Bones and Skeletal Tissues: Part B

Bone Development
- Osteogenesis (ossification)—bone tissue formation
- Stages
  - Bone formation—begins in the 2nd month of development
  - Postnatal bone growth—until early adulthood
  - Bone remodeling and repair—lifelong

Two Types of Ossification
1. Intramembranous ossification
   - Membrane bone develops from fibrous membrane
   - Forms flat bones, e.g. clavicles and cranial bones
2. Endochondral ossification
   - Cartilage (endochondral) bone forms by replacing hyaline cartilage
   - Forms most of the rest of the skeleton

Endochondral Ossification
- Uses hyaline cartilage models
- Requires breakdown of hyaline cartilage prior to ossification

Postnatal Bone Growth
- Interstitial growth:
  - ↑ length of long bones
- Appositional growth:
  - ↑ thickness and remodeling of all bones by osteoblasts and osteoclasts on bone surfaces

Growth in Length of Long Bones
- Epiphyseal plate cartilage organizes into four important functional zones:
  - Proliferation (growth)
  - Hypertrophic
  - Calcification
  - Ossification (osteogenic)
Hormonal Regulation of Bone Growth
• Growth hormone stimulates epiphyseal plate activity
• Thyroid hormone modulates activity of growth hormone
• Testosterone and estrogens (at puberty)
  • Promote adolescent growth spurts
  • End growth by inducing epiphyseal plate closure

Bone Deposit
• Occurs where bone is injured or added strength is needed
• Requires a diet rich in protein; vitamins C, D, and A; calcium; phosphorus; magnesium; and manganese

Bone Deposit
• Sites of new matrix deposit are revealed by the
  • Osteoid seam
    • Unmineralized band of matrix
  • Calcification front
    • The abrupt transition zone between the osteoid seam and the older mineralized bone

Bone Resorption
• Osteoclasts secrete
  • Lysosomal enzymes (digest organic matrix)
  • Acids (convert calcium salts into soluble forms)
• Dissolved matrix is transcytosed across osteoclast, enters interstitial fluid and then blood

Control of Remodeling
• What controls continual remodeling of bone?
  • Hormonal mechanisms that maintain calcium homeostasis in the blood
  • Mechanical and gravitational forces

Hormonal Control of Blood Ca$^{2+}$
• Calcium is necessary for
  • Transmission of nerve impulses
  • Muscle contraction
  • Blood coagulation
  • Secretion by glands and nerve cells
• Cell division

**Hormonal Control of Blood Ca\(^{2+}\)**
- Primarily controlled by parathyroid hormone (PTH)
  - Blood Ca\(^{2+}\) levels
    - Parathyroid glands release PTH
      - PTH stimulates osteoclasts to degrade bone matrix and release Ca\(^{2+}\)
        - Blood Ca\(^{2+}\) levels

**Hormonal Control of Blood Ca\(^{2+}\)**
- May be affected to a lesser extent by calcitonin
  - Blood Ca\(^{2+}\) levels
    - Parafollicular cells of thyroid release calcitonin
      - Osteoblasts deposit calcium salts
        - Blood Ca\(^{2+}\) levels
- Leptin has also been shown to influence bone density by inhibiting osteoblasts

**Response to Mechanical Stress**
- Wolff’s law: A bone grows or remodels in response to forces or demands placed upon it
- Observations supporting Wolff’s law:
  - Handedness (right or left handed) results in bone of one upper limb being thicker and stronger
  - Curved bones are thickest where they are most likely to buckle
  - Trabeculae form along lines of stress
  - Large, bony projections occur where heavy, active muscles attach

**Classification of Bone Fractures**
- Bone fractures may be classified by four “either/or” classifications:
  1. Position of bone ends after fracture:
     - Nondisplaced—ends retain normal position
     - Displaced—ends out of normal alignment
  2. Completeness of the break
     - Complete—broken all the way through
     - Incomplete—not broken all the way through

**Classification of Bone Fractures**
3. Orientation of the break to the long axis of the bone:
   • Linear—parallel to long axis of the bone
   • Transverse—perpendicular to long axis of the bone
4. Whether or not the bone ends penetrate the skin:
   • Compound (open)—bone ends penetrate the skin
   • Simple (closed)—bone ends do not penetrate the skin

Common Types of Fractures
• All fractures can be described in terms of
  • Location
  • External appearance
  • Nature of the break

Stages in the Healing of a Bone Fracture
1. Hematoma forms
   • Torn blood vessels hemorrhage
   • Clot (hematoma) forms
   • Site becomes swollen, painful, and inflamed

Stages in the Healing of a Bone Fracture
2. Fibrocartilaginous callus forms
   • Phagocytic cells clear debris
   • Osteoblasts begin forming spongy bone within 1 week
   • Fibroblasts secrete collagen fibers to connect bone ends
   • Mass of repair tissue now called fibrocartilaginous callus

Stages in the Healing of a Bone Fracture
3. Bony callus formation
   • New trabeculae form a bony (hard) callus
   • Bony callus formation continues until firm union is formed in ~2 months

Stages in the Healing of a Bone Fracture
4. Bone remodeling
   • In response to mechanical stressors over several months
   • Final structure resembles original

Homeostatic Imbalances
• Osteomalacia and rickets
  • Calcium salts not deposited
  • Rickets (childhood disease) causes bowed legs and other bone
deformities
• Cause: vitamin D deficiency or insufficient dietary calcium

Homeostatic Imbalances
• Osteoporosis
  • Loss of bone mass—bone resorption outpaces deposit
  • Spongy bone of spine and neck of femur become most susceptible to fracture
  • Risk factors
    • Lack of estrogen, calcium or vitamin D; petite body form; immobility; low levels of TSH; diabetes mellitus

Osteoporosis: Treatment and Prevention
• Calcium, vitamin D, and fluoride supplements
• ↑ Weight-bearing exercise throughout life
• Hormone (estrogen) replacement therapy (HRT) slows bone loss
• Some drugs (Fosamax, SERMs, statins) increase bone mineral density

Paget’s Disease
• Excessive and haphazard bone formation and breakdown, usually in spine, pelvis, femur, or skull
• Pagetic bone has very high ratio of spongy to compact bone and reduced mineralization
• Unknown cause (possibly viral)
• Treatment includes calcitonin and biphosphonates

Developmental Aspects of Bones
• Embryonic skeleton ossifies predictably so fetal age easily determined from X rays or sonograms
• At birth, most long bones are well ossified (except epiphyses)

Developmental Aspects of Bones
• Nearly all bones completely ossified by age 25
• Bone mass decreases with age beginning in 4th decade
• Rate of loss determined by genetics and environmental factors
• In old age, bone resorption predominates