17- Metabolic Bone Disorders

Objectives:

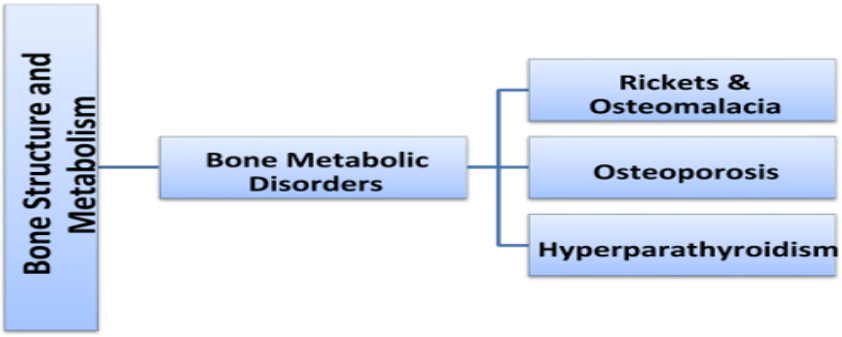
- To know about the function of the bone.
- To understand why metabolic disorders can happen.
- To learn about pathology and clinical picture of common metabolic bone disorders.
- To know possible complications of metabolic bone disorders.
- To understand principles of management of metabolic.

Team members: Meshal Aleiaidi, Rayan Al qarni, Sarah Alshamrani, Laila Mathkour, Amal AlQarni

Team leader: Mohammed Baqais, Nora AlSahli

Revised by: Abdulaziz Almohammed, Dina Aldossary

References: 435 team، Doctors' notes، 436 slides



Orthopedic surgeons and bones

- Orthopedic surgeons have to deal with all types of bone: healthy or diseased; and that's why they have to know about bone metabolism.
- Bones in the body protect vital organs.
- Bones give support to muscles and tendons.
- Bone may become weak in certain conditions.

★ Bone Is a Living Structure

- There is a continuous activity in bone during all stages of life.
- 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.
- That means bone is not only for protection and support, but its contents play an important part in blood homeostasis.
- Many factors are involved in this process.

★ Factors Controlling Bone Metabolism *Very Important ركزوا على هذي السلايد*

- Calcium and Phosphorus.
- Parathyroid and Thyroid glands.
- Estrogen and Glucocorticoid hormones.
- Intestinal absorption (patient with malabsorption such as celiac can't absorb calcium).
- Renal excretion.
- Diet.
- Vitamin D.
- Sun exposure.

★ Bone Structure

Bone is formed by:

- **Bone matrix:**
  - 40% organic: collagen type1 (responsible for tensile strength[1]).
  - 60% Minerals: **mainly** Calcium hydroxyapatite, Phosphorus, and traces of other minerals like zinc.
- **Cells in bone:** osteoblasts build bone, osteoclasts break bone, and osteocytes generate bone.

[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.

★ Plasma levels You **don't have** to memorize it, if we asked about it in the exam normal range will be given

- **Calcium**: 2.2-2.6 mmol/l
- **Phosphorus**: 0.9-1.3 mmol/l

} Both of them are absorbed and secreted by the kidney in urine

- **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 phosphate, elevated => hyperactive bone increased turnover
- **Vitamin D level**: 70-150 nmol/l
- **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.

- **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)

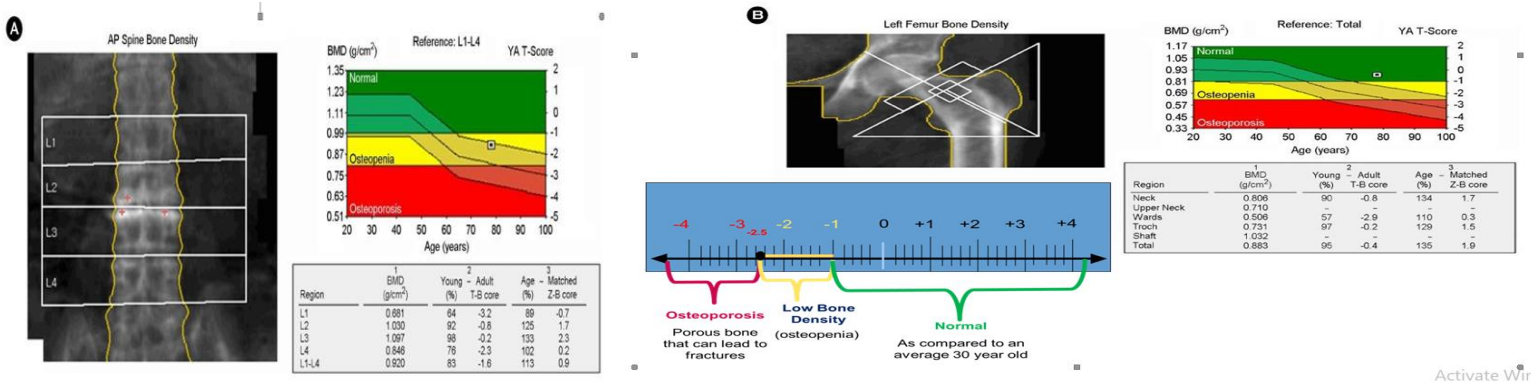
- Bone strength is affected by mechanical stress which means exercise and weight bearing.
- Bone strength gets reduced with menopause and advancing age.
- Reduced bone density on X rays is called Osteopenia. (The opposite is osteosclerosis)
- Osteopenia is also a term used to describe a degree of reduced 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 **densometry**).

★ Bone density

- Bone density is diagnosed at current time by a test done at radiology department called: **DEXA scan** (they do it in three areas: vertebrae, wrist, and neck of femur).
- DEXA is (Dual Energy X ray Absorbtionometry) to see how much radiation is absorbed. The more radiation absorbed (white) the bigger the muss 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.

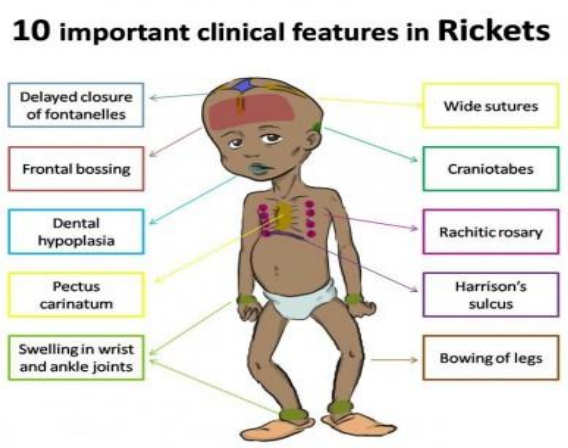
Rickets think about growth plate	**Osteomalacia**
Different expressions of the same disease, which is: **Inadequate** mineralization.	
Affects areas of endochondral growth in **children**	All skeleton is incompletely calcified in **adults**
Biochemistry: Hypocalcaemia, Hypocalciuria, High alkaline phosphatase	
Causes: ⇒ Calcium deficiency. ⇒ 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).	

Rickets

Osmosis high yield notes osmosis video
Toronto notes

★ Signs and Symptoms

- Child is restless, babies cry without obvious reason. (e.g. when changing diaper). هم دايم flu ولا tumor سواء عندهم more important is:
- **Failure to thrive.** "grow"
- Muscle weakness.
- In severe cases with very low calcium: tetany or convulsions.



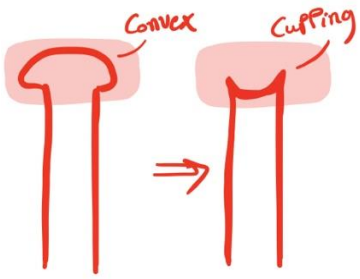
- Joint thickening (hypertrophy) especially around wrists and knees. Bc it is more obvious _the widening_ there more than for ex: shoulder since a lot of muscles are there
- **Lower limbs** are the most common site of clinical and radiological findings. Wrist is the most important X-ray to confirm the 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 أو الفالقس؟ متى ما جا استمر معه الديفورمتي
- Pigeon chest deformity, Rickety Rosary, **craniotabes(suture areas softening)**.

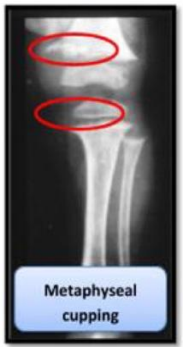
★ Biochemistry (most important investigation)

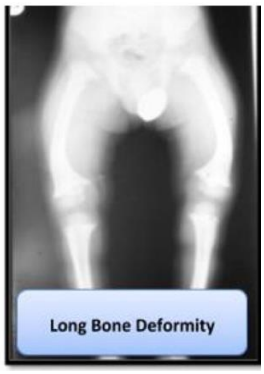
Hypocalcemia, Hypocalciuria, High alkaline phosphatase. (If alkaline phosphatase is normal, it is most likely not metabolic bone disease).

★ X-ray findings We like to **ask** about it

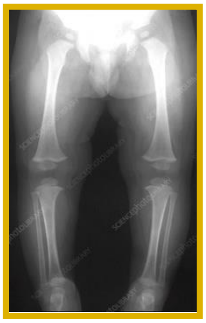
1. **Growth plate widening and thickening.**
2. Metaphyseal cupping should be convex **لكن يصير له** cupping
3. Long bone deformities.





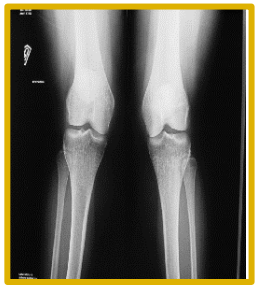


Normal Leg bones of 18-month-old infant **(Extra)**



★ 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).

Osteomalacia

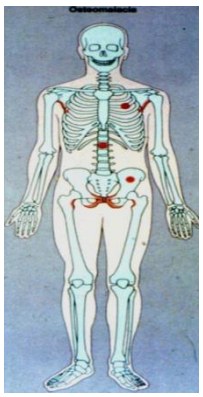
osmosis video **Toronto notes** **osmosis high yield notes**

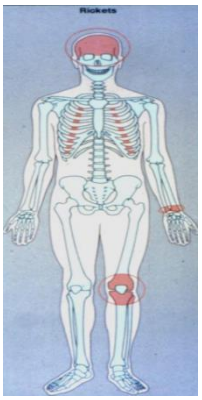
★ Signs and Symptoms

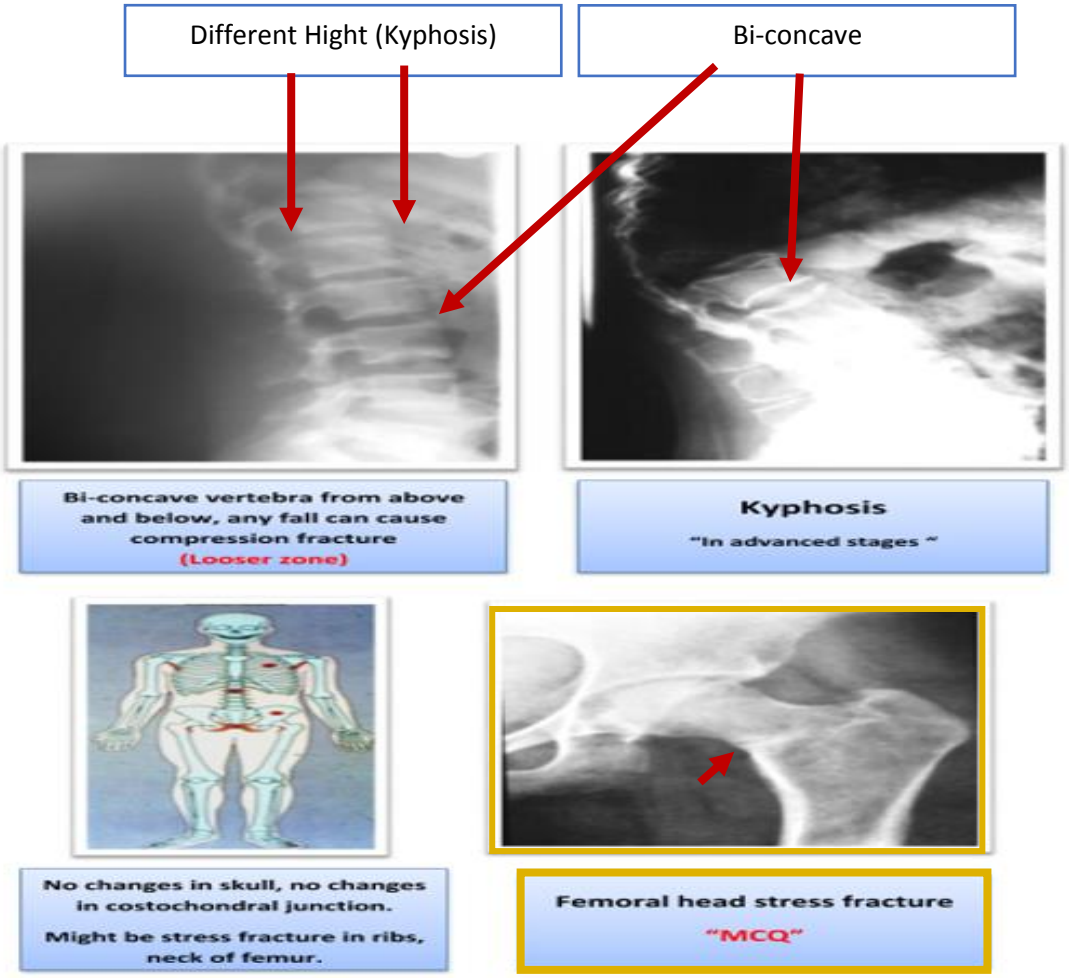
The difference here is that the growth is stopped in Adults unlike children so no growth-related symptoms here.

- Generalized bone , mainly backache (because the back bears body during walking).
- Muscle weakness.
- Reduced bone density.
- Vertebral changes (Typical): Bi-concave vertebra, vertebral collapse, and kyphosis.

- Stress fractures late stage: Loosers zones in scapula, ribs, pelvis, and proximal femur. Usually in neck of femur (stress area)







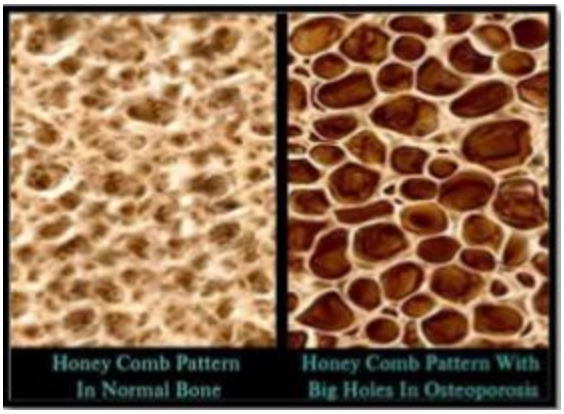
★ Treatment

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

Osteoporosis Asymptomatic

Osmosis video Toronto notes osmosis high yield notes

- Decreased bone mass: decreased amount of bone per unit volume and this causes reduced density (Loss of bone unite unlike osteomalacia which affects bone mineralization).
- Mineralization is not affected.
- Mainly post-menopausal (Drop in Estrogen levels) 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.



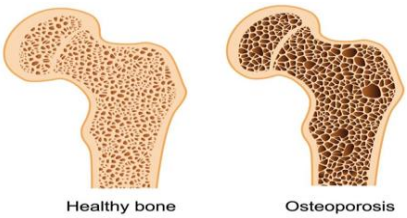
★ Primary Osteoporosis: (affect every bone)

	Postmenopausal Osteoporosis	Senile osteoporosis (Normal physiological process)
	• 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.	• Usually by 7th to 8th decades there is steady loss of at least 0.5% per year. • It is part of physiological manifestation of aging.
Risk factors	• Race (Caucasian) • Hereditary • Body build (thin people) • Early menopause • Smoking/ alcohol intake/ drug abuse • Calcium intake (low Ca)	• Male menopause (Decreased Testosterone) • Dietary: less calcium and vitamin D and protein. • Muscle weakness • Reduced activity

★ 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.



★ Clinical features of Osteoporosis

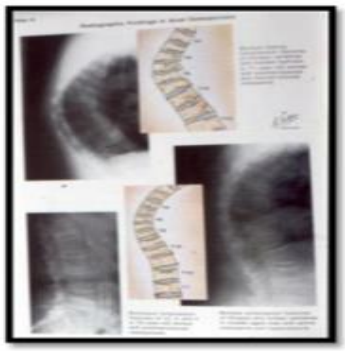
- Osteoporosis is a Silent disease Asymptomatic, so they present late & that makes the treatment difficult that's why it is serious
- Osteoporosis is Serious due to possible complications mainly fractures (common sites are dorsal spine, wrist, and neck of femur). The best way to treat osteoporosis is 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.
- 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 for

- They are Pathological fractures.
- Most common in osteoporotic compression fracture (OVC)of vertebra.
- Vertebral microfractures occur unnoticed (dull ache).
- Most serious is hip fractures (increased vascularity→ bleeding might cause death)
- Also common is wrist fractures (Colle`s fracture).

★ 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 (because of the side effect).

★ 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
- 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
- (2) 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 malignancies.

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

- Management of fracture:

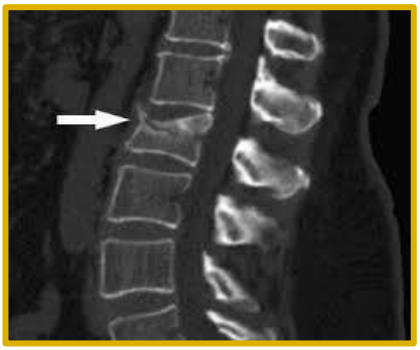
Use load shearing (brace) like Intramedullary nail

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

Osteomalacia	vs	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

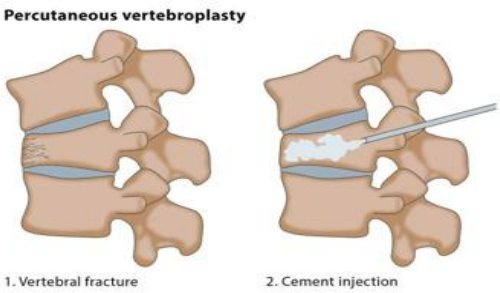
★ Management of Vertebral Osteoporotic Compression Fracture (OVC): I don't think anyone is gonna ask you about it ☺

- Pain relief
- Prevention of further fractures
- Prevention of instability
- Vertebroplasty
- Kyphoplasty



★ Vertebroplasty:

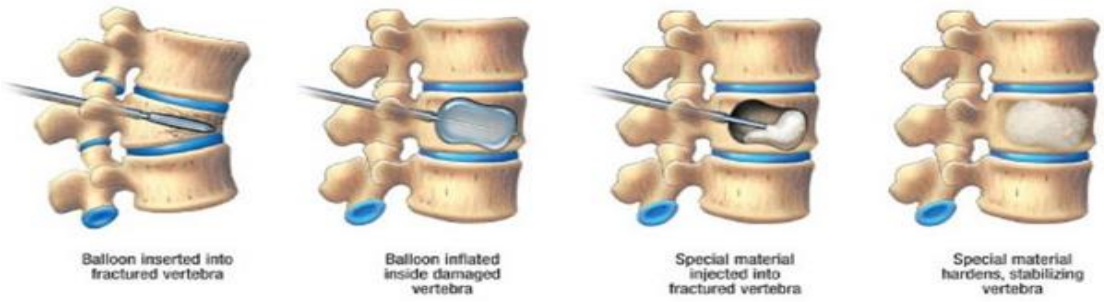
- It results in immediate pain relief
- Is the injection of bone cement into the collapsed vertebra.
- The injection is done under X ray control (image intensifier) by experienced orthopedist or interventional radiologist.
- It helps to prevent further OVF.
- Possible complication is leakage of cement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



★ Kyphoplasty: They go in & inject a material (bone cement) to elevate it, you don't need to know details I don't want you to know it

- 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



Hyperparathyroidism

Toronto and Kaplan notes

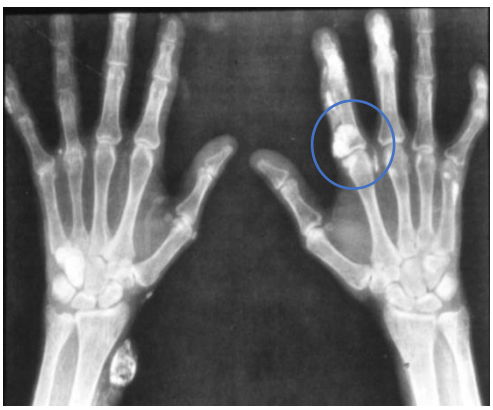
- Excessive PTH secretion: primary, secondary or tertiary:
  - **Primary:** Adenoma of the gland.
  - **Secondary:** as a result of low calcium (e.g. kidney and intestine problems)
  - **Tertiary:** as a result of prolonged or sustained stimulation = hyperactive nodule or hyperplasia.

مثلا كان عندك تسبب situation increasing the parathyroid hormone <= Then you correct the primary cause بعدها يعلّق، عاده
مايعلّق بمستوى مره عالي يكون slightly increased لكن برضو ستل يعتبر hyperactive

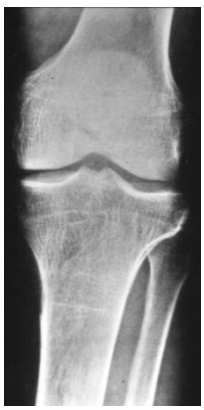
- Leads to increased bone resorption, sub periosteal erosions, osteitis manifested by fibrous replacement of bone.
- Significant feature is **hyper**calcemia.
- In severe cases: osteitis fibrosa cystica and formation of Brown tumors.

★ Radiological changes:

- Generalized decrease in bone density.
- Sub-periosteal bone resorption (scalloping of metacarpals and phalanges).
- 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 (wrist, knee, shoulder).

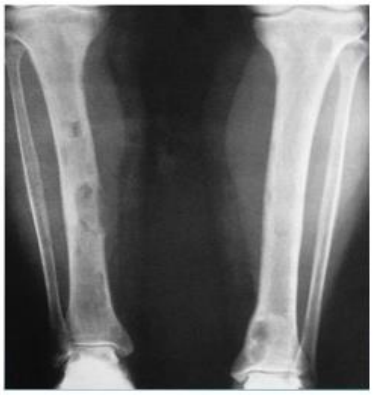


chondrocalcinosis



Early erosions

scalloped distal



Brown tumor

★ Management of Hyperparathyroidism (By treating the cause):

- Primary hyperparathyroidism due to neoplasm (adenoma or carcinoma) by excision.
- Secondary hyperparathyroidism by correcting the cause of hypocalcaemia.
- Tertiary hyperparathyroidism by excision of hyperactive (autonomous) nodule.
- Extreme care should be applied after surgery to avoid hypocalcaemia due hungry bones syndrome
  Very important: The bone when you treat hyperparathyroidism there is a phenomenon called hungry bone syndrome, اول ماتبدا تعالج وتعطي كالسيوم يقوم البون ياخذ كل شي ويسبب symptoms of hypocalcemia.