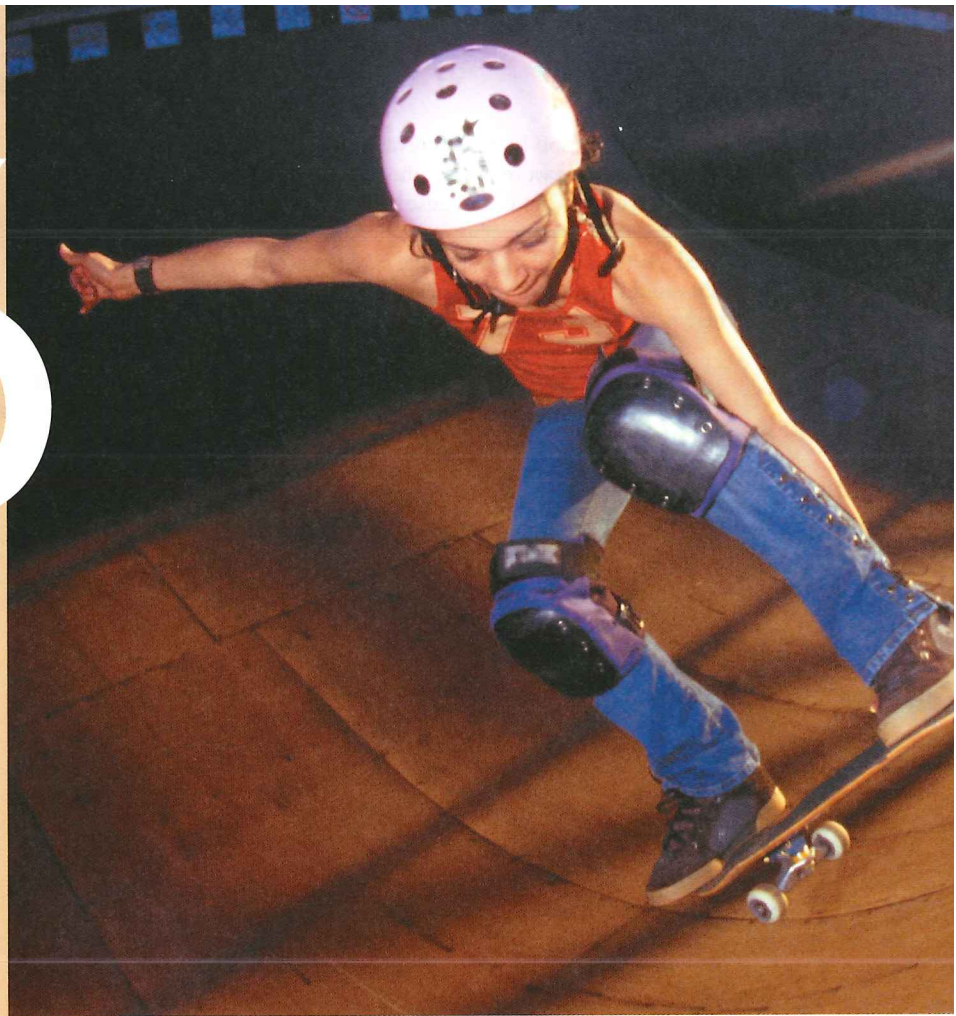


# 6



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# Bones and Skeletal Tissues

All of us have heard the expressions “bone tired” and “bag of bones”—rather unflattering and inaccurate images of one of our most phenomenal tissues and our main skeletal elements. Our brains, not our bones, convey feelings of fatigue. As for “bag of bones,” they are indeed more prominent in some of us, but without bones to form our internal skeleton we would all creep along the ground like slugs, lacking any definite shape or form. Along with its bones, the skeleton contains resilient cartilages, which we briefly discuss in this chapter. However, our major focus is the structure and function of bone tissue and the dynamics of its formation and remodeling throughout life.



## Skeletal Cartilages

- Describe the functional properties of the three types of cartilage tissue.
- Locate the major cartilages of the adult skeleton.
- Explain how cartilage grows.

The human skeleton is initially made up of cartilages and fibrous membranes, but most of these early supports are soon replaced by bone. The few cartilages that remain in adults are found mainly in regions where flexible skeletal tissue is needed.

### Basic Structure, Types, and Locations

A **skeletal cartilage** is made of some variety of *cartilage tissue*, which consists primarily of water. The high water content of cartilage accounts for its resilience, that is, its ability to spring back to its original shape after being compressed.

The cartilage, which contains no nerves or blood vessels, is surrounded by a layer of dense irregular connective tissue, the *perichondrium* (per"i-kon'dre-um; "around the cartilage"). The perichondrium acts like a girdle to resist outward expansion when the cartilage is compressed. Additionally, the perichondrium contains the blood vessels from which nutrients diffuse through the matrix to reach the cartilage cells. This mode of nutrient delivery limits cartilage thickness.

As we described in Chapter 4, there are three types of cartilage tissue in the body: hyaline, elastic, and fibrocartilage. All three types have the same basic components—cells called *chondrocytes*, encased in small cavities (lacunae) within an *extracellular matrix* containing a jellylike ground substance and fibers. The skeletal cartilages contain representatives from all three types.

**Hyaline cartilages**, which look like frosted glass when freshly exposed, provide support with flexibility and resilience. They are the most abundant skeletal cartilages. When viewed under the microscope, their chondrocytes appear spherical (see Figure 4.8g). The only fiber type in their matrix is fine collagen fibers (which, however, are not detectable microscopically). Colored blue in **Figure 6.1**, skeletal hyaline cartilages include (1) *articular cartilages*, which cover the ends of most bones at movable joints; (2) *costal cartilages*, which connect the ribs to the sternum (breastbone); (3) *respiratory cartilages*, which form the skeleton of the *larynx* (voicebox) and reinforce other respiratory passageways; and (4) *nasal cartilages*, which support the external nose.

**Elastic cartilages** look very much like hyaline cartilages (see Figure 4.8h), but they contain more stretchy elastic fibers and so are better able to stand up to repeated bending. They are found in only two skeletal locations, shown in green in Figure 6.1—the external ear and the epiglottis (the flap that bends to cover the opening of the larynx each time we swallow).

**Fibrocartilages** are highly compressible and have great tensile strength. The perfect intermediate between hyaline and elastic cartilages, fibrocartilages consist of roughly parallel rows of chondrocytes alternating with thick collagen fibers (see Figure 4.8i). Fibrocartilages occur in sites that are subjected to

both heavy pressure and stretch, such as the padlike cartilages (menisci) of the knee and the discs between vertebrae, colored red in Figure 6.1.

### Growth of Cartilage

Unlike bone, which has a hard matrix, cartilage has a flexible matrix which can accommodate mitosis. It is the ideal tissue to use to lay down the embryonic skeleton and to provide for new skeletal growth. Cartilage grows in two ways. In **appositional growth** (ap"o-zish'un-al; "growth from outside"), cartilage-forming cells in the surrounding perichondrium secrete new matrix against the external face of the existing cartilage tissue. In **interstitial growth** (in"ter-stish'al; "growth from inside"), the lacunae-bound chondrocytes divide and secrete new matrix, expanding the cartilage from within. Typically, cartilage growth ends during adolescence when the skeleton stops growing.

Under certain conditions—during normal bone growth in youth and during old age—calcium salts may be deposited in the matrix and cause it to harden, a process called calcification. Note, however, that calcified cartilage is not bone; cartilage and bone are always distinct tissues.

#### CHECK YOUR UNDERSTANDING

1. Which type of cartilage is most plentiful in the adult body?
2. What two body structures contain flexible elastic cartilage?
3. Cartilage grows by interstitial growth. What does this mean?

For answers, see Appendix G.

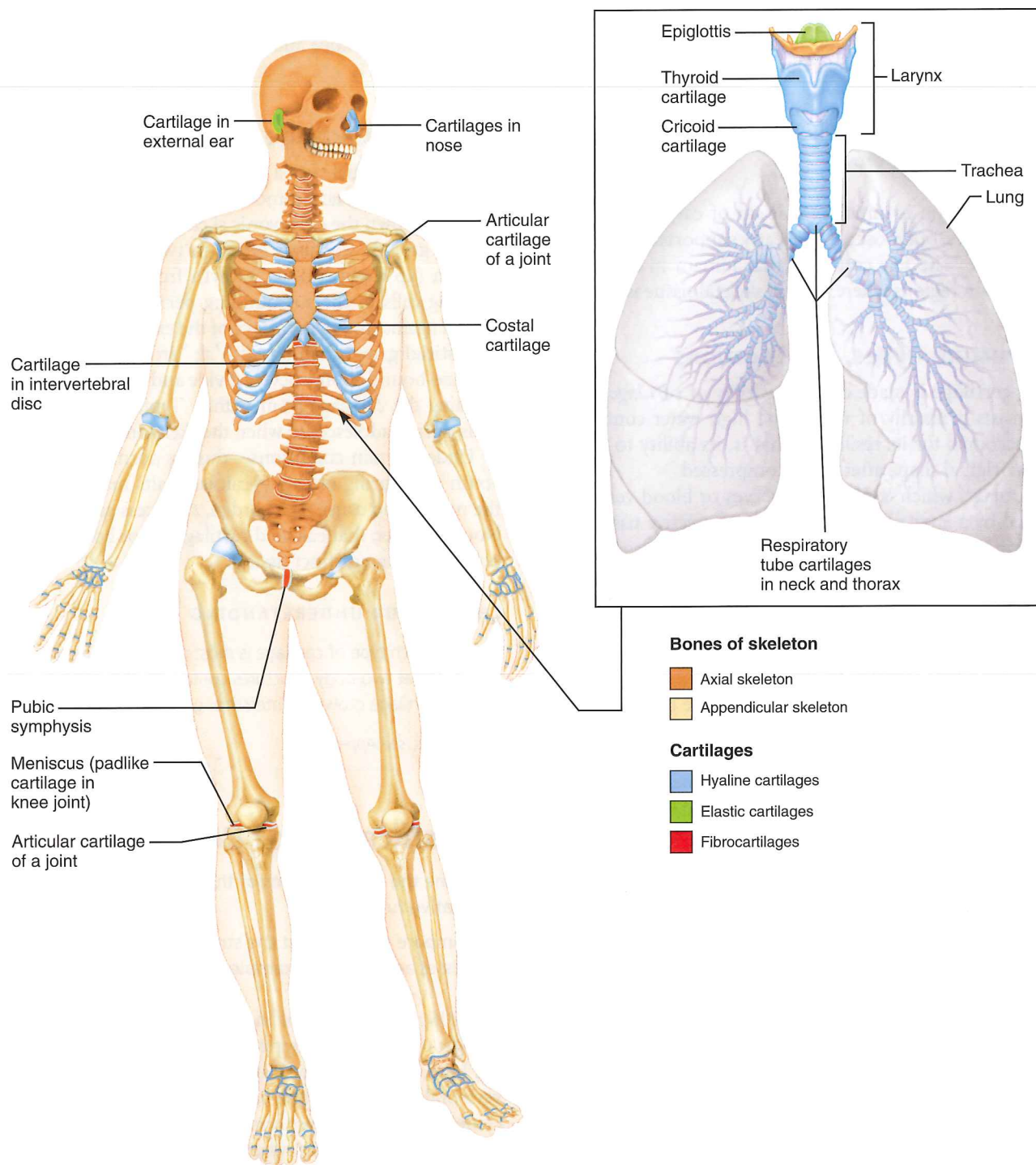
## Classification of Bones

- Name the major regions of the skeleton and describe their relative functions.
- Compare and contrast the structure of the four bone classes and provide examples of each class.

The 206 named bones of the human skeleton are divided into two groups: axial and appendicular. The **axial skeleton** forms the long axis of the body and includes the bones of the skull, vertebral column, and rib cage, shown in orange in Figure 6.1. Generally speaking these bones are most involved in protecting, supporting, or carrying other body parts.

The **appendicular skeleton** (ap'en-dik'u-lar) consists of the bones of the upper and lower limbs and the girdles (shoulder bones and hip bones) that attach the limbs to the axial skeleton. These bones are colored gold in Figure 6.1. Bones of the limbs help us to get from place to place (locomotion) and to manipulate our environment.

Bones come in many sizes and shapes. For example, the pisiform bone of the wrist is the size and shape of a pea, whereas the femur (thigh bone) is nearly 2 feet long in some people and has a large, ball-shaped head. The unique shape of each bone fulfills a particular need. The femur, for example, withstands great weight and pressure, and its hollow-cylinder design provides maximum strength with minimum weight.



**Figure 6.1 The bones and cartilages of the human skeleton.** The cartilages that support the respiratory tubes and larynx are drawn separately at the right.

For the most part, bones are classified by their shape as long, short, flat, and irregular (**Figure 6.2**).

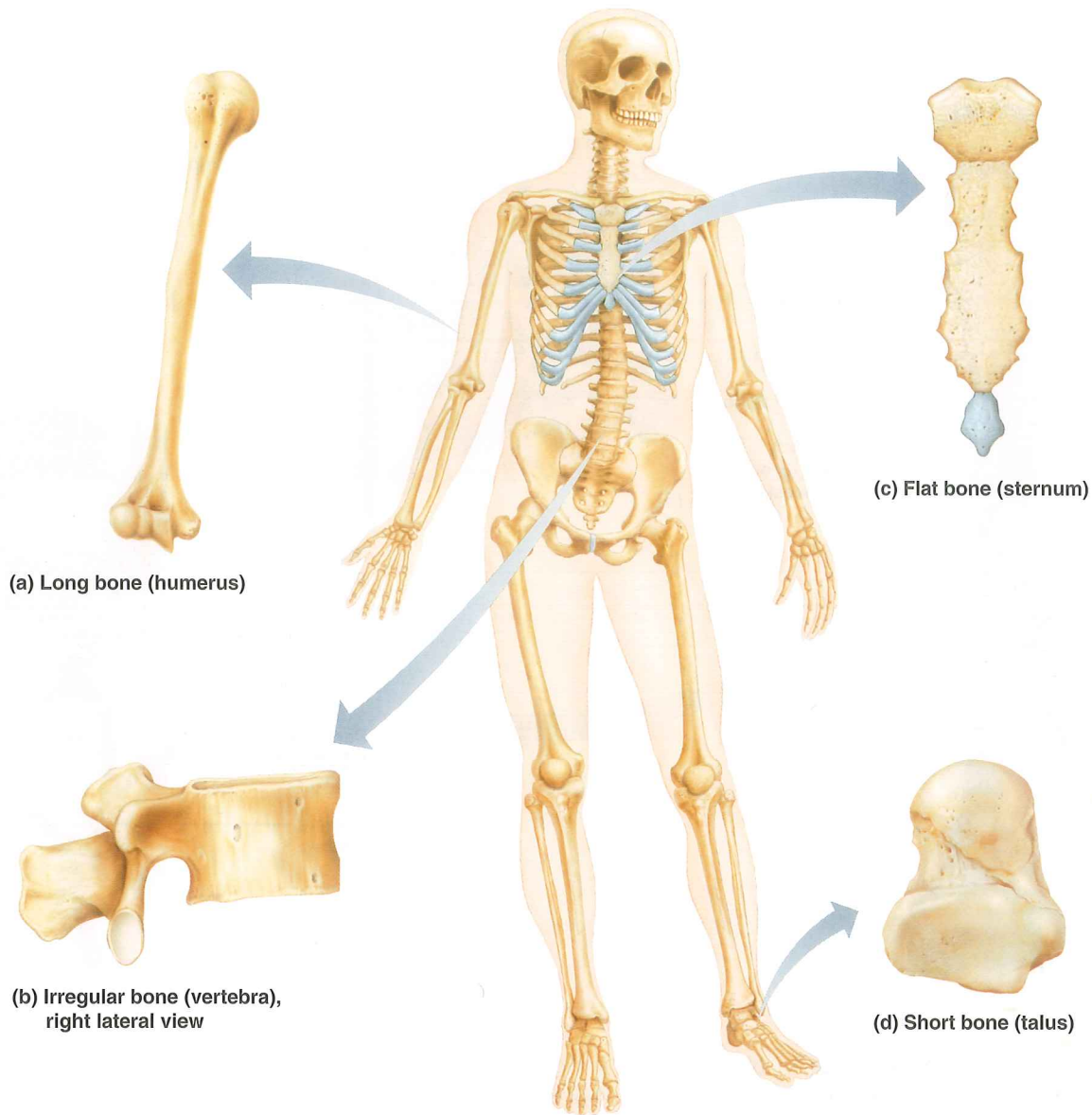
1. **Long bones**, as their name suggests, are considerably longer than they are wide (**Figure 6.2a**). A long bone has a shaft plus two ends. All limb bones except the patella (kneecap) and the wrist and ankle bones are long bones. Notice that these bones are named for their elongated

shape, *not* their overall size. The three bones in each of your fingers are long bones, even though they are very small.

2. **Short bones** are roughly cube shaped. The bones of the wrist and ankle are examples (**Figure 6.2d**).

**Sesamoid bones** (ses'ah-moid; "shaped like a sesame seed") are a special type of short bone that form in a tendon (for example, the patella). They vary in size and number in different individuals. Some sesamoid bones clearly act to





**Figure 6.2** Classification of bones on the basis of shape.

alter the direction of pull of a tendon. The function of others is not known.

- Flat bones** are thin, flattened, and usually a bit curved. The sternum (breastbone), scapulae (shoulder blades), ribs, and most skull bones are flat bones (Figure 6.2c).
- Irregular bones** have complicated shapes that fit none of the preceding classes. Examples include the vertebrae and the hip bones (Figure 6.2b).

#### CHECK YOUR UNDERSTANDING

- What are the components of the axial skeleton?
- Contrast the general function of the axial skeleton to that of the appendicular skeleton.
- What bone class do the ribs and skull bones fall into?

For answers, see Appendix G.

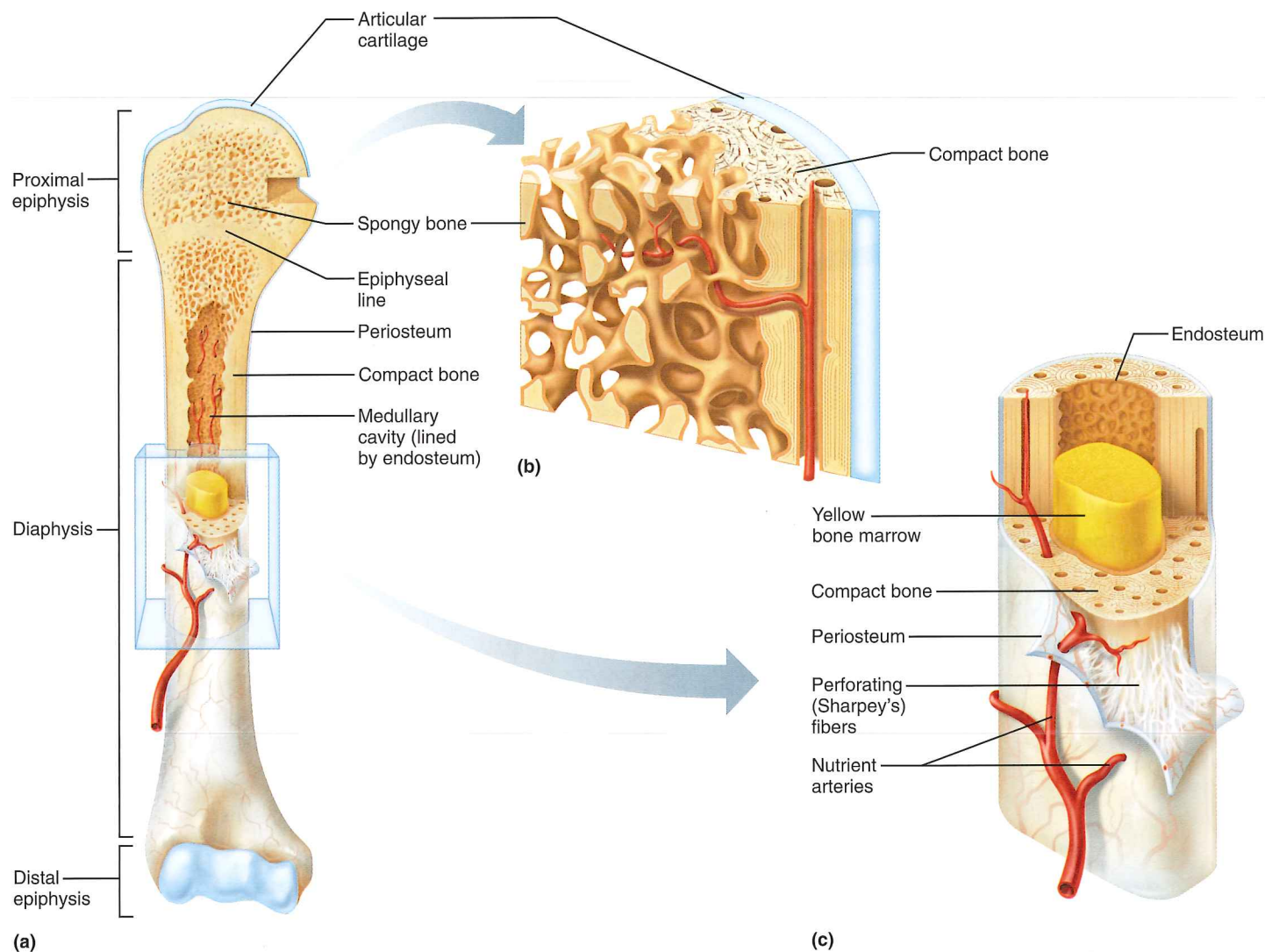
## Functions of Bones

- List and describe five important functions of bones.

Besides contributing to body shape and form, our bones perform several other important functions:

- Support.** Bones provide a framework that supports the body and cradles its soft organs. For example, bones of lower limbs act as pillars to support the body trunk when we stand, and the rib cage supports the thoracic wall.
- Protection.** The fused bones of the skull protect the brain. The vertebrae surround the spinal cord, and the rib cage helps protect the vital organs of the thorax.
- Movement.** Skeletal muscles, which attach to bones by tendons, use bones as levers to move the body and its parts. As a result, we can walk, grasp objects, and breathe. The design of joints determines the types of movement possible.





**Figure 6.3 The structure of a long bone (humerus of arm).** (a) Anterior view with bone sectioned frontally to show the interior at the proximal end. (b) Enlarged view

of spongy bone and compact bone of the epiphysis of (a). (See *A Brief Atlas of the Human Body*, Plates 20 and 21.) (c) Enlarged cross-sectional view of the shaft (diaphysis)

of (a). Note that the external surface of the diaphysis is covered by periosteum, but the articular surface of the epiphysis is covered with hyaline cartilage.

4. **Mineral and growth factor storage.** Bone is a reservoir for minerals, most importantly calcium and phosphate. The stored minerals are released into the bloodstream as needed for distribution to all parts of the body. Indeed, “deposits” and “withdrawals” of minerals to and from the bones go on almost continuously. Additionally, mineralized bone matrix stores important growth factors such as insulin-like growth factors, transforming growth factor, bone morphogenic proteins, and others.
5. **Blood cell formation.** Most blood cell formation, or **hematopoiesis** (hem’ah-to-poi-e’ sis), occurs in the marrow cavities of certain bones.
6. **Triglyceride (fat) storage.** Fat is stored in bone cavities and represents a source of stored energy for the body.

8. What two types of substances are stored in bone matrix?
9. What are two functions of a bone’s marrow cavities?

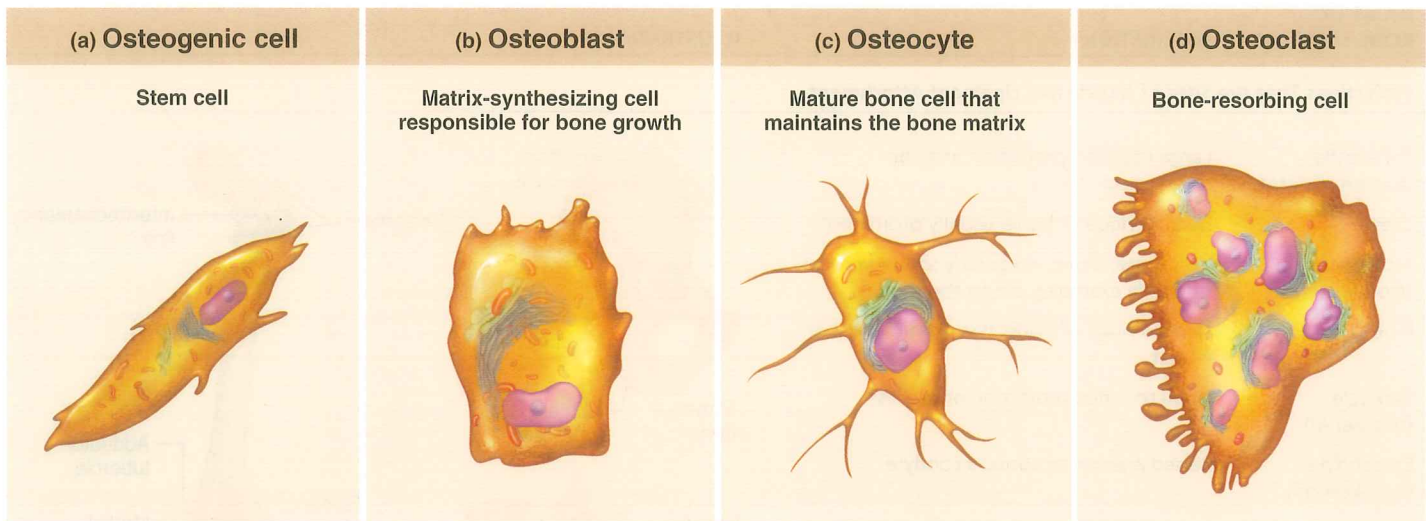
For answers, see Appendix G.

#### CHECK YOUR UNDERSTANDING

7. What is the functional relationship between skeletal muscles and bones?

## Bone Structure

- Indicate the functional importance of bone markings.
- Describe the gross anatomy of a typical long bone and a flat bone. Indicate the locations and functions of red and yellow marrow, articular cartilage, periosteum, and endosteum.
- Describe the histology of compact and spongy bone.
- Discuss the chemical composition of bone and the advantages conferred by the organic and inorganic components.



**Figure 6.4** Comparison of different types of bone cells.

Because they contain various types of tissue, bones are *organs*. (Recall that an organ contains several different tissues.) Although bone (osseous) tissue dominates bones, they also contain nervous tissue in their nerves, cartilage in their articular cartilages, fibrous connective tissue lining their cavities, and muscle and epithelial tissues in their blood vessels. We will consider bone structure at three levels: gross, microscopic, and chemical.

## Gross Anatomy

### Bone Markings

The external surfaces of bones are rarely smooth and featureless. Instead, they display projections, depressions, and openings that serve as sites of muscle, ligament, and tendon attachment, as joint surfaces, or as conduits for blood vessels and nerves. These **bone markings** are named in different ways.

Projections (bulges) that grow outward from the bone surface include heads, trochanters, spines, and others. Each has distinguishing features and functions. In most cases, bone projections are indications of the stresses created by muscles attached to and pulling on them or are modified surfaces where bones meet and form joints.

Depressions and openings include fossae, sinuses, foramina, and grooves. They usually serve to allow passage of nerves and blood vessels. The most important types of bone markings are described in [Table 6.1](#). You should familiarize yourself with these terms because you will meet them again as identifying marks of the individual bones studied in the lab.

### Bone Textures: Compact and Spongy Bone

Every bone has a dense outer layer that looks smooth and solid to the naked eye. This external layer is **compact bone** (Figures 6.3 and 6.5). Internal to this is **spongy bone** (also called *cancellous bone*), a honeycomb of small needle-like or flat pieces called **trabeculae** (trah-bek'u-le; "little beams"). In living bones the open spaces between trabeculae are filled with red or yellow bone marrow.

### Structure of a Typical Long Bone

With few exceptions, all long bones have the same general structure, which includes a shaft, bone ends, and membranes ([Figure 6.3](#)).

**Diaphysis** A tubular **diaphysis** (di-af'i-sis; *dia* = through, *physis* = growth), or shaft, forms the long axis of the bone. It is constructed of a relatively thick *collar* of compact bone that surrounds a central **medullary cavity** (med'u-lar-e; "middle"), or *marrow cavity*. In adults, the medullary cavity contains fat (yellow marrow) and is called the **yellow marrow cavity**.

**Epiphyses** The **epiphyses** (e-pif'i-sēz; singular: epiphysis) are the bone ends (*epi* = upon). In many cases, they are more expanded than the diaphysis. Compact bone forms the exterior of epiphyses, and their interior contains spongy bone. The joint surface of each epiphysis is covered with a thin layer of articular (hyaline) cartilage, which cushions the opposing bone ends during joint movement and absorbs stress. Between the diaphysis and each epiphysis of an adult long bone is an **epiphyseal line**, a remnant of the **epiphyseal plate**, a disc of hyaline cartilage that grows during childhood to lengthen the bone. The region where the diaphysis and epiphysis meet, whether it is the epiphyseal plate or line, is sometimes called the *metaphysis*.

**Membranes** A third structural feature of long bones is membranes. The external surface of the entire bone except the joint surfaces is covered by a glistening white, double-layered membrane called the **periosteum** (per'e-os'te-um; *peri* = around, *osteo* = bone). The outer *fibrous layer* is dense irregular connective tissue. The inner *osteogenic layer*, abutting the bone surface, consists primarily of bone-forming cells, called **osteoblasts** (os'te-o-blasts; "bone germinators"), which secrete bone matrix elements, and bone-destroying cells, called **osteoclasts** ("bone breakers"). In addition, there are primitive stem cells, **osteogenic cells**, that give rise to the osteoblasts ([Figure 6.4](#)).



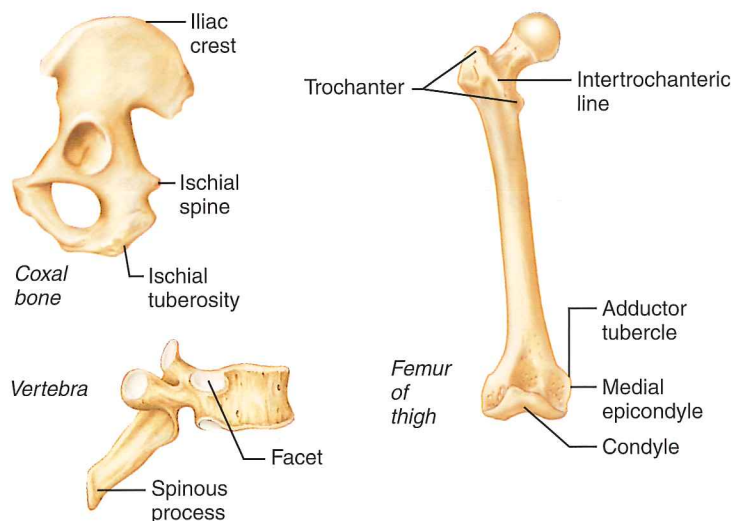
TABLE 6.1

## Bone Markings

NAME OF BONE MARKING	DESCRIPTION	ILLUSTRATIONS
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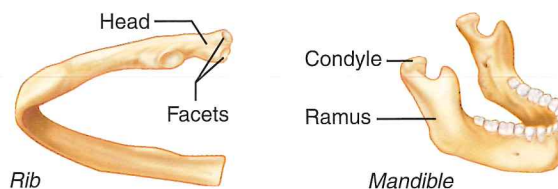
## Projections That Are Sites of Muscle and Ligament Attachment

Tuberosity (too'bĕ-ros'i-te)	Large rounded projection; may be roughened
Crest	Narrow ridge of bone; usually prominent
Trochanter (tro-kan'ter)	Very large, blunt, irregularly shaped process (the only examples are on the femur)
Line	Narrow ridge of bone; less prominent than a crest
Tubercle (too'ber-kl)	Small rounded projection or process
Epicondyle (ep'i-kon'dīl)	Raised area on or above a condyle
Spine	Sharp, slender, often pointed projection
Process	Any bony prominence



## Projections That Help to Form Joints

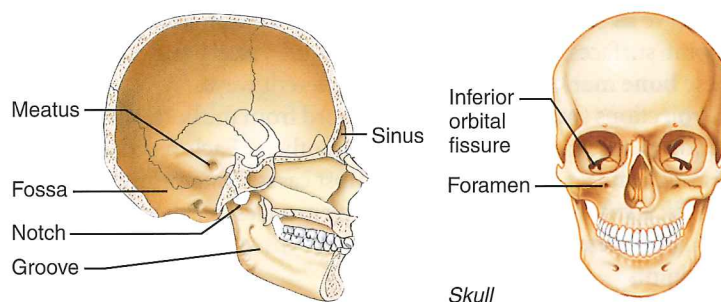
Head	Bony expansion carried on a narrow neck
Facet	Smooth, nearly flat articular surface
Condyle (kon'dīl)	Rounded articular projection
Ramus (ra'mus)	Armlike bar of bone



## Depressions and Openings

## For Passage of Blood Vessels and Nerves

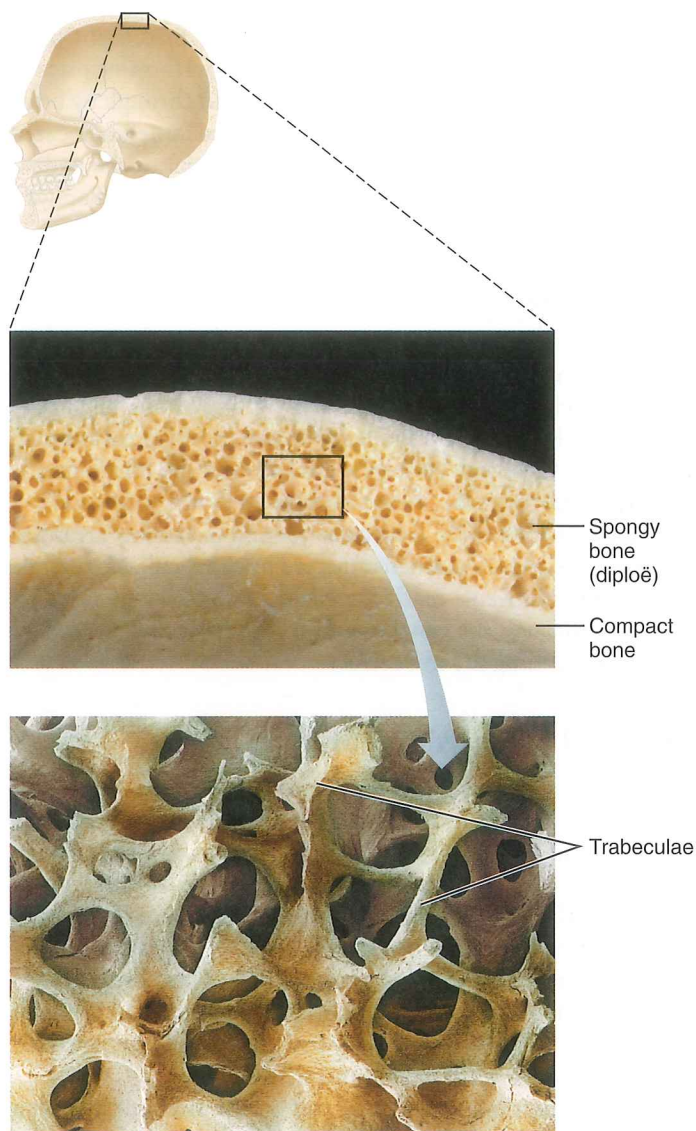
Groove	Furrow
Fissure	Narrow, slitlike opening
Foramen (fo-ra'men)	Round or oval opening through a bone
Notch	Indentation at the edge of a structure
Others	
Meatus (me-a'tus)	Canal-like passageway
Sinus	Cavity within a bone, filled with air and lined with mucous membrane
Fossa (fos'ah)	Shallow, basinlike depression in a bone, often serving as an articular surface



The periosteum is richly supplied with nerve fibers, lymphatic vessels, and blood vessels, which enter the diaphysis via **nutrient foramina** (fo-ra'me-nah; "openings").

The periosteum is secured to the underlying bone by *perforating (Sharpey's) fibers* (Figure 6.3), tufts of collagen fibers that extend from its fibrous layer into the bone matrix. The periosteum also provides anchoring points for tendons and ligaments. At these points the perforating fibers are exceptionally dense.

Internal bone surfaces are covered with a delicate connective tissue membrane called the **endosteum** (en-dos'te-um; "within the bone") (Figure 6.3). The endosteum covers the trabeculae of spongy bone and lines the canals that pass through the compact bone. Like the periosteum, the endosteum contains both bone-forming and bone-destroying cells.



**Figure 6.5** Flat bones consist of a layer of spongy bone sandwiched between two thin layers of compact bone. (Photomicrograph at bottom, 25 $\times$ .)

### Structure of Short, Irregular, and Flat Bones

Short, irregular, and flat bones share a simple design: They all consist of thin plates of periosteum-covered compact bone on the outside and endosteum-covered spongy bone within. However, these bones are not cylindrical and so they have no shaft or epiphyses. They contain bone marrow (between their trabeculae), but no significant marrow cavity is present.

**Figure 6.5** shows a typical flat bone of the skull. In flat bones, the spongy bone is called the **diploë** (dip'lo-e; "folded") and the whole arrangement resembles a stiffened sandwich.

### Location of Hematopoietic Tissue in Bones

Hematopoietic tissue, **red marrow**, is typically found within the trabecular cavities of spongy bone of long bones and in the diploë of flat bones. For this reason, both these cavities are often

referred to as **red marrow cavities**. In newborn infants, the medullary cavity of the diaphysis and all areas of spongy bone contain red bone marrow. In most adult long bones, the fat-containing medullary cavity extends well into the epiphysis, and little red marrow is present in the spongy bone cavities. For this reason, blood cell production in adult long bones routinely occurs only in the heads of the femur and humerus (the long bone of the arm).

The red marrow found in the diploë of flat bones (such as the sternum) and in some irregular bones (such as the hip bone) is much more active in hematopoiesis, and these sites are routinely used for obtaining red marrow samples when problems with the blood-forming tissue are suspected. However, yellow marrow in the medullary cavity can revert to red marrow if a person becomes very anemic and needs enhanced red blood cell production.

## Microscopic Anatomy of Bone

Essentially, four major cell types populate bone tissue: osteogenic cells, osteoblasts, osteocytes, and osteoclasts. These, like other connective tissue cells, are surrounded by an extracellular matrix of their making. The *osteogenic cells*, also called *osteoprogenitor cells*, are mitotically active stem cells found in the membranous periosteum and endosteum. Some of their progeny differentiate into **osteoblasts** (bone-forming cells) while others persist as bone stem cells to provide osteoblasts in the future. We describe the structure and function of the remaining two types of bone cells below.

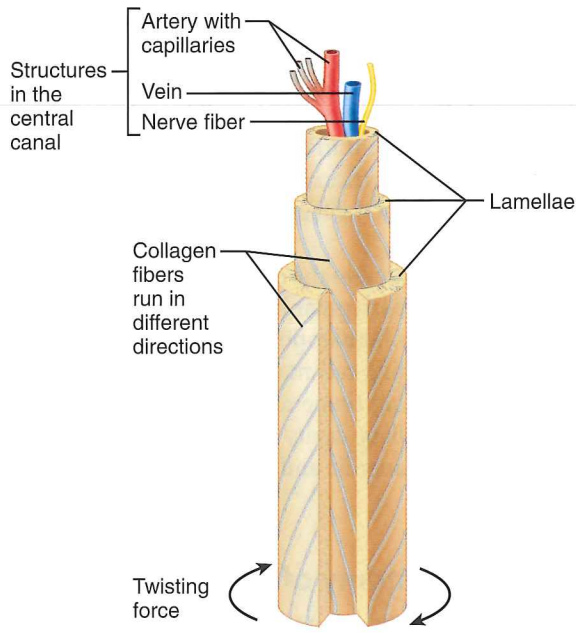
### Compact Bone

Although compact bone looks dense and solid, a microscope reveals that it is riddled with passageways that serve as conduits for nerves, blood vessels, and lymphatic vessels (see **Figure 6.7**). The structural unit of compact bone is called either the **osteon** (os'te-on) or the **Haversian system** (ha-ver'zhen). Each osteon is an elongated cylinder oriented parallel to the long axis of the bone. Functionally, osteons are tiny weight-bearing pillars.

As shown in the "exploded" view in **Figure 6.6**, an osteon is a group of hollow tubes of bone matrix, one placed outside the next like the growth rings of a tree trunk. Each matrix tube is a **lamella** (lah-mel'ah; "little plate"), and for this reason compact bone is often called **lamellar bone**. Although all of the collagen fibers in a particular lamella run in a single direction, the collagen fibers in adjacent lamellae always run in different directions. This alternating pattern is beautifully designed to withstand torsion stresses—the adjacent lamellae reinforce one another to resist twisting. You can think of the osteon's design as a "twister resister." Collagen fibers are not the only part of bone lamellae that are beautifully ordered. The tiny crystals of bone salts align with the collagen fibers and thus also alternate their direction in adjacent lamellae.

Running through the core of each osteon is the **central canal**, or **Haversian canal**, containing small blood vessels and nerve fibers that serve the needs of the osteon's cells. Canals of a sec-





**Figure 6.6 A single osteon.** The osteon is drawn as if pulled out like a telescope to illustrate the individual lamellae.

ond type called **perforating canals**, or **Volkman's canals** (folk'mahnz), lie at right angles to the long axis of the bone and connect the blood and nerve supply of the periosteum to those in the central canals and the medullary cavity (**Figure 6.7a**). Like all other internal bone cavities, these canals are lined with endosteum.

Spider-shaped **osteocytes** (Figures 6.4c and 6.7b) occupy **lacunae** (*lac* = hollow; *una* = little) at the junctions of the lamellae. Hairlike canals called **canaliculi** (kan"ah-lik'u-li) connect the lacunae to each other and to the central canal. The manner in which canaliculi are formed is interesting. When bone is being formed, the osteoblasts secreting bone matrix surround blood vessels and maintain contact with one another by tentacle-like projections containing gap junctions. Then, as the newly secreted matrix hardens and the maturing cells become trapped within it, a system of tiny canals—the canaliculi, filled with tissue fluid and containing the osteocyte extensions—is formed. The canaliculi tie all the osteocytes in an osteon together, permitting nutrients and wastes to be relayed from one osteocyte to the next throughout the osteon. Although bone matrix is hard and impermeable to nutrients, its canaliculi and cell-to-cell relays (via gap junctions) allow bone cells to be well nourished.

One function of osteocytes is to maintain the bone matrix. If they die, the surrounding matrix is resorbed. The osteocytes also act as stress or strain "sensors" in cases of bone deformation or other damaging stimuli. They communicate this information to the cells responsible for bone remodeling (osteoblasts and osteoclasts) so that countermeasures can be taken or repairs made. We discuss the bone-destroying **osteoclast** on p. 186 in conjunction with the topic of bone remodeling.

Not all the lamellae in compact bone are part of osteons. Lying between intact osteons are incomplete lamellae called

**interstitial lamellae** (in"ter-stish'al) (Figure 6.7c, right photomicrograph). They either fill the gaps between forming osteons or are remnants of osteons that have been cut through by bone remodeling (discussed later). **Circumferential lamellae**, located just deep to the periosteum and just superficial to the endosteum, extend around the entire circumference of the diaphysis (Figure 6.7a) and effectively resist twisting of the long bone.

### Spongy Bone

In contrast to compact bone, spongy bone looks like a poorly organized, even haphazard, tissue (see Figure 6.5 and Figure 6.3b). However, the trabeculae in spongy bone align precisely along lines of stress and help the bone resist stress as much as possible. These tiny bone struts are as carefully positioned as the flying buttresses that help to support a Gothic cathedral.

Only a few cells thick, trabeculae contain irregularly arranged lamellae and osteocytes interconnected by canaliculi. No osteons are present. Nutrients reach the osteocytes of spongy bone by diffusing through the canaliculi from capillaries in the endosteum surrounding the trabeculae.

### Chemical Composition of Bone

Bone has both organic and inorganic components. Its *organic components* include the cells (osteogenic cells, osteoblasts, osteocytes, and osteoclasts) and **osteoid** (os'te-oid), the organic part of the matrix. Osteoid, which makes up approximately one-third of the matrix, includes ground substance (composed of proteoglycans and glycoproteins) and collagen fibers, both of which are made and secreted by osteoblasts. These organic substances, particularly collagen, contribute not only to a bone's structure but also to the flexibility and great tensile strength that allow the bone to resist stretch and twisting.

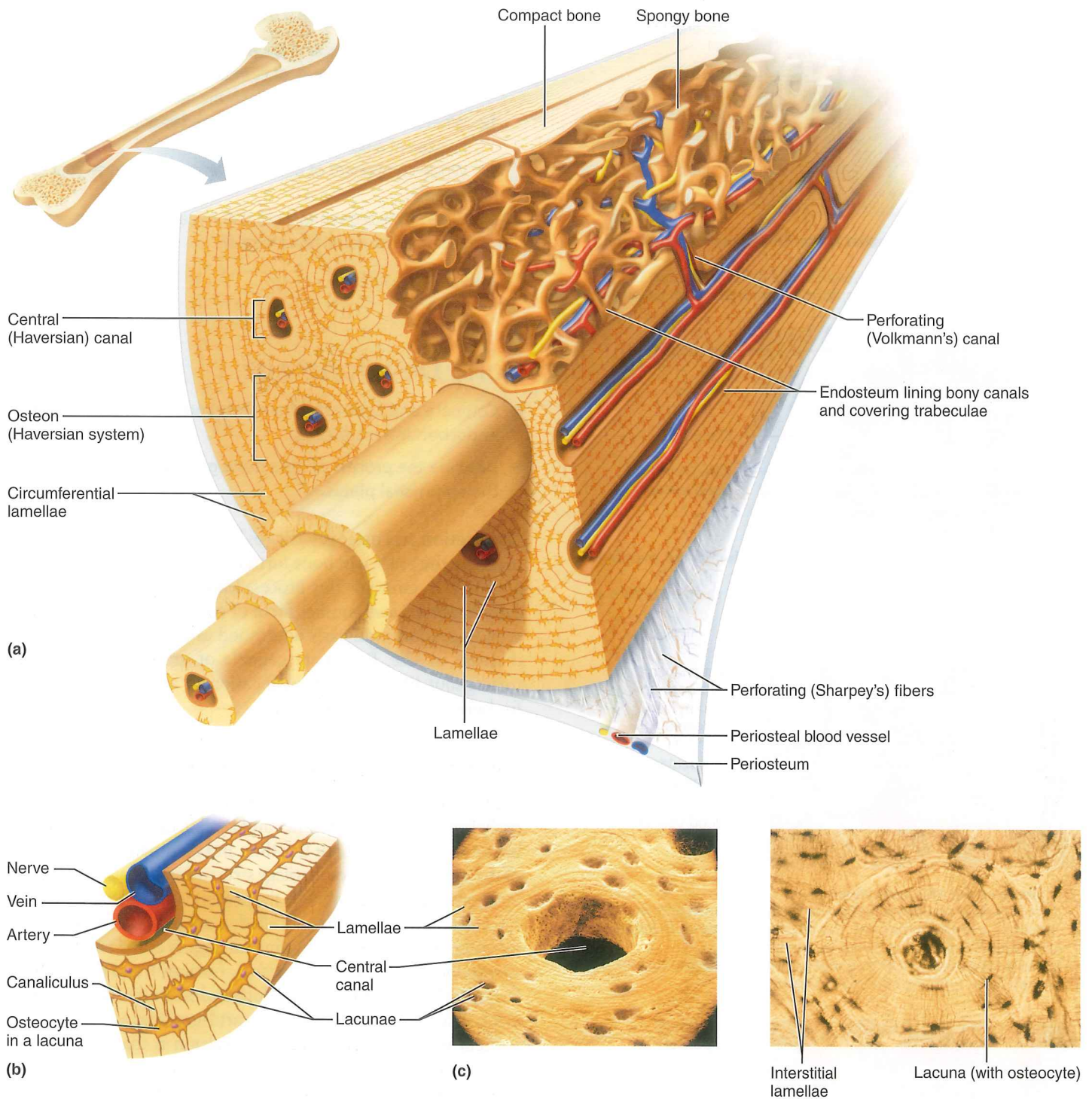
Bone's exceptional toughness and tensile strength has been the subject of intense research. It now appears that this resilience comes from the presence of *sacrificial bonds* in or between collagen molecules. These bonds break easily on impact, dissipating energy to prevent the force from rising to a fracture value. In the absence of continued or additional trauma, most of the sacrificial bonds re-form.

The balance of bone tissue (65% by mass) consists of inorganic **hydroxyapatites** (hi-drok"se-ap'ah-titz), or **mineral salts**, largely calcium phosphates present in the form of tiny, tightly packed, needle-like crystals in and around the collagen fibers in the extracellular matrix. The crystals account for the most notable characteristic of bone—its exceptional hardness, which allows it to resist compression.

The proper combination of organic and inorganic matrix elements allows bones to be exceedingly durable and strong without being brittle. Healthy bone is half as strong as steel in resisting compression and fully as strong as steel in resisting tension.

Because of the salts they contain, bones last long after death and provide an enduring "monument." In fact, skeletal remains many centuries old have revealed the shapes and sizes of ancient peoples, the kinds of work they did, and many of the ailments they suffered, such as arthritis.

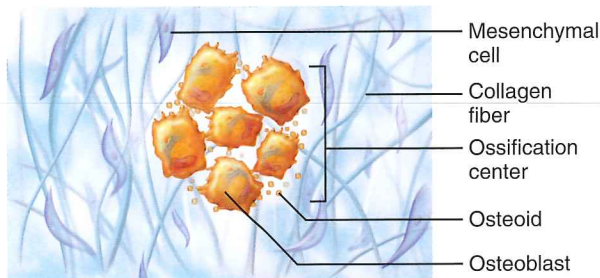




**Figure 6.7 Microscopic anatomy of compact bone.** (a) Diagrammatic view of a pie-shaped segment of compact bone. (b) Close-up of a portion of one osteon. Note the position of osteocytes in the lacunae. (c) SEM (left) of cross-sectional view of an osteon (180 $\times$ ). Light photomicrographs (right) of a cross-sectional view of an osteon (160 $\times$ ).

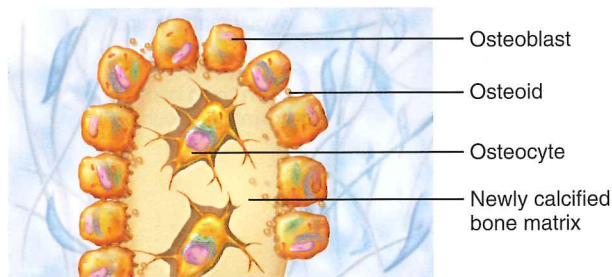
SOURCE: (c, left) Kessel and Kardon/Visuals Unlimited.





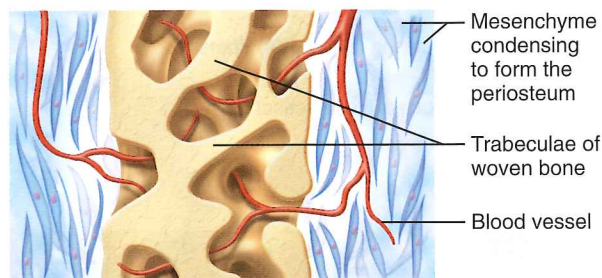
**① Ossification centers appear in the fibrous connective tissue membrane.**

- Selected centrally located mesenchymal cells cluster and differentiate into osteoblasts, forming an ossification center.



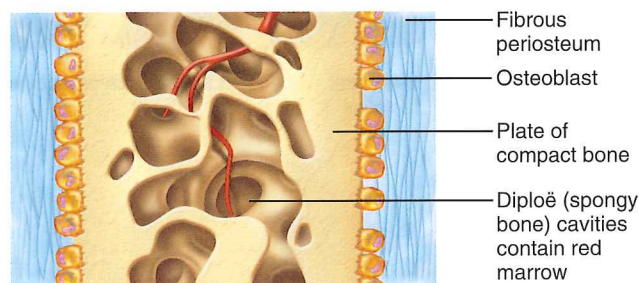
**② Bone matrix (osteoid) is secreted within the fibrous membrane and calcifies.**

- Osteoblasts begin to secrete osteoid, which is calcified within a few days.
- Trapped osteoblasts become osteocytes.



**③ Woven bone and periosteum form.**

- Accumulating osteoid is laid down between embryonic blood vessels in a random manner. The result is a network (instead of lamellae) of trabeculae called woven bone.
- Vascularized mesenchyme condenses on the external face of the woven bone and becomes the periosteum.



**④ Lamellar bone replaces woven bone, just deep to the periosteum. Red marrow appears.**

- Trabeculae just deep to the periosteum thicken, and are later replaced with mature lamellar bone, forming compact bone plates.
- Spongy bone (diploë), consisting of distinct trabeculae, persists internally and its vascular tissue becomes red marrow.

## CHECK YOUR UNDERSTANDING

- Are crests, tubercles, and spines bony projections or concavities?
- How does the structure of compact bone differ from that of spongy bone when viewed with the naked eye?
- What membrane lines the internal canals and covers the trabeculae of a bone?
- Which component of bone—organic or inorganic—makes it hard?
- What name is given to a cell that has a ruffled border and acts to break down bone matrix?

For answers, see Appendix G.

## Bone Development

- Compare and contrast intramembranous ossification and endochondral ossification.
- Describe the process of long bone growth that occurs at the epiphyseal plates.

**Ossification** and **osteogenesis** (os'te-o-jen'ě-sis) are synonyms meaning the process of bone formation (*os* = bone, *genesis* = beginning). In embryos this process leads to the *formation of the bony skeleton*. Later another form of ossification known as *bone growth* goes on until early adulthood as the body continues to increase in size. Bones are capable of growing in thickness throughout life. However, ossification in adults serves mainly for bone *remodeling* and repair.

### Formation of the Bony Skeleton

Before week 8, the skeleton of a human embryo is constructed entirely from fibrous membranes and hyaline cartilage. Bone tissue begins to develop at about this time and eventually replaces most of the existing fibrous or cartilage structures. When a bone develops from a fibrous membrane, the process is *intramembranous ossification*, and the bone is called a **membrane bone**. Bone development by replacing hyaline cartilage is called *endochondral ossification* (*endo* = within, *chondro* = cartilage), and the resulting bone is called a **cartilage**, or **endochondral bone**. The beauty of using structures (membranes and cartilages) that are flexible and resilient to fashion the embryonic skeleton is that they can accommodate mitosis. Were the early skeleton composed of bone tissue from the outset, growth would be much more difficult.

### Intramembranous Ossification

**Intramembranous ossification** results in the formation of cranial bones of the skull (frontal, parietal, occipital, and temporal bones) and the clavicles. Most bones formed by this process are flat bones. At about week 8 of development, ossification begins on fibrous connective tissue membranes formed by *mesenchymal*

**Figure 6.8 Intramembranous ossification.** Diagrams ③ and ④ represent much lower magnification than diagrams ① and ②.

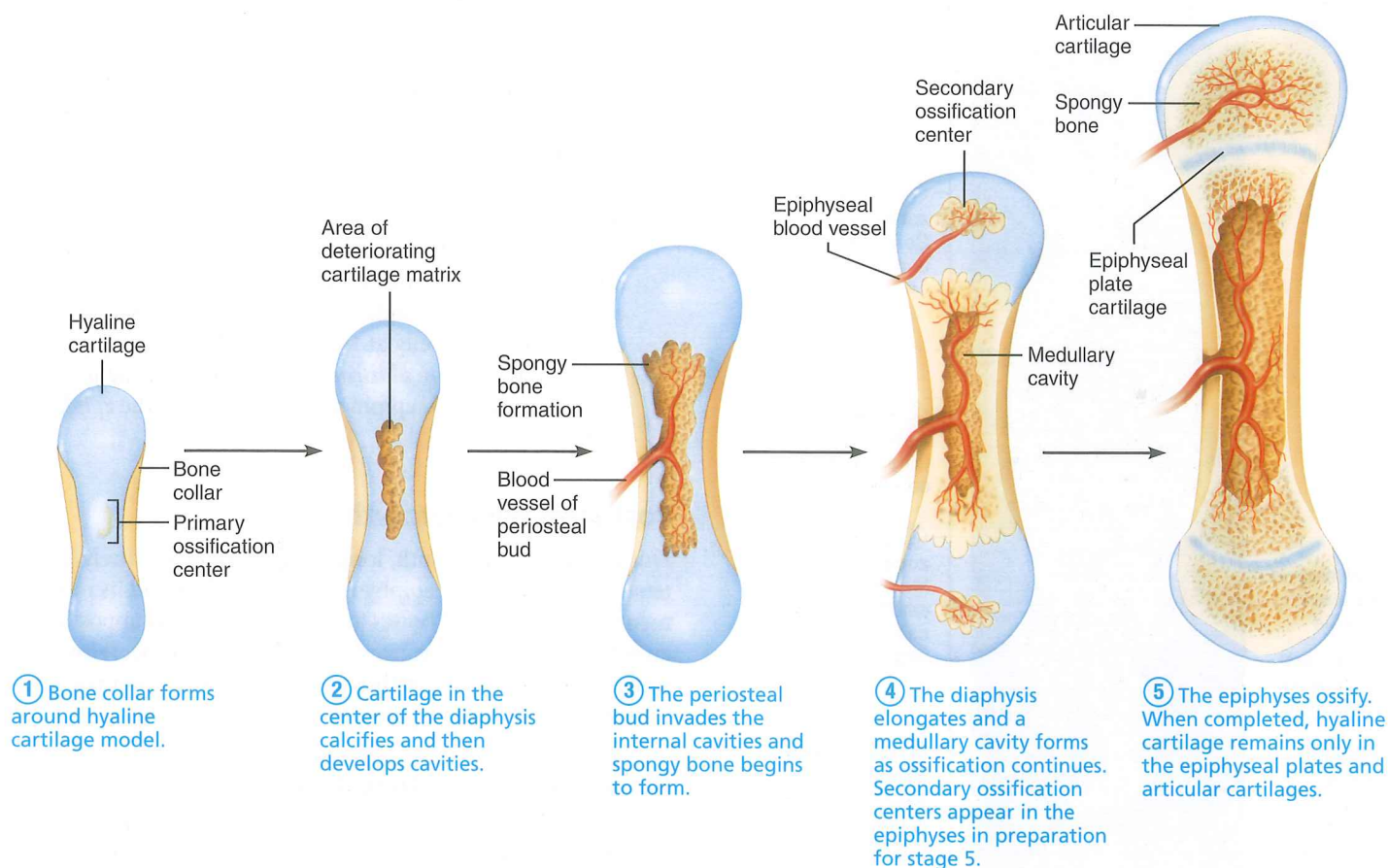


Week 9

Month 3

Birth

Childhood to adolescence



**Figure 6.9** Endochondral ossification in a long bone.

cells. Essentially, the process involves the four major steps depicted in **Figure 6.8**.

### Endochondral Ossification

Except for the clavicles, essentially all bones of the skeleton below the base of the skull form by **endochondral ossification** (en'do-kon'dral). Beginning in the second month of development, this process uses hyaline cartilage "bones" formed earlier as models, or patterns, for bone construction. It is more complex than intramembranous ossification because the hyaline cartilage must be broken down as ossification proceeds. We will use a forming long bone as our example.

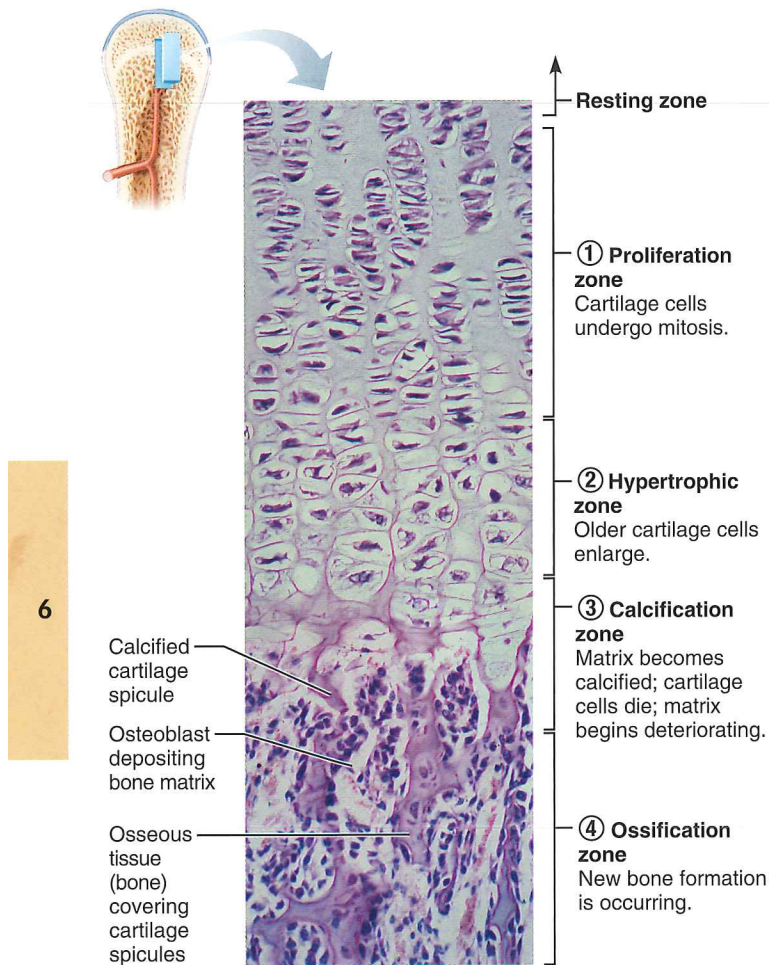
The formation of a long bone typically begins in the center of the hyaline cartilage shaft at a region called the **primary ossification center**. First, the perichondrium covering the hyaline cartilage "bone" is infiltrated with blood vessels, converting it to a vascularized periosteum. As a result of this change in nutrition, the underlying mesenchymal cells specialize into osteoblasts. The stage is now set for ossification to begin, as illustrated in **Figure 6.9**:

- 1** A bone collar is laid down around the diaphysis of the hyaline cartilage model. Osteoblasts of the newly converted

periosteum secrete osteoid against the hyaline cartilage diaphysis, encasing it in bone. This freshly formed layer of bone is called the *periosteal bone collar*.

- 2** **Cartilage in the center of the diaphysis calcifies and then develops cavities.** As the bone collar forms, chondrocytes within the shaft hypertrophy (enlarge) and signal the surrounding cartilage matrix to calcify. Then, because calcified cartilage matrix is impermeable to diffusing nutrients, the chondrocytes die and the matrix begins to deteriorate. This deterioration opens up cavities, but the hyaline cartilage model is stabilized by the bone collar. Elsewhere, the cartilage remains healthy and continues to grow briskly, causing the cartilage model to elongate.
- 3** **The periosteal bud invades the internal cavities and spongy bone forms.** In month 3, the forming cavities are invaded by a collection of elements called the **periosteal bud**, which contains a nutrient artery and vein, lymphatic vessels, nerve fibers, red marrow elements, osteoblasts, and osteoclasts. The entering osteoclasts partially erode the calcified cartilage matrix, and the osteoblasts secrete osteoid around the remaining fragments of hyaline cartilage, forming bone-covered cartilage trabeculae. In this way, the earliest version of spongy bone in a developing long bone forms.





**Figure 6.10 Growth in length of a long bone occurs at the epiphyseal plate.** The side of the epiphyseal plate facing the epiphysis (distal face) contains resting cartilage cells. The cells of the epiphyseal plate proximal to the resting cartilage area are arranged in four zones—proliferation, hypertrophic, calcification, and ossification—from the region of the earliest stage of growth ① to the region where bone is replacing the cartilage ④ (150 $\times$ ).

- ④ **The diaphysis elongates and a medullary cavity forms.** As the primary ossification center enlarges, osteoclasts break down the newly formed spongy bone and open up a medullary cavity in the center of the diaphysis. Throughout the fetal period (week 9 until birth), the rapidly growing epiphyses consist only of cartilage, and the hyaline cartilage models continue to elongate by division of viable cartilage cells at the epiphyses. Ossification “chases” cartilage formation along the length of the shaft as cartilage calcifies, is eroded, and then is replaced by bony spicules on the epiphyseal surfaces facing the medullary cavity.
- ⑤ **The epiphyses ossify.** At birth, most of our long bones have a bony diaphysis surrounding remnants of spongy bone, a widening medullary cavity, and two cartilaginous epiphyses. Shortly before or after birth, **secondary ossification centers** appear in one or both epiphyses, and the epiphyses gain bony tissue. (Typically, the large long bones form sec-

ondary centers in both epiphyses, whereas the small long bones form only one secondary ossification center.) The cartilage in the center of the epiphysis calcifies and deteriorates, opening up cavities that allow a periosteal bud to enter. Then bone trabeculae appear, just as they did earlier in the primary ossification center. (In short bones, only the primary ossification center is formed. Most irregular bones develop from several distinct ossification centers.)

Secondary ossification reproduces almost exactly the events of primary ossification, except that the spongy bone in the interior is retained and no medullary cavity forms in the epiphyses. When secondary ossification is complete, hyaline cartilage remains only at two places: (1) on the epiphyseal surfaces, as the *articular cartilages*, and (2) at the junction of the diaphysis and epiphysis, where it forms the *epiphyseal plates*.

## Postnatal Bone Growth

During infancy and youth, long bones lengthen entirely by interstitial growth of the epiphyseal plate cartilage and its replacement by bone, and all bones grow in thickness by appositional growth. Most bones stop growing during adolescence. However, some facial bones, such as those of the nose and lower jaw, continue to grow almost imperceptibly throughout life.

### Growth in Length of Long Bones

Longitudinal bone growth mimics many of the events of endochondral ossification. The cartilage is relatively inactive on the side of the epiphyseal plate facing the epiphysis, a region called the *resting* or *quiescent* zone. But the epiphyseal plate cartilage abutting the diaphysis organizes into a pattern that allows fast, efficient growth. The cartilage cells here form tall columns, like coins in a stack. The cells at the “top” (epiphysis-facing side) of the stack abutting the resting zone comprise the *proliferation* or *growth* zone (Figure 6.10). These cells divide quickly, pushing the epiphysis away from the diaphysis, causing the entire long bone to lengthen.

Meanwhile, the older chondrocytes in the stack, which are closer to the diaphysis (*hypertrophic* zone in Figure 6.10), hypertrophy, and their lacunae erode and enlarge, leaving large interconnecting spaces. Subsequently, the surrounding cartilage matrix calcifies and these chondrocytes die and deteriorate, producing the *calcification* zone. This leaves long slender spicules of calcified cartilage at the epiphysis-diaphysis junction, which look like stalactites hanging from the roof of a cave. These calcified spicules ultimately become part of the *ossification* or *osteogenic* zone, and are invaded by marrow elements from the medullary cavity. The cartilage spicules are partly eroded by osteoclasts, then quickly covered with new bone—called woven bone—by osteoblasts, and ultimately replaced by spongy bone. The spicule tips are eventually digested by osteoclasts, and in this way, the medullary cavity also grows longer as the long bone lengthens. During growth, the epiphyseal plate maintains a constant thickness because the rate of cartilage growth on its epiphysis-facing side is balanced by its replacement with bony tissue on its diaphysis-facing side.



Longitudinal growth is accompanied by almost continuous remodeling of the epiphyseal ends to maintain the proper proportions between the diaphysis and epiphyses (Figure 6.11). Bone remodeling involves both new bone formation and bone resorption (destruction). It is described in more detail later in conjunction with the changes that occur in adult bones.

As adolescence ends, the chondroblasts of the epiphyseal plates divide less often and the plates become thinner and thinner until they are entirely replaced by bone tissue. Longitudinal bone growth ends when the bone of the epiphysis and diaphysis fuses. This process, called *epiphyseal plate closure*, happens at about 18 years of age in females and 21 years of age in males. However, as noted earlier, an adult bone can still increase in diameter or thickness by appositional growth if stressed by excessive muscle activity or body weight.

### Growth in Width (Thickness)

Growing bones widen as they lengthen. As with cartilages, bones increase in thickness or, in the case of long bones, diameter, by appositional growth. Osteoblasts beneath the periosteum secrete bone matrix on the external bone surface as osteoclasts on the endosteal surface of the diaphysis remove bone (Figure 6.11). However, there is normally slightly less breaking down than building up. This unequal process produces a thicker, stronger bone but prevents it from becoming too heavy.

### CHECK YOUR UNDERSTANDING

15. Bones don't begin as bones. What do they begin as?
16. When describing endochondral ossification, some say "bone chases cartilage." What does that mean?
17. Where is the primary ossification center located in a long bone? Where is (are) the secondary ossification center(s) located?
18. As a long bone grows in length, what is happening in the hypertrophic zone of the epiphyseal plate?

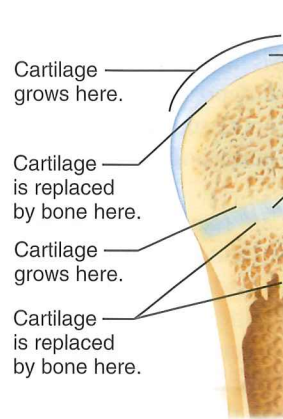
For answers, see Appendix G.

### Hormonal Regulation of Bone Growth

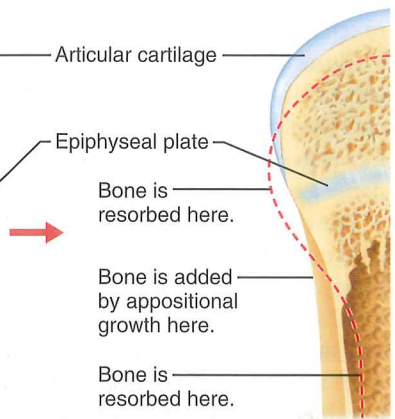
The growth of bones that occurs until young adulthood is exquisitely controlled by a symphony of hormones. During infancy and childhood, the single most important stimulus of epiphyseal plate activity is *growth hormone* released by the anterior pituitary gland. Thyroid hormones modulate the activity of growth hormone, ensuring that the skeleton has proper proportions as it grows. At puberty, male and female sex hormones (testosterone and estrogens, respectively) are released in increasing amounts. Initially these sex hormones promote the growth spurt typical of adolescence, as well as the masculinization or feminization of specific parts of the skeleton. Later the hormones induce epiphyseal plate closure, ending longitudinal bone growth.

Excesses or deficits of any of these hormones can result in obviously abnormal skeletal growth. For example, hypersecretion of growth hormone in children results in excessive height (gigantism), and deficits of growth hormone or thyroid hormone produce characteristic types of dwarfism.

### Bone growth



### Bone remodeling



**Figure 6.11 Long bone growth and remodeling during youth.**

The events at the left depict endochondral ossification that occurs at the articular cartilages and epiphyseal plates as the bone grows in length. Events at the right show bone remodeling during long bone growth to maintain proper bone proportions.

## Bone Homeostasis: Remodeling and Repair

- Compare the locations and remodeling functions of the osteoblasts, osteocytes, and osteoclasts.
- Explain how hormones and physical stress regulate bone remodeling.
- Describe the steps of fracture repair.

Bones appear to be the most lifeless of body organs, and may even summon images of a graveyard. But as you have just learned, this appearance is deceiving. Bone is a dynamic and active tissue, and small-scale changes in bone architecture occur continually. Every week we recycle 5–7% of our bone mass, and as much as half a gram of calcium may enter or leave the adult skeleton each day! Spongy bone is replaced every three to four years; compact bone, every ten years or so. This is fortunate because when bone remains in place for long periods more of the calcium salts crystallize (see description below) and the bone becomes more brittle—ripe conditions for fracture. And when we break bones—the most common disorder of bone homeostasis—they undergo a remarkable process of self-repair.

### Bone Remodeling

In the adult skeleton, bone deposit and bone resorption (removal) occur both at the surface of the periosteum and the surface of the endosteum. Together, the two processes constitute **bone remodeling**, and they are coupled and coordinated by “packets” of adjacent osteoblasts and osteoclasts called *remodeling units* (with help from the stress-sensing osteocytes). In healthy young adults, total bone mass remains constant, an indication that the rates of bone deposit and resorption are essentially equal. Remodeling does not occur uniformly, however. For



example, the distal part of the femur, or thigh bone, is fully replaced every five to six months, whereas its shaft is altered much more slowly.

**Bone deposit** occurs wherever bone is injured or added bone strength is required. For optimal bone deposit, a healthy diet rich in proteins, vitamin C, vitamin D, vitamin A, and several minerals (calcium, phosphorus, magnesium, and manganese, to name a few) is essential.

New matrix deposits by osteocytes are marked by the presence of an *osteoid seam*, an unmineralized band of gauzy-looking bone matrix 10–12 micrometers ( $\mu\text{m}$ ) wide. Between the osteoid seam and the older mineralized bone, there is an abrupt transition called the *calcification front*. Because the osteoid seam is always of constant width and the change from unmineralized to mineralized matrix is sudden, it seems that the osteoid must mature for about a week before it can calcify.

The precise trigger for calcification is still controversial. However, one critical factor is the product of the local concentrations of calcium and phosphate ( $\text{P}_i$ ) ions (the  $\text{Ca}^{2+} \cdot \text{P}_i$  product). Initially the bone salts are laid down in a noncrystalline form, but when the  $\text{Ca}^{2+} \cdot \text{P}_i$  product reaches a certain level, tiny crystals of hydroxyapatite form spontaneously and then catalyze further crystallization of calcium salts in the area. Other factors involved are matrix proteins that bind and concentrate calcium, and the enzyme *alkaline phosphatase* (shed by the osteoblasts), which is essential for mineralization. Once proper conditions are present, calcium salts are deposited all at once and with great precision throughout the “matured” matrix. Normally, a small percentage of the calcified salts remain in the noncrystallized form to provide a readily available source of calcium ions when blood calcium levels decline toward nonhomeostatic values.

**Bone resorption** is accomplished by **osteoclasts**, giant multinucleate cells that arise from the same hematopoietic stem cells that differentiate into macrophages. Osteoclasts move along a bone surface, digging grooves as they break down the bone matrix. The part of the osteoclast that touches the bone is highly folded to form a ruffled membrane (see Figure 6.4d) that clings tightly to the bone, sealing off the area of bone destruction. The ruffled border secretes (1) *lysosomal enzymes* that digest the organic matrix and (2) *hydrochloric acid* that converts the calcium salts into soluble forms that pass easily into solution. Osteoclasts may also phagocytize the demineralized matrix and dead osteocytes. The digested matrix end products, growth factors, and dissolved minerals are then endocytosed, transported across the osteoclast (by transcytosis), and released at the opposite side where they enter first the interstitial fluid and then the blood. There is much to learn about osteoclast activation, but proteins secreted by T cells of the immune system appear to be important.

### Control of Remodeling

The remodeling that goes on continuously in the skeleton is regulated by two control loops that serve different “masters.” One is a negative feedback hormonal loop that maintains  $\text{Ca}^{2+}$  homeostasis in the blood. The other involves responses to mechanical and gravitational forces acting on the skeleton.

The hormonal feedback becomes much more meaningful when you understand calcium’s importance in the body. Ionic calcium is necessary for an amazing number of physiological processes, including transmission of nerve impulses, muscle contraction, blood coagulation, secretion by glands and nerve cells, and cell division. The human body contains 1200–1400 g of calcium, more than 99% present as bone minerals. Most of the remainder is in body cells. Less than 1.5 g is present in blood, and the hormonal control loop normally maintains blood  $\text{Ca}^{2+}$  within the very narrow range of 9–11 mg per dl (100 ml) of blood. Calcium is absorbed from the intestine under the control of vitamin D metabolites. The daily calcium requirement is 400–800 mg from birth until the age of 10, and 1200–1500 mg from ages 11 to 24.

**Hormonal Controls** The hormonal controls primarily involve **parathyroid hormone (PTH)**, produced by the parathyroid glands. To a much lesser extent **calcitonin** (kal’*si*-to’*ni*n), produced by parafollicular cells (C cells) of the thyroid gland, may be involved. As Figure 6.12 illustrates, PTH is released when blood levels of ionic calcium decline. The increased PTH level stimulates osteoclasts to resorb bone, releasing calcium to the blood. Osteoclasts are no respecters of matrix age. When activated, they break down both old and new matrix. Only osteoid, which lacks calcium salts, escapes digestion. As blood concentrations of calcium rise, the stimulus for PTH release ends. The decline of PTH reverses its effects and causes blood  $\text{Ca}^{2+}$  levels to fall.

In humans, calcitonin appears to be a hormone in search of a function because its effects on calcium homeostasis are negligible. When administered at pharmacological (abnormally high) doses, it does lower blood calcium levels temporarily.

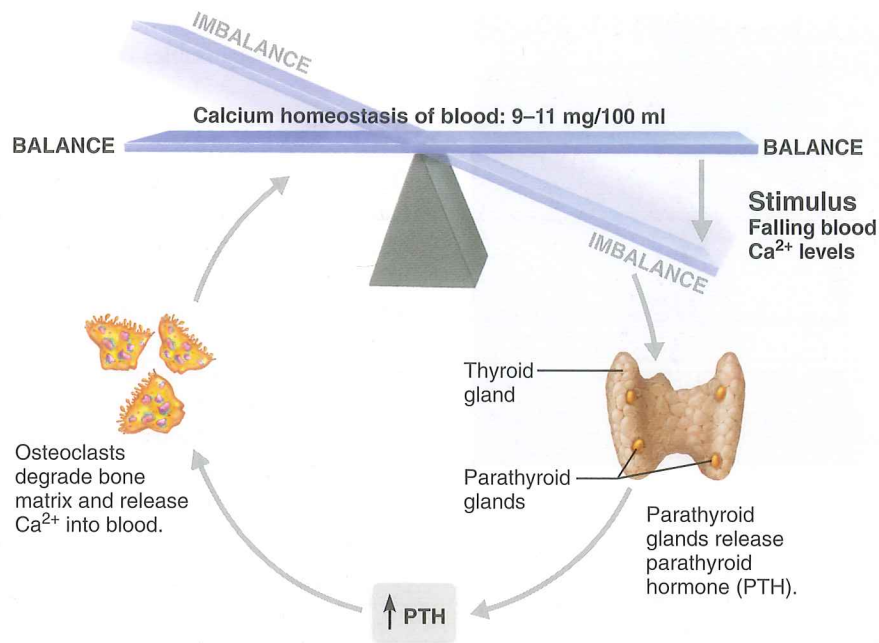
These hormonal controls act not to preserve the skeleton’s strength or well-being but rather to maintain blood calcium homeostasis. In fact, if blood calcium levels are low for an extended time, the bones become so demineralized that they develop large, punched-out-looking holes. Thus, the bones serve as a storehouse from which ionic calcium is drawn as needed.

### HOMEOSTATIC IMBALANCE

Minute changes from the homeostatic range for blood calcium can lead to severe neuromuscular problems ranging from hyperexcitability (when blood  $\text{Ca}^{2+}$  levels are too low) to nonresponsiveness and inability to function (with high blood  $\text{Ca}^{2+}$  levels). In addition, sustained high blood levels of  $\text{Ca}^{2+}$ , a condition known as *hypercalcemia* (hi’*per*-kal-se’*me*-ah), can lead to undesirable deposits of calcium salts in the blood vessels, kidneys, and other soft organs, which may hamper the functioning of these organs. ■

In addition to the hormones that regulate bone remodeling in response to blood calcium levels, it is now established that *leptin*, a hormone released by adipose tissue, plays a role in regulating bone density. Best known for its effects on weight and energy balance (see pp. 946–947), in animal studies leptin appears to inhibit osteoblasts through an additional pathway mediated by the hypothalamus which activates sympathetic nerves serving



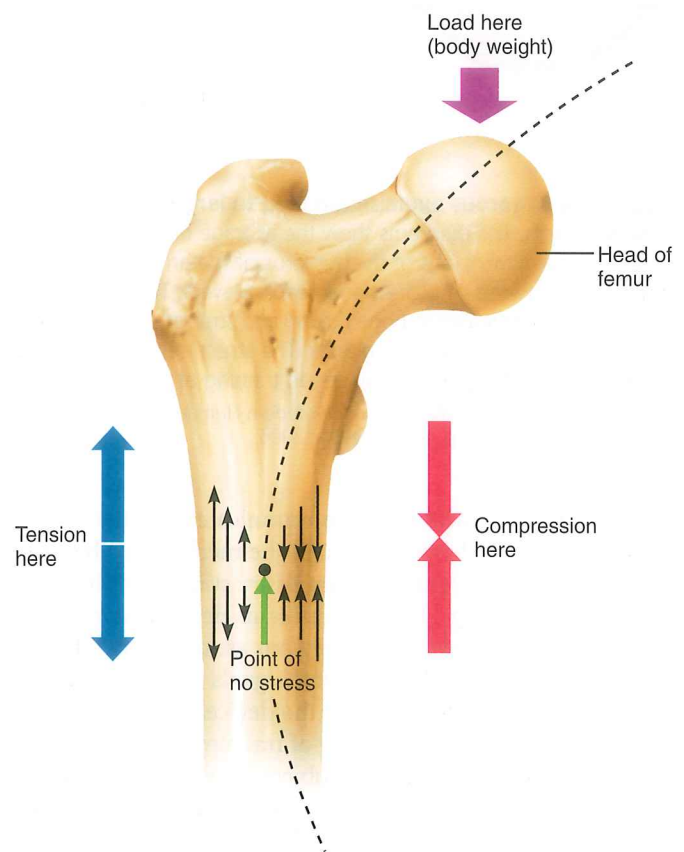


**Figure 6.12** Parathyroid hormone (PTH) control of blood calcium levels.

bones. However, the full scope of leptin's bone-modifying activity in humans is still being worked out.

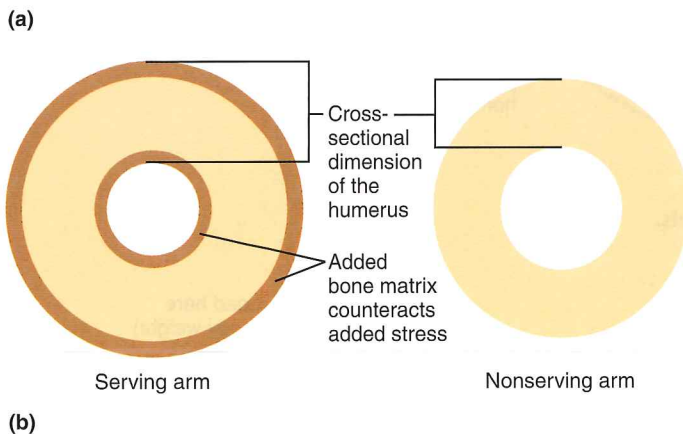
**Response to Mechanical Stress** The second set of controls regulating bone remodeling, bone's response to mechanical stress (muscle pull) and gravity, serves the needs of the skeleton by keeping the bones strong where stressors are acting. *Wolff's law* holds that a bone grows or remodels in response to the demands placed on it. The first thing to understand is that a bone's anatomy reflects the common stresses it encounters. For example, a bone is loaded (stressed) whenever weight bears down on it or muscles pull on it. This loading is usually off center, however, and tends to *bend* the bone. Bending compresses the bone on one side and subjects it to tension (stretching) on the other (**Figure 6.13**). As a result of these mechanical stressors, long bones are thickest midway along the diaphysis, exactly where bending stresses are greatest (bend a stick and it will split near the middle). Both compression and tension are minimal toward the center of the bone (they cancel each other out), so a bone can “hollow out” for lightness (using spongy bone instead of compact bone) without jeopardy.

Other observations explained by Wolff's law include these: (1) Handedness (being right or left handed) results in the bones of one upper limb being thicker than those of the less-used limb, and vigorous exercise of the most-used limb leads to large increases in bone strength (**Figure 6.14**). (2) Curved bones are thickest where they are most likely to buckle. (3) The trabeculae of spongy bone form trusses, or struts, along lines of compression. (4) Large, bony projections occur where heavy, active muscles attach. (The bones of weight lifters have enormous thickenings at the attachment sites of the most-used muscles.) Wolff's law also explains the featureless bones of the fetus and the atrophied bones of bedridden people—situations in which bones are not stressed.



**Figure 6.13** Bone anatomy and bending stress. Body weight transmitted to the head of the femur (thigh bone) threatens to bend the bone along the indicated arc, compressing it on one side (converging arrows on right) and stretching it on the other side (diverging arrows on left). Because these two forces cancel each other internally, much less bone material is needed internally than superficially.





**Figure 6.14 Vigorous exercise can lead to large increases in bone strength.** The diagrams show the average difference in the cross-sectional dimensions of the humerus of the arm in the serving and nonserving arms of professional tennis players. The data revealed average increases in bone rigidity and strength of 62% and 45%, respectively, in the serving arms. The structural changes were more pronounced in players who began training at an early age.

SOURCE: C. B. Ruff, "Gracilization of the Modern Human Skeleton," *American Scientist* 94(6): p. 513, Nov–Dec 2006.

How do mechanical forces communicate with the cells responsible for remodeling? Although the mechanisms by which bone responds to mechanical stimuli are still uncertain, we do know that deforming a bone produces an electrical current. Because compressed and stretched regions are oppositely charged, it has been suggested that electrical signals direct remodeling. This principle underlies some of the devices currently used to speed bone repair and the healing of fractures.

The skeleton is continuously subjected to both hormonal influences and mechanical forces. At the risk of constructing too large a building on too small a foundation, we can speculate that the hormonal loop determines *whether* and *when* remodeling occurs in response to changing blood calcium levels, and mechanical stress determines *where* it occurs. For example, when bone must be broken down to increase blood calcium levels, PTH is released and targets the osteoclasts. However, mechanical forces determine *which* osteoclasts are most sensitive to PTH

stimulation, so that bone in the *least* stressed areas (which is temporarily dispensable) is broken down.

## Bone Repair

Despite their remarkable strength, bones are susceptible to **fractures**, or breaks. During youth, most fractures result from exceptional trauma that twists or smashes the bones (sports injuries, automobile accidents, and falls, for example). Excessive intake of vitamin A appears to increase fracture risk in some people. Elevated blood levels of the amino acid derivative homocysteine were also believed to increase fracture risk, but recent studies indicate that it is actually a marker of low bone density and bone frailty. In old age, most fractures occur as bones thin and weaken.

Fractures may be classified by

1. Position of the bone ends after fracture. In *nondisplaced fractures* the bone ends retain their normal position; in *displaced fractures* the bone ends are out of normal alignment.
2. Completeness of the break. If the bone is broken through, the fracture is a *complete fracture*; if not, it is an *incomplete fracture*.
3. Orientation of the break relative to the long axis of the bone. If the break parallels the long axis, the fracture is *linear*; if the break is perpendicular to the bone's long axis, it is *transverse*.
4. Whether the bone ends penetrate the skin. If so, the fracture is an *open (compound) fracture*; if not, it is a *closed (simple) fracture*.

In addition to these four either-or classifications, all fractures can be described in terms of the location of the fracture, the external appearance of the fracture, and/or the nature of the break. **Table 6.2** summarizes the various descriptions.

A fracture is treated by *reduction*, the realignment of the broken bone ends. In *closed (external) reduction*, the bone ends are coaxied into position by the physician's hands. In *open (internal) reduction*, the bone ends are secured together surgically with pins or wires. After the broken bone is reduced, it is immobilized either by a cast or traction to allow the healing process to begin. For a simple fracture the healing time is six to eight weeks for small or medium-sized bones in young adults, but it is much longer for large, weight-bearing bones and for bones of elderly people (because of their poorer circulation).

Repair in a simple fracture involves four major stages (**Figure 6.15**):

- ① **A hematoma forms.** When a bone breaks, blood vessels in the bone and periosteum, and perhaps in surrounding tissues, are torn and hemorrhage. As a result, a **hematoma** (he"mah-to'mah), a mass of clotted blood, forms at the fracture site. Soon, bone cells deprived of nutrition die, and the tissue at the site becomes swollen, painful, and inflamed.
- ② **Fibrocartilaginous callus forms.** Within a few days, several events lead to the formation of soft *granulation tissue*, also called the *soft callus* (kal'us; "hard skin"). Capillaries grow into the hematoma and phagocytic cells invade the area and



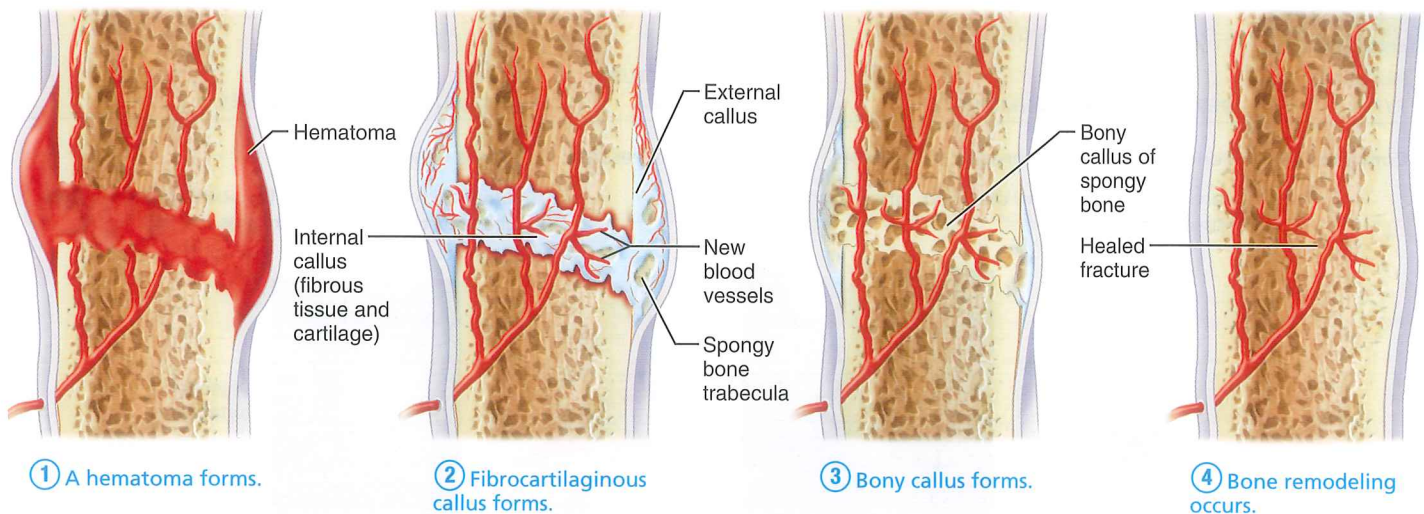


Figure 6.15 Stages in the healing of a bone fracture.

begin cleaning up the debris. Meanwhile, fibroblasts and osteoblasts invade the fracture site from the nearby periosteum and endosteum and begin reconstructing the bone. The fibroblasts produce collagen fibers that span the break and connect the broken bone ends, and some differentiate into chondroblasts that secrete cartilage matrix. Within this mass of repair tissue, osteoblasts begin forming spongy bone, but those farthest from the capillary supply secrete an externally bulging cartilaginous matrix that later calcifies. This entire mass of repair tissue, now called the **fibrocartilaginous callus**, splints the broken bone.

- ③ **Bony callus forms.** Within a week, new bone trabeculae begin to appear in the fibrocartilaginous callus and gradually convert it to a **bony (hard) callus** of spongy bone. Bony callus formation continues until a firm union is formed about two months later.
- ④ **Bone remodeling occurs.** Beginning during bony callus formation and continuing for several months after, the bony callus is remodeled. The excess material on the diaphysis exterior and within the medullary cavity is removed, and compact bone is laid down to reconstruct the shaft walls. The final structure of the remodeled area resembles that of the original unbroken bony region because it responds to the same set of mechanical stressors.

#### CHECK YOUR UNDERSTANDING

19. If osteoclasts in a long bone are more active than osteoblasts, what change in bone mass is likely?
20. Which stimulus—PTH (a hormone) or mechanical forces acting on the skeleton—is more important in maintaining homeostatic blood calcium levels?
21. How does an open fracture differ from a closed fracture?
22. How do bone growth and bone remodeling differ?

For answers, see Appendix G.

## Homeostatic Imbalances of Bone

- Contrast the disorders of bone remodeling seen in osteoporosis, osteomalacia, and Paget's disease.

Imbalances between bone deposit and bone resorption underlie nearly every disease that affects the adult skeleton.

### Osteomalacia and Rickets

**Osteomalacia** (os'te-o-mah-la'she-ah; "soft bones") includes a number of disorders in which the bones are inadequately mineralized. Osteoid is produced, but calcium salts are not deposited, so bones soften and weaken. The main symptom is pain when weight is put on the affected bones.

**Rickets** is the analogous disease in children. Because young bones are still growing rapidly, rickets is much more severe than adult osteomalacia. Bowed legs and deformities of the pelvis, skull, and rib cage are common. Because the epiphyseal plates cannot be calcified, they continue to widen, and the ends of long bones become visibly enlarged and abnormally long.



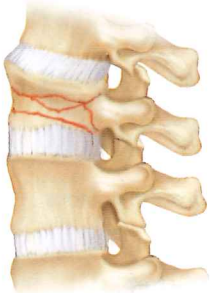
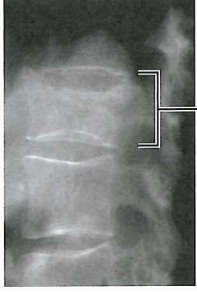





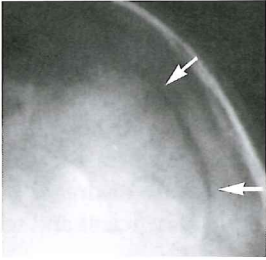


Osteomalacia and rickets are caused by insufficient calcium in the diet or by a vitamin D deficiency. For this reason, drinking vitamin D–fortified milk and exposing the skin to sunlight (which spurs the body to form vitamin D) usually cure these disorders. Although the seeming elimination of rickets in the United States has been heralded as a public health success, rickets still rears its head in isolated situations. For example, if a mother who breast-feeds her infant becomes vitamin D deficient because of dreary winter weather, the infant too will be vitamin D deficient and will develop rickets.

### Osteoporosis

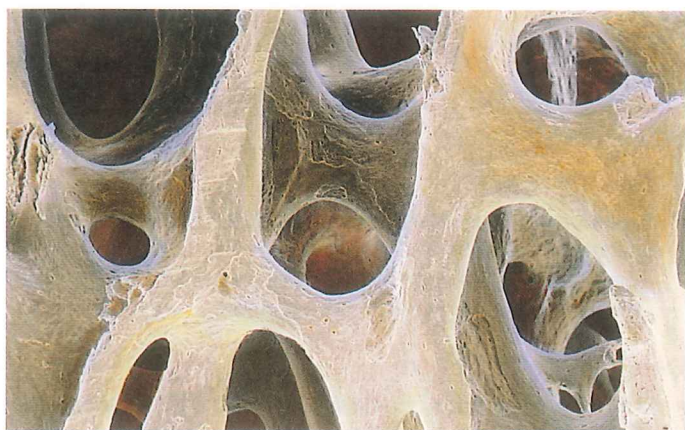
For most of us, the phrase "bone problems of the elderly" brings to mind the stereotype of a victim of osteoporosis—a hunched-over old woman shuffling behind her walker.



**TABLE 6.2** Common Types of Fractures

FRACTURE TYPE	DESCRIPTION AND COMMENTS	FRACTURE TYPE	DESCRIPTION AND COMMENTS
<b>Comminuted</b>	<p>Bone fragments into three or more pieces.</p> <p>Particularly common in the aged, whose bones are more brittle</p>	<b>Compression</b>	<p>Bone is crushed.</p> <p>Common in porous bones (i.e., osteoporotic bones) subjected to extreme trauma, as in a fall</p>
 		 	
<b>Spiral</b>	<p>Ragged break occurs when excessive twisting forces are applied to a bone.</p> <p>Common sports fracture</p>	<b>Epiphyseal</b>	<p>Epiphysis separates from the diaphysis along the epiphyseal plate.</p> <p>Tends to occur where cartilage cells are dying and calcification of the matrix is occurring</p>
 		 	
<b>Depressed</b>	<p>Broken bone portion is pressed inward.</p> <p>Typical of skull fracture</p>	<b>Greenstick</b>	<p>Bone breaks incompletely, much in the way a green twig breaks. Only one side of the shaft breaks; the other side bends.</p> <p>Common in children, whose bones have relatively more organic matrix and are more flexible than those of adults</p>
 		 	





(a) Normal bone



(b) Osteoporotic bone

**Figure 6.16** The contrasting architecture of normal versus osteoporotic bone. Scanning electron micrographs, 300 $\times$ .

**Osteoporosis** (os'te-o-po-ro'sis) refers to a group of diseases in which bone resorption outpaces bone deposit. The bones become so fragile that something as simple as a hearty sneeze or stepping off a curb can cause them to break. The composition of the matrix remains normal but bone mass is reduced, and the bones become porous and light (**Figure 6.16**). Even though osteoporosis affects the entire skeleton, the spongy bone of the spine is most vulnerable, and compression fractures of the vertebrae are common. The femur, particularly its neck, is also very susceptible to fracture (called a *broken hip*) in people with osteoporosis.

Osteoporosis occurs most often in the aged, particularly in postmenopausal women. Although men develop it to a lesser degree, 30% of American women between the ages of 60 and 70 have osteoporosis, and 70% have it by age 80. Moreover, 30% of all Caucasian women (the most susceptible group) will experience a bone fracture due to osteoporosis. Sex hormones, particularly estrogen, help to maintain the health and normal density of the skeleton by restraining osteoclast activity and by promoting deposit of new bone. After menopause, however, estrogen secretion wanes, and estrogen deficiency is strongly implicated in osteoporosis in older women. Other factors that contribute to

osteoporosis include a petite body form, insufficient exercise to stress the bones, immobility, a diet poor in calcium and protein, abnormal vitamin D receptors, smoking (which reduces estrogen levels), and hormone-related conditions such as hyperthyroidism, low blood levels of thyroid-stimulating hormone (better known for its role in stimulating the secretion of thyroid hormones), and diabetes mellitus. In addition, recent research indicates that a particular gene, dubbed *LRP5*, may play a role in osteoporosis. It inhibits release of serotonin by cells of the gut. Because serotonin inhibits osteoblast growth, reducing its synthesis increases bone density.

Osteoporosis has traditionally been treated with calcium and vitamin D supplements, weight-bearing exercise, and *hormone (estrogen) replacement therapy (HRT)*. Frustratingly, HRT only slows the loss of bone but does not reverse it. Additionally, because of the increased risk of heart attack, stroke, and breast cancer associated with estrogen replacement therapy, it is a controversial treatment these days.

Newer drugs are available. These include alendronate (Fosamax), a drug that decreases osteoclast activity and number, and shows promise in reversing osteoporosis in the spine; and selective estrogen receptor modulators (SERMs), such as raloxifene, dubbed "estrogen light" because it mimics estrogen's beneficial bone-sparing properties without targeting the uterus or breast. Additionally, *statins*, drugs used by tens of thousands of people to lower cholesterol levels, have been shown to have an unexpected side effect of increasing bone mineral density up to 8% over four years. Although not a substitute for HRT, estrogenic compounds in soy protein (principally the isoflavones daidzein and genistein) offer a good addition or adjunct for some patients.

How can osteoporosis be prevented (or at least delayed)? The first requirement is to get enough calcium while your bones are still increasing in density (bones reach their peak density during early adulthood). Second, drinking fluoridated water hardens bones (as well as teeth). Conversely, excessive intake of carbonated beverages leaches minerals from bone and decreases bone density. Finally, getting plenty of weight-bearing exercise (walking, jogging, tennis, etc.) throughout life will increase bone mass above normal values and provide a greater buffer against age-related bone loss.

### Paget's Disease

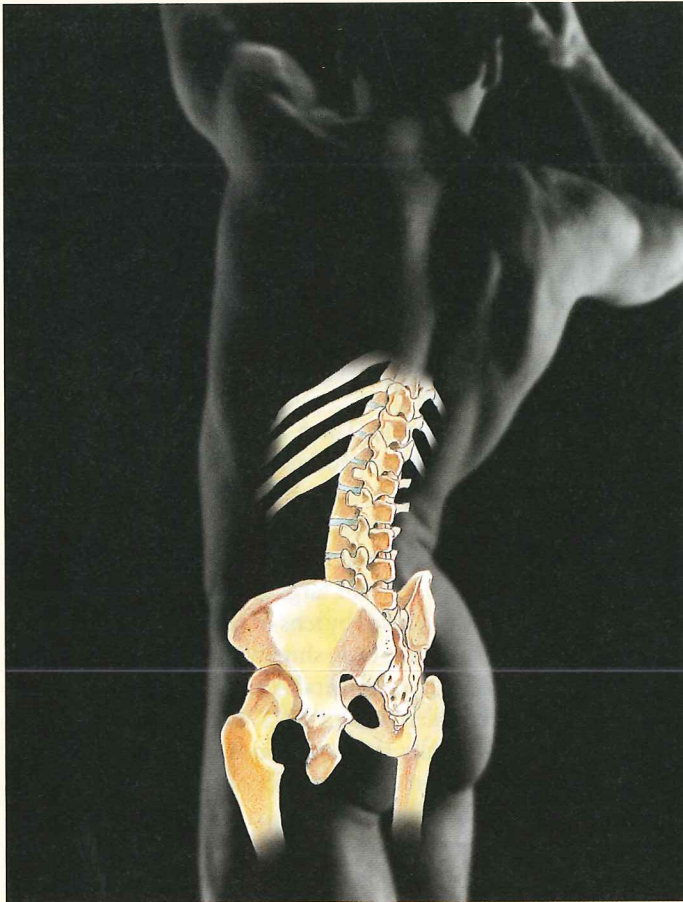
Often discovered by accident when X rays are taken for some other reason, **Paget's disease** (paj'ets) is characterized by excessive and haphazard bone deposit and resorption. The newly formed bone, called *Pagetic bone*, is hastily made and has an abnormally high ratio of spongy bone to compact bone. This, along with reduced mineralization, causes a spotty weakening of the bones. Late in the disease, osteoclast activity wanes, but osteoblasts continue to work, often forming irregular bone thickenings or filling the marrow cavity with Pagetic bone.

Paget's disease may affect any part of the skeleton, but it is usually a localized condition. The spine, pelvis, femur, and skull are most often involved and become increasingly deformed and painful. It rarely occurs before the age of 40, and it affects about 3% of North American elderly people. Its cause is unknown, but



## System Connections

### Homeostatic Interrelationships Between the Skeletal System and Other Body Systems



6

#### Integumentary System

- Skeletal system provides support for body organs including the skin
- Skin provides vitamin D needed for proper calcium absorption and use

#### Muscular System

- Skeletal system provides levers plus ionic calcium for muscle activity
- Muscle pull on bones increases bone strength and viability; helps determine bone shape

#### Nervous System

- Skeletal system protects brain and spinal cord; provides depot for calcium ions needed for neural function
- Nerves innervate bone and joint capsules, providing for pain and joint sense

#### Endocrine System

- Skeletal system provides some bony protection; stores calcium needed for second-messenger signaling mechanisms
- Hormones regulate uptake and release of calcium from bone; promote long bone growth and maturation

#### Cardiovascular System

- Bone marrow cavities provide site for blood cell formation; matrix stores calcium needed for cardiac muscle activity
- Cardiovascular system delivers nutrients and oxygen to bones; carries away wastes

#### Lymphatic System/Immunity

- Skeletal system provides some protection to lymphatic organs; bone marrow is site of origin for lymphocytes involved in immune response
- Lymphatic system drains leaked tissue fluids; immune cells protect against pathogens

#### Respiratory System

- Skeletal system protects lungs by enclosure (rib cage)
- Respiratory system provides oxygen; disposes of carbon dioxide

#### Digestive System

- Skeletal system provides some bony protection to intestines, pelvic organs, and liver
- Digestive system provides nutrients needed for bone health and growth

#### Urinary System

- Skeletal system protects pelvic organs (urinary bladder, etc.)
- Urinary system activates vitamin D; disposes of nitrogenous wastes

#### Reproductive System

- Skeletal system protects some reproductive organs by enclosure
- Gonads produce hormones that influence the form of the skeleton and epiphyseal closure



## Closer Connections

## The Skeletal System and Interrelationships with the Muscular, Endocrine, and Integumentary Systems

Our skeleton supports us, protects our “innards” (the protection our brain gets from the skull is indispensable), gives us stature (for some reason, tall people get more respect), contributes to our shape (women are shaped differently than men), and allows us to move. Obviously, the skeletal system has important interactions with many other body systems, not the least of which are the endocrine and integumentary systems. However, its most intimate and mutually beneficial relationship is with the muscular system, so we will consider that first.

### Muscular System

The codependence of the skeletal and muscular systems is striking—as one system goes, so goes the other. If we participate in weight-bearing exercise (run, play tennis, do aerobics) regularly, our muscles become more efficient and exert more force on our bones. As a result, our bones stay healthy and strong and increase their mass to assume the added stress.

Since both spongy and compact bone reach peak density during midlife, weight-bearing exercise during youth is important, especially in females who have less bone mass than males and lose it faster.

Regular exercise also stretches the connective tissues binding bones to muscles and to other bones, and reinforcing joints. Since this increases overall flexibility, we have fewer injuries, allowing us to stay active well into old age. (Pain makes couch potatoes.)

### Endocrine System

Although mechanical factors are undeniably important in shaping the skeleton and helping to keep it strong, hormones acting individually and in concert direct skeletal growth during youth, and enhance (or impair) skeletal strength in adults. Growth hormone is essential for normal skeletal growth and maintenance throughout life, whereas thyroid and sex hormones ensure that normal skeletal proportions are established during childhood and adolescence. Conversely, PTH serves not the skeleton but a different master—homeostasis of blood calcium levels. Any interference with normal hormonal functioning is soon apparent as a skeletal abnormality or malproportion.

### Integumentary System

The skeletal system is absolutely dependent on the integumentary system (the skin) for the calcium that keeps the bones hard and strong. The relationship is indirect: In the presence of sunlight, a vitamin D precursor is produced in the dermal capillary blood. It is activated elsewhere, and (among its other roles) it regulates the carrier system that absorbs calcium from ingested foods into the blood. Because calcium is required for so many body functions, and bones provide the “calcium bank,” the bones become increasingly soft and weak in the absence of vitamin D because no daily rations of calcium are allowed to enter the blood from the digestive tract.

## Clinical Connections

### Skeletal System

**Case study:** Remember Mrs. DeStephano? When we last heard about her she was being admitted for further studies. Relative to her skeletal system, the following notes have been added to her chart.

- Fracture of superior right tibia (shinbone of leg); skin lacerated; area cleaned and protruding bone fragments subjected to internal (open) reduction and casted
- Nutrient artery of tibia damaged
- Medial meniscus (fibrocartilage disc) of right knee joint crushed; knee joint inflamed and painful

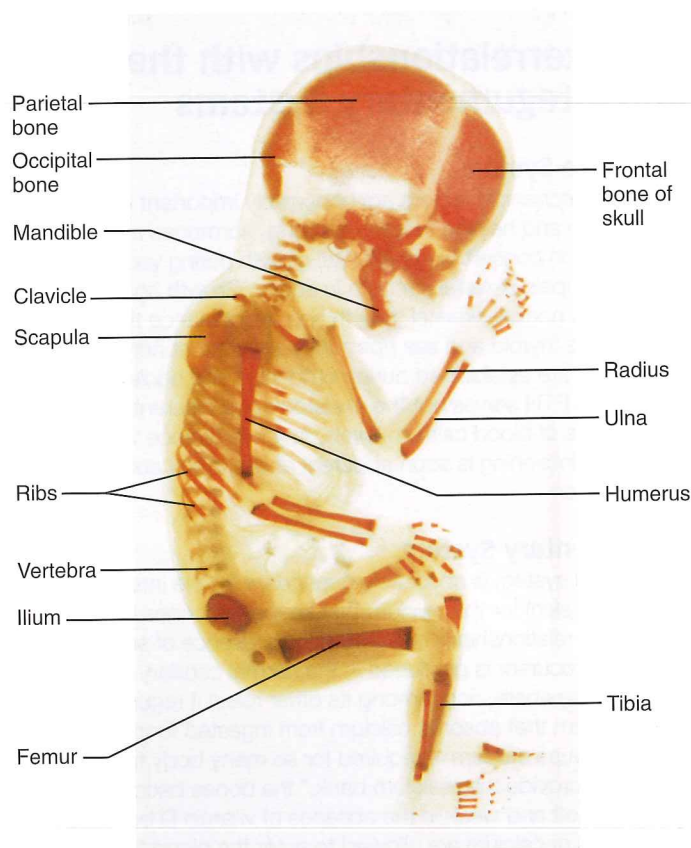
Relative to these notes:

1. What type of fracture does Mrs. DeStephano have?
2. What problems can be predicted with such fractures and how are they treated?

3. What is internal reduction? Why was a cast applied?
4. Given an uncomplicated recovery, approximately how long should it take before Mrs. DeStephano has a good solid bony callus?
5. What complications might be predicted by the fact that the nutrient artery is damaged?
6. What new techniques might be used to enhance fracture repair if healing is delayed or impaired?
7. How likely is it that Mrs. DeStephano's knee cartilage will regenerate? Why?

(Answers in Appendix G)





**Figure 6.17 Fetal primary ossification centers at 12 weeks.** The darker areas indicate primary ossification centers in the skeleton of a 12-week-old fetus.

it may be initiated by a virus. Drug therapies include calcitonin (now administered by a nasal inhaler), and the newer bisphosphonates (etidronate, alendronate, and others) which have shown success in preventing bone breakdown.

#### CHECK YOUR UNDERSTANDING

23. Which bone disorder is characterized by excessive deposit of weak, poorly mineralized bone?
24. What are three measures that may help to maintain healthy bone density?
25. What name is given to “adult rickets”?

For answers, see Appendix G.

## Developmental Aspects of Bones: Timing of Events

- Describe the timing and cause of changes in bone architecture and bone mass throughout life.

Bones are on a precise schedule from the time they form until death. The mesoderm germ layer gives rise to embryonic

mesenchymal cells, which in turn produce the membranes and cartilages that form the embryonic skeleton. These structures then ossify according to an amazingly predictable timetable that allows fetal age to be determined easily from either X rays or sonograms. Although each bone has its own developmental schedule, most long bones begin ossifying by 8 weeks after conception and have well-developed primary ossification centers by 12 weeks (**Figure 6.17**).

At birth, most long bones of the skeleton are well ossified except for their epiphyses. After birth, secondary ossification centers develop in a predictable sequence. The epiphyseal plates persist and provide for long bone growth all through childhood and the sex hormone-mediated growth spurt at adolescence. By the age of 25 years, nearly all bones are completely ossified and skeletal growth ceases.

In children and adolescents, bone formation exceeds bone resorption. In young adults, these processes are in balance, and in old age, resorption predominates. Despite the environmental factors (discussed earlier) that influence bone density, genetics still plays the major role in determining how much a person's bone density will change over a lifetime. A single gene that codes for vitamin D's cellular docking site helps determine both the tendency to accumulate bone mass during early life and a person's risk of osteoporosis later in life.

Beginning in the fourth decade of life, bone mass decreases with age. The only exception appears to be in bones of the skull. Among young adults, skeletal mass is generally greater in males than in females, and greater in blacks than in whites. Age-related bone loss is faster in whites than in blacks (who have greater bone density to begin with) and faster in females than in males. Qualitative changes also occur: More osteons remain incompletely formed, mineralization is less complete, and the amount of nonviable bone increases, reflecting a diminished blood supply to the bones in old age. These age-related changes are also bad news because fractures heal more slowly in old people. Daily ultrasound treatments are helpful in hastening repair of fractures, and electrical stimulation of fracture sites dramatically increases the speed of healing. (Presumably electrical fields inhibit PTH stimulation of osteoclasts and induce formation of growth factors that stimulate osteoblasts at the fracture site.)

#### CHECK YOUR UNDERSTANDING

26. What is the status of bone structure at birth?
27. The decrease in bone mass that begins in the fourth decade of life affects nearly all bones. What are the exceptions?

For answers, see Appendix G.

Skeletal cartilages and bones—their architecture, composition, and dynamic nature—have been examined in this chapter. We have also discussed the role of bones in maintaining overall body homeostasis, as summarized in *Making Connections*. Now we are ready to look at the individual bones of the skeleton and how they contribute to its functions, both collectively and individually.



## RELATED CLINICAL TERMS

**Achondroplasia** (a-kon''dro-pla'ze-ah; *a* = without; *chondro* = cartilage; *plasi* = mold, shape) A congenital condition involving defective cartilage and endochondral bone growth so that the limbs are too short but the membrane bones are of normal size; a type of dwarfism.

**Bony spur** Abnormal projection from a bone due to bony overgrowth; common in aging bones.

**Ostealgia** (os''te-al'je-ah; *algia* = pain) Pain in a bone.

**Osteitis** (os''te-i'tis; *itis* = inflammation) Inflammation of bony tissue.

**Osteogenesis imperfecta** Also called brittle bone disease, a disorder in which the bone matrix contains inadequate amounts of collagen, putting it at risk for shattering.

**Osteomyelitis** (os''te-o-mi''ē-l-i'tis) Inflammation of bone and bone marrow caused by pus-forming bacteria that enter the body via a wound (e.g., compound bone fracture), or spread from an infection near the bone. Commonly affects the long bones, causing acute pain and fever. May result in joint stiffness, bone destruction, and shortening of a limb. Treatment involves antibiotic

therapy, draining of any abscesses (local collections of pus) formed, and removal of dead bone fragments (which prevent healing).

**Osteosarcoma** (os''te-o-sar-ko'mah) A form of bone cancer typically arising in a long bone of a limb and most often in those 10–25 years of age. Grows aggressively, painfully eroding the bone; tends to metastasize to the lungs and cause secondary lung tumors. Usual treatment is amputation of the affected bone or limb, followed by chemotherapy and surgical removal of any metastases. Survival rate is about 50% if detected early.

**Pathologic fracture** Fracture in a diseased bone involving slight (coughing or a quick turn) or no physical trauma. For example, a hip bone weakened by osteoporosis may break and cause the person to fall, rather than breaking because of the fall.

**Traction** ("pulling") Placing sustained tension on a body region to keep the parts of a fractured bone in proper alignment; also prevents spasms of skeletal muscles, which would separate the fractured bone ends or crush the spinal cord in the case of vertebral column fractures.

## CHAPTER SUMMARY

**Skeletal Cartilages** (p. 173)**Basic Structure, Types, and Locations** (p. 173)

1. A skeletal cartilage exhibits chondrocytes housed in lacunae (cavities) within the extracellular matrix (ground substance and fibers). It contains large amounts of water (which accounts for its resilience), lacks nerve fibers, is avascular, and is surrounded by a fibrous perichondrium that resists expansion.
2. Hyaline cartilages appear glassy; the fibers are collagenic. They provide support with flexibility and resilience and are the most abundant skeletal cartilages, accounting for the articular, costal, respiratory, and nasal cartilages.
3. Elastic cartilages contain abundant elastic fibers, in addition to collagen fibers, and are more flexible than hyaline cartilages. They support the outer ear and epiglottis.
4. Fibrocartilages, which contain thick collagen fibers, are the most compressible cartilages and are resistant to stretch. They form intervertebral discs and knee joint cartilages.

**Growth of Cartilage** (p. 173)

5. Cartilages grow from within (interstitial growth) and by addition of new cartilage tissue at the periphery (appositional growth).

**Classification of Bones** (pp. 173–175)

1. Bones are classified as long, short, flat, or irregular on the basis of their shape and their proportion of compact or spongy bone.

**Functions of Bones** (pp. 175–176)

1. Bones give the body shape; protect and support body organs; provide levers for muscles to pull on; store calcium and other minerals; and are the site of blood cell production.

**Bone Structure** (pp. 176–182)**Gross Anatomy** (pp. 177–179)

1. Bone markings are important anatomical landmarks that reveal sites of muscle attachment, points of articulation, and sites of blood vessel and nerve passage.
2. A long bone is composed of a diaphysis (shaft) and epiphyses (ends). The medullary cavity of the diaphysis contains yellow marrow; the epiphyses contain spongy bone. The epiphyseal line is the remnant of the epiphyseal plate. Periosteum covers the diaphysis; endosteum lines inner bone cavities. Hyaline cartilage covers joint surfaces.
3. Flat bones consist of two thin plates of compact bone enclosing a diploë (spongy bone layer). Short and irregular bones resemble flat bones structurally.
4. In adults, hematopoietic tissue (red marrow) is found within the diploë of flat bones and occasionally within the epiphyses of long bones. In infants, red marrow is also found in the medullary cavity.

**Microscopic Anatomy of Bone** (pp. 179–180)

5. The structural unit of compact bone, the osteon, consists of a central canal surrounded by concentric lamellae of bone matrix. Osteocytes, embedded in lacunae, are connected to each other and the central canal by canaliculi.
6. Spongy bone has slender trabeculae containing irregular lamellae, which enclose red marrow-filled cavities.

**Chemical Composition of Bone** (pp. 180–182)

7. Bone is composed of living cells (osteogenic cells, osteoblasts, osteocytes, and osteoclasts) and matrix. The matrix includes osteoid, organic substances that are secreted by osteoblasts and give the bone tensile strength. Its inorganic components, the hydroxyapatites (calcium salts), make bone hard.



**Bone Development** (pp. 182–185)**Formation of the Bony Skeleton** (pp. 182–184)

1. Intramembranous ossification forms the clavicles and most skull bones. The ground substance of the bone matrix is deposited between collagen fibers within the fibrous membrane to form woven bone. Eventually, compact bone plates enclose the diploë.
2. Most bones are formed by endochondral ossification of a hyaline cartilage model. Osteoblasts beneath the periosteum secrete bone matrix on the cartilage model, forming the bone collar. Deterioration of the cartilage model internally opens up cavities, allowing periosteal bud entry. Bone matrix is deposited around the cartilage remnants but is later broken down.

**Postnatal Bone Growth** (pp. 184–185)

3. Long bones increase in length by interstitial growth of the epiphyseal plate cartilage and its replacement by bone.
4. Appositional growth increases bone diameter/thickness.

**Bone Homeostasis: Remodeling and Repair** (pp. 185–189)**Bone Remodeling** (pp. 185–188)

1. Bone is continually deposited and resorbed in response to hormonal and mechanical stimuli. Together these processes constitute bone remodeling.
2. An osteoid seam appears at areas of new bone deposit; calcium salts are deposited a few days later.
3. Osteoclasts release lysosomal enzymes and acids on bone surfaces to be resorbed. The dissolved products are transcytosed to the opposite face of the osteoclast for release to the extracellular fluid.
4. The hormonal controls of bone remodeling serve blood calcium homeostasis. When blood calcium levels decline, PTH is released

and stimulates osteoclasts to digest bone matrix, releasing ionic calcium. As blood calcium levels rise, PTH secretion declines.

5. Mechanical stress and gravity acting on the skeleton help maintain skeletal strength. Bones thicken, develop heavier prominences, or rearrange their trabeculae in sites where stressed.

**Bone Repair** (pp. 188–189)

6. Fractures are treated by open or closed reduction. The healing process involves formation of a hematoma, a fibrocartilaginous callus, a bony callus, and bone remodeling, in succession.

**Homeostatic Imbalances of Bone** (pp. 189–191, 194)

1. Imbalances between bone formation and resorption underlie all skeletal disorders.
2. Osteomalacia and rickets occur when bones are inadequately mineralized. The bones become soft and deformed. The most frequent cause is inadequate vitamin D.
3. Osteoporosis is any condition in which bone breakdown outpaces bone formation, causing bones to become weak and porous. Postmenopausal women are particularly susceptible.
4. Paget's disease is characterized by excessive and abnormal bone remodeling.

**Developmental Aspects of Bones: Timing of Events**

(p. 194)

1. Osteogenesis is predictable and precisely timed.
2. Longitudinal long bone growth continues until the end of adolescence. Skeletal mass increases dramatically during puberty and adolescence, when formation exceeds resorption.
3. Bone mass is fairly constant in young adulthood, but beginning in the 40s, bone resorption exceeds formation.

**REVIEW QUESTIONS****Multiple Choice/Matching**

(Some questions have more than one correct answer. Select the best answer or answers from the choices given.)

1. Which is a function of the skeletal system? (a) support, (b) hematopoietic site, (c) storage, (d) providing levers for muscle activity, (e) all of these.
2. A bone with approximately the same width, length, and height is most likely (a) a long bone, (b) a short bone, (c) a flat bone, (d) an irregular bone.
3. The shaft of a long bone is properly called the (a) epiphysis, (b) periosteum, (c) diaphysis, (d) compact bone.
4. Sites of hematopoiesis include all but (a) red marrow cavities of spongy bone, (b) the diploë of flat bones, (c) medullary cavities in bones of infants, (d) medullary cavities in bones of a healthy adult.
5. An osteon has (a) a central canal carrying blood vessels, (b) concentric lamellae, (c) osteocytes in lacunae, (d) canaliculi that connect lacunae to the central canal, (e) all of these.
6. The organic portion of matrix is important in providing all but (a) tensile strength, (b) hardness, (c) ability to resist stretch, (d) flexibility.
7. The flat bones of the skull develop from (a) areolar tissue, (b) hyaline cartilage, (c) fibrous connective tissue, (d) compact bone.
8. The remodeling of bone is a function of which cells? (a) chondrocytes and osteocytes, (b) osteoblasts and osteoclasts, (c) chondroblasts and osteoclasts, (d) osteoblasts and osteocytes.
9. Bone remodeling in adults is regulated and directed mainly by (a) growth hormone, (b) thyroid hormones, (c) sex hormones, (d) mechanical stress, (e) PTH.
10. Where within the epiphyseal plate are the dividing cartilage cells located? (a) nearest the shaft, (b) in the marrow cavity, (c) farthest from the shaft, (d) in the primary ossification center.
11. Wolff's law is concerned with (a) calcium homeostasis of the blood, (b) the thickness and shape of a bone being determined by mechanical and gravitational stresses placed on it, (c) the electrical charge on bone surfaces.
12. Formation of the bony callus in fracture repair is followed by (a) hematoma formation, (b) fibrocartilaginous callus formation, (c) bone remodeling to convert woven bone to compact bone, (d) formation of granulation tissue.
13. The fracture type in which the bone ends are incompletely separated is (a) greenstick, (b) compound, (c) simple, (d) comminuted, (e) compression.
14. The disorder in which bones are porous and thin but bone composition is normal is (a) osteomalacia, (b) osteoporosis, (c) Paget's disease.
15. Compare bone to cartilage tissue relative to its resilience, speed of regeneration, and access to nutrients.
16. Describe in proper order the events of endochondral ossification.

**Short Answer Essay Questions**