Metabolic bone diseases

The skeletal system is composed of 206 bones that vary in size and shape and are interconnected by a variety of joints that allow for a wide range of movement and promote structural stability.

STRUCTURE OF BONE

• Composition of Bone

① Cellular component

Osteoblasts: Large cells with basophilic cytoplasm; lay down osteoid

Osteocytes: Inactive osteoblasts trapped within formed bone; small cells with dark nuclei

Osteoclasts: Multinucleated cell with "ruffled border;" resorbs bone

② Osteoid (type I collagen matrix) which becomes mineralized by deposition of calcium hydroxyapatite

• Arrangment of Bone

Rigid outer shell of compact bone (cortex) surrounding central medullary area filled with thin bone trabeculae and hematopoietic marrow**.**

Osteoporosis

Definition: decrease mass of normally mineralized bone with a subsequent increase in the risk for fractures. Osteoporosis can be localized to one or a few bones (because of disuse) or generalized (involving a majority of the skeletal system). Osteoporosis can be a primary disorder, or it may be secondary to endocrine abnormalities, nutritional, or neoplasia).

Etiology**:** is multifactorial, the two most common forms are *senile osteoporosis* due to aging related losses of osteoblast function, and *postmenopausal osteoporosis* due to increased osteoclastic activity caused by the relative absence of estrogen**.**

Morphology**:** *Bones show* thinner and fewer trabeculae; thin cortex; widened Haversian systems

Clinical features: In its early stages, osteoporosis is asymptomatic. Later, patients may present with compression fractures of the vertebrae, femoral head fractures, and slow healing of fractured bones.

Osteomalacia and rickets

Definition: disorders characterized by softening of the bones as a result of vitamin D deficiency or abnormal vitamin D and phosphate metabolism. Rickets (in children) and osteomalacia (in adults) characterized by defective matrix mineralization.

Pathophysiology: Osteoblasts normally produce osteoid, which is then mineralized with calcium and phosphate to form bone. While in ***osteomalacia and rickets,*** Vitamin D deficiency → ↓ $Ca2^{+}$ absorption → ↓ calcification of osteoid matrix

Causes of osteomalacia and rickets include the following:

a. Dietary deficiency of vitamin D

b. Malabsorption syndromes

c. Inadequate vitamin D synthesis (i.e., lack of sun exposure)

d. Inadequate activation of vitamin D (i.e., kidney or liver disease)

e. Inborn errors of vitamin D metabolism, such as those causing end-organ resistance "vitamin D-resistant rickets".

Signs and symptoms

① Osteomalacia. Patients may complain of bone pain, but in adults, symptoms are rare.

②Rickets. Children present with gross skeletal changes, such as bowing of the legs, enlargement of the costochondral junctions ("rachitic rosary"), and bosselation of the cranium ("rachitic tabes").

Gout

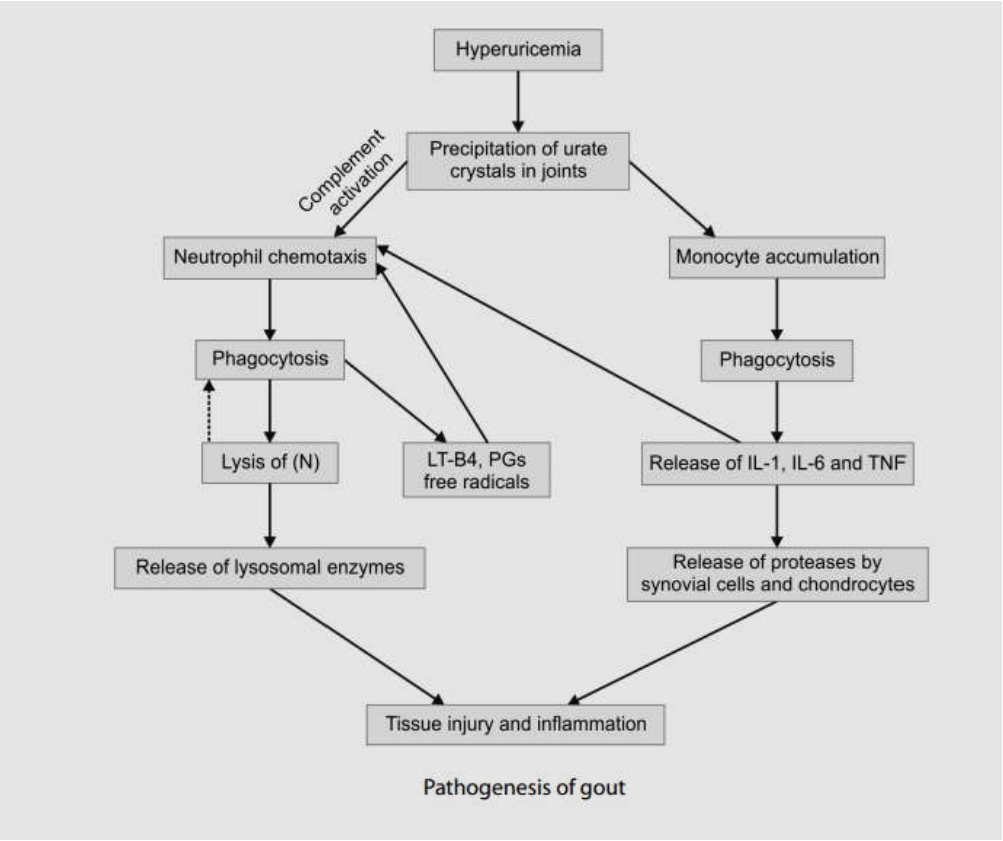
Definition: Gout is a metabolic disease characterized by hyperuricemia (>7 mg/dL) and deposition of urate crystals in various sites, most often joints, subcutaneous soft tissues, and kidneys.

Pathogenesis

• Hyperuricemia can be due to overproduction or reduced renal excretion (humans lack uricase to degrade uric acid).

① Overproduction (10% of cases): Most cases are associated with increased cell nucleic acid turnover e.g., cancer, psoriasis, tumor lysis. Others can be related to deficiency of hypoxanthine guanine phosphoribosyl transferase (HGPRT), an enzyme involved in the purine metabolism.

② Reduced renal excretion (90% of cases): either idiopathic decrease in uric acid excretion (75% of cases of clinical gout) or impaired uric acid excretion secondary to thiazide diuretics, chronic renal failure, etc.



Pathogenesis of gout

Morphology

The morphological changes in gout are as follows:

1. Acute arthritis

Acute inflammation: characterized by edema, congestion and dense infiltration of synovium by neutrophils. Few lymphocytes, plasma cells, and macrophages may also be seen. Monosodium urate (MSU) crystals are long, slender, and needle shaped.

2. Repeated attacks of acute gouty arthritis eventually lead to chronic tophaceous gouty arthritis, where the affected joint is damaged and function is impaired. Tophi: Cluster of urate crystals surrounded by fibroblasts, lymphocytes, and giant cells located in cartilage or soft tissues