Bone metabolism and its regulation

- Bone Cells
  - Osteoblasts
    - Produces bone matrix
  - Osteocytes
    - Respond to the mechanical stimuli
    - Initiate remodeling process
  - Osteoclasts
    - Resorbs mineralized tissues

- Bone mass vs. Age
  - The total bone mass of humans peaks at 25-35 years of age
  - Men have more bone mass than women
  - A gradual decline occurs in both genders with aging, but women undergo an accelerated loss of bone due to increased resorption during perimenopause
  - Bone resorption exceeds formation

- Metabolic functions of bone
  - Mineral reservoir
    - Bones act as homeostatic reservoir of minerals important for the body, calcium and phosphorus in form of crystalline hydroxyapatite \( \text{[Ca}\text{10(PO}_4\text{)}_6(\text{OH})_2] \)
  - Growth factor storage
    - Mineralized bone matrix stores important growth factors, such as insulin-like growth factors, transforming growth factor, bone morphogenetic proteins and other insulin-like growth factors
  - Fat storage
    - Yellow bone marrow acts as a storage reserve of fatty acids
  - Acid-base balance
    - Bone tissues buffer the body against excessive pH changes by absorbing or releasing alkaline salts
  - Detoxification
    - Bone tissues can also store heavy metals and other foreign elements, removing them from the blood and reducing their effects on other tissues
    - These can later be gradually released for excretion
  - Endocrine function
    - Bone controls metabolism of phosphate by releasing fibroblast growth factor (FGF-23), which acts on kidneys to reduce phosphate reabsorption
  - Calcium balance
    - The process of bone resorption by the osteoclasts releases stored calcium into the systemic circulation and is an important process in regulating calcium balance.
The definition and spectrum of metabolic bone diseases

The clinical features and management of metabolic disorder affecting bone

- **Vitamin D deficiency**
  - Decrease in Ca/PO$_4$ ratio
  - Increase in alkaline phosphatase
  - Decrease in calcium excretion
  - Treatment
    - Focus on repairing the deficiency in vitamin D, whether by increased sunshine (enhancing the skin’s ability to make vitamin D) and/or through dietary supplements.
  - In children
    - Rickets
      - First appears in 6- to 24-month-old children, but can manifest at any time until the closure of the bones’ epiphyseal growth plates
      - Characterized by impaired mineralization of the growing bones with accompanying bone pain, muscular tenderness, and hypocalcemic tetany
      - Tooth eruption may be delayed, the fontanelle may close late, and knees and wrists may appear swollen.
    - Affected children develop deformations of their softened, weight-bearing bones
      - Particularly those of the legs and arms
      - Hence, the characteristic leg signs:
        - Bow leg
        - Knock knee
        - Sabre tibia, which occur in nearly half of cases
    - Radiography reveals
      - Enlarged epiphyseal growth plates resulting from their failure to mineralize and continue growth
      - Rickets is most frequently associated with low dietary intakes of calcium, as in the lack of access to or avoidance of milk products
  - In adults
    - Osteomalacia
      - Causes
        - Most common cause: severe, prolonged vitamin D deficiency
        - Drugs that can cause osteomalacia
          - Longterm anticonvulsant therapy (mechanism: phenytoin, phenobarbital, and carbamazepine induce cytochrome P450 system → increased vitamin D conversion to inactive metabolites)
          - Prevented with vitamin D$_3$ from 1,000 to 4,000 units per day
      - Pathophysiology
        - In osteomalacia, normal bone resorption and formation
        - Osteomalacia is characterized by the body’s inability to fully mineralize the newly formed osteoid tissue, resulting in decreased bone strength
      - Treatment
        - High dose vitamin D
      - Diagnosis
        - Blood
          - Decreased serum calcium or phosphorus
          - Decreased serum 25-hydroxyvitamin D
          - Elevated alkaline phosphatase
        - X-Rays
          - Show loosers transformation zone
            - Ribbons of decalcification in bone