Parathyroid glands (1)

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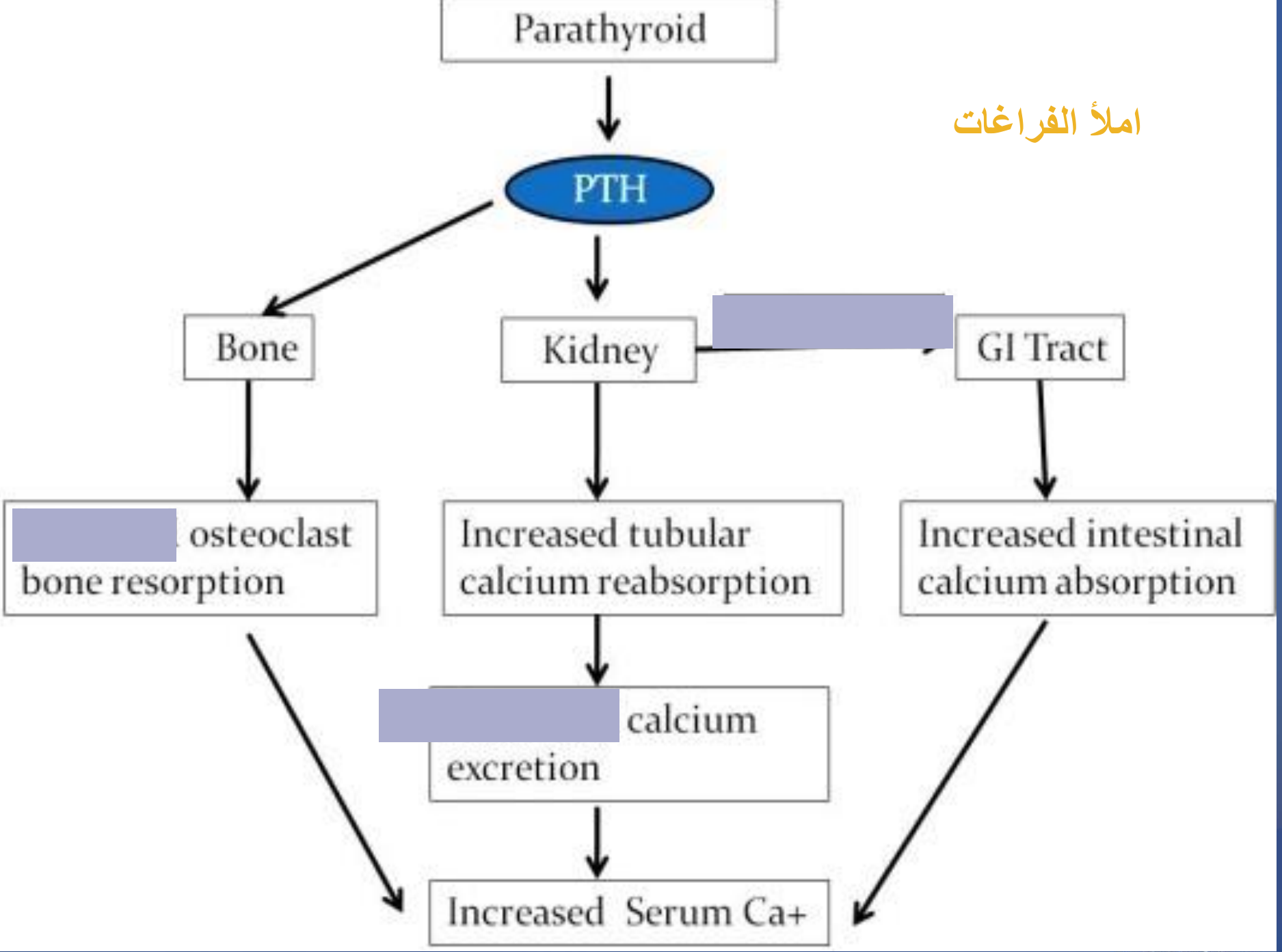
أ. م. د. زينب العرفي

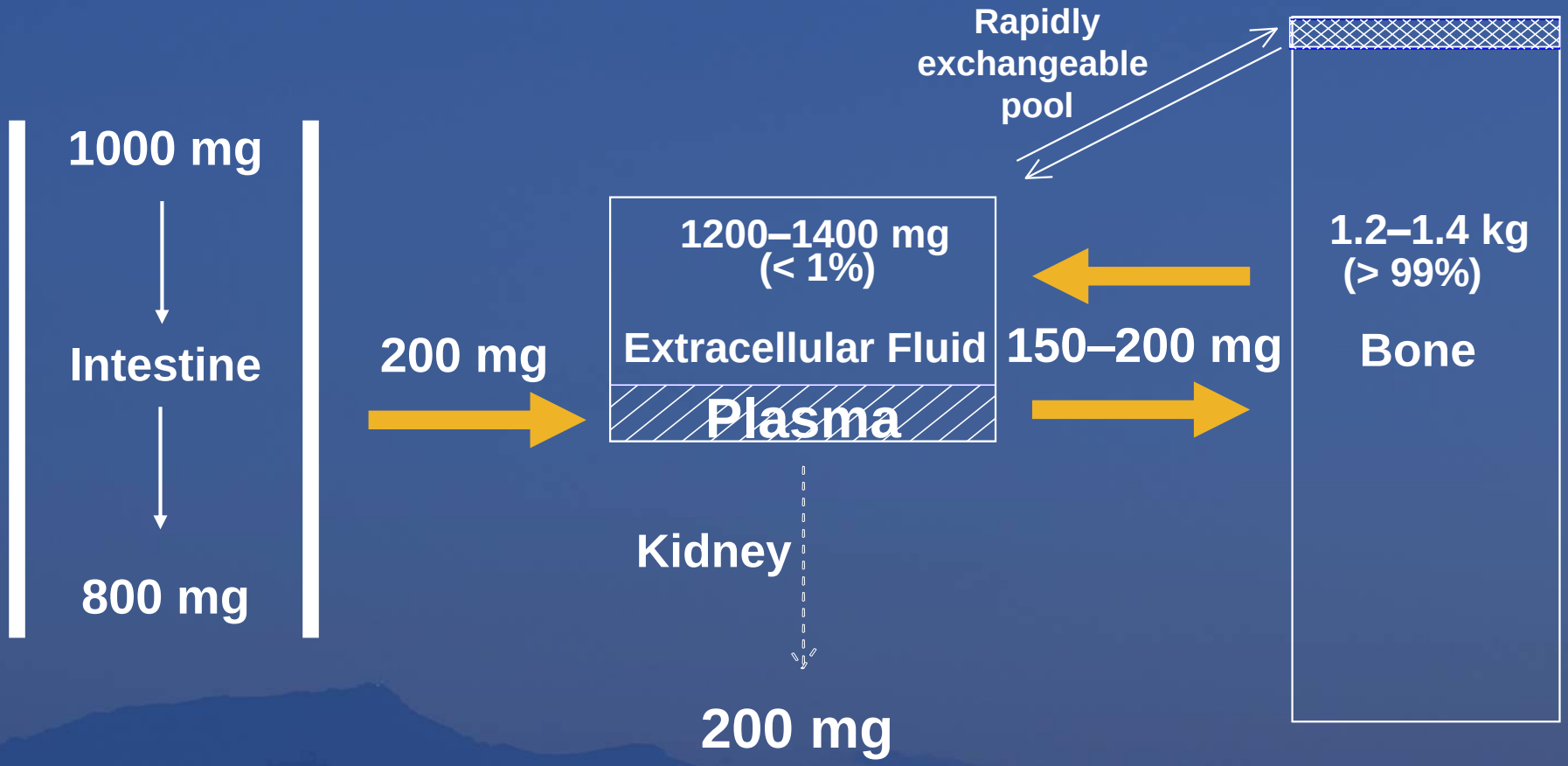
الكالسيوم

- استتباب الكالسيوم:
  - هرمون جارات الدرق
  - الكالسيتونين
  - ٢٥ هدروكسي فيتامين د

املأ الفراغات

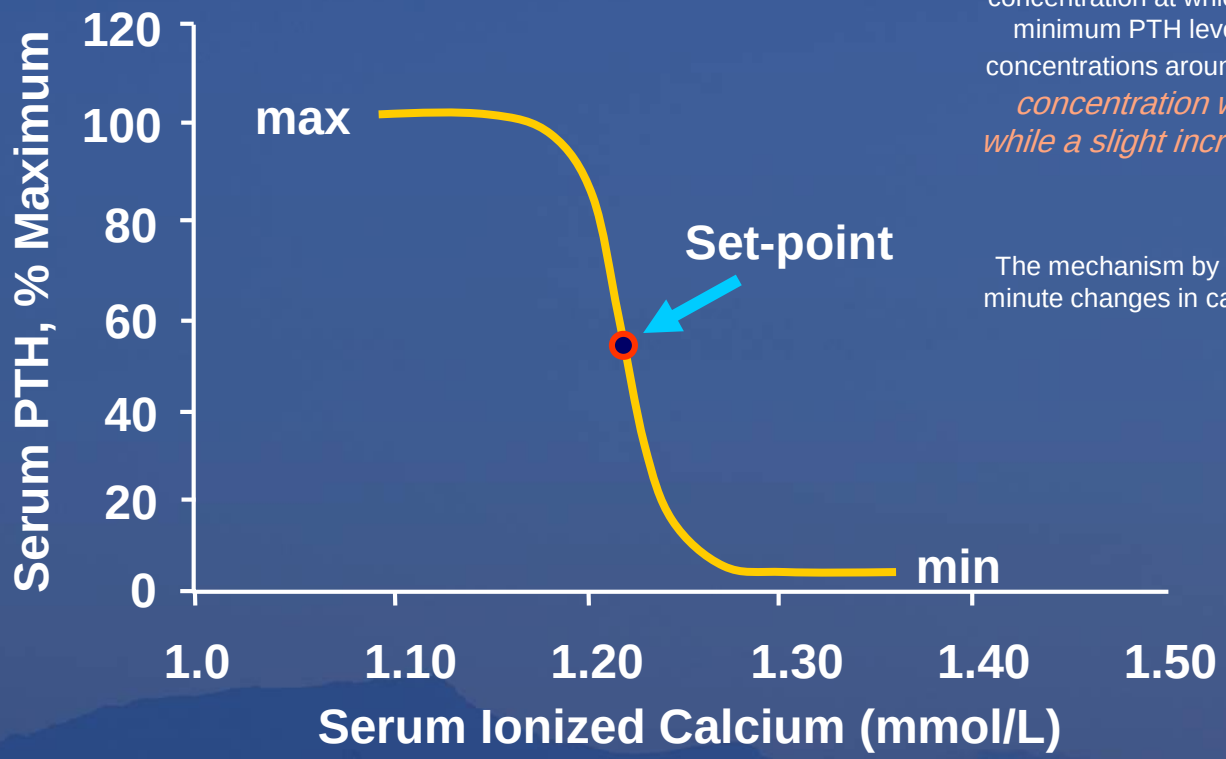


Normal Calcium Homeostasis



Goodman WG. *Med Clin North Am.* 2005;89:631-647.

Calcium Is a Sensitive Regulator of PTH Secretion

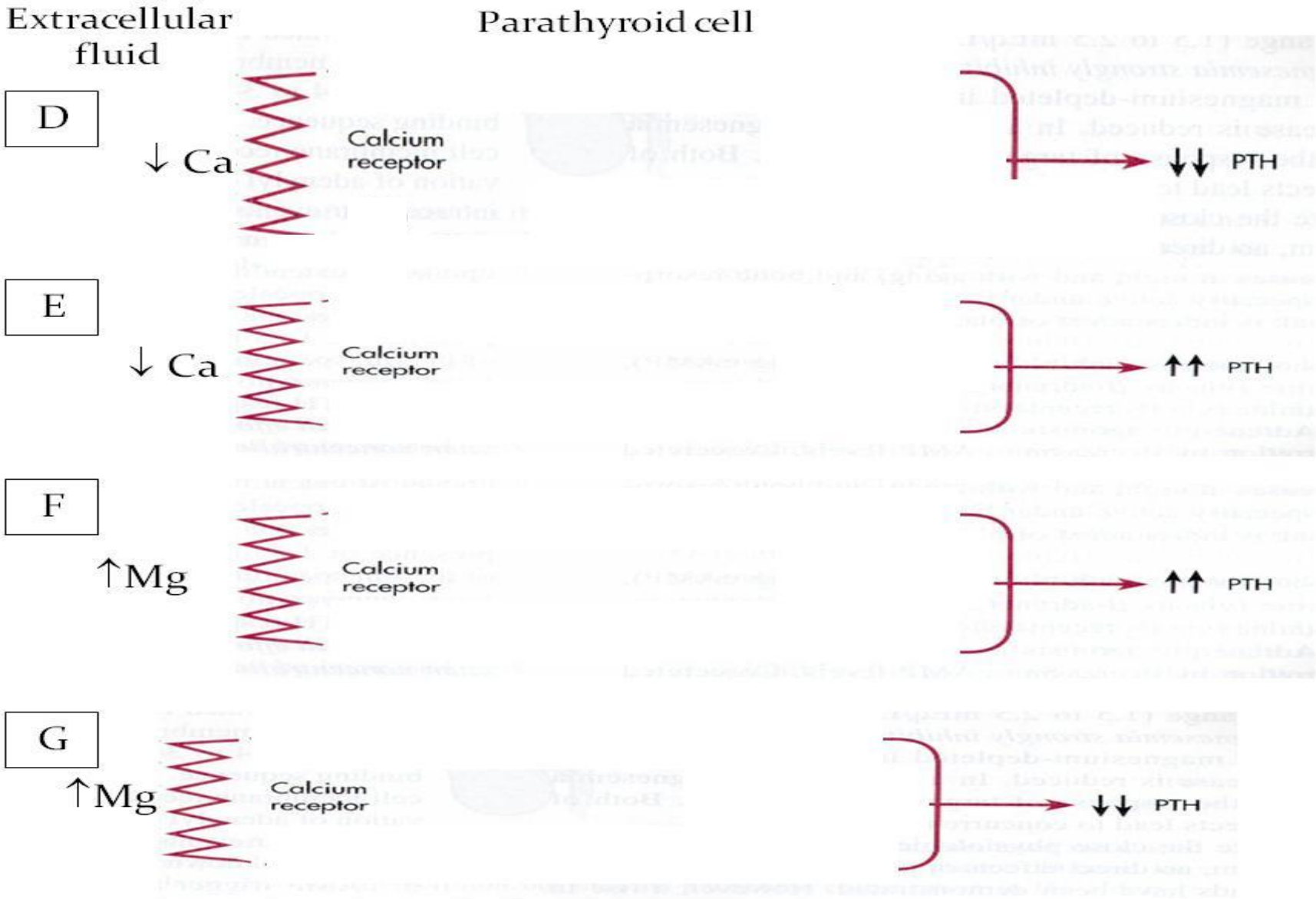


The set-point for calcium-regulated PTH release represents the calcium concentration at which PTH values are midway between the maximum and minimum PTH levels achieved.[2] Within a very narrow range of calcium concentrations around the set-point, *very slight decreases in calcium concentration will trigger a sharp rise in serum PTH levels, while a slight increase in calcium rapidly decreases serum PTH levels.*

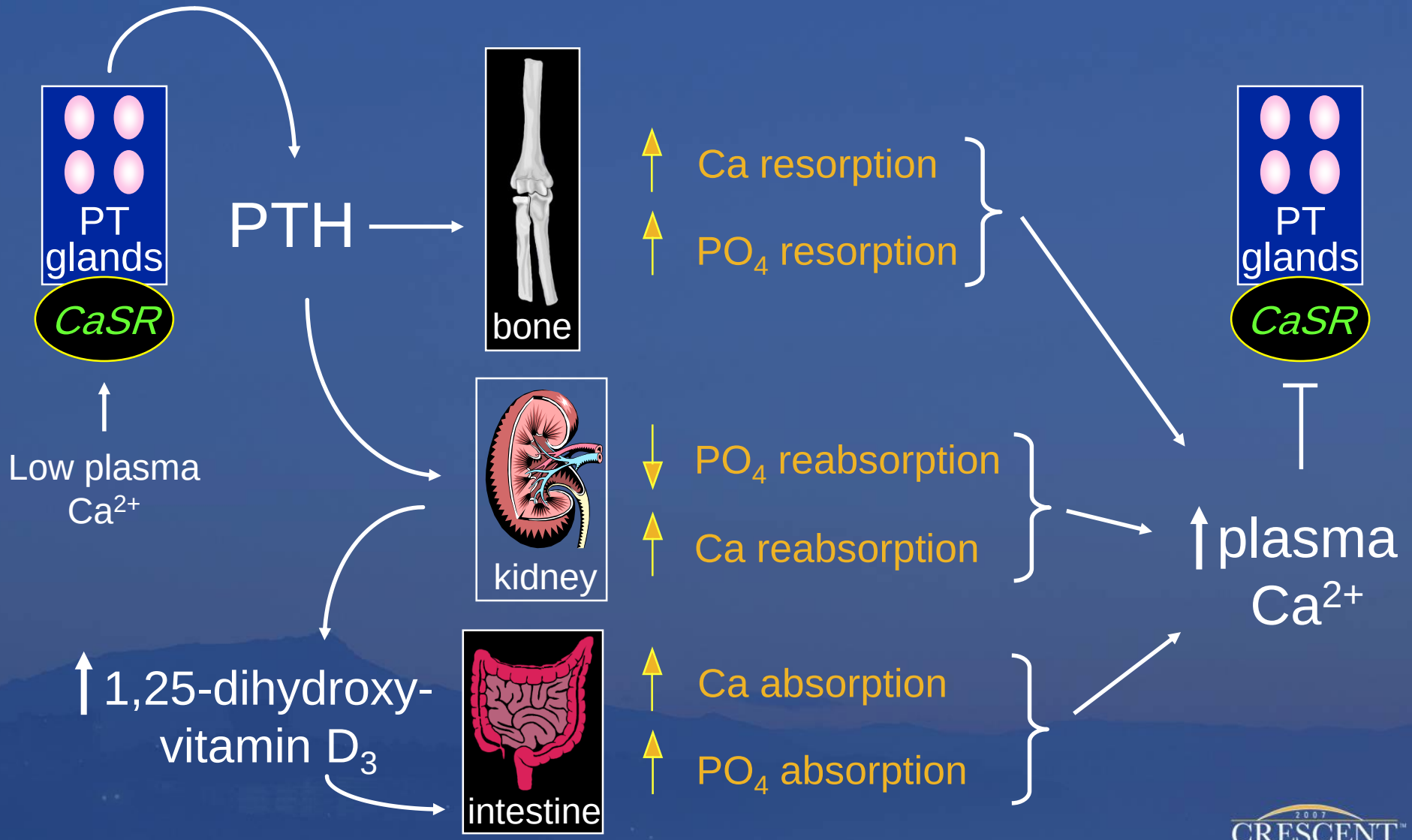
The mechanism by which the parathyroid cell is able to respond rapidly to minute changes in calcium concentration has been identified as the calcium sensing receptor (CaSR).

Adapted from Goodman WG, et al. *Kidney Int*. 1996;50:1834-1844.

أي من الأشكال التالية صحيح؟



Regulation of Plasma Calcium



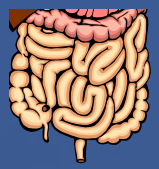
Adapted from E. Nemeth.

PTH Regulates Calcium and Phosphorus Homeostasis

↓ Serum Ca^{2+}

PTG

↑ PTH



Gut

↑ Ca absorption

↑ PO_4 absorption

Kidney

↑ Reabsorption of Ca

↑ $1,25(OH)_2D$ synthesis

↓ PO_4 reabsorption

Bone

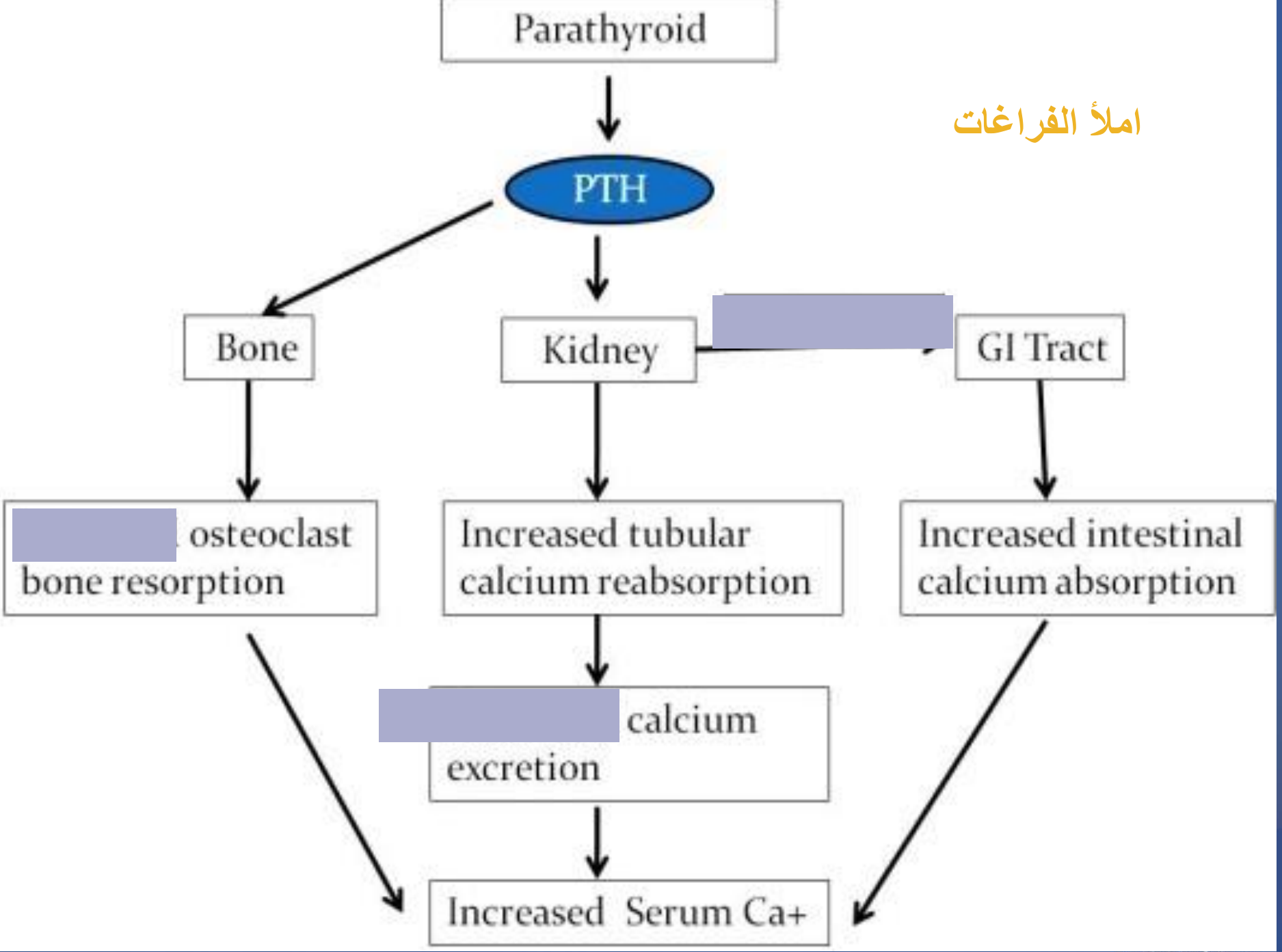
↑ Ca resorption

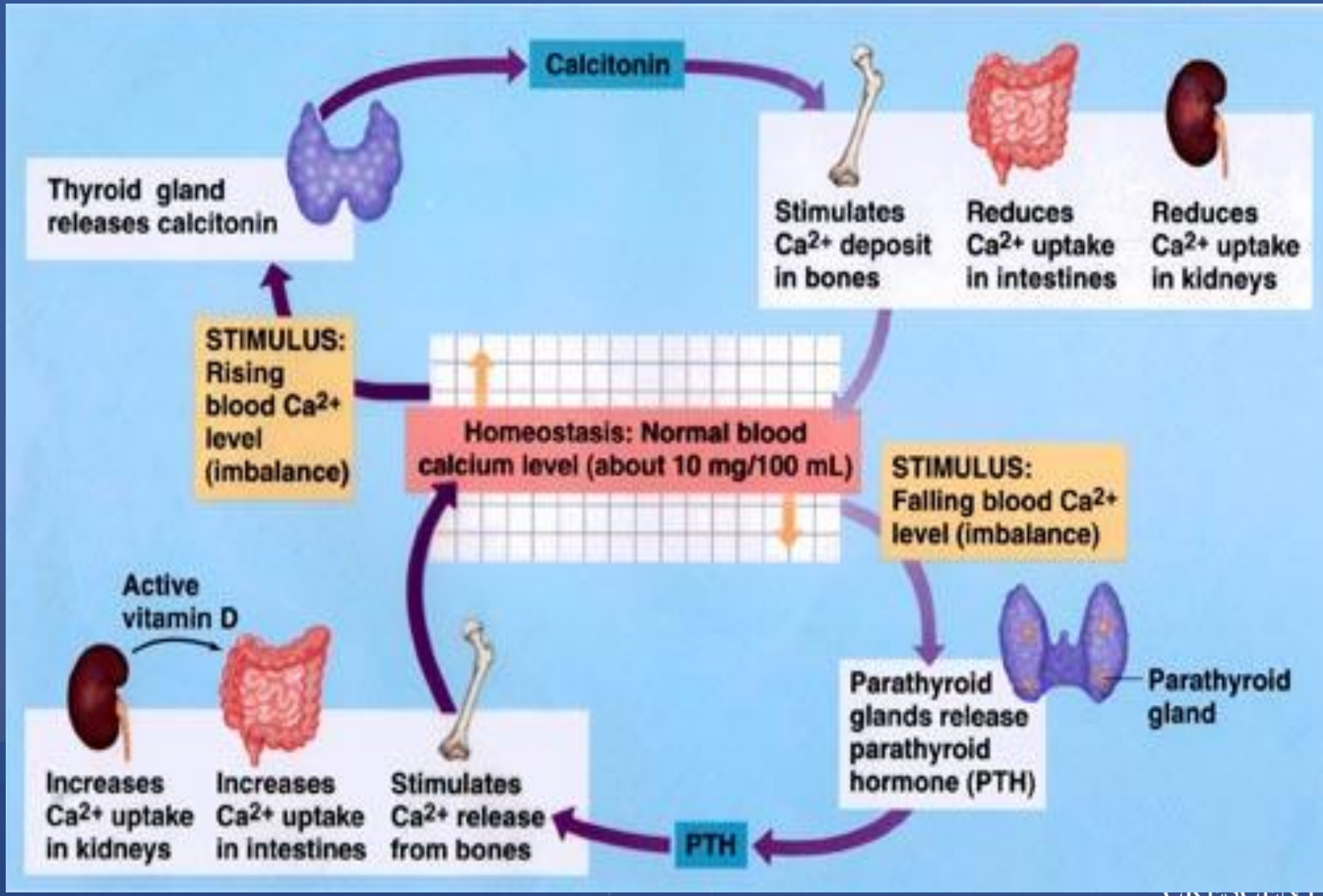
↑ PO_4 resorption

Serum $[Ca^{2+}]$ increased

Adapted from Chen RA, Goodman WG. *Am J Physiol Renal Physiol.* 2004;286:F1005-F1011.

املأ الفراغات




Calcitonin
Thyroid gland releases calcitonin
Stimulates Ca^{2+} deposit in bones
Reduces Ca^{2+} uptake in intestines
Reduces Ca^{2+} uptake in kidneys
STIMULUS: Rising blood Ca^{2+} level (imbalance)
Homeostasis: Normal blood calcium level (about 10 mg/100 mL)
STIMULUS: Falling blood Ca^{2+} level (imbalance)
Active vitamin D
Parathyroid glands release parathyroid hormone (PTH)
Parathyroid gland
Increases Ca^{2+} uptake in kidneys
Increases Ca^{2+} uptake in intestines
Stimulates Ca^{2+} release from bones
PTH

- **Normal Calcium Homeostasis**
- Dietary calcium intake varies widely from person to person (shown as 1000 mg).[1] Approximately 5% of the ingested amount is absorbed passively from the intestines, whereas a larger but variable amount is actively absorbed, principally under control of calcitriol. At steady state, the amount of calcium absorbed each day (shown as 200 mg) is excreted by the kidneys.

- Calcitriol (1,25-dihydroxyvitamin D_3 [$1,25(OH)_2D_3$]) alters the calcium balance to increase plasma Ca^{2+} levels. Its most important mechanism is in the small intestine, where it increases calcium absorption.[1] Specialized epithelial Ca^{2+} channels are located in intestinal epithelial cells and renal tubule cells, where they mediate uptake of Ca^{2+}.[2] These channels, which are members of the transient receptor potential (TRP) superfamily, include TRP vanilloid-5 (TRPV-5) and TRP vanilloid-6 (TRPV-6).[3] Calcitriol induces expression of these proteins as well as the calbindin family of cytosolic calcium-binding proteins. These results suggest intestinal and renal mechanisms whereby calcitriol regulates serum Ca^{2+}.

- Calcitriol also affects the release of Ca^{2+} from bone.[1] At high concentrations, calcitriol stimulates osteoclast-mediated bone resorption, thus increasing the Ca^{2+} release from bone. Taken together, these mechanisms contribute to the calcitriol-mediated increase in plasma Ca^{2+}.

PTH Regulates Calcium and Phosphorus Homeostasis

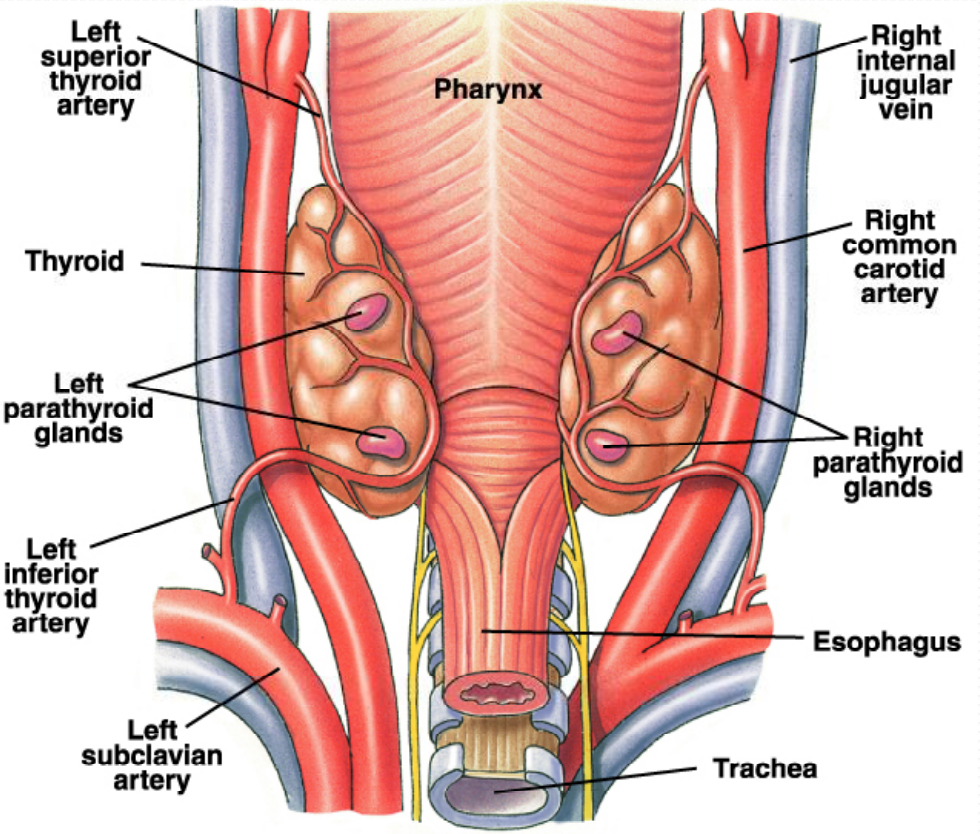
PTH produces a variety of actions that are primarily designed to restore plasma Ca^{2+} into the normal range.[1] The effects of PTH on phosphate levels are secondary. PTH stimulates bone resorption leading to Ca^{2+} as well as phosphate efflux from bone and into the extracellular fluid compartment. PTH acts in the kidney to enhance Ca^{2+} reabsorption while promoting phosphate excretion, and it enhances renal 1α-hydroxylase activity to increase calcitriol synthesis. In turn, calcitriol acts in the small intestine to stimulate calcium absorption and, to a lesser extent, phosphate absorption. As plasma Ca^{2+} normalizes, the higher Ca^{2+} and calcitriol levels play a negative regulatory role in the parathyroid gland, suppressing PTH production and secretion.

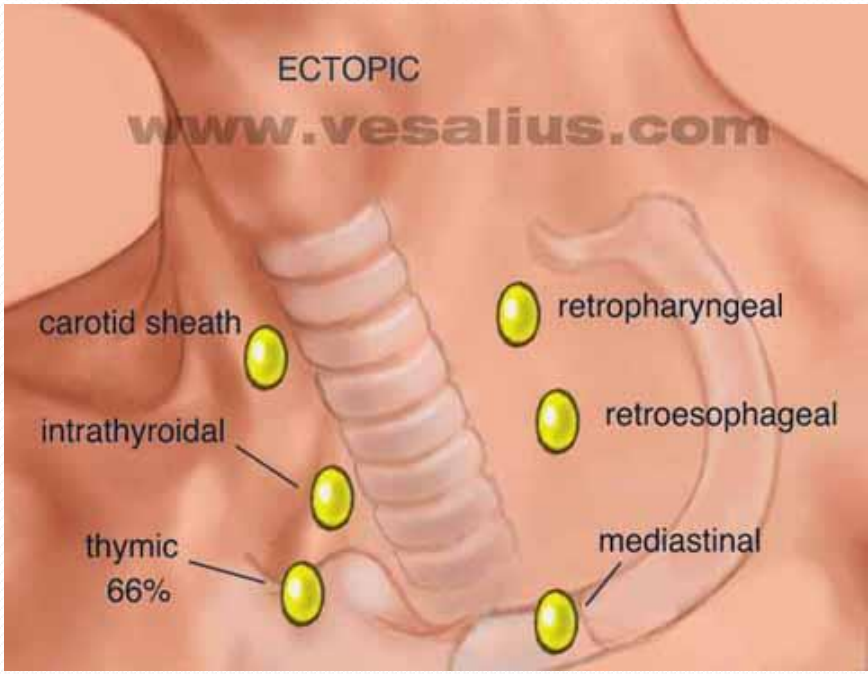
Regulation of Plasma Calcium

This slide, adapted from E. Nemeth, shows that Plasma Ca^{2+} must be maintained within a very narrow concentration range because of the key role it plays in a diverse array of physiological processes, including intracellular signal transduction, smooth muscle contraction, and neuronal transmission. Regulation of plasma Ca^{2+} depends on the secretion of parathyroid hormone (PTH) by the parathyroid glands.[1]

The calcium-sensing receptor (CaSR) located on the cell membrane of parathyroid chief cells detects decreases in plasma Ca^{2+} below normal and responds by rapidly stimulating PTH secretion.[1] PTH acts on bone – the major reservoir of calcium in the body – to increase resorption, thereby shifting Ca^{2+} from bone to blood. PTH also acts in the kidneys to increase Ca^{2+} reabsorption and phosphate (PO_4) excretion, but more importantly, it stimulates synthesis of 1,25-dihydroxyvitamin D_3 ($1,25(OH)_2D_3$) (calcitriol). Calcitriol, in turn, acts on the intestines to increase absorption of Ca^{2+} and PO_4 from the diet.[2] These direct and indirect effects of PTH serve to rapidly restore plasma Ca^{2+} to normal. Moreover, the higher Ca^{2+} and calcitriol levels provide a negative feedback signal to limit further PTH secretion.[1,2]

Parathyroid glands





مريض سكري عمره ٧٠ سنة، سكر الدم ٣٥٠ ملغ/دل والخلون ايجابي. راجع بشكوى ألم بطني وغثيان واقياء. عيار الكالسيوم بالدم ١١ ملغ/دل. ناقش ما يلي:

- لدى هذا المريض فرط كالسيوم وهو بحاجة لتخفيضه اسعافياً لأنه مسن.
- نسأل هل يوجد لديه شكاية من بوال وسهاف أو خدر ونمل باليدين وحول الفم أو زيادة المقوية العضلية أو اسهال أو آلام بالخاصرتين سلبية ما سبق يدل على أنه ليس لدى هذا المريض فرط كالسيوم.
- رقم الكالسيوم مناسب لعمر المريض
- لدى المريض فرط نشاط جارات درق ثانوي

رجل ٦٥سنة راجع بكسر عفوي في الساعد، ويشكو من تعب منذ حوالي السنة مترقٍ مع آلام شرسوفية قرحية مع نقص وزن حوالي ١٠ كغ خلال الأشهر الثلاثة الماضية دون تبدل في الشهية .

بالفحص السريري: شحوب . الضغط الشرياني ١٦٠/٩٥ ، النبض: ١٢٠/د منتظم

Calcium (total) – 11.9 mg/dL	(normal ~ 8.5-10.2 mg/dL)
Phosphate 3·4 mg/dL	(normal ~ 2.0-4.3 mg/dL)
Albumin – 3.8 g/dL	(normal ~ 3.5-5.0 g/dL)
PTH – 275 pg/mL	(normal ~ 10-60 pg/mL)
Creatinine – 1.2 mg/dL	

ما هو التشخيص الأرجح:

A- كارسينوما جارات الدرق B- فرط كلس الدم العائلي C - الانسمام بفيتامين د

D -أدينوما جارات الدرق E - ارتفاع كلس الدم بسبب خباثة يجب البحث عنها

ماهي الخطوة التشخيصية التالية:

A -تصوير طبقي محوري للعنق B - مرنان للعنق C - إيكو للعنق

D-إيكو للعنق ثم ومضان ب Technetium-99m sestamibi E – فحوصات أخرى؟

ما هو العلاج الصحيح:

A -تخفيض الكالسيوم اسعافياً. B - جراحة لجارات الدرق بيد خبيرة C -استئصال تام للدرق وجاراتها

D- معالجة محافظة بالمدرات الثيازيدية والسوائل السكرية والكورتيزول

E-زيادة تناول السوائل وإعطاء المدرات الثيازيدية وإجراء تمارين رياضية.

بحال راجعت المريضة بكالسيوم ١٤ ملغ/دل ما هو أول إجراء:

A -زيادة الوارد الفموي من السوائل B – إعطاء سيروم سكري ٥% وريدياً C – إعطاء سيروم ملحي ٠,٩% وريدياً

D -إعطاء الفوسفات وريديا E – مدرات العروة F- إعطاء سيروم ملحي وهدروكلورثيازايد

Mr. H is a 74 year old man with a past history significant for hypertension and COPD from smoking 2 packs per day for the last 40 years. He presented to an urgent pulmonary clinic appointment with 2 months of increased cough and 5 days of "mild" hemoptysis. Upon further obtaining further history, he reports feeling fatigued, nauseous, and chronically thirsty for several weeks. His exam is significant for bilateral rhonchi (no change from baseline lung exam) and absent reflexes. Stat labs are ordered from clinic:

He lost 20 kg during the last 3 months

Sodium – 138 meq/L
Potassium – 3.7 meq/L
Magnesium – 1.8 mg/dL
Calcium (total) – 13.1 mg/dL
Phosphate – 1.3 mg/dL
Creatinine – 2.8 mg/dL (baseline creatinine = 1.1)

CBC, PT/PTT – WNL
PTH - Pending
Albumin – 4 g/dL

ما هي قيمة PTH المتوقعة؟

Signs / Symptoms

Asymptomatic	
Symptomatic	
Bones	Bone pain, #'s, arthralgia
Renal	Stones, polyuria
G.I.	Pain, duodenal ulcer, pancreatitis
Neuro.	Depression, apathy
Cardiac	Hypertension, heart block

Symptom	%
Asymptomatic hypercalcemia	50
Renal stones	28
Arthralgia	5
Peptic Ulcer	4
Hypertension	4
Bone disease / MEN 1 / others	9

Hyperparathyroidism

Xrays:

sub-periosteal resorption

pepper pot skull

rugger jersey spine

cystic brown tumours

Hyperparathyroidism

Xrays:

pepper pot skull

Hyperparathyroidism

Xrays:

rugger jersey spine

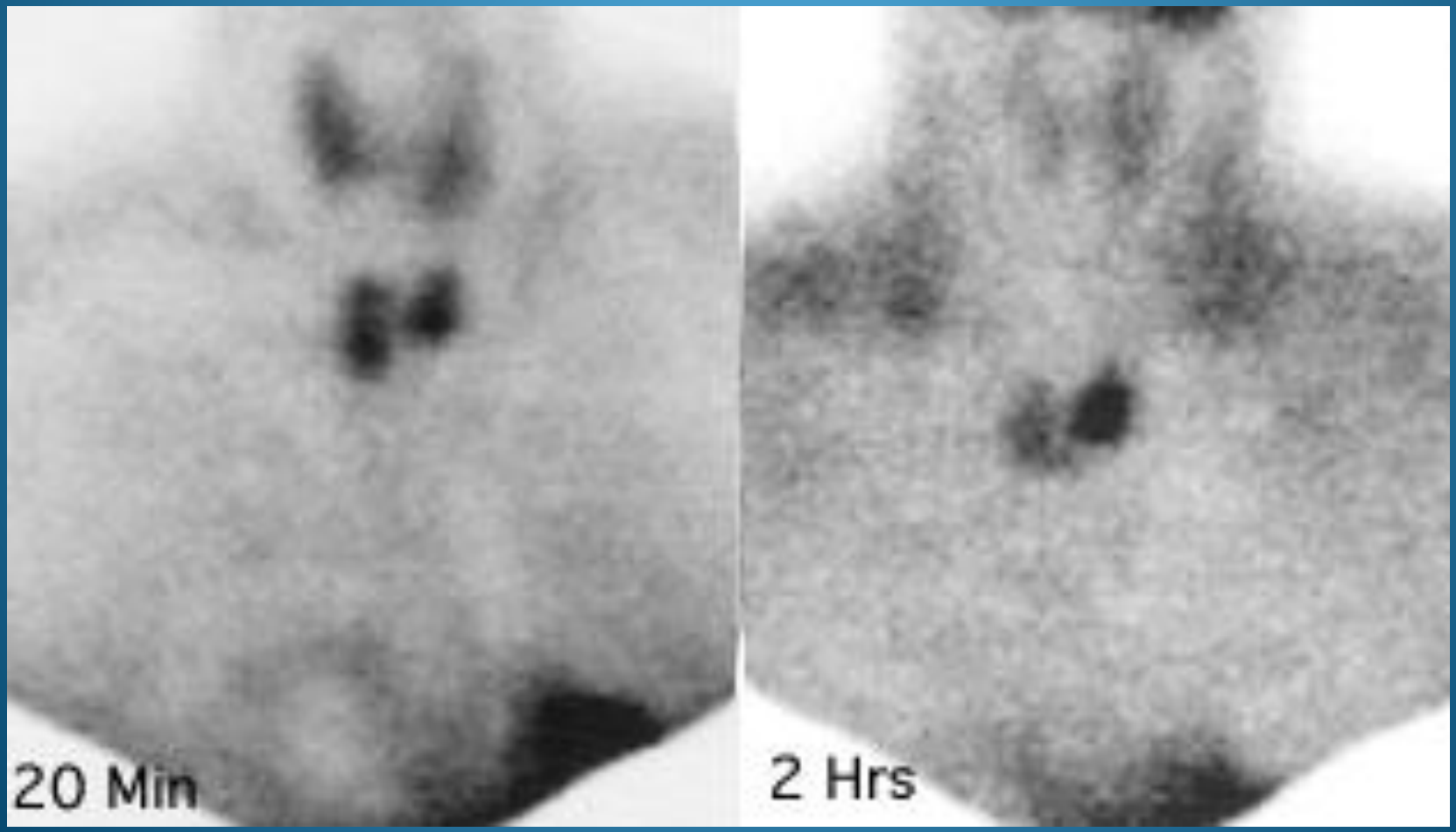
Hyperparathyroidism

Xrays:

cystic brown tumours

Hyperparathyroidism

Sestamibi scan



Treatment

- Confirmation of diagnosis is by

LABORATORY

- Radiological investigation is for localisation only

- First line treatment is surgery

Indications for Surgery

Symptomatic hyperparathyroidism

Serum Ca > 1 mg above upper limits of normal

Reduced creatinine clearance by 30 %

Renal stones

Hypercalciuria (>400mg day)

Reduced cortical bone density

Young patient (< 50 y.o.)

NIH Consensus Development Conference Statement - Ann Intern. Med. , 1991

SURGERY

- Until 15 years ago – bilateral neck exploration.
- **Radiological localization** of hyperfunctioning PTH tissue has enabled less traumatic surgery
- **Surgical experience is very important**

وظيفة: ما هي المقاربة الصحيحة ؟

لمريض لديه بوال وسهاف وحصيات كلوية وعقدة مثبتة للسيستاميبي تحاليله المخبرية

Ca = 9,5 mg/dl (normal: 8.5-10.5)

Albumin = 4 g/dl

PTH = 38 pg/ml (normal: 10 – 65)


شكراً
لإصغائكم