METABOLIC BONE DISEASES

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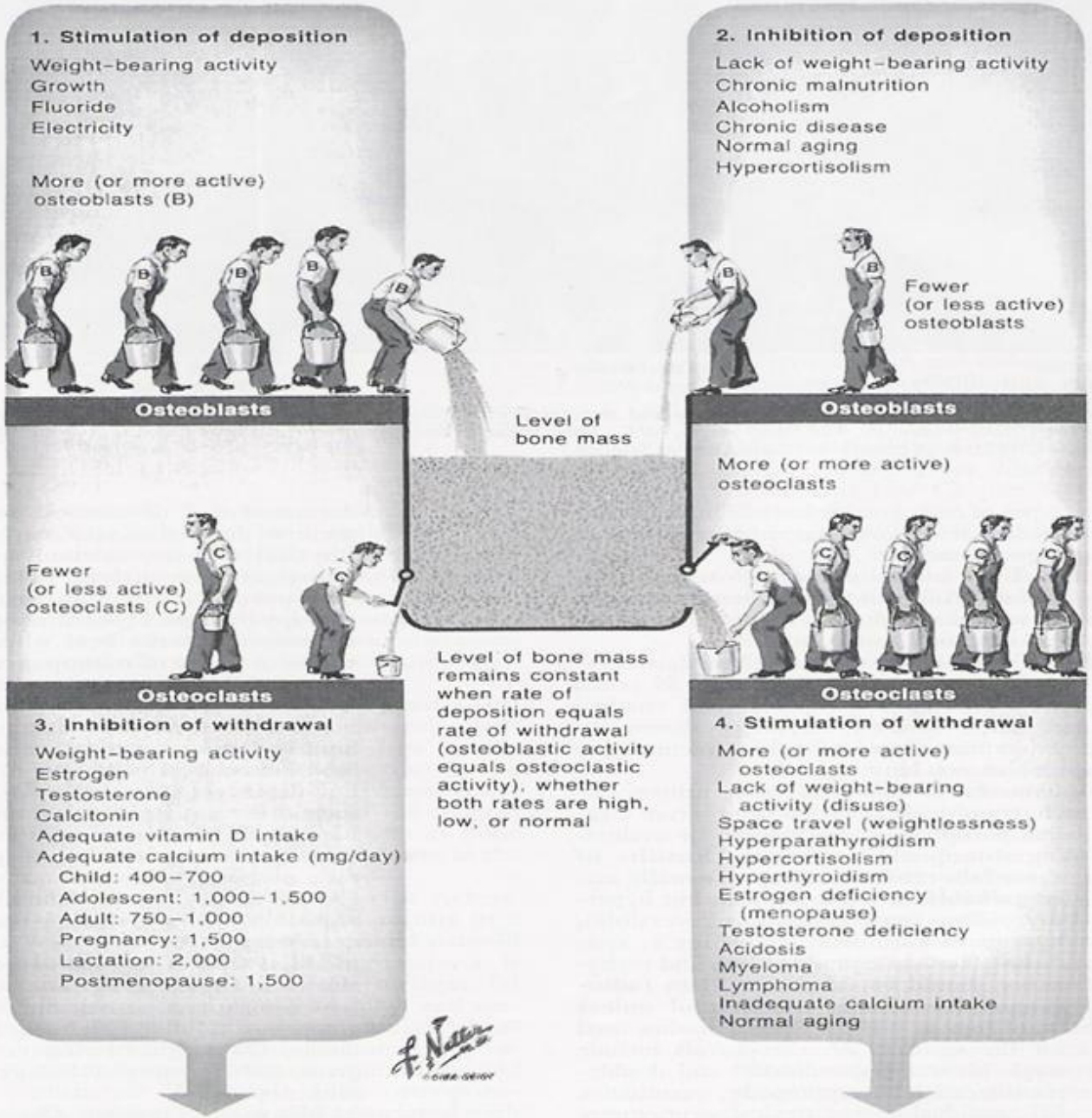
PHYSIOLOGY

- Calcium
- Phosphate
- PTH
- Vitamin D
- Calcitonin

Four Mechanisms of Bone Mass Regulation



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Calcium

- > 99% in bone
- Muscle and nerve function
- Clotting mechanisms
- Free plasma Ca = Bound plasma Ca

Calcium Requirement

- 600 mg/day in children
- 1300 mg/day in adolescents and young adults
- 750 mg/day in adults
- 1500 mg/day in pregnant women
- 2000 mg/day in lactating women
- 1500 mg/day in postmenopausal women and patients with fractures

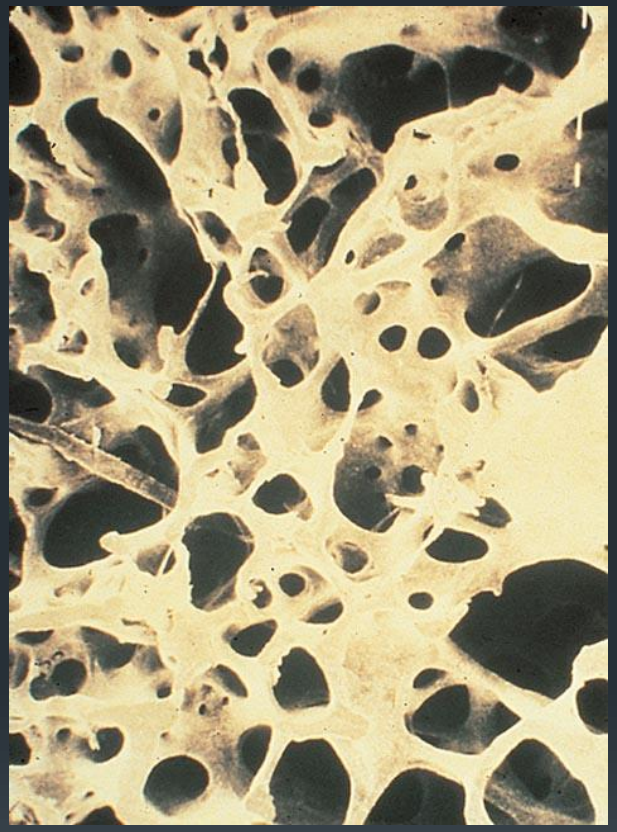
PHOSPHATE

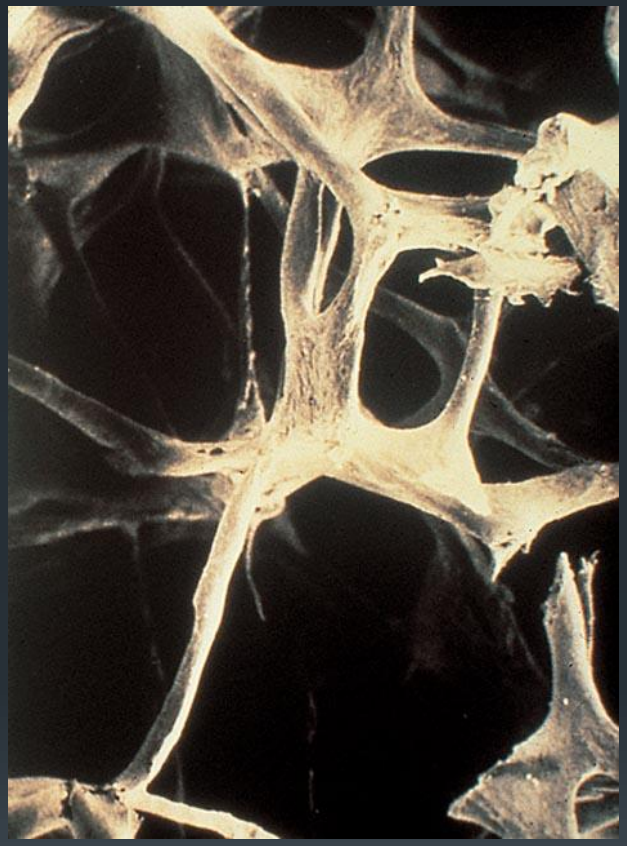
- Key component of bone mineral
- Enzyme systems and molecular interactions
- 85% in bone
- Plasma Phosphate is mostly unbound
- 1000-1500 mg/day

Diseases of bone

- Increased density
- Decreased density

Osteoporosis





Reduction in bone mass leading to increase risk of fracture

Ratio of mineralised bone: matrix is normal

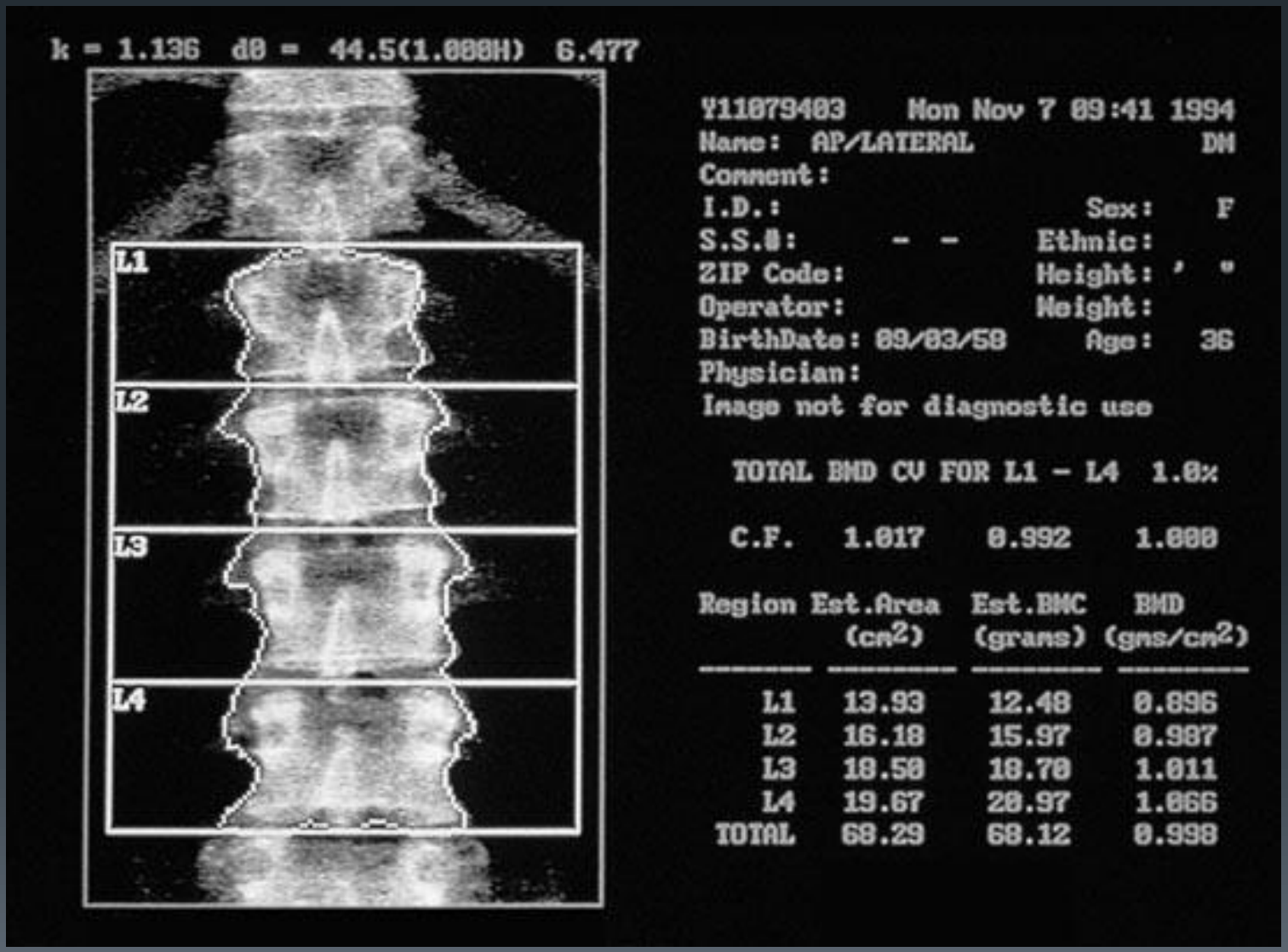
Imbalance of bone remodelling

Osteoporosis

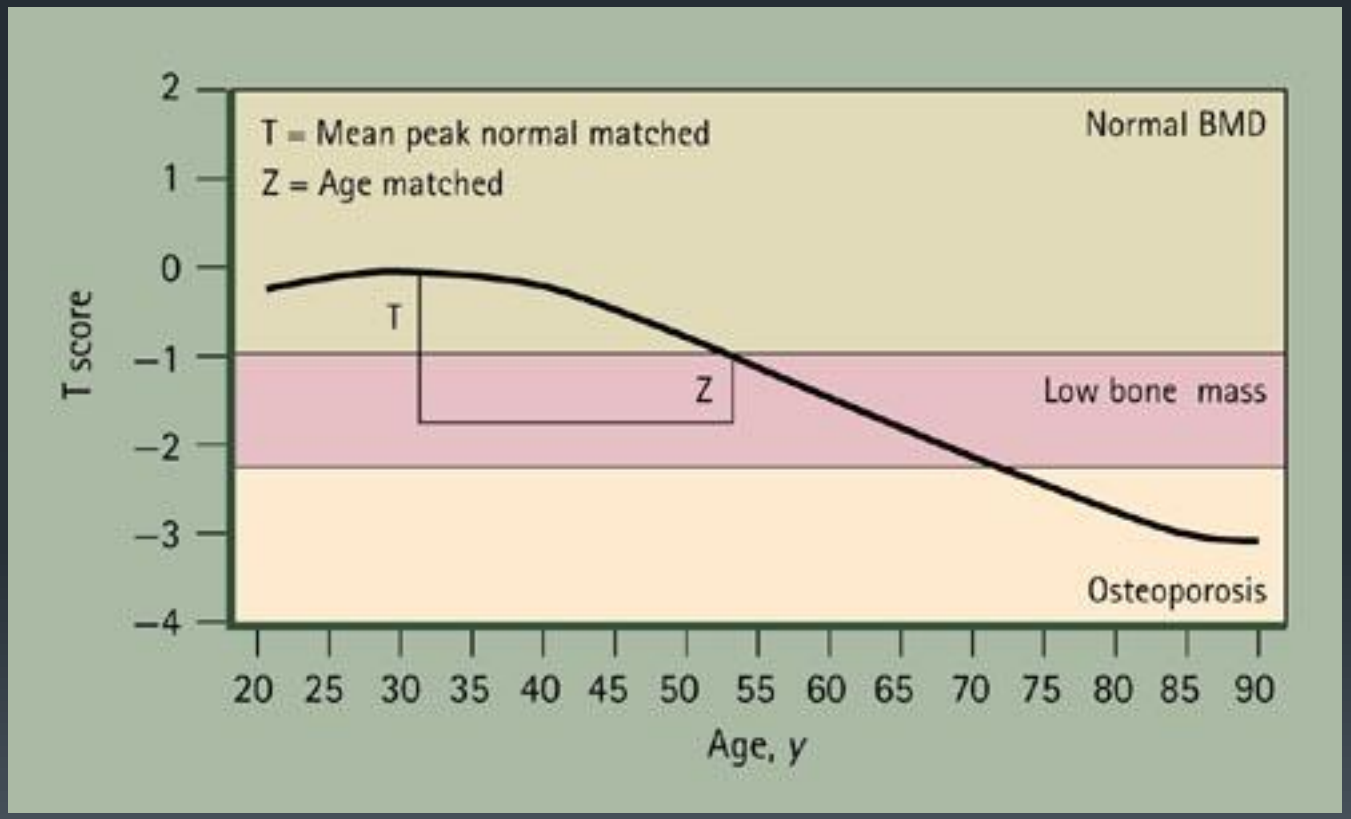
- Decrease in bone mass
- Women / smokers / EtOH
- Fractures: Hip, distal radius and vertebrae
- DEXA
- Treatment: Bisphosphonates
- Estrogen-progesterone therapy should be started within 6 years of menopause

Osteoporosis

DEXA


k = 1.136 d0 = 44.5(1.000H) 6.477
L1
L2
L3
L4
Y11079403 Mon Nov 7 09:41 1994
Name: AP/LATERAL DM
Comment:
I.D.: Sex: F
S.S.#: - - Ethnic:
ZIP Code: Height: ' "
Operator: Weight:
BirthDate: 09/03/58 Age: 36
Physician:
Image not for diagnostic use
TOTAL BMD CV FOR L1 - L4 1.0%
C.F. 1.017 0.992 1.000
Region Est.Area (cm2) Est.BMC (grams) BMD (gms/cm2)
L1 13.93 12.48 0.896
L2 16.18 15.97 0.987
L3 18.50 18.70 1.011
L4 19.67 20.97 1.066
TOTAL 68.29 68.12 0.998

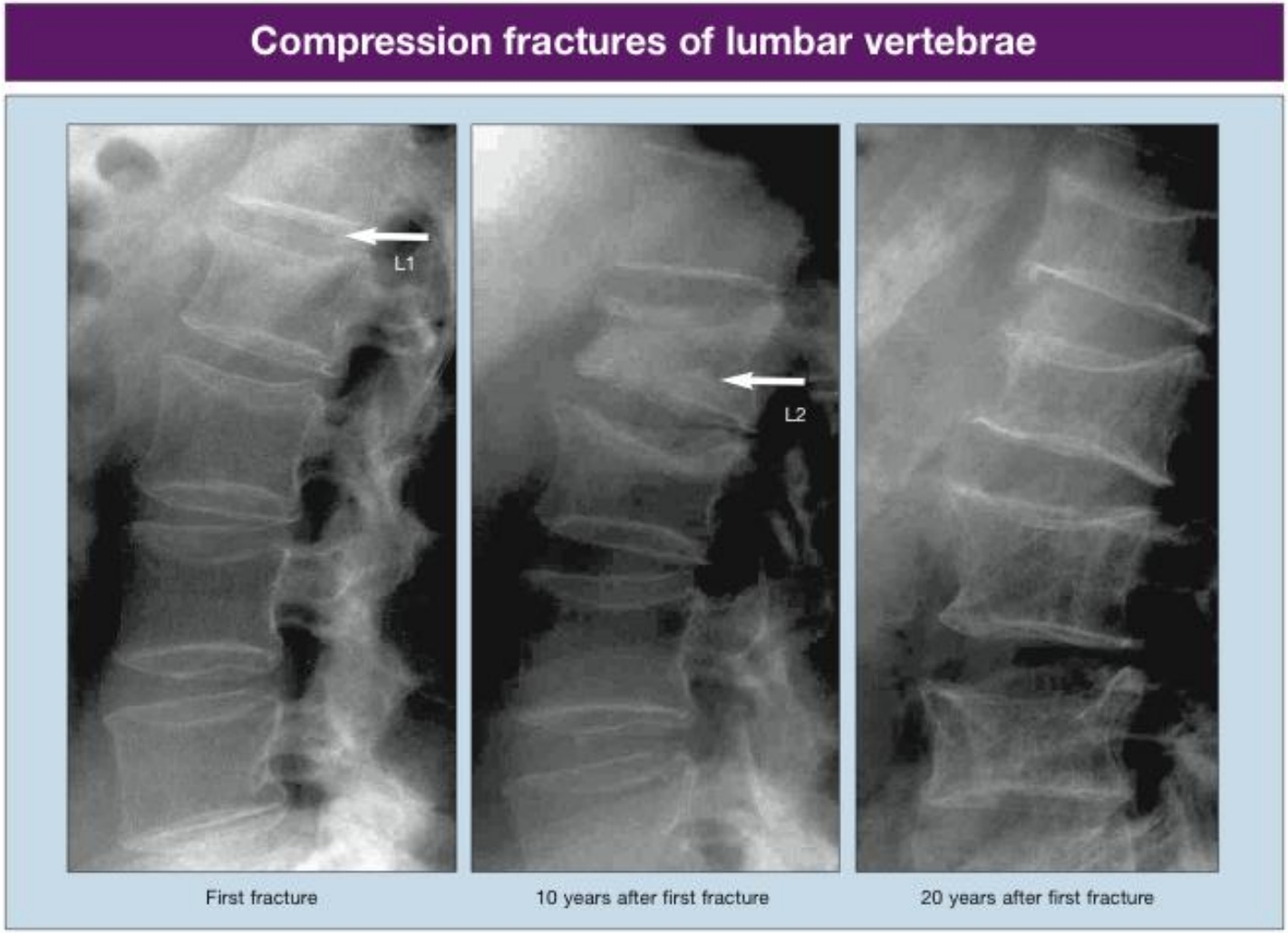
T scores


T = Mean peak normal matched
Z = Age matched
Normal BMD
Low bone mass
Osteoporosis
T
Z
T score
2
1
0
−1
−2
−3
−4
20 25 30 35 40 45 50 55 60 65 70 75 80 85 90
Age, y

World Health Organization criteria for the diagnosis of osteoporosis

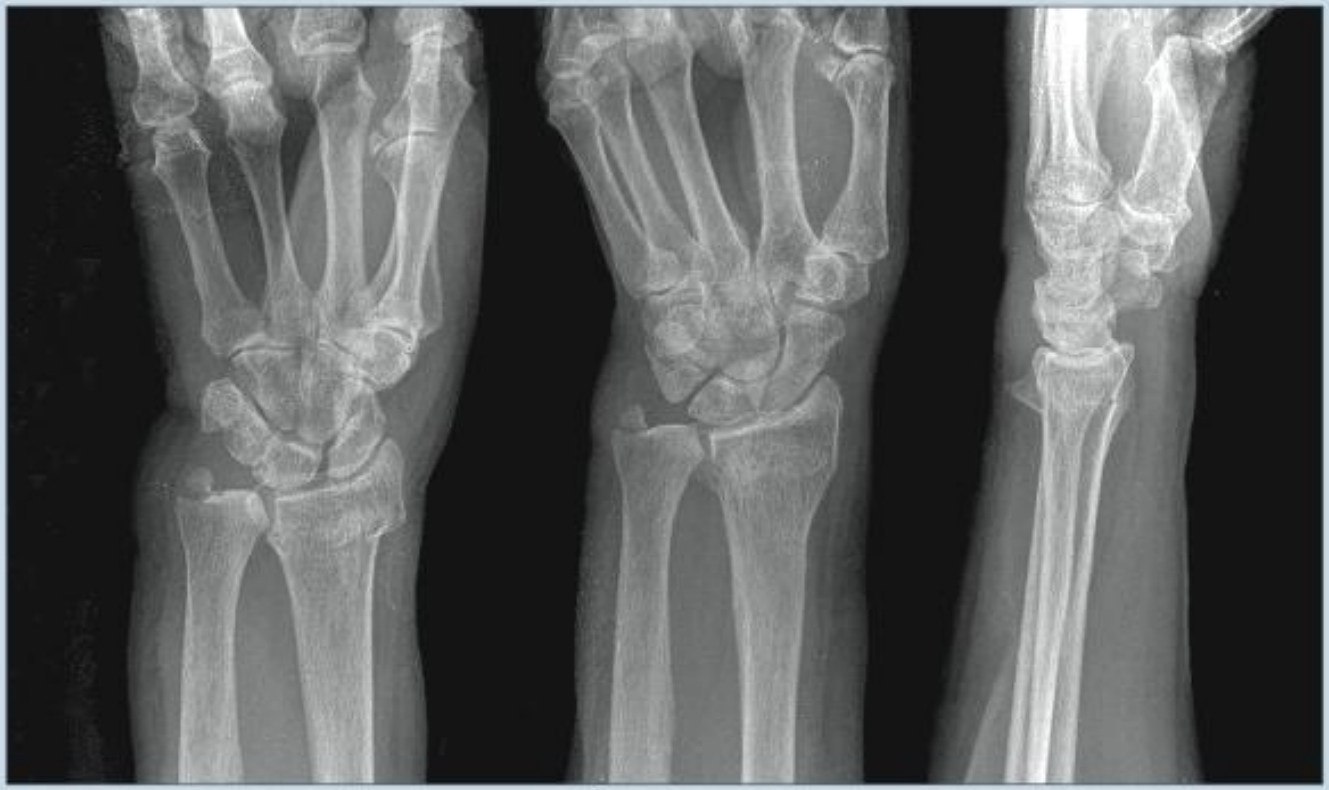
	T-score
Normal	⩾–1.0
Osteopenia	–1 to –2.5
Osteoporosis	⩽–2.5
'Established' osteoporosis	⩽–2.5 + presence of one or more fractures

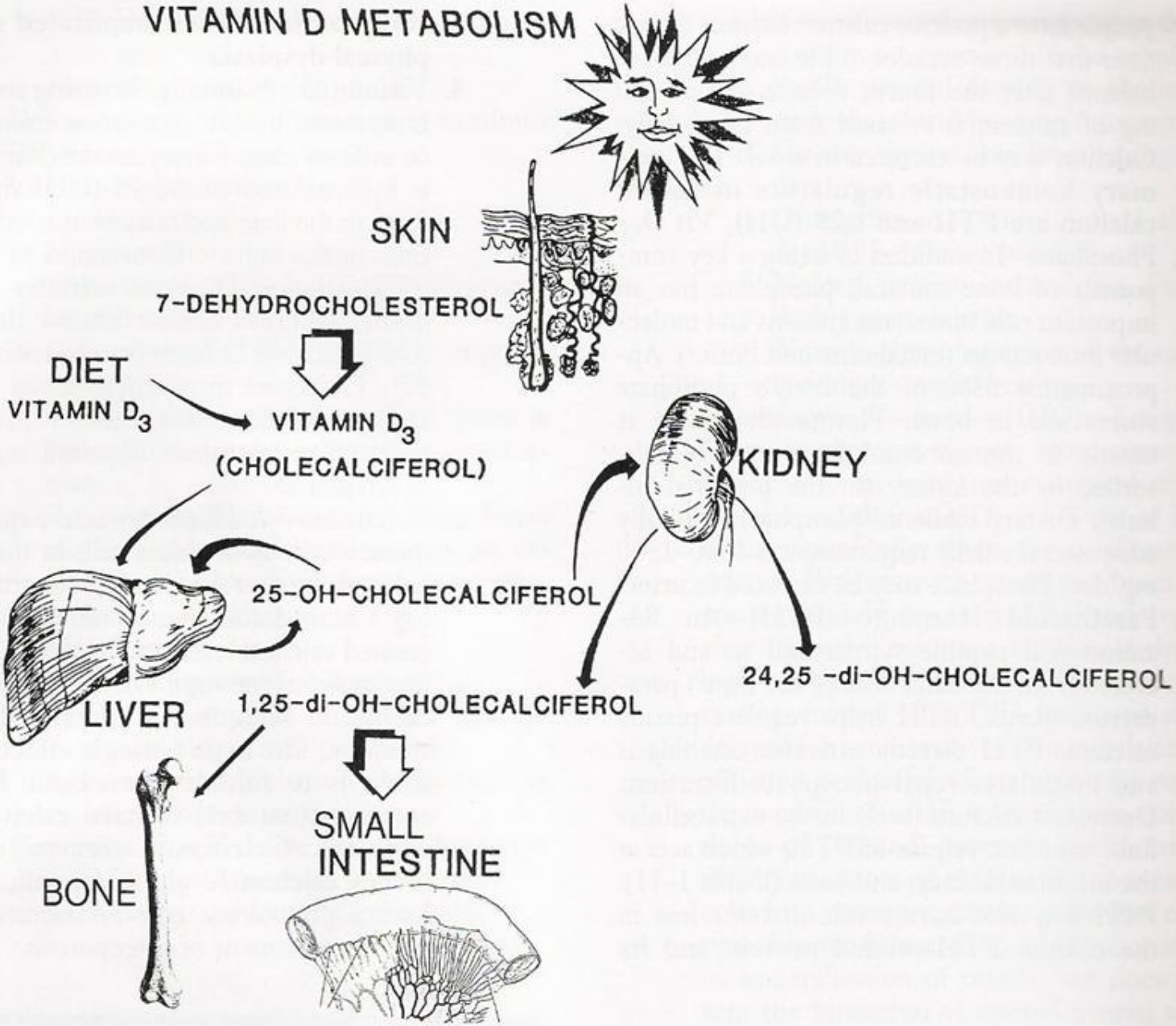
OP fractures



Femoral neck fracture

Colles' fracture of the wrist





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Rickets / Osteomalacia

- Increased width and disorientation in the physis
- Cortical thinning and bowing
- Retarded bone growth
- Muscle hypotonia
- Dental disease
- Pathologic fractures

Rickets / Osteomalacia

- Low normal Ca (maintained by high PTH)
- Low P
- High PTH
- Low vitamin D

Osteomalacia

- Rickets of adulthood
- Deficiency or resistance to Vit D OR Phosphate handling problem
- Defective mineralization of bone
- Proximal myopathy, Bony pain, malaise
  - Deformities much less common than with ri

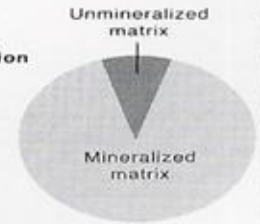
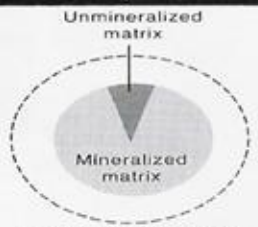
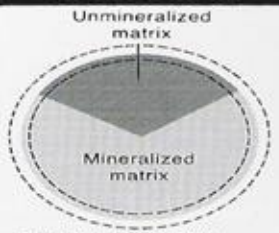
Loosers zones

Rickets

Causes of osteomalacia/rickets

- **Reduced availability of Vit D**
  - Diet: oily fish, eggs, breakfast cereals
  - Elderly individuals with minimal sun exposure
  - skin covering when outside
  - Fat malabsorption syndromes
  - Kidney failure
  - Epilepsy: phenytoin, phenobarbitones
  - Genetic disease(Malabsorption, RTA, hypophosphatasia)

Comparison of Osteoporosis and Osteomalacia

		Osteoporosis	Osteomalacia
Definition	 Normal	 Bone mass decreased, mineralization normal	 Bone mass variable, mineralization decreased
Age at onset	 Generally elderly, postmenopause	 Any age	
Etiology	Endocrine abnormality, age, idiopathic, inactivity, disuse, alcoholism, calcium deficiency	Vitamin D deficiency, abnormality of vitamin D pathway, hypophosphatemic syndromes, renal tubular acidosis, hypophosphatasia	
Symptomatology	 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^{++}	Normal	Low or normal (high in hypophosphatasia)	
Serum P,	Normal $Ca^{++} \times P, > 30$	Low or normal $Ca^{++} \times P, < 30$ if albumin normal (high in renal osteodystrophy)	
Alkaline phosphatase	Normal	Elevated, except in hypophosphatasia	
Urinary Ca^{++}	High or normal	Normal or low (high in hypophosphatasia)	
Bone biopsy	Tetracycline labels normal	Tetracycline labels abnormal	

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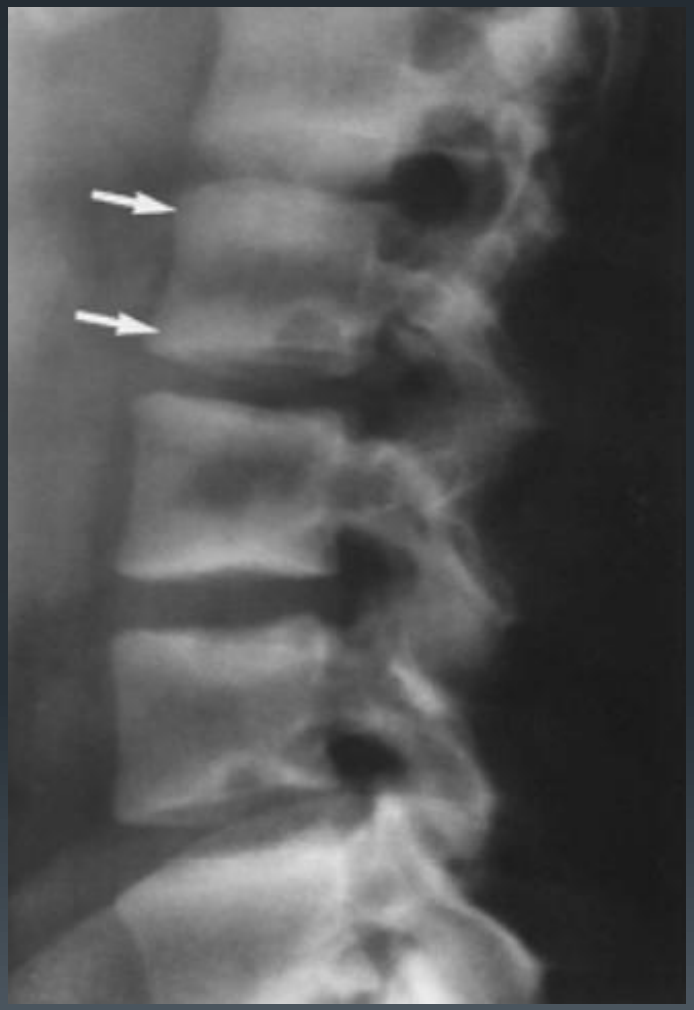
Hyperparathyroidism

- Primary
  - Often an incidental finding
- Secondary
  - Compensates for chronic low Ca
  - eg. Renal failure or malabsorption
  - $[Ca^{2+}]$ and $[PO_4^{2-}]$ normal PTH high
- Tertiary
  - Hyperplasia in longstanding secondary disease



Primary Hyperparathyroidism

- Parathyroid adenoma
- Increased plasma calcium and decreased phosphate
- Increased osteoclastic resorption
- Osteopenia, fibrous replacement, brown tumors and chondrocalcinosis
- Surgical parathyroidectomy

Sub periosteal bone resorption

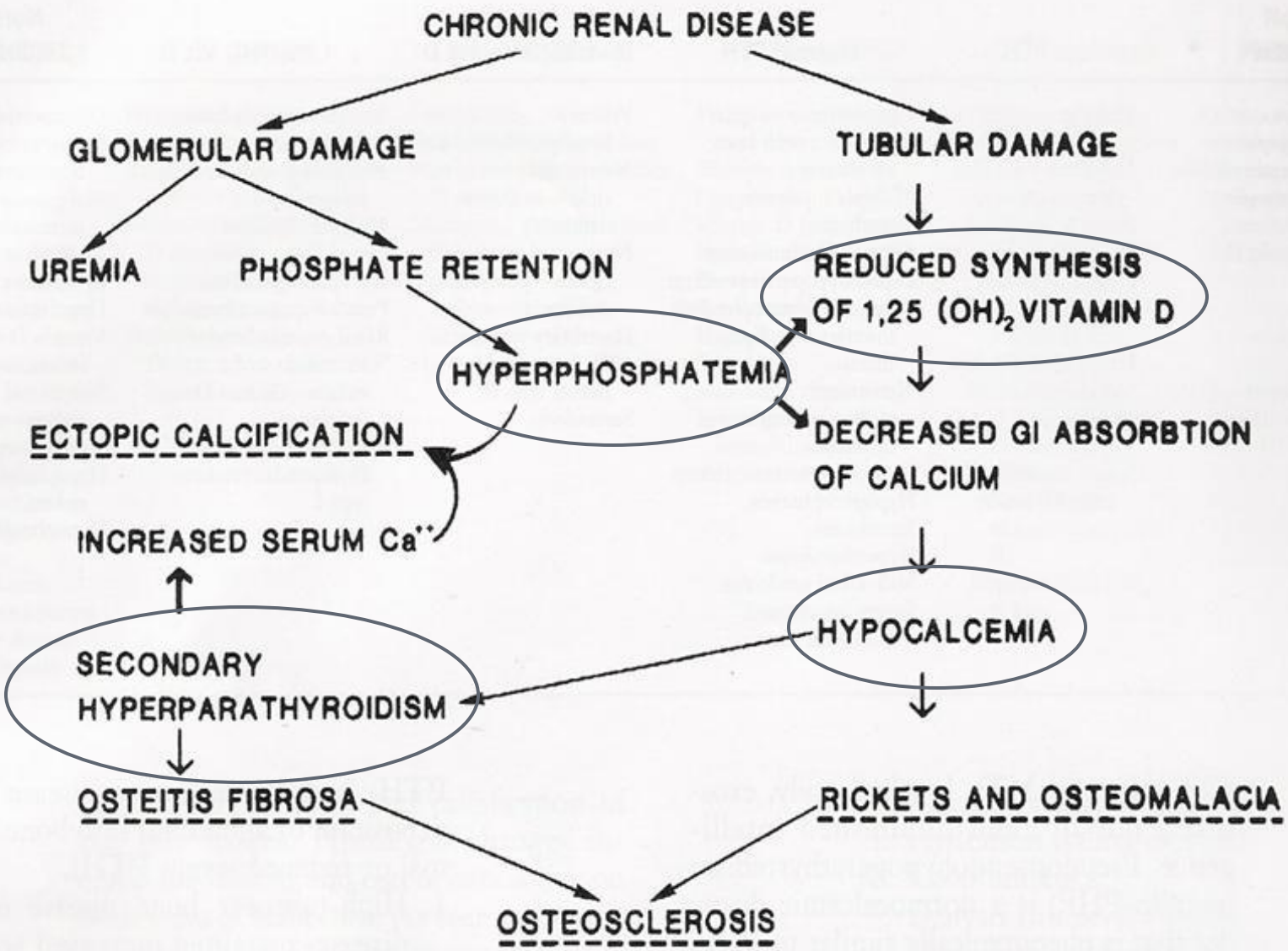
B

A

Renal Osteodystrophy

- Effect on bone of disordered calcium homeostasis
- May be osteomalacia, hyperparathyroidism
- Leads to
  - Bone pain
  - Skeletal deformity
  - Muscular weakness
  - Ectopic calcification
  - Growth retardation

MECHANISM OF BONE CHANGES IN RENAL OSTEODYSTROPHY



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Acromegaly

- calvarial thickening, enlarged sinuses, and an enlarged sella turcica.
- jaw is prognathic
- distal phalanges become hypertrophied and have a so-called spade appearance

Hyper-thyroidism

- thyroid acropachy
- only after prior thyroidectomy
- A characteristic-appearing periostitis
- ulnar aspect of the fifth metacarpal

Myelofibrosis

- progressive fibrosis of the marrow
- osteosclerosis is seen in a patient older than 50

Osteopetrosis

- Marble bone disease
- Congenital osteogenensis disease
- Severely sclerotic bones
- Fragile bones but rapidly cured

Pyknodysostosis

- congenital abnormality
- acroosteolysis with sclerosis

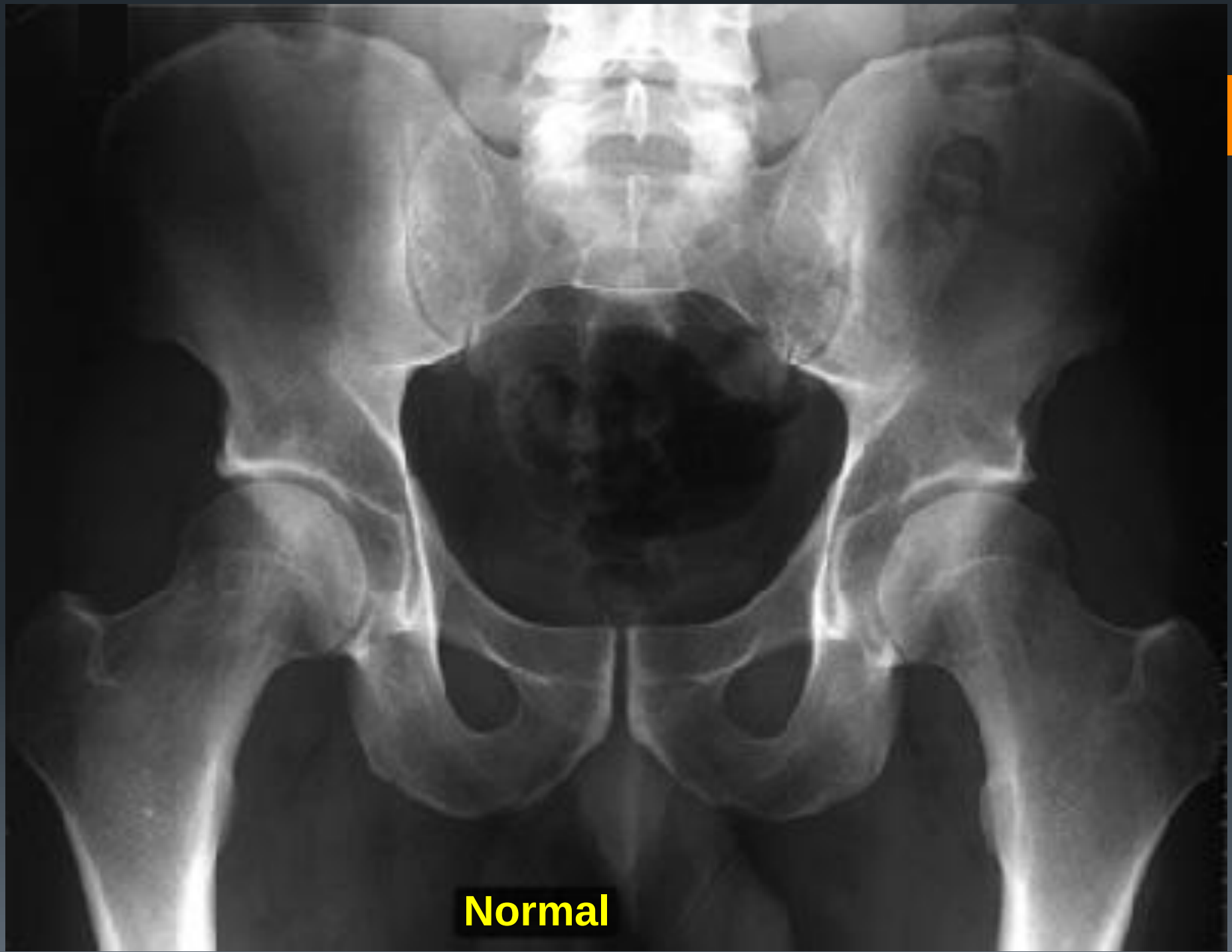
Paget disease

- Disease of bone remodeling
- Accelerated bone resorption and formation

- Fractures
- Deafness
- Nerve entrapment
- Spinal stenosis
- Cardiac failure
- Osteogenic sarcoma

Paget's Disease: investigations

- Radiology
  - cortical thickening
  - osteolytic, osteosclerotic and mixed lesions


Normal

Thank you