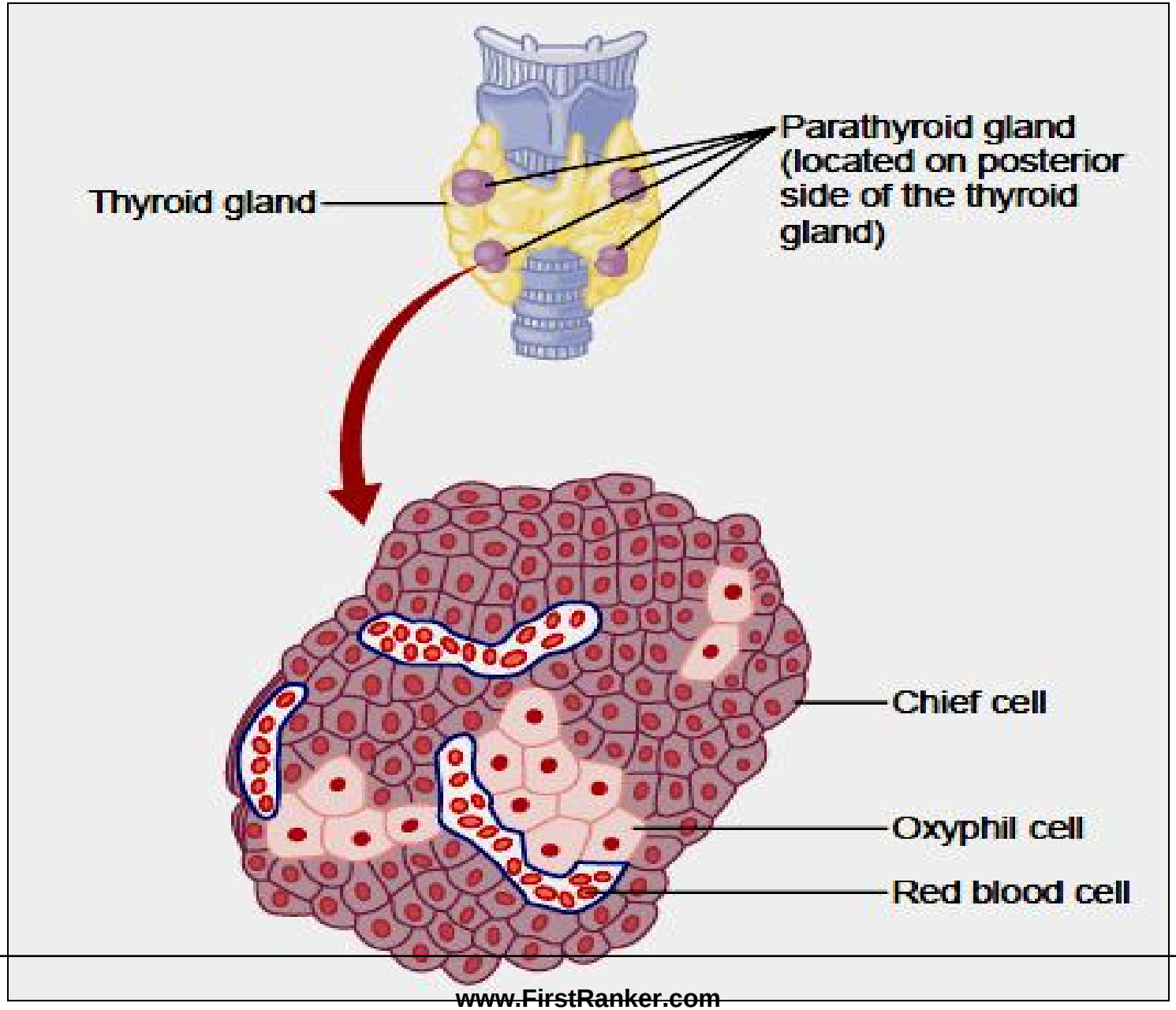
Parathyroid hormone from parathyroid glands



Anatomy

Humans have 4 parathyroid glands.

- 2 in superior pole of thyroid and 2 in its inferior pole.
- Contain 2 distinct cells

chief cells: contains golgi apparatus +ER + secretory granules.

➢ Secreates **PTH**.

Oxyphil cells : contains numerous mitochondria +oxyphil granules.

➢ Seen before puberty and no. ↑es with age.

➢ Function unknown

Parathyroid hormone

- Polypeptide hormone
- Secreted by parathyroid glands

Preprohormone (110 A.As)ER

prohormone (90 A.As)Golgi apparatus

hormone (84 A.As - ---->packed in secretory granules)

➢Normal level of PTH in plasma 10-55pg/ml.
Half life approx. 10 min , removed by liver.

Physiological actions

↑plasma calcium level (by its effect on bone, kidney, intestine)

On bone :-

- Stimulates osteoclastic activity (*indirect action*) bone resorption.
- PTH stimulates precursor cells(monocyte,macrophages,etc;)into osteoclast.
- *Hydroxyproline excretion in urine is an index of osteoclastic activity*
- fast Ca^{2+} efflux into the plasma from the small labile pool

Contd.

- Stimulation of osteolysis: PTH activate the process of osteocytic osteolysis.

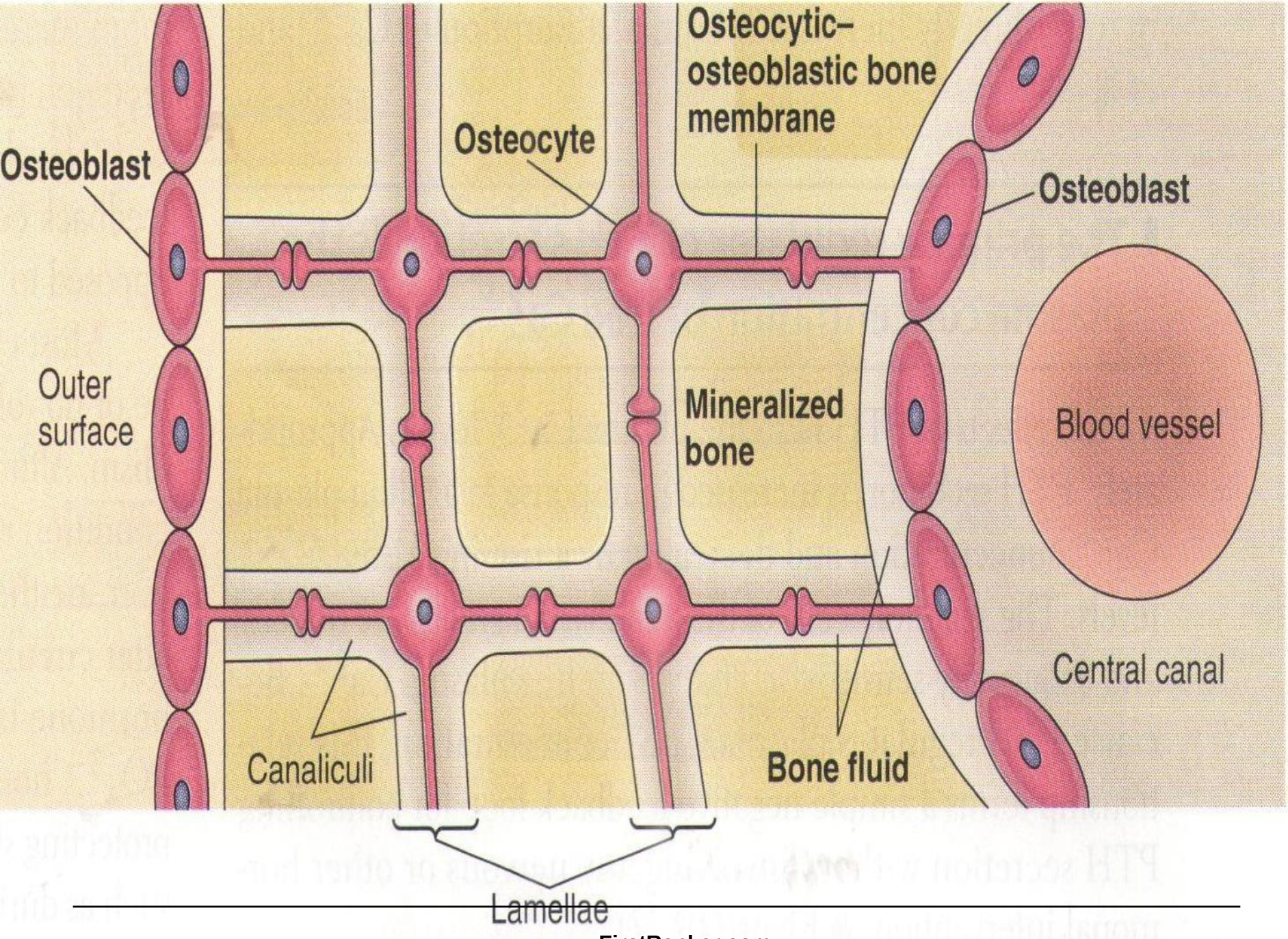
Ca from bone fluid → Osteocyte

↓

ECF ← Osteoblasts

- PTH also inhibits the synthesis of collagen by osteoblasts.

➢ **Net effect** is ↑ in bone mass in low conc. And ↓ in bone mass in high conc.



On kidney

- ↑es Ca^{2+} reabsorption (**late DCT, collecting tubule, ascending limb of Henle's loop) by** *regulating the expression of* ***TRPV5*** *channels)*
- ↑esPO_4^{3-} excretion (PCT)---> *phosphaturia by inhibiting* Na-Pi II a

enhances the activation of vitamin D by kidney

On intestine

- Indirectly increases both Calcium and Phosphate absorption from the small intestine by activating vitamin D.

Final effect :↑ed plasma calcium; ↓ed phosphate

Regulation of PTH secretion

Plasma concentration of ionized Calcium .

- Inverse relationship
- parathyroid glands hypertrophy :-*rickets,pregnancy, lactation*
- *Recently,**calcium sensing receptors(CaSR**) has been identified on **chief cells**.*
- *CaSR is a G- protein coupled receptor attached to **phospholipase C** and on binding to Ca generates IP3 &DAG.*
- *IP3 & DAG release Ca from cytosolic store and activate **protein kinase C** that inhibits PTH secretion.*

- Vitamin D : ↓es formation of preproPTH
- Plasma phosphate

  Rise in plasma phosphate : stimulates PTH
- Other factors :

  cAMP, βagonists, dopamine, histamine - ↑level

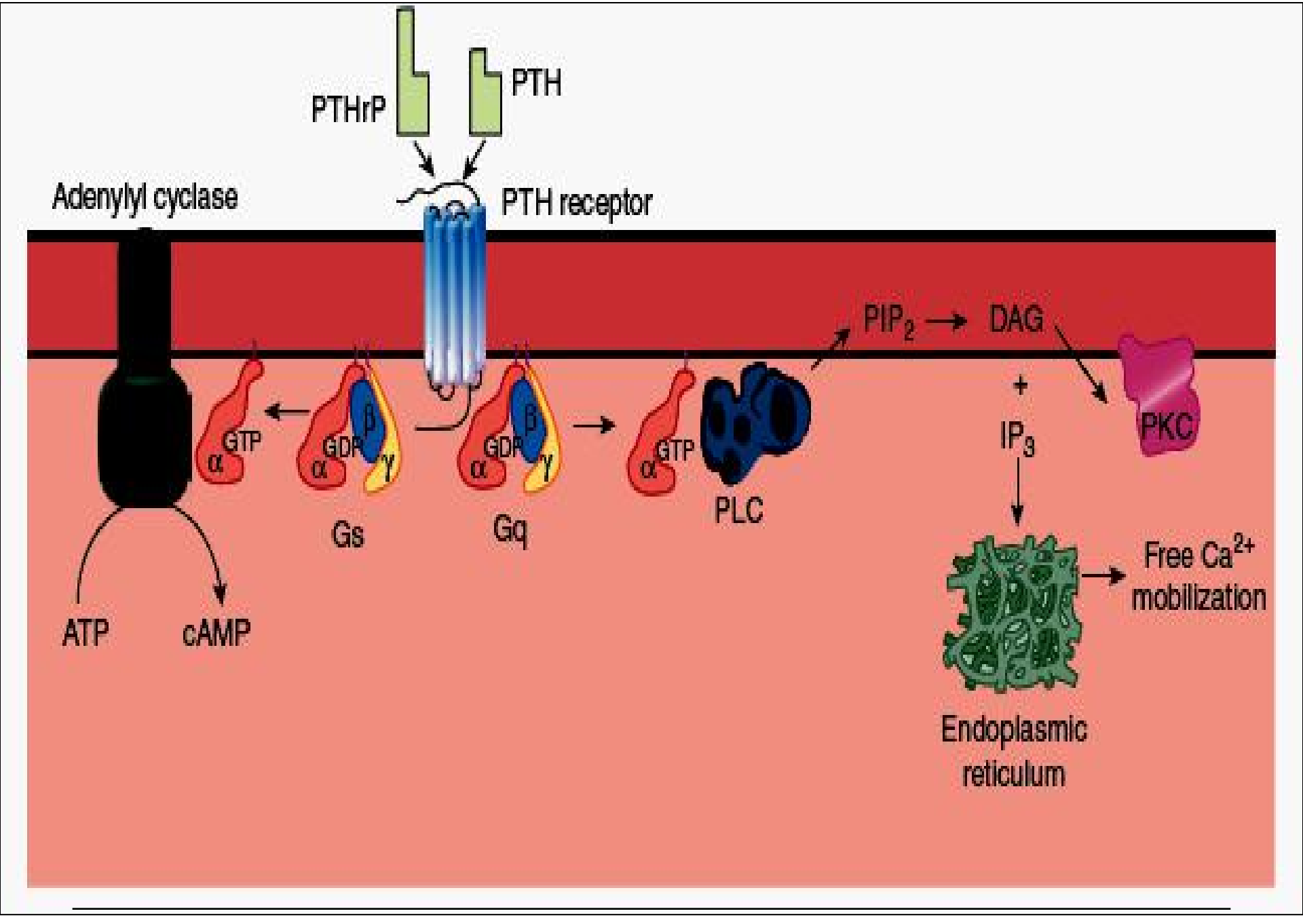
  α agonists, prostaglandins - ↓level

Mechanism of action:-

3 receptors:-

1. hPTH/PTHrP receptor. :binds to PTH &PTHrP,main receptor to regulate plasma calcium.
2. PTH2 (hPTH2-R) : binds to PTH, but not to PTHrP . Found in brain, placenta & pancreas
3. CPTH which reacts with the carboxyl terminal rather than the amino terminal of PTH.

PTH binds to its receptors and activates both **adenylyl cyclase** and **phospholipase C pathway**



PTHrP

- Another protein with PTH activity..
- Has 140 amino acid, encoded by gene on ch.12 whereas PTH by ch.11.
- Although **both bind on same receptor** hPTH/PTrP, yet their physiological actions are different.
- PTHrP acts close to where it is formed (paracrine factor).
- Has effect on cartilage ,brain,placenta ,smooth muscle in utero.
- It is also present in enamel epithelium of teeth.

Applied physiology

Hyperparathyroidism

Hypoparathyroidism

Hyperparathyroidism → primary

Hyperparathyroidism → secondary

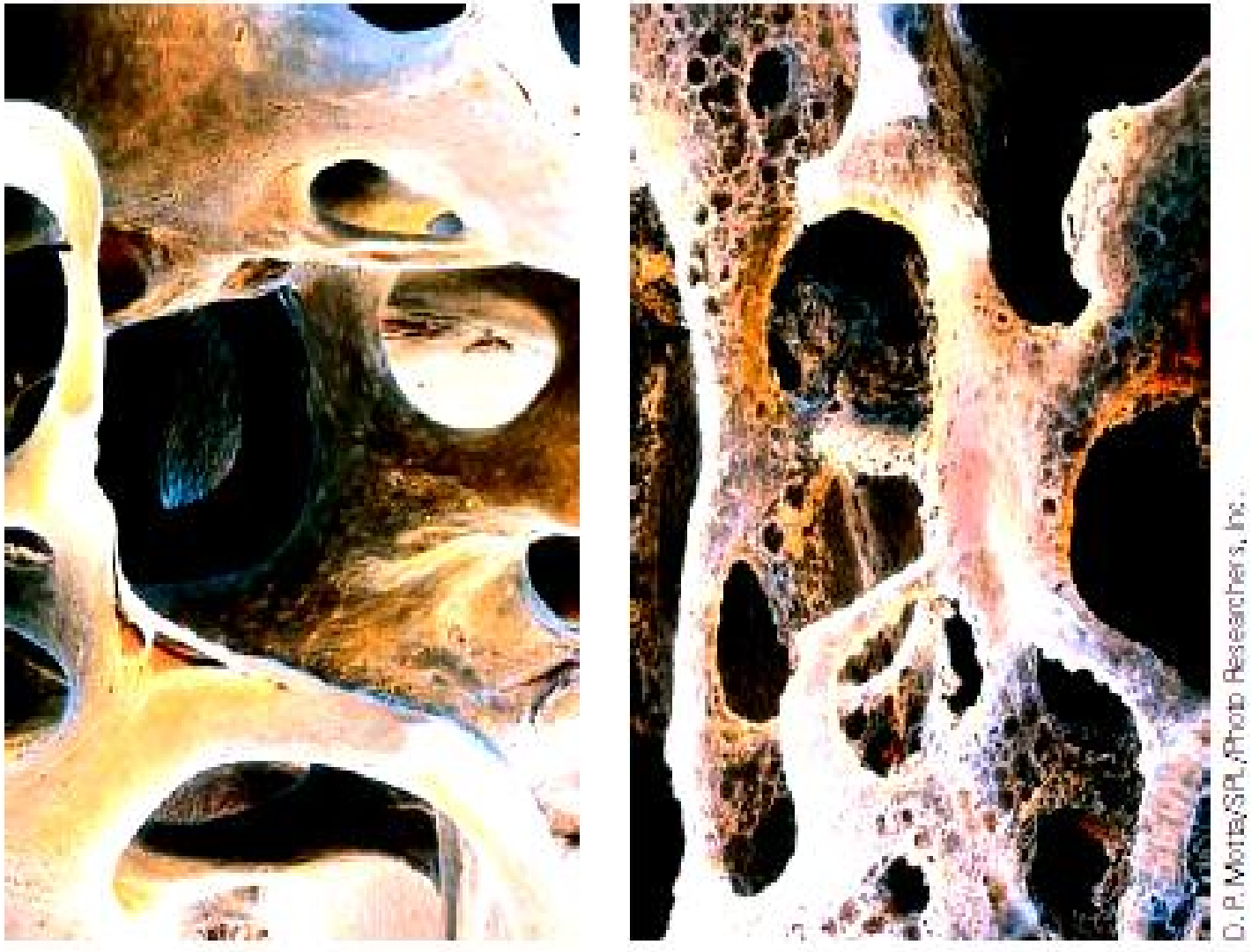
Primary hyperparathyroidism

Tumor of parathyroid gland

Features :-

hypercalcemia, hypophosphatemia, demineralisation of bone, hypercalciuria, renal stones

Extreme PTH : parathyroid poisoning, metastatic calcification



- *high level of plasma alkaline phosphatase --- an important diagnostic finding*
- **Secondary hyperparathyroidism**
  - Seen in chronic renal disease, rickets.
  - In these diseases ,the chronic hypocalcemia causes ↑PTH secretion.

Hypoparathyroidism

True hypoparathyroidism

- m/c : damage to glands/their blood supply/inadvertent removal e.g;.during thyroidectomy.

Pseudo-hypoparathyroidism

- PTH level normal/elevated

Defect : receptors/ post-receptor

Features :-

- hypocalcemia (6-7mg/dL)
- Hyperphosphatemia (6-16mg/dL)

Tetany

- Carpopedal spasm
- Laryngeal spasm leading to asphyxia
- Convulsions & seizures

•Paraesthesia

CVS :-

- dilatation of heart
- arrhythmias
- prolonged ST &QT intervals
- hypotension
- heart failure

Latent tetany : subclinical tetany

- Neuromuscular hyperexcitability d/t hypocalcemia
- Provocative tests:-
  - Chvostek's sign
  - Trousseau's sign

Management of hypoparathyroidism

- PTH
- Vitamin D (100,000units/day) along with calcium (1-2gms/day)
- Injections of calcium salts

??????

- Is parathyroid gland essential for life?
- Why hypoparathyroidism is common after thyroid surgery and its effects ?
- What is the role of plasma calcium & vit D in the regulation of PTH secretion?
- Difference between primary and secondary hyperparathyroidism ?
- In hypocalcemic tetany ,hyperexitibility is due to …….
- List physiological actions of PTH.

- Hypercalcemia of malignancy?
- Local osteolytic hypercalcemia?