12

Bone Tissue and Homeostasis

Dr. Sujay Bisht
Assistant Professor, L.N.I.P.E,
N.E.R.C, Guwahati (Assam)
sujaybisht@gmail.com

Abstract

Bone tissue is a dynamic, living structure that undergoes continuous remodelling to maintain structural integrity, support bodily functions, and regulate mineral homeostasis, particularly calcium balance. This chapter explores the macroscopic and microscopic anatomy of bone, including compact and spongy bone, cellular components like osteoblasts, osteocytes, and osteoclasts, and processes such as intramembranous and endochondral ossification. It further discusses bone growth and remodelling under mechanical stress (e.g., exercise vs. microgravity), fracture repair stages, hormonal influences (PTH, calcitonin), and disorders such as osteoporosis, rickets, and osteomalacia, emphasising the interplay among mechanical loading, nutrition, and hormones for optimal bone health.

Keywords: *Bone tissue, homeostasis, remodelling, ossification, osteoblasts, osteoclasts, calcium regulation, osteoporosis, bone structure, fracture repair*

Introduction

The bone tissue is a living and complex tissue that is dynamic in nature. It constantly develops new bone and removes the old bone, a process known as bone remodelling. In the early space exploration, physically fit and healthy people came back to space and shocked their doctors. These astronauts also lost as much as 20 percent of their bone density as determined by physical tests. Their bones were not strained much by the weightless space and the minimal movement they did by the small spaces they resided in. Conversely, the athletes exert much strain on the bones due to the heavy forces they experience. There is an increase in bone mass and density of successful athletes. What is the mechanism of bone response to various mechanical loads? Why does high

activity and bone tissue challenge bone health lead to bone health improvement? In order to comprehend how the bones grow, age as well as the impact of exercise on bone density and strength, this chapter will cover the various components of the bones.

Structure of Bone

We now look at the macroscopic structure of bone.A long bone, say the humerus (arm bone) may be used to investigate the macroscopic structure of bones.

The parts of a normal long bone are as under:

1.The primary shaft of the bone is the diaphysis that is long and cylindrical.

2.The ends of the bone are the epiphyses, which is close to the top and bottom.

3.The diaphys and epiphys spaces between the diaphysis and epiphyses are known as the metaphyses. Each metaphysis in a growing bone has an epiphyseal plate, a layer of hyaline cartilage which enables the bone to grow in length. When a bone has ceased to grow, the bone replaces the cartilage in the epiphyseal plate creating the epiphyseal line.

4.The articular cartilage is a thin film of hyaline cartilage covering the area of the epiphysis between the bone to another bone at a joint. This cartilage serves to relieve friction as well as taking up shock at the mobile joints. It does not easily repair damage as it does not contain a perichondrium or a blood vessels.

5.The periosteum is a dense connective tissue layer which encases the bones with the exceptions of those which are lined by articular cartilage. It comprises two, the outer fibrous layer and the inner cell layer which assist the growth of the bone in thickness. It also secures the bone, aids in healing of fractures, provides nutrients, and provides points of attachment of ligaments and tendons. The periosteum is connected with the bone by a type of fibers known as perforating or Sharpey fibers.

6.The medullary cavity is a cavity within the diaphysis, which houses the yellow bone marrow and the blood vessels. This hole allows the bone to shed some of its total weight by making the bone in regions where it is unnecessary to be less dense. Long bones are tubular in shape which ensures maximum strength with minimum weight.

7.The endosteum is a thin membrane which covers the medullary cavity. It is made of one layer of bone forming cells and a little connective tissue.

Functions of Bone

Bone is an organ that consists of a variety of different tissues that interact, that is, bone tissue, cartilage, dense connective tissue, epithelium, adipose tissue, and nervous tissue. The bones and their

cartilage form the skeletal system structure. Bone disorders and the study of bones are known as osteology. The skeletal system has a number of functions:

1.Support. The body is supported by the skeleton, which maintains soft tissues in place and holds them, and also, the skeleton gives most of the skeletal muscles attachment sites.

2.Protection. The skeleton protects the key internal organs. As an example, brain is safeguarded by the cranial bones, and heart and lungs are safeguarded by rib cage.

3.Assistance in movement. A majority of skeletal muscles attach to the bones and when they contract they pull the bones to cause movement.

4.Mineral homeostasis. Approximately 18 percent of the body weight comprises of bone tissue, which contains minerals such as calcium and phosphorus. The body has 99 percent of the calcium stored in the bone. Bone releases these minerals into the blood when the need arises to ensure that there is a balance of minerals in the body besides the supply of these minerals to other parts of the body.

5.Blood cell production. There are some bones called red bone marrow, which produces red blood cells, white blood cells, and platelets a process known as hemopoiesis. Red bone marrow has developing blood cells, fat cells, fibroblasts and the macrophages. It is found in growing bones of fetus and in certain bones of an adult such as hip, ribs, sternum, vertebrae, skull and ends of the humerus and femur. Every bone marrow in infants is red and it is engaged in the production of blood cells. On aging, a lot of the red marrow degenerates into yellow marrow.

6.Triglyceride storage. The yellow bone marrow contains mostly triglycerides in the form of fat cells which could be a potential source of chemical energy.

Histology of Bone Tissue

Now we take a look at the microscopic structure of bone. Bone or the osseous tissue, as it is also called, consists of a considerable quantity of extracellular matrix that surrounds cells that are spaced far apart,Just as in other connective tissue, bone is composed of extracellular matrix. It consists of about 15 percent water, 30 per cent. collagen fibers, and 55 per cent. crystallized mineral salts. Calcium phosphate is the most prevalent mineral in this mixture and is a salt. The mixture of calcium phosphate and other mineral salt, calcium hydroxide, results in the creation of crystals called hydroxyapatite. As these crystals form, they combine with such ions as magnesium, fluoride, potassium, sulfate, and other mineral salts as calcium carbonate. These

crystallized mineral salts, are deposited between the structure created by the collagen fibers and this results in the hardening of the tissue. This is known as the process of calcification.

The process of calcification first starts with the cells known as osteoblasts which are the ones that form bone.Previously, they thought that the body was able to naturally get to a place where it has enough mineral salt to build crystals. Today we understand that the presence of collagen fibers is critical to this process occurring. Mineral salts start crystallizing in the small crevices between the collagen strands. The mineral crystals are formed around the collagen strands as the spaces between the strands are filled. The characteristics of bone are based on the interplay of the collagen fibres and the mineral salts crystals.

The bone provides the bone with flexibility through the collagen and hardness through the mineral salts like reinforcing rods in concrete, which gives the bone organic tensile strength, the capacity to withstand extension or fracture. A bone that is dipped in acidic solution, e.g., vinegar, turns to be rubbery and pliable as the mineral salts are washed off. You will later learn that bone cells known as osteoclasts secret acids and enzymes, which dissolve collagen fibers as well as the mineral salts in the bone tissue, when required to break down or build up bone.

There are four main cell types in bone tissue: osteoprogenitor cells, osteoblasts, osteocytes, and osteoclasts.

1. Osteoprogenitor cells are undifferentiated bone precursor cells which derive out of mesenchyme, the tissue that constitutes the bone forming practically all of the connective tissues. It is only these cells, which divide to create osteoblasts. The osteoprogenitor cells are located on the endosteum which is the interior section of the periosteum and within the blood vessel linings of the bone.

2. Osteoblasts are cells that form bone and initiate the process of calcification.They produce and release collagen fibers and other substances required to construct the extra cellular matrix of bone. Osteocytes are developed when osteoblasts get entraped within the extracellular matrix they produce. The name of a bone cell has a suffix -blast which implies that it produces the extra cellular matrix.

3. The chief bone tissue cells are osteocytes, which carried out an everyday metabolic activity, including nutrient and waste exchange with the blood. Osteocytes do not divide as their counterparts, osteoblasts do. The ending of a cell name -cyte means that the cell preserves and checks the tissue.

4. The osteoclasts are large cells located in the endosteum and are formed as the result of the fusion of 50 monocytes,

which is a form of white blood cell.The plasma membrane of an osteoclast is folded into a ruffled border that is directed towards the bone surface. Osteoclasts destroy the extracellular bone by releasing strong lysosomal enzymes and acids. This is called bone resorption which is a natural process of bone growth, maintenance, and repair. Osteoclasts also aid in the regulation of the blood calcium level depending on some hormones.

In order to memorize new or unknown information, you may apply the help of a mnemonic. the mnemonic you may use to remember all the functions osteoblasts and osteoclasts perform is as follows: osteoclasts break the bone down; osteoblasts build it up.

The bone is not hard but contains numerous tiny spaces between the cells and the components of the bone matrix.Some of this space is filled by blood vessels which supply nutrients to cells in the bone. Other regions save red bone marrow. The size and distribution of the spaces can be of compact or spongy regions of a bone.

Compact bone tissue is the strongest type of bone tissue and has the fewest gaps.

It contains the greater part of the long bone shafts (diaphysis), and underneath the periosteum of every bone. Compact bone is protective, stable and resistant to both movement and weight strain. Compact bone tissue is composed of structural components known as haversian systems, or osteons. Every osteon consists of concentric lamellae enclosing a central canal full of blood vessels and nerves. These lamellae are circular formations of mineralized extracellular matrix which protrude outwards similar to the rings of a tree. These cylindrical units are usually parallel to the long axis of the bone in long bones. In small spaces between the concentric lamellae are found osteocytes in small pockets known as lacunae. These tube-like structures of bone are usually arranged in a series of parallel cylinders which are parallel to the length of the bone in case of a long bone. The lacunae are small openings between the concentric lamellae tiny canaliculi radiate out of the lacunae in every direction and are filled with extracellular fluid. The canaliculi contain finger-like structures within them, which are composed of osteocytes. Gap junctions enable the osteocytes that surround each other to interact with each other. The canaliculi form a complex, fine system of interconnection of the canals that traverse the bone by connecting lacunae to the main canals and to the other ones. This system provides many avenues of clearance of waste and provision of nutrients and oxygen to the osteocytes.

Osteons in compact bone tissues run parallel to the length of the diaphysis and they are in the same direction. Due to this reason, a long bone cannot bend or break even in case of the great pressure on both ends. Compact bone tissue normally appears in the areas of a bone in which the stresses are exerted in the relatively limited number of directions. The lines of stress of a bone are dynamic. They change following regular strenuous physical activity, such as weight lifting, and as an individual learns to walk. The lines of stress can also be affected by fractures and physical deformity of a bone as a consequence, therefore, the osteon organization is dynamic and modifies towards the physical needs of the skeletal system with time.

Lamellae which harbor the canaliculi and osteocyte lacunae are found in the spaces between the osteons called interstitial lamellae. Interstitial lamellae are fragments of earlier osteons that have partially been damaged during the growth or rebuilding of the bone, and through which blood vessels and periosteal nerves pass through the compact bone by transverse interosteonic (or perforating) canals. The arteries and nerves of the interosteonic canals are linked to the medullary cavity, periosteum and central canals.

Circumferential lamellae are lamellae which are placed about the entire outer and inner circumference of the shaft of a long bone. They are created at the initial phases of the bone formation. The circumferential lamellae which run directly perpendicular to the periosteum are external circumferential lamellae. Their attachment to the periosteum is done via perforating (Sharpey) fibers. The circumferential lamellae that are located on the edge of the medullary cavity are known as internal circumferential lamellae.

Spongy Bone Tissue

Unlike compact bone tissue, there are no osteons within the spongy bone tissue or trabecular or cancellous bone tissue. The interior part of a bone is always spongy bone tissue and covered by compact bone. It consists of narrow columns known as trabeculae which are lamellae, placed in irregular arrangement (tra-BEK-ū-lē = small beams; plural trabecula).The spaces that are in between trabeculae can be seen by the unaided eye. These macroscopic spaces in bones which form blood cells, are filled with red bone marrow; in other bones they are filled by yellow bone marrow (adipose tissue). Great numbers of small blood capillary nourish the osteocytes in both types of bone marrow. Each trabecula is composed of concentric lamellae, osteocytes which are located in lacunae, and canaliculi that extend outward of the lacunae. Sponge bone tissue forms the majority of the inner bone tissue in short and flat bones as well as in irregularly

shaped bones which are called sesamoid bones. It forms a variably narrow rim which borders the medullary cavity of the diaphysis and forms the core of the epiphyses in long bones under the paper-thin layer of compact bone.Compact bone always surrounds spongy bone to keep it intact.

The porous bone tissue may first have visible trabeculae that are less organized in their composition than the osteons of compact bone tissue. But when they are suitably placed on stress lines they can convey force and can resist loads without fracture. Sponge bone is usually observed where the stress on the bones is not high or where stresses are exerted in a many-directional manner. The trabeculae are not given their final form until they are thoroughly mastered in motility. actually as lines of stress move over with a deformity or a fracture that has not healed properly the layout can even move.

There are two differences between compact bone tissue and spongy bone tissue. One,the spongy bone tissue is light in nature and therefore the total weight of a bone is reduced. Due to such weight loss, the bone may move when it is pulled by a skeletal muscle with ease. Second, the trabeculae of the spongy bone tissue support and protect the red bone marrow. The bones used to store the red bone marrow are the hip bones, ribs, sternum (breastbone), the vertebrae and the ends of the humerus and femur that are closest to the heart. This is the region where the hemopoiesis or blood cell formation occurs in the adults.

Bone Formation

The formation of bone is called the process of Ossification. Osteogenic process or shun There are four general situations in which the bone grows:

The formation of bones in a fetus and embryo, formation of bones in childhood, adolescence and infancy until they reach adult size, bone remodelling (replacement of old bone by new bone tissue), and bone fractures (bone breaks) healing throughout life are all examples of bone formation.

Initial Bone Formation in an Embryo and Fetus

First we shall consider the formation of bones in embryos and fetuses. In the sixth week of embryonic life, the skeletal cartilage and bone formation occurs in the embryonic skeleton that is initially composed of mesenchyme in its approximate form of bones. The formation of bones is controlled by one of two patterns.

Both forms of producing bone, called replacement, whereby the existing connective tissue is replaced with bone do not lead to the difference in the form of the mature bone, rather, they are just different means through which the bones

are formed. The first form of ossification is intramembranous ossification. It is there that bone is directly growing in membrane, organized in membrane-like sheetlike layers. The second type is endochondral ossification. Bone is formed in hyaline cartilage which is a product of mesenchymes.

Intramembranous Ossification

The less complicated of the two bone-formation processes is intramembranous ossification. It is in this way that the mandible (lower jawbone), the medial part of the clavicle (collar bone), the flat bones of the skull, and most of the bones of the face, are formed. Also, the pliant points of the skull of the fetus through which the birth canal easily passes later hardens due to intramembranous ossification, whereby the process works as follows:

1. Differentiation of the ossification center - Due to some chemical signals at the point where bone is going to develop, the mesenchyme cells gathered and differentiate, first into osteoblasts after developing into the osteoprogenitor cells. Such a cluster is found in an ossification centre. Osteoblasts release the organic extracellular matrix of the bone until it surrounds them.

2. Calcification- The cells have become called osteocytes and they are now located in lacunae and extend their short cytoplasmic processes into canaliculi that radiate in all directions when the extracellular matrix production ceases. Calcification (hardening) of the extracellular matrix is done in days as calcium and other salt minerals are deposited.

3. Development of trabeculae - The extracellular matrix of the bone will develop around the network of blood arteries in the tissue and develop into trabeculae, which will later fuse to become spongy bones. Diffusion between red bone marrow and connective tissue that is attached to the blood vessels in the trabeculae is performed.

4. Development of the periosteum - The mesenchyme narrows at the bone periphery and develops to the periosteum as the trabeculae develops. The spongy bone does breakdown into a thin coating of compact bone on the surface layers but the spongy bone remains in the middle. With the transformation of the bone to the adult size and shape, much of the newly formed bone is remodeled, or destroyed and reformed.

Endochondral Ossification

Bone replacements cartilage is referred to as endochondral ossification. Although that is the way most of the bones in the body are formed, it is most easily observed in a long bone. It goes like this:

1. Development of the cartilage model-At the site of bone formation, mesenchymal

cells are attracted in the rough outline of the eventual bone and then they end up becoming chondroblasts. It is a cartilage model (in the future called diaphysis) that is produced by the chondroblasts and is composed of hyaline cartilage and is excreted by the chondroblasts as cartilage extracellular matrix. Relying on the model around the cartilage, a layer called the perichondrium develops.

2. Cartilage model formation- Chondroblasts are called chondrocytes when they are firmly embedded in cartilage extra cellular matrix. The length of the cartilage model is enhanced by the continued Chondrocyte cell division which is followed by the production of more cartilage extracellular matrix. This type of cartilaginous growth is referred to as interstitial (endogenous) growth (growth frominside), and increases the length. Conversely, the thickening of the cartilage by the deposition on the cartilage surface of the model of extracellular matrix material, mainly, is due to new chondroblasts which are formed in the perichondrium. The growth occurring at the external surface is calledappositional (exogenous) growth. With cartilage model development, the extracellular matrix surrounding the cartilage begins to calcify and the chondrocytes in the mid region of the cartilage hypertrophy (increase in size). Due to the impossibility of rapid diffusion of nutrients through the extracellular matrix, other chondrocytes in the calcifying cartilage die. The death of these chondrocytes leaves the spaces behind which subsequently join together to create small holes referred to as lacunae.

3. Development of the primary ossification center - The primary ossification begins on the outer side of the bone and inwards. A nutritional artery pierces the perichondrium and the calcifying cartilage model breaks osteoprogenitor cells of the perichondrium into osteoblasts through a nutrientforamen in the centre of the cartilage model. Once the perichondrium starts forming bone it is called the periosteum. The proliferation of periosteal capillaries into the calcified cartilage to the centre of the model will result in the formation of a primary ossification centre and most of the cartilage will be replaced by bone tissue. Then, osteoblasts begin enwrapping the pieces of the calcified cartilage with bone extracellular matrix forming spongy bone trabeculae. It is based on this central location where primary ossification is extended to the two extremes of the cartilage model.

4. Lengthening of the medullary (marrow) cavity -The osteoclasts dismantle a portion of the newly formed spongy bone trabeculae as an expansion of the main ossification center to the extremities of the bone occurs.

This activity leaves a hole in the diaphysis (shaft) in the form of a medullary (marrow) hollow. Majority of the diaphysis wall is replaced by the compact bone.

5. Formation of the secondary ossification centers - Secondary ossification centers are formed when branches of the epiphyseal artery penetrate the epiphyses, which normally occurs at or about the birthdate. Bone formation is likened to that of primary ossification centres. However, in the secondary ossification centres (no medullary canals are formed here), there is still spongy bone within the epiphyses. In contrast to primary ossification, secondary ossification migrates away, later on, at the centre of the epiphysis towards the periphery of the bone.

6. Differentiation of the articular cartilage and the epiphyseal (growth) plate - The articular cartilage forms out of the hyaline cartilage that coats the epiphyses. Before adulthood, hyaline cartilage is found in between the diaphysis and epiphysis referred to as epiphyseal layer. It is the area in which long bones grow in length that is known as the (growth) plate on which you will hear more later.

Bone Growth during Infancy, Childhood, and Adolescence

All of the body's bones thicken due to appositional growth during infancy, youth, and adolescence, and long bones lengthen due to the addition of bone material on the diaphyseal side of the interstitial development of the epiphyseal plate.

Growth in Length:

There are two primary processes that cause the lengthening of the long bones, which include (1) formation of interstitial cartilage in the epiphyseal side of the epiphyseal plate and (2) replacement of cartilage by bone through endochondral ossification in the diaphyseal side of the epiphyseal plate. The details of the structure of the epiphyseal plate in order to understand the process by which a bone extends. A growing bone metaphysis has a layer of hyaline cartilage referred to as epiphyseal (growth) plate that is subdivided into four zones.

1. The resting cartilage zone. This is the nearest layer to epiphysis composed of small chondrocytes scattered about. The cells are said to be resting because they are not engaged in the formation of bones. They are used instead to fasten the epiphyseal plate to the epiphysis of the bone.

2. Zone of proliferating cartilage.during this phase, somewhat larger chondrocytes are aggregated in a coin-likefashion. These chondrocytes divide and lose extracellular matrix which causes interstitial growth. The chondrocytes in this area differentiate in

order to insert the ones that perish in the diaphyseal side of epiphyseal plate.

3. The zone of cartilage hypertrophy. This layer is formed by large and developing chondrocytes assembled in columns.

4. Zone of calcified cartilage. The final area of epiphyseal plate is just a few cells and is mostly composed of dead chondrocytes as a result of calcification of the extracellular space surrounding the cell type. The diaphytic osteoblasts and capillaries penetrate the region when the osteoclasts dissolve the calcified cartilage. The osteoblasts substitute the cartilage by calcified osteo-bones that are produced through the process of endochondral ossification. It is important to remember that bone replaces cartilage by a process called endochondral ossification. As a result, the calcified cartilage area is formed into the new diaphysis that is firmly fixed to the other diaphysis of the bone.

Growth in thickness

Like the cartilage, bone can grow in thickness (diameter) only by appositional growth

- Periosteal cells then differentiate into osteoblasts towards the bone surface, and the osteoblasts release the organic compounds and collagen fibres that comprise the extracellular matrix of the bone. The osteoblasts become enclosed in extra cellular matrix, they grow up to be osteocytes... This process forms bone ridges on either side of a periosteal blood artery. The ridges also become widened slowly and give the blood vessel passing in the periosteum a groove.
- The groove continues to develop into a tunnel which engulfs the blood artery as the ridges fold and fuse up. The periodontal tissue previously becomes the endosteum which borders the tube.
- Osteoblasts deposits bone extracellular matrix in the endosteum forming new concentric lamellae. They then form more concentric lamellae as they approach the periosteal blood vessel up this way a new osteon is created when the tunnel fills up.
- Osteoblasts under the periosteum also develop further circumferential lamellae in the formation of an osteon, which also gradually increase the thickness of the bone. Further expansion in this process occurs with additional blood vessels of the periosteal origin being enclosed, like in step 1

It is important to remember that osteoclasts in the endosteum disintegrate the bone tissue that is lining the medullary cavity as new bone tissue forms on the bone surface. This way,

there is an increase in the medullary cavity when the bone thickness increases.

Remodeling of Bone

Bone just like skin grows before birth but continually grows after birth. This constant process of replacement of old bone with new bone is referred to as bone remodelling. One of them is bone resorption which entails the addition of minerals and collagen fibres to bone by osteoblasts and the removal of minerals and collagen fibres in bone by osteoclasts. Hence, bone deposition leads to the formation of bone extracellular matrix, and the bone resorption leads to its destruction. About 5 percent of all the bone mass in the body is in remodelling at a particular time. Besides, the process of remodelling is slower in certain body parts as compared to others. In comparison, every 4 months, the lower section of the femur is substituted.Alternatively, the life of a person will not lead to complete replacement of bone in certain areas of the femur shaft. During the growth of bones, even after they attain their adult proportions and shapes, old bone is constantly broken down and replaced in a continuous process, by new bone.

The process of remodelling also regenerates lost bone to new bone. Some of the factors that may lead to remodeling include exercise, sedentary lifestyles and changes in diet. Remodelling has many other benefits. In case the new bone that is produced is exposed to high loads, it will become thicker and stronger than the old bone because the level of stress is related to the level of bone strength. Besides, the shape of a bone may also be modified to the related help in the case of the stress patterns which are observed during the process of rebuilding. Finally, although of least importance, young bone is stronger in withstanding the breaking compared to old bones.

To create a leakproof seal at the boundaries of its ruffled border, an osteoclast adheres to the bone surface on its endosteum or periosteum in the process of bone resorption. Then it leaks different acids and lysosomal enzymes which destroy the proteins into the compartment that is sealed. The enzymes disintegrate the collagen strands and other organic materials as the acids disintegrate the minerals that constitute the bones. Five or six osteoclasts acting in parallel excavate a small tunnel out of the old bone. The disaggregated bone proteins and the extra-cellular matrix minerals (mostly calcium and phosphorus) pass through an osteoclast on the other side of the ruff-led boundary by endocytosis, across the cell by vesicles, and by exocytosis. The wastes of bone resorption are currently leaked to neighboring blood capillaries in the interstitial fluid. After a small Osteoclasts have vacated the resorbed region of the bone, osteoblasts get in to replace the lost bone.

Factors Affecting Bone Growth and Bone Remodeling

Normal bone metabolism is influenced by a number of variables, such as bone remodelling among adults and development among children. These are adequate amounts of vitamins and minerals in the food, and a number of hormones.

- Minerals - Smaller contents of magnesium, fluoride, and manganese are needed in growth of the bones, but very high contents of calcium and phosphorus are needed. The minerals are also required during boneremodelling.
- Vitamins- Vitamin A activates osteoblast activity. The main protein of bone, the collagen, is produced with the assistance of vitamin C. Vitamin D as you will soon see helps in building up bone by increasing the uptake of calcium into the blood stream by the digestive system. Vitamins K and B12 are also needed to produce bone protein.
- The hormones - Insulin-like growth factors (IGFs), produced by both bone tissue and the liver, are the most important hormones in the growth of the bones in children. IGFs more than doubles the synthesis of the proteins that are involved in the formation of new bone, osteoblast stimulation, and cell proliferation in the periosteum and at the epiphyseal plate. IGFs stimulation is done in response to the secretion of growth hormone (GH) by the pituitary glands anterior lobe. The T3 and T4 hormones of the thyroid gland also help in the formation of new bone by the activation of the osteoblasts. Moreover, the pancreatic hormone insulin enhances the growth of bone proteins that subsequently activates the growth of bones.

The sex hormones released in puberty play a major role in bone formation. The production of estrogens is done by the ovaries and the production of the androgens is done by the testes such as testosterone. These are the sex hormones. There are low levels of androgens in females and low levels of estrogens in males although females have far higher levels of estrogens and males have much higher levels of androgens. The adrenal glands produce both sexes androgens, which may be turned into estrogens through other tissues such as adipose tissue. All these hormones cause increased osteoblast activity, bone extracellular matrix production, and the sudden growth spurt which occurs in adolescence.

Also, estrogens promote skeletal development that is typical of women such as an increased pelvis size. Lastly, the sex hormones of both sexes, especially estrogens, prevent the growth at the epiphyseal (growth) plates that prevent

the lengthening of the bones. Since males possess smaller amounts of estrogen than females, bone growth typically halts earlier in females due to the action of sex hormones during adulthood that promote deposition of new bone, and prevent the breakdown of old bone. One way oestrogens reduce resorption is osteoclast apoptosis or programmed death. There are also other hormones that may affect bone remodelling among them being parathyroid hormone, calcitriol (active form of vitamin D) and calcitonin as you will soon see in a moment. Moderate weight bear exercises provide sufficient dense load on the bones to sustain and increase the bone density.

Fracture and Repair of Bone

A fracture is any division in a bone. The degree of the fracture, where or what the fracture line is or what the doctor who first identified it used to call it can all have an impact on the naming of the fracture. A stress fracture is a series of minuscule bone cracks that do not show any signs of harm to the surrounding tissues. Intense exercises such as sprinting, jumping or aerobic dance when done repeatedly and intensely can lead to stress fracture in healthy individuals. Besides being highly painful, stress fractures are also brought about by diseases such as osteoporosis which disrupts normal bone calcification (explained in Disorders: Homeostatic Imbalances at the end of this chapter). Approximately 25 percent of all stress fractures are tibia stress fractures which can be seen on a bone scan, but not on normal x-ray images.The bone fracture repair process goes through the following stages:

- Phase of reactivity - This step is a primitive phase of inflammation. The vessels of the blood are torn as they cross the fracture line. The development of a mass of blood (it is usually clotted) that develops around the fracturing point as the blood oozes out of the torn ends of the arteries. This is known as a fracture hematoma, and it normally presents itself 6-8hours following the injuries. The cells of the bones surrounding the fracture hematoma are killed due to lack of blood circulation in the area. Swelling and inflammation of bone cells leads to increased cellular waste.The osteoclasts and phagocytes (macrophages and neutrophils) begin to remove the dead or damaged tissue within and surrounding the fracture hematoma. This period may last several weeks.

- Two things occur during the reparative phase - A fibrocartilaginous callus forms and a bony callus fills the gap. between the fractured end of the bones. When blood vessels dilate into the fracture hematoma, phagocytes begin to destroy dead bone. Periosteum

fibroblasts enter the fracture site forming collagen fibers. Also there is a development of periosteumcells and they begin forming fibrocartilage in this region. A fibrocartilaginous (soft) is a mass of healing tissue of collagen fibers and cartilage that fills the fractured ends of the bone. Thefibrocartilaginous callus is developed in about three weeks.

- Stage of repair - formation of the bone callus. Osteoprogenitor cells develop into osteoblasts in areas surrounding healthy and well-vascularized bone tissue and these cells begin to develop spongy bone.
- Trabeculae. The trabeculae bind the living and the dead part of the original bones. The fibrocartilage will eventually become spongy bone, where the callus is referred to as a bony (hard) callus. The bone callus takes approximately three or four months.
- Phase of bone remodeling - The final stage of the healing of fractures is bone remodeling in the callus. Progressively, Osteoclasts reabsorb the dead fragments of the original broken bone. SmallAround the edge of the fracture, the bone starts growing instead of the spongy bone.Sometimes, the mending process is so thorough that even a radiograph (x-ray) is unable to show the line of the fracture. However, there is still a fatter patch on the surface of the bone that is the evidence that the fracture is healed.

Bone's Role in Calcium Homeostasis

Bone contains the 99 percent of the calcium in the body making it the first level of calcium storage. One of the ways of maintaining the amount of calcium in the blood is the rate at which calcium is reabsorbed out of the bone into the blood. To optimally work, muscle as well as nerve cells demand a constant level of calcium ions (Ca^{2+}) in extracellular fluid. Blood coagulation also requires Ca^{2+}. Besides, Ca^{2+} is a cofactor, a supplementary substance needed to have an enzymatic reaction, with a number of enzymes. Due to this, the concentration of Ca^{2+} in blood plasma is highly regulated with a normal concentration of 9-11mg/100 ml with anything above this or below this leading to death of the patient (cardiac arrest) or the loss of breathing (respiratory arrest). To regulate the homeostasis of calcium, bone assists in the solution of the blood Ca^{2+} by using osteoclasts to release Ca^{2+} into blood plasma when it is low, and osteoblasts to take it up when it is high.

- Hormones regulate the trade of Ca^{2+} with parathyroid hormone (PTH) that is discharged by parathyroid gland being the most important. This hormone increases the concentration

of Ca2+ in the blood. The cyclic adenosine monophosphate mechanism is a negative feedback systemA substance known as cyclic adenosine monophosphate is generated in larger amounts by the parathyroid gland cells (receptors) in response to a stimulation that reduces the blood Ca2+ level. The PTH gene of a cell in the parathyroid gland (the control center) senses the intracellular increase of the cyclic AMP (the input). Consequently, an increase in PTH (the output) is released into the blood and PTH production is raised. An increase in PTH levels will hasten bone resorption by increasing the number and activity of osteoclasts, or eff ectors. The Ca2+ level in the blood is restored to normal through release of Ca2+ into the blood by the subsequent release of Ca2+ by the bone.

- PTH also influences the kidneys (effectors) to secrete less Ca2+ in their urine in order to hold more of it in circulation. Also, PTH stimulates the synthesis of calcitriol, which is the active form of vitamin D, a hormone that stimulates the uptake of calcium in food by the gastrointestinal tract into the blood. Also, the two processes lead to the rise of the blood Ca2+ levels. Another hormone decreases the blood Ca2+ level. When the blood Ca2+ level of the blood increases and reaches an abnormal level, the parafollicular cells in the thyroid gland secrete calcitonin (CT) (kal-si-TO-) into the blood. CT elevates bone uptake of Ca2+, accelerates bone deposition of Ca2+, and inhibits osteoclastic activity.Ultimately, CT reduces the level of blood Ca2+ and bone growth. Irrespective of these effects, it is not clear how CT will lead to the right calcium homeostasis since it may completely be absent and cause no effects at all. Nevertheless, a salmon derived drug known as Miacalcin is effective in the treatment of osteoporosis because it retards bone resorption.

Disorders: Homeostatic Imbalances

BONE SCAN

A bone scan is a diagnostic method, which makes use of the fact that bone is a living tissue. A radioactive tracer substance that is easily taken up by bone is injected in a small amount intravenously. The extent of absorption of the tracer is dependent on the blood flow to the bone. A radiation produced by the bones is then scanned by a measuring device (gamma camera), which is then translated into an image that is displayed on a monitor like an x-ray. The normal bone tissue takes the radioactive tracer in even amounts and hence it has the same Grayhue everywhere. Lighter and darker spots might indicate the presence of something wrong in the bones.Since there

is more blood flow, darker spots, also referred to as hot spots, absorb more of the radioactive tracer. The presence of hot spots may indicate aberrant bone growth, inappropriate fracture healing or bone malignancy. lighter areas or due to decreased blood flow, "cold spots," or less metabolic areas, take up less of the radioactive tracer. Cold spots may indicate degenerative bone disease, rheumatoid arthritis, fractures, bone infections, decalcified bone or Paget's disease. A bone scan subjects the patient to lesser amounts of radiation and is able to detect abnormalities three to six months before a normal x-ray method. A bone scan is considered to be the gold standard of assessing bone density, particularly where osteoporosis is suspected in a woman.

OSTEOPOROSIS

Osteoporosis -One in every ten million individuals in the US are afflicted with the disease, which literally means porous bones annually. More so, osteopenia or low bone mass exposes 18 million people to osteoporosis. The basic problem is that there is a greater deposition (building) of the bones than resorption (dissolution). It is largely brought about by the fact that the body excretes more calcium in the form of sweat, urine, and feces, than in consuming food. During mechanical stress of everyday living, the bone mass is diminished to the extent that the bones often fracture spontaneously. An example is that sitting down can easily lead to a hip fracture because of osteoporosis that affects over 1.5 million people every year in the US. Osteoporotic individuals are the entire skeleton. Besides fractures, osteoporosis causes bone soreness, stooped back, loss of height and shrinkage of the vertebra. Eighty percent of the persons with osteoporosis are women in their middle and old age. Estrogens and testosterone stimulate osteoblast activity and bone matrix formation (the fact that women have smaller bones and older men experience less testosterone, the main androgen, production) led to the fact that osteoporosis is more common in older women than in men. Other risk factors that contribute to osteoporosis besides gender include a family history of osteoporosis, being of European or Asian descent, having a thin or small body build, smoking cigarettes, poor lifestyle, low calcium and vitamin D intake in diet among others and taking more than two alcoholic beverages per day.

Diagnosis of osteoporosis is done by bone mineral density (BMD) test and family history. The bone density is assessed by BMD tests, which are carried out in the same manner as x-rays. They are also applicable in monitoring the outcomes of treatment, estimating bone loss rate and confirming an osteoporosis diagnosis. Also in the fairly recent utility exists is FRAX 4 which is an accurate estimation

of the risk of fractures based on non-bone mineral density risk factors. The data provided by the patients through online questionnaire are used to estimate the probability of the person experiencing a hip fracture or another major bone fracture in the spine, hip, or forearm within the next ten years due to osteoporosis by the FRAX -12. Osteoporosis can be treated in a number of ways. The body requires vitamin D in order to utilize calcium in terms of nutrition to reduce the risk of fracture. It is proved that a regularity of weight-bearing exercises can be helpful to maintain and even gain bone mass. Some of these exercises include walking, jogging, trekking, climbing stairs, playing tennis as well as dancing. Muscle mass and bone strength are also enhanced by resistance training such as weights lifting.

Two major types of drugs: (1) antireabsorptive drugs, which reduce the rate of bone loss, and (2) bone-building drugs, which encourage the bone to build new bone mass, are used to treat osteoporosis: (1) bisphosphonates, which inhibit osteoclasts (Fosamax 700 mg, Actonel 1000 mg, Boniva 1000 mg, and 1000 mg of calcitonin); (2) selective estrogen receptor modulators, which im ERT helps to preserve bone mass and develop it after menopause. Women who are on ERT are slightly at risk of stroke and blood clots. Moreover, HRT stimulates and maintains bone density.One of the drugs that develop bone is the parathyroid hormone (PTH) which stimulates osteoblasts to build new bone (Forteo 3). Others are being developed.

RICKETS AND OSTEOMALACIA

Osteomalacia and rickets are two forms of the same disease, which are caused by lack of sufficient calcification of the extracellular bone membrane, normally due to a deficiency of vitamin D. Rickets children develop soft or stretchy growing bones which are liable to destruction. The common ones are bowing legs and malformation of the skull, rib cage and pelvis, where the new bone formed at the epiphyseal (growth) plates fails to ossify.The adult counterpart to rickets is osteomalacia. Due to the inability of the new bone formed in remodeling to calcify, the individual experiences different levels of bone pain and discomfort especially in the hip and legs. Small trauma may also lead to bone fractures. To reduce the occurrence and treatment of osteomalacia and rickets, one should have enough vitamin D, which is exposure to moderate amounts of solar radiation.

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