Calcium Homeostasis

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Physiological Importance of Calcium

- Calcium salts in bone provide structural integrity of the skeleton.
- Calcium ions in **extracellular** & **cellular fluids** is essential to normal function of biochemical processes:
  - Neuoromuscular excitability.
  - Blood coagulation.
  - Hormonal secretion.
  - Enzymatic regulation.
- ↑carbonated beverages is associated with increased loss of calcium from the body.
- Because normal bone function requires weight-bearing exercise , ↑immobility & total bed-rest cause bones to lose calcium.

Calcium in blood

- total Ca^{++} concentration in blood is **≈10 mg/dl** (range 8.5-10 mg/dl)
- **Present in two forms:**

The free ionized Ca^{++} is about 50% of the total blood Ca^{++} = 5mg/dl .

- It is the only form of Ca^{++} which is biologically active.

non-free , unionized calcium →

- (i) Protein-bound calcium →around 40% of total ECF calcium .

Most of this calcium is bound to albumin , & much smaller fraction is bound to globulin.

- (ii) present as complexed salt (mainly bound to serum citrate & phosphate), around 10% of blood calcium .

- Binding of calcium to albumin is pH-dependent.

- Acute respiratory alkalosis increases calcium binding to protein → thereby decreases ionized calcium level.
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- When ionized calcium falls below normal, permeability of neuronal cell-membranes to sodium increases → depolarization → hyperexcitability of the nervous system → patients become prone to develop tetanic muscle contractions & seizures .

Phosphate

- Phosphorous is an essential mineral necessary for ATP, cAMP second messenger systems, and other roles.
- PO_4 plasma concentration is ≈ 4 mg/dL.
- Ionized (diffusible) → around 50% of total.
- The remainder (50%) is un-ionized (non-diffusible) and protein- bound.
- Calcium is tightly regulated with Phosphorous in the body.

Hormonal Regulation of Calcium

- 3 principal hormones regulate serum Ca^{++} level .

- 2 of them increase it :

(1) Vitamin D3 (1,25-dihydroxy) (taken in food & synthesized in the skin)

(2) Parathyroid hormone (PTH): polypeptide hormone secreted by Parathyroid Glands .

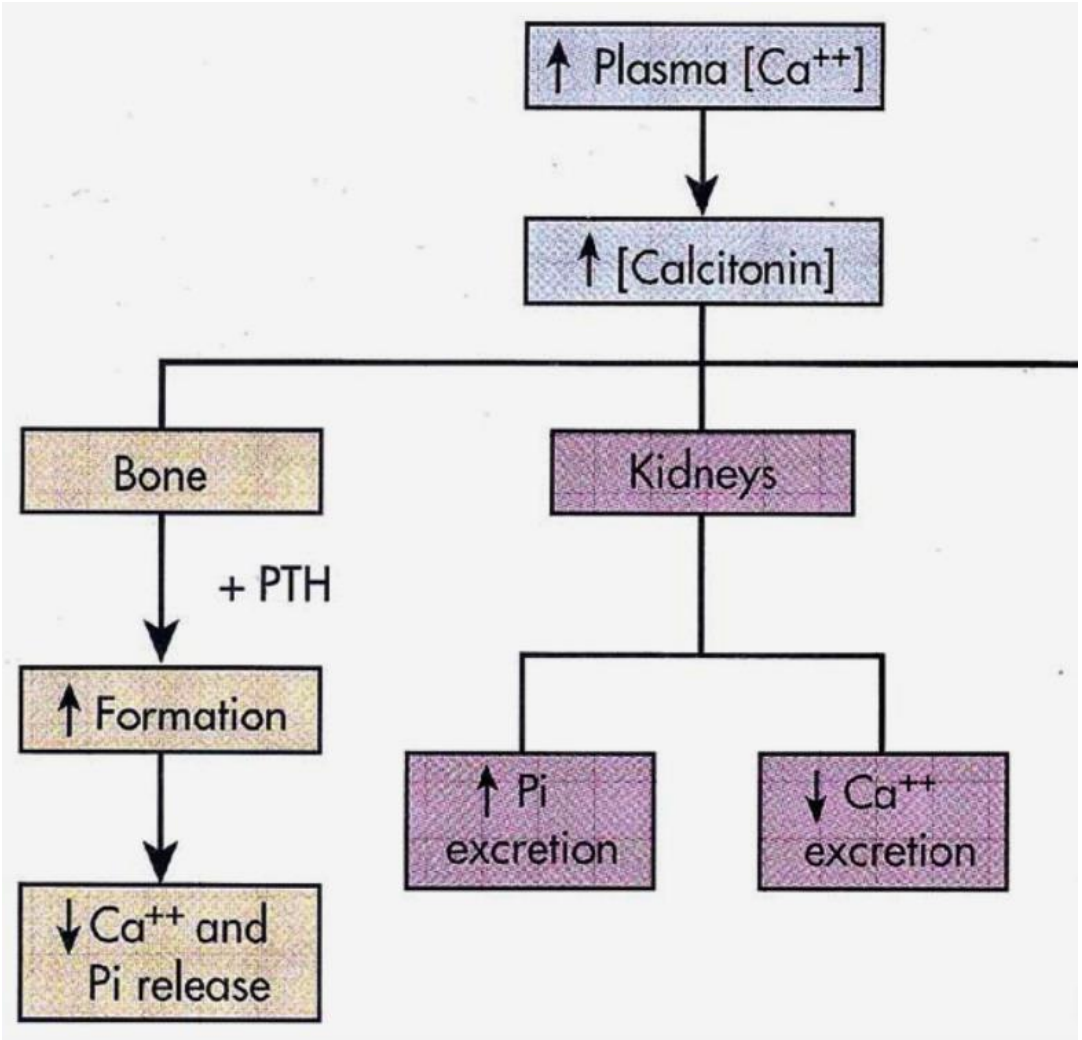
- And the third one decreases it :

(3) Calcitonin: polypeptide hormone secreted by Parafollicular (C) cells of Thyroid Gland

NB : While PTH and vitamin D act to increase plasma Ca^{++} → only calcitonin causes a decrease in plasma Ca^{++}.

- High plasma Ca^{++} leads to → increased Calcitonin secretion
- The main action of this calcitonin is to inhibits osteoclasts → inhibition of bone resorption → (1) increases bone formation (2) decreases blood Ca^{++} level .
- Thus calcitonin plays a central role in bone re-modelling .

Calcitonin



Calcitonin

Actions:

On bone

[1] ↑ Ca deposition of bone by:

↓ osteolysis.

↑ osteoblastic activity

[2] ↓↓ Bone resorption:

inhibition of osteoclasts.

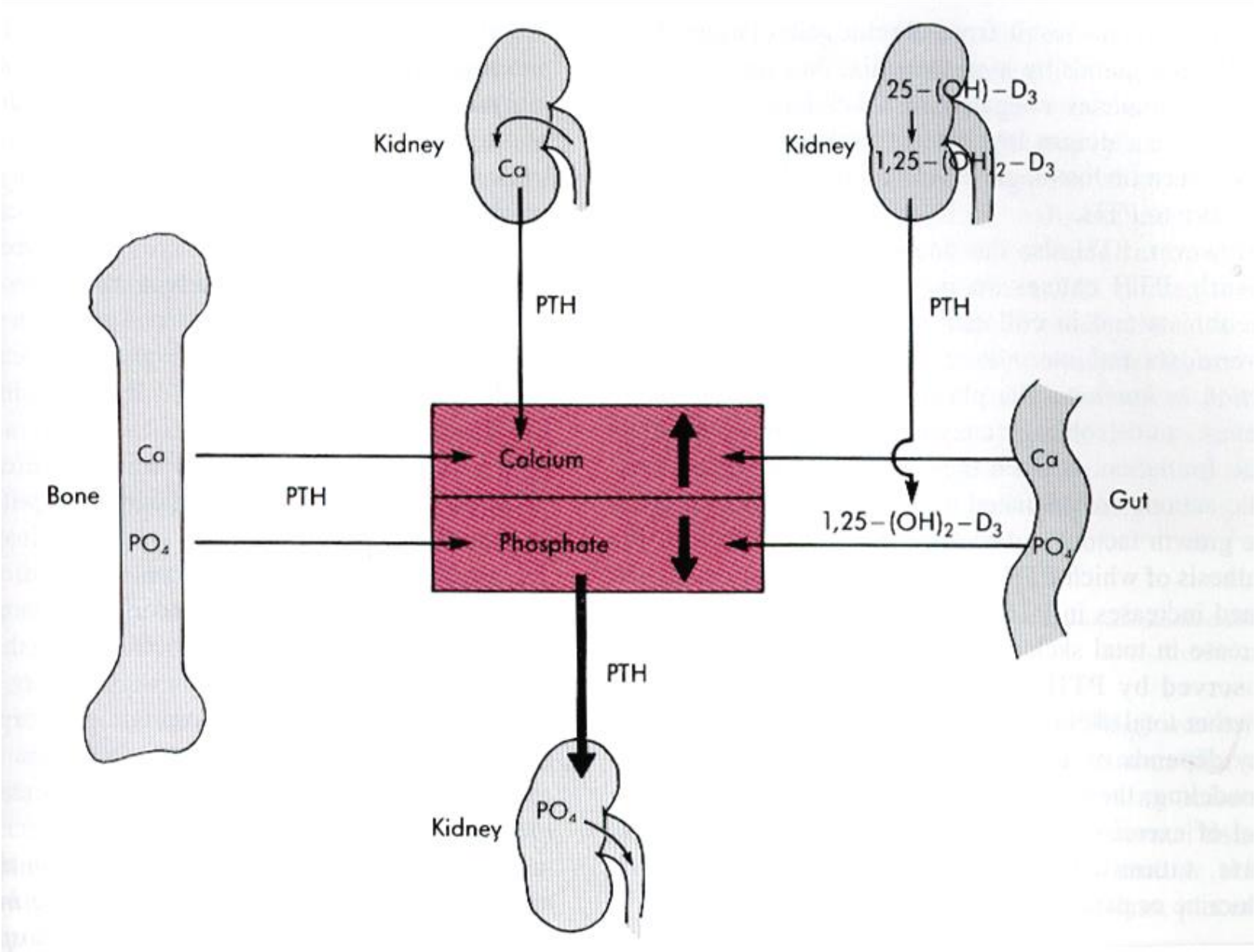
↓ formation of osteoclasts

On kidney

↓↓ Ca reabsorption

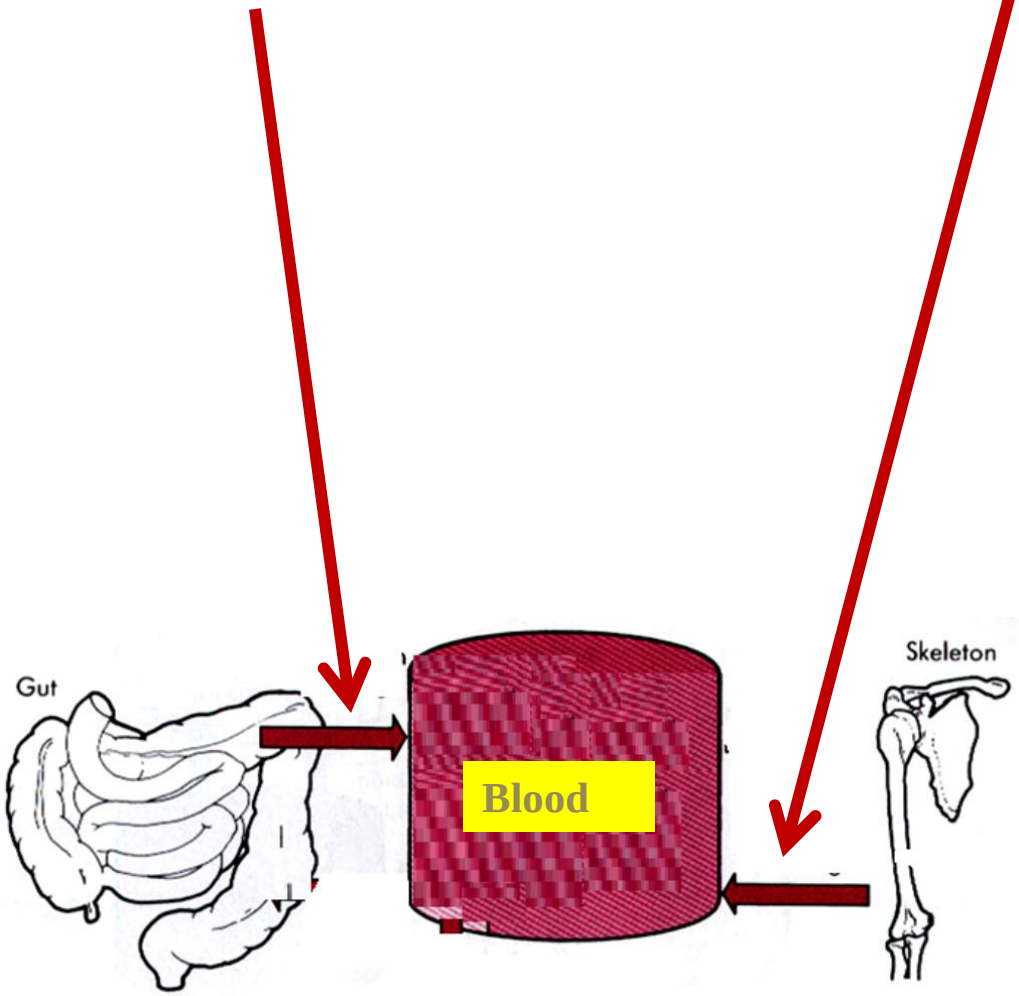
↑↑ Ca excretion (in addition to phosphate)

Calcium & Phosphorus



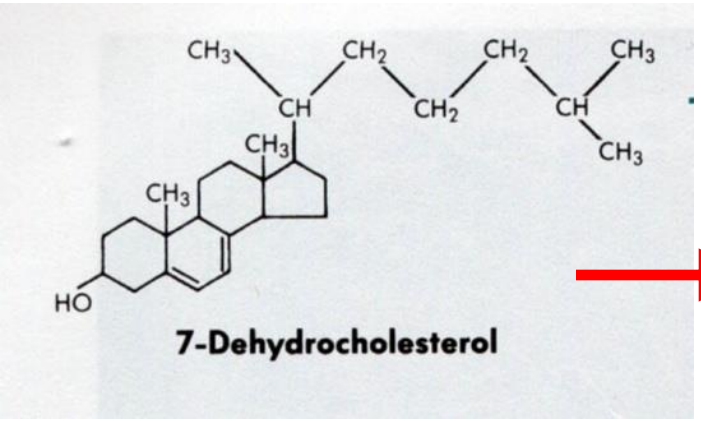
- Vitamin D3 increases Ca^{++} level by :
- (1) Ca^{++} absorption from the intestine , &

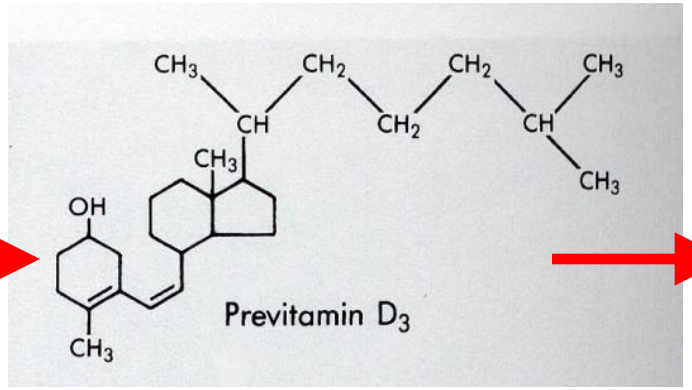
(2) Ca^{++} resorption from the bone (by increasing osteoclastic number & activity)

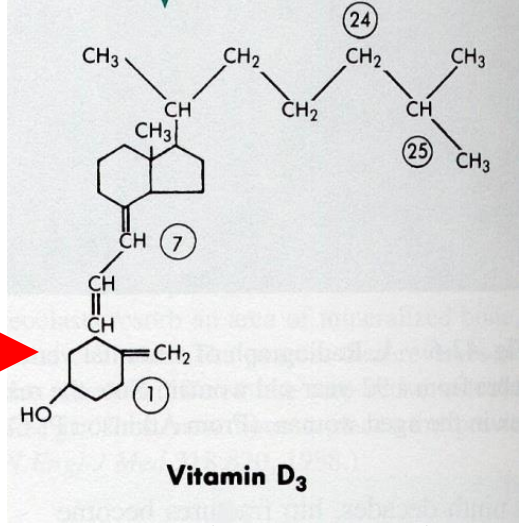


(3) Some believe that it also increases Ca^{++} reabsorption by the kidney

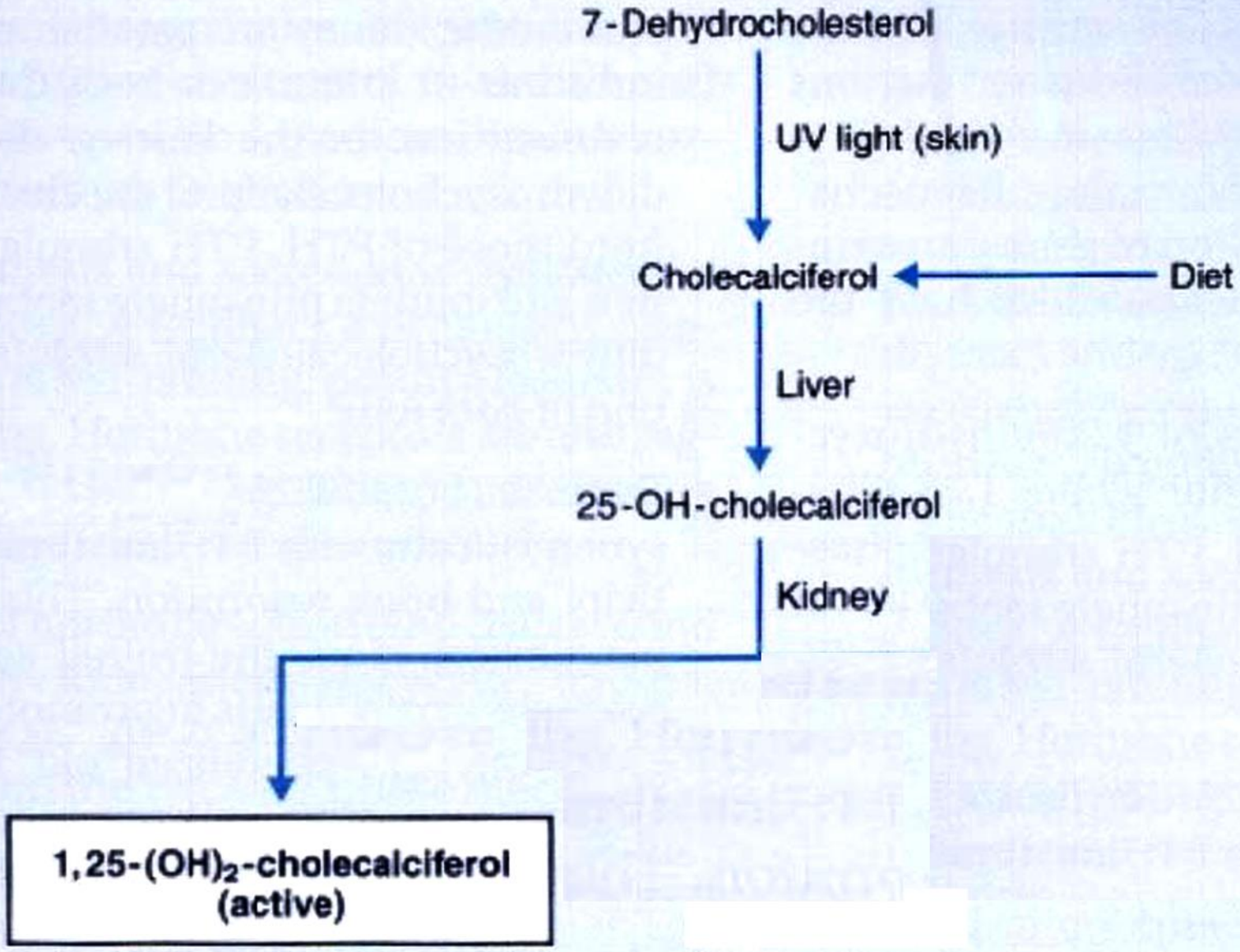
Humans acquire vitamin D from two sources →
(1) Ingestion in diet (food)
(2) Skin : Vitamin D is produced in the skin by ultraviolet light .







- Keratinocytes in the skin synthesize 7-dehydrocholesterol .
- 7-dehydrocholesterol is photoconverted (by UV light in skin) to Cholecalciferol (previtamin D3).
- This form of Vitamin D is inactive, it requires modification to the active metabolite, 1,25-dihydroxy-D → by two hydroxylation reactions → the 1st occurs in liver and the 2nd in kidney
- Limited exposure to the sun , dietary vitamin D is essential . If there is no sufficient exposure to the sun , or if there is dietary deficiency in vitamin D → Rickets (in children) or Osteomalacia (in adults) occur .
- PTH stimulates Vit D synthesis.


7-Dehydrocholesterol
UV light (skin)
Cholecalciferol
Diet
Liver
25-OH-cholecalciferol
Kidney
1,25-(OH)2-cholecalciferol
(active)

- Vitamin D deficiency leads to a disease characterized by softening of bone

- If it occurs in children → it is called Rickets

- If it occurs in adults → it is called Osteomalacia

- Most affected areas :
- Metaphyses of long bones subjected to stress →
- Wrists
- Knees
- Ankles

- Clinical Features
  - Delayed dentition (delayed teething)
  - Bowed legs

    (Due to the effect of weight bearing on the legs)
  - Swelling of wrists and ankles
  - Short stature

Metaphyseal widening in wrists & knees + signs of bone rarfaction

Bowed legs (Bowing of legs)

Osteomalacia : an adult disease characterized by a gradual softening and bending of the bones