College of Dentistry
Second year
Academic year/ 2019-2020

Title:- Histology

Subject: Bone Lec. no.3

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Bone

- **Bone** is a **specialized form of connective tissue, consists of cells and extracellular matrix**.
- The feature **that distinguishes bone** from other connective tissues is the **mineralization of its matrix**, which produces an **extremely hard tissue capable of providing support** and **protection**.
- The mineral is calcium phosphate in the form of **hydroxyapatite crystals** [Ca10(PO4)6(OH)2].
- **Because mineralized bone matrix, nutrients and metabolites cannot freely diffuse through it to the osteocytes. Consequently, bone is very vascular.**

Functions of Bone

- 1. Support and Protection
- 2. Storage of minerals (calcium)
- 3. Storage of lipids (yellow marrow)
- 4. Blood cell production (red marrow)

Bone matrix

- **Bone matrix contains mainly type I collagen (MAJOR) along with other matrix proteins** (noncollagenous) proteins **(MINOR).**
- The **major structural component** of **bone matrix** is **type I collagen** and, to a lesser extent, **type V collagen**. Trace amounts of other types such as (**type III, XI, and XIII collagens)** have also been found in the matrix.
- **All collagen molecules constitute about 90%** of the total weight of the bone matrix proteins.
- **COLLAGENOUS MOLECULES 90%.**

Bone Matrix

- **The minor structural component :-** (Noncollagenous) proteins.
- They constituting only 10% of the total weight of bone matrix proteins, they are essential to bone **development, growth, remodeling, and repair**.
- **(Noncollagenous)proteins 10%**

Noncollagenous proteins

- The four main groups of **noncollagenous proteins** found in the bone matrix are the following:
- 1.**Proteoglycan macromolecules:-** contain a **core protein** with various numbers of covalently attached side chains of **glycosaminoglycans.** They contribute to the **compressive strength of bone**.
- 2.**Multiadhesive glycoproteins:-** are **responsible for attachment of bone cells and collagen fibers to the mineralized ground substance**., included:
- **Osteonectin**
- **Sialoproteins** such as **osteopontin and sialoprotein I and II.**

Noncollagenous proteins

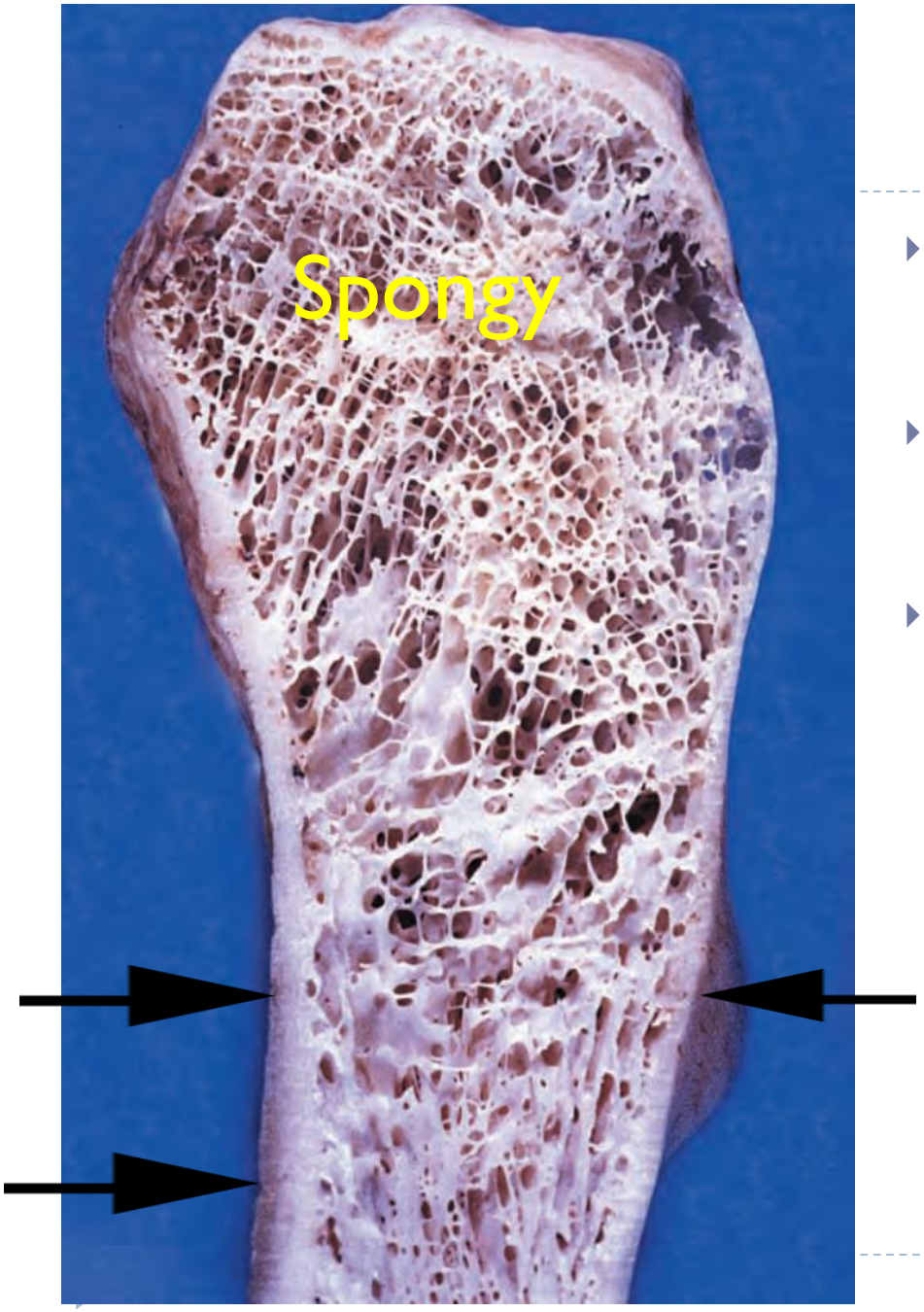
- **3. Growth factors** and **cytokines**:- which are small regulatory proteins including **insulin like growth factors (IGFs), tumor necrosis factor alpha (TNF-), transforming growth factor beta (TGF-), platelet-derived growth factors (PDGFs), bone morphogenic proteins (BMPs)**, and **interleukins (IL-1, IL-6)**. The most unique members of this group are **BMPs,** because they ***induce the differentiation of mesenchymal cells into osteoblasts.***
- 4. **Vitamin K–dependent proteins**, such as **osteocalcin** (which captures calcium from the circulation and stimulates osteoclasts in bone remodeling).

Bone and bone tissue

- **Bones are the organs of the skeletal system; bone tissue is the structural component of bones.**
- Typically, a bone consists of **bone tissue and other connective tissues, including hemopoietic tissue, fat tissue, blood vessels, and nerves.**
- **Bone tissue is classified as either compact (dense) or spongy (cancellous).**

Compact bone and spongy bone

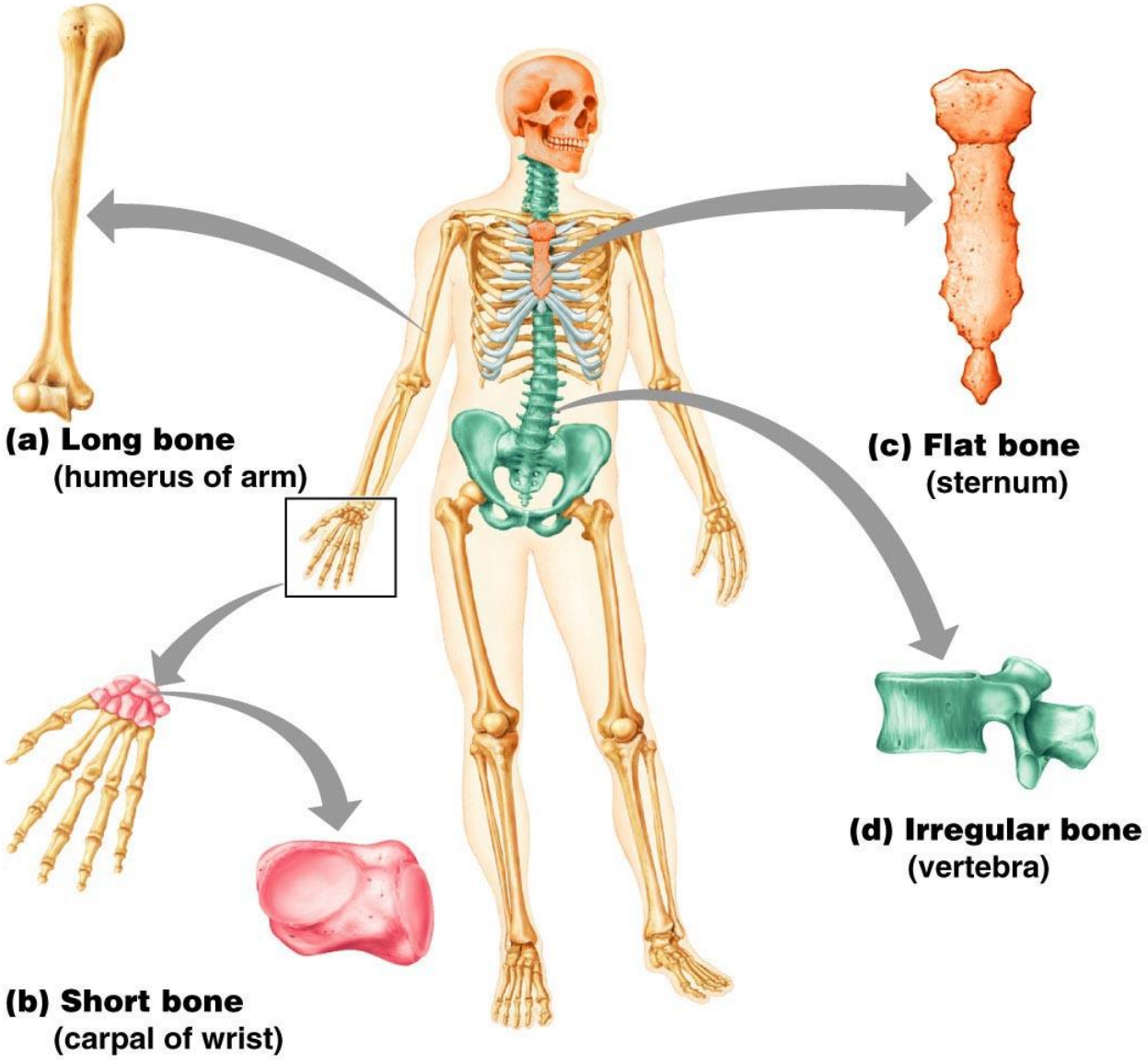
- If a bone is cut, two distinct structural arrangements of bone tissue can be recognized.
- **Compact bone:-** Dense layer **forms the outside of the bone**.
- **Spongy bone:-** Sponge-like meshwork consisting of **trabeculae** forms **the interior of the bone**.
- The **spaces within the meshwork** are filled by **marrow and blood vessels**.



- **An adult long bone.**
  This photo shows a longitudinally sectioned of a long bone.
- The outer portion of the bone has a solid structure (*arrows*) and represents compact (dense) bone.
- The interior of the bone exhibits a spongy configuration and represents spongy (cancellous) bone.

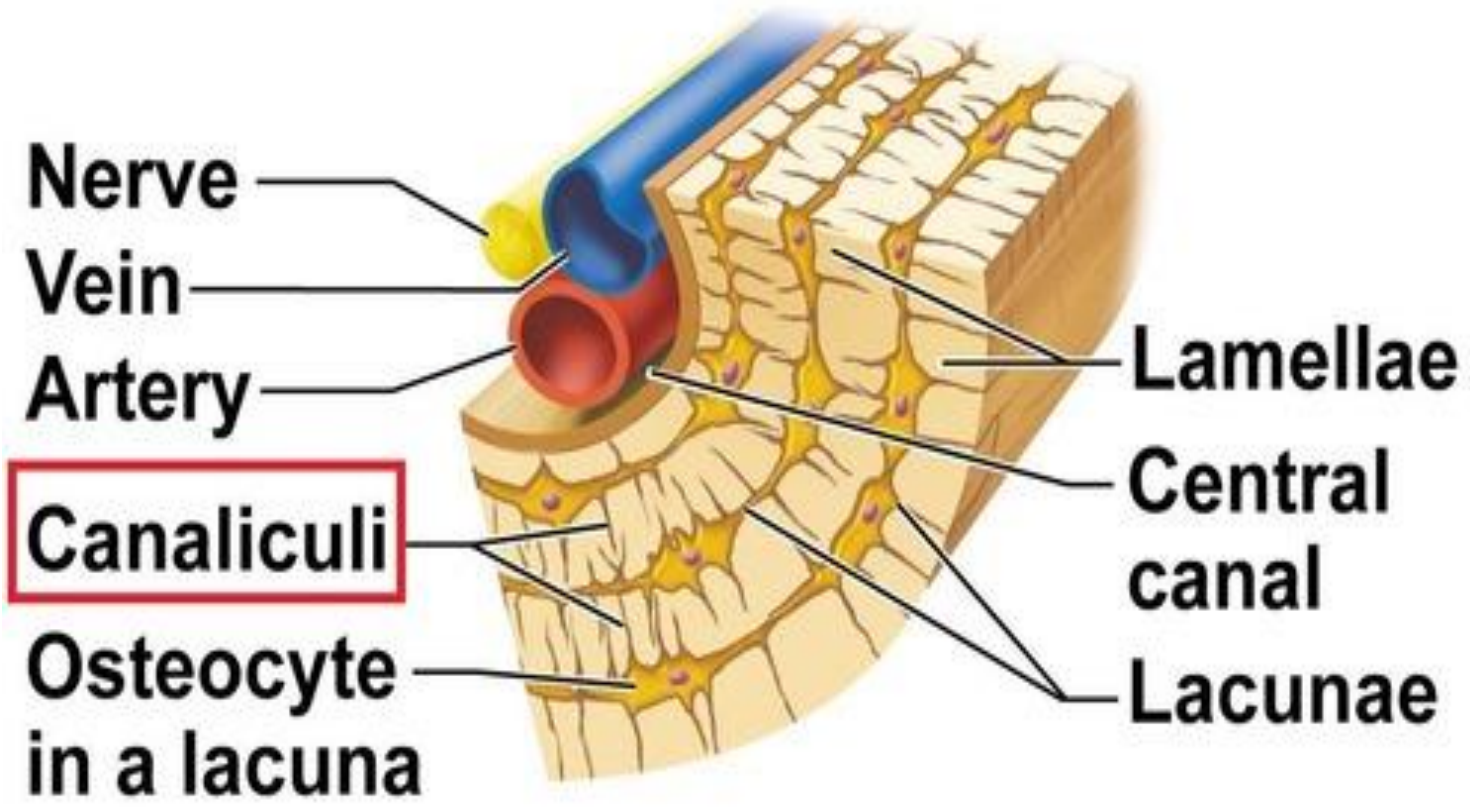
- **Bones are classified according to shape into four groups:-**

1. **Long bones** are longer in one dimension than other bones and consist of a shaft and two ends (e.g., the tibia and the metacarpals).
2. **Short bones** are nearly equal in length and diameter (e.g., the carpal bones of the hand).
3. **Flat bones** are thin and plate like (e.g., the bones of the calvaria [skull cap] and the sternum).
4. **Irregular bones** have a shape that does not fit into any one of the three groups just described; the shape may be complex (e.g., a vertebra, ethmoid bone).



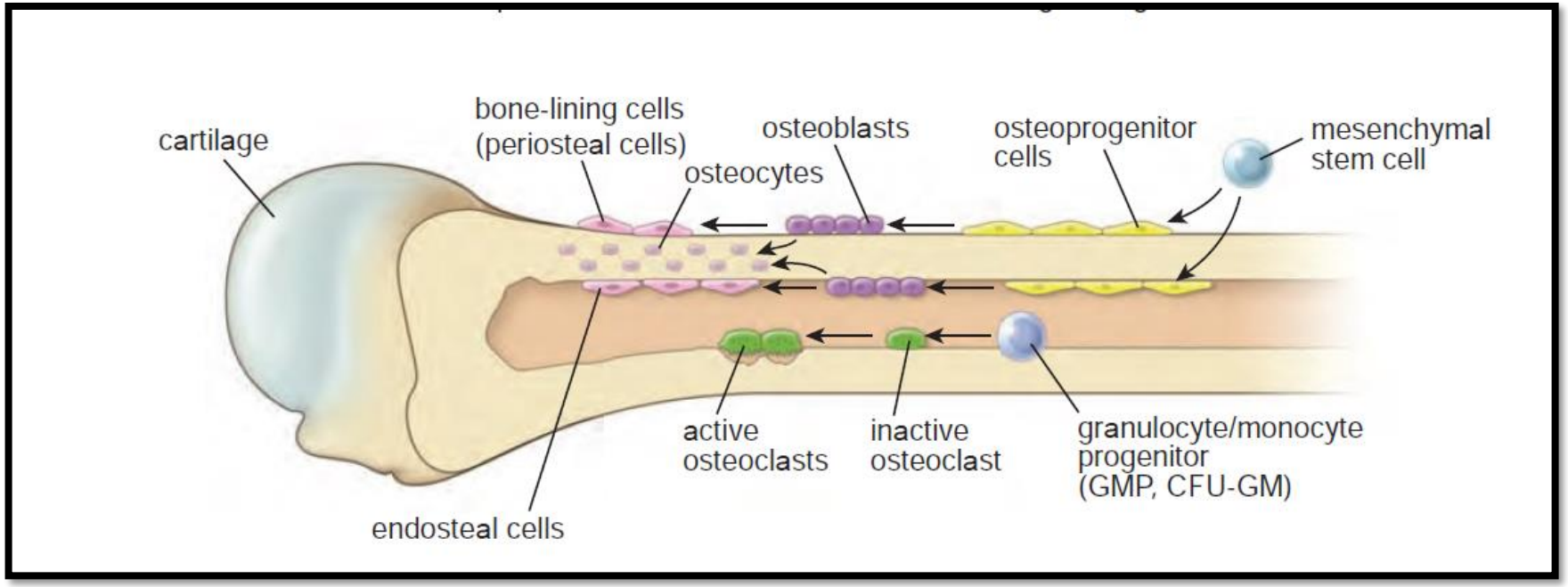
Lacunae

- Within the bone matrix are spaces called **lacunae** (sing., *lacuna*), each of which contains a bone cell, or **osteocyte**. (Never contains more than one osteocyte).
- The osteocyte extends many processes into small tunnels called **canaliculi**.
- **Canaliculi** going through the mineralized matrix, connecting **adjacent lacunae** and allowing contact between of neighboring osteocytes. (***The canaliculi provide routes by which nutrients can reach the osteocytes and waste products can leave them***).


Nerve
Vein
Artery
Canaliculi
Osteocyte in a lacuna
Lamellae
Central canal
Lacunae

CELLS OF BONE TISSUE

- Five designated cell types are related with bone tissue: **osteoprogenitor cells, osteoblasts, osteocytes, bone-lining cells, and osteoclasts.**
- With the **exception of the osteoclast**, each of these cells are differentiated form of the same basic cell type (Fig.).
- In contrast, the osteoclast originates from a different cell line.



Schematic drawing of cells associated with bone. All cells except osteoclasts originate from the mesenchymal stem cells, which differentiate into osteoprogenitor cells, osteoblasts, and finally osteocytes and bone-lining cells. Bone-lining cells on external bone surfaces are part of the periosteum, hence the term periosteal cells. Bone-lining cells on internal bone surfaces are frequently called endosteal cells. Note that osteoprogenitor cells and bone-lining cells have a similar microscopic appearance and are often difficult to distinguish from each other. Osteoclasts originate from hemopoietic progenitor cells, which differentiate into bone resorbing cells.

Osteoprogenitor Cells

- **Derived from mesenchymal stem cells.**
- The **key factor** that triggers differentiation of ***osteoprogenitor cells*** is a ***transcription factor*** called **core binding factor alpha-1 (CBFA1)**.
- **Can differentiate into an osteoblast.**
- Found on the ***external and internal*** surfaces of bones.

Osteoblast

- **The osteoblast also called bone-forming cell that secretes or synthesis new bone matrix (**osteogenesis**).**
- It secretes both **type I collagen** (which constitutes 90% of the protein in bone) and **bone matrix proteins (BMPs)**.
- The osteoblast is also responsible for the calcification of bone matrix.

- **The bone matrix proteins produced by the osteoblast include:-**

1. Calcium-binding proteins such as osteocalcin and osteonectin.

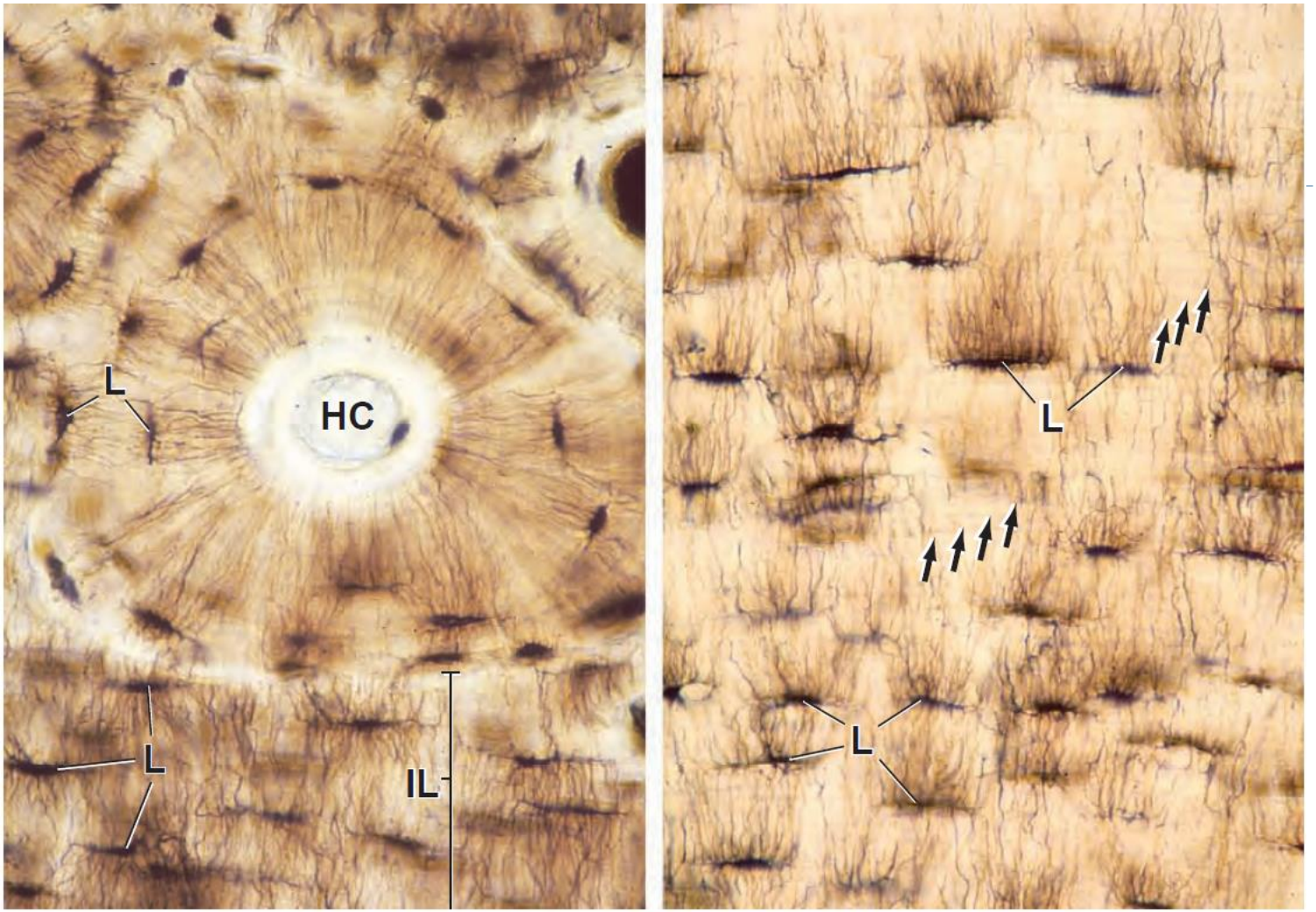
2. Multiadhesive glycoproteins such as bone sialoproteins I and II, osteopontin.

3. Alkaline phosphatase (ALP).

- ***Circulating levels of ALP and osteocalcin are used clinically as markers of osteoblast activity.***

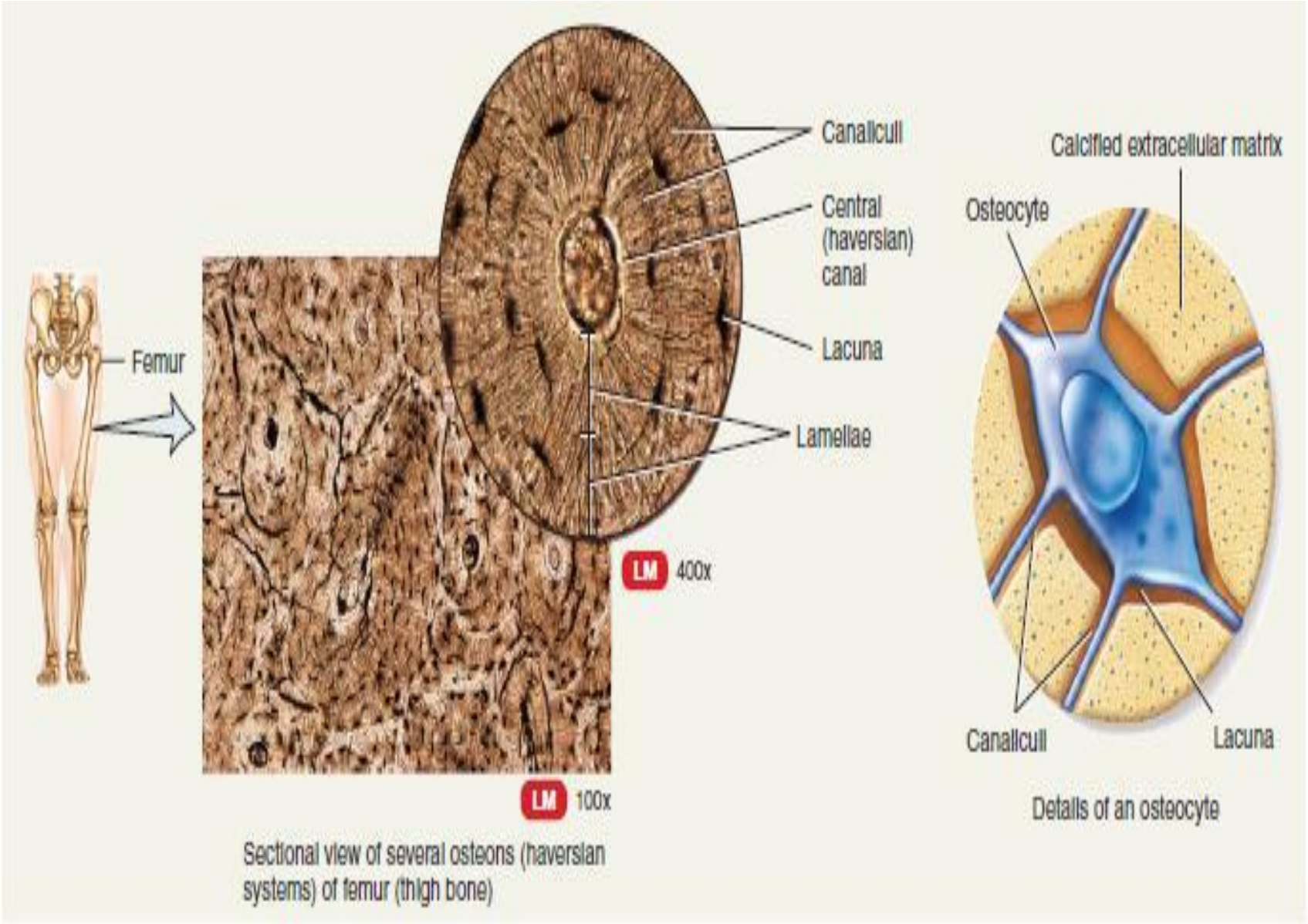
Osteocytes (mature bone cells)

- **Osteocytes** are the mature form of osteoblasts and are the principal cells of the bone; they are also smaller than osteoblasts.
- **Osteocytes** lie in lacunae and are very close to a blood vessel.
- Because **mineralized bone matrix** (hard matrix), nutrients and metabolites cannot freely diffuse through it to the osteocytes.
- Consequently, bone is very vascular and possesses a unique system of channels or tiny canals called **canaliculi**, which open into the osteons.
- **Canaliculi** containing the processes of osteocytes are generally arranged in a radial pattern with respect to the canal for the passage of substances between the osteocytes and blood vessels.



Key:-

HC, Haversian canal, **L**, lacuna, **IL**, Interstitial lamella


Femur
Canaliculi
Central (haversian) canal
Lacuna
Lamellae
LM 400x
LM 100x
Sectional view of several osteons (haversian systems) of femur (thigh bone)
Calcified extracellular matrix
Osteocyte
Canaliculi
Lacuna
Details of an osteocyte

Osteoclasts

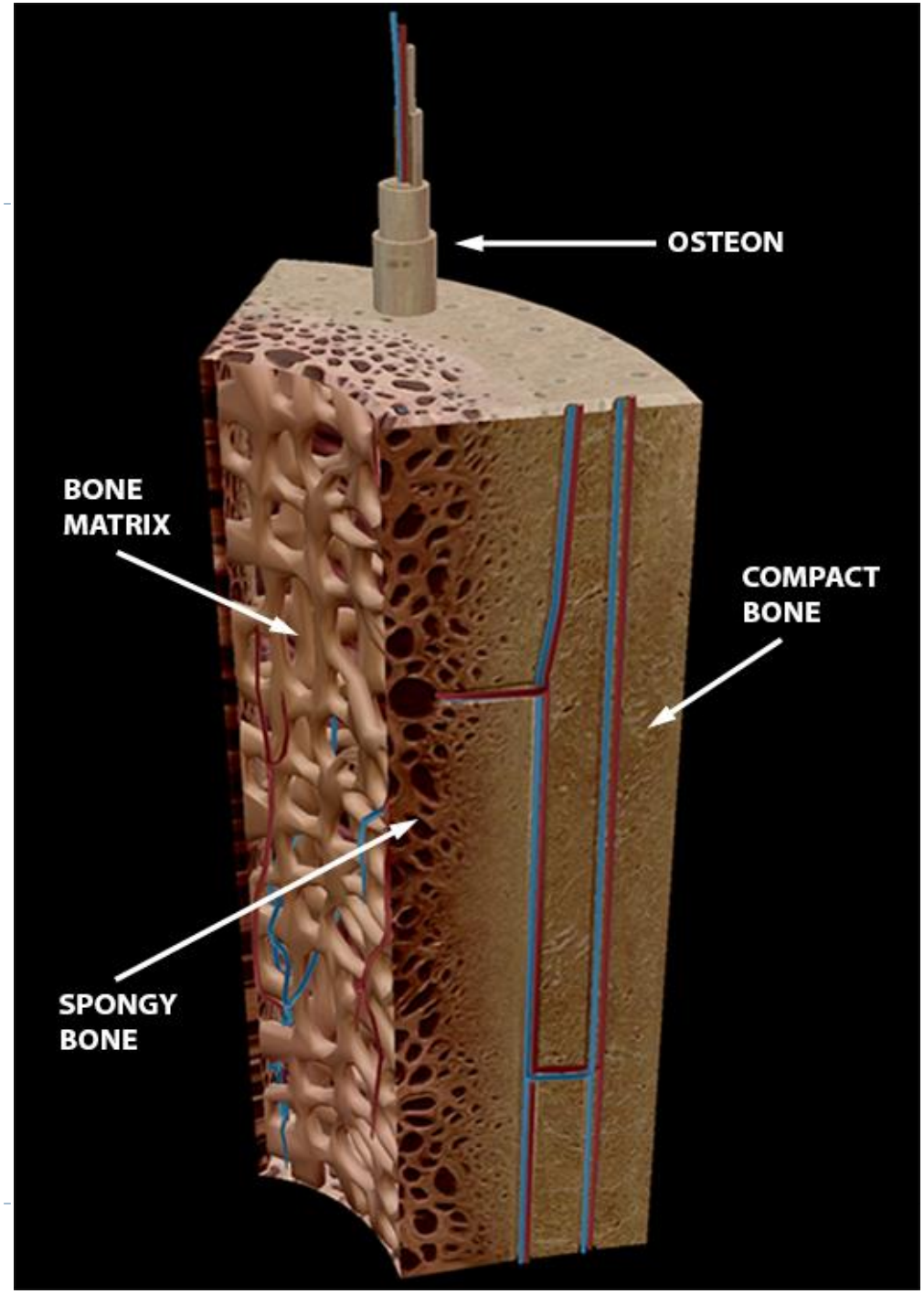
- **Osteoclasts** are large, multinucleated cells found along bone surfaces.
- They do not belong to the osteoprogenitor cell line.
- Instead, the osteoclasts originate from the fusion of **blood or hemopoietic progenitor cells that belong to the mononuclear macrophage-monocyte cell line** of the bone marrow.
- The main function of osteoclasts is bone resorption(during remodeling (renewal or restructuring).
-

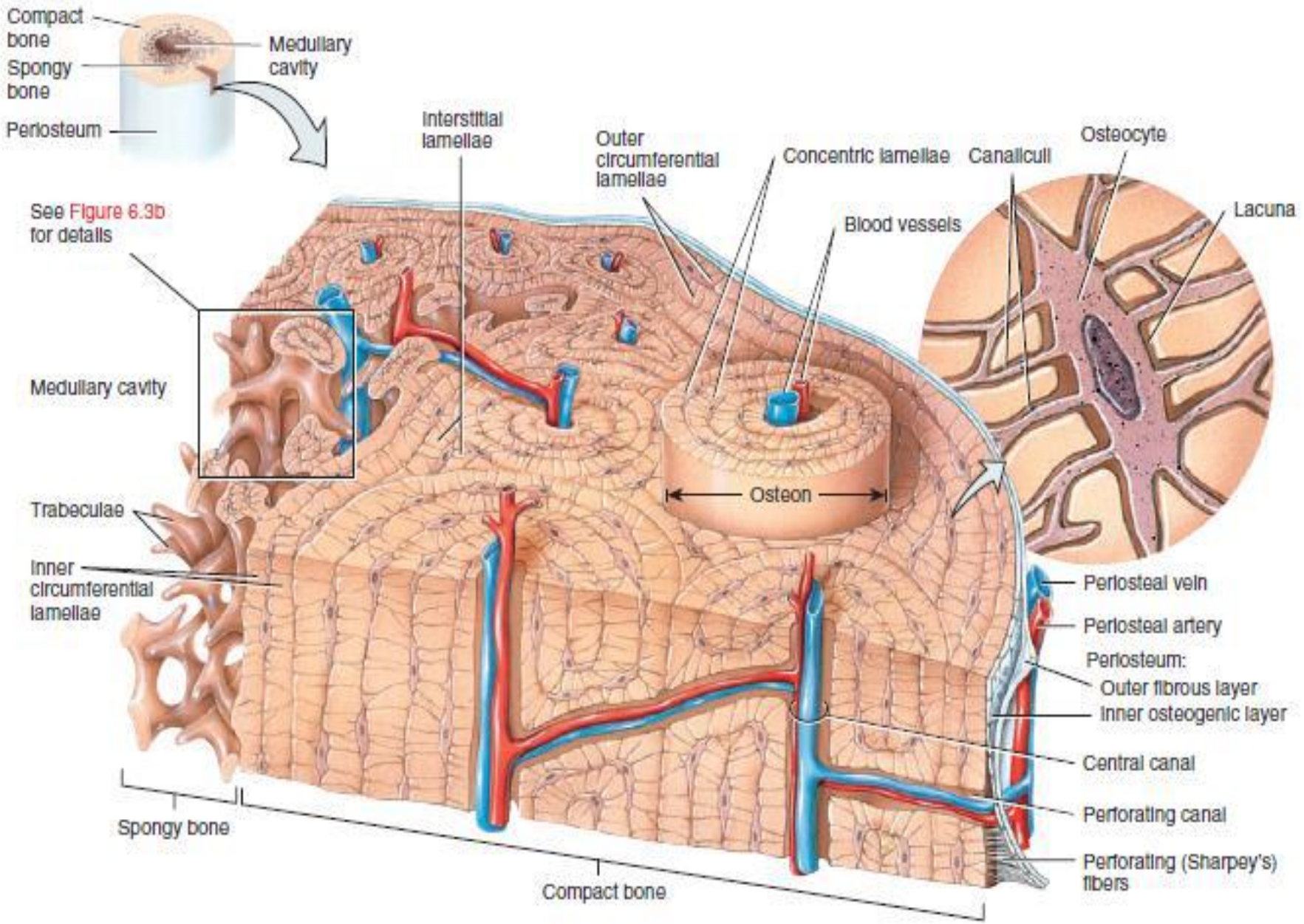
Bone-Lining Cell

- **Bone-lining cells are derived from osteoblasts and cover bone.**
- Bone-lining cells on external bone surfaces are called **periosteal cells**, and those lining internal bone surfaces are often called **endosteal cells.**

Compact bone tissue

- The strongest form of bone tissue.
- Provides protection and support and resists the stresses produced by weight and movement.
- Composed of repeating structural units called osteons, or Haversian systems (ha-VER-shan).
- Osteons **(Haversian systems)** consist of (1)**concentric lamellae** (sing., *lamella*) of bone matrix surrounding a central canal, (2) **osteonal (Haversian) canal**, which contains the vascular and nerve supply of the osteon, (3) **lacunae contain osteocytes and (4) canaliculi.**


OSTEON
BONE MATRIX
COMPACT BONE
SPONGY BONE



(a) Osteons (haversian systems) in compact bone and trabeculae in spongy bone

FIGURE 4.17 ■ Dry, compact bone: ground, transverse section. Low magnification.

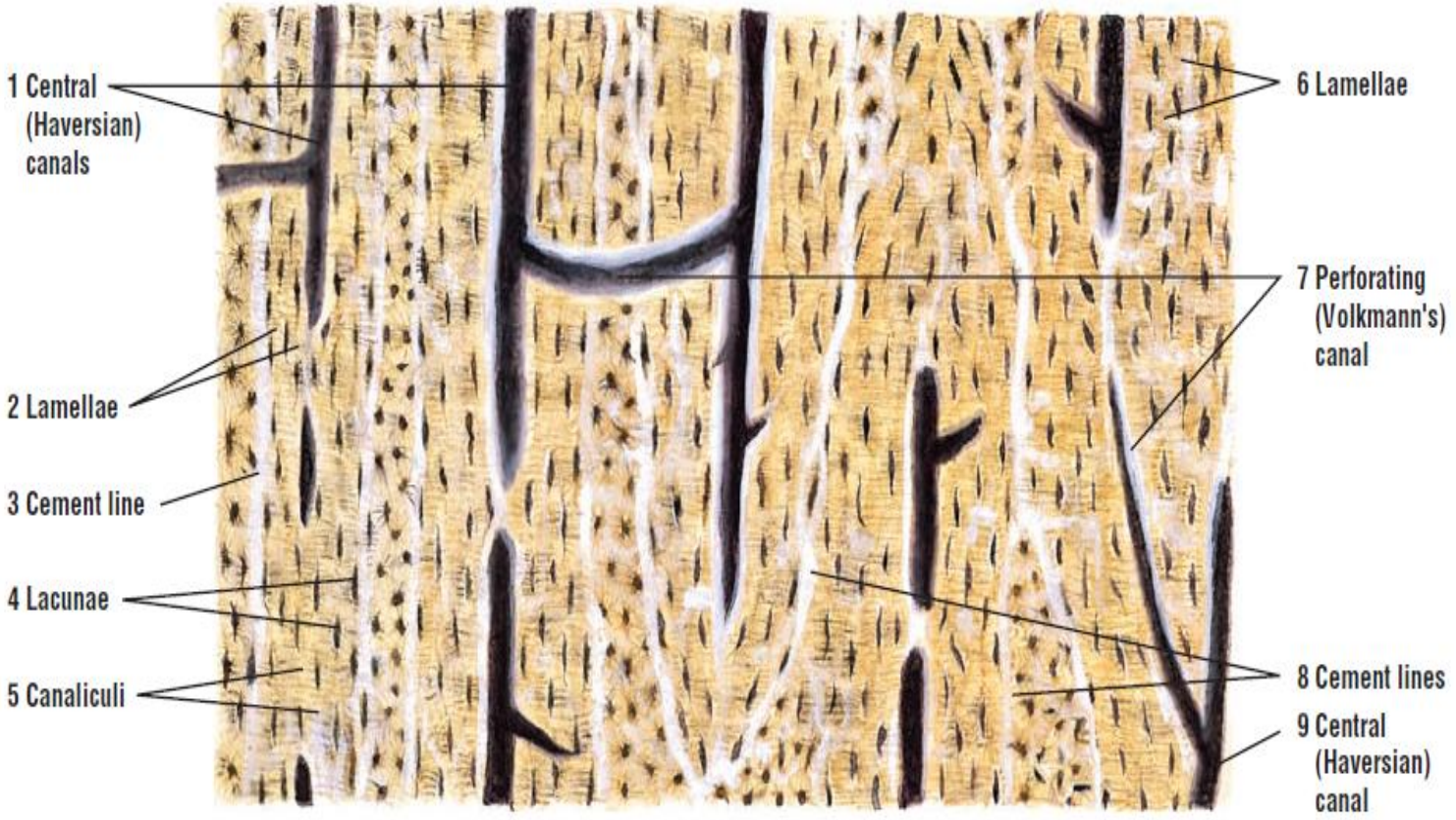


FIGURE 4.18 ■ Dry, compact bone: ground, longitudinal section. Low magnification.

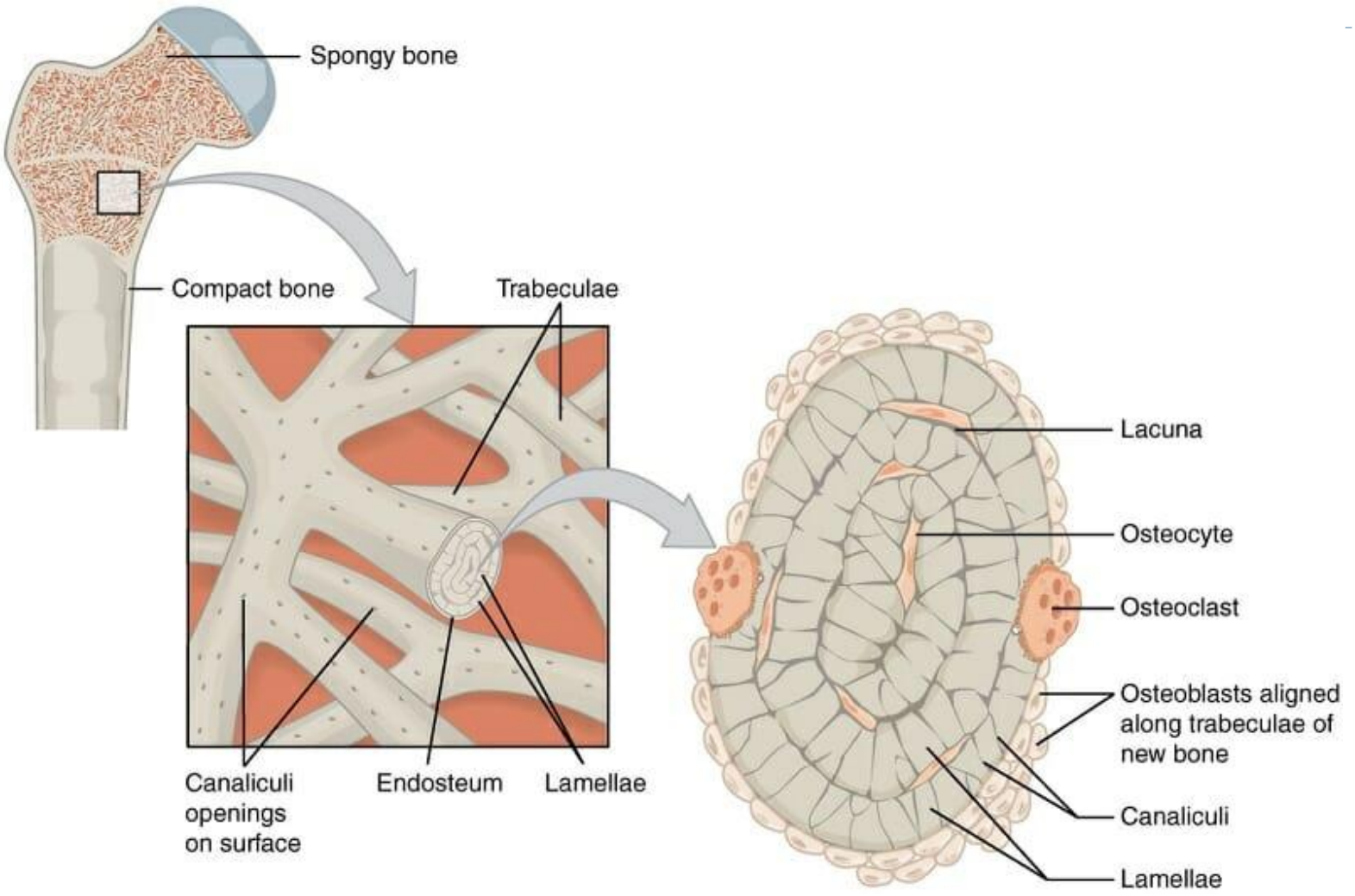
FIGURE 4.19 ■ Dry, compact bone: an osteon, transverse section. High magnification.

Spongy Bone Tissue

In contrast to compact bone tissue, **spongy bone tissue,** also referred to as **trabecular or cancellous** bone tissue, **does not contain osteons**.

- It consists of **lamellae** that are arranged in an **irregular type** called **trabeculae**.
- Between the trabeculae are spaces that are visible by unaided eye.
- These macroscopic spaces are **filled with red bone marrow in bones that produce blood cells, and yellow bone marrow (adipose tissue) in other bones.**
- **Each trabecula consists of concentric lamellae, osteocytes that lie in lacunae, and canaliculi that radiate outward from the lacunae .**

- Site of Erythropoiesis
- Storage of bone marrow


Spongy bone
Compact bone
Trabeculae
Canaliculi openings on surface
Endosteum
Lamellae
Lacuna
Osteocyte
Osteoclast
Osteoblasts aligned along trabeculae of new bone
Canaliculi
Lamellae

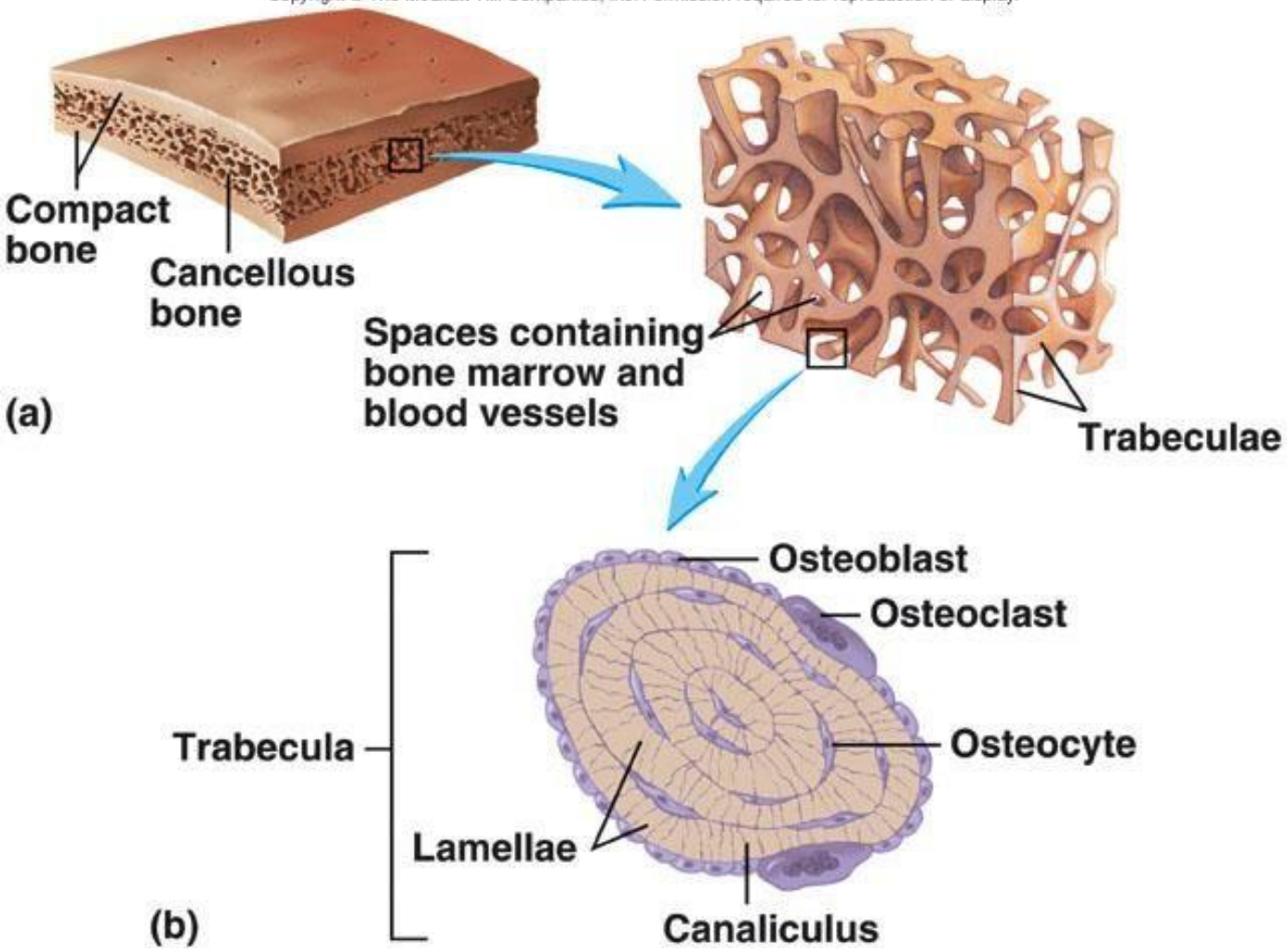


FIGURE 4.15 ■ Cancellous bone with trabeculae and bone marrow cavities: sternum (decalcified bone, transverse section). Stain: hematoxylin and eosin. Low magnification.

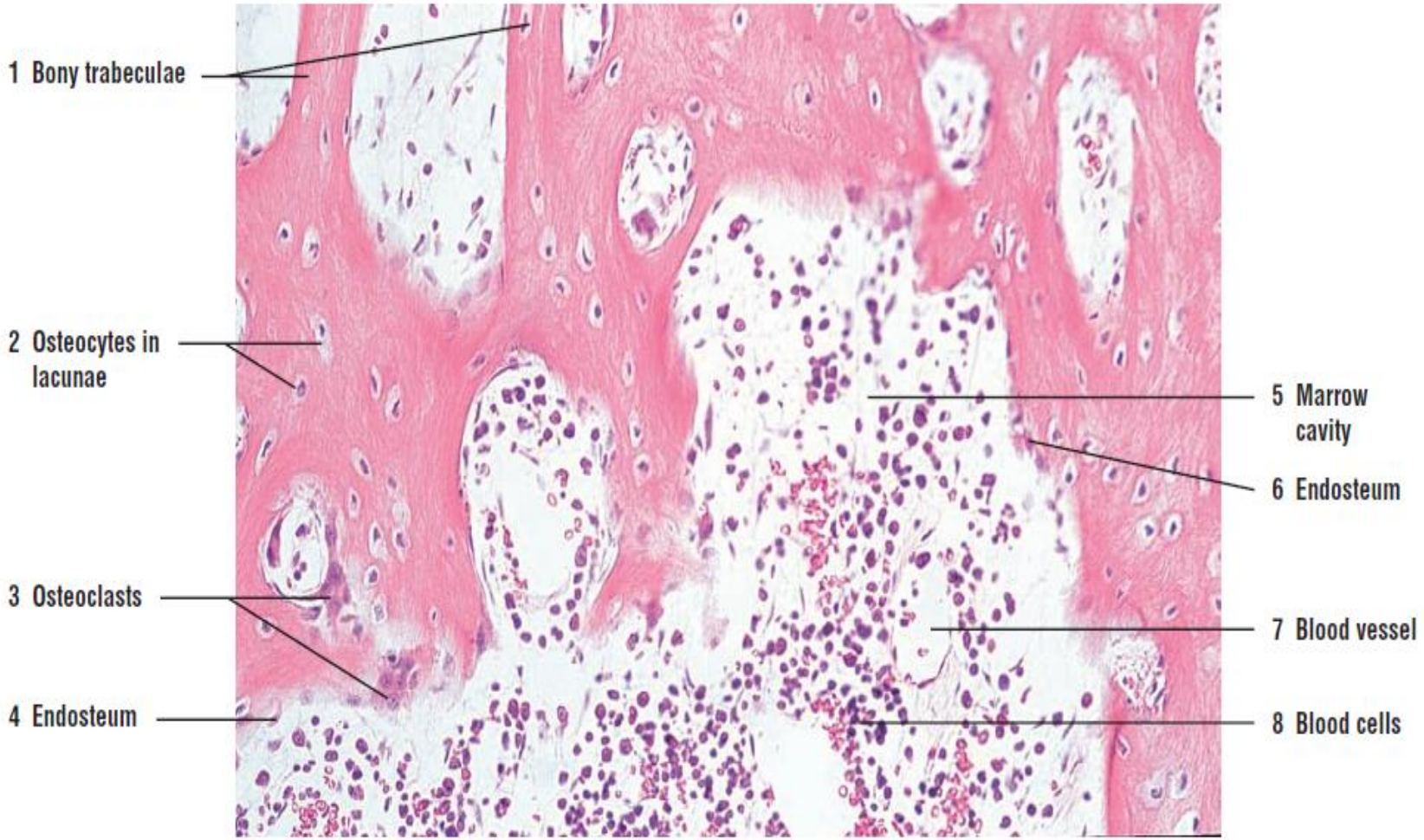


FIGURE 4.16 ■ Cancellous bone: sternum (decalcified bone, transverse section). Stain: hematoxylin and eosin. ×64.

GENERAL STRUCTURE OF BONES

- **Outer Surface of Bones**
- Bones are covered by a **periosteum (a sheath of dense fibrous connective tissue)** except in areas where they articulate with another bone. In this case, the articulating surface is covered by **cartilage**.
- **Periosteum** consists of an **outer fibrous layer** that similar to other dense connective tissues and **an inner, more cellular layer that contains the osteoprogenitor cells**.

GENERAL STRUCTURE OF BONES

Bone Cavities

- Endosteum, a layer of connective tissue cells that contains osteoprogenitor cells.
- The endosteum is often only one cell layer thick of osteoprogenitor cells that can differentiate into bone matrix–secreting cells (the osteoblasts) and bone-lining cells.
- Osteoprogenitor cells and bone-lining cells are difficult to distinguish at the microscopic level.
- They are both flattened in shape with elongated nuclei and indistinguishable cytoplasmic features. Because of their location within the bone cavities they are frequently called **endosteal cells.**

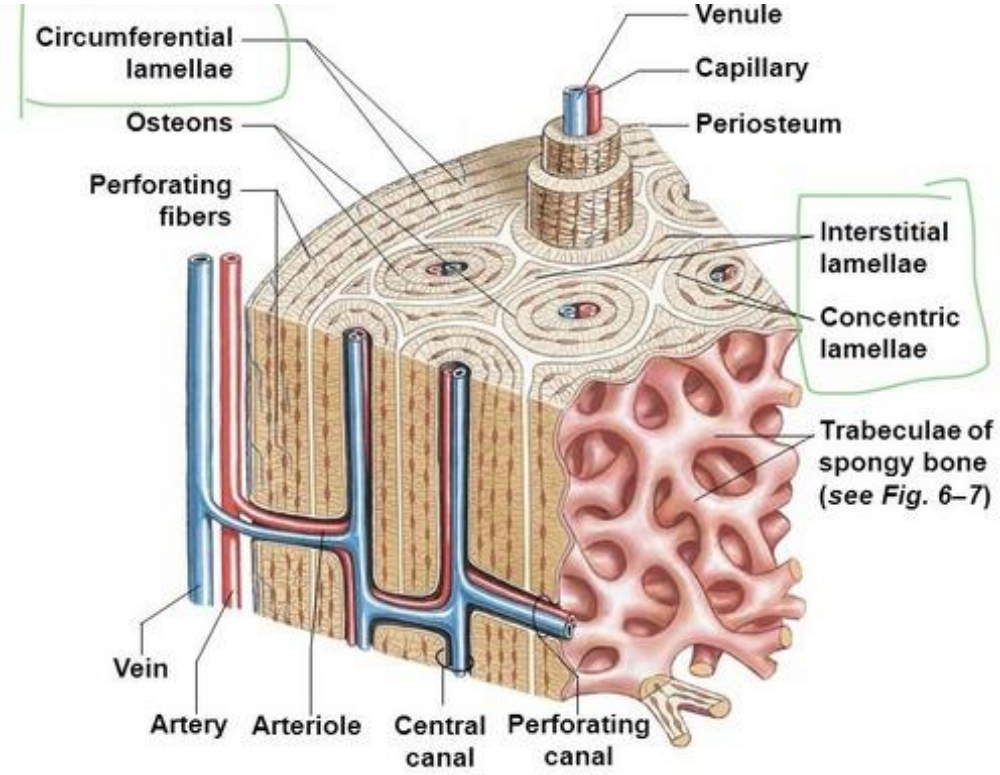
Surface Covers of Bone

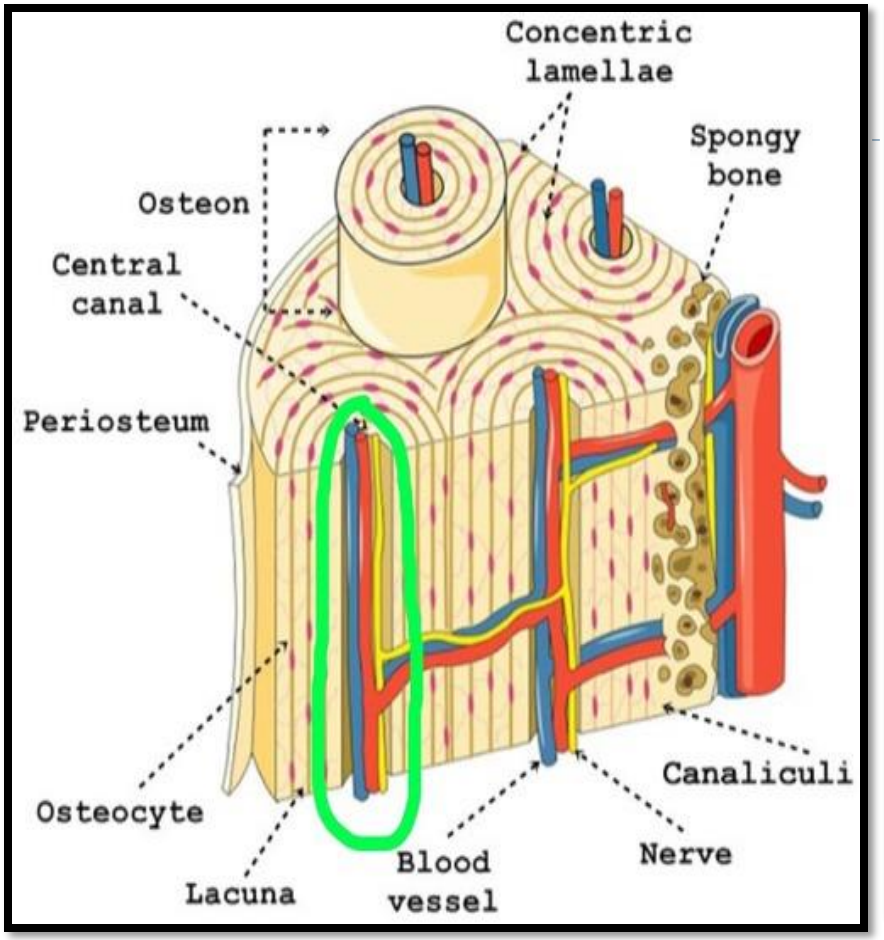
- **Periosteum: Double layer** of connective tissue surrounding the outer surface of bones, except for articular surfaces.
- **Layers of Periosteum**
- **1.OUTER Fibrous layer**. Outer layer of dense connective tissue.
- **2.INNER Osteogenic layer**. Inner, more cellular layer, contains **osteoprogenitor cells**
- **Endosteum**
- lines all interior surfaces of bone.

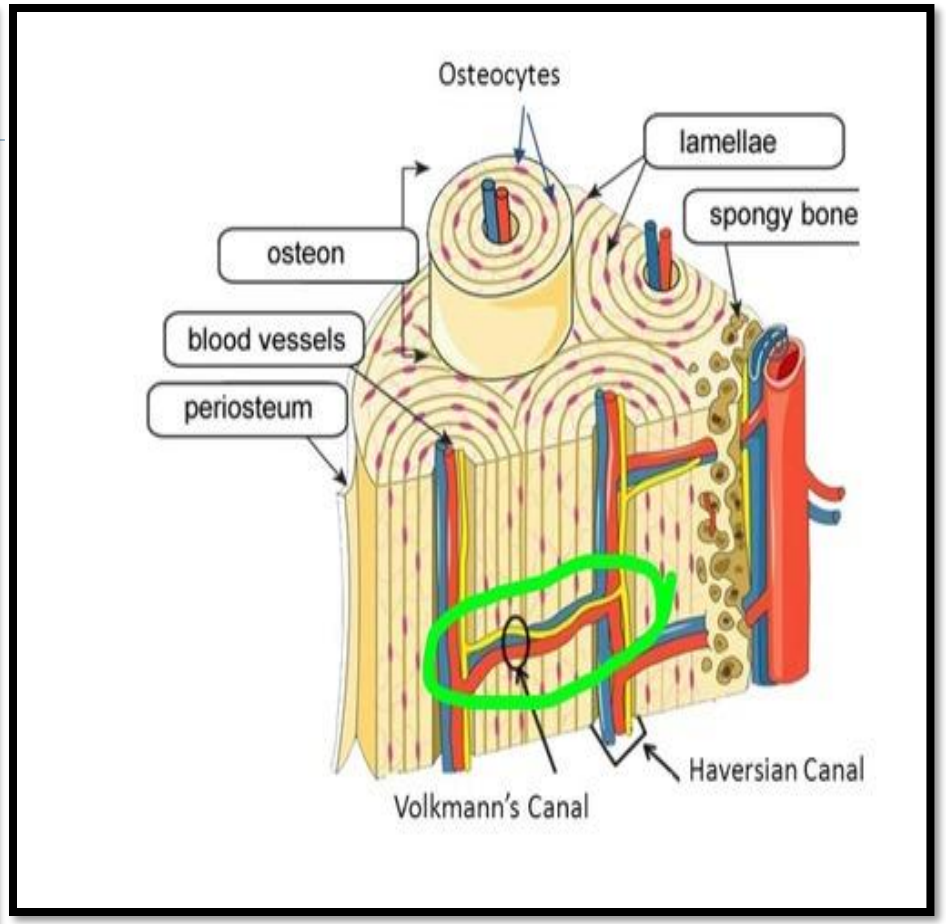
Mature Bone

- **Mature bone is composed of structural units called osteons (Haversian systems).**
- Between the osteons also found lamellae of collagen called **interstitial lamellae.**
- The collagen fibers in the **concentric lamellae** in an osteon are parallel to one another in any lamella but in different directions in adjacent lamellae.
- This arrangement imparts great strength to the osteon.

- **Circumferential lamellae** in entire inner and outer circumferences of the shaft of a long bone.
- **Perforating canals (Volkmann's canals)** horizontal opening that holds blood vessels and nerves **and** travel them from the periosteal and endosteal surfaces to reach the osteonal canal; they also connect osteonal canals to one another.
- Volkmann's canals are not surrounded by concentric lamellae, a key feature in their histologic identification.


Circumferential lamellae
Osteons
Perforating fibers
Venule
Capillary
Periosteum
Interstitial lamellae
Concentric lamellae
Trabeculae of spongy bone (see Fig. 6–7)
Vein
Artery
Arteriole
Central canal
Perforating canal


Concentric lamellae
Spongy bone
Osteon
Central canal
Periosteum
Osteocyte
Lacuna
Blood vessel
Nerve
Canaliculi


Osteocytes
lamellae
spongy bone
osteon
blood vessels
periosteum
Haversian Canal
Volkmann's Canal

Immature Bone

- The first bone to appear in a skeleton of fetus development and in fracture repair (**usually temporary**), is replaced in adults by secondary bone tissue.
- Differ from mature bone in several aspects:

1. Does not display an organized lamellated appearance. (**nonlamellar or woven bone**) because of the interlacing(mix) arrangement of the collagen fibers.
2. The cells in immature bone tend to be randomly arranged, whereas cells in mature bone are usually arranged with their long axes in the same direction as the lamellae.

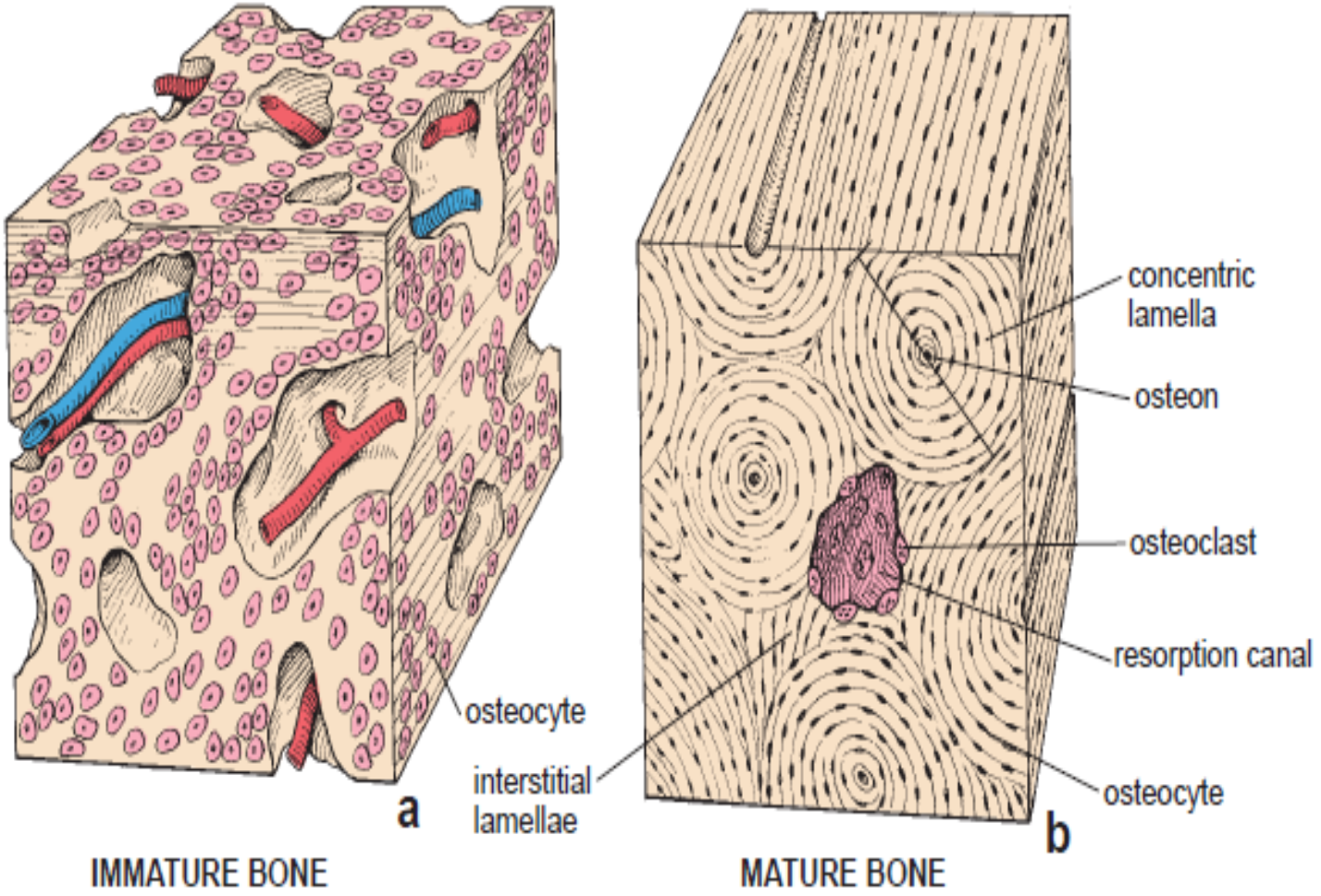


Diagram of immature and mature bone. Immature bone does not display an organized lamellar appearance because of the interlacing arrangement of the collagen fibers. The cells tend to be randomly arranged, whereas the cells in mature bone are organized in a circular fashion that reflects the lamellar structure of the Haversian system

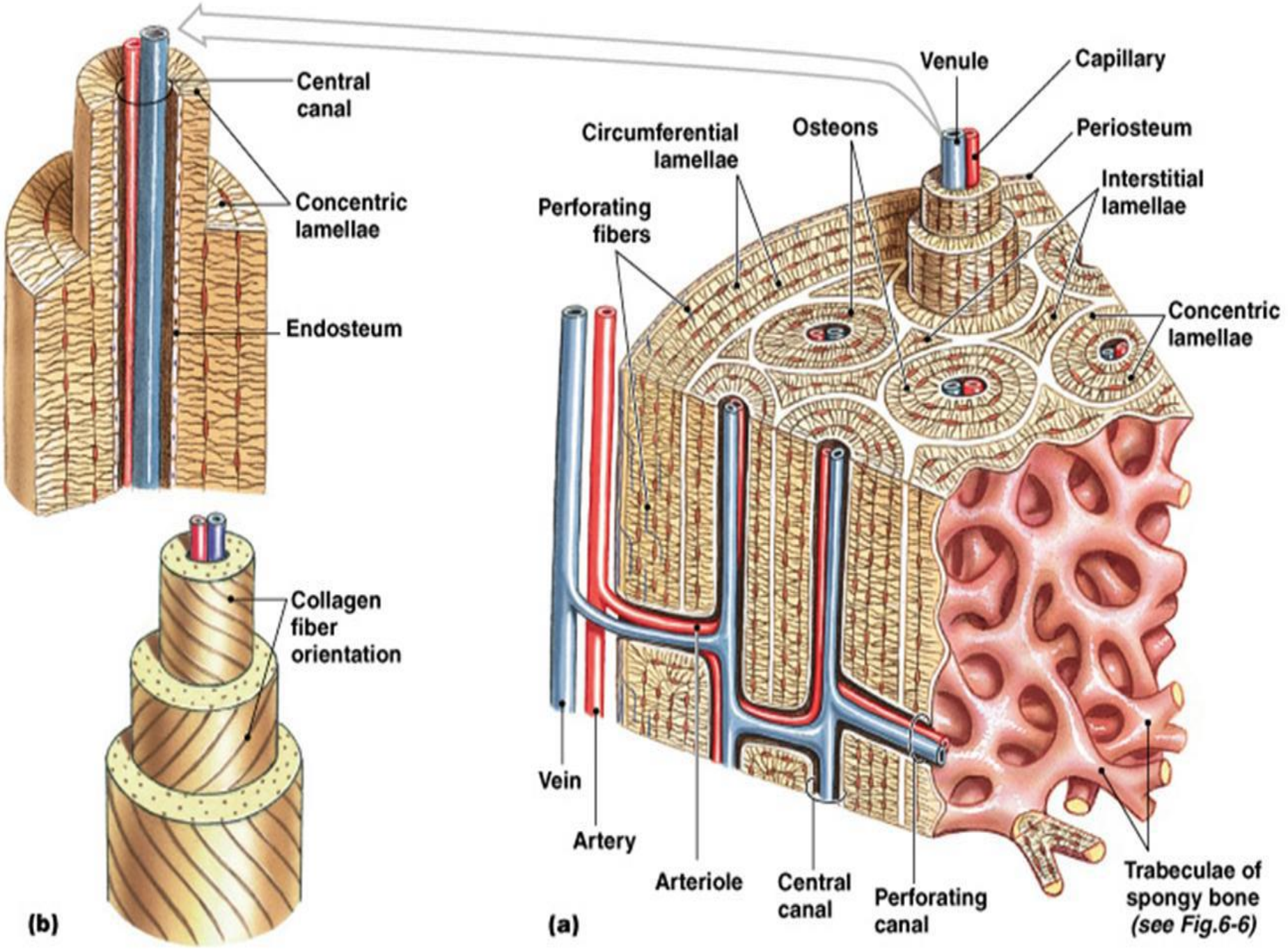
Immature bone

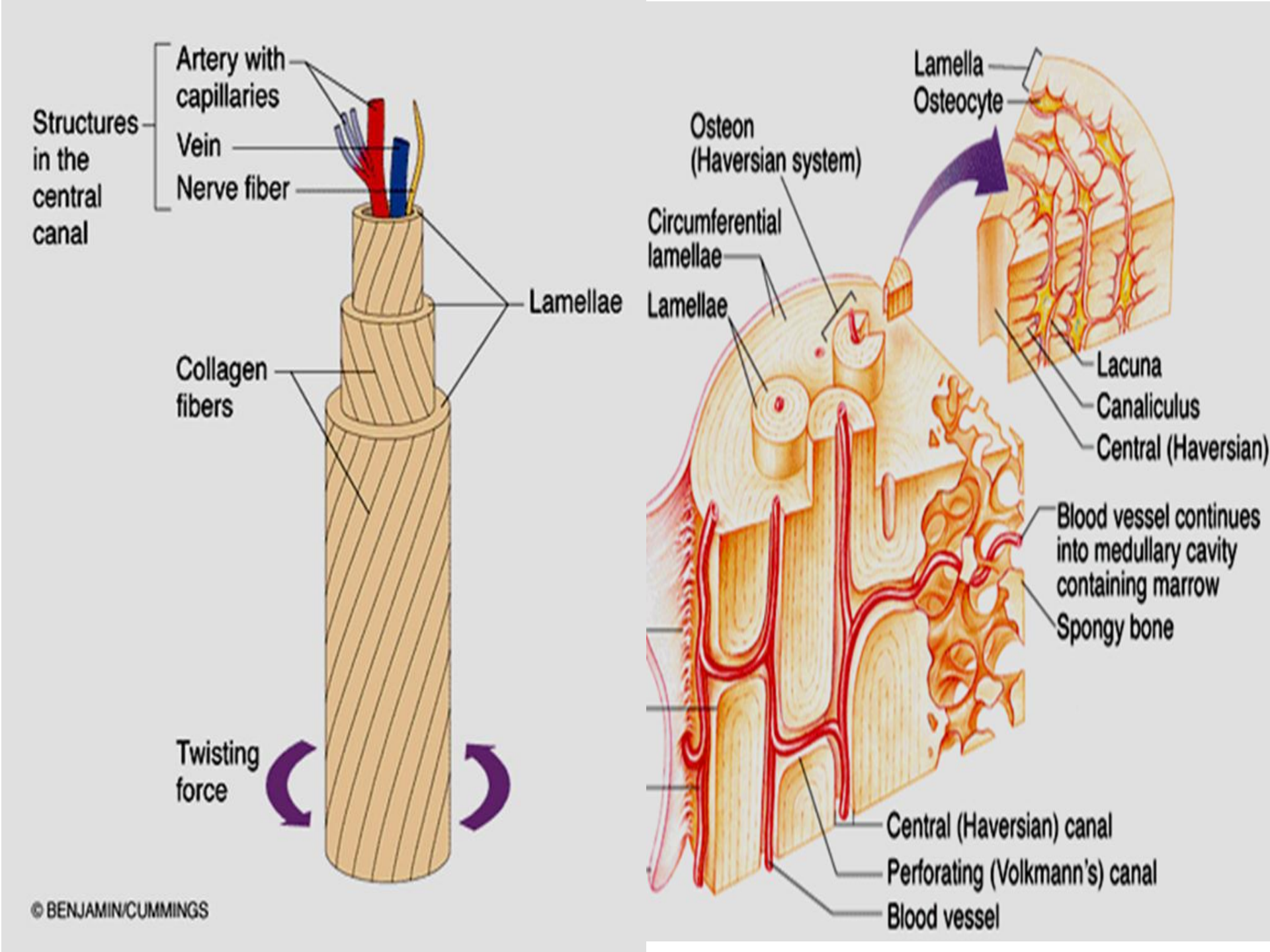
- Although mature bone is clearly the major bone type in the adult and immature bone is the major bone type in the developing fetus, areas of immature bone are present in adults, especially where bone is being remodeled. Areas of immature bone are common in the alveolar sockets of the adult oral cavity. It is this immature bone in the alveolar sockets that makes it possible to make orthodontic corrections even in adults.

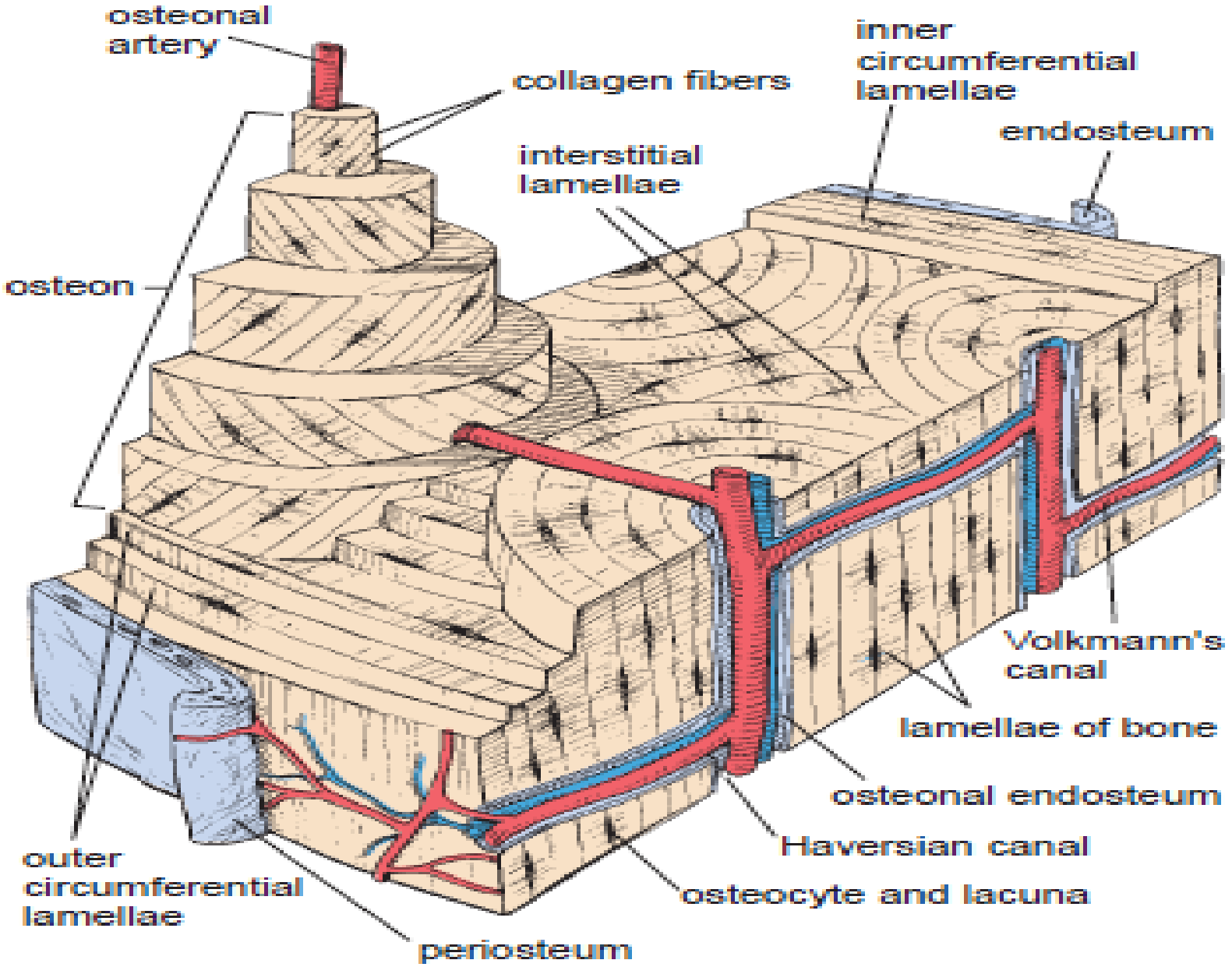
BONE MARROW

- **The marrow cavity and the spaces in spongy bone contain bone marrow.**
- **Red bone marrow** consists of **blood cells in different stages of development** and a network of reticular cells and fibers that serve as a supporting framework for the developing blood cells.
- In later stages of growth and in adults, when the rate of blood cell formation has diminished, the tissue in the marrow cavity consists mostly of fat cells; it is then called **yellow marrow.**

- In the adult, red marrow is normally restricted to the spaces of spongy bone in a few locations such as the sternum and the iliac crest.
- Diagnostic bone marrow samples and marrow for transplantation are obtained from these sites.


Central canal
Concentric lamellae
Endosteum
Collagen fiber orientation
(b)
Venule
Capillary
Circumferential lamellae
Osteons
Periosteum
Interstitial lamellae
Perforating fibers
Concentric lamellae
Vein
Artery
Arteriole
Central canal
Perforating canal
Trabeculae of spongy bone
(see Fig.6-6)
(a)


Structures in the central canal
Artery with capillaries
Vein
Nerve fiber
Lamellae
Collagen fibers
Twisting force
© BENJAMIN/CUMMINGS
Lamella
Osteocyte
Osteon (Haversian system)
Circumferential lamellae
Lamellae
Lacuna
Canaliculus
Central (Haversian)
Blood vessel continues into medullary cavity containing marrow
Spongy bone
Central (Haversian) canal
Perforating (Volkmann's) canal
Blood vessel

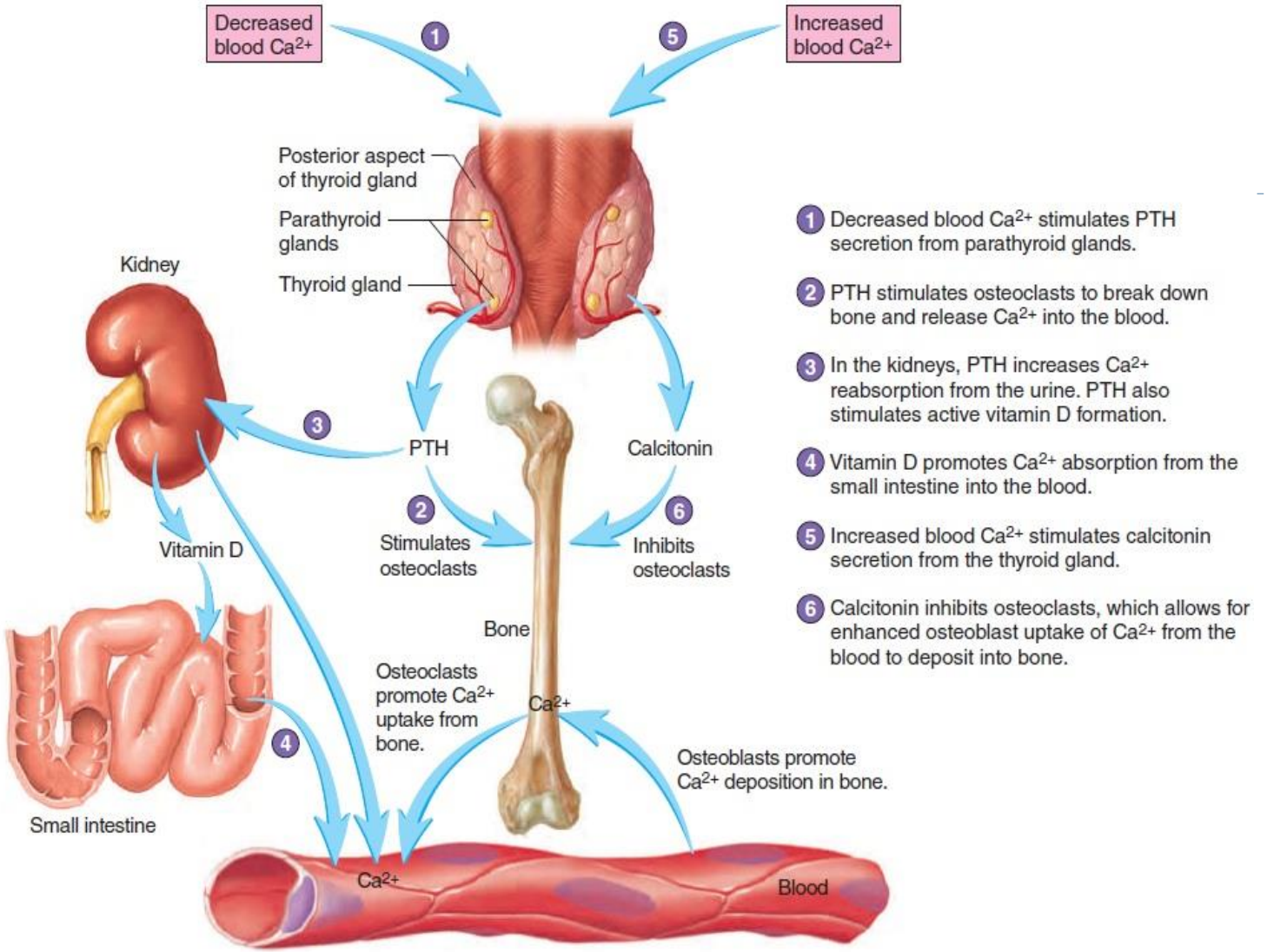

osteonal artery
collagen fibers
inner circumferential lamellae
endosteum
interstitial lamellae
osteon
Volkmann's canal
lamellae of bone
osteonal endosteum
Haversian canal
osteocyte and lacuna
outer circumferential lamellae
periosteum

PHYSIOLOGIC ASPECTS OF BONE

Bone serves as a reservoir for body calcium

- Keeping of **normal blood calcium** levels is critical to health and life.
- Calcium may be delivered from the bone matrix to the blood if the circulating blood levels of calcium fall below a critical point (**physiologic calcium concentration in the human ranges from 8.9 to 10.1 mg/dL**).
- Conversely, excess blood calcium may be removed from the blood and stored in bone.
- These processes are regulated by **parathyroid hormone (PTH)**, secreted by the parathyroid gland, and **calcitonin**, secreted by the parafollicular cells or C- cells of the thyroid gland.
- **PTH** acts on the bone to *raise low blood calcium levels* to normal.
- **Calcitonin** acts to *lower elevated blood calcium levels* to normal.

- When the calcium level falls below normal, **parathyroid hormone**, released from the parathyroid glands, stimulates osteoclasts to resorb the bone matrix. This action releases more calcium into the blood.
- When the calcium level is above normal, a hormone called **calcitonin**, released by parafollicular cells in the thyroid gland, inhibits osteoclast activity and decreases bone resorption.



PROCESS Figure 6.9 Calcium Homeostasis

Best regards
Dr. Reyadh Salim