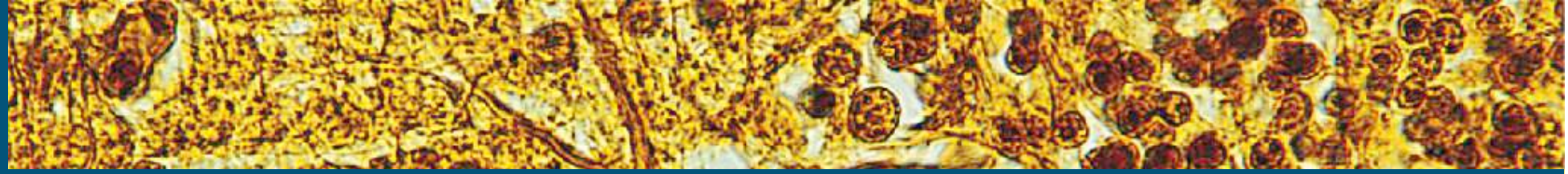


Bone

Textbook of Histology, 4th ed.

Gartner

Bone

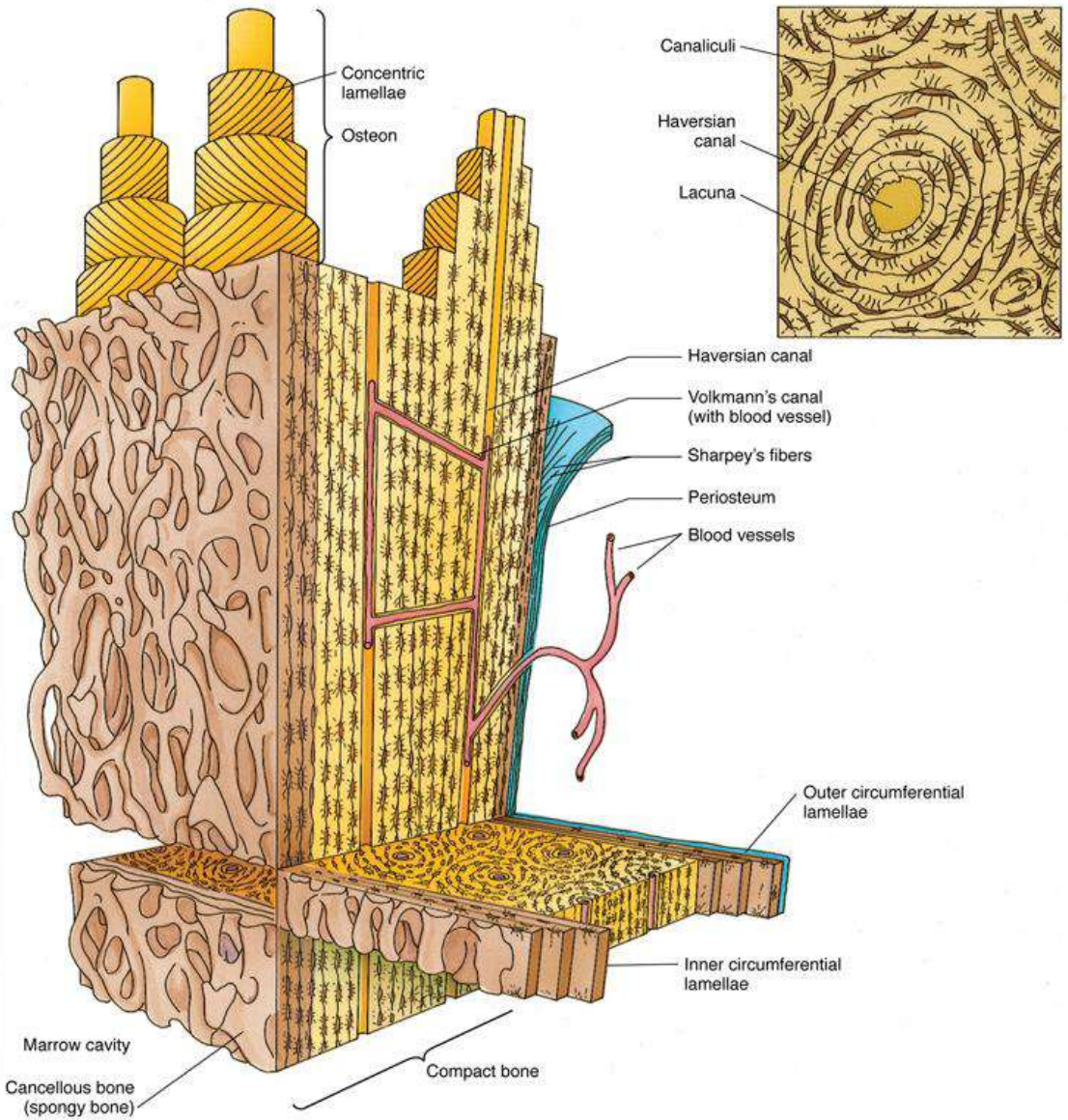


Diagram of bone illustrating compact cortical bone, osteons, lamellae, Volkmann's canals, haversian canals, lacunae, canaliculi, and spongy bone.

Bone, one of the hardest substances of the body, is the primary structural framework for support and protection of the organs of the body, including the brain and spinal cord.

Bones also serve as levers for the muscles attached to them, thereby multiplying the force of the muscles to attain movement.

Bone is a reservoir for several minerals of the body; for example, it stores about 99% of the body's calcium. Bone contains a central cavity, the **marrow cavity**, which houses the **bone marrow**, a hemopoietic organ.

Bone

Bone is a rigid inflexible connective tissue in which the ECM has become impregnated with salts of calcium and phosphate by a process called **mineralization**. Bone is highly vascularized and metabolically very active.

The functions of bone are:

1. Support and protection of the body and its organs.

2. A reservoir for calcium and phosphate ions.

Bone

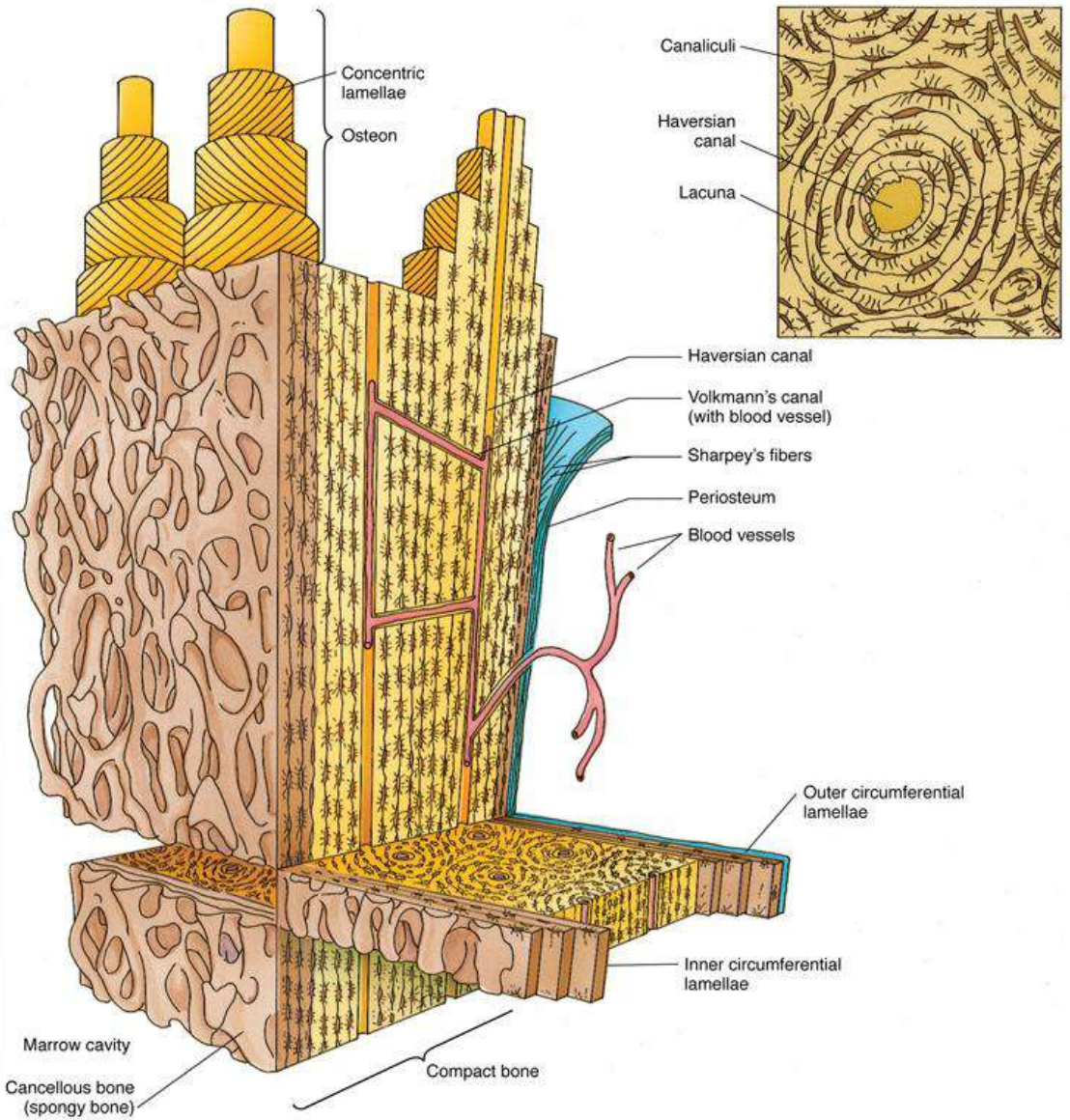


Diagram of bone illustrating compact cortical bone, osteons, lamellae, Volkmann's canals, haversian canals, lacunae, canaliculi, and spongy bone.

Bone is covered on its external surface, except at synovial articulations, with a **periosteum,** which consists of an outer layer of **dense fibrous connective tissue** and an inner cellular layer containing osteoprogenitor (osteogenic) cells.

The central cavity of a bone is lined with **endosteum**, a specialized thin connective tissue composed of a monolayer of **osteoprogenitor cells** and **osteoblasts**.

Bone

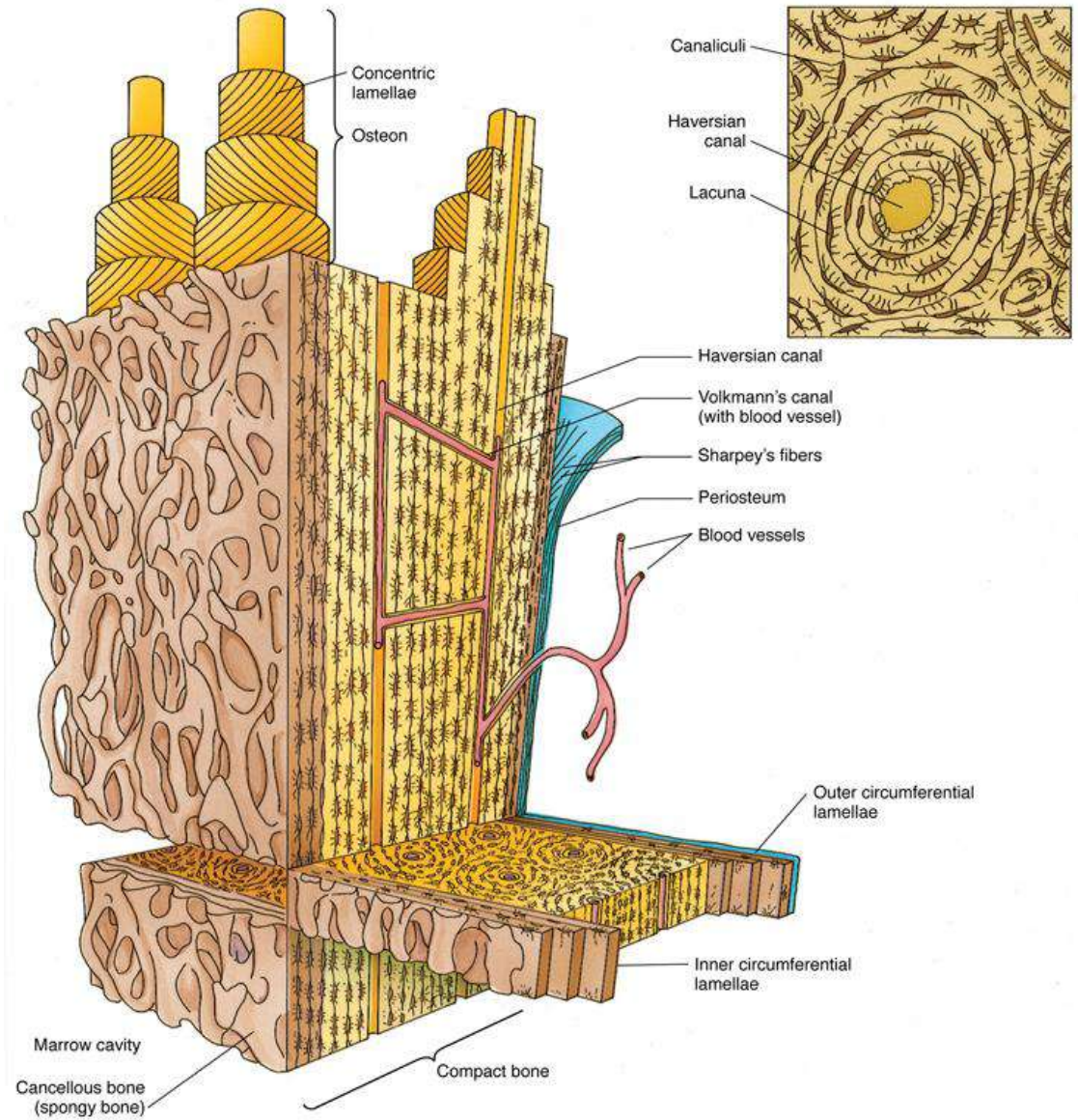
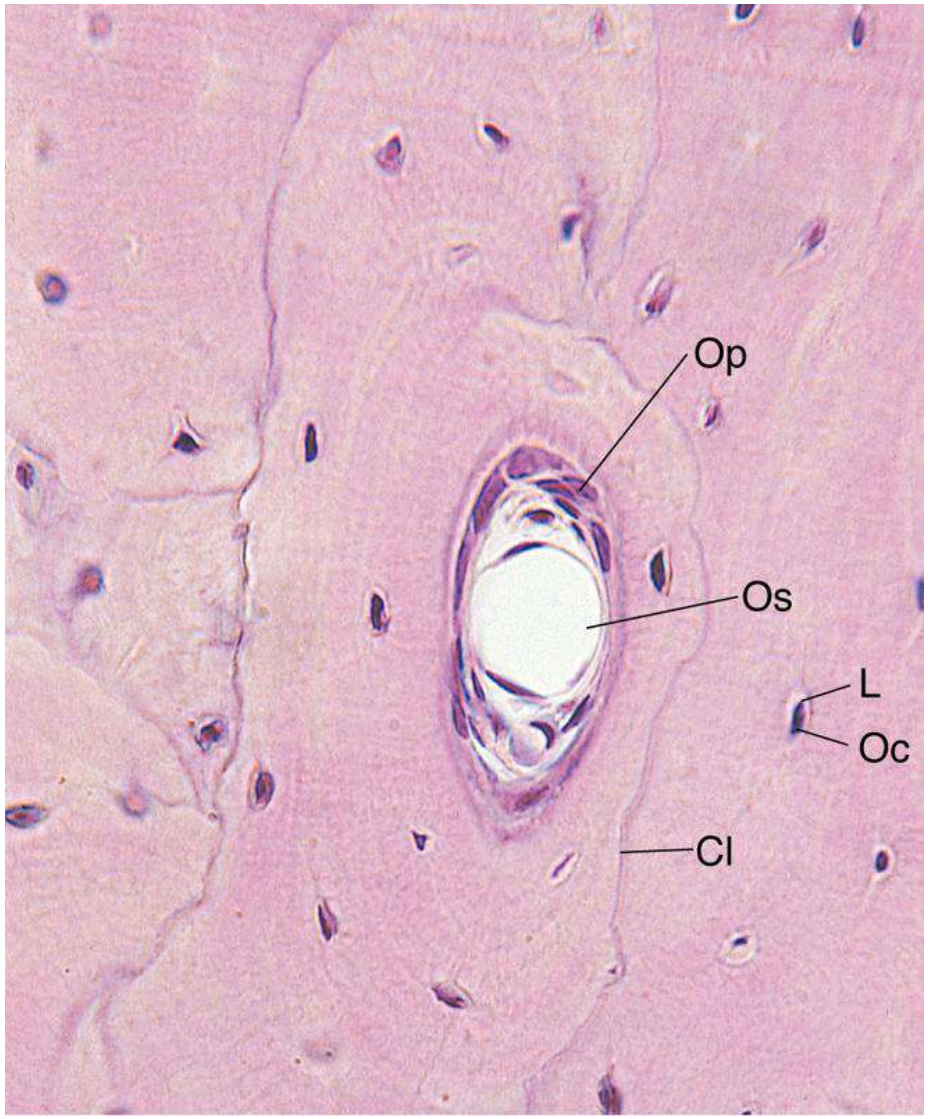


Diagram of bone illustrating compact cortical bone, osteons, lamellae, Volkmann's canals, haversian canals, lacunae, canaliculi, and spongy bone.

Bone is composed of cells lying in an extracellular matrix that has become calcified. The calcified matrix is composed of fibers and ground substance. The fibers constituting bone are primarily type I collagen. The ground substance is rich in proteoglycans with chondroitin sulfate and keratan sulfate side chains.

In addition, glycoproteins, such as osteonectin, osteocalcin, osteopontin, and bone sialoprotein, are present.

Cells of Bone



Light micrograph of decalcified compact bone (×540). Osteocytes (Oc) may be observed in lacunae (L). Also note the osteon (Os), osteoprogenitor cells (Op), and the cementing lines (Cl).

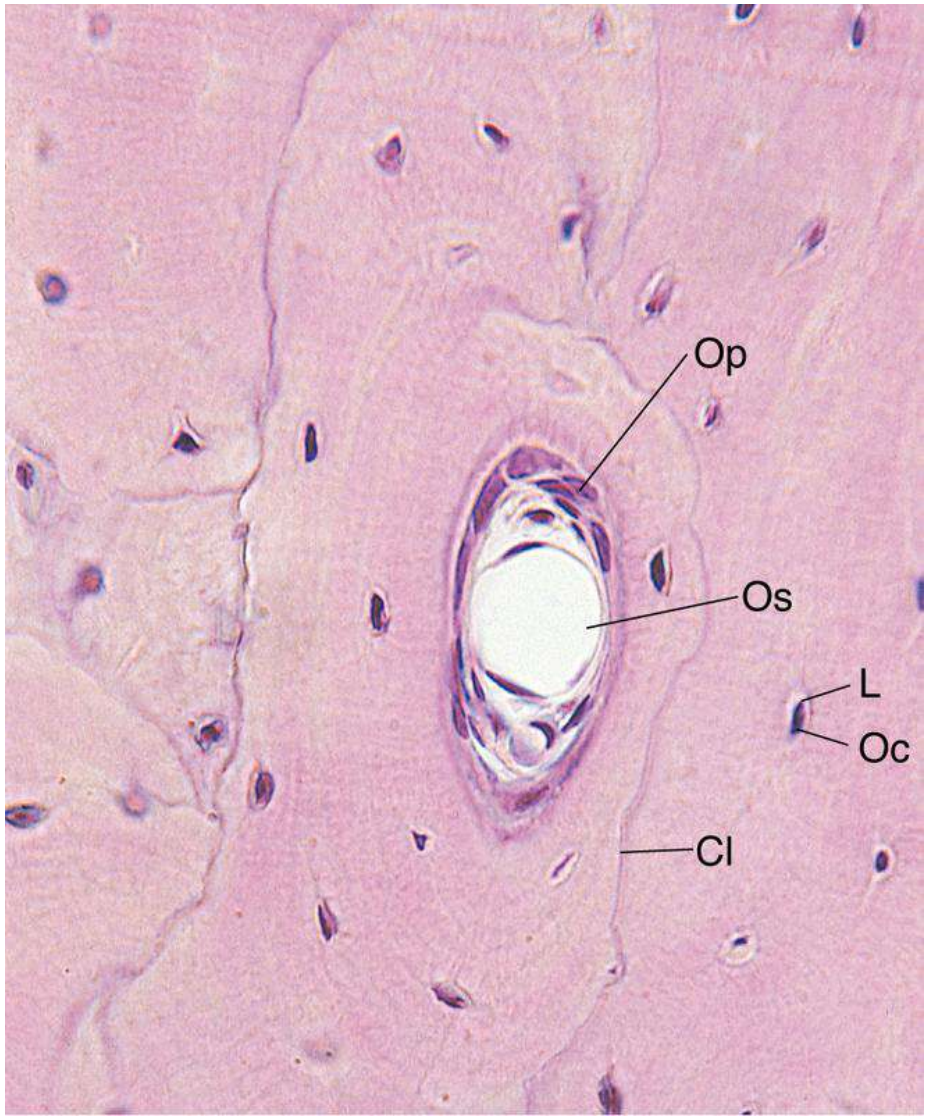
The cells of bone are:

- osteoprogenitor cells,
- osteoblasts,
- osteocytes,
- osteoclasts.

Osteoprogenitor cells are located in the inner cellular layer of the periosteum, lining haversian canals, and in the endosteum. These cells, derived from embryonic mesenchyme, can undergo mitotic division and have the potential to differentiate into osteoblasts.

Osteoblasts, derived from osteoprogenitor cells, are responsible for the synthesis of the organic components of the bone matrix, including collagen, proteoglycans, and glycoproteins.

Cells of Bone

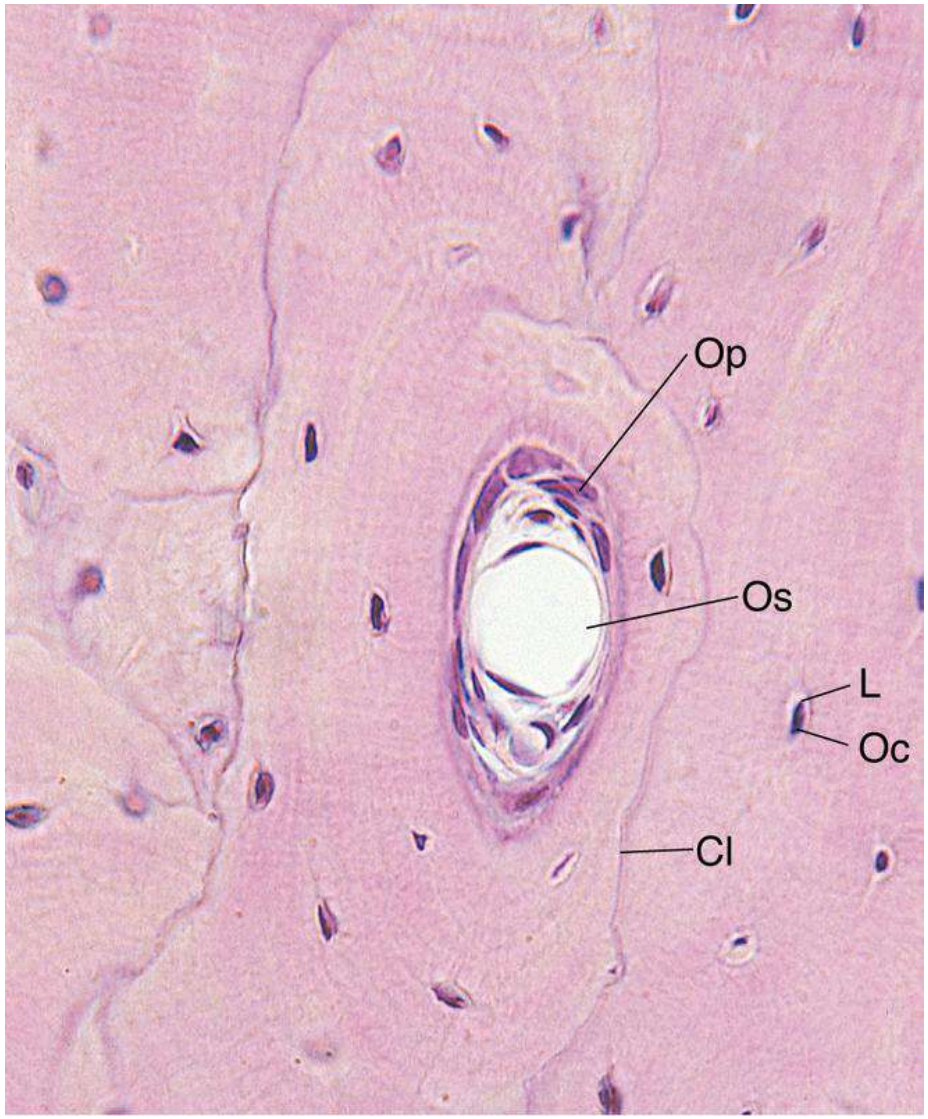


Light micrograph of decalcified compact bone (×540). Osteocytes (Oc) may be observed in lacunae (L). Also note the osteon (Os), osteoprogenitor cells (Op), and the cementing lines (Cl).

Osteoblasts are located on the surface of the bone in a sheet-like arrangement of cuboidal to columnar cells. When actively secreting matrix, they exhibit a basophilic cytoplasm.

Osteocytes conform to the shape of their lacunae. Their nucleus is flattened, and their cytoplasm is poor in organelles, displaying scant RER and a greatly reduced Golgi apparatus. Although osteocytes appear to be inactive cells, they secrete substances necessary for bone maintenance.

Cells of Bone



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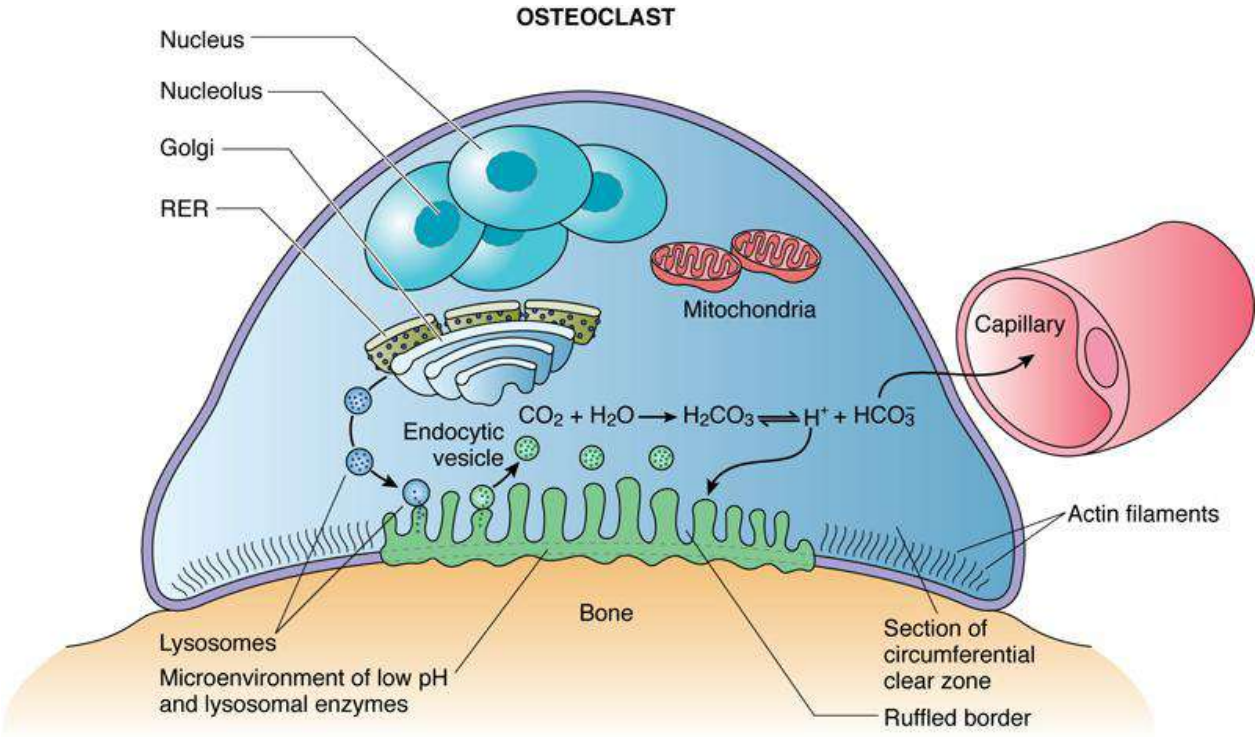
These cells have also been implicated in **mechanotransduction**, in that they respond to stimuli that place tension on bone by releasing cyclic adenosine monophosphate (cAMP), osteocalcin, and insulin-like growth factor. The release of these factors facilitates the recruitment of preosteoblasts to assist in the remodeling of the skeleton (adding more bone) not only during growth and development but also during the long-term redistribution of forces acting on the skeleton.

Osteoclasts resorb bone.

Osteoclasts



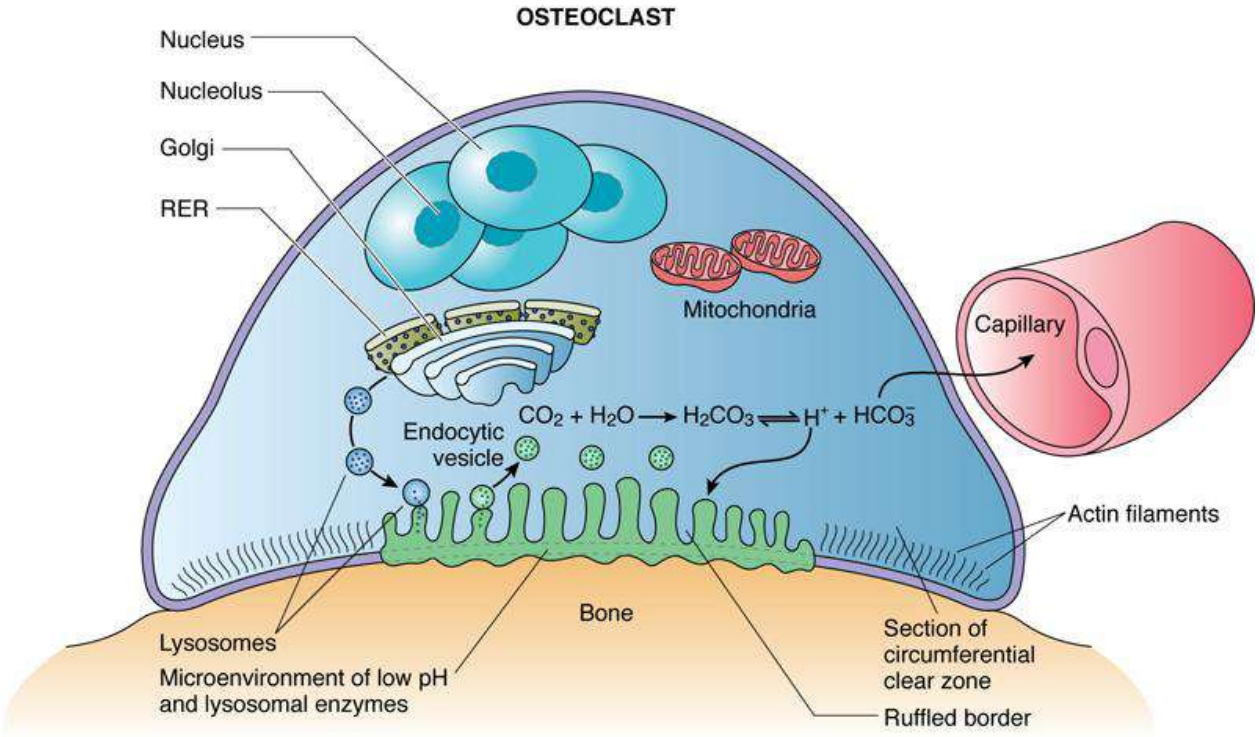
Osteoclastic function. RER, rough endoplasmic reticulum. *(From Gartner LP, Hiatt JL, Strum JM: Cell Biology and Histology [Board Review Series]. Philadelphia, Lippincott Williams & Wilkins, 1998, p 100.)*

The precursor of the **osteoclast** originates in the bone marrow.

Osteoclasts have receptors for osteoclast-stimulating factor, colony-stimulating factor-1, OPGL, osteoprotegerin, and calcitonin, among others.

These cells are responsible for resorbing bone; after they finish doing so, these cells probably undergo apoptosis.

Osteoclasts



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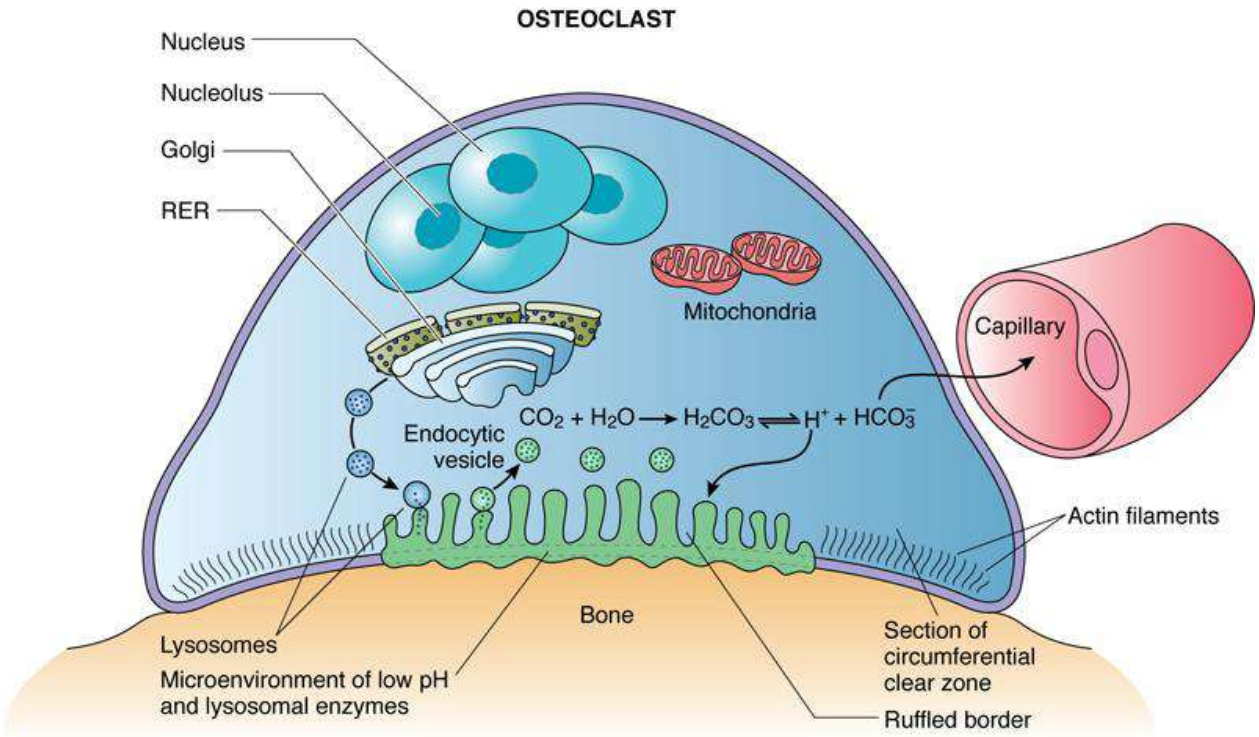
Osteoclasts are large, motile, multinucleated cells 150 μm in diameter; they contain up to 50 nuclei and have an acidophilic cytoplasm. Osteoclasts were once thought to be derived from the fusion of many blood-derived monocytes, but the newest evidence shows that they have a bone marrow precursor in common with monocytes, the **granulocyte-macrophage progenitor cell** (**GM-CFU**).

These precursor cells are stimulated by macrophage colony-stimulating factor and by OPGL to undergo mitosis. In the presence of bone, these osteoclast precursors fuse to produce the multinucleated osteoclast.

Osteoclasts



Osteoclastic function. RER, rough endoplasmic reticulum. *(From Gartner LP, Hiatt JL, Strum JM: Cell Biology and Histology [Board Review Series]. Philadelphia, Lippincott Williams & Wilkins, 1998, p 100.)*

Osteoclasts occupy shallow depressions, called **Howship's lacunae**, that identify regions of bone resorption.

An osteoclast active in bone resorption may be subdivided into four morphologically recognizable regions:

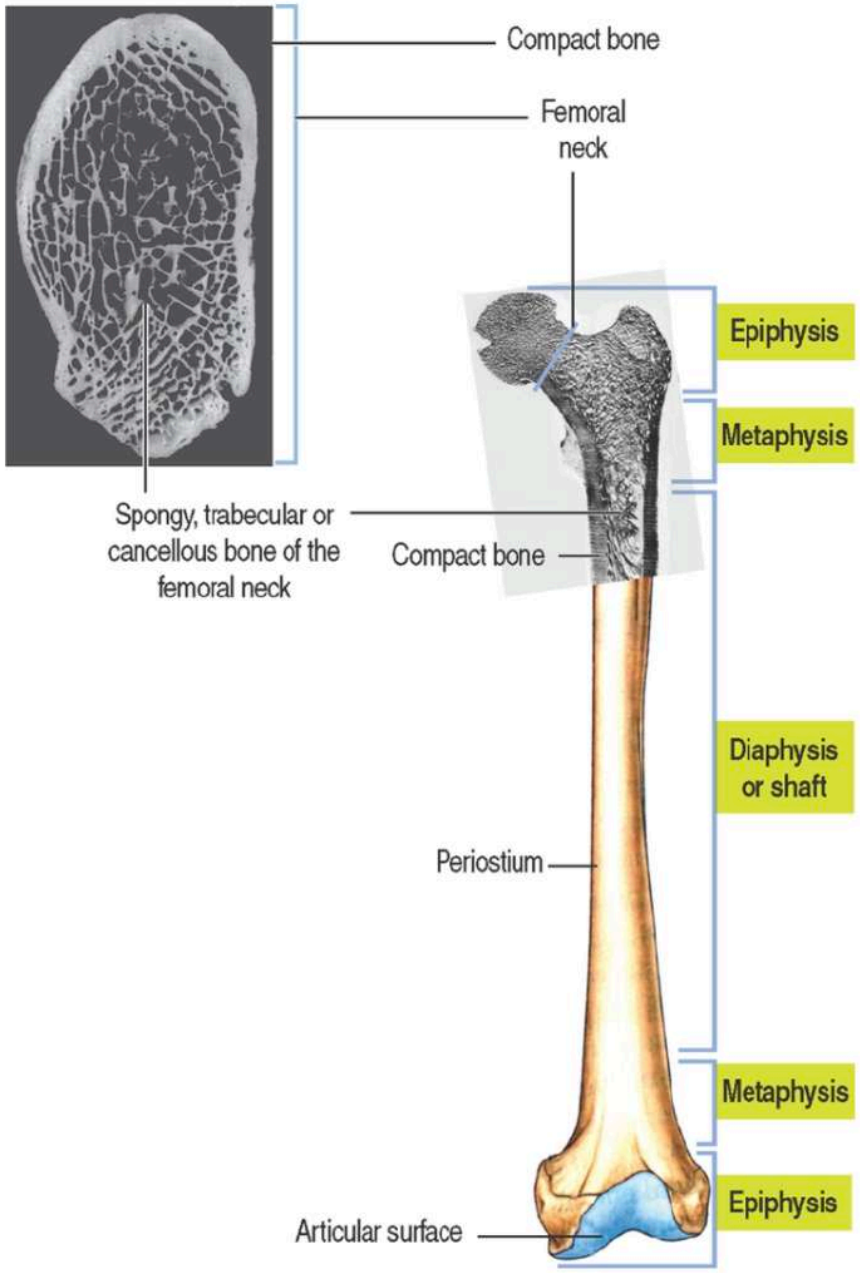
basal zone, clear zone, vesicular zone and ruffled border.

Ruffled Border: Highly folded plasma membrane facing the bone, formed by fusion of lysosomal vesicles, which increases surface area for secretion of HCl and lysosomal proteases.
Clear Zone (Sealing Zone): A dense area surrounding the ruffled border, rich in actin filaments and integrins, which anchors the osteoclast to the bone and seals off the resorption pit.
Vesicular Zone: Packed with numerous lysosomes, vesicles, and mitochondria that transport enzymes to the ruffled border and transport resorbed materials out of the cell.
Basal Zone (Basolateral Membrane): Located on the opposite side of the cell, it is involved in exocytosis of debris and contains high concentrations of transporters and ion channels

Two forms of bone can be distinguished based on the gross appearance:

- **Compact** or **dense bone**.
- **Spongy, trabecular** or **cancellous bone**

Macroscopic structure of mature bone

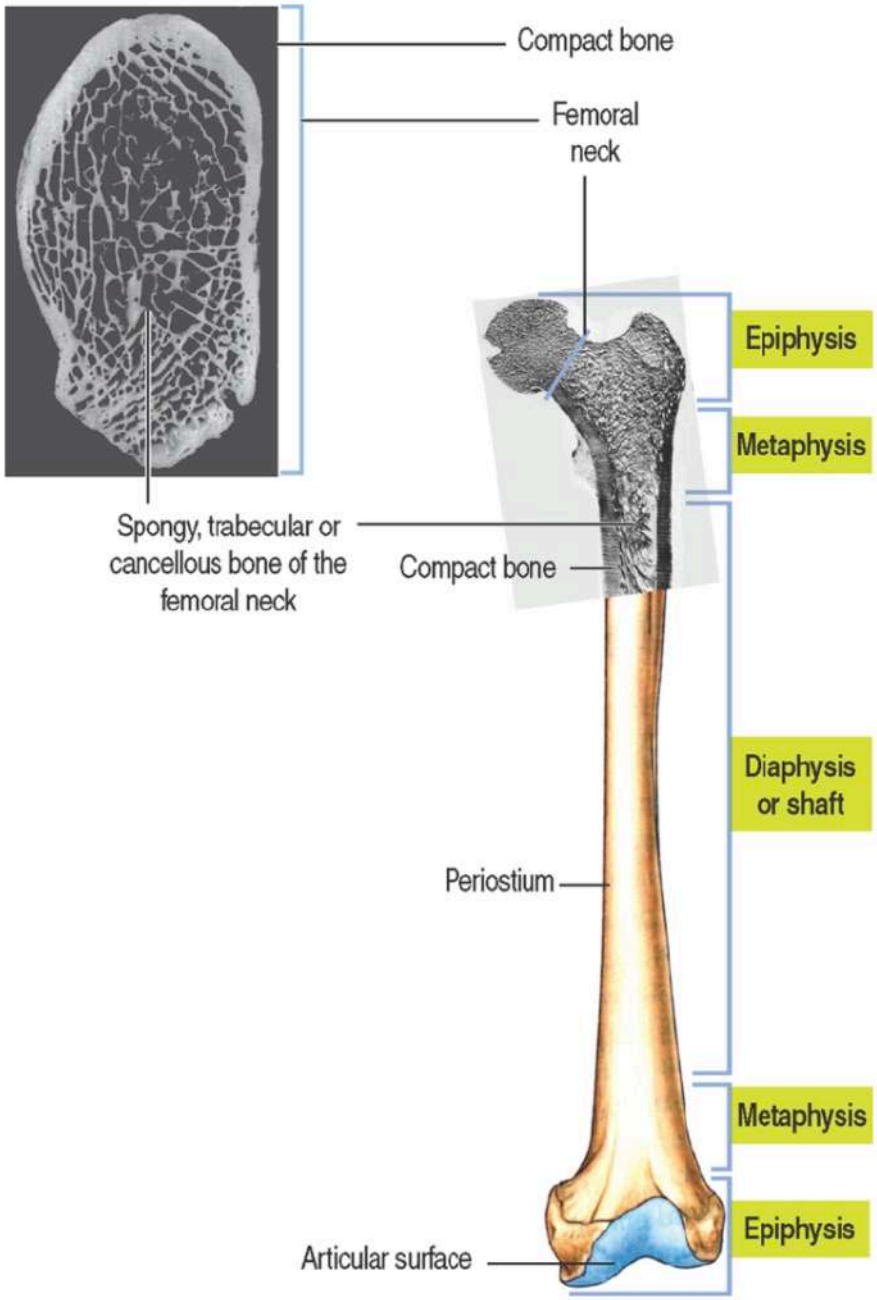


Compact bone appears as a solid mass. Spongy bone consists of a network of bony spicules or trabeculae delimiting spaces occupied by the bone marrow.

In long bones, such as the femur, the **diaphysis** consists of compact bone forming a hollow cylinder with a central marrow space, called the **marrow cavity**.

The ends of the long bones, called **epiphyses**, consist of spongy bone covered by a thin layer of compact bone.

Macroscopic structure of mature bone



In the growing individual, epiphyses are separated from the diaphysis by a cartilaginous **epiphyseal plate**, connected to the diaphysis by spongy bone.
A transitional region, called the **metaphysis**, connects the epiphysis and the diaphysis.
*Both the epiphyseal plate and adjacent spongy bone represent the **growth zone**, responsible for the increase in length of the growing bone*.

The articular surfaces, at the ends of the long bones, are covered by **hyaline cartilage**, the articular cartilage. Except on the articular surfaces and at the insertion sites of tendons and ligaments, most bones are surrounded by the **periosteum**, a layer of specialized connective tissue with osteogenic potential.
The marrow wall of the diaphysis, the **endosteum**, and the spaces within spongy bone are lined by **osteoprogenitor cells**, with osteogenic potential.

Microscopic structure of mature bone

Two types of bone are identified on the basis of the microscopic three-dimensional arrangement of the collagen fibers:

1. **Lamellar or compact bone**, typical of the mature bone, displays a regular alignment of collagen fibers. This bone is mechanically strong and develops slowly.
2. **Woven bone**, observed in the developing bone, is characterized by an irregular alignment of collagen fibers. This bone is mechanically weak, is formed rapidly and is latter replaced by lamellar bone. Woven bone is produced during the repair of a bone fracture.

lamellar bone

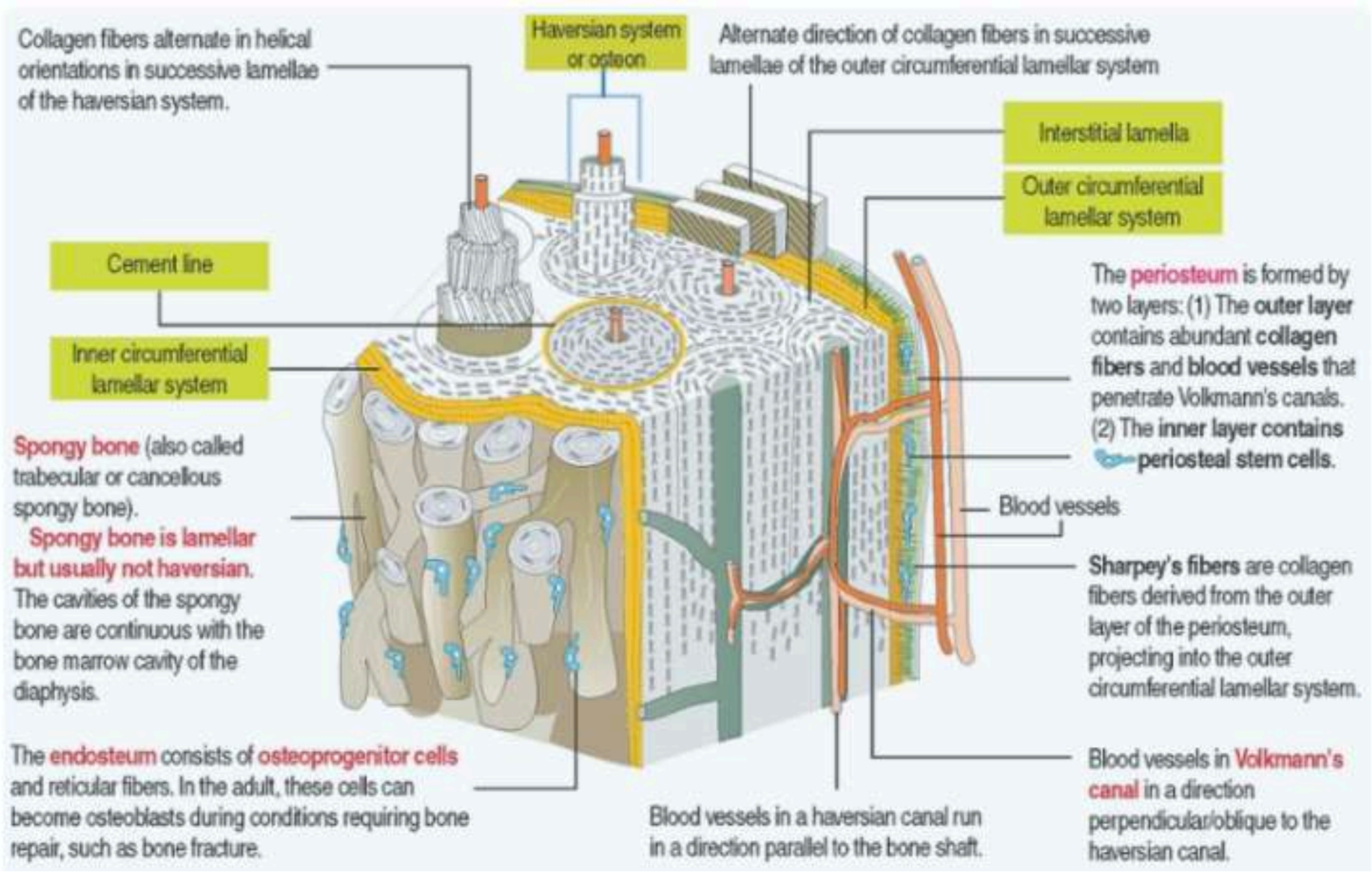
The **lamellar bone** consists of **lamellae**, largely composed of **bone matrix**, a mineralized substance deposited in layers, or lamellae, and **osteocytes**, each one occupying a cavity or **lacuna** with radiating and branching **canaliculi** that penetrate the lamellae of adjacent lacunae.

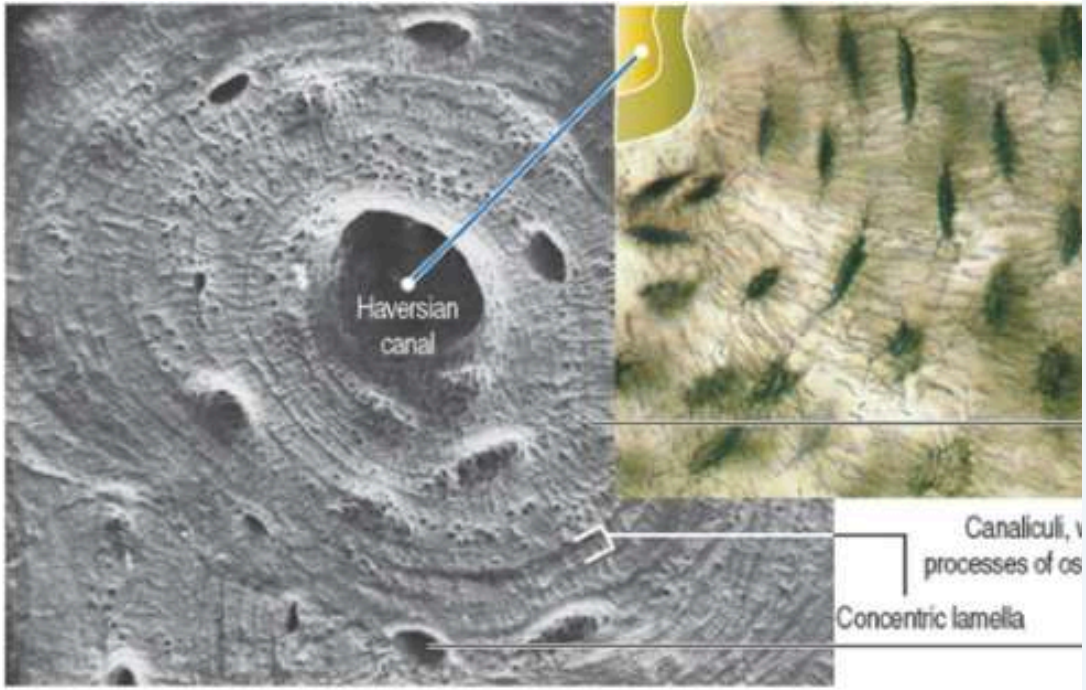
The lamellar bone displays four distinct patterns:

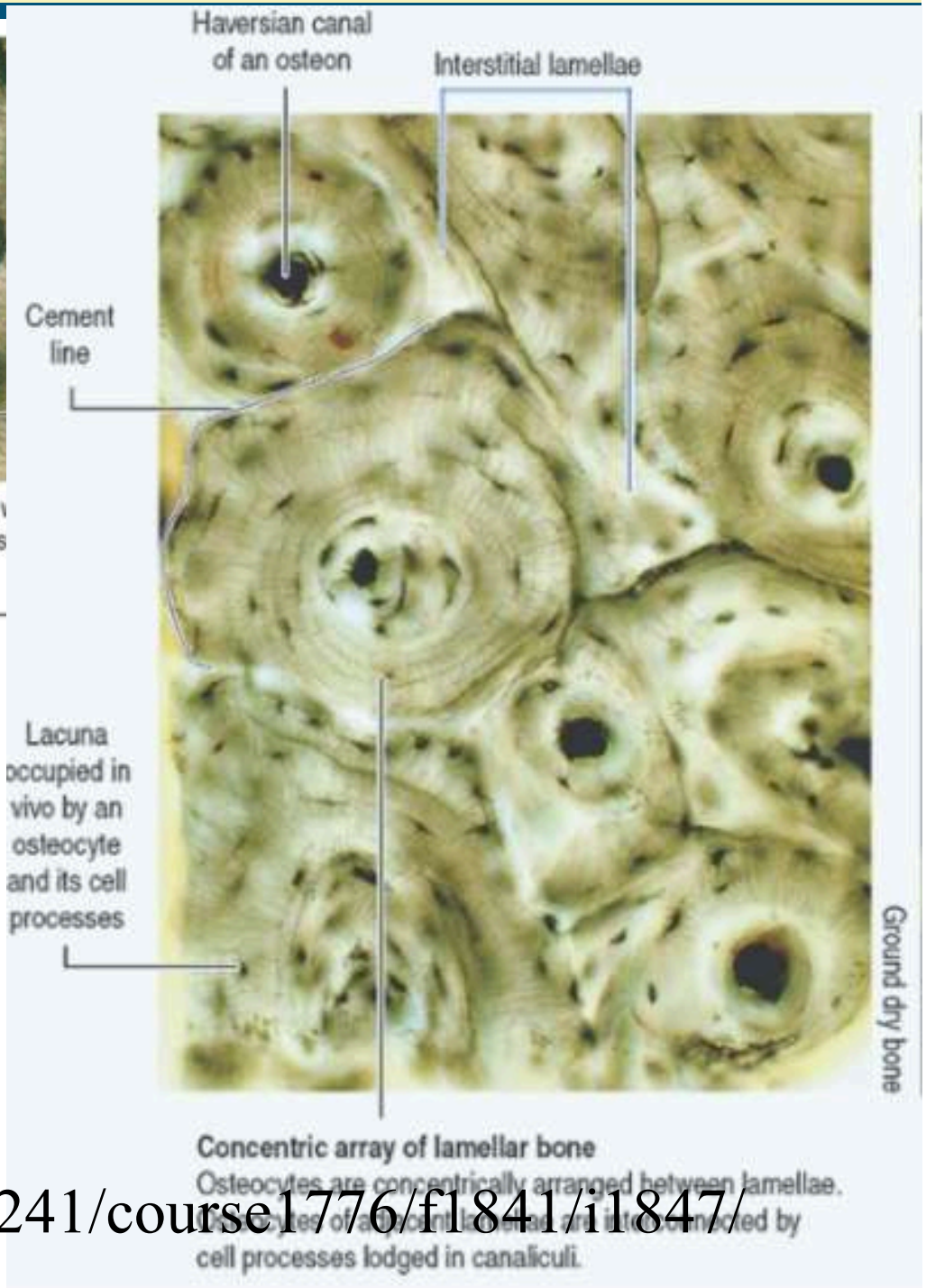
1. The **osteons** or **haversian systems**, formed by concentrically arranged lamellae around a longitudinal vascular channel. About 4 to 20 lamellae are concentrically arranged around the **haversian canal**.
2. The **interstitial lamellae**, observed between osteons and separated from them by a thin layer known as the **cement line**.
3. The **outer circumferential lamellae**, visualized at the external surface of the compact bone under the periosteum
4. The **inner circumferential lamellae**, seen on the internal surface subjacent to the endosteum.

The **vascular channels** in compact bone have two orientations with respect to the lamellar structures:

- The longitudinal **haversian canal**, housing capillaries and postcapillary venules in the center of the osteon
- The transverse or oblique **Volkmann's canals**, connecting haversian canals with one another, containing blood vessels derived from the bone marrow and some from the periosteum.







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Periosteum and endosteum

- During embryonic and postnatal growth the **periosteum** consists of:

- An **inner layer of osteoprogenitor cells**, in direct contact with bone. In the adult, the periosteum contains **periosteal stem cells (PSCs) that displays clonal multipotency and self-renewal**. PSCs give rise to bone-forming osteoblasts in response to injury.

- An **outer layer** rich in blood vessels, some of them entering Volkmann's canals, and thick anchoring collagen fibers, called **Sharpey's fibers**, that penetrate the outer circumferential lamellae.

Periosteum and endosteum

- The **endosteum** covers the spongy walls and extends into all the cavities of the bone, including the haversian and Volkmann's canals. It consists of osteoprogenitor cells, reticular stromal cells of the bone marrow and connective tissue fibers.
- Preosteoblasts and osteoblasts in the endosteum contribute to the hematopoietic cytokines to the bone marrow microenvironment, the endosteal niche, essential for hematopoietic stem cell proliferation and maturation.

Osteogenesis
(Bone development or ossification)

Bone can develop either directly from an initial cell condensation of the mesenchyme **(intramembranous ossification)** or by gradual replacement of a pre-existing tissue, the cartilage, which acts as a template **(endochondral ossification;** bone formation inside cartilage).

Osteogenesis
(Bone development or ossification)

- The initial mechanism of bone formation during intramembranous and endochondral ossification is essentially the same:
- **An initial trabecular network, called primary spongiosa, is first laid down and then transformed into mature bone**.

Intramembranous ossification

Intramembranous ossification of certain parts of the skull and the clavicle occurs in the following sequence:

1. The embryonic connective tissue (mesenchyme) becomes highly vascularized and mesenchymal stem cells aggregate while still embedded in an extracellular matrix containing collagen fibers and proteoglycans.

2. Aggregated mesenchymal stem cells **directly** differentiate into **osteoblasts** that begin to secrete **osteoid** or **bone matrix**.

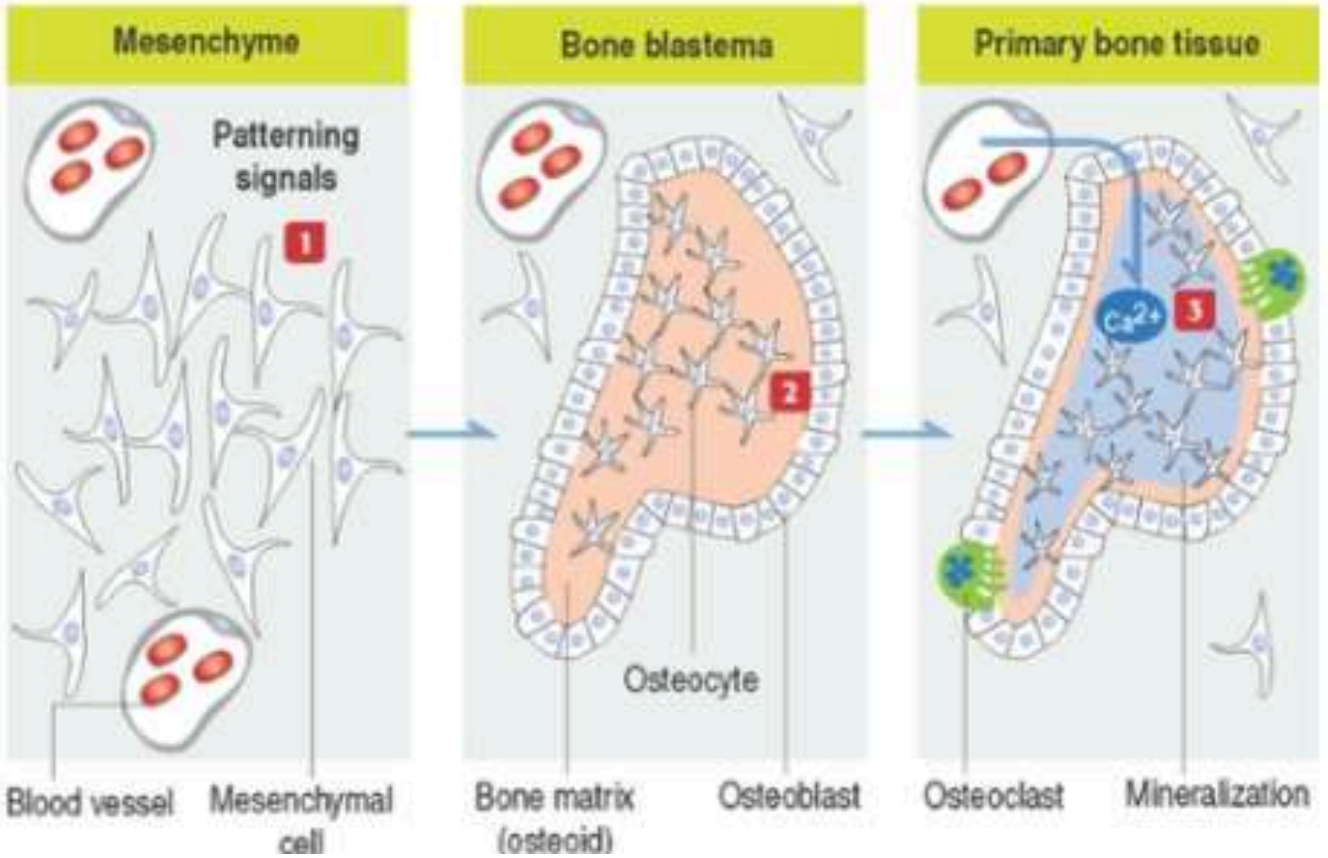
- Osteoid is the **unmineralized**, organic portion of the bone matrix.
- Numerous osteogenesis centers develop and eventually fuse, forming a network of anastomosing **trabeculae** resembling a sponge, the so-called **spongy bone**.

Intramembranous ossification

1 Mesenchymal cells aggregate without a cartilage intermediate. This process is controlled by patterning signals from polypeptides of the Wnt, hedgehog, fibroblast growth factor and transforming growth factor–β families.

2 Mesenchymal cells differentiate into osteoblasts. A bone blastema (**a mass of undifferentiated cells**) is formed. Osteocytes **within** the core of the blastema are interconnected by cell processes forming a functional syncytium. Osteoblasts line the **surface** of the bone blastema.

3 Bone matrix (osteoid) is deposited by osteoblasts. Later, Ca^{2+}, transported by blood vessels, is used in the mineralization process and primary bone tissue is formed. Osteoclasts initiate the modeling of the bone tissue.



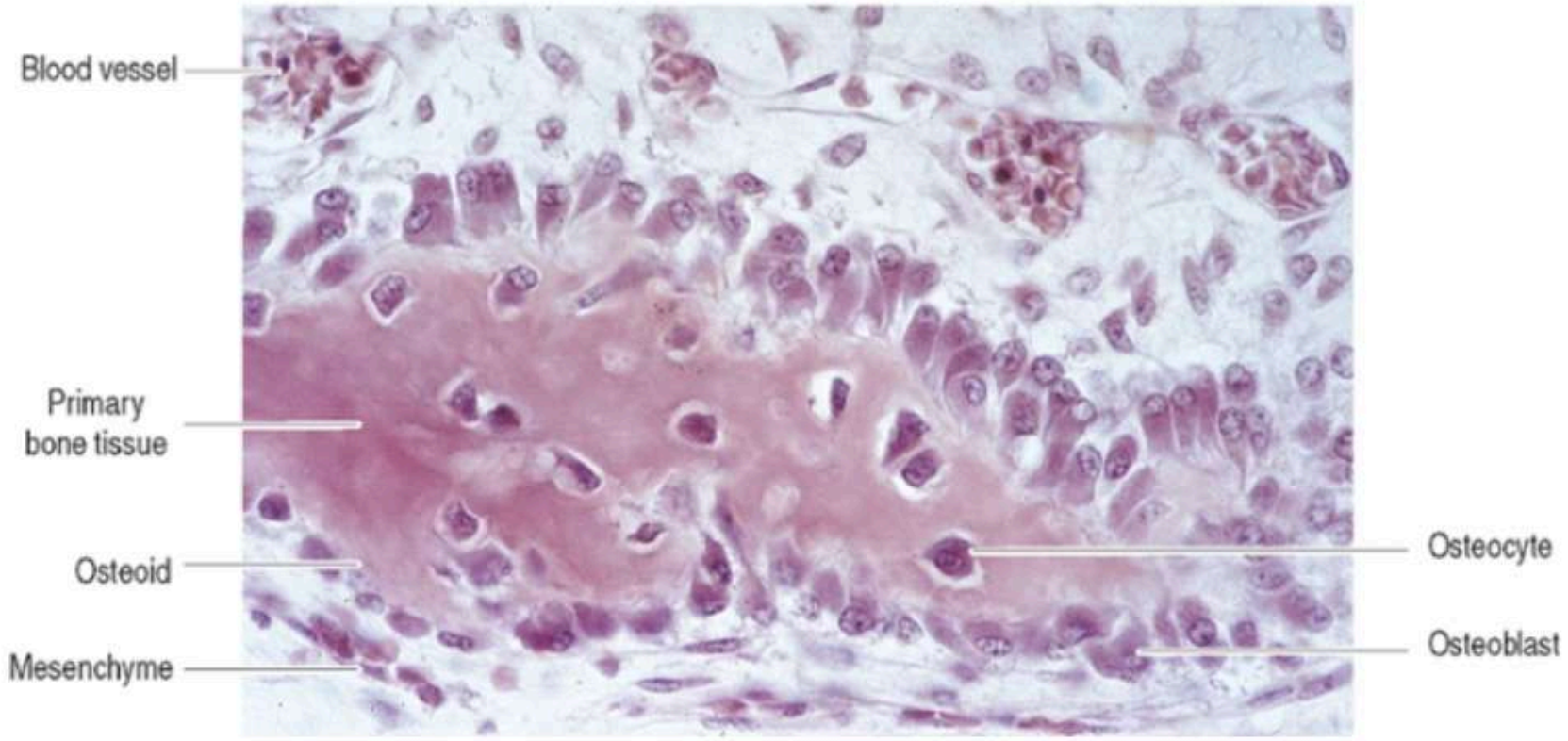
Organization of a primary center of ossification

Multiple individual trabeculae enlarge by appositional growth and eventually fuse together as a primary osteogenesis center organized during the first stage of intramembranous ossification.

Although primary bone tissue formation begins as an interstitial process, it soon becomes appositional.

Osteocytes become trapped within the calcified osteoid.

At the surface of the osteoid, osteoblasts continue the appositional deposit of matrix, mainly type I collagen and non-collagenous proteins.



Intramembranous ossification

3. Because collagen fibers in the newly formed trabeculae are **randomly** oriented, the early intramembranous bone is described as **woven bone**, in contrast with the **regularly** oriented collagen fibers of the **lamellar or compact bone** formed later during bone remodeling.

4. Calcium phosphate is deposited in the bone matrix or osteoid, which becomes **mineralized**. Osteoid is laid down by **apposition**. No interstitial bone growth occurs.

Intramembranous ossification

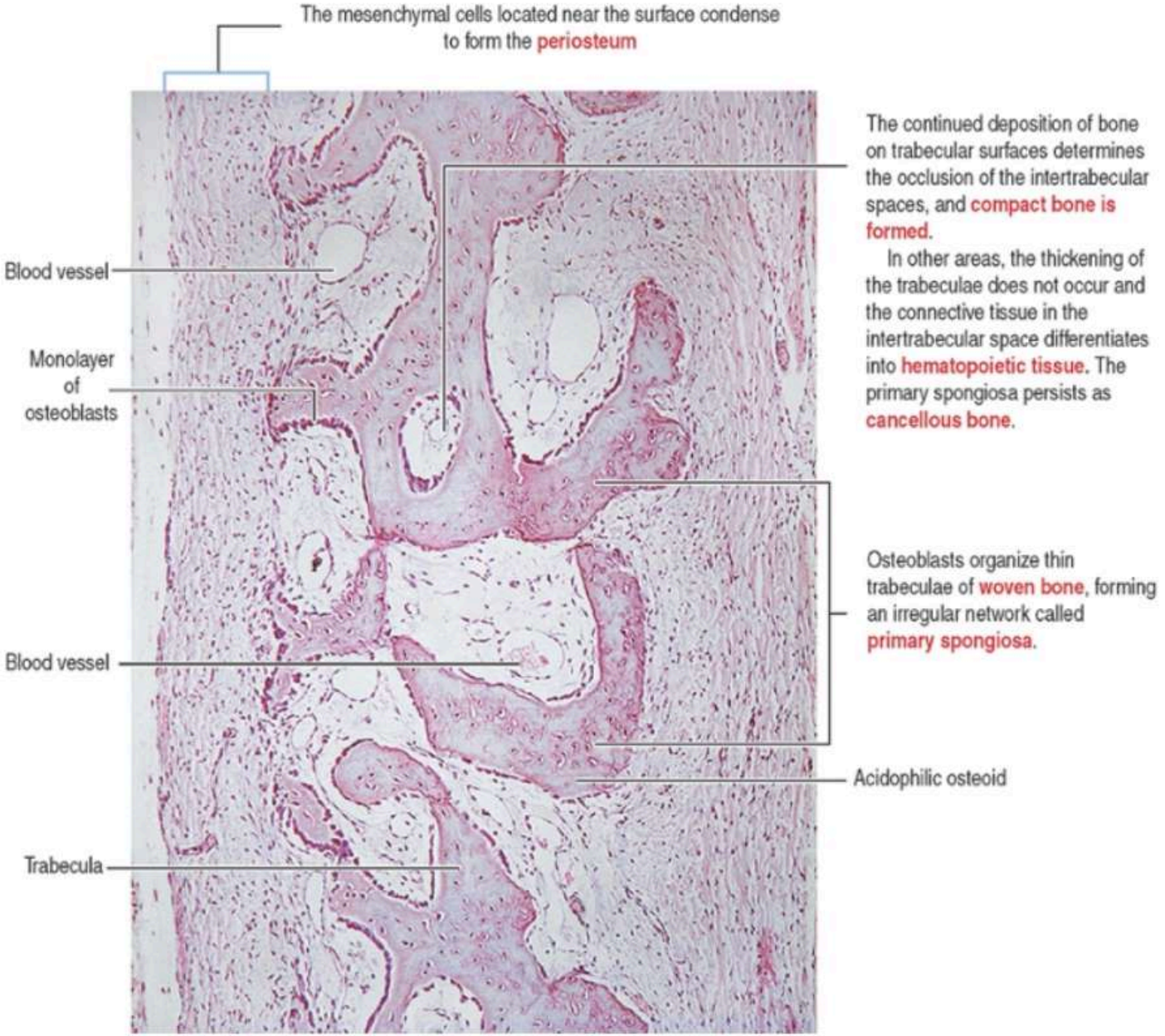
5. Bone matrix mineralization leads to two new developments the entrapment of osteoblasts as **osteocytes** within the mineralized bone matrix that is remodeled by the bone resorptive **osteoclasts** and the partial closing of the perivascular channels, which assume the new role of **blood formation** by conversion of mesenchymal stem cells into blood-forming cells.

Intramembranous ossification

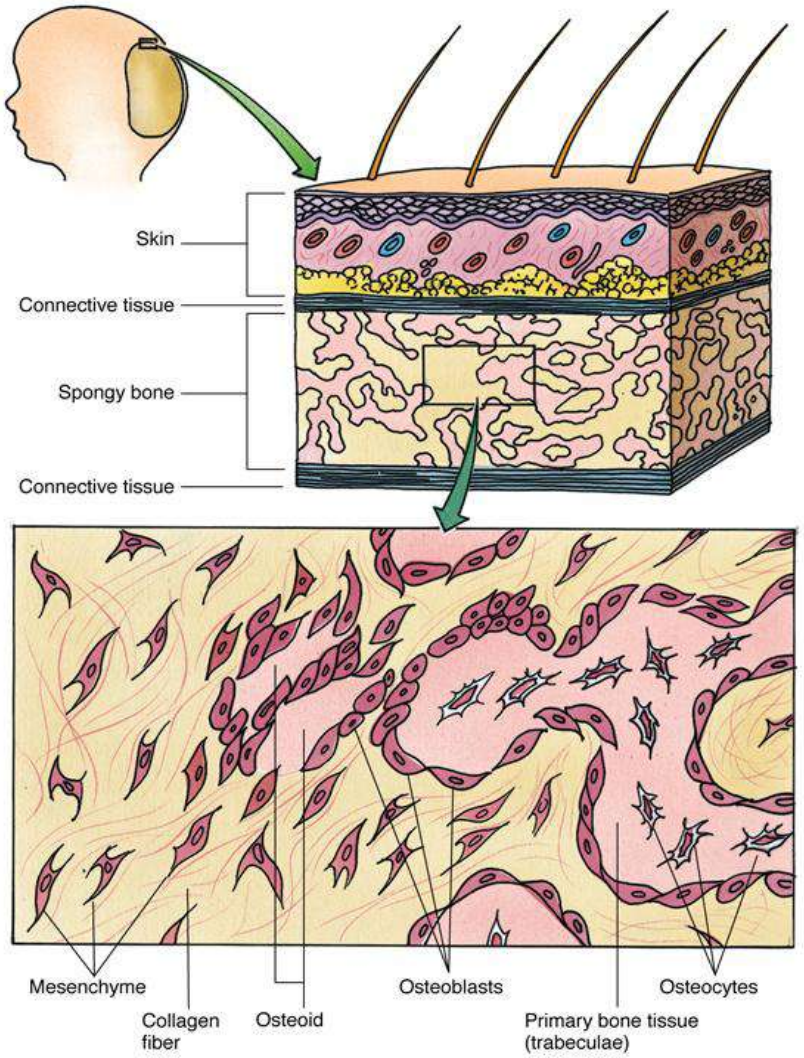
The frontal and parietal bones and parts of the occipital, temporal, mandible, and maxilla bones develop by intramembranous osteogenesis.

Intramembranous ossification is characterized by:

- A **well-vascularized primitive connective tissue**.
- Bone formation is **not preceded** by the formation of a **cartilage**.
- An aggregate of mesenchymal stem cells differentiates **directly** into osteoid-producing osteoblasts.



Intramembranous Bone Formation



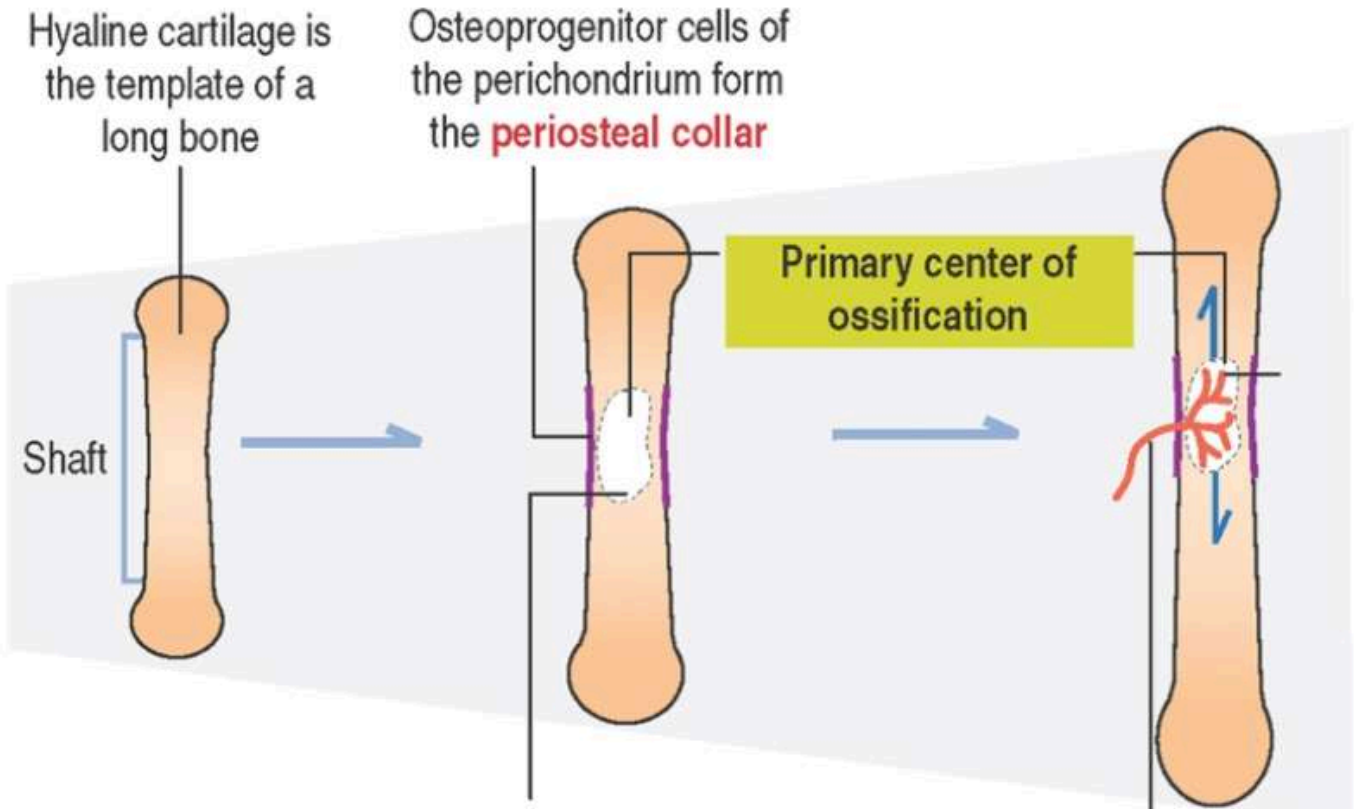
Intramembranous bone formation.

Most flat bones are formed by **intramembranous bone formation**. This process occurs in a richly vascularized mesenchymal tissue, whose cells make contact with each other via long processes.

Mesenchymal cells differentiate into **osteoblasts** that secrete **bone matrix**, forming a network of **spicules** and **trabeculae** whose surfaces are populated by these cells. This region of initial osteogenesis is known as the **primary ossification center**.

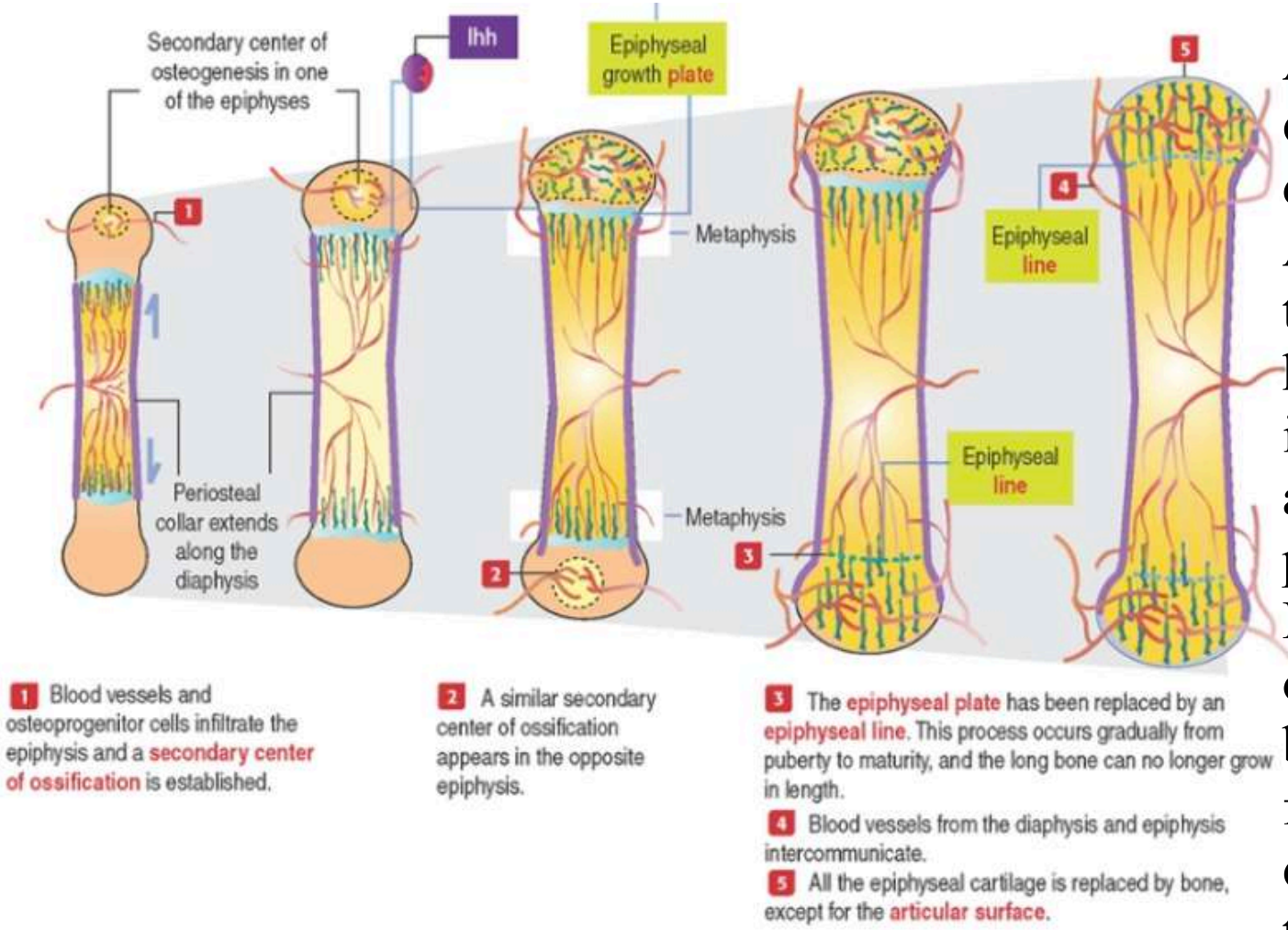
The collagen fibers of these developing spicules and trabeculae are randomly oriented as expected in primary bone. Calcification quickly follows osteoid formation, and osteoblasts trapped in their matrices become osteocytes. Continuous mitotic activity of mesenchymal cells provides a supply of undifferentiated **osteoprogenitor cells**, which form osteoblasts.

Endochondral Bone Formation



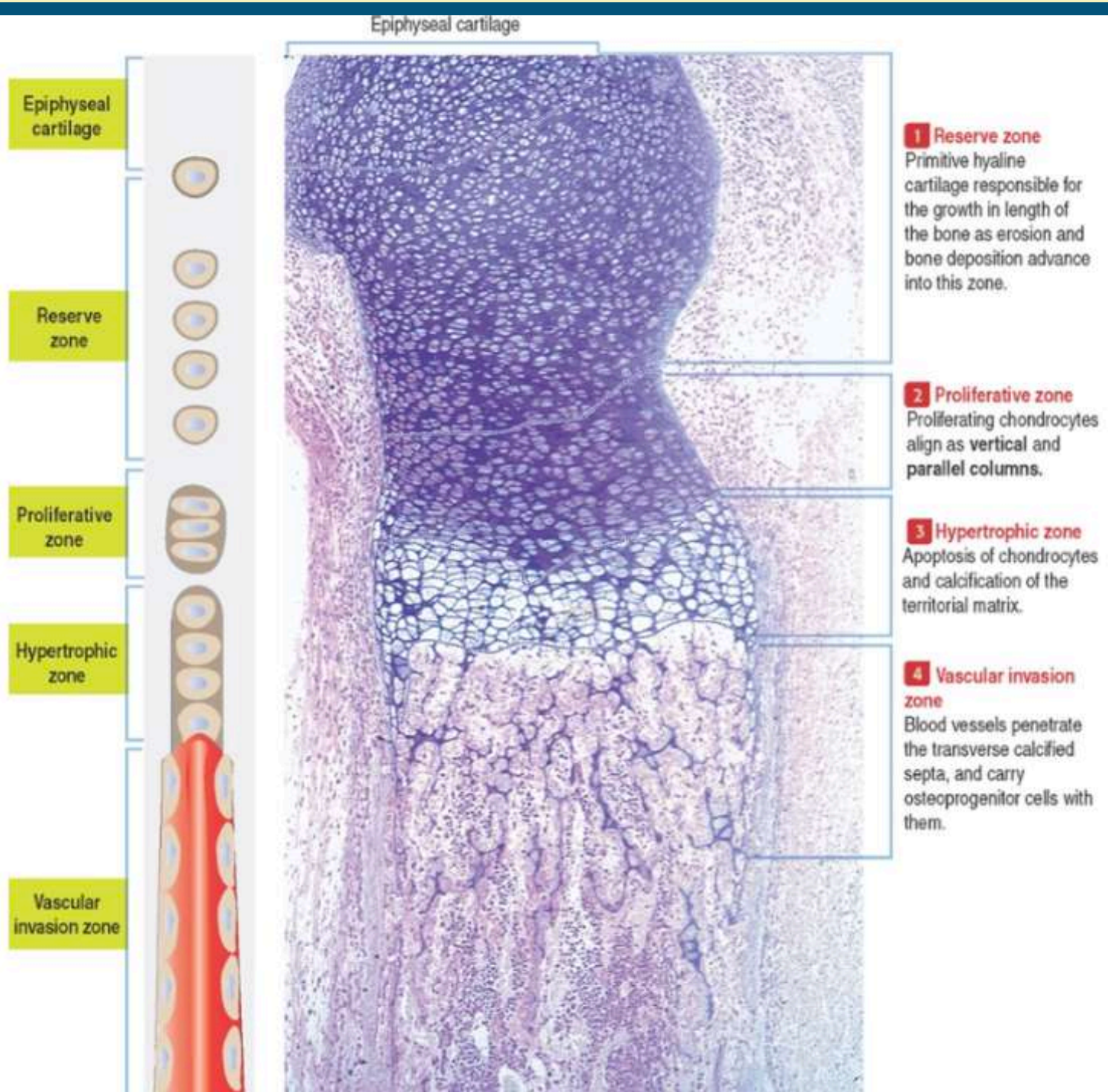
the development of primary centers of ossification in the diaphysis of long bones
occurs by the third month of fetal life.

Endochondral ossification: Secondary centers of ossification

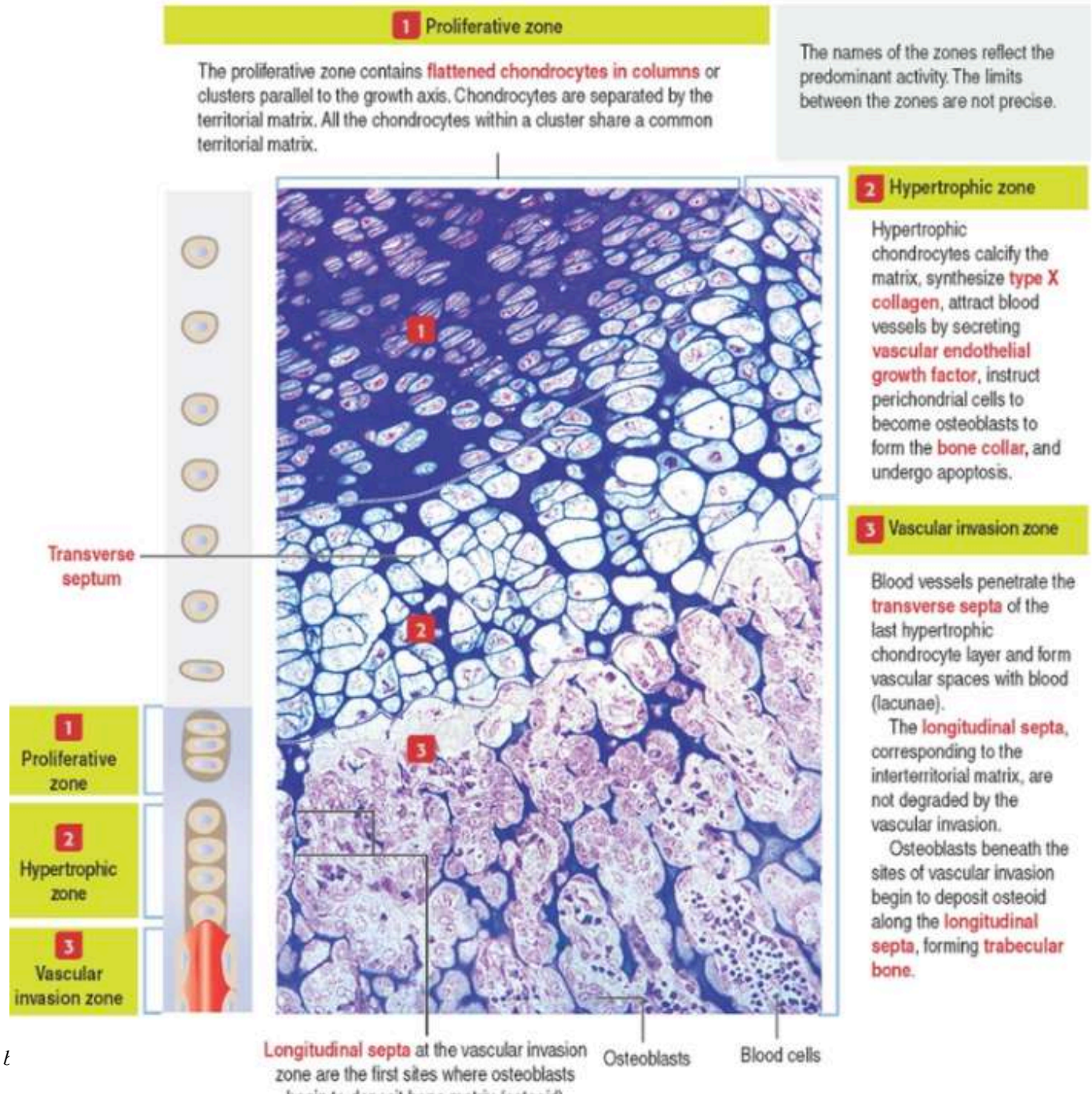


After birth, **secondary centers** of ossification develop in the **Epiphyses.**
As in the diaphysis, the space occupied by hypertrophic chondrocytes is invaded by blood vessels and preosteoblasts from the perichondrium.
Most of the hyaline cartilage of the epiphyses is replaced by the spongy bone, except for the **articular cartilage** and a thin disk, the **epiphyseal growth plate**, located between the epiphyses and the diaphysis.

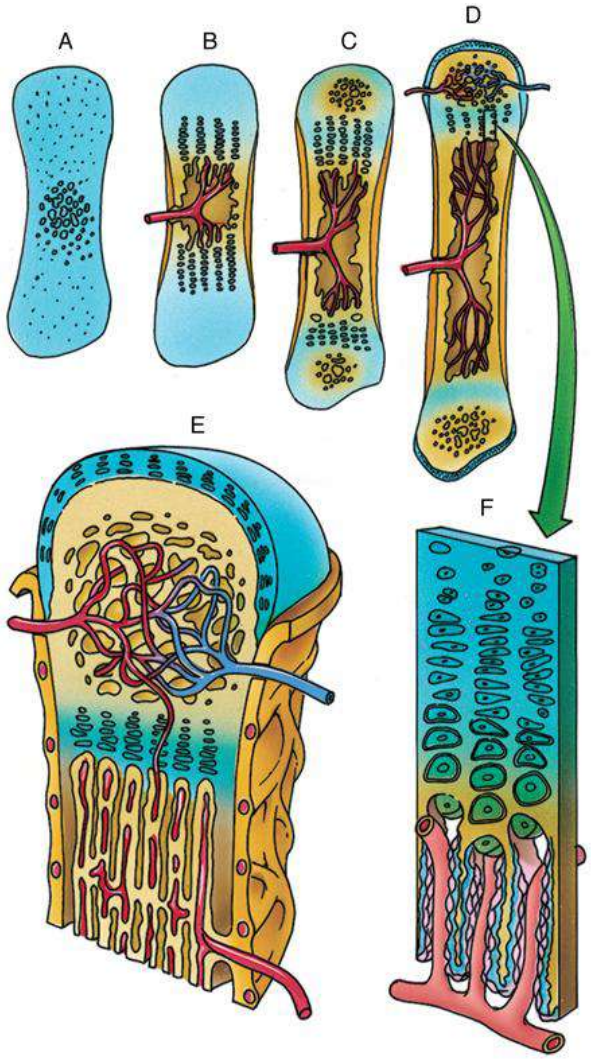
The epiphyseal growth plate is responsible for subsequent growth in length of the bone



Endochondral ossification- **The epiphyseal growth**



Endochondral Bone Formation



Endochondral bone formation. *Blue* represents the cartilage model upon which bone is formed. The bone then replaces the cartilage. **A,** Hyaline cartilage model. **B,** Cartilage at the midriff (diaphysis) is invaded by vascular elements. **C,** Subperiosteal bone collar is formed. **D,** Bone collar prevents nutrients from reaching cartilage cells so they die leaving confluent lacunae. Osteoclasts invade and etch bone to permit periosteal bud to form. **E,** Calcified bone/calcified cartilage complex at epiphyseal ends of the growing bone. **F,** Enlargement of the epiphyseal plate at the end of the bone where bone replaces cartilage.

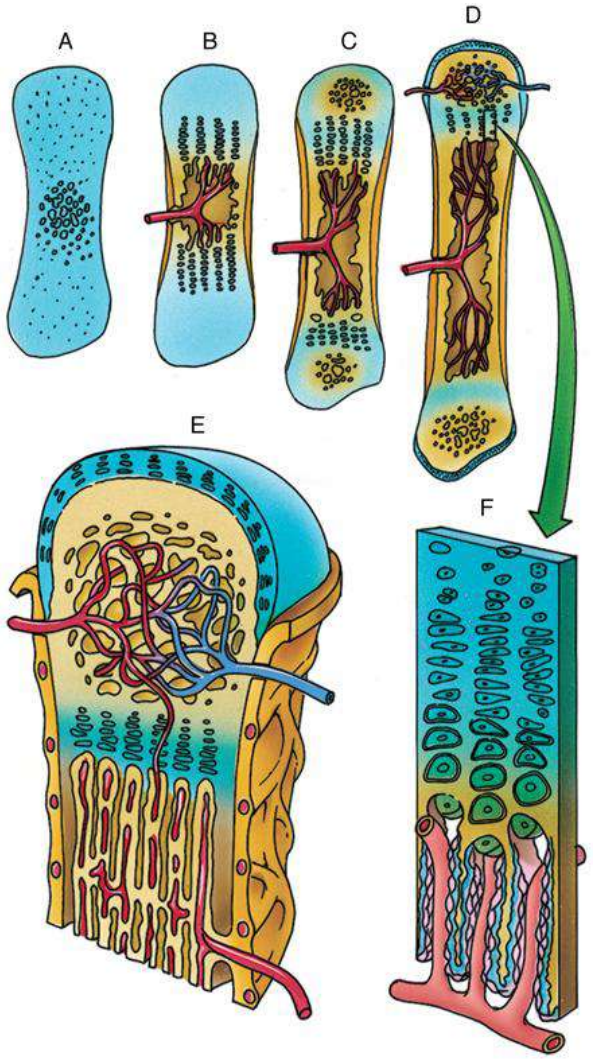
Most of the long and short bones of the body develop by **endochondral bone formation**.

1. In the region where bone is to grow within the embryo, a **hyaline cartilage model of that bone is developed** and it grows both appositionally and interstitially. Eventually, the chondrocytes in the center of the cartilage will undergo hypertrophy, their lacunae enlarge, and the intervening cartilage matrix septa become calcified.

2. Concurrently, the perichondrium at the **midriff of the diaphysis of cartilage becomes vascularized**. The chondrogenic cells become osteoprogenitor cells forming osteoblasts, and the overlying perichondrium becomes a periosteum.

3. The newly formed **osteoblasts** secrete bone matrix, forming the **subperiosteal bone collar** on the surface of the cartilage template by intramembranous bone formation.

Endochondral Bone Formation



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4. The hypertrophied chondrocytes within the core of the cartilage model die, resulting in the presence of empty, confluent lacunae forming the future marrow cavity.

5. Holes etched in the bone collar by osteoclasts permit a **periosteal bud** (osteogenic bud) to enter the concavities within the cartilage model.

6. Osteoprogenitor cells divide to form osteoblasts. These newly formed cells elaborate bone matrix on the surface of the calcified cartilage. The bone matrix becomes calcified to form a **calcified cartilage/calcified bone complex**.

7. As the subperiosteal bone becomes thicker and grows in each direction from the midriff of the diaphysis toward the epiphyses, osteoclasts begin resorbing the calcified cartilage/calcified bone complex, enlarging the marrow cavity.

Conversion of trabecular bone into osteons

As the bone grows in length, new layers of bone are laid down under the periosteum of the diaphysis by appositional growth.

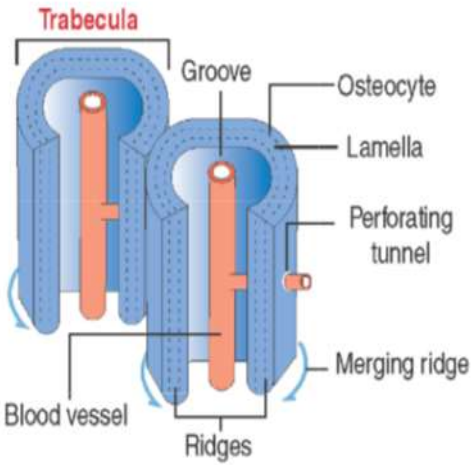
- The simultaneous gradual erosion of the inner wall of the diaphysis results in a width increase of the marrow cavity, but the walls do not increase proportionally in thickness.
- How does the trabecular organization of the developing bone by endochondral ossification change into the form of haversian systems or osteons?

- the newly formed bone during endochondral ossification consists of **spicules** that are changing into **trabeculae**.
- Remember that a spicule consists of a longitudinal core of calcified cartilage coated by osteoid produced by osteoblasts lining the surface. In contrast, a trabecula lacks the calcified cartilage core; instead it contains an osteocyte lamellar core lined by osteoblasts depositing osteoid on the surface. Keep in mind that blood vessels are in contact with the trabeculae.
- Once the spicules change into trabeculae, they need to organize osteons.

- Trabeculae are then converted into osteons, each consisting of a **bone cylinder** with a central longitudinal tunnel housing a blood vessel.

Sequence observed during **the trabecula–to–osteon conversion**

- The **longitudinal edges** of a trabecula are the boundary o a **groove**.
- The groove contains a blood vessel. The ridges and groov are lined by osteoblasts that continue depositing osteoid.
- As a result of the ridges growing toward one another, the groove is converted into a tunnel lined by osteoblasts and the blood vessel becomes trapped inside a tunnel. The blood vessel becomes the **longitudinal axis** of the newly formed osteon.
- The blood vessel interconnects with a similar vessel of an adjacent tunnel through perforating spaces leading to a **transverse-oriented Volkmann's canal**.

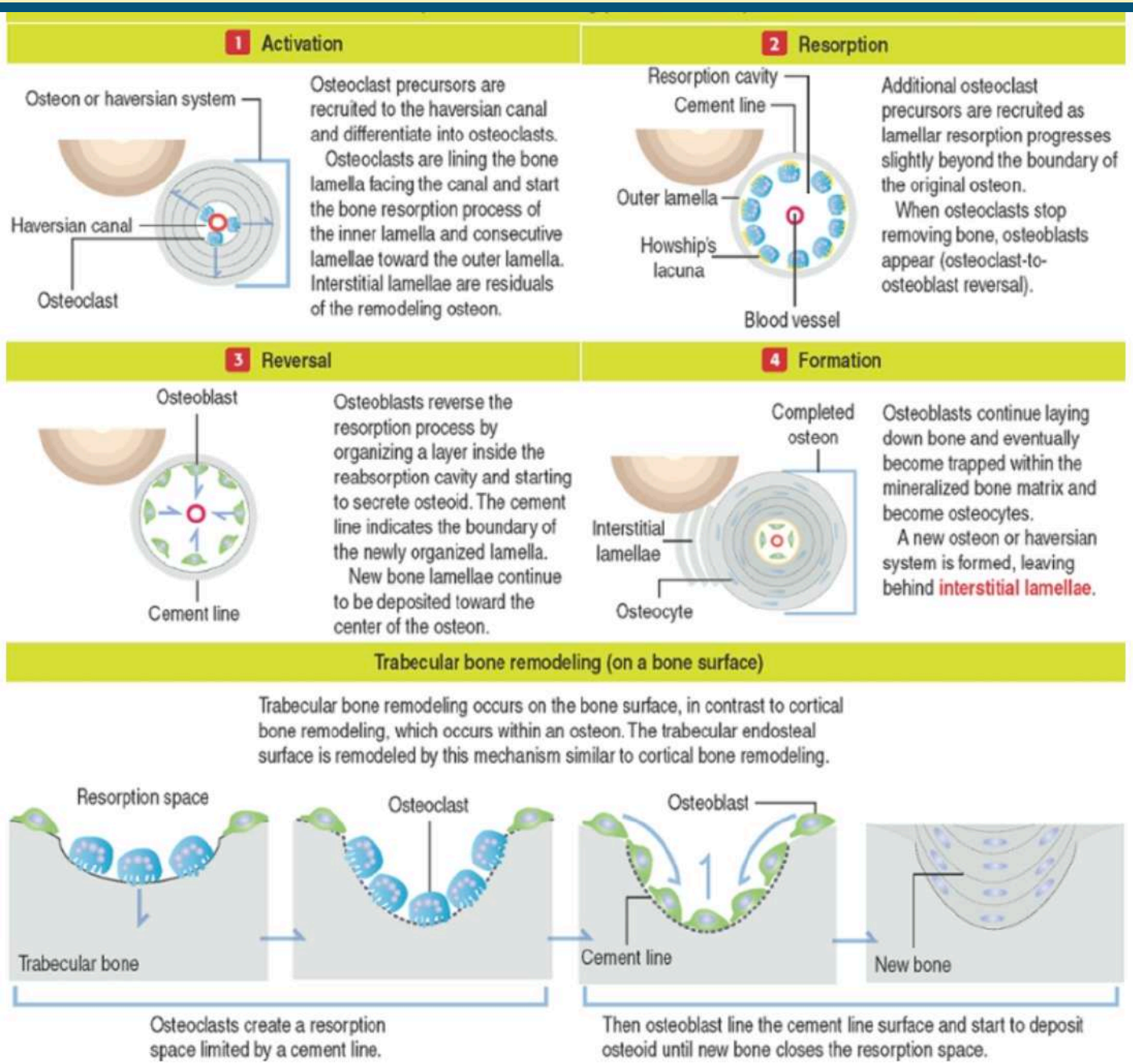


2.Osteoblasts lining the wall of the tunnel deposit by apposition new concentric lamellae and convert the structure into an osteon.

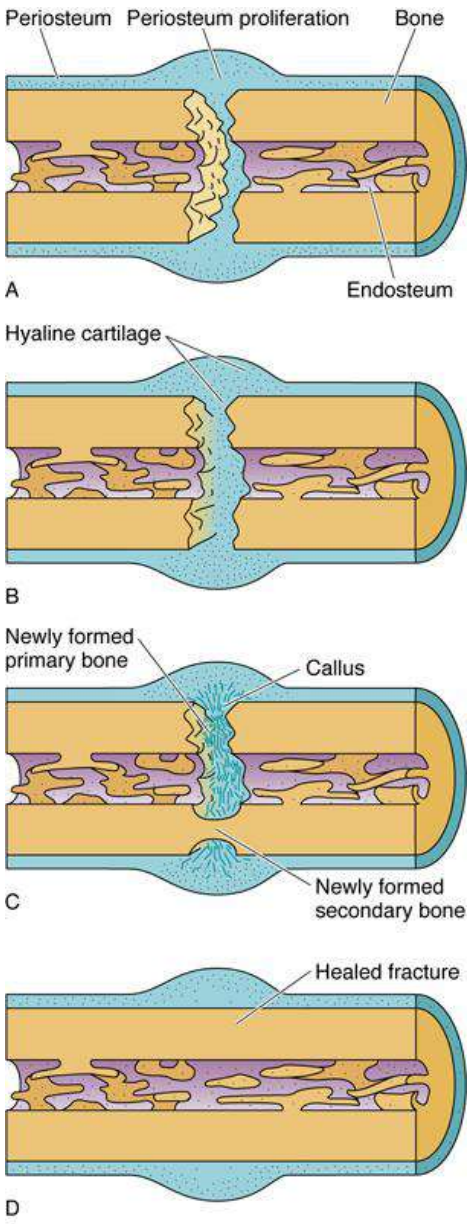
3.Appositional growth continues adding lamellae under the periosteum

A modeling-remodeling process occurs through the balancing activities of the bone-forming osteoblasts and the bone-resorbing osteoclasts. At the end of the process, the outer circumferential lamellae becomes the boundary of the multiple haversian systems and interstitial lamellae fill the spaces between the haversian systems or osteons.

4. Osteoblasts lining the inner surface of the bone, the **endosteum**, develop the **inner circumferential lamellae.**



Bone Repair- **Bone Fracture and Healing**

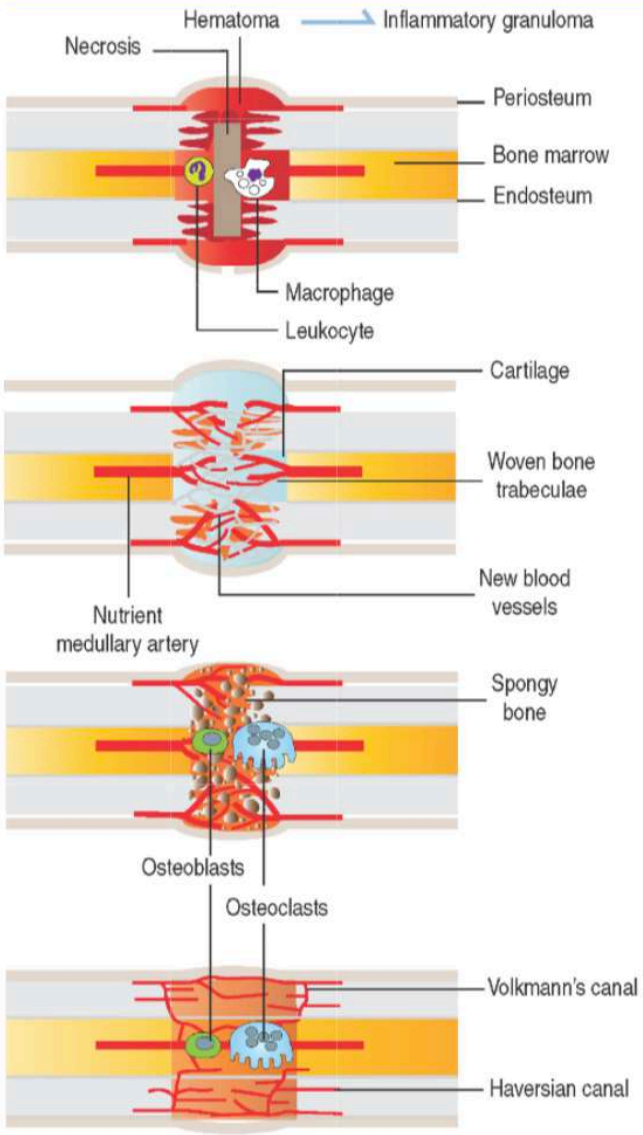


Events in bone fracture repair.

A bone fracture causes damage and destruction to the bone matrix, death of cells, tears in the periosteum and endosteum, and possible displacement of the ends of the broken bone (fragments). Because bone marrow and the periosteum are highly vascularized, the initial injury site in either of these two areas does not grow significantly, nor is there a notable increase in dead and dying cells much beyond the original injury site. Wherever the bone's haversian systems are without a blood supply, osteocytes become pyknotic and undergo lysis, leaving empty lacunae. The blood clot filling the site of the fracture is invaded by small capillaries and fibroblasts from the surrounding connective tissue, forming **granulation tissue**. A similar event occurs in the marrow cavities as a clot forms; the clot is soon invaded by osteoprogenitor cells of the endosteum and multipotential cells of the bone marrow, forming an **internal callus.** Osteoprogenitor cells build up and the deepest layer of proliferating osteoprogenitor cells of the periosteum (those closest to the bone), which are in the vicinity of capillaries, differentiate into osteoblasts and begin elaborating a collar of bone, cementing it to the dead bone about the injury site.

Traumatic bone fracture is common during childhood and in the elderly. With aging, cortical bone remains stable until mid-life, when estrogen deficiency in women and gradual sex steroid reduction in men begins to drive cortical bone loss.

Bone fracture and healing



1 Hematoma/inflammatory phase

Accumulation of blood between the fracture ends, under the periosteum and the bone marrow space. The periosteum opposite to the trauma impact site may be torn. Osteocytes and marrow cells undergo cell death and necrotic material is observed in the immediate fracture zone. An inflammatory response follows. Macrophages and polymorphonuclear leukocytes migrate into a fibrin scaffold and an inflammatory granuloma is formed. The fracture is stabilized.

2 Reparative phase: Soft callus formation

Periosteal stem cells and osteoprogenitor cells of the endosteum initiate the repair of the fracture. Periosteal-derived capillary buds extend into the inflammatory granuloma. The nutrient medullary artery also contributes capillaries. Cartilage is formed and a soft callus contributes to the stability of the bone fractured ends. Woven bone, in the form of trabeculae, gradually replaces the cartilage. Mineralization of the woven bone is observed.

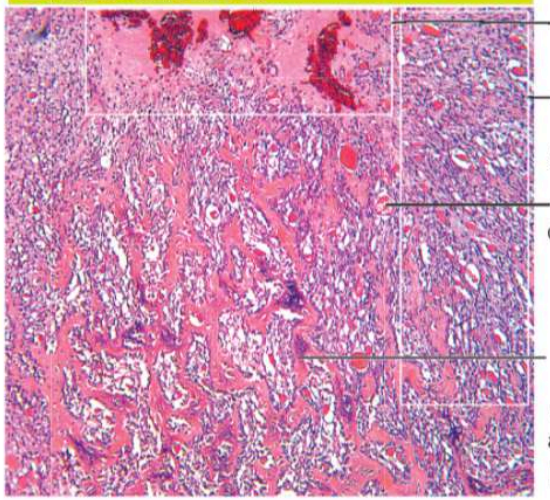
3 Reparative phase: Hard callus formation

Osteoblasts, derived from periosteal stem cells and osteoprogenitor cells derived from the endosteum, are active. The ends of the fracture become enveloped by the periosteal (external) and internal hard callus and a clinical union can be visualized. Yet, the reparative process is not complete: the necrotic ends of the fractured bone, and even portions of the hard callus, are being reabsorbed. In addition, woven bone needs to be replaced by compact bone.

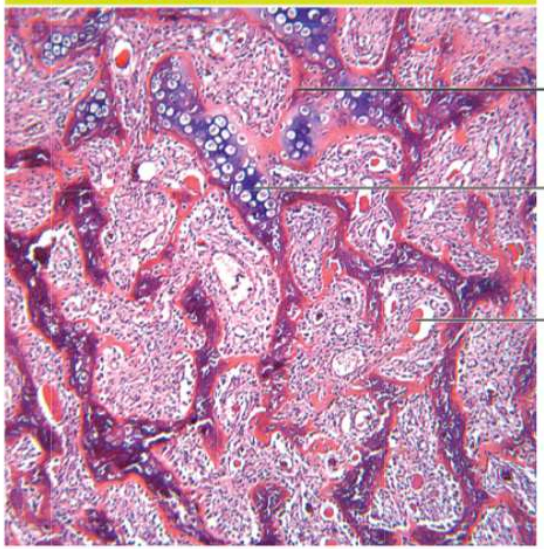
4 Remodeling phase

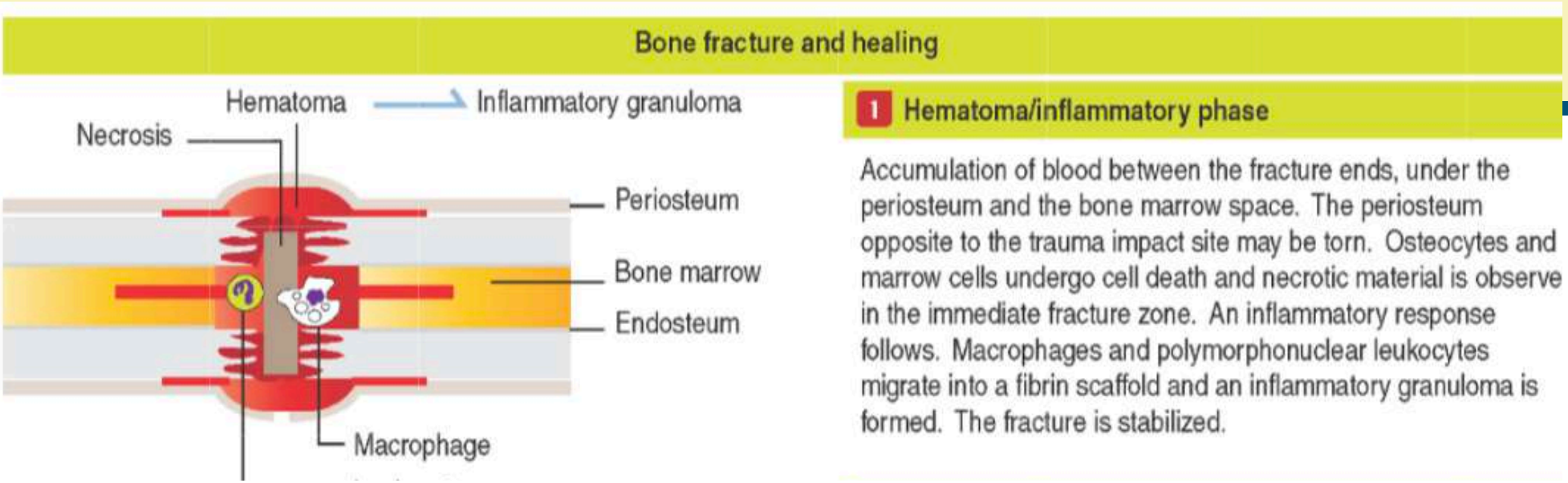
Osteoclasts reabsorb excessive and missplaced trabeculae and new bone is laid down by osteoblasts to construct compact bone along the stress lines. New haversian systems or osteons and Volkmann's canals are formed to house blood vessels.

2 Repair woven bone area



4 Hard callus formation



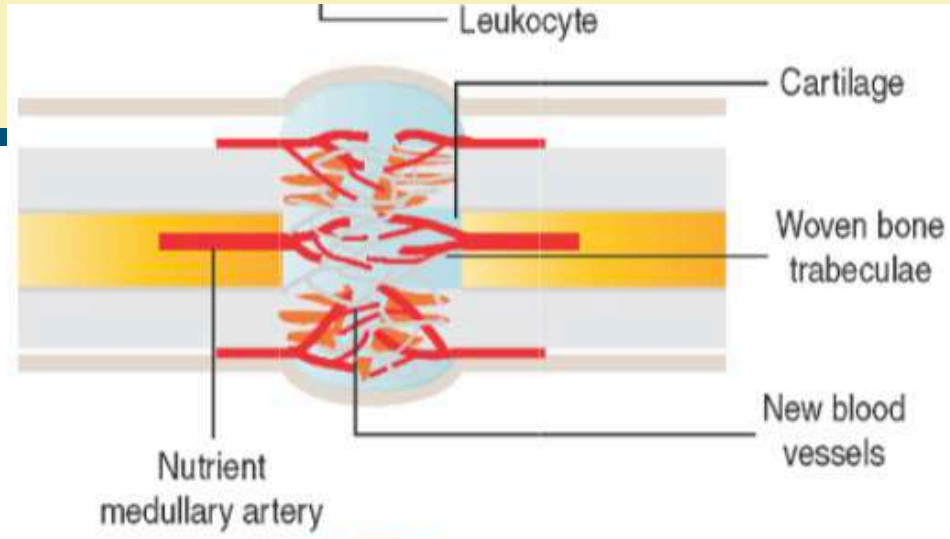


Hematoma/inflammatory phase. Bleeding and accumulation of blood at the fracture site occurs **(hematoma)** because of massive disruption of blood vessels housed in the haversian and Volkmann's canals.

Swelling, pain and an inflammatory process starts immediately. Macrophages, monocytes, lymphocytes and polymorphonuclear cells, as well as fibroblasts, are attracted to the fracture site.

The result is the formation of **granulation tissue** that bulges over the edges of the fractured bone and connects the fragments.

The development of this temporary granuloma is seen during the first week after fracture. Cytokines released by inflammatory cells and platelets recruit osteprogenitor cells from the periosteum and endosteum to the temporary granuloma, whose appropriate formation and stability require proper immobilization.



2 Reparative phase: Soft callus formation

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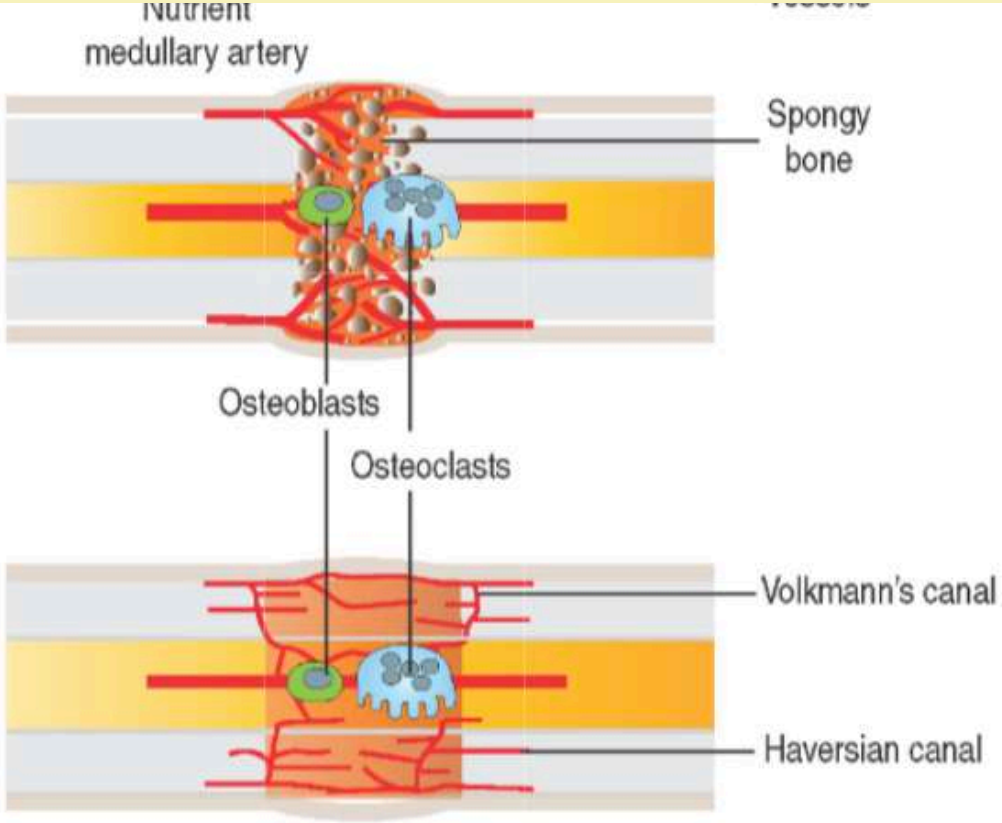
3 Reparative phase: Hard callus formation

Reparative phase: cartilagenous soft callus phase. Phagocytic cells start the removal of dead cells and damaged bone tissue.

A **soft callus**, consisting of **non-calcified cartilage**, connects the two ends of the fractured bone.

About 3 to 4 weeks after the injury, periosteal and endosteal-derived osteoblasts penetrate and replace the soft cartilaginous callus with **woven bone**.

Osteoblast penetration starts from each end of the fractured fragments and a distinct collar, consisting of woven bone typical of cancellous bone, is formed around the fragments.



3 Reparative phase: Hard callus formation

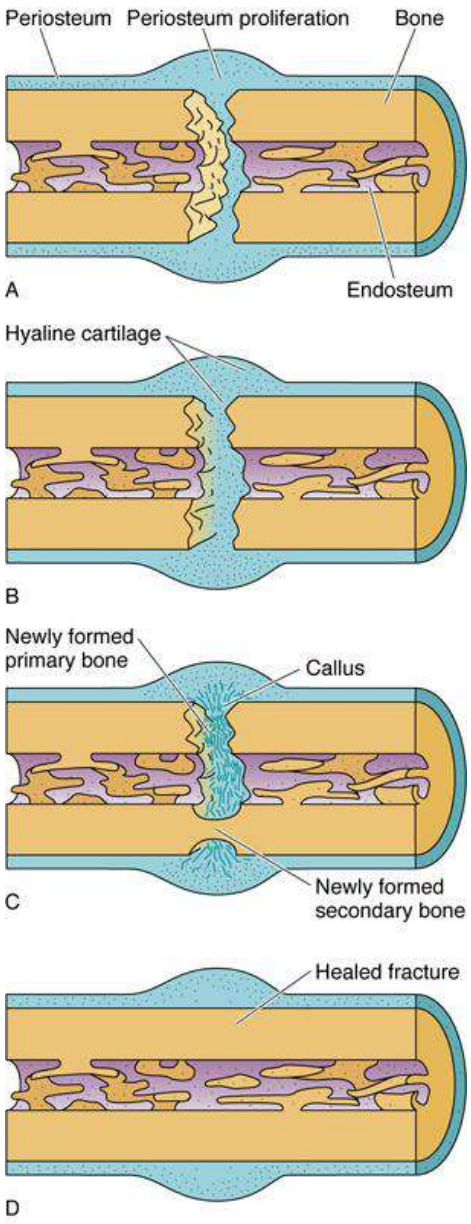
Osteoblasts, derived from periosteal stem cells and osteoprogenitor cells derived from the endosteum, are active. The ends of the fracture become enveloped by the periosteal (external) and internal hard callus and a clinical union can be visualized. Yet, the reparative process is not complete: the necrotic ends of the fractured bone, and even portions of the hard callus, are being reabsorbed. In addition, woven bone needs to be replaced by compact bone.

4 Remodeling phase

Osteoclasts reabsorb excessive and missplaced trabeculae and new bone is laid down by osteoblasts to construct compact bone along the stress lines. New haversian systems or osteons and Volkmann's canals are formed to house blood vessels.

3.Reparative phase: hard bone callus phase. The union of the fragments is achieved by the development of a **hard bone callus**. Osteoblasts deposit osteoid that is calcified and woven bone is formed.
4. Remodeling phase. This repair process is still in progress 2 to 3 months after the injury.

Bone Repair



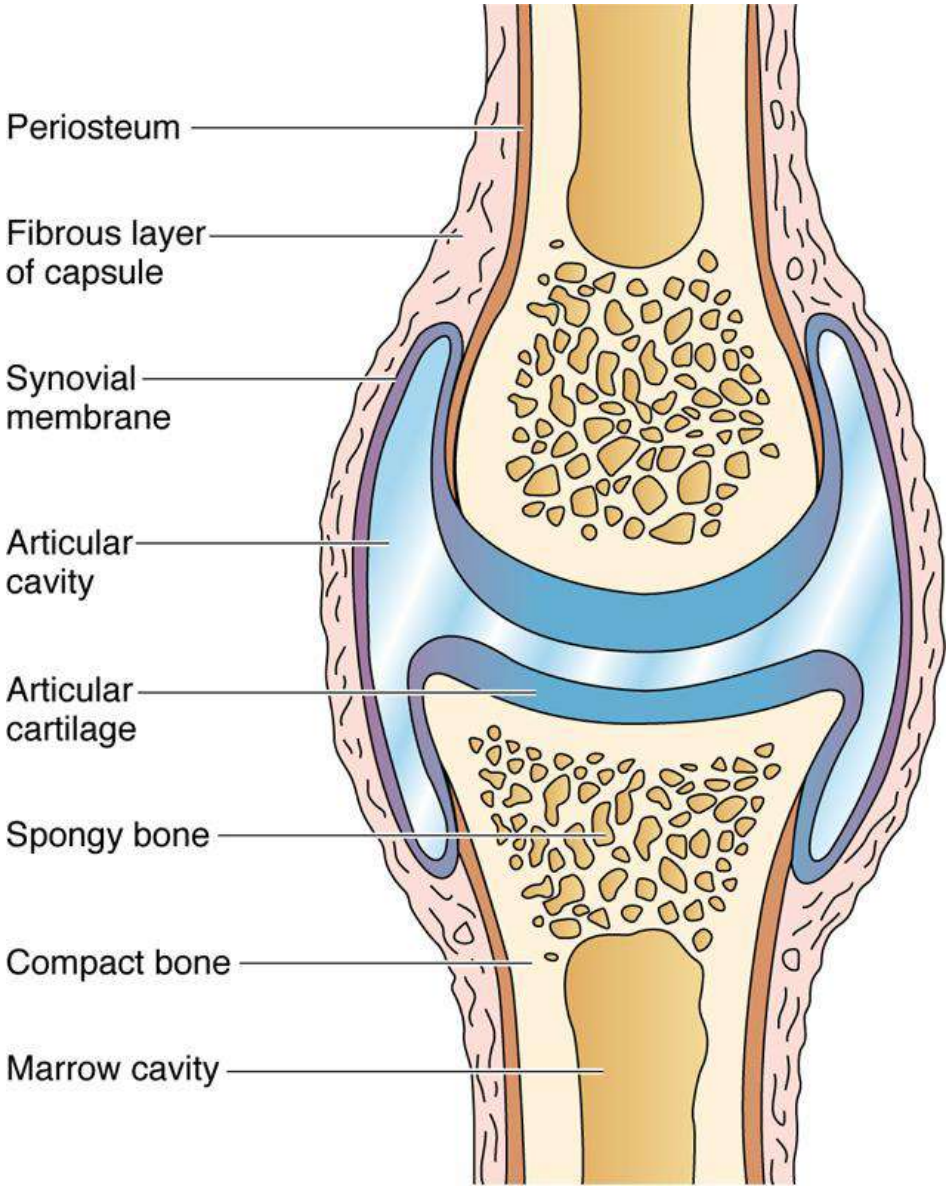
Events in bone fracture repair.

Osteoprogenitor cells in the middle of the proliferating mass are without a profuse capillary bed and these cells become chondrogenic cells, giving rise to chondroblasts that form cartilage in the outer parts of the collar.

The outermost layer of the proliferating osteoprogenitor cells proliferate as osteoprogenitor cells. Thus, the collar exhibits three zones that blend together: (1) a layer of new bone cemented to the bone of the fragment, (2) an intermediate layer of cartilage, and (3) a proliferating osteogenic surface layer. In the meantime, the collars formed on the ends of each fragment fuse into one collar, known as the **external callus**, leading to union of the fragments. Continued growth of the external collar is derived mainly from proliferation of osteoprogenitor cells and, to some degree, from interstitial growth of the cartilage in its intermediate zone.

The cartilage matrix adjacent to the new bone formed in the deepest region of the collar becomes calcified and is eventually replaced with cancellous bone. Ultimately, all of the cartilage is replaced with primary bone by endochondral bone formation.

Synovial Joint

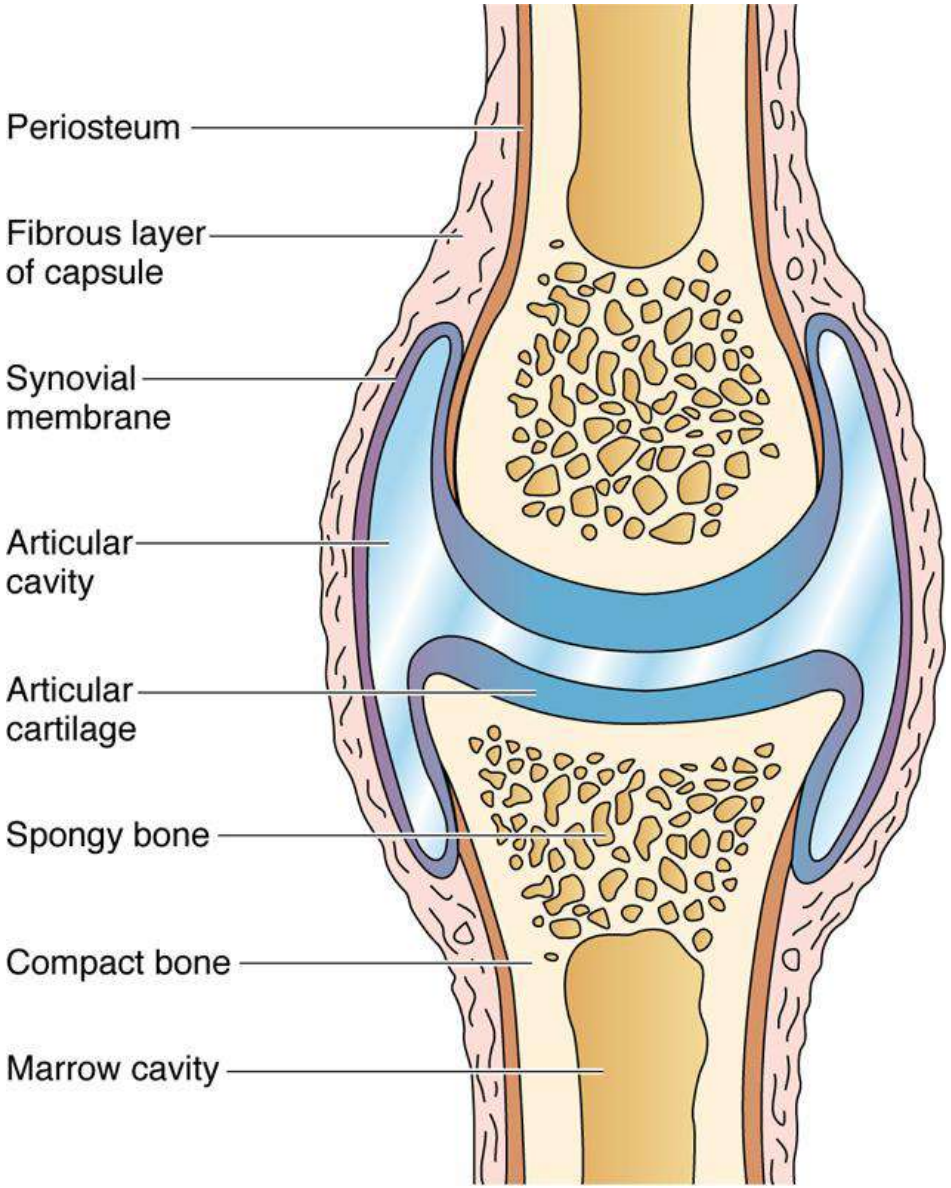


Anatomy of a diarthrodial joint.

Bones articulate or come into close proximity with one another at joints, which are classified according to the degree of movement available between the bones of the joint.

Those that are closely bound together with only a minimum of movement between them are called **synarthroses**; joints in which the bones are free to articulate over a fairly wide range of motion are classified as **diarthroses**.

Synovial Joint



Anatomy of a diarthrodial joint.

There are three types of **synarthrosis joints** according to the tissue making up the union:

1. Synostosis. There is little if any movement, and joint-uniting tissue is bone (e.g., skull bones in adults).

2. Synchondrosis. There is little movement, and joint-uniting tissue is hyaline cartilage (e.g., joint of first rib and sternum).

3. Syndesmosis. There is little movement, and bones are joined by dense connective tissue (e.g., pubic symphysis).

Most of the joints of the extremities are **diarthroses** (Fig. 7–21). The bones making up these joints are covered by persistent **hyaline cartilage**, or **articular cartilage**. Usually, ligaments maintain the contact between the bones of the joint, which is sealed by the **joint capsule** .

The **capsule** is composed of an outer **fibrous layer** of dense connective tissue, which is continuous with the periosteum of the bones, and an inner cellular **synovial layer**, which covers all nonarticular surfaces. Some prefer to call this a **synovial membrane**.