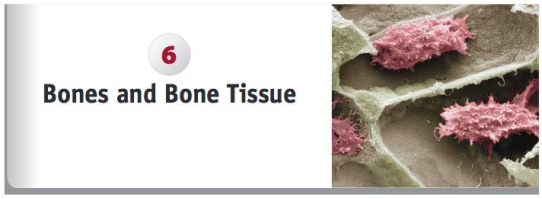

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MODULE 6.1: INTRODUCTION TO BONES AS ORGANS

SKELETAL SYSTEM

- **Skeletal system** includes:
  - Bones, joints, and their associated supporting tissues
  - **Bones** are main organs of this system:
    - Like any organ, they are composed of more than osseous tissue
    - Also composed of both *dense regular* and *irregular collagenous connective tissue* as well as **bone marrow**

FUNCTIONS OF THE SKELETAL SYSTEM

- **Functions of skeletal system** include:

1. **Protection**: certain bones, including skull, sternum (breastbone), ribs, and pelvis, *protect underlying organs*; example of **Structure-Function Core Principle**

Figure 6.1 Functions of the skeletal system.

FUNCTIONS OF THE SKELETAL SYSTEM

- **Functions of skeletal system** (continued):

2. **Mineral storage and acid-base homeostasis**: bone is most important storehouse in body for *calcium*, *phosphorus*, and *magnesium salts*; these minerals, also present in blood as electrolytes, acids, and bases; critical for electrolyte and acid-base maintenance

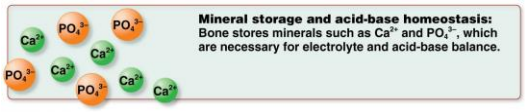


Figure 6.1 Functions of the skeletal system.

FUNCTIONS OF THE SKELETAL SYSTEM

- **Functions of skeletal system** (continued):

3. **Blood cell formation**: bones house **red bone marrow**; specialized connective tissue involved in *formation of blood cells* (**hematopoiesis**)

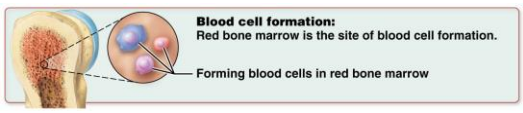


Figure 6.1 Functions of the skeletal system.

FUNCTIONS OF THE SKELETAL SYSTEM

- **Functions of skeletal system** (continued):

4. **Fat storage**: bones also contain **yellow bone marrow**; contains fat cells, or adipocytes, that *store triglycerides*; fatty acids from breakdown of triglycerides can be used for fuel by cells

Figure 6.1 Functions of the skeletal system.

FUNCTIONS OF THE SKELETAL SYSTEM

- **Functions of skeletal system** (continued):

5. **Movement**: bones serve as sites for *attachment for most skeletal muscles*; when muscles contract, they pull on bones; generates movement at a joint

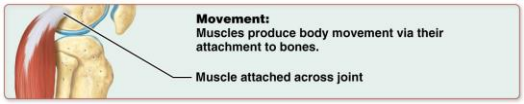


Figure 6.1 Functions of the skeletal system.

FUNCTIONS OF THE SKELETAL SYSTEM

- **Functions of skeletal system** (continued):

6. **Support**: skeleton *supports weight of body* and provides its *structural framework*

Figure 6.1 Functions of the skeletal system.

FUNCTIONS OF THE SKELETAL SYSTEM

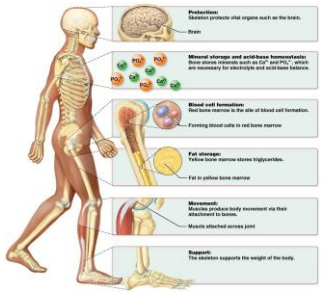


Figure 6.1 Functions of the skeletal system.

BONE STRUCTURE

- **Bone structure** can be organized into **5** classes despite diversity of bone appearance; all 206 bones fit into one of following categories based on shape (**Figure 6.2**):
  - **Long bones** – named for *overall shape*; not their actual size; longer than they are wide; include most bones in *arms* and *legs*

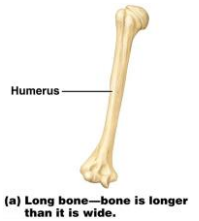


Figure 6.2a Classification of bones by shape.

BONE STRUCTURE

- **Bone categories** based on shape (**Figure 6.2**):
  - **Short bones** – also named for shape rather than size; roughly *cube-shaped* or about as long as they are wide; include bones of *wrist* or **carpals** and *ankle* or **tarsals** (**Figure 6.2b**)

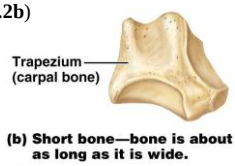


Figure 6.2b Classification of bones by shape.

BONE STRUCTURE

- **Bone categories** based on shape (continued):
  - **Flat bones** – *thin and broad bones*; include *ribs*, *pelvis*, *sternum* (breastbone), and most bones in *skull*

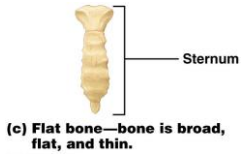


Figure 6.2c Classification of bones by shape.

BONE STRUCTURE

- **Bone categories** based on shape (continued):
  - **Irregular bones** – include *vertebrae* and certain *skull* bones; do not fit into other classes because of *irregular shapes*

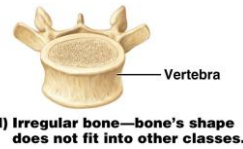


Figure 6.2d Classification of bones by shape.

BONE STRUCTURE

- **Bone categories** based on shape (continued):
  - **Sesamoid bones** – specialized bones located within *tendons*; usually small, flat, and oval-shaped; give tendons a *mechanical advantage*, which gives muscles better leverage; **patella** (kneecap) is an example of this class of bones

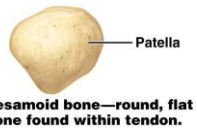


Figure 6.2e Classification of bones by shape.

BONE STRUCTURE

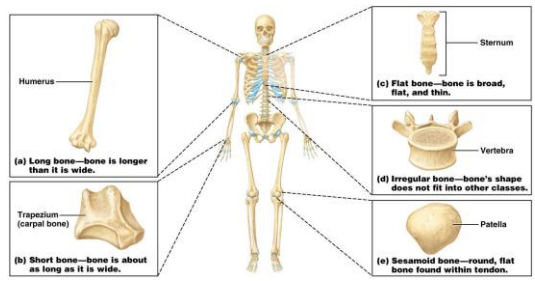


Figure 6.2 Classification of bones by shape.

BONE STRUCTURE

- **Structure of a long bone**:
  - **Periosteum** – membrane composed of *dense irregular collagenous connective tissue*; forms a covering, rich with blood vessels and nerves; surrounds outer surface of long bones
  - **Perforating fibers** (**Sharpey's fibers**) – made of collagen; *anchors periosteum* firmly to underlying bone surface by penetrating deep into bone matrix

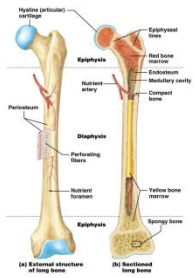


Figure 6.3 Structure of long bones.

BONE STRUCTURE

- **Structure of a long bone** (continued):
  - **Diaphysis** – *shaft of a long bone*; each end is its **epiphyses**; epiphysis is covered with a thin layer of *hyaline cartilage* (**articular cartilage**) found within joints (**articulations**) between bones
  - Within diaphysis is a *hollow cavity* known as **marrow cavity**; contains either **red** or **yellow bone marrow**, depending on bone and age of individual

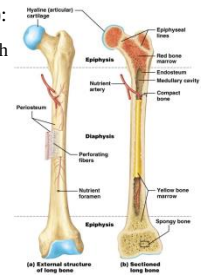


Figure 6.3 Structure of long bones.

BONE STRUCTURE

- **Structure of a long bone** (continued):
  - **Compact bone** – one of two *bone textures*; hard, dense outer region that allows bone to resist **linear compression** and **twisting forces** among other stresses
  - **Spongy bone** (**cancellous** bone) – second bone texture found inside cortical bone; *honeycomb-like framework* of bony struts; allows long bones to resist forces from many directions; provides a *cavity* for bone marrow

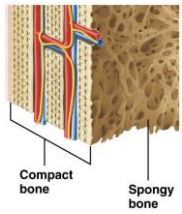


Figure 6.9 Structure of compact bone.

BONE STRUCTURE

- **Structure of a long bone** (continued):
  - *Bony struts* of spongy bone and all *inner surfaces* of bone are covered by a thin membrane called **endosteum**; contains different populations of bone cells involved in maintenance of *bone homeostasis*
  - **Epiphyseal lines** – found *separating* both proximal and distal epiphyses from diaphysis; remnants of **epiphyseal plates** (**growth plates**), a line of hyaline cartilage found in developing bones of children

BONE STRUCTURE

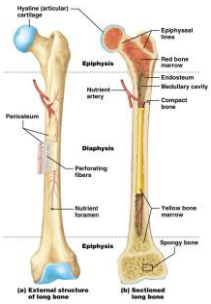


Figure 6.3 Structure of long bones.

BONE STRUCTURE

- **Structure of short**, **flat**, **irregular**, and **sesamoid bones**: these bones do not have diaphyses, epiphyses, medullary cavities, epiphyseal lines, or epiphyseal plates (**Figure 6.4**):
  - Covered by *periosteum*, with associated perforating fibers, blood vessels, and nerves, like long bones
  - Internal structure is composed of two *outer layers of thin compact bone* with a middle layer of *spongy bone*, called **diploë**, and its associated bone marrow
  - Some flat and irregular bones of skull contain hollow, air-filled spaces called **sinuses**, which *reduce bone weight*

BONE STRUCTURE

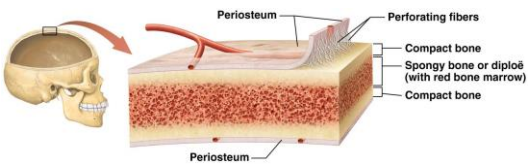


Figure 6.4 Structure of short, flat, irregular, and sesamoid bones.

BONE STRUCTURE

- **Blood and nerve supply to bone** – bones are well supplied with *blood vessels* and *sensory nerve fibers*:
  - Blood supply to short, flat, irregular, and sesamoid bones is provided mostly by vessels in *periosteum* that penetrate bone
  - Long bones get a *third* of their blood supply from periosteum; mostly supplies compact bone

Bone Structure

- **Blood and nerve supply to bone** (continued):
  - Remaining two-thirds is supplied by one or two **nutrient arteries**; enter bone through a small hole in diaphysis called **nutrient foramen**
  - Nutrient arteries *bypass* compact bone to *supply internal structures* of bone
  - Epiphyses receive some blood supply from nutrient arteries; majority comes from small blood vessels that enter and exit through small holes in their compact bone

Bone Structure

- **Red bone marrow** – consists of loose connective tissue that supports islands of *blood-forming hematopoietic cells*
  - *Amount* of red marrow decreases as a person ages
  - Red marrow in *adult* is found only in pelvis, proximal femur and humerus, vertebrae, ribs, sternum, clavicles, scapulae, and some bones of skull
  - Children need more red marrow to assist in their growth and development

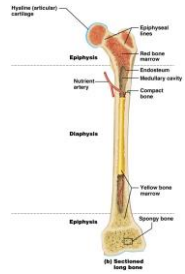


Figure 6.3b Structure of long bones.

Bone Structure

- **Yellow bone marrow** – composed of triglycerides, blood vessels, and adipocytes

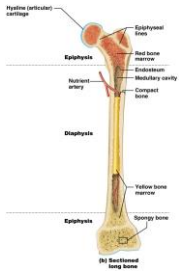


Figure 6.3b Structure of long bones.

Bone Marrow Transplantation

- Diseases of blood (leukemia, sickle-cell anemia, aplastic anemia) have *improperly functioning hematopoietic cells*; can therefore benefit from **bone marrow transplantation**
- Needle is inserted into pelvic bone of matching donor and *red marrow is withdrawn*; repeated until up to 2 quarts (about 2% of total) is removed
- Recipient's marrow is *destroyed* and donor marrow is given intravenously; cells travel to recipient's marrow cavities; *produce new blood cells* in 2–4 weeks if successful
- **Complications** – flu-like symptoms (first 2–4 weeks), *infection* or *transplant rejection*
- Many recipients can return to a healthy life if transplant "takes"

Module 6.2: Microscopic Structure of Bone Tissue

Microscopic Structure

- **Bone** or **osseous tissue** – primary tissue found in bone; composed mostly of *extracellular matrix* with a *small population of cells* scattered throughout
- **Extracellular matrix of bone** is *unique*:
  - **Inorganic matrix** – consisting of *minerals* makes up about 65% of bones total weight
  - **Organic matrix** – makes up remaining 35%; consists of collagen fibers and *usual ECM components* (**Figure 6.5**)

EXTRACELLULAR MATRIX

- **Inorganic matrix** – made up predominantly of *calcium salts*; bone stores around *85% of total calcium ions* in body as well as a large amount of *phosphorus*:
  - Calcium and phosphorus salts exist as large molecules of a mineral called **hydroxyapatite crystals** [$Ca_{10}(PO_4)_6(OH)_2$]
  - *Crystalline structure* makes bone one of *hardest substances in body*; makes it strong and resistant to compression
  - Allows bone to be both *protective* and *supportive*; demonstrates **Structure-Function Core Principle**
  - *Bicarbonate*, *potassium*, *magnesium*, and *sodium* are also found in inorganic matrix

EXTRACELLULAR MATRIX

- **Organic matrix** – known as **osteoid**; consists of *protein fibers*, *proteoglycans*, *glycosaminoglycans*, *glycoproteins*, and *bone-specific proteins*
  - **Collagen** – predominant protein fiber; forms *cross-links* with one another; helps bone *resist torsion* (twisting) and *tensile* (pulling or stretching) *forces*
  - Collagen fibers also *align themselves* with hydroxyapatite crystals; enhances hardness of bone

EXTRACELLULAR MATRIX

- **Osteoid** (continued):
  - Glycosaminoglycans and proteoglycans create an *osmotic gradient* that draws water into osteoid; helps tissue resist *compression*
  - Glycoproteins in osteoid *bind* all of different components of osteoid and inorganic matrix together

EXTRACELLULAR MATRIX

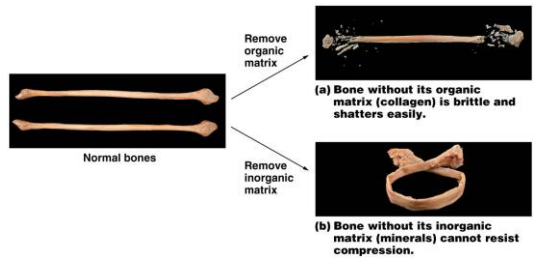


Figure 6.5 The importance of bone matrices.

BONE CELLS

- Bone is a *dynamic tissue*; continually changing as older bone is *broken down* for raw materials to *build new bone*; three types of **bone cells** are responsible for bone's dynamic nature (**Figures 6.6**, **6.7**, **6.8**):
  - **Osteoblasts**
  - **Osteocytes**
  - **Osteoclasts**

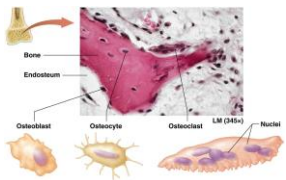


Figure 6.6 Types of bone cells.

BONE CELLS

- **Osteoblasts** – metabolically active bone cells found in periosteum and endosteum:
  - **Osteogenic cells** – flattened cells that differentiate into osteoblasts when stimulated by specific chemical signals
  - Osteoblasts are bone-building cells that perform *bone deposition*
  - **Bone deposition** – process where osteoblasts secrete organic matrix materials and assist in formation of inorganic matrix

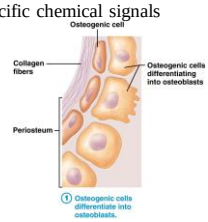


Figure 6.7.1 Functions of osteoblasts and osteocytes.

BONE CELLS

- **Osteocytes**
  - Osteoblasts eventually *surround themselves* with bone matrix in a small cavity known as a **lacuna**; become **osteocytes** that are no longer *actively synthesizing bone matrix*

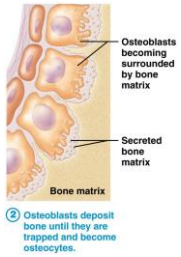


Figure 6.7.2 Functions of osteoblasts and osteocytes.

BONE CELLS

- **Osteocytes** (continued)
  - No longer as <u>metabolically active</u> except for local need for *maintaining bone extracellular matrix* (**Figure 6.7.3**)
  - Appear to have ability to *recruit osteoblasts* to build up or *reinforce bone* under tension

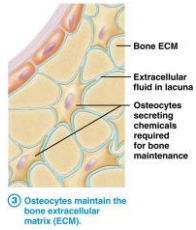


Figure 6.7.3 Functions of osteoblasts and osteocytes.

BONE CELLS

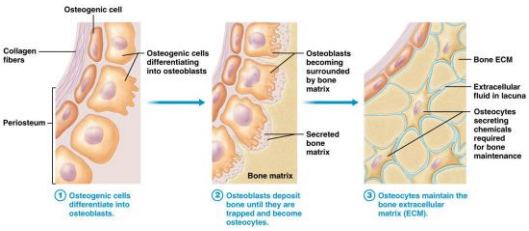


Figure 6.7 Functions of osteoblasts and osteocytes.

BONE CELLS

- **Osteoclasts**
  - Responsible for *bone resorption*; process where cell secretes **hydrogen ions** and **enzymes** that *break down bone matrix*
  - Have a completely different overall cell structure than other two cell types; *large multinucleated cells*; resemble jellyfish; derived from *fusion of cells* from bone marrow (**Figure 6.8**)
  - Eventually located in *shallow depressions* on internal and external surfaces of bone

BONE CELLS

- **Osteoclasts** (continued)
  - **Hydrogen ions** dissolve components of *inorganic matrix*; **enzymes** break down *organic matrix*
  - Liberated substances from breakdown of bone include nutrients, minerals, amino acids, and sugars; *absorbed* by various transport methods into *osteoclast cytosol*
  - Substances can be *released into blood* where they might be *reused* or *excreted* from the body as waste products

BONE CELLS

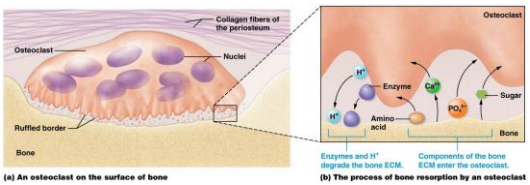


Figure 6.8 Functions of osteoclasts.

HISTOLOGY OF BONE

- **Histology of bone tissue** is quite <u>different</u> between *hard* outermost compact bone and *porous* inner spongy bone (**Figures 6.9**, **6.10**)
- Both gross and histological differences can be attributed to *different functions* each region performs; **Structure-Function Core Principle**

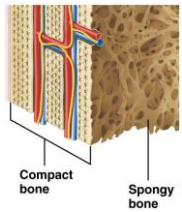


Figure 6.9 Structure of compact bone.

HISTOLOGY OF BONE

- **Structure** of **compact bone** is continuously subjected to a great deal of *stress*; tends to *strain or deform objects* like bone; must be able to withstand these forces or suffer damage:
  - Compact bone, in cross section, resembles *forest of tightly packed trees* where each tree is a unit called an **osteon** or a Haversian system
  - Rings of each tree are made up of *thin layers of bone* called **lamellae**

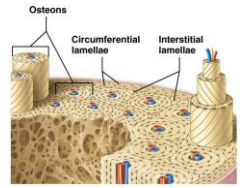


Figure 6.9 Structure of compact bone.

HISTOLOGY OF BONE

- **Osteon structure** consists of following components:
  - Each osteon contains between 4 and 20 **lamellae** arranged in layered ring structures also known as **concentric lamellae**
  - Lamellar arrangement is very *stress resistant*
  - Collagen fibers of neighboring lamellae run in *opposite directions*; resist twisting and bending forces placed on bone from a variety of directions

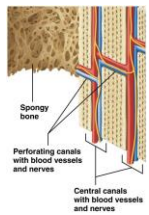


Figure 6.9 Structure of compact bone.

HISTOLOGY OF BONE

- **Osteon structure** (continued):
  - **Central canal** – *endosteum-lined hole* found in center of each osteon where blood vessels and nerves reside to supply bone
  - Osteocytes reside in **lacunae** – *small cavities* found between lamellae; filled with *extracellular fluid*

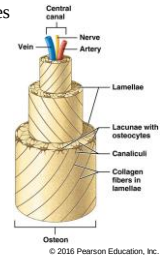


Figure 6.9 Structure of compact bone.

HISTOLOGY OF BONE

- **Osteon structure** (continued):
  - Neighboring lacunae are *connected to one another* by a network of small passageways or canals in matrix called **canaliculi**; *cytoplasmic extensions* of osteocytes extend through these networks allowing neighboring cells to *share resources* and *communicate* with one another

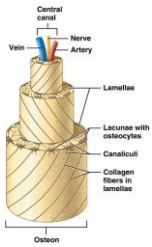


Figure 6.9 Structure of compact bone.

HISTOLOGY OF BONE

- **Overall compact bone structure**:
  - Osteons *are <u>not</u> permanent structures*; osteoclasts break down and osteoblasts rebuild bone matrix depending on needs of bone or body; process leaves behind *characteristic features* in compact bone:
    - **Interstitial lamellae** – found filling the spaces <u>between</u> circular osteons and represent *remnants* of old osteons

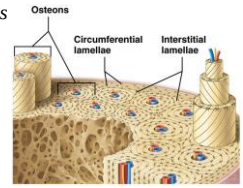


Figure 6.9 Structure of compact bone.

HISTOLOGY OF BONE

- **Overall compact bone structure** (continued):
  - **Circumferential lamellae** – outer and inner layers of lamellae *just inside periosteum* and at *boundary with spongy bone*; add strength to bone
  - **Perforating canals** (**Volkmann's canals**) originate from blood vessels in periosteum and travel at *right angles* (*perpendicular*) *to central canals* of neighboring osteons; serve to *connect them* with one another

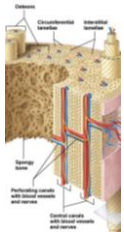


Figure 6.9 Structure of compact bone.

HISTOLOGY OF BONE

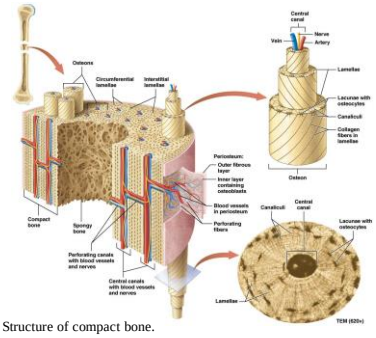


Figure 6.9 Structure of compact bone.

HISTOLOGY OF BONE

- **Structure of spongy bone**:
  - Spongy bone – usually <u>not</u> *weight-bearing* like compact bone so is much <u>less</u> *densely packed*
  - Network of struts reinforce strength of compact bone by resisting forces from a *variety of directions*
  - Provide a *protective structure* for bone marrow tissue

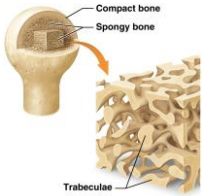


Figure 6.10 Structure of spongy bone.

HISTOLOGY OF BONE

- **Structure of spongy bone** (continued):
  - Struts or ribs of bone are called **trabeculae**; covered with endosteum and usually *not arranged into osteons*
  - **Trabeculae** – composed of *concentric lamellae* between which lacunae are found containing osteocytes; communicate with each other through canaliculi
  - <u>No</u> central or perforating canals supplying blood to trabeculae; obtain their blood supply from *vessels in bone marrow*

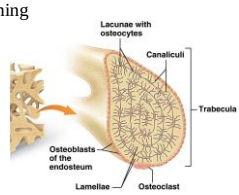


Figure 6.10 Structure of spongy bone.

HISTOLOGY OF BONE

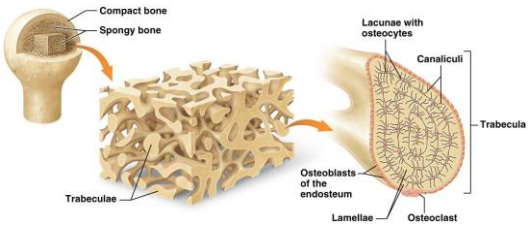


Figure 6.10 Structure of spongy bone.

OSTEOPETROSIS

- Primary defect in **osteopetrosis** ("marble bone disease") is *defective osteoclasts*; do not properly degrade bone; causes *bone mass* to *increase* and become weak and brittle
- Main forms:
  - **Infantile** – predominately inherited, more severe form; openings of skull and marrow cavities *fail to enlarge* with growth; traps nerves causing *blindness* and *deafness* and <u>decreases</u> *blood* cell *production*; can be fatal; must be treated with drugs to stimulate osteoclasts and red marrow
  - **Adult** – also inherited; develops during *adolescence or later*; symptoms: *bone pain*, *recurrent fractures*, *nerve trapping*, *joint pain*; treated symptomatically only

6.3: Bone Formation: Ossification

Ossification

- Process of bone formation is called **ossification** or **osteogenesis**; begins in embryonic period and continues through childhood with most bones completing the process by age 7:
  - Can proceed by two different mechanisms but both have *similar features* including:
    - First bone formed is *immature primary* or *woven bone*; consists of irregularly arranged collagen bundles, osteocytes, and sparse inorganic matrix
    - Usually primary bone is broken down by osteoclasts and replaced with *mature secondary* or *lamellar bone*; has more inorganic matrix and increased strength

Ossification

- **Ossification** or **osteogenesis** (continued):
  - Bones formed by **intramembranous ossification** are built on a model (starting material) made of a *membrane of embryonic connective* tissue
  - Bones formed by **endochondral ossification** are built on a model of *hyaline cartilage*

Intramembranous Ossification

- **Intramembranous ossification** – forms many flat bones, including bones of skull and clavicles, during fetal development (**Figure 6.11**):
  - Primary bone – formed within a *mesenchymal membrane* composed of embryonic connective tissue; richly supplied with blood and populated with mesenchymal cells
  - Recall that *flat bone structure* essentially is two outer layers of compact bone with an inner or middle layer of spongy bone
  - Middle layer of spongy bone ossifies before outer compact bone layers; begins from region called **primary ossification center**

Intramembranous Ossification

- **Intramembranous ossification** (continued):
  - Begins at primary ossification center and proceeds through *following steps* (**Figure 6.11**):
    - Mesenchymal cells differentiate into **osteogenic cells** then **osteoblasts** at primary ossification site
    - Osteoblasts secrete *organic matrix* of bone; calcium salts and other inorganic matrix components are *deposited in trabeculae* over a few days (process called **calcification**); *hardens* primary bone; osteoblasts get trapped in lacunae and become **osteocytes**

Intramembranous Ossification

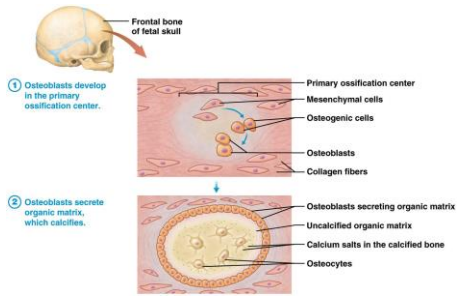


Figure 6.11 The process of intramembranous ossification.

INTRAMEMBRANOUS OSSIFICATION

- **Intramembranous ossification** (continued):
  - Early spongy bone is formed as osteoblasts continue to lay down new bone to form trabeculae; smaller trabeculae can *merge* forming larger structures
  - Some mesenchymal cells differentiate and *form periosteum*; some of vascular tissue in early spongy bone will *become bone marrow*
  - Spongy bone *deep to periosteum* becomes *heavily calcified* and its structure is rearranged to form immature compact bone

INTRAMEMBRANOUS OSSIFICATION

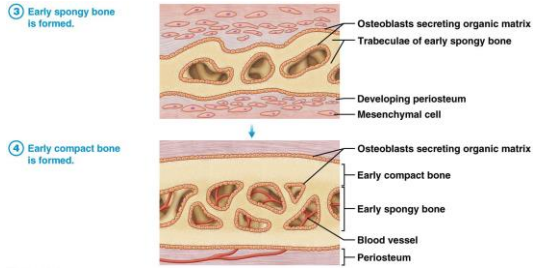


Figure 6.11 The process of intramembranous ossification.

INTRAMEMBRANOUS OSSIFICATION

- **Intramembranous ossification** (continued):
  - Larger bones have more *than one* primary ossification center
  - Leads to pieces of bone that must *fuse to one another* over time
  - An example of early incomplete ossification is **fontanels** (soft spots) in *skulls of newborn babies*

ENDOCHONDRAL OSSIFICATION

- **Endochondral ossification** (**Figure 6.12**):
  - Bone development for all bones below head except *clavicles*
  - Begins in *fetal stage* of development for most bones; some bones (wrist and ankle) ossify *much later*
  - Many bones *complete ossification* by age 7

ENDOCHONDRAL OSSIFICATION

- Endochondral ossification occurs from within a model of *hyaline cartilage*; serves as a scaffold for developing bone:
  - Hyaline cartilage model is composed of *chondrocytes, collagen, and ECM* all surrounded by a connective tissue membrane called **perichondrium** and immature cartilage cells called **chondroblasts**
  - Begins at a *primary ossification center* where primary bone is first synthesized; then replaced with secondary bone
  - Long bones have *secondary ossification centers* found in their epiphyses; ossify by a similar pattern

ENDOCHONDRAL OSSIFICATION

- Once cartilage model is completed, endochondral ossifications occur in following steps (**Figure 6.12**):
  - Chondroblasts in perichondrium differentiate first into osteogenic cells then osteoblasts and periosteum is formed
  - Bone begins to form where osteoblasts have built a **bone collar** on *external surface of bone*
  - At same time bone collar forms, *internal cartilage begins to calcify* and *chondrocytes die off* as their connection to blood supply is severed; calcified cartilage and tiny cavities are left behind

Endochondral Ossification

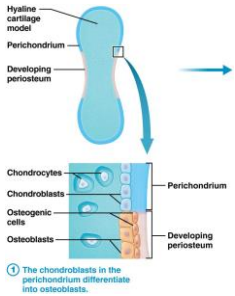


Figure 6.12 The process of endochondral ossification.

Endochondral Ossification

- Endochondral ossification steps (continued):
  - In primary ossification center, osteoblasts replace calcified cartilage with early spongy bone; *secondary ossification* centers and *medullary cavity* begin development
  - As medullary cavity enlarges, *remaining cartilage is replaced by bone*; epiphyses finish ossifying

Endochondral Ossification

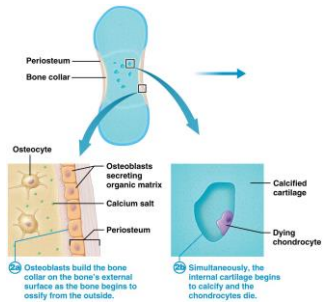


Figure 6.12 The process of endochondral ossification.

Endochondral Ossification

- Endochondral ossification steps (continued):
  - Medullary cavity is *filled with bone marrow*
  - Cartilage only *persists in two places*; epiphyseal plates and articular surfaces where bones interact at a joint (called **articular cartilage**)
  - Articular cartilage *persists into adulthood* while epiphyseal plates are *eventually filled in*, once bone is finished growing in length

Endochondral Ossification

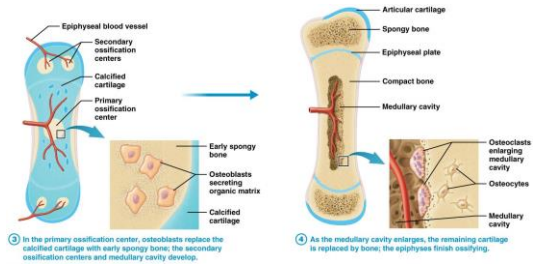
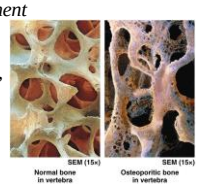


Figure 6.12 The process of endochondral ossification.

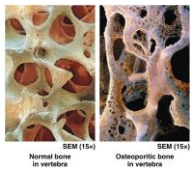
Osteoporosis and Healthy Bones

- Most common bone disease in United States; bones become weak and brittle due to inadequate inorganic matrix; increases risk of fractures with decreased rate of healing
- Diagnosed by *bone density measurement*
- **Causes** – *dietary* (calcium and/or vitamin D deficiency), *female* gender, advanced age, lack of *exercise*, hormonal (lack of *estrogen* in postmenopausal women), genetic factors, and other diseases



Osteoporosis and Healthy Bones

- **Prevention** – balanced diet, with supplementation as needed, weight-bearing exercise, and estrogen replacement if appropriate
- **Treatment** – drugs that *inhibit osteoclasts* or *stimulate osteoblasts*



Module 6.4: Bone Growth in Length and Width

Growth in Length

- Long bones lengthen by a process called **longitudinal growth**; involves division of chondrocytes (not osteocytes or osteoblasts) in epiphyseal plate
- Bone growth takes place at epiphysis on side *closest to diaphysis* (**Figure 6.13**)

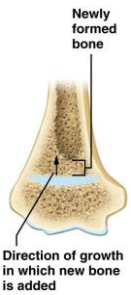


Figure 6.14 Growth at the epiphyseal plate.

Growth in Length

- **Epiphyseal plate**, composed of hyaline cartilage that did not ossify *zones of cells*, each with a distinctive appearance:
  - **Zone of reserve cartilage** – (found closest to epiphysis) contains cells that are <u>not</u> directly involved in bone growth but *can be recruited* for cell division if need arises
  - **Zone of proliferation** (next region) consists of *actively dividing chondrocytes* by endochondral ossification, contains *five different* lacunae

Growth in Length

- **Epiphyseal plate zones** (continued):
  - **Zone of hypertrophy and maturation** (next region closer to diaphysis) contains *mature chondrocytes*
  - **Zone of calcification** (second to last region) contains dead chondrocytes, some of which have been calcified
  - **Zone of ossification** (last region) consists of *calcified chondrocytes and osteoblasts*

Growth in Length

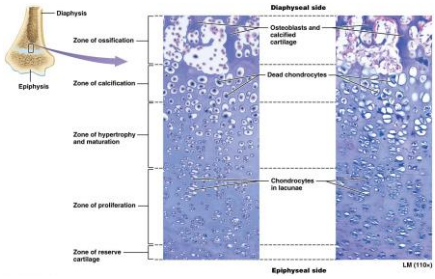


Figure 6.13 Structure of the epiphyseal plate.

GROWTH IN LENGTH

- Each zone of epiphyseal plate, except zone of reserve cartilage, is *actively involved in longitudinal growth*; proceeds in following sequence of events (**Figure 6.14**):
  - *Chondrocytes divide* in zone of proliferation forcing cells ahead of them into next zones, moving toward diaphysis
  - Chondrocytes that reach zone of hypertrophy and maturation *enlarge and stop dividing*

GROWTH IN LENGTH

- Process of longitudinal growth (continued):
  - Chondrocytes that reach zone of calcification *die and their matrix calcifies*
  - *Calcified cartilage is replaced with bone* in zone of ossification; osteoblasts invade calcified cartilage and begin to lay down bone
  - Eventually calcified cartilage and primary bone is resorbed by osteoclasts and completely *replaced with mature bone*

GROWTH IN LENGTH

- Longitudinal growth continues at epiphyseal plate as long as *mitosis continues* in zone of proliferation:
  - Mitotic rate slows around ages of 12–15 years old while *ossification continues*; causes epiphyseal plates to *shrink* as zone of proliferation is *overtaken* by zone of calcification and ossification
  - Between ages of 18–21, zone of proliferation is *completely ossified*, longitudinal growth stops, and epiphyseal plate is considered **closed**
  - **Epiphyseal line** is a *calcified remnant* of epiphyseal plate

GROWTH IN LENGTH

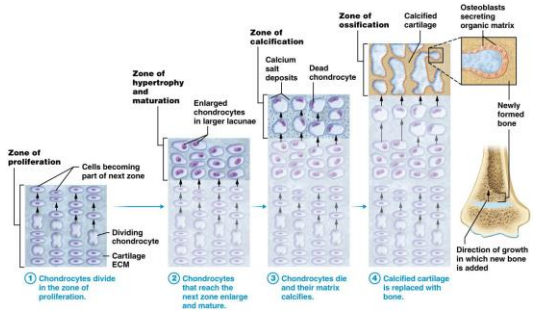


Figure 6.14 Growth at the epiphyseal plate.

GROWTH IN WIDTH

- Bones not only grow in length, they also grow in width; process called **appositional growth**
  - Osteoblasts, found in between periosteum and bone surface, *lay down new bone*
  - Appositional growth does not result in immediate formation of osteons; instead, *new circumferential lamellae* are formed

GROWTH IN WIDTH

- **Appositional growth** (continued):
  - As new lamellae are added, older deeper circumferential lamellae are either *removed or restructured into osteons*
  - Bones may *continue to increase in width* even after epiphyseal plates have *closed* and bone is no longer *lengthening*

Achondroplasia

- Most common cause of **dwarfism**; gene defect *inherited* from a parent or caused by *new mutation*
- Defective gene produces an *abnormal growth factor receptor* on cartilage; interferes with hyaline cartilage model used in endochondral ossification; also articular and epiphyseal cartilage
- Bones form and grow abnormally; results in *short limbs*, a disproportionately long trunk and *facial abnormalities*
- Long-term problems include joint disorders, respiratory difficulties, and spinal cord compression; may be managed with medications

Role of Hormones in Bone Growth

- Multiple factors play a role in *how much cell division* occurs in epiphyseal plate and *how long process remains active*:
  - One of *main factors* affecting bone growth is a group of chemicals called **hormones**
  - Hormones are *secreted* by cells of **endocrine glands**; example of **Cell-Cell Communication Core Principle**

Role of Hormones in Bone Growth

- **Growth hormone** – secreted by *anterior pituitary gland*; enhances protein synthesis and cell division in nearly all tissues, including bone
- Has following effects on both *longitudinal and appositional growth*:
  - It increases *rate of cell division of chondrocytes* in epiphyseal plate
  - It increases *activity of the osteogenic cells*, including their activity in zone of ossification
  - It *directly stimulates osteoblasts* in periosteum; triggers appositional growth

Role of Hormones in Bone Growth

- Male sex hormone **testosterone** has a pronounced effect on bone growth:
  - Increases appositional growth causing bones in males to *become thicker* with more calcium salt deposition than in females
  - Increases *rate of mitosis in epiphyseal plate*; leads to "growth spurts" in teenage years
  - *Accelerates closure* of epiphyseal plate

Role of Hormones in Bone Growth

- Female sex hormone **estrogen** also plays a role in bone growth:
  - Increases *rate of longitudinal bone growth* and inhibits *osteoclast activity*
  - When estrogen levels spike in teen years an accompanying "growth spurt" occurs in females
  - Accelerates closure of epiphyseal plate at a much *faster rate than testosterone*; leads to *average height differences* between genders

Gigantism and Acromegaly

- *Excess growth* hormone can produce two conditions, depending on when in life it develops; both generally caused by a *tumor* that secretes hormone; treated by tumor removal
- **Childhood** – condition is **gigantism**; epiphyseal growth plates have yet to close; individuals get *very tall* due to excessive longitudinal and appositional bone growth
- **Adulthood** – condition is **acromegaly**; epiphyseal growth plates have closed; no increase in height, but enlargement of bone, cartilage, and soft tissue
  - Skull, bones of face, hands, feet, and tongue affected
  - Can cause heart and kidney malfunction; associated with development of diabetes

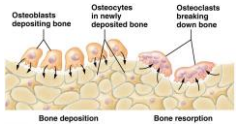
MODULE 6.5: BONE REMODELING AND REPAIR

BONE REMODELING

- Once bone has finished growing in length it is far from inactive; undergoes a continuous process of formation and loss called **bone remodeling**; new bone is formed by **bone deposition** and old bone is removed by **bone resorption**; cycle occurs for following reasons:
  - Maintenance of *calcium ion homeostasis*
  - *Replacement* of primary bone with secondary bone
  - Bone *repair*
  - *Replacement* of old brittle bone with newer bone
  - *Adaptation* to tension and stress

BONE REMODELING

- **Bone remodeling** (**Figures 6.15**, **6.16**):
  - In healthy bone of adults, process of formation and loss *occur simultaneously*; bone *breakdown* by osteoclasts matches bone *formation* by osteoblasts
  - In childhood deposition proceeds at a *much faster rate* than resorption; once epiphyseal plates close and longitudinal growth is complete, deposition and resorption become *roughly equivalent*



BONE REMODELING

- **Bone deposition**:
  - Carried out by **osteoblasts**
    - Found in both *periosteum* and *endosteum*; make organic matrix and facilitate formation of inorganic matrix
    - Secrete proteoglycans and glycoproteins that *bind to calcium ions*
    - Secrete vesicles containing *calcium ions*, *ATP*, and *enzymes*; bind to collagen fibers; calcium ions eventually crystallize, rupturing vesicle and *beginning calcification process*

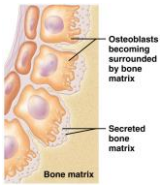


Figure 6.7 Functions of osteoblasts and osteocytes.

BONE REMODELING

- **Bone resorption**:
  - Osteoclasts secrete **hydrogen ions** on bone ECM
    - Hydroxyapatite crystals in inorganic matrix are pH-sensitive; *break down in acidic environment* created by osteoclasts
    - Calcium ions and other liberated minerals can be *reused elsewhere* in body

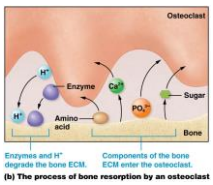


Figure 6.8 Functions of osteoclasts.

BONE REMODELING

- **Bone resorption** (continued):
  - Osteoclasts secrete enzymes
    - *Degrade organic matrix*, including: proteoglycans, glycosaminoglycans, and glycoproteins
    - Breakdown products of these molecules are *taken up by osteoclast* for recycling

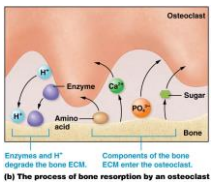


Figure 6.8 Functions of osteoclasts.

BONE REMODELING

- **Bone remodeling in response to tension and stress**: heavier loads (compression) increase tissue deposited in that bone; tension and pressure also affect remodeling
  - **Compression** – squeezing or pressing together; occurs when bones are pressed between body's weight and ground; *stimulates bone deposition*
  - **Tension** – stretching force; *bone deposition occurs* in regions of bone exposed to tension
  - **Pressure** – continuous downward force; *bone resorption is stimulated* in regions of bone exposed to continuous pressure

BONE REMODELING

- **Other factors influencing bone remodeling**:
  - **Hormones** – Testosterone promotes *bone deposition* while estrogen inhibits *osteoclast activity*
  - **Age** – As individual ages growth hormone and sex hormones decline; decreases protein synthesis in bone
  - **Calcium ion intake** from diet must be *adequate to support bone deposition*
  - **Vitamin D intake** from diet must be adequate to *promote calcium ion absorption* from gut and prevents *calcium ion loss* in urine

BONE REMODELING

- **Other factors influencing bone remodeling** (continued):
  - **Vitamin C intake** from diet must be adequate for *synthesis of collagen*
  - **Vitamin K intake** from diet must be adequate for *synthesis of calcium ion-binding glycoproteins* secreted by osteoblasts
  - **Protein intake** from diet must be adequate for osteoblasts to *synthesize collagen fibers* found in organic matrix

BONE REMODELING

- **Bone remodeling and calcium ion homeostasis**:
  - Bone stores most of *calcium ions in body*
  - Stored calcium ions are not only used for bone deposition and remodeling; used throughout body for *several critical processes* such as muscle contraction
  - A negative feedback loop maintains *calcium ion homeostasis* in blood (**Figure 6.15**); example of **Feedback Loops Core Principle**

BONE REMODELING

- **Bone remodeling and calcium ion homeostasis** (continued):
  - Negative feedback loop (**Figure 6.15**):
    - Calcium ion levels in blood are *closely monitored*; both high and low levels of calcium ions can lead to major disruptions in homeostasis and even death
    - **Stimulus and receptor**: when calcium ion level drops in blood it is detected by **parathyroid cells**
    - **Control center and effector**: parathyroid cells act as control center and secrete **parathyroid hormone** (**PTH**)

Figure 6.15 Structure of the epiphyseal plate.

BONE REMODELING

- **Bone remodeling and calcium ion homeostasis** (continued):
  - Negative feedback loop (continued):
    - **Effect/response**: PTH stimulates effects that increase *blood calcium ion levels*
      - Increases osteoclast activity; breaks down the inorganic matrix of bone releasing calcium ions from hydroxyapatite crystals
      - Increases *absorption* of calcium from gut
      - Inhibits calcium *loss* in urine

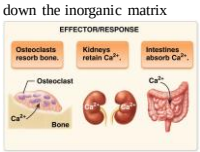


Figure 6.15 Structure of the epiphyseal plate.

BONE REMODELING

- **Bone remodeling and calcium ion homeostasis** (continued):
  - Negative feedback loop (continued):
    - **Homeostasis and negative feedback**: As calcium ion levels *return to normal* in blood, change is detected by parathyroid cells and they reduce secretion of PTH, closing feedback loop

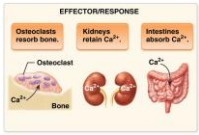


Figure 6.15 Structure of the epiphyseal plate.

BONE REMODELING

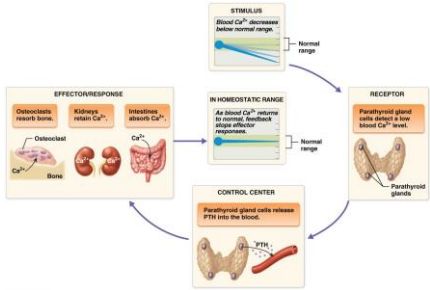


Figure 6.15 Structure of the epiphyseal plate.

BONE REMODELING

- **Bone remodeling and calcium ion homeostasis** (continued):
  - Negative feedback loop (continued):
    - An increase in blood calcium levels triggers a different negative feedback loop; first response is a drop in PTH secretion by parathyroid gland
    - **Calcitonin** is secreted by thyroid gland and has basically opposite effects as PTH; leads to *bone deposition*; pulls calcium ions out of blood to manufacture inorganic bone matrix; calcitonin is most active during *bone growth* and less so in adulthood
    - **Vitamin D** is important for calcium ion homeostasis due to its effects on the *absorption of calcium ions* from the gut

BONE REMODELING

- **Factors influencing bone remodeling are summarized**:

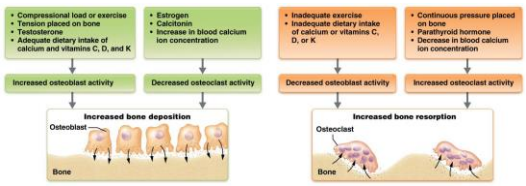


Figure 6.16 Factors that influence bone remodeling.

BONE REPAIR

- Bones are *commonly injured* while performing their protective and supportive functions
- Most dramatic bone injury is a **fracture** (broken bone) (**Table 6.1**):
  - **Simple fractures** – skin and tissue around fracture *remain intact*
  - **Compound fractures** – skin and tissues around fracture are *damaged*

BONE REPAIR

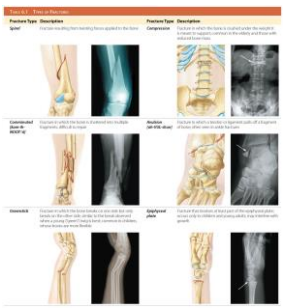


Table 6.1 Types of Fractures.

BONE REPAIR

- General process of fracture healing involves:
  - **Hematoma (blood clot) fills in gap between bone fragments**; mass of *blood cells and proteins* form in an injury due to ruptured blood vessels
  - **Fibroblasts and chondroblasts infiltrate hematoma and form a soft callus**; mixture of hyaline cartilage and collagenous connective tissue

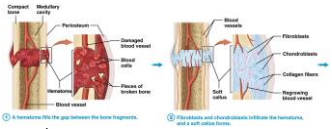


Figure 6.17 The process of fracture repair.

BONE REPAIR

- General process of fracture healing (continued):
  - **Osteoblasts build a bone callus** (hard callus); collar of primary bone made by osteoblasts residing in periosteum
  - **Bone callus is remodeled and primary bone is replaced with secondary bone**

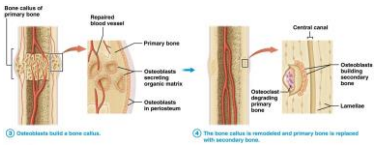


Figure 6.17 The process of fracture repair.