Lecture 21

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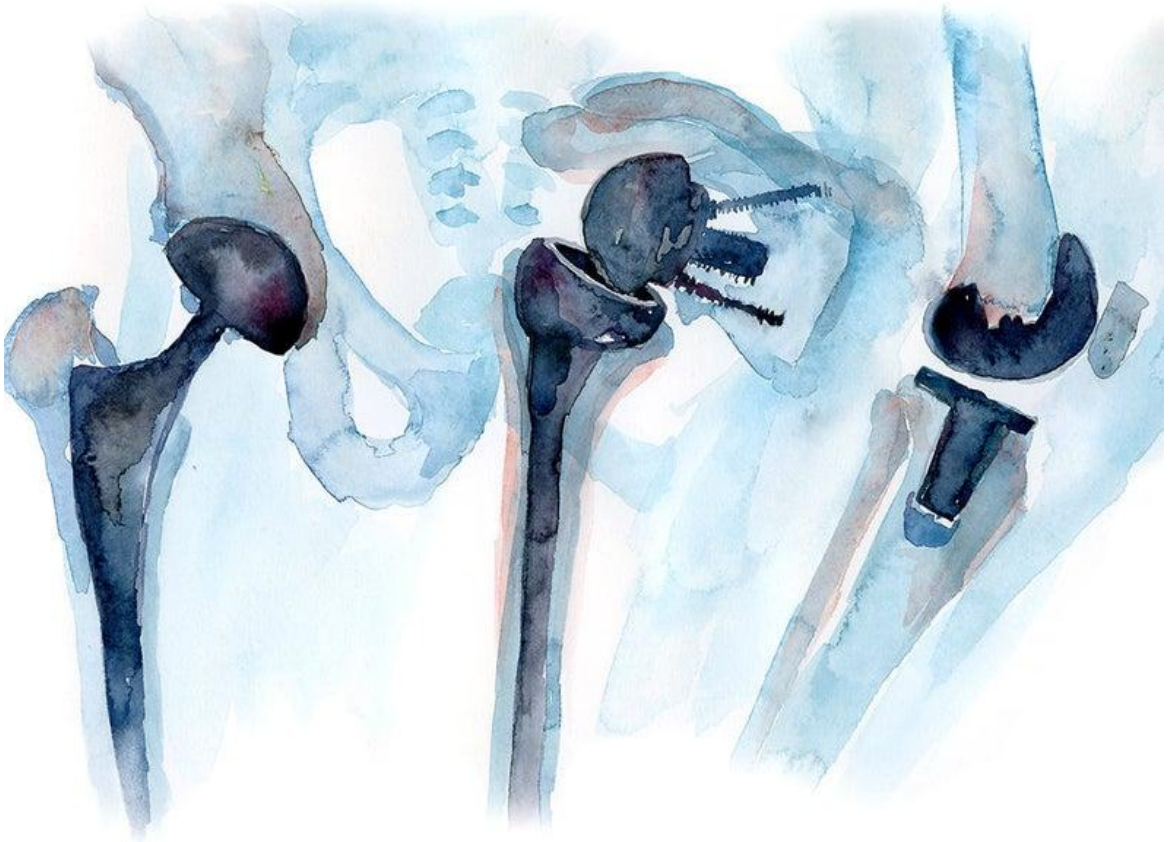


Metabolic Bone Disorders

Dr. Hisham Al Sanawi

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.

Color Index:

Original text | Doctor's notes | Text book
Important | Golden notes | Extra

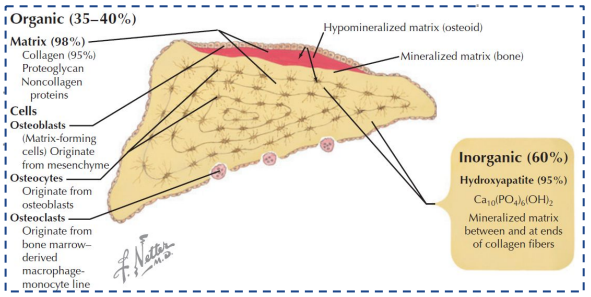
Bones:

Orthopedic Surgery

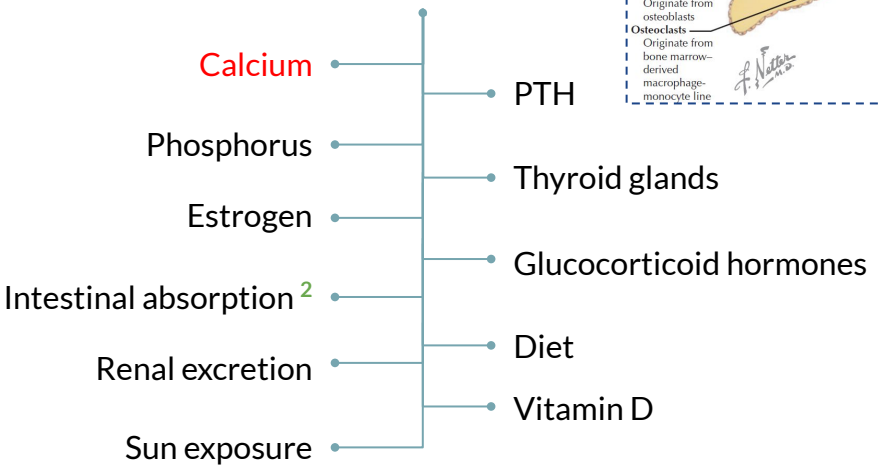
- Orthopedic surgeons have to deal with all types of bone: healthy or diseased; and that's why they have to know about bone metabolism.
- Bones in the body protect vital organs.
- Bones give support to muscles and tendons.
- Bone may become weak in certain conditions.

Bone as 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. [1]
- Bones not only protects and support the body, they also play an important role in blood homeostasis.
- Many factors are involved in this process.



Factors Controlling Bone Metabolism



Bone Structure

- **Bone matrix:** (collagen → tension; minerals (Ca^{2+}) → compression)
  - ➔ **40% Organic**: mainly collagen type 1 (responsible for tensile strength [1]) and cells.
    - There are other types but the **majority** of it in the bone are type 1
    - Tensile strength is the measurement of the force required to pull something
  - ➔ **60% Minerals**: mainly Calcium hydroxyapatite, Phosphorus, and traces of other minerals like zinc. (provides compressive strength)
- **Cells in bone:** osteoblasts , osteoclasts , and osteocytes.

1- 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. Any imbalance in this process will lead to disease

2- Patients with intestinal problems such as celiac have poor calcium absorption.

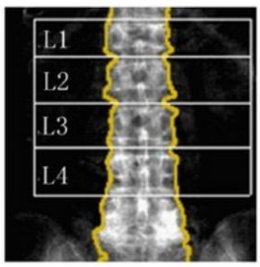
Bones Strength and Density:

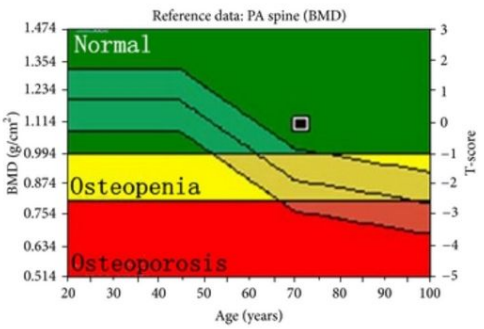
Bone Strength

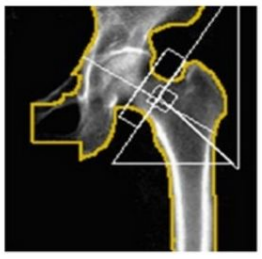
- Minerals resist compression, collagen resist tension.[1]
- Bone strength is affected by mechanical stress which means exercise and weight bearing strengthen the bone. (Wolff's Law)
- Bone strength gets reduced with menopause and advancing age.
- Reduced bone density on X rays is called osteopenia.
- Osteopenia is also a term used to describe a degree of reduced bone density, which if advanced becomes Osteoporosis.
- X-ray is not accurate
- You can't diagnose a patient with osteoporosis with an X Ray alone. You must use a bone densitometry to accurately check the bones density.

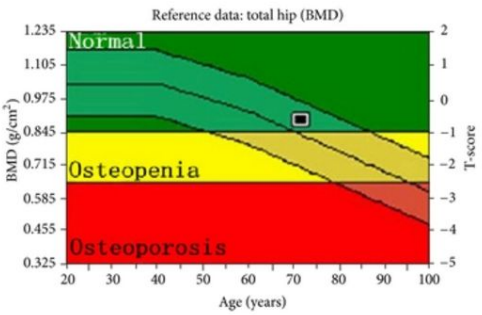
Bone Density

- Bone density is measured nowadays by a DEXA scan [2](Dual Energy X-ray Absorptiometry)
- They do it in three areas: vertebrae, wrist (distal of radius), and neck of femur; these bones get affected first and might get fractured easily (we need to protect them)
- **DEXA** is measured radiation absorption (more absorption → more density)
- 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 measurement of bone density will be expressed as a T score (see image)



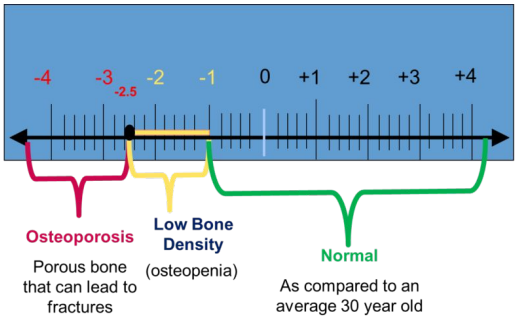






T 2. World Health Organization classification of Bone Mineral Density (15).

Classification	T-score
Normal	-1.0 or greater
Osteopenia	Between -1.0 and -2.5
Osteoporosis	-2.5 or less
Severe Osteoporosis	-2.5 or less with a fragility fracture



1- Minerals protect the bone from compressive forces (Push), while collagen protects the bone form tensile forces (Pull).
2- It's very important to learn how to read the graph, you may be asked to do so.

Hormonal Regulations:

Plasma Levels

! There are normal plasma levels in osteoporosis

- **Calcium** : 2.2-2.6 mmol/l
- **Phosphorus** : 0.9-1.3 mmol/l
  - ➔ Both absorbed by intestine and secreted by kidney in urine.
- **Vitamin D** : 70-150 nmol/l (promotes Ca absorption from kidney and intestines.
- **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)

Calcitonin

! Not used in treatment due to its side effects

- Is secreted by **C cells** of thyroid gland.
- Its secretion is regulated by serum calcium.
- It decreases serum calcium by inhibiting bone resorption and increasing its excretion.
  - ➔ Inhibit reabsorption from kidney & intestine and trying to bring it back to the bone, used to be given as supplement but not anymore b/c of its side effects.

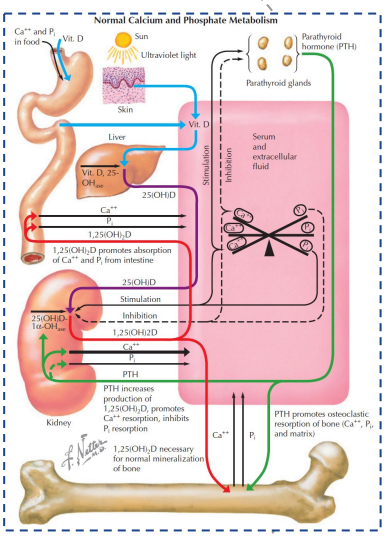
Parathyroid Hormone

- Production levels are related to serum calcium levels,

Action of PTH → (↓ Ca^{2+} → ↑ PTH)

1. Increasing osteoclastic activity to release Ca^{2+} from the bones
2. Increases intestinal absorption from the intestines by activating Vit D
3. Increases Ca+ reabsorption from the kidney and increases the excretion of phosphorus

- If the 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		
Primary	**Secondary**	**Tertiary**
Adenoma of the gland	Low Ca (e.g. renal failure)	Prolonged sustained stimulation = hyperactive nodule of hyperplasia

1- 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)
2- Irreversible clonal outgrowth of parathyroid glands, usually in long-standing inadequately treated chronic renal failure on dialysis

Bone Structure and Metabolism

Bone Metabolic Disorders

- Rickets and Osteomalacia
- Osteoporosis
- Hyperparathyroidism

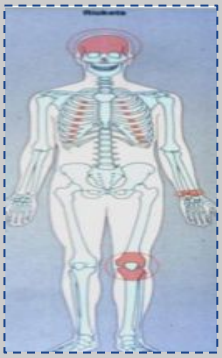
❶ Rickets and Osteomalacia

Rickets	Osteomalacia
• Different expressions of the same disease, which is: inadequate mineralization	
• Affects area of endochondral growth in children. (Ex: Proximal humerus and proximal femur)	• All skeleton is incompletely calcified in adults (slowly progressive)

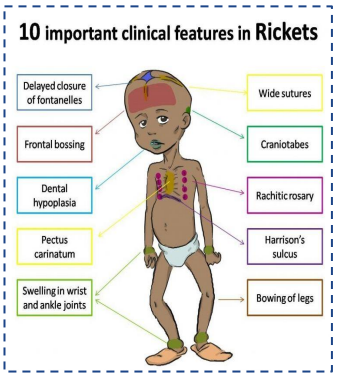
Biochemistry	• Hypocalcemia (always check Ca, PO4, Vit D and ALP levels) • Hypocalciuria • High alkaline phosphatase (If normal, it is mostly not a metabolic disease)
Causes	• Calcium deficiency (diet , malabsorption) • Hypophosphatemia (to deposit calcium you need phosphate) • Defect in Vitamin D metabolism: (nutritional, underexposure to sunlight, intestinal malabsorption, liver & kidney diseases

Rickets

Signs and Symptoms

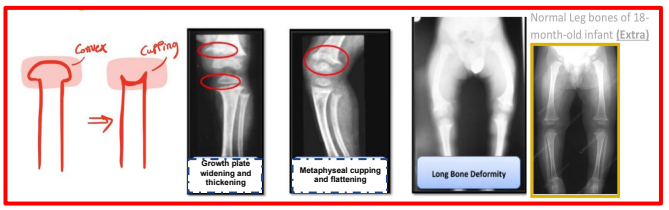


- Child is restless, babies cry without obvious reason
- Failure to thrive
- Muscle weakness.
- In severe cases with very low calcium: tetany or convulsions.
- Joint thickening (hypertrophy) especially around wrists and knees.
  - ➔ Wrist is the most important X-ray to confirm the diagnosis.
- Deformity of limbs
  - ➔ Late → the kid will have Valgus, early → Varus.
- Pigeon chest deformity, Rickety Rosary, craniotabes



X ray

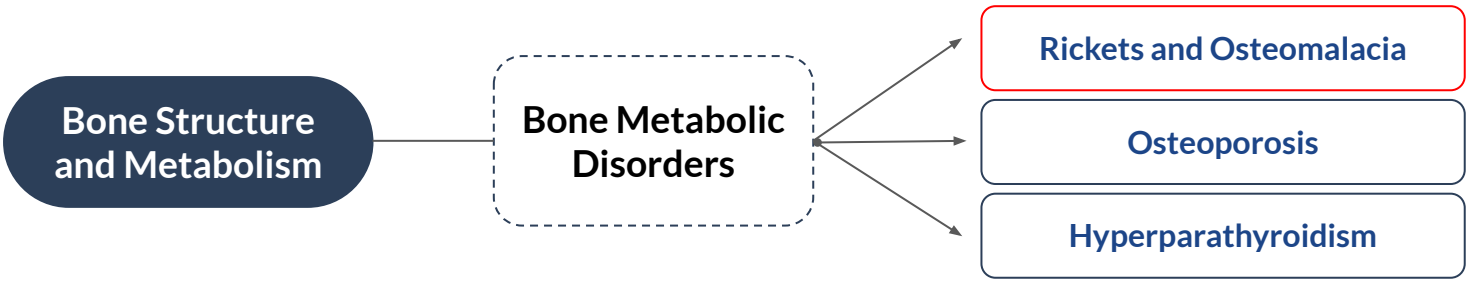
- Growth plate widening and thickening
- Metaphyseal cupping
- Long bones deformity



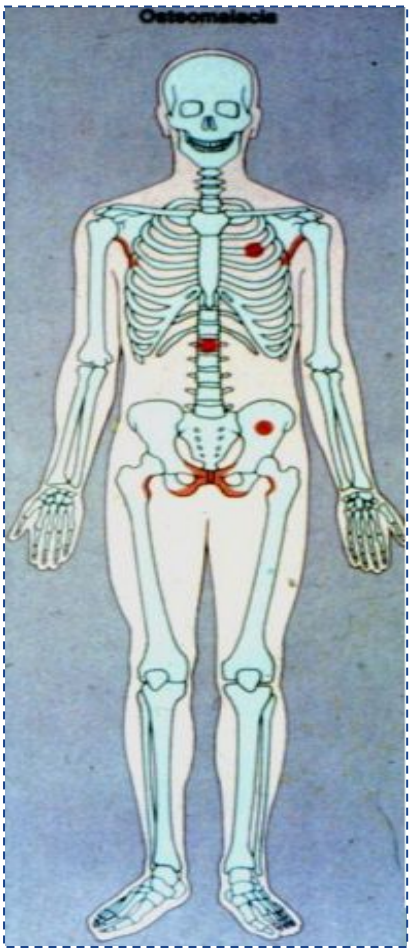
Treatment

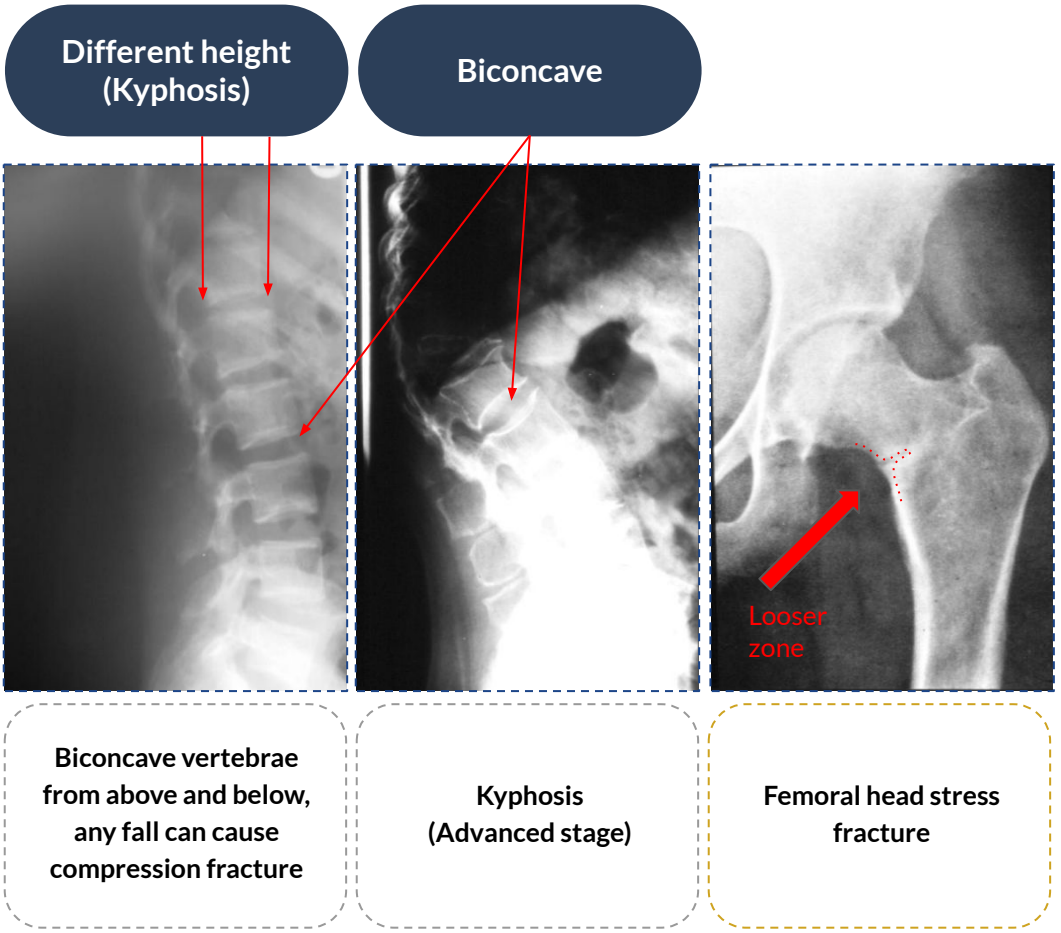
- Check if there's no systemic illness (treat the cause)
- Adequate Vitamin D replacement.
- Sun exposure.
- Correct (Post rachitic) deformities. (if persistent → corrective osteotomy)

➔ Don't perform surgery immediately bc the bone is still growing



Osteomalacia	
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 • Muscle weakness. • Reduced bone density • Vertebral changes: Bi-concave vertebrae, vertebral collapse, and kyphosis. • Stress fractures (late): Loosers zones in (scapula (neck), ribs, pelvis, and proximal femur (neck of femur)
Treatment	• Exclusion of other diseases • Vitamin D + Ca + lifestyle modification + exercise + Sun expose. • Fracture management • Correct deformity if needed. [1]





1- (Treating the complications is done only after treating the original cause)

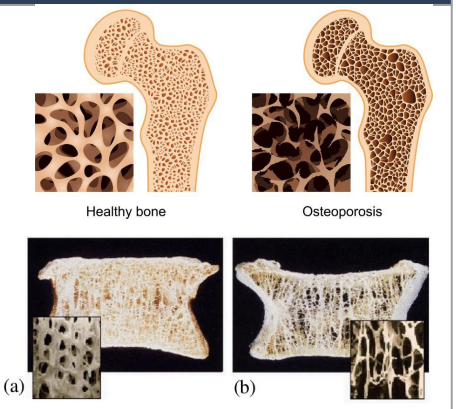
Bone Structure and Metabolism

Bone Metabolic Disorders

- Rickets and Osteomalacia
- Osteoporosis
- Hyperparathyroidism

❷ Osteoporosis Question comes as a routine check up

- Decreased bone mass : decreased amount of bone per unit volume (reduced density)
- Mineralisation 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.
- Osteoporosis can be primary or secondary



Primary Osteoporosis

Type	Postmenopausal	Senile
Description	• 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. • Low Calcium intake • Chronic lack of exercise	• Male menopause (Decreased Testosterone). • Dietary: less calcium and vitamin D and protein. • Muscle weakness • Reduced activity (exercise the best way to delay osteoporosis in men)
Clinical Features	• Osteoporosis is a silent disease (asymptomatic, until complications happen) • 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 due collapsed vertebrae • Osteoporosis is not osteoarthritis; but the two conditions may co-exist	

Bone Structure and Metabolism

Bone Metabolic Disorders

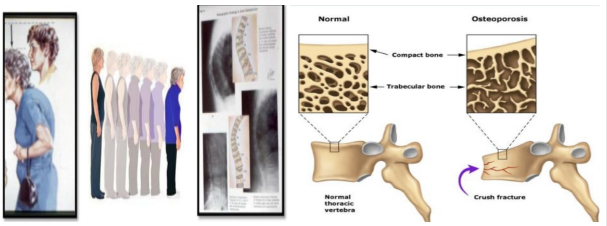
- Rickets and Osteomalacia
- Osteoporosis
- Hyperparathyroidism

❷ Osteoporosis

Secondary Osteoporosis

It happens most of the time in younger patient e.g. 45 years old (young patients), causes include:

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

Kyphosis and height loss	• With osteoporosis the anterior part of the vertebra narrows which leads to kyphosis and loss height. 
Fragility Fractures	• We must observe the hip and vertebra • They are Pathological fractures. • Most common in osteoporotic compression fracture (OVC) of vertebra. • Vertebral microfractures occur unnoticed (dull ache). • Most serious is hip fractures • Also common is wrist fractures (Colle`s fracture = distal radius).
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).
Prevention	• 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.

Bone Structure and Metabolism

Bone Metabolic Disorders

- Rickets and Osteomalacia
- Osteoporosis
- Hyperparathyroidism

❷ Osteoporosis

Management

Drug Therapy

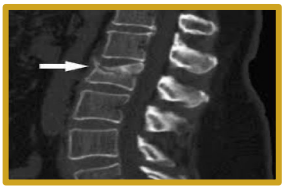
- Estrogen has a definite therapeutic effect and was used extensively as HRT but cannot be recommended now due to serious possible side effects (such as tumors and CV risks)
- Adequate intake of calcium and vitamin D is mandatory
- Drugs which inhibit osteoclast activities: as first line treatment
  - e.g. Bisphosphonates like sodium alendronate FOSAMAX , BONVIVA
- Denosumab human monoclonal IGG2 antibody that can be used
- Drugs that enhance osteoblast activities: bone stimulating agents like PROTELOS (strontium), FORTEO (teriparatide)
  - The problem in this type of medication is the risk of malignancy

Exercise

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

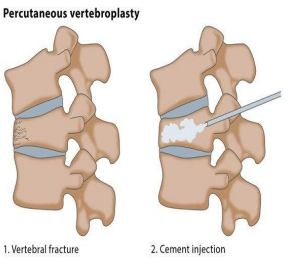
Management of Fractures

- Use load shearing (brace) in fracture internal fixation instead of plating
- Plates = load bearing | Screws (preferred) = load sharing
  - Like intramedullary nail → screws (load sharing)
- Pain relief
- Prevention of further fractures and instability
- Vertebroplasty and kyphoplasty



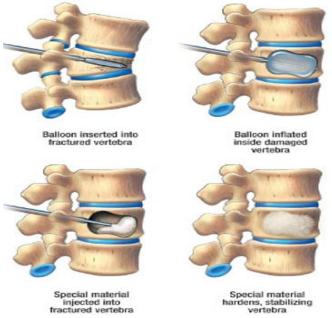
Vertebroplasty

- 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 IR.
- It helps to prevent further OVF.
- Possible complication is leakage of cement into spinal canal (nerve injury) or venous blood (cement PE).

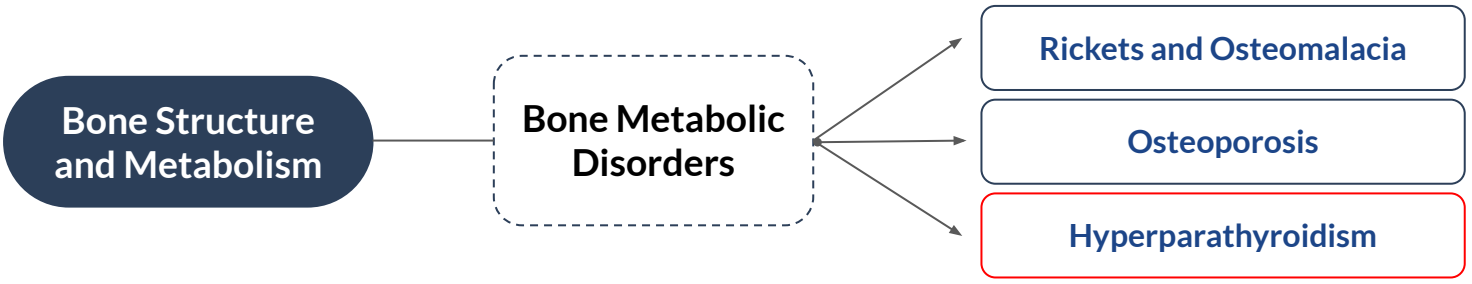


Kyphoplasty

- 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 correction of kyphosis is achieved.
- It is safer because cement is injected into a safe void. (low leakage risk)



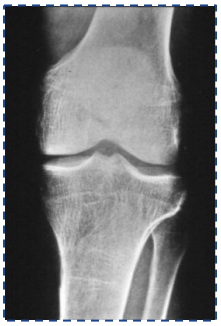
Osteomalacia	Osteoporosis
• Any age • Patient is ill • General ache • Weak muscles • Looser zones • ALP increased • PO4 decreased	• Post menopausal, old age • Not ill • Asymptomatic until fractures • Normal muscles • Late X ray changes • Normal ALP • Normal PO4



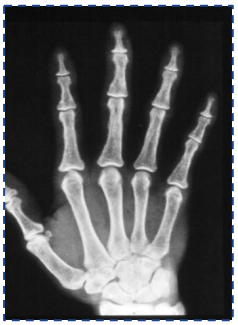
❸ Hyperparathyroidism

- Excessive PTH secretion : primary, secondary or tertiary
- 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 tumours

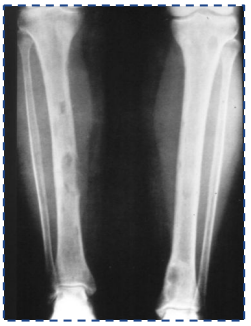
X ray	• Generalized decrease in bone density. • Subperiosteal bone resorption: scalloping of metacarpals and phalanges • Brown tumors (empty bone areas with bleeding caused by bone reuptake) • Chondrocalcinosis = calcification of cartilage (wrist, knee, shoulder).
Management	• Primary: excise neoplasm (adenoma or carcinoma) • Secondary: correct the cause of hypocalcemia (renal or intestinal issue) • Tertiary: excision of hyperactive (autonomous) nodule ★ Extreme care should be applied after surgery to avoid hypocalcaemia due hungry bones syndrome - The moment you correct hypothyroidism, the bone might absorb a lot of calcium leading to severe hypocalcemia (might cause cardiac problems)



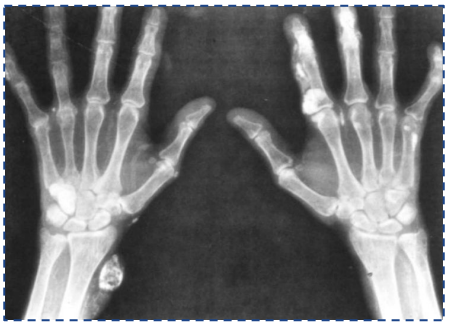
Early erosions



Scalloped distal phalanges



Brown tumors



Chondrocalcinosis

Extra:

Metabolic Bone Disease

Osteomalacia and Rickets

Definition
- 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 34. Clinical Features of Rickets and Osteomalacia

Rickets	Osteomalacia
Skeletal pain and deformities, bow-legged	Not as severe
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 35. 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 Renal Tubular Acidosis	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 (MBD) in Chronic Kidney Disease (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^{2+} in age-appropriate normal range in children

Extra:

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 (does not include fractures of fingers and toes)
  - 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 Hx 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 32, 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, and high-risk
5. for all patients being assessed for osteoporosis, encourage appropriate lifestyle changes (see Table 33, 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 totaling 30970 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%)

Extra:

Table 31. 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 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

Table 32. Osteoporosis Risk Stratification

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 pharmacotherapy: Additional vertebral fracture(s) identified on vertebral fracture assessment (VFA) or lateral spine x-ray Previous wrist fracture in individuals ≥65 yr 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 33. Treatment of Osteoporosis in Women and Men

Treatment for Both Men and Women	
Lifestyle	Diet: elemental calcium 1000-1200 mg/d; vitamin 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 fractures (Grade A): alendronate (PO), risedronate (PO), zoledronic acid (IV)
RANKL Inhibitors	Denosumab: 1st line in prevention of hip, nonvertebral, vertebral fractures (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
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 fractures (Grade A) Advantages: prevents osteoporotic fractures (Grade A to B evidence), improves lipid profile, decreased breast cancer risk Disadvantages: increased risk of deep vein thrombosis (DVT)//PE, stroke mortality, hot flashes, leg cramps
HRT: combined estrogen + progesterone (see Gynaecology, GY35)	Indicated for vasomotor symptoms of menopause For most women, risks > benefits Combined estrogen/progestin prevents hip, vertebral, total fractures Increased risks of breast cancer, cardiovascular events, and DVT/PE

Alendronate (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

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

Extra:

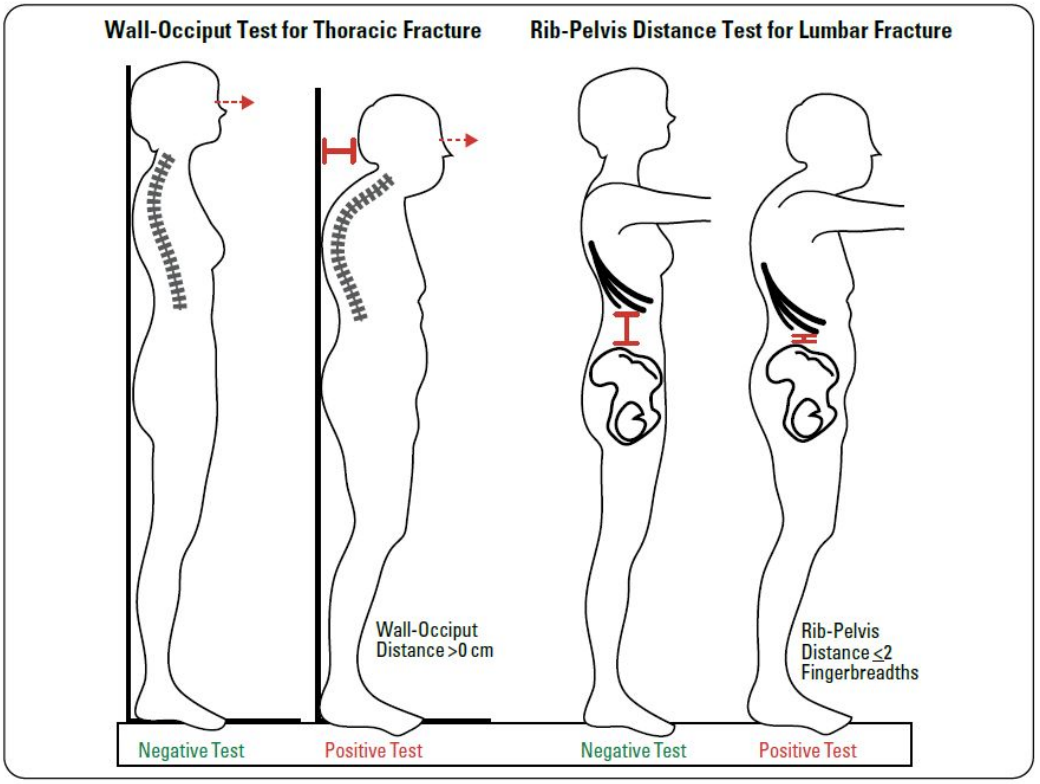


Figure 20. Physical examination test for vertebral fractures

Normal or ↑ PTH

Drugs: Lithium

Familial Hypocalciuric Hypercalcemia (FHH): Ca^{2+} receptor gene defect

Primary Hyperparathyroidism: Solitary adenoma (81%) Hyperplasia (15%) Carcinoma (4%) MEN 1 and 2a

Tertiary Hyperparathyroidism: Increased PTH after prolonged secondary hyperparathyroidism due to renal failure

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

Quiz

MCQ

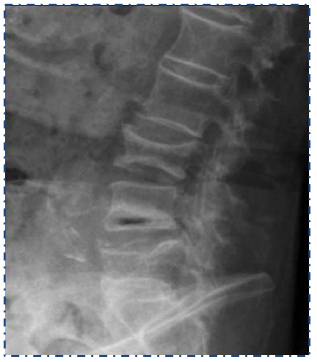
Q1: Which of the following is a sign of rickets on an X ray?

A. Gunstock deformity
B. Kyphoscoliosis
C. Metaphyseal cupping
D. Bone marrow expansion

Q2: 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. Family history of osteoporosis
D. Low Ca intake

Q3: 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 ray showed a compression fracture. What is the next step?



A. Start anti-osteoporotic medication
B. Admission and bed rest
C. Open reduction and internal fixation (ORIF)
D. 6 weeks of halo femoral traction

Q4: 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

SAQs

1. Discuss 2 factors involved in bone metabolism that you think are important and explain why?
   - Page 2

2. Sketch a tibia and draw two radiographic findings and label them
   - Page 5

Answers

Q1	Q2	Q3	Q4
C	B	A	B

THANK YOU

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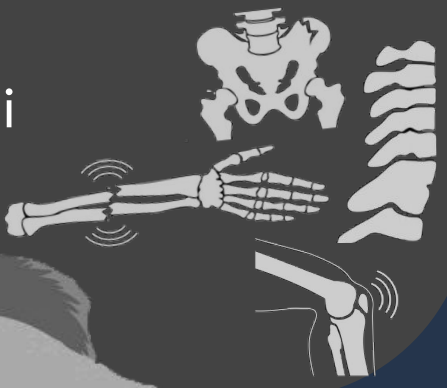

Congratulations!!

You just finished your orthopedics course!

I'd like to take a moment to thank everyone who participated in the making of this team, this has been a terribly unenjoyable journey filled with stress and headaches. Regardless, we managed to get it done.

We hope you enjoyed it tho?
If you deemed this work unhelpful or you think we could've somehow made it better, we wholeheartedly accept your feedback, please click here.

Nah fr this was easy and you should ace your exams.

Take care,
Group A1 academic leader
Badr Alshehri