ENDOCHONDRAL OSSIFICATION

Formation of the Bone Collar:

The first bone tissue appears as a collar surrounding the main shaft (diaphysis) of the cartilage model.

This collar is formed by active osteoblasts (bone-forming cells) within the surrounding perichondrium (membrane covering cartilage).

The collar restricts the diffusion of oxygen and nutrients to the underlying cartilage, promoting its degeneration. (Key Point)

Changes in the Cartilage:

Chondrocytes (cartilage cells) start producing an enzyme called alkaline phosphatase and become enlarged (hypertrophy), increasing the size of their cavities (lacunae). (Key Point)

These changes lead to:

Compression of the matrix (material between cartilage cells) into narrow columns called trabeculae. (Key Point)

Calcification (mineralization) of these trabeculae. (Key Point)

Death of Cartilage Cells and Bone Formation:

Cartilage cell death creates a structure consisting of remnants of calcified cartilage. (Key Point)

These remnants get covered by a layer of osteoblasts, which then initiate the process of building true bone tissue. (Key Point)

Woven Bone Formation and Blood Vessel Invasion:

Osteoblasts (bone-forming cells) attach to the remaining calcified cartilage matrix and produce a temporary bone type called woven bone. (Note: Woven bone is less organized than mature bone.)

At this stage, the calcified cartilage appears basophilic (stains blue with specific dyes), while the newly formed bone is more acidophilic (stains pink with specific dyes).

Blood vessels from the perichondrium (now called the periosteum) penetrate the bone collar, bringing osteoprogitor cells (precursor cells to osteoblasts) to the central region. (This increases the bone-forming activity.)

The process happening in the diaphysis (main shaft) forms the primary ossification center. This process can begin as early as the first trimester in many bones.

Secondary Ossification Centers and Epiphyseal Cartilage:

Secondary ossification centers appear later at the ends (epiphyses) of the cartilage model and develop similarly to the primary center.

Bone Marrow and Remodeling:

During their expansion and remodeling, both primary and secondary ossification centers create cavities that fill gradually with bone marrow and bony trabeculae (thin plates of bone).

Remaining Cartilage and Growth:

Even with the ossification centers, two regions of cartilage remain:

Articular Cartilage: This layer exists within joints and persists throughout adulthood. It does not contribute to bone growth.

Epiphyseal Cartilage (Growth Plate): This cartilage connects each epiphysis to the diaphysis and is responsible for bone growth in length. It disappears at adulthood ("epiphyseal closure"). This closure happens at different times for different bones, with all bones being completely closed by around age 20.

Bone Age Determination:

By examining X-rays of growing skeletons or using forensic techniques, it's possible to estimate the "bone age" of a young person by observing which epiphyses are open and which are closed. Once epiphyseal closure occurs, further bone growth in length is impossible, although some widening can still occur.

Zone	Description
Resting Zone	Hyaline cartilage with typical chondrocytes.
Proliferative Zone	Chondrocytes divide rapidly, forming columns stacked parallel to the bone's long axis.
Hypertrophic Cartilage Zone	Swollen, degenerative chondrocytes with glycogen accumulation. Hypertrophy compresses the matrix into thin septa.
Calcified Cartilage Zone	Chondrocytes die (apoptosis), and septa of cartilage matrix calcify by forming hydroxyapatite crystals.
Ossification Zone	Capillaries and osteoprogenitor cells invade cavities left by chondrocytes. Osteoblasts form a layer over calcified matrix septa, secreting osteoid and forming woven bone.

BONE FRACTURE

(a) Blood vessels torn within the fracture release blood that clots to produce a large fracture hematoma. This initial step creates a blood clot at the fracture site.

(b) Macrophages gradually remove the hematoma and replace it with a soft fibrocartilage-like mass of procallus tissue rich in collagen and fibroblasts. Clean-up begins as white blood cells (macrophages) remove the clot and prepare the area for healing. A soft, fibrous tissue called procallus forms.

(c) Regrowing blood vessels and osteoblasts invade the soft procallus. New blood vessels grow into the area, bringing essential nutrients and oxygen. Osteoblasts, specialized bone-forming cells, move in to begin building new bone.

(d) Over the next few weeks, the fibrocartilage is gradually replaced by trabeculae of woven bone (process that resembles a combination of endochondral and intramembranous ossification) forming a hard callus throughout the original area of fracture. The soft procallus is replaced with a stronger, woven bone structure called a callus. This process involves elements of both cartilage-based and direct bone formation.

(e) The woven bone is then remodeled as compact and cancellous bone in continuity with the adjacent uninjured areas and fully functional vasculature is reestablished. Finally, the woven bone is remodeled into the stronger forms of bone found in the body (compact and cancellous bone). This remodeled bone seamlessly connects with the healthy bone around the fracture. Additionally, a full network of blood vessels is restored in the healed area.