Prof. Suheil Zmeili, MD; PhD
Faculty of Medicine
Department of Pharmacology
University of Jordan

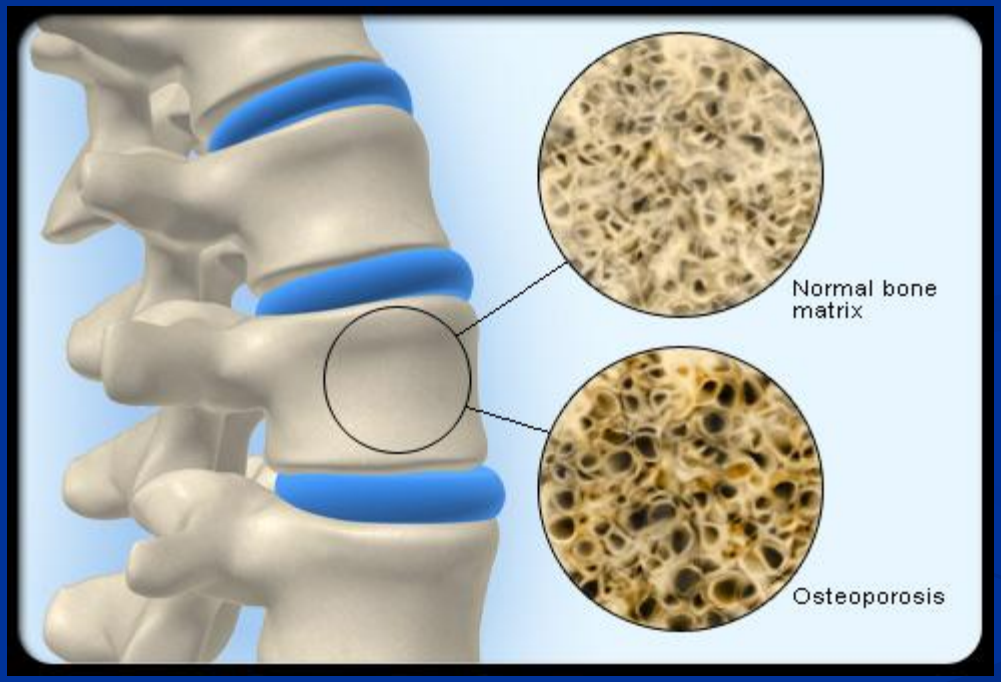
Osteoporosis

- Definitions:

- **Osteoblasts:** Fibroblasts essential for bone formation and mineralization of bone matrix
- **Osteoclasts:** Cells that break down bone and are responsible for bone resorption
- **Bone matrix:** The intercellular substance of bone formed by osteoblasts, consisting of collagenous fibers, ground substance, and inorganic salts
- **Bone resorption:** A process by which osteoclasts break down bone and release minerals resulting in transfer of Ca^{++} from bone to blood

- **Bone turnover=Bone remodeling:** Removal of old bone and its replacement by new bone. Bone is constantly being remodeled throughout adult life and in general, the processes of bone resorption and formation are "coupled" so that there is no net change in bone mass.

During growth osteoblast activity is more than that of osteoclsts (bone formation) but in diseases such as osteoporosis bone resorption is greater than bone formation, leading to a net decrease in bone mass


Normal bone matrix
Osteoporosis

- **Definition of osteoporosis:**

A reduction in bone mass per unit volume leading to fractures particularly the spine, distal radius and proximal femur

It is often known as " the silent thief "because bone loss occurs without symptoms

- **Etiology:**

- Hormone deficiencies

Estrogen deficiency in ♀'s; androgen deficiency in ♂'s

Postmenopausal osteoporosis is the most common form of osteoporosis

The greatest amount of bone density is lost during the first 5 years after the onset of menopause (start therapy early)

Other causes of osteoporosis:

- Thyrotoxicosis
- Hyperparathyroidism
- Alcohol consumption
- Smoking

Causes of osteoporosis (continue):

- Low Ca^{++} diet
- Malabsorption syndrome
- Drug-induced osteoporosis

Glucocorticoids (Cushing's syndrome)

GnRH agonists

Anticonvulsants

Heparin...

- **Osteoporosis risk factors:**

- Female, menopause (early menopause → high incidence)
- Family history of osteoporosis
- Limited physical activity
- Low Ca^{++} diet
- Low vit. D diet or limited exposure to sunlight

Osteoporosis risk factors (continue):

- Caffeine consumption
- Smoking
- Alcohol intake
- Chronic use of glucocorticoids or anticonvulsants

- **Diagnosis of osteoporosis:**

- Symptoms and signs

No symptoms in early stage

Fractures of vertebrae, hips, or wrist

Low back pain

Neck pain...

- lab. Tests

X-ray, bone mineral density (BMD; densitometry), blood biochemistry, bone biopsy if necessary...

- **Treatment of osteoporosis:**

Good outcome if started early

Late osteoporosis or patients with fracture 2º to osteoporosis resist R_x but therapy could limit further fractures

Effective drugs:

- Estrogen + progesterone (to ↓ incidence of uterine cancer)
- Androgen therapy

Treatment of osteoporosis (continue):

- Selective estrogen receptor modulators (SERM) e.g. Raloxifene (has estrogenic effects on bone & anti-estrogenic actions on the uterus and breast)
- Vit. D + Ca^{++}
- Biophpsphanates

Etidronate, Alendronate…

- Calcitonin (intranasal)
- Small dose of fluoride (slow release sodium fluoride)
- Synthetic rPTH (Teriparatide), recently approved by FDA in the management of osteoporosis

Treatment of osteoporosis (continue):

- Denosumab (given SC every 6 months)

An inhibitor to Receptor activator of nuclear factor kappa-B ligand (RANKL) recently approved for use in postmenaupausal osteoporosis, drug-induced bone loss and in bone metastasis

RANKL is a protein present on osteoblasts and activates activity of osteoclasts ⟶ osteoporosis

Associated with many side effects:

Hypocalcemia, serious infections-skin, bladder, heart=endocarditis, high blood cholesterol levels, pain in jaws and back...

- **Postmenopausal osteoporosis R_x or prophylaxis:**

- Estrogen + alendronate + Ca^{++}& vit. D + intranasal calcitonin
- Raloxifene + alendronate + Ca^{++}& vit. D + calcitonin
- Estrogen + progesterone
- Raloxifene + alendronate
- Teriparatide (rPTH) (S.C)
- Denosumab