Bone Formation:
Ossification
• Scientifically called: **Ossification or Osteogenesis**
• Before week 8 of development, human embryo skeletons are entirely **mesenchyme (fibrous membranes)** and **hyaline cartilage**.
• Ossification begins after week 8 in utero
Bone Formation: Intramembranous Ossification

Intramembranous Ossification

- Intramembranous Ossification:
  - Bone develops from within a fibrous membrane
  - All bones formed by this are flat bones.
  - Examples: Forms the cranial bones of the skull and the clavicle (collar bone).
Bone Formation: Endochondral Ossification

- **Endochondral Ossification:**
  - “endo”=within, “chondro”=cartilage
  - Bone develops by replacing hyaline cartilage
    - Forms essentially all bones below the base of the skull except the clavicles.
    - Begins second month of development.
Before ossification can occur in LONG BONES:

- Blood vessels infiltrate the membrane that surrounds the cartilage (perichondrium).
  - a. This membrane is now periosteum.
  - b. This change causes the mesenchymal cells to differentiate (change) into osteoblasts.
Bone Formation: Intramembranous Ossification

Steps:
1. OSTEOBLASTS FORM in the mesenchyme (fibrous connective tissue membrane).
   a. cells cluster and differentiate (change) into osteoblasts, forming an ossification center
Bone Formation: Intramembranous Ossification

Steps:
2. BONE IS BUILT: The Bone matrix (osteoid) is created within the fibrous membrane.
   a. Osteoblasts lay the bone matrix using collagen fibers called osteoid,
   b. The osteoid attracts Ca\(^+\) minerals and hardens.
   b. This traps the osteoblasts, turning into osteocytes.

osteoblast  osteoid  osteocyte  mesenchyme
3. Woven Bone and Periosteum Form

a. As osteoid accumulates it gets laid down between blood vessels, forming a random network of trabeculae.

- This advanced tissue is called **woven bone** (osteoid is “woven” around the vessels)

b. Mesenchymal condenses along the outside of this woven bone to form the periosteum.
Bone Formation: Intramembranous Ossification

4. Bone Collar of Compact Bone forms and Red Marrow Appears

   a. Trabeculae just under the periosteum thickens and is soon replaced with compact bone, called a bone collar
   
   b. Spongy Bone stays on the inside and red marrow fills in the spaces.
Bone Formation: Endochondral Ossification

Steps:

1. Bone collar forms around the diaphysis of the cartilage.
   - The new osteoblasts in the periosteum secrete osteoid (bone matrix) against the cartilage, wrapping it in a bone collar.
Bone Formation: Endochondral Ossification

**Steps:**

2. Cartilage in the center of the diaphysis calcifies and creates a cavity.
   - Chondrocytes (cartilage cells) in the diaphysis enlarge and signal the cartilage around it to calcify.
   - Nutrients cannot support the large cells and they die. This causes the matrix to deteriorate, creating a cavity.
   - Cartilage in the epiphysis remains healthy and grows quickly causing the bone to lengthen.
Bone Formation: Endochondral Ossification

3. Periosteal bud invades the cavity and spongy bone forms.
   – This happens in the third month in utero.
   – A nutrient artery and vein grow from the periosteum into the cavity creating the **periosteal bud**
   – The artery carries hemaopoietic tissue to form red marrow.
   – **Spongy bone forms:** Osteoclasts break down the calcified cartilage and then osteoblasts secrete osteoid around remaining hyaline cartilage fragments, forming more trabeculae.
Bone Formation: Endochondral Ossification

4. Diaphysis elongates and Medullary Cavity forms.

- As the ossification center grows, osteoclasts break down this spongy bone and form the medullary cavity.
- Cartilage cells at the epiphyses divide rapidly.
5. Epiphyses ossify.
   – Shortly before or after birth, *secondary ossification centers* appear in one or both epiphyses, so they get bone tissue.
   – This then goes through the same steps as in the diaphysis, except the spongy bone stays in the epiphysis instead of being broken down forming the medullary cavity.
Bone Formation: Endochondral Ossification

From birth until about the 21st birthday the cartilage is completely replaced by bone except:

1. On the surfaces of the epiphyses (articulating surface)
2. At the epiphyseal plate—the junction of the diaphysis and epiphysis.

At the end of growth the epiphyseal plate is ossified creating the epiphyseal line.
Bone Growth After Birth: at the epiphyseal plate

- Long bones must still lengthen and thicken
- Most bones stop growing during adolescence
- Some facial bones continue to grow throughout most of life
Bone Growth After Birth

• Lengthen:
  – On epiphysis side of epiphyseal plate, cartilage does not reproduce much.
  – On diaphysis side, cartilage organized to allow rapid growth—forms tall columns
Resting zone

**Growth zone** — cartilage cells dividing quickly

**Hypertrophic zone** — older cartilage cells enlarge and lacunae erode

**Calcification zone** — cartilage matrix calcifies and chondrocytes die

**Ossification zone** — cartilage partly eroded by osteoclasts then covered with bone matrix by osteoblasts
Bone Growth After Birth

• Thicken through bone remodeling:
  – Osteoblasts beneath the periosteum secrete osteoid on the outside of the bone
  – Slightly less breaking down than building up
    =thicker, stronger bones but not too heavy
Bone Growth After Birth

• Regulated by hormones
  – Growth hormone from anterior pituitary gland
    • GH regulated by thyroid hormones
  – Puberty: sex hormones (testosterone and estrogen)—promote growth spurt and masculine or feminine skeletal features
  – Later, sex hormones promote the closing or calcification of the epiphyseal plate, ending bone growth