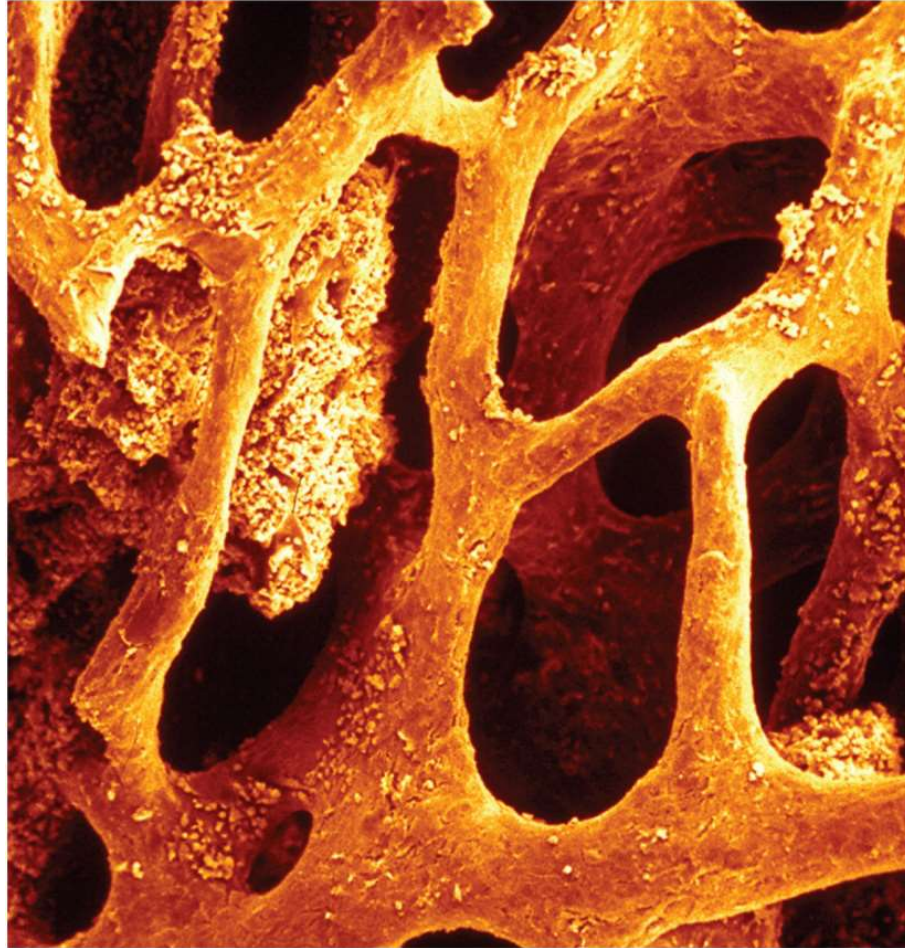


Chapter 7.1

Bone Tissue



Bones and Osseous Tissue



- Bone is also called osseous tissue
 - Bone is a type of connective tissue. An engineer would describe bone as a composite. A composite material is a solid material that results when two or more different substances, each with its own characteristics, are combined to create a new substance whose properties are superior to those of the original components in a specific application.
 - Bone consists of cells and a matrix. The matrix is the composite. It is made up of collagen fibers and calcium-phosphate crystals. Collagen fibers are flexible and calcium-phosphate crystals are hard. Bone exhibits both of these characteristics in the bone matrix.
 - Bone is one of the most metabolically active tissue in the body and constantly remodels itself in response to mechanical forces.
 - Bone has many nerves and blood vessels, which attests to its sensitivity and metabolic activity

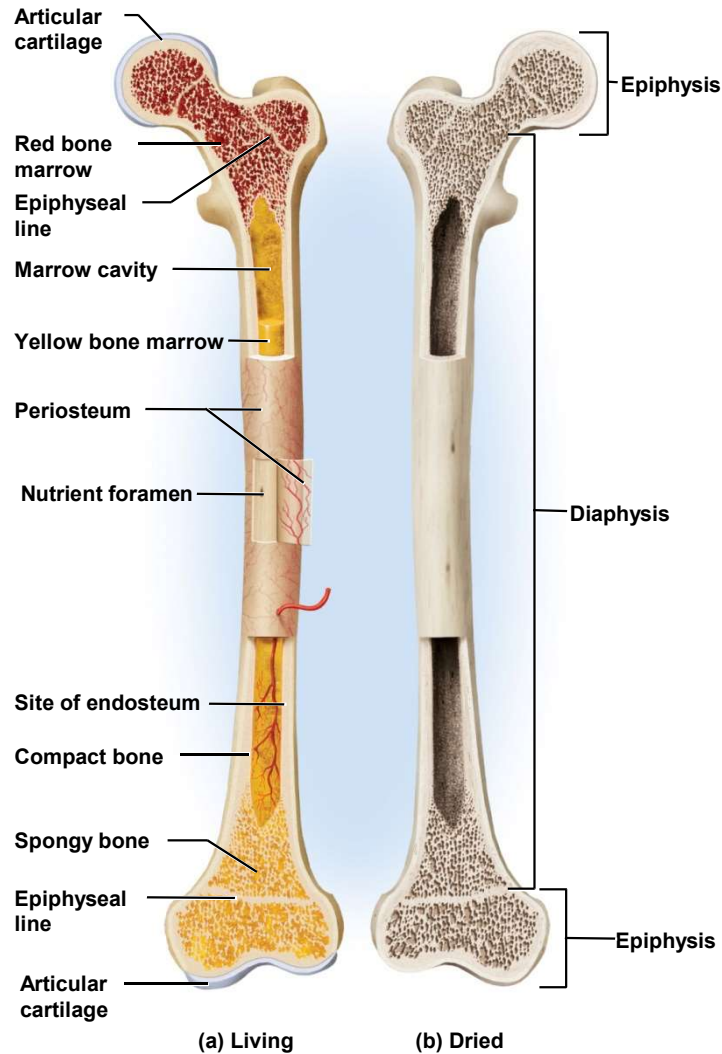
Functions of the Skeleton

- **support** – hold the body up, supports muscles, mandible and maxilla support teeth
- **protection** – brain, spinal cord, heart, lungs
- **movement** – limb movements, breathing, action of muscle on bone
- **electrolyte balance** – calcium and phosphate ions
- **acid-base balance** – buffers blood against excessive pH changes
- **blood formation** – red bone marrow is the chief producer of blood cells

Bones and Osseous Tissue

- An individual bones consist of:
 - bone
 - bone marrow
 - cartilage
 - adipose tissue
 - nervous tissue
 - fibrous connective tissue
 - blood vessels and nerves

Structure of a Long Bone



- epiphyses and diaphysis
- compact and spongy bone
- marrow cavity
- articular cartilage
- periosteum

General Features of Bones

- **compact (dense) bone** // Superficial layer of long bone // **functional unit = osteon**
- **diaphysis** (shaft) // cylinder of compact bone to provide leverage
- **medullary cavity** (marrow cavity) // space in middle of diaphysis
 - contains bone marrow
 - Yellow marrow = fat
 - red marrow = hemopoetic
- **epiphyses** // enlarged ends of a long bone // enlarged to strengthen joint and attach ligaments and tendons

General Features of Bones

- spongy (cancellous) bone
 - covered by more durable compact bone
 - skeleton about three-fourths compact and one-fourth spongy bone by weight
 - spongy bone found in ends of long bones, and the middle of nearly all others
- nutrient foramina
 - minute holes in the bone surface
 - allows blood vessels to penetrate bone to distribute blood to osteons and medullary cavity
- articular cartilage
 - a layer of **hyaline cartilage**
 - covers the joint surface where one bone meets another
 - allows joint to move more freely and friction free

General Features of Bones



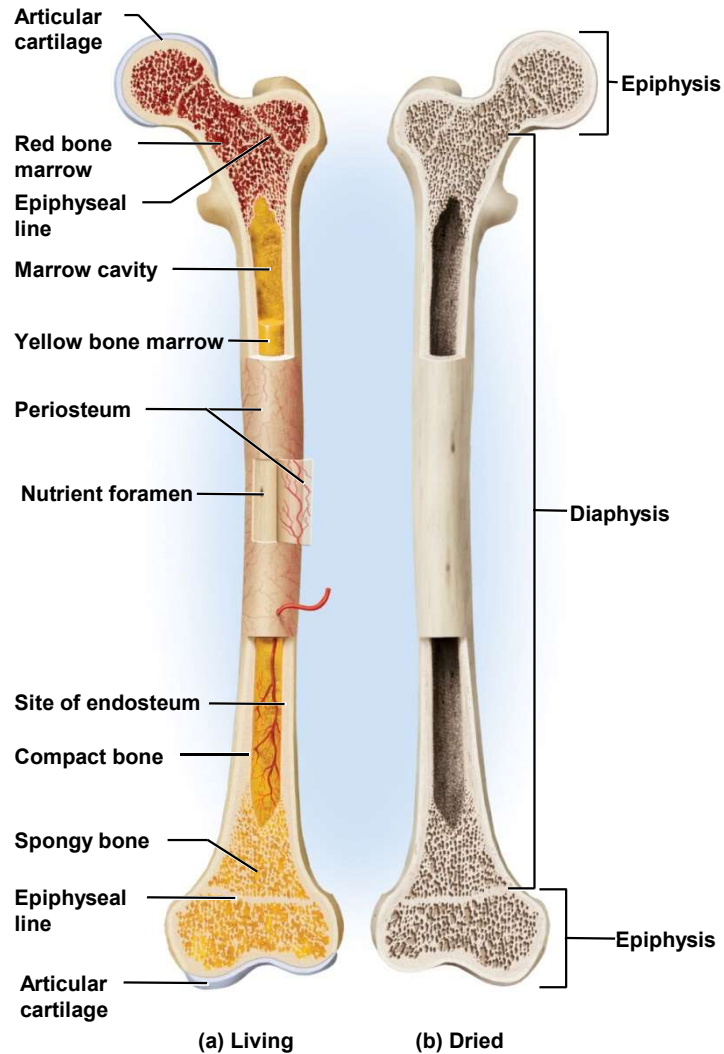
- **Periosteum** // external sheath that covers bone
 - outer fibrous membrane = dense irregular
 - some outer fibers (collagen fibers) continuous with the tendons that attach muscle to bone
 - perforating (Sharpey's) fibers –fibers on inner surface of periosteum which penetrate into the bone matrix
 - strong attachment and continuity from muscle to tendon to bone
 - inner osteogenic layer of bone forming cells // important to growth of bone and healing of fractures
 - not present on articular surfaces (hyalin cartilage)

General Features of Bones



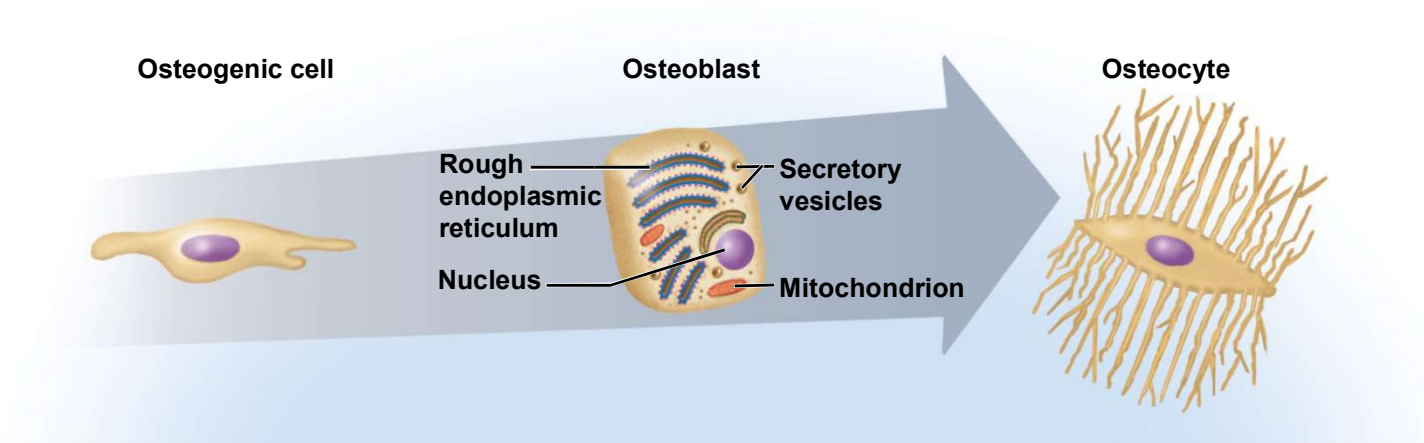
- **endosteum**
 - connective tissue membrane lining marrow cavity
 - Between membrane and bone there are osteogenic cells (osteoblast and osteoclast)
- **epiphyseal plate** (growth plate)
 - area of hyaline cartilage that separates the marrow spaces of the epiphysis and diaphysis
 - enables growth in length
- **epiphyseal line**
 - in adults, a bony scar that marks where growth plate used to be

Structure of a Long Bone



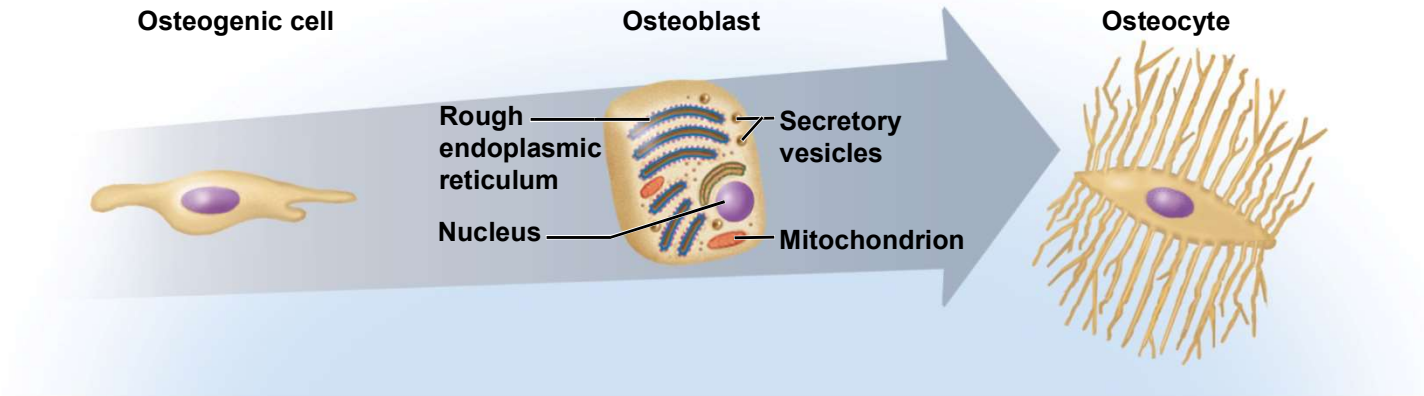
- epiphyses and diaphysis
- compact and spongy bone
- marrow cavity
- articular cartilage
- periosteum

Histology of Osseous Tissue



- **bone** is connective tissue that consists of cells, fibers and ground substance
- **four principal types** of bone cells (know function of these cell types!)
 - **osteogenic (osteoprogenator) cells**
 - **osteoblasts**
 - **osteocytes**
 - **Osteoclasts // formed by union of macrophage**

Osteogenic (osteoprogenator) cells



- stem cells found in endosteum, periosteum, and in central canals
- arise from embryonic mesenchymal cells
- multiply continuously to produce new osteoblasts

Osteoblasts



- bone forming cells
- line up as single layer of cells under endosteum and periosteum // are non-mitotic
- synthesize extracellular fiber = collagen / exocytosis / forms matrix
- calcium phosphate crystals form in collagen fibers // comes from blood and regulated by hormones
- stress and fractures stimulate osteogenic cells to multiply more rapidly and increase number of osteoblasts to reinforce or rebuild bone

Osteoclasts



- **bone-dissolving cells** found on the bone surface
- osteoclasts develop from same bone marrow stem cells that give rise to blood cells / modified macrophage
- different origin from rest of bone cells
- unusually large cells formed from the fusion of several stem cells / typically have 3 to 4 nuclei, may have up to 50
- ruffled border – side facing bone surface
 - several deep infoldings of the plasma membrane which increases surface area and resorption efficiency
- resorption bays (Howship lacunae) – pits on surface of bone where osteoclasts reside
- remodeling – results from combined action of the bone-dissolving osteoclasts and the bone-depositing osteoblasts

Osteocytes



- Osteoblast transforms itself into an osteocyte
- Osteoblast become surrounded by the matrix they have deposited
- **lacunae** – tiny cavities where osteocytes reside
- **canaliculi** – little channels that connect lacunae
- cytoplasmic processes of osteocyte reach into canaliculi
- contribute to homeostatic mechanism of bone density and calcium and phosphate ions
- when stressed, produce biochemical signals that regulate bone remodeling
- If lamella eroded back to the osteocyte / can once again become an osteoblast

The Matrix



- **Bone's matrix is a composite**
 - combines optimal mechanical properties of each component
 - bone combines the polymer, collagen, with the ceramic, hydroxyapatite and other minerals
 - ceramic portion allows the bone to support the body weight, and the protein portion gives bone some degree of flexibility
- **rickets** – soft bones due to deficiency of calcium salts
- **osteogenesis imperfecta** - brittle bone disease // excessively brittle bones due to lack of the protein fiber collagen

The Matrix

- matrix of osseous tissue by dry weight
 - about one-third organic
 - two-thirds inorganic matter
- organic matter
 - synthesized by osteoblasts
 - collagen fibers, carbohydrate – protein complexes, such as glycosaminoglycans, proteoglycans, and glycoproteins
- inorganic matter
 - 85% hydroxyapatite (crystallized calcium phosphate salt)
 - 10% calcium carbonate
 - other minerals (fluoride, sodium, potassium, magnesium)
 - *Calcium is a critical component to many different physiological events. Homeostatic mechanisms regulate blood calcium levels. Hormones are used to adjust blood calcium levels by using bone as a type of “bank” where calcium maybe added to bone (lower blood concentration) or subtracted from bone (increase blood calcium levels) to adjust blood calcium levels.*

Compact Bone

- **Osteon (haversian system)** – the structural unit of compact bone
 - formed by a **central canal** and its **concentric lamella**
 - connected to each other by **canaliculi**
 - organized as cylinder of tissue around a central canal
 - **perforating (Volkmann) canals** are transverse or diagonal passages along the length of the osteon
 - **collagen fibers** “corkscrew” down the matrix of the lamella giving it a helical arrangement
 - helices coil in one direction in one lamella and in the opposite direction in the next lamella for added strength

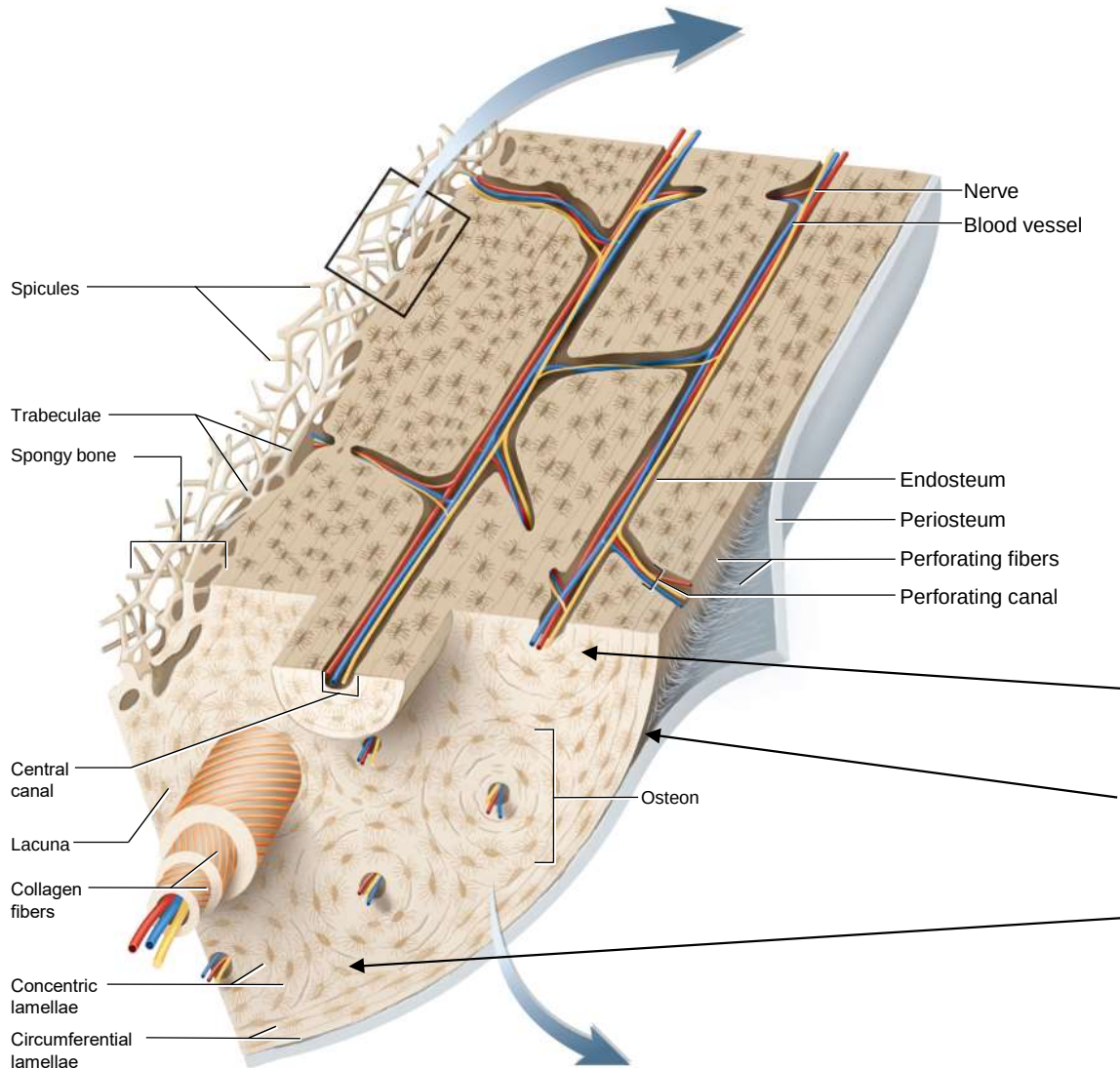
Compact Bone

- blood flow - skeleton receives about half a liter of blood per minute
- nutrient foramina – on the surface of bone tissue that allow blood vessels and nerves to enter the bone
 - open into the perforating canals that cross the matrix and feed into the central canals
 - innermost osteocytes near central canal receive nutrients and pass them along through their gap junction to neighboring osteocytes
 - they also receive wastes from their neighbors and transfer them to the central canal maintaining a two-way flow of nutrients and waste

Three Types of Lamellae in Compact Bone

- **concentric lamellae** // forms matrix around central canal
- **circumferential lamellae** // inner and outer boundaries of dense bone // run parallel to bone surface
- **interstitial lamellae** // remains of old osteons // as bone is remodeled some osteons are “eroded” // the fragments of old osteons are referred to as interstitial lamellae
- (see next slide)

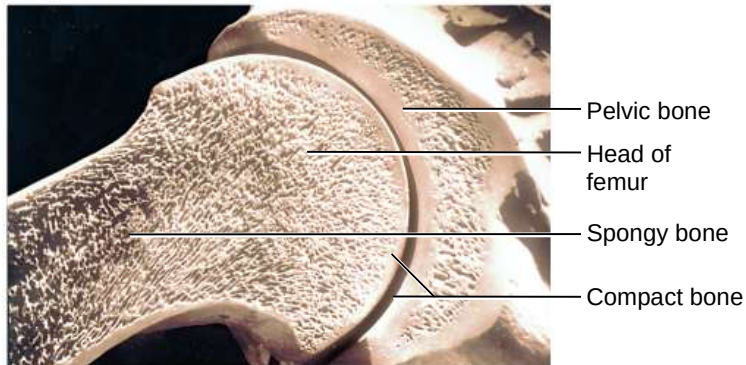
Blood Vessels of Compact Bone



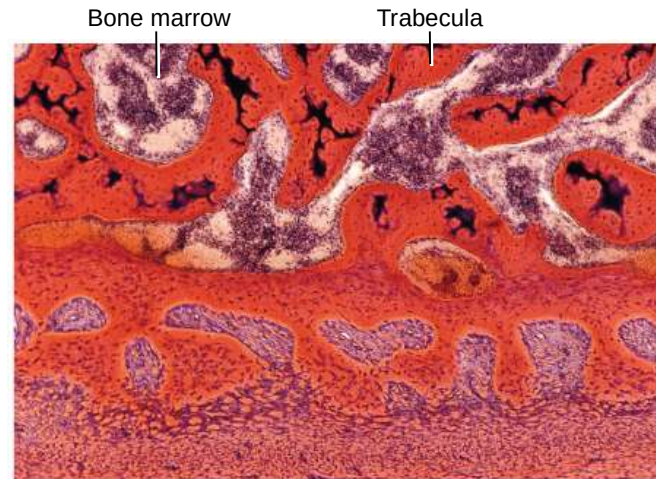
- **nutrient foramina** // on bone surface
- **perforating (Volkmann's) canals** // transverse or diagonal canals
- **central canals** // vertical canals
- **concentric lamellae**
- **circumferential lamellae**
- **interstitial lamellae**

(b)

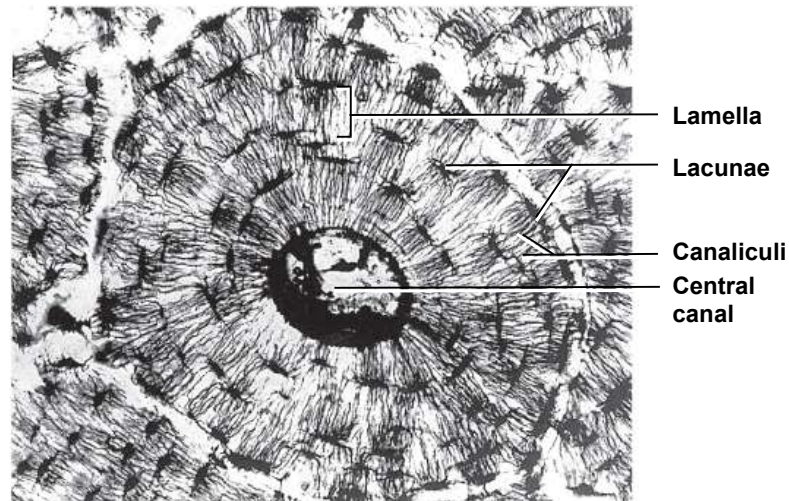
Histology of Compact and Spongy Bone



(a)



(c)



(d)

20 μm

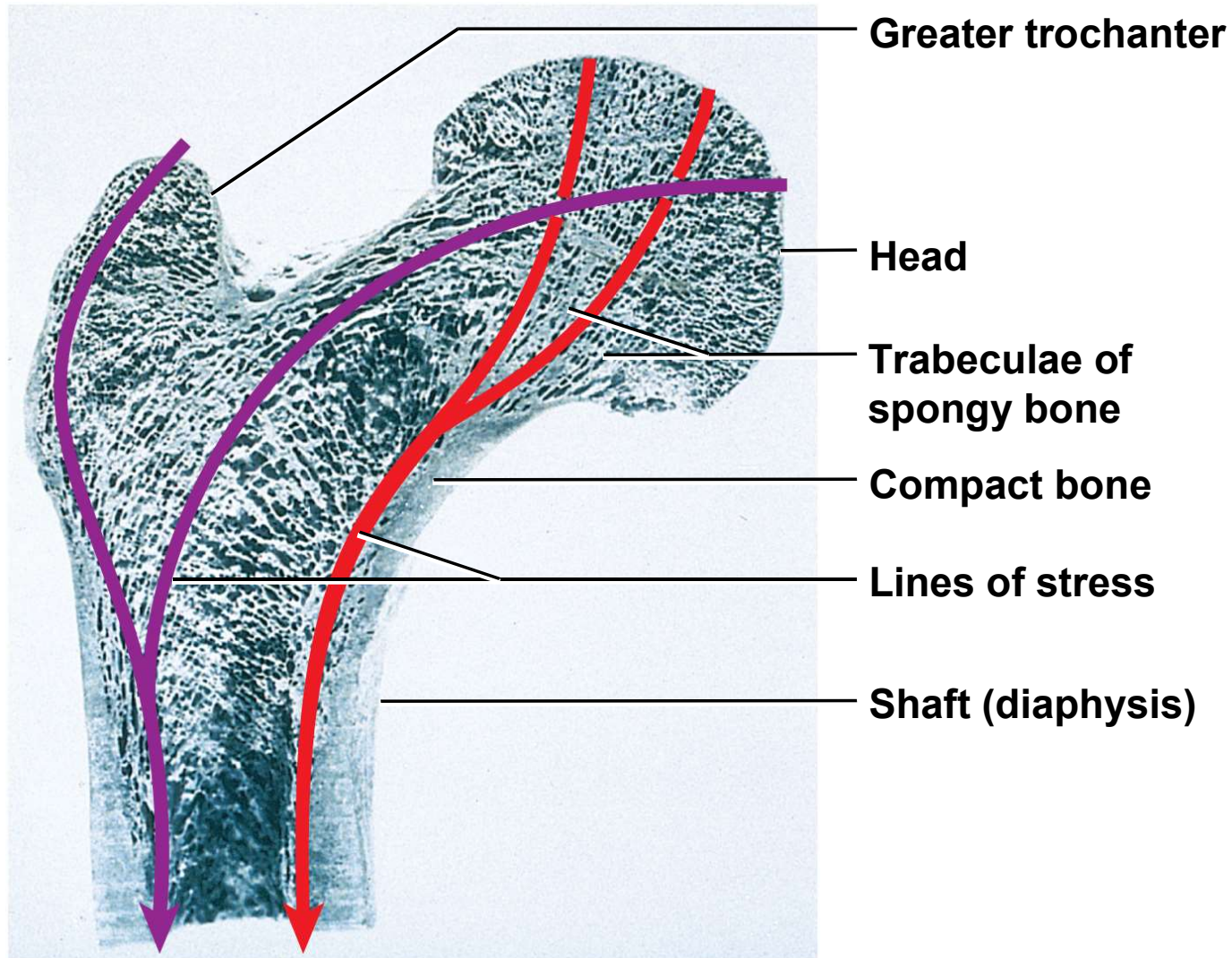
a,c: © Dr. Don W. Fawcett/Visuals Unlimited; d: Visuals Unlimited

Spongy Bone (Cancellous Bone)

- sponge-like appearance // but as hard as compact bone
- spongy bone consists of:
 - slivers of bone called **spicules**
 - thin plates of bone called **trabeculae**
 - spaces filled with **bone marrow**
- fewer osteons and no central canals
- all osteocytes close to bone marrow
- provides strength with minimal weight // trabeculae develop along bone's lines of stress

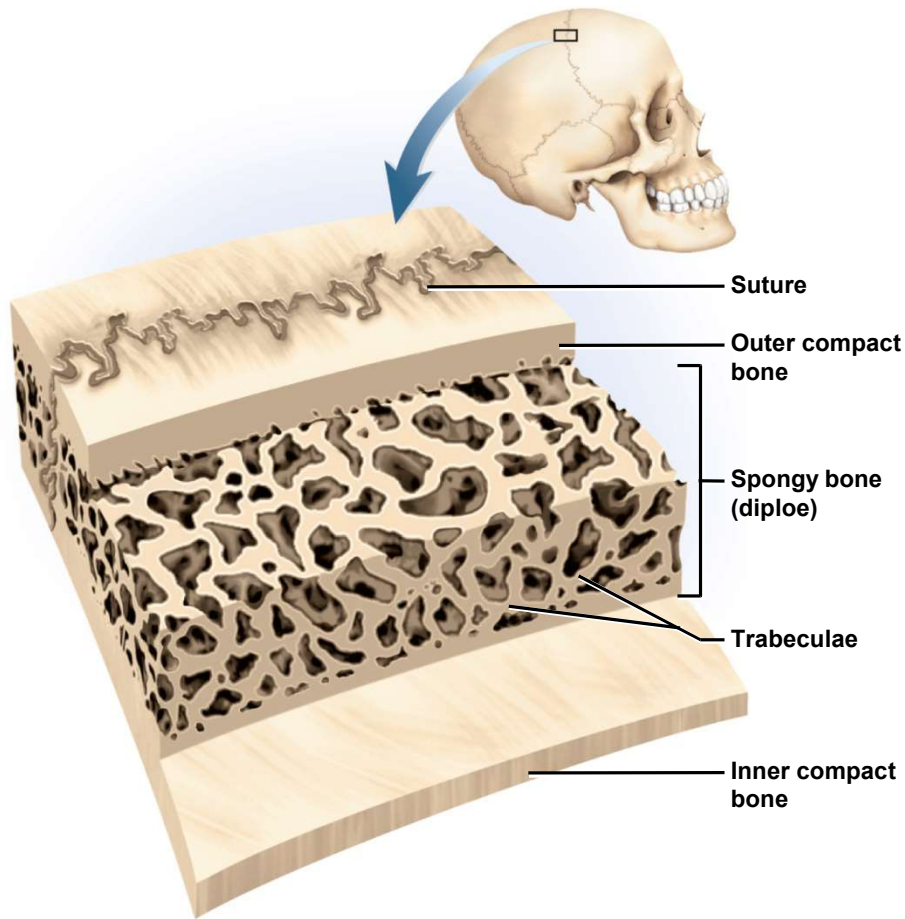
Design of Spongy Bone

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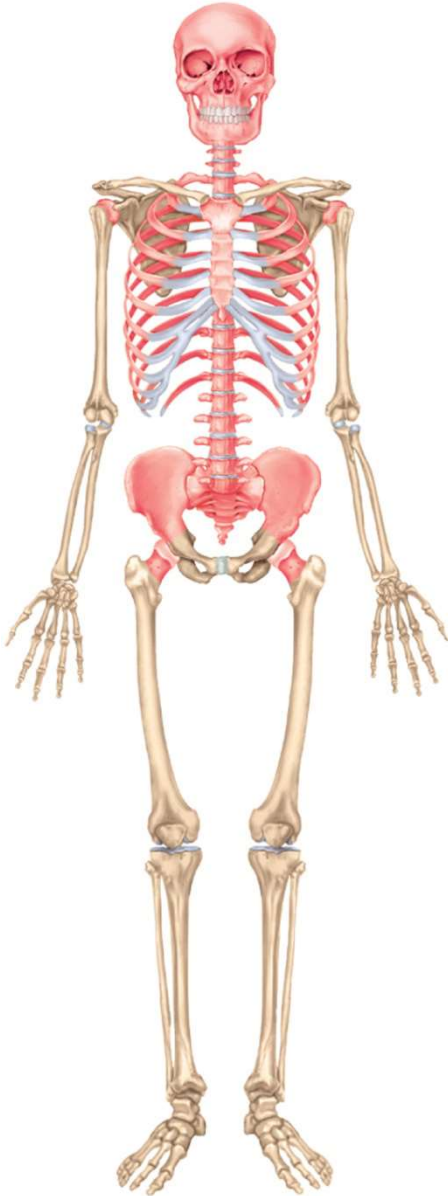
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Structure of a Flat Bone



- sandwich-like construction
- two layers of compact bone enclosing a middle layer of spongy bone
 - both surfaces of flat bone covered with periosteum
- **diploe** – spongy layer in the cranium
 - absorbs shock
 - marrow spaces lined with endosteum

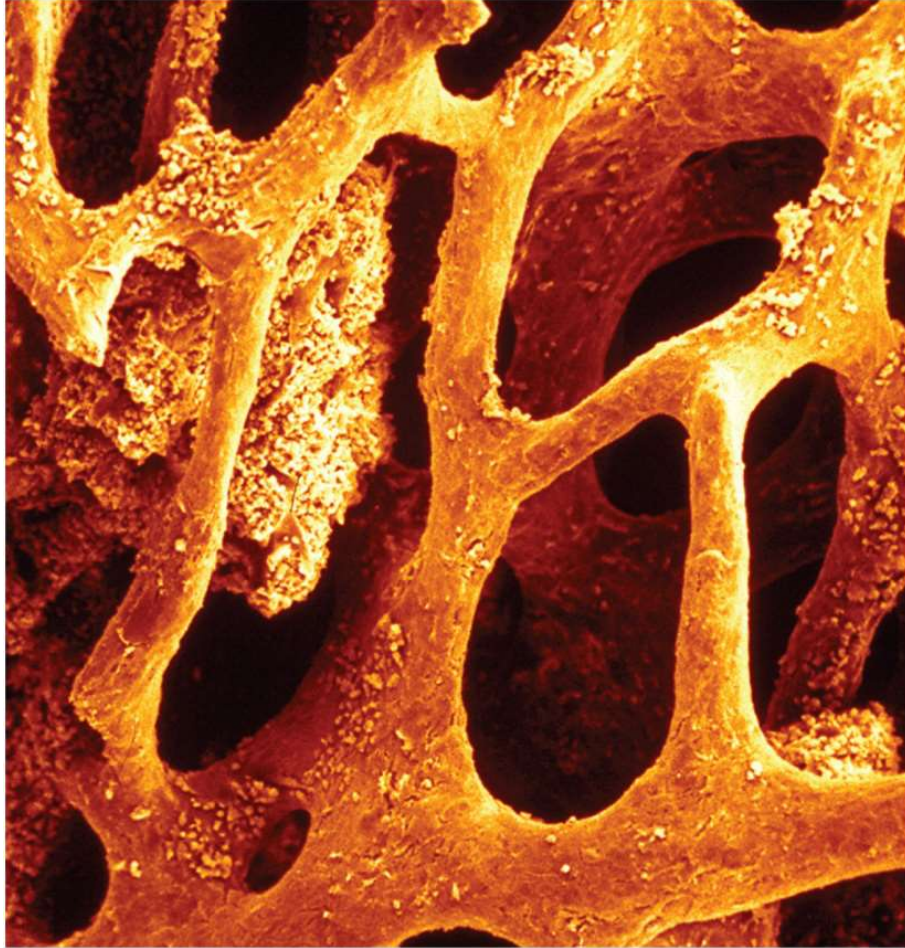
Bone Marrow



- **bone marrow** – general term for soft tissue that occupies the marrow cavity of a long bone and small spaces amid the trabeculae of spongy bone
- **red marrow (myeloid tissue)**
 - in nearly every bone in a child
 - **hemopoietic tissue** - produces blood cells and is composed of multiple tissues in a delicate, but intricate arrangement that is an organ to itself
 - in adults, found in **skull, vertebrae, ribs, sternum, part of pelvic girdle, and proximal heads of humerus and femur**
- **yellow marrow** found in adults
 - most red marrow turns into fatty yellow marrow
 - no longer produces blood

Chapter 6

Bone Development



Bone Development in Fetal Growth



- **Ossification or osteogenesis** = the formation of new bone
- Bone grows differently during fetal-infant and adult stages
- **In fetal and infant bone growth occurs by:**
 - intramembranous ossification
 - endochondral ossification
- **In adults bone growth occurs by:**
 - interstitial ossification – increases length (stop at 20yr)
 - appositional ossification – increases diameter (continues throughout life)

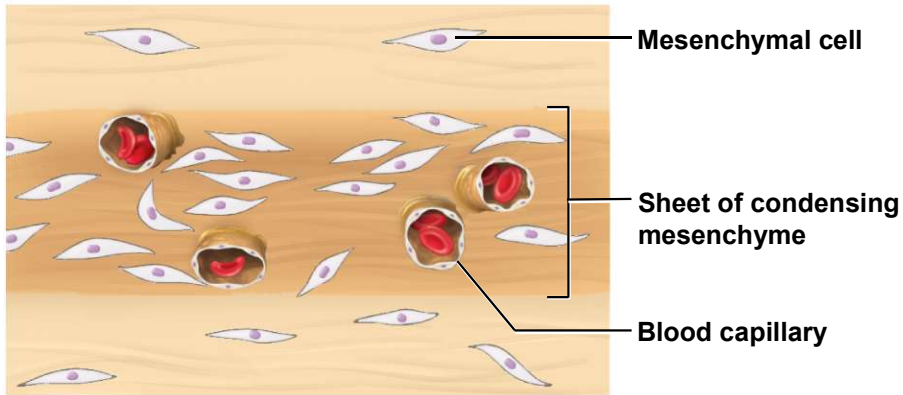
Intra-membranous Ossification

- these bones develop within a **fibrous membrane similar to the epidermis** of the skin (**dermal bones**)
 - **mesenchyme** – embryonic connective tissue condenses into a layer of soft tissue with dense supply of blood capillaries
 - **mesenchymal cells** differentiate into **osteogenic cells**
 - regions of mesenchyme become a network of soft sheets
 - **trabeculae**
 - osteogenic cells differentiate into **osteoblasts**
 - these cells deposit organic matrix – **osteoid tissue**

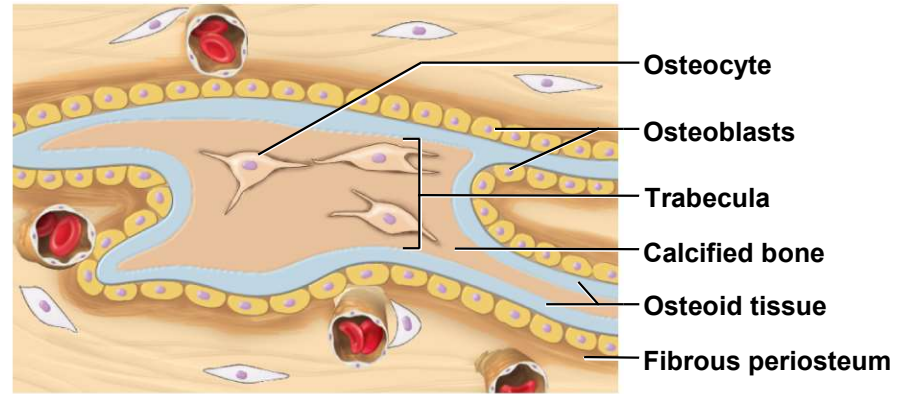
Intramembranous Ossification

- as trabeculae grow thicker, calcium phosphate is deposited in the matrix
- mesenchyme close to the surface of a trabecula remains uncalcified // becomes denser and more fibrous, forming periosteum
- osteoblasts continue to deposit minerals // producing a honeycomb of bony trabeculae
 - some persist as permanent spongy bone
 - osteoclasts resorb and remodel others to form a marrow cavity in the middle of bone
- trabeculae at the surface continue to calcify until the spaces between them are filled in, converting spongy bone to compact bone

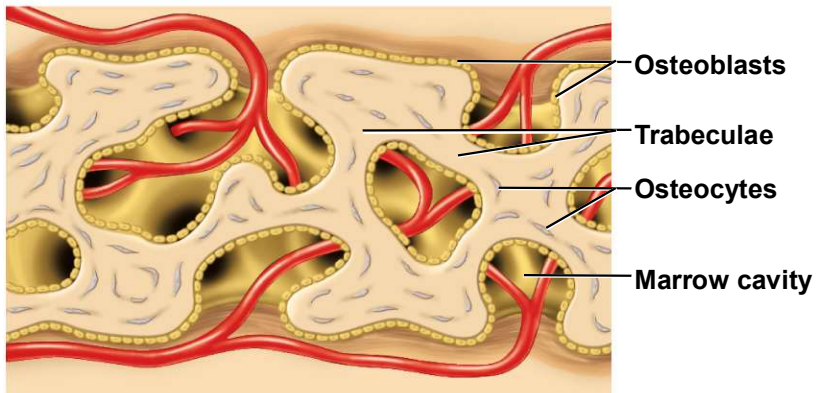
Intramembranous Ossification



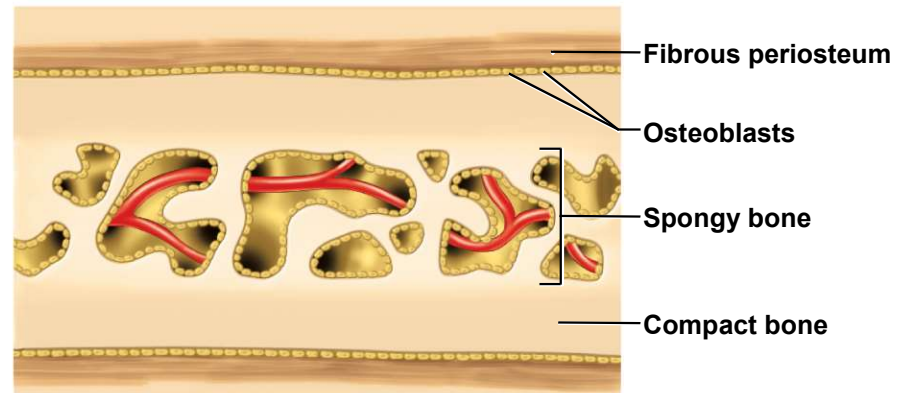
1 Condensation of mesenchyme into soft sheet permeated with blood capillaries



2 Deposition of osteoid tissue by osteoblasts on mesenchymal surface; entrapment of first osteocytes; formation of periosteum



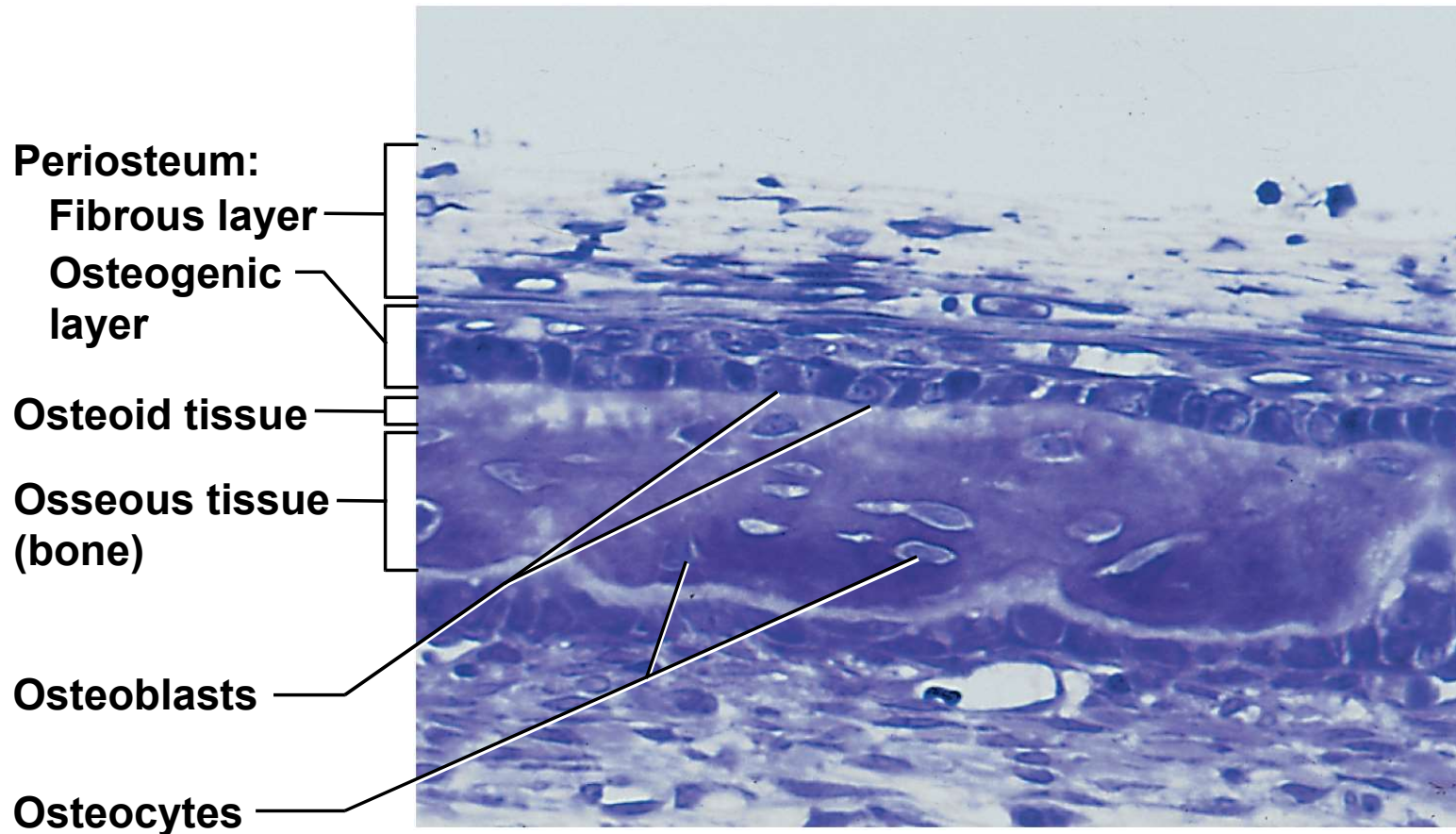
3 Honeycomb of bony trabeculae formed by continued mineral deposition; creation of spongy bone



4 Surface bone filled in by bone deposition, converting spongy bone to compact bone. Persistence of spongy bone in the middle layer.

e.g. // produces flat bones of skull and clavicle

Intramembranous Ossification



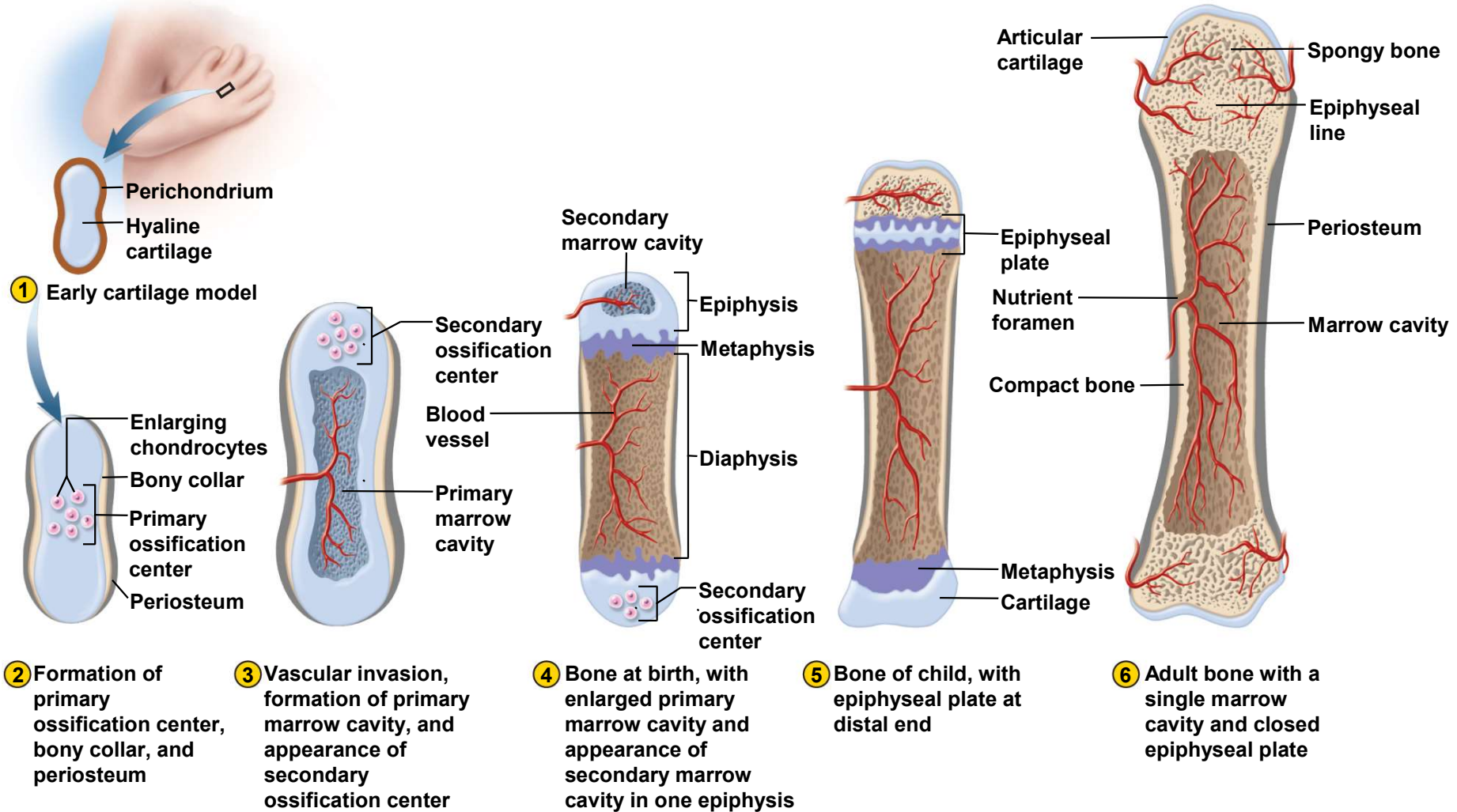
© Ken Saladin

note the periosteum and osteoblasts

Endochondral Ossification

- process in which **bone develops from pre-existing hyaline cartilage model**
 - beginning the 6th fetal week and ending in early 20's
 - most bones develop by this process
- mesenchyme develops into a body of **hyaline cartilage** in location of future bone
 - covered with fibrous **perichondrium** /// perichondrium produces chondrocytes initially, and later produces osteoblasts
 - osteoblasts form a bony collar around middle of cartilage model
 - former perichondrium is now considered to be **periosteum**

Stages of Endochondral Ossification

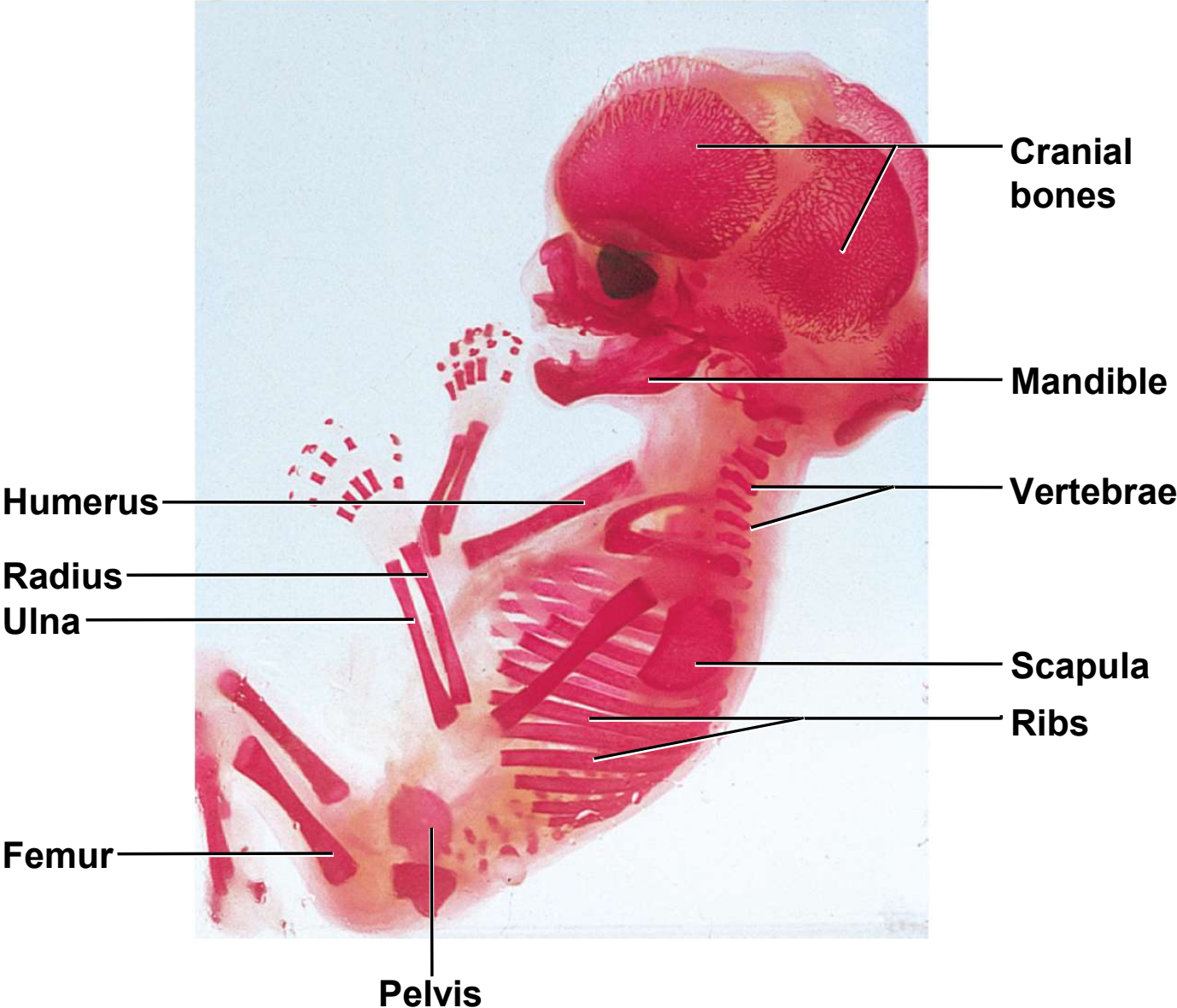


Endochondral Ossification

- **primary ossification center** - chondrocytes in the middle of the model enlarge
 - matrix between lacunae are reduced to thin walls
 - walls of this thin matrix ossify and block nutrients from reaching chondrocytes
 - they die and their lacunae merge into a single cavity in the middle of the model
- blood vessels penetrate the bony collar and invade primary ossification center
 - **primary marrow cavity** – forms from blood and stem cells filling hollow cavity

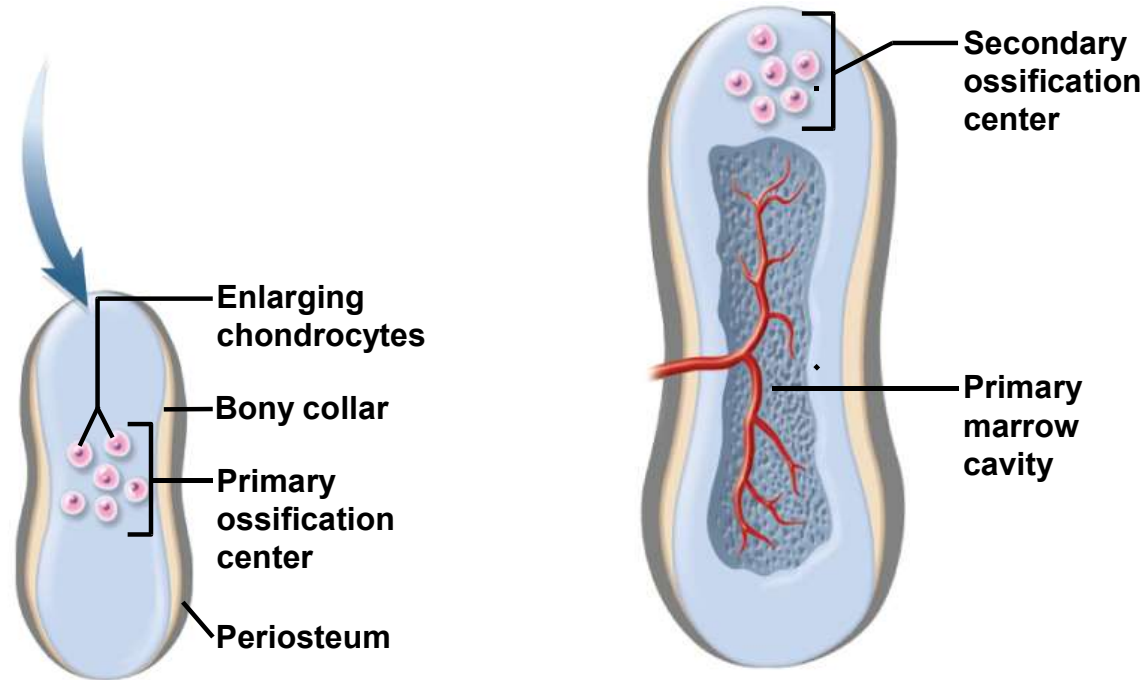
Fetal Skeleton at 12 Weeks

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Primary Ossification Center and Primary Marrow Cavity



2 Formation of primary ossification center, bony collar, and periosteum

3 Vascular invasion, formation of primary marrow cavity, and appearance of secondary ossification center

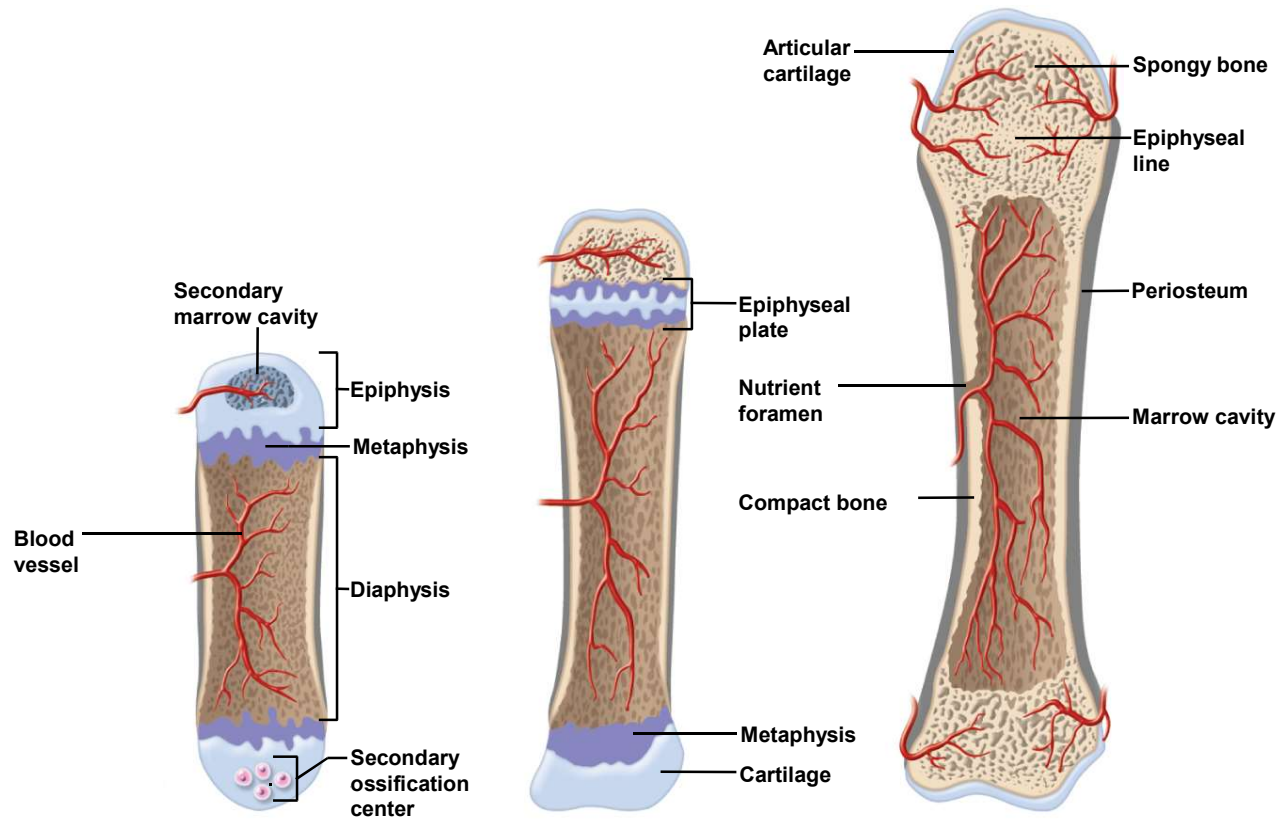
Endochondral Ossification

- blood vessels penetrate the bony collar and invade **primary ossification center**
 - **primary marrow cavity** – forms from blood and stem cells filling hollow cavity
 - stem cells give rise to osteoblasts and osteoclasts
 - osteoblasts line cavity and deposit osteoid tissue and calcify it
 - forming temporary network of trabeculae
 - wave of cartilage death progresses toward the ends
 - osteoclasts follow the wave dissolving the cartilage remnants enlarging the marrow cavity
 - **metaphysis** – region of transition from cartilage to bone at each end of primary marrow cavity

Endochondral Ossification

- **secondary ossification center** – created by chondrocyte enlargement and death in the epiphyses
 - become hollowed out by the same process generating a **secondary marrow cavity** in epiphyses
 - cavity expands outward from the center in all directions

Secondary Ossification Centers and Secondary Marrow Cavities

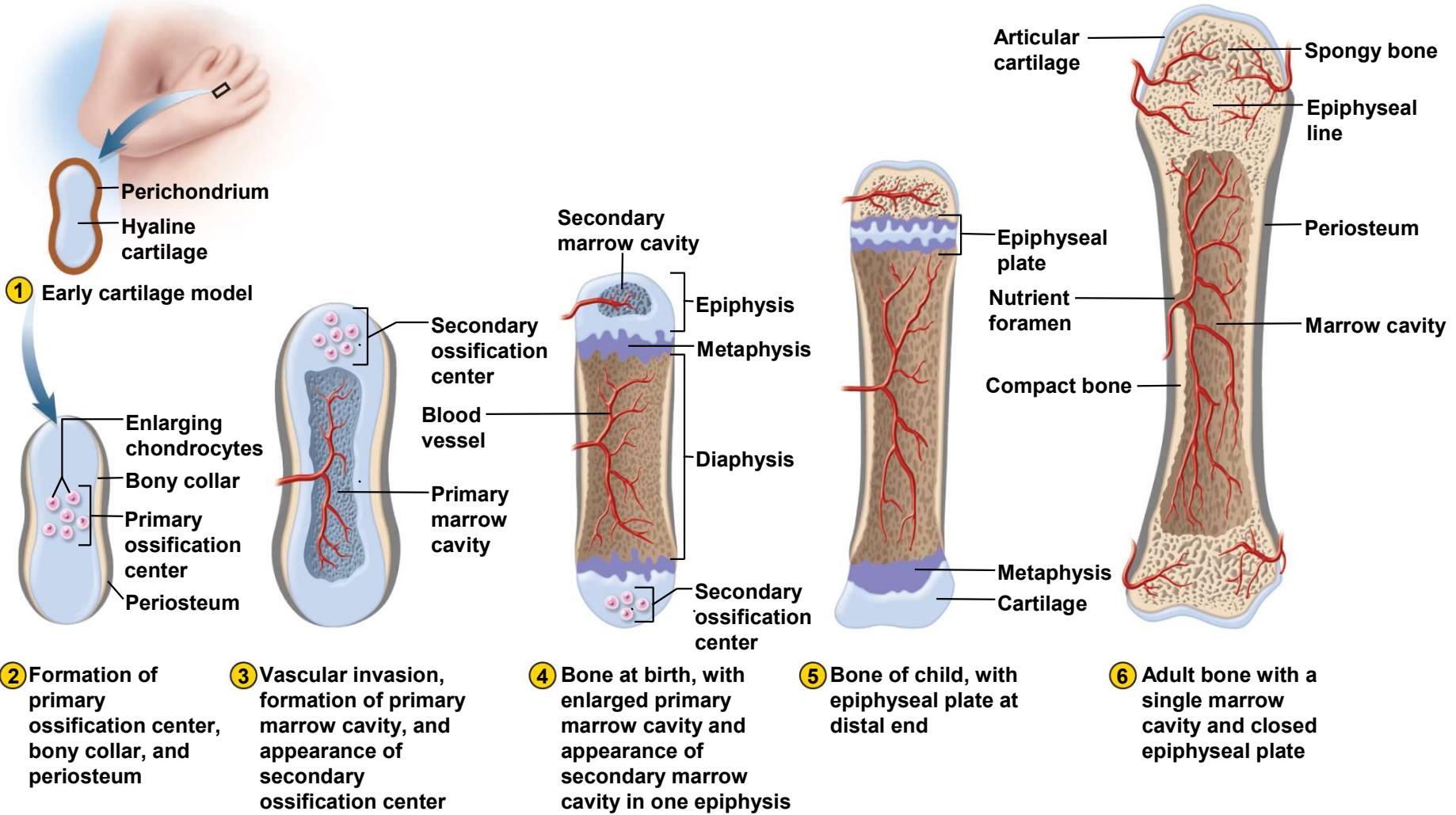


4 Bone at birth, with enlarged primary marrow cavity and appearance of secondary marrow cavity in one epiphysis

5 Bone of child, with epiphyseal plate at distal end

6 Adult bone with a single marrow cavity and closed epiphyseal plate

Stages of Endochondral Ossification



2 Formation of primary ossification center, bony collar, and periosteum

3 Vascular invasion, formation of primary marrow cavity, and appearance of secondary ossification center

4 Bone at birth, with enlarged primary marrow cavity and appearance of secondary marrow cavity in one epiphysis

5 Bone of child, with epiphyseal plate at distal end

6 Adult bone with a single marrow cavity and closed epiphyseal plate

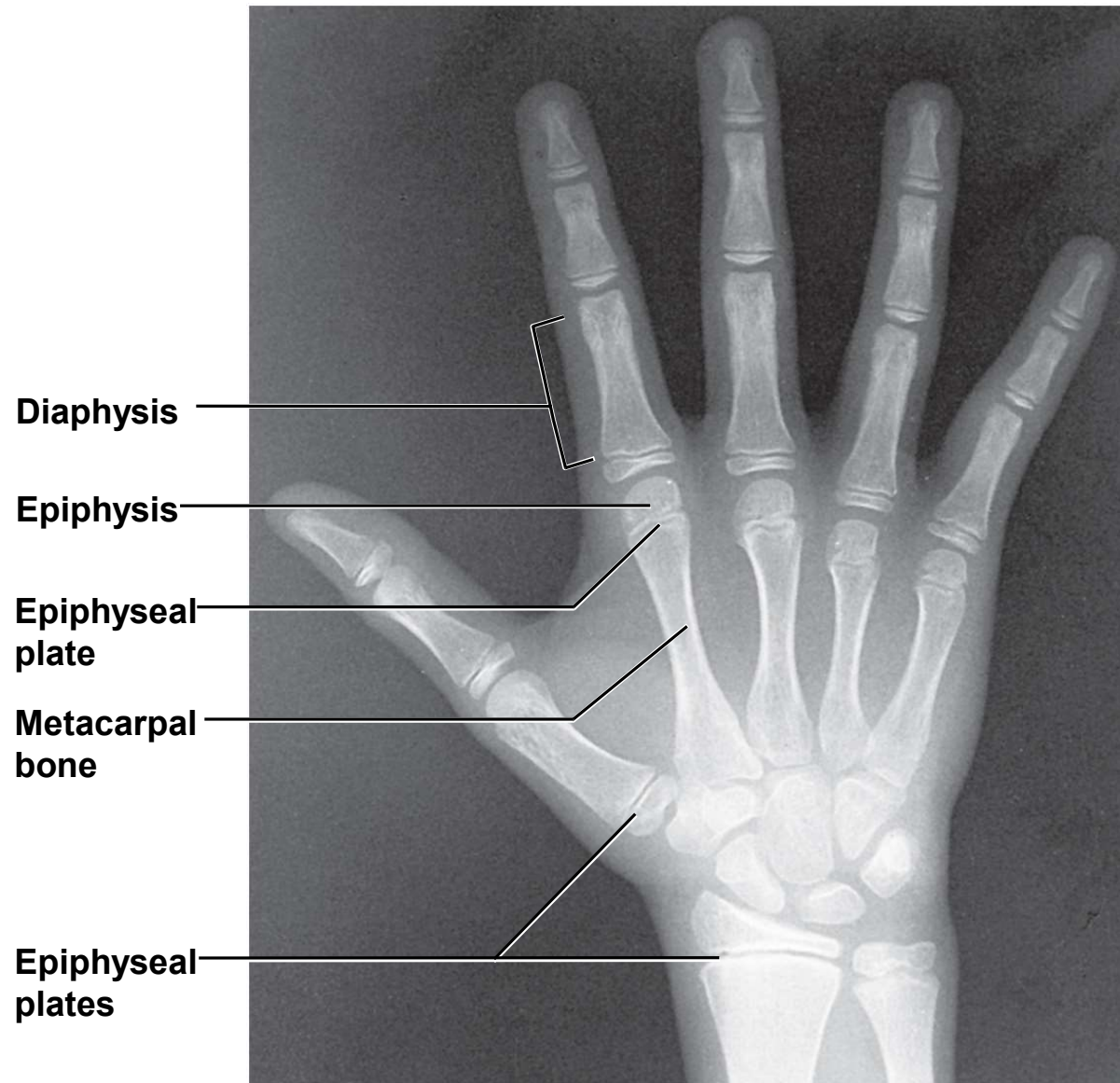
Postpartum Bone Growth

- During infancy and childhood, the hyaline epiphyses fill with spongy bone
- As bone matures the cartilage limited to the **articular cartilage** covering each joint surface, and to the **epiphyseal plate**
 - a thin wall of cartilage separating the primary and secondary marrow cavities
 - epiphyseal plate **persists through childhood** and adolescence
 - serves as a growth zone for bone elongation

Postpartum Bone Growth

- **By late teens to early twenties**, all remaining cartilage in the epiphyseal plate is generally calcified
 - gap between epiphyses and diaphysis closes
 - primary and secondary marrow cavities unite into a single cavity
 - *bone can no longer grow in length*
 - **epiphyseal line** “remains” as shadow of old epiphyseal plate

Cartilaginous Epiphyseal Plates



Bone Growth and Remodeling After Birth

- ossification continues throughout life with the growth and remodeling of bones
 - bones grow in two directions
 - length (interstitial) – stops in early 20's
 - width (appositional) – continues throughout
 - elongation occurs at epiphyseal plate
 - after it closes, bone can still remodel itself by changing the width and/or shape of long bones

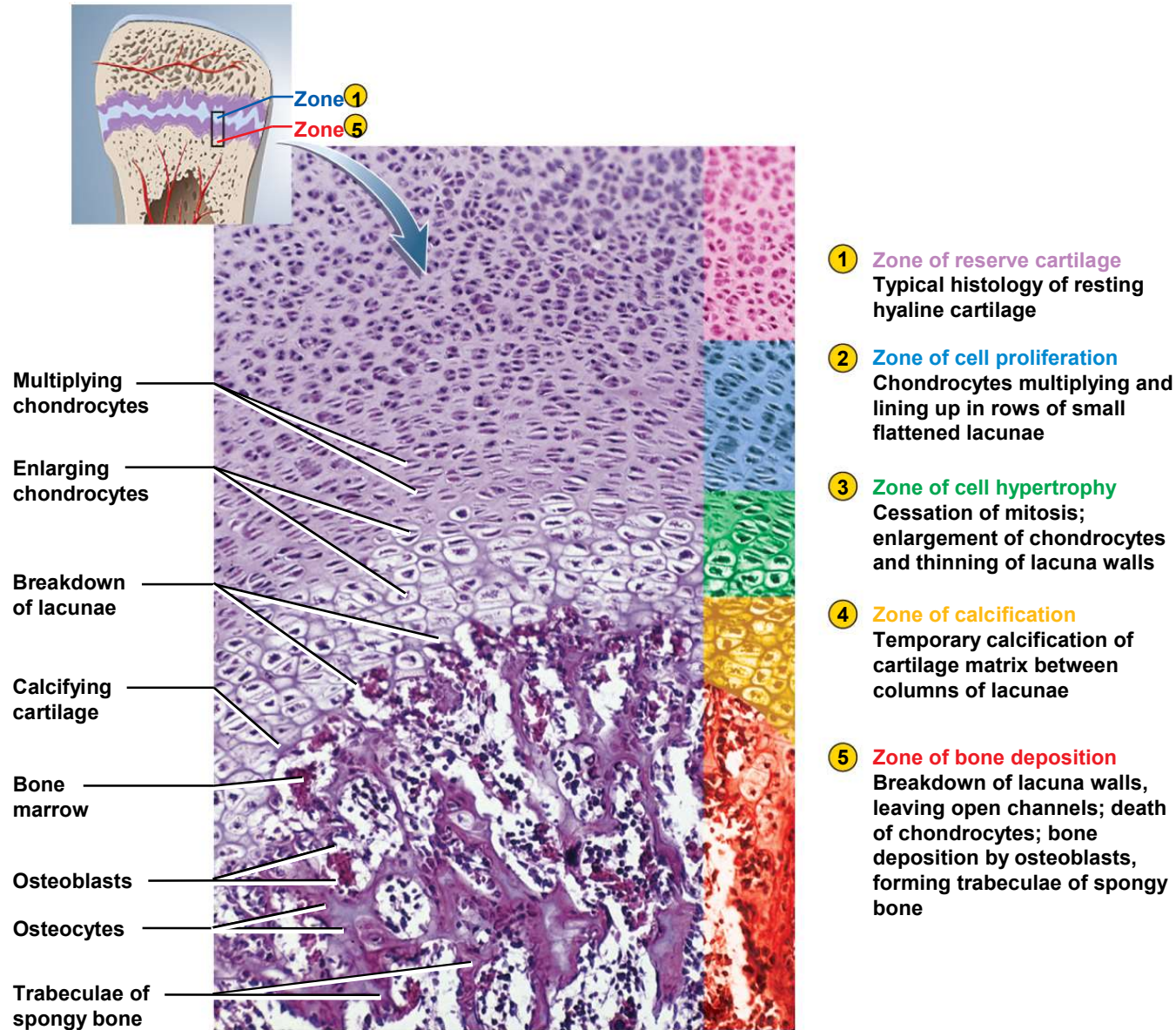
Bone Growth and Remodeling After Birth

- interstitial growth = bone elongation
 - epiphyseal plate – a region of transition from cartilage to bone
 - functions as growth zone where the bones elongate
 - consists of typical hyaline cartilage in the middle
 - with a transition zone on each side where cartilage is being replaced by bone
 - **metaphysis** is the zone of transition facing the marrow cavity

Bone Growth and Remodeling After Birth

- interstitial growth
 - bones increase in length
 - bone elongation is really a result of cartilage growth within epiphyseal plate
 - epiphyses close when cartilage is gone forming the **epiphyseal line**
 - length-wise growth is completed // occurs at different ages in different bones

Zones of the Metaphysis



Victor Eroschenko

Bone Growth and Remodeling After Birth

- **Appositional Growth**
 - bones increase in width throughout life
 - the deposition of new bone at the surface
 - osteoblasts on deep side of periosteum deposit osteoid tissue / become trapped as tissue calcifies
 - **circumferential lamellae** = matrix in layers parallel to surface
 - forms over surface
 - osteoclasts under endosteum enlarge marrow cavity

Bone Growth and Remodeling



- **Bone remodeling** occurs throughout life - 10% per year
 - repairs microfractures, releases minerals into blood, reshapes bones in response to use and disuse
 - **Wolff's Law of Bone**
 - architecture of bone determined by mechanical stresses placed on it and bones adapt to withstand those stresses
 - remodeling is a collaborative and precise action of osteoblasts and osteoclasts
 - bony processes grow larger in response to mechanical stress
 - Tendons' pull on periosteum and matrix produce “stress” and osteoblasts and osteoclast respond to physical forces

Dwarfism



- **Achondroplastic dwarfism**

- long bones stop growing in childhood // **normal torso, short limbs / more common**

- failure of cartilage growth in metaphysis

- spontaneous mutation produces mutant dominant allele

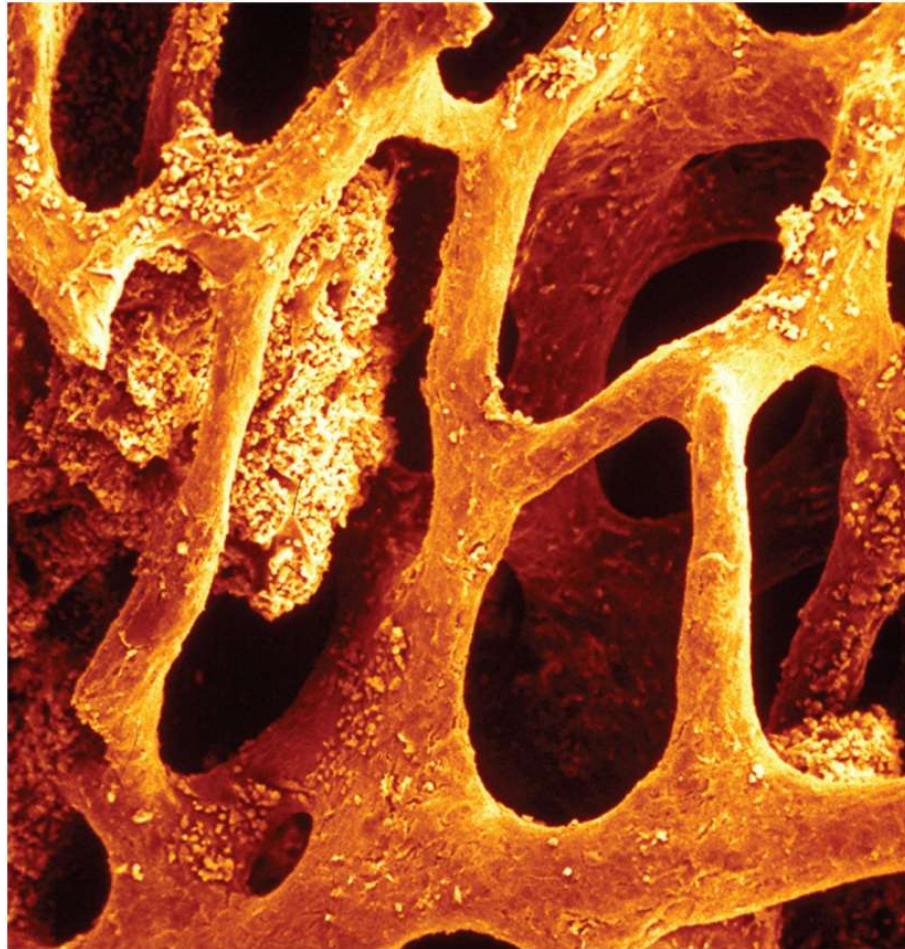
- **Pituitary dwarfism**

- lack of growth hormone

- **normal proportions with short stature**

Chapter 6

Bone Fracture & Repair



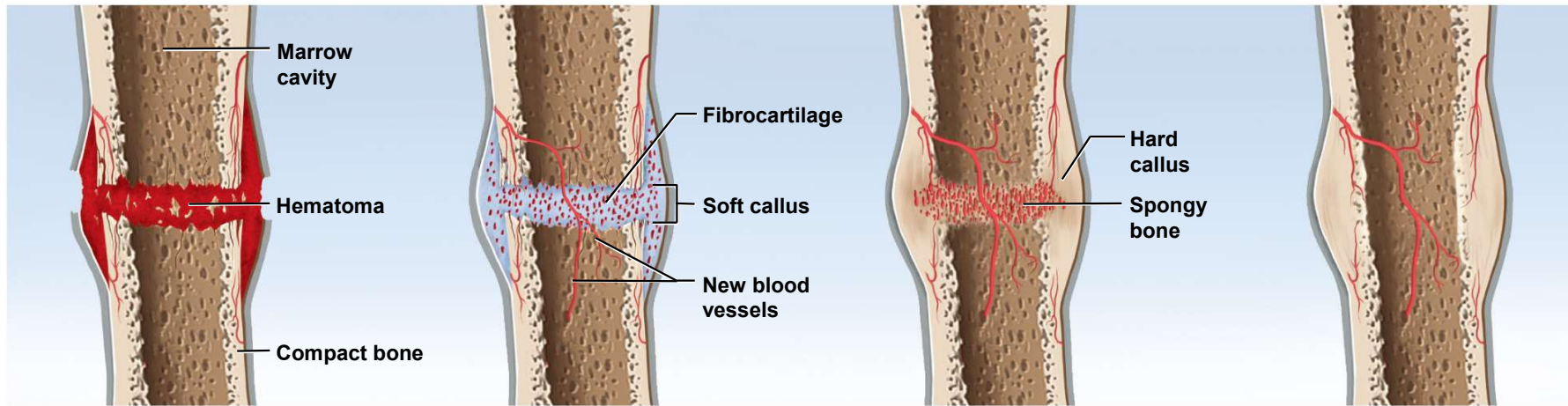
Fractures and Their Repair

- **stress fracture** – break caused by abnormal trauma to a bone
 - falls, athletics, and military combat
- **pathological fracture** – break in a bone weakened by some other disease
 - bone cancer or osteoporosis
 - usually caused by stress that would not break a healthy bone
- **fractures** classified by structural characteristics
 - direction of fracture line
 - break in the skin
 - multiple pieces
- uncomplicated fractures
 - normally take **8 - 12 weeks to heal**
 - longer in elderly



Stages in Healing of Fractures

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1 Hematoma formation
The hematoma is converted to granulation tissue by invasion of cells and blood capillaries.

2 Soft callus formation
Deposition of collagen and fibrocartilage converts granulation tissue to a soft callus.

3 Hard callus formation
Osteoblasts deposit a temporary bony collar around the fracture to unite the broken pieces while ossification occurs.

4 Bone remodeling
Small bone fragments are removed by osteoclasts, while osteoblasts deposit spongy bone and then convert it to compact bone.

Stages of Healing Bone Fractures (#1)

- Fracture results in hematoma followed by development of granulation tissue
 - bleeding of a broken bone forms a clot – fracture hematoma // immune cells like neutrophils and macrophage enter area
 - granulation tissue – soft fibrous mass is produced includes new capillary networks growing into hematoma
 - cellular invasion // after about 48 hours after injury // chondrocytes enter area
 - fibroblasts, osteoclasts, and osteogenic cells follow chondroblast enter area to further develop granulation tissue

Stages of Healing Bone Fractures (#2)

– Soft callus formation

- formed by fibroblasts and chondroblasts depositing collagen and fibrocartilage into granulation tissue

Stages of Healing Bone Fractures (#3)

– Conversion to hard callus

- osteoblasts produce a bony collar in 6 weeks called a hard callus
- hard callus is cemented to dead bone around the injury site and acts as a temporary splint to join broken ends together
- 4 - 6 weeks for hard callus to form and immobilization is necessary

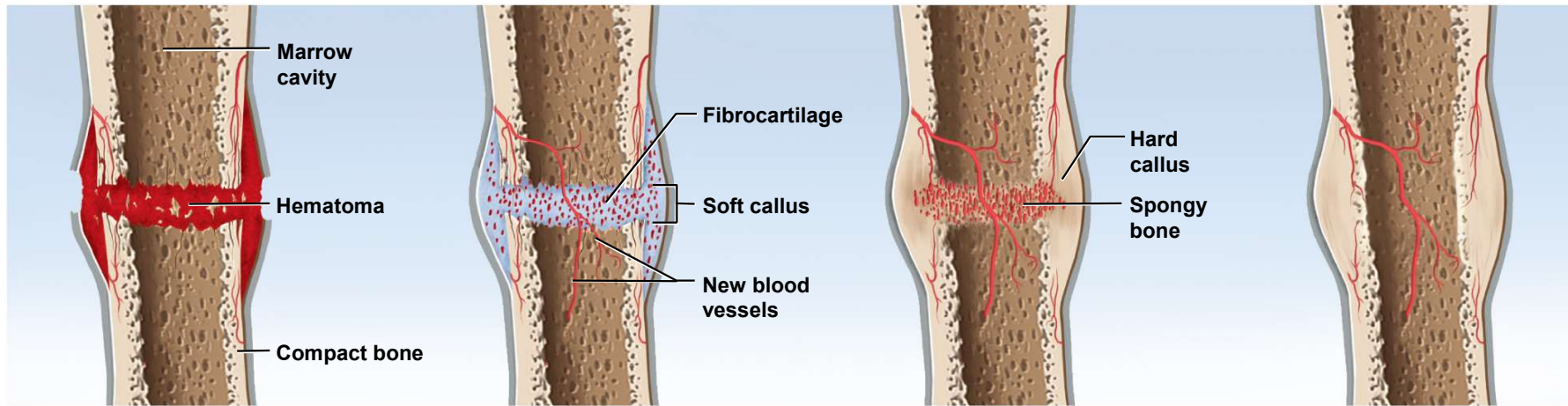
Stages of Healing Bone Fractures (#4)

– Remodeling

- hard callus persists for 3 – 4 months
 - osteoclasts dissolve fragments of broken bone
 - osteoblasts deposit spongy bone to bridge to gap between the broken ends, transformed gradually into compact bone that is thicker in fracture area
- **Note: Vitamin A, vitamin C, and vitamin D are required nutritional factors for growth and repair**

Healing of Fractures

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Treatment of Fractures

- **closed reduction**
 - procedure in which the bone fragments are manipulated into their normal positions without surgery
- **open reduction**
 - involves surgical exposure of the bone and the use of plates, screws, or pins to realign the fragments

Treatment of Fractures

- cast – normally used to stabilize and immobilize healing bone
- electrical stimulation accelerates repair // suppresses the effects of parathyroid hormone
- orthopedics – the branch of medicine that deals with prevention and correction of injuries and disorders of the bones, joints, and muscles

Treatment of Fractures

- traction used to treat fractures of the femur in children
 - aligns bone fragments by overriding force of the strong thigh muscles
 - risks long-term confinement to bed
 - rarely used for the elderly
 - hip fractures are usually pinned in elderly and early ambulation (walking) is encouraged to promote blood circulation and healing

Types of Bone Fractures



(a) Nondisplaced



(c) Comminuted



(d) Greenstick

X-Ray of Fractures and Their Repairs



Osteoporosis

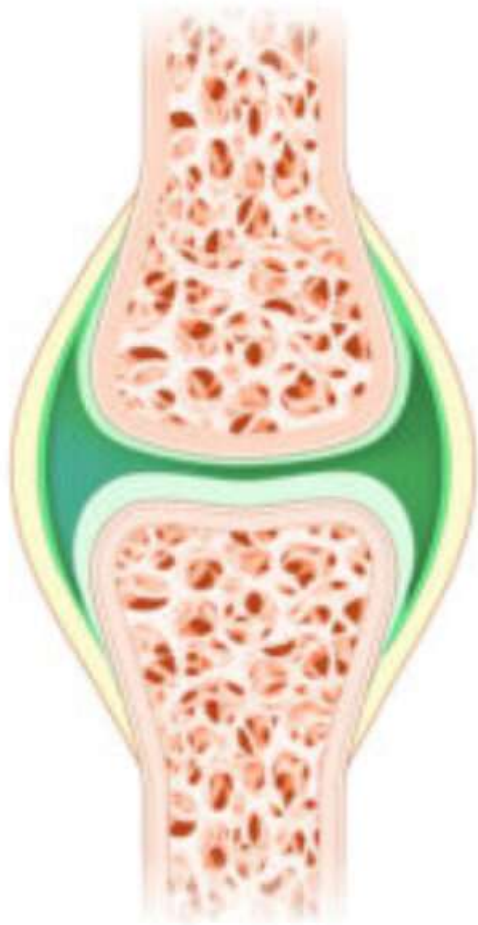
A medical condition in which the bones become brittle and fragile from loss of tissue, typically as a result of hormonal changes, or deficiency of calcium or vitamin D.

Estrogen inhibits osteoclast. After menopause, the ovaries no longer secrete estrogen. Osteoclast become more active and erode bone mass especially the spongy bone

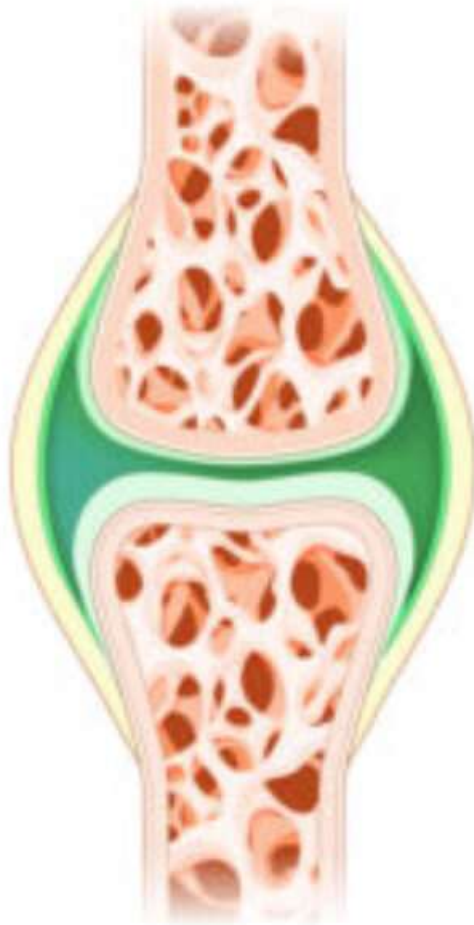
Five Symptoms:

- > Fragility-related fractures. These occur when even mild impact causes a fracture of the wrist, back, hip or other bones.
- > Height loss. More than two inches in height can be lost over time.
- > Receding gums. ...
- > A curved, stooped shape to the spine. ...
- > Lower back pain.

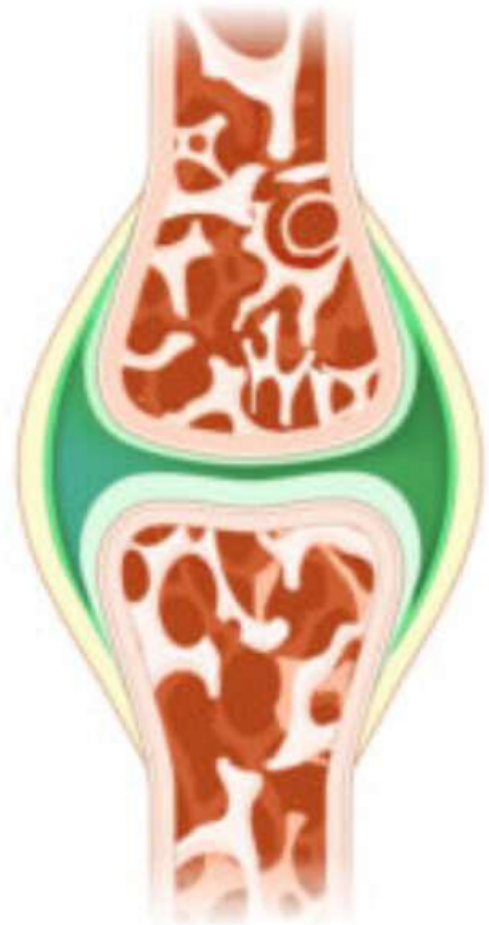
Stages of osteoporosis



Healthy bone

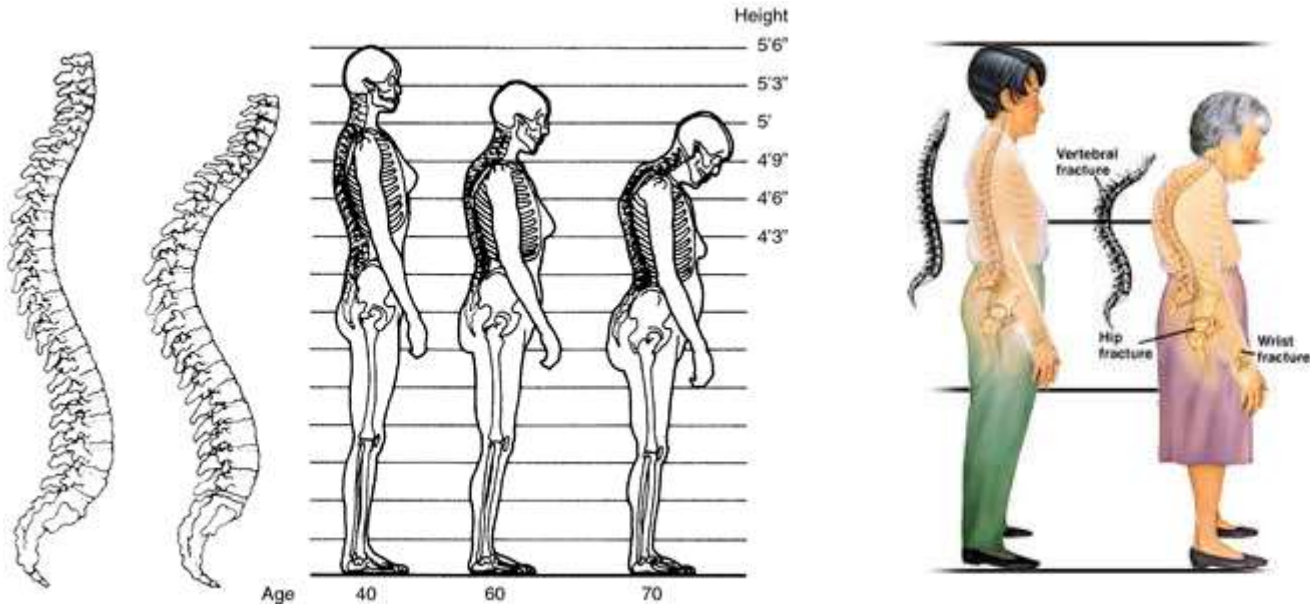


Osteoporosis



Severe osteoporosis

Osteoporosis



Osteoporosis

