BONE

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OUTLINES

- Functions of bone tissue
- Structure of bone
- Types of bone
- Osteogenesis
- Bone growth, remodeling & repair
- Joints
FUNCTIONS OF BONE TISSUE

1. It provides solid support for the body.
2. It protects vital organs such as those in the cranial and thoracic cavities.
3. It harbors cavities containing bone marrow where blood cells are formed.
4. It also serves as a reservoir of calcium, phosphate, and other ions.
5. Bones form a system of levers that multiply the forces generated during skeletal muscle contraction and transform them into bodily movements.
Bone is a specialized connective tissue composed of:

1. Calcified bone matrix, and
2. Three major cell types, namely osteoblasts, osteocytes & osteoclasts.

All bones are lined on both internal and external surfaces by layers of connective tissue containing osteogenic cells-
estosteum on the internal surface surrounding the marrow cavity and periosteum on the external surface.
FIGURE 8-1

(a) Section of humerus

(b) Compact bone

(c) Spongy bone

Diaphysis of humerus
Central canal
Perforating canals
Osteon
External circumferential lamellae
Perforating fibers
Interstitial lamellae
Cellular fibrous layer
Periosteum
Internal circumferential lamellae
Endosteum
Lamellae
Canalicular opening at surface
Canalicular opening at surface
Canaliculi
Nerve
Artery
Canaliculi
Central canal
Concentric lamellae
Lacuna
Osteocyte
Canaliculi
Osteoclast
Osteoclast
Osteocyte in lacuna
Space for bone marrow
Trabeculae
Trabeculae of spongy bone
Osteoblasts aligned along trabecula of new bone
Because bone is such a hard tissue, two methods are employed to prepare it for study.

1. **Decalcified sections:** can be prepared by decalcifying the bone in an acid solution to remove the calcium salts.
   - The tissue can then be embedded, sectioned, and routinely stained for study.
   - **Disadvantage:** osteocytes are distorted by the decalcifying acid bath.

2. **Ground sections:** are prepared by sawing the bone into thin slices, followed by grinding the sections with abrasives between glass plates.
   - When the section is sufficiently thin for study with light microscope, it is mounted for study.
   - **Disadvantage:** the cells are destroyed, and the lacunae and canaliculi are filled in with bone debris.
# BONE CELLS

<table>
<thead>
<tr>
<th>Osteoblasts</th>
<th>Osteocytes</th>
<th>Osteoclasts</th>
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</table>
| • Synthesize the organic components of the matrix. | • Found in lacunae between bone matrix layers.  
• Have cytoplasmic processes extending into small canaliculi between lamellae. | • Multinucleated, giant cells.  
• Involved in the resorption and remodeling of bone tissue. |
FIGURE 8-2
OSTEOBLASTS

- Osteoblasts synthesize and secrete the organic components of bone matrix (osteoid), which include:
  1. Type I collagen fibers.
  2. Proteoglycans.
  3. Several glycoproteins such as osteonectin.

- Viable osteoblasts are required for deposition of the inorganic components of bone.
OSTEOBLASTS (cont’d)

- Mature osteoblasts are located exclusively at the surfaces of bone matrix, usually side by side in a layer somewhat resembling a simple epithelium.
- When actively engaged in matrix synthesis, osteoblasts have a cuboidal to columnar shape and basophilic cytoplasm.
- When their synthesizing activity declines, they flatten and basophilia is reduced.
- Inactive osteoblasts represent most of the flattened bone lining cells in both the endosteum and periosteum.
OSTEOBLASTS (cont’d)

During matrix synthesis, osteoblasts have the ultrastructure of cells actively synthesizing proteins for secretion.
OSTEObLASTS (cont’d)

- Osteoblasts are polarized cells, producing a layer of new (but not yet calcified) material called osteoid between the osteoblast layer and the preexisting bone surface.

- This process of bone appositional growth is completed by subsequent deposition of calcium salts into the newly formed matrix.
From their ends adjacent to the matrix, osteoblasts secrete type I collagen, several glycoproteins, and proteoglycans.

Some of these factors, notably osteocalcin and certain glycoproteins, bind $\text{Ca}^{2+}$ with high affinity, thus raising the local concentration of these ions.

Osteoblasts also release very small membrane-enclosed matrix vesicles with which alkaline phosphatase and other enzymes are associated.

These enzymes hydrolyze $\text{PO}_4^-$ ions from various macromolecules, creating a high concentration of these ions locally.
OSTEOBLASTS (cont’d)

- The high ion concentrations cause calcified nanocrystals to form in and around the matrix vesicles.
- The crystals grow and mineralize further with formation of small growing masses of calcium hydroxyapatite \([\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2]\), which surround the collagen fibers and all other macromolecules.
- Eventually the masses of hydroxyapatite merge as a confluent solid bony matrix as calcification of the matrix is completed.
FIGURE 8-4

Osteoblasts release matrix vesicles

Released matrix vesicles and collagen fibers

Early mineralization around vesicles

Matrix becoming confluent between vesicles

Osteoblasts

Osteoid layer

Mineralized bone
1. **Primary bone tumor:**
   - Cancer originating directly from bone cells.
   - It is fairly uncommon (0.5% of all cancer deaths), although a cancer called **osteosarcoma** can arise in osteoprogenitor cells.

2. **Secondary bone tumors:**
   - The skeleton is often the site of secondary, metastatic tumors.
   - They arise when cancer cells move into bones via small blood or lymphatic vessels from malignancies in other organs, most commonly the breast, lung, prostate gland, kidney, or thyroid gland.
OSTEOCYTES

- As osteoblasts secrete the matrix, they become gradually surrounded by it and differentiate further as osteocytes.

- Osteocytes are enclosed singly within the lacunae that are regularly spaced throughout the mineralized matrix.

- In the transition from osteoblasts to osteocytes, the cells extend many long dendritic processes, which also become surrounded by calcifying matrix.

- Osteocytic processes thus come to occupy the many canaliculi, 250-300 nm in diameter, that radiate from each lacuna.
OSTEOCYTES (cont’d)

- **Diffusion of metabolites** between osteocytes and blood vessels occurs through the small amount of extracellular fluid between the bone matrix and the osteocytes and their processes.

- Osteocytes also communicate with one another via **gap junctions** on the dendritic processes in the canaliculi and on osteoblasts and bone lining cells.
When compared with osteoblasts, the flat, almond-shaped osteocytes exhibit significantly less RER, smaller Golgi complexes, and more condensed nuclear chromatin.
OSTEOCYTES (cont’d)

- These cells maintain the bony matrix, and their death is followed by rapid matrix resorption.

- Osteocytes express a different array of genes compared to osteoblasts, and osteocyte products such as the protein sclerostin and certain cytokines help regulate bone remodeling.

- The extensive lacunar-canalicular network of osteocytes and their communication with all other bone cells suggest additional roles for osteocytes in calcium homeostasis and as sensors for detection of mechanical stresses on bone, which is also important in directing bone remodeling.
The network of dendritic processes extending from osteocytes acts as a sensor detecting mechanical stresses on bone, monitoring areas within bones where loading has been increased or decreased, and maintaining the adjacent bone matrix accordingly.

Lack of exercise or the weightlessness experienced by astronauts leads to decreased bone density.
OSTEOCLASTS

- Osteoclasts are **very large, motile cells with multiple nuclei**.
- They play a major role in **matrix resorption** during bone growth and remodeling.
- The large size and multinucleated condition of osteoclasts are due to their origin from the fusion of **bone marrow–derived cells**.
- Osteoclast development requires **two polypeptides produced by osteoblasts**: macrophage-colony–stimulating factor (M-CSF) and the receptor activator of nuclear factor-κB ligand (RANKL).
OSTEOCLASTS (cont’d)

- In areas of bone undergoing resorption, osteoclasts lie within enzymatically etched cavities in the matrix known as resorption cavities (also called Howship lacunae).

- In active osteoclasts, the surface against the bone matrix is folded into irregular projections, forming a ruffled border surrounded by a cytoplasmic zone rich in actin filaments, which is the site of adhesion to the matrix.

- This circumferential adhesion zone creates a microenvironment between the osteoclast and the matrix in which bone resorption occurs.
FIGURE 8-6

Osteoclast

Bone matrix
OSTEOCLASTS (cont’d)

- Into this subcellular pocket the osteoclast secretes collagenase, cathepsin K, and other enzymes and pumps protons to produce an acidic environment locally for dissolving hydroxyapatite and promoting the localized digestion of matrix proteins.
- Osteoclast activity is controlled by local signaling factors and hormones.
- Osteoclasts have receptors for calcitonin.
- Osteoblasts activated by parathyroid hormone (PTH) produce M-CSF, RANKL, and other factors that regulate the formation and activity of osteoclasts.
**MEDICAL APPLICATION**

- **Osteopetrosis**, is a genetic disease characterized by dense, heavy bones ("marble bones").
- The osteoclasts lack ruffled borders and bone resorption is defective.
- This disorder results in overgrowth and thickening of bones, often with obliteration of the marrow cavities, depressing blood cell formation and causing anemia and the loss of white blood cells.
- The defective osteoclasts in most patients have mutations in genes for the cells’ proton-ATPase pumps or chloride channels.
Case courtesy of Dr Wael Nemattalla, Radiopaedia.org, rID: 7417
**Osteoporosis**, frequently found in **immobilized patients** and in **postmenopausal women**, is an **imbalance in skeletal turnover** so that bone resorption exceeds bone formation.

- This leads to **calcium loss from bones** and **reduced bone mineral density (BMD)**.
- Individuals at risk for osteoporosis are routinely tested for BMD by dual-energy x-ray absorptiometry (**DXA scans**).
1. **Inorganic matrix:**

- Represents about **50%** of the dry weight of bone matrix.

- **Calcium hydroxyapatite** is most abundant, but bicarbonate, citrate, magnesium, potassium, and sodium ions are also found.

- Significant quantities of **amorphous (non-crystalline) calcium phosphate** are also present.

- The surface ions of **hydroxyapatite crystals are hydrated**; the layer of water around the crystal facilitates the exchange of ions between the mineral and body fluids.
2. **Organic matrix:**

- It is embedded in the calcified matrix & includes **type I collagen**, **proteoglycan aggregates**, and **bone specific multiadhesive glycoproteins** such as **osteonectin**.

- Calcium-binding glycoproteins, notably **osteocalcin**, and the **phosphatases** released in matrix vesicles by osteoblasts promote calcification of the matrix.

- Other tissues containing type I collagen do not contain osteocalcin or matrix vesicles and are not normally calcified.
Because of its high collagen content, decalcified bone matrix is usually acidophilic.

The association of minerals with collagen fibers during calcification is responsible for the hardness and resistance of bone tissue.

After a bone is decalcified, its shape is preserved, but it becomes as flexible as a tendon.
1. The periosteum:

- Is a **double-layered** tissue with bone-forming cells covering the external surface of bone.

- **The outer layer** is **dense connective tissue**, with small blood vessels, collagen bundles, and fibroblasts.

- Bundles of periosteal collagen fibers, called **perforating (or sharpey) fibers**, penetrate the bone matrix, binding the periosteum to bone.

- **The inner layer** of periosteum is a **more cellular** layer containing bone lining cells, **osteoblasts**, and mesenchymal stem cells called **osteoprogenitor cells**.
PERIOSTEUM & ENDOSTEUM (cont’d)

- Osteoprogenitor cells play a prominent role in bone growth and in bone repair, as they have the potential to proliferate and differentiate into osteoblasts.

- The principal functions of periosteum are to nourish the osseous tissue and provide a continuous supply of new osteoblasts for appositional bone growth or repair.

2. The Endosteum:

- It covers small trabeculae of bony matrix that project into the marrow cavities.

- Endosteum is a connective tissue composed of a monolayer of osteoprogenitor cells and osteoblasts.
FIGURE 8-3

- Osteoblast
- Osteoclast
- Osteocyte
- Mesenchyme
- Bone matrix
- Newly formed matrix (osteoid)
Grossly, cross section shows two bone types:

1. **Compact (cortical) bone**: a dense area near the surface & represents 80% of the total bone mass.

2. **Cancellous (trabecular or spongy) bone**: deeper areas with numerous interconnecting cavities, constituting about 20% of total bone mass.
The distribution of compact & cancellous bones:

- **In long bones**, the epiphyses are composed of spongy bone covered by a thin layer of compact bone.
- The diaphysis is almost totally composed of compact bone, with a thin region of spongy bone on the inner surface around the central marrow cavity.
- **Short bones** usually have cores of spongy bone surrounded completely by compact bone.
- **The flat bones** have two layers of compact bone called plates, separated by a thicker layer of spongy bone called the diploë.
Microscopic examination of bone tissue shows two types of organization:

1. **Lamellar bone**: mature bone.

2. **Woven bone**: which is usually more immature than lamellar bone.
I. LAMELLAR BONE

- **Most bone in adults**, compact or cancellous, is organized as lamellar bone, characterized by **multiple layers or lamellae of calcified matrix**, each 3-7 μm thick.

- The lamellae are organized either **parallel to each other** or **concentrically around a central canal**.

- In each lamella, **type I collagen fibers are aligned in parallel**, with the pitch of the fibers’ orientation shifted orthogonally (by about 90 degrees) in successive lamellae.

- This highly ordered organization of collagen within lamellar bone is **visible under the polarizing light microscope** as birefringence; **alternating bright and dark layers** are due to the changing orientation of collagen fibers in the lamellae.
Bone Lamellae

- Osteon
- Interstitial Lamellae
- Circumferential Lamellae
An osteon (or Haversian system) refers to the complex of concentric lamellae surrounding a small central canal that contains blood vessels, nerves, loose connective tissue, and endosteum.

Between successive lamellae are lacunae, each with one osteocyte, interconnected by canaliculi containing the cells’ dendritic processes.

Processes of adjacent cells are in contact via gap junctions, and all cells of an osteon receive nutrients and oxygen from the microvasculature in the central canal.

The outer boundary of each osteon is a more collagen-rich layer called the cement line.
OSTEON (HAVERSIAN SYSTEM) cont’d

- Each osteon is a long, sometimes bifurcated, cylinder generally parallel to the long axis of the diaphysis.
- It consists of a central canal surrounded by 4-10 concentric lamellae.
- The central canals communicate with the marrow cavity and the periosteum and with one another through transverse perforating canals (or Volkmann canals).
- The transverse canals have few, if any, concentric lamellae.
- All central osteonic canals and perforating canals come into existence when matrix is laid down around areas with preexisting blood vessels.
**INTERSTITIAL LAMELLAE**

- **Interstitial lamellae** are numerous irregularly shaped groups of parallel lamellae, scattered among the intact osteons.

- These structures are lamellae remaining from osteons partially destroyed by osteoclasts during growth and remodeling of bone.
CIRCUMFERENTIAL LAMELLAE

- In compact bone (e.g., the diaphysis of long bones) besides forming osteons, the lamellae also exhibit a typical organization consisting of multiple external circumferential lamellae and often some inner circumferential lamellae.

- **Inner circumferential lamellae** are located around the marrow cavity.

- **External circumferential lamellae** are located immediately beneath the periosteum.
FIGURE 8-1

(a) Section of humerus

Diaphysis of humerus

Central canal

Osteon

External circumferential lamellae

Perforating fibers

Perforating canals

Central canal

(b) Compact bone

Concentric lamellae

Nerve

Artery

Canaliculi

Internal circumferential lamellae

Interstitial lamellae

Lacuna

Osteocyte

Canaliculi

Inner circumferential lamellae

Trabeculae of spongy bone

(c) Spongy bone

Space for bone marrow

Trabeculae

Canaliculi opening at surface

Osteoclast

Osteoblasts aligned along trabecula of new bone

Canaliculi opening at surface

Endosteum

Osteocyte in lacuna
Bone remodeling is continuous throughout life and involves a process of bone resorption and bone formation.

In compact bone, remodeling resorbs parts of old osteons and produces new ones.

Osteoclasts often work in groups to remove old bone in tunnel-like cavities having the approximate diameter of new osteons.
Such tunnels are quickly invaded by many osteoprogenitor cells from the endosteum or periosteum and sprouting loops of capillaries.

Osteoblasts develop, line the wall of the tunnels, and begin to secrete osteoid in a cyclic manner, forming the concentric lamellae of bone with trapped osteocytes.

In healthy adults 5%-10% of the bone turns over annually.
FIGURE 8-11

Old bone

Osteoclasts tunneling into old bone

Osteoblast

Endothelial cell

Mesenchymal cell

Growing capillary

Newly calcified bone

Osteoid

Lacunae with osteocytes

Quiescent osteoblast

Cutting cone

Reversal zone

Closing cone
FIGURE 8-11

- Forming resorption cavity
- Resorption cavity
- Closing osteon
- Osteon
2. WOVEN BONE

- Woven bone is non-lamellar and characterized by random disposition of type I collagen fibers and is the first bone tissue to appear in embryonic development and in fracture repair.

- Woven bone tissue is usually temporary and is replaced in adults by lamellar bone, except in a very few places in the body, for example, near the sutures of the calvaria and in the insertions of some tendons.

- This type of bone has a lower mineral content (it is more easily penetrated by x-rays) and often a higher proportion of osteocytes than mature lamellar bone.

- These features reflect the fact that woven bone forms more quickly but has less strength than lamellar bone.
### TABLE 8–1  Summary of bone types and their organization.

<table>
<thead>
<tr>
<th>Type of Bone</th>
<th>Histological Features</th>
<th>Major Locations</th>
<th>Synonyms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Woven bone, newly calcified</td>
<td>Irregular and random arrangement of cells and collagen; lightly calcified</td>
<td>Developing and growing bones; hard callus of bone fractures</td>
<td>Immature bone; primary bone; bundle bone</td>
</tr>
<tr>
<td>Lamellar bone, remodeled from woven bone</td>
<td>Parallel bundles of collagen in thin layers (lamellae), with regularly spaced cells between; heavily calcified</td>
<td>All normal regions of adult bone</td>
<td>Mature bone; secondary bone</td>
</tr>
<tr>
<td>Compact bone, ~80% of all lamellar bone</td>
<td>Parallel lamellae or densely packed osteons, with interstitial lamellae</td>
<td>Thick, outer region (beneath periosteum) of bones</td>
<td>Cortical bone</td>
</tr>
<tr>
<td>Cancellous bone, ~20% of all lamellar bone</td>
<td>Interconnected thin spicules or trabeculae covered by endosteum</td>
<td>Inner region of bones, adjacent to marrow cavities</td>
<td>Spongy bone; trabecular bone; medullary bone</td>
</tr>
</tbody>
</table>
Bone development or osteogenesis occurs by one of two processes:

1. **Intramembranous ossification**, in which osteoblasts differentiate directly from mesenchyme and begin secreting osteoid.

2. **Endochondral ossification**, in which a preexisting matrix of hyaline cartilage is eroded and invaded by osteoblasts, which then begin osteoid production.

- The bone forms initially; in both processes, is **temporary woven bone**, which is **soon replaced by stronger lamellar bone**.
- During growth of all bones, areas of woven bone, areas of bone resorption, and areas of lamellar bone all exist contiguous to one another.
Osteogenesis imperfecta, or “brittle bone disease,” refers to a group of related congenital disorders in which the osteoblasts produce deficient amounts of type I collagen or defective type I collagen due to genetic mutations.

Such defects lead to significant fragility of the bones.
I. INTRAMEMBRANOUS OSSIFICATION

- Intramembranous ossification, is so called because it takes place within condensations ("membranes") of embryonic mesenchymal tissue.

- Most flat bones begin to form by this type of ossification e.g., the frontal and parietal bones of the skull, parts of the occipital and temporal bones and the mandible and maxilla.
I. INTRAMEMBRANOUS OSSIFICATION

- The starting points for bone formation within the mesenchyme are called **ossification centers**.

- In these areas **mesenchymal cells differentiate into osteoprogenitor cells** which proliferate and form incomplete layers of osteoblasts around a network of developing capillaries.

- The polarized **osteoblasts secrete the osteoid** components from their surfaces facing away from these blood vessels, that **later calcify** and form trabeculae of **woven bone**.
I. INTRAMEMBRANOUS OSSIFICATION

- Differentiating osteocytes now enclosed within lacunae retain intercellular contacts via their cytoplasmic processes within canaliculi.

- Continued matrix secretion, calcification, and trabecular growth lead slowly to the fusion of neighboring ossification centers and gradually produce layers of compact bone that broadly enclose a region of cancellous bone with marrow and larger blood vessels.
1. INTRAMEMBRANOUS OSSIFICATION

- In cranial flat bones, bone formation predominates over bone resorption at both the internal and external surfaces.

- Thus, two layers of compact bone (internal and external plates) arise, while the central portion (diploë) maintains its cancellous, spongy nature.

- The fontanelles or “soft spots” on the heads of newborn infants are areas in the skull that correspond to parts of the connective tissue that are not yet ossified.

- Regions of the connective tissue that do not undergo ossification give rise to the endosteum and the periosteum of the new bone.
2. ENDOCHONDRAL OSSIFICATION

- Endochondral ossification takes place within a piece of hyaline cartilage whose shape resembles a small version, or model, of the bone to be formed.

- This type of ossification is principally responsible for initiating most bones of the body and is especially well studied in developing long bones.

- The first bone tissue appears as a collar surrounding the diaphysis of the cartilage model.
FIGURE 8-14

1. Fetal hyaline cartilage model develops.
2. Cartilage calcifies, and a periosteal bone collar forms around diaphysis.
3. Primary ossification center forms in the diaphysis.
4. Secondary ossification centers form in epiphyses.
5. Bone replaces cartilage, except the articular cartilage and epiphyseal plates.
6. Epiphyseal plates ossify and form epiphyseal lines.
2. ENDOCHONDRAL OSSIFICATION

- This bone collar is produced by osteoblasts that form within the surrounding perichondrium.
- The collar impedes diffusion of oxygen and nutrients into the underlying cartilage, promoting its degeneration.
- The chondrocytes begin to produce alkaline phosphatase and hypertrophy, enlarging their lacunae.
- These changes both compress the matrix into narrow trabeculae and lead to calcification in these structures.
- Death of the chondrocytes creates a porous structure consisting of calcified cartilage remnants which become covered by a layer of osteoblasts.
2. ENDOCHONDRAL OSSIFICATION

- **Blood vessels** from the perichondrium (now the periosteum) penetrate through the bone collar, bringing **osteoprogenitor cells** to the porous central region.

- Next, osteoblasts adhere to the remnants of calcified cartilage matrix and produce **woven bone**.

- The **calcified cartilage** at this stage appears **basophilic**, and the **new bone** is more **acidophilic**.

- This process in the **diaphysis** forms the **primary ossification center**, beginning in many bones as early as the **fist trimester**.
2. ENDOCHONDRAL OSSIFICATION

- Secondary ossification centers appear later at the epiphyses of the cartilage model.

- During their expansion and remodeling, the primary and secondary ossification centers produce cavities that are gradually filled with bone marrow and trabeculae of cancellous bone.

- With the primary and secondary ossification centers, two regions of cartilage remain:
  1. Articular cartilage covering the articular surfaces in joints.
  2. Epiphyseal cartilage: between the epiphysis and the diaphysis, responsible for elongation of bone till the age of 20, where it is closed and transformed into epiphyseal line.
FIGURE 8-16

a X-ray of a hand

Epiphyses
Diaphysis

Epiphyses
Diaphyses

Epiphyseal plates
Epiphyseal plates
2. ENDOCHONDRAL OSSIFICATION

- An epiphyseal growth plate shows five distinct zones of cellular activity, starting from the thin region of normal cartilage:

1. The resting zone consists of hyaline cartilage with typical chondrocytes.

2. In the proliferative zone, chondrocytes begin to divide rapidly and form columns of stacked cells parallel to the long axis of the bone.

3. The hypertrophic cartilage zone contains swollen, degenerative chondrocytes whose cytoplasm has accumulated glycogen. This hypertrophy compresses the matrix into thin septa between the chondrocytes.
FIGURE 8-16

b Epiphyseal plate

| Zone 1: Zone of resting cartilage |
| Zone 2: Zone of proliferating cartilage |
| Zone 3: Zone of hypertrophic cartilage |
| Zone 4: Zone of calcified cartilage |
| Zone 5: Zone of ossification |
2. ENDOCHONDRAL OSSIFICATION

4. In the calcified cartilage zone, loss of the chondrocytes by apoptosis is accompanied by calcification of the septa of cartilage matrix by the formation of hydroxyapatite crystals.

5. In the ossification zone, bone tissue first appears.

   Capillaries and osteoprogenitor cells originally from the periosteum invade the cavities left by the chondrocytes.

   Many of these cavities will be merged and become the marrow cavity.

   Osteoblasts settle in a layer over the septa of calcified cartilage matrix and secrete osteoid over these structures, forming woven bone.
FIGURE 8-16

Zone 1: Zone of resting cartilage

Zone 2: Zone of proliferating cartilage

Zone 3: Zone of hypertrophic cartilage

Zone 4: Zone of calcified cartilage

Zone 5: Zone of ossification

b Epiphyseal plate
Calcium deficiency in children can lead to rickets, a disease in which the bone matrix does not calcify normally and the epiphyseal plate can become distorted by the normal strains of body weight and muscular activity.

Ossification processes are consequently impeded, which causes bones to grow more slowly and often become deformed.

The deficiency can be due either to insufficient calcium in the diet or a failure to produce the steroid prohormone vitamin D, which is important for the absorption of Ca²⁺ by cells of the small intestine.

In adults, calcium deficiency can give rise to osteomalacia (osteon + gr. malakia, softness), characterized by deficient calcification of recently formed bone and partial decalcification of already calcified matrix.
BONE GROWTH, REMODELING, & REPAIR

- Osteogenesis and bone growth involves the partial resorption of old bone tissue, while simultaneously forming new bone at a rate exceeding that of bone removal.

- The rate of bone turnover is very active in young children, where it can be 200 times faster than that of adults.

- The constant remodeling of bone ensures that, despite its hardness, this tissue remains plastic and capable of adapting its internal structural in the face of changing stresses.

- A well known example of bone plasticity is the ability to modify the positions of teeth by the lateral pressures produced by orthodontic appliances.
Bone forms on the side where traction is applied and is resorbed on the opposite side where pressure is exerted.

In this way, teeth are moved within the jaw while the bone is being remodeled.

Cranial bones grow mainly because of the formation of bone tissue by the periosteum between the sutures and on the external bone surface.

At the same time, resorption takes place on the internal surface.

The plasticity of bone allows it to respond to the growth of the brain and form a skull of adequate size.

The skull is small if the brain does not develop completely and larger than normal in a person with hydrocephalus.
Because it contains **osteoprogenitor stem cells** in the periosteum, endosteum, and marrow and is very **well vascularized**, bone normally has an excellent capacity for repair.
Bone fractures are repaired through fibrocartilage formation and osteogenic activity of the major bone cells.

Bone fractures disrupt blood vessels, causing bone cells near the break to die.

The damaged blood vessels produce a localized hemorrhage or hematoma.

Clotted blood & tissue debris is removed by macrophages and damaged bone is resorbed by osteoclasts.

The periosteum and the endosteum produce a soft callus of fibrocartilage-like tissue that surrounds the fracture and covers the extremities of the fractured bone.
The fibrocartilaginous callus is gradually replaced in a process of combined endochondral and intramembranous ossification.

This produces a hard callus of woven bone around the fractured ends of bone.

Stresses imposed on the bone during repair and during the patient’s gradual return to activity serve to remodel the bone callus.

The immature, woven bone of the callus is gradually resorbed and replaced by lamellar bone, thus restoring the original bone structure.
(a) A fracture hematoma forms.

(b) A fibrocartilaginous (soft) callus forms.

(c) A hard (bony) callus forms.

(d) The bone is remodeled.
MEDICAL APPLICATION

- PTH, calcitonin, and several other hormones act on bone.
- The anterior pituitary synthesizes growth hormone, which stimulates the liver to produce insulin-like growth factor-1 (IGF-1).
- IGF has a growth-promoting effect, especially on the epiphyseal cartilage.
- Consequently, lack of growth hormone during the growing years causes pituitary dwarfism; an excess of growth hormone causes excessive growth of the long bones, resulting in gigantism.
- Adult bones cannot increase in length even with excess IGF because they lack epiphyseal cartilage, but they do increase in width by periosteal growth.
- In adults, an increase in GH causes acromegaly, a disease in which the bones—mainly the long ones—become very thick.
Joints are regions where adjacent bones are capped and held together firmly by connective tissues.

The type of joint determines the degree of movement between the bones.

Those that are closely bound together with only a minimum of movement between them are called synarthroses.

Joints in which the bones are free to articulate over a fairly wide range of motion are classified as diarthroses.
There are three types of synarthrosis joints according to the tissue making up the union:

1. **Synostosis**: There is no movement, and joint-uniting tissue is bone (e.g., skull bones in adults).

2. **Synchondrosis**: There is little movement, and joint-uniting tissue is hyaline cartilage (e.g., joint of first rib and sternum).

3. **Syndesmosis**: There is little movement, and bones are joined by fibrocartilage (e.g., pubic symphysis).
**JOINTS (cont’d)**

- **Diarthroses** such as the elbow and knee generally unite long bones and allow great mobility.

- In a diarthrosis, *ligaments* and a *capsule* of dense connective tissue maintain proper alignment of the bones.

- The capsule encloses a sealed *joint cavity* that contains *synovial fluid*, a clear, viscous liquid.

- The joint cavity is lined by a specialized connective tissue called the *synovial membrane* that extends folds and villi into the cavity and secretes the lubricant *synovial fluid*.
a Typical synovial joint

- Periosteum
- Yellow bone marrow
- Fibrous layer
- Synovial membrane
- Articular capsule
- Joint cavity (containing synovial fluid)
- Articular cartilage
- Ligament
• **Synovial fluid** is derived from blood plasma, but with a high concentration of **hyaluronan** produced by cells of the synovial membrane.

• In different diarthrotic joints the **synovial membrane** may have prominent regions with dense connective tissue or fat.

• However the **tissue’s surface** region is usually **well vascularized**, with many porous (fenestrated) capillaries.
The synovial membrane contains cells of connective tissue proper and a changing population of leukocytes, is characterized by two specialized cells with distinctly different functions and origins:

1. Macrophage-like synovial cells, also called type A cells.
2. Fibroblastic synovial cells, or type B cells.
JOINTS (cont’d)

1. Type A cells:
   - Are modified macrophages derived from blood monocytes and remove wear-and-tear debris from the synovial fluid.
   - These cells represent approximately 25% of the cells lining the synovium, are important in regulating inflammatory events within diarthrotic joints.

2. Type B cells:
   - Produce abundant hyaluronan and other extracellular components.
   - Much of this material is transported by water from the capillaries into the synovial fluid, which lubricates the joint, reducing friction on all internal surfaces, and supplies nutrients and oxygen to the articular cartilage.
FIGURE 8-20

- Macrophage-like type A cell
- Ground substance
- Fibroblast-like type B cell
- Fenestrated blood capillary
- Collagen fibrils
- Fibroblast
In the hyaline articular cartilage, collagen fibers are disposed as arches with their tops near the exposed surface, which is not covered by perichondrium.

This arrangement of collagen helps distribute the forces generated by pressure on joints.

The resilient articular cartilage is also an efficient absorber of the intermittent mechanical pressures.
In **rheumatoid arthritis**, chronic inflammation of the synovial membrane causes its thickening and stimulates the macrophages to release collagenases and other hydrolytic enzymes.

Such enzymes eventually cause **destruction of the articular cartilage**, allowing direct contact of the bones projecting into the joint.
JOINTS (cont’d)

- **Intervertebral discs:**
  - They are thick discs of fibrocartilage between successive vertebral bodies.
  - These joints facilitate movements of the vertebral column.
  - **The disc is composed of two parts:**
    1. **The annulus fibrosus:** has an external layer of dense connective tissue but is mainly composed of overlapping laminae of fibrocartilage in which collagen bundles are orthogonally arranged in adjacent layers.
    - The multiple lamellae provide the disc with unusual resilience and enable it to withstand pressures generated by the vertebrae.
2. The **nucleus pulposus**: is situated in the center of the annulus fibrosus and allows each disc to function as a shock absorber within the vertebral column.

- It typically contains scattered, vacuolated cells (the only cells derived from the embryonic notochord), but it is largely composed of water in a gel-like matrix rich in hyaluronan and fibers of **type II collagen**.

- The nucleus pulposus is large in children, but these structures gradually become smaller with age and are partially replaced by fibrocartilage.
Within an intervertebral disc, collagen loss or other degenerative changes in the annulus fibrosus are often accompanied by displacement of the nucleus pulposus, a condition variously called a slipped or herniated disc.

This occurs most frequently on the posterior region of the intervertebral disc where there are fewer collagen bundles.

The affected disc frequently dislocates or shifts slightly from its normal position.

If it moves toward nerve plexuses, it can compress the nerves and result in severe pain and other neurologic disturbances.

The pain accompanying a slipped disc may be perceived in areas innervated by the compressed nerve fibers—usually the lower lumbar region.
Thank You