Bone

Ossification
Bone ossification and callus formation

Objectives: Students must be able to identify:

- Types of ossifications and their cells.
- Osteogenesis.
- Bone Fracture.
- Callus formation (bone healing).
- Clinical disorders.
Ossification = Osteogenesis
Ossification = Osteogenesis

- Parts of the fetal skeleton form during the first few weeks after conception
- By the end of the 8th week, the skeletal pattern is formed: cartilage & connective tissue membranes
Bone Formation - Ossification

All embryonic CT begins as mesenchyme
- provides template for ossification

Two types of ossification:

Intramembranous ossification:
- bone forms directly from or within fibrous CT membranes

Endochondral ossification:
- bone forms from hyaline cartilage models
Intramembranous ossification

- Begins with osteoblast differentiation
- Dermal bones produced
- Begins at ossification center
Intramembranous Ossification

Forms flat bones of skull & mandible

**Ossification center:** forms from mesenchyme that become osteoprogenitor cells
- change into osteoblasts that deposit matrix
- matrix surrounds osteoblasts that calcify to form osteocytes

Osteoblast depositing new bone matrix
Intramembranous Ossification, cont.

Calcifying matrix centers join to form bridges of trabeculae, becoming spongy bone with red marrow

Mesenchyme on the bone surface condenses into periosteum

Compact bone replaces superficial layers of spongy bone
**Intramembranous Ossification**

**STEP 1:**
Mesenchymal cells aggregate, differentiate, and begin the ossification process. The bone expands as a series of spicules that spread into surrounding tissues.

**STEP 2:**
As the spicules interconnect, they trap blood vessels within the bone.

**STEP 3:**
Over time, the bone assumes the structure of spongy bone. Areas of spongy bone may later be removed, creating marrow cavities. Through remodeling, spongy bone formed in this way can be converted to compact bone.
Intramembranous Ossification

1. Development of ossification center
2. Calcification
3. Formation of trabeculae
4. Development of the periosteum
1. Development of cartilage model
2. Growth of cartilage model
3. Development of primary ossification center
4. Development of the medullary cavity
5. Development of secondary ossification center
6. Formation of articular cartilage and epiphyseal plate
Endochondral ossification

- Cartilage model gradually replaced by bone
  - Increasing bone length
- Growth occurs by interstitial & Appositional
- Appositional growth increases bone diameter
- Stages of Ossification are:
  1. proliferation
  2. hypertrophy
  3. calcified zone
  4. chondrocyte die
  5. ossification zone epiphyseal plate: connect the two epiphyses and diaphysis and responsible for the growth in length of the bone
1. Development of Cartilage Model

Mesenchyme forms cartilage model of bone during development.
Growth of the cartilage template

• Two mechanisms:
  • Appositional growth \(\rightarrow\) by chondroblasts
    new cartilage is added on the surface by
    recruiting chondroblasts from the inner layer
    of the perichondrium
  • Interstitial growth \(\rightarrow\) by chondrocytes
    new cartilage is formed within the cartilaginous
    template by chondrocytes dividing and
    producing additional matrix
2. Growth of Cartilage Model

Chondrocytes divide and matrix forms
- **Interstitial growth**: in length

New matrix forms on periphery by perichondrium
- **Appositional growth**: in width

Cells in mid-region burst & lower pH
- triggers calcification
- destroys chondrocytes
Step 1: Bone formation at the surface of the bone produces ridges that parallel a blood vessel.

Step 2: The ridges enlarge and create a deep pocket.

Step 3: The ridges meet and fuse, trapping the vessel inside the bone.

Steps 4-6: Bone deposition then proceeds inward toward the vessel, creating a typical osteon. Meanwhile, additional circumferential lamellae are deposited and the bone continues to increase in diameter. As it does, additional blood vessels will be encased.

(a) Steps in appositional bone growth
Appositional Growth

Periosteal ridges
Periosteum
Periosteal blood vessel
Perforating canal
Groove
Endosteum
Foramen
Tunnel
Central (haversian) canal
Circumferential lamellae
Periosteum
New osteon

Appositional Bone Growth animation
Appositional Bone Growth

**STEP 5:**
Capillaries and osteoblasts migrate into the epiphyses, creating secondary ossification centers.

**STEP 6:**
Soon the epiphyses are filled with spongy bone. An articular cartilage remains exposed to the joint cavity; over time it will be reduced to a thin superficial layer. At each metaphysis, an epiphysial cartilage separates the epiphysis from the diaphysis.
Interstitial Growth

4 Zones of Epiphyseal Plate:
- Zone of resting cartilage
- Zone of proliferating cartilage
- Zone of hypertrophic cartilage
- Zone of calcified cartilage
Chondrocytes are produced by mitosis on the **epiphyseal side** of plate

Will be replaced by bone on the **diaphyseal side** of plate

Plate closes between ages 18-25
- chondrocytes stop dividing
- bone replaces cartilage
  (**epiphyseal line**)
Zones of Growth, cont.

Zone of hypertrophic cartilage
- cells enlarge & remain in columns

Zone of calcified cartilage
- thin zone of mostly dead cells
- osteoclasts remove matrix
- osteoblasts & capillaries build bone over calcified cartilage
Zones of Growth, cont.

Zone of hypertrophic cartilage
- cells enlarge & remain in columns

Zone of calcified cartilage
- thin zone of mostly dead cells
- osteoclasts remove matrix
- osteoblasts & capillaries build bone over calcified cartilage
• oseopetrosis: a disease caused by a defect in osteoclast function that results in overgrowth, thickening, and hardening of bones.

• Obesity imposes significant strain on the articular cartilage, accelerating its degeneration, joint problems are far more frequent in obesity individuals.

• Chondroplastic dwarfism: results from the chondrocytes in multiplication and hypertrophy zones fail to multiply, the long bone grow slowly and stop growing early
Bone Fracture

• There are three processes involved in the healing of fractures - inflammatory, reparative and remodelling phases or 6 stages - the hematoma stage, inflammatory stage, formation of granulation tissue, soft and 'hard' callus formation, and remodelling.

• Their duration depends on age, health and nutritional status.

• Hematoma Stage: Hemorrhage, clot formation - within hours to days.

• Inflammatory Stage: Begins within 48 hours, inflammatory cells appear.
Organization and resorption of

• Granulation Tissue: From 2 days. Presence of - 12 mesenchymal cells, fibroblasts, new capillaries.

• Soft Callus: One week to several months. Callus grows and bridges the fracture site; cartilage and trabecular bone laid down.

• Hard Callus: One week to several months. When callus has sealed the bone ends. Trabecular bone.

• Remodelling: Continues for several months. Reorganization of bon.
Stages in the Healing of a Bone Fracture

• Hematoma formation
  – Torn blood vessels hemorrhage
  – A mass of clotted blood (hematoma) forms at the fracture site
  – Site becomes swollen, painful, and inflamed
Stages in the Healing of a Bone Fracture

Fibrocartilaginous callus forms

Granulation tissue (soft callus) forms a few days after the fracture
- Capillaries grow into the tissue and phagocytic cells begin cleaning debris
Stages in the Healing of a Bone Fracture

- Bony callus formation
- New bone trabeculae appear in the fibrocartilaginous callus
- Fibrocartilaginous callus converts into a bony (hard) callus
- Bone callus begins 3-4 weeks after injury, and continues until firm union is formed 2-3 months later
Stages in the Healing of a Bone Fracture

Bone remodeling
- Excess material on the bone shaft exterior and in the medullary canal is removed
- Compact bone is laid down to reconstruct shaft walls
Fracture Repair

1. Formation of fracture hematoma
2. Fibrocartilaginous callus formation
3. Bony callus formation
4. Bone remodeling
normal bone
haematoma and granulation tissue
cartilaginous callus
bony callus and cartilaginous remnants
re-modelling
healed fracture
How does a broken bone heal?

1. Blood flow increases to the area of the break. This allows nutrients and oxygen to help the healing process.

2. As bone becomes deposited, it grows stronger, and eventually remodels itself.
Aging & Bone Tissue

The loss of Ca\(^{+2}\) from bone matrix (demineralization)
- may result in osteoporosis
- rapid in women age 40-45
  (when estrogen levels decrease)
- begins after age 60 in men

Decreased rate of protein synthesis
- less collagen production
- less growth hormone
- brittle bones more likely to fracture
(a) Normal bone

(b) Osteoporotic bone
Red Marrow

- Forms Erythrocytes:
- Forms Leucocytes:
- Forms Thrombocytes:

Red color is due to hemoglobin

Location:
- Skull
- Sternum
- Clavicles
- Vertebrae
- Pelvis
- Ribs
Figure 7.4
Note the stained, developing bones of this fourteen-week fetus.
Clinical Forms

- Rickets
- Arthritis
- Gouty Arthritis (GOUT)
- Osteoporosis
- Osteosarcoma
Rickets:

- **Vitamin D deficiency** in growing children
- Unable to absorb calcium and phosphate from gut
- Inorganic bone matrix (mineral salts) lacks calcium-
- Bones deform
Clinical Forms of Arthritis

• Osteoarthritis
  – Most common chronic arthritis
  – Probably related to normal aging processes

• Rheumatoid arthritis
  – An autoimmune disease – the immune system attacks the joints
  – Symptoms begin with bilateral inflammation of certain joints
  – Often leads to deformities
Gouty Arthritis (GOUT)

- Inflammation of joints is caused by a deposition of urate (URIC ACID) crystals from the blood
- Can usually be controlled with diet
- Hereditary as it runs in families.
- This is very painful!!
Osteoporosis......

Cause is related to calcium loss due to the following dietary and behavioral patterns......

- High meat protein diets
- Phosphorylated soft drinks
- Smoking
- Lack of exercise
- High caffeine intake

Treatment:

- elimination of risk factors
- exercise
- calcium supplements
- estrogen administration
Osteosarcoma

- Most common and most malignant form of bone cancer
- Tumors arise beneath periosteum and elevate it as they grow
- Penetrate cortical bone
- Rapid spreading - cure rate is low
summary

. Bone formation by two different ways, intramembranous and endochondral ossification, and how calcium phosphate is deposited in the matrix.

. There are differences between cartilage and bone cells. Chondroplastic dwarfism and osteopetrosis are bone diseases.

. Bone fracture and formation of Soft and hard callus, aging & bone tissue and some examples of disease.
Bone Growth at an Epiphyseal Cartilage