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UNIT 2: BONES AND CARTILAGE
STRUCTURE AND TYPES 0F BONES AND CARTILAGE
OSSIFICATION
BONE GROWTH AND RESORPTION

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STRUCTURE AND TYPES 0F BONES

The bones in the skeleton are not all solid. The outside cortical bone is solid bone with only a few small canals.

The insides of the bone contain trabecular bone which is like scaffolding or a honey-comb.

The spaces between the bone are filled with fluid bone marrow cells, which make the blood, and some fat cells

A bone is a rigid organ that constitutes part of the vertebrate skeleton in animals. Bones protect the various organs of the body, produce red and white blood cells, store minerals, provide structure and support for the body, and enable mobility. Bones come in a variety of shapes and sizes and have a complex internal and external structure. They are lightweight yet strong and hard, and serve multiple functions

Bone tissue (osseous tissue) is a hard tissue, a type of dense connective tissue. It has a honeycomb-like matrix internally, which helps to give the bone rigidity. Bone tissue is made up of different types of bone cells.

Osteoblasts and osteocytes are involved in the formation and mineralization of bone; osteoclasts are involved in the resorption of bone tissue. Modified (flattened) osteoblasts become the lining cells that form a protective layer on the bone surface.

The mineralised matrix of bone tissue has an organic component of mainly collagen called ossein and an inorganic component of bone mineral made up of various salts.

Bone tissue is a mineralized tissue of two types, cortical bone and cancellous bone. Other types of tissue found in bones include bone marrow, endosteum, periosteum, nerves, blood vessels and cartilage

In the human body at birth, there are approximately 270 bones present; many of these fuse together during development, leaving a total of 206 separate bones in the adult, not counting numerous small sesamoid bones.

The largest bone in the body is the femur or thigh-bone, and the smallest is the stapes in the middle ear

Structure

Bone is not uniformly solid, but consists of a flexible matrix (about 30%) and bound minerals (about 70%) which are intricately woven and endlessly remodeled by a group of specialized bone cells. Their unique composition and design allows bones to be relatively hard and strong, while remaining lightweight.

Bone matrix is 90 to 95% composed of elastic collagen fibers, also known as ossein, and the remainder is ground substance. The elasticity of collagen improves fracture resistance. The matrix is hardened by the binding of inorganic mineral salt, calcium phosphate, in a chemical arrangement known as calcium hydroxylapatite. It is the bone mineralization that give bones rigidity.

Bone is actively constructed and remodeled throughout life by special bone cells known as osteoblasts and osteoclasts. Within any single bone, the tissue is woven into two main patterns, known as cortical and cancellous bone, and each with different appearance and characteristics.

Cortical bone

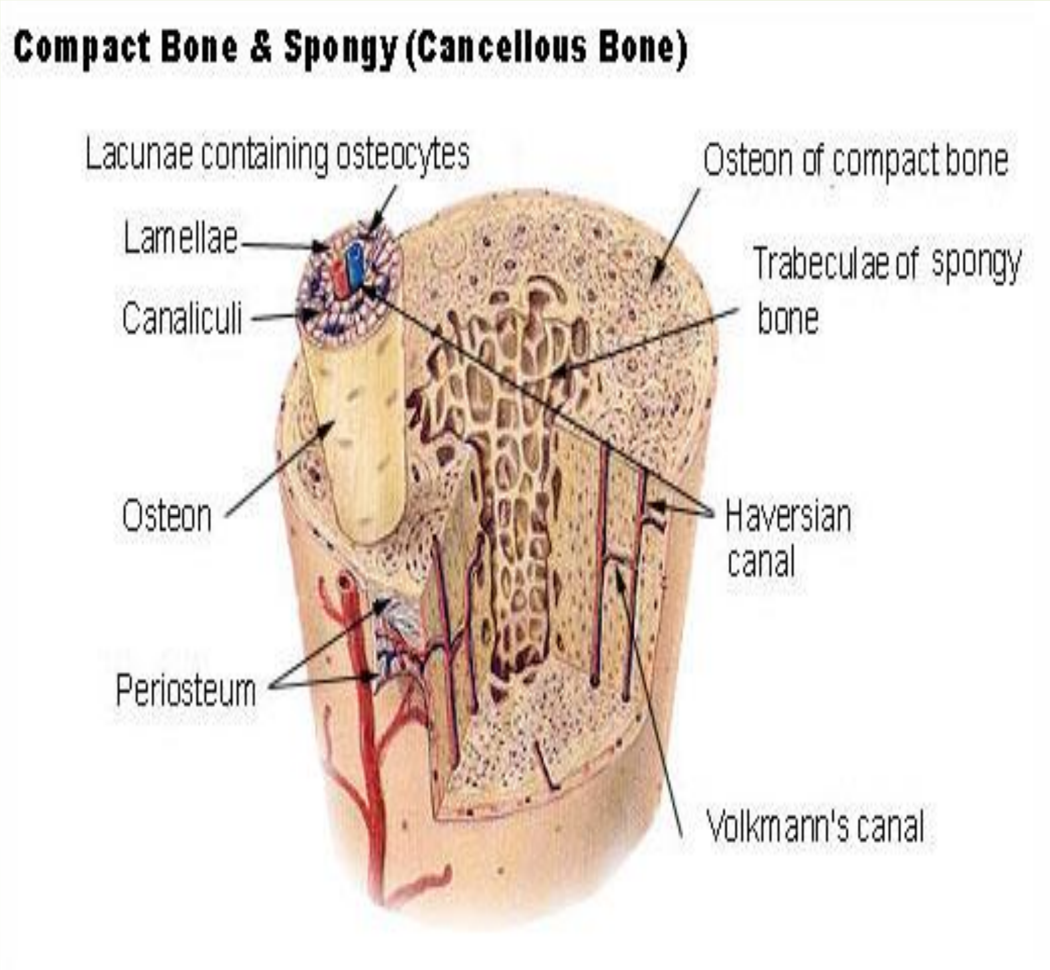
The hard outer layer of bones is composed of cortical bone, which is also called compact bone as it is much denser than cancellous bone. It forms the hard exterior (cortex) of bones.

The cortical bone gives bone its smooth, white, and solid appearance, and accounts for 80% of the total bone mass of an adult human skeleton. It facilitates bone's main functions—to support the whole body, to protect organs, to provide levers for movement, and to store and release chemical elements, mainly calcium.

It consists of multiple microscopic columns, each called an osteon or Haversian system. Each column is multiple layers of osteoblasts and osteocytes around a central canal called the haversian canal. Volkmann's canals at right angles connect the osteons together.

The columns are metabolically active, and as bone is reabsorbed and created the nature and location of the cells within the osteon will change. Cortical bone is covered by a periosteum on its outer surface, and an endosteum on its inner surface.

The endosteum is the boundary between the cortical bone and the cancellous bone. The primary anatomical and functional unit of cortical bone is the osteon.



Cross-section details of a long bone

Cancellous bone

Cancellous bone, also called trabecular or spongy bone, is the internal tissue of the skeletal bone and is an open cell porous network. Cancellous bone has a higher surface-area-to-volume ratio than cortical bone and it is less dense. This makes it weaker and more flexible.

The greater surface area also makes it suitable for metabolic activities such as the exchange of calcium ions. Cancellous bone is typically found at the ends of long bones, near joints and in the interior of vertebrae.

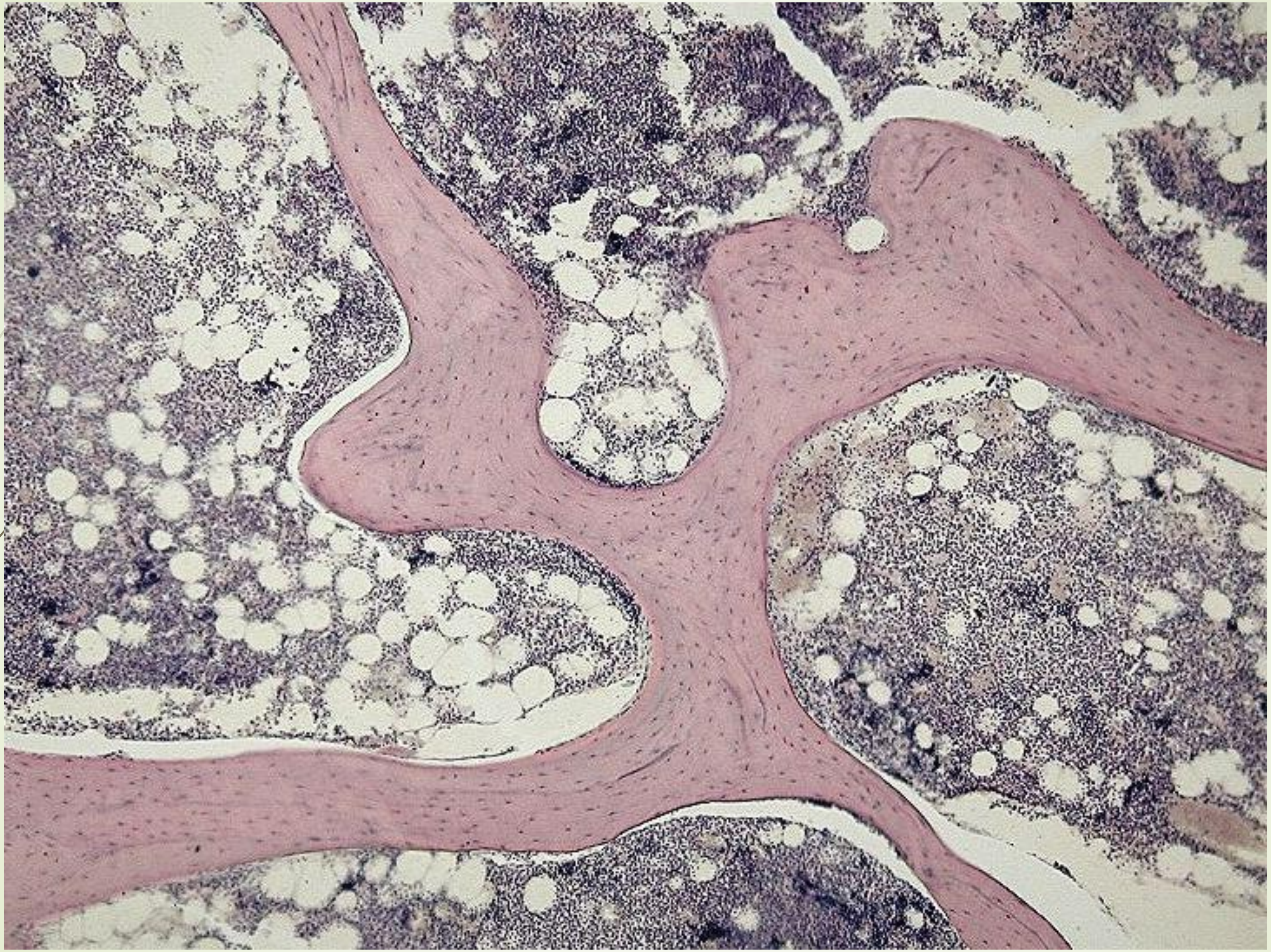
Cancellous bone is highly vascular and often contains red bone marrow where hematopoiesis, the production of blood cells, occurs. The primary anatomical and functional unit of cancellous bone is the trabecula.

The trabeculae are aligned towards the mechanical load distribution that a bone experiences within long bones such as the femur. As far as short bones are concerned, trabecular alignment has been studied in the vertebral pedicle.

Thin formations of osteoblasts covered in endosteum create an irregular network of spaces, known as trabeculae. Within these spaces are bone marrow and hematopoietic stem cells that give rise to platelets, red blood cells and white blood cells.

Trabecular marrow is composed of a network of rod- and plate-like elements that make the overall organ lighter and allow room for blood vessels and marrow. Trabecular bone accounts for the remaining 20% of total bone mass but has nearly ten times the surface area of compact bone.

The words cancellous and trabecular refer to the tiny lattice-shaped units (trabeculae) that form the tissue. It was first illustrated accurately in the engravings of Crisóstomo Martinez.



Micrograph of cancellous bone

Bone marrow

Bone marrow, also known as myeloid tissue in red bone marrow, can be found in almost any bone that holds cancellous tissue.

In newborns, all such bones are filled exclusively with red marrow or hematopoietic marrow, but as the child ages the hematopoietic fraction decreases in quantity and the fatty/yellow fraction called marrow adipose tissue (MAT) increases in quantity.

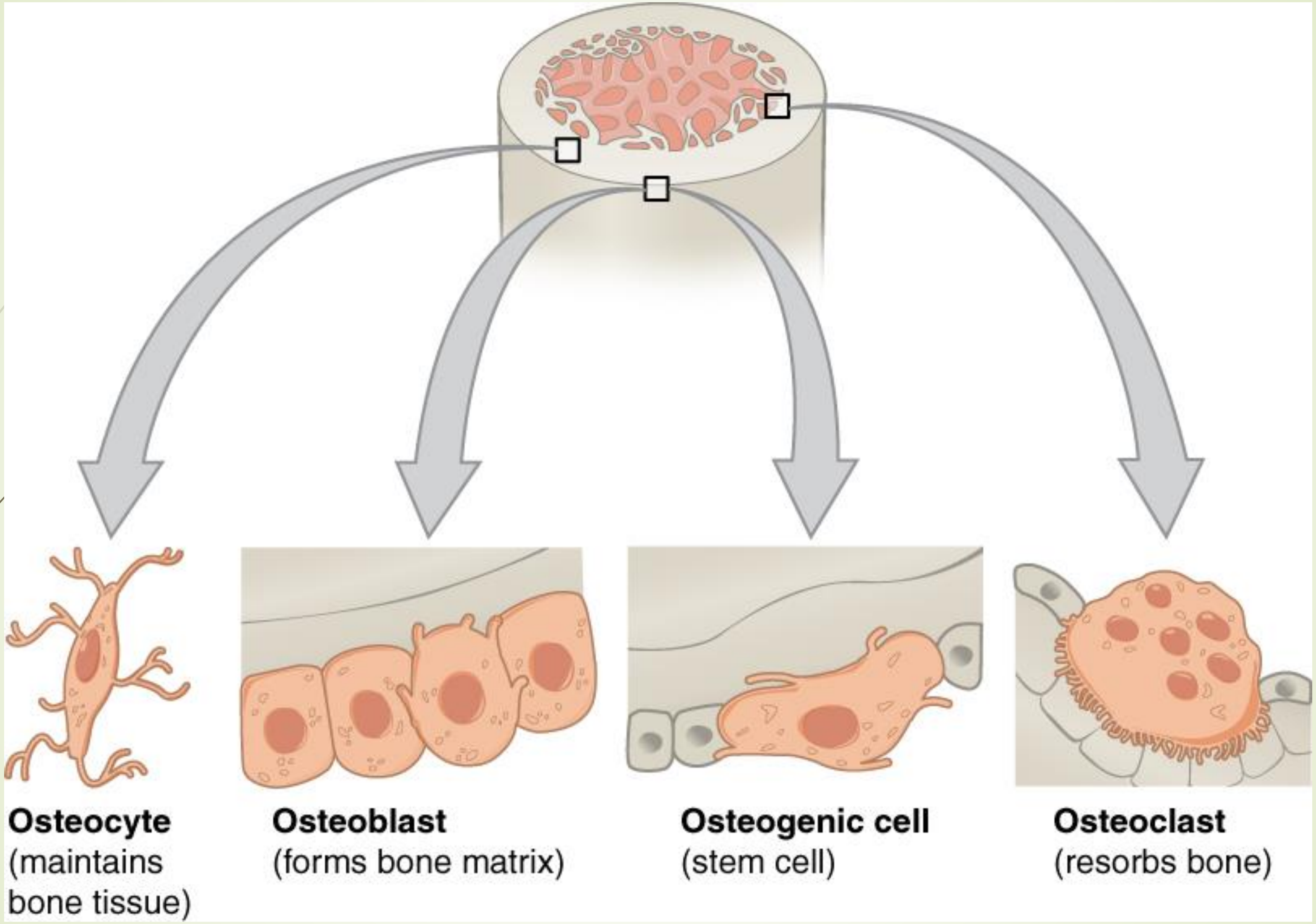
In adults, red marrow is mostly found in the bone marrow of the femur, the ribs, the vertebrae and pelvic bones

Bone cells

Bone is a metabolically active tissue composed of several types of cells. These cells include osteoblasts, which are involved in the creation and mineralization of bone tissue, osteocytes, and osteoclasts, which are involved in the reabsorption of bone tissue.

Osteoblasts and osteocytes are derived from osteoprogenitor cells, but osteoclasts are derived from the same cells that differentiate to form macrophages and monocytes.

Within the marrow of the bone there are also hematopoietic stem cells. These cells give rise to other cells, including white blood cells, red blood cells, and platelets


Osteocyte
(maintains
bone tissue)
Osteoblast
(forms bone matrix)
Osteogenic cell
(stem cell)
Osteoclast
(resorbs bone)

Bone cells

Osteoblast

Osteoblasts are mononucleate bone-forming cells. They are located on the surface of osteon seams and make a protein mixture known as osteoid, which mineralizes to become bone .

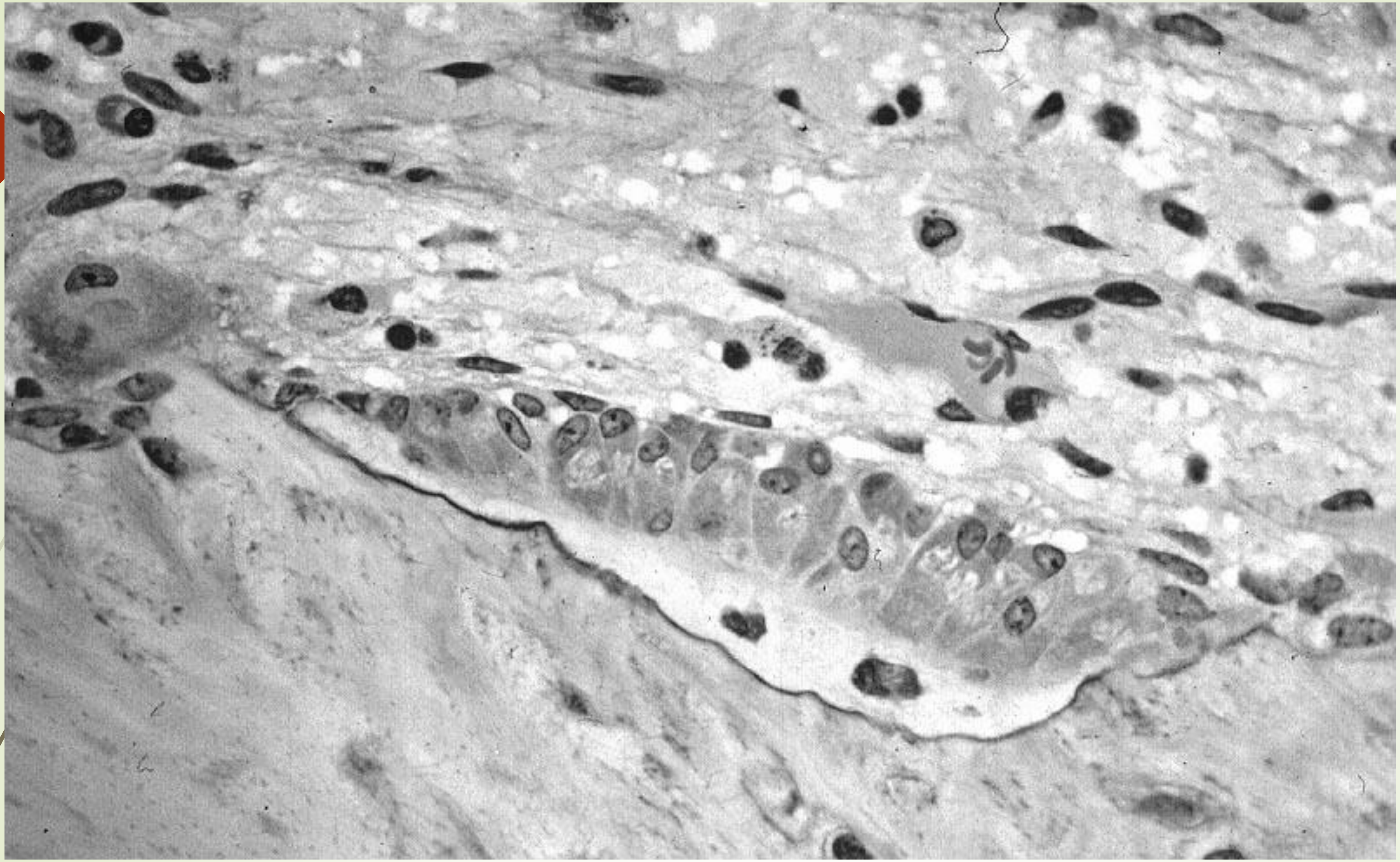
The osteoid seam is a narrow region of newly formed organic matrix, not yet mineralized, located on the surface of a bone. Osteoid is primarily composed of Type I collagen.

Osteoblasts also manufacture hormones, such as prostaglandins, to act on the bone itself. The osteoblast creates and repairs new bone by actually building around itself. First, the osteoblast puts up collagen fibers.

These collagen fibers are used as a framework for the osteoblasts' work. The osteoblast then deposits calcium phosphate which is hardened by hydroxide and bicarbonate ions.

The brand-new bone created by the osteoblast is called osteoid. Once the osteoblast is finished working it is actually trapped inside the bone once it hardens.

When the osteoblast becomes trapped, it becomes known as an osteocyte. Other osteoblasts remain on the top of the new bone and are used to protect the underlying bone, these become known as lining cells.



Light micrograph of decalcified cancellous bone displaying osteoblasts actively synthesizing osteoid, containing two osteocytes

Osteocyte

Osteocytes are mostly inactive osteoblasts. Osteocytes originate from osteoblasts that have migrated into and become trapped and surrounded by bone matrix that they themselves produced.

The spaces they occupy are known as lacunae.

Osteocytes have many processes that reach out to meet osteoblasts and other osteocytes probably for the purposes of communication.

Osteocytes remain in contact with other cells in the bone through gap junctions—coupled cell processes—which pass through small channels in the bone matrix called the canaliculi

Osteoclast

Osteoclasts are very large multinucleate cells that are responsible for the breakdown of bones by the process of bone resorption. New bone is then formed by the osteoblasts.

Bone is constantly remodelled by the resorption of osteoclasts and created by osteoblasts.

Osteoclasts are large cells with multiple nuclei located on bone surfaces in what are called Howship's lacunae (or resorption pits).

These lacunae are the result of surrounding bone tissue that has been reabsorbed. Because the osteoclasts are derived from a monocyte stem-cell lineage, they are equipped with phagocytic-like mechanisms similar to circulating macrophages.

Osteoclasts mature and/or migrate to discrete bone surfaces. Upon arrival, active enzymes, such as tartrate-resistant acid phosphatase, are secreted against the mineral substrate. The reabsorption of bone by osteoclasts also plays a role in calcium homeostasis

Composition : Extracellular matrix

Bones consist of living cells embedded in a mineralized organic matrix. This matrix consists of organic components, mainly type I collagen—"organic" referring to materials produced as a result of the human body—and inorganic components, primarily hydroxyapatite and other salts of calcium and phosphate.

Above 30% of the acellular part of bone consists of the organic components, and 70% of salts.The collagen fibers give bone its tensile strength, and the interspersed crystals of hydroxyapatite give bone its compressive strength. These effects are synergistic.

The inorganic composition of bone (bone mineral) is primarily formed from salts of calcium and phosphate, the major salt being hydroxyapatite ($Ca_{10}(PO_4)_6(OH)_2$) .

The exact composition of the matrix may be subject to change over time due to nutrition and biomineralization, with the ratio of calcium to phosphate varying between 1.3 and 2.0 (per weight), and trace minerals such as magnesium, sodium, potassium and carbonate also being found

Type I collagen composes 90–95% of the organic matrix, with remainder of the matrix being a homogenous liquid called ground substance consisting of proteoglycans such as hyaluronic acid and chondroitin sulfate, as well as non-collagenous proteins such as osteocalcin, osteopontin or bone sialoprotein.

Collagen consists of strands of repeating units, which give bone tensile strength, and are arranged in an overlapping fashion that prevents shear stress. The function of ground substance is not fully known.

Two types of bone can be identified microscopically according to the arrangement of collagen: woven and lamellar.

Woven bone (also known as fibrous bone), which is characterized by a haphazard organization of collagen fibers and is mechanically weak.

Lamellar bone, which has a regular parallel alignment of collagen into sheets ("lamellae") and is mechanically strong.

Woven bone is produced when osteoblasts produce osteoid rapidly, which occurs initially in all fetal bones, but is later replaced by more resilient lamellar bone. In adults woven bone is created after fractures or in Paget's disease.

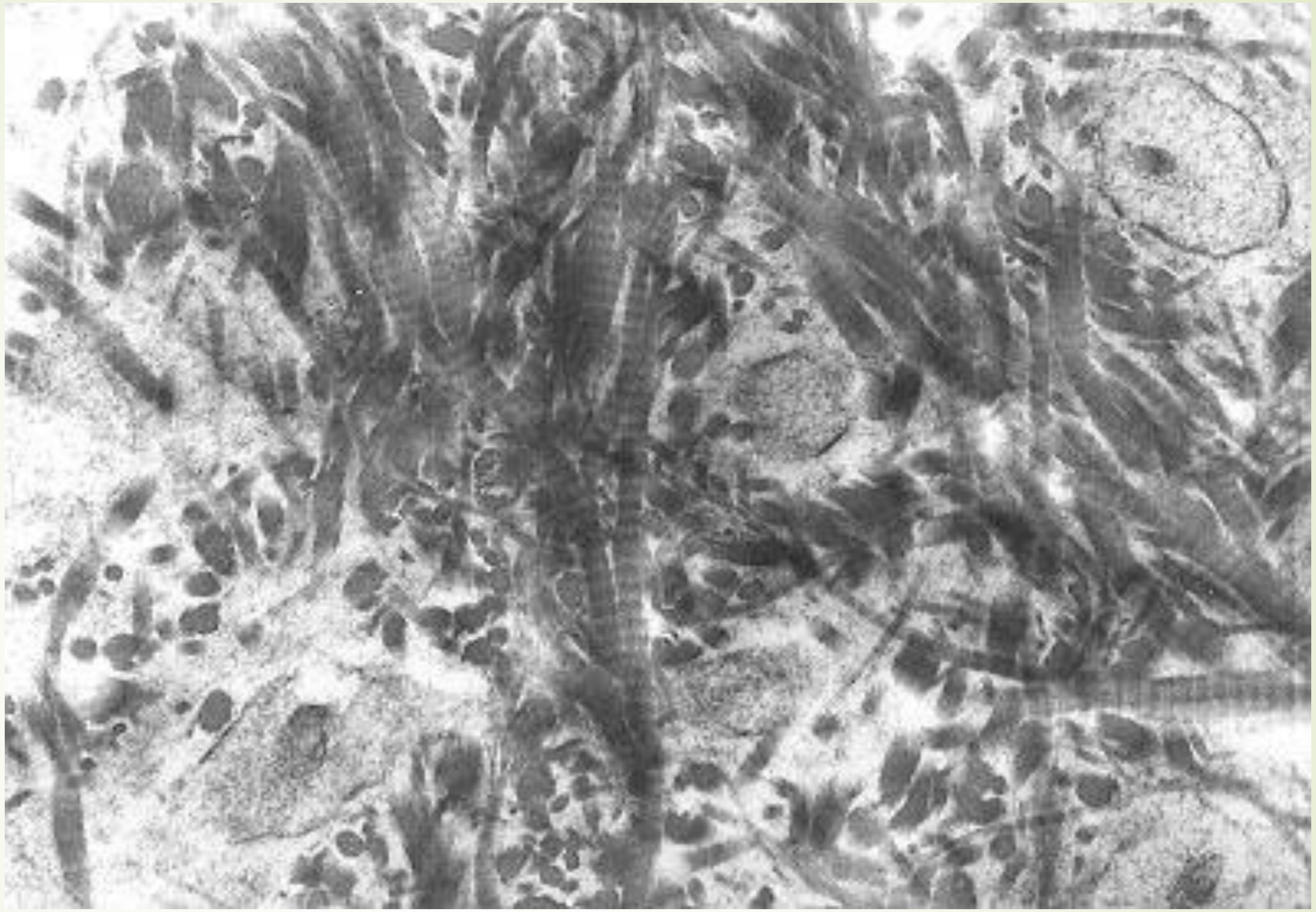
Woven bone is weaker, with a smaller number of randomly oriented collagen fibers, but forms quickly; it is for this appearance of the fibrous matrix that the bone is termed woven. It is soon replaced by lamellar bone, which is highly organized in concentric sheets with a much lower proportion of osteocytes to surrounding tissue.

Lamellar bone, which makes its first appearance in humans in the fetus during the third trimester, is stronger and filled with many collagen fibers parallel to other fibers in the same layer (these parallel columns are called osteons).

In cross-section, the fibers run in opposite directions in alternating layers, much like in plywood, assisting in the bone's ability to resist torsion forces.

After a fracture, woven bone forms initially and is gradually replaced by lamellar bone during a process known as "bony substitution." Compared to woven bone, lamellar bone formation takes place more slowly.

The orderly deposition of collagen fibers restricts the formation of osteoid to about 1 to 2 μm per day. Lamellar bone also requires a relatively flat surface to lay the collagen fibers in parallel or concentric layers.



Transmission electron micrograph of decalcified woven bone matrix displaying characteristic irregular orientation of collagen fibers

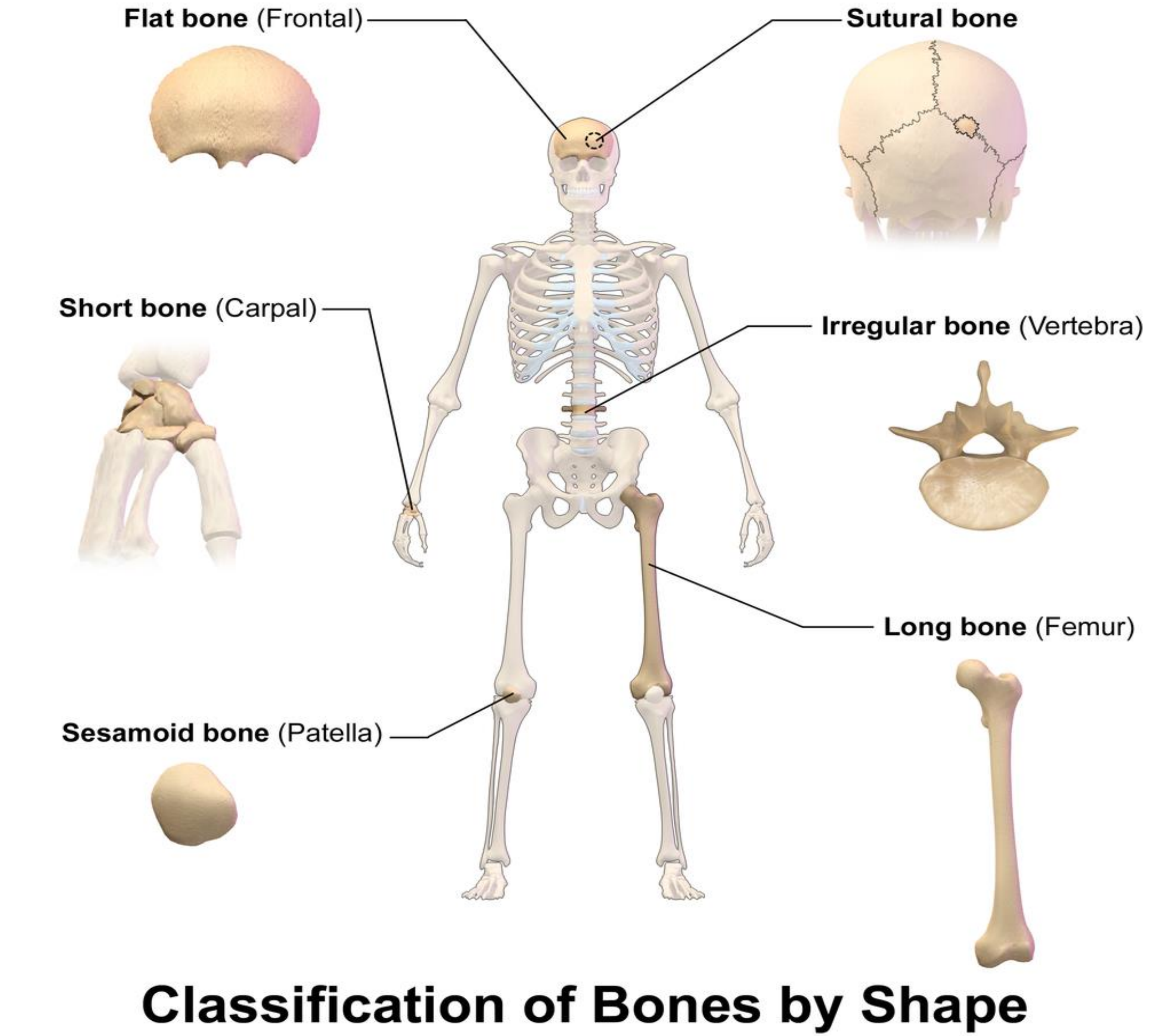
Deposition

The extracellular matrix of bone is laid down by osteoblasts, which secrete both collagen and ground substance. These synthesise collagen within the cell, and then secrete collagen fibrils.

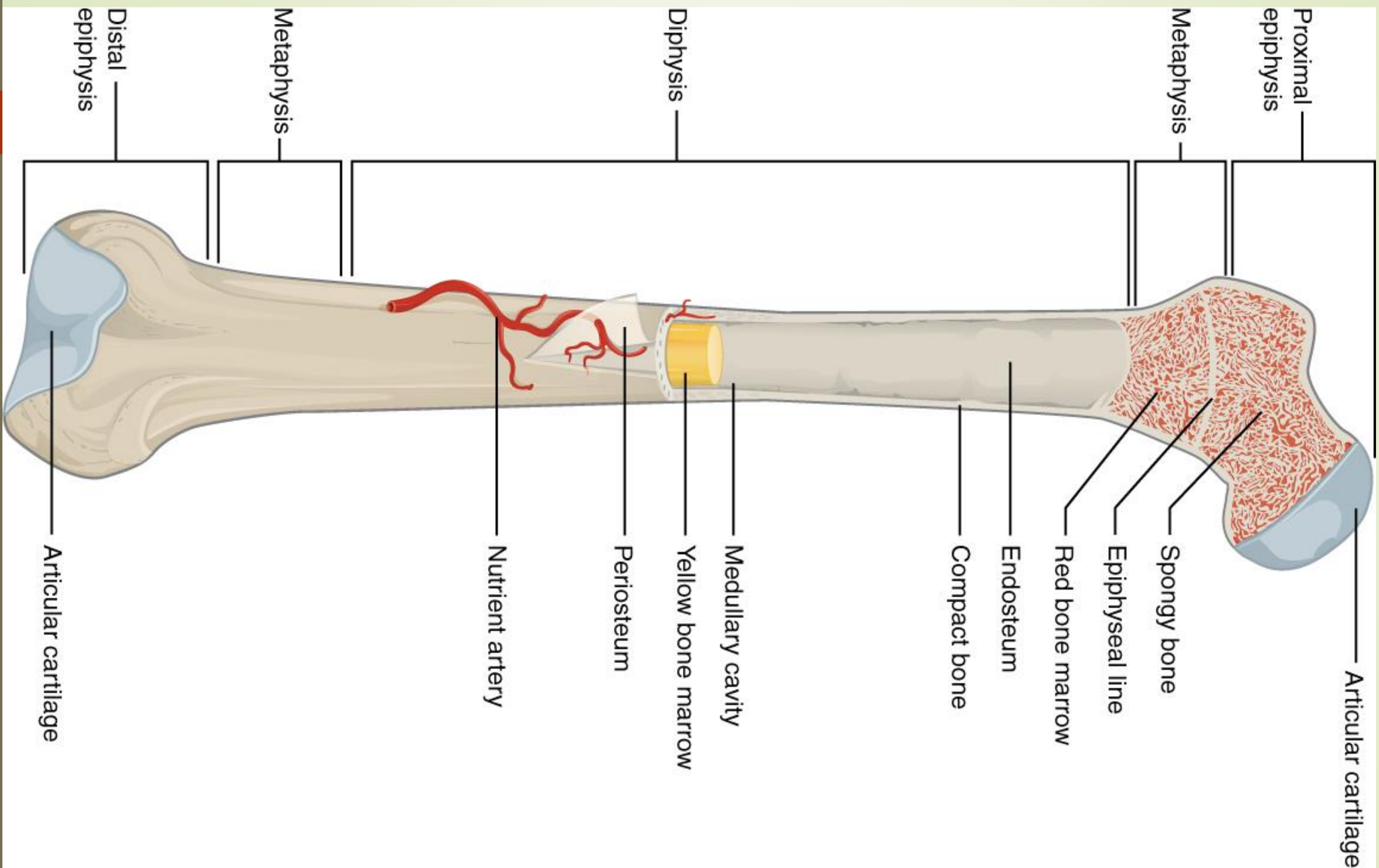
The collagen fibers rapidly polymerise to form collagen strands. At this stage they are not yet mineralised, and are called "osteoid". Around the strands calcium and phosphate precipitate on the surface of these strands, within days to weeks becoming crystals of hydroxyapatite.

In order to mineralise the bone, the osteoblasts secrete vesicles containing alkaline phosphatase. This cleaves the phosphate groups and acts as the foci for calcium and phosphate deposition. The vesicles then rupture and act as a centre for crystals to grow on. More particularly, bone mineral is formed from globular and plate structures

Types OF BONES



Structure of a long bone



There are five types of bones in the human body: long, short, flat, irregular, and sesamoid

Long bones are characterized by a shaft, the diaphysis, that is much longer than its width; and by an epiphysis, a rounded head at each end of the shaft.

They are made up mostly of compact bone, with lesser amounts of marrow, located within the medullary cavity, and areas of spongy, cancellous bone at the ends of the bones.

Most bones of the limbs, including those of the fingers and toes, are long bones. The exceptions are the eight carpal bones of the wrist, the seven articulating tarsal bones of the ankle and the sesamoid bone of the kneecap. Long bones such as the clavicle, that have a differently shaped shaft or ends are also called modified long bones.

Short bones are roughly cube-shaped, and have only a thin layer of compact bone surrounding a spongy interior. The bones of the wrist and ankle are short bones.

Flat bones are thin and generally curved, with two parallel layers of compact bones sandwiching a layer of spongy bone. Most of the bones of the skull are flat bones, as is the sternum.

Sesamoid bones are bones embedded in tendons. Since they act to hold the tendon further away from the joint, the angle of the tendon is increased and thus the leverage of the muscle is increased. Examples of sesamoid bones are the Patella.

Irregular bones do not fit into the above categories. They consist of thin layers of compact bone surrounding a spongy interior.

As implied by the name, their shapes are irregular and complicated. Often this irregular shape is due to their many centers of ossification or because they contain bony sinuses.

The bones of the spine, pelvis, and some bones of the skull are irregular bones. Examples include the ethmoid and sphenoid bones

STRUCTURE AND TYPES 0F CARTILAGE

Cartilage is a semi-rigid but flexible avascular connective tissue found at various sites within the body.

With a pliable structure composed primarily of water, this tissue type is also extremely tough.

Cartilage is found throughout the human body in areas such as the joints, nose, airway, intervertebral discs of the spine, and the ear

structure

Cartilage is a resilient and smooth elastic tissue, a rubber-like padding that covers and protects the ends of long bones at the joints and nerves, and is a structural component of the rib cage, the ear, the nose, the bronchial tubes, the intervertebral discs, and many other body components.

It is not as hard and rigid as bone, but it is much stiffer and much less flexible than muscle. The matrix of cartilage is made up of glycosaminoglycan, proteoglycans, collagen fibers and, sometimes, elastin.

Because of its rigidity, cartilage often serves the purpose of holding tubes open in the body. Examples include the rings of the trachea, such as the cricoid cartilage and carina.

Cartilage is composed of specialized cells called chondrocytes that produce a large amount of collagenous extracellular matrix, abundant ground substance that is rich in proteoglycan and elastin fibers.

Cartilage is classified in three types, elastic cartilage, hyaline cartilage and fibrocartilage, which differ in relative amounts of collagen and proteoglycan.

Cartilage does not contain blood vessels (it is avascular) or nerves (it is aneural). Nutrition is supplied to the chondrocytes by diffusion. The compression of the articular cartilage or flexion of the elastic cartilage generates fluid flow, which assists diffusion of nutrients to the chondrocytes.

Compared to other connective tissues, cartilage has a very slow turnover of its extracellular matrix and is documented to repair at only a very slow rate relative to other tissues

The Main Ingredients of Cartilage

Cartilage is made up of highly specialized cells called chondrocytes and chondroblasts (chondro refers to cartilage), and other extracellular material which forms the cartilage matrix.

All connective tissue types within the human body are derived from the embryonal mesoderm. Bone, the strongest of the connective tissues, is the last to form and can remain in cartilage form well after birth.

Increased cartilage to bone ratio enables a flexible and pliable new-born to exit the birth canal. A new-born has 300 bones, as opposed to the 206 of the normal adult, and all of these originate from cartilage.

From the seventh week of embryonic life, the process of ossification or osteogenesis slowly replaces cartilage with bone. This process continues into early childhood. Cartilage grows in two ways.

In interstitial growth, chondrocytes proliferate and divide, producing more matrix inside existing cartilage throughout childhood and adolescence. In appositional growth, fresh layers of matrix are added to existing matrix surface by chondroblasts in the perichondrium.

The perichondrium is a dense layer of connective tissue which surrounds most cartilage sites. Its outer layer contains collagen-producing fibroblasts, while the inner layer houses large numbers of differentiated fibroblasts called chondroblasts.

Chondroblasts

As long as they are free to move, chondroblasts produce the elements of the extracellular matrix (ECM). This cell type first forms a matrix of hyaluronic acid, chondroitin sulphate, collagen fibers, and water during embryonal development. Chondroblasts eventually become immobile after becoming surrounded by the matrix, and are then referred to as chondrocytes.

Chondrocytes

Chondrocytes are the immobile form of chondroblasts. They are surrounded by the matrix and contained within allotted spaces called lacunae. A single lacuna can contain one or more chondrocytes. Chondrocytes have varying roles according to the type of cartilage they are found in. In articular cartilage, found in the joints, chondrocytes increase joint articulation. At growth plates, chondrocytes regulate epiphyseal plate growth. While chondroblasts are ECM manufacturers, chondrocytes maintain the existing ECM and are a less active form of the same cell.

Fibroblasts

Fibroblasts are found in all types of connective tissue. In cartilage, these cells produce type I collagen. In certain situations, fibroblasts transform into chondrocytes.

Extracellular Matrix

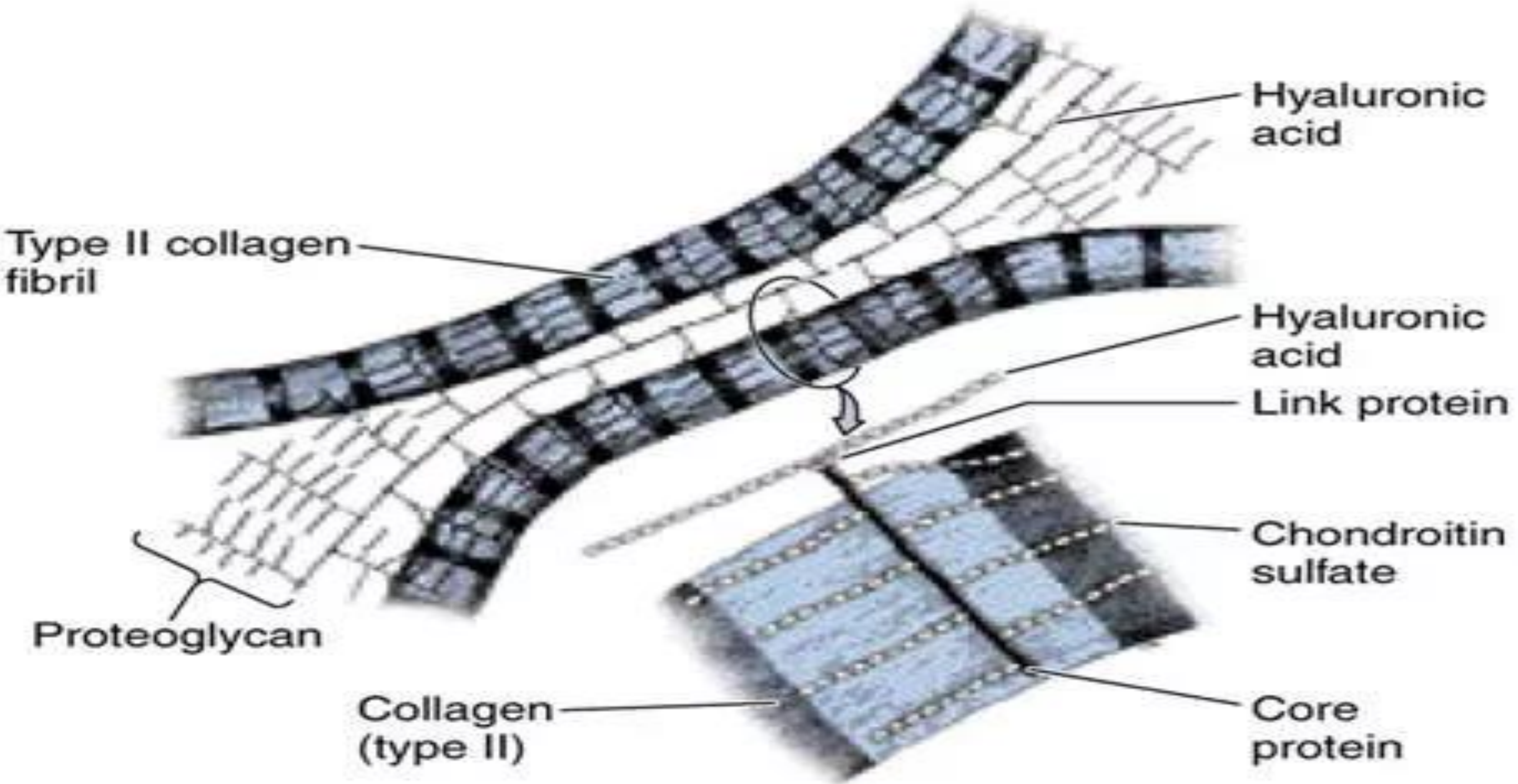
There is significantly more matrix than cells in cartilage structure, as the low oxygen environment and lack of vasculature do not allow for larger numbers. Because of this, there is little metabolic activity, and little to no new growth in cartilage tissue – one of the reasons the elderly commonly suffer from degenerative joint pain. Cartilage does continue to grow slowly, however. This can be seen in the larger ears and noses of older individuals.

Collagen

A protein-based collagen matrix gives form and strength to cartilage tissue through a mesh-like structure of fibrils. Although there are many different forms of collagen in the human body, the collagen found in cartilage is primarily type II, with an attached FACIT (short for fibril-associated collagen with interrupted triple helix) XIV collagen which determines the diameter of these fibers.

Proteoglycans

Proteoglycans are large molecules that bind with water, providing flexibility and cushioning qualities. Proteoglycan monomers bond to hyaluronic acid by way of link proteins, as is the case with the large proteoglycan Aggrecan (chondroitin sulphate proteoglycan 1), seen below.



Collagen and aggrecan in hyaline cartilage

The high numbers of negative charges such constructions provide, together with a large surface area, make it possible for proteoglycans to bind to large amounts of water. This creates high osmotic pressure, increases load-bearing, and constitutes the gel-like consistency of the ECM.

Noncollagenous Proteins

Noncollagenous elements of the ECM are small in number and supposed to play a role in maintenance and organization of the cartilage structure on a macromolecular level.

Types of Cartilage

There are three cartilage types in the human body. Although their components are very similar, the quantities of each component differ, providing different qualities to each type. Accordingly, each type has a particular location.

Hyaline Cartilage

The most common form of cartilage is hyaline cartilage. Hyalos is the Greek word for glass, which describes the appearance of this type of connective tissue – translucent, blueish-white, and shiny

Hyaline cartilage is usually only 2 – 4 mm thick (all cartilage must be thin, as there is no vascularization in this tissue type, and nutrients and oxygen must be obtained through diffusion). It is the embryonic form of cartilage, and also found in the ribs, joints, nose, larynx and trachea.

Hyaline cartilage collagen fibers are primarily type II, extremely thin, and invisible to the microscope due to similar refractory properties to that of the matrix itself.

Fibrocartilage

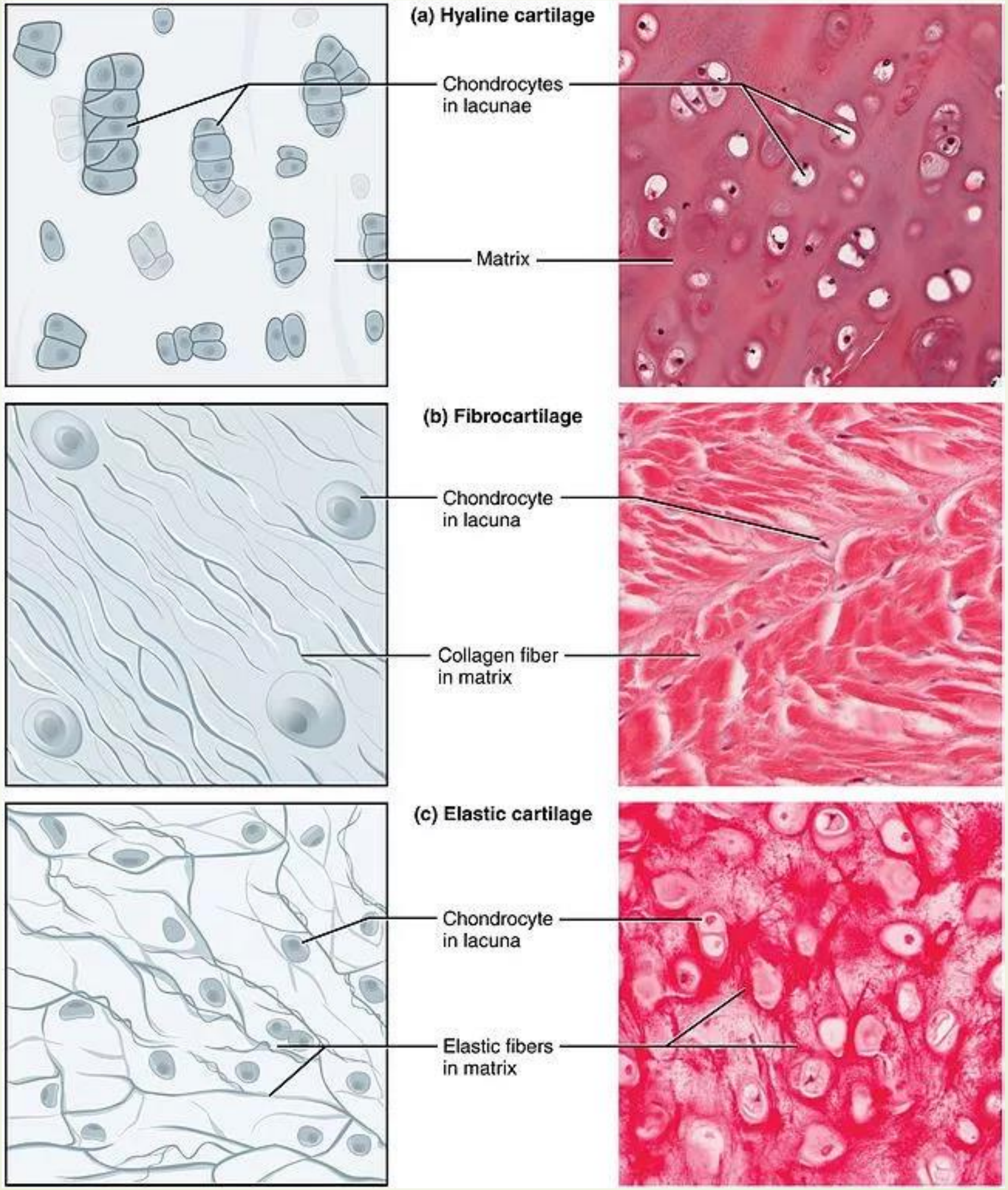
Found where tendons and ligaments meet bone, at the pubic symphysis, in the menisci, the sternoclavicular joint, and the annulus fibrosus (the center of the intervertebral disc), fibrocartilage is a very strong and pliable connective tissue.

It is reinforced with collagen fiber bundles that run parallel to each other, allowing a low level of stretch. Because of the abundance of collagen fibers, fibrocartilage is white in appearance. It lacks a perichondrium and is composed of type II and type I collagen fibers. The image below shows the smooth, white horseshoe shape of the fibrocartilaginous menisci.

Elastic Cartilage

Elastic cartilage is primarily found in the external ear (auricle or pinna), the Eustachian tube, and the epiglottis. These parts of the anatomy are required to always spring back into the original shape. Elastic cartilage's role is purely structural, offering flexibility and resilience due to a mixture of elastic fibers and type II collagen fibers. It is yellow in color, and without the organized structure of fibrocartilage when viewed on a microscope slide.

Types of Cartilage



OSSIFICATION

Ossification (or osteogenesis) in bone remodeling is the process of laying down new bone material by cells called osteoblasts.

It is synonymous with bone tissue formation. There are two processes resulting in the formation of normal, healthy bone tissue:

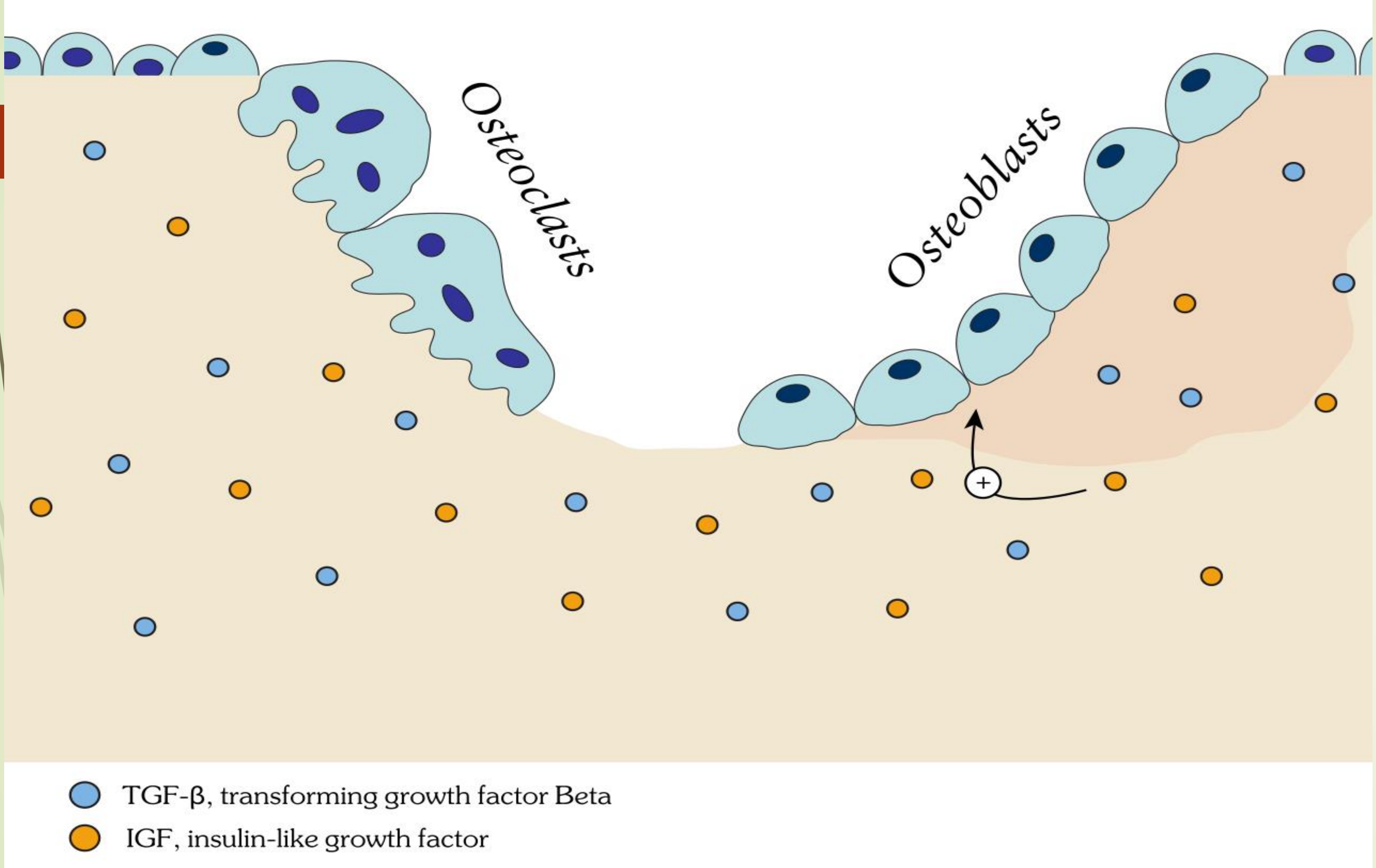
Intramembranous ossification is the direct laying down of bone into the primitive connective tissue (mesenchyme), while endochondral ossification involves cartilage as a precursor.

In fracture healing, endochondral osteogenesis is the most commonly occurring process, for example in fractures of long bones treated by plaster of Paris, whereas fractures treated by open reduction and internal fixation with metal plates, screws, pins, rods and nails may heal by intramembranous osteogenesis.

Heterotopic ossification is a process resulting in the formation of bone tissue that is often atypical, at an extraskeletal location.

Calcification is often confused with ossification. Calcification is synonymous with the formation of calcium-based salts and crystals within cells and tissue. It is a process that occurs during ossification, but not necessarily vice versa.

The exact mechanisms by which bone development is triggered remains unclear, but it involves growth factors and cytokines in some way



Bone is broken down by osteoclasts, and rebuilt by osteoblasts, both of which communicate through cytokine (TGF-β, IGF) signalling.

Intramembranous ossification

Intramembranous ossification forms the flat bones of the skull, mandible and hip bone

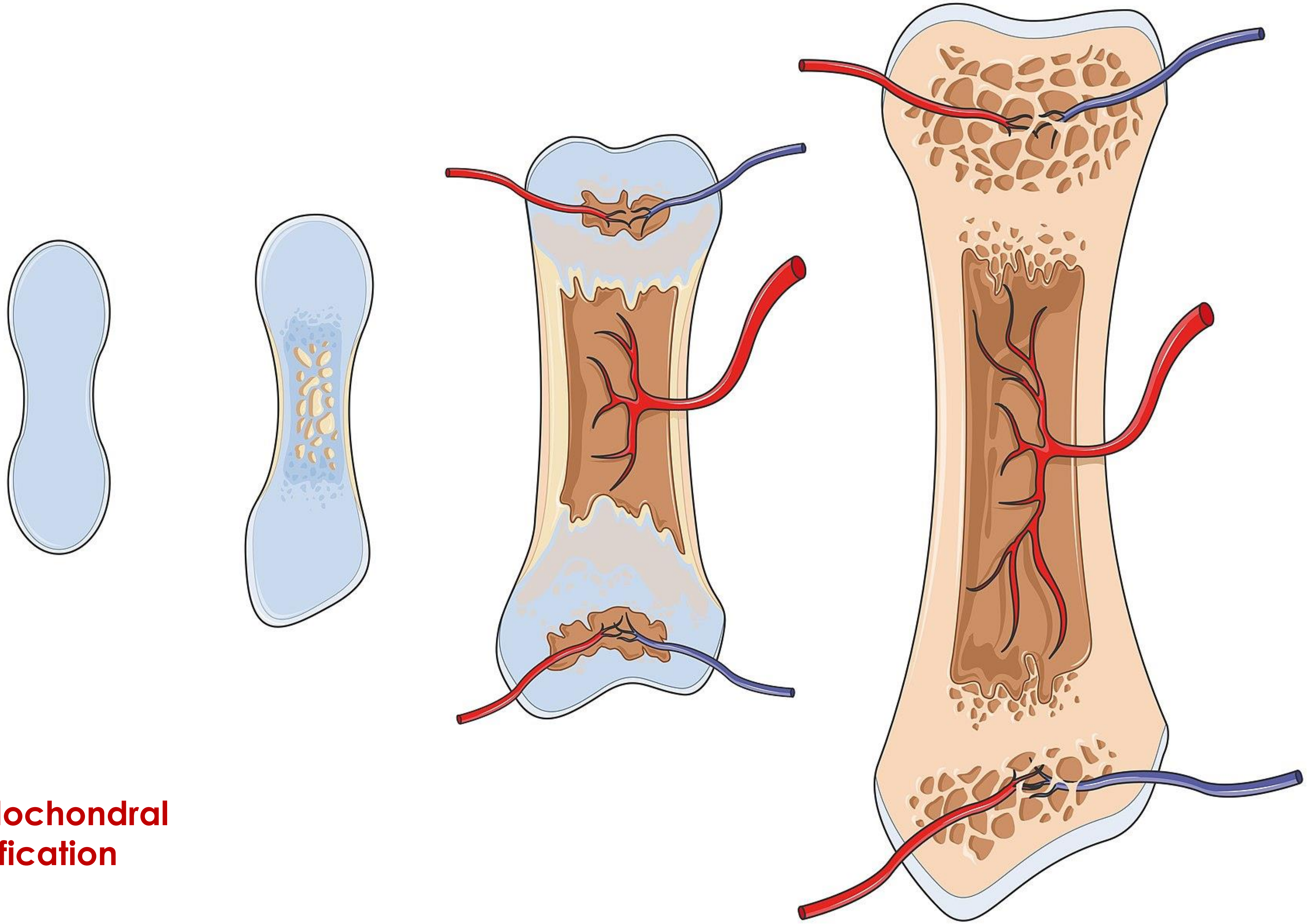
Endochondral ossification

Diagram showing stages of endochondral ossification
Endochondral ossification is the formation of long bones and other bones. This requires a hyaline cartilage precursor. There are two centers of ossification for endochondral ossification

The primary center

In long bones, bone tissue first appears in the diaphysis (middle of shaft). Chondrocytes multiply and form trebeculae. Cartilage is progressively eroded and replaced by hardened bone, extending towards the epiphysis.

A perichondrium layer surrounding the cartilage forms the periosteum, which generates sperm cells that then go on to make a collar that encircles the outside of the bone and remodels the medullary cavity on the inside.



endochondral ossification

The nutrient artery enters via the nutrient foramen from a small opening in the diaphysis.

It invades the primary center of ossification, bringing osteogenic cells (osteoblasts on the outside, osteoclasts on the inside.) The canal of the nutrient foramen is directed away from more active end of bone when one end grows more than the other.

When bone grows at same rate at both ends, the nutrient artery is perpendicular to the bone.

Most other bones (e.g. vertebrae) also have primary ossification centers, and bone is laid down in a similar manner.

Secondary centers

The secondary centers generally appear at the epiphysis. Secondary ossification mostly occurs after birth (except for distal femur and proximal tibia which occurs during 9th month of fetal development).

The epiphyseal arteries and osteogenic cells invade the epiphysis, depositing osteoblasts and osteoclasts which erode the cartilage and build bone. This occurs at both ends of long bones but only one end of digits and ribs.

Timetable for human ossification [edit]

Time period[2]	Bones affected[2]
Third month of fetal development	Ossification in long bones beginning
Fourth month	Most primary ossification centers have appeared in the diaphyses of bone.
Birth to 5 years	Secondary ossification centers appear in the epiphyses
5 years to 12 years in females, 5 to 14 years in males	Ossification is spreading rapidly from the ossification centers and various bones are becoming ossified.
17 to 20 years	Bone of upper limbs and scapulae becoming completely ossified
18 to 23 years	Bone of the lower limbs and os coxae become completely ossified
23 to 26 years	Bone of the sternum, clavicles, and vertebrae become completely ossified
By 25 years	Nearly all bones are completely ossified

BONE GROWTH

Introduction

Bone is living tissue that is the hardest among other connective tissues in the body, consists of 50% water. The solid part remainder consisting of various minerals, especially 76% of calcium salt and 33% of cellular material.

Bone has vascular tissue and cellular activity products, especially during growth which is very dependent on the blood supply as basic source and hormones that greatly regulate this growth process. Bone-forming cells, osteoblasts, osteoclast play an important role in determining bone growth, thickness of the cortical layer and structural arrangement of the lamellae.

Bone continues to change its internal structure to reach the functional needs and these changes occur through the activity of osteoclasts and osteoblasts.

The bone seen from its development can be divided into two processes: first is the intramembranous ossification in which bones form directly in the form of primitive mesenchymal connective tissue, such as the mandible, maxilla and skull bones.

Second is the endochondral ossification in which bone tissue replaces a preexisting hyaline cartilage, for example during skull base formation. The same formative cells form two types of bone formation and the final structure is not much different.

Bone growth depends on genetic and environmental factors, including hormonal effects, diet and mechanical factors.

The growth rate is not always the same in all parts, for example, faster in the proximal end than the distal humerus because the internal pattern of the spongiosum depends on the direction of bone pressure.

The direction of bone formation in the epiphysis plane is determined by the direction and distribution of the pressure line. Increased thickness or width of the bone is caused by deposition of new bone in the form of circumferential lamellae under the periosteum.

If bone growth continues, the lamella will be embedded behind the new bone surface and be replaced by the haversian canal system.

2. Bone cells and matrix

Bone is a tissue in which the extracellular matrix has been hardened to accommodate a supporting function. The fundamental components of bone, like all connective tissues, are cells and matrix.

Although bone cells compose a small amount of the bone volume, they are crucial to the function of bones. Four types of cells are found within bone tissue: osteoblasts, osteocytes, osteogenic cells, and osteoclasts.

They each unique functions and are derived from two different cell lines (Figure 1 and Table 1) [1, 2, 3, 4, 5, 6, 7].

Osteoblast synthesizes the bone matrix and are responsible for its mineralization. They are derived from osteoprogenitor cells, a mesenchymal stem cell line.

Osteocytes are inactive osteoblasts that have become trapped within the bone they have formed.

Osteoclasts break down bone matrix through phagocytosis. Predictably, they ruffled border, and the space between the osteoblast and the bone is known as Howship's lacuna.

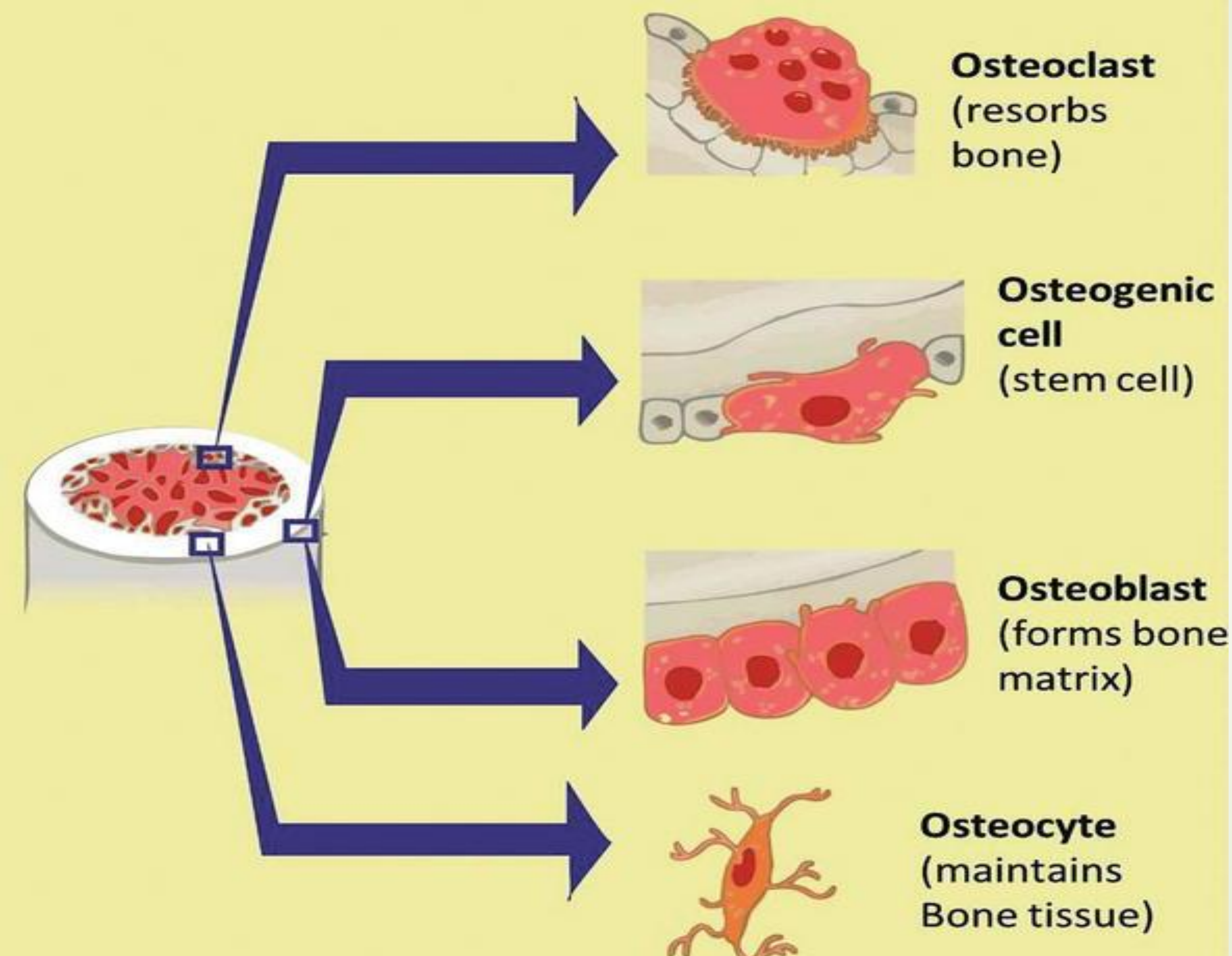


Figure 1. Development of bone precursor cells. Bone precursor cells are divided into developmental stages, which are

1. mesenchymal stem cell,
2. . pre-osteoblast
3. , . osteoblast, and
4. mature osteocytes, and
5. 5. osteoclast.

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

Table 1.
Bone cells, their function, and location

The balance between osteoblast and osteoclast activity governs bone turnover and ensures that bone is neither overproduced nor overdegraded. These cells build up and break down bone matrix, which is composed of:

Osteoid, which is the unmineralized matrix composed of type I collagen and gylcosaminoglycans (GAGs).

Calcium hydroxyapatite, a calcium salt crystal that give bone its strength and rigidity.

Bone is divided into two types that are different structurally and functionally. Most bones of the body consist of both types of bone tissue

Compact bone, or cortical bone, mainly serves a mechanical function. This is the area of bone to which ligaments and tendons attach. It is thick and dense.

Trabecular bone, also known as cancellous bone or spongy bone, mainly serves a metabolic function. This type of bone is located between layers of compact bone and is thin porous. Location within the trabeculae is the bone marrow.

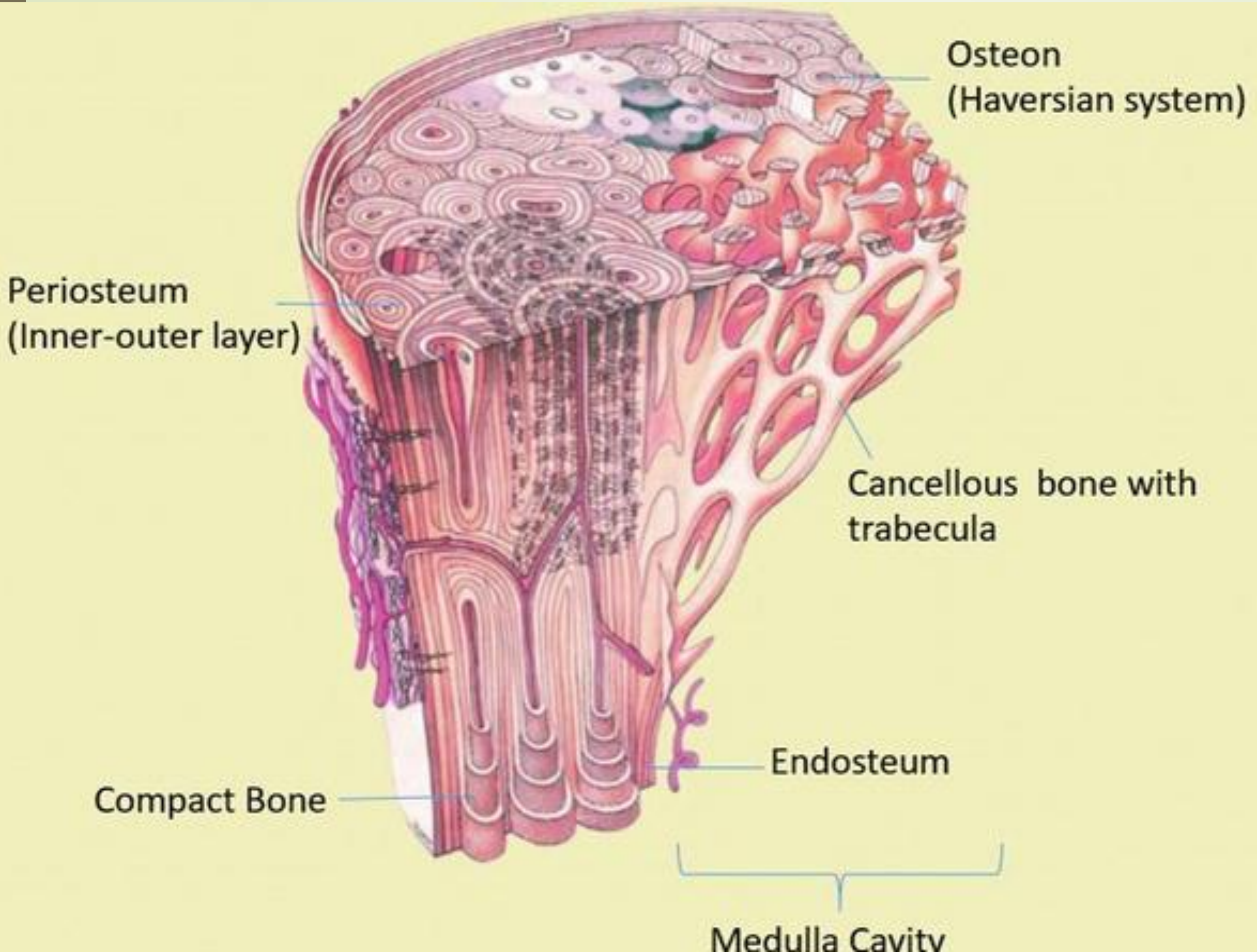


Figure 2. Structure of a long bone.

BONE RESORPTION

Bone resorption is the process by which osteoclasts break down the bone tissue. This process is critical in the maintenance of blood calcium levels.

Abnormal increases in the activity of osteoclasts that produce an increase in bone resorption cause osteoporosis and other bone loss-associated diseases.

Bone resorption is resorption of bone tissue, that is, the process by which osteoclasts break down the tissue in bones and release the minerals, resulting in a transfer of calcium from bone tissue to the blood.

The osteoclasts are multi-nucleated cells that contain numerous mitochondria and lysosomes.

These are the cells responsible for the resorption of bone. Osteoclasts are generally present on the outer layer of bone, just beneath the periosteum.

Attachment of the osteoclast to the osteon begins the process.

The osteoclast then induces an infolding of its cell membrane and secretes collagenase and other enzymes important in the resorption process.

High levels of calcium, magnesium, phosphate and products of collagen will be released into the extracellular fluid as the osteoclasts tunnel into the mineralized bone.

Osteoclasts are prominent in the tissue destruction found in psoriatic arthritis and rheumatological disorders.

The human body is in a constant state of bone remodeling. Bone remodelling is a process which maintains bone strength and ion homeostasis by replacing discrete parts of old bone with newly synthesized packets of proteinaceous matrix.

Bone is resorbed by osteoclasts, and is deposited by osteoblasts in a process called ossification.

Osteocyte activity plays a key role in this process. Conditions that result in a decrease in bone mass can either be caused by an increase in resorption or by a decrease in ossification.

During childhood, bone formation exceeds resorption. As the aging process occurs, resorption exceeds formation

Bone resorption rates are much higher in post-menopausal older women due to estrogen deficiency related with menopause.

Common treatments include drugs that increase bone mineral density. Bisphosphonates, RANKL inhibitors, SERMs—selective oestrogen receptor modulators, hormone replacement therapy and calcitonin are some of the common treatments.

Light weight bearing exercise tends to eliminate the negative effects of bone resorption.

Regulation

Bone resorption is highly stimulated or inhibited by signals from other parts of the body, depending on the demand for calcium.

Calcium-sensing membrane receptors in the parathyroid gland monitor calcium levels in the extracellular fluid. Low levels of calcium stimulates the release of parathyroid hormone (PTH) from chief cells of the parathyroid gland.

In addition to its effects on kidney and intestine, PTH increases the number and activity of osteoclasts. The increase in activity of already existing osteoclasts is the initial effect of PTH, and begins in minutes and increases over a few hours.

Continued elevation of PTH levels increases the abundance of osteoclasts. This leads to a greater resorption of calcium and phosphate ions

High levels of calcium in the blood, on the other hand, leads to decreased PTH release from the parathyroid gland, decreasing the number and activity of osteoclasts, resulting in less bone resorption. Vitamin D increases absorption of calcium and phosphate in the intestinal tract, leading to elevated levels of plasma calcium, and thus lower bone resorption.

Calcitriol (1,25-dihydroxycholecalciferol) is the active form of vitamin D3. It has numerous functions involved in blood calcium levels. Recent research indicates that calcitriol leads to a reduction in osteoclast formation, and bone resorption.

It follows that an increase in vitamin D3 intake should lead to a decrease in bone resorption — it has been shown that oral administration of vitamin D does not linearly correlate to increased serum levels of calcifediol, the precursor to calcitriol.

Calcitonin is a hormone secreted by the thyroid in humans. Calcitonin decreases osteoclast activity, and decreases the formation of new osteoclasts, resulting in decreased resorption. Calcitonin has a greater effect in young children than in adults, and plays a smaller role in bone remodeling than PTH.

In some cases where bone resorption outpaces ossification, the bone is broken down much faster than it can be renewed.

The bone becomes more porous and fragile, exposing people to the risk of fractures. Depending on where in the body bone resorption occurs, additional problems like tooth loss can arise.

This can be caused by conditions such as hyperparathyroidism and hypovitaminosis D or even decreased hormonal production in the elderly. Some diseases with symptoms of decreased bone density are osteoporosis, and rickets.

Some people who experience increased bone resorption and decreased bone formation are astronauts. Due to the condition of being in a zero-gravity environment, astronauts do not need to work their musculoskeletal system as hard as when on earth.

Ossification decreases due to a lack of stress, while resorption increases, leading to a net decrease in bone density

Thank you