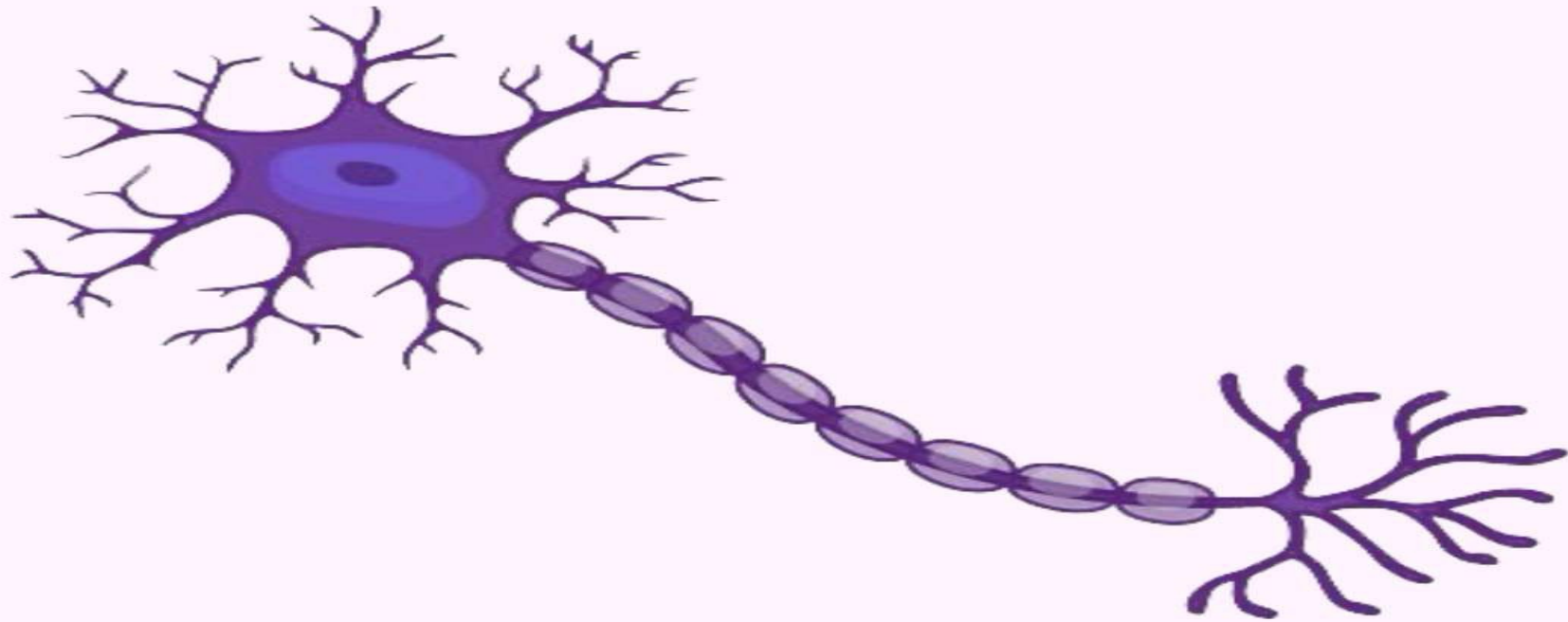




PHYSIOLOGY



LEC NO. : 18
DONE BY : Nour Al-amoush.

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



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:

Calcium functions:

1. Blood clotting هو مراحل أساسية في عملية تكوين الجلطة، العيل أدوية تفتح الدم تعمل على تكسير Ca

2. Muscle contraction

3. Neurotransmission برحوضتان يطلق Ach.

and Neuromuscular transmission.

4. Enzymatic reactions معظم التفاعلات تحتاج إلى Ca

5. Formation of milk, bone and teeth

6. Mechanism of secretion e.g. Hormone secretion

الهرمونات الموجودة في حويصلات ما يتطاع إلى تخزين Ca

7. Acts as 2nd messenger ← لأنه هو الهرمون مو قادر يدخل الخلية

(e.g. mediates hormonal action)

8. Stabilization of cell membrane

عامل زي الاسمنت و يقفل أي فتحة في 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.

← العظام نسيج متجدد
بعضه يتلصق ويكون خلايا
جديدة ، لها يتلصق يطرح
Ca ، ذأنا محتاجه دائماً .

Skeletal storage: 99% of total body calcium in bone

Plasma Ca²⁺ : -

The normal range of Ca²⁺ in plasma is ○

9-11 mg%; presents as: ○

50% : ionized; **biologically active form.** (free form)

10%: complexed in nonionic & unfilterable form (such

as CaHCO₃). (not free form) → ما بقدر أذ نتموه من
الأمعاء لأنه ما بقدر

40% is bound to proteins, mainly albumin. plasma protein

WHAT IS THE DAILY CA²⁺ REQUIREMENT?

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

Childhood → - لأنه هون في مرحلة النمو محتاج في العظام و الأسنان

Pregnancy → - لأنه الجنين بياخذ ال Ca من الأم

- **Lactation**

Absorption of Ca²⁺:

Ca²⁺ can be absorbed from all parts of small intestine especially **duodenum** by an **active transport mechanism** controlled by vit

ينظم عملية Ca امتصاص

→ **D** (w is activated in the **kidney** by **parathormone**).

vit D ينشط

Liver⁺

تعداد امتصاص

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.

Ca Balance lie في 8

FACTORS AFFECTING CALCIUM ABSORPTION AND EXCRETION

- **Calcium absorption is affected by:**

Hormones: → ↑ed by **vit D, PTH** and **GH**. → ^{Parathormone} ^{Growth hormone} يساعد في تكوين Bones

Ca²⁺ absorption decreases in: -

Vit D deficiency •

Renal failure • لأنهم لا يتم تنشيط vit D

Intestinal malabsorption • سوء امتصاص الأمعاء

Presence of unabsorbed fatty acid

in the intestine

• fatty acids + Ca
↓
- يتحدوا مع بعض ما بغير الامتصاص filtration في ما في امتصاصه لاله.

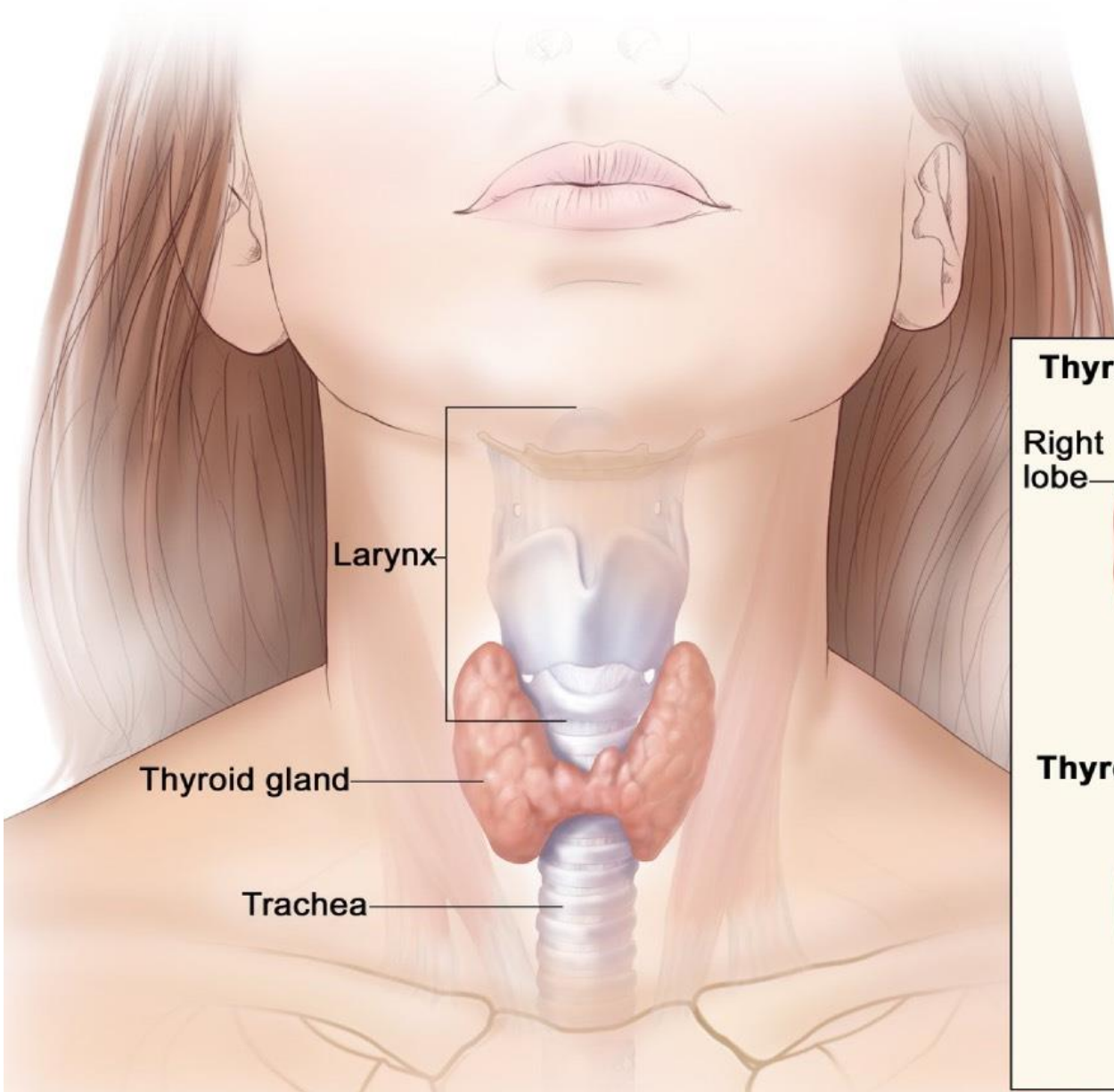
excretion of Ca²⁺ in urine: 80-400

mg/day

PARATHYROID GLANDS

- ◉ They are 4 glands present at the back of thyroid glands. (*posterior aspect*)
- ◉ 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

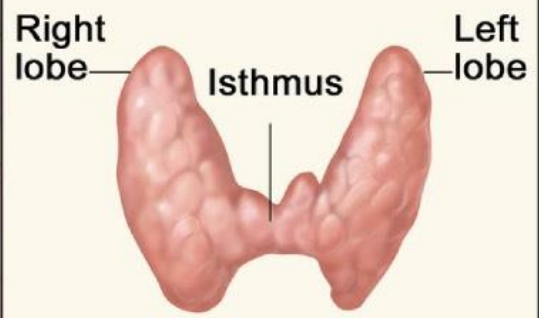


Larynx

Thyroid gland

Trachea

Thyroid gland (front view)

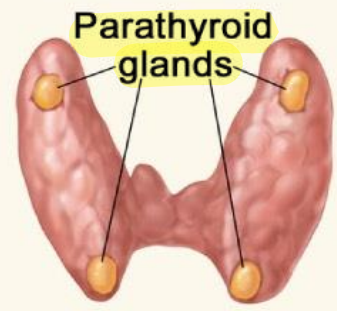


Right lobe

Isthmus

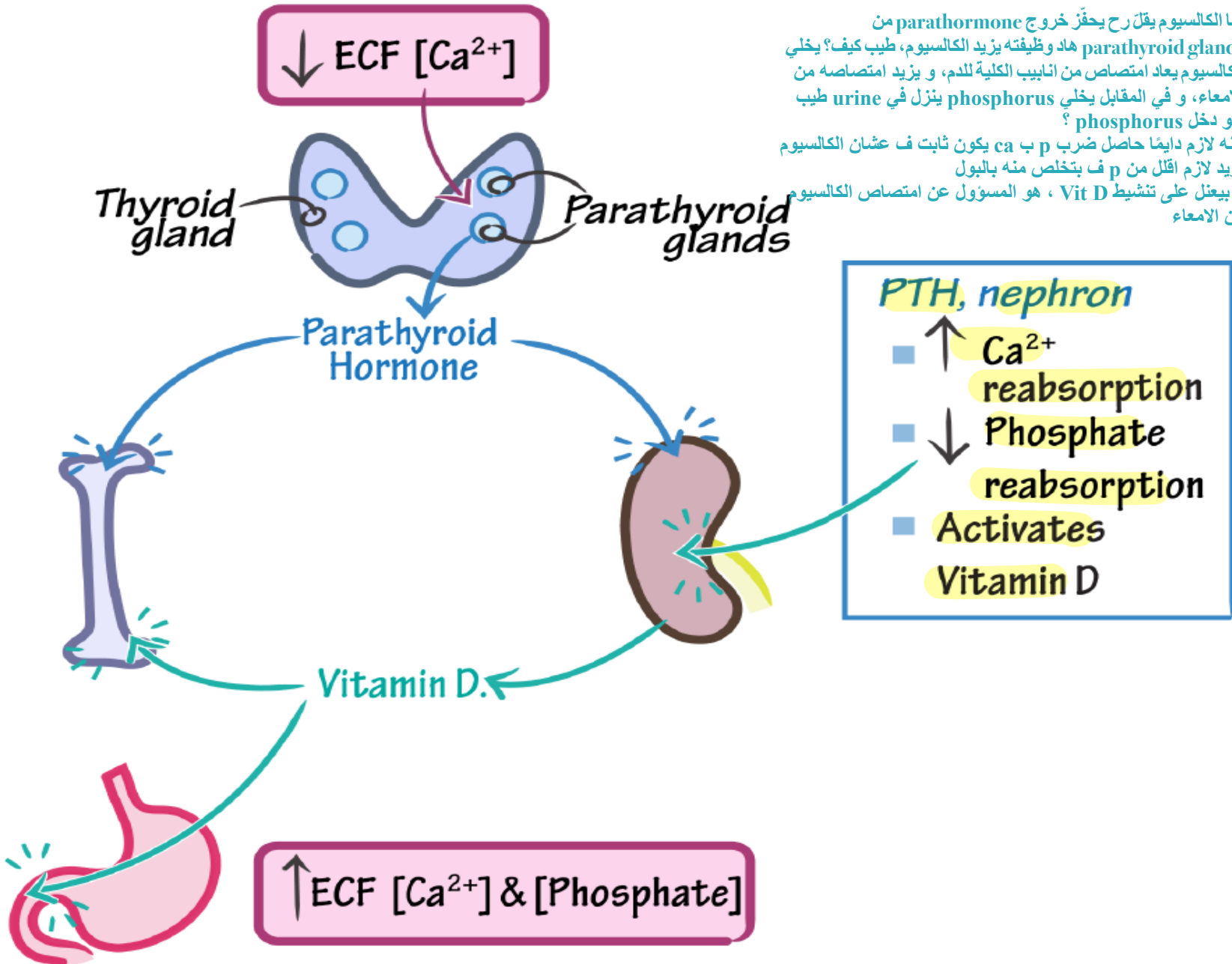
Left lobe

Thyroid gland (back view)



Parathyroid glands

Calcium Homeostasis



لما الكالسيوم يقلّ رح يحفّز خروج parathormone من parathyroid glands هاد وظيفته يزيد الكالسيوم، طيب كيف؟ يخلي الكالسيوم يعاد امتصاص من انابيب الكلية للدم، و يزيد امتصاصه من الامعاء، و في المقابل يخلي phosphorus ينزل في urine طيب شو دخل phosphorus؟
لانه لازم دائما حاصل ضرب p ب ca يكون ثابت ف عشان الكالسيوم يزيد لازم اقلل من p ف بتخلص منه بالبول و بيعمل على تنشيط Vit D ، هو المسؤول عن امتصاص الكالسيوم من الامعاء

Parathyroid hormone (pth) = parathormone

Functions:

- ◉ **The prime function of PTH is to keep Ca^{++} level (9 – 11 mg%).** *Normal level*
- ◉ Normally, the plasma inorganic phosphate is *علاقة عكسية* inversely related to Ca^{++} concentration & **the product $\text{Ca}^{++} \times \text{Po}_4^- = \text{constant}$** (solubility product).
- ◉ **The function of parathormone is to \uparrow plasma Ca^{++} & \downarrow 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. \uparrow Ca^{++} absorption

- This action is mediated by active vitamin D.

B. \uparrow phosphate & Mg^{++} absorption

2- On the bone: الشرح على الرسمة

حرارة / تحرر

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

3- On the kidney:

- \uparrow Ca^{++} & Mg^{++} reabsorption.

- \uparrow phosphate excretion التخلّص

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

DISORDERS OF THE PARATHYROID GLAND

1- Hypo-para-thyroidism → *parathyroid gland* يعني *↓ Ca level* موشالة وهذا يعني

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^{+} .** - يعني الإشارة تمر من العصب إلى العضلة بسرعة بدون محفّر و

Leading to tetany. *Action potential* *Na Channels* على طول مفتوحة ويتصل تعمل بدون محفّر و
↓
تشنجات عصبية

TETANY (التشنجات العصبية)

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

Cause: Factors that decrease Ca

1. Hypoparathyroidism

2. Renal failure due to phosphate retention.

3. Alkalaemia due to precipitation of ionized Ca^{++} الأحماض تذوب Ca بينما القواعد تتجمع Ca وتعمل complex لا يمكن امتصاصه

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 إسهال



→ wrist flexed
hand metacarpophalangeal flexed
hands extended
Thumb adducted

→ Toes flexed

TETANY

Manifestations:

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

I- Manifest tetany عنده نقص كبير	II- Latent tetany عنده نقص بس مش أوي
- Occurs if Ca^{++} is markedly ↓ i.e. < 7 mg%	- Ca^{++} isn't markedly ↓ () 7&9 mg%

Manifestations:

1- In adults, carpopedal spasm:

a) In the hands, carpal spasm:

- Flexion of the wrist & metacarpophalangeal joint.
- Extension of the interphalangeal joint.
- Adduction of the thumb.

b) In the feet, pedal spasm:

- Dorsiflexion of the ankle & plantar flexion of the toes.

2- In children : may be convulsions تشنجات

3- In infants : may be laryngeal spasm →

- No carpopedal spasm except if the person is exposed to stress. تشخيصه راجع

- The patient may feel numbness & heat flushings خدر أو تنميل في الأطراف

مكان يصير اختناق

TETANY

Treatment of tetany

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

لأنه parathormone لها أخذة على قرآن جديدة بتكون Anti bodies بتلصق به.

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

هاد المحفز

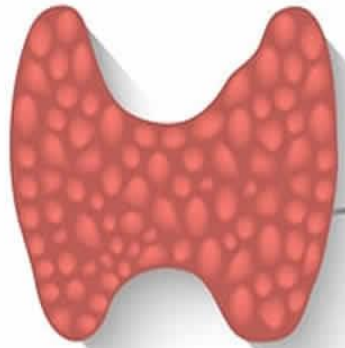
- ↑ serum Ca^{++} by 1 mg% → ↑ calcitonin release

about 10 times. *para hormone* يعمل تقريباً عكس

2. Ingestion of food :

- ingestion of food → ↑ calcitonin release.

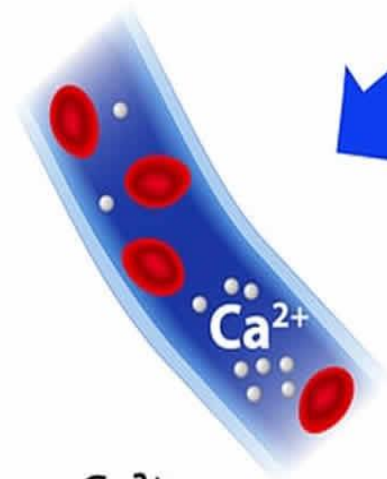
Thyroid gland



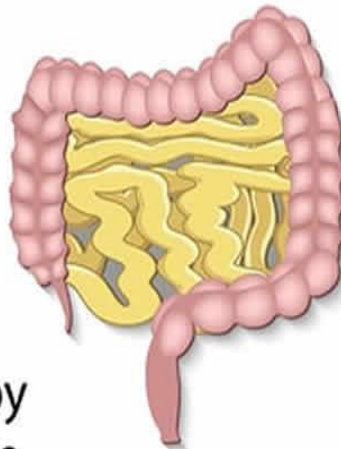
- نکلنے سے ہوتا ہے



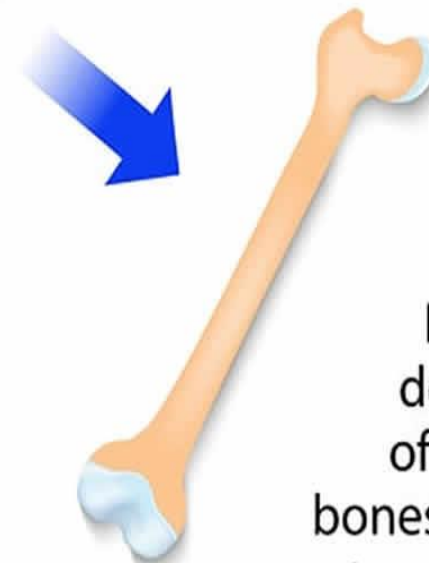
Inhibits Ca^{2+} reabsorption in the kidney (excreted in the urine)



Lowers Ca^{2+} levels in blood



Inhibits Ca^{2+} absorption by the intestines



Promotes deposition of Ca^{2+} into bones (inhibits osteoclasts and stimulates osteoblasts)

1- On the intestine:

- ↓ Ca^{++} absorption & P_{04}^{-}

2- On the bone :

يُكَبِّدُ أَصْلًا تَانِيَةً تَكْسِرُ بONE وَتَطْبَخُ Ca

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

3- On the kidney:

- ↑ urinary excretion of Ca^{++} & P_{04}^{-}
- Inhibits renal $\alpha 1$ -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, → يرضو بقل منه

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 ^① vitamin D, ^② estrogens and ^③ androgens, ^④ glucocorticoids, ^⑤ thyroid hormones, and ^⑥ growth hormone.
from adrenal gland

*بالعقد
تأثير وبناء
العظام.* 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 : *تأخذ* function to resorb bone

1- VITAMIN D → same action as parathormone

- **Vitamin D** have both **dietary & endogenous precursors** :
 - I. **Vitamin D₂** (ergo-calciferol) formed in plants
 - II. **Vitamin D₃** (chole-calciferol) formed in the skin by the ultra-violet rays (UVR)

Actions:

1- On the intestine :

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

عشان يترسبوا في
• Bones

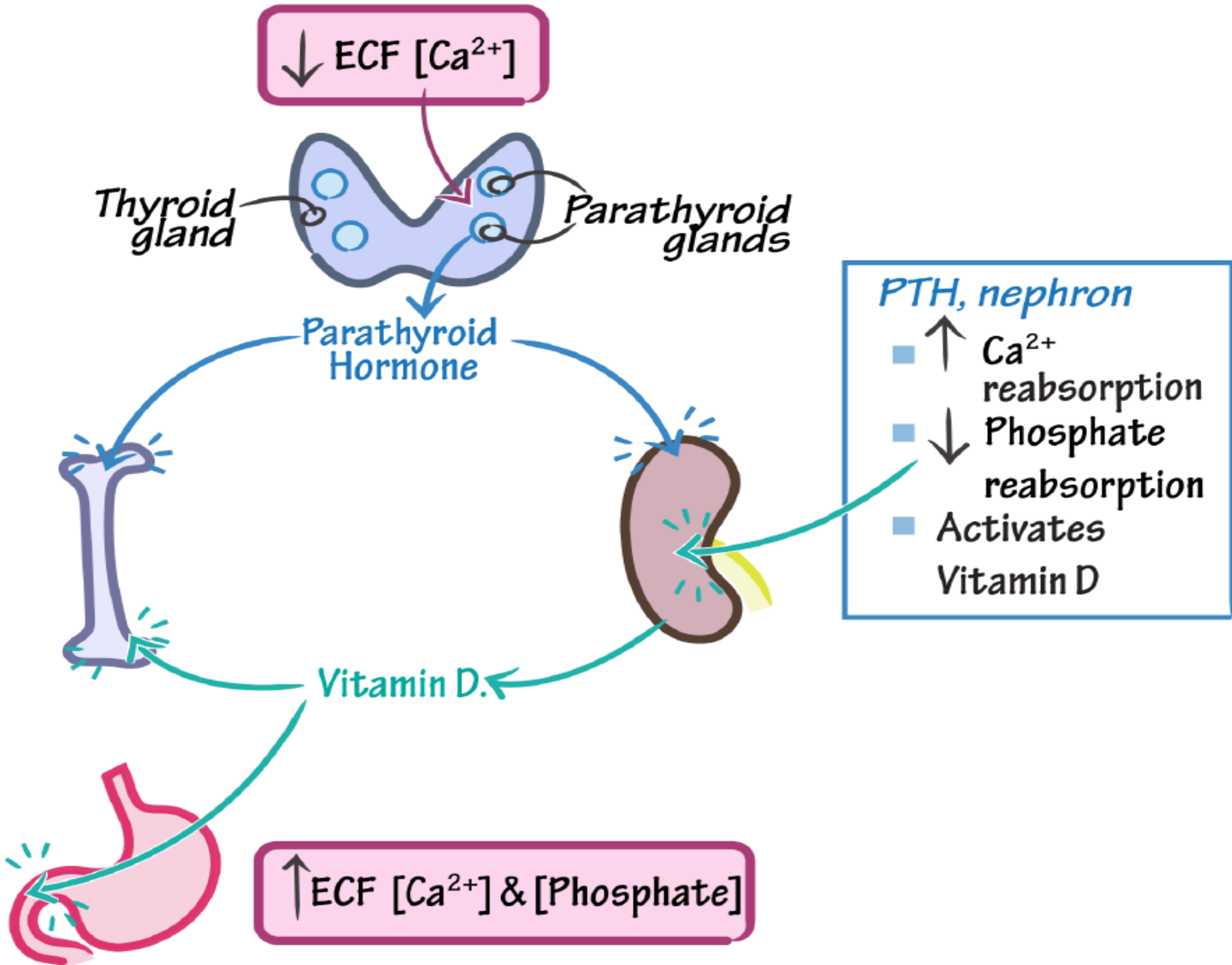
2- On the kidney:

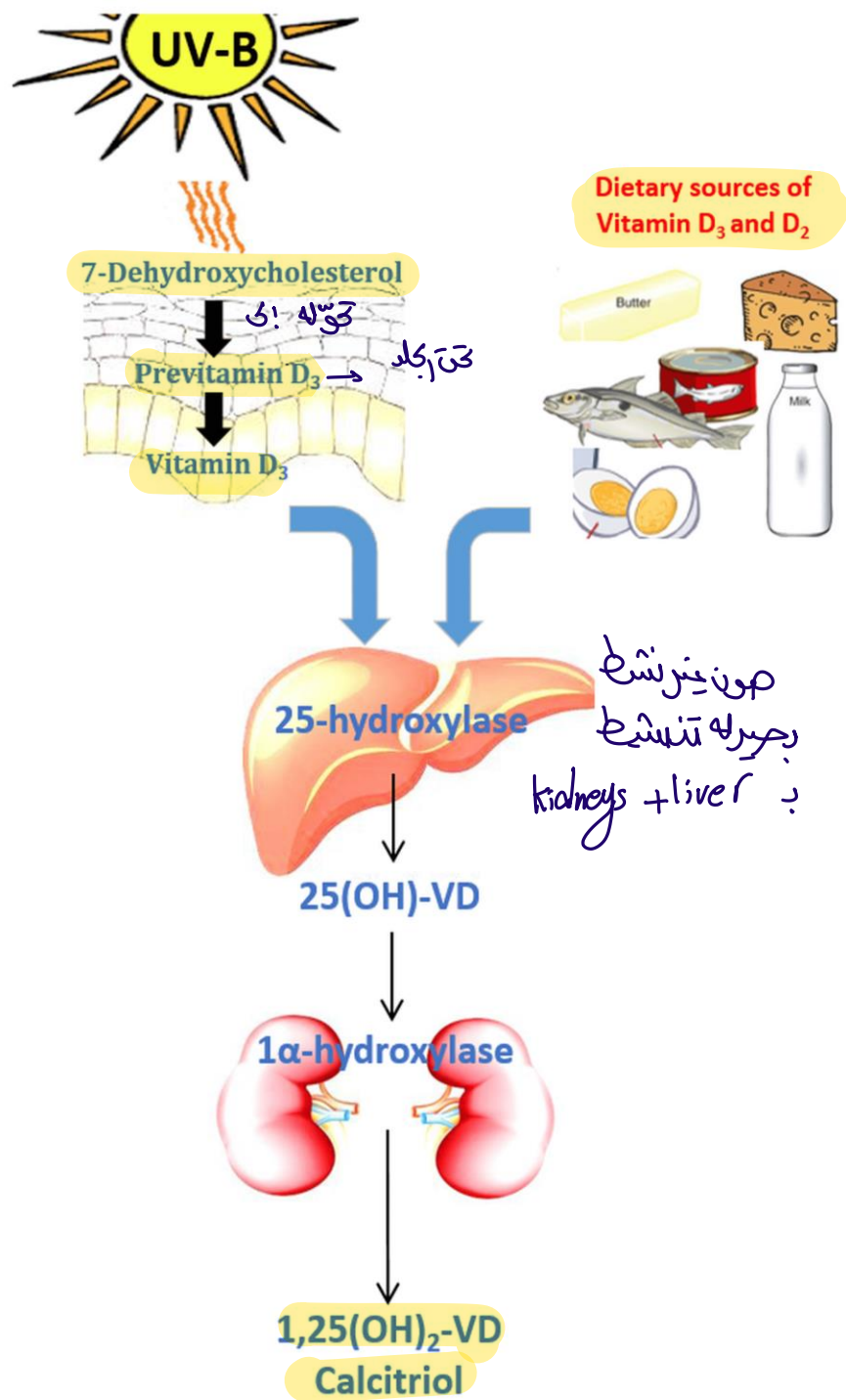
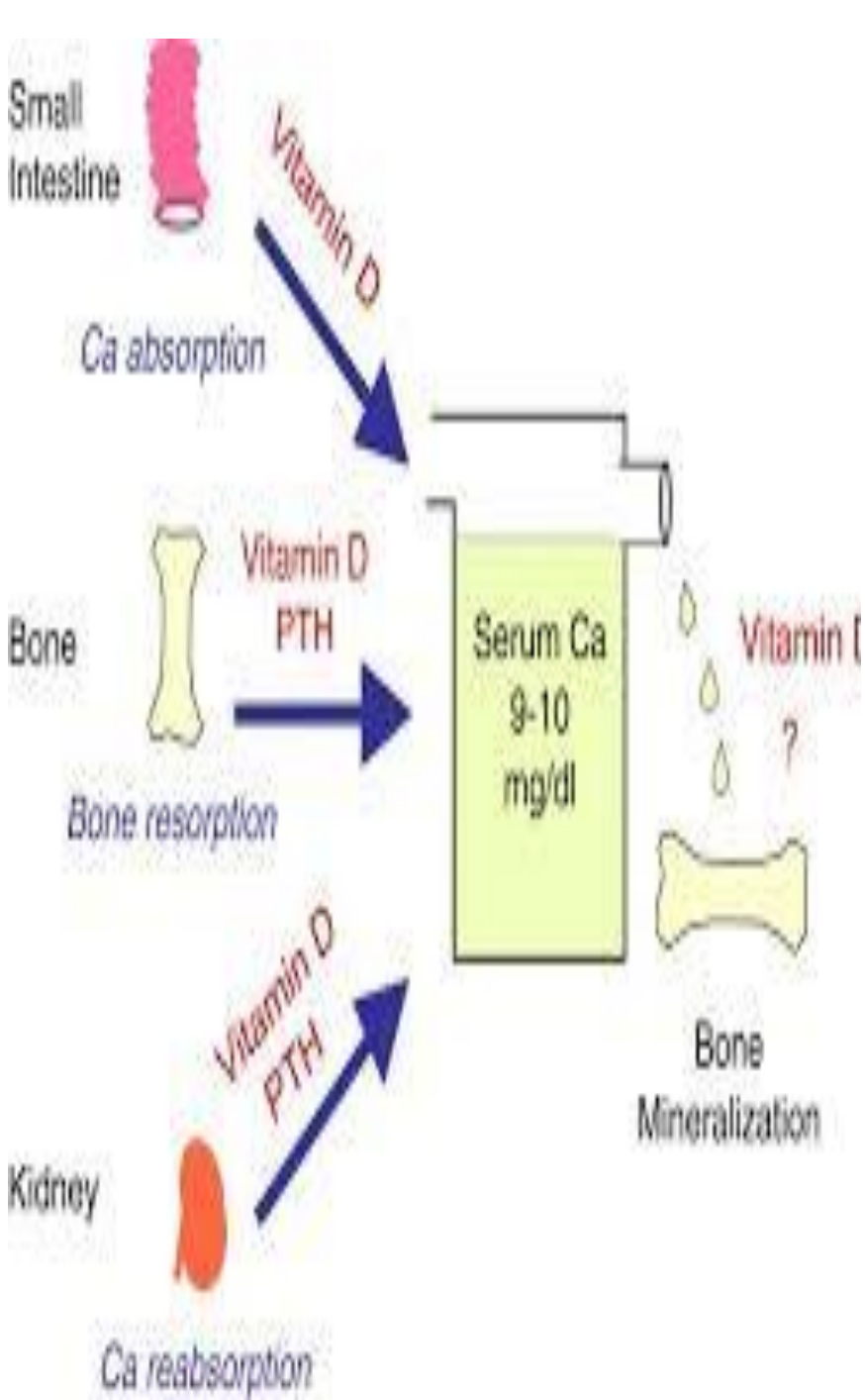
- it stimulates re-absorption of both Ca^{++} & phosphate.

3- On the bone:

- it provides Ca^{++} & phosphate needed for bone formation.
- it promotes differentiation of monocyte precursors to monocytes & macrophages.

Calcium Homeostasis





Females

Males

2- ESTROGENS & ANDROGENS

- Have a role in childhood & ^{البلوغ} puberty.
- These hormones **favours bone formation** over resorption.
- **In the female estrogen protect the skeleton from development of osteoporosis.**
- عند females لا ينقطع الكالسيوم ما يكون في estrogen في العظام عندها تضعف هشاشة العظام

3- GLUCOCORTICOIDS

- I. At **physiological** levels they are essential for skeletal growth.
- II. At **high level** they have deleterious effect on Ca^{++} homeostasis.
تأثير ضار

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 → Indirect action

- 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

عشان يترسب في
Bone

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)