Osteoporosis

Osteopenia refers to decreased bone mass**,**
Osteoporosis is defined as osteopenia that is severe enough to significantly increase the risk of fracture.
The disorder may be localized or generalized (involving the entire skeleton).
most osteoporosis is primary and can be secondary to endocrine disorders (e.g., hyperthyroidism), gastrointestinal disorders (e.g., malnutrition), or drugs (e.g., corticosteroids).
The most common forms of osteoporosis are the senile and postmenopausal types.

Pathogenesis

Peak bone mass is achieved during young adulthood. Its magnitude is influenced by hereditary factors, Physical activity, muscle strength, diet, and hormonal state.
After maximal skeletal mass is attained, bone turnover continues with a net deficit in bone formation resulting in an average loss of 0.7% of bone mass per year.
• Age-related changes. Osteoblasts from older individuals have reduced proliferative and biosynthetic potential and reduced response to growth factors compared to osteoblasts in younger individuals. The net result is a diminished capacity to make bone. This form of osteoporosis, known as senile osteoporosis, is categorized as a low-turnover osteoporosis.
• Reduced physical activity. The decreased physical activity that is associated with normal aging contributes to senile osteoporosis. Mechanical forces stimulate normal bone remodeling as evidenced by bone loss in an immobilized or paralyzed extremity. Resistance exercises such as weight training are more effective stimuli for increasing bone mass than repetitive endurance activities such as bicycling.
• Calcium nutritional state. Adolescents (particularly girls) tend to have low dietary calcium intake, a factor that restricts peak bone mass. Calcium deficiency, increased PTH concentrations, and reduced levels of vitamin D also may play a role in the development of senile osteoporosis.
• Hormonal influences. In the decade after menopause, yearly reductions in bone mass may be as much as 2% of cortical bone and 9% of medullary bone. Estrogen deficiency plays the major role in this phenomenon and close to 40% of postmenopausal women are affected by osteoporosis. Decreased estrogen levels after menopause increase both bone resorption and formation but the latter does not keep up with the former, leading to high-turnover osteoporosis. The decreased estrogen may increase secretion of inflammatory cytokines by monocytes. These cytokines stimulate osteoclast recruitment and activity by increasing the levels of RANKL, diminishing the expression of OPG, and preventing osteoclast apoptosis.

Cytokines such as IL-6, TNF-α, and IL-1 also have been implicated in postmenopausal osteoporosis, either independently or as downstream mediators of estrogen signaling.

Morphology: The hallmark of osteoporosis is histologically normal bone that is decreased in quantity.

Clinical Course:

The clinical manifestations of osteoporosis depend on which bones are involved. Vertebral fractures that frequently occur in the thoracic and lumbar regions are painful, and, when multiple, can cause significant loss of height and various deformities, including lumbar lordosis and kyphoscoliosis.

Hyperparathyroidism

Excess production and activity of parathyroid hormone (PTH) result in increased osteoclast activity, bone resorption, and osteopenia.

Pathogenesis

Parathyroid hormone plays a central role in calcium homeostasis through the following effects:

• Osteoclast activation, increasing bone resorption, and calcium mobilization. PTH mediates the effect indirectly by increased RANKL expression on osteoblasts.
• Increased resorption of calcium by the renal tubules.
• Increased urinary excretion of phosphates.
• Increased synthesis of active vitamin D, 1,25(OH)2-D, by the kidneys, which in turn enhances calcium absorption from the gut and mobilizes bone calcium. The net result of the actions of PTH is an elevation in serum calcium, which, under normal circumstances, inhibits further PTH production. However, excessive or inappropriate levels of PTH can result from autonomous parathyroid secretion (primary hyperparathyroidism) or can occur in the setting of underlying renal disease (secondary hyperparathyroidism).

Morphology: Symptomatic, untreated primary hyperparathyroidism manifests with three interrelated skeletal abnormalities: **osteoporosis, brown tumors,** and **osteitis fibrosa cystica.**

Paget Disease (Osteitis Deformans)

Common disorder of unknown etiology in which there is a localized increase in bone turnover. (there is disorderly bone remodeling).

Characterized by repetitive episodes of increased, regional osteoclastic activity and bone resorption (osteolytic stage), followed by exuberant bone formation (mixed

osteoclastic-osteoblastic stage), and finally by an apparent exhaustion of cellular activity (osteosclerotic stage). The net effect of this process is a gain in bone mass; however, the newly formed bone is disordered and lacks strength. Rare before mid-adulthood & becomes progressively more common thereafter.

Pathogenesis

Current evidence suggests that a paramyxovirus infection ultimately underlies Paget disease. As Electron microscopic studies have demonstrated probable viral inclusions in the nuclei of osteoclasts.
Other pathogenic mechanisms are suggested by the observations that osteoclasts in Paget disease appear to be intrinsically hyper-responsive to activating agents such as vitamin D.

Morphology

Paget disease may present as a solitary lesion (monostotic) or may occur at multiple sites in the skeleton (polyostotic).

In the initial lytic phase, osteoclasts are numerous and abnormally large. Osteoclasts persist in the mixed phase, but the bone surfaces become lined by prominent osteoblasts. The newly formed bone may be woven or lamellar. The pathognomonic histologic feature is a mosaic pattern of lamellar bone due to prominent cement lines that haphazardly anneal units of lamellar bone.

Complications: • deformities • bone pain • fractures • nerve or spinal cord compression • deafness • osteosarcoma• heart failure.