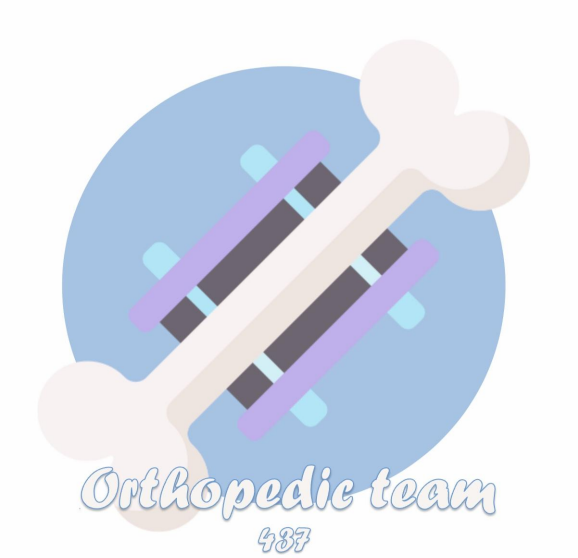
METABOLIC BONE DISORDERS



Lecture objectives:

1. To know about the function of the bone.
2. To understand why metabolic disorders can happen.
3. To learn about pathology and clinical picture of common metabolic bone disorders.
4. To know possible complications of metabolic bone disorders.
5. To understand principles of management of metabolic.

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References: Doctor's slides + Team 436 + Toronto notes 2020

★Orthopedic surgeons and bones:

O Orthopedic surgeons have to deal with all types of bone: healthy or diseased; and that's why they have to know about bone metabolism.

O Bones in the body protect vital organs.

O Bones give support to muscles and tendons.

O Bone may become weak in certain conditions.

★ Bone is a living structure:

O There is a continuous activity in bone during all stages of life.

O There is continuous bone resorption and bone formation as well as remodeling. While osteoblasts are forming new bones, osteoclasts are removing the dead or aged ones. This process accelerates with aging and when estrogen levels drop (Ex, menopause) the rate of formation decrease and the rate of loss increase. Opposite happens in the childhood where bone formation is higher than resorption.

O That means bone is not only for protection and support, but its contents play an important part in blood homeostasis long bones don't do much as flat bones, so that why when have pt with fracture and has problem affect ability of healing so for that need supply the fracture with some stimulus to help in healing likening bone grafting mostly take from iliac crest which is most active bone.

O Many factors are involved in this process.

★ Factors controlling bone metabolism:

1. Calcium.
2. Phosphorus.
3. Parathyroid
4. Thyroid glands.
5. Estrogen
6. Glucocorticoid hormones.
7. Intestinal absorption (patient with malabsorption such as celiac can't absorb calcium).
8. Renal excretion.
9. Diet.
10. Vitamin D.
11. Sun exposure.

★ Bone structure **Bone is formed by:**

- **Bone matrix:** Collagen important in tension while minerals (Ca) important in compression.
  - 40% organic: collagen type 1 (responsible for tensile strength[1]), there are other types but **majority** type 1 in bone.
  - 60% Minerals: mainly Calcium hydroxyapatite, Phosphorus, and traces of other minerals like zinc.
- **Cells in bone: osteoblasts (build bone), osteoclasts (break bone), and osteocytes.**

★ Plasma levels: You don't have to memorize the ranges, normal range will be given in exam.

➢ **Calcium:** 2.2-2.6 mmol/l

➢ **Phosphorus:** 0.9-1.3 mmol/l

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1. Is a measurement of the force required to pull something such as rope, wire, or a structural beam to the point where it breaks.

- **Alkaline phosphatase:** 30-180 units/l is elevated in bone increased activity like during growth or in metabolic bone disease or destruction. Indicator of bone metabolism, how active is the bone, so if there is any disease that cause either fast or slow metabolism check alkaline phosphatase, elevated => hyperactive bone increased turnover, like in bone tumor and fractures.
- **Vitamin D level:** 70-150 nmol/l. Vit D promotes Ca reabsorption from kidney and absorption from intestine.
- **Parathyroid hormone (PTH):** **Not** very friendly to the bone.
  - Production levels are related to serum calcium levels.
  - PTH secretion is increased when serum calcium is low.
  - **Action of PTH:** it increases calcium levels in the blood by osteoclastic activity increasing its release from bone & increase absorption from the intestine & and increase reabsorption from the kidney (also increase secretion of phosphorus). Have direct effect on the bone if you have any problem with parathyroid hormone => check it effect on bone (**This is really really important**); If parathyroid hormone is high due to a body demand, that's mean calcium is low we need to increase it how? From the bone (readily available) so basically you will sacrifice the bone for the seek of heart, brain & vital organs. So, it works as a storage for calcium.
  - Hyperparathyroidism:

1. Primary: adenoma of the gland.
2. Secondary: as a result of low calcium.
3. Tertiary: as a result of prolonged or sustained stimulation = hyperactive nodule or hyperplasia.

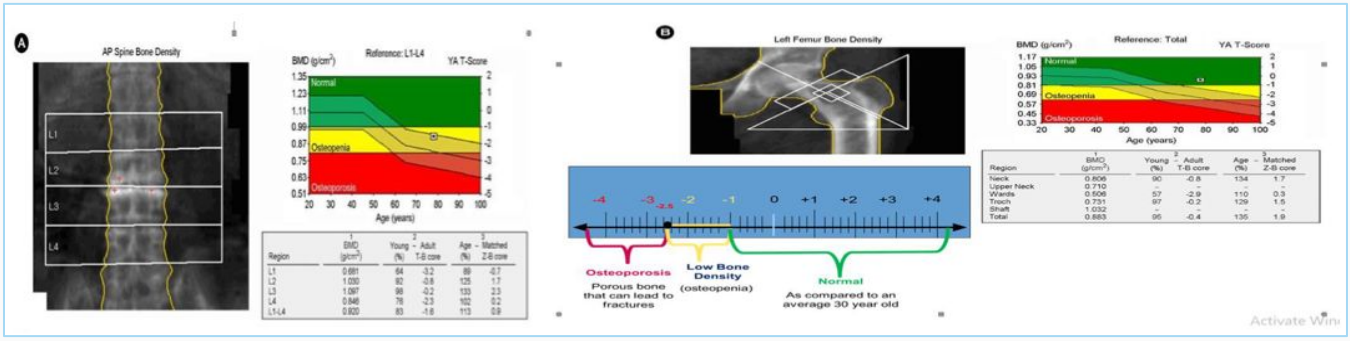
- **Calcitonin:** Bone friendly.
  - Is secreted by C cells of thyroid gland.
  - Its secretion is regulated by serum calcium.
  - Its action is to cause inhibition of bone resorption and increasing calcium excretion by this it causes lowering of serum calcium. Inhibit reabsorption from kidney & intestine trying to bring it back to the bone, used to be given as supplement but not anymore bc of the side effects.

★ Bone Strength:

- Minerals resist compression, collagen resist tension (when you applying force part of the bone will be under compression and part will be under tension)
- Bone strength is affected by mechanical stress which means exercise and weight bearing.
- Bone strength gets reduced with menopause and advancing age.
- Reduced bone density on X rays is called Osteopenia, the opposite is osteosclerosis, someone in cast has osteopenia.
- Osteopenia is also a term used to describe a degree of reduced bone density, which if advanced becomes Osteoporosis.
- X-ray is not accurate because sometimes the technician put overexposure or underexposure
- When you see an x-ray with reduced density of the bone, we don't call it osteoporosis you can't say that bc you can't diagnose it without checking the mass of the bone & compare it to the normal (Done by densitometry).

★ Bone density:

- Bone density is diagnosed at current time by a test done at radiology department called: DEXA scan (Dual Energy X ray Absorptiometry), they do it in three areas: vertebrae, wrist (distal of radius), and neck of femur; these bones most commonly affected first and can get fracture easily so need to detect them first to protect them.
- DEXA is to see how much radiation is absorbed. The more radiation absorbed (white) the bigger the mass of the bone.
- However: increased bone density does not always mean increased bone strength, as sometimes in Brittle bone disease (which is a dense bone) is not a strong bone but fragile bone, which may break easily.

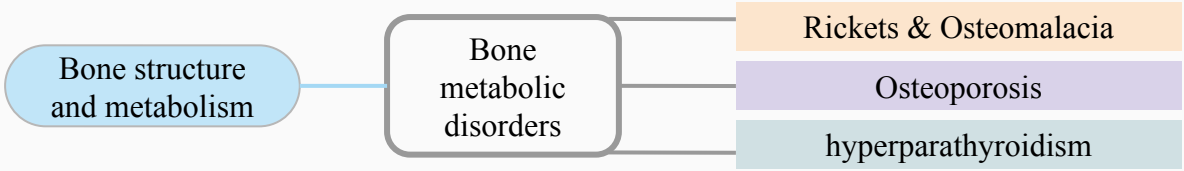


The T-score is the relevant measure when screening for osteoporosis. It is the bone mineral density (BMD) at the site when compared to the young normal reference mean. It is a comparison of a patient's BMD to that of a healthy 30-year-old. The US standard is to use data for a 30-year-old of the same sex and ethnicity, but the WHO recommends using data for a 30-year-old white female for everyone. Values for 30-year-olds are used in post-menopausal women and men over age 50 because they better predict risk of future fracture.[8] The criteria of the World Health Organization are]

Normal is a T-score of −1.0 or higher.

Osteopenia is defined as between −1.0 and −2.5

Osteoporosis is defined as −2.5 or lower, meaning a bone density that is two and a half standard deviations below the mean of a 30-year-old man/woman

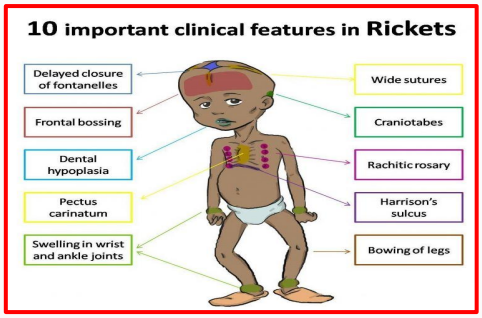


OSMOSIS VIDEO

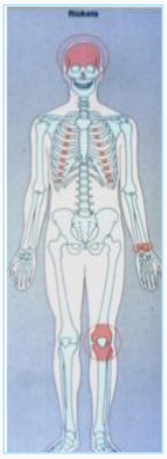
Rickets (think about growth plate)	**Osteomalacia** (Slow process)
Different expressions of the same disease, which is: Inadequate mineralization.	
Affects areas of endochondral growth (b/c it is hyperactive area) in children	All skeleton is incompletely calcified in adults
Biochemistry: Hypocalcaemia, Hypocalciuria, High alkaline phosphatase (bones try to build bone (in hyperactive state) but the problem is in supplies of bone (If alkaline phosphatase is normal, it is most likely not metabolic bone disease).	
Causes: • Calcium deficiency diet , malabsorption. • Hypophosphatemia. You need to deposit calcium, that's only done by phosphate. • Defect in Vitamin D metabolism: (nutritional, underexposure to sunlight, intestinal malabsorption, liver & kidney diseases, also exercise affects on metabolism of vit D, ppl who not exercise or live sedentary lifestyle suffer from either deficits vit D or low normal).	

RICKETS DISEASE الكساح

★ Signs and Symptoms:



- Child is restless, babies cry without obvious reason. (e.g. when changing diaper) more important is:
- Failure to thrive "grow" look small.
- Muscle weakness. You should ask the parents (How do you compare your kid to their peers?)
- In severe cases with very low calcium: tetany or convulsions.
- Joint thickening (hypertrophy) especially around wrists and knees. Most of growth in LL is around knee (distal femur and tibia), so kid with Rickets has wide knee, in UL most of growth is away from elbow (it is in proximal humerus and distal radius), but wide it is more obvious in wrist more than shoulder because of deltoid/a lot of muscles are there; lower limbs are the most common site of clinical and radiological findings. Wrist is the most important X-ray to confirm the diagnosis.
- Deformity of limbs, mostly Genu varum or Genu Valgum. Late → the kid will have Valgus, early → Varus.

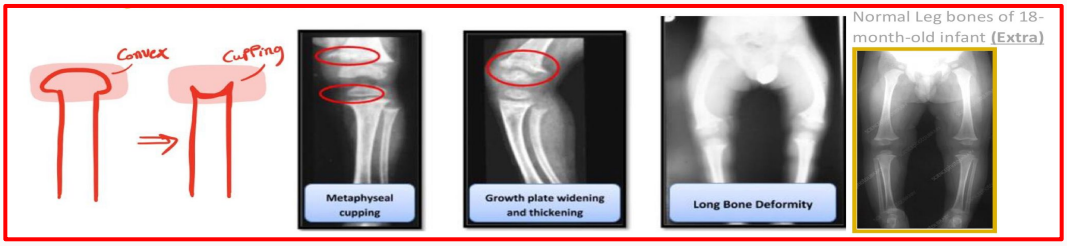


تذكرون وش قلنا بمحاضرة د خلود؟ حسب متى يجي المرض هل وقت سن الفارز الطبيعي او الفاقس؟ متى ماجا استمر معه الديفورمتي

- Pigeon chest deformity, Rickety Rosary the area of attache cartilage with rib is large, craniotabes = suture areas softening.

★ X-ray findings:

1. Growth plate widening and thickening. it grows while there is not enough Ca to calcify it so still growing in both directions which become widened and thickening.
2. Metaphyseal cupping.
3. Long bone deformities.



★ Treatment:

You have to make sure first that the patient does not have systemic disease like malabsorption in intestine or kidney disease (Because there is no point of treatment without treating the primary cause).

- Adequate Vitamin D replacement.
- Sun exposure.
- Correct residual (Post rachitic) deformities. (If there is Genu varum or Genu Valgum and did not improve after the treatment we do corrective osteotomy).

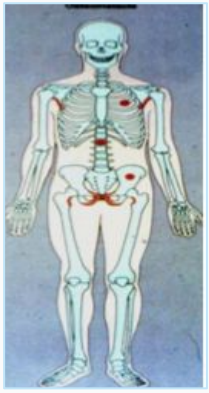
➔ If kid has rickets with deformity, wait before correct deformity surgically why?

1- Bones are very weak and can't hold, so may loss the fixation after a while.

2- Kids still have potential to correct deformity by give them supplements and treat underlying cause, they may correct deformity partially, and when undergo to surgery there is not much difficulties.

OSTEOMALACIA تلين العظام

OSMOSIS HIGH YIELD NOTES

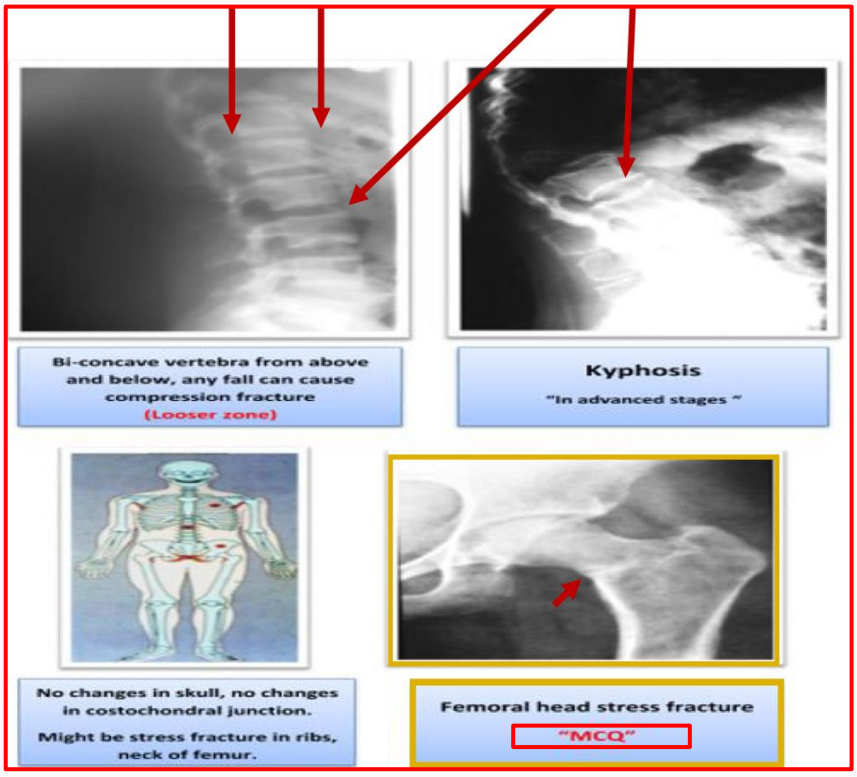


★ Signs and Symptoms:

The difference here is that the growth is stopped in Adults unlike children so no growth-related symptoms here.

- Generalized bone pain, mainly backache (because the back bears body during walking).
- Muscle weakness.
- Reduced bone density.
- Vertebral changes (Typical): Bi-concave vertebrae, vertebral collapse, and kyphosis.
- Stress fractures late stage: Loosers zones in (scapula (neck), ribs, pelvis, and proximal femur usually in neck of femur (stress area)).

Different Height (Kyphosis)	Bi-concave



★ Treatment:

- Exclusion of other diseases.
- Vitamin D + Ca + lifestyle modification + exercise + Sun expose.
- Fracture management.
- Correct deformity if needed.

OSTEOPOROSIS هشاشة العظام

OSMOSIS VIDEO

General Notes

- Decreased bone mass: decreased amount of bone per unit volume and this causes reduced density.
- Mineralization is not affected.
- Mainly post-menopausal and age related.
- The danger is not in osteoporosis itself but in the complications that it might cause.
- Osteoporosis is painless disease unless it causes fracture.
- Osteoporotic fracture nowadays is called fragility fracture.
- Case scenario(typical presentation): Elderly pt was presented to the ER and he was not complaining from anything before he presented to the ER and all of the sudden he had a minor trauma and he developed a fracture bc of this minor trauma and we did some investigation he had Osteoporosis.
- Osteoporosis can be primary or secondary

Primary Osteoporosis: (affect every bone)

Postmenopausal Osteoporosis:

- Due to rapid decline in estrogen level.
- This results in increased osteoclastic activity.
- Normal bone loss usually 0.3% per year.
- Post-menopausal bone loss 3% per year.

Senile osteoporosis:

- Usually by 7th to 8th decades there is steady loss of at least 0.5% per year.
- t is part of physiological manifestation of aging.

Risk factors:

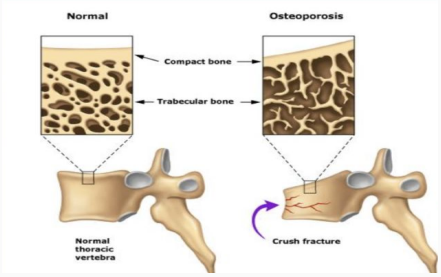
- Race (Caucasian) more common in whait and female (whait lady).
- Hereditary
- Body build (thin people).
- Early menopause.
- Smoking/ alcohol intake/ drug abuse.
- Calcium intake (low Ca).

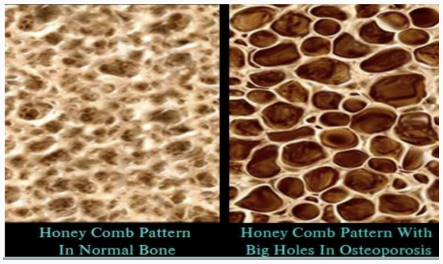
Risk factors:

- Male menopause (Decreased Testosterone).
- Dietary: less calcium and vitamin D and protein.
- Muscle weakness
- Reduced activity

★ Clinical features:

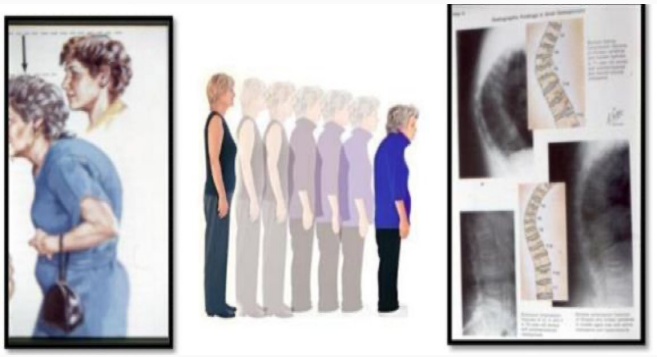
- Osteoporosis is a Silent disease (Asymptomatic, so they present late & that makes the treatment difficult that's why it is serious).
- Osteoporosis is serious due to possible complications mainly fractures (common sites are dorsal spine, wrist, and neck of femur).
- The best way to treat osteoporosis is to prevent it in the first place.
- Osteoporosis does not cause pain usually.
- Osteoporosis causes gradual increase in dorsal kyphosis.
- Osteoporosis leads to loss of height. It is a sign of asymptomatic osteoporosis.
- Osteoporosis is not osteoarthritis; but the two conditions may co-exist.

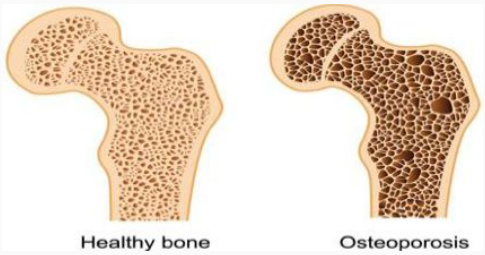




★ How does kyphosis and loss of height occur?

With osteoporosis the anterior part of the vertebra narrows which leads to kyphosis and loss of height.





★ Osteoporotic fractures (fragility fractures):

- 1- hip 2- vertebral fracture we must observe.
- They are Pathological fractures.
- Most common in osteoporotic compression fracture (OVC)of vertebra.
- Vertebral microfractures occur unnoticed (dull ache). Tiny fracture in the vertebra that do not cause collapse and it looks normal from outside but the patient is complaining of pain.
- Most serious is hip fractures bc pt become immobilized and leads consequences of complications like infection.(increased vascularity→ bleeding might cause death).
- Also common is wrist fractures (Colle`s fracture = distal radius fractures).

★ Secondary osteoporosis:

It happens most of the time in younger patient e.g. 45 years old, so in younger patient with osteoporosis suspect a secondary cause.

- **Drug induced:** steroids, alcohol,smoking, phenytoin, heparin
- Hyperparathyroidism, hyperthyroidism, Cushing's syndrome, gonadal disorders, malabsorption, malnutrition.
- **Chronic diseases:** RA, renal failure, tuberculosis.
- **Malignancy:** multiple myeloma, leukemia, metastasis.

★ Disuse Osteoporosis:

- Occurs locally adjacent to immobilized bone or joint.
- May be generalized in bedridden patients.
- Awareness of and attempts for prevention are helpful (by moving the limb from time to time).

★ Prevention of Osteoporosis:

- Prevention of osteoporosis should start from childhood.
- Healthy diet, adequate sunshine, regular exercise, avoidance of smoking or alcohol, caution in steroid use.
- At some time in the past there was a recommendation of HRT (Hormone replacement Therapy) for post-menopausal women? And men; but now this is discontinued.

Management

Drug Therapy, Exercise, Management of Fractures:

Drug therapy:

- Estrogen has a definite therapeutic effect and was used extensively as HRT but cannot be recommended now due to serious possible side effects (such as tumors) **Forget about it**.
- Adequate intake of calcium and vitamin D is mandatory it is **NOT** a treatment it is supplement.
- Drugs which inhibit osteoclast activities: as first line treatment (bc the problem is in osteoclast) e.g. Bisphosphonates like sodium alendronate FOSAMAX (70 mg Tablet once weekly), BONVIVA
- Denosumab = PROLIA (s/c injection every 6 months) = human monoclonal IGG2 antibody.
- Drugs that enhance osteoblast activities: If problem progress & you need to treat this faster bone stimulating agents like PROTELOS, FORTEO. The problem in this type of medication is the risk of malignancy

Exercise in osteoporosis:

- Resistive exercises.
- Weight bearing exercises.
- Exercise should be intelligent to avoid injury which may lead to fractures.

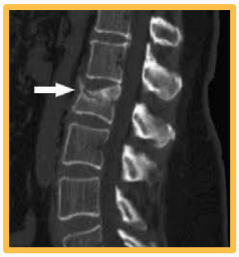
Management of fracture:

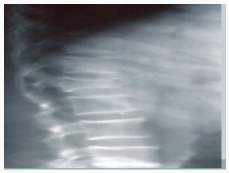
Use load shearing (brace) like Intramedullary nail Not load bearing which is => Plate & screw implants in fracture internal fixation instead of plating. كل البليت اللود عليه البون ما يشارك بعكس النيل اللي يسمح للبون يشارك معاه في اللود

Load sharing = share some of the weight of pt with bone, like in shaft fractures. Has features: area of fracture is not spur 53:20, help in healing and save dense of bone.

Load bearing = minimal sharing with bone, this kind of fixation not encourage in LL, except in some cases like distal femur.

Management of Vertebral Osteoporotic Compression Fracture (OVC):

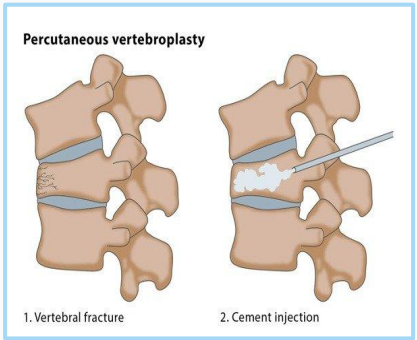




- Pain relief.
- Prevention of further fractures.
- Prevention of instability bc vertebra very collapsed could causes stress in nerves and spinal cord.
- Vertebroplasty.
- Kyphoplasty.

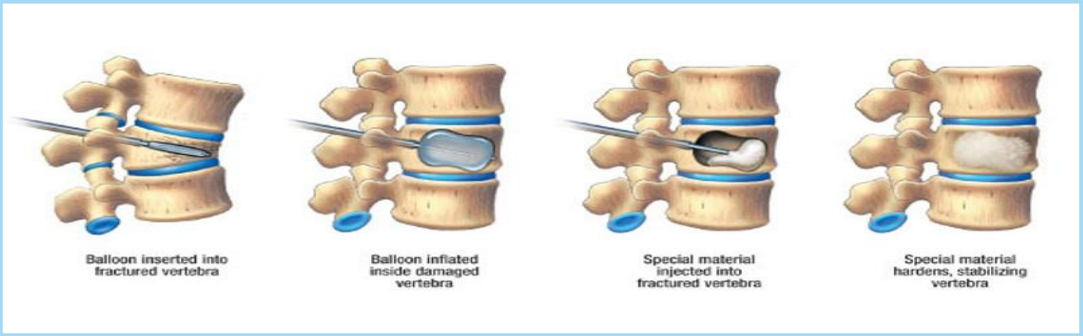
★ Vertebroplasty:

- It results in immediate pain relief
- Is the injection of bone cement into the collapsed vertebra.
- The injection is done under X ray control (image intensifier) by experienced orthopedist or interventional radiologist.
- It helps to prevent further OVF.
- Possible complication is leakage of cement into spinal canal (nerve injury) or venous blood (cement PE).



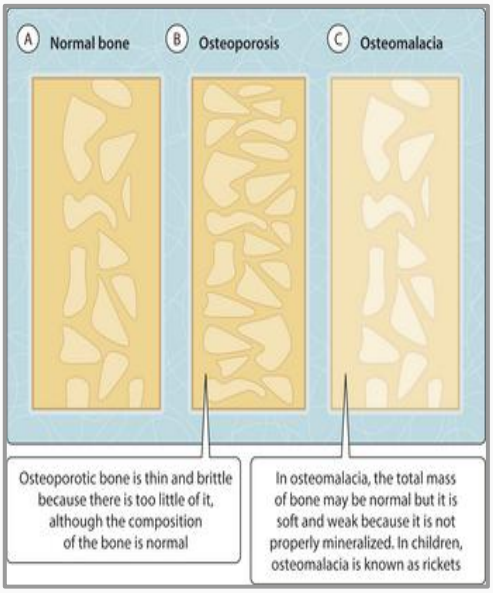
★ Kyphoplasty:

- Is the injection of bone cement into the collapsed vertebra AFTER inflating a balloon in it to correct collapse and make a void (empty space) into which cement is injected.
- It is possible that some correction of kyphosis is achieved.
- It is safer because cement is injected into a safe void. So risk of leakage is much less.



Osteomalacia	Osteoporosis
Any age	Post-Menopausal, old age
Patient is ill	Not ill
General ache	Asymptomatic until fracture
Weak muscles	Normal
Looser zones	Nil
Alkaline Ph increased	Normal
PO4 decreased	Normal

Extra



Toronto notes

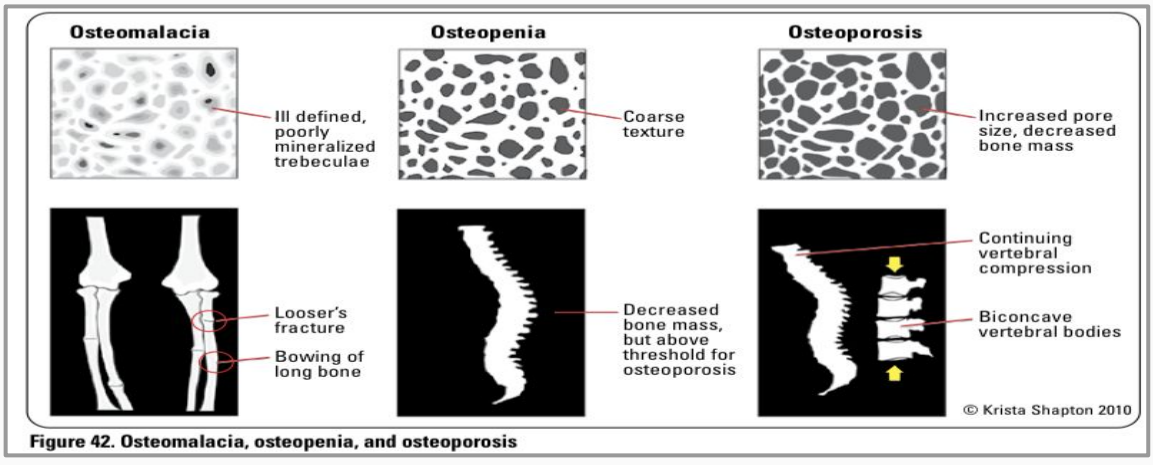


Figure 42. Osteomalacia, osteopenia, and osteoporosis

HYPERPARATHYROIDISM

فرط إفراز الدريقة

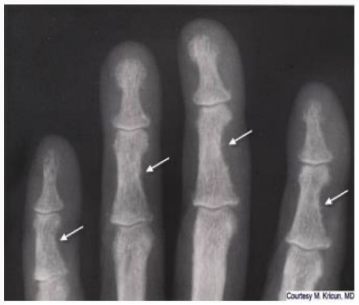
General Notes

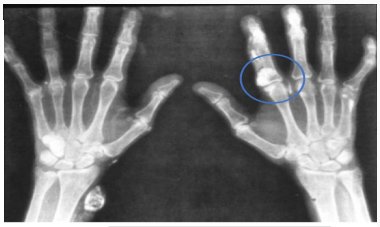
Excessive PTH secretion:

- primary, secondary or tertiary :
- Primary: Adenoma of the gland.
- Secondary: as a result of low calcium (e.g. kidney and intestine problems)
- Tertiary: as a result of prolonged or sustained stimulation = hyperactive nodule or hyperplasia. عاده، قيعل بعدها Then you correct the primary cause >= increasing the parathyroid hormone تسبب situation ك عند كان مثال مايعلّق بمستوى مره عالي يكون increased slightly لكن برضو ستل يعتبر hyperactive
- Leads to increased bone resorption, subperiosteal erosions, osteitis manifested by fibrous replacement of bone.
- Significant feature is hypercalcemia.
- In severe cases: osteitis fibrosa cystica and formation of Brown tumors.

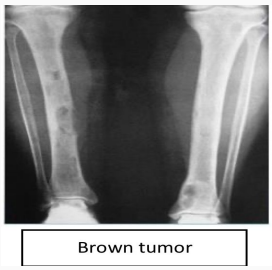
Radiological changes:

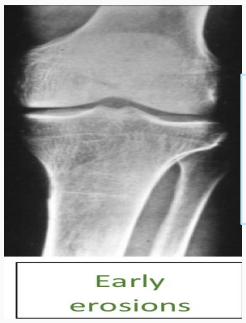
- Generalized decrease in bone density.
- Sub-periosteal bone resorption (scalloping of metacarpals and phalanges very common in these areas).
- Brown tumors (too much bone reuptake causing areas of empty bone with bleeding, this blood will accumulate like paste forming what calls brown tumors).
- Chondrocalcinosis = calcification of cartilage (wrist, knee, shoulder).





Severe hyperparathyroidism





Replaced by fibrous tissue

★ Management of Hyperparathyroidism (By treating the cause):

- Primary hyperparathyroidism due to neoplasm (adenoma or carcinoma) by excision.
- Secondary hyperparathyroidism by correcting the cause of hypocalcemia.
- Tertiary hyperparathyroidism by excision of hyperactive (autonomous) nodule. Surgically by excising hyperactive part if doesn't response to medical treatment.
- Extreme care should be applied after surgery to avoid hypocalcaemia due hungry bones syndrome, bone with low Ca and low density, the moment when you correct hypoparathyroidism, the bone take Ca which lead to severe hypocalcemia due to a rapid increase in bone remodeling and may cause cardiac problem.

Osteomalacia and Rickets

- osteopenia with disordered calcification leading to a higher proportion of osteoid (unmineralized) tissue prior to epiphyseal closure: rickets (in childhood), osteomalacia (in adulthood)

Etiology and Pathophysiology

Vitamin D Deficiency

- deficient uptake or absorption
  - nutritional deficiency
  - malabsorption: post-gastrectomy, small bowel disease (e.g. Celiac sprue), pancreatic insufficiency
- defective 25-hydroxylation
  - liver disease
  - anticonvulsant therapy (phenytoin, carbamazepine, phenobarbital)
- loss of vitamin D binding protein
  - nephrotic syndrome
- defective 1-α-25 hydroxylation
  - hypoparathyroidism
- renal failure
- pathophysiology: leads to secondary hyperparathyroidism and hypophosphatemia

Mineralization Defect

- abnormal matrix
  - osteogenesis imperfecta
- enzyme deficiency
  - hypophosphatasia (inadequate ALP bioactivity)
- presence of calcification inhibitors
  - aluminum, high dose fluoride, anticonvulsants

Table 35. Clinical Features of Rickets and Osteomalacia

Rickets	Osteomalacia
Skeletal pain and deformities, bow legged	Not as dramatic
Fracture susceptibility	Diffuse skeletal pain
Weakness and hypotonia	Bone tenderness
Disturbed growth	Fractures
Ricketic rosary (prominent costochondral junctions)	Gait disturbances (waddling)
Harrison's groove (indentation of lower ribs)	Proximal muscle weakness
Hypocalcemia	Hypotonia

Investigations

Table 36. Laboratory Findings in Osteomalacia and Rickets

Disorder	Serum Phosphate	Serum Calcium	Serum ALP	Other Features
Vitamin D deficiency	Decreased	Decreased to normal	Increased	Decreased calcitriol
Hypophosphatemia	Decreased	Normal	Decreased to normal	
Proximal RTA	Decreased	Normal	Normal	Associated with hyperchloremic metabolic acidosis
Conditions associated with abnormal matrix formation	Normal	Normal	Normal	

- radiologic findings
  - pseudofractures, fissures, narrow radiolucent lines – thought to be healed stress fractures or the result of erosion by arterial pulsation
  - loss of distinctness of vertebral body trabeculae; concavity of the vertebral bodies
  - changes due to secondary hyperparathyroidism: subperiosteal resorption of the phalanges, bone cysts, resorption of the distal ends of long bones
  - others: bowing of tibia, coxa profundus hip deformity
- bone biopsy: usually not necessary but considered the gold standard for diagnosis

Treatment

- definitive treatment depends on the underlying cause
- vitamin D supplementation
- PO_4^{3-} supplements if low serum PO_4^{3-}, Ca^{2+} supplements for isolated calcium deficiency
- bicarbonate if chronic metabolic acidosis

KDIGO 2017 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease
Kidney Inter Suppl 2017;7(1):1-60

Recommendations for Metabolic Bone Disease in CKD

Screening
- In CKD patients with evidence of CKD-MBD and/or risk factors for osteoporosis, perform BMD testing to assess fracture risk if results will impact treatment decisions
- In patients with CKD-BMD, it is reasonable to perform a bone biopsy if knowledge of the type of renal osteodystrophy will impact treatment decisions

Management
- Treatment of CKD-MBD should be based on serial assessments of PO_4^{3-}, Ca^{2+} and PTH levels, considered together
- Suggest lowering elevated PO_4^{3-} levels towards the normal range
- Avoid hyperglycemia in adult patients and maintain serum Ca^{+} in age-appropriate normal range in children

Osteomalacia/Rickets

- reduction in bone mineral density; normal amount of bone, but reduced mineralization of normal osteoid
- usually due to vitamin D deficiency, resulting in softening and bowing of long bones
- similar to osteoporosis, initial radiological appearance of osteopenia (coarse and poorly defined bone texture)
- "fuzzy", ill-defined trabeculae
- insufficiency fractures
- Looser's zones (pseudofracture)
  - characteristic radiologic feature
  - fissures or clefts at right angles to long bones and extending through cortex
  - DDx: chronic renal disease, fibrous dysplasia, hyperthyroidism, Paget's, osteodystrophy, X-linked hypophosphatemia

Metabolic Bone Disease

- see 2010 Clinical Practice Guidelines for the Diagnosis and Management of Osteoporosis for details

Osteoporosis

Definition

- a condition characterized by decreased bone mass and microarchitectural deterioration with a consequent increase in bone fragility and susceptibility to fracture
- BMD is measured at hip and lumbar spine, BMD T-score ≤-2.5 is indicative of osteoporosis
- osteopenia (low bone mass): BMD with T-score between –1.0 and –2.5

ETIOLOGY AND PATHOPHYSIOLOGY

Secondary Osteoporosis

- gastrointestinal diseases
  - gastrectomy
  - malabsorption (e.g. celiac disease)
  - chronic liver disease
- bone marrow disorders
  - multiple myeloma
  - lymphoma
  - leukemia
- endocrinopathies
  - Cushing's syndrome
  - hyperparathyroidism
  - hyperthyroidism
  - premature menopause
  - DM
  - hypogonadism
- malignancy
  - secondary to chemotherapy
  - myeloma
- drugs
  - corticosteroid therapy
  - phenytoin
  - chronic heparin therapy
  - androgen deprivation therapy
  - aromatase inhibitors
  - rheumatologic disorders
    - rheumatoid arthritis
    - SLE
    - ankylosing spondylitis
  - renal disease
  - poor nutrition
  - immobilization
- COPD (due to disease, tobacco, and glucocorticoid use)

Clinical Features

- commonly asymptomatic
- height loss due to collapsed vertebrae
- fractures: most commonly in hip, vertebrae, humerus, and wrist
  - fragility fractures: fracture with fall from standing height or less
  - Dowager's hump: collapse fracture of vertebral bodies in mid-dorsal region
  - x-ray: vertebral compression fractures (described as wedge fractures, require a minimum of 20% height loss), "codfishing" sign (weakening of subchondral plates and expansion of intervertebral discs)
- pain, especially backache, associated with fractures

Approach to Osteoporosis

1. assess risk factors for osteoporosis on history and physical
2. decide if patient requires BMD testing with dual-energy x-ray absorptiometry (DEXA): men and women ≥65 yr (or younger if presence of risk factors, see Table 33, E44)
3. initial investigations
   - all patients with osteoporosis: calcium corrected for albumin, CBC, creatinine, ALP, TSH
   - also consider serum and urine protein electrophoresis if vertebral fractures, celiac workup, and 24 h urinary Ca^{2+} excretion to rule out additional secondary causes
   - 25-OH-Vitamin D level should only be measured after 3-4 mo of adequate supplementation and should not be repeated if an optimal level ≥75 nmol/L is achieved
   - lateral thoracic and lumbar x-ray if clinical evidence of vertebral fracture (or in individuals at moderate risk of fracture to help decide if they require medical therapy)
4. assess 10-yr fracture risk by combining BMD result and risk factors
   1) WHO Fracture Risk Assessment Tool (FRAX)
   2) Canadian Association of Radiologists and Osteoporosis Canada Risk Assessment Tool (CAROC)
      - approach to management guided by 10-yr risk stratification into low, medium, high risk
5. for all patients being assessed for osteoporosis, encourage appropriate lifestyle changes (see Table 34, E44)

Corticosteroid Therapy is a Common Cause of Secondary Osteoporosis
Individuals receiving ≥7.5 mg of prednisone daily for over 3 mo should be assessed for bone-sparing therapy
Mechanism: increased resorption + decreased formation + increased urinary calcium loss + decreased intestinal calcium absorption + decreased sex steroid production

Calcium Plus Vitamin D Supplementation and Risk of Fractures. Osteoporosis
Int 2015;27:367-376
Purpose: To review trials of Vitamin D and Calcium therapy for reducing fracture risk in osteoporosis.
Study: Systematic review searching 2011-2015, inclusive, identified 8 RCTs totalling 30,970 participants. RCTs reviewed included healthy adults and ambulatory older adults with medical conditions (excluding cancer). Vitamin D and Calcium combination therapy was compared to placebo.
Results: Analysis of RCT data revealed that calcium plus vitamin D supplementation produced a statistically significant reduction in risk of total fractures (0.85; CI:0.73-0.98) and in hip fractures (0.70; CI:0.56-0.87). Subgroup analysis was significant for community dwelling or institutionalized patients.
Conclusions: Systematic analysis suggests that Vitamin D and calcium therapy significantly decreases fracture risk. This study did not specifically look at individuals with osteoporosis. However, it still supports that Vitamin D and calcium should continue to be used as preventative treatment for individuals at increased risk of fractures.

Clinical Signs of Fractures or Osteoporosis
- Height loss >3 cm (Sn 92%)
- Weight <51 kg
- Kyphosis (Sp 92%)
- Tooth count <20 (Sp 92%)
- Grip strength
- Armspan-height difference >5 cm (Sp 76%)
- Wall-occiput distance >0 cm (Sp 87%)
- Rib-pelvis distance ≤2 finger breadth (Sn 88%)

Table 32. Indications for BMD Testing

Older Adults (age ≥50 yr)	Younger Adults (age <50 yr)
All women and men age ≥65 yr Menopausal women, and men aged 50-64 yr with clinical risk factors for fracture: Fragility fracture after age 40 Prolonged glucocorticoid use Other high-risk medication use (aromatase inhibitors, androgen deprivation therapy) Parental hip fracture Vertebral fracture or osteopenia identified on x-ray Current smoking High alcohol intake Low body weight (<60 kg) or major weight loss (>10% of weight at age 25 yr) Rheumatoid arthritis Other disorders strongly associated with osteoporosis: primary hyperparathyroidism, T1DM, osteogenesis imperfecta, uncontrolled hyperthyroidism, hypogonadism or premature menopause (<45 yr), Cushing's disease, chronic malnutrition or malabsorption, chronic liver disease, COPD, and chronic inflammatory conditions (e.g. inflammatory bowel disease)	Fragility fracture Prolonged use of glucocorticoids Use of other high-risk medications (aromatase inhibitors, androgen deprivation therapy, anticonvulsants) Hypogonadism or premature menopause Malabsorption syndrome Primary hyperparathyroidism Other disorders strongly associated with rapid bone loss and/or fracture

Aledronate (10 mg/d)

1° Prevention – Vertebral (Gold)	45% RRR, 2% ARR
1° Prevention – Hip	Not significant
1° Prevention – Wrist	Not significant
2° Prevention – Vertebral (Gold)	45% RRR, 6% ARR
2° Prevention – Hip (Gold)	53% RRR, 1% ARR
2° Prevention – Wrist (Gold)	50% RRR, 2% ARR

Etidronate (400 mg/d)

1° Prevention – Vertebral	Not significant
1° Prevention – Hip	Not significant
1° Prevention – Wrist	Not significant
2° Prevention – Vertebral (Silver)	47% RRR, 5% ARR
2° Prevention – Hip	No benefit
2° Prevention – Wrist	No benefit

Risedronate (5 mg/d)

1° Prevention – Vertebral	Not significant
1° Prevention – Hip	Not significant
1° Prevention – Wrist	Not significant
2° Prevention – Vertebral (Gold)	39% RRR, 5% ARR
2° Prevention – Hip (Silver)	26% RRR, 1% ARR
2° Prevention – Wrist	Not significant

Table 33. Osteoporosis Risk Stratification

Low Risk 10 yr fracture risk <10%	Unlikely to benefit from pharmacotherapy; encourage lifestyle changes Reassess risk in 5 yr
Medium Risk 10 yr fracture risk 10-20%	Discuss patient preference for management and consider additional risk factors Factors that warrant consideration for pharmacological therapy: Additional vertebral fracture(s) identified on vertebral fracture assessment (VFA) or lateral spine x-ray Previous wrist fracture in individuals ≥65 or with T-score ≤–2.5 Lumbar spine T-score much lower than femoral neck T-score Rapid bone loss Men receiving androgen-deprivation therapy for prostate cancer Women receiving aromatase-inhibitor therapy for breast cancer Long-term or repeated systemic glucocorticoid use (oral or parenteral) that does not meet the conventional criteria for recent prolonged systemic glucocorticoid use Recurrent falls (defined as falling 2 or more times in the past 12 mo) Other disorders strongly associated with osteoporosis Repeat BMD and reassess risk every 1-3 yr initially
High Risk 10 yr fracture risk >20%; OR Prior fragility fracture of hip or spine; OR More than one fragility fracture	Start pharmacotherapy

Treatment of Osteoporosis

Table 34. Treatment of Osteoporosis in Women and Men

Treatment for Both Men and Women	
Lifestyle	Diet: Elemental calcium 1000-1200 mg/d; Vit D 1000 IU/d Exercise: 3x30 min weight-bearing exercises, balance exercise, and aerobic exercise/wk Cessation of smoking, reduce caffeine intake Stop/avoid osteoporosis-inducing medications
Drug Therapy	
Bisphosphonate: inhibitors of osteoclast binding	1st line in prevention of hip, nonvertebral, and vertebral # (Grade A): alendronate (PO), risedronate (PO), zoledronic acid (IV)
RANKL Inhibitors	Denosumab: 1st line in prevention of hip, nonvertebral, vertebral # (Grade A) *Denosumab should not be abruptly stopped/administration delayed. Increased risk of vertebral fractures due to increased bone turnover on discontinuation
Parathyroid Hormone (teriparatide)	18-24 mo duration, followed by long-term anti-resorptive therapy with bisphosphonate or RANKL inhibitor, followed by long-term anti-resorptive therapy with bisphosphonate or RANKL inhibitor
Treatment Specific to Post-Menopausal Women	
SERM (selective estrogen-receptor modulator): agonistic effect on bone but antagonistic effect on uterus and breast	Raloxifene: 1st line in prevention of vertebral # (Grade A) +ve: prevents osteoporotic # (Grade A to B evidence), improves lipid profile, decreased breast cancer risk -ve: increased risk of DVT/PE, stroke mortality, hot flashes, leg cramps
HRT: combined estrogen + progesterone (see Gynecology, GY34)	1st line in prevention of hip, nonvertebral, and vertebral # (Grade A) For most women, risks > benefits Combined estrogen/progestin prevents hip, vertebral, total # Increased risks of breast cancer, cardiovascular events, and DVT/PE

Factors Necessary for Mineralization

- Quantitatively and qualitatively normal osteoid formation
- Normal concentration of calcium and phosphate in ECF
- Adequate bioactivity of ALP
- Normal pH at site of calcification
- Absence of inhibitors of calcification

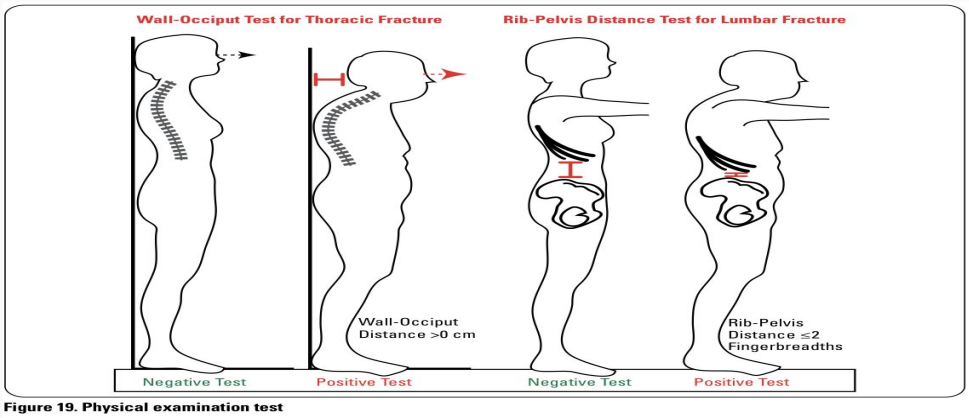


Figure 19. Physical examination test

Osteoporosis

- reduction in amount of normal bone mass; fewer and thinner trabeculae; diffuse process affecting all bones
- DEXA: gold standard for measuring bone mineral density
  - T-score: the number of standard deviations from the young adult mean, most clinically valuable
    - osteopenia: −2.5< T-score <−1
    - osteoporosis: T-score ≤−2.5
  - Z-score: the number of standard deviations from the age-matched mean, helpful in diagnosing secondary osteoporosis
  - risk of fracture: related to bone mineral density, age, history of previous fractures, steroid therapy
  - diagnostic sensitivity of DEXA highest when bone mineral density measured at lumbar spine and proximal femur
- appearance on plain film (not sensitive; changes detectible only after large reduction in bone mineral density)
  - osteopenia: reduced bone density on plain films
    - may also be seen with osteomalacia, hyperparathyroidism, and disuse
  - compression of vertebral bodies
  - "codfish vertebra" (biconcave vertebral bodies), "picture frame vertebra" (cortical loss), "ghost vertebra" (trabecular loss)
  - long bones have appearance of thinned cortex and increased medullary cavity
    - look for complications of osteoporosis (e.g. insufficiency fractures: hip, vertebrae, sacrum, pubic rami)

see Endocrinology, E43

Osteoporosis
Reduced amount of bone

OsteoMalacia
Normal amount of bone, but reduced Mineralization of normal osteoid

Hyperparathyroidism

- most common cause is renal failure (secondary hyperparathyroidism)
- chondrocalcinosis is a common complication
- calcium crystal deposition in hyaline cartilage or fibrocartilage (including arteries and peri-articular soft tissue)
- resorption of bone typically in hands (subperiosteal and at tufts), sacroiliac joints (subchondral), skull ("salt and pepper" appearance), subligamentous resorption (ischial tuberosity, trochanters, and clavicle), osteoclastoma (brown tumours)
- "rugger jersey spine": band-like osteosclerosis at superior/inferior margins of vertebral bodies

Primary Hyperparathyroidism
Increased PTH secretion commonly due to parathyroid adenoma, lithium therapy; less often due to parathyroid carcinoma or parathyroid hyperplasia

Secondary Hyperparathyroidism
Partial resistance to PTH action leads to parathyroid gland hyperplasia and increased PTH secretion, often in patients with renal failure and osteomalacia (due to low or low normal serum calcium levels)

Tertiary Hyperparathyroidism
Irreversible clonal outgrowth of parathyroid glands, usually in long-standing inadequately treated chronic renal failure on dialysis

KAPLAN NOTES

Hyperparathyroidism is most commonly found by serendipitous discovery of high serum calcium in blood tests (rarely seen in the full florid "disease of stones, bones, and abdominal groans"). Repeat calcium determinations, look for low phosphorus, and rule out cancer with bone metastases. If findings persist, do parathyroid hormone (PTH) determination (and interpret in light of serum calcium levels).

- Asymptomatic patients become symptomatic at a rate of 20% per year; thus elective intervention is justified.
- Ninety percent have single adenoma.
- Removal is curative (sestamibi scan may help localize the culprit gland before surgery).

MCQS

1-which of the following is a sign of rickets?
A. Gunstock deformity
B. Widening nasal bridge
C. Kyphoscoliosis
D. Wide growth plate

2-A 41 Y/O lady presented to the clinic with a long Hx of diarrhea, amenorrhea, bilateral hip pain, Lateral lumbar spine X-ray was done and showed bone thinning. What is the next Ix?
A. Ca, Po4, Vit-D serum levels
B. DEXA

3 -A child comes to your clinic presenting with Rickets, X-ray shown. Identify the sign present on the X-ray?
A. Widened epiphysis
B. Looser's zone
C. Rickets Rosary

4- a 45-year-old osteoporotic lady presented for check up. She smokes 10 cigarettes per day and reached menopause at the age of 41, Her mother had a hip fracture at the age of 61. Which of the following is the major risk factor for her to develop osteoporosis?
A-Smoking
B-Early menopause
C-Low calcium intake
D-Family history of osteoporosis

5-55 years old lady came to osteoporotic clinic follow up she has history of fracture DEXA scan for hip was2.5 she has no family history of osteoporosis but her mom had hip fracture at age of 65, nonsmoker, her menopause at 41 year old, low dairy intake . Which one of the following increase her risk for fracture?
A-Premature menopause.
B-Low dairy milk product.
C-Family history of fracture.
D-Low calcium intake

6-Which one of the following is a sign on rickets that you might see in clinical observation?
A-Pectus excavatum.
B-Craniotabes.

7-An 82-year-old woman presented with back pain. There was no history of trauma, fever or weight loss. Physical examination showed mild thoraco-lumbar kyphosis but no tenderness. Neurologic examination is normal. X-rays are shown below.

A-Start anti-osteoporotic medications

B-Admission and bed-rest.

C-Open reduction and internal fixation

D-6 weeks of halo-femoral traction

8- 46 yrs. Lady has a wedge fracture how would you manage her? Brace and analgesia.

9-Patient has a rheumatoid arthritis how to investigate him? Mineral density.

10-Which of the following is the most common site of clinical and radiological findings in established diagnosis of rickets ?

A-Cranium

B-Lower limb

C-Upper limb

D-Thoracic cage

Answers:

1. D
2. B
3. A
4. B
5. A
6. B
7. A
10. B