Cartilage
DANIL
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**Chrondrocyte**

- are the only cells found in healthy cartilage.
- They produce and maintain the cartilaginous matrix, which consists mainly of collagen and proteoglycans.
Skeletal Cartilage

- Contains **no blood vessels or nerves**
- **Surrounded by the perichondrium** (dense irregular connective tissue) that resists outward expansion
- **Three types** –
  - hyaline
  - elastic
  - fibrocartilage
Types of Cartilage

- **Hyaline**
  - **Smooth** (but not totally flat!), bluish color
  - **Articular cartilage** and Cartilaginous Endplate
  - Larynx, trachea, bronchi, ribs, articular surface of bones
  - – Epiphyseal plate

- **Elastic**
  - More flexible than hyaline
  - Epiglottis, external ear
  - Elastic fibers for resiliency

- **Fibrocartilage**
  - Fibrous tissues
  - Annulus Fibrosus (intervertebral discs), Meniscus, pubic symphysis
  - Type I collagen fibers for tensile strength, frictional forces
  - Between cartilage and connective tissue –,
Hyaline Cartilage

- Provides support, flexibility, and resilience
- Is the most abundant skeletal cartilage
- Is present in these cartilages:
  - **Articular** – covers the ends of long bones
  - **Costal** – connects the ribs to the sternum
  - **Respiratory** – makes up larynx, reinforces air passages
  - **Nasal** – supports the nose

la = lacuna (chondrocytes shrunken or lost as artifact of slide preparation)
c = chondrocyte
Articular Cartilage is a specialised form of hyaline cartilage. It transforms the articulating ends of the bones into lubricated, wear-proof, slightly compressible surfaces, which exhibit very little friction.

It is not surrounded by a perichondrium and is partly vascularised.

It is, depending on the arrangement of chondrocytes and collagenous fibres, divided into several zones:
**Hyaline Cartilage**

**Matrix** (amorphous & glassy)

- hyaluronic acid
- chondroitin sulfate
- keratin sulfate
- H₂O (60-78%)

**Fibers** - collagenous

(invisible due to same refractive index as matrix)

**Typical Locations**

- intercostals (connect ribs to the sternum)
- wall of trachea & bronchii
- articular cartilage of bone
- epiphyseal plate
- fetal axial skeleton

[Image of Hyaline Cartilage with labeled parts: chondrocyte nucleus, matrix, lacuna]

[Image of Hyaline Cartilage (SEM)]
Elastic Cartilage

- Similar to hyaline cartilage, but contains elastic fibers
- Found in the external ear and the epiglottis
Elastic Cartilage

Matrix
- hyaluronic acid
- chondroitin sulfate
- keratin sulfate

Fibers
- elastic (elastin)

Typical Locations
- external ear
- walls of external auditory canal and eustachian tubes
- epiglottis & larynx
- bridge of nose

Properties
- resiliency and pliability
Fibrocartilage

- Highly compressed with great tensile strength
- Contains collagen fibers type I in addition to type II
- Found in menisci of the knee and in intervertebral discs, TMJ, Pubic symphysis
Fibrous Cartilage H&E

fibrous matrix

chondrocytes

Fibrous Cartilage H&E

chondrocytes

fibrous matrix
Fibrocartilage, intervertebral disc

- Cortex
- Rows of chondrocytes
- Lacunae
- Medulla
- Intervereval disc, H&E 400x

Collagen (periosteum)

- Fibrocartilage
- Bone

The pubic symphysis with its fibrocartilagenous joint
Fibrocartilage

Matrix
- hyaluronic acid
- chondroitin sulfate
- keratin sulfate

Fibers
- dense collagenous bundles

Typical Locations
- intervertebral discs
- pubic symphysis
- meniscus of knee joint
- attach tendons to bone

Properties
- resistance to compression and shear forces

Fibrocartilage- longitudinal section

Fibrocartilage- transverse section

Fibrocartilage- SEM
Cartilage

Properties of Cartilage

1. Avascular
2. Permeable
   (conducts nutrients and water)
3. Flexible but Weight-Bearing
   (resistance to compression)
4. Elasticity and Resiliency
5. Resistance to Shear Forces
6. Slippery
   (low friction at articular joints)
7. Poor Regenerative Capacity
Bones and Cartilages of the Human Body

Figure 6.1

Key:
- Brown = Bones of axial skeleton
- Yellow = Bones of appendicular skeleton
- Blue = Hyaline cartilages
- Green = Elastic cartilages
- Red = Fibrocartilages
Distribution of The Various Types Of Cartilage

**Hyaline Cartilage**
- Most bones of the embryonic skeleton
- Articular cartilage (synovial jt)
- Epiphyseal Plate
- Costal Cartilage
- Xiphoid process
- Nasal Cartilages
- Most Laryngeal Cartilages
- Tracheal Ring Cartilages
- Cartilage plates in large and medium bronchi

**Elastic Cartilage**
- Pinna
- External Auditory tube
- Eustachian Tube
- Epiglottis
- Laryngeal Cartilages (2)
- Cartilage plates in small bronchi

**Fibrocartilage**
- Symphyses
- - Intervertebral disks
- - Pubic symphysis
- - Menisci
GENERAL CHARACTERISTICS OF CARTILAGE

- Growth: appositional and interstitial
- Perichondrium
  - Two layers:
    - Outer fibrous (type 1 collagen)
    - Inner chondrogenic (appositional growth)
  - Not found in articular cartilage and fibrocartilage
- Cells = chondrogenic cells, chondroblasts, and chondrocytes
- Matrix (ground substance and collagen)
  - Territorial matrix, rich in GAG’s = basophilic, surrounds
  - lacunae (also called “capsular” matrix)
  - Interterritorial matrix, less basophilic
  - Matrix binds water (negatively charged GAG’s attract Na+, H2O)
  - follows); resistant to compression
- Avascular (nourished by diffusion)
Components of Cartilage

- Water
  - 70%
- Collagen Type II, IX, XI
  - 10-20%
  - Tensile strength
  - Shear strength
- Proteoglycans
  - 5-10%
  - Compressive strength
- Chondrocytes
  - Cells ~5%
  - Maintenance of tissue
Collagen Types

Major type of collagen in articular cartilage (~80%)

Stabilizes and forms core of the collagen type II fibril

<table>
<thead>
<tr>
<th>Collagen Type</th>
<th>Molecular Structure*</th>
<th>Tissues</th>
<th>Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type I</td>
<td>[α1(I)]₂ α2(I)</td>
<td>Bone, tendon, ligament,</td>
<td>Support tensile loads</td>
</tr>
<tr>
<td>Type II</td>
<td>[α1(II)]₃</td>
<td>Cartilage</td>
<td>Support tensile loads; primary collagenous constituent of articular cartilage</td>
</tr>
<tr>
<td>Type VI</td>
<td>α1(VI) α2(VI) α3(VI)</td>
<td>Cartilage</td>
<td>Pericellular adhesion molecule</td>
</tr>
<tr>
<td>Type IX</td>
<td>α1(IX) α2(IX) α3(IX)</td>
<td>Cartilage</td>
<td>Fibril association; stabilizes Type II</td>
</tr>
<tr>
<td>Type X</td>
<td>[α1(X)]₃</td>
<td>Cartilage</td>
<td>Hypertrophic zone of growth plate; role in calcification postulated</td>
</tr>
<tr>
<td>Type XI</td>
<td>α1(XI) α2(XI) α1(II)</td>
<td>Cartilage</td>
<td>Core of Type II; controls fibril growth</td>
</tr>
<tr>
<td>Tissue</td>
<td>Water</td>
<td>Proteoglycans</td>
<td></td>
</tr>
<tr>
<td>--------------</td>
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<td>-----------------------</td>
<td></td>
</tr>
<tr>
<td>Articular Cartilage</td>
<td>68-85%</td>
<td>10-20% (type I)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>5-10%</td>
<td></td>
</tr>
<tr>
<td>Meniscus</td>
<td>60-70%</td>
<td>15-25% (type II)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>1-2%</td>
<td></td>
</tr>
</tbody>
</table>
Purpose of Cartilage

- Connective tissue
  - Transmit load from one bone to another
    - Load bearing surface about 2-3mm thick
  - Allows bones to articulate – or move with respect to one another
    - Friction
Bone Development

- **Osteogenesis and ossification** –
  - the process of bone tissue formation, which leads to:
    - The formation of the bony skeleton in embryos
    - Bone growth until early adulthood
    - Bone thickness, remodeling, and repair
Fetal Primary Ossification Centers

- Parietal bone
- Occipital bone
- Mandible
- Clavicle
- Scapula
- Radius
- Ulna
- Humerus
- Ribs
- Vertebra
- Ilium
- Femur
- Tibia

<<fetal spine>>
Growth of Cartilage

- **Appositional** – cells in the perichondrium secrete matrix against the external face of existing cartilage
- **Interstitial** – lacunae-bound chondrocytes inside the cartilage divide and secrete new matrix, expanding the cartilage from within
- **Calcification of cartilage occurs**
  - During normal bone growth
  - During old age
Growth plate

Resting cartilage
Multiplying cartilage
Maturing cartilage
Calcified cartilage
Mature bone

Direction of bone growth

Growth plate zones
- Changes in chondrocytes
- Reserve zone
- Matrix production
- Proliferative zone
- Mitosis
- Maturation and hypertrophy
- Lipids, glycogen, and alkaline phosphatase accumulate; matrix calcifies
- Calcified matrix
- Cell death

Metaphysis
- Zone of ossification
- Primary spongiosa
- Secondary spongiosa
Cartilage grows by appositional and interstitial growth

- **Resting (quiescent) zone**: Cartilage cells undergo mitosis.
- **Growth (proliferation) zone**: Older cartilage cells enlarge.
- **Hypertrophic zone**: Matrix becomes calcified; cartilage cells die; matrix begins deteriorating.
- **Calcification zone**: New bone formation is occurring.
- **Perichondrium**: (new cartilage is added to the surface of the cartilage by chondroblasts from the inner layer of the perichondrium)
- **Chondroblast**: Lacuna
- **Chondrocyte**: Nucleus
- **Interstitial growth**: Chondrocytes that have divided produce additional matrix.

Fig. 6.1
Osteogenesis (a.k.a. ossification) is the process of bone tissue formation.

In embryos this leads to the formation of the bony skeleton.

In children and young adults, ossification occurs as part of bone growth.

In adults, it occurs as part of bone remodeling and bone repair.
Formation of the Bony Skeleton

- Begins at week 8 of embryo development

- **Intramembranous ossification** – bone develops from a fibrous membrane
  - Formation of most of the flat bones of the skull and the clavicles
  - Fibrous connective tissue membranes are formed by mesenchymal cells

- **Endochondral ossification** – bone forms by replacing hyaline cartilage

- By age 25, nearly all bones are completely ossified

- In old age, bone resorption predominates

- A single gene that codes for vitamin D docking determines both the tendency to accumulate bone mass early in life, and the risk for osteoporosis later in life
Developmental Aspects of Bones

- **Mesoderm** gives rise to embryonic mesenchymal cells, which produce membranes and cartilages that form the embryonic skeleton.
- The embryonic skeleton ossifies in a predictable timetable that allows fetal age to be easily determined from sonograms.
- At birth, most long bones are well ossified (except for their epiphyses).
Intramembranous Ossification

- Some bones of the skull (frontal, parietal, temporal, and occipital bones), the facial bones, the clavicles, the pelvis, the scapulae, and part of the mandible are formed by intramembranous ossification.
- Prior to ossification, these structures exist as fibrous membranes made of embryonic connective tissue known as mesenchyme.
Mesenchymal cells first cluster together and start to secrete the organic components of bone matrix which then becomes mineralized through the crystallization of calcium salts. As calcification occurs, the mesenchymal cells differentiate into osteoblasts.

The location in the tissue where ossification begins is known as an ossification center.

Some osteoblasts are trapped w/i bony pockets. These cells differentiate into osteocytes.

The developing bone grows outward from the ossification center in small struts called spicules.

Mesenchymal cell divisions provide additional osteoblasts.

The osteoblasts require a reliable source of oxygen and nutrients. Blood vessels trapped among the spicules meet these demands and additional vessels branch into the area.

These vessels will eventually become entrapped within the growing bone.
Intramembranous Ossification

- Formation of most of the flat bones of the skull and the clavicles
- Fibrous connective tissue membranes are formed by mesenchymal cells

Stages of Intramembranous Ossification

- An ossification center appears in the fibrous connective tissue membrane
- Bone matrix is secreted within the fibrous membrane
- Woven bone and periosteum form
- Bone collar of compact bone forms, and red marrow appears
Stages of Intramembranous Ossification

1. An ossification center appears in the fibrous connective tissue membrane.
   - Selected centrally located mesenchymal cells cluster and differentiate into osteoblasts, forming an ossification center.

2. Bone matrix (osteoid) is secreted within the fibrous membrane.
   - Osteoblasts begin to secrete osteoid, which is mineralized within a few days.
   - Trapped osteoblasts become osteocytes.

3. Woven bone and periosteum form.
   - Accumulating osteoid is laid down between embryonic blood vessels, which form a random network. The result is a network (instead of lamellae) of trabeculae.
   - Vascularized mesenchyme condenses on the external face of the woven bone and becomes the periosteum.

4. Bone collar of compact bone forms and red marrow appears.
   - Trabeculae just deep to the periosteum thicken, forming a woven bone collar that is later replaced with mature lamellar bone.
   - Spongy bone (diploë), consisting of distinct trabeculae, persists internally and its vascular tissue becomes red marrow.
Endochondral Ossification

- Begins in the second month of development
- Uses hyaline cartilage “bones” as models for bone construction
- Requires breakdown of hyaline cartilage prior to ossification
Stages of Endochondral Ossification

- Formation of bone collar
- Cavitation of the hyaline cartilage
- Invasion of internal cavities by the periosteal bud, and spongy bone formation
- Formation of the medullary cavity; appearance of secondary ossification centers in the epiphyses
- Ossification of the epiphyses, with hyaline cartilage remaining only in the epiphyseal plates
Stages of Endochondral Ossification

1. Formation of bone collar around hyaline cartilage model.
2. Cavitation of the hyaline cartilage within the cartilage model.
3. Invasion of internal cavities by the periosteal bud and spongy bone formation.
4. Formation of the medullary cavity as ossification continues; appearance of secondary ossification centers in the epiphyses in preparation for stage 5.
5. Ossification of the epiphyses; when completed, hyaline cartilage remains only in the epiphyseal plates and articular cartilages.
Endochondral Ossification

- Begins with the formation of a hyaline cartilage model which will later be replaced by bone.
- Most bones in the body develop via this model.
- More complicated than intramembranous because the hyaline cartilage must be broken down as ossification proceeds.
- We’ll follow limb bone development as an example.
Endochondral Ossification

Endochondral ossification is a process by which a bone develops from cartilage. It involves the following steps:

1. **Proliferation** (a): This is the initial stage where cartilage cells divide and produce new cells.

2. **Condensation** (b): The newly formed cells condense into a mass, forming a cartilage model of the bone.

3. **Hypertrophy, bone collar and vascularization** (c): The cartilage cells hypertrophy, and blood vessels invade the model, bringing nutrients and oxygen.

4. **Growth axes and bone marrow compartment** (d): Longitudinal growth occurs along the growth axes, and a bone marrow compartment develops.

5. **Maturation of ossification centres** (e): The cartilage model is replaced by bone as osteoblasts lay down bone matrix.

6. **Adult bone** (f): The bone continues to grow and mature, with the addition of trabecular bone and cortical bone.

During this process, osteoclasts break down the newly formed spongy bone and open up a medullary cavity in the center of the shaft. As the osteoblasts move towards the epiphyses, the epiphyseal cartilage is growing as well. Thus, even though the shaft is getting longer, the epiphyses have yet to be transformed into bone.
Around birth, most long bones have a bony diaphysis surrounding remnants of spongy bone, a widening medullary cavity, and 2 cartilaginous epiphyses.

At this time, capillaries and osteoblasts will migrate into the epiphyses and create secondary ossification centers.

The epiphysis will be transformed into spongy bone.

However, a small cartilaginous plate, known as the epiphyseal plate, will remain at the juncture between the epiphysis and the diaphysis.
Growth of Cartilage

- **fibroblasts** and collagen form a matrix.
- **Perichondrium** and **blood vessels** facilitate growth.

**Appositional Growth**
- Peripheral mitosis and differentiation of fibroblasts.

**Interstitial Growth**
- Mitosis of chondrocytes and deposition of new matrix.

Diagram illustrating the transition from cartilage to bone with stages labeled A to J.
Growth in Bone Length

- Epiphyseal cartilage (close to the epiphysis) of the epiphyseal plate divides to create more cartilage, while the diaphyseal cartilage (close to the diaphysis) of the epiphyseal plate is transformed into bone.
- This increases the length of the shaft.
As a result osteoblasts begin producing bone faster than the rate of epiphyseal cartilage expansion. Thus the bone grows while the epiphyseal plate gets narrower and narrower and ultimately disappears. A remnant (epiphyseal line for adult) is visible on X-rays (do you see them in the adjacent femur, tibia, and fibula?)

At puberty, growth in bone length is increased dramatically by the combined activities of growth hormone, thyroid hormone, and the sex hormones.
BONE ANATOMY

Epiphysis and Metaphysis

- articular cartilage
- epiphyseal plate
- foramen
- epiphysis
- metaphysis
- diaphysis
- cancellous (spongy) bone
- compact bone
- marrow cavity
- growth plate
- compact bone
- spongey bone and trabeculae
Epiphyseal plate
three year old boy

growth plate
clavicle
scapula
humerus

anterior-posterior view
Growth in Bone Thickness

- Osteoblasts beneath the periosteum secrete bone matrix on the external surface of the bone. This obviously makes the bone thicker.
- At the same time, osteoclasts on the endosteum break down bone and thus widen the medullary cavity.
- This results in an increase in shaft diameter even though the actual amount of bone in the shaft is relatively unchanged.

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Growth in Width (Thickness)

- Growing bones widen as they lengthen
- **Increases in thickness by appositional growth**
Postnatal Bone Growth

- **Growth in length of long bones**
  - Cartilage on the side of the **epiphyseal plate closest to the epiphysis is relatively inactive**
  - Cartilage abutting the shaft of the bone organizes into a pattern that allows fast, efficient growth
  - Cells of the epiphyseal plate proximal to the resting cartilage form three functionally different zones: growth, transformation, and osteogenic
Functional Zones in Long Bone Growth

- **Growth zone** – cartilage cells undergo mitosis, pushing the epiphysis away from the diaphysis

- **Transformation zone** – older cells enlarge, the matrix becomes calcified, cartilage cells die, and the matrix begins to deteriorate

- **Osteogenic zone** – new bone formation occurs
Long Bone Growth and Remodeling

- **Growth in length** – cartilage continually grows and is replaced by bone as shown

- **Remodeling** – bone is resorbed and added by appositional growth as shown
Growth in Length of Long Bone

Figure 6.9

- Resting (quiescent) zone
- Growth (proliferation) zone
  - Cartilage cells undergo mitosis
- Hypertrophic zone
  - Older cartilage cells enlarge
- Calcification zone
  - Matrix becomes calcified; cartilage cells die; matrix begins deteriorating
- Ossification (osteogenic) zone
  - New bone formation is occurring

- Calcified cartilage spicule
- Osteoblast depositing bone matrix
- Osseous tissue (bone) covering cartilage spicules
Growth
Bone grows in length because:

1. Cartilage grows here
2. Cartilage replaced by bone here
3. Cartilage grows here
4. Cartilage replaced by bone here

Remodeling
Growing shaft is remodeled by:

1. Bone resorbed here
2. Bone added by appositional growth here
3. Bone resorbed here
During infancy and childhood, epiphyseal plate activity is stimulated by growth hormone.

During puberty, testosterone and estrogens:
- Initially promote adolescent growth spurts
- Cause masculinization and feminization of specific parts of the skeleton
- Later induce epiphyseal plate closure, ending longitudinal bone growth
Bone Remodeling

- **Remodeling units** – adjacent osteoblasts and osteoclasts deposit and resorb bone at periosteal and endosteal surfaces.
**Bone Deposition**

- Occurs where bone is injured or added strength is needed
- Requires a diet rich in protein, vitamins C, D, and A, calcium, phosphorus, magnesium, and manganese
- Alkaline phosphatase is essential for mineralization of bone

- Sites of new matrix deposition are revealed by the:
  - **Osteoid seam** – unmineralized band of bone matrix
  - **Calcification front** – abrupt transition zone between the osteoid seam and the older mineralized bone
Bone Resorption

- Accomplished by osteoclasts
- Resorption bays – grooves formed by osteoclasts as they break down bone matrix
- Resorption involves osteoclast secretion of:
  - Lysosomal enzymes that digest organic matrix
  - Acids that convert calcium salts into soluble forms

Dissolved matrix is transcytosed across the osteoclast’s cell where it is secreted into the interstitial fluid and then into the blood
The bone remodelling process.
Bone is continuously remodelled at discrete sites in the skeleton in order to maintain the integrity of the tissue. During this process, old bone is resorbed by osteoclasts and replaced with new osteoid, secreted by osteoblasts. First osteoclasts are activated, and the resorption phase takes approximately 10 days. Following resorption, unclassified macrophage-like cells are found at the remodelling site in the intermediate, or reversal phase. Osteoblast precursors are then recruited, which proliferate and differentiate into mature osteoblasts, before secreting new bone matrix. The matrix then mineralises to generate new bone and this completes the remodelling process. Copyright BTR©
Bone Resorption

- Dissolved matrix is transcytosed across the osteoclast’s cell where it is secreted into the interstitial fluid and then into the blood.

Response to Mechanical Stress

- Trabeculae form along lines of stress
- Large, bony projections occur where heavy, active muscles attach

Stress effects

- Bone formation
- Bone reabsorption
- Osteoblasts
- Osteoclasts

Stress increases bone density
Bone Remodeling

A. More force stimulates osteoblasts.

B. Osteoblasts deposit bone on the inside curvature and osteoclasts remove bone from the outside curvature.

C. Weight is evenly distributed.

Compressive Force
Fracture occurrence
Blood vessel disruption
Hematoma formation

Chemotactic invasion of osteoprogenitor
Mitogenic and osteogenic molecules released
Cellular proliferation begins
Formation of granulation tissue
Neovascularization

Soft callus is formed
Differentiation starts

Remodeling
Hard callus is formed