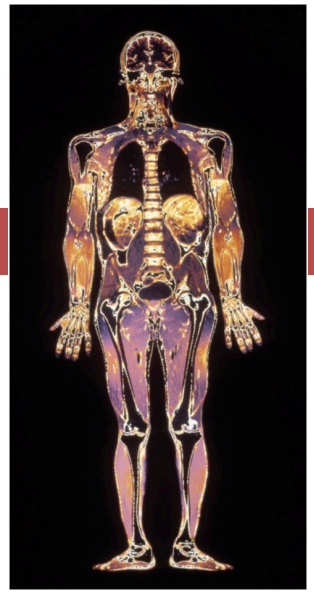
The Skeletal system I

Al-Farabi Kazakh National University
Higher School of Medicine



LEARNING OUTCOMES

As a result of the lesson you will be able to:

- *State functions of the skeletal system;*
- *Describe the general features of a long bone and a flat bone;*
- *Describe briefly the process of bone formation in the fetus, and summarize the events of bone remodeling throughout life.*
- *Discuss the role of the bones in Mineral Homeostasis.*
- *Name the main hormones that regulate bone physiology, and describe their effects;*

Bone Tissue

- tissues and organs of the skeletal system
- histology of osseous tissue
- bone development
- physiology of osseous tissue
- bone disorders

Bone as a Tissue

- **osteology** – the study of bone
- **skeletal system** - composed of bones, cartilages, and ligaments
  - form strong flexible framework of the body
  - **cartilage** – forerunner of most bones
    - covers many joint surfaces of mature bone
- **ligaments** – hold bones together at the joints
- **tendons** – attach muscle to bone

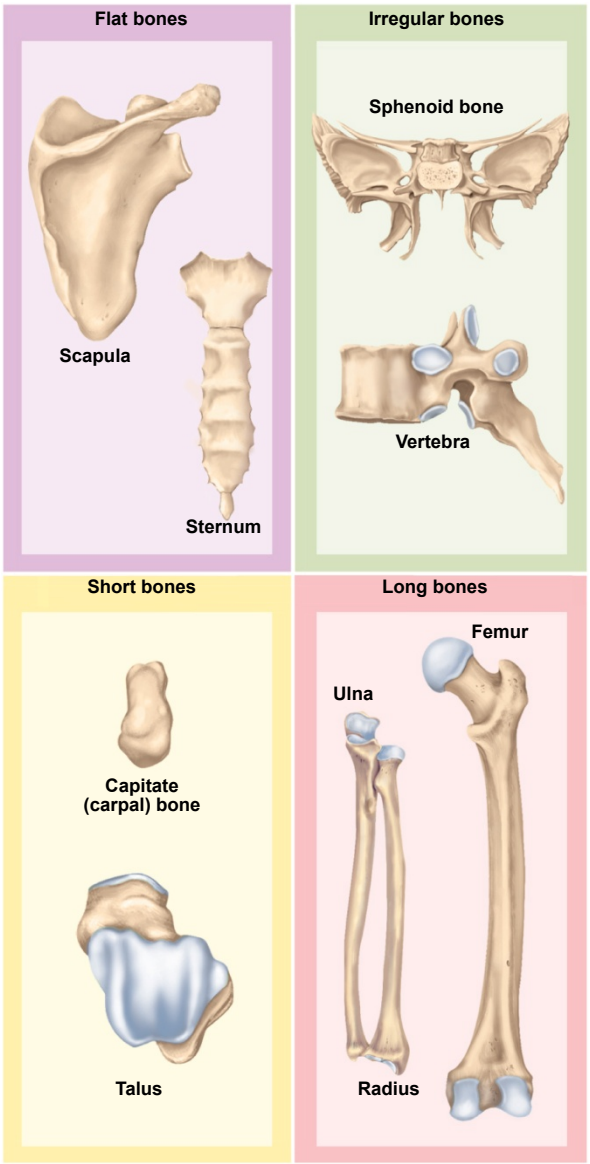
Functions of the Skeleton

- **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

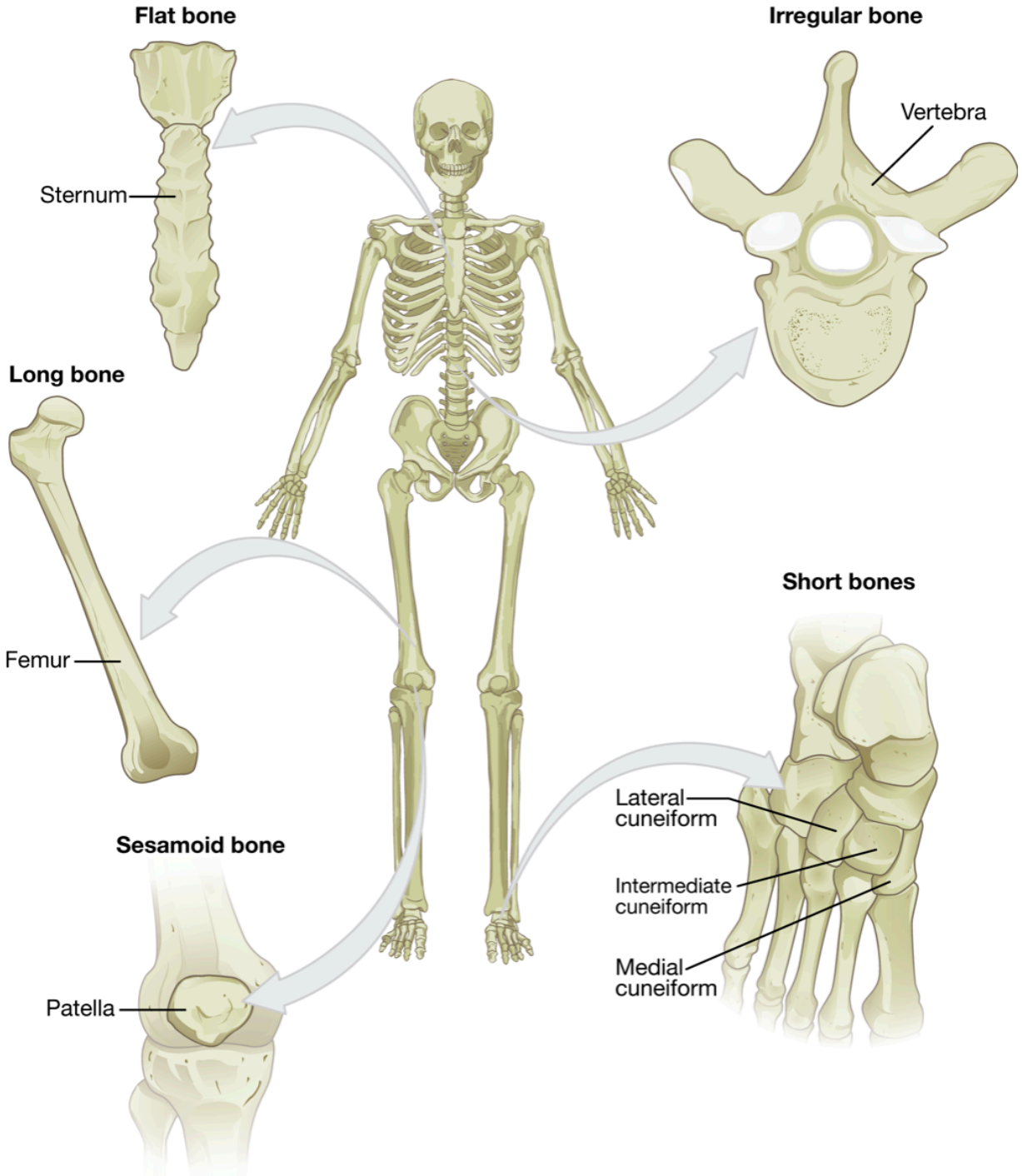
- **bone** (osseous tissue) - connective tissue with the matrix hardened by calcium phosphate and other minerals
- **mineralization** or **calcification** – the hardening process of bone
- individual bones consist of bone tissue, bone marrow, cartilage, adipose tissue, nervous tissue, and fibrous connective tissue
- continually remodels itself and interacts physiologically with all of the other organ systems of the body
- permeated with nerves and blood vessels, which attests to its sensitivity and metabolic activity

Shapes of Bones



- **long bones**
  - longer than wide
  - rigid levers acted upon by muscles
- **short bones**
  - equal in length and width
  - glide across one another in multiple directions
- **flat bones**
  - protect soft organs
  - curved but wide & thin
- **irregular bones**
  - elaborate shapes that don't fit into the other categories

Figure 7.1


Flat bone
Sternum
Irregular bone
Vertebra
Long bone
Femur
Short bones
Lateral cuneiform
Intermediate cuneiform
Medial cuneiform
Sesamoid bone
Patella

General Features of Bones

- **compact (dense) bone** – outer shell of long bone
- **diaphysis** (shaft) - cylinder of compact bone to provide leverage
- **medullary cavity** (marrow cavity) - space in the diaphysis of a long bone that contains bone marrow
- **epiphyses** - enlarged ends of a long bone
  - enlarged to strengthen joint and attach ligaments and tendons
- **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
- **articular cartilage** – a layer of hyaline cartilage that covers the joint surface where one bone meets another
  - allows joint to move more freely and relatively friction free
- **nutrient foramina** – minute holes in the bone surface that allows blood vessels to penetrate

General Features of Bones

- **periosteum** – external sheath that covers bone except where there is articular cartilage
  - **outer fibrous layer** of collagen
    - some outer fibers continuous with the tendons that attach muscle to bone
    - **perforating (Sharpey's) fibers** – other outer fibers that 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
- **endosteum** – thin layer of reticular connective tissue lining marrow cavity
  - has cells that dissolve osseous tissue and others that deposit it
- **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

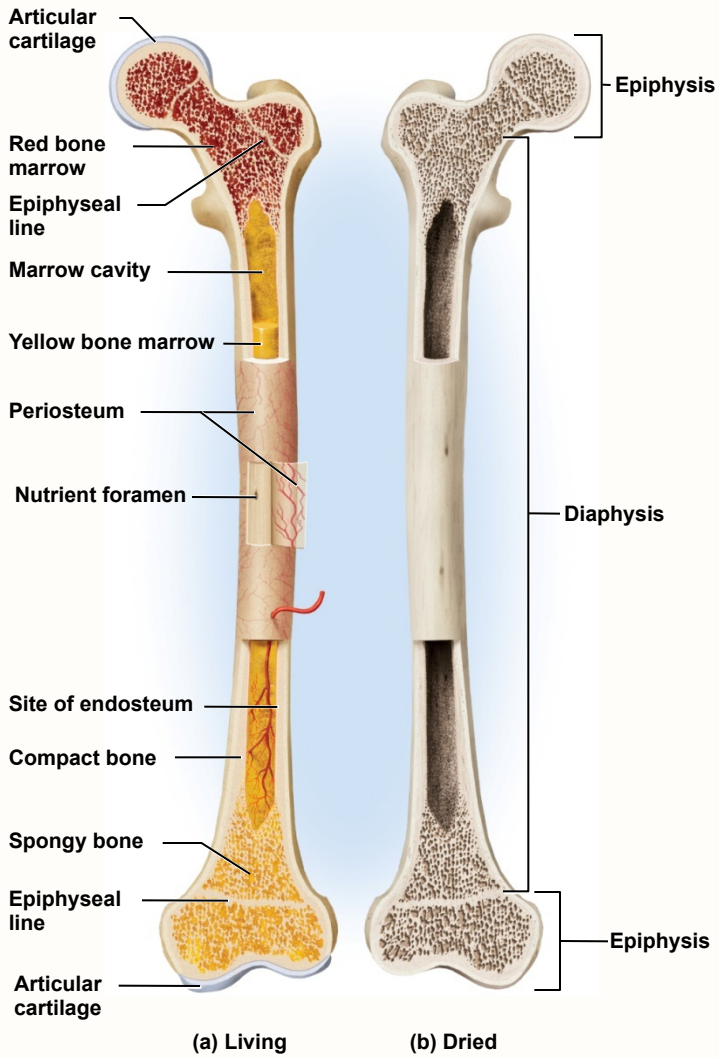


Figure 7.2

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

Structure of a Flat Bone

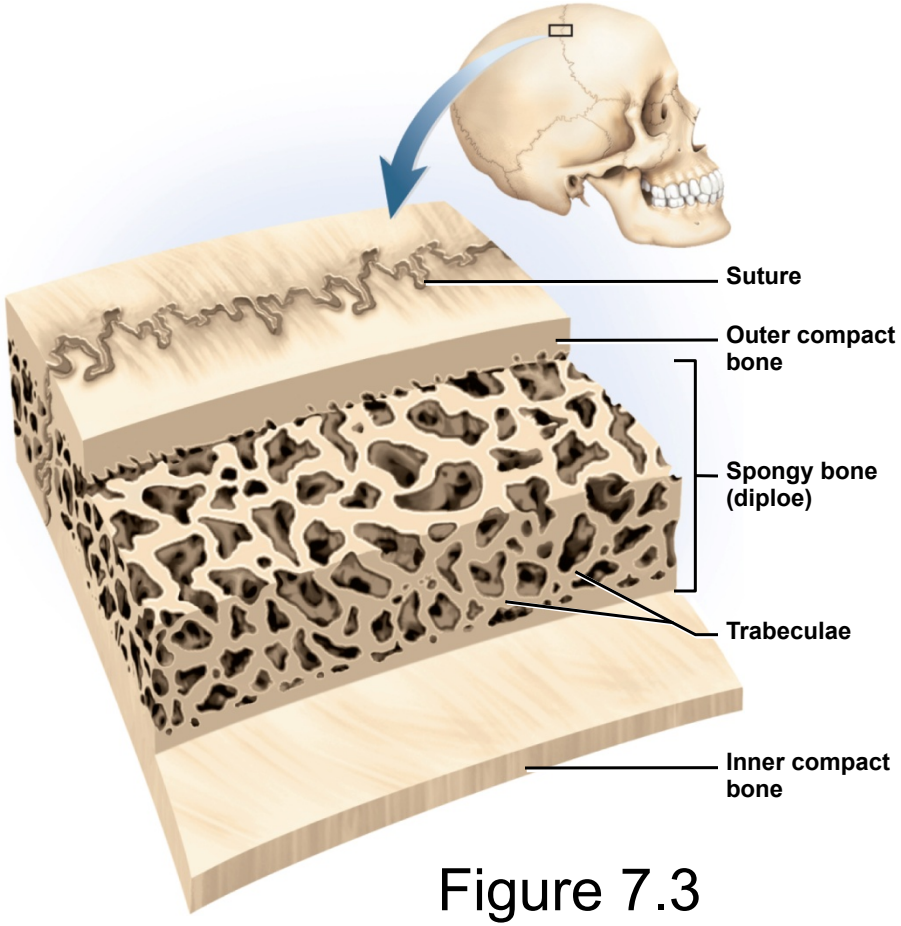


Figure 7.3

- 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

Histology of Osseous Tissue

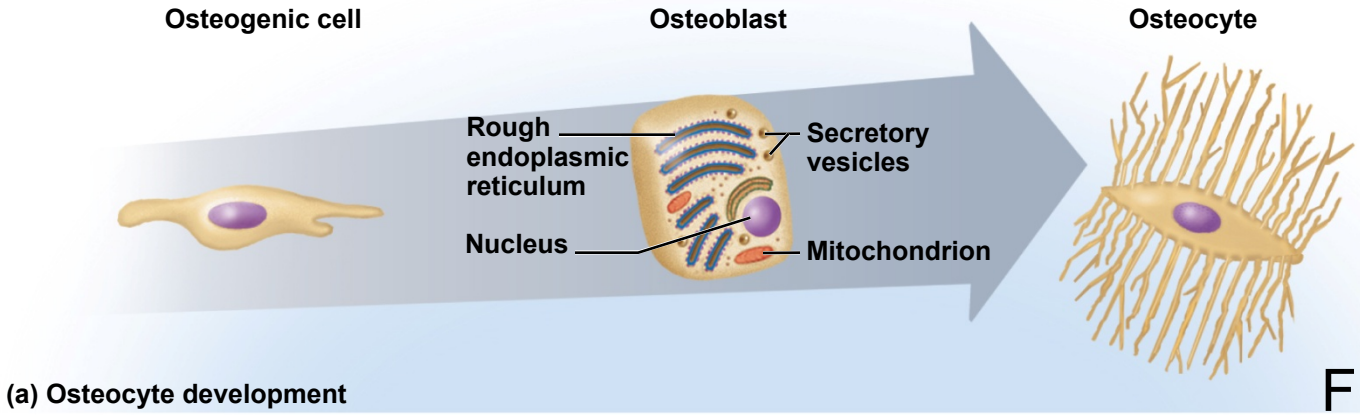


Figure 7.4a

- **bone** is connective tissue that consists of cells, fibers and ground substance

- **four principal types** of bone cells
  - **osteogenic (osteoprogenator) cells**
  - **osteoblasts**
  - **osteocytes**
  - **osteoclasts**

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

Histology of Osseous Tissue

- **osteoblasts** – bone forming cells
  - line up as single layer of cells under endosteum and periosteum
  - are nonmitotic
  - synthesize soft organic matter of matrix which then hardens by mineral deposition
  - stress and fractures stimulate osteogenic cells to multiply more rapidly and increase number of osteocytes to reinforce or rebuild bone
  - secrete **osteocalcin** – thought to be the structural protein of bone
    - stimulates insulin secretion of pancreas
    - increases insulin sensitivity in adipocytes which limit the growth of adipose tissue

- **osteocytes** – former osteoblasts that have become trapped in the matrix they have deposited
  - **lacunae** – tiny cavities where osteocytes reside
  - **canaliculi** – little channels that connect lacunae
  - **cytoplasmic processes** reach into canaliculi
  - some osteocytes reabsorb bone matrix while others deposit it
  - contribute to homeostatic mechanism of bone density and calcium and phosphate ions
  - when stressed, produce biochemical signals that regulate bone remodeling

Cells of Osseous Tissue

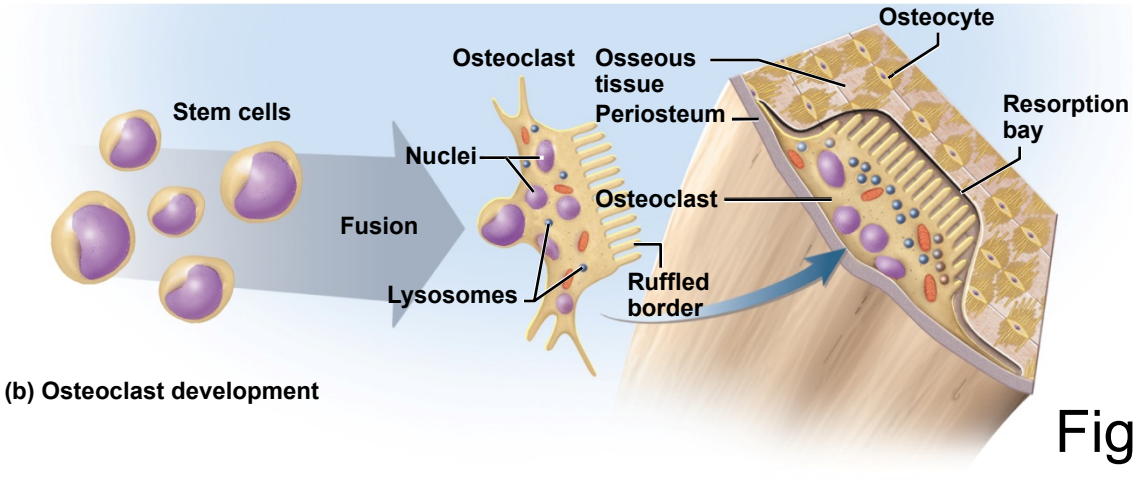


Figure 7.4b

- **osteoclasts** – bone-dissolving cells found on the bone surface
  - osteoclasts develop from same bone marrow stem cells that give rise to blood cells
  - 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

The Matrix

- **matrix of osseous tissue** is, by dry weight, about one-third organic and two-thirds inorganic matter

- **organic matter** – synthesized by osteoblasts
  - collagen, 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)

- bone is **a composite** – combination of two basic structural materials, a ceramic and a polymer
  - 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 protein portion gives bone some degree of flexibility

- **rickets** – soft bones due to deficiency of calcium salts

- **osteogenesis imperfecta** or brittle bone disease – excessively brittle bones due to lack of protein, collagen

Bone Marrow

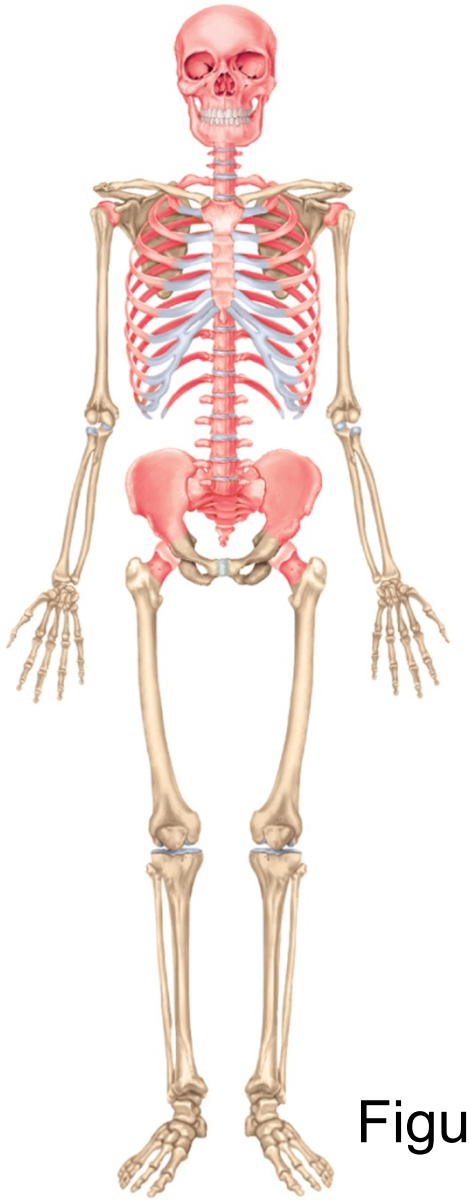


Figure 7.7

- **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

Bone Development

- **ossification or osteogenesis** – the formation of bone

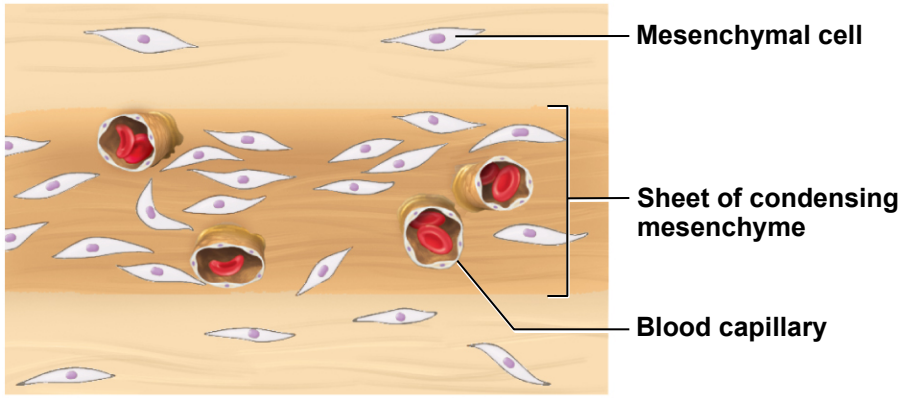
- in the human fetus and infant, bone develops by **two methods**:
  - **intramembranous ossification**
  - **endochondral ossification**

Intramembranous Ossification

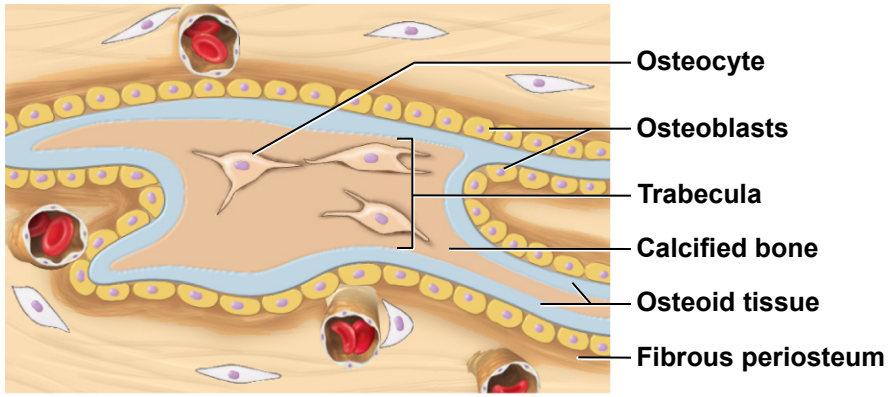
- **intramembranous ossification** – produce the flat bones of the skull and most of the clavicle (collar bone)

- these bones develop within a fibrous sheet similar to 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**
  - 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
  - gives rise to the sandwich-like arrangement of mature flat bone

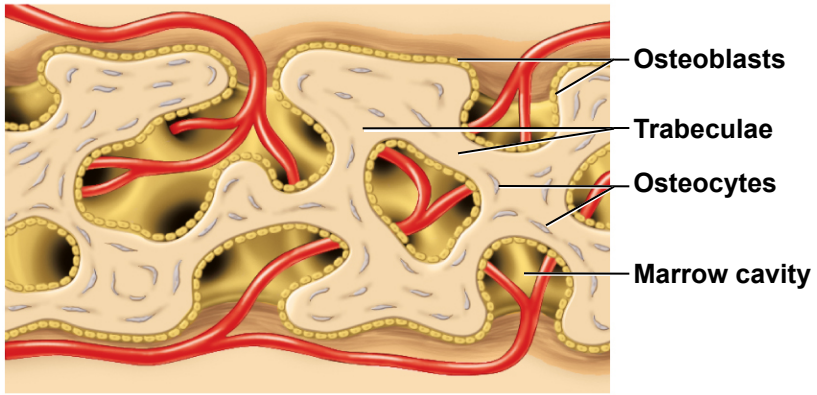
Intramembranous Ossification



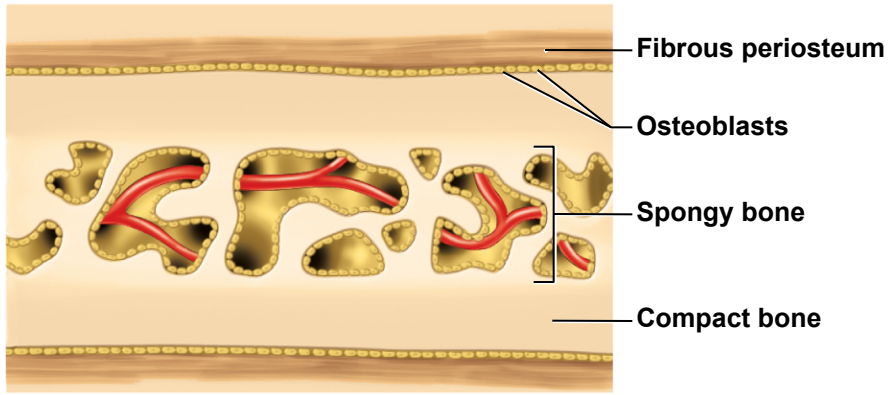
1 Condensation of mesenchyme into soft sheet permeated with blood capillaries



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

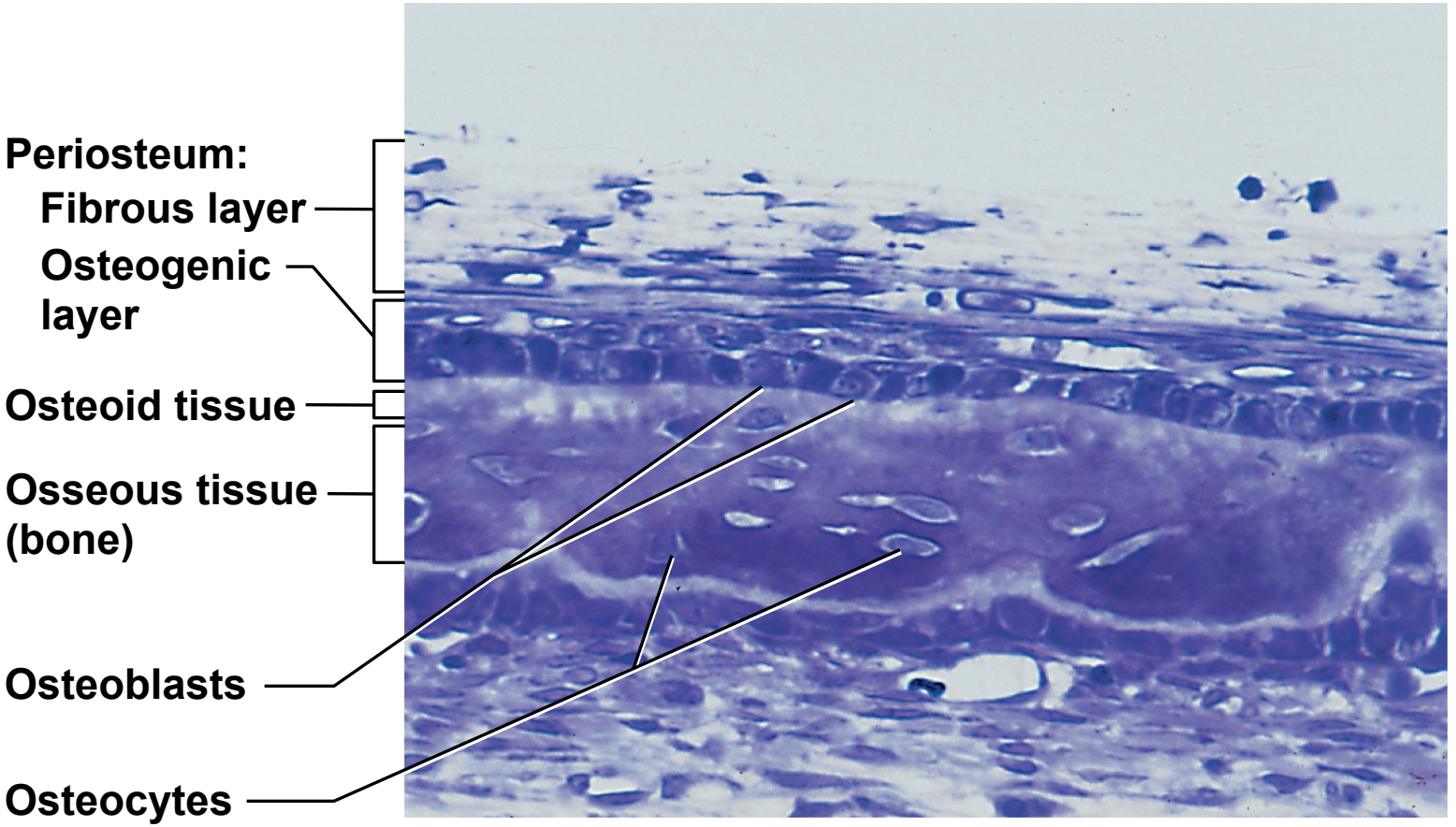


4 Surface bone filled in by bone deposition, converting spongy bone to compact bone. Persistence of spongy bone in the middle layer.

Figure 7.8

produces flat bones of skull and clavicle

Intramembranous Ossification



© Ken Saladin

Figure 7.9

note the periosteum and osteoblasts.

Endochondral Ossification

- **endochondral ossification** – process in which bone develops from pre-existing 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**
  - **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

Primary Ossification Center and Primary Marrow Cavity

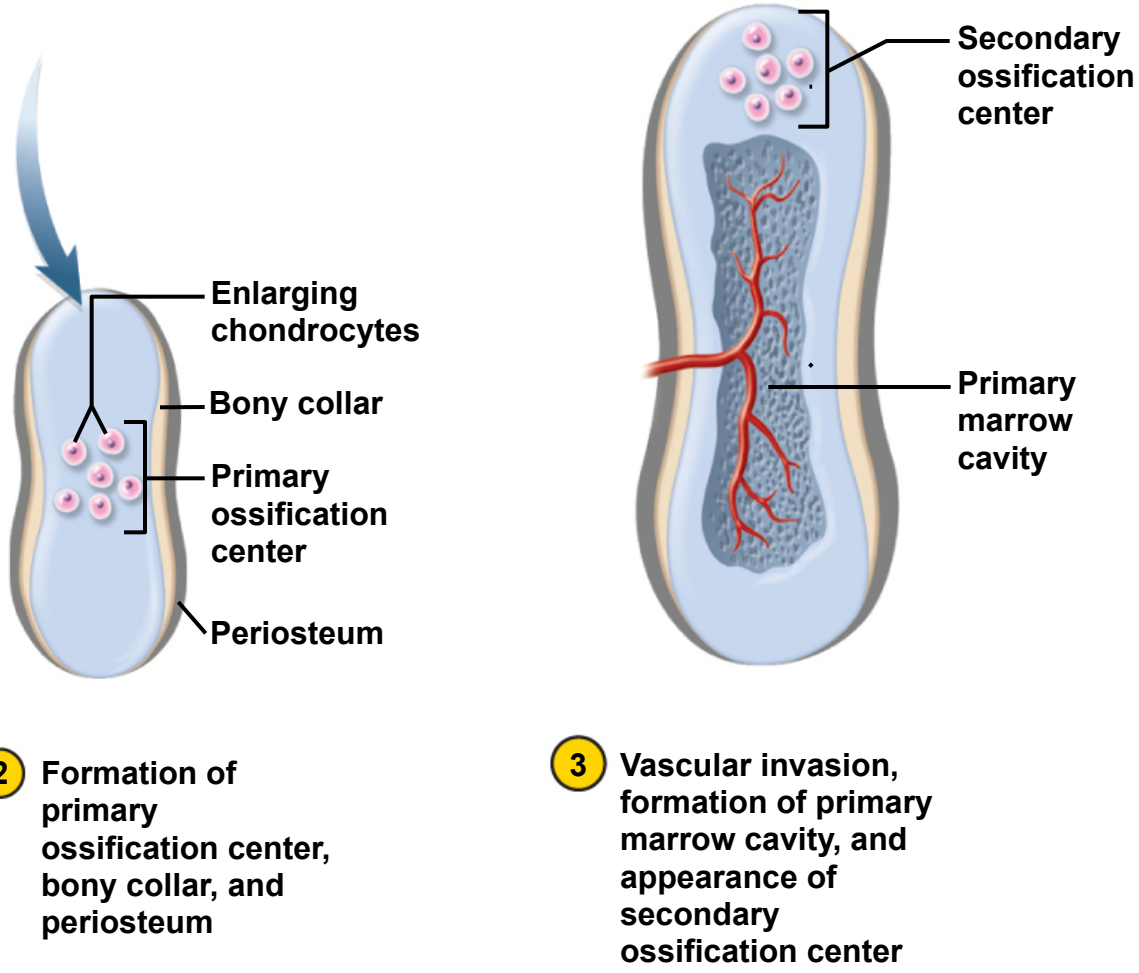


Figure 7.10 (2-3)

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
- **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

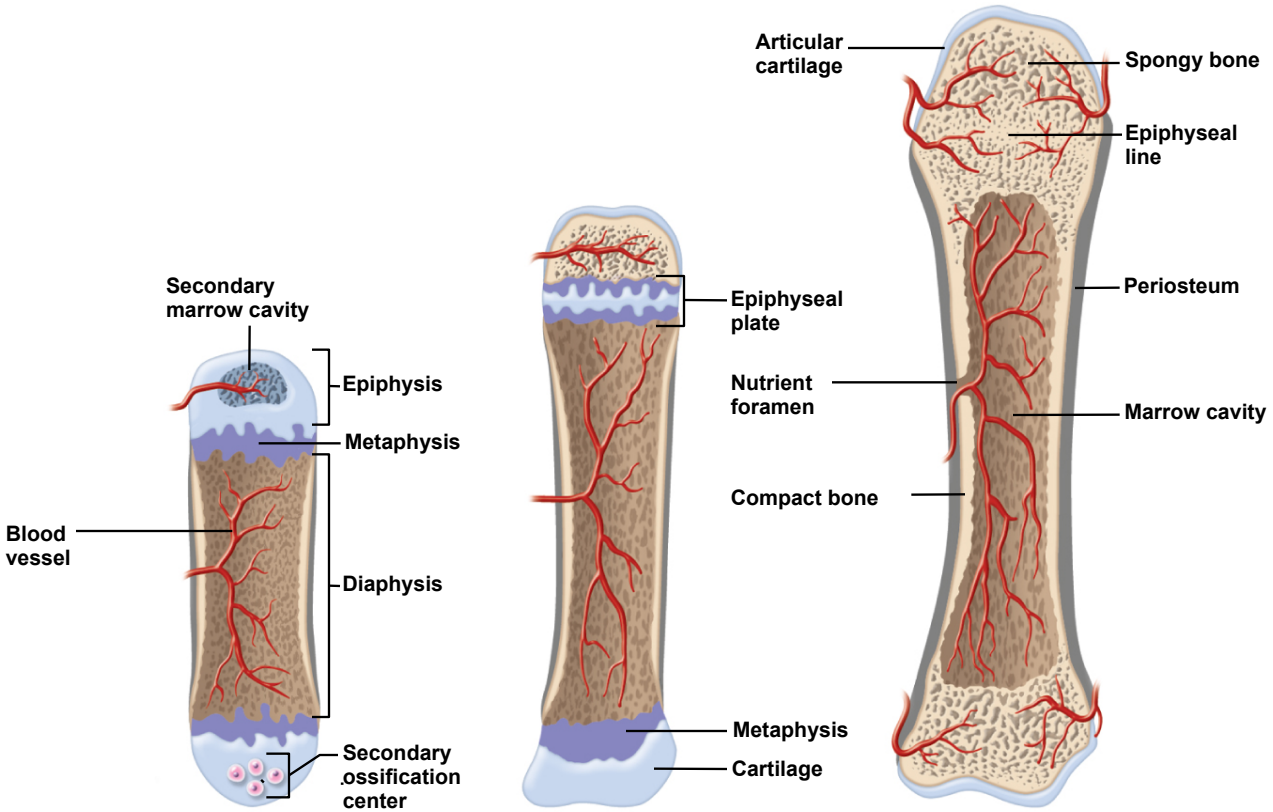


Figure 7.10 (4-6)

Endochondral Ossification

- during infancy and childhood, the epiphyses fill with spongy bone
- 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
- by late teens to early twenties, all remaining cartilage in the epiphyseal plate is generally consumed
  - gap between epiphyses and diaphysis closes
  - primary and secondary marrow cavities unite into a single cavity
  - bone can no longer grow in length

Stages of Endochondral Ossification

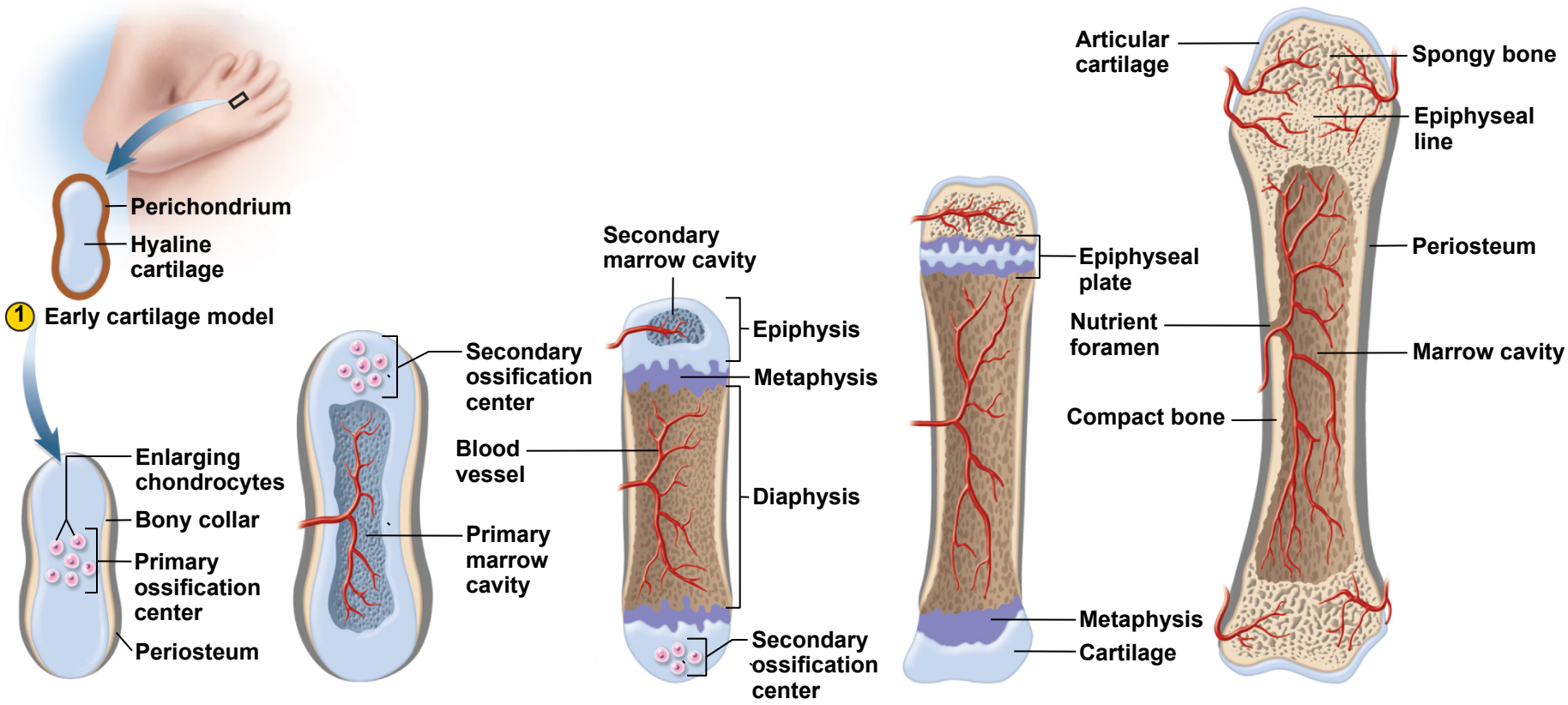


Figure 7.10

Cartilaginous Epiphyseal Plates

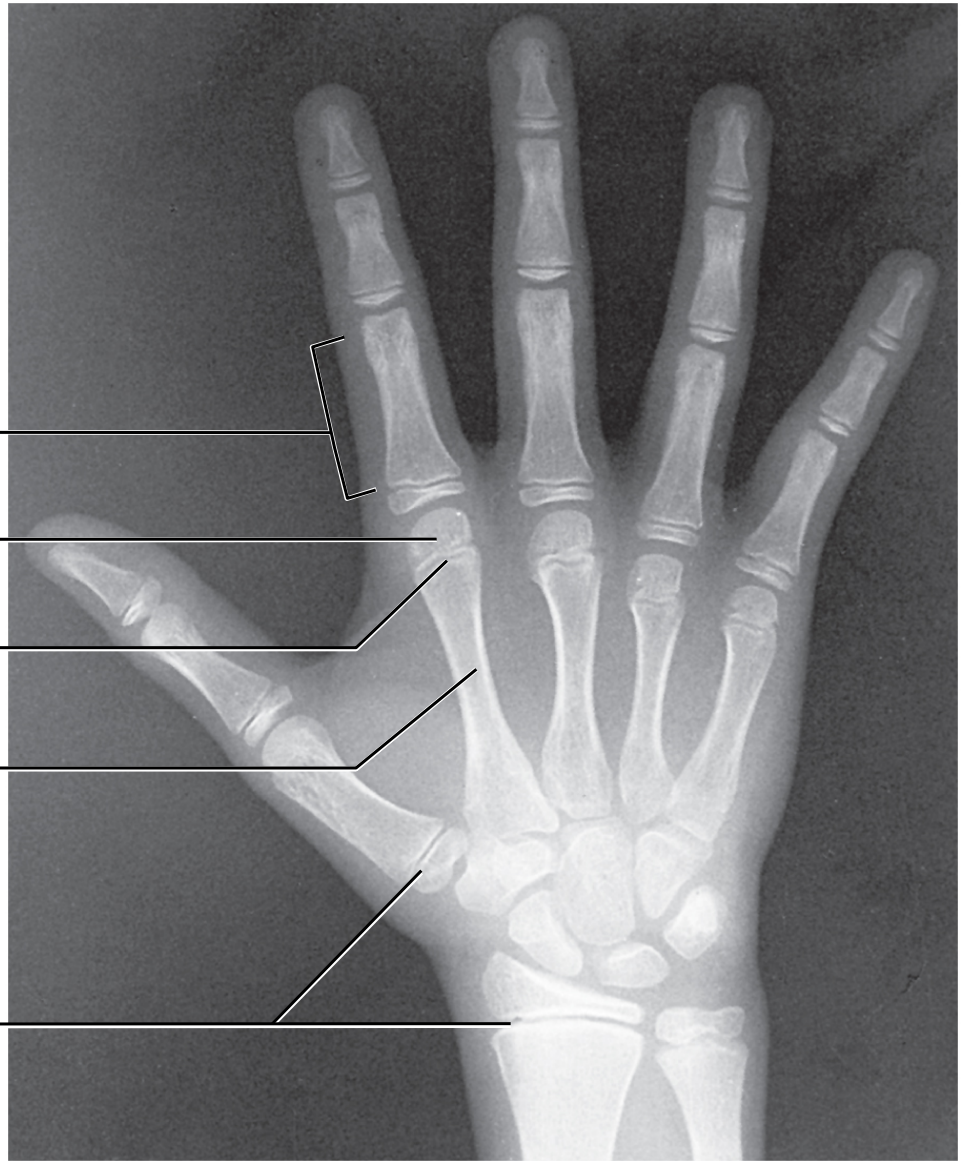


Figure 7.12

Courtesy of Utah Valley Regional Medical Center, Department of Radiology

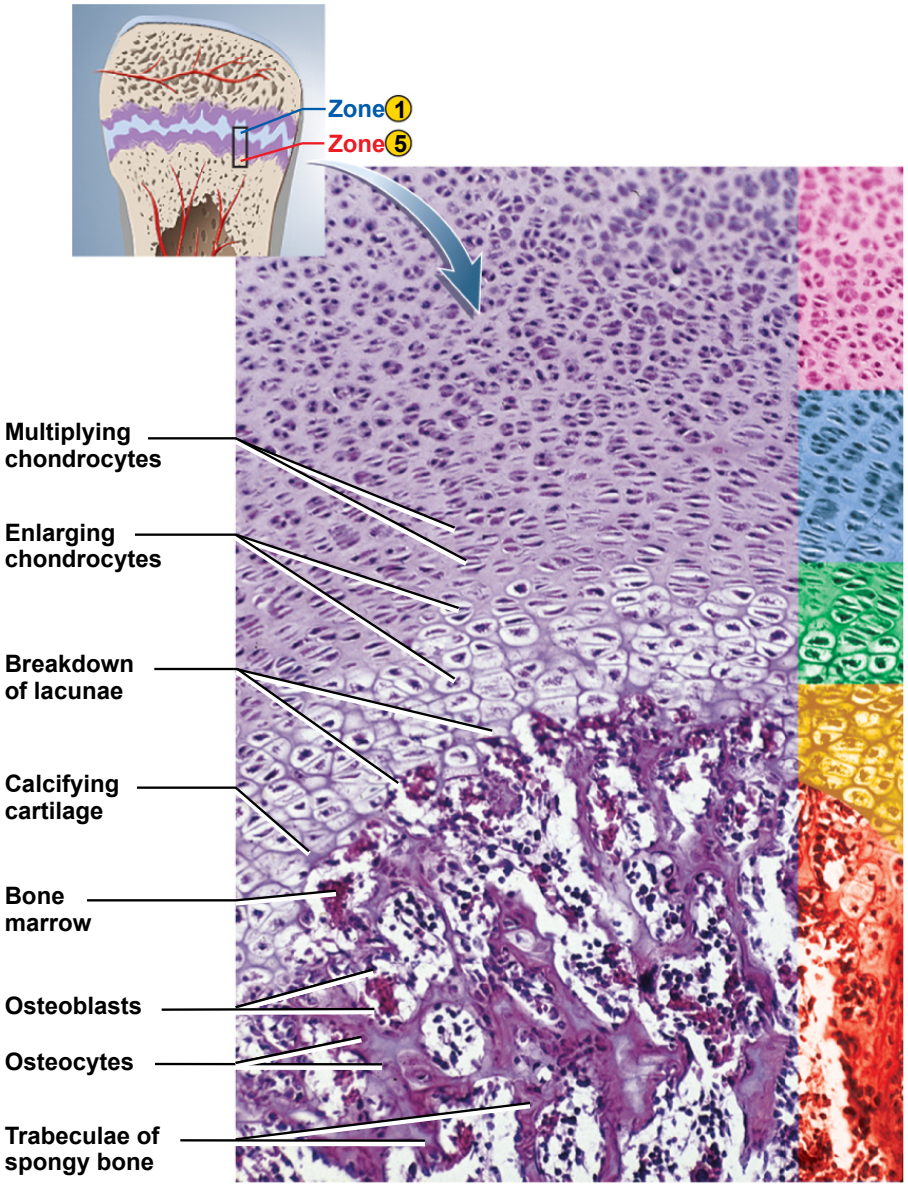
Bone Growth and Remodeling

- **ossification** continues throughout life with the growth and remodeling of bones
- bones grow in two directions: **length** and **width**
- **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

Histology of Metaphysis

- **zone of reserve cartilage**
  - typical hyaline cartilage farthest from marrow cavity
  - shows no sign of transforming into bone
- **zone of proliferation**
  - chondrocytes multiply forming columns of flat lacunae
- **zone of hypertrophy**
  - chondrocyte enlargement
  - matrix between lacunae become very thin
- **zone of calcification**
  - mineral deposited in the matrix between columns of lacunae
  - temporary support for cartilage
- **zone of bone deposition**
  - chondrocytes die, longitudinal columns fill with osteoblasts and blood vessels, osteoclasts dissolve the calcified cartilage
  - osteons and spongy bone are created by osteoblasts

Zones of the Metaphysis



1. **Zone of reserve cartilage**
   Typical histology of resting hyaline cartilage
2. **Zone of cell proliferation**
   Chondrocytes multiplying and lining up in rows of small flattened lacunae
3. **Zone of cell hypertrophy**
   Cessation of mitosis; enlargement of chondrocytes and thinning of lacuna walls
4. **Zone of calcification**
   Temporary calcification of cartilage matrix between columns of lacunae
5. **Zone of bone deposition**
   Breakdown of lacuna walls, leaving open channels; death of chondrocytes; bone deposition by osteoblasts, forming trabeculae of spongy bone

Figure 7.13

Victor Eroschenko

Structure of a Long Bone

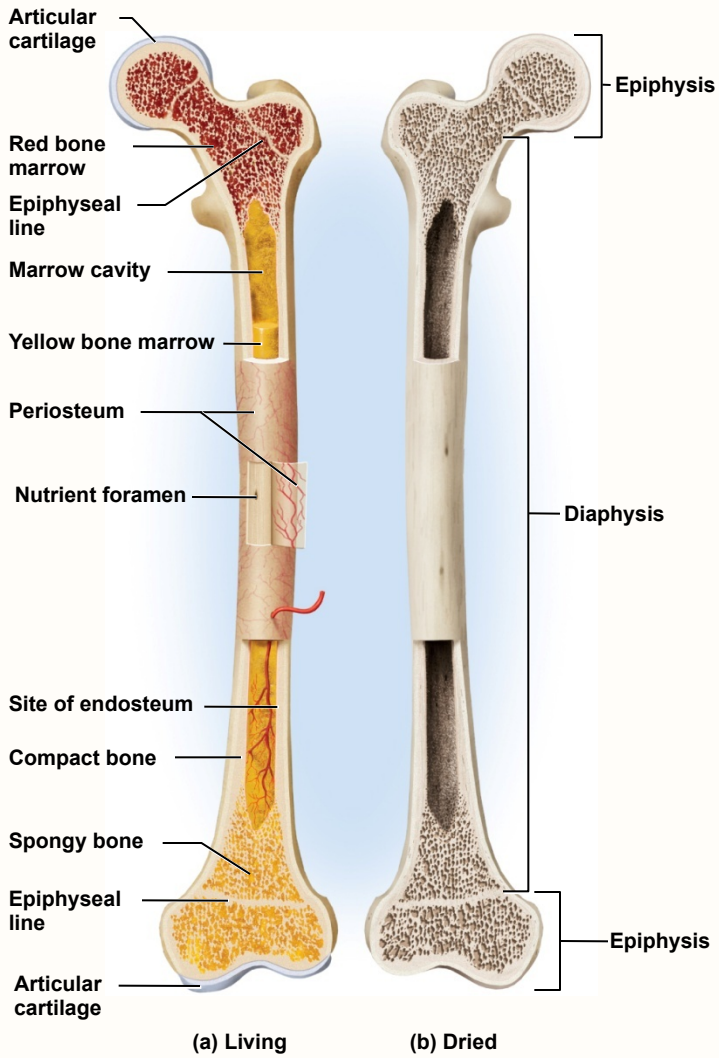


Figure 7.2

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

Fetal Skeleton at 12 Weeks

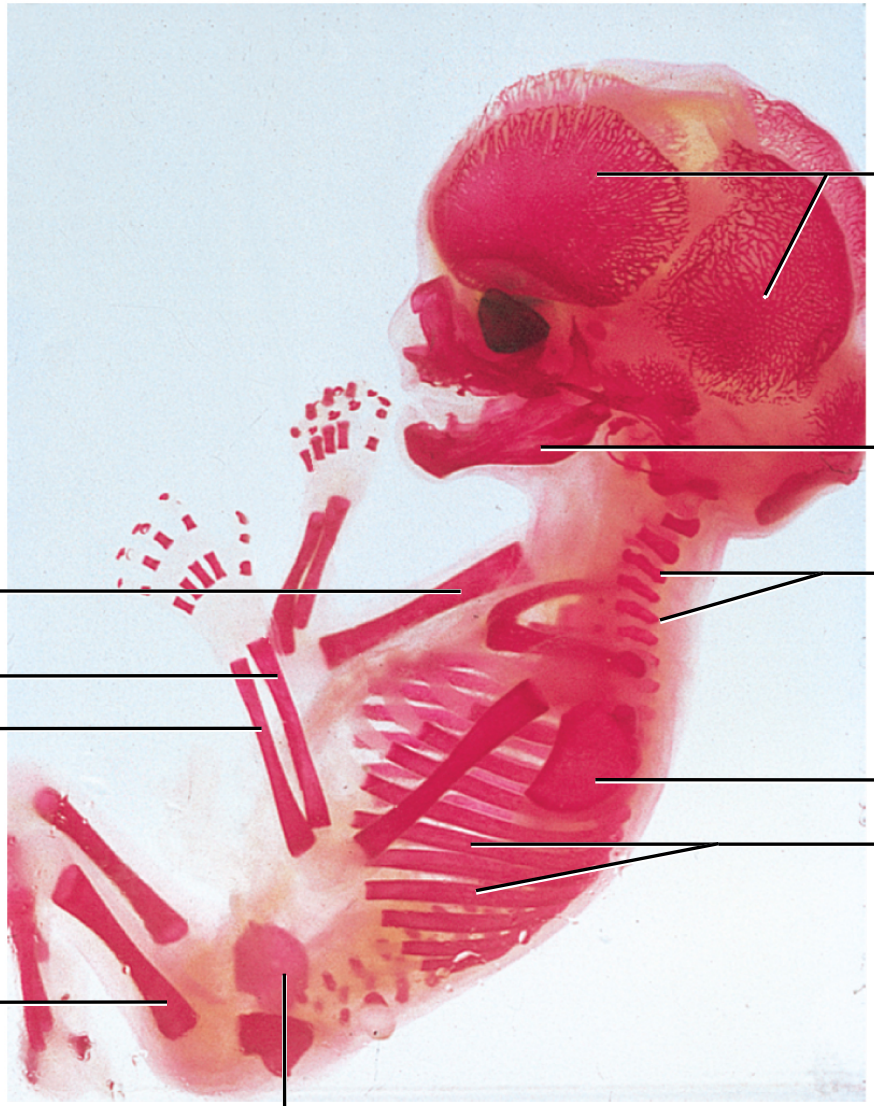


Figure 7.11

Bone Growth and Remodeling

- **interstitial growth** - bones increase in length
  - bone elongation is really a result of cartilage growth within epiphyseal plate
  - epiphyses close when cartilage is gone – **epiphyseal line**
  - length-wise growth is finished
    - occurs at different ages in different bones
- **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
  - lay down matrix in layers parallel to surface
    - forms **circumferential lamellae** over surface
      - osteoclasts of endosteum enlarge marrow cavity
- **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

Dwarfism

Figure 7.14

achondroplastic dwarfism

- long bones stop growing in childhood
  - normal torso, short limbs
- failure of cartilage growth in metaphysis
- spontaneous mutation produces mutant dominant allele

pituitary dwarfism

- lack of growth hormone
- normal proportions with short stature

Physiology of Osseous Tissue

- **a mature bone remains a metabolically active organ**
  - involved in its own maintenance of growth and remodeling
  - exerts a profound influence over the rest of the body by exchanging minerals with tissue fluid
    - disturbance of **calcium homeostasis** in skeleton disrupts function of other organ systems
      - especially nervous and muscular

Mineral Deposition

- **mineral deposition** (mineralization) - a crystallization process in which calcium phosphate, and other ions are taken from the blood plasma and deposited in bone tissue
  - **osteoblasts** produce collagen fibers that spiral the length of the osteon
  - fibers become encrusted with minerals that harden the matrix
    - calcium and phosphate (hydroxyapatite) from blood plasma are deposited along the fibers
    - the calcium and phosphate ion concentration must reach a critical value called the **solubility product** for crystal formation to occur
    - most tissues have **inhibitors** to prevent this so they do not become calcified
    - osteoblasts **neutralize these inhibitors** and allow salts to precipitate in the bone matrix
    - first few crystals (**seed crystals**) attract more calcium and phosphate from solution
- **abnormal calcification** (**ectopic ossification**)
  - may occur in lungs, brain, eyes, muscles, tendons or arteries (arteriosclerosis)
  - **calculus** – calcified mass in an otherwise soft organ such as the lung

Mineral Resorption

- **mineral resorption** – the process of dissolving bone and releasing minerals into the blood
  - performed by **osteoclasts** at the "**ruffled border**"
  - **hydrogen pumps** in membrane secrete hydrogen into space between the osteoclast and bone surface
  - **chloride ions** follow by electrical attraction
  - **hydrochloric acid** (pH 4) dissolves bone minerals
  - **acid phosphatase** enzyme digests the collagen
- **orthodontic appliances** (braces) reposition teeth
  - tooth moves because **osteoclasts** dissolve bone ahead of the tooth, where the pressure on the bone is the greatest
  - **osteoblasts** deposit bone more slowly in the low-pressure zone behind the tooth

Calcium Homeostasis

- calcium and phosphate are used for much more than bone structure
- phosphate is a component of DNA, RNA, ATP, phospholipids, and pH buffers
- calcium needed in neuron communication, muscle contraction, blood clotting, and exocytosis
- minerals are deposited in the skeleton and withdrawn when they are needed for other purposes
- about 1100g of calcium in adult body
  - 99% in the skeleton
    - as easily exchangeable calcium ions and more stable hydroxyapatite reserve
    - 18% of adult skeleton exchanged with blood each year
- normal calcium concentration in blood plasma is normally **9.2 to 10.4 mg/dl –** 45% as Ca^{2+} can diffuse across capillary walls and affect other tissues – rest in reserve, bound to plasma proteins
  - **hypocalcemia** - blood calcium deficiency
    - causes excess excitability of muscle, tremors, spasms or tetany (inability to relax)
      - Na^{+} enters cells too easily and excites nerves and muscles
  - **hypercalcemia** - blood calcium excess
    - sodium channels less responsive and nerve and muscle less excitable than normal (sluggish reflexes, depression)

Carpopedal Spasm

Figure 7.15

hypocalcemia demonstrated by muscle spasm of hands and feet

Ion Imbalances

- **hypercalcemia** is rare
- **hypocalcemia** has a wide variety of causes
  - vitamin D deficiency
  - diarrhea
  - thyroid tumors
  - underactive parathyroids
  - pregnancy and lactation
  - accidental removal of parathyroid glands during thyroid surgery
- **calcium homeostasis** depends on a balance between dietary intake, urinary and fecal loses, and exchanges between osseous tissue
- calcium homeostasis is regulated by three hormones:
  - ***calcitriol, calcitonin, and parathyroid hormone***

Hormonal Control of Calcium

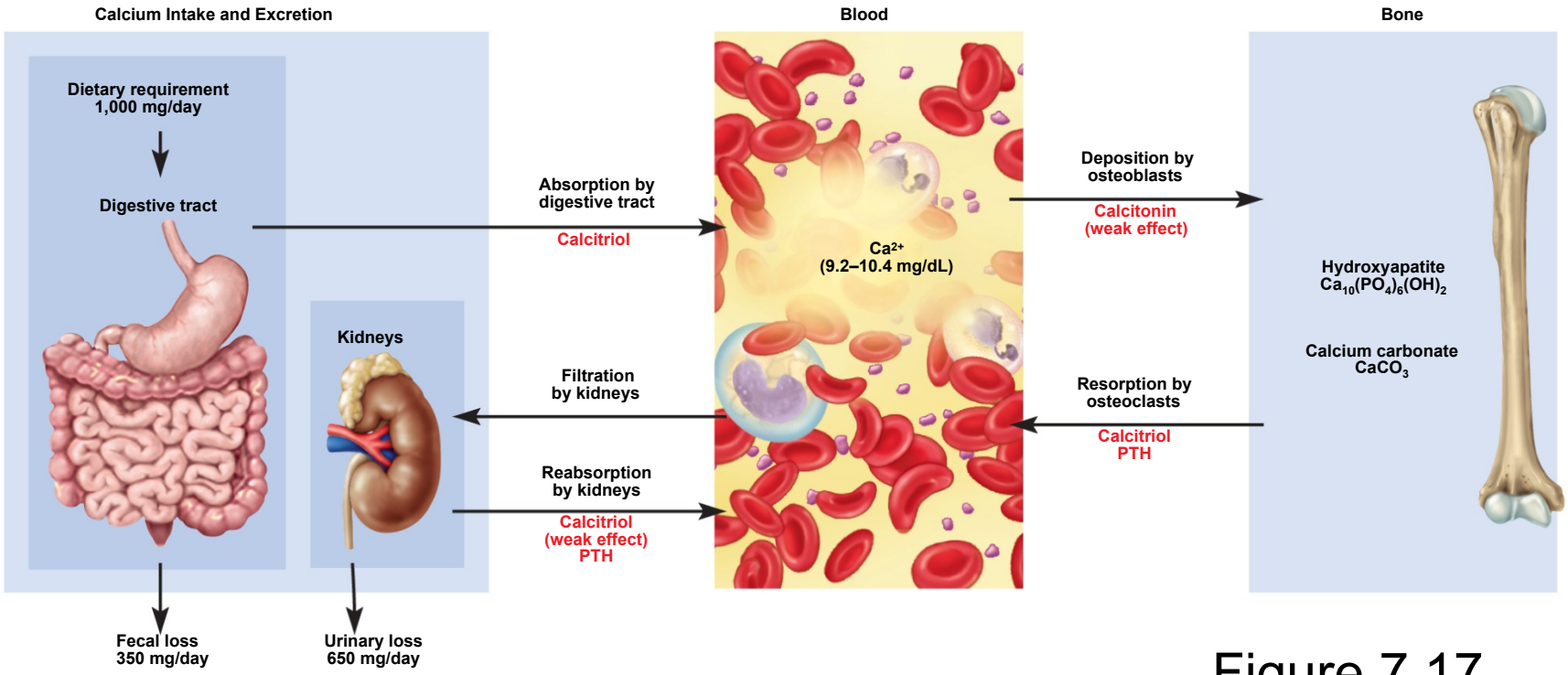


Figure 7.17

calcitriol, calcitonin, and PTH maintain normal blood calcium concentration

Calcitriol (Activated Vitamin D)

- **calcitriol** – a form of vitamin D produced by the sequential action of the skin, liver, and kidneys
- produced by the following process:
  - **epidermal keratinocytes** use UV radiation to convert a steroid, ***7-dehydrocholesterol*** to ***previtamin D_3***
  - **liver** adds a hydroxyl group converting it to **calcidiol**
  - **kidneys** adds another hydroxyl group, converting that to ***calcitriol*** (most active form of vitamin D) – also from fortified milk
- calcitriol behaves as a **hormone** that **raises blood calcium concentration**
  - increases calcium absorption by small intestine
  - increases calcium resorption from the skeleton
    - increases stem cell differentiation into osteoclasts which liberates calcium and phosphate from bone
  - promotes kidney reabsorption of calcium ions, so less lost in urine
- necessary for bone deposition – need adequate calcium and phosphate
- abnormal softness of bones (**rickets**) in children and (**osteomalacia)** in adults without adequate vitamin D

Calcitriol Synthesis and Action

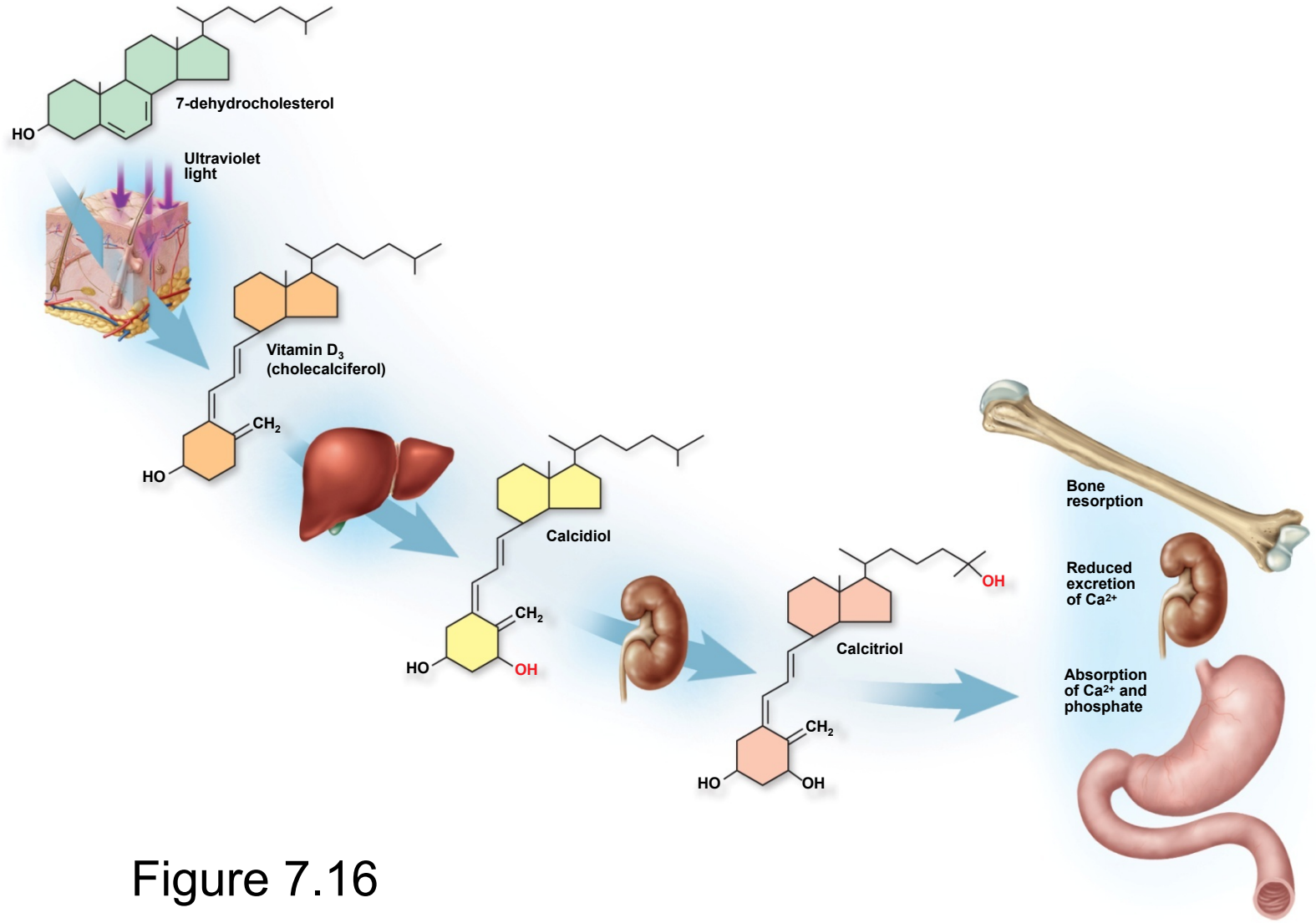
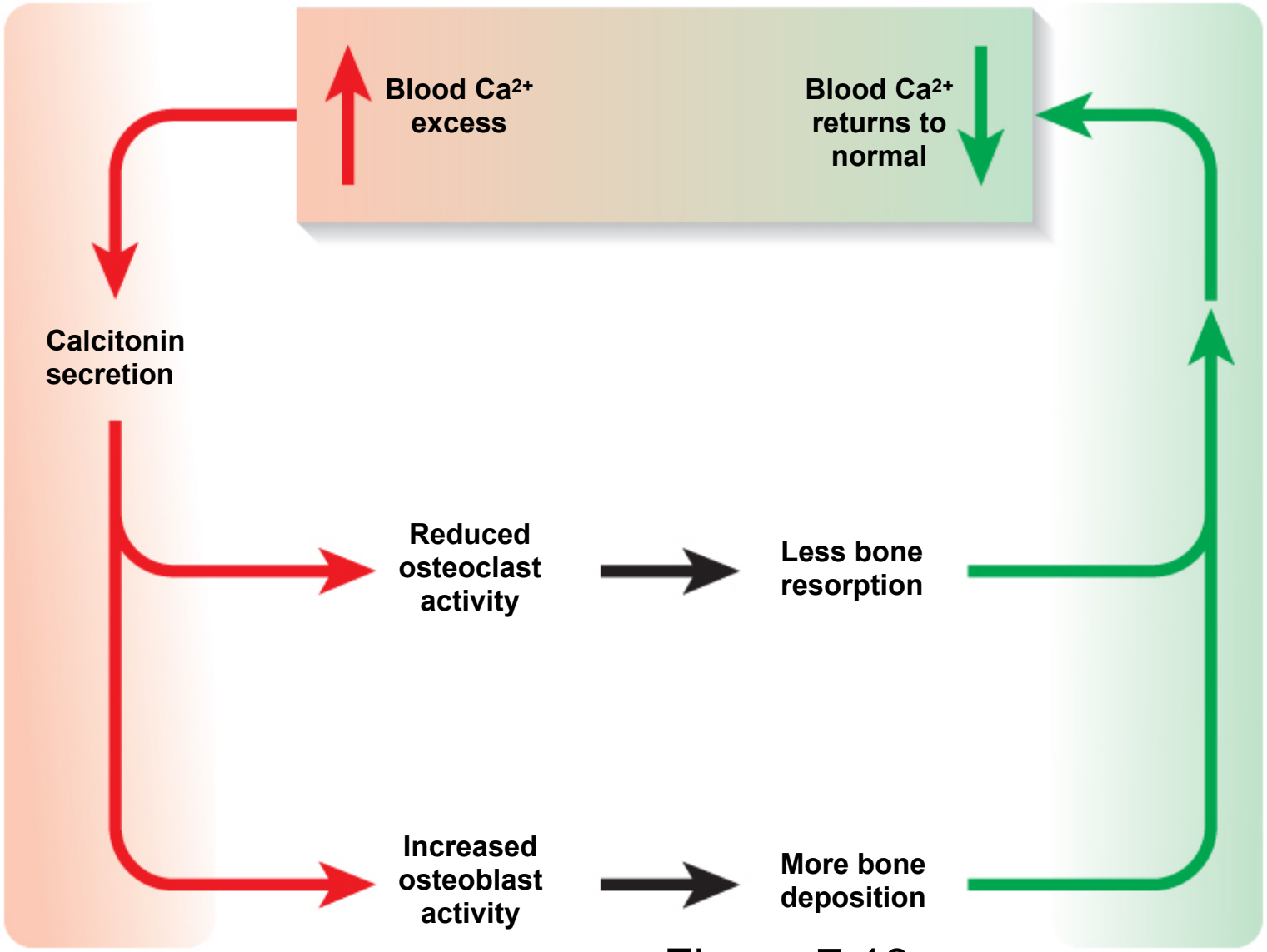


Figure 7.16

Calcitonin

- **calcitonin** - secreted by **C cells** (clear cells) of the **thyroid gland** when calcium concentration rises **too high**
- **lowers blood calcium concentration** in two ways:
  - **osteoclast inhibition**
    - reduces osteoclast activity as much as 70%
    - less calcium liberated from bones
  - **osteoblast stimulation**
    - increases the number and activity of osteoblasts
    - deposits calcium into the skeleton
- important in children, weak effect in adults
  - osteoclasts more active in children due to faster remodeling
  - deficiency does not cause disease in adults
- reduces bone loss in women during pregnancy & lactation

Correction for Hypercalcemia



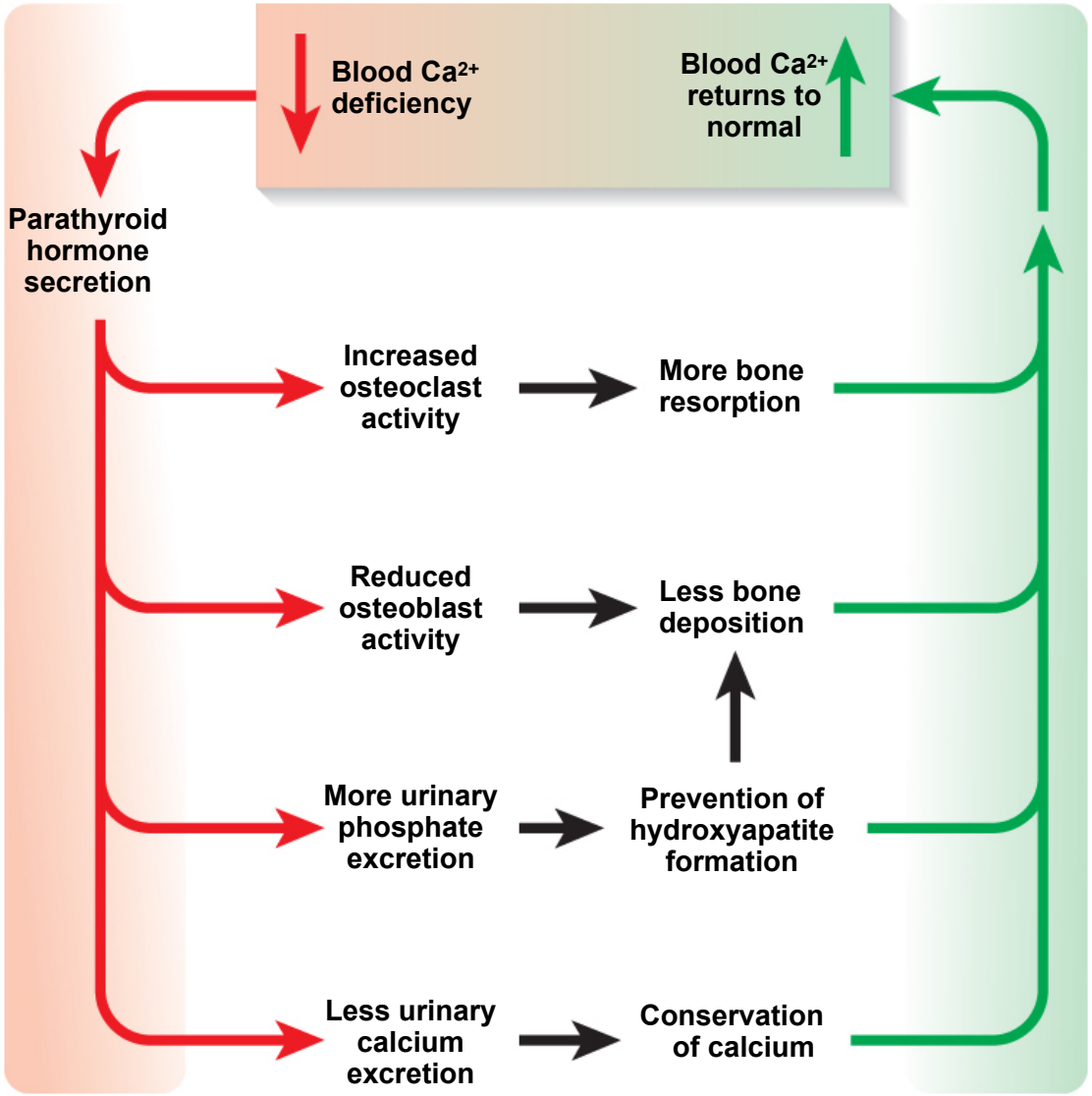
(a) Correction for hypercalcemia

Figure 7.18a

Parathyroid Hormone

- **parathyroid hormone** (PTH) – secreted by the parathyroid glands which adhere to the posterior surface of thyroid gland
- PTH released with low calcium blood levels
- **PTH raises calcium blood level** by four mechanisms
  - binds to receptors on osteoblasts
    - stimulating them to secrete RANKL which raises the osteoclast population
  - promotes calcium reabsorption by the kidneys, less lost in urine
  - promotes the final step of calcitriol synthesis in the kidneys, enhancing calcium raising effect of calcitriol
  - inhibits collagen synthesis by osteoblasts, inhibiting bone deposition
- sporadic injection or secretion of low levels of PTH causes bone deposition, and can increase bone mass

Correction for Hypocalcemia



(b) Correction for hypocalcemia

Figure 7.18b

Phosphate Homeostasis

- average adult has 500 – 800 g of phosphorus
- 85-90% of phosphate is in the bones
- normal plasma concentration is **3.5 – 4.0 mg/dl**
- occurs in **two principal forms**:
  - **HPO_4^{2-}** and **$H_2PO_4^-$** (monohydrogen & dihydrogen phosphate ions)
- phosphate levels are not regulated as tightly as calcium levels
  - no immediate functional disorders
- calcitriol promotes its absorption by small intestine & promotes bone deposition
- PTH lowers blood phosphate level by promoting its urinary excretion

Other Factors Affecting Bone

- at least 20 or more hormones, vitamins, and growth factors affect osseous tissue

- bone growth especially rapid in puberty & adolescence
  - surges of growth hormone, estrogen, and testosterone occur and promote ossification
  - these hormones stimulate multiplication of osteogenic cells, matrix deposition by osteoblasts, and chondrocyte multiplication and hypertrophy in metaphyses
  - girls grow faster than boys and reach full height earlier
    - estrogen stronger effect than testosterone on bone growth
  - males grow for a longer time and taller

- **anabolic steroids** cause growth to stop
  - epiphyseal plate “closes” prematurely
  - results in abnormally short adult stature

Osteoporosis

- **osteoporosis** – the most common bone disease
  - severe loss of bone density
- bones lose mass and become brittle due to loss of organic matrix and minerals
  - affects spongy bone the most since it is the most metabolically active
  - subject to pathological fractures of hip, wrist and vertebral column
  - **kyphosis** (widow's hump) – deformity of spine due to vertebral bone loss
  - complications of loss of mobility are pneumonia and thrombosis
- postmenopausal white women at greatest risk
  - begin to lose bone mass as early as 35 yoa
    - by age 70, average loss is 30% of bone mass
  - risk factors - race, age, gender, smoking, diabetes mellitus, diets poor in calcium, protein, vitamins C and D

Osteoporosis

- estrogen maintains density in both sexes inhibits resorption by osteoclasts
  - testes and adrenals produce estrogen in men
  - in women, rapid bone loss after menopause since estrogen blood level drops below 30 ng/mL
- osteoporosis is common in young female athletes with low body fat causing them to stop ovulating and ovarian estrogen secretion is low
- treatments
  - **estrogen replacement therapy** (ERT) slows bone resorption, but increases risk of breast cancer, stroke and heart disease
  - drugs **Fosamax/Actonel** destroys osteoclasts
  - **PTH** slows bone loss if given as daily injection
    - **Forteo** (PTH derivative) increases density by 10% in 1 year
      - may promote bone cancer so use is limited to 2 years
  - best treatment is **prevention** - exercise and calcium intake (1000 mg/day) between ages 25 and 40

Spinal Osteoporosis

(a)

(b)

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Figure 7.22 a-b