ENDOCRINE REGULATION OF CA^{++} & PHOSPHATE METABOLISM

CALCIUM HOMEOSTASIS

Calcium homeostasis refers to the maintenance of a constant concentration (9-11 mg/dL) of calcium ions in the extracellular fluid.

Calcium is involved in the following biological processes:

1. ***Blood clotting***
2. ***Muscle contraction***
3. ***Neurotransmission and Neuromuscular transmission.***
4. ***Enzymatic reactions***
5. ***Formation of milk, bone and teeth***
6. ***Mechanism of secretion e.g. Hormone secretion***
7. ***Acts as 2nd messenger (e.g. mediates hormonal action)***
8. ***Stabilization of cell membrane***

NORMAL DISTRIBUTION OF CALCIUM

Total body calcium in a young adult is about 1 kg.

After the 3rd decade of life, bone resorption exceeds bone formation, and there is a slow but progressive loss of bone occurs which is greater in women than in men.

Skeletal storage: 99% of total body calcium

Plasma Ca^{2+} :

The normal range of Ca^{2+} in plasma is

9-11 mg%; presents as:

50% : ionized; biologically active form.

10%: complexed in nonionic & unfilterable form (such as $CaHCO_3$).

40% is bound to proteins, mainly albumin.

WHAT IS THE DAILY CA2+ REQUIREMENT?

- ***400 mg for adults, with greater amounts in:***

Childhood –

Pregnancy –

- ***Lactation***

- ***Absorption of Ca2+:***

  Ca2+ can be absorbed from all parts of small intestine especially duodenum by an active transport mechanism controlled by vit D (w is activated in the kidney by parathormone).

  Urinary excretion of calcium: About 9 gm Ca2+ pass daily into the glomerular filtrate. Most of this is reabsorbed by the tubules and in normal people the urinary excretion is 80-400 mg/day.

FACTORS AFFECTING CALCIUM ABSORPTION AND EXCRETION

- ***Calcium absorption is affected by:***

Hormones: → ↑ed by vit D, PTH and GH. –

Ca2+ absorption decreases in: –

Vit D deficiency •

Renal failure •

Intestinal malabsorption •

Presence of unabsorbed fatty acid •

in the intestine

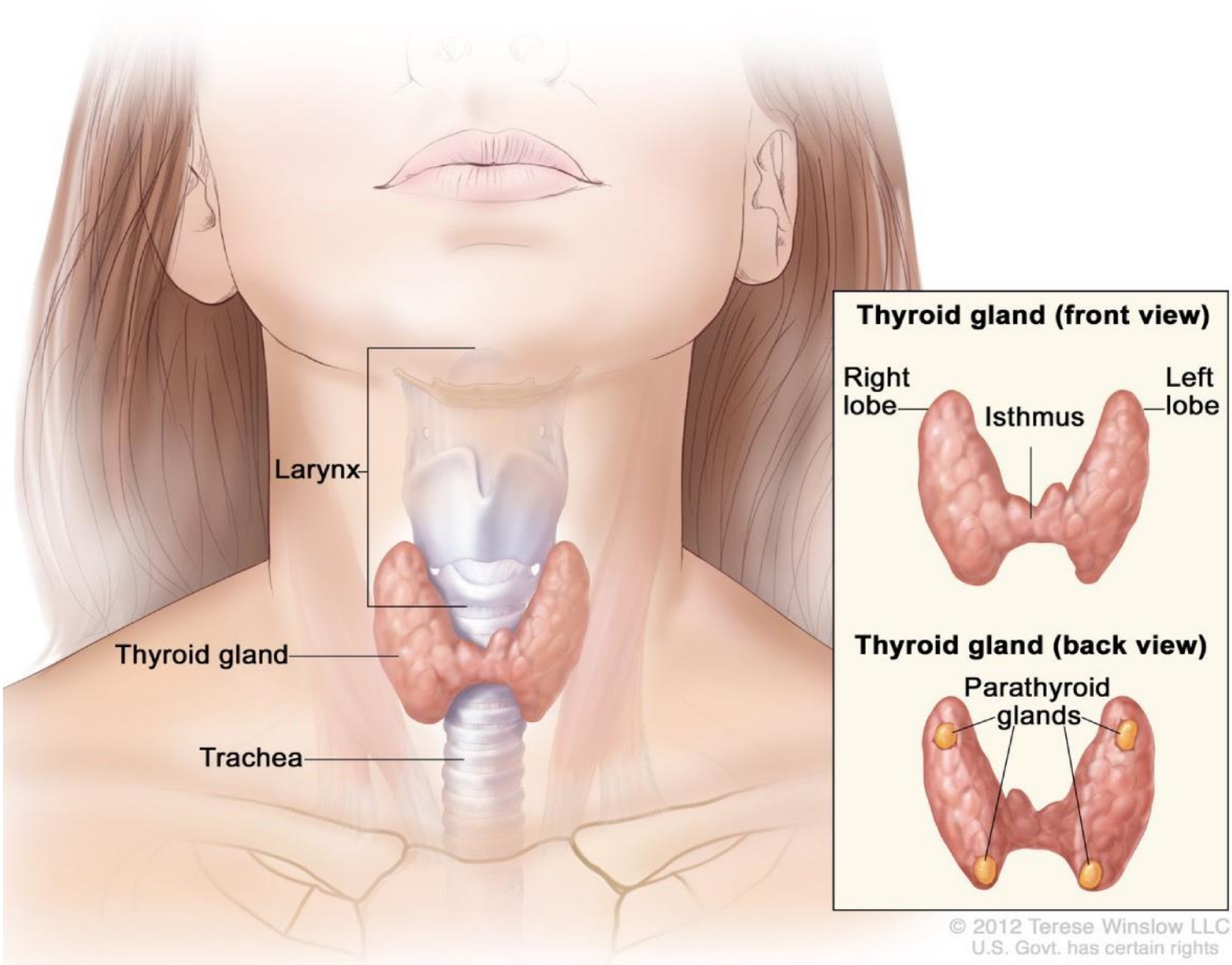
excretion of Ca2+ in urine: ***80-400***

mg/day

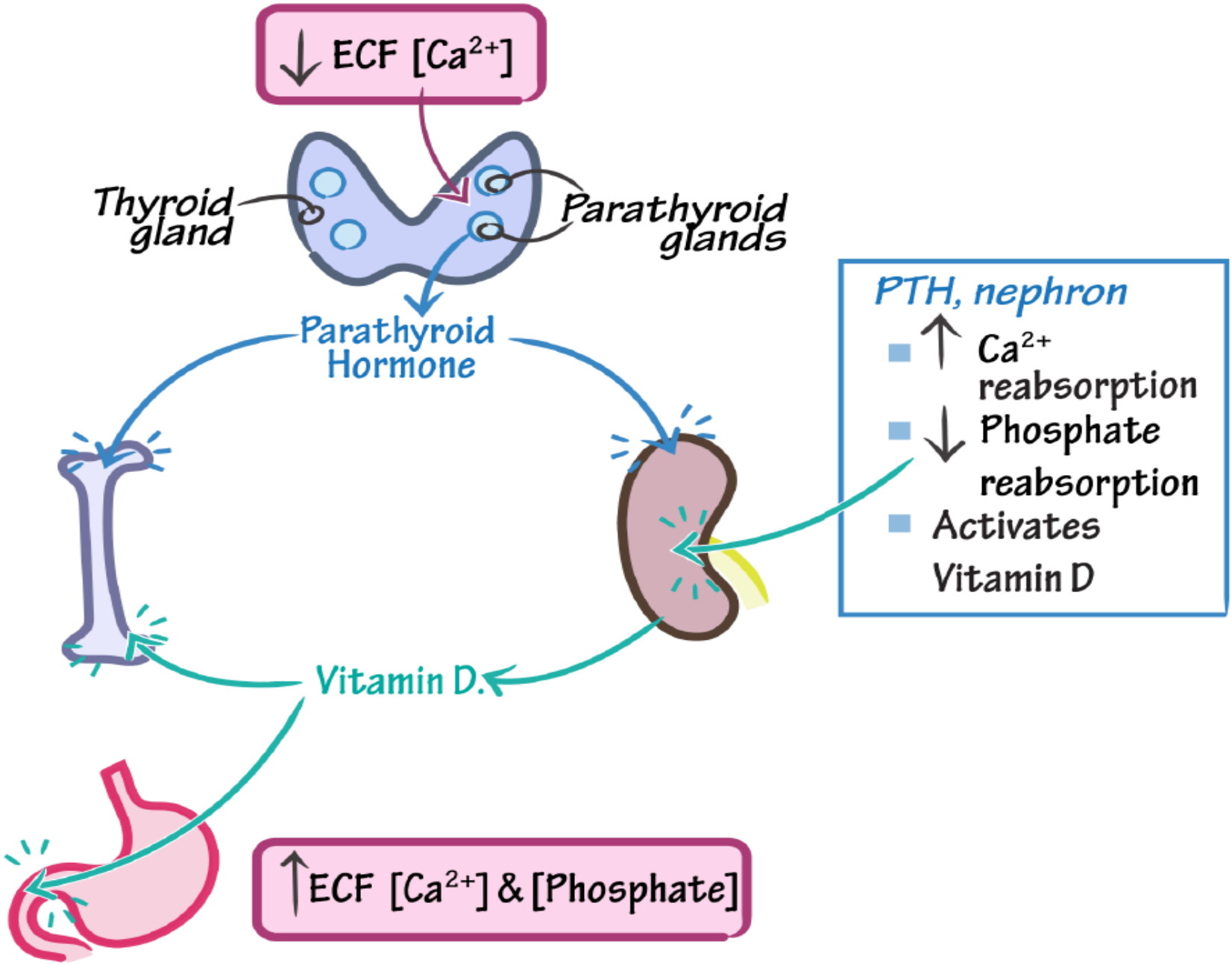
PARATHYROID GLANDS

- **They are 4 glands present at the back of thyroid glands**.
- Each measures **4 mm in diameter & their combined weight** = 120 mg.
- They secrete parathyroid hormone (**parathormone**) which is **essential for life.**

Anatomy of the Thyroid and Parathyroid Glands



Calcium Homeostasis



Parathyroid hormone (pth) = parathormone

Functions:

- **The prime function of PTH is to keep Ca^{++} level (9 – 11 mg%).**
- Normally, the plasma inorganic phosphate is inversely related to Ca++ concentration **& the product $Ca^{++} \times Po_4^-$ = constant** (solubility product).
- **The function of parathormone is to ↑ plasma Ca^{++} & ↓ plasma PO_4^- thus maintain the solubility product constant.**

Parathyroid hormone (PTH) raises the lowered Ca^{++} level through acting on:

1- On the intestine :

A. ↑ Ca^{++} absorption

- This action is mediated by active vitamin D.

B. ↑ phosphate & Mg^{++} absorption

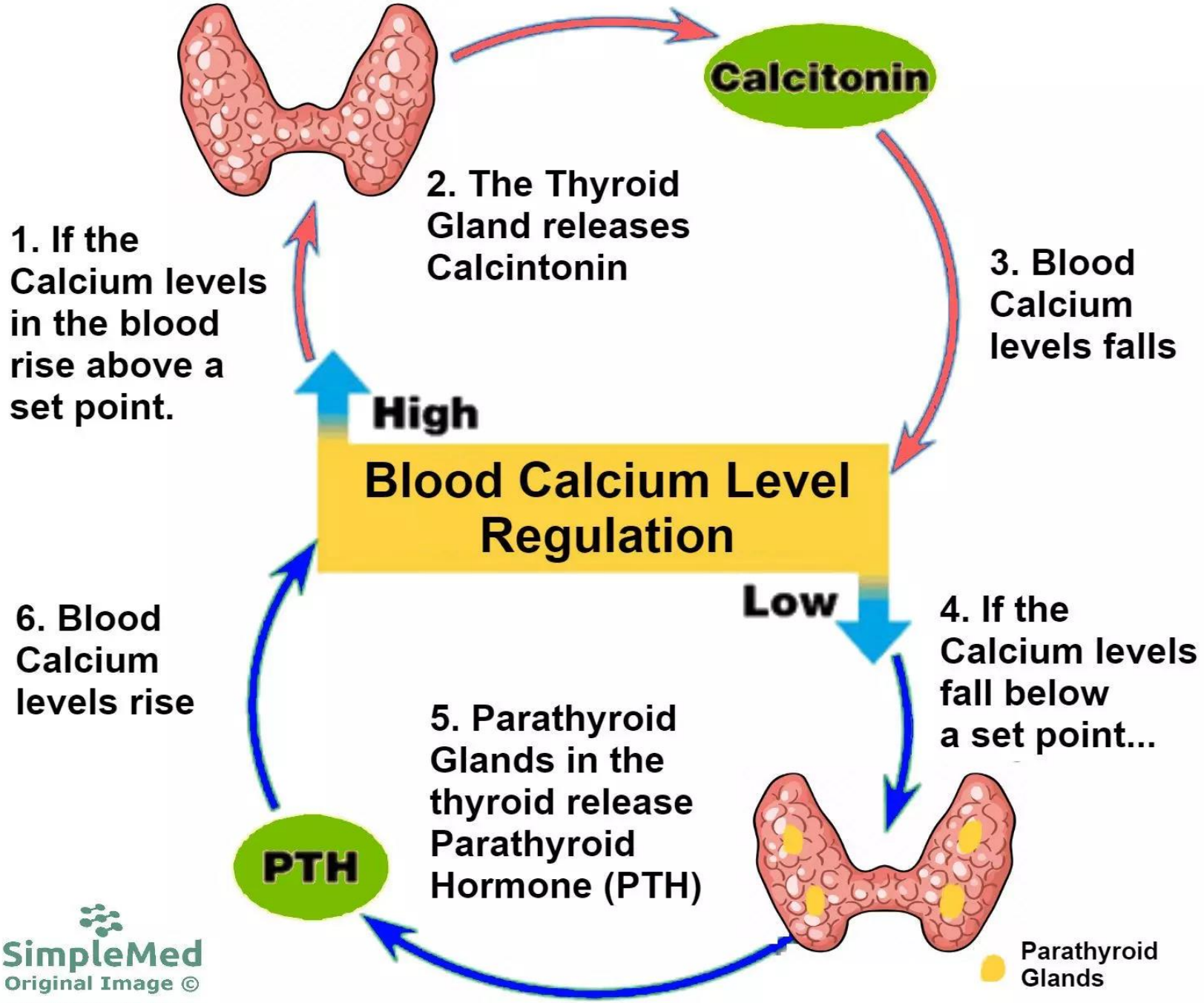
2- On the bone:

- **↑ Ca^{++} mobilization from bone by activating osteoclasts (bone destroying cells)** → release of Ca^{++} & phosphate into the blood stream .

3- On the kidney:

- **↑ Ca^{++} & Mg^{++} reabsorption.**
- ↑ phosphate excretion

4- ↓ Ca^{++} excretion in milk to maintain its blood levels high.



DISORDERS OF THE PARATHYROID GLAND

1- Hypo-para-thyroidism

Cause :

- **Accidental damage or removal of the parathyroid gland during thyroid surgery**.
- **Hypoparathyroidism** is characterized by **hypocalcemia due to decrease ionized** Ca^{++}.
- **hypocalcemia** is associated with **increased neuromuscular excitability due increased membrane permeability to Na^{+}. Leading to tetany.**

TETANY

- **Is a disease characterized by increased neuromuscular excitability caused by reduction of blood levels of ionized Ca^{++}.**

Cause :

1. Hypoparathyroidism
2. **Renal failure due t phosphate retention.**
3. Alkalaemia due to precipitation of ionized Ca^{++}.
4. **Decreased Ca^{++} absorption from the intestine due to :**
   I. **Low dietary Ca^{++} intake.**
   II. **Vitamin D deficiency.**
   III. steatorrhea (fatty diarrhea) which ↓ Ca^{++} absorption

TETANY

Manifestations:

- Manifestations of tetany depends on the degree of Ca^{++} lowering:

I- Manifest tetany	II- Latent tetany
- Occurs if Ca++ is **markedly** ↓ i.e. < 7 mg%	- Ca++ **isn't marked ly** ↓ ( )7&9 mg%
Manifestations:	
*1- **In adults, carpopedal spasm**:* *a) In the hands, **carpal spasm**:* - ***Flexion of the wrist & metacarpo-phalangeal joint.*** - ***Extension of the interphalangeal joint.*** - ***Adduction of the thumb.*** *b) In the feet, **pedal spasm**:* - ***Dorsiflexaion of the ankle & plantar** flexion of the toes.* *2- **In children** : may be **convulsions*** *3- **In infants :** may be **laryngeal spasm***	- **No** carpopedal spasm **except** if the person is **exposed to stress.** - The pateint may feel **numbness & heat flushings**

TETANY

Treatement of tetany

1. Intravenous **Ca^{++} gluconate** stops immediately the spasm.
2. **Diet rich in Ca^{++} & vitamin D.**
3. **Acidifying salts** e.g. ammonium Cl^{-} (↑) Ca^{++} solubilit in GT)
4. **Dihydro-tachysterol: has similar effects to parathormone but doesn't produce antibodies like exogenous parathormone.**

CALCITONIN HORMONE (= THYRO-CALCITONIN)

Calci= calcium, tonin = lowering

Nature :

- Polypeptide hormone

Source :

- **Parafollicular C cells of the thyroid gland.**

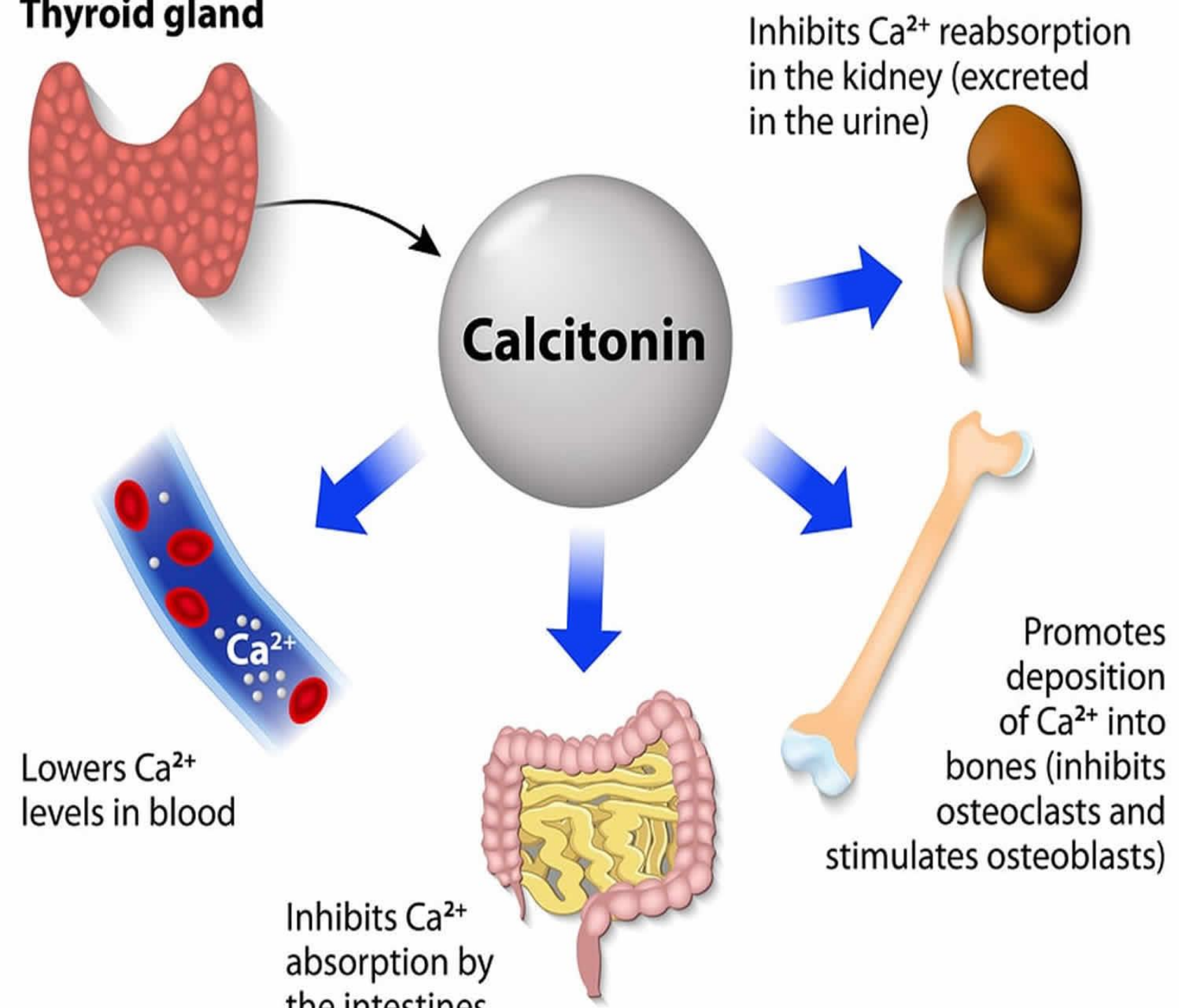
Control of release:

1. **Rise of serum Ca++, the major stimulus**

   - ↑ serum Ca++ by 1 mg% →↑ calcitonin release about 10 times.

2. **Ingestion of food :**

   - ingestion of food →↑ calcitonin release.


Thyroid gland
Inhibits Ca^{2+} reabsorption in the kidney (excreted in the urine)
Calcitonin
Ca^{2+}
Lowers Ca^{2+} levels in blood
Promotes deposition of Ca^{2+} into bones (inhibits osteoclasts and stimulates osteoblasts)
Inhibits Ca^{2+} absorption by the intestines

1- On the intestine:

- **↓ Ca^{++} absorption & P_{o4}^{-}**

2- On the bone :

- **It inhibits osteoclastic activity →↓ bone resorption & mobilization of Ca^{++} from bone into the blood**

3- On the kidney:

- ↑ urinary excretion of Ca^{++} &P_{o4}^{-}
- **Inhibits** renal **α1-hydroxylase enzyme** which activate vit D.

4- It act as physiological antagonist to parathormone as regards Ca^{++}, and its has the same effect as regards phosphate,

OTHER HORMONES AFFECTING BONE & CALCIUM METABOLISM

- **Although parathormone and calcitonin are the major calcium**
- **regulating hormones,** a number of other hormones are known to have an important influence on the bone and mineral metabolism.
- **These include vitamin D, estrogens and androgens, glucocorticoids, thyroid hormones, and growth hormone.**
- **Bone remodeling** is a process which continues throughout life, long **after epiphyseal fusion and cessation of linear growth of bone.**
- Remodeling consists of **bone formation and bone resorption**

I. **Osteoblasts : are the primary cells concerned with synthesis of new bone.**

II. **Osteoclasts :** function to **resorb** bone

1- VITAMIN D

- **Vitamin D have both dietary & endogenous precursors** :
  I. **Vitamin D_2 (ergo-calciferol) formed in plants**
  II. **Vitamin D_3 (chole-calciferol) formed in the skin by the ultra-violet rays (UVR)**

Actions:

1- On the intestine :

- it stimulates absorption of both Ca^{++} & phosphate.

2- On the kidney:

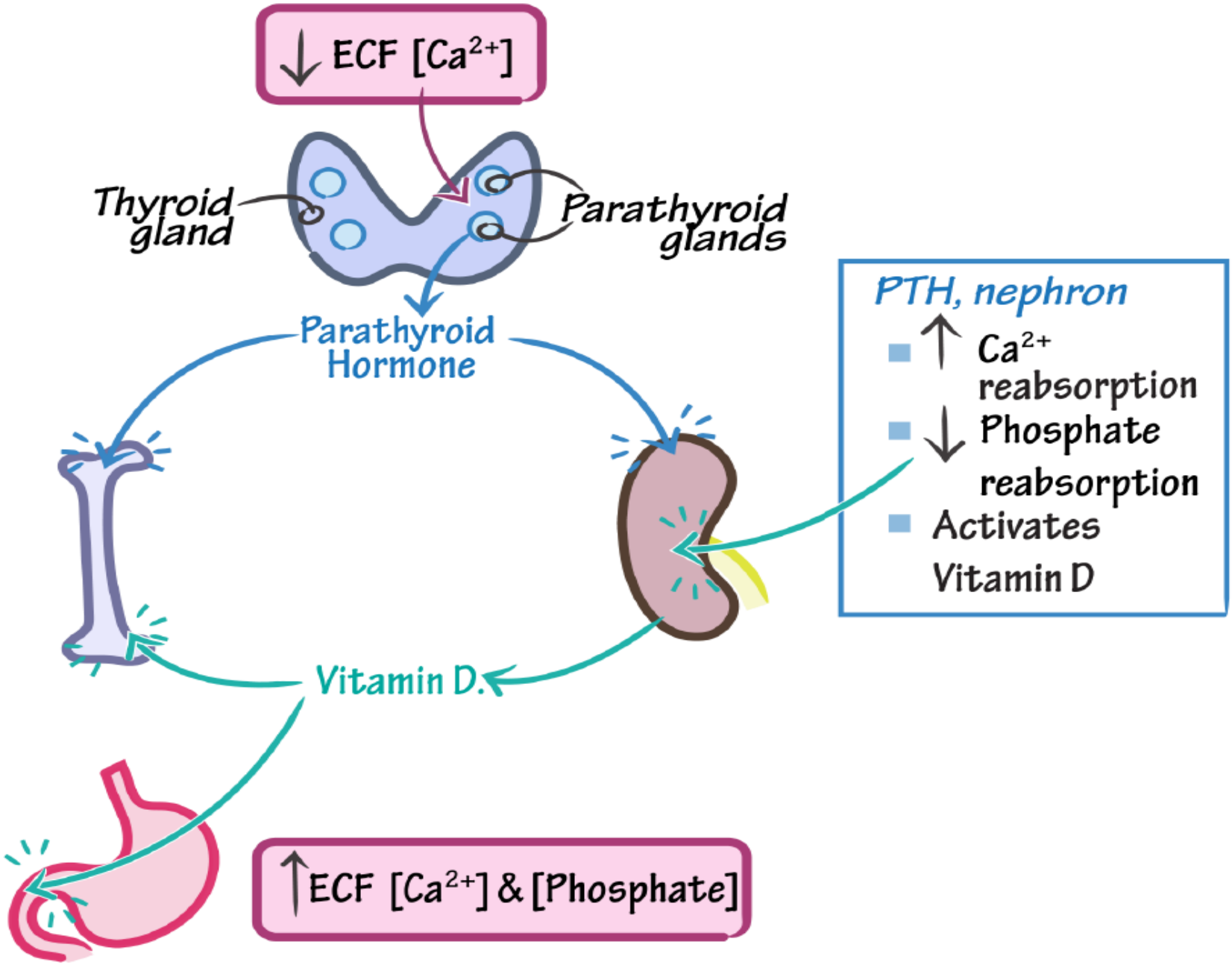
- it stimulates re-absorption of both Ca^{++} & phosphate.

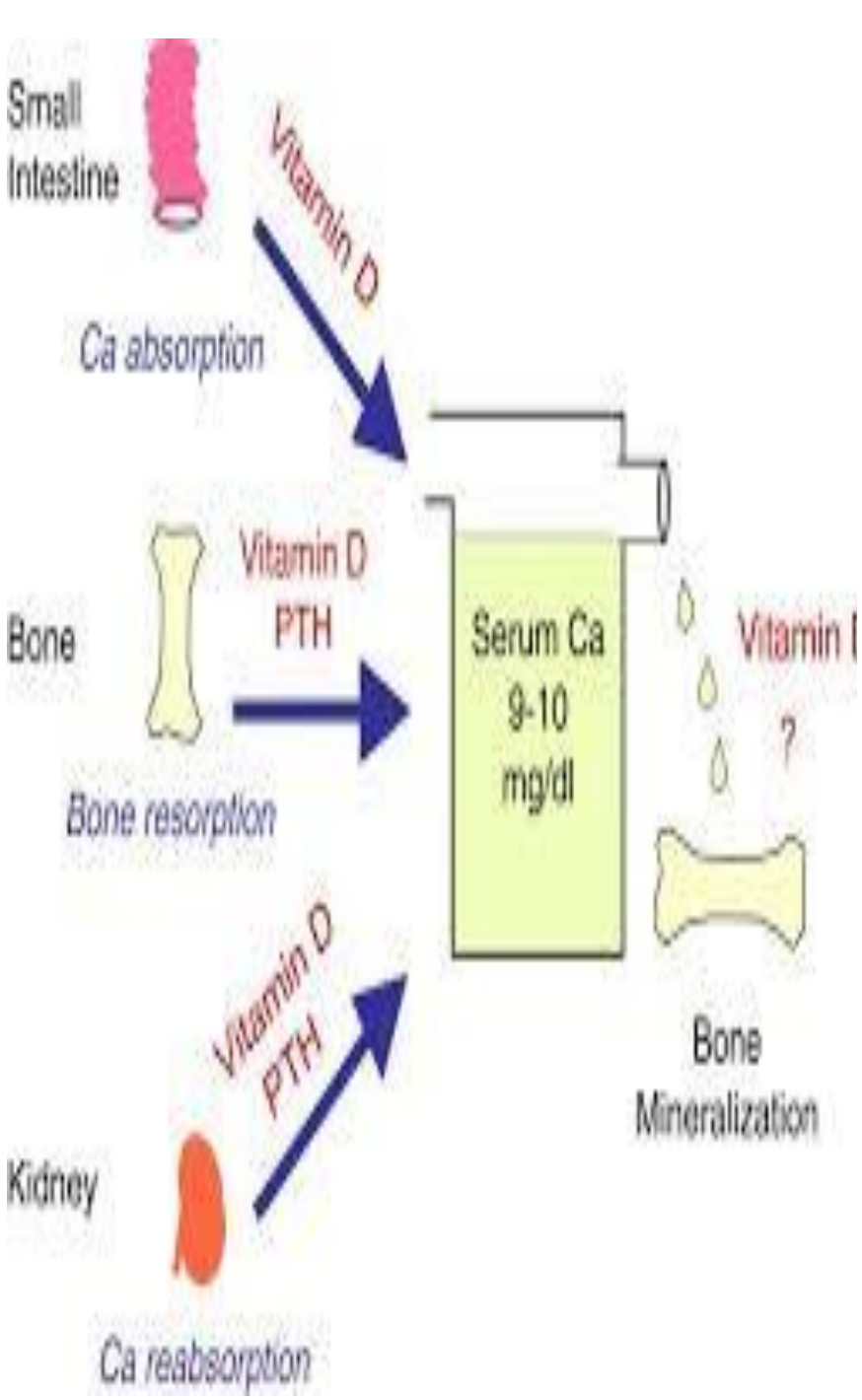
3- On the bone:

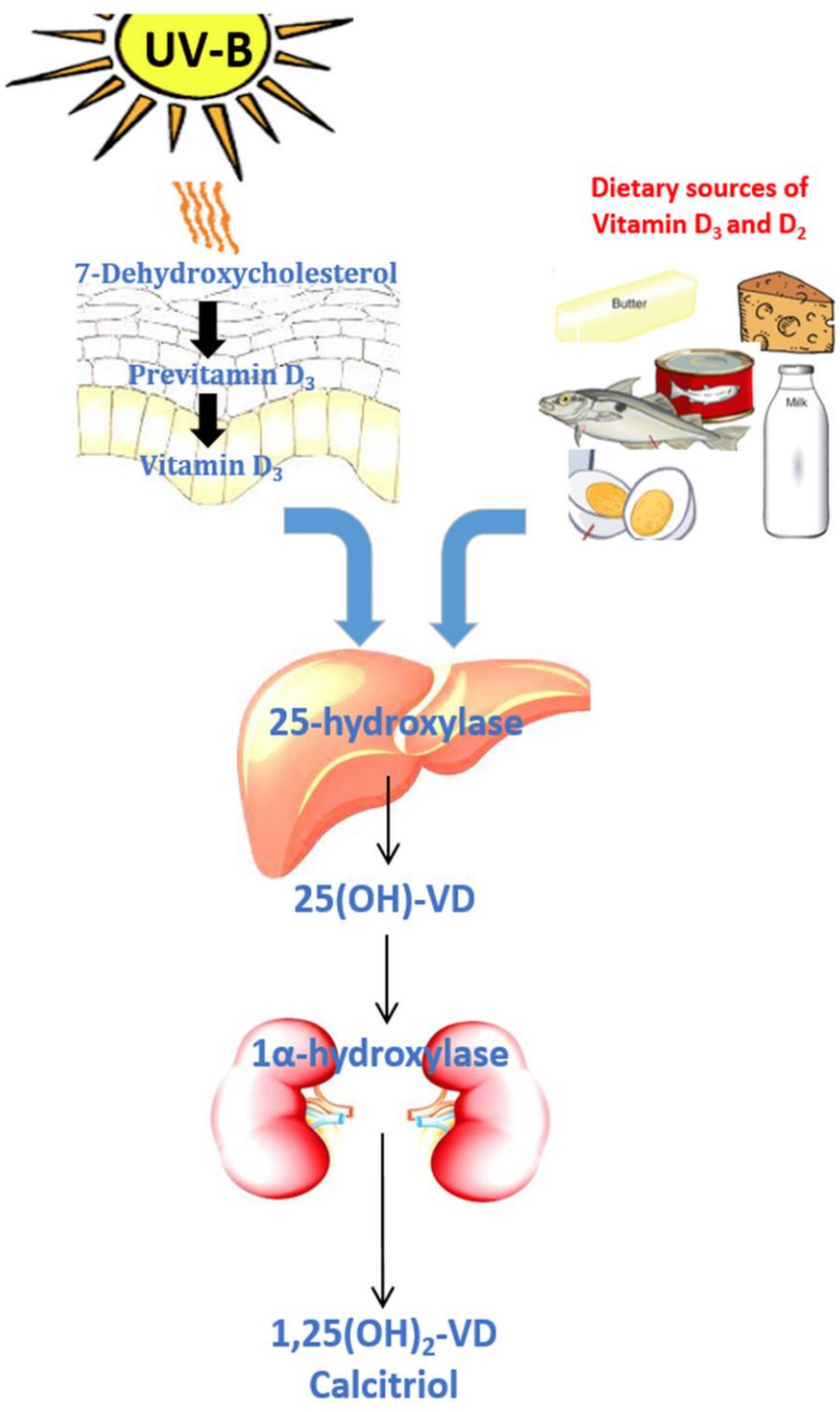
- it provides Ca^{++} & phosphate needed for bone formation.

- **it promotes differentiation of monocyte precursors to monocytes & macrophages**.

Calcium Homeostasis




Small Intestine
Vitamin D
Ca absorption
Bone
Vitamin D
PTH
Bone resorption
Serum Ca
9-10
mg/dl
Vitamin D
?
Bone
Mineralization
Vitamin D
PTH
Kidney
Ca reabsorption


UV-B
7-Dehydroxycholesterol
Previtamin D_3
Vitamin D_3
Dietary sources of Vitamin D_3 and D_2
Butter
Milk
25-hydroxylase
25(OH)-VD
1α-hydroxylase
1,25$(OH)_2$-VD
Calcitriol

2- ESTROGENS & ANDROGENS

- Have a role in childhood & puberty.
- These hormones **favours bone formation** over resorption.
- **In the female estrogen protect the skeleton from development of oesteoporosis.**

3- GLUCOCORTICOIDS

I. At **physiological** levels they are essential for skeletal growth.

II. **At high level they have deleterious effect on Ca^{++} homeostasis**.

4- THYROID HORMONES

I. **At physiological levels they are essential for skeletal growth**..
II. At **high level** e.g. in hyperthyroidism they cause bone **resorption**.
III. **Also, in hypothyroidism bone growth is retarded.**

5- GROWTH HORMONE

I. Has strong stimulatory effect on **bone growth** dependent on somatomedins.
II. **It increase intestinal Ca^{++} absorption through vit D**
III. **It increase also renal phosphate reabsorption**

1-WHICH IS THE VALUE OF CALCIUM LEVEL IN SERUM?

4-5% (a

1-3% (b

9-11% (c

15% (d

20% (e

2- Which of these hormones mediates the action of parathormone in calcium absorption by intestine?

Growth hormone (a

Vitamin D (b

Calcitonin (c

Estrogen (d

Cortisol (e

4- WHICH OF THESE HORMONES DECREASES BLOOD CALCIUM LEVEL?

Estrogen (a

Parathormone (b

Progestrone (c

VitaminD (d

Calcitonin (e

4-WHICH OF THESE CONDITIONS CAUSES A DISEASE CHARACTERIZED BY INCREASED NEUROMUSCULAR EXCITABILITY ?

Hyperparathyroidism (a

Increased dietary calcium (b

Acidemia (c

Vit d deficiency (d

Decreased phosphorus (e

6-TETANY IS MANIFESTED BY WHICH OF THESE MANIFESTATIONS?

Extension of the wrist (a

Flexion of interphalangeal joint (b

Extension of metacarpophalangeal joint (c

Dorsiflexion of the ankle and planter flexion of the toes (d

Abduction of the thumb (e