# Bones: Fundamentals of Anatomy for Physicians

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**The skeletal system has important functions as protection and support during movements, for the mineral balance, blood production, and the storage of triglycerides. Bones (Latin: *os*, greek: *ost*-, *oste*- or *osteo*-) provide stability and shape. How many bones do humans have? This is easily answered numerically: 206.**

## Structure and Function of Bone

It is possible to assess and describe the macroscopic bone structure of single bone segments through a close examination of the long bones (e.g., humerus or femur). Hollow bone or long bone is longer than it is wide and is composed of the following elements:

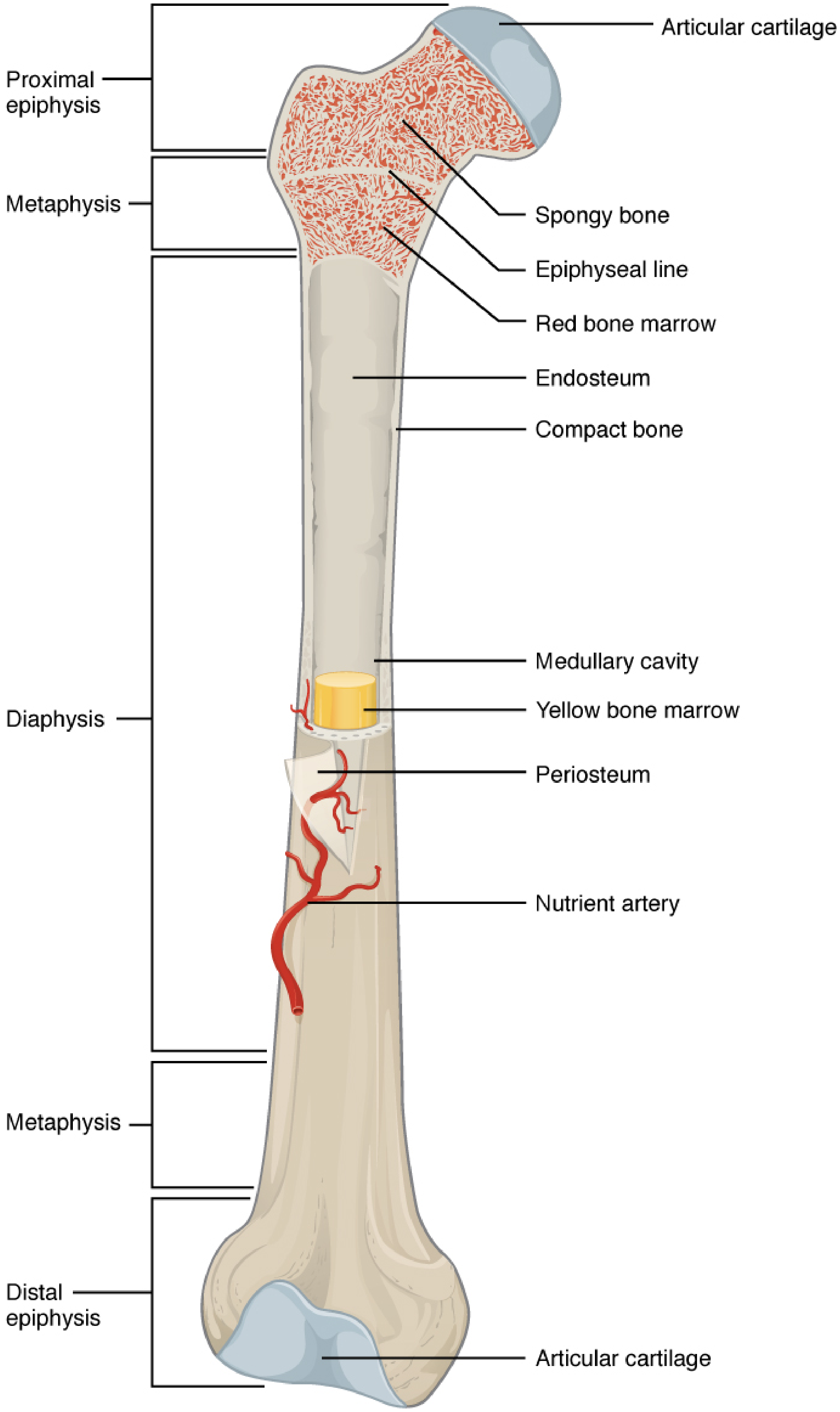


Image: A typical long bone shows the gross anatomic characteristics of bone. By Phil Schatz. License: CC BY 4.0.

# Bone formation

Collagen deposition ⇒ Ground substance ⇒ Crystal seeding ⇒ Maturation

Each bone contains a small organic part and a larger inorganic part. A bone consist of the following parts:

| Component (% by weight) | Composition |
|---|---|
| Organic (30%) | Cells (2%)<br>Collagen + Type 1 (93%)<br>Ground substance (5%) |
| Inorganic (70%) | Ca2+ and PO43- |

Cells, blood vessels, nerves, ground substance, and a dense network of collagen form the organic substance. Calcium phosphate is the main component of the inorganic substances. Calcium carbonate and magnesium salts are found in large amounts, while there are numerous other minerals and trace elements found in smaller amounts.

Considering the minerals calcium, phosphate, and magnesium, bones represent by far the largest storage organ of the human body. Approximately 1.2 kg (2.65 lb) or 98% of the entire body's calcium is stored in our bones.

# Diaphysis

The **diaphysis** is the major part of the bone, and is long and cylindrical in nature. It consists of a bony sheath made up of layers of bone *lamellae* and **compact bone**, also known as cortical bone, which is dense and rigid. These parts come together to enclose a large hollow space known as the medullary cavity. This is the innermost cavity of the bone shafts, storing two types of bone marrow: red and yellow. The red bone marrow is vascular in nature and the yellow marrow is composed of adipose tissue.

# Epiphysis

The **epiphyses** are the proximal and distal ends of a bone. They are covered with cartilage. The epiphysis of a long bone should **NOT** be confused with the **endocrine gland epiphysis** (pineal gland) of the brain.

The transition area between the ends of the diaphysis and each epiphysis is also called growth plate, epiphyseal plate, and metaphysis.

The epiphyses also have an outer sheath of compact bone better known as **spongy bone**, which consists of delicate *trabeculae* and *lamellae*, making it appear spongy. The bone trabeculae are not arranged randomly, but follow lines of pressure to provide the bone with maximum stability. The resulting hollow spaces of the spongy bone make room for the hematopoietic bone marrow.

The special conformation of the spongy bone, consisting of numerous hollow spaces such as the large medullary cavities, contributes considerably to reducing its weight. The strength and resilience of bone remain despite this 'lightweight' construction.

# Metaphysis

The **metaphysis** consists of one layer of hyaline cartilage, which is responsible for the longitudinal growth of the diaphysis. At the age of approximately 18–21 years, bones stop growing. During this time, the cartilage of the epiphyseal plate is replaced with bone and the resulting line is called an epiphyseal line.

## Articular cartilage

The **articular cartilage** (*cartilago articularis*) consists of a thin layer of hyaline cartilage, which covers the end of each epiphysis, thus forming a joint. The main function of the articular cartilage is to absorb impact forces on the joints as well as to reduce friction between bones.

## Periosteum

The **periosteum** covers the bone in places where it is not protected by articular cartilage. It consists of thin, irregular connective tissue. The periosteum consists of dense irregular connective tissue divided into an outer ‘fibrous layer’ and an inner ‘cambium layer’ (or ‘osteogenic layer’). The fibrous layer contains fibroblasts, while the cambium layer contains progenitor cells that develop into osteoblasts. The periosteum is responsible for growth in diameter, because bone-forming cells ordinarily can only make a bone thicker but not longer. Therefore, the periosteum serves to protect the bone, to maintain support during fracture repair, to supply nutrition to the bone, and to provide insertion for tendons and ligaments.

## Medullary cavity

Inside the hollow space of the diaphysis is the **medullary cavity**, which contains the hematopoietic bone marrow. Starting from early adulthood, the bone marrow slowly converts into fatty tissue due to excess capacity and the red bone marrow becomes yellow fatty tissue. The yellow fatty marrow has similar properties as red marrow because it provides nutrients and protection. However, under special circumstances (e.g., large blood loss or leukemia), it can be converted back to red bone marrow. It is important to mention that the **red bone marrow** does not take on any functions of the immune system but serves only as the site of **blood formation**.

## Endosteum

The **endosteum** (endo = within) surrounds the medullary cavity and consists of a thin membrane. It contains a small amount of connective tissue and consists of a simple layer of bone-forming cells.

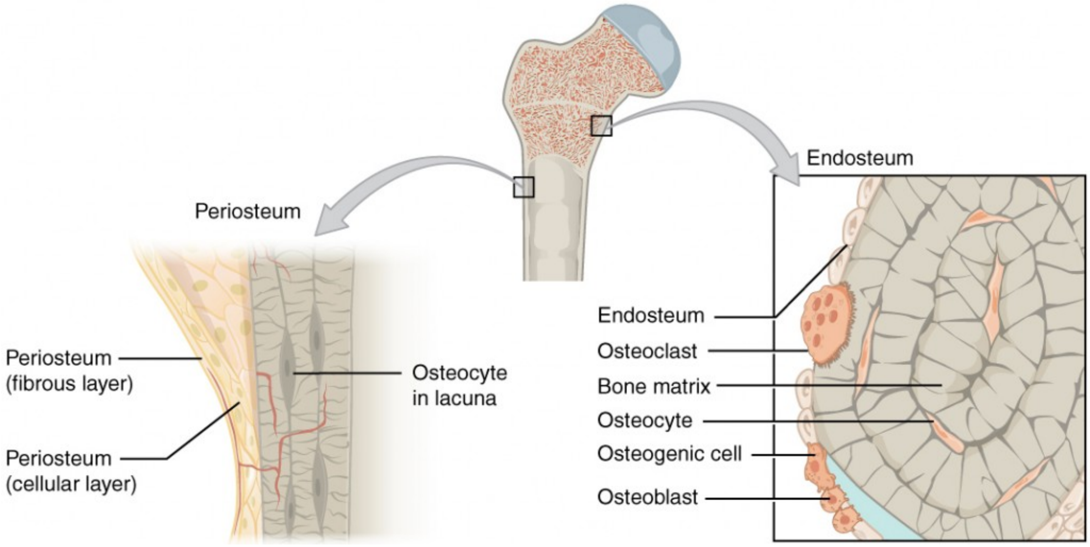


Image: The periosteum forms the outer surface of the bone, and the endosteum lines the medullary cavity. By Phil Schatz. License: CC BY 4.0.

## The Histology of Bony Tissue

Bony tissue is a type of connective tissue in the body. The formation and maintenance of normal connective tissue only need one single type of cell, the fibrocyte or, rather, fibroblast.

The bone requires one more cell type for the degradation of the organic matrix and the dissolving of inorganic calcium phosphate crystals (apatite). This happens in the course of a continuous conversion process.

The following types of bone cells can be differentiated:

- Osteoblasts
- Osteocytes
- Osteoclasts

**Remember:** 'Osteo**b**lasts **b**uild **b**ones.'

Osteoblasts are cells that build bones and are needed especially for the formation of the extracellular matrix. Osteoblasts are found mainly within the outer and inner surface of the bone, integrated in the cambium layer of the periosteum. They synthesize and secrete collagen fibers and other organic components. They are also important to initiate calcification. A high concentration of participating ions is necessary to produce calcium phosphate for the process of calcification. This is achieved by the protein osteocalcin and by membrane-surrounded vesicles outside the osteoblasts, which contain enzymes that can split off phosphate. These matrix vesicles are extracellular round spherical bodies of about 100 nm in size that act as initial sites for hydroxyapatite crystal deposition. Crystals are formed with the help of calcium ions that have already been gathered inside the osteoid (organic ground substance). Further apatite crystals are accumulated until the whole osteoid is calcified.

With time, enough extracellular matrix accumulates around the osteoblasts until they are embedded in it and develop into osteocytes.

**Remember: 'Osteocytes maintain the tissue.'**

Osteocytes are the main cells of bony tissue. They carry out their daily metabolism by exchanging nutrients with the blood. Just like osteoblasts, the mature bone cells are not able to divide.

**Remember:** ‘Osteo**c**lasts **c**hew bones.’

Their task is to degrade the extracellular matrix. This is a process that goes hand in hand with the coordination of osteoblasts because they also secrete a series of messenger substances. This is part of the normal development, maintenance, and repair process of bones.

Osteoclasts are specialized macrophages or giant cells. They are concentrated inside the endosteum and consist of up to 50 monocytes. **The second essential function of osteoclasts is the maintenance of the serum calcium level.** When degrading bones, the bound calcium and phosphate are released and their serum levels increase.

## What Are Osteons?

Bones have numerous small gaps between their cells and the components of the extracellular matrix (among others, collagen fibers, water, electrolytes, and glycosaminoglycans). As we have learned, bone consists of periosteum, compact bone, spongy bone, endosteum, and bone marrow.

The smallest units of bones are found inside the compact bone. Through the concentrated arrangement of bone *lamellae*, several thin long cylinders are formed. These are called **osteons or Havers’ system**.

The concentrated *lamellae* proceed around a recess along the longitudinal axis of the bone, which is called the Haversian canal or **central canal (*canales centrales*)**. Inside this centrally located Haversian canal, blood vessels and single nerves proceed through the bone surrounded by a bony sheath. These bony sheaths contain osteocytes that are necessary for maintaining the structure. Perpendicular to the Haversian canals is the Volkmann’s canals (*canales perforantes*). They contain arteries, veins, and nerves from the periosteum, which proceed to the center of the osteons.

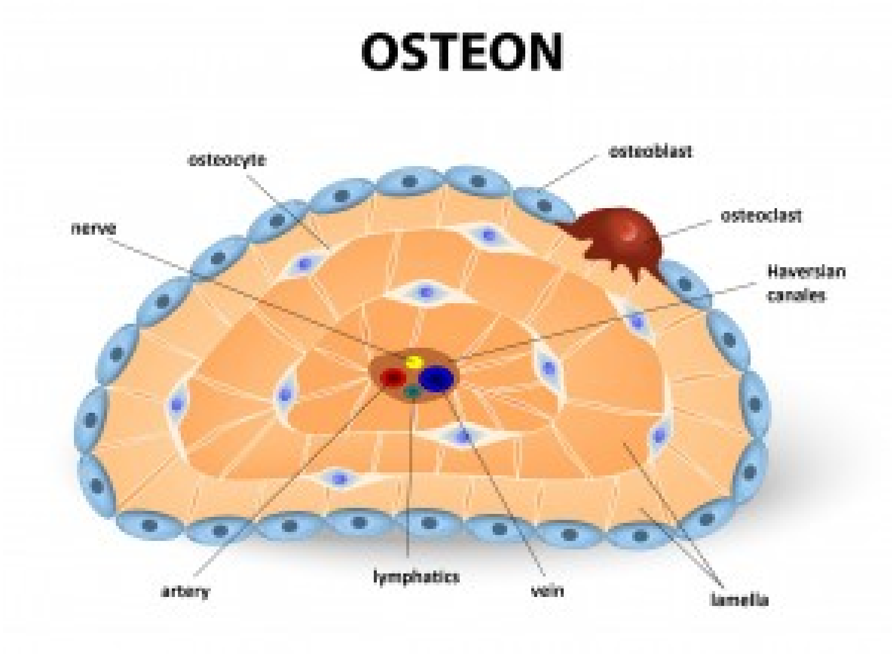


Image: Labeled diagram of an osteon. By Lecturio.

## Stability of the Compact Bone

Lacunas (*lacunae* = small lake) are small gaps between the *lamellae* that contain osteocytes. From the lacunas, which are filled with extracellular fluid, small canals (*canaliculi*) radiate in all directions. Finger-shaped extensions of osteocytes are located inside the *canaliculi*, which connect the lacunas and the central canals. Neighboring osteocytes communicate via so-called gap junctions. These are complicated networks of tiny, interconnected canals, found across the whole bone. This network forms a network for the supply of nutrients and oxygen as well as the removal of metabolic products.

The stability of a compact bone is achieved through continuously repeating units, the osteons, which consist of a central canal with arranged *lamellae*, lacunas, osteocytes, and *canaliculi*. Osteons of a long bone can be compared to a tree trunk. An immense amount of strength is required to break through a tree trunk, attributed to their well-formed circular structure made of hard material. The same is found in the system of bones and osteons. To meet the requirements of continuous stress such as running or weight lifting, the load line of bones change and the bone reconfigures itself to match the stress lines.

## Bone Formation

The process of **bone formation** is called **ossification** (*os* = bone, and *fiacre* = to make) or osteogenesis. It is differentiated between the following two processes:

- **Chondral** (endochondral) ossification
- **Desmal** (membranous) ossification

They represent two different methods of bone development or ossification.

### Chondral ossification—from cartilage to bone

In the case of chondral ossification, the formation of bones mainly starts after birth from preformed hyaline cartilage, which has been developed out of mesenchyme (embryonic connective tissue).

During growth and ossification of the cartilage of short and flat bones, which can be found among others at the wrist and tarsal bones as well as in the manubrium of the sternum, **ossification** occurs in two ways:

- **Perichondrally**
- **Enchondrally**

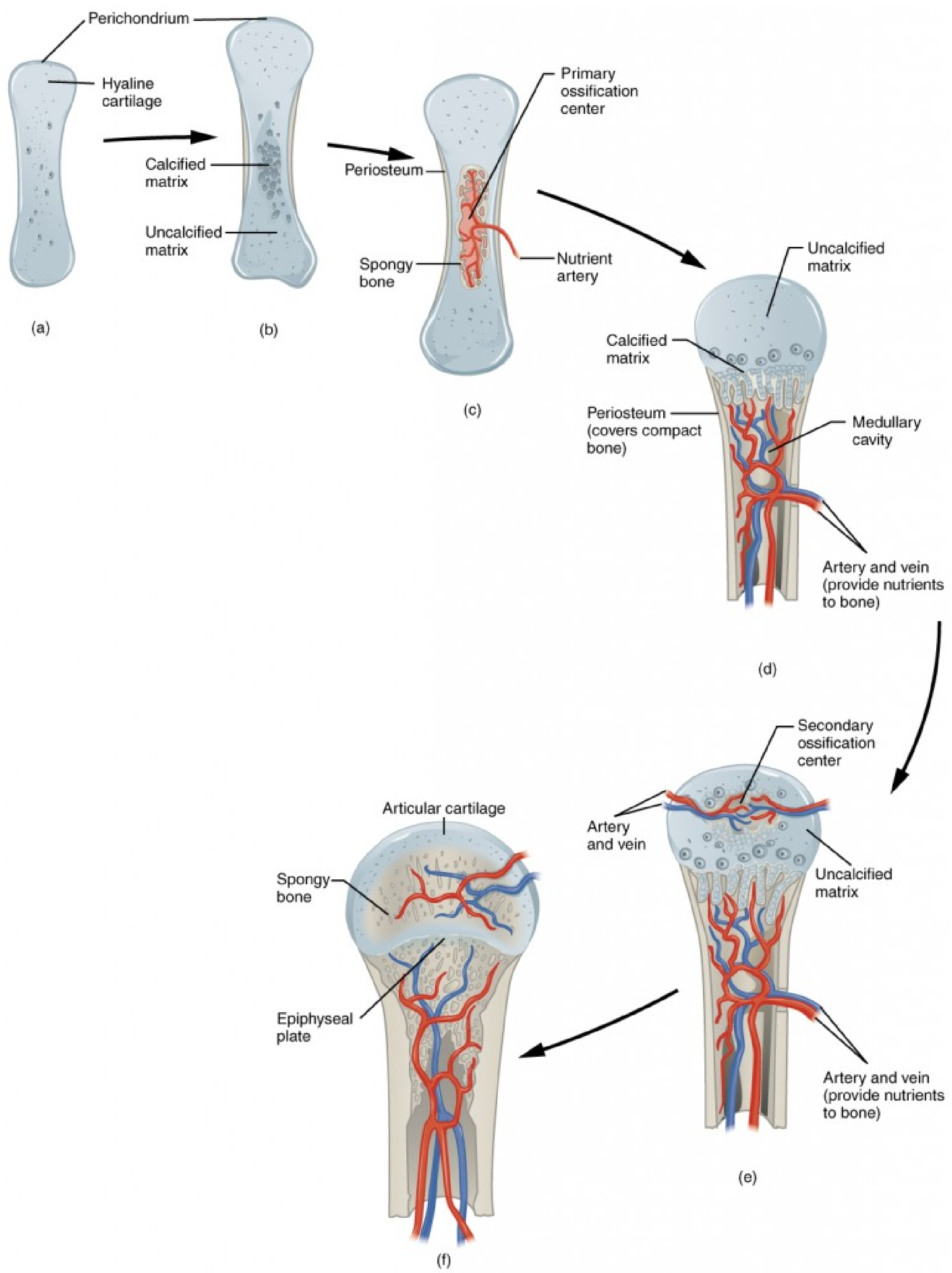


Image: Endochondral ossification follows five steps. By Phil Schatz. License: .

# 1. Perichondral ossification

In the case of **perichondral ossification**, the ossification starts from the outside, which means on the surface, with the formation of osteoblasts from perichondral connective tissue in the area of the diaphysis. Due to the extension toward the epiphyses, a bony shell is formed that encloses the cartilage matrix like a cuff or splint.

The cartilage is separated from its surroundings, which leads to the initiation of the conversion process of cartilage to bone (endochondral ossification). Finally, the perichondrium becomes the periosteum.

# 2. Endochondral ossification

In the case of **endochondral ossification**, the ossification process starts from the middle of the cartilage matrix inside the bone.

Blood vessels reach into the cartilage and are accompanied by mesenchymal cells. To gradually convert the cartilage tissue into bone, mesenchymal cells are changed into chondroclasts and chondroblasts.

**This type of ossification occurs in growing bones in the area of the epiphyseal plate and can be observed best in long bones**.

The longitudinal growth of a long bone starts in defined growth areas such as the epiphyseal plates (growth plates, physes), part of the metaphysis (located between the diaphysis and the two epiphyses). Hyaline cartilage is produced inside the epiphyseal plate and after its ‘completion,’ it is gradually shifted toward the diaphysis, which therefore gets longer. The primary centrum of ossification of a long bone is located in the diaphysis.

The newly built cartilage is initially arranged in columns to produce larger, bubble-shaped cells in the direction of the diaphysis. The ‘oldest’ structures, the ones in the middle of the diaphysis, start the process of ossification. This process has only been performed by cartilage but now deposition of calcium salts begins. Toward the end of puberty, the metaphysis changes into spongy bone, the growth plate ossifies, and the inner structure of the diaphysis is reabsorbed, forming a medullary cavity. The cartilage degenerates and leaves hollow spaces behind that are expanded to the medullary cavities (see below).

While the bone matrix grows, the cartilage matrix is continuously degraded by chondroclasts and replaced with the help of osteoblasts.

The epiphyseal plate is an exception.

Until the end of puberty, calcium-free cartilage is only found in the epiphyseal plate, because the epiphyses themselves increasingly ossify. Due to the high serum growth hormone level during the growth spurt at the end of puberty, ossification is closed and no more physical growth is possible.

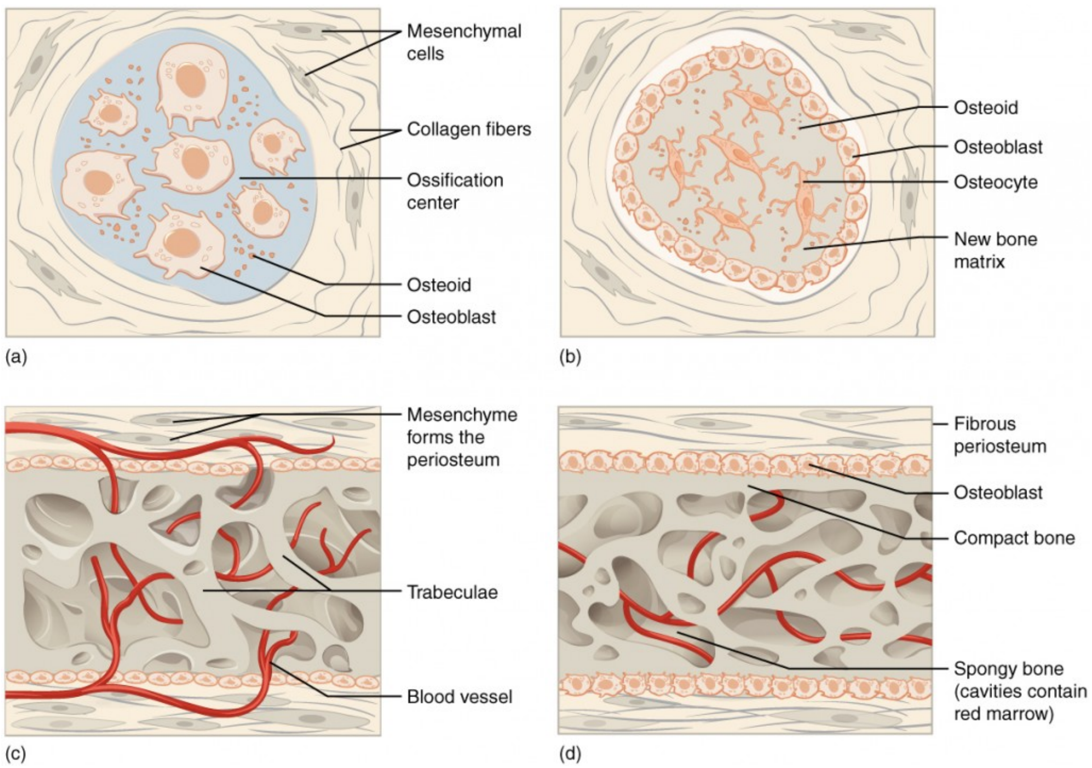


Image: Intramembranous ossification follows four steps. By Phil Schatz. License: CC BY 4.0.

## Desmal ossification—bone formation from mesenchyme

**Desmal ossification** is the easiest type of ossification.

In the case of this direct type of ossification, bones are not converted from preformed cartilage but built directly from embryonic connective tissue, the mesenchyme. During this process, the mesenchyme differentiates into osteoprogenitor cells, which mature into osteoblasts and form a preliminary stage of a bone, the osteoid. Bone bridges are formed through the calcification of the osteoid, which finally results in the skeleton.

For instance, the cranial bones and the sternum are created this way.

Desmal ossification differs from chondral ossification. For example, osteoblasts are created from progenitor cells of connective tissue (osteoprogenitor cells) instead of being created from chondroblasts. Apart from that, the mechanism of bone formation is mostly the same as the mechanism of chondral ossification.

## Bone Remodeling

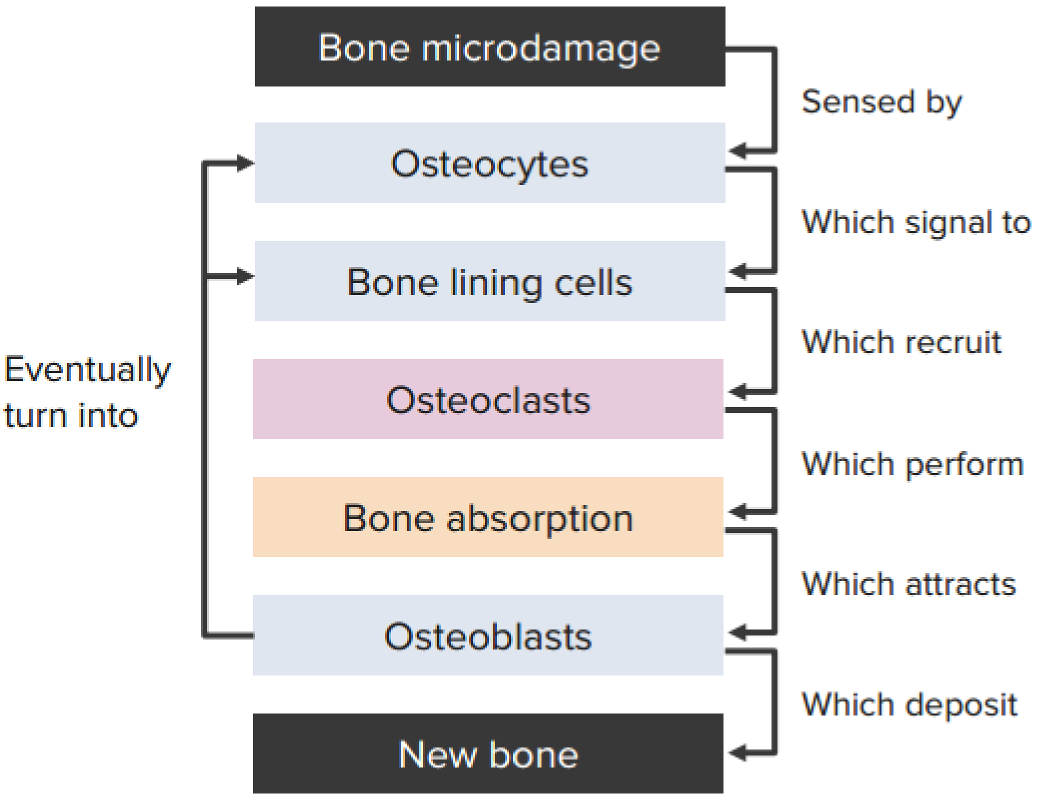


Image by Lecturio.

## Bone remodeling cycle

| Signaling microdamage | Activation | Osteoclast precursor recruitment |
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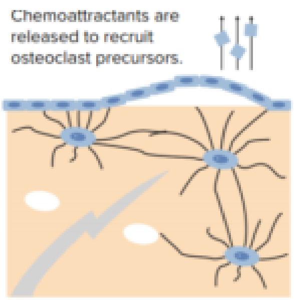
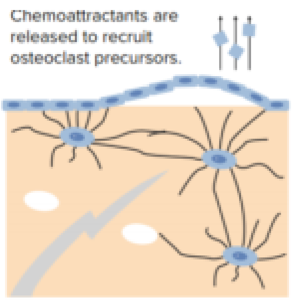
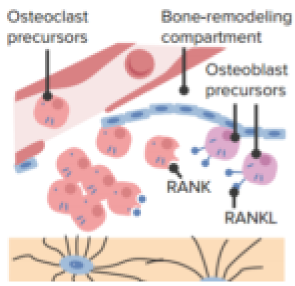
|   |   |   |
| Osteocytes at the site of microdamage undergo apoptosis. | Bone-lining cells digest underlying osteoid to expose mineral and then lift off the surface. | Osteoclast precursors bind receptor activator of nuclear factor kappa B ligand (RANKL) and coalesce to form an osteoclast. |
| **Absorption** | **Deposition** | **New bone** |

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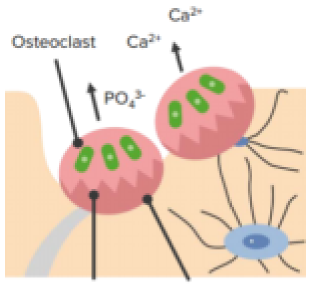
<td>
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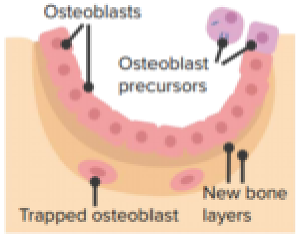
<td>
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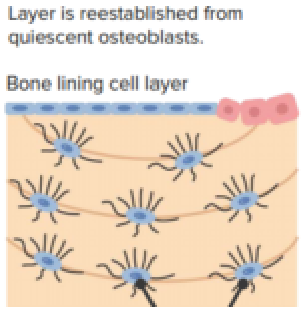
<td>
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<tr>
<td>Osteoclasts digest minerals with acid, releasing $Ca^{2+}$ and $PO_4^{3-}$.</td>
<td>Osteoblast precursors become osteoblasts and lay down new osteoid. Osteoid mineralizes and forms new bone.</td>
<td>Trapped osteoblasts become osteocytes and extend dendrites.</td>
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## Control and regulation of calcium and phosphorus

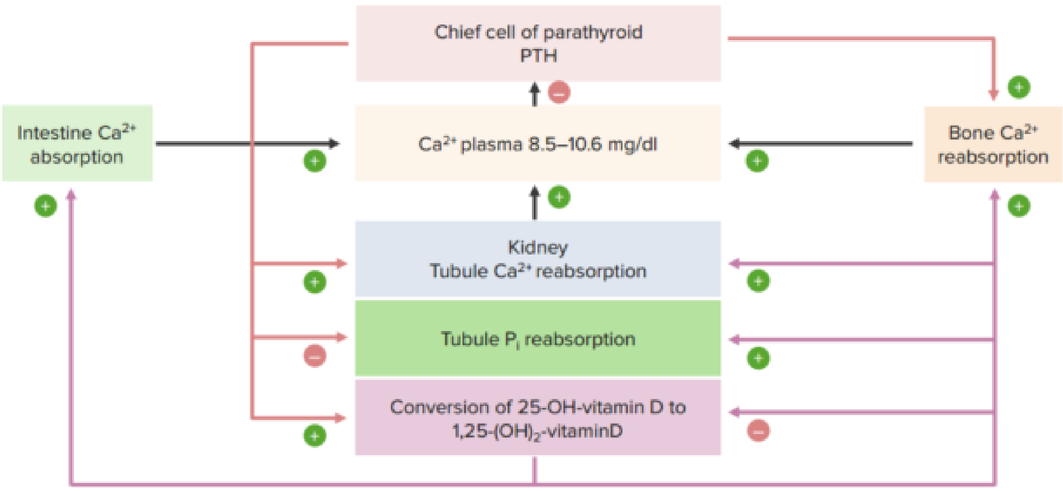



Image: Control and regulation of calcium and phosphorus. By Lecturio.

# Hematopoiesis (Formation of Blood Cells)

**Note:** Hematopoiesis includes erythropoiesis, leukopoiesis, and thrombopoiesis.

Blood cells and platelets have a limited lifespan, so they need to be continually replaced. Hematopoiesis (hemopoiesis) occurs in the bone marrow. The hematopoietic stem cell (pluripotent stem cell) can differentiate into all the blood cell lineages.

**Several progenitor stem cell types arise from a hematopoietic stem cell (HSC)**

Two major colonies arising from the HSC are as follows:

**Common lymphoid progenitor cells:** These differentiate into T cells, B cells, and natural killer (NK) cells.

**Common myeloid progenitor cells:** These differentiate into specific lineage-restricted progenitors under the influence of cytokines and growth factors including colony-stimulating factors (CSFs), as follows:

- Megakaryocyte/erythrocyte progenitor (MEP)

- Granulocyte/monocyte progenitor (GMP)

## Erythropoiesis (erythrocytes)

The megakaryocyte/erythrocyte progenitor (MEP) provides erythrocyte-committed progenitors.

**Stages of erythropoiesis**

1. Proerythroblast
2. Basophilic erythroblast
3. Polychromatophilic erythroblast
4. Orthochromatophilic erythroblast
5. Polychromatophilic erythrocyte or reticulocyte
6. Erythrocyte

## Thrombopoiesis

The megakaryocyte has a multi-lobed nucleus and can measure 70 µm in diameter.

Platelets are derived from invaginations of the plasma membrane, which initiates the shedding of these cytoplasmic fragments (platelets).

## Granulopoiesis (granulocytes)

The granulocyte/monocyte progenitor (GMP) produces granulocytes and monocytes.

**Stages of granulopoiesis, e.g., a neutrophil**

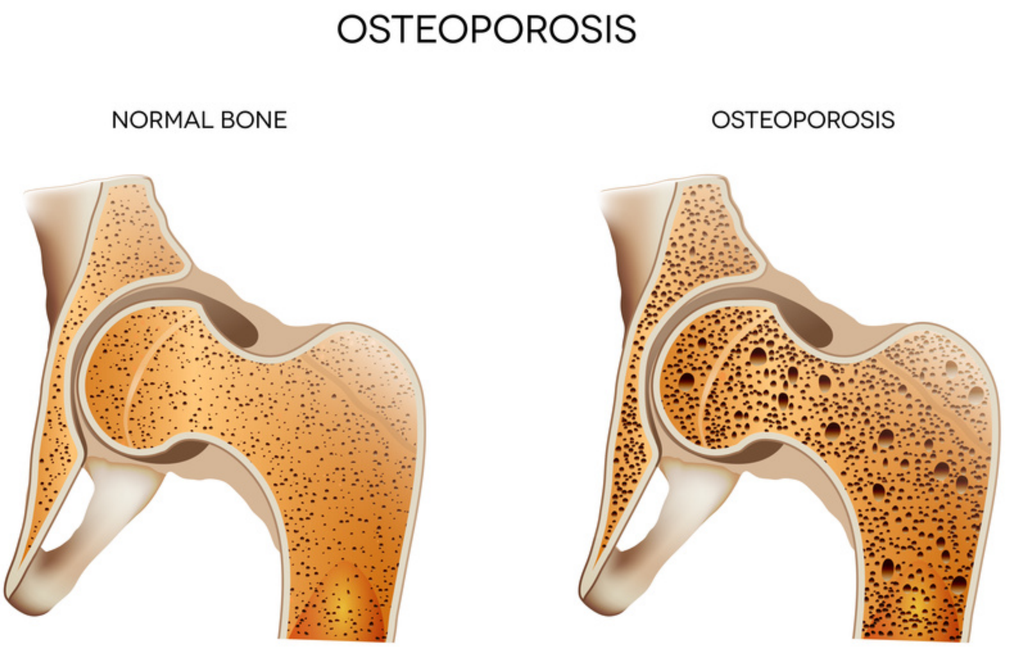
1. Myeloblast
2. Promyelocyte
3. Myelocyte
4. Metamyelocyte
5. Band (stab) cell
6. Neutrophil

# Bone Diseases

The entirety of bone and cartilage forms the skeletal system. Bones and joints perform hard labor and can be damaged by inactivity or unhealthy dietary practices.

One well-known bone disease is osteoporosis.

## Osteoporosis




In the case of osteoporosis (*osteon* = bone, *poros* = pore), the bone resorption dominates in relation to the bone formation, which means that the body loses more calcium than it can deposit in the bone. In a porous bone, bone mass is reduced to such an extent that bones break more often and spontaneous fractures can occur.

Osteoporosis is found especially in the areas of the hip, wrist, and vertebral bodies. Height reduction of vertebral bodies, loss of body height, distortion of the spinal column, or bone pain are results of this disease. People with osteoporosis are usually of middle to old age, with women being more affected (approximately 80%) because their bones are thinner than the bones of men.

The activity of osteoblasts and the production of the extracellular bony matrix is stimulated by estrogens and testosterone. A woman's production of estrogen decreases rapidly during menopause. The testosterone in men, however, only decreases slowly and slightly by comparison.

Risk factors for a homeostatic imbalance can be a positive family anamnesis, being of European or Asian origin, having a thin physical build, performing little activity, smoking, drinking alcohol, having decreased vitamin D/calcium intake, and taking certain medications.

In the case of increased osteoporosis risk factors, special emphasis should be put on prevention. Regular physical activity and continuous intake of calcium, particularly for younger women, have a better effect than medication alone or calcium substitution in older people.

## Further Bone Diseases (Osteopathies)

- Achondroplasia
- Fibrodysplasia ossificans progressiva
- Fracture
- Hypophosphatasia
- Bone marrow edema

- Ahlbäck’s disease
- Paget’s disease (osteodystrophia deformans)
- Osteochondrosis dissecans
- Osteogenesis imperfecta
- Osteomyelitis (inflammation of the bone)
- Spongy bone edema

# References

Deng, H., & Liu, Y. (2005). *Current topics in bone biology*. Hackensack, NJ: World Scientific.

Fundamentals of anatomy. (1938). *Journal of the American Medical Association,110*(22), 1863. doi:10.1001/jama.1938.02790220065044

Halsey, J. (2012). *Bone anatomy*. Delhi: Orange Apple.

Pritchard, J. (1956). General anatomy and histology of bone. *The Biochemistry and Physiology of Bone,*1–25. doi:10.1016/b978-1-4832-3286-7.50005-1



Notes