FUNCTIONS OF THE SKELETAL SYSTEM
1. The skeletal system consists of bone, cartilage, ligaments (attach bone to another bone), and tendons (attach muscle to bone).

2. Functions.
   A. Support. Bone helps to maintain body shape.
   
   B. Protection. Various structures are encased in bone, e.g., brain (cranial vault), spinal cord (vertebral column), and the lungs and heart (thoracic cage).
   
   C. Movement. Bones and their associated joints make movement possible when acted upon by skeletal muscle.
   
   D. Storage.
   1) Excess minerals such as calcium and phosphate are removed from the blood and stored in bone. When mineral levels are low (e.g., in pregnancy), they are released from bone into the blood.
   
   2) Fat is stored within the cavities of bones.
   
   E. Blood cells production. Blood cells are produced within the cavities of bones.

CARTILAGE
Hyaline Cartilage
1. The three kinds of cartilage are hyaline cartilage, fibrocartilage, and elastic cartilage (see chapter 4).

2. Hyaline cartilage is the most abundant cartilage in the body. Examples include cartilage in joints, costal cartilage of the ribs, cartilage of the respiratory system, nasal cartilages, cartilage in growing bones, and the embryonic skeleton.

2. Structure.
   A. Cartilage is produced by cells called chondroblasts, which produce the cartilage matrix. When the chondroblasts are completely surrounded by matrix they are called chondrocytes. A chondrocyte is located in a space called the lacuna.
   
   B. The matrix contains collagen fibers, which provide strength, and proteoglycans, which trap water and make cartilage resilient (returning back to its original shape).
   
   C. Cartilage is surrounded by a membrane, the perichondrium, which consists of dense, irregular connective tissue. Blood vessels and nerves that supply the cartilage are found in the perichondrium, but there are no blood vessels in the cartilage itself. Therefore cartilage repairs slowly when damaged.
Explain why cartilage normally is found as thin sheets of tissue.

D. Articular cartilage is cartilage that covers the ends of bones in a joint. Articular cartilage does not have a perichondrium.

Explain why articular cartilage in joints does not have a perichondrium.

3. Cartilage growth.

**FIGURE 6.1**

A. **Appositional growth.** Chondroblasts in the perichondrium lay down new matrix, adding to the outside of the cartilage.
B. **Interstitial growth.** Chondrocytes within the cartilage divide and lay down new matrix.

![Cartilage](image)

**BONE**

**Bone Shape**

Bones can be classified as **long bones** (longer than wide), **short bones** (approximately same length and width), **flat bones** (thin, flat shape), and **irregular bones** (everything else).

**Structure of a Long Bone**

1. A long bone consists of a **diaphysis** (shaft) and the **epiphyses** (ends; singular epiphysis).
2. Two kinds of bone are present: **cancellous bone** in the epiphyses has many small spaces; **compact bone** in the diaphysis and the outer surface of the bone is denser than cancellous bone and has fewer spaces.
3. The diaphysis has an enlarged space called the **medullary cavity**.
4. The **periosteum** is a connective tissue membrane on the outer surface of the bone. It is the site of bone growth in diameter. The **endosteum** lines cavities within the bone. It can be a source of new bone during bone remodeling.
5. **Articular cartilage** covers the part of the epiphyses within joints.
6. The **epiphyseal plate** is hyaline cartilage within the epiphyses. It is the site of bone growth in length. After bone growth stops, the epiphyseal plate becomes bone and is called the **epiphyseal line**.
7. Spaces with bone are filled with **bone marrow**.

FIGURE 6.2

FIGURE 6.3

FIGURE 6.4
A. **Red marrow** is connective tissue where blood cells are produced. **Yellow marrow** is stored fat.

B. In children, red marrow is in cancellous bone and the medullary cavities of long bones.

C. In adults, some of the red marrow has been replaced with yellow marrow. The red marrow is in the cancellous bone of the trunk and proximal epiphyses of the limbs, and yellow marrow is in the skull and limbs.

☞ If you wanted to take a red marrow sample, where would be a good place?

**Structure of Flat, Short, and Irregular Bones**

FIGURE 6.5

1. Flat bones, short bones, and irregular bones are cancellous bone between two layers of compact bone.

2. There is no diaphysis, but some bones have short processes that have epiphyseal plates, e.g., vertebrae.

**BONE HISTOLOGY**

**Bone Matrix**

1. Bone matrix is 35% organic (primarily collagen fibers) and 65% inorganic mineral (primarily a calcium phosphate crystal called **hydroxyapatite**).

2. Flexible strength is provided by the collagen fibers. Weight-bearing strength is provided by the mineral component.

☞ In elderly persons, the proportion of collagen fibers to hydroxyapatite decreases. What effect does this have on the bone?
Bone Cells
1. **Osteoblasts** produce bone.

2. **Osteocytes** are osteoblasts that have become surrounded by bone matrix.

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**FIGURE 6.7**

A. The process of forming bone matrix is called **ossification** or **osteogenesis**. Osteoblast extend cell process that join the cell processes of other osteoblasts. Matrix is then produced.

B. Matrix formed around the cell body of the osteocyte results in a **lacuna** (a cavity) in which the osteocyte cell body is located. Matrix formed around the cell processes results in **canaliculi** (tiny canals) in which the cell processes are located.

**Why does bone have canaliculi, but cartilage does not?** (Hint: bone is a **dense**, **thick** tissue compared to cartilage)

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3. **Osteoclasts** breakdown bone.

**Origin of Bone Cells**
1. Mesenchyme forms stem cells, which have the ability to replicate and become more specialized types of cells. **Osteochondral progenitor cells** are stem cells that can become osteoblasts or chondroblasts.

2. Osteoblasts become osteocytes.

3. Osteoclasts are derived from stem cells in red bone marrow that also give rise to blood cells that become macrophages.

**WOVEN AND LAMELLAR BONE**
1. **Woven bone** has a matrix in which the collagen fibers are oriented in many different directions. It is first formed during fetal development or bone repair following a fracture.

2. In **bone remodeling**, osteoclasts break down woven bone and osteoblasts produce new bone in which the collagen fibers are organized parallel to each other, forming layers of bone called **lamellae**. This mature bone is called **lamellar bone**.
Which type of bone, woven bone or lamellar bone, is the most mechanically strong? Explain. (Hint: tendons and dermis of the skin)

CANCELLOUS AND COMPACT BONE
1. Depending on the amount of space within the tissue, woven bone and lamellar bone can be classified as cancellous or compact bone.

2. Cancellous bone has more space than bone matrix, whereas compact bone has more bone matrix than space.

3. The spaces are not empty in life. The spaces in cancellous and compact bone can be filled with blood vessels and loose connective tissue. In addition, the spaces in cancellous bone can contain red or yellow bone marrow.

Cancellous Bone

FIGURES 6.8 and 6.9

1. Trabeculae are beams of bone with spaces in-between. Cancellous bone is sometimes called spongy bone. The spaces are filled with blood vessels and marrow.

2. Most trabeculae are thin, consisting of several lamellae with osteocytes located between the lamellae. Osteoblasts on the surface of trabeculae can lay down new bone, and osteoclasts can break down the trabeculae.

3. Trabeculae are arranged along lines of stress, so even though the bone tissue is not completely solid, it is strong.

Compact Bone

FIGURE 6.10

1. The basic unit of compact bone is the osteon (haversian system) which consists of concentric lamellae surrounding a central canal containing blood vessels.
2. The outer surface of compact bone consists of **circumferential lamellae**.

3. **Interstitial lamellae** are remnants of older osteons and circumferential lamellae found between newer, functional osteons.

4. Route of delivery of materials to osteocytes: Blood vessel in periosteum - **perforating canal** (Volkmann's canal) - central canal - canaliculi - osteocyte.

Why does compact bone have osteons but cancellous bone does not?

**BONE DEVELOPMENT**

1. **Intramembranous** (within membrane) **ossification** involves the formation of a connective tissue membrane that is replaced by bone. Many skull bones and the diaphysis of the clavicle are formed by intramembranous ossification.

2. **Endochondral** (within cartilage) **ossification** involves the formation of a cartilage model that is replaced by bone. Bones of the base of the skull and most of the remaining bones of the trunk are formed by endochondral ossification.

3. Both types of ossification produce cancellous and compact bone.

4. The bone produced by both types of ossification is the same.

**Intramembranous Ossification**

**FIGURE 6.11**

1. A connective tissue membrane is formed by mesenchymal cells. The membrane consists of delicate collagen fibers.
2. Bone begins to be formed at **centers of ossification**. Osteochondral progenitor cells become osteoblasts and lay down bone along the fibers of the membrane, forming trabeculae.

![Image of Bone on collagen fiber]

3. The trabeculae grow together to form cancellous bone. Cells trapped in the cancellous bone space become red marrow. A periosteum forms outside the cancellous bone and produces a layer of compact bone around the cancellous bone.

![Image of Compact bone and Cancellous bone]

4. More and more membrane is replaced by cancellous and compact bone. The cancellous and compact bone is woven bone that is remodeled.

5. **Fontanels**, or soft spots, are portions of the membrane that have not ossified at birth.

**FIGURE 6.12**

**Endochondral Ossification**

**FIGURE 6.13**

You need to carefully look at each part of the illustration and understand the important events occurring at each step of the process. Pay attention to the colors.

1. A **cartilage model** is formed.

2. The perichondrium becomes the periosteum and a **bone collar** is formed. **Calcified cartilage** forms as chondrocytes hypertrophy (enlarge), the matrix is mineralized, and the chondrocytes die.

3. A **primary ossification center** forms (about the end of the second month) when blood vessels and osteoblasts from the periosteum invade the calcified cartilage and produce woven bone on the calcified matrix.
4. The cartilage model enlarges and the process of bone collar formation, cartilage calcification, and woven bone formation continues toward the epiphyses. Osteoclasts, from the periosteum are brought into the primary ossification center by blood vessels. The osteoclasts remove bone to form the medullary cavity. Remodeling converts woven bone to lamellar bone.

5. **Secondary ossification centers** form (about eight months to 18-20 years) in the epiphyses.

6. The original cartilage model is ossified except for the **epiphyseal plate** (site of future growth) and **articular cartilage** (smooth covering over the ends of bones).

7. In mature bone the epiphyseal plate becomes ossified to form the **epiphyseal line**. Except for the articular cartilage, all the cartilage in the bone is ossified.

**BONE GROWTH**

Unlike cartilage, which can grow by interstitial and appositional growth, bone can only growth by appositional growth, the formation of new bone on another surface such as cartilage or older bone. Explain why bone does cannot undergo interstitial growth.

**Growth in Bone Length**

1. Growth at the epiphyseal plate is responsible for the increase in length of long bones and bony processes.

2. The epiphyseal plate is a sequence of cells undergoing change. Like the strata of the epidermis, this continuum of cells can be subdivided into zones.
3. Growth at the epiphyseal plate involves two processes.
   A. The formation of cartilage by interstitial growth followed by calcification of the cartilage matrix.
      (1) The zone of resting cartilage is on the epiphyseal side of the epiphyseal plate and contains chondrocytes that do not often divide.

      (2) The zone of proliferation contains condrocytes that divide and form new matrix. Note that this is interstitial cartilage growth.

      (3) The zone of hypertrophy contains enlarged chondrocytes.

      (4) In the zone of calcification the matrix is calcified and the chondrocytes are dead. Note that zones 3 and 4 are the same steps that take place in endochondral ossification.

   B. Appositional growth of bone occurs as blood vessels grow into the calcified cartilage and osteoblasts lay down bone matrix on the calcified cartilage.

4. The growth of cartilage in the epiphyseal plate results in the increase in length. The formation of cartilage on the epiphyseal side of the epiphyseal plate occurs at the same rate as the formation of bone on the diaphyseal side of the plate. Therefore the thickness of the epiphyseal plate does not change.

5. The epiphyseal plate becomes the epiphyseal line (12 - 25 years of age depending on the bone) and growth of the bone in length stops.

**Growth at Articular Cartilage**

1. The area between the articular cartilage and the bone of the epiphyses is much like the epiphyseal plate.

2. Increase in the size of epiphyses results from interstitial cartilage growth followed by bone apposition. Short bones, which do not have epiphyseal plates, also increase in size by this process.
After bone growth ceases, why doesn’t the articular cartilage become ossified.

**Growth in Bone Width**
1. Bone growth in width (diameter) of long bones and bone growth in thickness of other bones occurs by appositional growth beneath the periosteum.

2. Osteochondral progenitor cells from the periosteum become osteoblasts and lay down new bone matrix.

3. Rapid bone growth in width (diameter) or thickness:

   ![Figure 6.17](image1)

   A. Osteoblast form bone ridges. The valley between the ridges is lined with periosteum and contains blood vessels.

   B. The ridges grow together to form a tunnel. What was the periosteum is now the endosteum because it is inside the bone.

   C. Through appositional growth, osteoblast lay down a layer of bone to form a concentric lamella.

   D. Additional concentric lamellae are formed, resulting in an osteon. Analogy: The concentric lamellae are like the growth rings in a tree, but they are formed in the opposite direction.

4. Slow bone growth in width (diameter) or thickness. Instead of ridges, a "flat" layer of bone is laid down to form a circumferential lamella.

**Factors Affecting Bone Growth**
1. The potential shape and size of an individual’s bones are genetically determined.

2. Nutrition and hormones modify the genetic potential.
Nutrition

1. **Vitamin D** is necessary for normal absorption of calcium from the small intestine.

   **Rickets** is a disease in children resulting from inadequate vitamin D. Bones become soft and bend, producing bowlegs and malformations of the chest, head, and pelvis. Explain why this occurs.

2. **Vitamin C** is necessary for normal collagen synthesis. Lack of vitamin C can result in **scurvy** in which the teeth fall out because the ligaments (dense, regular collagenous connective tissue) that hold the teeth in place break down.
Hormones
1. **Growth hormone** is produced by the pituitary gland in the brain.
   A. **Dwarfism** results from too little growth hormone as a child.
   
   B. **Giantism** results from too much growth hormone as a child.
   
   C. **Acromegaly** results from too much growth hormone as an adult.

   ✎ What symptoms would you expect to see in acromegaly? Explain.

2. **Sex hormones** (estrogen and testosterone) both stimulate bone growth and both cause the epiphyseal plate to become the epiphyseal line (estrogen causes earlier conversion than testosterone).

   ✎ Why do both males and females experience a spurt of growth at puberty? Why, on the average, are women shorter than men?

   ✎ Eunuchs are males who, as boys, were castrated. This procedure removes the testes, the site of testosterone production. Lack of testosterone results in lack of sex drive. A side effect of this procedure was a taller than average height in the eunuchs when they became adults. Explain how this occurs.
BONE REMODELING
1. **Bone remodeling** is the removal of bone by osteoclasts followed by the addition of new bone by osteoblasts.

2. The breakdown of concentric or circumferential lamellae by osteoclasts is sometimes incomplete and small parts of the lamellae remain and become interstitial lamellae.

3. Functions of bone remodeling.
   A. Bone repair (more later).
   B. Calcium ion regulation (more later)
   C. Bone growth and changes in bone shape.

   **FIGURE 6.18**

1) After bone is formed through endochondral growth in the epiphyseal plate or epiphyses it is remodeled to form cancellous or compact bone.

2) As the diaphysis of a bone increases in diameter as a result of appositional growth on the outside of the bone, osteoclasts remove bone from the medullary cavity. This increases the size of the medullary cavity and makes the bone lighter.

D. Bone remodeling allows bone to adjust to stress. Old bone is removed and new bone, i.e., new matrix is formed that is strongest along the lines of stress.

1) Increased stress increases osteoblast activity.

2) Decreased stress decreases osteoblast activity while having little affect on osteoclast activity.

Assume that two identical twins have identical breaks in the femur (thigh bone). If one is bedridden and the other has a walking cast, which twin's fracture heals faster? Explain.
Because astronauts are in a weightless environment their bones degenerate. Explain why. How can they try to prevent the bone degeneration from happening?

In Paget's disease, for unknown reasons the lamellar bone reverts to woven bone in which the bone fibers run randomly in all directions. What symptoms would you expect to observe?

BONE REPAIR

FIGURE 6.19

1. Following damage, blood vessels in the periosteum and the bone bleed and a hematoma (blood clot) is formed. The hematoma stops the bleeding and is a temporary, very weak bridge holding the broken bone together.

2. A callus is a mass of tissue that forms at a fracture site.
   A. The internal callus forms between the ends of the broken bone. It replaces the hematoma and is a stronger bridge holding the broken bone together.
   1) Blood vessels and cells from the periosteum and the endosteum invade the hematoma.

   2) The hematoma is removed by macrophages and dead bone is broken down by osteoclasts.

   3) The hematoma is replaced with a fibrous collagen network (produced by fibroblasts) containing islets of cartilage (produced by chondroblasts). Some bone is also formed by osteoblasts.

B. The external callus forms a collar around the broken bone. Osteoblast produce bone and chondroblasts produce cartilage.
3. In callus ossification, the collagen network and cartilage of the internal callus and the cartilage of the external callus are replaced by woven bone.

4. The woven bone is remodeled to become stronger lamellar bone. If the break is in the diaphysis, the internal callus is removed, reestablishing the medullary cavity.

CALCIUM HOMEOSTASIS

1. Blood calcium levels must be maintained because calcium is necessary for normal muscle and nerve function (more later this semester).

2. Osteoclasts and osteoblasts are involved in maintaining blood calcium levels.

   If osteoblast activity > osteoclast activity = Blood calcium levels decrease
   If osteoblast activity < osteoclast activity = Blood calcium levels increase

3. Parathyroid hormone (PTH) is produced by the parathyroid glands and increases blood calcium levels by indirectly stimulating osteoclast activity, increasing calcium reabsorption from urine, and promoting the formation of vitamin D, which increases calcium absorption from the small intestine.

   \[ \text{PTH} \uparrow, \text{blood Ca}^{2+} \uparrow \]

4. Calcitonin is produced by the thyroid glands and decreases blood calcium levels by inhibiting osteoclast activity.

   \[ \text{Calcitonin} \uparrow, \text{blood Ca}^{2+} \downarrow \]

5. Parathyroid hormone and calcitonin will be considered in greater detail with the endocrine system next semester.

PRACTICE PROBLEM

1. Osteoporosis is a disorder of bone tissue. There are two kinds of osteoporosis.
   A. Age-related osteoporosis affects women and men. Starting at age 35, humans start to lose bone mass at a rate of 0.3%-0.5% a year. The cause of age-related osteoporosis is unknown.

   B. Postmenopausal osteoporosis affects women 50 to 65 years of age. There can be a bone loss of 3%-5% a year, which is ten times higher than age-related bone loss. Postmenopausal osteoporosis is associated with decreased estrogen production at menopause. Estrogen inhibits the stimulatory effect of PTH on osteoclast activity.
2. In osteoporosis bone resorption (breakdown) is greater than bone formation. Osteoblast still produce collagen and calcium salts, but less than normal. Also, proportionately less collagen than normal compared to salt production.

If postmenopausal osteoporosis occurs in a bone, what does the bone look like?

Is the bone too brittle or too flexible? Explain.

If calcium absorption in the small intestine is below normal, what would you recommend to remedy the situation?

Can you suggest any other therapy that might be useful to treat osteoporosis?