears and from the eyeball fluid (aqueous humor) just behind the cornea. Also, the lack of blood vessels means that cells of the immune system are completely excluded from the cornea. This makes it possible to transplant a cornea from a donor into a patient with irreversible corneal scarring.

Another common operation involving the cornea is LASIK surgery (Laser ASsIsted Keratomileusis). In this procedure, a thin flap of the anterior cornea is created with a scalpel and lifted off the rest of the cornea. Then the remaining portions of the cornea beneath this flap are sculpted with a laser beam. When the overlying flap is allowed to fall back into place, it will heal and cover the new contours of the cornea. This procedure can dramatically affect vision because about 90 percent of the refractive power of the eye is due to light passing through the cornea from the outside of the eye.

After passing through the cornea, light enters the eye via an opening (pupil) in a disk-shaped plate (iris) at the front of the eye. The color of the iris is determined by the number of pigment-producing cells, called melanocytes,

that are present in it. Brown-eyed people have more melanocytes in the iris than blue-eyed people. Albinos are individuals having melanocytes that lack the ability to produce the brown pigment, melanin. Hence, the irises of albinos will appear pink, due to the color of the blood vessels present in the iris.

Light that enters the eye through the pupil then passes through the lens, a structure composed of very peculiar, closely packed cells called lens fibers. The proteins found in lens fibers, as well as the proteins found in the cornea, are positioned next to each other with extreme regularity. The regular spacing of these protein molecules, analogous to the spacing of atoms in a crystal, is another factor that allows for the transparency of the lens and cornea.

The lens is held in place by small fibers of a protein called fibrillin that attach the lens to a vascular mass of tissue called the ciliary body. The ciliary body, in addition to anchoring the lens, also produces a watery fluid called aqueous humor that percolates forward, around the lens, and beneath the cornea. This fluid is slowly drained from the eyeball by passing into a small tubular structure called the canal of Schlemm, located at the junction between the cornea and sclera. If this fluid does not drain properly, an increased intraocular pressure results, forming a condition called *glaucoma*.

There is a ring-shaped mass of muscle within the ciliary body that surrounds the lens. When these muscles contract, the diameter of this ring shrinks, and the tension on the fibers attached to the lens is diminished. This allows the lens to "round up" and focus light from nearby objects more accurately upon the retina. Prolonged reading may cause the ciliary muscles to tire, resulting in "eyestrain."

As light continues through the lens, it passes through a more viscous mass of fluid in the back of the eye called vitreous humor, and then finally strikes the retina. The retina contains specialized, light-sensitive neurons called rods (one hundred million in human eyes) and cones (seven million). Rods are mainly sensitive to dim light and allow us to see at nighttime; cones can distinguish between red, green, and blue colors, and are mainly concentrated in the fovea, a depression in the center of the retina. Information from these photoreceptors is processed by other nerve cells in the retina, and finally leaves the retina via bundles of axons that form the optic nerve. There are no photoreceptor cells at the spot where the optic nerve leaves the retina, so no light can be detected there. This forms the so-called "blind spot" in our visual field that can be detected by gazing at one finger and moving a finger on your other hand slowly to one side of it. Normally, our brains and retinas routinely "ignore" this insensitive area of the retina so that we are not even aware of it.

One challenge in understanding the eye is the question of how such a complex structure ever evolved. What were the precursors of the eye, and did they function as some kind of more primitive eyes? Moreover, flies, octopuses, and mammals all have eyes with very different-appearing structures. Did they evolve independently? Even Darwin was troubled by these questions. More recently, however, it has been determined that all creatures with eyes, even jellyfish with very primitive light-sensing organs, seem to share the same kinds of genes with all other visual organisms. So, it appears that the cells of eyes did only evolve once, in a very simple form, and became incorporated into more complex organs as evolution proceeded.

The Ear

The ear is divisible into three portions: the outer ear (pinna), which directs sound into the auditory canal; the middle ear, which consists of three bones suspended in an air-filled cavity; and the inner ear, a collection of fluid-filled sacs surrounded by bone.

The function of the outer ear is obvious: to convey sound vibrations to the eardrum, which transmits them to other parts of the ear. However, it is not as easy to explain why the human middle ear contains three tiny bones. These bones convey sound vibrations from the eardrum (tympanic membrane) to another membrane covering the so-called oval window, which then transmits vibrations into the fluid of the inner ear. What is the advantage of this complicated arrangement? Why not transmit sound directly from the eardrum to the inner ear and dispense with the middle ear altogether?

The three bones of the middle ear are called the malleus (hammer), attached to the eardrum, the incus (anvil), and the stapes (stirrup). Not all animals possess all three ossicles: fish, for example, have only a single stapes that connects the eardrum to the oval window. The two additional bones—the malleus and incus—appear to have been derived, during evolution, from small bones of the jaw that were displaced into the ear. Movements between these two additional bones exert further leverage upon the eardrum and increase the sound-induced force upon it.

The hole above the footplate of the stapes (obturator foramen) is formed by the passage of a small artery (stapedial artery) through the bone. In humans, but not in some mammals, this artery disappears during embryogenesis.

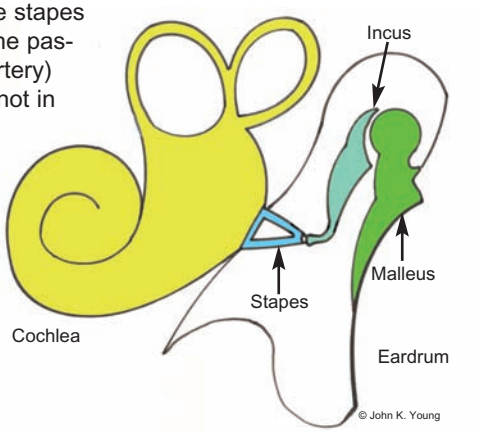

Fig. 18

Diagram of the middle and inner portions of the ear.

The functional reason for the existence of middle ear structures relates to the higher viscosity of fluid relative to air. Sound travels through air easily. In fluid, however, the transmission of vibrations is more attenuated and requires more energy. The resistance of fluid to sound transmission is called *impedence*. The inner ear ossicles have the function of impedence matching between air and inner ear fluid. Sound striking the tympanum exerts a force across some 60 mm^2. This energy is transmitted by the ossicles onto the membrane covering the oval window, which is much smaller (3.2 mm^2). Thus, a sound exerts a much greater force per square millimeter on the oval window than on the eardrum, and so can overcome the greater impedence of fluid for the transmission of vibrations. The air cavity within the middle ear communicates with that of the nasopharynx via a tube called the Eustachian tube (pharyngotympanic tube). The opening of this tube is normally closed, unless it is tugged on by a muscle called the tensor palati during swallowing or yawning.

The eye and inner ear have some functional features in common. The eye has two tasks to fulfill: a simple task (the presence or absence of light), and a more complex function of determining the frequency (color) and directionality of light. Similarly, the inner ear is devoted to a simple, primitive function of detecting vibrations in fluid that are caused by shifting the positions of the head and also to a more complex function of detecting fluid vibrations caused by sound and determining the frequency and directionality of that sound. Unlike in the eye, the primitive and sophisticated functions of the ear are carried out by two anatomically distinct divisions of the inner ear, the vestibular apparatus and the cochlea, respectively.

The cochlea contains three tubules, filled with fluid, that are closely adjacent to each other. In reptiles, these tubules lie side-by-side next to each other in a straight line and stick out to form a structure rather like a tiny ice-cream cone. In mammals, these tubules have gotten much longer, and to save space, they have become coiled into a spiral resembling a snail shell.

One tube within the cochlea contains about thirty-five hundred sensory cells called inner hair cells that respond to sound waves. Their reactions are detected by about thirty thousand nerve cells that live within the cochlea and produce axons that form the auditory nerve. This is a much smaller number of nerves than in the optic nerve, which contains about one million axons. Cells at the base of the cochlea are responsive to high-frequency sounds, whereas cells at the tip of the cochlea respond to low-frequency sounds. As the cells age, they accumulate damage, die, and are not normally replaced in mammals because adjacent supporting cells do not divide to replace them. Thus, age-related deafness is one of the largest causes of disability in older people. Curiously, in birds, damaged hair cells *can* be replaced by nearby cells. If this ability for hair-cell replacement could be recovered, a possible treatment for deafness could be achieved.

The other portion of the inner ear, adjacent to the cochlea, is called the vestibule. The vestibule contains sensory cells that react to currents and movements of fluid that occur upon movements of the head or body. Some sensory cells are located beneath long, looping tubules that form the so-called semicircular canals. These cells react to rotational movements of the head. Other cells are located in patches called maculae. These cells react when the head is accelerated forward or dropped downwards. Cells of the vestibule are innervated by their own set of nerve cells, which send axons to the vestibular portion of the auditory nerve.

The evolution of the ear from simpler structures is a bit easier to understand than the evolution of the eye. Nevertheless, questions persist. Did the primitive ear arise only once in our ancestors and then become modified in different types of animals? Recent data have shown that, surprisingly, the same sets of proteins that are required to create our ears are found in the sound-sensitive structures on the antennae of insects. It seems likely that the creation of ears was a very ancient event, occurring before the ancestors of insects had diverged from the ancestors of vertebrate animals.

FOR GREATER UNDERSTANDING

Questions

Inner ear infections (otitis media) are extremely common in young children and account for one-third of all visits to pediatricians. Why do you think that young children would be more susceptible to this than adults?

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Lecture 8:
Upper Digestive System

The Suggested Reading for this lecture is Elaine N. Marieb, Jon Mallatt, and Patricia Brady Wilhelm's *Human Anatomy* (chapter 22).

Oral Cavity

The upper digestive system of mammals begins with the lips, which evolved primarily to provide infants with the ability for suckling. Other animals, such as reptiles, amphibians, birds, and fish, do not suckle and lack lips. Lips also provide humans with the ability to modulate sounds and create speech.

Behind the lips, there are thirty-two teeth embedded either into the mandible or maxilla. In humans, the teeth have different forms that coincide with different functions: incisors for cutting, canines for stabbing, and molars for chewing. Animals like sharks that have a simpler mode of eating have teeth that all look the same. The outer covering of tooth enamel contains no cells; almost all of it (96 percent) is composed of a specialized type of calcium phosphate that is harder than steel. The underlying dentin is softer (70 percent mineralized), and contains long, thin processes of cells called odontoblasts that produce it. These cells live in the interior of the tooth, at the border of the dentin and the innermost pulp cavity. Reactions of these cells to heat and pressure are probably responsible for the sensations you feel in a dentist's chair.

Tooth cavities form when oral bacteria digest food remnants (plaque) that adhere to the teeth. The end products for food digestion by bacteria are acids, which dissolve the calcium phosphate in the enamel. Teeth are held in their sockets by bands of connective tissue that form periodontal ligaments. If bacteria enter these ligaments and damage them (periodontitis), this can cause a loosening and loss of teeth.

The tongue is covered on all surfaces by a layer of epithelial cells. Prominent upfoldings of this epithelium form so-called lingual papillae. Four types of lingual papillae exist. Filliform papillae are the most abundant type, and form hundreds of tiny spear-shaped projections from the surface of the tongue. These are analogous to the teeth of a file and make the surface of the tongue rougher for better manipulation of food. Filiform papillae are unusually well developed on the rough surface of the tongue of cats, for example. The remaining three types of lingual papillae are more mushroom shaped and consist of small fungiform and foliate papillae and larger vallate papillae, which are found in a V-shaped line demarcating the anterior two-thirds of the tongue from the posterior one-third of the tongue. These papillae often possess taste buds, onion-shaped masses of sensory cells that convey the taste of food molecules dissolved in saliva. If you look in a mirror, you can see this line of ten to twelve vallate papillae at the back of the tongue.

The tongue itself contains a mass of intrinsic muscles that modulate its shape, as well as portions of three extrinsic muscles. One such extrinsic muscle, the genioglossus, attaches to the inside of the anterior jaw and

assists in protruding the tongue. If it is paralyzed or injured, the tongue falls to the back of the mouth and can cause suffocation. Another muscle, the hyoglossus, attaches the base of the tongue to the hyoid bone, located in the pharynx just above the larynx. When you stick out your tongue, you can feel the hyoid bone move.

The roof of the mouth, the palate, is composed of the anterior hard (bony) palate and the more posterior soft palate. Muscles pull on the soft palate to elevate it during swallowing, so that food does not enter the nasal cavity from behind.

In about one out of seven hundred newborns, the structures on both sides of the face that form the palate fail to fuse completely during development, leading to a condition called cleft palate. This is usually correctable with surgery after about ten weeks of age. One cause of cleft palate is an abnormality in a DNA-binding protein called IRF6, which instructs cells in the developing palate to migrate and to form fused structures of the palate.

Like most facial structures, the oral cavity sends sensory information up nerve branches of cranial nerve five (trigeminal nerve). As its name suggests, the trigeminal nerve has three major branches that innervate the face. The first (opthalmic) branch innervates the forehead and eye region; the second branch (maxillary division) innervates the upper jaw and maxillary area, and the third branch (mandibular) divides to innervate the tongue and lower jaw. When anesthesia is injected by a dentist to anesthetize the mandibular nerve, numbness may thus be felt in the tongue and cheeks as well as in the lower teeth.

The trigeminal nerve also supplies motor innervation to chewing muscles like the temporalis, masseter, and the buccinator muscle, which forms the lateral wall of the oral cavity. The other muscles of the face (muscles of facial expression) receive motor innervation from another cranial nerve, the facial (seventh) nerve.

Esophagus and Stomach

Food and fluids are passed from the mouth to the esophagus, which rhythmically contracts in a pattern called peristalsis to move food down to the stomach. The wall of the esophagus contains thick layers of muscle that accomplish this. Muscle contractions are stimulated and coordinated by millions of nerve cells present in ganglia located throughout the walls of the gastrointestinal tract. This system of nerve cells is extensive and relatively sophisticated, and contains more neurons than the spinal cord itself.

The esophagus passes down through the thoracic cavity behind the heart and pierces through the diaphragm via an opening called the esophageal hiatus. Occasionally, this opening can weaken and allow the stomach to protrude up into the thoracic cavity (hiatal hernia). A consequence of this is excessive exposure of the lining of the esophagus to stomach acid, which can damage it.

The stomach is a muscular sac that stores food and initiates digestion of food. Much of the digestion that takes place in the stomach is due to secretion by the stomach of hydrochloric acid, which breaks proteins down into amino acids that can be more easily absorbed by the intestines. The stomach has the capacity to hold about one liter (roughly a quart) of fluid. In recent

decades, surgery to reduce the capacity of the stomach (gastric bypass surgery) has become a popular approach for reducing obesity. In this procedure, the stomach is divided into two portions with staples. The upper portion, which joins the esophagus, is reduced to a thumb-sized sac that only holds 15 ml. This restricts the size of meals that can be taken. This reduced sac is reconnected to the small intestine to allow for the passage of food through the gastrointestinal system. About one hundred forty thousand gastric bypass surgeries are performed each year in the United States.

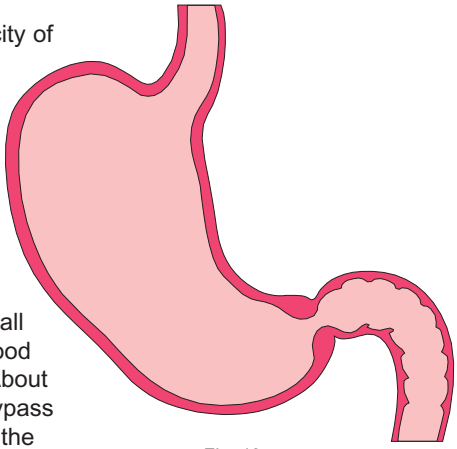

Fig. 19

Diagram of the stomach.

Some types of animals, like certain fish, eat such small particles of food that the food can be directly passed to the intestines, so these fish have no stomachs at all. On the other hand, in some animals, such as cows and sheep, the stomach has developed constrictions that divide it into four distinct pouches that help digest grass. In actuality, three of these pouches have a microscopic structure similar to that of the esophagus, and only one of these "four" stomachs has cells that produce acid and enzymes like the stomachs of most animals. The other three portions of the stomach are big fermentation tanks containing specialized bacteria that can break down the cellulose of grass into molecules the cow can use. The stomach of a cow can account for 25 percent of the entire body weight of the animal.

Stomach ulcers arise when damage to the lining epithelium of the stomach exposes the underlying tissues to acid, causing damage and bleeding. For many years, a so-called psychogenic cause of ulcers was proposed, in which psychological stress had a major role in enhancing stimulation of acid secretion in the stomach by the vagus nerve. In spite of the failure of this approach to satisfactorily treat ulcers, it was nevertheless stubbornly adhered to, until the 1980s. At that time, a completely novel explanation for ulcers was proposed by two Australian researchers, Barry Marshall and Robin Warren. Marshall and Warren found that most ulcer patients were suffering from infection of the digestive system by a bacterium called *Helicobacter pylorii* that damages the stomach epithelium and allows damage by stomach acid. To convince skeptics of their proposal, Marshall deliberately infected himself with the bacterium to show that it could cause acute gastric illness. Marshall and Warren were awarded the Nobel Prize for medicine in 2005 for their work. These bacteria can be killed by administration of the antibiotic, clarithromycin, in the presence of an inhibitor (like Prilosec) of the hydrogen transporter. These treatments kill the bacteria and lower the acidity of the stomach, leading to a cure for ulcers.

FOR GREATER UNDERSTANDING

Questions

1. Distension of the stomach by food is one of the signals that limit appetite. How is this signal communicated to the brain?
2. What other signals might alert the brain that sufficient food has been ingested?

Suggested Reading

Marieb, Elaine N., Jon Mallatt, and Patricia Brady Wilhelm. *Human Anatomy*. 5th ed. New York: Benjamin Cummings, 2007.

Articles of Interest

Knight, A.S., et al. “Developmental Expression Analysis of the Mouse and Chick Orthologues of *IRF6*: The Gene Mutated in Van der Woude Syndrome.” *Developmental Dynamics*. Vol. 235, pp. 1441–1447, 2006.

Lecture 9:
Lower Digestive System

The Suggested Reading for this lecture is Elaine N. Marieb, Jon Mallatt, and Patricia Brady Wilhelm's *Human Anatomy* (chapter 22).

Small Intestine

After food leaves the stomach, it passes into the small intestine, which in humans is about fifteen feet long. The small intestine is divisible into three portions: the duodenum, a short (one foot long) portion of the intestine that passes beneath the stomach and partly encircles the pancreas; the jejunum (about six feet long); and the ileum (about eight feet long). The duodenum is firmly anchored to the back of the abdominal wall, but the remainder of the small intestine is suspended four to five inches away from the posterior abdominal wall by thin sheets of tissue called mesenteries.

All of the portions of the small intestine are specialized for the digestion and absorption of food molecules. One sign of this specialization is the presence of millions of tiny, finger-like projections called *villi* from the epithelium lining the intestine. All of these villi greatly increase the surface area of the intestinal lining and enhance the absorption of food molecules. The cells lining the intestine have enzymes attached to their cell membranes that break proteins and starches into smaller amino acids and sugars, respectively. In addition, the pancreas secretes powerful digestive enzymes into the duodenum to aid in food digestion. Also, the enzyme-containing fluid secreted by the pancreas has a strongly basic pH, so that it counteracts the strong acids entering the intestine from the stomach. Additional basic fluid is produced by glands called Brunner's glands that are found only in the duodenum.

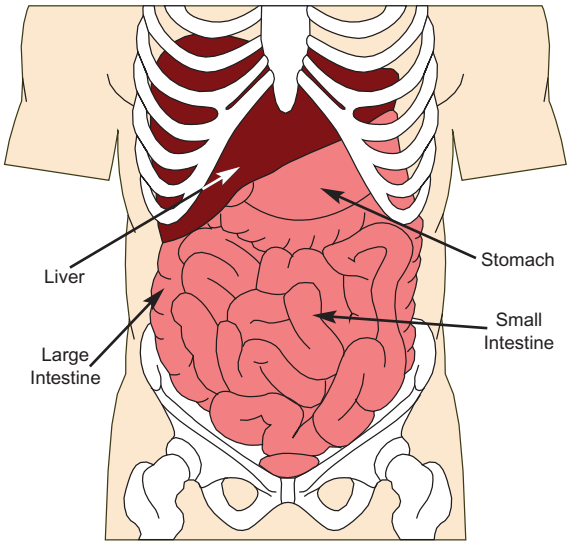

Fig. 20
Diagram of the gastrointestinal organs.

The blood vessels associated with the intestines are unusual. The arteries supplying oxygenated blood to the stomach, small intestines, and large

intestines originate from three large branches of the abdominal aorta: the celiac trunk, the superior mesenteric artery, and the inferior mesenteric artery, respectively. These arteries provide blood to capillary networks in these digestive organs. Blood collected from the intestines does not take a normal route back to the heart. Intestinal blood is collected into superior and inferior mesenteric veins that, together with a vein from the spleen, forms the so-called portal vein. This vein, instead of leading back to the heart, dives into the liver and delivers blood to a *second* bed of sinusoidal capillaries. The cells of the liver adjust the contents of this blood, and then allow the blood to leave the liver via the hepatic veins to finally return to the heart. This situation, in which two capillary beds rather than one are interposed between an artery and a vein, is called a *portal system*.

In embryonic life, oxygen- and nutrient-rich blood from the placenta traveled via the umbilical vein to the portal vein, and thence to the liver and to the rest of the body. At birth, the umbilical vein is clamped off, and its connection to the portal vein is gradually lost.

After most of the nutrients and water have been absorbed, food passes through the large intestines (colon). There are three parts of the colon: the ascending colon, on the right side of the abdominal cavity, the transverse colon, just beneath the stomach, and the descending colon, which eventually terminates in the rectum.

In humans, the main task of the colon is to absorb remaining water from food. Although almost nine liters of fluid/day enter the gut, the vast majority of this fluid is reabsorbed, so that only 100 ml of fluid eventually leave the body in the stool.

Some animals, like shrews, moles, and whales, ingest a diet that does not require food processing in the large intestine, so these animals entirely lack this organ. On the other hand, in grass-eating animals like rabbits and horses, the colon has become larger than that of humans and is specialized for the digestion of cellulose. Bacteria in the large intestines of these animals help digest cellulose into nutrients like fatty acids. So, in some animals, the large intestine carries out a function similar to the four-chambered stomachs of cows. This bacteria-aided digestive process produces 70 percent of the calories needed by cows, for example. In humans, however, intestinal bacteria probably provide us with only 10 percent of our needed daily calories. Nevertheless, the human gut has been estimated to contain some one hundred trillion bacteria.

In addition to absorbing water, the cells of the large intestine secrete large amounts of mucus that lubricates the intestinal contents. As a consequence of water absorption, the gut contents steadily become less liquid and more solid and exert more friction upon the lining epithelium. To counteract this, specialized cells called goblet cells of the large intestine secrete more mucus.

The appendix is a small, worm-shaped organ located near the junction of the small intestine with the colon. It contains an unusually large number of lymphocytes and may have some immune function. When its connection with the rest of the intestine becomes blocked, the appendix fills with mucus and swells. Eventually this compresses the blood vessels leading to it and the

appendix becomes inflamed and infected. At this point, it must be surgically removed before it bursts and contaminates the abdominal cavity with bacteria.

Liver and Gall Bladder

The liver is one of the largest organs in the body, and receives about one-quarter of the blood flowing throughout the cardiovascular system. It functions rather like a filter interposed between the gut and the rest of the body. Helpful materials, such as foods, can be stored in the liver or converted to other molecules. For example, after the ingestion of a solution of glucose, about 65 percent of this glucose is immediately converted to a storage form (glycogen) and stored in the liver for emergencies, so that only 35 percent of this sugar directly reaches the other tissues of the body. Also, if we eat a large, protein-rich meal, only a portion of absorbed amino acids reach the tissues; the remainder of these molecules are converted to other types of molecules and burned by the liver. One problem for this process of amino acid metabolism is that, in the first step, ammonia is generated when NH_2 groups are cleaved from the amino acids. Ammonia is so toxic that, if it were then released from the liver into the bloodstream, it would be lethal. Instead, the liver combines two ammonia molecules into a less toxic molecule called urea, which will later be extracted from the blood by the kidneys and excreted into the urine.

Harmful materials absorbed from the gut are metabolically destroyed in the liver before they can reach the rest of the body. These include drugs such as phenobarbital, toxins in foods, and alcohols. A family of fifty-seven types of related proteins called cytochrome-P450 enzymes accomplish many of these chemical transformations. One type of enzyme, called alcohol dehydrogenase, breaks down ingested alcohol into less toxic chemicals.

Chronic alcoholism, experienced by almost ten million Americans, causes this liver enzyme to become more abundant and active. This can be helpful when it breaks down alcohol, but can cause damage when it breaks down other materials into toxic chemicals. Alcohol can thus cause cirrhosis of the liver, in which liver cells react to toxins by secreting tough fibers of collagen that accumulate abnormally and fill up the spaces within the liver. This can impede blood flow through and into the liver. As a result, one of the veins (left gastric vein) that normally delivers blood into the portal vein experiences a backflow of blood that goes up along the stomach until it fills the veins of the esophagus. These may swell and burst as a result. Alcoholics should not use the pain-killing drug acetaminophen, because it can be turned into a toxic chemical by alcohol dehydrogenase and damage the liver.

When the liver is damaged, it fortunately has an unusually strong ability to recover and regenerate. For example, if half the liver is removed from a rat, within a month the remaining portion enlarges until it completely replaces the missing part. Even more importantly, the liver does not *continue* to grow and normally stops when regeneration is complete. Recently, an important DNA-binding protein that regulates overall organ size has been identified. If this DNA-binding protein, called YAP, is experimentally activated in the liver of a mouse, the liver may grow to five times its normal size.

In addition to storing food molecules, the liver also secretes many important molecules into the blood. These include blood-clotting proteins and choles-

terol. Finally, the liver manufactures bile and secretes it into a duct connected to the gall bladder and duodenum. Bile is a mixture of waste products and bile salts that are eventually secreted into the intestine. Bile salts are the most abundant components of bile. When they reach the small intestine, they function as detergent-like molecules that break up fats into smaller droplets that are more easily digested. A much smaller component of bile is a waste product, derived from the breakdown of hemoglobin, called bilirubin. This is a highly colored chemical that gives bile its yellow-green appearance. If the excretion of bilirubin in the bile is prevented, by a blocked duct or by liver disease, it accumulates in the blood stream and can provoke a yellowish tinge to the skin and eyeballs. This condition is called *jaundice*.

The liver can be severely affected by a very common genetic disorder called hereditary hemochromatosis. In this disease, which affects one out of four hundred people, iron accumulates in the liver, pancreas, and brain because of a flaw in a protein that regulates the absorption of iron from the blood into cells. Iron overload can have a very damaging effect on the liver and other organs. Fortunately, there is a simple cure: removal of blood from the body rapidly depletes iron stores in all organs and, if done judiciously, can reverse the symptoms of hemochromatosis.

Gall Bladder

The gall bladder is a small bag-shaped organ attached to the bile duct that stores and concentrates bile for delivery into the small intestine. By removing water from bile, it can concentrate it five-fold and store enough for the demands of daily meals.

Over time, cholesterol in bile precipitates to form insoluble masses called gallstones. By age sixty, 15 to 20 percent of the total population will have experienced gallstones. If these enlarge enough to block the bile duct, that can cause jaundice, infections of the gall bladder, and very painful symptoms. Surgical removal of the gall bladder cures these problems, and leaves intact a trickle of bile from the liver directly to the small intestine that is usually sufficient for digestive processes.

FOR GREATER UNDERSTANDING

Questions

1. Why have grass-eating animals developed larger colons?
2. What is the relationship between alcohol, liver enzymes, and cirrhosis?

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Lecture 10:
Exocrine and Endocrine Glands

The Suggested Reading for this lecture is Elaine N. Marieb, Jon Mallatt, and Patricia Brady Wilhelm's *Human Anatomy* (chapters 22 and 25).

Glands are assemblies of epithelial cells specialized for secretion. Some glands secrete specialized molecules into ducts that connect to hollow organs. These glands are defined as exocrine glands. Other glands—endocrine glands—secrete molecules termed hormones directly into the bloodstream. Exocrine molecules are often proteins like enzymes. Hormones, on the other hand, bind to cell structures and modulate cell activity. These two classes of glands can be examined separately.

Exocrine Glands

One important exocrine gland is the lacrimal gland that bathes the surface of the eyeball in tears. Tears are a complex fluid containing some 491 proteins. Many of these proteins fight bacteria or protect the cornea from the damaging effects of high levels of atmospheric oxygen. The watery fluid of tears also lubricates the eye and prevents it from drying out.

In a common disorder, Sjögren's syndrome, the immune system attacks the cells of exocrine glands, particularly the lacrimal glands and salivary glands. This disease is the second-most common autoimmune disease, and can affect 5 percent of all women over the age of sixty-five (the disease is nine times more common in women than in men). For many patients, symptoms are not too serious—dry eyes and a dry mouth. In some, however, the dryness can be so severe that serious problems with vision develop, and artificial tears have to be constantly applied to the surface of the eye. The reasons why the immune system would attack specific types of exocrine glands are not known.

Three major salivary glands can be identified surrounding the mouth. The largest one lies anterior to the ear, and derives its name, the parotid gland, from its location (*par* = near, and *otid* = ear, in Latin). Its duct penetrates the cheek muscles and delivers saliva into the mouth near the second upper molar. The parotid gland is particularly vulnerable to infection by a virus that causes the swelling and discomfort found in *mumps*. Usually, these symptoms last for several days but cause no permanent damage in most infected patients. The submandibular gland, located beneath the angle of the jaw, sends saliva via a duct to the bottom of the mouth. Similarly, the sublingual gland, which lies beneath the tongue, sends saliva via many tiny ducts to the bottom of the mouth. About three hundred proteins can be identified in saliva. The bulk of these proteins are enzymes like amylase that digest starch, or proteins of the immune system that fight bacteria. Other proteins bind to the surface of teeth and maintain the integrity of tooth enamel.

Salivary gland function can be damaged in Sjögren's syndrome. Also, treatment of oral cancers with radiation can damage salivary tissue and lead to dry-mouth syndromes. About forty thousand cases of oral cancer are treated with radiation each year, so this can be a common problem. One result of diminished saliva production is an explosion of dental cavities that can lead to loss of teeth.

Smaller, specialized salivary glands can be found throughout the oral cavity, but have no specific names in general. One type of salivary gland is found near the taste buds, and functions to continually bathe the taste buds of the tongue with fluid so that food molecules are washed off and the cells are freed to react with other tastants.

Another major exocrine gland is the pancreas, which delivers its secretions into the duodenum via the pancreatic duct. The fluid secreted by the pancreas has a basic pH, which greatly helps to neutralize the powerful acids leaving the stomach and entering the duodenum. Also, the pancreas secretes numerous enzymes that help digest the proteins, sugars, fats, and DNA and RNA molecules that are present in foods. Most of the cells in the pancreas are exocrine cells, but a few of them form clusters of endocrine cells.

Endocrine Glands

Endocrine Pancreas

About 4 percent of the cells of the pancreas are organized into small, spherical clusters called islets of Langerhans that secrete hormones into the bloodstream. The two major hormones of these islets are glucagon and insulin. Glucagon is a protein hormone, formed from a chain of amino acids, which primarily functions to stimulate the release of glucose from the liver into the bloodstream during times of fasting. Insulin, on the other hand, is a protein hormone that stimulates the uptake of glucose from the bloodstream by muscle and fat cells.

In diabetes mellitus, interference with this effect of insulin causes elevations in blood glucose and many medical problems. Elevated blood glucose is associated with damaged kidney and heart function, increased risks of retinal bleeding and cataract formation, and poor circulation and wound healing that can necessitate amputations of the toes. About 5 percent of Americans currently have diabetes mellitus, and the risk for diabetes is increasing in step with increasing rates of obesity. What causes diabetes mellitus?

About 10 percent of diabetics have type I diabetes, in which symptoms are due to an attack upon islet cells by the immune system that reduces the ability of islets to make insulin. The exact causes for this attack are uncertain, but they may involve abnormalities in nerves that innervate the islets.

The remaining 90 percent of diabetics have type II diabetes, in which islets at first have a relatively normal ability to produce insulin, but for uncertain reasons, muscle and fat cells are less responsive to insulin. Release of a variety of molecules from fat cells may partly explain this condition. Also, strains of mice and rats that develop diabetes-like symptoms have an abnormal function of a specific cluster of neurons—the arcuate nucleus—in the hypothalamus. So this type of diabetes may result from an abnormal function of both the pancreas and the brain.

Diabetes can be controlled by taking drugs that increase insulin release from the pancreas or by taking injections of insulin itself.

Adrenal Gland

The adrenal glands are located close to the pancreas and sit on the top of each kidney. They are actually composed of two portions, an outer cortex and an inner medulla, that contain two completely different types of cells and which secrete two completely different types of hormones.

The outer adrenal cortex secretes hormones like cortisol that stimulate the release of glucose from the liver and which suppress the function of the immune system. Cortisol is a steroid hormone, derived from the cholesterol molecule, and is chemically very different from protein hormones. In patients suffering from an excessive activity of the immune system, as in severe arthritis, administration of a cortisol precursor called prednisone can temporarily relieve symptoms. However, chronic doses of prednisone, or overproduction of cortisol by the adrenal gland, can have very harmful effects. Excessive cortisol secretion causes Cushing's syndrome, in which weight gain, thinned skin, and immunosuppression are prominent.

The inner adrenal medulla produces hormones made of modified amino acids called epinephrine and norepinephrine. These hormones can stimulate heart rate and increase blood pressure. In addition, the medulla secretes a peptide hormone called enkephalin that binds to opioid receptors of neurons of the nervous system. Enkephalin functions as an endogenous morphine-like substance and can reduce the perception of pain. Many of the hormones of the adrenal gland help the body adjust to dangerous or stressful situations.

Thyroid Gland

The thyroid gland is wrapped around a portion of the larynx called the thyroid cartilage, from which it gets its name. It secretes two hormones, thyroxine and calcitonin. Thyroxine increases the heart rate and the overall metabolic rate of the body. An overactive thyroid gland produces a swelling in the neck called a goiter and can have harmful effects on the body. One curious symptom of hyperthyroidism is a protrusion of the eyeballs forwards in their sockets, a condition called exopthalmos. This easily perceptible symptom of hyperthyroidism is due to a swelling of muscles and fat that lie behind the eyeball. Hyperthyroidism is often treated by the administration of radioactive iodine, which accumulates in the thyroid and kills overactive cells.

The other thyroid hormone, calcitonin, stimulates bone cells to release less calcium into the blood.

Parathyroid Gland

The four small parathyroid glands are located behind the thyroid, on its dorsal surface. They secrete a hormone called parathyroid hormone that stimulates bone to release more calcium into the bloodstream. This gland is essential for life, since the normal function of muscles and nerves requires specific levels of extracellular calcium. If the parathyroid glands are removed accidentally during thyroid surgery, a fatal condition of uncontrollable muscle contractions called *tetany* occurs.

Pituitary Gland

The pituitary gland hangs suspended from the brain by a thin process called the infundibular stalk. It is supported on its ventral surface by a cavity in the sphenoid bone called the *sella turcica* (Latin for "Turkish saddle"). This gland is actually two glands, formed from tissues that originate from two different sites. The anterior lobe of the pituitary originates from oral epithelial cells in the embryo. The posterior lobe appears as a downgrowth from the brain that migrates toward the anterior pituitary and envelopes it.

The anterior pituitary makes hormones that stimulate the functions of the testis and ovary (FSH and LH), the adrenal cortex (ACTH), and the thyroid gland (TSH). It also secretes growth hormone, which increases the growth of bones. Rarely, a tumor of the anterior pituitary will secrete too much growth hormone, resulting in gigantism. Finally, the anterior pituitary makes prolactin, a hormone that stimulates milk synthesis in mammary glands.

The posterior pituitary is a reservoir for two hormones synthesized in the brain and carried down for storage in nerve endings. These hormones are oxytocin, which stimulates milk release from mammary glands, and vasopressin, which stimulates increases in blood pressure.

FOR GREATER UNDERSTANDING

Questions

1. Exocrine and endocrine glands both secrete proteins, but the targets of exocrine proteins are different from the targets of endocrine proteins. What are these targets?
2. In a certain sense, endocrine molecules can be viewed as signals that communicate information throughout the body. What other main type of communication system exists in the body? How do the signals originating in this second system differ from endocrine signals?

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Lecture 11:
The Respiratory System

The Suggested Reading for this lecture is Elaine N. Marieb, Jon Mallatt, and Patricia Brady Wilhelm's *Human Anatomy* (chapter 21).

Nasal Cavity

The respiratory system begins at the nose and nasal cavity, which are the structures that warm and moisten air before its conduction into the lungs. Air rushing into the nasal cavity first passes between three flattened bones that project from the lateral wall of the cavity. These bones, called nasal conchae, are covered by a highly vascular mucosa that warms and moistens inhaled air.

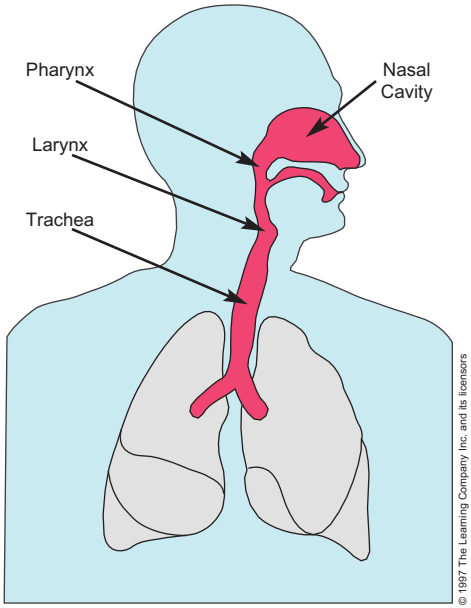

Fig. 21
Diagram of the respiratory system.

These flaps of bone also cover over openings (meatuses) in the lateral walls of the nasal cavity that let air into the so-called *paranasal sinuses*, air-filled cavities that project away from the nasal cavity. These hollow spaces form within the frontal bone over the eyebrows, in the sphenoid bone below the pituitary, in the ethmoid bone in the lateral wall of the nasal cavity, and in the maxillary bones (within the cheeks). Paranasal sinuses provide a helpful function during the growth of the face from infancy to adulthood: they enlarge the dimensions of the upper jaw and provide room for larger, adult teeth, but do not add substantial weight to the skull. Infections of the nasal cavity can lead to swelling that obstructs the openings to these sinuses. In this situation, sinuses can become filled with infected mucus, leading to facial pain. Such infections are usually treated with antibiotics. Occasionally, pain originating from a maxillary sinus infection can become confused with a toothache, since nerves from the upper teeth pass close to the maxillary sinus.

In many animals, small sensory organs called vomeronasal organs are located alongside the vomer bone that helps form the nasal septum, the midline wall of the nasal cavities. Vomeronasal organs in rodents and many monkeys respond to olfactory stimuli called pheromones; such stimuli have profound effects upon the secretion of reproductive hormones in these animals. In humans, a small vomeronasal organ can also be found, but most

studies suggest that it is nonfunctional. The palatine bone forms the floor of the nasal cavity.

As air passes through the nasal conchae, it arrives at the back of the nose, or nasopharynx, which passes downwards to become continuous with the oral pharynx. The pharynx is the gateway to both the digestive and respiratory systems. Flaps of tissue in the palate and covering the larynx direct food toward the esophagus and air toward the trachea. The back of the pharynx is formed by three muscles called pharyngeal constrictors. These three muscles are anchored to the base of the skull, the hyoid bone just above the larynx, and to the larynx itself.

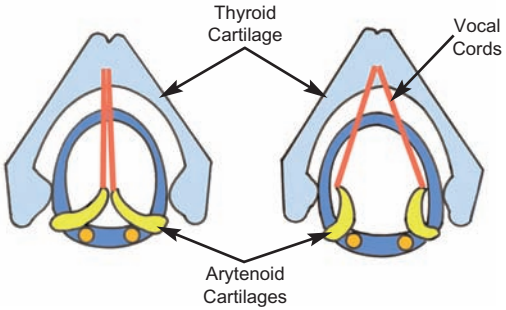

Fig. 22

Diagram of the larynx as seen from above. This shows how the swiveling of the arytenoid cartilages causes the opening of the glottis (space between vocal cords).

When air leaves the pharynx, it passes into the respiratory system via the larynx. This is a complicated structure suspended from the hyoid bone and containing six cartilaginous structures. The opening to the larynx is covered by a flap, the epiglottis, formed from flexible elastic cartilage. Two cylinders of cartilage—the thyroid and cricoid cartilages—make up the bulk of the larynx, together with the smaller arytenoid, corniculate, and cunieform cartilages. The vocal cords stretch between the arytenoid cartilages and the inside of the thyroid cartilage. Each arytenoid cartilage can be made to rotate (pivot) by muscles, thus opening and closing the aperture between the vocal cords. In the open position, the vocal cords allow the free passage of air and no sound is produced. In the closed position, air is forced through a slit between the vocal cords, making them vibrate. The frequency of the vibration and the pitch of the sound can be made to vary by altering the tension upon the vocal cords. Males have a lower voice because testosterone causes an enlargement of the thyroid cartilage and a lengthening of the vocal cords.

Most animals have a larynx that is positioned higher up in the throat than in humans. The extreme of this is seen in snakes, which can elevate the larynx into a position near the tongue in the mouth. This allows the snake to breathe even when it is slowly swallowing a large portion of prey at the same time. The lower position of the larynx in human throats allows for more resonance of sounds and improves our vocal abilities. Birds lack a larynx altogether and produce birdsong via a completely different structure called the syrinx, which is located at the bottom of the trachea rather than at the top.

As air leaves the larynx, it passes into a flexible tube, the trachea. During embryogenesis, a tube connecting the pharynx with the thoracic cavity becomes divided into a ventral portion, the trachea, and a dorsal portion, the esophagus. This event depends upon a DNA-binding protein (a homeotic protein) called Nkx2.1; if it is blocked, the cells composing the trachea and lungs fail to develop properly. The structure of the trachea is ideal for air conduction. Its walls contain rings of cartilage separated from each other by flexible areas

of connective tissue. This prevents the trachea from collapsing in response to lowered air pressure during breathing, but still allows the trachea the flexibility needed for bending the neck. This anatomy of the trachea, rather like a flexible drinking straw, is created in response to local accumulations of a protein called Sonic Hedgehog that stimulate the development of cartilage rings.

The bottom of the trachea divides into two large, primary bronchi that provide air to the right and left lungs. The right bronchus is a bit shorter, wider, and straighter, so that an accidentally inhaled object is more likely to fall into the right bronchus and lodge in the right lung. The main primary bronchi divide into three lobar bronchi on the right and two lobar bronchi in the left lung, which supply the so-called five lobes of the lungs. Each lobe receives smaller and smaller branches of the bronchi and are further subdivided into regions called bronchopulmonary segments. Air passes from bronchi into smaller tubules called bronchioles, in which the cartilage has been replaced by smooth muscle. Finally, air arrives at tiny, thin-walled sacs called alveoli. Each alveolus is surrounded by masses of capillaries that exchange oxygen for carbon dioxide across the thin wall of the alveolus.

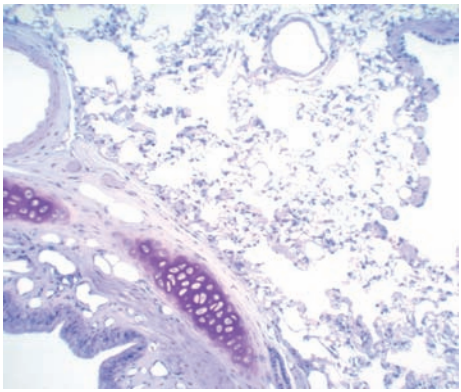

Fig. 23

View of a lung through the microscope, illustrating the pink-stained cartilage surrounding a bronchus (lower left) and the delicate alveolar sacs of the lung.

Not all animals, of course, utilize lungs for respiration. Fish, for example, use gills to extract oxygen from water. Frogs and salamanders have small or even absent lungs; these animals primarily absorb oxygen dissolved in water directly through their thin skins. This isn't possible for us, because living on dry land, we would quickly lose all of our body fluids. So, oxygen exchange must take place within the moist cavities of the lungs.

Inhalation takes place when the diaphragm contracts, lengthening and enlarging the thoracic cavity. The lungs expand to fill this cavity. When the diaphragm relaxes, abundant elastic fibers present in the lungs cause the lungs to "recoil" and partially collapse, expelling air. If air is introduced into the fluid-filled space between the lungs and the thoracic wall (pleural cavity), a lung will collapse completely and become inactive. This was actually done deliberately at the turn of the century as a therapy for tuberculosis of the lung; now that antibiotic-resistant strains of tuberculosis are appearing, this approach may be adopted once more.

The warm, moist environment of the lungs is also, unfortunately, an ideal place for the reproduction of bacteria, so the lungs are particularly vulnerable to infections that cause pneumonia. Various types of chronic lung disorders affect thirty-five million Americans and are a significant cause of death.

One lung disorder is particularly important for the health of newborns. This is the so-called Respiratory Distress Syndrome, which causes impaired breathing in newborns and is the cause of one-third of all infant deaths. Its cause is an insufficient production of a substance called *surfactant* by specialized lung cells. Surfactant is a lipid-rich substance that reduces the surface tension of fluids in the lungs. Without surfactant, lung fluids cause the collapse of lung alveoli and impair respiration. Male babies are 50 percent more likely to develop this condition than females, because testosterone impairs the production of surfactant.

Lung cancer is a particularly serious form of cancer; only 12 percent of patients who develop lung cancer survive longer than five years after diagnosis. Although lung cancer can arise from many causes, smokers are twenty times more likely to develop the disease than non-smokers.

Asthma affects about 7 percent of the adult population. In asthma, the smooth muscle surrounding the bronchioles and bronchi constricts, narrowing air passages and making breathing difficult. One way of treating asthma is via inhaling drugs that act on cellular receptors for epinephrine (albuterol). These drugs cause smooth muscle cells of the respiratory system to relax. Another approach is inhalation of corticosteroid hormones, which suppress the activity of immune cells. The bronchoconstriction of asthma seems initiated by some type of immune reaction to inhaled allergens, so corticosteroids are an effective mode of therapy.

One of the most common genetic diseases, cystic fibrosis, affects the lungs. This disorder is present in about one in twenty-four hundred people. A chloride transporter protein is abnormal in this disease. This causes an excessive accumulation of salt (sodium plus chloride) in many secretory passages of the body. Among these passages are the bronchi; in cystic fibrosis, the mucus secreted into the bronchi becomes too thick and viscous. In addition, dying cells add their DNA to the mucus, which makes it even thicker. One treatment for this condition is the inspiration of aerosols containing an enzyme, DNAase, which breaks the viscous DNA down into smaller molecules.

Another common lung malady is called emphysema, in which the elastic recoil of the lung is reduced and the lungs expand. This makes exhalation and breathing in general difficult. Emphysema seems to be due to an excessive action in the lungs of an enzyme called *elastase*, which destroys the elastic fibers of the lung. This condition also seems to be stimulated by smoking.

Finally, the lungs can be severely affected by a medical condition that does not even arise in the lungs. In about 10 to 20 percent of patients who undergo leg surgery, blood clots can form during or after surgery that lodge in the large veins of the leg. If these clots break off of the lining of the vein, they travel via larger veins through the heart and come to rest in the pulmonary circulation. Once in the lungs (pulmonary embolism), these clots can block off the circulation to portions of the lungs and cause death of lung cells.

The lungs and other delicate organs within the thoracic cavity are protected by the rib cage, which is covered over by the intercostal muscles (*costal* = rib in Latin). These muscles help elevate the ribs during inspiration, which assists the action of the diaphragm in enlarging the thoracic cavity.

FOR GREATER UNDERSTANDING

Questions

The amount of blood entering the lungs is equal to the amount of blood flowing through the rest of the body. Thus, the two sides of the heart pump the same volume of blood. Why, then, is the right side of the heart, which supplies the lungs with blood, smaller and less muscular than the left side of the heart?

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Lecture 12:
The Urinary System

The Suggested Reading for this lecture is Elaine N. Marieb, Jon Mallatt, and Patricia Brady Wilhelm's *Human Anatomy* (chapter 23).

Kidney

The development of the kidney in the human embryo is rather peculiar and is related to the evolution of the urinary system. A fetus develops two types of functioning kidneys. The first one, called the mesonephros, functions during the first three months of life. It is a long, sausage-shaped organ that extends all along the backbone and which receives blood vessels from most of the descending aorta. It somewhat resembles the type of kidney seen in sharks and other fish. Urine produced by this early kidney is collected into the so-called mesonephric duct, which directs urine toward the bladder.

At about five weeks of life, a second type of kidney, the metanephros, sprouts from the lower portions of the urinary system. The metanephros will grow into the adult kidney. As it grows, it ascends into the abdominal cavity from the pelvic cavity. Simultaneously, most of the mesonephros begins to degenerate, until it largely disappears. Occasionally, the two metanephric kidneys will not successfully ascend from the pelvis, and may fuse together to form a so-called horseshoe kidney (incidence: one out of six hundred people). Usually, this abnormal kidney anatomy does not have medical consequences.

The kidneys have a challenging task to fulfill. They receive almost 20 percent of the blood flowing out of the heart, and must filter 125 ml/min of fluid to form urine. However, if all of this fluid were to reach the bladder, the body would lose most of its water within minutes. Hence, most of the fluid and many essential molecules must be also recovered from urine by the kidneys, so that the final volume of urine that leaves each kidney amounts to less than 1 ml/min.

The basic functional units of the kidneys are called nephrons. Each nephron is divisible into two portions. The first portion is a hollow, spherical structure called a renal corpuscle, which filters blood and forms urine. The second portion is a long tubule that receives urine from the renal corpuscle and modifies it. This long tubule, in turn, is divisible into distinct regions with distinct functions. The region of the tubule closest to the renal corpuscle is called the *proximal tubule*. This proximal tubule extends throughout the outermost *cortex* of the kidney, and at its end, it dives down into the innermost *medulla* of the kidney. As it does so, it changes its name to the *loop of Henle*. The loop of Henle makes a hairpin turn in the medulla, and heads on back up into the cortex to form the *distal tubule*. The distal tubule wanders around in the cortex and connects to so-called collecting ducts, which convey urine from the cortex, through the medulla, and out of the kidney to the ureter.

Filtration of fluid escaping from the leaky capillaries inside each renal corpuscle is the simplest and easiest part of urine formation. The difficult part is

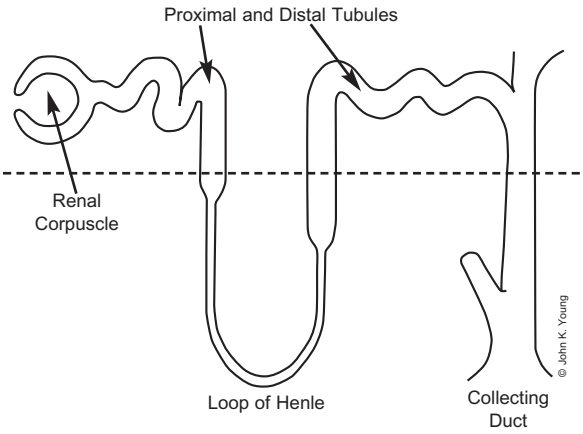

Fig. 24

Diagram of the components of a nephron.

the recovery of most of the water and essential molecules that would otherwise be lost in the urine. About 80 percent of this reabsorption takes place in the proximal tubule, which is correspondingly larger than the other tubular portions of the nephron (the proximal tubule is six times longer than the distal tubule, for example). Cells in the proximal tubule pump water, sodium, glucose, amino acids, and other small molecules out of the tubular lumen, across the epithelial lining cells, and into the tissue surrounding the tubule. The energy requirements for all of this activity are enormous, so these cells are packed full of the energy-producing organelles, mitochondria.

In diabetes mellitus, the concentration of glucose within the blood (and presumptive urine) becomes so elevated that the proximal tubule cells cannot retrieve all of it. Because of this, glucose and associated water is lost in the urine in diabetes. The term “diabetes mellitus” originally referred to the overproduction of a “sweet” urine that is a symptom of the disease.

Besides reabsorbing molecules from the urine, the proximal tubule also has additional tasks. The urine contains small proteins that pass through the filtration barrier in the renal corpuscles. These proteins, though small, are nevertheless too large to be reabsorbed intact into proximal tubule cells. Instead, the proteins become attached to long lines extending from the surface of the cell composed of a protein called megalin. Once these megalin “fishing lines” become fully loaded with small proteins, the entire line is reeled into the cell and destroyed. The kidney is thus a major site for the destruction of bloodborne proteins. In some kidney diseases, which compromise this function, many small proteins tend to accumulate in the bloodstream because they are not destroyed as quickly as normal. One final function of the proximal tubule is to secrete waste molecules such as urea into the urine.

The function of the next part of the nephron, the loop of Henle, is to make it possible for the kidney to remove more water from the urine. As urine passes down into the loop of Henle and upwards again, cells in this part of the nephron extract atoms of sodium from the urine. This sodium remains suspended around the loop of Henle, and in the innermost part of the medulla may attain concentrations four-fold higher than in the rest of the kidney. This means that when collecting ducts pass through the medulla to deliver urine to the ureter, they are located in a very salty environment. The salt in this environment tends to draw water out of the collecting tubules by a process called osmosis. This is the same process that causes a salty sausage to swell up when placed into water: water tends to move across a membrane so that

concentrations of salt on both sides of the membrane become more equal. In the kidney, the high-salt environment of the medulla draws water out of the urine in the collecting ducts.

This function of the loop of Henle can be controlled by drugs and hormones. For example, a drug called Lasix (furosemide) is one of the most commonly prescribed drugs in the United States. This drug is transported into the urine and binds to the sodium transporters in the loop of Henle. It prevents the accumulation of sodium in the renal medulla. As a consequence, water is not withdrawn from the urine, but leaves the body as an increased urine flow. This drug can be used to decrease swelling (edema) that occurs in many abnormal conditions of water retention by the body.

A hormone called antidiuretic hormone (ADH, or vasopressin) also regulates kidney function and urine flow. This hormone, which is secreted from the posterior pituitary, makes the cells of the collecting ducts permeable to water. This allows the withdrawal of water from the collecting ducts and makes it possible to produce a concentrated urine. Alcoholic drinks diminish the secretion of ADH, and thus result in the production of an increased amount of dilute urine.

The distal tubule also reabsorbs small amounts of water and sodium from the urine. Its function can be stimulated by a hormone secreted from the adrenal cortex called aldosterone. Loss of aldosterone from the body, because of damage or tuberculosis of the adrenal gland (Addison's disease), can have fatal consequences, since in the absence of aldosterone, sodium is gradually lost from the body. This can result in a collapse in circulatory function and death.

Specialized cells in the distal tubule function as sensors that monitor the sodium and chloride content of the urine. These sodium-sensitive cells form a small patch in the distal tubule called the macula densa. If the body becomes too dehydrated, or if too much sodium has been lost in sweat, the macula densa is activated to stimulate the renal production of an enzyme called renin. What does renin do?

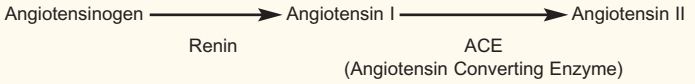

Fig. 25

Steps in the production of angiotensin II, a powerful stimulant for increased blood pressure.

Renin is an enzyme that converts an inactive blood protein, angiotensinogen, into an intermediate protein called angiotensin I. Angiotensin I, in turn, is converted to an active protein called angiotensin II by an enzyme (ACE) found in the lungs. The result of all this is the production of angiotensin II, a powerful hormone that causes contraction of blood vessels and stimulates the production of aldosterone by the adrenal gland. Both of these effects result in an elevation in blood pressure. So the macula densa of the distal tubule reacts to low urinary sodium by causing the production of a hormone that conserves body levels of sodium and which elevates blood pressure.

The generation of angiotensin II provides physicians with a powerful tool to modulate blood pressure. New types of drugs called ACE inhibitors have few side effects but are very effective in reducing blood pressure, and can be used to treat hypertension.

Many Americans experience high blood pressure, or hypertension, and have to take a variety of drugs, including ACE inhibitors, to combat it. The reasons why some people experience high blood pressure are uncertain. One recent finding is that hypertensive patients have 50 percent fewer nephrons in their kidneys than normal (seven hundred thousand per kidney vs. 1.4 million in control patients). Perhaps an anatomical abnormality in the kidney is a major factor in the genesis of hypertension.

Another peculiar feature of cells of the distal tubules and collecting ducts is that each cell lining these structures has a single cilium, which seems to function as a sensor of fluid flow down the tubule. If this cilium does not function properly, the tubules react as if urine is not being produced, and enlarge. A defect in this sensory function is now known to be the cause of polycystic kidney disease, in which many cysts appear in the kidneys, leading to kidney failure. This genetic disorder is relatively common, affecting about six hundred thousand Americans (about one in five hundred people). Now that its basis is known, perhaps some treatment can be determined.

The collecting ducts deliver urine into hollow, cup-shaped spaces in the kidney termed the *minor* and *major calyces*. These, in turn, drain into a large space called the renal pelvis, which represents the beginning of the ureter. Not infrequently, calcium and phosphate will precipitate within these spaces to form crystalline aggregations called kidney stones. Such stones may affect as many as 12 percent of men at some stages of their lives (women are less prone to this disorder). Large stones may grow to fill up the major calyces, and are termed “staghorn” stones because of their shape on x-rays. Stones can block the outflow of urine and lead to damaging, increased fluid pressure within the kidneys. Passage of stones via the urethra to the bladder can be very painful. For small stones, the current treatment of choice is to partly submerge a patient in water and bombard the stones with high-frequency sound waves (lithotripsy), which break up the stones and allow them to pass out of the body. The reasons why stones form in the first place are unclear. Some investigators believe they form around the calcified shells covering tiny bacteria that invade the urinary system.

The urinary bladder stores urine until it can be voided from the body via the urethra. This important function of the bladder can be adversely affected by diabetes, which damages the nerves to the bladder, and also by direct damage to the portions of the spinal cord that innervate the bladder. In addition, some patients can be born with urinary bladders that are too small or which contract too much, reducing the capacity to store urine. For such cases, it now seems possible to grow new bladders in vitro by recovering epithelial and muscle cells from a patient, allowing them to multiply in a dish, and combining them to form a new bladder wall that can be added surgically to the deformed bladder already in place. This is the first example of how it may someday be possible to grow replacement organs outside of the body.

FOR GREATER UNDERSTANDING

Questions

Patients with kidney stones can be cautioned to limit their intakes of alcoholic beverages. Why might this be helpful in maintaining healthy kidney function?

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Lecture 13:
The Male Reproductive System

The Suggested Reading for this lecture is Elaine N. Marieb, Jon Mallatt, and Patricia Brady Wilhelm's *Human Anatomy* (chapter 24).

The male reproductive system is composed of the testis, a series of tubular structures that convey seminal fluid away from the testis, and several glands that contribute molecules to seminal fluid. Each portion of the system can be discussed individually.

Testis

The testis begins its existence as a ventral swelling on the embryonic kidney, called the mesonephros. This kidney portion becomes transformed into either a male or female gonad under the influence of a DNA binding protein called steroidogenic factor 1 that turns on at least fifteen other genes needed for the construction of gonads. If this gene is disabled in mice, they are born without gonads. In males, the developing testis becomes attached to a duct, the mesonephric duct, which formerly delivered urine to the bladder. As the rest of the mesonephros degenerates, this duct changes its function to containing seminal fluid from the testis, and changes its name to the epididymis.

Although the structure of the testis forms from the mesonephros, this is not the site of origin for developing germ cells that will eventually form sperm cells. These primordial germ cells in fact originate in another embryological structure called the yolk sac, and migrate from there into the body and into the gonadal ridge of the mesonephros.

As the testis matures, it is drawn caudally from its origin in the abdominal cavity down toward the developing scrotal sac. This is due to tension exerted upon the testis by a ligament called the gubernaculum. This tension, and testicular movement, is stimulated by a hormone produced in the testis called insulin-3. Why would this intraabdominal organ migrate to this extraabdominal sac?

The reasons for testicular descent relate to temperature. For unknown reasons, sperm cells cannot form properly unless they are exposed to temperatures about three degrees (Celsius) cooler than the rest of the body. Inside the scrotal sac, temperatures are lower, both because of the location outside of the abdomen and also because a plexus of veins (pampiniform plexus) surrounds the testicular artery and cool it before heated arterial blood can enter the testis.

One consequence of this testicular migration is the formation of a passageway, the inguinal canal, through the abdominal musculature into the scrotum. Fluids flowing to and from the testis must pass through the inguinal canal, which is a site of weakness of the abdominal musculature. This weakness can result in an *inguinal hernia*, in which portions of the intestines protrude down into the inguinal canal. Men are twenty-five times more likely

than women to experience this injury, which affects about 5 percent of the general population.

In about 5 percent of newborn boys, one or both testes fail to completely descend into the scrotum, a condition called cryptorchidism. This must be surgically corrected to allow the normal development of sperm cells in the testis.

The testis itself is covered by a thick layer of connective tissue that protects its more delicate interior. The interior of the testis contains about two hundred fifty seminiferous tubules, in which sperm cells mature. The tissue surrounding the seminiferous tubules contains Leydig cells, which are specialized for the production of the male sex hormone, testosterone. As sperm cells mature, they are conveyed into a series of tubules that exit the testis. Sperm first enter a tubular structure in the midline of the testis called the rete testis, and then leave via a series of efferent ductules. Finally, they are collected in a long, tortuous tubule called the epididymis.

Ducts and Glands of the Male Reproductive System

Cells in the epididymis resorb much of the water present in seminal fluid and also modify its content of chloride. This particular function makes the epididymis vulnerable to an inherited disease, cystic fibrosis (see lecture 11). In this disease, an abnormal chloride transporter is inherited. This causes a dysfunction and even degeneration of the epididymis. Such an event is serious, since the epididymis is a site critical for the maturation of sperm. Sperm cells that are isolated from the seminiferous tubules of the testis appear normal anatomically, but do not swim well (impaired motility). In order to acquire the full capacity to swim, sperm must be exposed to unknown molecules in both the epididymis and female reproductive tract (this maturational stage is known as *sperm capacitation*). So males with cystic fibrosis do not produce normal sperm and are infertile. An impaired production of sperm results in infertility in about 3 to 4 percent of all men.

After leaving the epididymis, seminal fluid passes into the vas deferens, a tubular organ that ascends into the abdominal cavity via the inguinal canal. Large amounts of smooth muscle in this structure contract during sexual intercourse and ejaculation to force seminal fluid further forward in the male reproductive tract. The terminal portions of the vas deferens penetrate into a walnut-sized, midline gland called the prostate gland. At this point, each vas deferens becomes known as an ejaculatory duct. At the point of contact with the prostate gland, additional glands called seminal vesicles connect to the ejaculatory ducts and contribute their own molecules and fluids to the seminal fluid.

The prostate gland secretes fluid and enzymes into seminal fluid. The enzymes have a role in maintaining the fluidity of seminal fluid, which otherwise tends to rapidly coagulate. One of these enzymes, prostate specific antigen (PSA) has long had a role in the diagnosis of prostate cancer.

Prostate cancer is the most commonly diagnosed cancer in men and is the second leading cause of cancer death in men. Cancerous growth in the prostate is stimulated by testosterone, so one treatment for it involves drugs that slow the production of testosterone. Abnormal prostate enlargement is diagnosed both by rectal examinations and by measurement of PSA levels in the blood. Elevated PSA levels may indicate prostate cancer. However, these

measurements are only about 65 percent accurate in detecting cancer, and can show erroneous “false positives.” A new, improved blood test for cancer involves the detection of another protein called Early Prostate Cancer Antigen (EPCA). Early trials of such a test show that it is 95 percent accurate in diagnosing prostate cancer.

Penis

The penis is a muscular tube containing the penile urethra and three masses of highly vascular tissue called erectile tissue. A single vascular corpus spongiosum surrounds the urethra and is accompanied by two cylindrical masses called corpora cavernosa in the dorsal portion of the penis. During sexual intercourse, these vascular tissues become filled with blood, enlarge, and are responsible for penile erection. How do these events occur?

In response to sexual stimuli, nerve terminals innervating the smooth muscle of the venous sinuses of the corpora cavernosa release an unusual, *gaseous* neurotransmitter called nitric oxide. Nitric oxide is produced by an enzyme, nitric oxide synthase, that is synthesized in nerve cells of the lumbar spinal cord in response to testosterone. Nitric oxide stimulates the production of a molecule called cyclic GMP (cGMP) in smooth muscle cells surrounding the venous sinuses. This causes the muscle cells to relax and the venous sinuses become engorged with blood.

Between the ages of eighteen and sixty, blood concentrations of testosterone slowly decline by about 20 percent, for uncertain reasons. Consequently, the testosterone-sensitive neurons of the CNS that normally stimulate penile erection are less active, leading to erectile dysfunction. A knowledge of the molecules involved in penile erection, however, has allowed a treatment for this condition.

Following ejaculation, intracellular cGMP is degraded, allowing for a renewed contraction of vascular smooth muscle and a return of the penis to the flaccid state. This degradation of cGMP is performed by an enzyme called phosphodiesterase. At least seven different forms of phosphodiesterase exist in the body; the most abundant form in the corpus cavernosum is phosphodiesterase V. This particular enzyme has become a target for pharmaceutical intervention. Sildenafil (Viagra), an inhibitor of phosphodiesterase V, can prevent the degradation of cGMP and thus can enhance and prolong penile erection in older men, in spite of relatively lower blood levels of testosterone. This drug has been used by millions to enhance sexual activity.

One drawback of sildenafil is that it can also affect the activity of other forms of phosphodiesterase present elsewhere, for example, in coronary arteries or in the retina. If taken along with other drugs such as nitroglycerine, sildenafil can cause a dangerous fall in blood pressure. It can also affect color perception and retinal function, since cGMP has an important role in visual physiology.

FOR GREATER UNDERSTANDING

Questions

Patients with kidney stones can be cautioned to limit their intakes of alcoholic beverages. Why might this be helpful in maintaining healthy kidney function?

Suggested Reading

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Lecture 14:
The Female Reproductive System

The Suggested Reading for this lecture is Elaine N. Marieb, Jon Mallatt, and Patricia Brady Wilhelm's *Human Anatomy* (chapter 24).

Organs of the female reproductive system include the ovaries, oviducts, uterus, vagina, and mammary glands. Each are discussed separately.

Ovaries

The ovaries are almond-shaped organs suspended in the pelvic cavity by a fold of connective tissue called the mesovarium. The mesovarium, in turn, is just a portion of a wide sheet of connective tissue called the broad ligament of the uterus that anchors the uterus to the surrounding pelvic wall. The ovaries function to produce fertilizable egg cells, or oocytes, and the female sex hormones, estrogen and progesterone. The most important functional units of the ovaries are assemblies of cells called ovarian follicles.

Ovarian follicles are composed of developing egg cells (oocytes) and the accessory cells that surround them. Just as in the testis, the primordial germ cells that become oocytes do not actually originate within the ovary, but migrate to it from another embryonic structure, the yolk sac. When the germ cells arrive at the ovary, they produce a protein called Growth Determining Factor-9 that induces cells already in the ovary to surround the oocytes and form follicles.

A young woman will have about three hundred thousand follicles within each ovary. The vast majority of these follicles will degenerate, or undergo *atresia*. Only a few are somehow selected by an uncertain, mysterious process to undergo further development. Large, highly developed follicles contain an enormously enlarged oocyte and are ready for the process of *ovulation.* During ovulation, a surge in pituitary hormones (LH and FSH) causes the follicle to rupture and release the oocyte into the surrounding peritoneal fluid. The released oocyte moves into the oviduct, where it may be fertilized by a sperm cell.

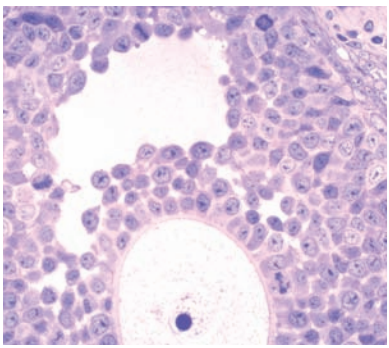

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Fig. 26

View of an ovarian follicle. An enormous oocyte (bottom) is surrounded by hundreds of accessory cells of the follicle.

The onset of ovulation in young girls at puberty is termed *menarche*. The exact reasons why this takes place at all are still uncertain. Most research points to a role of a part of the brain called the hypothalamus that regulates the release of stimulatory hormones from the pituitary gland. The hypothalamus, in turn, is regulated by hormones from fat cells in the body that signal that there is sufficient body fat to maintain a pregnancy. Starvation eliminates this hormonal signal from fat cells and can

delay or prevent puberty and normal ovarian function.

In many animals (rats, mice, rabbits), twelve to fifteen follicles will reach the final stages of maturation at once, so that twelve to fifteen eggs may be ovulated and litters of twelve to fifteen newborns will develop. Humans and other animals, like horses, in contrast, usually ovulate only one egg cell at a time. This is probably because in humans, a single, enlarging follicle (dominant follicle) can have a suppressive influence upon the development of other follicles in the ovary. One molecule released from the dominant follicle that may be responsible for this suppressive effect is called anti-Mullerian hormone. Because of the presence of a dominant follicle in an ovary, the other follicles in that ovary tend to be small. Consequently, successive ovulations tend to switch between ovaries.

Besides causing the release of an egg cell, the ovulatory surge of pituitary hormones also has a transforming effect upon the cells that remain in the ovary. Before ovulation, follicular cells mainly secrete a hormone called estrogen, which stimulates a thickening of the lining of the uterus. After ovulation, the remaining cells of an ovulated follicle form a new structure called a corpus luteum, which secretes a different hormone, progesterone. Progesterone further prepares the uterine lining for a possible pregnancy and also suppresses LH and FSH release from the pituitary, so that further ovulations are suppressed for a while. For uncertain reasons, an ovarian corpus luteum only secretes progesterone for about fourteen days, and then degenerates. This event has drastic effects upon the uterus.

The name for the menstrual or ovarian cycle are related to the Latin word *mensis* (month), which in turn relates to the Greek *mene* (moon). The ovarian cycle repeats about every twenty-eight days, a period which is similar to the interval between full moons (twenty-nine days). There is no obvious reason why the human ovarian cycle is of this length; in animals like rats, the ovarian cycle repeats every four to five days. It is possible that variations in nighttime illumination might have influenced the reproductive cycle of our nocturnal ancestors long ago. It is known that variations in day length or intensities of ambient light do have an influence upon the regulation of sex hormones by the brain in many animals.

Ovarian function and ovulation decline with aging and finally cease between the ages of fifty to fifty-five in women, an event called the menopause. The reasons for this, like the reasons for puberty, are uncertain, but once again may be connected to a functional change in the hypothalamus. The pregnancy rate for women younger than twenty-nine is about 14 percent, whereas the pregnancy rate for women older than forty is about 3 percent. The reduction in ovarian estrogen production after menopause may provoke a variety of symptoms. One prominent symptom is the “hot flush,” a transient sensation of heat that provokes sweating. One previous treatment for these symptoms was the administration of estrogen to menopausal women; however, since this was found to increase the risks for breast cancer and blood clots, it is not currently advised.

Oviduct (Fallopian Tube)

Following ovulation, the oocyte is conducted into the oviduct, where it might become fertilized by a sperm cell. Generally, a fertilized ovum moves into the

uterus and implants into the uterine wall (endometrium). However, in about 1 percent of all pregnancies, the fertilized ovum implants into the oviduct. This is unfortunate, since the thin-walled oviduct is too delicate to sustain the growth of a fetus and will thus rupture and cause extensive and potentially dangerous bleeding.

Uterus

The uterus is a hollow organ composed of two layers of tissue. The interior of the uterus is lined by an epithelium and connective tissue that make up a layer called the endometrium. The outer portions of the uterus are mainly composed of smooth muscle that makes up the myometrium. Both layers are very responsive to a variety of hormones.

Estrogen causes a thickening of the endometrium. Progesterone causes an increased activity of endometrial glands. When blood levels of both hormones fall ten to fourteen days after ovulation, hormone-sensitive blood vessels in the endometrium start to spasmodically contract, cutting off the blood supply to the endometrial cells. These layers of cells die, and then are disrupted when blood transiently flows back into the endometrium. Eventually, most of the endometrial layer is disrupted in the process of menstruation.

If a pregnancy occurs, the continuous production of progesterone (first by the ovaries and then by the placenta) thickens the uterus, stimulates the enlargement of the myometrium, and reduces myometrial contractility. Much later, labor and the birth of a baby occur when the myometrial muscle forcefully contracts. One factor that influences this contraction is a hormone called oxytocin. The oxytocin responsible for labor is produced within the endometrium of the uterus itself.

What initiates all of these dramatic events of labor? Recent evidence suggests that the signal for labor comes from the baby itself, in the form of lung surfactant molecules that are shed into the amniotic fluid. These molecules stimulate the migration of cells called macrophages from the baby, into the placenta, and finally into the uterus. These cells initiate an inflammatory response that hastens labor.

In about 20 percent of pregnancies, the placenta does not invade into the uterine endometrium sufficiently, so that the blood supply to the placenta and baby from the mother is inadequate. The placenta responds by secreting uncharacterized molecules into the bloodstream that drastically increase blood pressure. This may have positive results for the placenta and baby, but can be very dangerous for the mother. This condition is called *pre-eclampsia*. The cause of pre-eclampsia now appears to be a circulating molecule that binds growth factors required for placental growth. This molecule, called sFlt-1, is three-fold higher in the blood of pre-eclamptic mothers than in normal mothers, and appears to interfere with the normal growth of placental blood vessels. Bed-rest and an early delivery of the baby are the main treatments for this condition.

In order to maintain the early stages of pregnancy, cells of the placenta secrete a hormone that is much like LH. This hormone, human chorionic gonadotropin (hCG) stimulates the corpus luteum so that it continues to secrete progesterone for the first three months of pregnancy. Blood levels of

hCG rise sharply in the early stages of pregnancy and become so high that the kidney cannot recover all of these molecules. hCG thus becomes detectable in the urine and forms the basis for a pregnancy test.

The portion of the uterus adjacent to the vagina is termed the cervix. This uterine region is particularly prone to cancer. Cervical cancer is the fifth most lethal cancer in women; about one out of one hundred fifty women may experience this disease. A major risk factor for developing this cancer is infection with human papilloma virus. Widescale administration of vaccines against this virus is now being undertaken with the goal of drastically reducing the risk for this type of cancer.

Vagina and External Genitalia

The vagina is a thin-walled, muscular tube that allows access to the uterus for spermatozoa present in the female reproductive tract. It is lubricated by glands that secrete a mucus-rich fluid during sexual intercourse. The orifice of the vagina is surrounded laterally by the labia minora and majora, which originate from the same tissues during embryogenesis as the scrotal sac. The clitoris originates from the same tissue as the penis during embryogenesis.

Mammary Glands

The mammary glands are secretory organs embedded in large amounts of fat just beneath the nipples. Throughout most of life, these glands are undeveloped and consist of a few, scattered, tubular structures. Their cellular structure very much resembles that of sweat glands; it is thought that both sweat glands and mammary glands developed during evolution to cool off warm-blooded bodies and to provide nourishment for warm-blooded offspring with a high metabolic rate. Hormones secreted during pregnancy, like estrogen and prolactin, stimulate them to develop blind pockets called secretory alveoli that synthesize milk.

Milk is a complex mixture of sugars (lactose), fats, and proteins (a major one is a calcium-binding protein called casein). Milk is secreted from the glands in response to suckling, which triggers a reflex release of oxytocin from the pituitary gland and an action of contractile cells surrounding the secretory alveoli that expresses milk onto the nipple. The milk secreted in the first few days after delivery is particularly rich in antibody molecules that "jump start" the immune system of the newborn and help protect a baby against infections.

Cancer of mammary gland cells is common—about one in ten women may experience this disease over the course of a lifetime. A number of factors increase the risk for breast cancer. In rare cases, an abnormality in a gene called BRCA1 enhances the development of cancer. Having children reduces the risk by about 10 percent, probably because, for uncertain reasons, blood levels of prolactin rise briefly during nursing and then fall to significantly lower levels later than in women who had never had a pregnancy. In mice, a mammary tumor virus specifically binds to proteins on mammary cells and can provoke cancer. Studies are ongoing to determine if such a virus may be involved in carcinogenesis of the breast in humans. Treatments for breast cancer include removal of cancerous tissue, exposure to cancer-killing radiation and chemotherapies, and administration of anti-estrogen drugs.

FOR GREATER UNDERSTANDING

Questions

What evolutionary factors might have been involved in determining how many oocytes are ovulated every month in our primate ancestors?

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