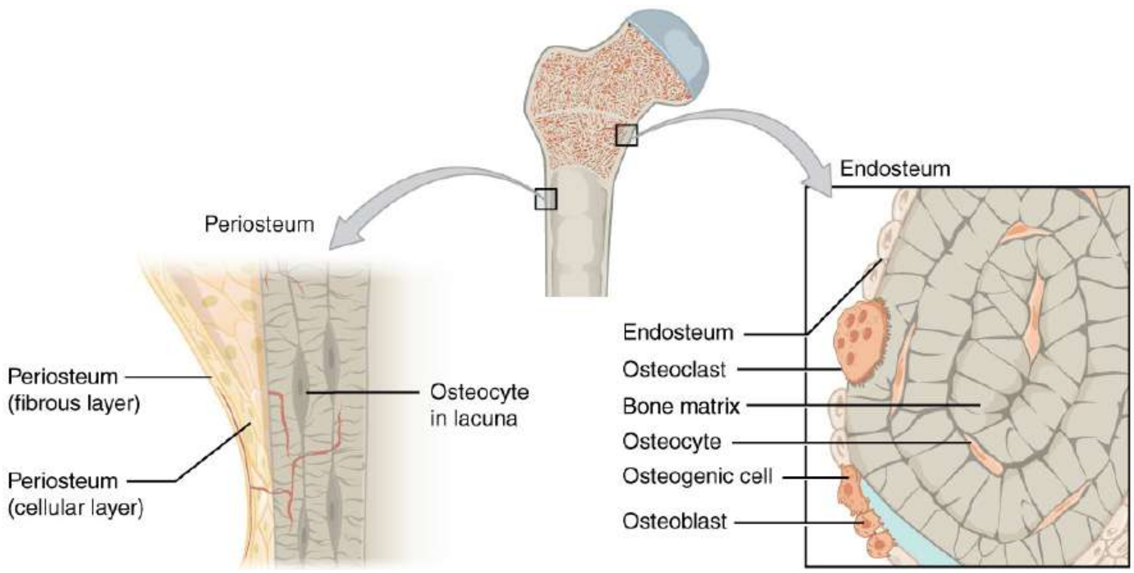
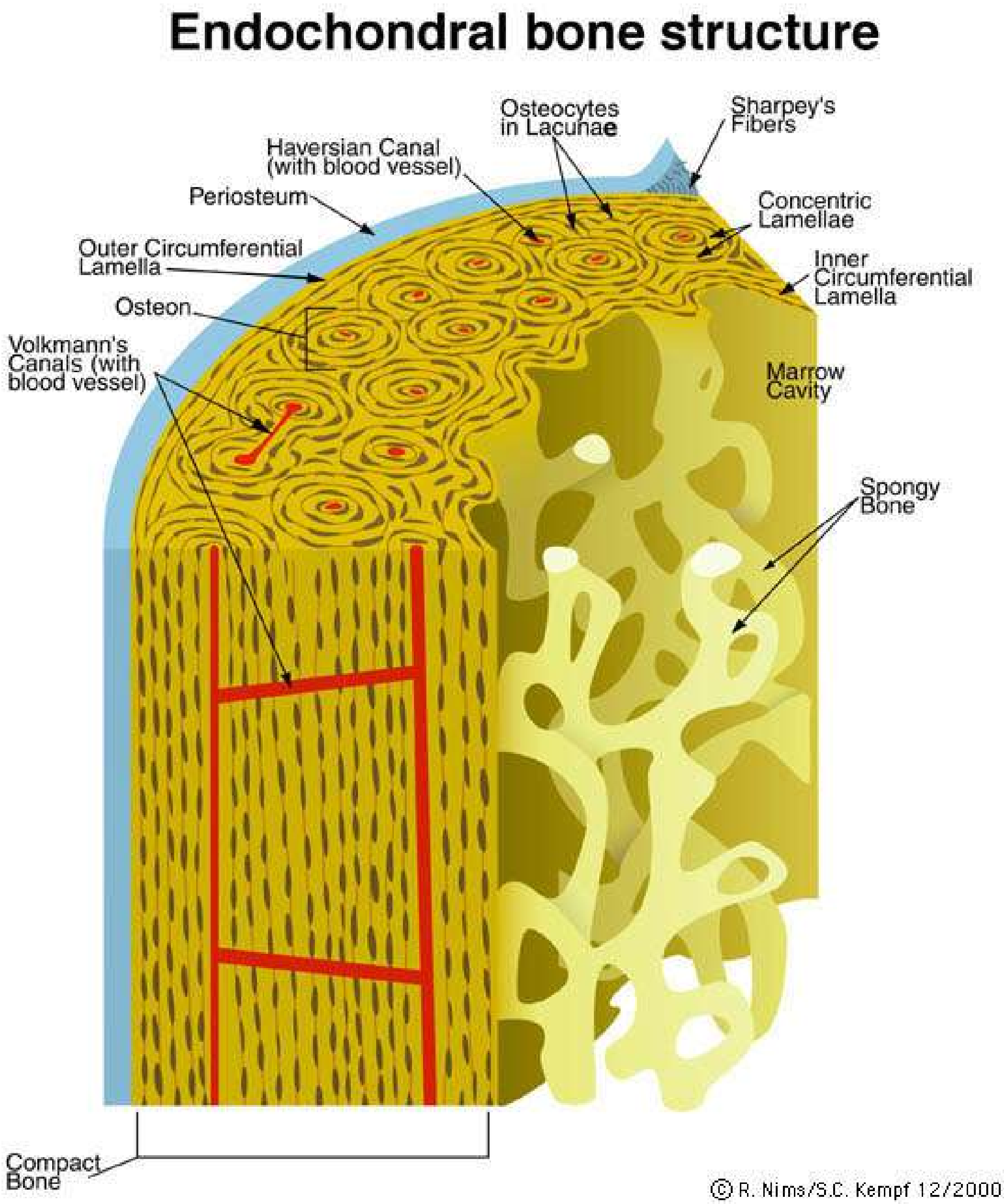
BONE/UG/SEM3 HONS/SDG

Bone is one of the hardest substances in the body, bone is a living tissue composed of cells and their associated extracellular matrix.

IT IS A CONNECTIVE TISSUE



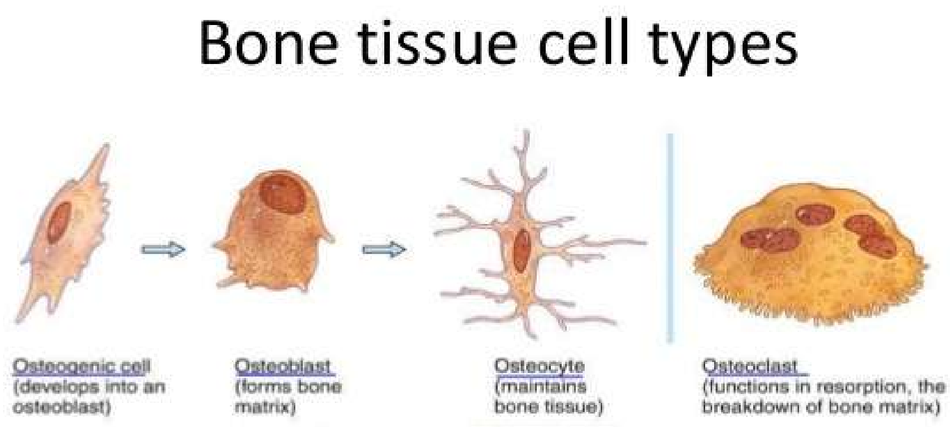
Bone structure

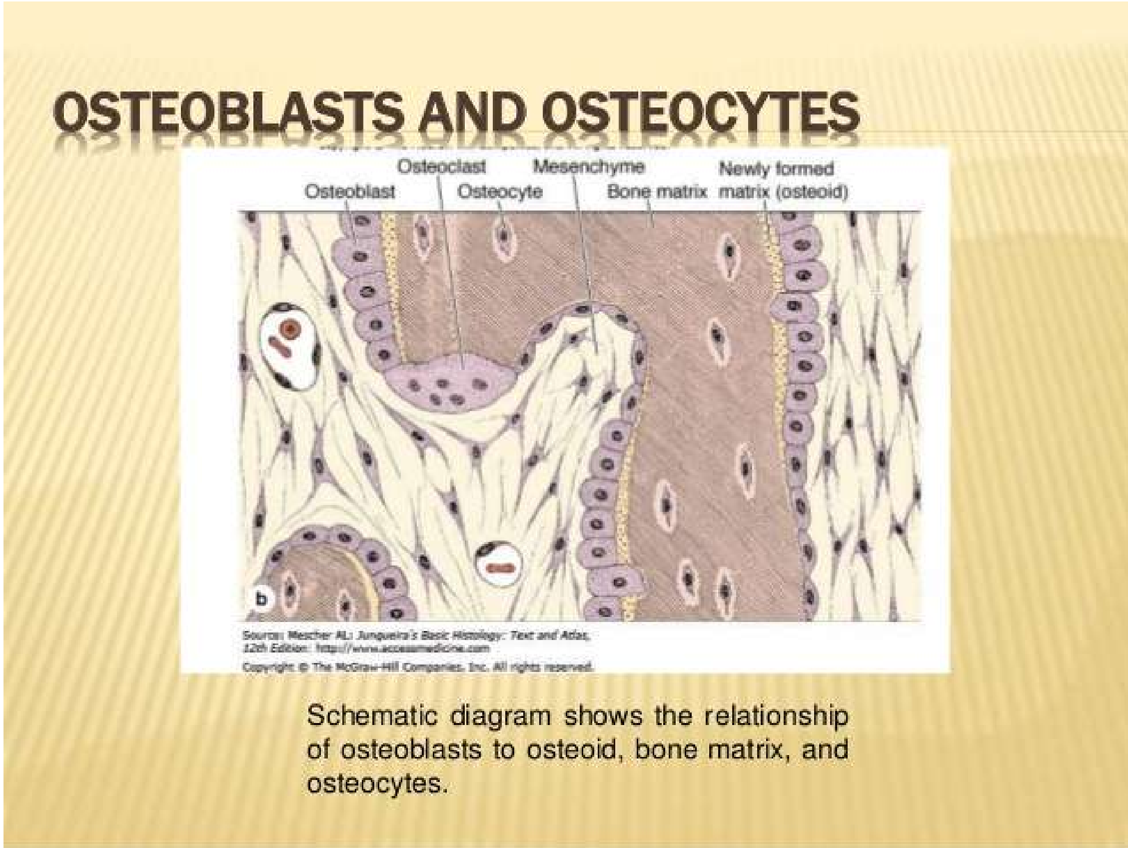


1. **periosteum** - a layer of connective tissue that covers the bone containing a high concentration of collagen fibers.
   Two distinct layers. External layer very fibrous, while internal layer is more cellular and vascularized.
   Some of the collagen fibers penetrate the calcified bone matrix and bind the periosteum to the bone. These fibers are called Sharpey'sFibers.
   Cells of this connective tissue play important roles in bone histogenesis and in the healing of fractures.

2. endosteum – similar to the periosteum, but only one cell thick. Lines the internal surfaces of bone.

Important roles of the periosteum and endosteumare nutrition of bone cells and provision of osteoblasts for bone histogenesis and repair.





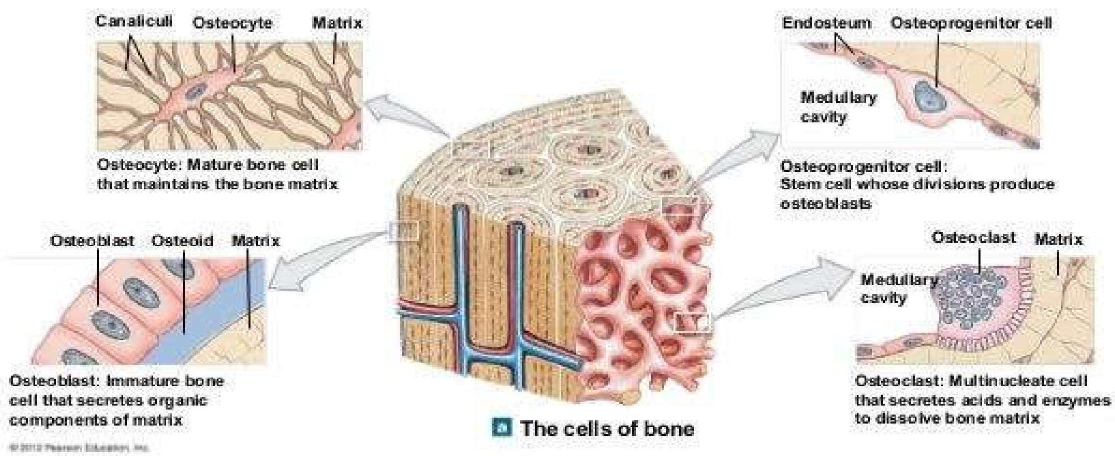
There are 3 different bone cell types.

1. **osteoblasts** - immature bone cells that synthesize and secrete the osteoid matrix that will calcify to form the bones extracellular matrix. This matrix is composed of glycoproteins and collagen. In areas where these cells occur, they are located on the surfaces of forming bone and are not yet embedded in the extracellular matrix. These cells have cytoplasmic processes that bring them into contact with neighboring osteoblasts, as well as nearby osteocytes. Ultrastructure shows organelle systems typical of secretory cells.

2. **osteocytes** - mature bone cells. These cells are osteoblasts that have become embedded in calcified bone matrix. They reside in lacunae within the matrix and are in contact with neighboring osteocytes via cytoplasmic processes that extend through small tunnels called canaliculi. Contacting cytoplasmic processes form gap junctions. This communication between osteocytes is important in the tranfer of nutrients to these cells and wastes out of them since they may be far removed from blood capillaries. The cells are flattened and their internal organelles exhibit the characteristics of cells that have reduced synthetic activity.

3. **osteoclasts** - these are large, multinucleate cells that act to reabsorb bone during specific stages in bone formation and healing, and during the continual reworking of internal bone architecture that occurs throughout life.

Figure 5.1a Histological Structure of a Typical Bone



a The cells of bone

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Bone matrix - 50% inorganic components composed mainly of various calcium salts. The organic matter composing the other 50% of the matrix is made-up of 95% collagen and a mixture of various glycosaminoglycans associated with proteins.

HISTOGENESIS OF SKELETAL STRUCTURE

Two modes of bone formation

1. **Endochondral** - cartilage template formed that is replaced by bone (e.g. vertebral column, long bones of limbs – most bones in body)

2. **Intramembranous** - direct formation of bone structure with no cartilagenous template (e.g. flat bones of skull)

In the embryo, **osteoblasts** are derived from mesenchymal cells. These cells either aggregate where bones are to form (**intramembranous bone formation**) and lay down the matrix that will later become calcified, or they migrate into pre-existing cartilage "models)" of the presumptive bone and replace the cartilage with a calcareous matrix (**endochondral bone formation**). Long bone growth is also endochondral in nature. Osteoblasts are different than the chondroblasts that begin the histogenesis of cartilage and should not be confused with them.

As the primordial bone matrix is layed down, the osteoblasts become entrapped in lacunae within the matrix and are then known as mature osteocytes. As bone is being formed, there is also localized removal of the bone matrix by another set of connective tissue cells known as **osteoclasts**. These cells are thought to differentiate from monocytes and are responsible, in part, for the internal architecture of bones in that they excavate localized portions of the forming bone and make passageways for such things as blood vessels nerves. Osteoclasts will continue to remodel the bone throughout a person's life.

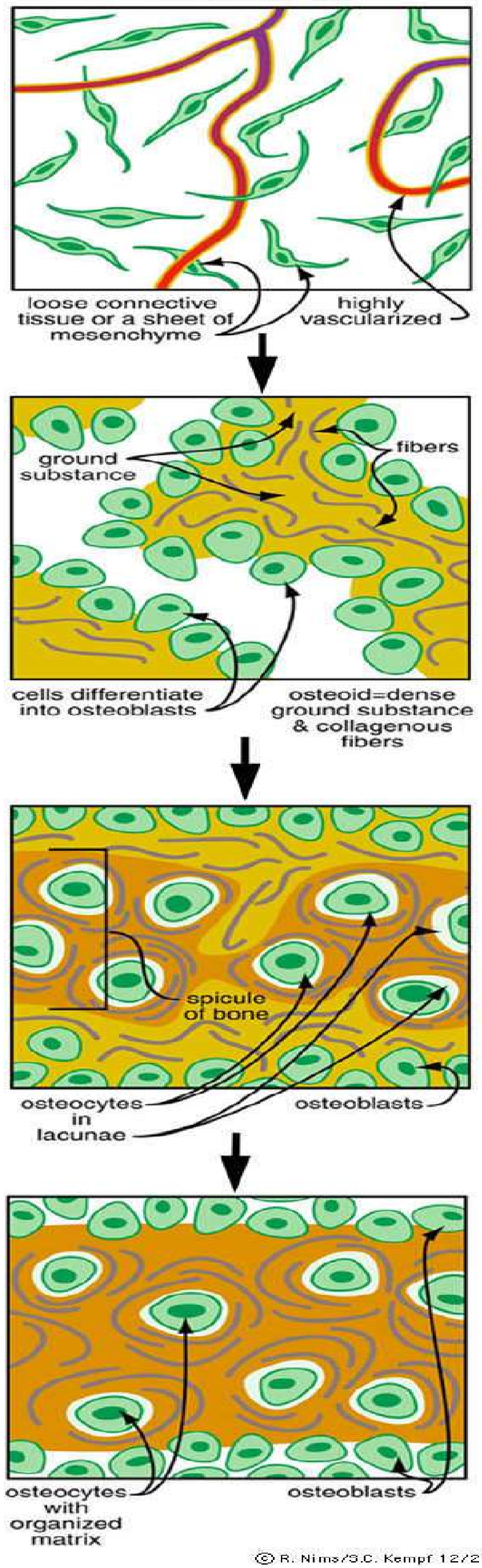
A third population of cells involved in bone formation are the cells of the marrow. These are the stem cells for blood cells and all their progeny.

Bone Cells

Cell type	**Function**	**Location**
Osteogenic cells	Develop into osteoblasts	Deep layers of the periosteum and the marrow
Osteoblasts	Bone formation	Growing portions of bone, including periosteum and endosteum
Osteocytes	Maintain mineral concentration of matrix	Entrapped in matrix
Osteoclasts	Bone resorption	Bone surfaces and at sites of old, injured, or unneeded bone

INTRAMEMBRANOUS BONE FORMATION

Intramembranous Bone Formation



Occurs mainly in bones of the skull.

Mesenchymal cells aggregate and begin to secrete matrix that is characterized by bundles of collagenous fibers.

The secreted osteoid matrix has a high affinity for calcium salts, that are brought into the area of bone formation by the circulatory system.

These deposit within and on the matrix to form calcified bone. As this calcification takes place, the mesenchymal cells undergo morphological changes.

They loose the appearance of mesenchymal cells and round up becoming true osteoblasts. The osteoblasts become oriented in epithelial-like layers along the forming bone. The osteoblasts and the collagen and other components of the intercellular matrix form the organic osteoid framework of the bone.

As a strand of matrix is invested with inorganic salts it forms a spicule of bone. The spicules will merge to form larger calcified structures called trabeculae. These will thicken with the deposition of more osteoid matrix and inorganic salts as the osteoblasts continue their secretion in an appositional manner. This secretion by the osteoblasts is cyclic and results in layers of bone material called lamellae. The deposition of lamellae traps some of the osteoblasts within the osteoid matrix. Once trapped they are considered mature osteocytes. Osteocytes are characterized by cytoplasmic processes that contact similar processes of adjacent osteocytes.

Gap juctions form at points of contact allowing transfer of small molecules between cells. This transfer is important in co-ordinating bone growth and in the nourishment of osteocytes which may be separated from blood vessels by a considerable amount of calcified bone. Channals through which cytoplasmic processes of osteocytes extend are called canaliculi.

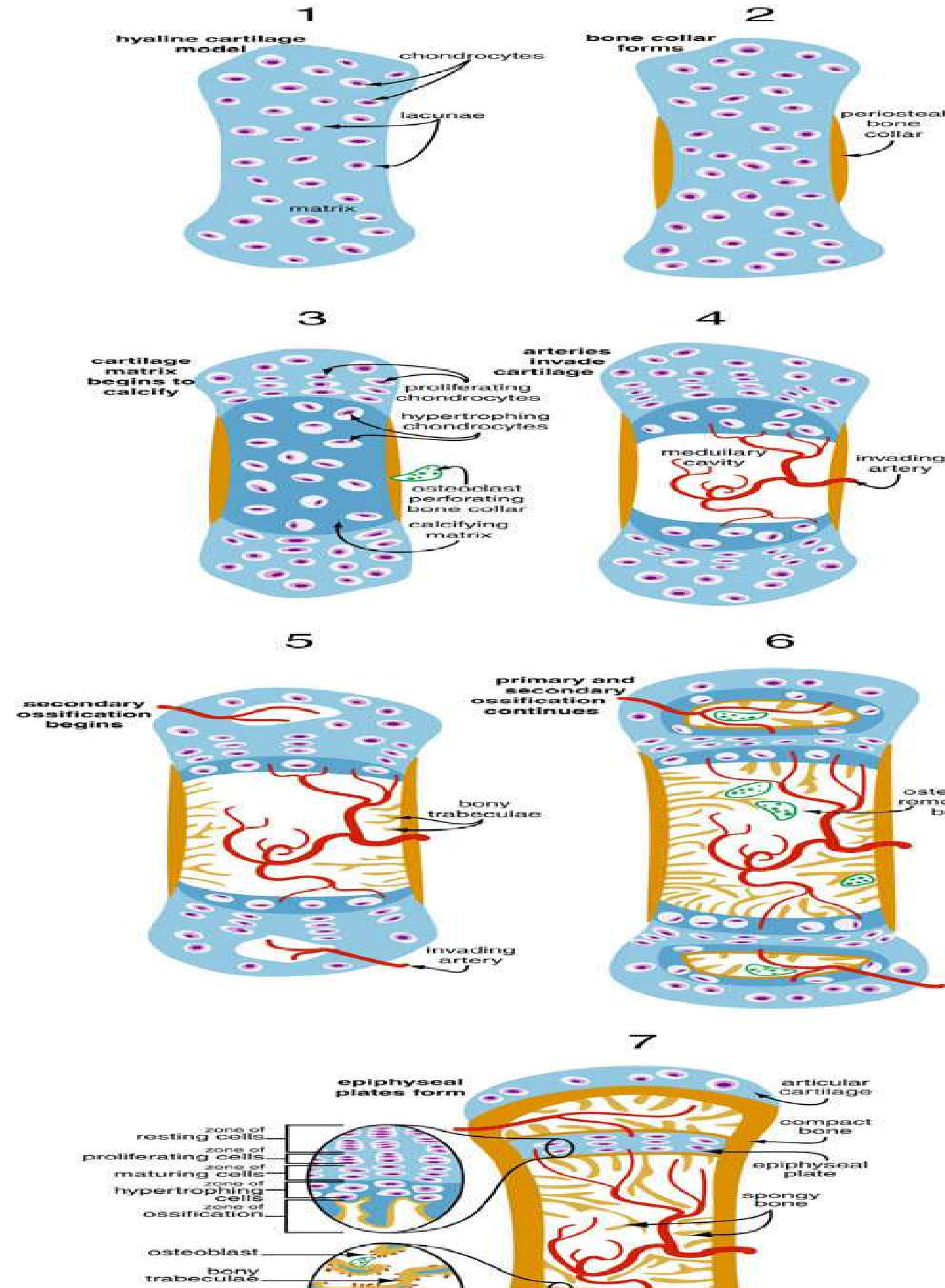
Growing adjacent trabeculae will contact and fuse forming the structure of the mature bone.

As intramembranous bones grow, selective reabsorption of bone material is also occurring due to the activities of osteoclast cells.

This results in the formation of much of the internal architecture of the bones, providing spaces for blood vessels and marrow.

ENDOCHONDRAL BONE FORMATION

Endochondral bone formation



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Most of the bones in the mammalian body are initially formed by endochondral means. That is to say, a template of hyaline cartilage that is in the shape of a miniature of the bone is layed down prior to the bone's formation. This deposition of cartilage is accomplished by the action of chondroblasts functioning in both interstitial and appositional growth capacities.

The typical examples that are used to describe endochondral bone formation are the long bones of the limbs.

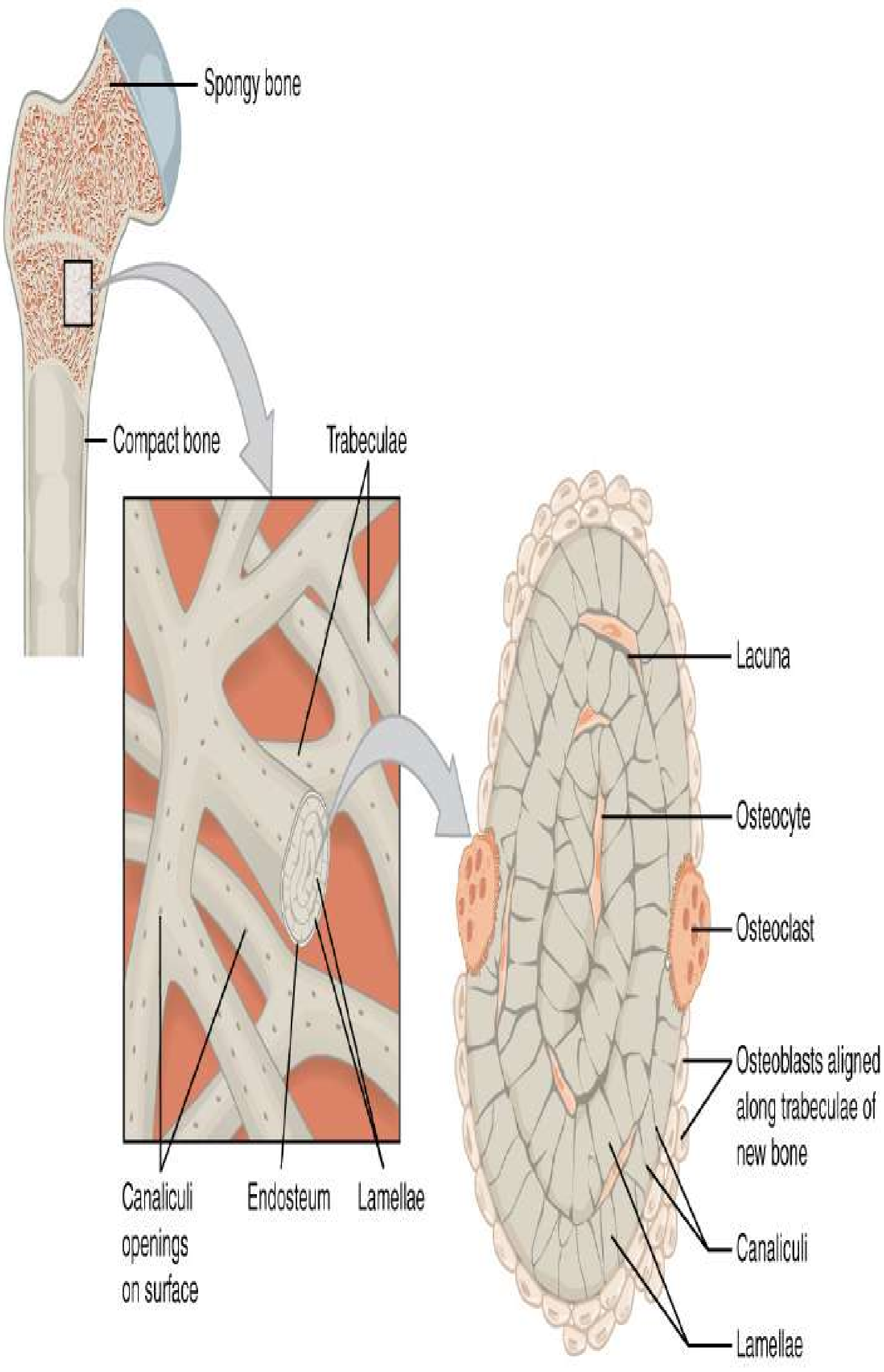
Bones of the body, including the long bones may be considered a rigid form of connective tissue. The cells of this tissue are embedded within a matrix that consists of organic and inorganic components.

The organic matrix, or ground substance, consists of collagen fibers for the most part. The inorganic component mostly consists of calcium salts, calcium phosphate (85%), calcium carbonate (10%), and small amounts of calcium and magnesium flouride.

Two types of bone tissue can be distingished. These are cancellous, or spongy, bone that lies centrally within the shaft of long bones, and compact or dense bone that lies more peripherally.The actual mineralized matrix of these two types of bone is the same. It contains embedded osteocytes that are in communication via gap junctions at their contacting cytoplasmic processes.

The difference between spongy and compact bone lies simply in the size of open spaces within the mineralized bone.

The spongy bone consists of slender, irregular trabeculae with large spaces between them where blood vessels, nerves, and marrow cells are located.



Compact bone appears solid, no large cavities within it.

Since the actual mineralized matrix of both types of bone is the same, there is no distinct boundary between spongy and compact bone.

The shaft of a long bone consists of a medullary or central volume of spongy bone surrounded by a thick cortical layer of compact bone. The compact layer can be subdivided into an outer series of sub-layers called periosteal lamellae that were secreted by the periosteal cells during its development and growth, and an inner component consisting of multiple concentric sub-layers surrounding the halversian canals. Radial cavities called Volkmann's canals also extend through the compact bone. These radial cavities and halversian canals form a network within the compact bone that is continuous with the cavities of the spongy bone. Blood vessels and nerves extend through the channels of this network.

STEPS:

The first step in endochondral bone formation is the histogenesis of a cartilage miniature of the bone. This takes place as discussed above via the action of chondroblasts that have migrated to the area. The chondroblasts secrete a cartilagenous matrix that is laid down both interstitially and appossitionally. The end result is a cartilage template of the bone in miniature that contains chondrocytes embedded within the cartilage matrix.

Actual osteogenesis (bone ossification) begins with the establishment of a periosteum on the shaft (or diaphysis) of the cartilage template and the laying down of an intramembranous collar of bone on the circumference of the cartilage diaphysis. This is followed by hypertrophy (they get bigger) and eventual death of the chondrocytes within the cartilage matrix. As the chondrocytes degenerate they reabsorb some of the surrounding cartilage matrix causing enlargement of the lacunae in which they reside. This process is known as **hypertrophication**. As this occurs, the chondrocytes loose their ability to maintain the remaining cartilage matrix and it becomes partially calcified. The end result is an area of porous calcified cartilage within the central regions of the diaphysis. As this is occurring, osteoclasts that have arrived in the area via the circulatory system, begin excavating passageways or tunnels through the intramembranous collar surrounding the diaphysis. These passageways provide a means through which blood vessels, nerves and undifferentiated mesenchymes cells can enter into the lacunae (spaces) in the remnants of the cartilage matrix that have been left by the degenerating chondrocytes.

The mesenchyme cells will differentiate into osteoblasts and hematopoietic stem cells that are distributed within the bone.

The osteoblasts, blood vessels, and nerves form the osteogenic bud that comes to lie more or less centrally within the diaphysis of the forming bone.

As the invading cells spread out within the diaphysis of the cartilage template and ossification begins, this central volume of active bone deposition is called a primary ossification center.

The osteoblasts begin to secrete osteoid matrix on the remnants of calcified cartilage. The osteoid matrix becomes mineralized forming cancellous bone in the shaft of the diaphysis. Some of the osteoblasts become trapped within the mineralized bone and become mature bone cells, osteocytes. These cells maintain contact with other osteocytes and/or with osteoblasts via contacting cytoplasmic processes that extend through canaliculi the mineralized matrix.

As the cancellous bone is layed down, chondroclasts (which are the cartilagenous equivalent of osteoclasts) reabsorb the calcified cartilage as it is replaced by osteoid matrix (i.e., the calcified chondroid matrix does not form bone!). At this point, it is important to note that this means the actual bone tissue, matrix and mineralization, is the result of the action of a new group of cells, the osteoblasts.

The primary ossification center rapidly extends longitudinally within the diaphysis as the shaft of the cartilage template is completely replaced by cancellous bone tissue. As the ossification center extends longitudinally, so does the calcified outer collar of bone layed down by the periostial osteocytes.

As ossification proceeds in the diaphysis, secondary ossification centers form in the cartilage of the bulbuous ends, or epiphyses, at either end of the long bone shaft. Osteogenic tissues in these regions also act to form mineralized bone. This process is similar to the primary ossification we've just discussed with one difference. Since there is no periosteum on the surface of the epiphyses, there is no periostial external collar of bone.

What we have just discussed is endochondral bone formation. This involved the deposition of cancellous, or spongy bone, within a cartilage matrix. This is not the final step in bone formation. In fact, there really is no such thing as a final step in this process.

During and after endochondral bone formation, there is considerable internal remodeling of the architecture of the bone. This is accomplished by the efforts of osteoblasts, osteocytes, and osteoclasts.

Osteoclasts act to reabsorb much of the cancellous bone that has been layed down during endochondral bone formation. As this occurs, channels are hollowed out within the spongy bone structure. These are in addition to the cavities already formed in spongy bone. In more peripheral regions where compact bone will be present, these channels will give rise to the halversian systems as compact or dense bone is laid down within them.

As these peripheral channels are hollowed out, osteoblasts from the marrow invade the channels and form an epithelium on the channel's inner wall. These osteoblasts lay down cyclical layers of osteoid matrix which becomes mineralized and decrease the diameter of the channels. As this occurs, some of the osteoblasts are trapped within the matrix and become osteocytes with the characteristic long cytoplasmic processes that extend through canaliculi in the mineralized bone and contact each other. As this ossification takes place, large cavities like those present in spongy bone are not formed, thus, this kind of bone is called compact or dense bone. Since there is no cartilage precursor to the compact bone, it may be considered intramembranous as far as its mode of formation is concerned.

The final result of this ossification process is the replacement of much of the spongy bone within the shaft of the diaphysis with compact bone which has many halversian canals running through it. Osteoclasts hollow out Volkmann's canals that extend radially between haversian canals.

The reabsorption and redeposition of compact and spongy bone continues throughout life.

Functions of Bones

Bone is often stereotyped as simply a protective and supportive framework for the body. Though it does perform these functions, bone is actually a very dynamic organ that is constantly remodeling and changing shape to adapt to the daily forces placed upon it. Moreover, bone stores crucial nutrients, minerals, and lipids and produces blood cells that nourish the body and play a vital role in protecting the body against infection. All these functions make the approximately 206 bones of the human body an organ that is essential to our daily existence.

Bones have many functions, including the following:

- *Support:* Bones provide a framework for the attachment of muscles and other tissues.
- *Protection:* Bones such as the skull and rib cage protect internal organs from injury.
- *Movement:* Bones enable body movements by acting as levers and points of attachment for muscles.
- *Mineral storage:* Bones serve as a reservoir for calcium and phosphorus, essential minerals for various cellular activities throughout the body.
- *Blood cell production:* The production of blood cells, or hematopoiesis, occurs in the red marrow found within the cavities of certain bones.
- *Energy storage:* Lipids, such as fats, stored in adipose cells of the yellow marrow serve as an energy reservoir.