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## **Chapter 7**

## \*Lecture PowerPoint

#### **Bone Tissue**

\*See separate *FlexArt PowerPoint* slides for all figures and tables preinserted into PowerPoint without notes.

## Introduction

## In this chapter we will cover:

- Bone tissue composition
- How bone functions, develops, and grows
- How bone metabolism is regulated and some of its disorders

## Introduction

- Bones and teeth are the most durable remains of a once-living body and the most vivid reminder of life
- Living skeleton is made of dynamic tissues, full of cells, permeated with nerves and blood vessels
- Osteology is the study of bone

# Tissues and Organs of the Skeletal System

#### Expected Learning Outcomes

- Name the tissues and organs that compose the skeletal system.
- State several functions of the skeletal system.
- Distinguish between bones as a tissue and as an organ.
- Describe the four types of bones classified by shape.
- Describe the general features of a long bone and a flat bone.

# Tissues and Organs of the Skeletal System

- Osteology—the study of bone
- Skeletal system—composed of bones, cartilages, and ligaments
  - Form strong, flexible framework of the body
  - Cartilage—forerunner of most bones
    - Covers many joint surfaces of mature bone
- Ligaments—hold bones together at the joints
- Tendons—attach muscle to bone

## **Functions of the Skeleton**

- Support—holds up the body, supports muscles, mandible and maxilla support teeth
- Protection—brain, spinal cord, heart, lungs
- Movement—limb movements, breathing, action of muscle on bone
- Electrolyte balance—calcium and phosphate ions
- Acid-base balance—buffers blood against excessive pH changes
- Blood formation—red bone marrow is the chief producer of blood cells

## **Bones and Osseous Tissue**

- Bone (osseous tissue)—connective tissue with the matrix hardened by calcium phosphate and other minerals
- Mineralization or calcification—the hardening process of bone
- Individual bones consist of bone tissue, bone marrow, cartilage, adipose tissue, nervous tissue, and fibrous connective tissue
- Continually remodels itself and interacts physiologically with all of the other organ systems of the body
- Permeated with nerves and blood vessels, which attests to its sensitivity and metabolic activity

#### Flat bones

- Protect soft organs
- Curved but wide and thin

#### Long bones

- Longer than wide
- Rigid levers acted upon by muscles

#### Short bones

- Equal in length and width
- Glide across one another in multiple directions

#### Irregular bones

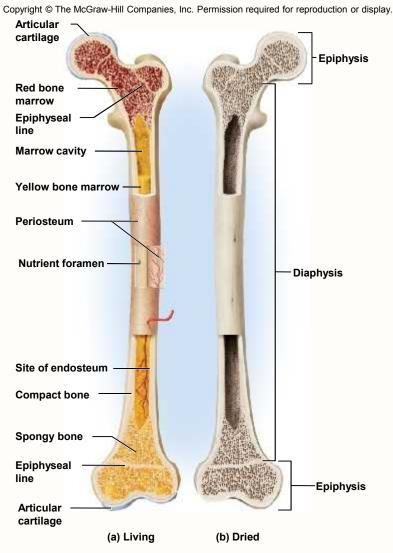
Elaborate shapes that do not fit into other categories

- Compact (dense) bone—outer shell of long bone
- Diaphysis (shaft)—cylinder of compact bone to provide leverage
- Medullary cavity (marrow cavity)—space in the diaphysis of a long bone that contains bone marrow
- Epiphyses—enlarged ends of a long bone
  - Enlarged to strengthen joint and attach ligaments and tendons
- Spongy (cancellous) bone—covered by more durable compact bone
  - Skeleton three-fourths compact and one-fourth spongy bone by weight
  - Spongy bone in ends of long bones, and middle of nearly all others

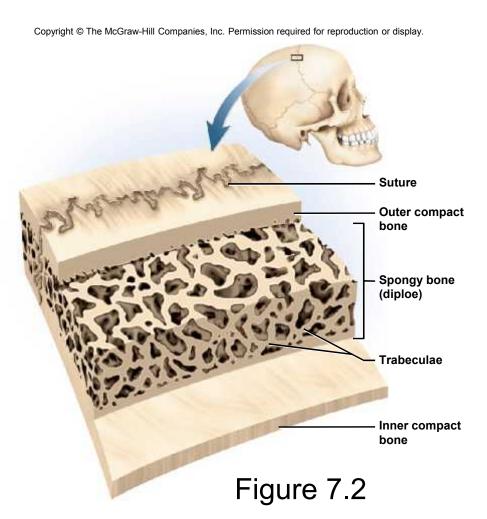
- Spongy (cancellous) bone—covered by more durable compact bone
  - Skeleton three-fourths compact and one-fourth spongy bone by weight
  - Spongy bone in ends of long bones, and middle of nearly all others
- Articular cartilage—layer of hyaline cartilage that covers the joint surface where one bone meets another; allows joint to move more freely and relatively friction free
- Nutrient foramina—minute holes in the bone surface that allows blood vessels to penetrate

- Periosteum—external sheath that covers bone except where there is articular cartilage
  - Outer fibrous layer of collagen
    - Some outer fibers continuous with the tendons that attach muscle to bone
    - Perforating (Sharpey) fibers—other outer fibers that penetrate into the bone matrix
    - Strong attachment and continuity from muscle to tendon to bone
  - Inner osteogenic layer of bone-forming cells
    - Important to growth of bone and healing of fractures

- Endosteum—thin layer of reticular connective tissue lining marrow cavity
  - Has cells that dissolve osseous tissue and others that deposit it
- Epiphyseal plate (growth plate)—area of hyaline cartilage that separates the marrow spaces of the epiphysis and diaphysis
  - Enables growth in length
  - Epiphyseal line—in adults, a bony scar that marks where growth plate used to be



- Epiphyses and diaphysis
- Compact and spongy bone
- Marrow cavity
- Articular cartilage
- Periosteum

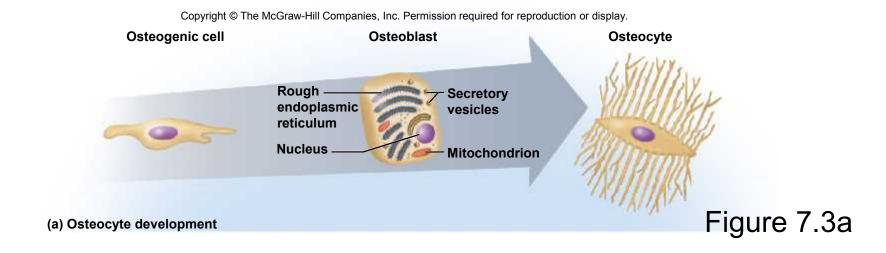


- Sandwich-like construction
- Two layers of compact bone enclosing a middle layer of spongy bone
  - Both surfaces of flat bone covered with periosteum
- Diploe—spongy layer in the cranium
  - Absorbs shock
  - Marrow spaces lined with endosteum

## **Histology of Osseous Tissue**

#### Expected Learning Outcomes

- List and describe the cells, fibers, and ground substance of bone tissue.
- State the importance of each constituent of bone tissue.
- Compare the histology of the two types of bone tissue.
- Distinguish between the two types of bone marrow.



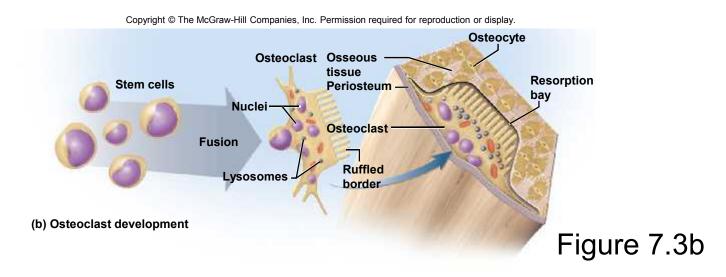
- Bone is connective tissue that consists of cells, fibers, and ground substance
- Four principal types of bone cells
  - Osteogenic cells; osteoblasts; osteocytes; osteoclasts

- Osteogenic (osteoprogenitor) cells—stem cells found in endosteum, periosteum, and in central canals
  - Arise from embryonic mesenchymal cells; multiply continuously to produce new osteoblasts
- Osteoblasts—bone-forming cells
  - Line up as single layer of cells under endosteum and periosteum
  - Nonmitotic
  - Synthesize soft organic matter of matrix which then hardens by mineral deposition

#### Cont.

- Stress and fractures stimulate osteogenic cells to multiply more rapidly and increase number of osteocytes to reinforce or rebuild bone
- Secrete osteocalcin—thought to be the structural protein of bone
  - Stimulates insulin secretion of pancreas
  - Increases insulin sensitivity in adipocytes which limit the growth of adipose tissue

- Osteocytes—former osteoblasts that have become trapped in the matrix they have deposited
  - Lacunae—tiny cavities where osteocytes reside
  - Canaliculi—little channels that connect lacunae
  - Cytoplasmic processes reach into canaliculi
  - Some osteocytes reabsorb bone matrix while others deposit it
  - Contribute to homeostatic mechanism of bone density and calcium and phosphate ions
  - When stressed, produce biochemical signals that regulate bone remodeling



- Osteoclasts—bone-dissolving cells found on the bone surface
  - Osteoclasts develop from same bone marrow stem cells that give rise to blood cells
  - Different origin from rest of bone cells
  - Unusually large cells formed from the fusion of several stem cells
    - Typically have 3 to 4 nuclei, may have up to 50

- Ruffled border—side facing bone surface
  - Several deep infoldings of the plasma membrane which increases surface area and resorption efficiency
- Resorption bays (Howship lacunae)—pits on surface of bone where osteoclasts reside
- Remodeling—results from combined action of the bone-dissolving osteoclasts and the bonedepositing osteoblasts

## The Matrix

- Matrix of osseous tissue is, by dry weight, about onethird organic and two-thirds inorganic matter
- Organic matter—synthesized by osteoblasts
  - Collagen, carbohydrate—protein complexes, such as glycosaminoglycans, proteoglycans, and glycoproteins
- Inorganic matter
  - 85% hydroxyapatite (crystallized calcium phosphate salt)
  - 10% calcium carbonate
  - Other minerals (fluoride, sodium, potassium, magnesium)

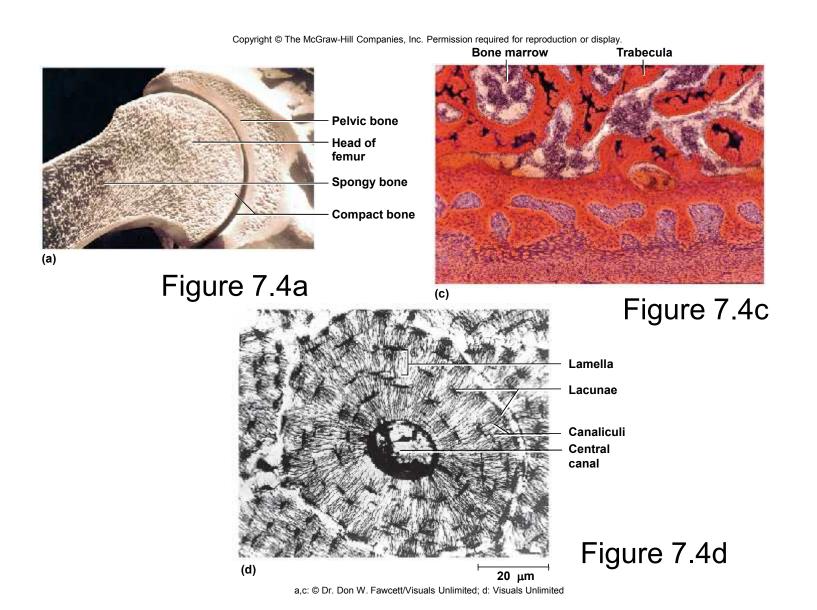
## The Matrix

- Bone is a composite—combination of two basic structural materials, a ceramic and a polymer
  - Combines optimal mechanical properties of each component
  - Bone combines the polymer, collagen, with the ceramic, hydroxyapatite and other minerals
  - Ceramic portion allows the bone to support the body weight,
     and protein portion gives bone some degree of flexibility

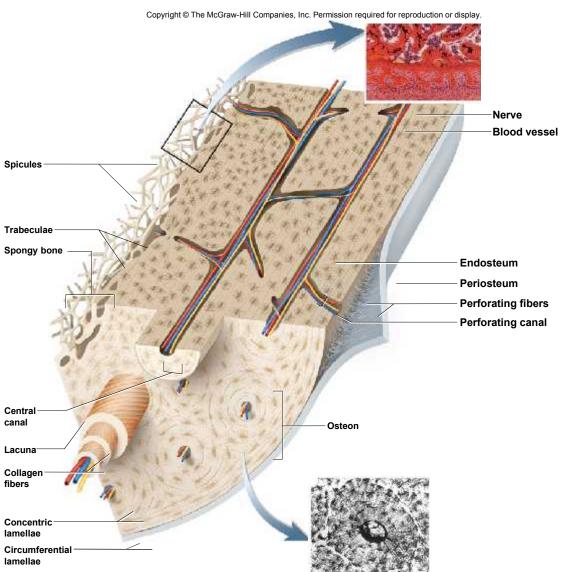
## The Matrix

- Rickets—soft bones due to deficiency of calcium salts
- Osteogenesis imperfecta or brittle bone disease excessively brittle bones due to lack of protein, collagen

## **Histology of Osseous Tissue**



## **Histology of Osseous Tissue**



- Nutrient foramina on bone surface
- Perforating
   (Volkmann) canals—
   transverse or diagonal
   canals
- Central canals vertical canals
- Circumferential lamellae
- Interstitial lamellae

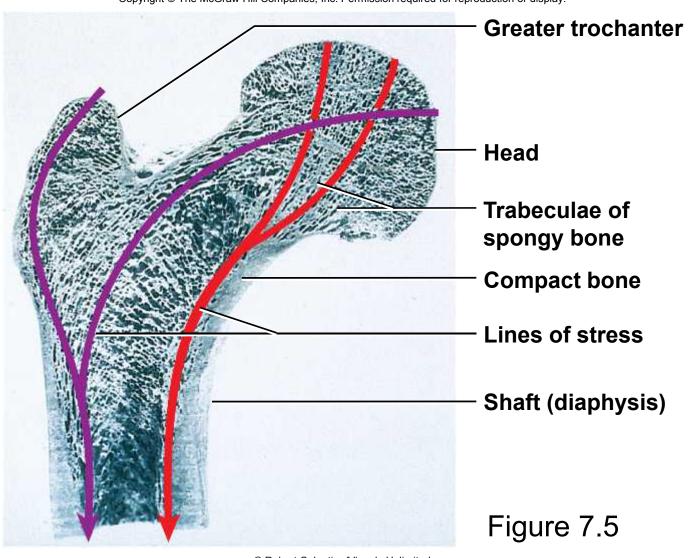
(b)

## **Spongy Bone**

- Spongelike appearance
- Spongy bone consists of:
  - Slivers of bone called spicules
  - Thin plates of bone called trabeculae
  - Spaces filled with red bone marrow
- Few osteons and no central canals
  - All osteocytes close to bone marrow
- Provides strength with minimal weight
  - Trabeculae develop along bone's lines of stress

## Spongy Bone Structure in Relation to Mechanical Stress

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## **Bone Marrow**

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Bone marrow—general term for soft tissue that occupies the marrow cavity of a long bone and small spaces amid the trabeculae of spongy bone

## **Bone Marrow**

- Red marrow (myeloid tissue)
  - In nearly every bone in a child
  - Hemopoietic tissue—produces blood cells and is composed of multiple tissues in a delicate, but intricate arrangement that is an organ to itself
  - In adults, found in skull, vertebrae, ribs, sternum, part of pelvic girdle, and proximal heads of humerus and femur
- Yellow marrow found in adults
  - Most red marrow turns into fatty yellow marrow
  - No longer produces blood

## **Bone Development**

#### Expected Learning Outcomes

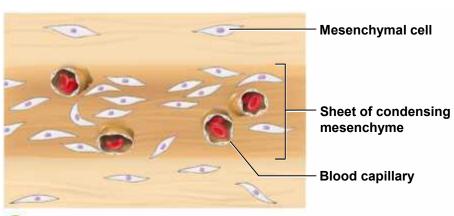
- Describe two mechanisms of bone formation.
- Explain how mature bone continues to grow and remodel itself.

## **Bone Development**

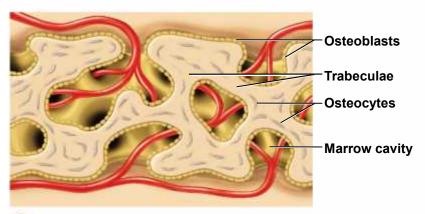
- Ossification or osteogenesis—the formation of bone
- In the human fetus and infant, bone develops by two methods
  - Intramembranous ossification
  - Endochondral ossification

## Intramembranous Ossification

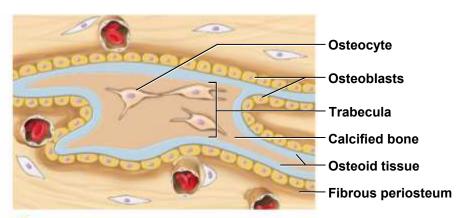
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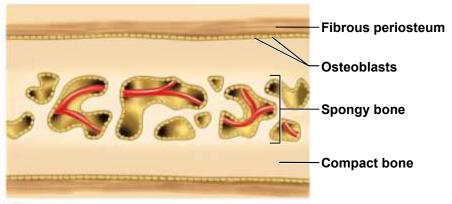
1 Condensation of mesenchyme into soft sheet permeated with blood capillaries



3 Honeycomb of bony trabeculae formed by continued mineral deposition; creation of spongy bone



2 Deposition of osteoid tissue by osteoblasts on mesenchymal surface; entrapment of first osteocytes; formation of periosteum



4 Surface bone filled in by bone deposition, converting spongy bone to compact bone. Persistence of spongy bone in the middle layer.

Figure 7.7

Produces flat bones of skull and clavicle

## Intramembranous Ossification

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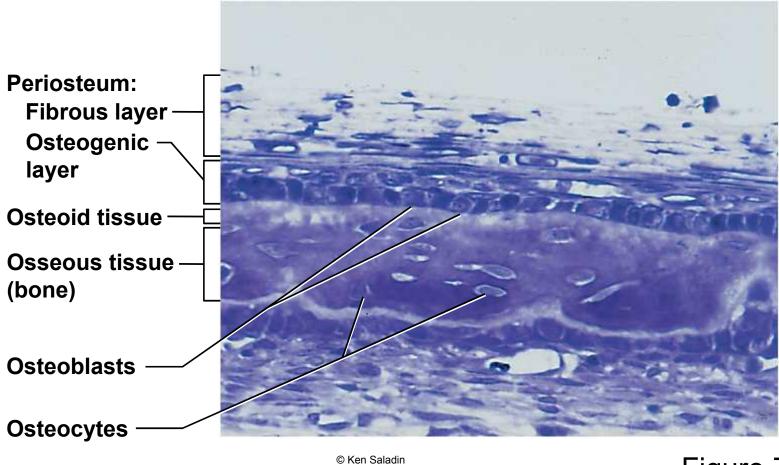


Figure 7.8

7-34

Note the periosteum and osteoblasts

## **Endochondral Ossification**

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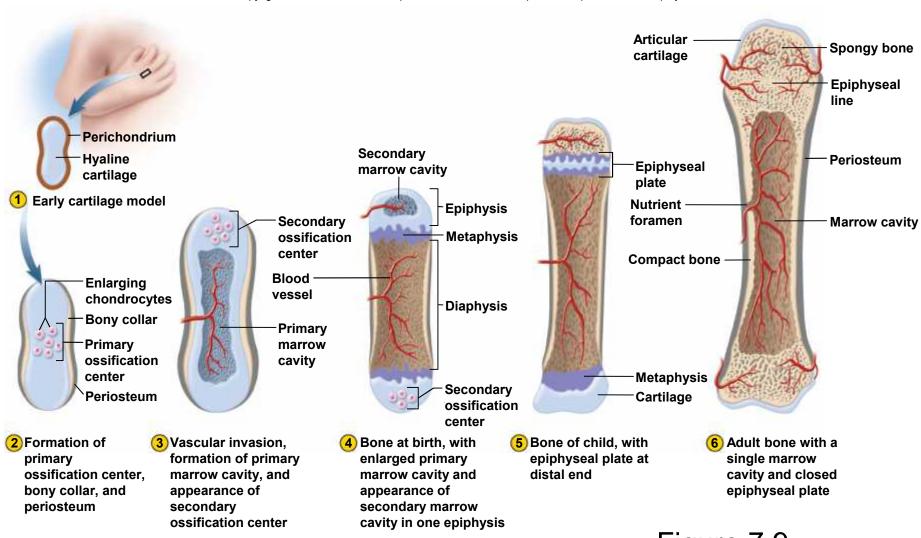


Figure 7.9

## **Endochondral Ossification**

- During infancy and childhood, the epiphyses fill with spongy bone
- Cartilage limited to the articular cartilage covering each joint surface, and to the epiphyseal plate
  - A thin wall of cartilage separating the primary and secondary marrow cavities
  - Epiphyseal plate persists through childhood and adolescence
  - Serves as a growth zone for bone elongation

#### **Endochondral Ossification**

- By late teens to early 20s, all remaining cartilage in the epiphyseal plate is generally consumed
  - Gap between epiphyses and diaphysis closes
  - Primary and secondary marrow cavities unite into a single cavity
  - Bone can no longer grow in length

#### The Fetal Skeleton at 12 Weeks

Copyright © The McGraw-Hill Companies, Inc. Permission required for reproduction or display. Cranial bones **Mandible Vertebrae Humerus Radius** Ulna-Scapula **Ribs Femur** Figure 7.10 **Pelvis** © Biophoto Associates/Photo Researchers, Inc.

## **Bone Growth and Remodeling**

- Ossification continues throughout life with the growth and remodeling of bones
- Bones grow in two directions
  - Length
  - Width

### **Bone Elongation**

- Epiphyseal plate—a region of transition from cartilage to bone
  - Functions as growth zone where the bones elongate
  - Consists of typical hyaline cartilage in the middle
  - With a transition zone on each side where cartilage is being replaced by bone
  - Metaphysis is the zone of transition facing the marrow cavity

### X-Ray of Child's Hand Epiphyseal Plates

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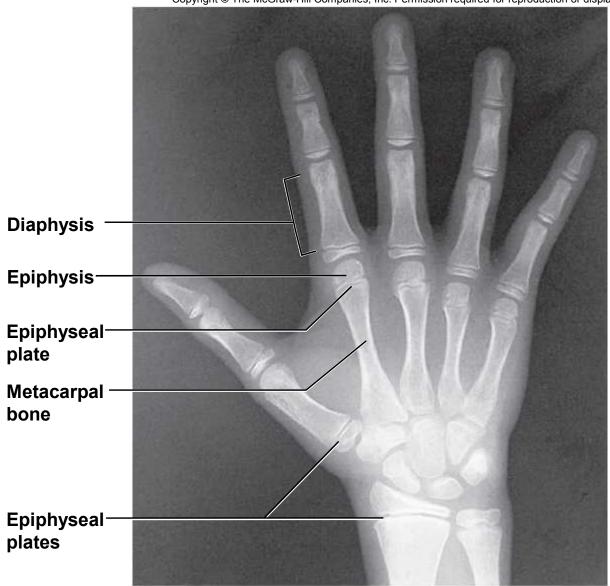
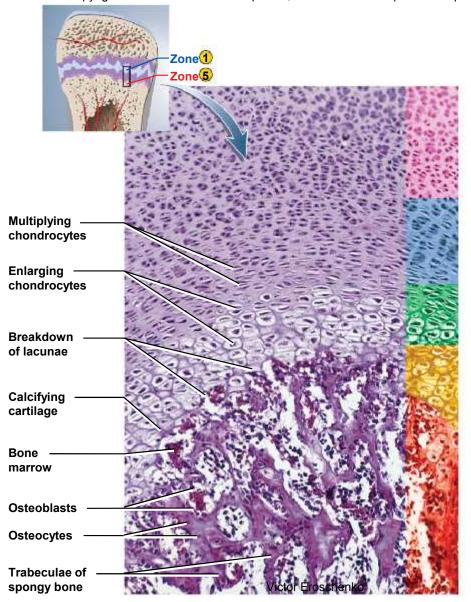


Figure 7.11

### **Zones of the Metaphysis**

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- 1 Zone of reserve cartilage
  Typical histology of resting
  hyaline cartilage
- Zone of cell proliferation Chondrocytes multiplying and lining up in rows of small flattened lacunae
- 3 Zone of cell hypertrophy Cessation of mitosis; enlargement of chondrocytes and thinning of lacuna walls
- Zone of calcification
  Temporary calcification of
  cartilage matrix between
  columns of lacunae
- 5 Zone of bone deposition
  Breakdown of lacuna walls,
  leaving open channels; death
  of chondrocytes; bone
  deposition by osteoblasts,
  forming trabeculae of spongy
  bone

Figure 7.12

# **Bone Widening and Thickening**

- Interstitial growth—bones increase in length
  - Bone elongation is really a result of cartilage growth within the epiphyseal plate
  - Epiphyses close when cartilage is gone—epiphyseal line
  - Lengthwise growth is finished
    - Occurs at different ages in different bones

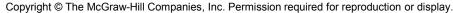
## **Bone Widening and Thickening**

- Appositional growth—bones increase in width throughout life
  - Deposition of new bone at the surface
  - Osteoblasts on deep side of periosteum deposit osteoid tissue
    - Become trapped as tissue calcifies
  - Lay down matrix in layers parallel to surface
    - Forms circumferential lamellae over surface
      - Osteoclasts of endosteum enlarge marrow cavity

### **Bone Remodeling**

- Bone remodeling occurs throughout life—10% per year
  - Repairs microfractures, releases minerals into blood, reshapes bones in response to use and disuse
  - Wolff's law of bone: architecture of bone determined by mechanical stresses placed on it and bones adapt to withstand those stresses
    - Remodeling is a collaborative and precise action of osteoblasts and osteoclasts
    - Bony processes grow larger in response to mechanical stress

#### **Dwarfism**





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#### Achondroplastic dwarfism

- Long bones stop growing in childhood
  - Normal torso, short limbs
- Failure of cartilage growth in metaphysis
- Spontaneous mutation produces mutant dominant allele

#### Pituitary dwarfism

- Lack of growth hormone
- Normal proportions with short stature

# **Physiology of Osseous Tissue**

#### Expected Learning Outcome

- Describe the processes by which minerals are added to and removed from bone tissue.
- Describe the role of the bones in regulating blood calcium and phosphate levels.
- Name several hormones that regulate bone physiology and describe their effects.

# Physiology of Osseous Tissue

- A mature bone remains a metabolically active organ
  - Involved in its own maintenance of growth and remodeling
  - Exerts a profound influence over the rest of the body by exchanging minerals with tissue fluid
    - Disturbance of calcium homeostasis in skeleton disrupts function of other organ systems
      - Especially nervous and muscular

- Mineral deposition (mineralization)—crystallization process in which calcium phosphate and other ions are taken from the blood plasma and deposited in bone tissue
  - Osteoblasts produce collagen fibers that spiral the length of the osteon
  - Fibers become encrusted with minerals that harden the matrix
    - Calcium and phosphate (hydroxyapatite) from blood plasma are deposited along the fibers

#### Cont.

- Calcium and phosphate ion concentration must reach a critical value called the solubility product for crystal formation to occur
- Most tissues have inhibitors to prevent this so they do not become calcified
- Osteoblasts neutralize these inhibitors and allow salts to precipitate in the bone matrix
- First few crystals (seed crystals) attract more calcium and phosphate from solution

- Abnormal calcification (ectopic ossification)
  - May occur in lungs, brain, eyes, muscles, tendons, or arteries (arteriosclerosis)
  - Calculus: calcified mass in an otherwise soft organ such as the lung
- Mineral resorption—the process of dissolving bone and releasing minerals into the blood
  - Performed by osteoclasts at the ruffled border
  - Hydrogen pumps in membranes secrete hydrogen into space between the osteoclast and bone surface

#### Cont.

- Chloride ions follow by electrical attraction
- Hydrochloric acid (pH 4) dissolves bone minerals
- Acid phosphatase enzyme digests the collagen
- Orthodontic appliances (braces) reposition teeth
  - Tooth moves because **osteoclasts** dissolve bone ahead of the tooth, where the pressure on the bone is the greatest
  - Osteoblasts deposit bone more slowly in the lowpressure zone behind the tooth

- Calcium and phosphate are used for much more than bone structure
- Phosphate is a component of DNA, RNA, ATP, phospholipids, and pH buffers
- Calcium needed in neuron communication, muscle contraction, blood clotting, and exocytosis
- Minerals are deposited in the skeleton and withdrawn when they are needed for other purposes

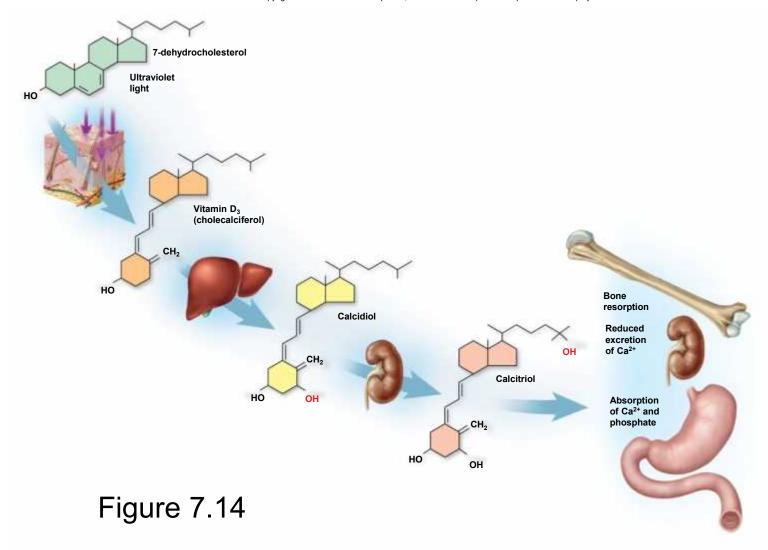
- About 1,100 g calcium in adult body
  - 99% in the skeleton
    - As easily exchangeable calcium ions and more stable hydroxyapatite reserve
    - 18% of adult skeleton exchanged with blood each year
- Normal calcium concentration in blood plasma is 9.2 to 10.4 mg/dL—45% as Ca<sup>2+</sup> can diffuse across capillary walls and affect other tissues; rest in reserve, bound to plasma proteins

- Hypocalcemia has a wide variety of causes, blood calcium excess
  - Vitamin D deficiency
  - Diarrhea
  - Thyroid tumors
  - Underactive parathyroids
  - Pregnancy and lactation
  - Accidental removal of parathyroid glands during thyroid surgery

- Calcium homeostasis depends on a balance between dietary intake, urinary and fecal losses, and exchanges between osseous tissue
- Calcium homeostasis is regulated by three hormones:
  - Calcitriol, calcitonin, and parathyroid hormone

### **Calcitriol Synthesis and Action**

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### **Calcitriol**

- Calcitriol—a form of vitamin D produced by the sequential action of the skin, liver, and kidneys
- Produced by the following process
  - Epidermal keratinocytes use UV radiation to convert a steroid, 7-dehydrocholesterol to previtamin D<sub>3</sub>
  - Liver adds a hydroxyl group converting it to calcidiol
  - Kidneys add another hydroxyl group, converting that to calcitriol

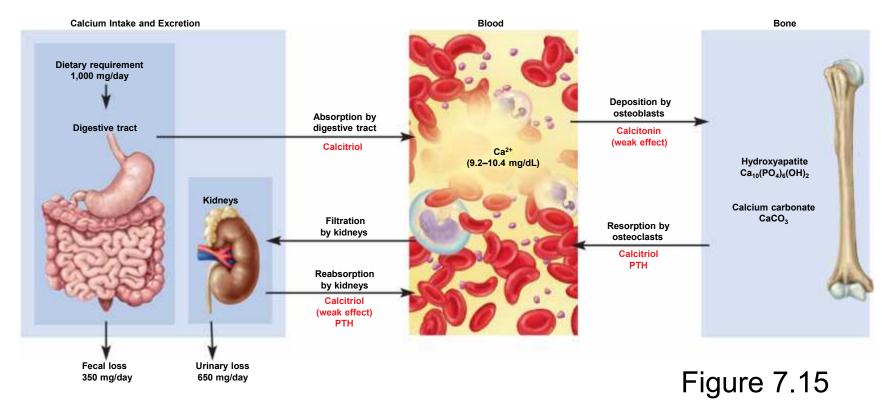
(most active form of vitamin D); also from fortified milk

### **Calcitriol**

#### Cont.

- Calcitriol behaves as a hormone that raises blood calcium concentration
  - Increases calcium absorption by small intestine
  - Increases calcium resorption from the skeleton
  - Promotes kidney reabsorption of calcium ions, so less lost in urine
- Necessary for bone deposition—need adequate calcium and phosphate
- Abnormal softness of bones in children (rickets) and in adults (osteomalacia) without adequate vitamin D

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Calcitriol, calcitonin, and PTH maintain normal blood calcium concentration

#### **Calcitonin**

- Calcitonin—secreted by C cells (clear cells) of the thyroid gland when calcium concentration rises too high
- Lowers blood calcium concentration in two ways
  - Osteoclast inhibition
    - Reduces osteoclast activity as much as 70%
    - Less calcium liberated from bones
  - Osteoblast stimulation
    - Increases the number and activity of osteoblasts
    - Deposits calcium into the skeleton

#### **Calcitonin**

- Important in children, weak effect in adults
  - Osteoclasts more active in children due to faster remodeling
  - Deficiency does not cause disease in adults
- Reduces bone loss in women during pregnancy and lactation

### **Parathyroid Hormone**

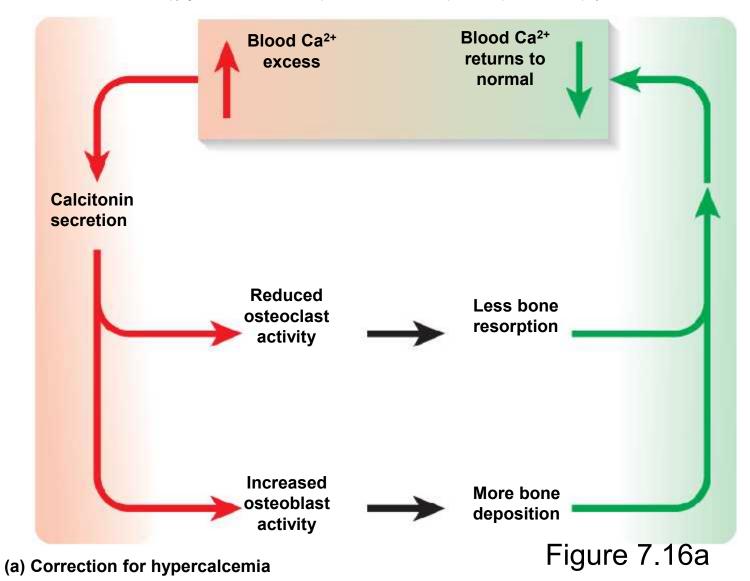
- Parathyroid hormone (PTH)—secreted by the parathyroid glands which adhere to the posterior surface of thyroid gland
- PTH released with low calcium blood levels
- PTH raises calcium blood level by four mechanisms
  - Binds to receptors on osteoblasts
    - Simulating them to secrete RANKL which raises the osteoclast population

## **Parathyroid Hormone**

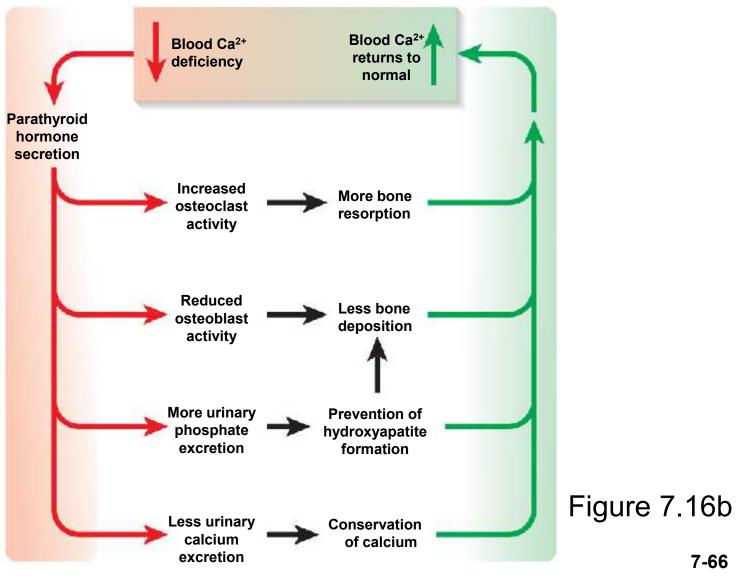
#### Cont.

- Promotes calcium reabsorption by the kidneys, less lost in urine
- Promotes the final step of calcitriol synthesis in the kidneys, enhancing calcium-raising effect of calcitriol
- Inhibits collagen synthesis by osteoblasts, inhibiting bone deposition
- Sporadic injection or secretion of low levels of PTH causes bone deposition, and can increase bone mass

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(b) Correction for hypocalcemia

### **Phosphate Homeostasis**

- Average adult has 500 to 800 g phosphorus
- 85% to 90% of phosphate is in the bones
- Normal plasma concentration is 3.5 to 4.0 mg/dL
- Occurs in two principal forms
  - HPO<sub>4</sub><sup>2-</sup> and H<sub>2</sub>PO<sub>4</sub><sup>-</sup> (monohydrogen and dihydrogen phosphate ions)

### **Phosphate Homeostasis**

- Phosphate levels are not regulated as tightly as calcium levels
  - No immediate functional disorders
- Calcitriol promotes its absorption by small intestine and promotes bone deposition
- PTH lowers blood phosphate level by promoting its urinary excretion

## Other Factors Affecting Bone

- At least 20 or more hormones, vitamins, and growth factors affect osseous tissue
- Bone growth especially rapid in puberty and adolescence
  - Surges of growth hormone, estrogen, and testosterone occur and promote ossification
  - These hormones stimulate multiplication of osteogenic cells, matrix deposition by osteoblasts, and chondrocyte multiplication and hypertrophy in metaphyses

## Other Factors Affecting Bone

#### Cont.

- Girls grow faster than boys and reach full height earlier
  - Estrogen stronger effect than testosterone on bone growth
- Males grow for a longer time and taller
- Anabolic steroids cause growth to stop
  - Epiphyseal plate "closes" prematurely
  - Results in abnormally short adult stature

### **Bone Disorders**

### Expected Learning Outcomes

- Name and describe several bone diseases.
- Name and describe the types of fractures.
- Explain how a fracture is repaired.
- Discuss some clinical treatments for fractures and other skeletal disorders.

### **Bone Disorders**

- Orthopedics—originated as the name implies, as the treatment of skeletal deformities in children
- Deals with the prevention and correction of injuries and disorders of bones, joints, and muscles
- Includes the design of artificial joints and limbs and the treatment of athletic injuries

## Fractures and Their Repair

- Stress fracture—break caused by abnormal trauma to a bone
  - Falls, athletics, and military combat
- Pathological fracture—break in a bone weakened by some other disease
  - Bone cancer or osteoporosis
  - Usually caused by stress that would not break a healthy bone
- Fractures classified by structural characteristics
  - Direction of fracture line
  - Break in the skin
  - Multiple pieces

### **Types of Bone Fractures**

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(a) Nondisplaced





(c) Comminuted



(d) Greenstick

Figure 7.17

7-74

### **Healing of Fractures**

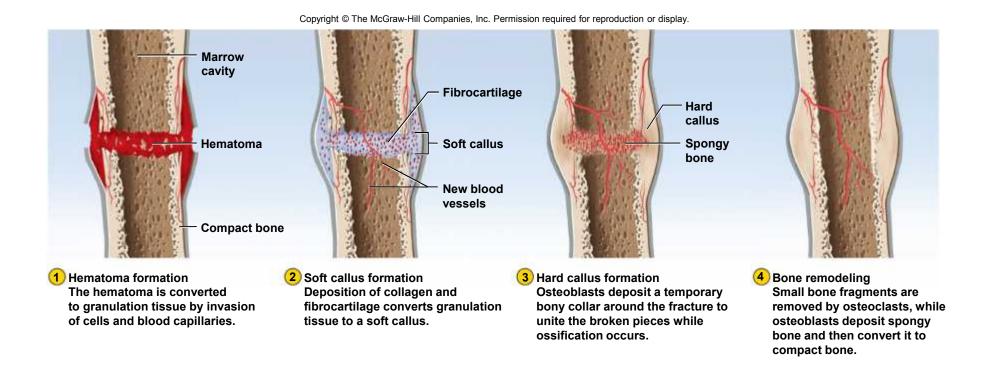


Figure 7.18

#### The Treatment of Fractures

- Closed reduction—procedure in which the bone fragments are manipulated into their normal positions without surgery
- Open reduction—involves surgical exposure of the bone and the use of plates, screws, or pins to realign the fragments
- Cast—normally used to stabilize and immobilize healing bone

### The Treatment of Fractures

- Traction—used to treat fractures of the femur in children
  - Aligns bone fragments by overriding force of the strong thigh muscles
  - Risks long-term confinement to bed
  - Rarely used for the elderly
  - Hip fractures are usually pinned in elderly and early ambulation (walking) is encouraged to promote blood circulation and healing
- Electrical stimulation accelerates repair
  - Suppresses effects of parathyroid hormone
- Orthopedics—branch of medicine that deals with prevention and correction of injuries and disorders of the bones, joints, and muscles

### **Open Reduction of an Ankle Fracture**

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Figure 7.19

#### Other Bone Disorders

- Osteoporosis—the most common bone disease
  - Severe loss of bone density
- Bones lose mass and become brittle due to loss of organic matrix and minerals
  - Affects spongy bone the most since it is the most metabolically active
  - Subject to pathological fractures of hip, wrist, and vertebral column
  - Kyphosis (widow's hump)—deformity of spine due to vertebral bone loss
  - Complications of loss of mobility are pneumonia and thrombosis

## **Osteoporosis**

- Estrogen maintains density in both sexes; inhibits resorption by osteoclasts
  - Testes and adrenals produce estrogen in men
  - In women, rapid bone loss after menopause since ovaries cease to secrete estrogen
- Osteoporosis is common in young female athletes with low body fat causing them to stop ovulating and ovarian estrogen secretion is low

# **Osteoporosis**

#### Cont.

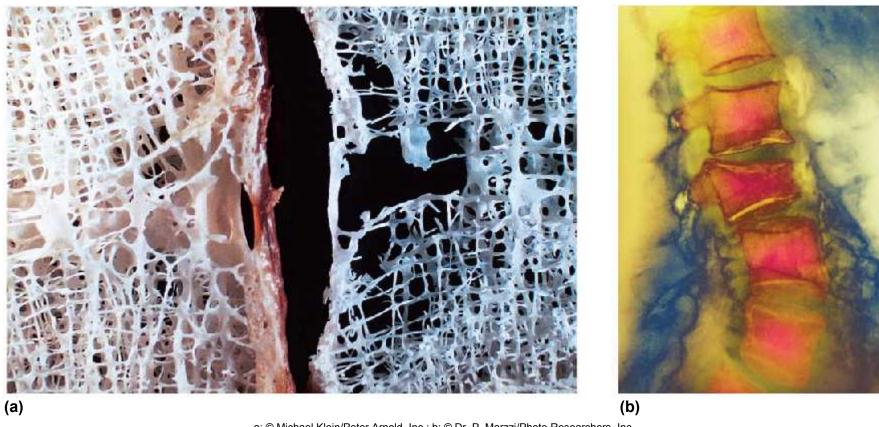
- Treatments
  - Estrogen replacement therapy (ERT) slows bone resorption, but increases risk of breast cancer, stroke, and heart disease
  - Drugs Fosamax, Actonel destroy osteoclasts
  - PTH slows bone loss if given as daily injection
    - Forteo (PTH derivative) increases density by 10% in 1 year
      - May promote bone cancer so use is limited to 2 years
  - Best treatment is prevention: exercise and a good bonebuilding diet between ages 25 and 40

#### **Other Bone Disorders**

- Postmenopausal white women at greatest risk
  - Begin to lose bone mass as early as age 35
    - By age 70, average loss is 30% of bone mass
  - Risk factors: race, age, gender, smoking, diabetes mellitus, diets poor in calcium, protein, vitamins C and D

# **Spinal Osteoporosis**

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Figure 7.20a,b