Osteoporosis

Dr. Mohammad Hamdan

Why important

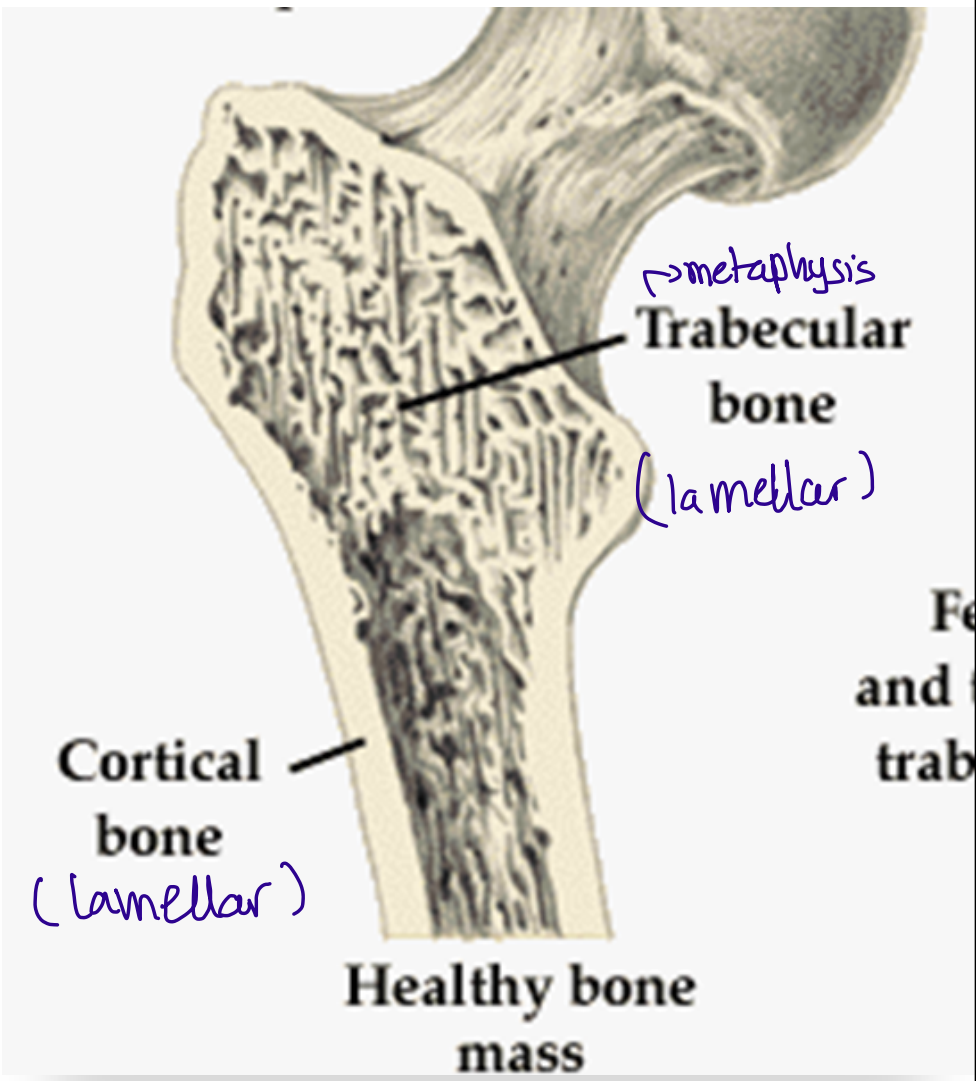
- 10 million Americans and 200 million people worldwide have osteoporosis
- 1.5 million osteoporotic fractures occur each year
- Hip Fx mortality 20%
- Vertebra Fx mortality 15%

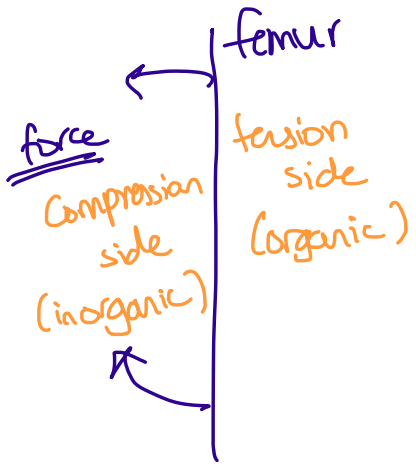
↑ burden

↑ challenge

Types

* bone
  - woven: disorganized newly-formed bone
    - i.e callus
  - lamellar
    - ↳ trabecular
    - ↳ cortical





COMPOSITION OF BONE

EXTRACELLULAR MATTER

ORGANIC MATRIX
(Osteoid Tissue)
Collagen fibrins bound by amorphus mucopolysaccharide substance

tension resistant

INORGANIC MATRIX
(Bone Mineral)
Ca^{++}
Calcium phosphate
(hydroxyapatite)
OH^- phosphate

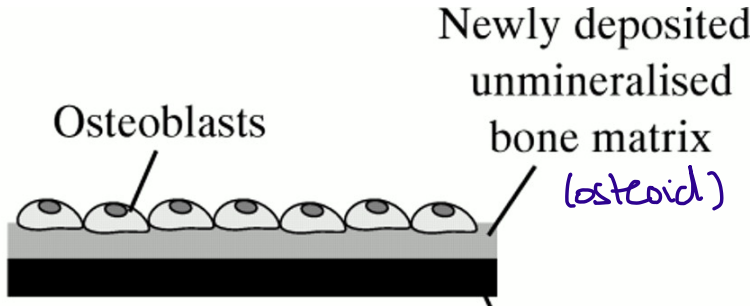
Compression resistant

CELLULAR COMPONENT

OSTEOBLASTS
OSTEOCLASTS
OSTEOCYTES
↓
homeostasis of bone

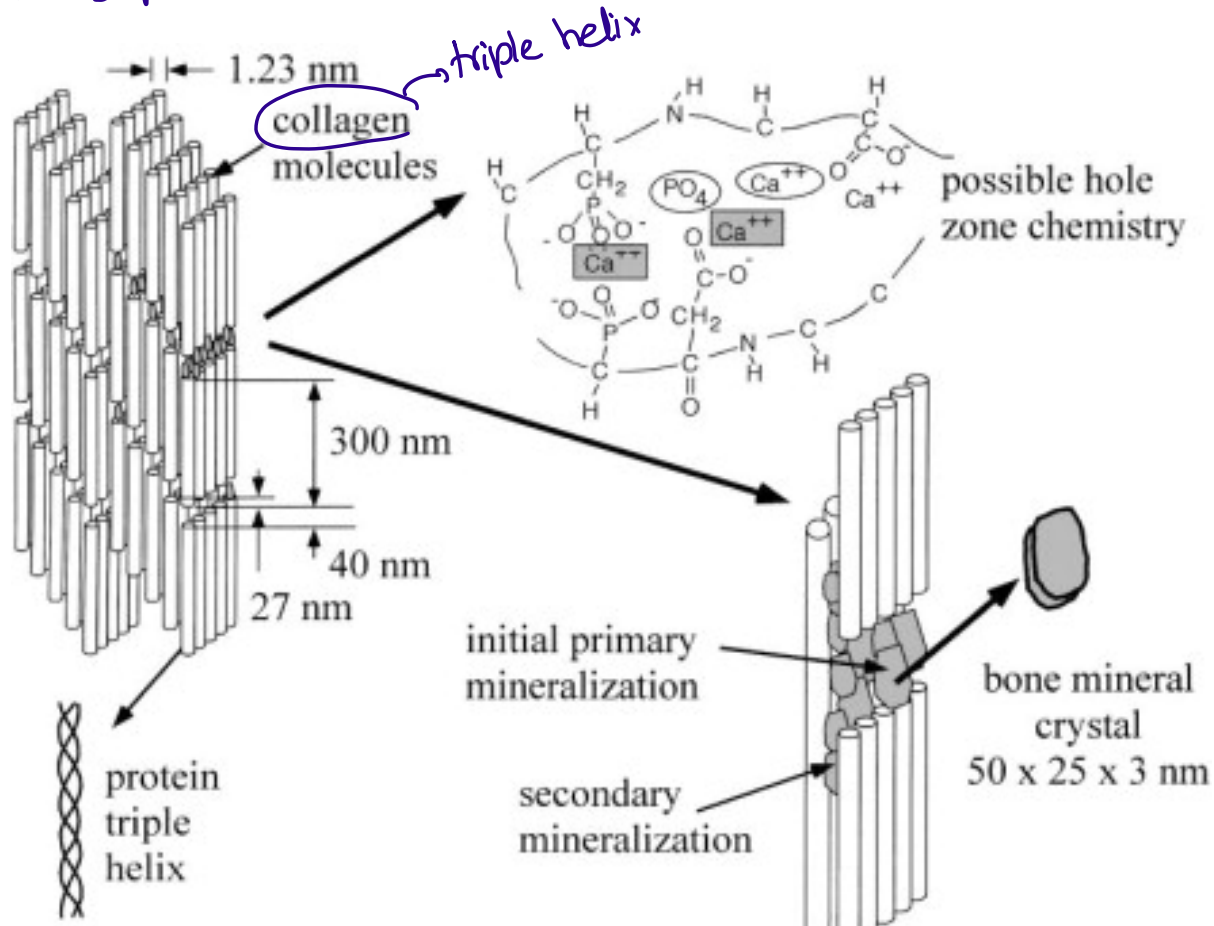
holes & pores

Step 1:
Deposition of
osteoid

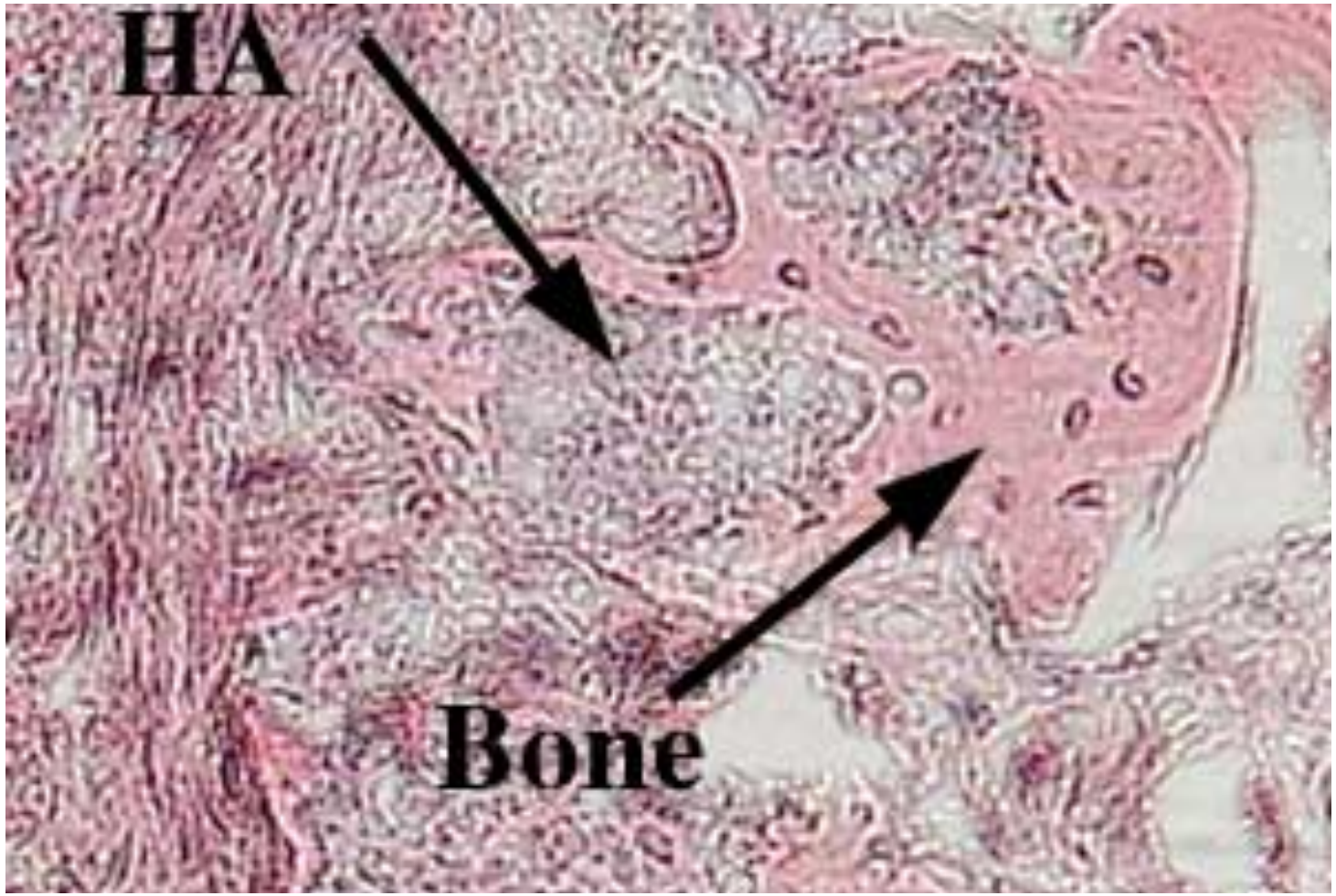


Step 2:
Mineralisation

bone



* Mineralization *

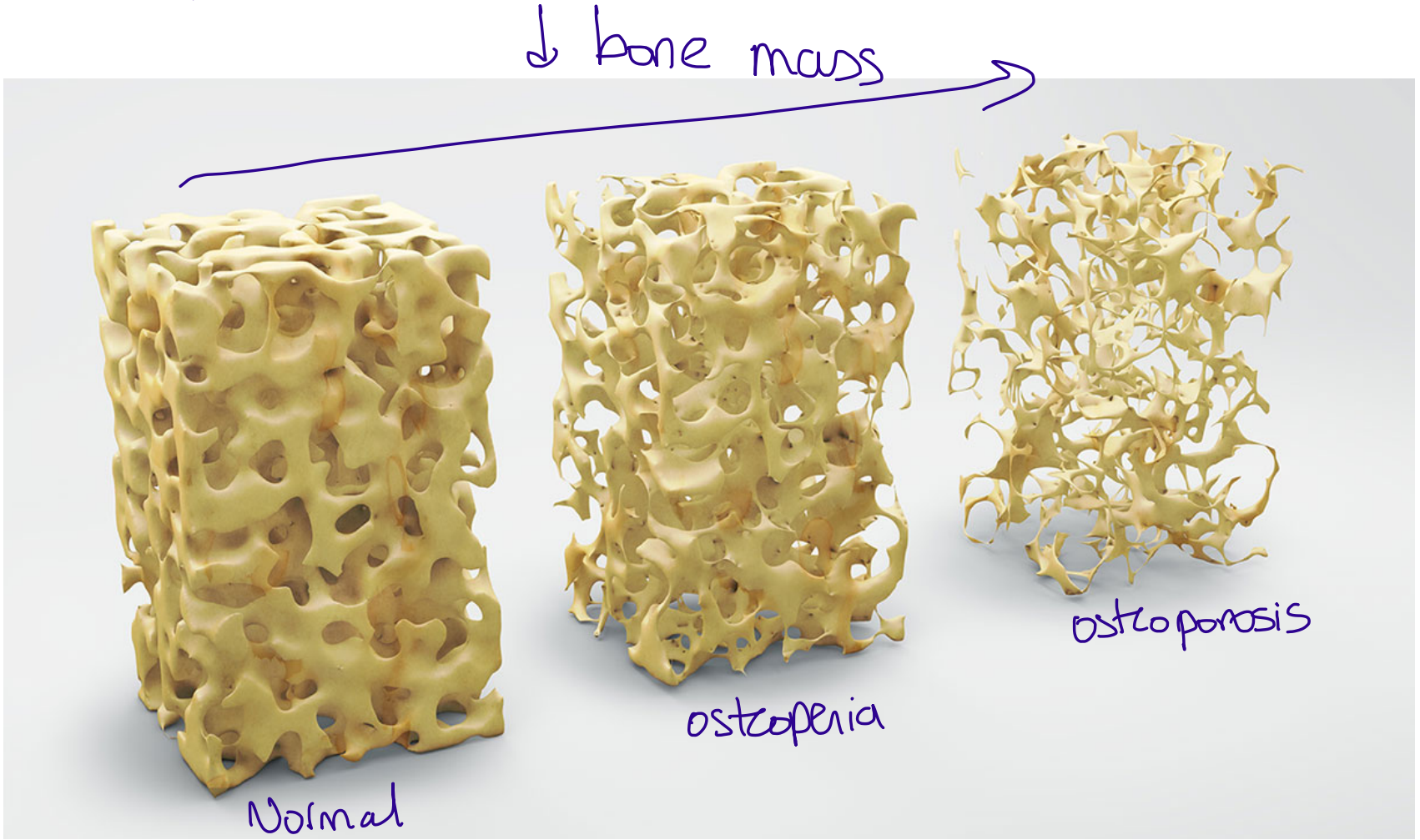

HA
Bone

Osteoporosis is…

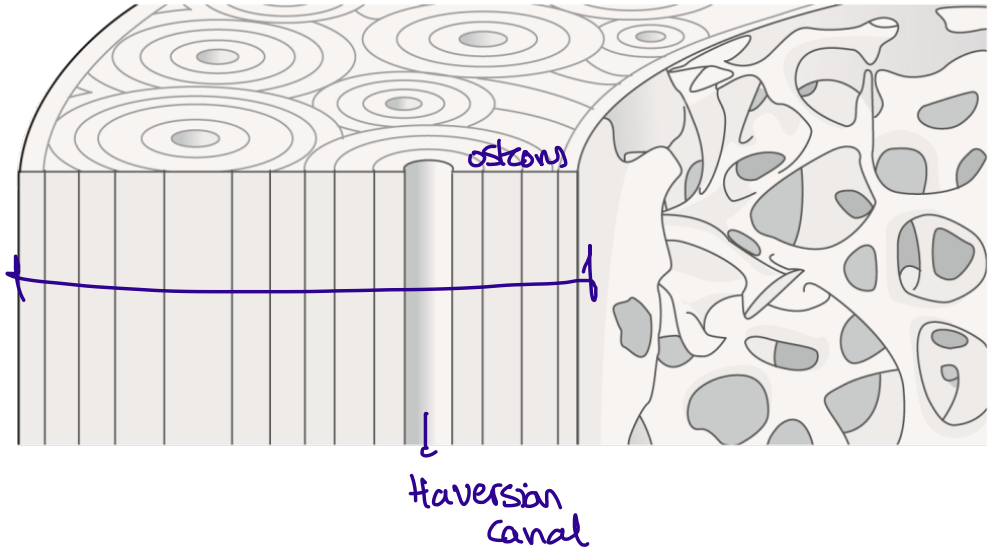
"...a systemic skeletal disease characterized by **low bone mass** and **microarchitectural deterioration** with a consequent increase in bone fragility with susceptibility to fracture..."

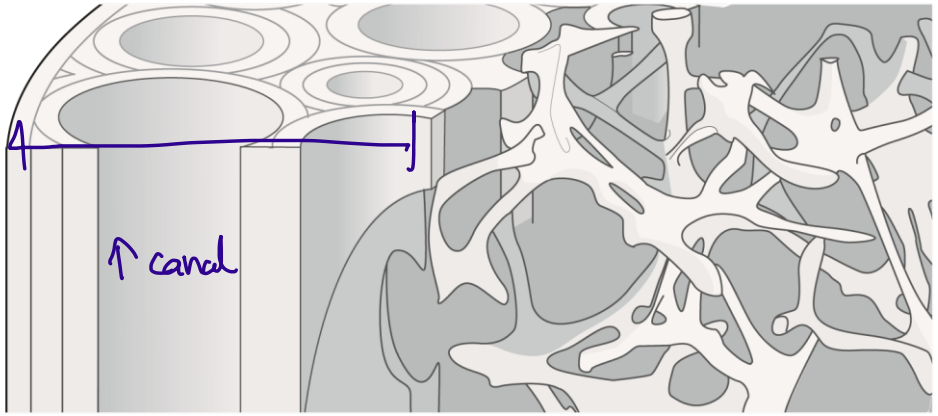
Definition from WHO

Trabecular bone



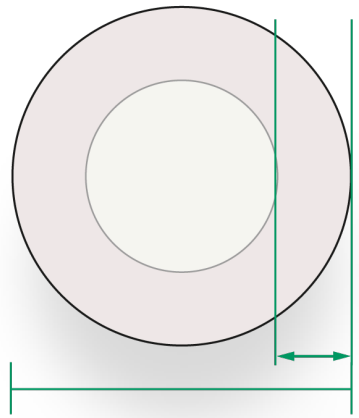
cortical bone

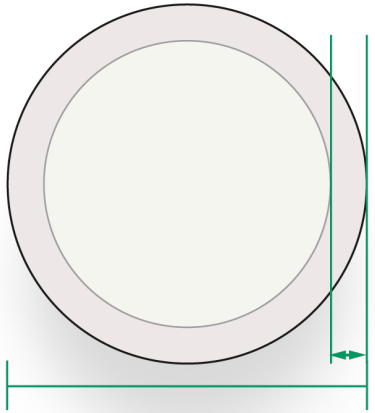


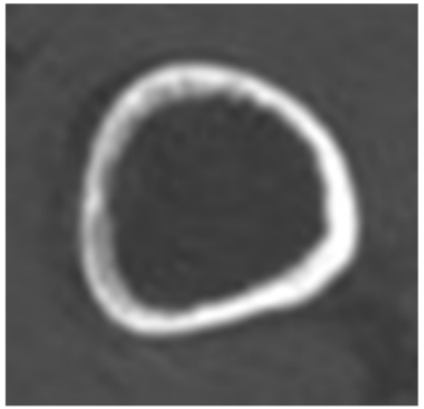


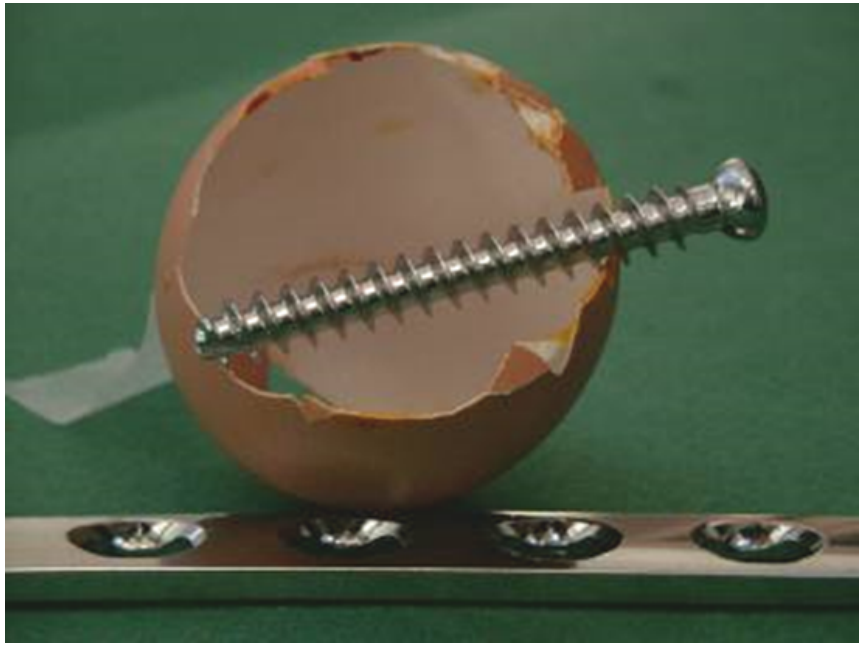
↑ ↓ thickness

Cortical bone



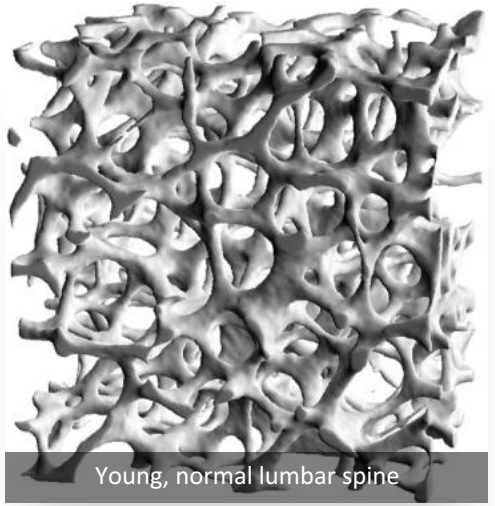




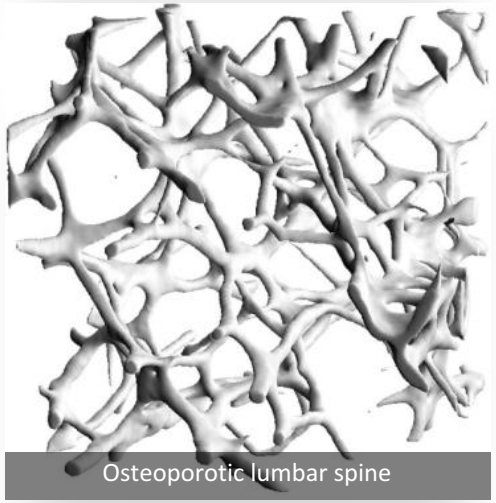


Cancellous bone

Less and thinner trabeculae with fewer, often broken interconnections



Young, normal lumbar spine



Osteoporotic lumbar spine

Types

Primary Osteoporosis

Primary: Is the more common form and is due to the typical age-related loss of bone from skeleton.

Type 1 (Postmenopausal Osteoporosis)
- Due to decrease in estrogen or testosterone deficiency

Type 2 (Senile Osteoporosis)
- Inability to produce adequate vitamin D3
- Decrease in bone formation

Secondary Osteoporosis

Secondary: Results from the presence of other diseases or conditions that predispose to bone loss.

- Medications
- Hyperparathyroidism
- Excess Alcohol
- Smoking

* estrogen normally
↑ osteoblast
↓ osteoclast

first 6 years after menopause

MC

anticoagulants
anticonvulsants
furosemide

Location of fractures

* osteoporosis alone : usually asymptomatic
* fractured osteoporosis : painful

- vertebral body > hip > wrist fractures
  (axial)

Risk factors

Thin, smoker and alcoholic old Caucasian white female with freckles and fair hair known to have RA on steroid

F more than M

Medications

- Steroid
- Phenytoin
- LMWH
- Omeprazole

Diseases

- Malabsorption syndromes
- Hyperthyroidism
- DM1
- Hypogonadisim
- Cancers

Risk factors

Symptoms and Signs

Patients with osteoporosis are asymptomatic unless a fracture has occurred

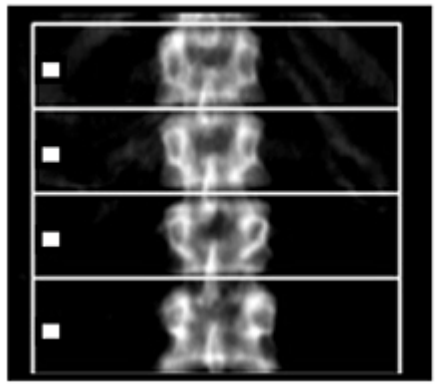
Signs follow the same rule

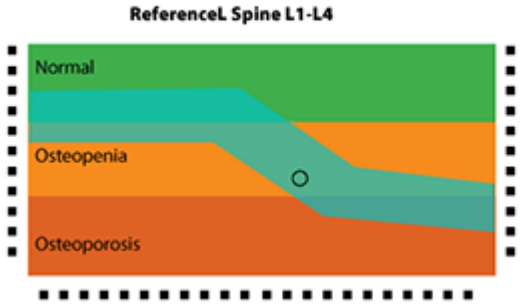
Diagnosis

* Peak of bone density ⇒ at the age of 25.

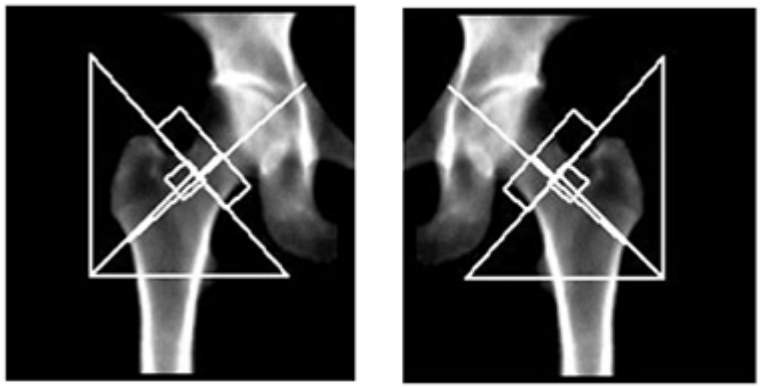
- Dexa Scan (Dual Energy Xray Absorptiometry)

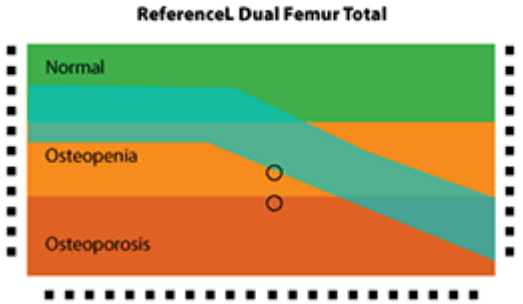
Vertebrae



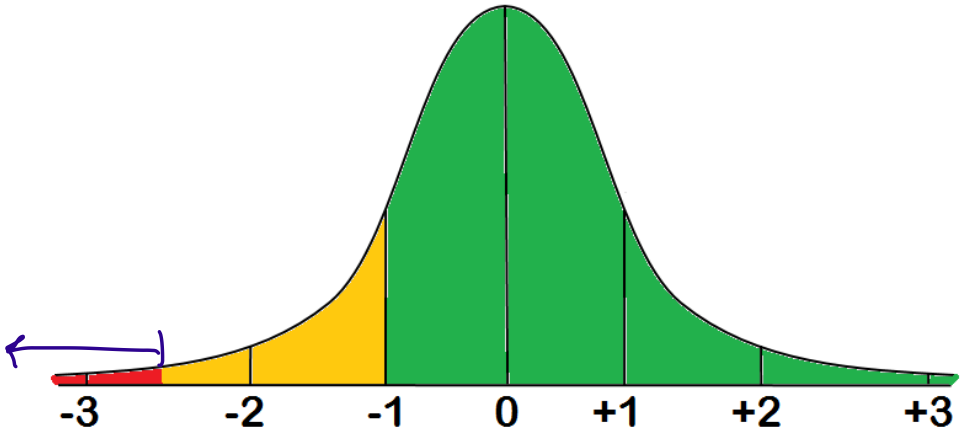


hip



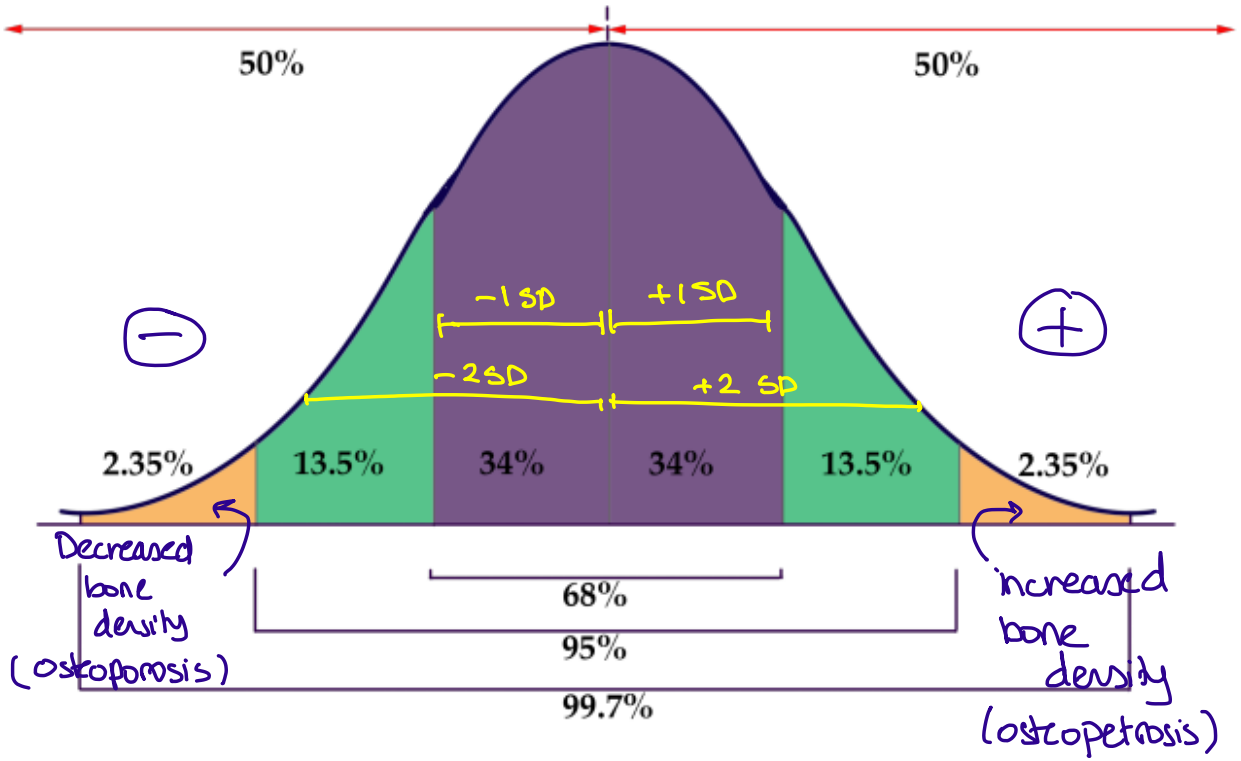


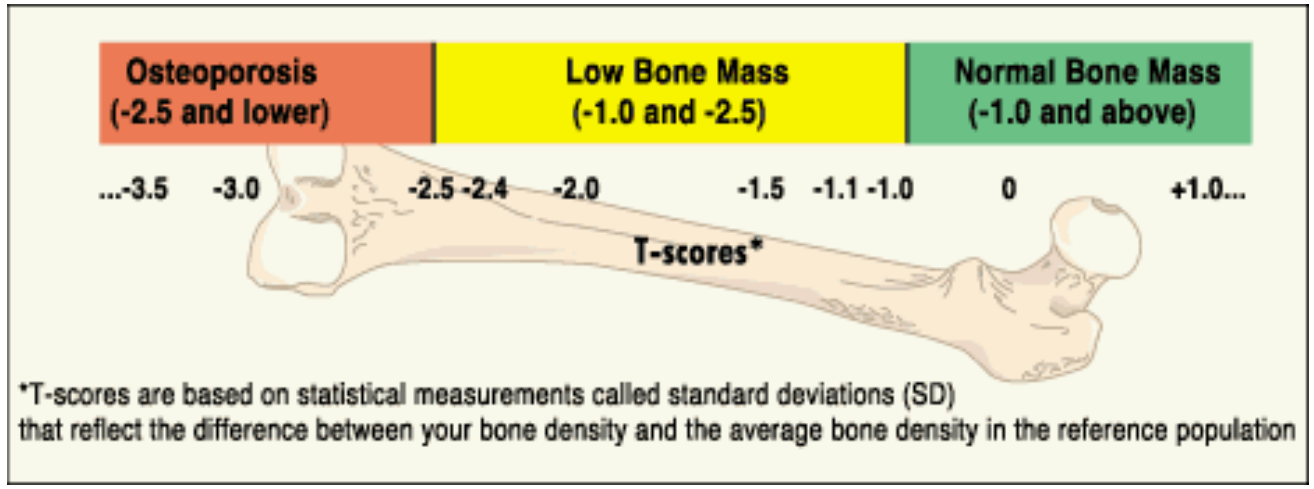
DEXA T-Scores



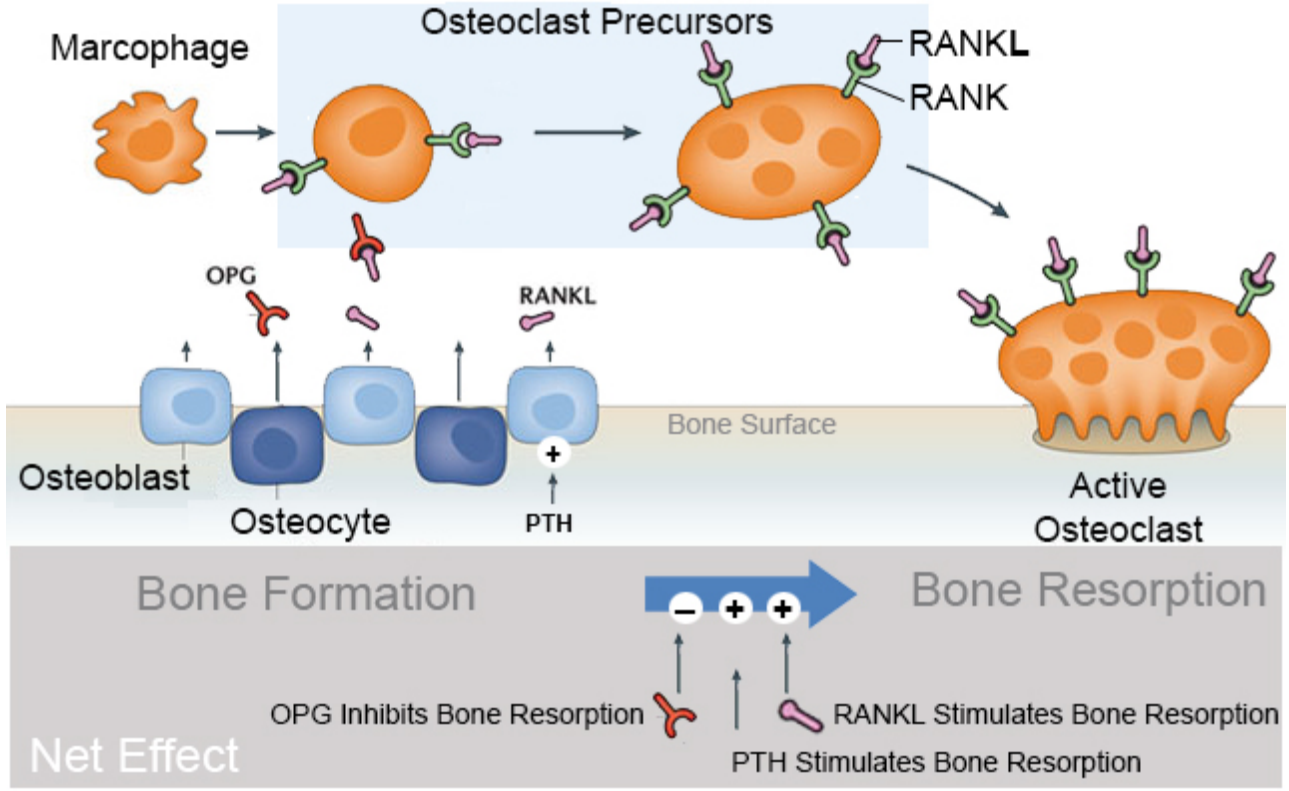
Osteopenia: -1 to -2.5

Osteoporosis: ≤ -2.5





Bone signaling



Treatment

lifestyle modification

pharmacologic treatment

calcium and Vitamin D

Bisphosphonates

* Raloxifene → CA. breast tx

* Denosumab

monoclonal Ig

تبتعطم الـ rough border ←

تبع الـ osteoclast

↓ bone resorption

it mimics estrogen (anabolic role)

* Osteoporosis (quantitative bone loss)
↓ ECM
↓ organic
↓ inorganic

Osteomalacia (qualitative bone loss)

↳ only ↓ in inorganic matrix
↑ organic matrix (osteoid)

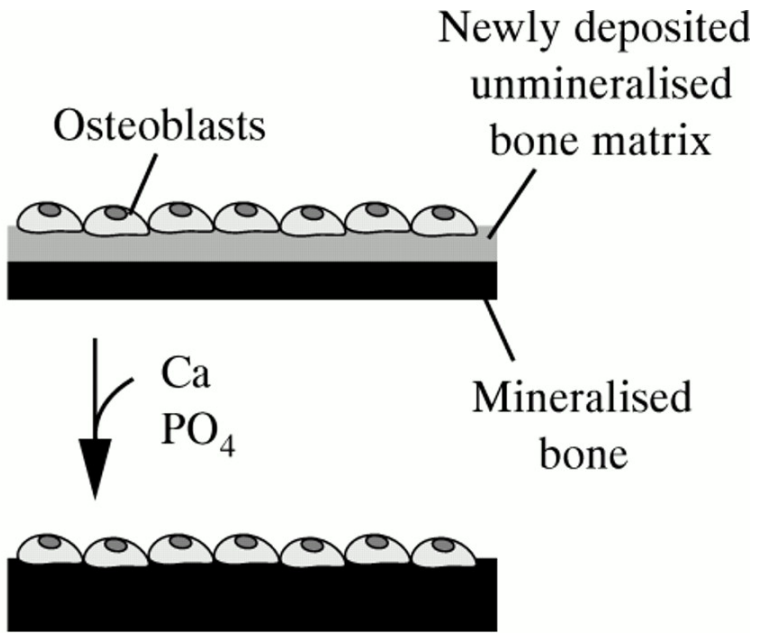
A metabolic bone disease where defective mineralization results in a large amount or unmineralized osteoid

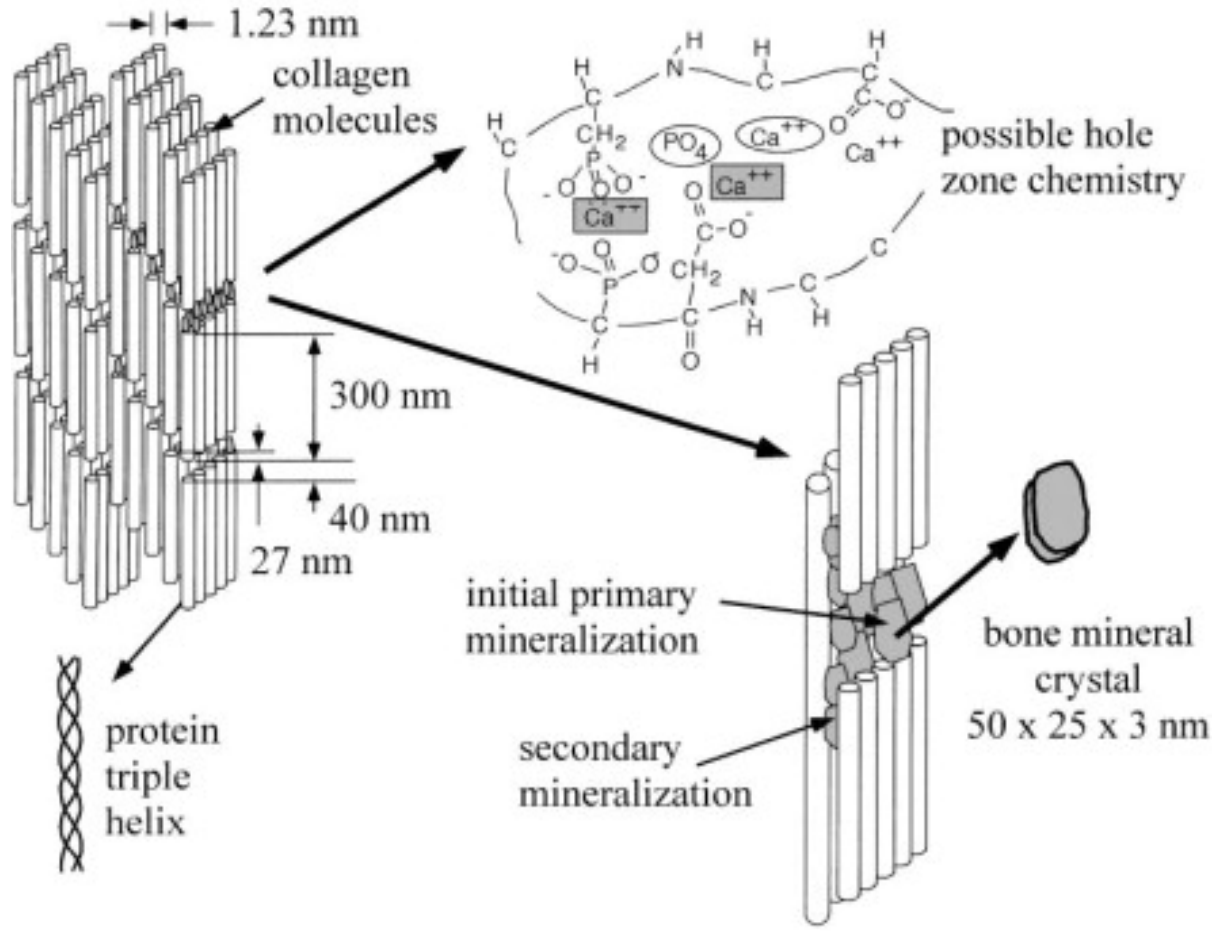
Osteomalacia = Rickets

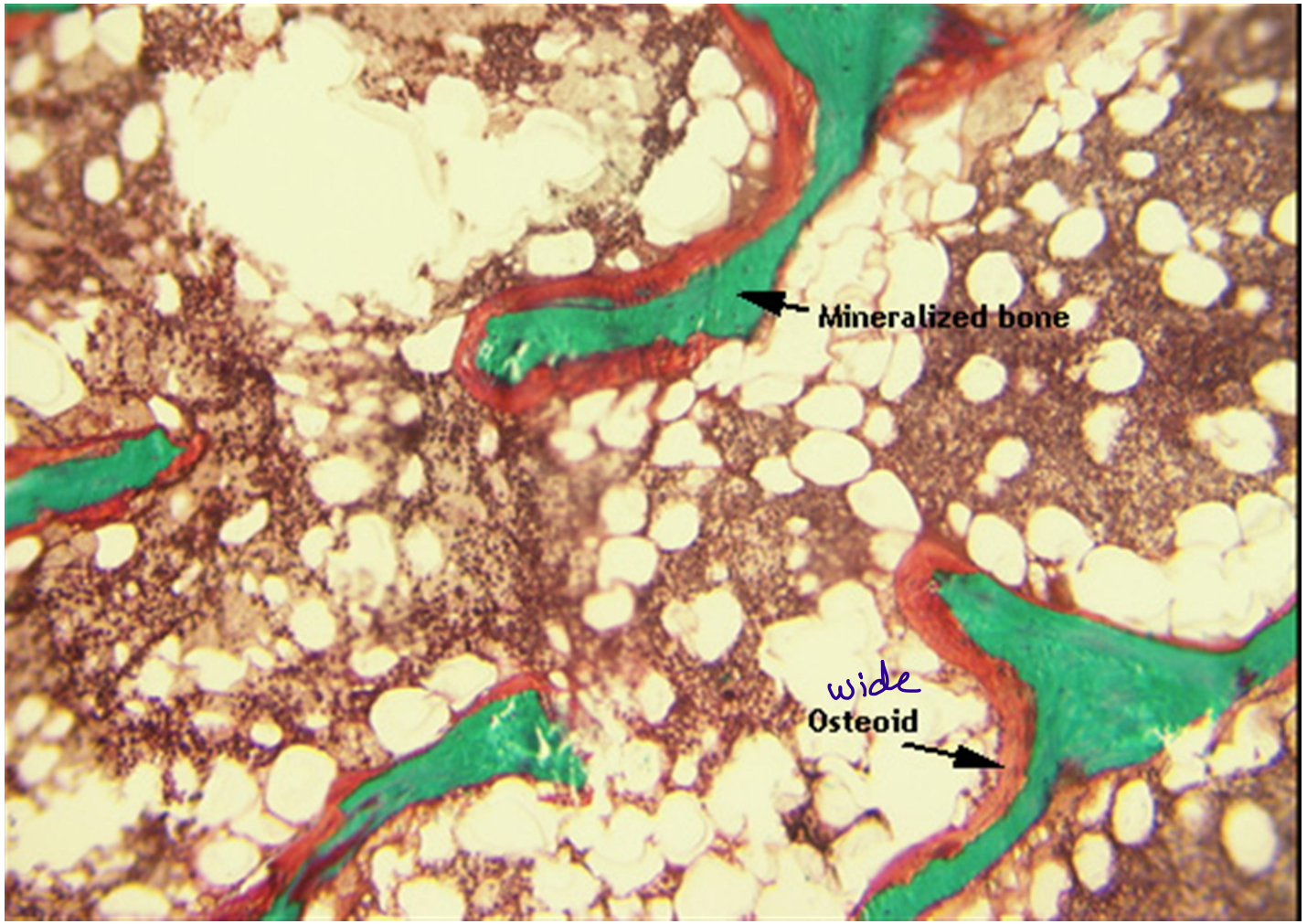
rickets is found in children (open physis)	osteomalacia is found in adults (closed physis)

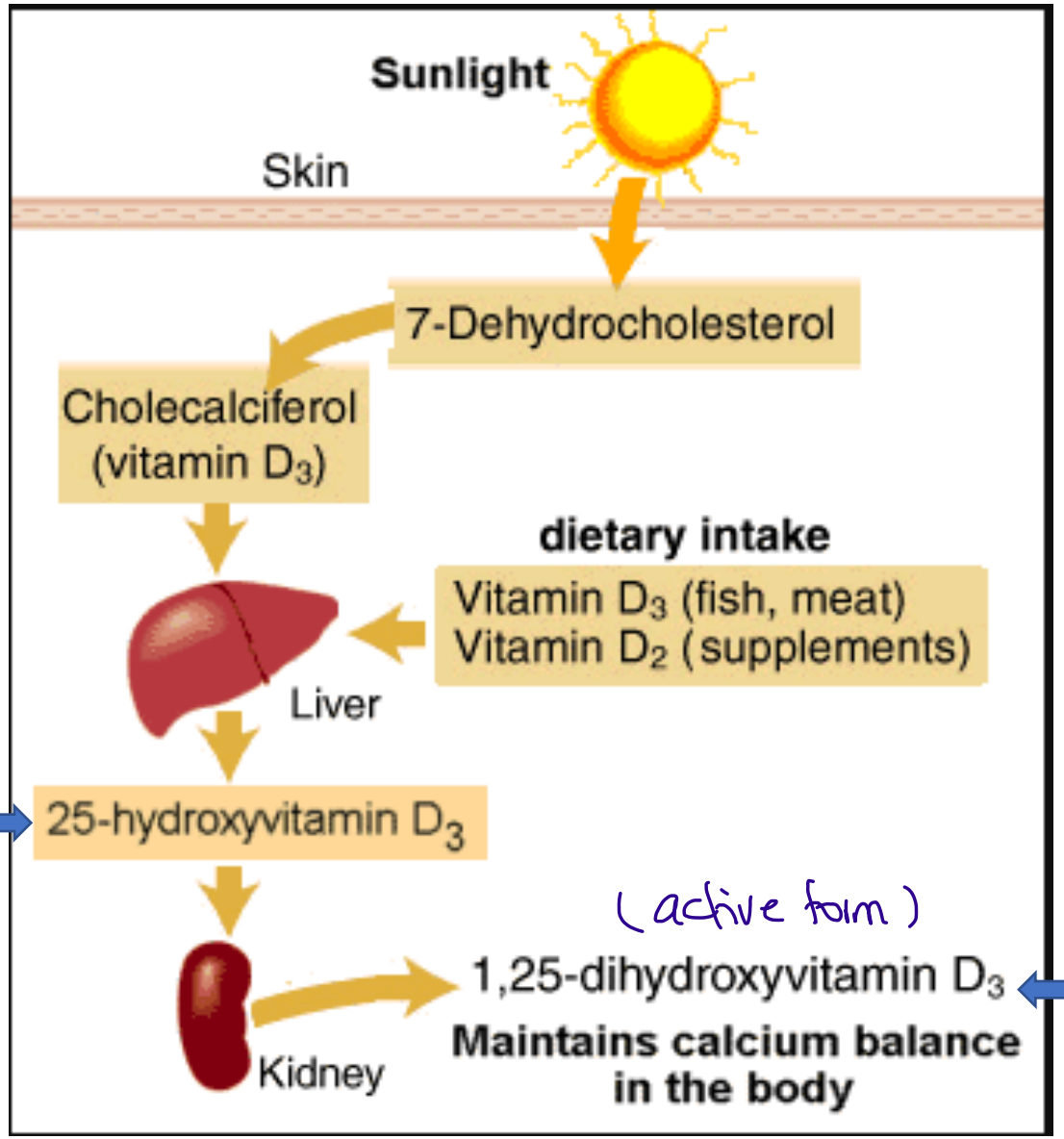
Step 1:
Deposition of
osteoid

Step 2:
Mineralisation



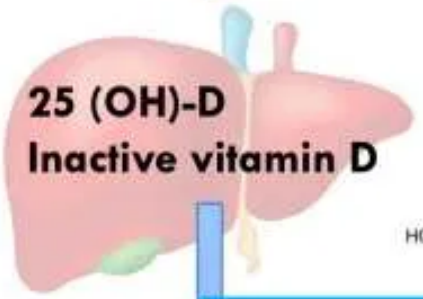



Mineralized bone
wide
Osteoid

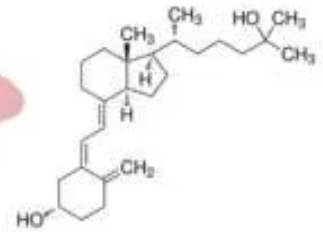

Sunlight
Skin
7-Dehydrocholesterol
Cholecalciferol
(vitamin D3)
dietary intake
Vitamin D3 (fish, meat)
Vitamin D2 (supplements)
Liver
25-hydroxyvitamin D3
(active form)
1,25-dihydroxyvitamin D3
Kidney
Maintains calcium balance
in the body

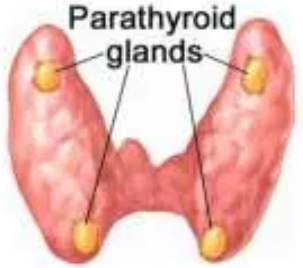
Overview of Ca & Phos metabolism

Diet, sun exposure



25 (OH)-D
Inactive vitamin D

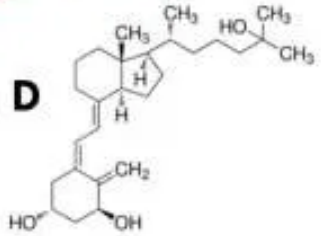




Regulation of 1-a hydroxylation in kidney
- ⇑ **Hypophosphatemia,** ⇓ **Hyperphosphatemia**
- ⇑ PTH
- ⇓ 1,25 (OH)-D
- ⇓ Renal failure

Regulation of parathyroid hormone synthesis
- ⇑⇑ by **Hypocalcemia**
- ⇓ 1,25 (OH)-D
- (magnesium required)

1,25 (OH)-D
Activated vitamin D

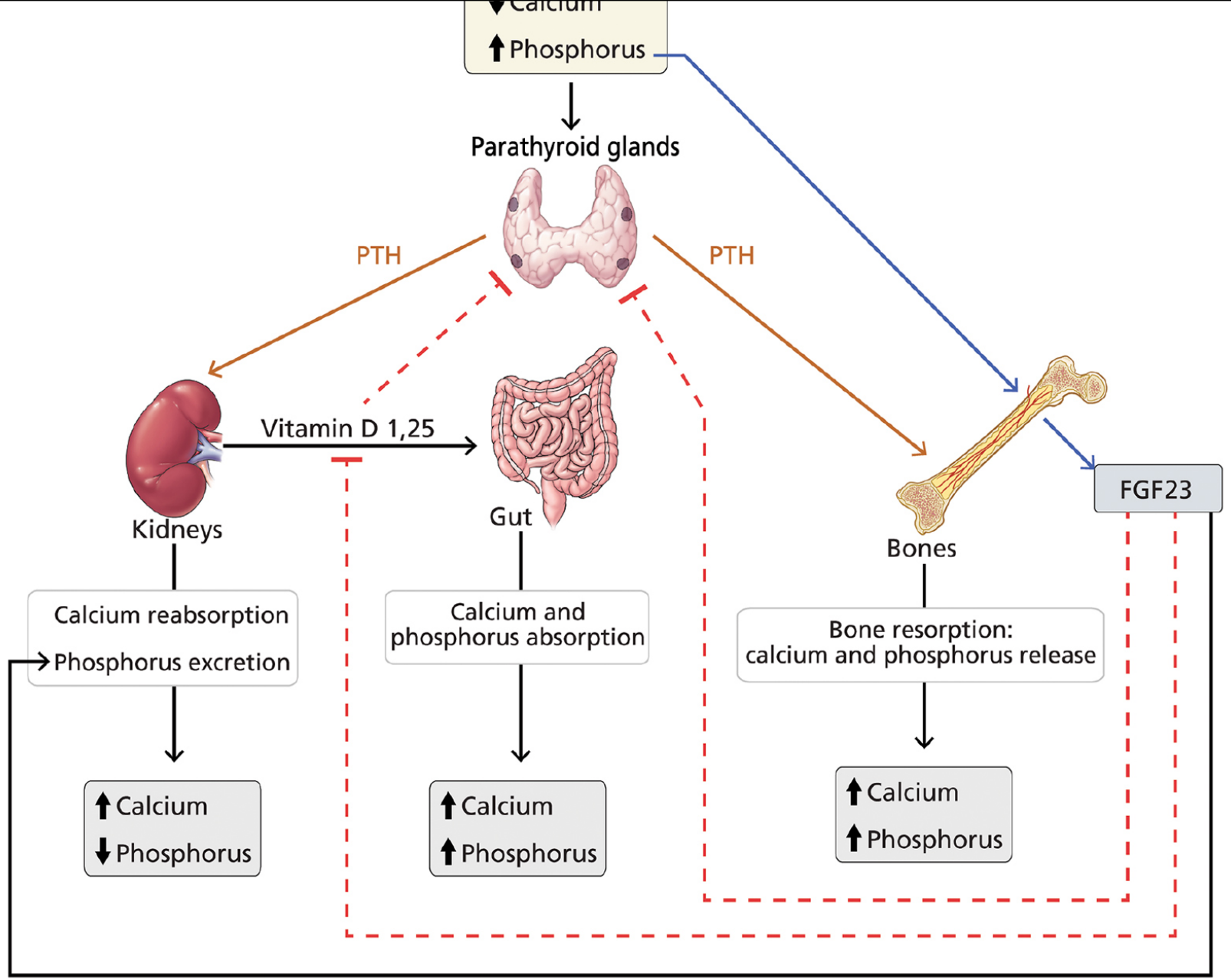


Parathyroid hormone (PTH)

⇑ **Renal calcium absorption**
⇑ **Gut absorption of Ca & Phos**
Overall effect: ⇑ Ca, ⇑ Phos

⇑ **Renal calcium absorption**
⇑ **Renal phosphate excretion**
⇑ **Bone reabsorption**
Overall effect: ⇑ Ca, ⇓ Phos

The Internet Book of Critical Care, by @PulmCrit


Calcium
Phosphorus
Parathyroid glands
PTH
PTH
Vitamin D 1,25
Kidneys
Gut
Bones
FGF23
Calcium reabsorption
Phosphorus excretion
Calcium and phosphorus absorption
Bone resorption: calcium and phosphorus release
Calcium
Phosphorus
Calcium
Phosphorus
Calcium
Phosphorus

↓ Ca or ↓ PO4

↓ mineralization of bone

(inorganic matrix)
(hydroxyapatite)

risk factors

Vitamin-D deficient diets

malabsorption e.g. celiac disease

renal osteodystrophy

hypophosphatemia

chronic alcoholism

tumors (tumor-induced osteomalacia)

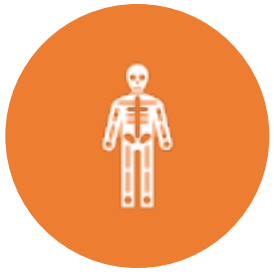
phosphatonin

↳ excretes phosphate

Drugs

- Phenytoin
- Glucocorticoids
- Ifosfamide
- etidronate

Symptoms



GENERALIZED BONE AND MUSCLE PAIN

(stress)

FRACTURES OF LONG BONES, RIBS AND VERTEBRAE

PROXIMAL MUSCLE WEAKNESS WEAKNESS

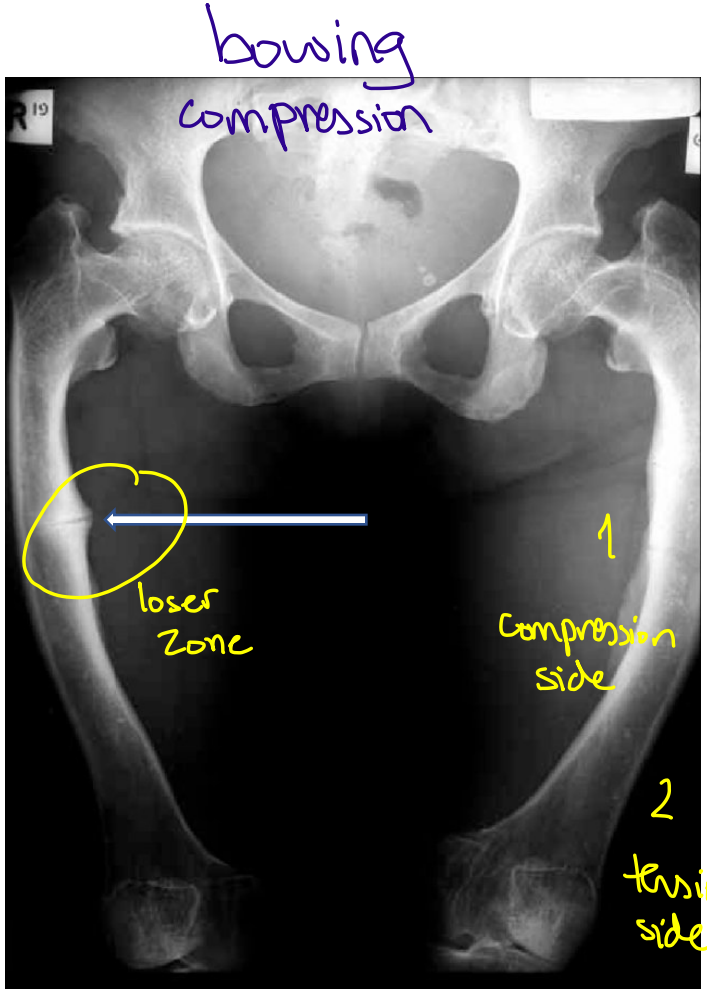
FATIGUE

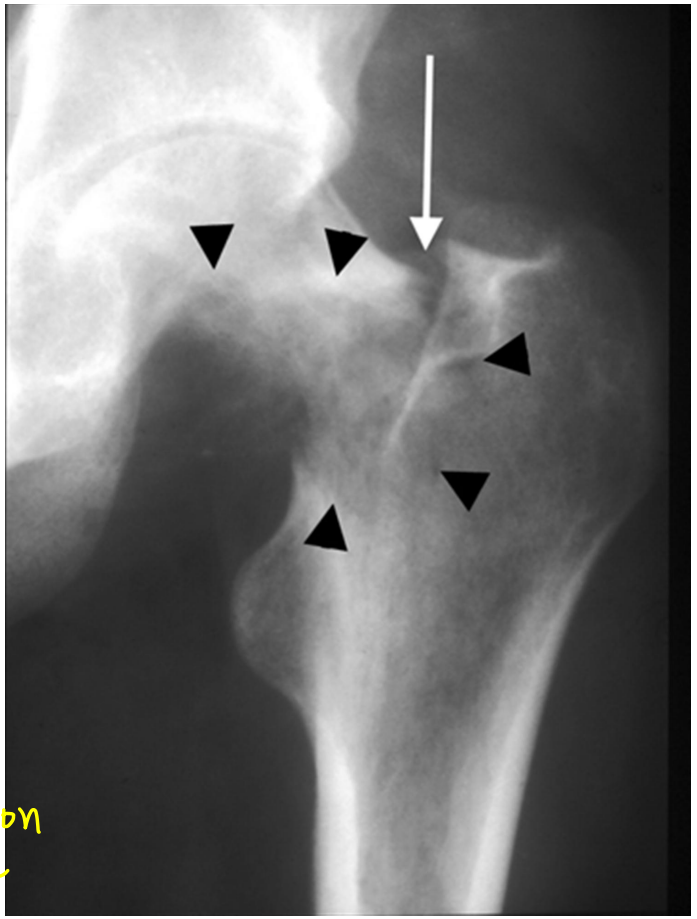
Physical exam

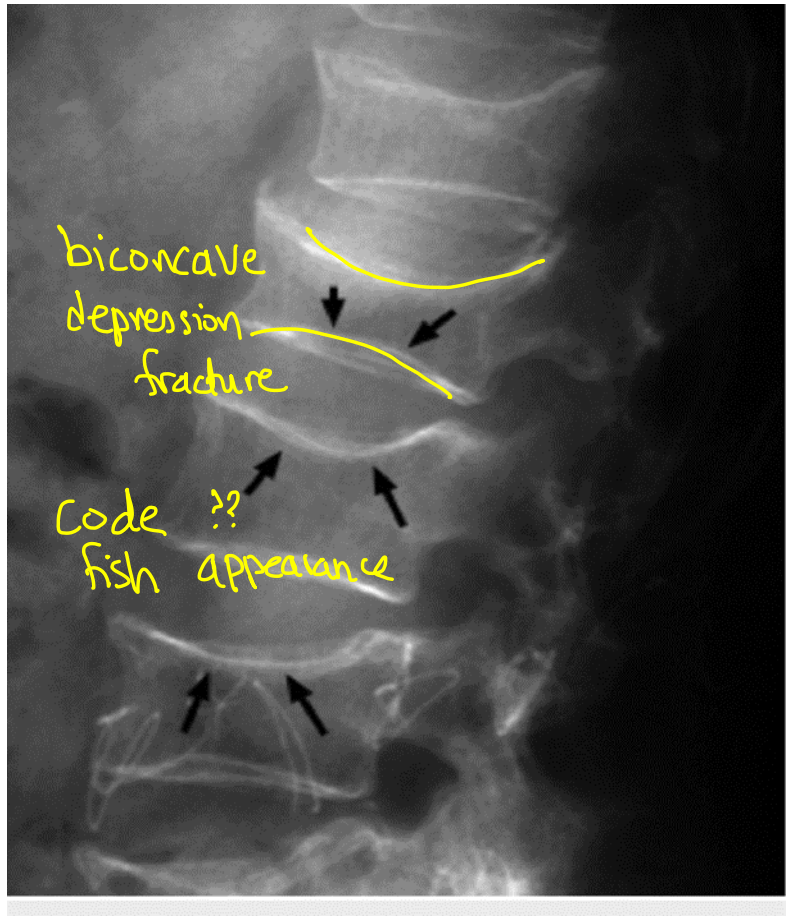
waddling gait

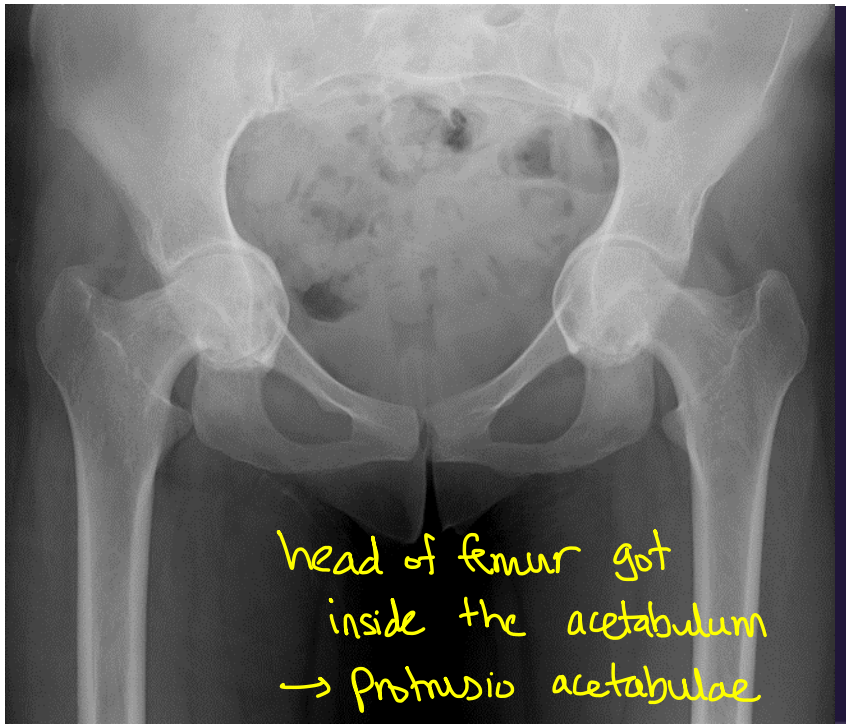
difficulty rising from chair and climbing stairs

Imaging

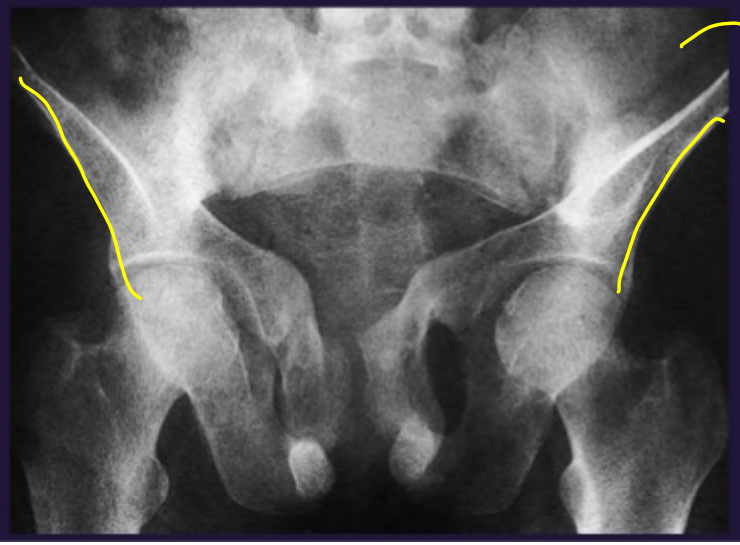

bowing
compression
loser
zone
1
compression
side
2
tension
side




biconcave
depression
fracture
Code ??
fish appearance



Trefoil Pelvis



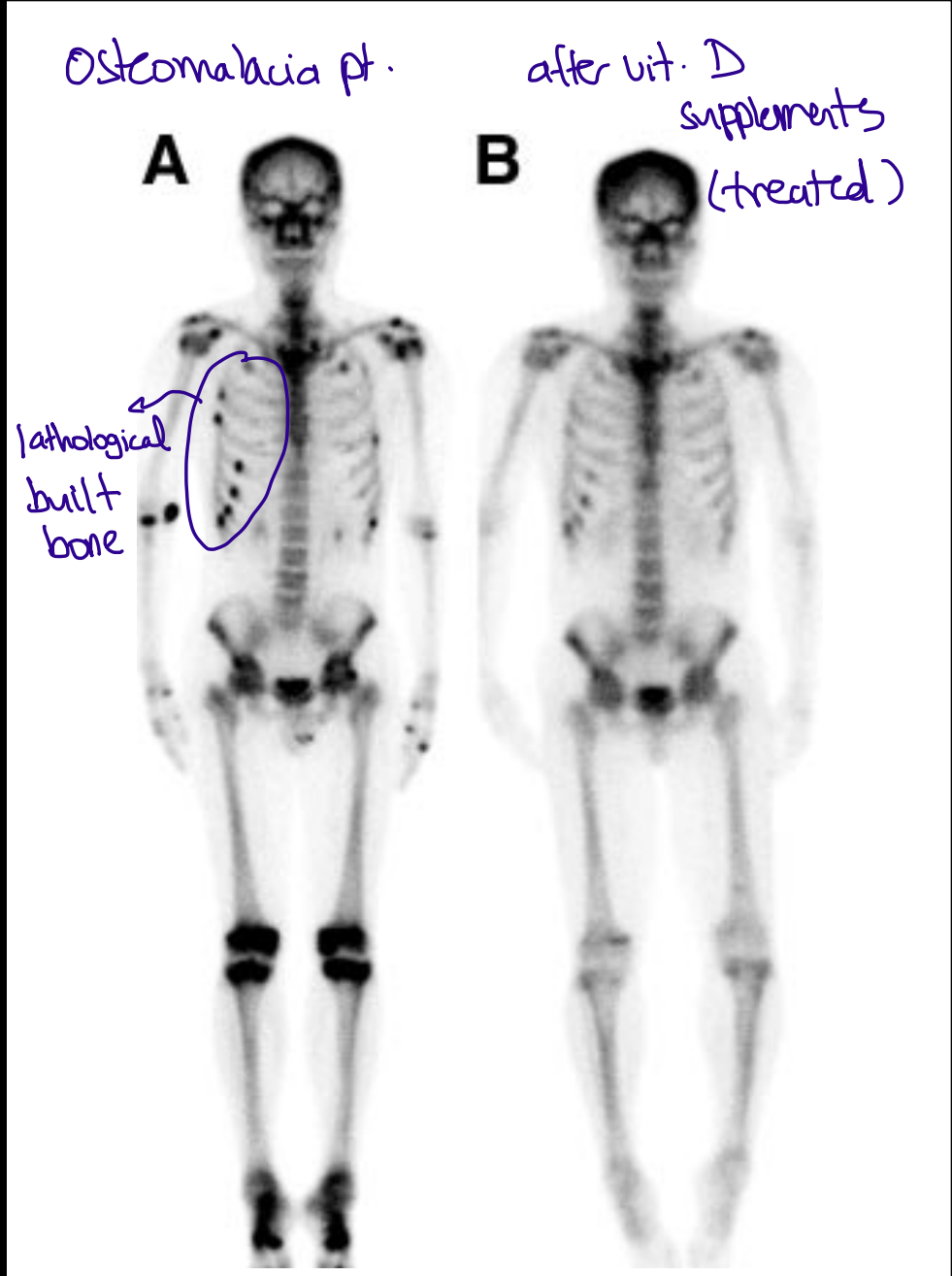
iliac wing
ميل أكثر من
الثاني

Bone scan

- osteomalacia is an active process
  - ↳ osteoid is being formed but NOT mineralized.
  - as a compensation → more osteoid formation (active process)

- hot spots → symmetrical
  - if unilateral → Pathological

- Symmetrical bone density.
  - (hot nodules)



Treatment

large doses of oral vitamin D (1000IU/day), treat underlying cause

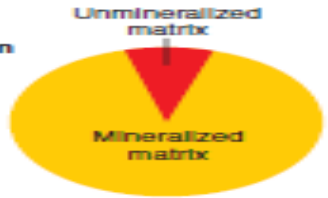
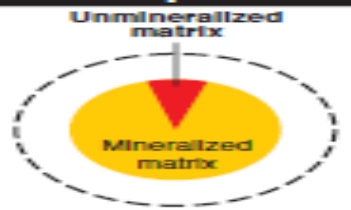
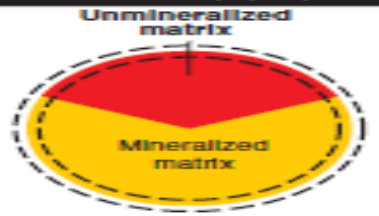
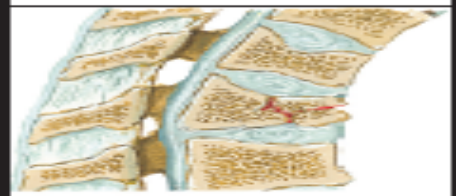
↑ Ca
↑ PO4

Most Pts

specific subgroups of patients

on long-term anticonvulsant therapy	with hepatobiliary disease	with renal disease
• supplement with 400-800IU/day of vitamin D	• supplement with 25(OH)-vit D	• supplement with 1,25(OH)2 vit D

Comparison of Osteoporosis and Osteomalacia

	Osteoporosis	Osteomalacia
Definition	 Normal	 Bone mass decreased, mineralization normal	 Bone mass variable, mineralization decreased
Age at onset	Generally in old age, after menopause	Any age
Etiology	Endocrine abnormality, age, idiopathic cause, inactivity, disuse, alcoholism, calcium deficiency	Vitamin D deficiency, abnormality of vitamin D pathway, hypophosphatemic syndromes, renal tubular acidosis, hypophosphatasia
Symptoms	Pain referable to fracture site	Generalized bone pain
Signs	Tenderness at fracture site	Tenderness at fracture site and generalized tenderness
Radiographic features	 Axial predominance	Often symmetric; pseudofractures or completed fractures Appendicular predominance
Laboratory findings		
Serum Ca^{2+}	Normal	Low or normal (high in hypophosphatasia)
Serum P_i	Normal	Low or normal
$Ca^{2+} \times P_i$	>30	>30 if albumin normal (high in renal osteodystrophy)
Alkaline phosphatase	Normal	Elevated, except in hypophosphatasia
Urinary Ca^{2+}	High or normal	Normal or low (high in hypophosphatasia)
Bone biopsy	Tetracycline labels normal	Tetracycline labels abnormal

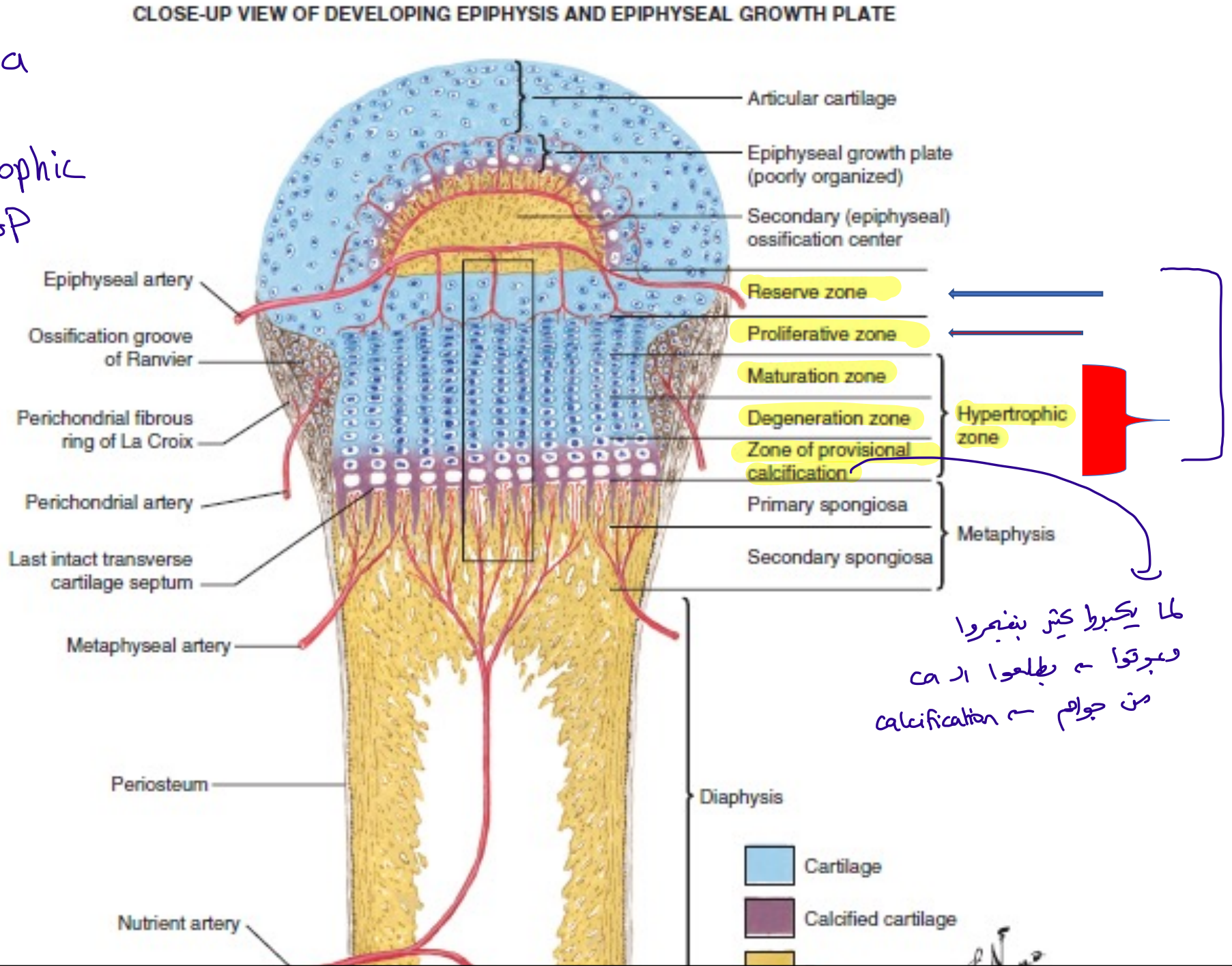
indicates bone activity (organic phosphate)

	Serum Ca	*Serum P*	*Alk phos*	*PTH*	*25-(OH)vit D*	*1,25-(OH)vit D*	*Urinary Ca*
Osteomalacia	low	low	high	high	low	low	low
Osteoporosis (NL labs)	normal	normal	variable	normal	normal	normal	normal
Tumor induced	low	very low	low	low	low	low	low

due to phosphatonin

the tumor disrupted the normal bone (↓ bony activity)

* osteomalacia affects the hypertrophic zone of GP


CLOSE-UP VIEW OF DEVELOPING EPIPHYSIS AND EPIPHYSEAL GROWTH PLATE

growth Plate

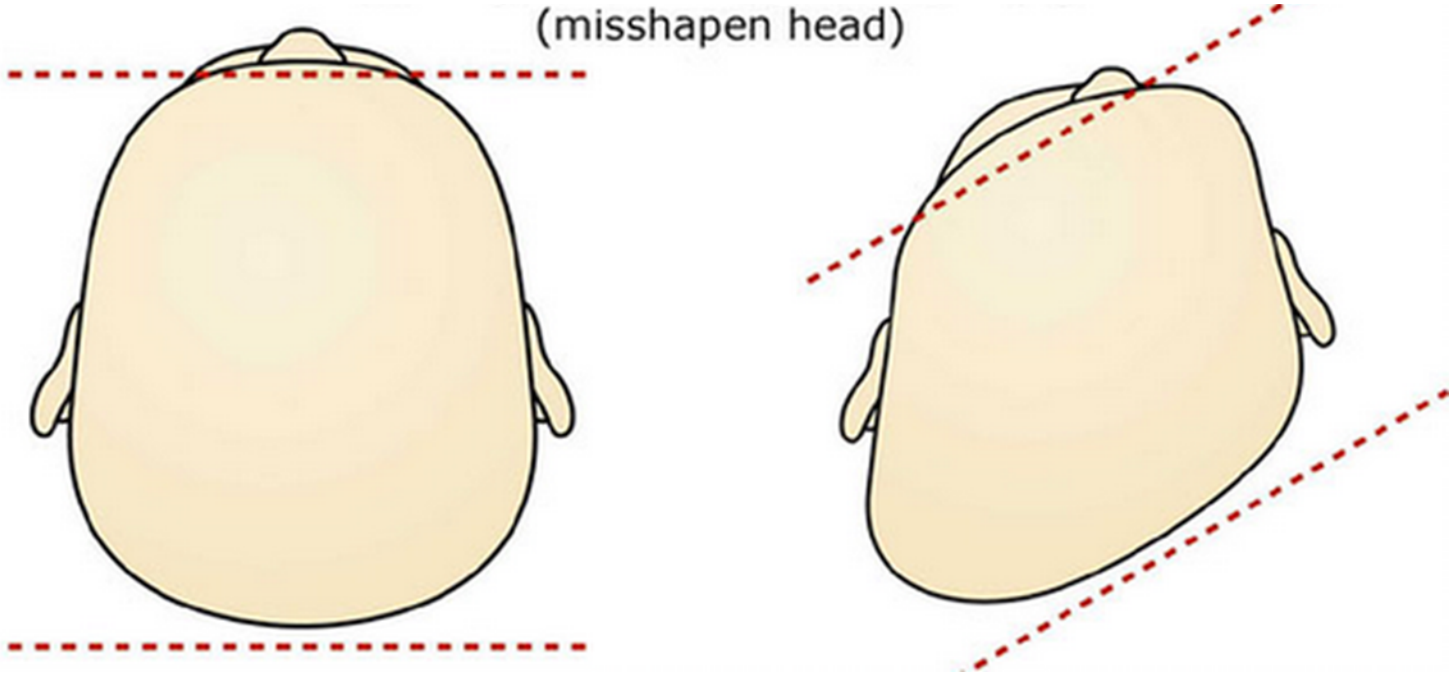
لما يكبروا كثير بنفجروا
وبموتوا ← بطلعوا ال ca
من جوام ← calcification

No mineralization

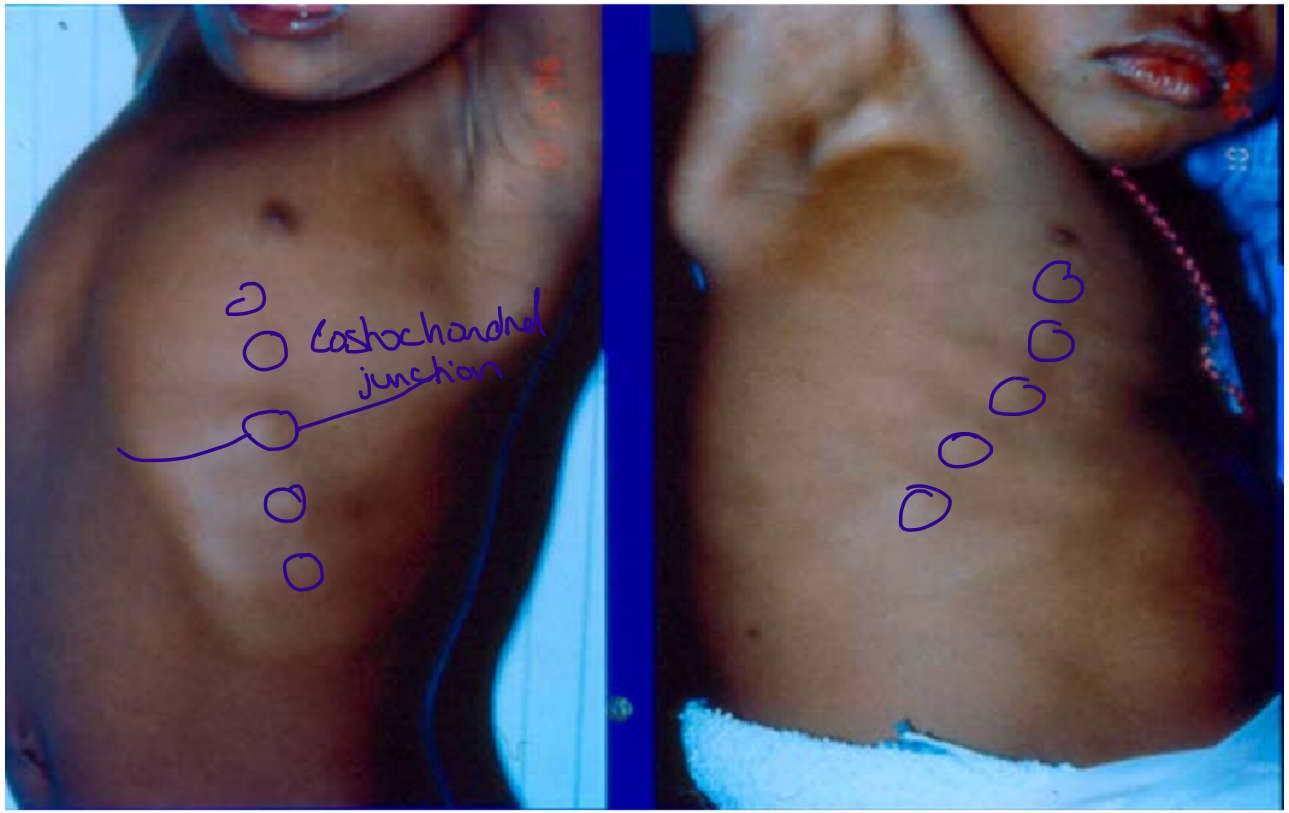
ما كبر محل
cupping

bowing

flat skull

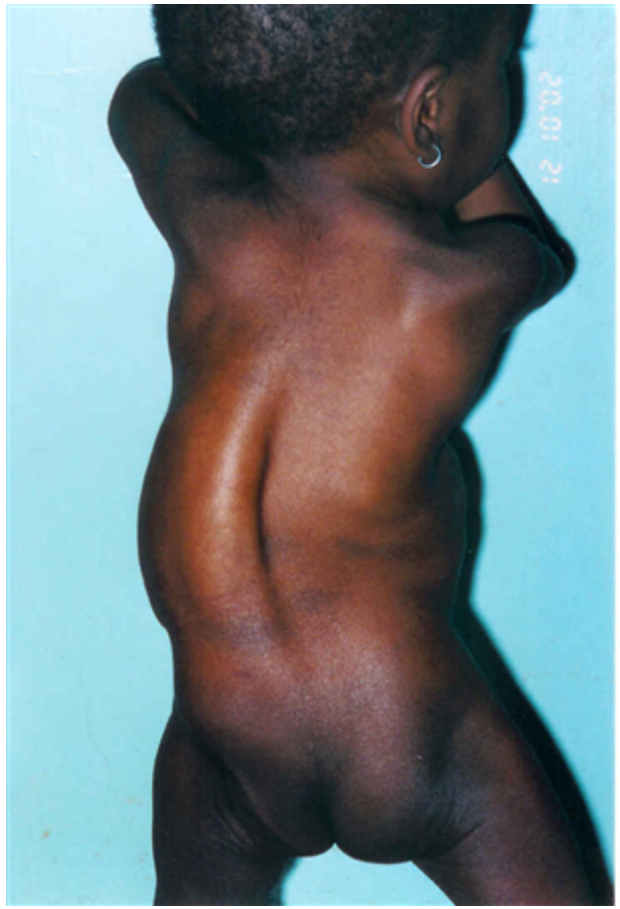


Rosary bead sign (Rachitic beads)



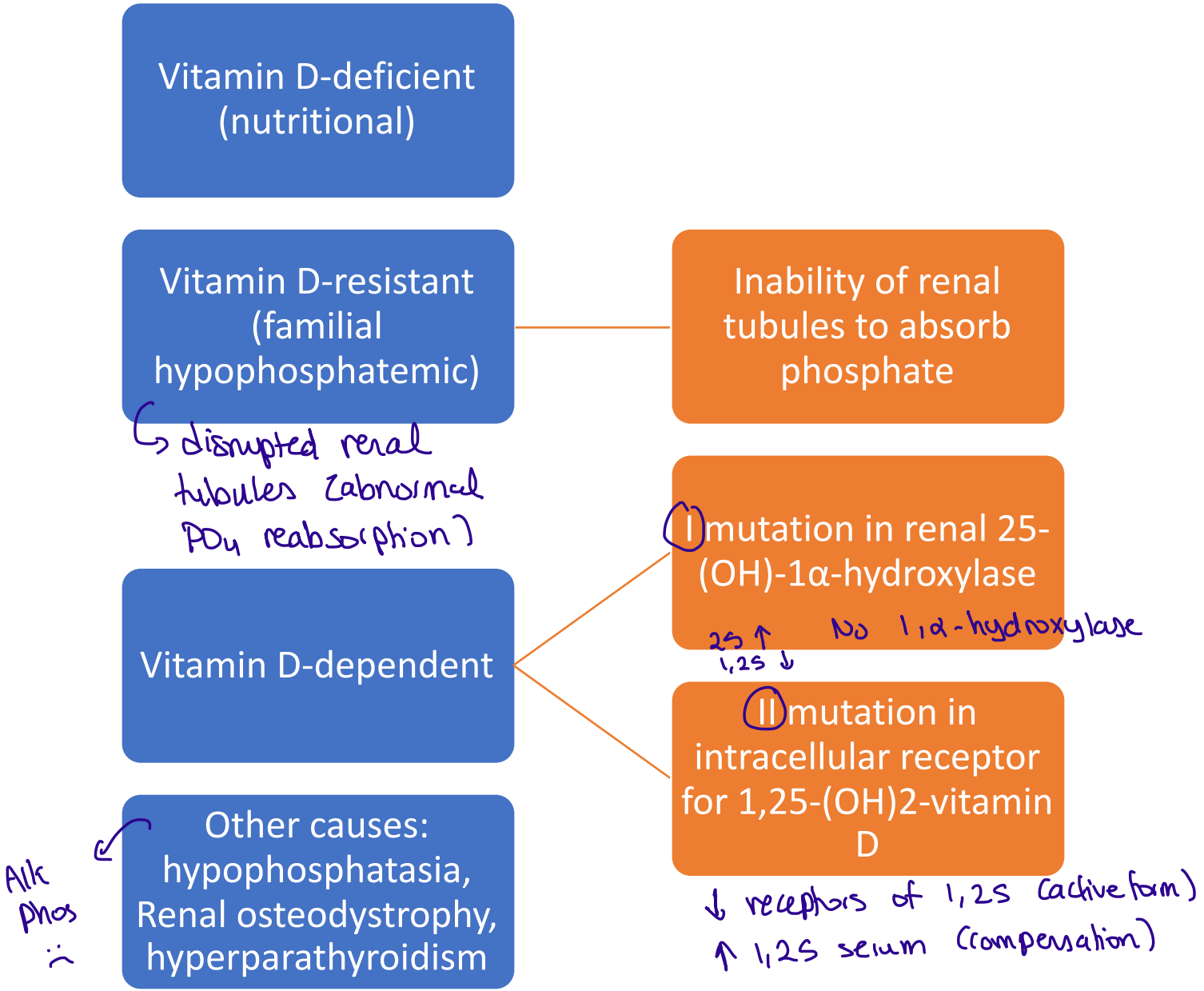
Kyphosis

* cat back



Classification

Rickets



Condition	Genetics	Ca	Phos.	Alk Phos	PTH	Vit D	1,25 (OH)VitD
Vitamin D Resistant Rickets (Hypophosphatemic)	X linked dominant	–	↓	↑	–	–	
Vitamin D Deficiency Rickets (Nutritional)	Nutritional	–↓	↓	↑	↑	↓	
Type I Vitamin D Dependent	Auto. Recessive	↓	↓	↑	↑		↓↓
Type II Vitamin D Dependent	Auto. Recessive	↓	↓	↑			↑↑
Hypophosphatasia	Auto. Recessive	↑	↑	↓↓	–	–	
Renal Osteodystrophy	Renal Disease	↓	↑	↑	↑		
Hyperparathyroidism	90% adenoma	↑	↓	↑	↑		

Treatment

- Calcitriol → active vit. D_3
- phosphate replacement
- Vitamin D
- corrective surgery (severe bowing)