Skeletal System

Bone

Bone is one of the hardest tissues of the human body and is second only to cartilage in its ability to withstand stress. As the main constituent of the skeleton, it supports fleshy structures, protects vital organs (such as those in the cranial and thoracic cavities) and also contains marrow, where the blood cells are formed.

Besides these three functions, bones form a system of levers which multiply the forces generated during muscle contraction, transforming them into body movements.

Bone is composed of intercellular calcified material, the bone matrix and different cell types.

1) Osteocytes which are found in cavities (lacuna) within the matrix. These are basically mature bone cells that have encased themselves in bony matrix.

2) Osteoblasts which synthesize the organic components of the matrix. Once these cells surround themselves with bony matrix they become osteocytes.

3) Osteoclasts which are multinucleated giant cells involved in the resorption of bone tissue.

Osteoblasts and osteoclasts both participate in the bone remodeling process. In short Osteoblasts make bone and Osteoclasts eat bone.

The internal and external surfaces of bones are covered by layers of connective tissue named endosteum and periosteum. Bone surfaces that are not covered by connective tissue or by osteoblasts are subject to resorption through the activity of osteoclasts which appear in the region. For this reason, special attention is given to the periosteum and endosteum during surgery.

The periosteum is a layer of dense connective tissue that is very fibrous externally but more cellular and vascular near the bone tissue.

Periosteal collagenous fibers are called perforating (Sharpey's) fibers. They bind the periosteum to the underlying bone tissue.

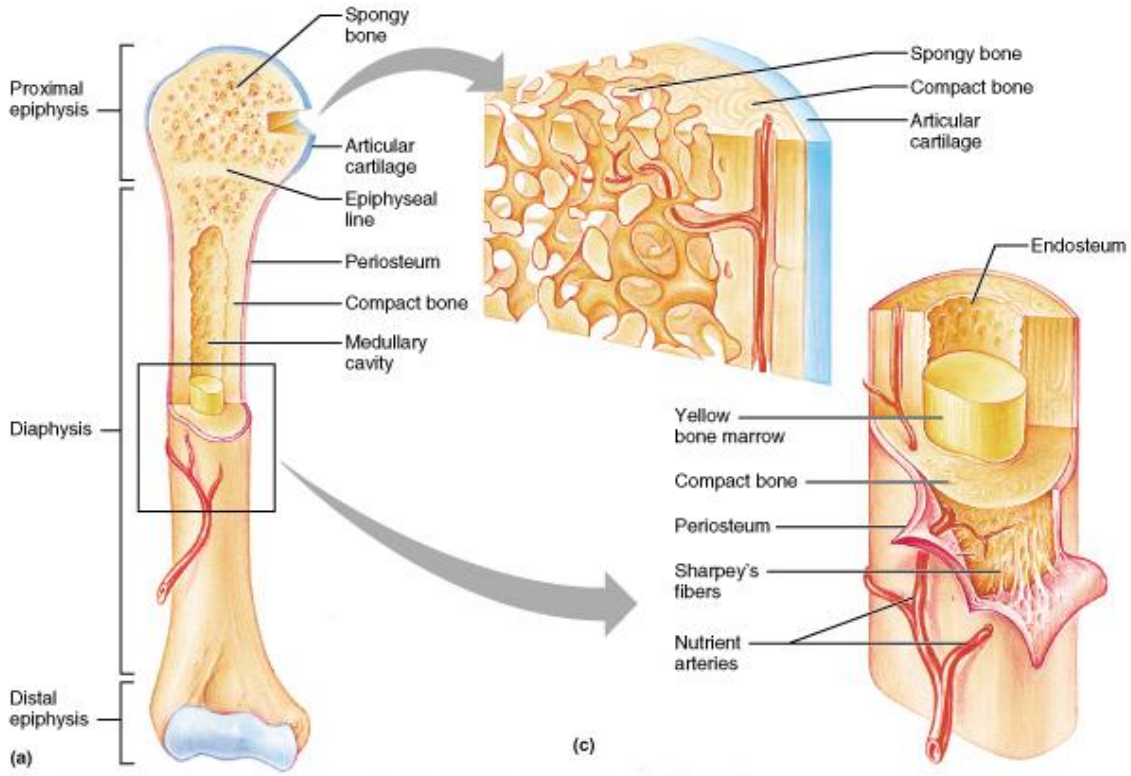
Periosteal cells with morphologic characteristics of fibroblasts are easily transformed into osteoblasts and then, through mitosis, into other osteoblasts. These periosteal cells play a prominent role in bone growth and repair.

The endosteum has the same components as the periosteum and nearly the same structure, but it is considerably thinner, and does not have two layers as the periosteum does.

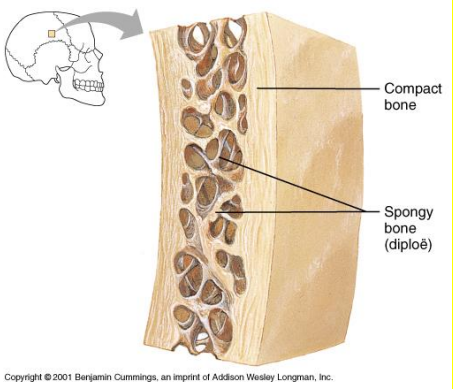
Long bones – represent many of the bones of the extremities. These bones are well designed to act a level bars.

Long bones have a shaft known as the diaphysis. It is almost totally composed of compact bone with a small component of spongy bone in an inner position around the marrow cavity.

On the ends of the shaft we find the epiphyses, which are spongy bone covered with a thin layer of compact bone.



Flat bones - form the calvarium (or skull), the ribs and sternum, the scapula, and the bones that fuse to form the os coxa. In flat bones there are two layers of compact bone called plates, with a layer of spongy bone (called diploe) in between. The design of flat bones makes them very light but also very resistant to compression. They are able to withstand a high amount of compressive force, but will snap very easily if subjected to bending forces. This makes them useless as levers.



Think about it. Why is it necessary to have compact bone and spongy bone? Why not have all bones in the body be made of compact bone? Why not have all bones of the body be made of spongy bone?

Histologically there are two types of bone tissue

1) primary (immature or woven bone)
2) secondary (mature or lamellar bone)

Primary bone - is the first bone tissue to appear both in formation and repair. It is temporary and is replaced in adults by
secondary bone, except near the sutures of the flat bones of the skull, in tooth sockets, and in the insertions of some tendons.

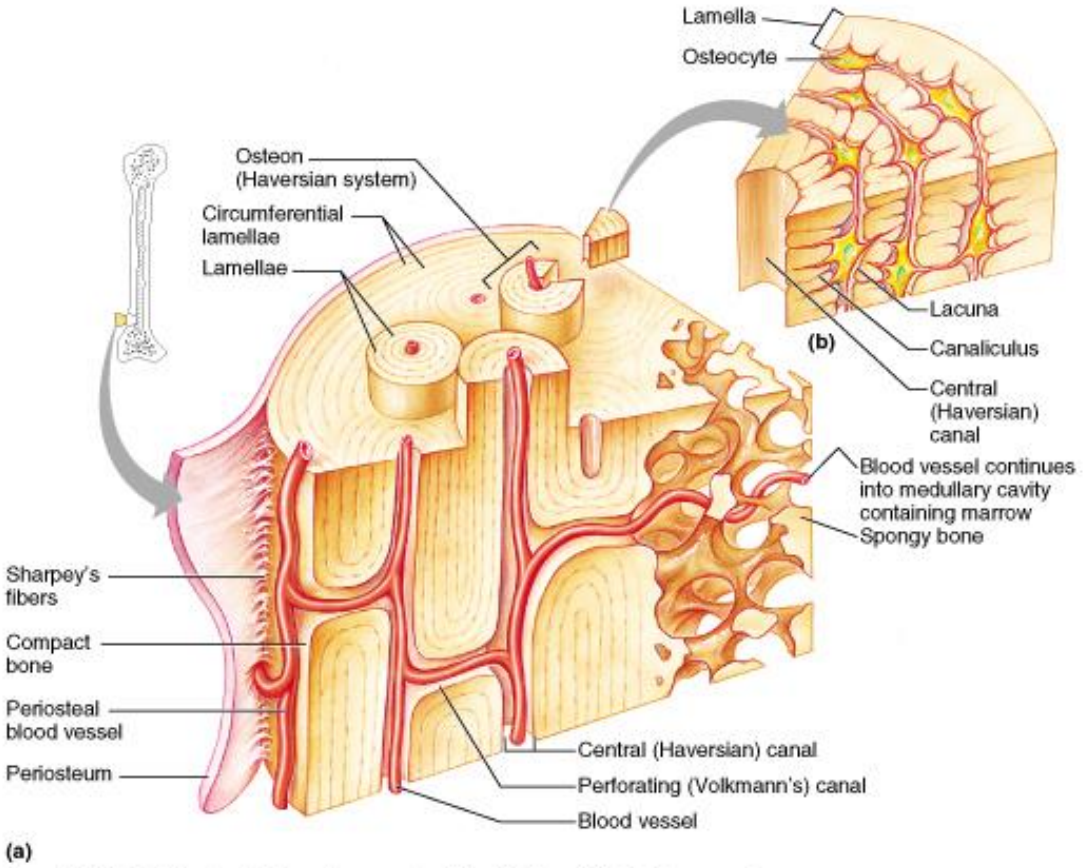
Secondary Bone (in adults)

has collagenous fibers arranged in concentric lamella organized around a vascular canal.

The whole complex of concentric lamellae surrounding a canal containing blood vessels, nerves, and loose connective tissue is called an osteon (or Haversian system, named for the histologist by which it was first described).

Each osteon is a long, often bifurcated cylinder parallel to the diaphyses. It consists of a central canal (of Havers) surrounded by 4 - 20 concentric lamellae. These central (Haversian) canals communicate with the marrow cavity, with the periosteum, and with each other through transverse or oblique canals called perforating canals (Volkmann's canals).

The osteocytes found within lacuna communicate with each other via canaliculi.



Formation of bone

Bone tissue is formed by either intramembranous ossification or by endochondral ossification. In either case the bone tissue which appears first is primary or immature bone. It is also VERY important to realize that the osteoid substance (mainly hydroxyapatite crystals) must be deposited along some preexisting framework. It cannot form bone on its own.

Intramembranous Ossification - is so named because it takes place within membranes of connective tissue. The primary cell type found within connective tissue is known as a fibroblast. As the name of the cell implies, the cell makes fibers. These may be collagen fibers, elastic fibers, reticular fibers, or any combination of the above. In intramembranous ossification cells resembling young fibroblasts differentiate into osteoblasts. These osteoblasts lay down osteoid and calcium along the fibers of the membrane. Eventually the osteoblast will surround themselves with osteoid, at which time they become osteocytes. This happens in several groups so that the fusion of the matrix spicules gives a spongy structure.

The frontal, parietal, parts of the occipital and temporal bones of the skull and the mandible and maxilla are formed by intramembranous ossification.

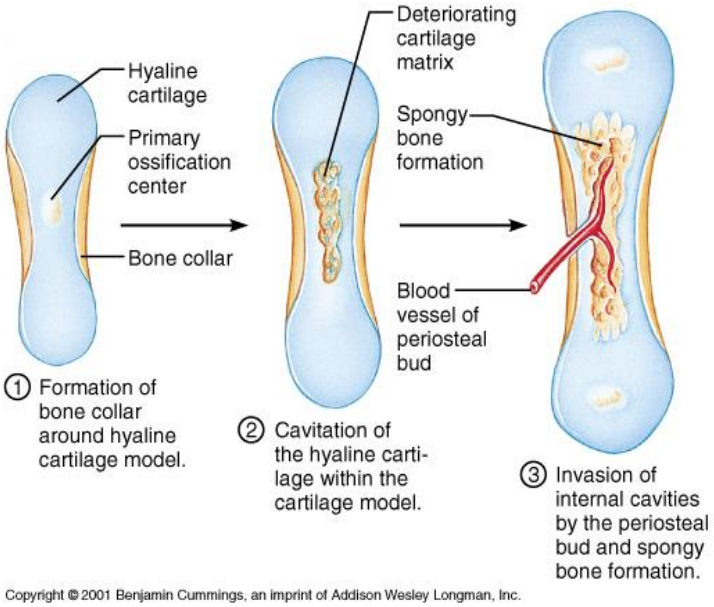
Endochondral Ossification – as its name implies, takes place within a piece of cartilage. This is hyaline cartilage whose shape resembles a small model of the bone to be formed.

This type of ossification principally forms the long bones and short bones of the body.

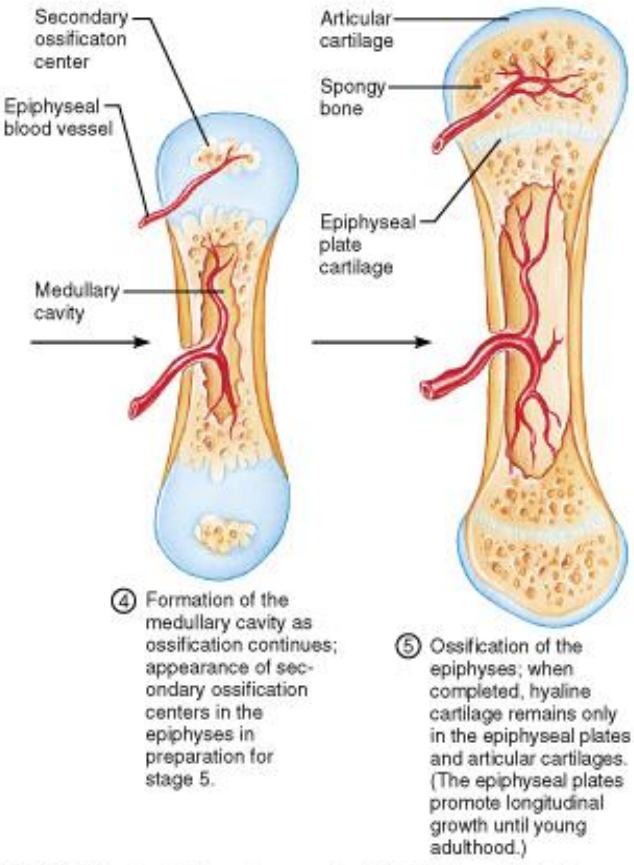
Basically endochondral ossification consists of 2 processes. The first process is hypertrophy and destruction
of the chondrocytes of the model of the bone, leaving cavities separated by the septa of a calcified cartilage matrix. In the second process, undifferentiated mesenchymal cells and blood capillaries penetrate into the spaces left by the destroyed chondrocytes. The undifferentiated cells give rise to osteoblasts which form an osseous matrix on the remnants of the calcified cartilage matrix. In this way, bone tissue appears at the site where there was cartilage, but there is no transformation of cartilage into bone tissue.

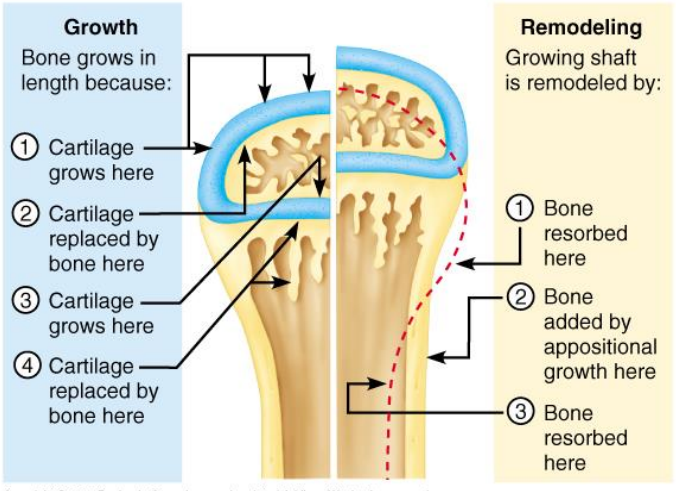
<u>Primary Ossification Center</u>

In the diaphyses of a long bone the first bone tissue to form appears by intramembranous ossification in the perichondrium surrounding the diaphyses. This produces a <u>bone collar</u> around the diaphyses. The cartilage cells of this cartilage model below the bony collar increase their size and degenerate, leaving large cavities. The cartilage matrix becomes reduced to slender calcified partitions. Osteoclasts in the bone collar make holes through which blood vessels from the periosteum can enter the matrix. These invading vessels carry with them undifferentiated mesenchymal cells, which proliferate and give rise to osteoblasts and bone marrow stem cells. These form a continuous layer over the calcified cartilagenous matrix and start to synthesize bone matrix. A secondary ossification center arises at each epiphyses. The function of these centers is similar to



the primary centers but the growth is radial rather than longitudinal. In secondary ossification centers no bone collar is formed because the articular cartilage (the cartilage within the joint) does not have a perichondrium.





The Epiphyseal plate is a cartilaginous disc that separates the diaphysis of a long bone from the epiphysis. This feature is essential for the longitudinal growth (increase in length) of a long bone. There are 4 events that are occurring simultaneously during the longitudinal growth of a long bone. The cartilage on the diaphyseal side of the epiphyseal plate is being replaced by bone while the epiphyseal side is growing (via mitosis) more cartilage. The epiphyseal side of the articular cartilage is being replaced by bone while the

joint surface of the articular cartilage is growing (via mitosis). If we proceed with just this simple explanation, we could rationalize a never ending longitudinal growth of long bones. We know that people do not continue to increase the length of their long bones over the entire duration of their lives. Can we provide an explanation for the termination of this longitudinal growth? The explanation is initially very simple. The mitosis that is occurring within the cartilage of the epiphyseal plate is proceeding at a slower rate than the rate at which we are replacing that cartilage with bony matrix. Eventually the ossification overtakes the cartilage and at that point no further longitudinal growth can take place.

This is a good time to introduce the condition known as dwarfism. There are two types of dwarfism; pituitary dwarfism and achondroplastic dwarfism. It is generally easy to distinguish which type of dwarfism a person has simply by looking at the individual.

Pituitary dwarfism is caused by insufficient amounts of growth hormone from the anterior pituitary gland. This hormone is responsible for telling all of the cells of your body to grow. Without enough growth hormone the individual will not reach a normal adult size, but since all areas of the body were equally affected, they maintain normal body/limb proportions.

It is helpful to understand some terminology in order to understand achondroplasia. Chondral essentially refers to cartilage. Placing the prefix "a" in front of a word means "without." So if "chondral" means cartilage, "achondral" means without cartilage. So a person who is an acondroplastic dwarf did not reach their adult size due to the fact that they did not have sufficient cartilage to replace with bone. The cartilage that does not grow correctly in these individuals is the cartilage of the epiphyseal plate. Think about it. If the cartilage of the epiphyseal plates does not proliferate (grow), what bones will not be able to grow in length? Which bone would not be affected? The long bones of the extremities would not be able to reach their adult size, but the bones of the skull, thoracic cage, and vertebral column would be unaffected. Individuals with achondroplasia (acondroplastic dwarfism) have a normal size torso and head, but short upper and lower extremities. At a glance you can see that they do not have normal body to limb ratios.

The cartilage of a growing epiphyseal plate is divided into 5 zones:

- 1) Resting zone - hyaline cartilage
- 2) Proliferative zone - chondrocytes divide rapidly and form parallel rows of stacked cells along the long axis of the bone
- 3) Zone of Hypertrophy - large chondrocytes whose cytoplasm has accumulated glycogen. The matrix is reduced to thin septa between the chondrocytes
- 4) Zone of Calcification - death of chondrocytes, thin septa of cartilage become calcified by deposition of hydroxyapatite
- 5) Zone of Ossification - bone tissue appears

Appositional bone growth refers to growth in the width of a bone. In this process there are mesenchymal cells located in the periosteum that give rise to osteoblasts. These osteoblasts, essentially located on the surface of the bone, can lay down new bone matrix along the inner fibers of the periosteum, this adding width to the bone.

Fracture repair

When a bone is fractured, the damage suffered by the blood vessels produces a localized hemorrhage with the formation of a blood clot. Although we have not learned about clot formation, one of the first things to occur during clot formation is the production of fibers. This is an essential step in knitting the broken pieces of bone together. Think about it. Based on what we have learned earlier in this lecture, why is the formation of these fibers essential to fracture repair? Destruction of bone matrix and death of bone cells adjoining the fracture also occur.

During repair, the blood clot, the remaining cells, and the damaged bone matrix are removed. The periosteum and endosteum around the fracture respond with intense proliferation of their fibroblasts and other undifferentiated cells which form a cellular tissue surrounding the fracture, and penetrate between the extremities of the fractured bone. Some of these cells differentiate into macrophages which engulf the remains of the damaged tissue and the blood clot.

Immature bone is then formed by endochondal ossification of small fragments of cartilage appearing in the connective tissue that develops first in the fracture. It is also formed by means of intramembranous ossification. Therefore, areas of cartilage, areas of intramembranous ossification, and areas of endochondral ossification are encountered simultaneously when repair is taking place. Repair progresses in such a way that, after a period of time, irregularly formed trabeculae of immature bone temporarily unite the extremities of the fractured bone forming a bone callus.

Normal stress imposed on the bone during repair and during the patients gradual return to activity serves to remodel the bone callus. The remodeling of the bone callus reconstitutes the bone as it was prior to fracture. The primary bone tissue of the callus is gradually resorbed and replaced by lamellar bone, resulting in restoration of the original bone structure.

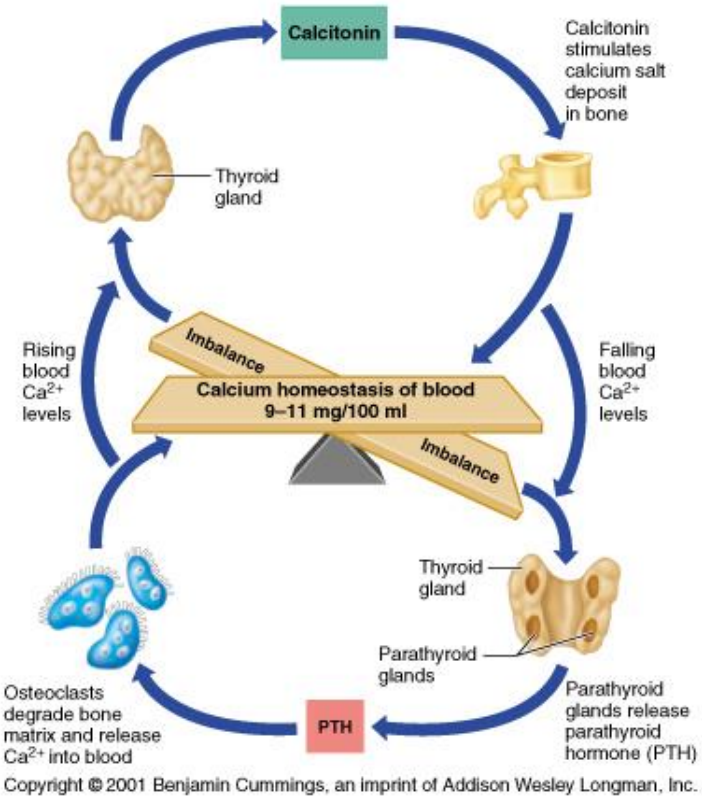
Plasticity of bone

Bone is capable of remodeling its internal structure according to the different stresses to which it is subjected. This is how orthodontic appliances (braces) work. Bone formation takes place on the side where traction is applied and is resorbed on the side when pressure is exerted (the opposite side).

Calcium reserve

The skeleton contains 99% of the bodies calcium and acts as a calcium reservoir. The concentration of calcium in the blood and tissue is held quite stable, this means that calcium taken in through the diet usually goes into storage in the bones or is excreted in the feces and urine.

Calcium can be mobilized from the bone in 2 ways



1) a simple transfer of ions from hydroxyapatite crystals to interstitial fluid, where calcium can pass quickly into the blood.

2) parathyroid hormone (produced in the parathyroid glands) activates and increases the number of osteoclasts thus promoting resorption (reabsorption) of the bone matrix, with the consequent liberation of calcium.

Calcitonin (produced in the thyroid) inhibits matrix resorption and calcium mobilization. Thus its action is the opposite of parathyroid hormone.

Nutrition

Calcium deficiency may be due to lack of calcium in the diet or the lack of vitamin D which is important for the absorption of calcium by the small intestine.

Calcium deficiency in children results in rickets.

Calcium deficiency in adults results in osteomalacia. This condition may be evident during pregnancy since the developing fetus requires a great deal of calcium. As calcium is removed from bone it may leave open spaces within the bone. Depending on the degree of bone loss a patient may be diagnosed with osteopenia or osteoporosis.

Vitamin A also plays a role in balancing the production and resorption of bone. Deficiency of vitamin A results in osteoblasts not synthesizing the bone matrix normally, thus the individual may not reach their normal stature.

Vitamin C is essential for the production of collagen by cells including osteoblasts. Deficiency interferes with bone growth and hinders repair of fractures.

Hormones

Growth hormone from the anterior lobe of the pituitary stimulates overall growth. Lack of growth hormone during the growing years results in pituitary dwarfism. Excess growth hormone during the growing years causes gigantism due to excess growth in the long bones. In adults, since long bones can no longer increase in length (no epiphyseal cartilage) they increase in width by periosteal (appositional) growth. This causes a condition known as acromegaly.

Sex hormones both male and female, have very complex effects on bone growth, but are, in general, stimulators of bone growth.