Medical Biology

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BONE TISSUE

Bone tissue is a supporting connective tissue and is the main element of the skeletal tissue. It is composed of cells and an extracellular matrix in which fibers are embedded. Bone tissue is unlike other connective tissues in that the extracellular matrix becomes calcified.

FUNCTIONS OF BONE TISSUE

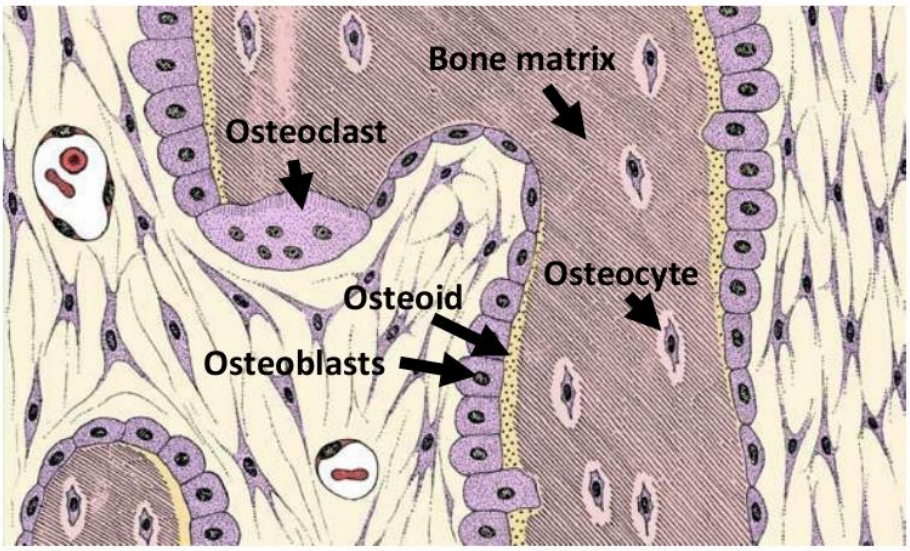
1. The skeleton is built of bone tissue. Bone provides the internal support of the body and provides sites of attachment of tendons and muscles, essential for locomotion.
2. Bone provides protection for the vital organs of the body: the skull protects the brain; the ribs protect the heart and lungs. The hematopoietic bone marrow is protected by the surrounding bony tissue.
3. The main store of calcium and phosphate is in the bone. Bones have several metabolic functions, especially in calcium homeostasis.

Bones are a hard, but brittle tissue. Bone is a dynamic tissue, which throughout life bone tissue is continually being formed and resorbed.

BONE CELLS

4 different cell types are found in developing bones:

1. Osteoprogenitor cells
2. Osteoblasts
3. Osteocytes
4. Osteoclasts



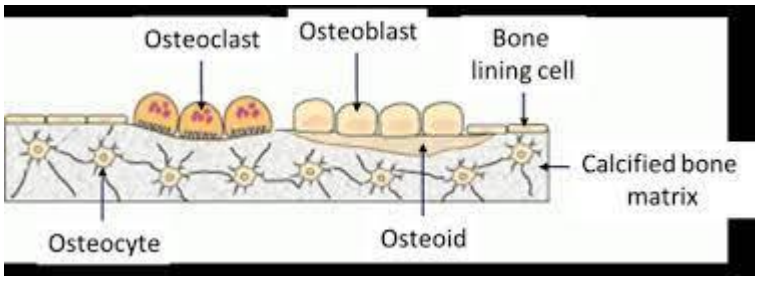
Osteoprogenitor cells

Bones, like other connective tissue in the embryo, are derived from mesenchymal cells. After birth, flattened, poorly differentiated, mesenchyme-like cells, are found in the periosteum and endosteum. These cells can divide (mitosis) and differentiate into bone cells (osteogenic potential) and as a result are known as osteoprogenitor cells.

Osteoblasts

The first cells to develop from the osteoprogenitor cells are the osteoblasts. Osteoblasts are involved in the formation of bone and are found on the boundaries of developing and growing bones. The cells are typically cuboidal, and the cytoplasm is fairly basophilic. These cells are very active in synthesizing and secreting the components of the bone matrix and have well-developed rough endoplasmic reticulum (RER). Osteoblasts are rich in the enzyme alkaline phosphatase, which plays a major role in the formation of the mineral deposits in the matrix. The collagen fibers are synthesized and secreted by the osteoblasts.

The matrix closest to the osteoblasts is not yet calcified and is known as osteoid or prebone. This osteoid is rich in collagen fibers. Small membrane-bound matrix vesicles (not visible by light microscopy) are budded off processes of the osteoblast cell membrane and secreted to the matrix. These play an important role in the calcification process of the matrix. When their synthetic activity is completed, some osteoblasts differentiate as osteocytes entrapped in matrix bound lacunae, some flatten and cover the matrix surface as *bone lining cells*, and the majority undergo apoptosis.

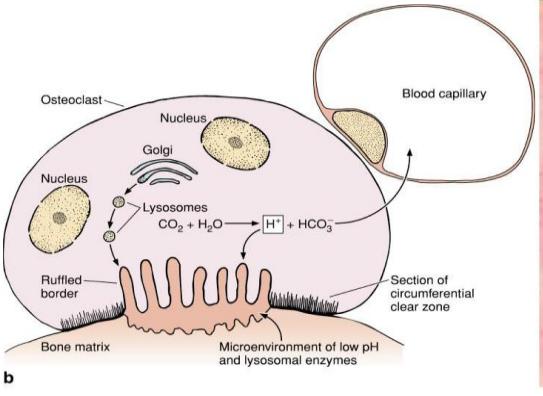


Osteocytes

Osteocytes are mature bone cells that develop from osteoblasts and are located in almond shaped lacunae within the bony matrix. Osteocytes have cytoplasmic processes located in canaliculi, which penetrate the bony matrix. Cytoplasmic processes from one osteocyte make contact with the processes from neighboring osteocytes and can communicate via gap junctions. Because the bony matrix is calcified there is no possibility of diffusion except via the network of canaliculi.

Osteoclasts

Osteoclasts are the largest of the bone cells and are multinuclear (with up to 50 nuclei). Osteoclasts are involved in bone resorption and can be found on the eroding surfaces of bone, often in cavities known as Howship's lacunae. The osteocytic cell membrane closest to the bone undergoing resorption has multiple invaginations and is known as the "ruffled border". These cells are metabolically very active, possess large numbers of mitochondria (resulting in the acidophilia of regular staining) and have well developed Golgi bodies.



Osteoclasts originate from monocytes and are included in the **mononuclear phagocyte system.**

Clinical Notes:

In the genetic disease *osteopetrosis*, which is characterized by dense, heavy bones ("*marble bones*"), the osteoclasts lack ruffled borders and bone resorption is defective. This disorder results in overgrowth and thickening of bones, often with obliteration of marrow cavities, depressing blood cell formation and causing anemia and the loss of white blood cells.

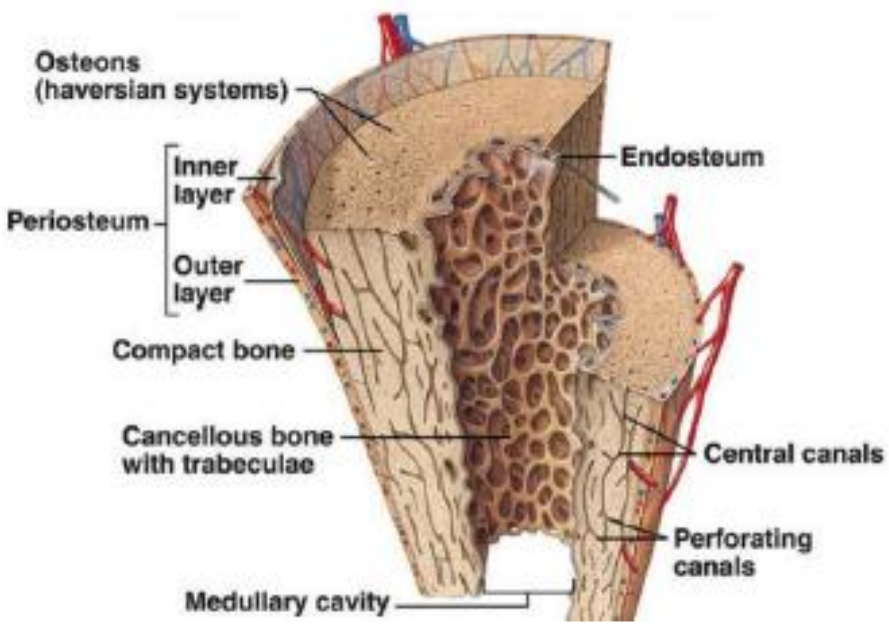
Bone Matrix

About 50% of the dry weight of bone matrix is inorganic materials. Calcium hydroxyapatite is the most abundant, but bicarbonate, citrate, magnesium, potassium, and sodium ions are

also found. Significant quantities of noncrystalline calcium phosphate are also present. The surface of hydroxyapatite crystals is hydrated, facilitating the exchange of ions between the mineral and body fluids.
The organic matter embedded in the calcified matrix is 90% type I collagen but also includes mostly small proteoglycans and multiadhesive glycoproteins such as *osteonectin*. Calcium-binding proteins, notably osteocalcin, and the phosphatases released from cells in matrix vesicles promote calcification of the matrix. Other tissues rich in type I collagen lack osteocalcin and matrix vesicles and therefore do not normally become calcified.
The association of minerals with collagen fibers during calcification provides the hardness and resistance required for bone function. If a bone is decalcified by a histologist, its shape is preserved but it becomes soft and pliable like other connective tissues. Because of its high collagen content, decalcified bone matrix is usually acidophilic.

Clinical notes:
Osteogenesis imperfecta, or "*brittle bone disease*," refers to a group of related congenital disorders in which the osteoblasts produce deficient amounts of type I collagen or defective type I collagen due to genetic mutations. Such defects lead to a spectrum of disorders, all characterized by significant fragility of the bones. Fragility reflects the deficit in normal collagen, which normally reinforces and adds a degree of resiliency to the mineralized bone matrix.

Periosteum & Endosteum
External and internal surfaces of bone are covered by connective tissue called periosteum and endosteum.
The ***periosteum*** consists of an outer layer of collagen fibers and fibroblasts. Bundles of periosteal collagen fibers, called Sharpey's fibers, penetrate the bone matrix, binding the periosteum to bone. The inner, more cellular layer of the periosteum is composed of fibroblast-like cells called osteoprogenitor cells, with the potential to divide by mitosis and differentiate into osteoblasts. Osteoprogenitor cells play a prominent role in bone growth and repair.



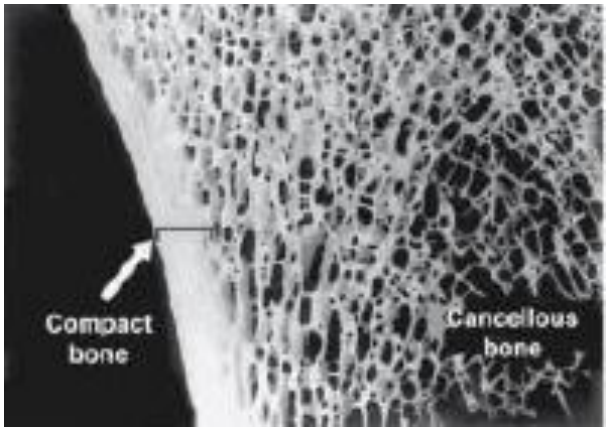
The ***endosteum*** lines all internal cavities within the bone and is composed of a single layer of flattened osteoprogenitor cells and a very small amount of connective tissue. The endosteum is therefore considerably thinner than the periosteum.
The principal functions of periosteum and endosteum are nutrition of osseous tissue and provision of a continuous supply of new osteoblasts for repair or growth of bone.

Types of Bone

Anatomical classification of **bones**: long, short, flat, & irregular bones.

Macroscopic classification of **bone tissue**: compact bone, cancellous bone (microscopically they are almost identical).

Developmental classification of bone tissue: primary & secondary.



Macroscopic classification of bone tissue:

Compact bone:

Here, bone tissue forms a solid mass of bone with no cavities. In a long bone, compact bone tissue forms the bone shaft (diaphysis) around the bone marrow cavity, & the outer layer of the metaphysis & epiphysis.

Under microscope, compact bone matrix is made of bone layers (lamellae) having small cavities (lacunae) between them that contain osteocytes. Osteocytes are oval cells with many slender cytoplasmic processes that occupy small tunnels (canaliculi) connecting adjacent lacunae. As mentioned above, inside each canaliculus, cytoplasmic processes of adjacent osteocytes contact each other by gap junctions.

In compact bone, lamellae are arranged as follows:

- Outer circumferential lamellae: large in number, occupy the outer zone, beneath & parallel to the periosteum

- Inner circumferential lamellae: less in number, occupy the inner zone parallel to the endosteum.

- Osteons (Haversian systems): longitudinal cylinders of bone made of concentric lamellae with a central narrow canal "***the central (Haversian) canal***" filled with loose connective tissue. Osteons fill the zone between the outer & inner circumferential lamellae & are parallel to the long axis of the bone. Central canals are connected to each other by several transverse or oblique canals "***perforating (Volkmann's) canals***", that also connect central canals to the outer & inner surfaces of the bone.

- Interstitial lamellae: short parallel lamellae that fill the small triangular spaces between osteons.

Notes:

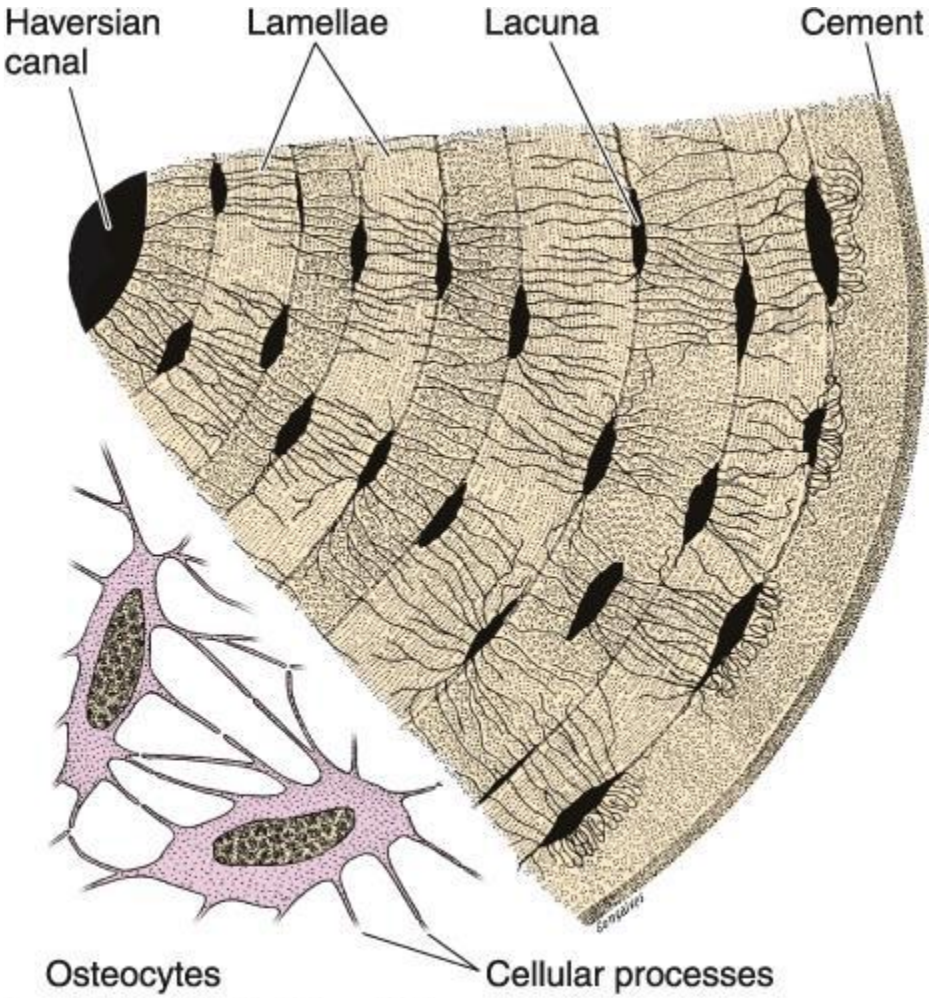
 In each lamella, collagen fibers are arranged spirally, in a direction opposite that of the collagen fibers of the adjacent lamella.

 Osteons are in a continuous renewal process; therefore, they differ in diameter & number of lamellae.

 Surrounding each osteon is a layer of amorphous material called the **cementing substance** that consists of mineralized matrix with few collagen fibers.

 Perforating canals are not surrounded by concentric lamellae; they perforate the lamellae of haversian systems. Perforating canals are lined with endosteum & filled with loose connective tissue.

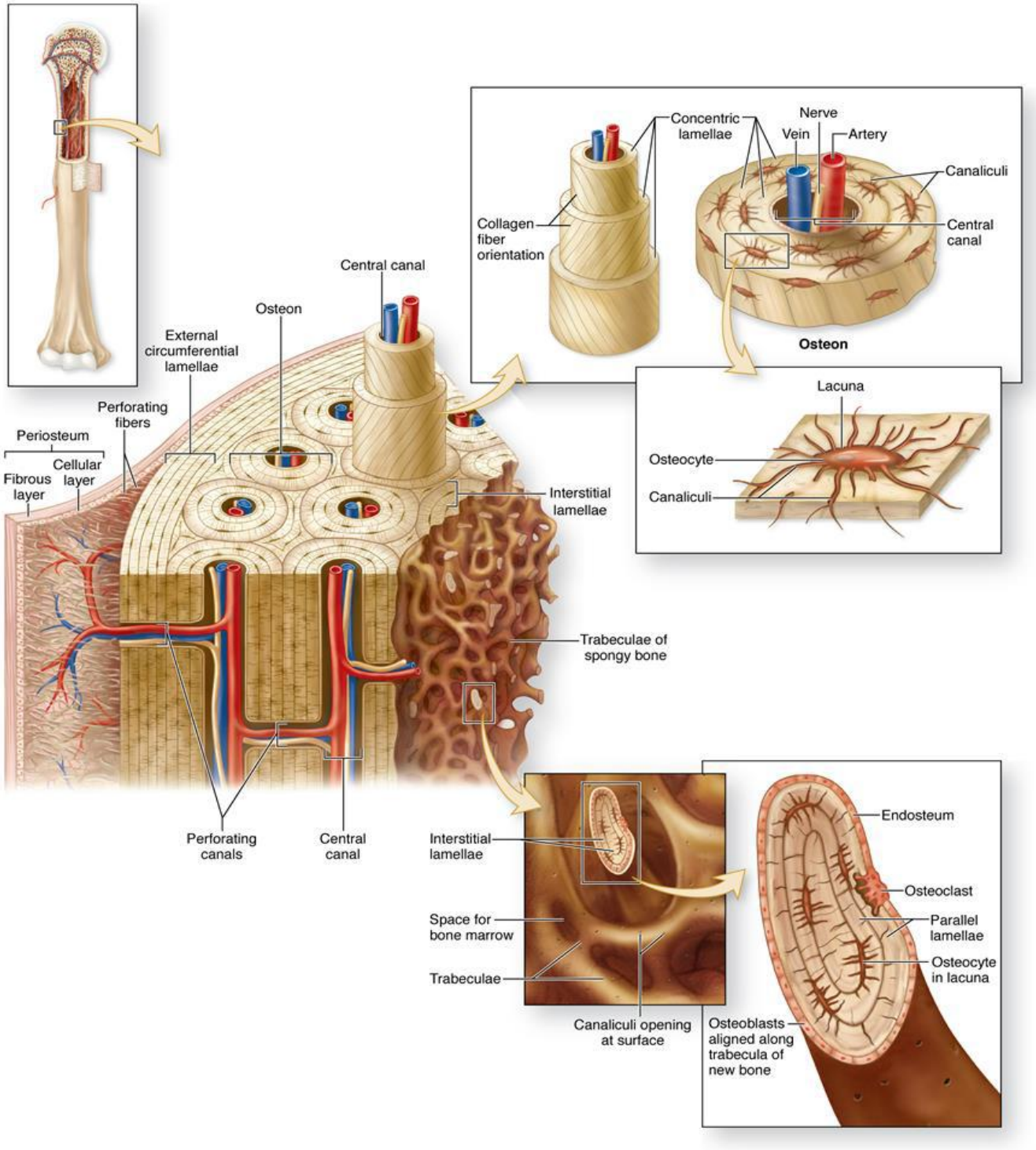
 Blood vessels & nerves enter the bone via foramina & are distributed through all central & perforating canals.



Cancellous bone:

Cancellous (spongy, trabecular) bone fills the epiphysis & metaphysis of long bones & form a thin zone on the inner surface of diaphysis around the marrow cavity. In short & irregular bones, cancellous bone forms the core & compact bone makes the outer layer of the bone. In flat bones, 2 plates of compact bone sandwich a thin zone of cancellous bone called the diploe.

Cancellous bone is made of bony trabeculae separated by extensively interconnected cavities, just like a sponge. Histologically, it is similar to compact bone in being made by concentric lamellae with lacunae containing osteocytes, but the lamellae are not perforated by central or perforating canals. On the surface of the bony trabeculae, osteoblasts are present, together with fewer osteoclasts, all surrounded by thin endosteum.



Developmental classification of bone tissue:

Primary bone tissue:

Primary (immature, woven) bones are the first bone tissue to appear in embryonic development and in fracture repair and other repair processes. It is characterized by random disposition of fine collagen fibers, a lower mineral content and a higher proportion of osteocytes than in secondary bone tissue. Primary bone tissue is usually temporary, it is replaced in adults by secondary bone tissue except in few places (near the sutures of the flat bones of the skull, in tooth sockets, and in the insertions of some tendons).

Secondary bone tissue:

Secondary (mature, lamellar) bone tissue is usually found in adults. It shows collagen fibers arranged in lamellae forming compact or cancellous bone tissue (discussed above).

Clinical Notes:
Cancer originating directly from bone cells (a primary bone tumor) is uncommon (0.5% of all cancer death), although a cancer called *osteosarcoma* can arise in osteoprogenitor cells. The skeleton is often the site of secondary, metastatic tumors, however, arising when cancer cells move into bones via small blood or lymphatic vessels from malignancies in other organs, most commonly the breast, lung, prostate gland, kidney, or thyroid gland.