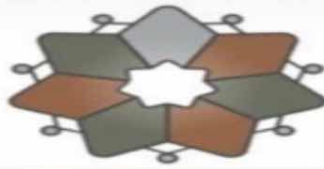


جائزة الخسین
بن عبد الله الثاني
للقمل التطوعي

AL HUSSEIN BIN ABDULLAH II
AWARD FOR VOLUNTARY WORK



النادي الطبي
Medical Club



General Surgery



Subject: _____

Parathyroid disease

Group no: _____

Done by: _____

Sadeel Alfaqeer

Parathyroid Disease

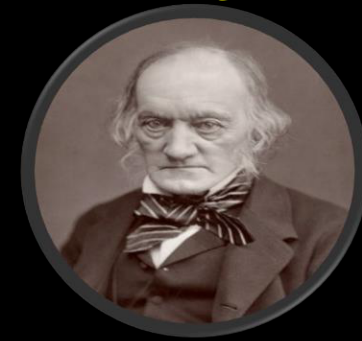
- ↳ Primary hyperparathyroidism
- ↳ Secondary hyperparathyroidism
- ↳ Tertiary hyperparathyroidism

Dr Sohail Bakkar MD, Ph D

Asst. Prof. Endocrine & General Surgery (Hashemite University)

Parathyroid Glands

The last human organs to be discovered
↳ Glands of Owen

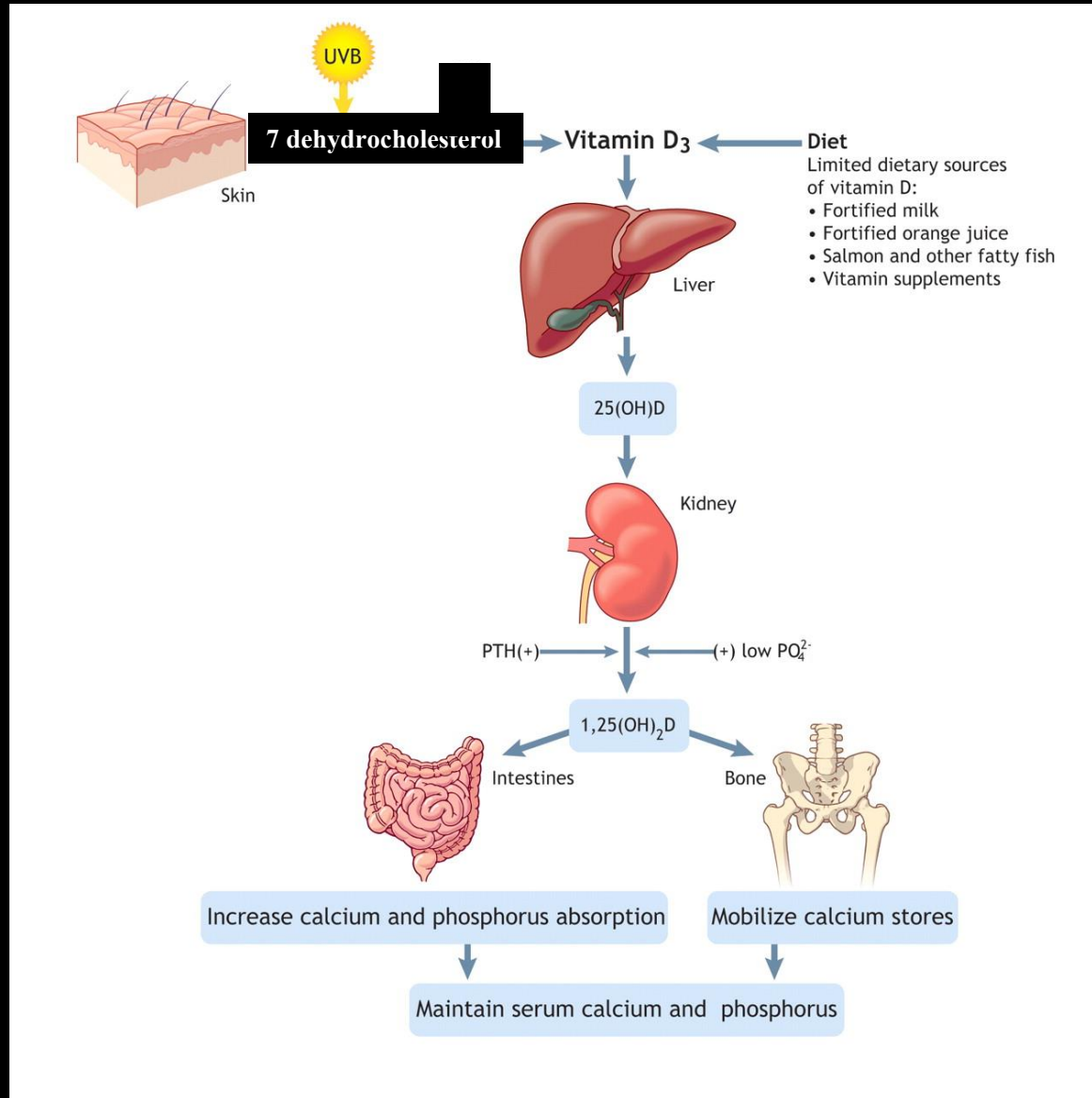


1862

العالم البريطاني Richard Owen كان
يدرس تشريح حيوان الـ rhinoceros
(وحيد القرن). أثناء التشريح، لاحظ وجود
غدد صغيرة جداً خلف الغدة الدرقية ما
كانت معروفة قبل. هاي كانت أول مرة يتم
فيها وصف الـ parathyroid glands.

Modarai B, Sawyer A, Ellis H. The glands of Owen. J R Soc Med 2004; 97(10):494-495.

Vitamin D metabolism



* in general, Calcium homeostasis is controlled by 3 hormones: parathyroid glands

Vitamin D

Calcitonin

* major source of Vit D is solar irradiation of skin which convert 7 dehydrocholesterol in $\sim$ to active form of Vit D which is known as Vit D₃ or cholecalciferol

2 phases of activation:

1. in liver, undergoes its first hydroxylation & converted to 25 hydroxycholecalciferol
 2. then in kidney $\rightarrow$ converted into 1,25 dihydroxycholecalciferol (final & active form)

The enzyme that is responsible of Hydroxylation of Vit D₃ in kidney is Renal 1 alpha Hydroxylase & The catalyst of this enzyme is PTH, so both are imp
 (تسرع)

Bone mineralization

Calcium homeostasis is regulated by three main hormones:

Parathyroid hormone (PTH)

Vitamin D (Calcitriol)

Calcitonin

Vitamin D synthesis:

The major source of Vitamin D is sunlight (UVB).

UVB converts 7-dehydrocholesterol in the skin into Vitamin D3 (cholecalciferol).

Activation of Vitamin D occurs in two steps:

In the liver:

Vitamin D3 is converted to 25-hydroxycholecalciferol (25-OH Vitamin D)

In the kidney:

It is converted to the active form:

1,25-dihydroxycholecalciferol (Calcitriol)

Key enzyme:

The renal enzyme responsible is 1-alpha hydroxylase

Role of PTH:

PTH stimulates 1-alpha hydroxylase

→ increases production of active Vitamin D (Calcitriol)

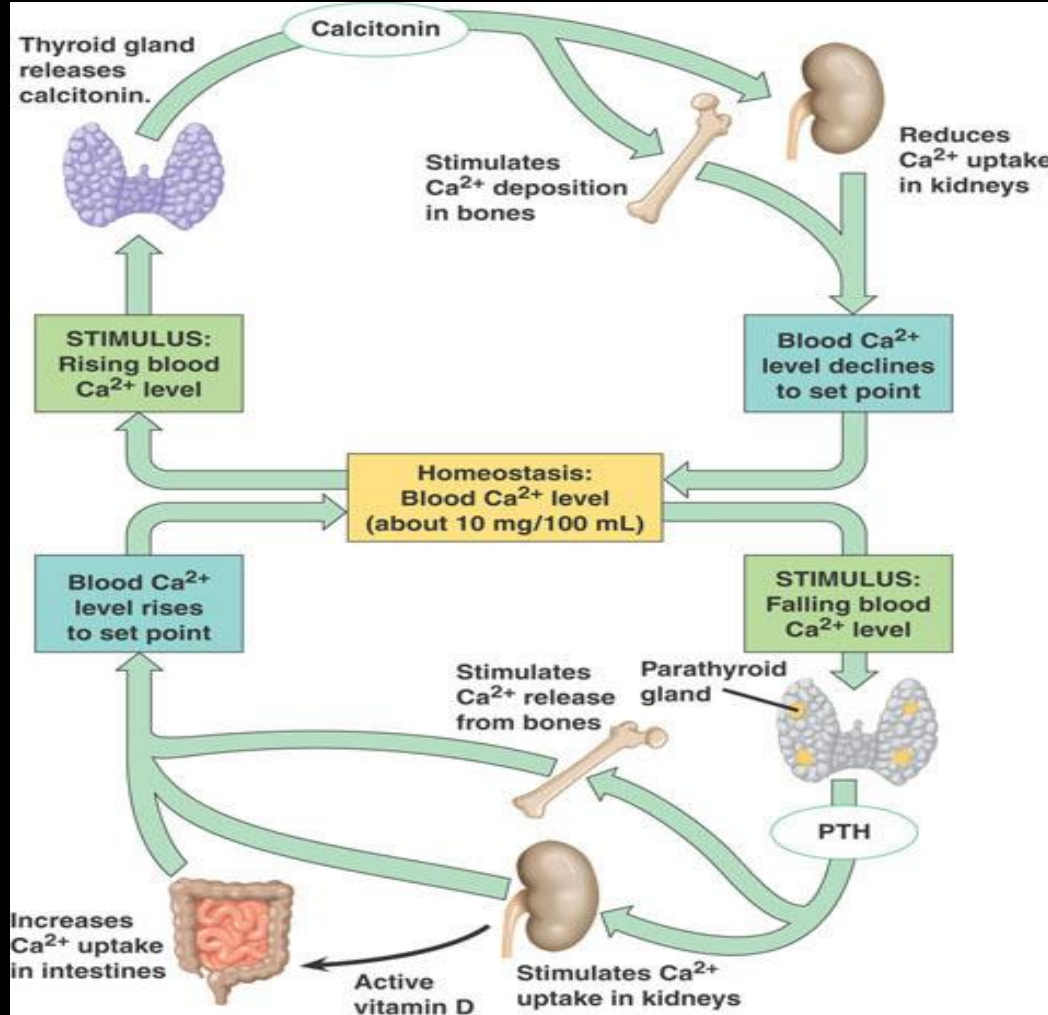
Summary:

PTH and Vitamin D work together to increase blood calcium levels.

Main role of active vit D3 is to increase absorption of Dietary calcium from intestine, any deficiency in vit D3 → you will have deficiency in calcium
Remember: one of major causes of 2ndry hyperparathy is Vit D deficiency

Calcitonin is a hormone secreted by the parafollicular (C) cells of the thyroid gland in response to elevated serum calcium levels. Its primary action is to lower blood calcium by directly inhibiting osteoclast activity, thereby reducing bone resorption and limiting the release of calcium from bone stores. It also has a minor effect on the kidneys by increasing urinary calcium excretion. However, in humans—especially adults—its role in overall calcium homeostasis is relatively limited compared to parathyroid hormone (PTH) and vitamin D. This is evidenced by the fact that absence of calcitonin does not result in significant disturbances in calcium balance. Thus, calcitonin functions mainly as a protective, short-term regulator against hypercalcemia rather than a primary controller of calcium homeostasis

Calcium Homeostasis



3 hormones:

* **Active form of vit D**

1, 25 Dihydroxy cal--

* **PTH**

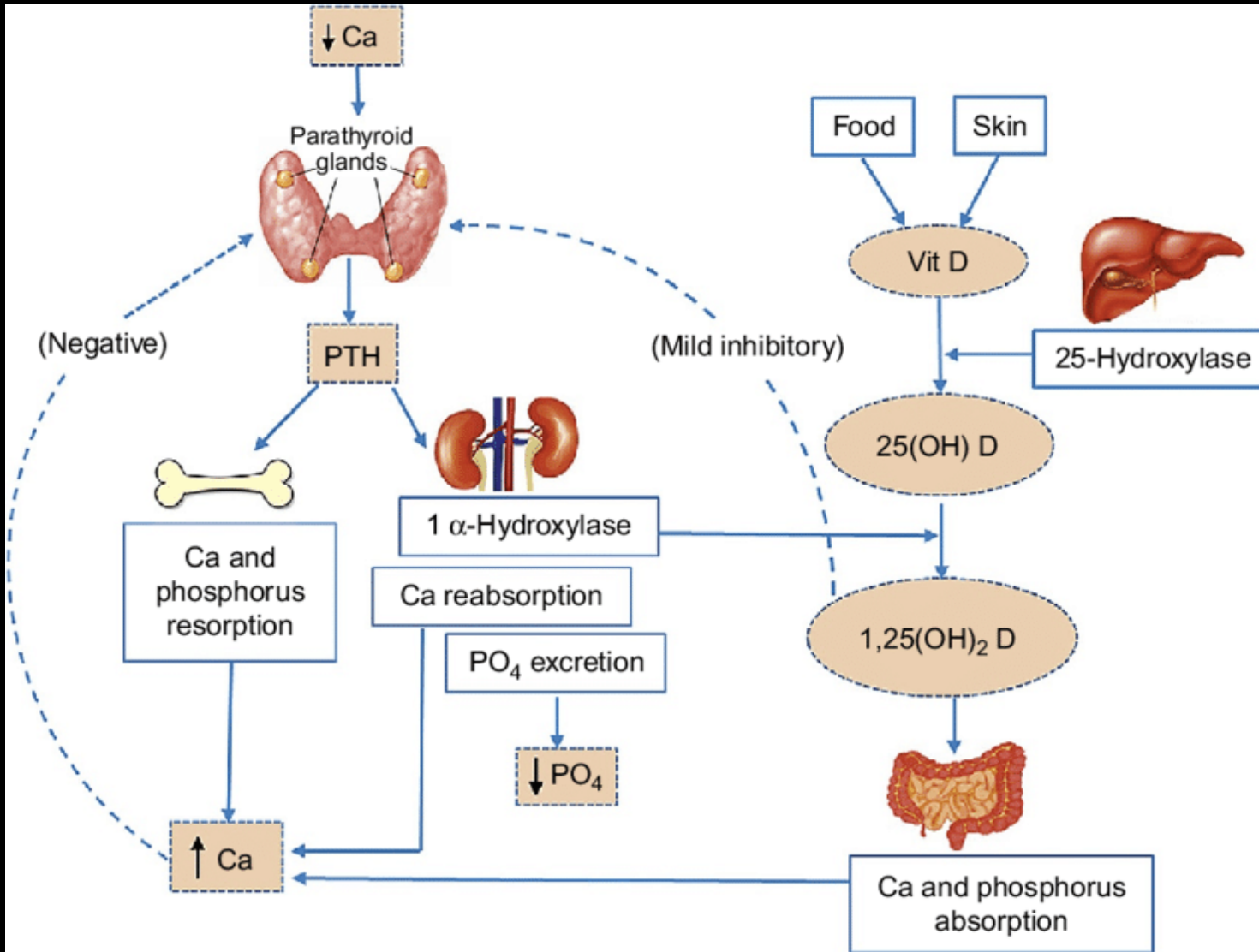
↳ only endocrine glands that not controlled by hypothalamic pituitary axis

* **Calcitonin**

major regulator of calcium homeostasis
it has role opposite to PTH ($\downarrow$ Ca level)

↳ active form
it's controlled by ionized serum calcium levels, if $\downarrow \rightarrow$ Parathy. stimulating & vice versa.

Calcium Homeostasis



Calcium forms:

- ★ **50% free (ionized)**
active that regulate PTH secretion
- ★ **40% albumin bound**
inactive
- ★ **10% Anion bound (Phosphorous, citrate)**
inactive

When active Ca $\downarrow\downarrow$, This will stimulate the 4 parathyroid glands to release PTH, PTH affects bones & $\uparrow\uparrow$ Ca & phosphorus resorption to $\uparrow\uparrow$ serum concentration of Ca^{2+} , It goes to kidney & catalyst of 2nd Hydroxylation of vit D_3 by stimulating renal 1 α Hydroxylase. to produce more of active vit D to $\uparrow$ abs.. of calcium & Phosphorus.

Primary = problem is in gland (Parathyroid adenomas or all 4 glands being hyperplastic)

Hypoparathyroidism

Secondary: 2ndry to some problem that caused Ca deficiency

In Primary --> the gland is autonomously releasing it's product in excess, without Ca def. in blood $\uparrow\text{PTH}$, $\uparrow\text{Ca}$

In 2ndry is the excess release of PTH is the compensatory mechanism is 2ndry to some factor that has $\downarrow$ or drop in serum Ca

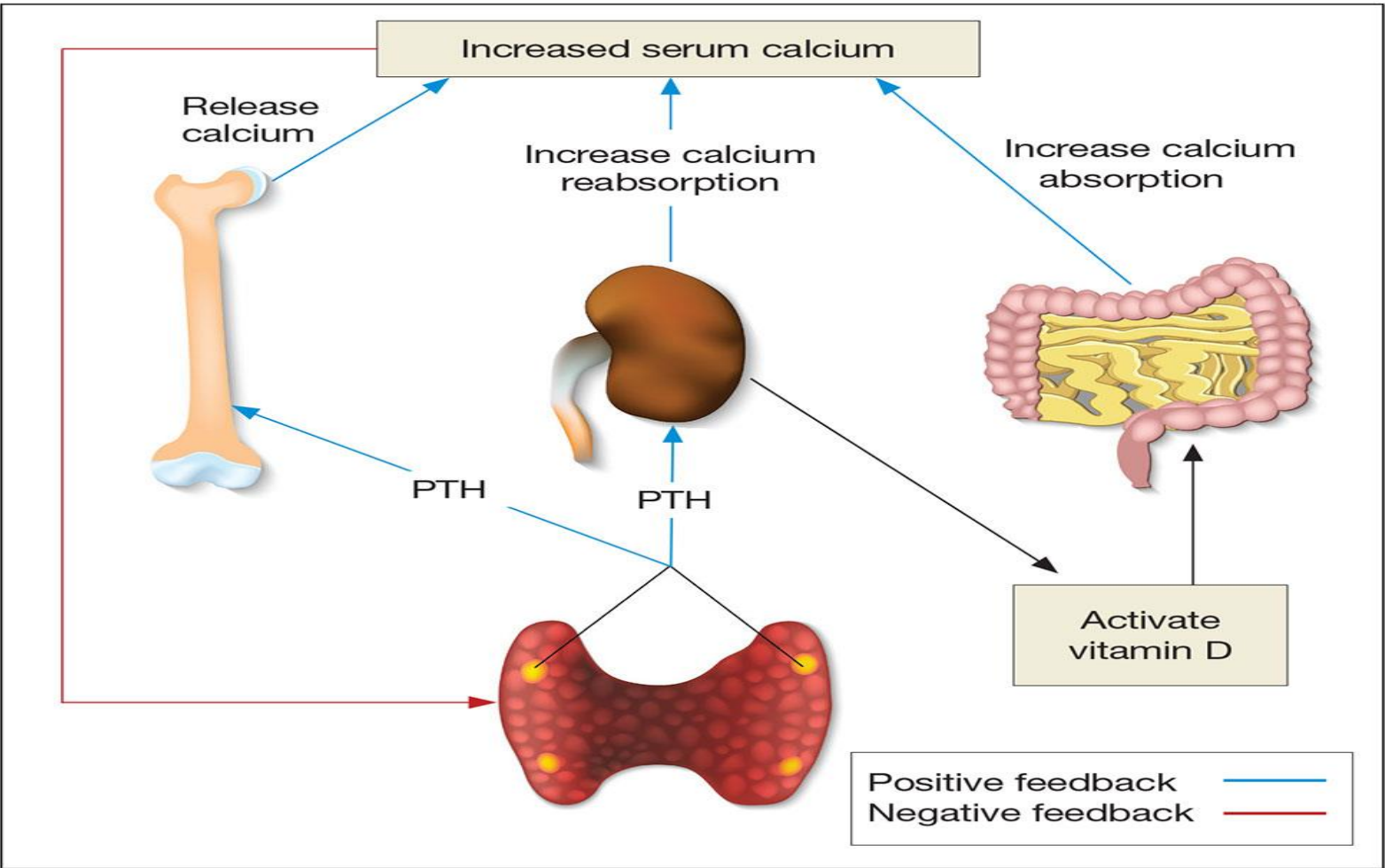
serum Ca: normal or $\downarrow\downarrow$
PTH: $\uparrow\uparrow$

$\rightarrow$ vit D deficiency $\rightarrow$ $\downarrow\downarrow\downarrow$ absorption of Ca from intestine

$\rightarrow$ Renal failure CKD: Renal $\propto$ 1 α Hydroxylase

$\downarrow\downarrow\downarrow$ Ca $\leftarrow$ No active Vit D_3 $\leftarrow$ No 2nd Hydroxylation of Vit D_3

Parathyroid Hormone – Calcium Feedback



The parathyroid glands (unlike other endocrine glands) are not controlled by the hypothalamic-pituitary axis. They are controlled by ionized serum calcium levels (active form of calcium).

Ionized calcium receptors on parathyroids are G-protein membrane receptors
act on para-glands

Serum calcium levels are modulated by PTH secretion by action on bone, kidneys, and intestines. PTH stimulates osteoclastic release of calcium directly into the blood. Kidneys are stimulated to increase reabsorption of calcium and convert 25-hydroxy-vitamin D to the active form of vitamin D. Vitamin D prompts gastrointestinal calcium absorption. All three pathways in the positive feedback loop result in increased serum calcium levels. In the negative feedback loop, high serum levels suppress PTH secretion; low levels stimulate PTH secretion.

Sources: Kapustin and Schofield. *Nurse Pract.* 2012³; Michels and Kelly. *Am Fam Physician.* 2013.⁸

Calcium Homeostasis

	PTH	Calcitriol	Calcitonin
Stimulus for secretion	$\downarrow$ serum $[\text{Ca}^{2+}]$ $\uparrow$ serum $[\text{PO}_4^{3-}]$ $\downarrow$ serum [calcitriol]	$\downarrow$ serum $[\text{Ca}^{2+}]$ $\downarrow$ serum $[\text{PO}_4^{3-}]$ $\uparrow$ PTH	$\uparrow$ serum $[\text{Ca}^{2+}]$
Actions:			
Bone	$\uparrow$ resorption of bone	$\uparrow$ resorption of bone	$\downarrow$ resorption of bone
Kidney	$\uparrow$ Ca^{2+} reabsorption $\downarrow$ phosphate reabsorption	$\uparrow$ Ca^{2+} and phosphate reabsorption $\uparrow$ Ca^{2+} and phosphate absorption	$\uparrow$ excretion of Ca^{2+} and phosphate
Intestines	$\uparrow$ Ca^{2+} absorption (via activation of calcitriol)		None
Net effect	$\uparrow$ serum $[\text{Ca}^{2+}]$ $\downarrow$ serum $[\text{PO}_4^{3-}]$	$\uparrow$ serum $[\text{Ca}^{2+}]$ $\uparrow$ serum $[\text{PO}_4^{3-}]$	$\downarrow$ serum $[\text{Ca}^{2+}]$

Causes of Hyperparathyroidism

Primary	Secondary- In response to hypocalcemia	Tertiary
90% tend to be benign couldn't be palpable as neck mass. But if aggressive could be palpable •Parathyroid Adenoma, Hyperplasia, Carcinoma ↳ 4 glands dx •MEN 1 or MEN 2a ↳ 3 pts ↳ pheochr... ↳ MTC ↳ hyperparathy... •Familial hypocalciuric hypercalcemia •Hyperparathyroid-jaw tumor (HPT-JT) syndrome •Familial isolated hyperparathyroidism (FIHPT)	•Renal Failure ✗ -Impaired calcitriol production impaired 1α hydroxylase -Hyperphosphatemia ↳ Anion bind to Ca → convert it to inactive ↓ hypocalcemia •Decreased calcium -Low oral intake -Vit D deficiency ✗ -Malabsorption -renal calcium loss – lasix •Inhibition of bone resorption -Bisphosphonates -Hungry Bone Syndrome	•Autonomous hypersecretion of parathyroid hormone -chronic secondary hyperparathyroidism -After renal transplantation ↳ in 3% the glands became Autonomously secreted PTH, ↑ Ca ↳ even with new kidney. 2dy هم كانوا - بعد التقليل من الكالسيوم - منطلقوا Tertiary

Parathyroid carcinoma accounts for only 1% of cases of primary hyperparathyroidism

	Primary Hyperparathyroidism	Secondary Hyperparathyroidism	Tertiary Hyperparathyroidism
Calcium	↑	↓/N	↑
PTH	↑	↑	↑↑
Phosphate	↓	↑/N	↑

Manifestations of Primary Hyperparathyroidism

System	Signs and symptoms	Mechanism
<u>Renal</u>	Nephrolithiasis, nephrocalcinosis, recurrent urinary tract infections, renal impairment Polyuria, dehydration	Hypercalcemia, hypercalciuria, and hyperphosphaturia Calcium phosphate precipitates in alkaline urine, calcium oxalate stones form; stones formed in the renal pelvis or collecting ducts are associated with increased risk of infection Hypercalcemia has a direct effect on renal tubules, causing a decreased response to antidiuretic hormone
<u>Musculoskeletal</u>	Osteoporosis, osteitis fibrosa cystica, fractures, muscle weakness, myalgia Arthralgia, arthritis	Excess PTH excretion leads to metabolic acidosis, bone resorption, and myopathic changes Hyperuricemia leads to gout, pseudogout
<u>Gastrointestinal</u>	Abdominal pain, constipation, anorexia, nausea, vomiting Peptic ulcer disease Pancreatitis (less common)	Hypercalcemia decreases gastrointestinal motility, stimulates the central vomiting center, and increases gastrin secretion Hypercalcemia stimulates elevated hydrochloric acid secretion Exact mechanism unknown; gastrin weakly stimulates pancreatic enzymes and gallbladder contraction
<u>Neurologic/psychiatric</u>	Memory impairment, depression, anxiety, confusion, stupor, coma	Hypercalcemia induces neuropathy, electroencephalographic changes
<u>Cardiovascular</u>	Hypertension	Hypercalcemia has direct effect on arterial smooth muscle and elevates plasma renin activity

Sources: Brashers et al. *Pathophysiology*. 2015⁶; Michels and Kelly. *Am Fam Physician*. 2013⁸; Bilezikian et al. *J Clin Endocrinol Metab*. 2014.¹⁹

Hypercalcemia / Hyperparathyroidism Signs



knowmedge

Mnemonic: "Bones, Stones, Groans, Moans"

Painful Bones	Painful bone condition (Classically osteitis fibrosa cystica) Osteoporosis, osteitis fibrosa cystica, fractures, muscle weakness, myalgia
Renal Stones	Kidney Stones (Can ultimately lead to Renal failure) <i>Ca oxalate no Ca phosphate stones</i>
Abdominal Groans	GI symptoms: Nausea, Vomiting, Constipation, Indigestion <i>epigastric pain (as PUD) → ↑PTH → ↑ basal acid secret.</i>
Psychiatric Moans	Effects on nervous system: lethargy, fatigue, memory loss, psychosis, depression <i>↑ anxiety → over excitability of reflexes</i>

Most cases of primary hyperparathyroidism are asymptomatic

Accuracy of Imaging Studies

Not for diagnosis (Diagnosed biochemically)...
for localization pre operatively.

Imaging Study	Sensitivity, % (95% CI) <i>* قد يش الفحص قادر - محدد الموضع</i>	Specificity, % (95% CI) <i>* قد يش الشغف بطول +ve للشغف الصواب في تحليل السليم</i>	Positive Predictive Value, % (95% CI)
MIBI	69 (66-73)	<u>92</u> (90-94)	89 (85-92)
<u>1.</u> US	<u>63</u> (59-67)	<u>90</u> (87-92)	89 (86-92)
MIBI and US imaging positive for same site (concordant)	56 (51-60) <i>طبعيا ينزل لا يش بدنا الـ 2 يكونوا صحيح بعض</i>	<u>60</u> (56-64)	<u>99</u> (97-100) <i>properly localisation الـ 2 في اتفقوا على نفس المكان فخله اكله قريب الـ 100 يكونه الكامع</i>

بعد ما نشيل ما بنهي العليه بنسب
بما 5 د الـ 10 و PTH و HbA1c بنسب الـ
PTH level بنسب 15-65

Targeted or (minimally) go to operate
invasive to remove this gland
Parathyroid surgery

(Normal PTH level 15-65) if it is 100 it should go to normal level after removal

2014 Guidelines for Surgery in Asymptomatic Primary Hyperparathyroidism (Bilezikian et al. JCEM, 2014)

Recommended Index

Serum calcium (above normal)

Skeletal

Renal

Age

3rd Int'l Workshop
(Bilezikian et al. JCEM 2009)

اكتر من الطبيعي
→
>0.25 mmol/L
or >1 mg/dL

DXA: T-Score < -2.5 at any site; any fragility fracture

هشاشة العظام

كيف نحسب؟
هو عبارة عن عدد (SD) standard deviations عن المتوسط.
• إذا T-score = 0 طبيعي تمامًا (مثل الشخص الشاب)
• إذا T-score = -1 أقل شوي
• إذا T-score = -2.5 أقل بكثير (وهنا الخطورة)

التصنيف المعتمد عالميًا (WHO):
• Normal: ≥ -1
• Osteopenia: بين -1 و -2.5
• Osteoporosis: ≤ -2.5

eGFR < 60 mL/min

24 hr urine: Not recommended

بس بال 2014 تغير

<50

4th Int'l Workshop
(Bilezikian et al., 2014)

> 0.25 mmol/L

DXA: T-Score < -2.5 at any site;

Vert Fx by X-ray or VFA Fracture

eGFR < 60 mL/min

Stone by X-ray, CT, or ultrasound or KUB

Urinary calcium: >10 mmol/d plus other urinary biochemical indices of increased stone risk

< 50

Primary Hyperpar--

