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M1 Musculoskeletal Sequence
Histology
Bone Formation and Remodeling

Fall 2009
Bone

**Cells:** Osteoblasts, Osteocytes, Osteoclasts

**Fibers:** Type 1 Collagen

**Bone Matrix:**

- Ground Substance
  - GAGs: Hyaluronan, Chondroitin & Keratan Sulfate
  - Proteoglycans: short core proteins and relatively fewer GAG side chains than in cartilage.

Hydroxyapatite crystals \([\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2]\): Calcium phosphate
Haversian system or osteon

Bony spicules or trabeculae

Compact and spongy bone

Haversian system (osteon)
Differentiation of chondrogenic cells

- **Perichondrium**
- **Chondroblasts**
- **Chondrocytes**
- **Isogenous group**

Diagram:

1. Surrounding connective tissue
2. Perichondrium (fibrous layer)
3. Lacuna

Kierszenbaum, p. 115
Inner and outer circumferential lamellae

Forming osteon or Haversian system (osteoblasts, osteoid)

Outer circumferential lamellae

Osteon

Volkmann's canal

Haversian canal

Inner circumferential lamellae

Resorption cavity

Interstitial lamellae

Osteon

HC

Inner Circumferential Lamellae

Bone Marrow

Weiss, 6th ed., p. 222
Sponge, cancellous or trabecular Bone

Bony spicules form trabeculae or trabecular network

Cells of bone
Bone Formation

**Intramembranous Ossification:** Forms directly from the embryonic mesenchyme.

(Most flat bones of the skull and face)

**Endochondral Ossification:** Initially hyaline cartilage model is formed, which is replaced by bone.

(Long bones of the extremities)
Basic Mechanism of Bone Formation

The process of bone deposition is the same in both endochondral and intramembranous ossifications – osteoblasts laying down layers of bone.

Both endochondrial and intramembranous bone formations can make spongy and compact bone.

Long bones start as cartilage and so form endochondrally. Flat bones do not begin as cartilage but rather form intramembranously.

In both types of formation, however, at the cellular level, bone is deposited appositionally.
BMP7 induces the expression of Cbfa1.

BMP: bone morphogenetic protein

Cbfa 1: core binding factor family gene

Kierszenbaum, p. 125
Vitamin D₃ (1α,25-dihydroxycholecalciferol) regulates the expression of osteocalcin, a protein with high binding affinity for hydroxyapatite.

5 Vitamin D₃

Alkaline phosphatase

Parathyroid hormone

Growth hormone (from the hypophysis)

Liver

Insulin-like growth factor-1 (IGF-1) (also called somatomedin C)

3 Type 1 collagen

4 Noncollagenous proteins

Osteocalcin
Osteonectin
Osteopontin
Bone sialoprotein
Osteoprotegerin
Macrophage-colony stimulating factor

© PD-INEL Kierszenbaum p. 122
Mesenchymal cells and Center of Osteogenesis

[Image of a diagram showing mesenchyme, bone blastema, osteoblasts, and primary bone tissue.]
Intramembranous Bone Formation

- periosteum
- Forming bone trabeculae
Intramembranous Bone Formation

Periosteum

osteoblasts
Sharpey’s Fibers

Periosteum

Periosteum
Bone forming cells and bone modeling

- Active osteoclasts
- Inactive osteoblasts
- Osteoid
- Periosteum
- Osteoclasis
EM of Active Osteoblasts
Unmineralized (osteoid) and Mineralized Bone

Osteocalcin – Ca^{++}
Matrix vesicles: alkaline phosphatase and pyrophosphatase – PO_4^{-}
Crystalization of CaPO_4

\[ \text{[Ca}_{10}(\text{PO}_4)_6(\text{OH})_2] \]
Osteoclasts

Howship’s lacuna
Osteoclast (EM)

Note the ruffled border of the cell and resorbing bone matrix
Osteoclast and Bone Resorption

Image of osteoclast physiologic activity removed

Original source: Kierszenbaum, p. 124
Formation of Bone Trabeculae
Conversion of trabecular bone to compact bone
Formation of Osteons
Immature and Mature Bone
(nonlamellar, bundle, or woven bone)
Intramembranous ossification of facial (maxillary) bone
Long bones start as cartilage and so form endochondrally. Flat bones form intramembranously and do not begin as cartilage.
Endochondral Bone Formation

Hyaline cartilage remains:
1. articular surface
2. epiphyseal (growth) plate
Formation of Bone Collar

Bone Growth

Source Undetermined
Periosteal Bud

Bone Growth

Source Undetermined
Periosteal Bud
New bone is deposited on the outer surface of the diaphysis by successive generations of osteoblasts arising from osteogenic cells of the periosteum.

To compensate this growth and prevent bone from becoming too thick and heavy, older bone on the inner surface of the shaft is resorbed by osteoclasts so as to widen the marrow cavity.
Epiphyseal Plate and Secondary Ossification Center

Bone Growth

Wheater's 5th ed., p. 199
Epiphyseal Plate and Growth in Length of Long Bones

Wheater's 5th ed., p. 199

Junqueira & Carneiro, 10th ed., p. 150
Secondary Ossification Center, Epiphyseal Plate and Metaphysis

Source Undetermined

Wheater’s 5th ed., p. 199
Epiphyseal Plate: Zone of

1. Resting Cartilage
2. Proliferation
3. Hypertrophy
4. Calcified Cartilage and Bone Deposition
Zone of:

- Proliferation

- Hypertrophy

- Calcification and Bone deposition

Tide mark
Bone Growth in Length and Diameter
Mature Bone
Mature (adult) Bone
Repair of Fractured Bone

Modified from Junqueira & Carneiro 10th ed., p. 154
Bone Remodeling

Bone remodeling occurs continuously. It is the process whereby bone is being resorbed by osteoclasts and is then replaced by new bone deposited by ostoblasts. The activity of the two cell types is coupled and balanced to maintain the normal internal structure and shape of a bone.

Remodeling:
- Structural remodeling during bone growth.
- Internal remodeling to replace worn out bone.
- Compensatory remodeling in responses to prevailing stresses, injury or changes in metabolic activities.
Intramembranous ossification of facial (maxillary) bone
Bone Remodeling
Erosion (resorption) Tunnel
Resorption tunnel

[Diagram of the resorption tunnel with labeled parts: Cutting Cone, Reversal Zone, Closing Cone, A, B, C, D, E, O, G, I, II, III, IV.]

- Forming Resorption Cavity
- Resorption Cavity
- Forming Haversian System
- Completed Haversian System

Weiss, 6th ed., p. 243
Bone Remodeling

Intermediate, or interstitial, lamellae

First-generation haversian system
Second-generation haversian system
Third-generation haversian system

Modified from Junqueira & Carneiro 10th ed., p. 147
Osteons (os) and Interstitial lamellae (il)
Age-related Bone Loss

Osteoporosis

Bone Resorption > Deposition

Weiss, 5th ed., p. 245
Nutritional Effects on Bone

**Scurvy:** Insufficient level of dietary vitamin C leading to inadequate hydroxylation of proline of collagen (unable to form triple-helix).

**Rickets:** In the absence of an adequate level of vitamin D, ossification of epiphyseal cartilage is disturbed, leading to formation of a mixture of uncalcified cartilage and poorly calcified bone matrix in the metaphysis.

**Osteomalacia (adult rickets):** Accumulation of an excessive amount of uncalcified osteoid due to a prolonged deficiency of calcium and vitamin D.
Regulation of Blood Calcium Level

When the blood level of calcium falls:
secretion of parathyroid hormone is increased.

The hormone acts on osteoblasts to suppress their bone deposition and induce the secretion of osteoclast-stimulating factor.
Activated osteoclasts resorb bone, releasing calcium into the blood to restore the normal level.

When the blood level of calcium increases:
secretion of parathyroid hormone is suppressed.

Osteoblasts continue deposition of bone.
secretion of calcitonin (a thyroid hormone) is increased. Calcitonin acts directly on the osteoclasts to inhibit bone resorption.
Bone formation and remodeling
Learning objectives - 1

• Be able to describe, as well as recognize in section, the process of **intramembranous bone formation**, including the process whereby cancellous bone is converted into compact bone.

• Be able to recognize osteoblasts, osteocytes and osteoclasts and know their role in the process of intramembranous bone formation and conversion of cancellous bone to compact bone.

• Be able to recognize mature and immature (mottled or woven) bone.

• Understand the process of **endochondral bone formation** and know how a cartilage model is broken down and replaced by bone (e.g. formation of a bony collar, chondrocyte death, invasion of an osteogenic bud from the periosteum, etc.).

• Understand how the diameter of a long bone increases.
Bone formation and remodeling
Learning objectives - 2

- Understand how the epiphyseal growth mechanism results in elongation of a long bone.

- Be able to recognize the different zones of a cartilage growth plate and describe the processes of osteogenesis taking place in each zone (e.g. zone of resting cartilage, proliferation, hypertrophy, calcification and ossification).

- Be able to describe the process and types of bone remodeling and to recognize cells and structures involved in the process.

- Be able to describe how fracture repair resembles the process of endochondral bone formation.
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