Stages of Intramembranous Ossification

- Results in the formation of cranial bones of the skull (frontal, perietal, occipital, and temporal bones) and the clavicles.
- All bones formed this way are flat bones
- An ossification center appears in the fibrous connective tissue membrane
- Bone matrix is secreted within the fibrous membrane
- Woven bone and periosteum form
- Bone collar of compact bone forms, and red marrow appears
Stages of Intramembranous Ossification

1. An ossification center appears in the fibrous connective tissue membrane.
   - Selected centrally located mesenchymal cells cluster and differentiate into osteoblasts, forming an ossification center.
2. Bone matrix (osteoid) is secreted within the fibrous membrane.
   - Osteoblasts begin to secrete osteoid, which is mineralized within a few days.
   - Trapped osteoblasts become osteocytes.
Stages of Intramembranous Ossification

3 Woven bone and periosteum form.
   • Accumulating osteoid is laid down between embryonic blood vessels, which form a random network. The result is a network (instead of lamellae) of trabeculae.
   • Vascularized mesenchyme condenses on the external face of the woven bone and becomes the periosteum.
Stages of Intramembranous Ossification

Figure 6.7.4

Bone collar of compact bone forms and red marrow appears.

- Trabeculae just deep to the periosteum thicken, forming a woven bone collar that is later replaced with mature lamellar bone.
- Spongy bone (diploë), consisting of distinct trabeculae, persists internally and its vascular tissue becomes red marrow.
Endochondral Ossification

- Results in the formation of all of the rest of the bones
- Begins in the second month of development
- Uses hyaline cartilage “bones” as models for bone construction
- Requires breakdown of hyaline cartilage prior to ossification
- Formation begins at the primary ossification center
Endochondral Ossification

- The perichondrium covering the hyaline cartilage “bone” is infiltrated with blood vessels converting it to vascularized periosteum.

- This change in nutrition causes the underlying mesenchymal cells to specialize into osteoblasts.
Stages of Endochondral Ossification

- Formation of bone collar
- Cavitation of the hyaline cartilage
- Invasion of internal cavities by the periosteal bud, and spongy bone formation
- Formation of the medullary cavity; appearance of secondary ossification centers in the epiphyses
- Ossification of the epiphyses, with hyaline cartilage remaining only in the epiphyseal plates
Stages of Endochondral Ossification

Figure 6.8

1. Formation of bone collar around hyaline cartilage model.
2. Cavitation of the hyaline cartilage within the cartilage model.
3. Invasion of internal cavities by the periosteal bud and spongy bone formation.
4. Formation of the medullary cavity as ossification continues; appearance of secondary ossification centers in the epiphyses in preparation for stage 5.
5. Ossification of the epiphyses; when completed, hyaline cartilage remains only in the epiphyseal plates and articular cartilages.
Postnatal Bone Growth

- Growth in length of long bones
  - Cartilage on the side of the epiphyseal plate closest to the epiphysis is relatively inactive
  - Cartilage abutting the shaft of the bone organizes into a pattern that allows fast, efficient growth
  - Cells of the epiphyseal plate proximal to the resting cartilage form three functionally different zones: growth, transformation, and osteogenic
Details of Stages of Endochondral Ossification

- 1) Bone collar forms around the diaphysis of the hyaline cartilage model
  - Osteoblasts of the converted periosteum secrete osteoid against the hyaline cartilage diaphysis encasing it in a bone collar
Details of Stages of Endochondral Ossification

- 2) cartilage in the center of the diaphysis calcifies and then cavitates
  - Chondrocytes w/I the shaft hypertrophy & signal surrounding cartilage matrix to calcify.
  - Chondrocytes die due to lack of nutrients (impermeability of calcified matrix)
  - Matrix deteriorates thus opening up cavities
Details of Stages of Endochondral Ossification

3) Periosteal bud invades the internal cavities and spongy bone forms

- The forming cavities are invaded by a collection of elements
- Periosteal bud contains a nutrient artery and vein, lymphatics, nerve fibers, red marrow elements, osteoblasts, and osteoclasts
- Osteoclasts erode the calcified cartilage matrix & osteoblasts secrete osteoid around the remaining hyaline cartilage forming bone-covered cartilage trabeculae (the formation of spongy bone)
Details of Stages of Endochondral Ossification

4) The diaphysis elongates and a medullary cavity forms

- Osteoclasts open up a medullary cavity by breaking down the newly formed spongy bone
- Cartilage is growing, bones being calcified and eroded and then replaced by bony spicules on the epiphyseal surfaces facing the medullary cavity
Details of Stages of Endochondral Ossification

- 5) The epiphysis ossify
  - Secondary ossification centers appear in one or both epiphyses.
  - Steps 1-4 occur there except no medullary cavity forms
Details of Stages of Endochondral Ossification

- Finally, hyaline cavity remains at:

  - Epiphyseal surface (articular cartilage)
  - Epiphyseal plates (junction of the diaphysis and the epiphysis)
Functional Zones in Long Bone Growth

- Growth zone – cartilage cells undergo mitosis, pushing the epiphysis away from the diaphysis

- Transformation zone – older cells enlarge, the matrix becomes calcified, cartilage cells die, and the matrix begins to deteriorate

- Osteogenic zone – new bone formation occurs
Postnatal Bone Growth

- Long bones lengthen by interstitial growth of the epiphyseal plates, and increase thickness by appositional growth.
Long Bone Growth and Remodeling

- Growth occurs at the epiphyseal plate (the cartilage abutting the diaphysis) called the Growth Zone

- Cartilage cells stack and divide quickly **pushing the epiphysis away from the diaphysis** causing bone to lengthen

- The older chondrocytes die & deteriorate forming the Calcification Zone

- The resulting calcified spicules become part of the Ossification Zone and are invaded by marrow elements from the medullary cavity
Growth in Length of Long Bone

- **Resting (quiescent) zone**
- **Growth (proliferation) zone**
  - Cartilage cells undergo mitosis
- **Hypertrophic zone**
  - Older cartilage cells enlarge
- **Calcification zone**
  - Matrix becomes calcified; cartilage cells die; matrix begins deteriorating
- **Ossification (osteogenic) zone**
  - New bone formation is occurring
Long Bone Growth and Remodeling

Growth
Bone grows in length because:

1. Cartilage grows here
2. Cartilage replaced by bone here
3. Cartilage grows here
4. Cartilage replaced by bone here

Remodeling
Growing shaft is remodeled by:

1. Bone resorbed here
2. Bone added by appositional growth here
3. Bone resorbed here

Figure 6.10
Long Bone Growth and Remodeling

- Longitudinal growth is accompanied by remodelling which includes appositional growth to thicken bone

- Includes bone formation & reabsorption

- Bone growth stops around age 21 for males and 18 for females when the epiphysis & diaphysis fuse (epiphyseal plate closure)
Long Bone Growth and Remodeling

- Growth in width (thickness) via appositional growth
- Osteoblasts beneath the periosteum secrete bone matrix on the external bone surface as osteoclasts on the endosteal surface of the diaphysis remove bone
Hormonal Regulation of Bone Growth During Youth

- During infancy and childhood, epiphyseal plate activity is stimulated by growth hormone (released by the anterior pituitary).

- During puberty, testosterone and estrogens:
  - Initially promote adolescent growth spurts
  - Cause masculinization and feminization of specific parts of the skeleton
  - Later induce epiphyseal plate closure, ending longitudinal bone growth
Bone Remodeling

- Remodeling units – adjacent osteoblasts and osteoclasts deposit and resorb bone at peristomal and endostemal surfaces
Bone Deposition

- 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
- Alkaline phosphatase is essential for mineralization of bone
Bone Deposition

- Sites of new matrix deposition are revealed by the:
  - Osteoid seam – unmineralized band of bone matrix
  - Calcification front – abrupt transition zone between the osteoid seam and the older mineralized bone
Bone Resorption

- Accomplished by osteoclasts (giant, multinucleated cells that arise from the same stem cells that produce macrophages)
- Resorption bays – grooves formed by osteoclasts as they break down bone matrix
- The osteoclast membrane seals off the bone that is to be broken down
- Resorption involves osteoclast secretion of:
  - Lysosomal enzymes that digest organic matrix
  - Hydrochloric acid that converts calcium salts into soluble forms
  - The broken down products are endocytosed (transcytosed) and released into the interstitial fluid and blood
Control of Remodeling

- Two control loops regulate bone remodeling
  - Hormonal mechanism maintains calcium homeostasis in the blood (negative feedback)
  - Mechanical and gravitational forces acting on the skeleton
Hormonal Mechanism

- Rising blood Ca\(^{2+}\) levels trigger the thyroid to release calcitonin
- Calcitonin inhibits bone resorption and stimulates calcium salt deposit in bone
- Falling blood Ca\(^{2+}\) levels signal the parathyroid glands to release parathyroid hormone (PTH)
- PTH signals osteoclasts to degrade bone matrix and release Ca\(^{2+}\) into the blood
Hormonal Control of Blood Ca

Calcium homeostasis of blood: 9–11 mg/100 ml

Rising blood Ca\(^{2+}\) levels

Imbalance

Imbalance

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Figure 6.11
Hormonal Control of Blood Ca

Rising blood Ca\(^{2+}\) levels

Imbalance

Calcium homeostasis of blood: 9–11 mg/100 ml

Imbalance

Thyroid gland
Hormonal Control of Blood Ca

Thyroid gland

Rising blood Ca^{2+} levels

Calcitonin secreted

Calcium homeostasis of blood: 9–11 mg/100 ml

Imbalance
Hormonal Control of Blood Ca

Calcitonin secreted

Thyroid gland

Calcitonin stimulates calcium salt deposit in bone

Rising blood Ca\(^{2+}\) levels

Calcium homeostasis of blood: 9–11 mg/100 ml

Imbalance
Hormonal Control of Blood Ca

Figure 6.11

Calcitonin stimulates calcium salt deposit in bone

Thyroid gland

Calcitonin secreted

Rising blood Ca^{2+} levels

Calcium homeostasis of blood: 9–11 mg/100 ml
Hormonal Control of Blood Ca

Calcium homeostasis of blood: 9–11 mg/100 ml

Falling blood Ca^{2+} levels

Imbalance
Hormonal Control of Blood Ca

Parathyroid glands release parathyroid hormone (PTH) in response to falling blood calcium levels. Calcium homeostasis of blood: 9–11 mg/100 ml.

Figure 6.11
Hormonal Control of Blood Ca

Calcium homeostasis of blood: 9–11 mg/100 ml

Falling blood Ca$^{2+}$ levels

Parathyroid glands release parathyroid hormone (PTH)

PTH

Imbalance

Imbalance

Thyroid gland

Parathyroid glands

Figure 6.11
Hormonal Control of Blood Ca

Parathyroid glands release parathyroid hormone (PTH)

Thyroid glands release calcium (Ca) into blood

Osteoclasts degrade bone matrix and release Ca^{2+} into blood

Calcium homeostasis of blood: 9–11 mg/100 ml

Falling blood Ca^{2+} levels

Imbalance

Imbalance

Figure 6.11
Hormonal Control of Blood Ca
ERROR:

OFFENDING COMMAND:

STACK:

ERROR: undefined