Chapter 07
Lecture Outline

See separate PowerPoint slides for all figures and tables pre-inserted 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
- Living skeleton is made of dynamic tissues, full of cells, permeated with nerves and blood vessels
- Continually remolds itself and interacts with other organ systems of the body
- 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

• **Skeletal system**—composed of bones, cartilages, and ligaments
  – **Cartilage**—forerunner of most bones
    • Covers many joint surfaces of mature bone
  – **Ligaments**—hold bones together at joints
  – **Tendons**—attach muscle to bone
Functions of the Skeleton

- **Support**—limb bones and vertebrae support body; jaw bones support teeth; some bones support viscera.
- **Protection**—of brain, spinal cord, heart, lungs, and more.
- **Movement**—limb movements, breathing, and other movements depend on bone.
- **Electrolyte balance**—calcium and phosphate levels.
- **Acid–base balance**—buffers blood against large pH changes by altering phosphate and carbonate salt levels.
- **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 (organs) consist of bone tissue, bone marrow, cartilage, adipose tissue, nervous tissue, and fibrous connective tissue**
General Features of Bones

• **Flat bones**
  – Thin, curved plates
  – Protect soft organs

• **Long bones**
  – Longer than wide
  – Rigid levers acted upon by muscles; crucial for movement

• **Short bones**
  – Approximately equal in length and width
  – Glide across one another in multiple directions

• **Irregular bones**
  – Elaborate shapes that do not fit into other categories
General Features of Bones

- **Compact bone**—dense outer shell of bone
- **Spongy (cancellous) bone**—loosely organized bone tissue
  - Found in center of ends and center of shafts of long bones and in middle of nearly all others
  - Covered by more durable compact bone
- **Skeleton three-fourths compact and one-fourth spongy bone by weight**
- **Long bone features**
  - **Diaphysis**—shaft that provides leverage
    - **Medullary cavity (marrow cavity)**—space in the diaphysis of a long bone that contains bone marrow
  - **Epiphyses**—enlarged ends of a long bone
    - Strengthen joint and anchor ligaments and tendons
General Features of Bones

• **Articular cartilage**—layer of hyaline cartilage that covers joint surface; allows joint to move more freely

• **Nutrient foramina**—minute holes in bone surface that allows blood vessels to penetrate

• **Periosteum**—external sheath covering most of bone
  – **Outer fibrous layer** of collagen
    • Some fibers continuous with tendons
    • **Perforating fibers**—penetrate into bone matrix
  – **Inner osteogenic layer** of bone-forming cells
    • Important to bone growth 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
General Features of Bones

- **Epiphyseal plate (growth plate)**—area of **hyaline cartilage** that separates epiphyses and diaphyses of children’s bones
  - Enables growth in length
  - **Epiphyseal line**—in adults, a bony scar that marks where growth plate used to be
General Features of Bones

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

Figure 7.1
General Features of Bones

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

Figure 7.2
 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 Cells

- **Bone** is connective tissue that consists of cells, fibers, and ground substance

- **Four principal types** of bone cells
  - Osteogenic cells; osteoblasts; osteocytes; osteoclasts
Bone Cells

- **Osteogenic cells**—stem cells found in endosteum and inner layer of periosteum
  - Arise from embryonic mesenchymal cells
  - Multiply continuously and give rise to most other bone cell types

- **Osteoblasts**—bone-forming cells
  - Form single layer of cells under endosteum and periosteum
  - Nonmitotic
  - Synthesize soft organic matter of matrix which then hardens by mineral deposition
  - Stress stimulates osteogenic cells to multiply rapidly and increase the number of osteoblasts which reinforce bone
  - Secrete hormone **osteocalcin**
    - Stimulates insulin secretion of pancreas
    - Increases insulin sensitivity in adipocytes which limits the growth of adipose tissue
Bone Cells

- **Osteocytes**—former osteoblasts that have become trapped in the matrix they deposited
  - **Lacunae**—tiny cavities where osteocytes reside
  - **Canaliculi**—little channels that connect lacunae
  - Cytoplasmic processes of osteocytes reach into canaliculi and contact processes of neighboring cells
    - Gap junctions allow for passage of nutrients, wastes, signals
  - Some osteocytes reabsorb bone matrix while others deposit it
  - Act as strain sensors—when stressed, produce biochemical signals that regulate bone remodeling (shape and density changes that are adaptive)
• **Osteoclasts**—bone-dissolving cells found on bone surface
  – Osteoclasts develop from same bone marrow stem cells that give rise to blood cells (different origin from other bone cells)
  – Very large cells formed from fusion of several stem cells
    • Have multiple nuclei in each cell
  – **Ruffled border** (large surface area) faces bone
  – Cells often reside in **resorption bays** (pits in bone surface)
  – Dissolving bone is part of bone remodeling
The Matrix

- **Matrix of osseous tissue** is, by dry weight, about one-third 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 material**—a combination of a ceramic and a polymer
  – Hydroxyapatite and other minerals are the ceramic and collagen (protein) is the polymer
  – Ceramic portion allows the bone to support body weight without sagging
    • Rickets is a disease caused by mineral deficiency and resulting in soft, deformed bones
  – Polymer (protein) gives some flexibility
    • Osteogenesis imperfecta (brittle bone disease) results from a defect in collagen deposition
Histology of Osseous Tissue

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Figure 7.4a,c,d

(a) Pelvic bone
(b) Head of femur
(c) Spongy bone
(d) Compact bone

(d) Lacunae
Canaliculi
Central canal
Lamella

20 µm

a: ©D.W. Fawcett/Visuals Unlimited; c: ©Science VU/Visuals Unlimited; d: ©Donald Fawcett/Visuals Unlimited
Compact bone

- Histology of compact bone reveals osteons (haversian systems)
  - Concentric lamellae surround a central (haversian) canal running longitudinally
  - Perforating (Volkmann) canals—transverse or diagonal passages
  - Circumferential lamellae fill outer region of dense bone
  - Interstitial lamellae fill irregular regions between osteons

Figure 7.4b,c,d
Spongy Bone

• **Spongy bone consists of:**
  – Lattice of bone covered with endosteum
    • 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

Figure 7.5

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Bone Marrow

• **Bone marrow**—soft tissue occupying marrow cavities of long bones and small spaces of spongy bone

• **Red marrow (myeloid tissue)**
  – Contains *hemopoietic tissue*—produces blood cells
  – In nearly every bone in a child
  – In adults, found in skull, vertebrae, ribs, sternum, part of pelvic girdle, and proximal heads of humerus and femur

• **Yellow marrow** found in adults
  – Fatty marrow that does not produce blood
  – Can transform back to red marrow in the event of chronic anemia

Figure 7.6
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

- Produces flat bones of skull and clavicle in fetus
- Thickens long bones throughout life
Intramembranous Ossification

- Note the periosteum and osteoblasts

Figure 7.8
Endochondral Ossification

1. Early cartilage model
   - Perichondrium
   - Hyaline cartilage

2. Formation of primary ossification center, bony collar, and periosteum
   - Enlarging chondrocytes
   - Bony collar
   - Primary ossification center
   - Periosteum

3. Vascular invasion, formation of primary marrow cavity, and appearance of secondary ossification center
   - Secondary ossification center
   - Blood vessel
   - Primary marrow cavity

4. Bone at birth, with enlarged primary marrow cavity and appearance of secondary marrow cavity in one epiphysis
   - Secondary ossification center
   - Epiphysis
   - Metaphysis
   - Diaphysis
   - Secondary marrow cavity

5. Bone of child, with epiphyseal plate at distal end
   - Epiphyseal plate
   - Nutrient foramen
   - Marrow cavity
   - Compact bone
   - Metaphysis
   - Cartilage

6. Adult bone with a single marrow cavity and closed epiphyseal plate
   - Articular cartilage
   - Spongy bone
   - Epiphyseal line
   - Periosteum
   - Marrow cavity

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

Figure 7.10

Cranial bones
Mandible
Vertebrae
Scapula
Ribs
Pelvis
Humerus
Radius
Ulna
Femur

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Bone Growth and Remodeling

- **Ossification** continues throughout life with the growth and remodeling of bones

- Bones grow in two directions
  - Length
  - Width
X-Ray of Child’s Hand
Epiphyseal Plates

Figure 7.11

Diaphysis
Epiphysis
Epiphyseal plate
Metacarpal bone
Epiphyseal plates

Courtesy of Utah Valley Regional Medical Center, Department of Radiology
Bone Elongation

- **Epiphyseal plate**—cartilage transitions to bone
  - Functions as *growth zone* where bone elongates
  - Has typical hyaline cartilage in the middle with transition zones on each side where cartilage is replaced by bone
  - **Metaphysis** is zone of transition facing the marrow cavity
- **This is interstitial growth**—growth from within
  - Bone elongation is a result of cartilage growth within the epiphyseal plate
  - Epiphyses close when cartilage is gone—**epiphyseal line** of spongy bone marks site of former epiphyseal plate
    - Lengthwise growth is finished
    - Occurs at different ages in different bones
Zones of the Metaphysis

1. **Zone of reserve cartilage**
   Typical histology of resting hyaline cartilage

2. **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

4. **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

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Dwarfism

• **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

Figure 7.13
Bone Widening and Thickening

- **Appositional growth**—occurs at bone surface
  - Continual growth in diameter and thickness
  - Intramembranous ossification
  - Osteoblasts of inner periosteum deposit osteoid tissue
    - Become trapped as tissue calcifies
  - Lay down matrix in layers parallel to surface
    - Forms *circumferential lamellae*
    - Osteoclasts of endosteum enlarge marrow cavity
Bone Remodeling

• **Bone remodeling** (absorption and deposition) occurs throughout life—10% of skeleton 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
    • Remodeling is a collaborative and precise action of osteoblasts and osteoclasts
    • Bony processes grow larger in response to mechanical stress
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 and Resorption

- Mineral deposition (mineralization)—process in which calcium, phosphate, and other ions are taken from blood and deposited in bone
  - Osteoblasts produce collagen fibers that spiral the length of the osteon
  - Fibers become encrusted with minerals
    - Hydroxyapatite crystals form at solubility product—critical level of calcium times phosphate concentration
    - First few crystals act as seed crystals that attract more calcium and phosphate from solution
  - Abnormal calcification (ectopic ossification)—formation of a calculus (calcified mass) in an otherwise soft organ such as a lung, brain, eye, muscle, tendon, or artery (arteriosclerosis)
Mineral Deposition and Resorption

- **Mineral resorption**—process of dissolving bone and releasing minerals into blood
  - Performed by **osteoclasts** at **ruffled border**
  - **Hydrogen pumps** in membranes secrete hydrogen into space between osteoclast and bone surface
  - **Chloride ions** follow by electrical attraction
  - **Hydrochloric acid** (pH 4) dissolves bone minerals
  - **Acid phosphatase** enzyme digests collagen

- **Orthodontic appliances (braces) reposition teeth through resorption and deposit**
  - Tooth moves because osteoclasts dissolve bone ahead of tooth; osteoblasts deposit bone behind the tooth
Calcium Homeostasis

• 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
Calcium Homeostasis

• Total of about 1,100 g of calcium in adult body with 99% of it in bones
  – Most exists as part of hydroxyapatite, but a little is in a form that is easily exchanged with the blood
  – About 18% of skeletal calcium is exchanged with blood each year

• Normal calcium concentration in blood plasma is 9.2 to 10.4 mg/dL
  – 45% as Ca$^{2+}$ that can diffuse across capillary walls and affect other tissues
  – Rest in reserve, bound to plasma proteins
Calcium Homeostasis

• **Hypocalcemia**—deficient calcium in blood
  – Changes membrane potentials and causes overly excitable nervous system and tetany (muscle spasms)
    • **Laryngospasm** can cause suffocation
  – Caused by vitamin D deficiency, diarrhea, thyroid tumors, underactive parathyroid glands
  – Pregnancy and lactation increase risk of hypocalcemia

• **Hypercalcemia**—excessive calcium levels
  – Makes ion channels less responsive and thus nerve and muscle are less excitable
    • Can cause emotional disturbance, muscle weakness, sluggish reflexes, cardiac arrest
  – Hypercalcemia rarely occurs
Calcium Homeostasis

• 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

- **Calcitriol**—most active form of vitamin D
- **Produced by actions of skin, liver, and kidneys**
  - Epidermal keratinocytes use UV radiation to convert 7-dehydrocholesterol to **previtamin D$_3$**; warm sun on skin converts this to **vitamin D$_3$**
  - Liver adds hydroxyl group converting that to **calcidiol**
  - Kidney adds hydroxyl group converting that to **calcitriol**
Calcitriol

• Calcitriol is a hormone that raises blood calcium level
  – Mainly, it increases calcium absorption by small intestine
  – It also increases calcium resorption from the skeleton
    • Stimulates osteoblasts to release RANKL, a chemical that stimulates production of more osteoclasts
  – It weakly promotes kidney reabsorption of calcium ions, so less lost in urine
Calcitriol Synthesis and Action

Figure 7.14
Calcitriol

- Calcitriol is also necessary for bone deposition—helping provide adequate calcium and phosphate
- Inadequate calcitriol results in abnormal softness of bones in children (rickets) and in adults (osteomalacia)
Calcium Homeostasis

Calcitriol, calcitonin, and PTH maintain normal blood calcium concentration

Figure 7.15
Calcitonin

• **Calcitonin**—secreted by C cells (clear cells) of thyroid gland when blood calcium levels rise too high

• **Lowers blood calcium concentration in two ways:**
  – Inhibits osteoclasts thereby reducing bone resorption
  – Stimulates osteoblasts to deposit calcium into bone

• **Important in children, weak effect in adults**
  – Osteoclasts more active in children due to faster remodeling

• **May inhibit bone loss in pregnant and lactating women**
Parathyroid Hormone

- Parathyroid hormone (PTH)—secreted by parathyroid glands on posterior surface of thyroid
- PTH released when calcium levels low in blood
- PTH raises calcium blood level by four mechanisms
  - Stimulates osteoblasts to secrete RANKL, thereby increasing osteoclast population and bone resorption
  - Promotes calcium reabsorption by kidneys, so 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
Calcium Homeostasis

(a) Correction for hypercalcemia

Figure 7.16a
Calcium Homeostasis

(b) Correction for hypocalcemia

Figure 7.16b
Phosphate Homeostasis

- Average adult has 500 to 800 g phosphorus with 85% to 90% of it in the bones
- Normal plasma concentration is 3.5 to 4.0 mg/dL
- Occurs in two main forms
  - $\text{HPO}_4^{2-}$ and $\text{H}_2\text{PO}_4^-$ (monohydrogen and dihydrogen phosphate ions)
- Phosphate levels are not regulated as tightly as calcium levels
- Calcitriol raises phosphate levels by promoting its absorption by small intestine
- PTH lowers blood phosphate levels 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

(Continued)

– Girls grow faster than boys and reach full height earlier
  • Estrogen has stronger effect than testosterone on bone growth
– Males grow for a longer time and also 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**—branch of medicine dealing with prevention and correction of injuries and disorders of bones, joints, and muscles
  – Name implies its origin as field treating skeletal deformities in children

• **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 (example: in a fall)

• Pathological fracture—break in a bone weakened by disease (such as bone cancer or osteoporosis)
  – Usually caused by a stress that would not break a healthy bone

• Fractures classified by structural characteristics
  – Direction of fracture line
  – Break in the skin
  – Multiple pieces
    • Example: comminuted—three or more pieces
Types of Bone Fractures

Figure 7.17

(a) Nondisplaced
(b) Displaced
(c) Comminuted
(d) Greenstick

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Healing of Fractures

Figure 7.18

1. **Hematoma formation**
The hematoma is converted to granulation tissue by invasion of cells and blood capillaries.

2. **Soft callus formation**
Deposition of collagen and fibrocartilage converts granulation tissue to a soft callus.

3. **Hard callus formation**
Osteoblasts deposit a temporary bony collar around the fracture to unite the broken pieces while ossification occurs.

4. **Bone remodeling**
Small bone fragments are removed by osteoclasts, while osteoblasts deposit spongy bone and then convert it to compact bone.

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The Treatment of Fractures

• **Closed reduction**—procedure in which 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

• Fractures of the femur in children often treated with **traction**
  – Aligns bone fragments by overriding force of the strong thigh muscles

• Hip fractures in older adults are usually pinned and early walking is encouraged
  – Fractures taking more than 2 months to heal may be treated with electrical stimulation which suppresses effects of parathyroid hormone
Open Reduction of an Ankle Fracture

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 bone density in both sexes; inhibits resorption by osteoclasts

- Postmenopausal white women at greatest risk
  - Ovaries cease to secrete estrogen
  - White women 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 which are poor in: calcium, protein, vitamins C and D

- Osteoporosis also seen in young female athletes with low body fat causing them to stop ovulating and decrease estrogen secretion
Osteoporosis (Continued)

• 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 bone-building diet between ages 25 and 40
Figure 7.20 a,b

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