Metabolic Bone Diseases

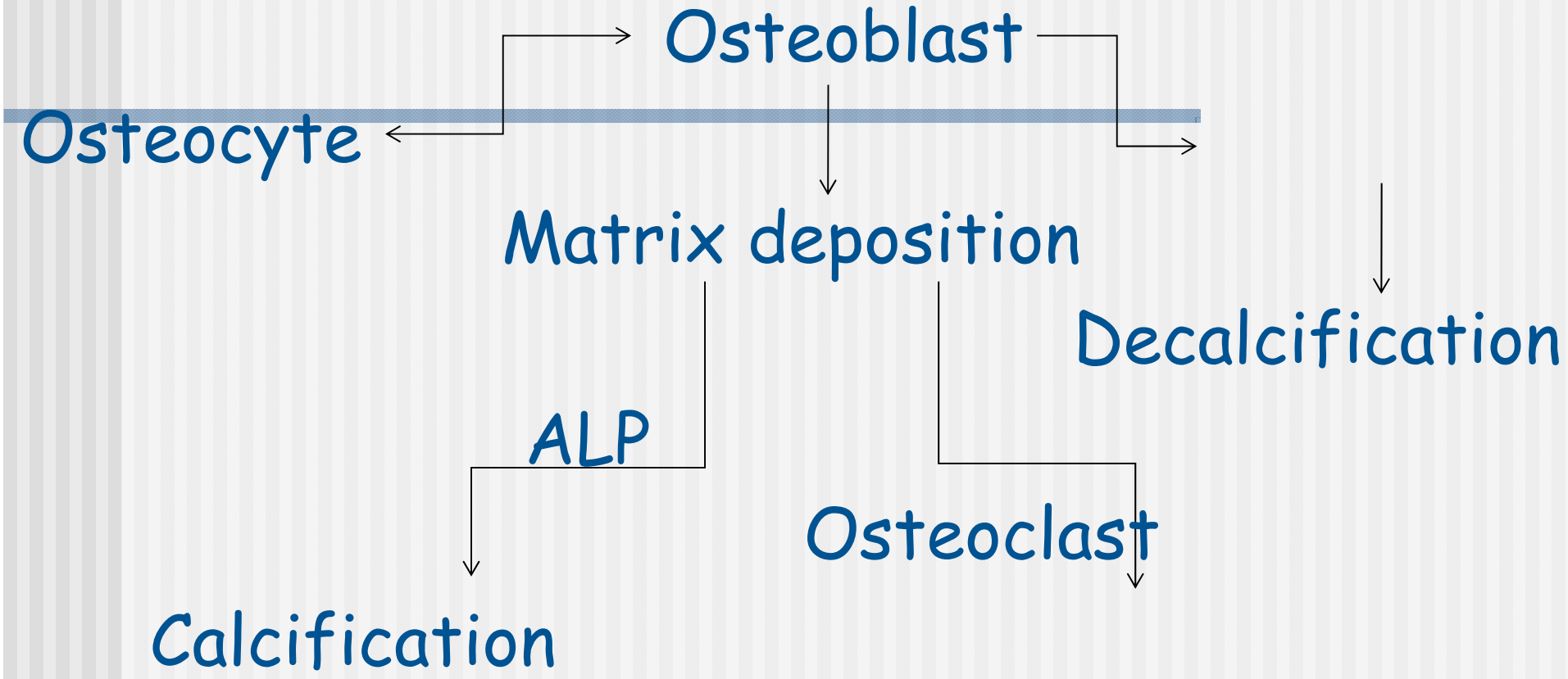
Normal bone n mineral metabolism

- Highly vascular (receives 10% CO)
- Dynamic (constt. remodeling throughout life)
- Compact-Cancellous arrangement
- Other vital functions…hematopoesis n homeostasis for S. Ca, Mg, PO_4

Normal bone n mineral metabolism

- Constituents:
  - Cells→ Osteoblasts, Osteoclasts, Osteocyte
    Hematopoetic cells
  - ECM→ Collagen(type I, fibrillary arrangement
    → Proteins (Fibronectin, Ca-binding prot
    Thromboplastin)
    → Minerals (Ca n PO_4 hydroxy-apatite)

Normal bone n mineral metabolism



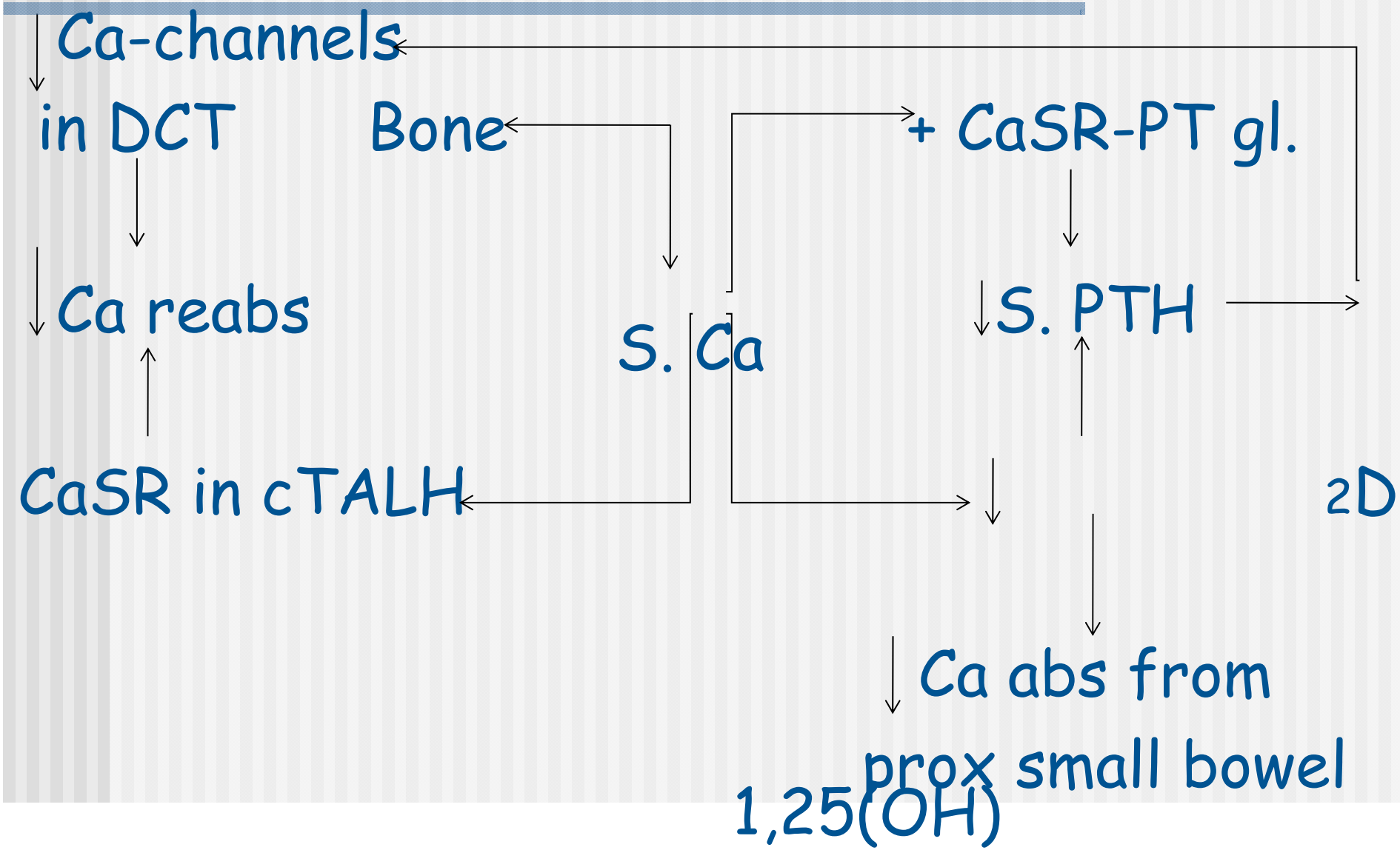
Osteoblast activity: ALP, Osteocalcin

Osteoclast activity: Collagen degradation pdt.

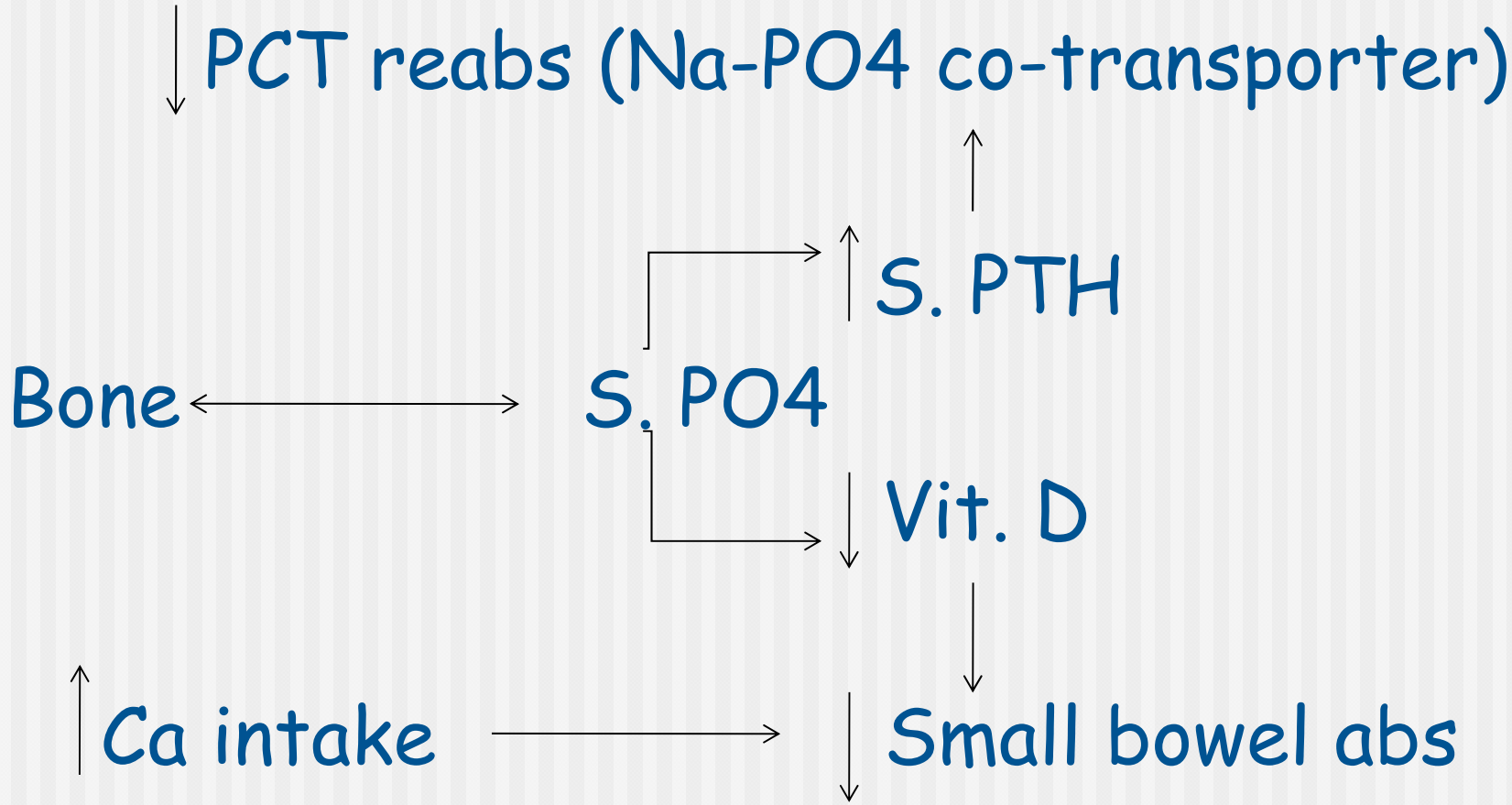
Calcium n Phosphorus metabolism

- Total Ca content of body = 1-2 Kg
- 99% of it in bones
- Vital for ….neuromuscular activity
  ….glandular secretions
  ….signal transduction (sec messanger)
- Total Phosphorus content of body = 500 mg
- 85% Of it in bones
- Vital for…ATP stores, NA, structural protein
  Enzymes, Co-factors

Calcium homeostasis



Phosphorus homeostasis



Calcium n Phosphorus homeostasis

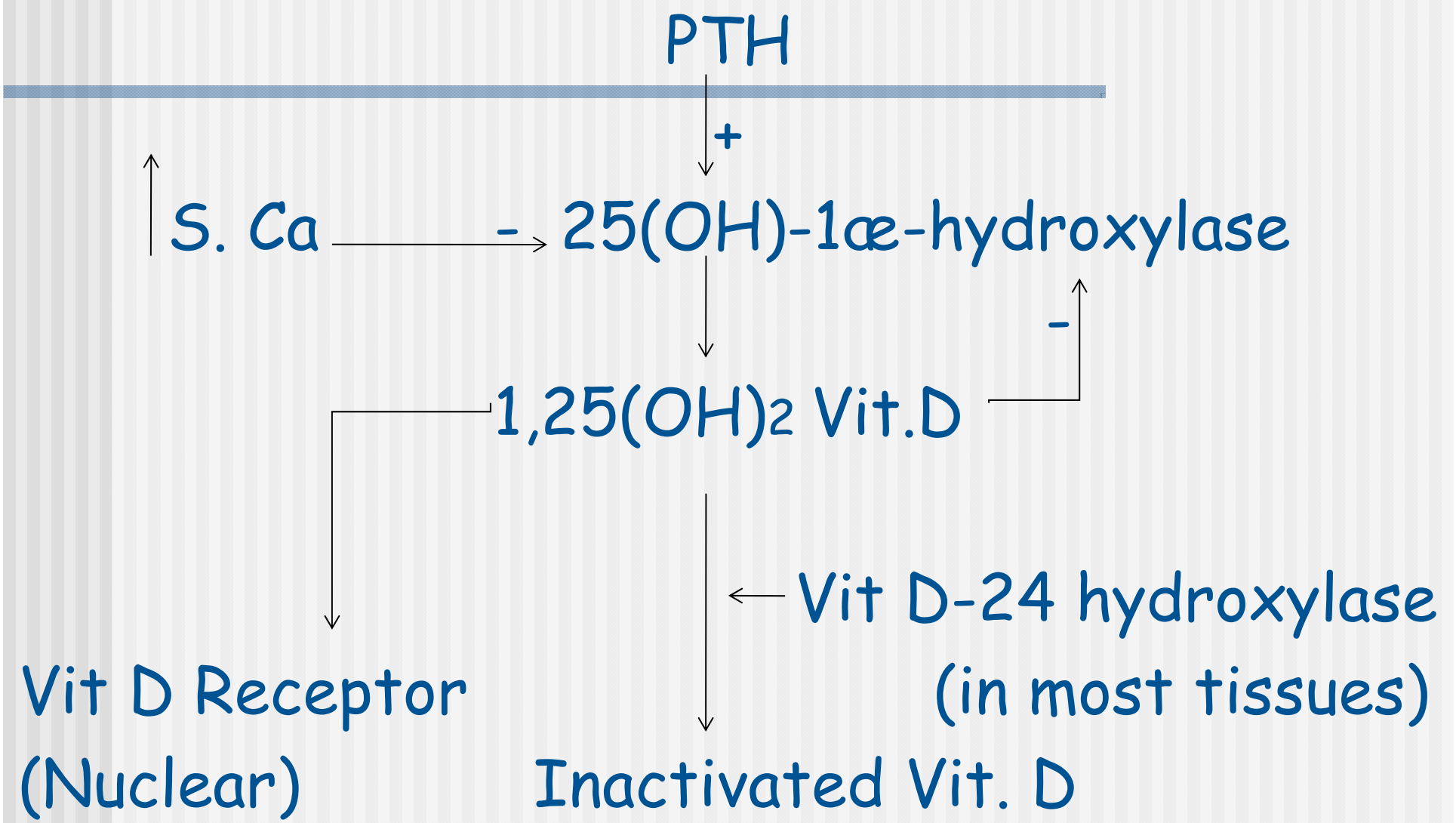
- Hence, perturbed Ca n PO4 homeostasis can result from

1. PTH disorders
2. Vit. D disorders
3. Renal disease
4. Small bowel ds & Achlorhydria

Vitamine D

- 7- DehydroCholesterol $\xleftrightarrow[\text{UV light}]{}$ Vitamine D_1
- Vitamine D_2: Plant source
- Vitamine D_3: Animal source
- Vitamine D_2 n D_3....equally effective
- 25(OH)D.the major circulating n storage form

Vitamine D metabolism



Vitamine D deficiency states

- Reduced Vit D

Intake…..dietary inadequacy

Production….sun exposure

Absorption…..malabsorption syndrome

- Excessive loss/break-down of Vit D

Catabolism….Phenytoin, R-cin, Barbiturates

Enterohepaic circulation….small bowel ds

or resection

Vitamine D deficiency states

- Impaired metabolism
  - 25-hydroxylation: Liver ds, INH
  - 1œ-hydroxylation: CKD, Hypoparathyroidism
    - 1œ-hydroxylase mutations
    - X-linked hypophosphatemic rickets
  - Target organ resis: VDR mutations

Vitamine D deficiency

- Clinical manifestations:
  - Hypocalcemia, tetany, seizures
  - Osteopenia, rickets, osteomalacia
  - Proximal myopathy
  - Pathologic bone fractures
- Diagnosis:
  - 25(OH)D (< 15 ng/mL)
  - Raised S. PTH
  - Low S. Ca, ↑ALP (bone-specific)
  - X-ray…Osteopenia, Pseudofractures

- Treatment:
  - Therapeutic dose = 40,00 IU/d
  - Prophylactic dose = 800 IU/d
  - Various formulations n doses

1. Clacitriol ($1,25(OH)_2D_3$) = 0.25-0.5 µg/d
2. Doxercalciferol ($1(OH)D_2$) = 2.5-5.0 µg/d
3. Calciferol (Vit D_2) = 50,000 IU wkly X 3 mth f/b 800 IU/d
4. Inj. Vit D = 2.5 MU deep i/m Biannually

- Always add Ca with Vit D supplementation
- Normocalcemia (<1 wk); ALP n PTH in 3-6 mth

Parathyroid related disorders

- Hyperparathyroidism:

1. Pr. Hyperparathyroidism

Solitary adenoma (80%)

MEN 1 (Wermer's synd: Pitutary n Pancreas)

MEN 2A (Medullary Ca thyroid + Pheochromo)

MEN 2B (Multiple Neuromas + MCT + PCC)

2. Sec. → CKD, Lithium therapy

- Familial hypocalciuric hypercalcemia

Pr. Hyperparathyroidism

- Clinical features:

i. Asymptomatic

ii. Bone, Stone, Groan, Mone

➢ Bone→ high turnover bone ds

→ Osteitis fibrosa cystica

→ X-ray: subperiosteal resorption

→ Histo: multinucleated osteocasts at bone surface pits

→ Formation/Resorption markers: ALP, Procollagen/Collagen telopeptide

Pr. Hyperparathyroidism

- Stone → Nephrocalcinosis
  → Nephrolithiasis
- Groan → Refractory gastritis
  → Zollinger-Ellison syndrome
  → Pancreatitis
- Mone → Neuropsychiatric manifestations
  → Neuropathy, Parathyroid myopathy

Pr. Hyperparathyroidism

- Diagnosis: Hypercalcemia with î S. PTH
- Treatment: Medical or Surgical ?

➢ Medical→ SERMs (Raloxifene)
→ Calcimimetics (CaSR +)

❖ Annual S. Creat, DEXA scan n Biannual S. Ca

Pr. Hyperparathyroidism

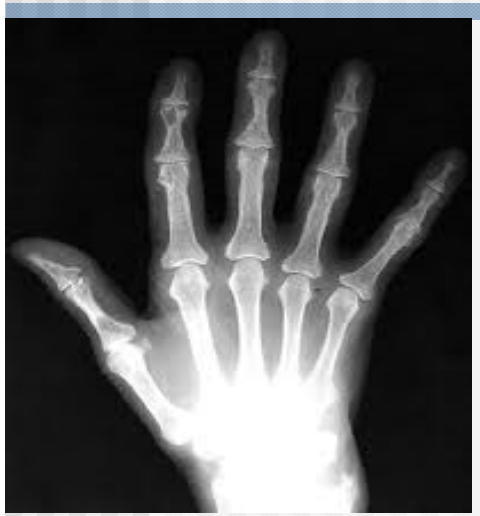
- Surgery

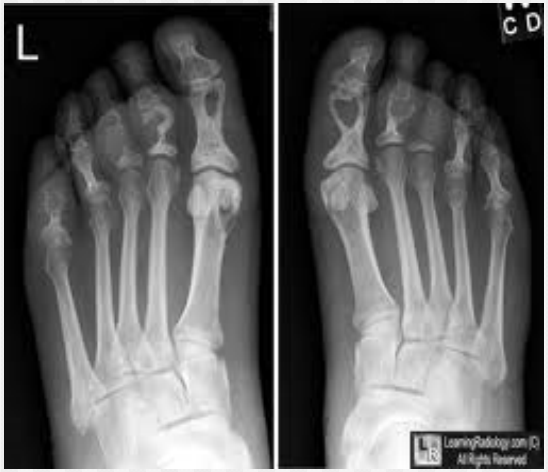
I. Severe hyperCa (>15 mg%)
   or hypercalciuria (>400 mg/d)
II. Asymp hyperPTH with age < 50 yrs
III. T-score < -2.5 at any site
IV. CCL reduced by 30% or more

- Pre-op Radiolabelled Tec SPECT & intra-operative S. PTH sampling (>50% decline; 5 min. post-removal) for better localization

Familial hypocalciuric hypercalcemia

- Mutation in CaSR in PTH gland n Kidney
- Usually asymptomatic
- Must be differentiated from Pr. hyperPTH as medical therapy or surgery not useful (*K)

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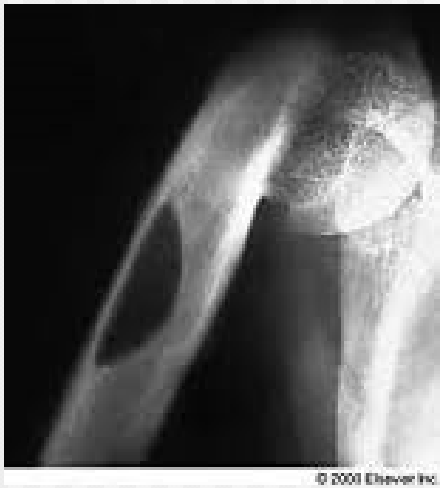
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