CHAPTER 6: BONES AND BONE TISSUE

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**

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

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**)

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

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

FUNCTIONS OF THE SKELETAL SYSTEM

- Functions of skeletal system (continued):

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

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*

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**)

BONE STRUCTURE

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

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*

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

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

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

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

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

- **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

- **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

BONE STRUCTURE

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

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

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**

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

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*

BONE CELLS

- **Osteocytes** (continued)
    - No longer as metabolically active 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

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

HISTOLOGY OF BONE

- **Histology of bone tissue** is quite different 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**

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**

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

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*

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

HISTOLOGY OF BONE

- **Overall compact bone structure:**
  - Osteons *are not 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 between circular osteons and represent *remnants* of old osteons

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

HISTOLOGY OF BONE

- **Structure of spongy bone:**
  - Spongy bone – usually not *weight-bearing* like compact bone so is much less *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

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
  - No central or perforating canals supplying blood to trabeculae; obtain their blood supply from *vessels in bone marrow*

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 decreases *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

- **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

- **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

- 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

- 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

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**)

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

- 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 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*

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

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

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**)

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

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

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:

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

- 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

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**