

## BONE

Bone is specialized dense connective tissue where matrix is impregnated with calcium salts making it hard and rigid. Calcium salts exist in form of *hydroxyapatite crystals* [ $\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$ ].

### Functions of bone:

1. Store-house of calcium
2. Bone marrow present in bones manufacture RBC, platelets
3. Attachment to muscles
4. Protects visceral organs

*The feature that distinguishes bone from other connective tissue is the mineralization of its matrix.*

**Cells of bones:** All cells of bone are derived from mesenchymal stem cells except *osteoclasts* which are derived from CFU-GM, a cell that gives rise to neutrophilic granulocytes (CFU-G) and monocytes (CFU-M).

- a. Osteoprogenitor cells:** These are derived from mesenchymal cells. These cells then differentiate into other bone cells. These cells are found on external and internal surface of bones. They are called **periosteal cells** that forms innermost layer of periosteum and **endosteal cells** that line marrow cavities, Haversian canals and perforating canals. These cells are *flat or squamous cells* with light staining, elongated or ovoid nuclei.
- b. Osteoblasts:** These are found where active bone is being formed. These are large **basophilic cells** with large rounded eccentric nuclei. Cells are cuboidal or polygonal shaped. These cells lay down fibers and matrix in areas of bone formation. They deposit osteoid (collagen I and proteoglycan).  
**Osteoid is unmineralized matrix.** Bone matrix proteins produced osteoblast include:
  - Calcium binding proteins, e.g. osteonectin, *osteocalcin*
  - Multiadhesive glycoproteins, e.g. sialoprotein I & II, osteopontin
  - Proteoglycans
  - Alkaline phosphatase: Circulating level of AP and osteocalcin are used clinically as markers of osteoblast activity

➤ They have receptors for PTH. When PTH binds to osteoblast, it stimulates osteoclastic activity.
- c. Osteocytes:** These are resting cells enclosed in bony matrix. They lie in spaces/lacunae in the matrix. Radiating in all directions from lacunae are branching tubular passages called canaliculi. These anastomose with similar canaliculi of adjacent lacunae. *These are main cells of mature bone.*
- d. Osteoclasts:** These are large, *multinucleated cells with acidophilic cytoplasm*. They rest directly on bone tissue where resorption is taking place. As a result of osteoclastic activity, a shallow bay can be observed directly under osteoclasts known as *Howship's lacunae* or *resorption bay*. *Cell is very prominent because of its large size and marked acidophilia.*

Osteoclasts resorb bone tissue by releasing protons and lysosomal hydrolases (e.g. cathepsin K, matrix metallo-proteinase). They degrade collagen and other proteins of bone matrix. Activated cells have ruffled border created by extensive folding of cell membrane.

### Bone matrix:

Bone matrix contains mainly **type I collagen (approx. 94%)** and other non-collagenous proteins. Because bone matrix is calcified, it is harder than cartilage. Diffusion is not possible through

calcified matrix; therefore bone matrix is highly vascularized. Bone matrix contains both organic and inorganic components. The inorganic component consists of calcium and phosphate in form of hydroxyapatite crystals. *Mineral component mainly resist compression.*

Organic component helps bone to resist tension. Major organic components of bone matrix are:

1. **Type I collagen**
2. **Proteoglycans:** Proteins and GAGs (hyaluronic acid, chondroitin sulfate, keratin sulfate)
3. **Multiadhesive glycoproteins**
  - a. **Osteonectin:** serve as glue between collagen and hydroxyapatite
  - b. **Sialoproteins:** helps attachment of cells to bone matrix. Also initiate Ca-phosphate formation
4. **Growth factors**

**Types of bones:** Bone tissue is classified as either compact (dense) or spongy (cancellous). In long bone, outer cylindrical part is dense compact bone. The inner surface, adjacent to marrow cavity is cancellous bone. Cancellous bone has sponge-like meshwork consisting of trabeculae.

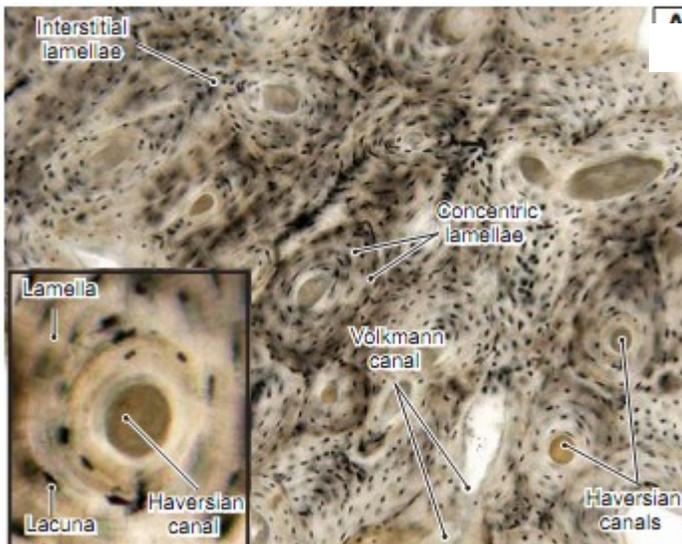
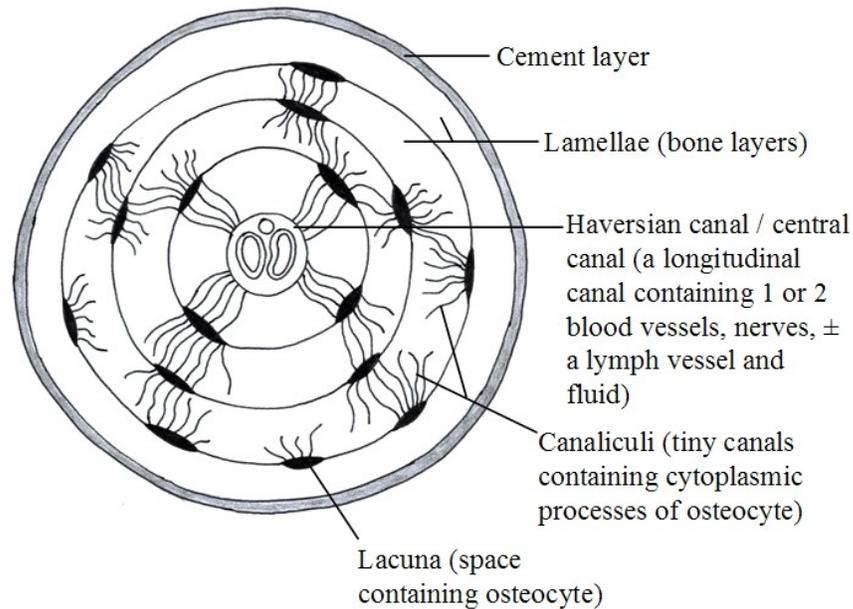
**General structure of bone:**

1. **Outer surface:** Bones are covered by periosteum, a sheath of dense fibrous CT containing osteoprogenitor cells. Bones are covered by periosteum except in areas where they articulate with another bone (covered by cartilage). Periosteum has two layers:
  - a. Outer fibrous layer
  - b. Inner cellular layer having osteoprogenitor cells called periosteal cells  
In general, collagen fibers of periosteum are arranged parallel to surface of bone in form of capsule. Areas where ligament & tendons are attached, collagen fibers extend into bone tissue at an angle. These are called *Sharpey's fibers*.
2. **Bone cavities:** Lined by endosteum that contains osteoprogenitor cells (endosteal cells). It is often only one cell thick. The marrow cavity and spaces in spongy bone contain bone marrow:
  - a. **Red marrow:**
    - i. It contains developing blood cells
    - ii. Network of reticular cells and fibers
  - b. **Yellow marrow:**
    - i. In adult, when rate of blood cell formation has diminished, tissue in bone marrow is replaced by fat cell. It is then called *yellow bone marrow*.
  - c. **Gelatinous marrow:** Generally seen in very old animals or in chronic diseases.

**Mature Bone:** It is composed of cylindrical units called **OSTEON (Haversian System)**. The boundary of an osteon is the **cement line**. It consists of:

- a. Central/Haversian canal: It contains nerve and blood vessels.
- b. Collagen fibers are arranged as lamellae called **concentric lamellae** surrounding central canal. In long bones, **outer circumferential lamellae** are present deep to periosteum and **inner circumferential lamellae** surrounds bone marrow cavity. Lamellae present between osteons are called **interstitial lamellae**.

- c. Lacunae containing osteocytes. Radiating from lacunae are canaliculi that penetrate and join canaliculi of adjacent lamellae. Thus, lacunae and canaliculi form an extensive system of inter-connecting passageway for transport of nutrients. **Because of presence of lamellae, mature bone is called LAMELLAR BONE.**
- d. Central canals are connected with each other and marrow cavity by transverse or horizontal channels called **perforating canals (VOLKMANN'S CANAL)**. These canals are not surrounded by concentric lamellae.



**Compact bone. Ground substance (unstained)**

**Cancellous Bone (Spongy)**

It consists of trabeculae that enclose irregular marrow cavities with blood vessels. Bony trabeculae are lined by a thin, inner layer of cells called endosteal cells. If trabeculae are sufficiently thick, they will contain osteons.

Diaphysis (shaft of long bone): Mostly compact bone, only small amount of spongy bone towards marrow cavity. Epiphysis: Spongy bone is extensive.

**Immature bone:**

Bone tissue initially formed in skeleton of a developing fetus is called immature bone. It differs from mature bone:

1. It is non-lamellar (known as **woven bone**). Woven bone is produced when osteoblasts produce osteoid rapidly. This occurs initially in all fetal bones, but the resulting woven bone is replaced by remodeling and the deposition of more resilient lamellar bone. In adults, woven bone is formed when there is very rapid new bone formation, as occurs in the repair of a fracture.
2. More cells per unit area than mature bone
3. Matrix has more ground substance and stain more intensely with Hematoxylin whereas the matrix of mature bone stains more intensely with eosin.

**Bone formation:** Classified as endochondral or intra-membranous. In **endochondral ossification**, cartilage model serve as precursor of the bone, which is absent in intra-membranous ossification.

The bones of extremities and vertebrae develop by endochondral ossification. The flat bones of skull, face, mandible, clavicle develop by intra-membranous ossification.

<b>Bone</b>	<b>Cartilage</b>
Hard, inelastic and tough	It is soft, elastic and flexible
Cells are called osteocytes	Cells are called chondrocytes
Osteocytes has protoplasmic processes	Chondrocytes lack protoplasmic processes
Vascular matrix	Non-vascular matrix, perichondrium has blood supply
Haversian system present	Haversian system absent
Matrix has protein called OSSEIN	Matrix has protein called CHONDRIN
Matrix has both organic and inorganic part	Matrix is entirely organic
Bone marrow is present	Marrow absent