Physiology of Osseous Tissue

By

Dr. Hassan Y. Hassan

2nd year

Lecture 1

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 and Resorption

- **Mineral deposition (mineralization)**—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

Mineral Deposition and Resorption

Cont.

- 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

Mineral Deposition and Resorption

- **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**—the process of dissolving bone and releasing minerals into the blood
  - Performed by **osteoclasts** at the **ruffled border**
  - **Hydrogen pumps** in membranes secrete hydrogen into space between the osteoclast and bone surface

Mineral Deposition and Resorption

Cont.

- **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

Calcium Homeostasis

- About 1,100 g 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 **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

Calcium Homeostasis

- **Hypocalcemia** has a wide variety of causes, blood calcium excess
  - Vitamin D deficiency
  - Diarrhea
  - Thyroid tumors
  - Underactive parathyroids
  - Pregnancy and lactation
  - Accidental removal of parathyroid glands during thyroid surgery

Calcium Homeostasis

- **Calcium homeostasis** depends on a balance between dietary intake, urinary and fecal losses, and exchanges between osseous tissue
- Calcium homeostasis is regulated by three hormones:
  - **Calcitriol, calcitonin,** and **parathyroid hormone**

Calcitriol Synthesis and Action

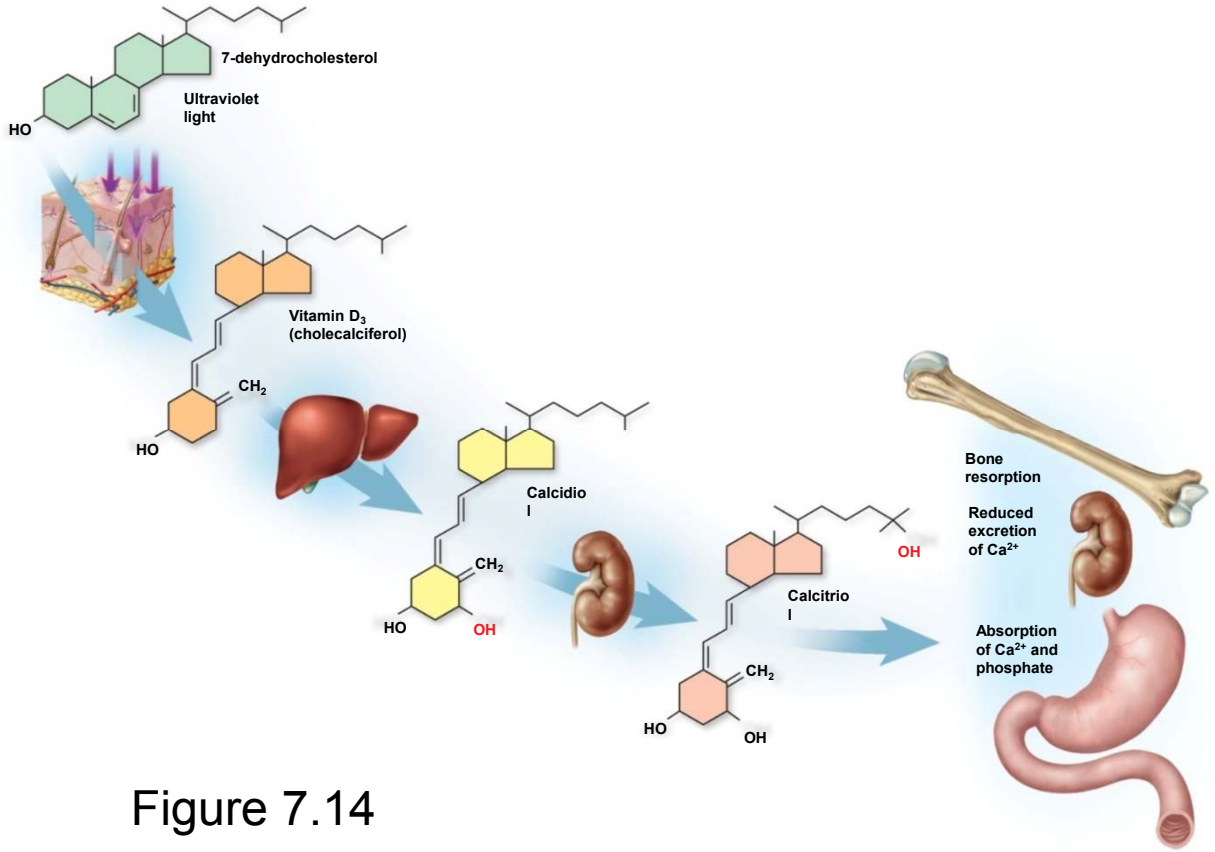


Figure 7.14

Calcitriol

- **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** add another hydroxyl group, converting that to **calcitriol**

    (most active form of vitamin D); also from fortified milk

Calcitriol

Cont.

- Calcitriol behaves as a **hormone** that **raises blood calcium concentration**
  - Increases calcium absorption by small intestine
  - Increases calcium resorption from the skeleton
  - Promotes kidney reabsorption of calcium ions, so less lost in urine
- Necessary for bone deposition—need adequate calcium and phosphate
- Abnormal softness of bones in children (**rickets**) and in adults (**osteomalacia**) without adequate vitamin D

Calcium Homeostasis

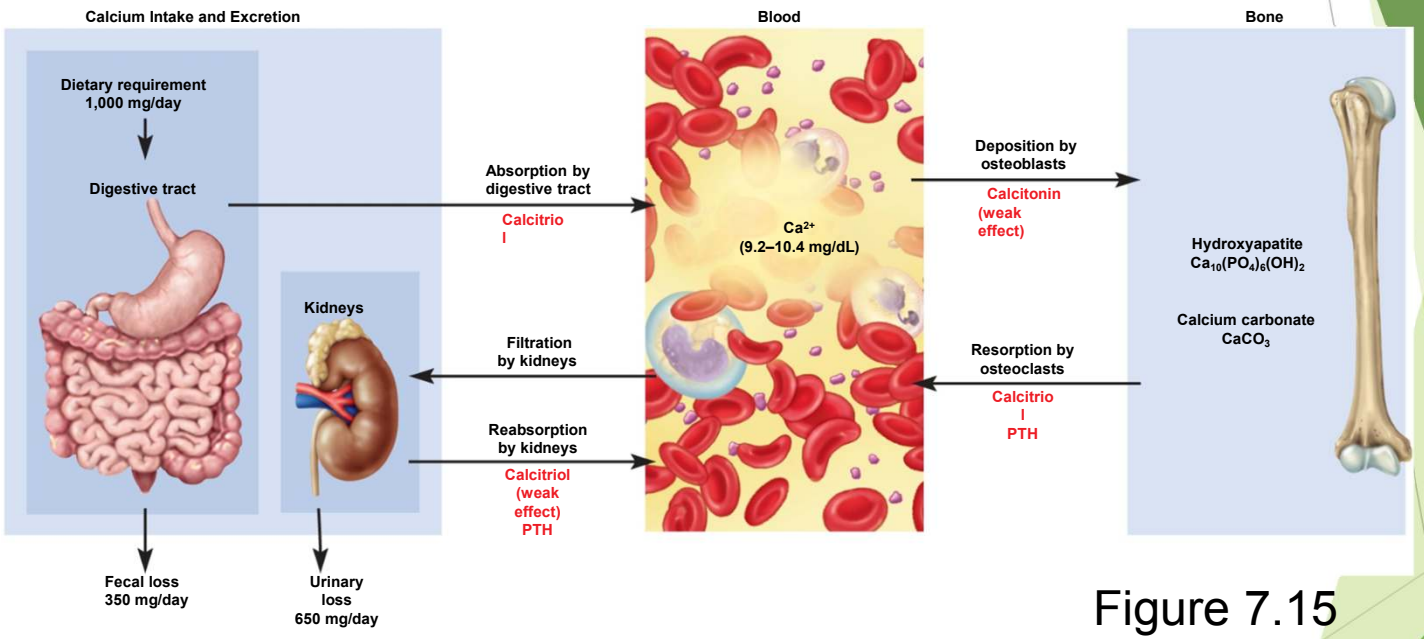


Figure 7.15

Calcitriol, calcitonin, and PTH maintain normal blood calcium concentration

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

Calcitonin

- 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 and lactation

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
    - Simulating them to secrete RANKL which raises the osteoclast population

Parathyroid Hormone

Cont.

- 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

Calcium Homeostasis

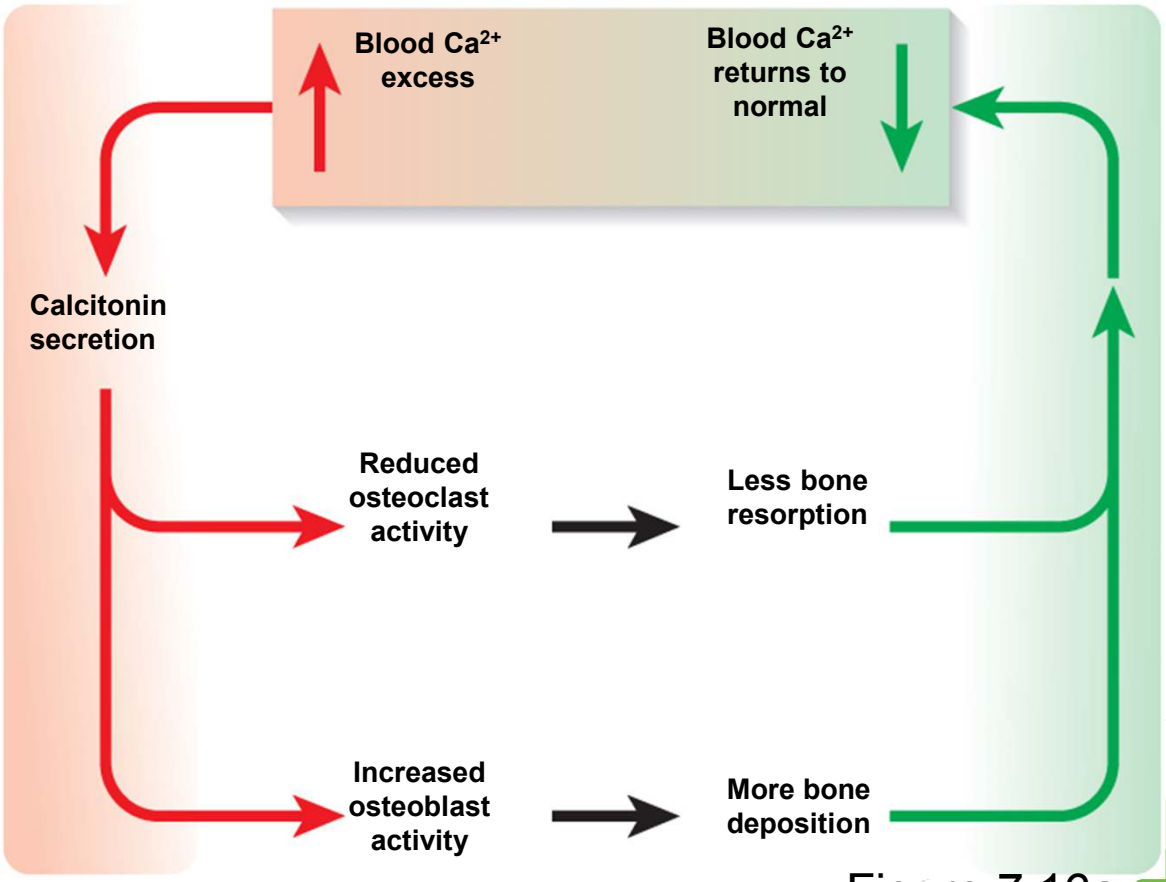
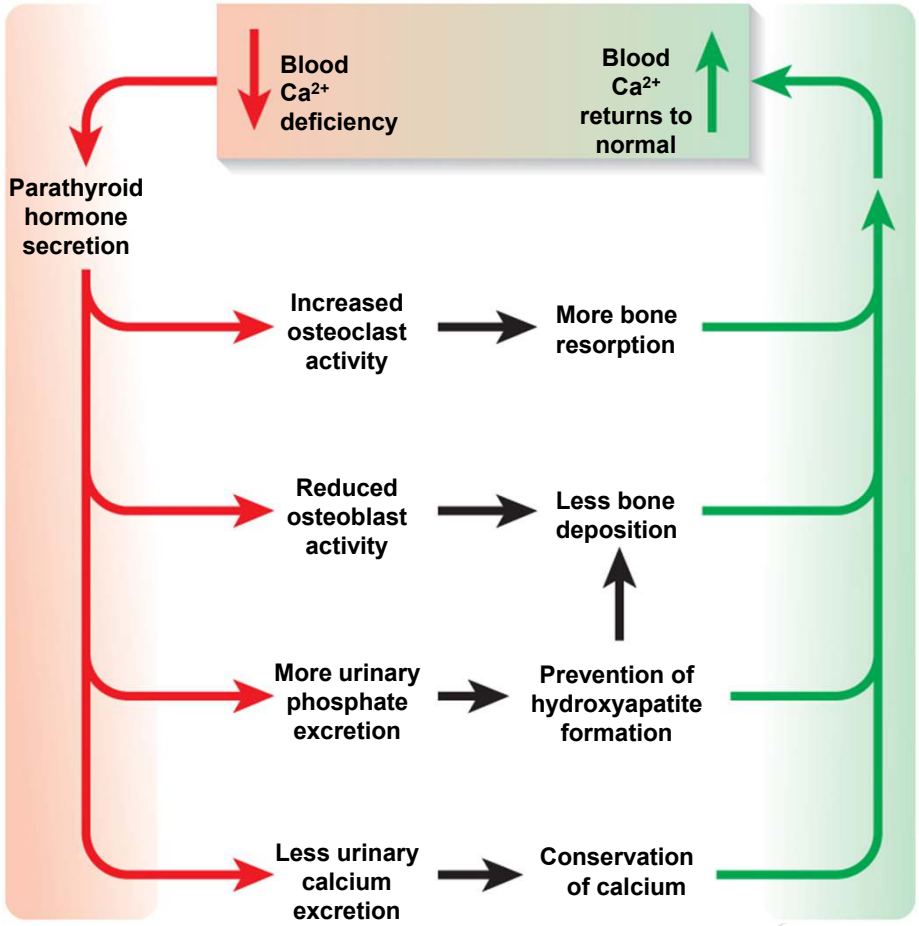


Figure 7.16a

Calcium Homeostasis



(b) Correction for

Figure 7.16b

Phosphate Homeostasis

- Average adult has 500 to 800 g phosphorus
- 85% to 90% of phosphate is in the bones
- Normal plasma concentration is **3.5 to 4.0 mg/dL**
- Occurs in **two principal forms**
  - **HPO_4^{2-}** and **$H_2PO_4^-$** (monohydrogen and dihydrogen phosphate ions)

Phosphate Homeostasis

- Phosphate levels are not regulated as tightly as calcium levels
  - No immediate functional disorders
- Calcitriol promotes its absorption by small intestine and 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 and 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

Other Factors Affecting Bone

Cont.

- 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