

PARATHYROID HORMONE

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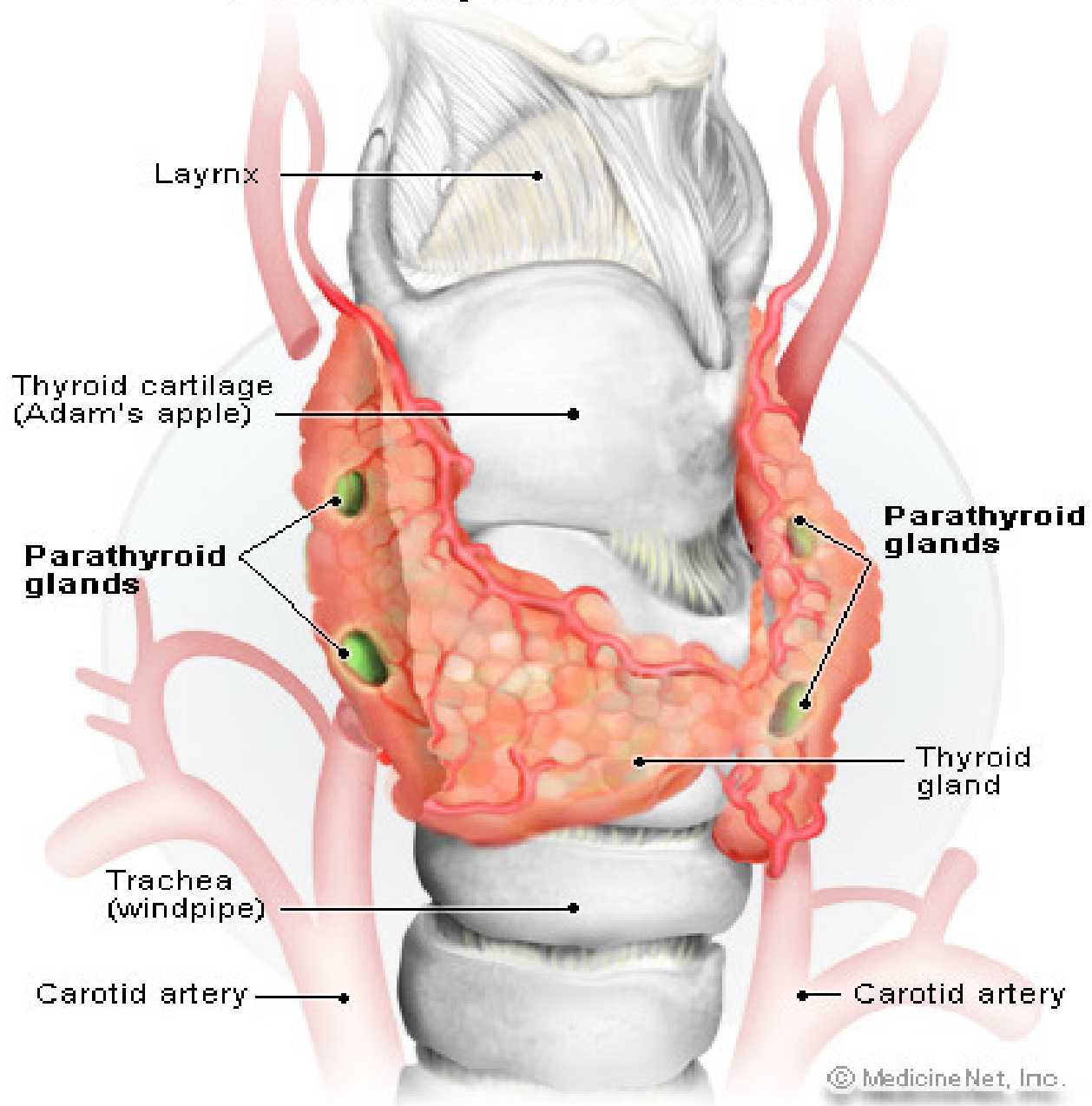
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Introduction

- ➔ **Parathyroid Hormone (PTH)**
→ Peptide hormone secreted by parathyroid glands, which are located to the thyroid gland
- ➔ Alters serum calcium via actions on three target organs : bone, intestinal mucosa and kidney.
- ➔ Contain 84 amino acids , coded by a gene on chromosome 11
- ➔ Full biology activity of hormone : the first 34 amino acids

Parathyroid Glands



Function of PTH

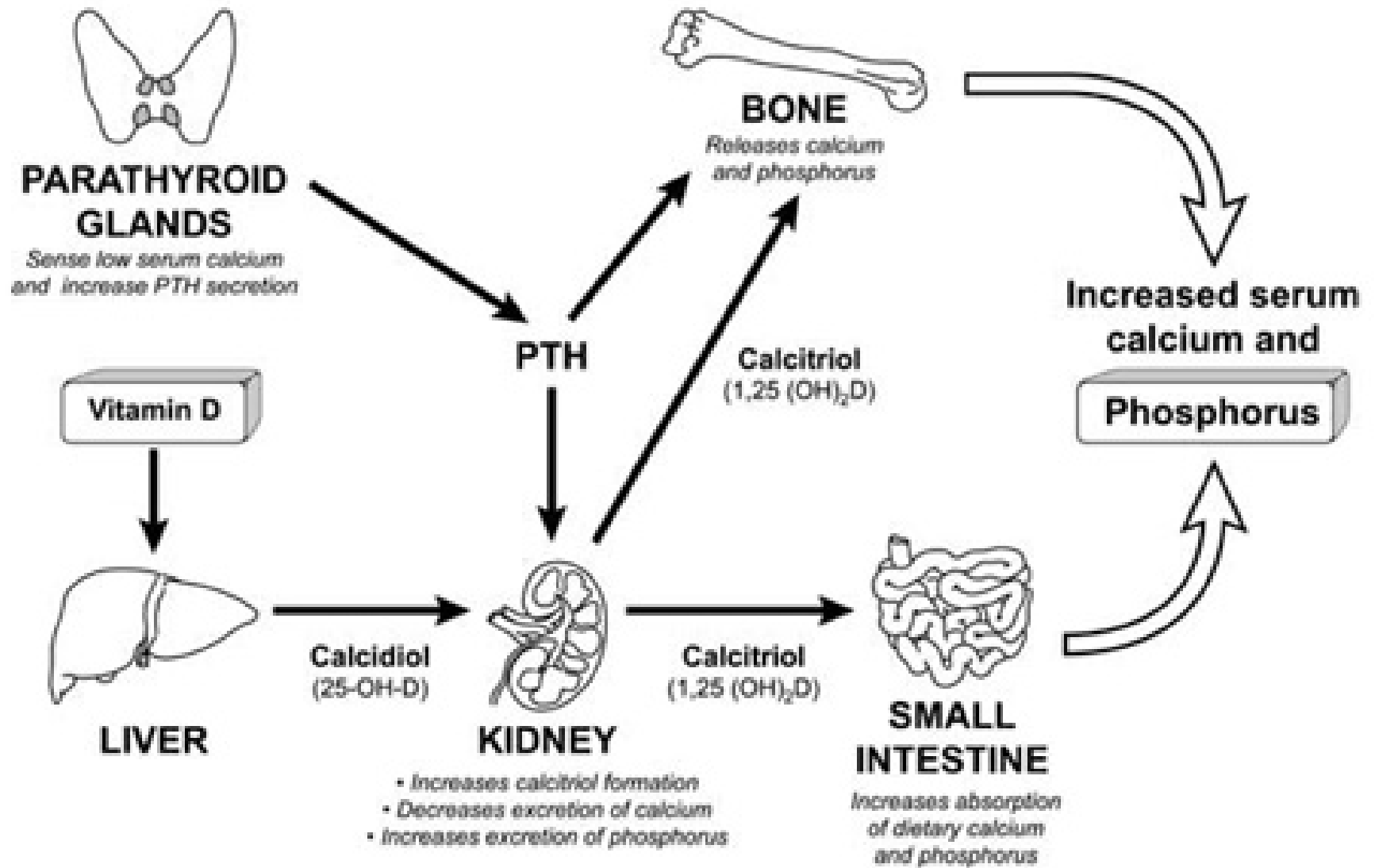
➤ **Kidney**

- **Promote calcium reabsorption on distal tubule**
- **Decrease phosphate absorption on proximal tubule**

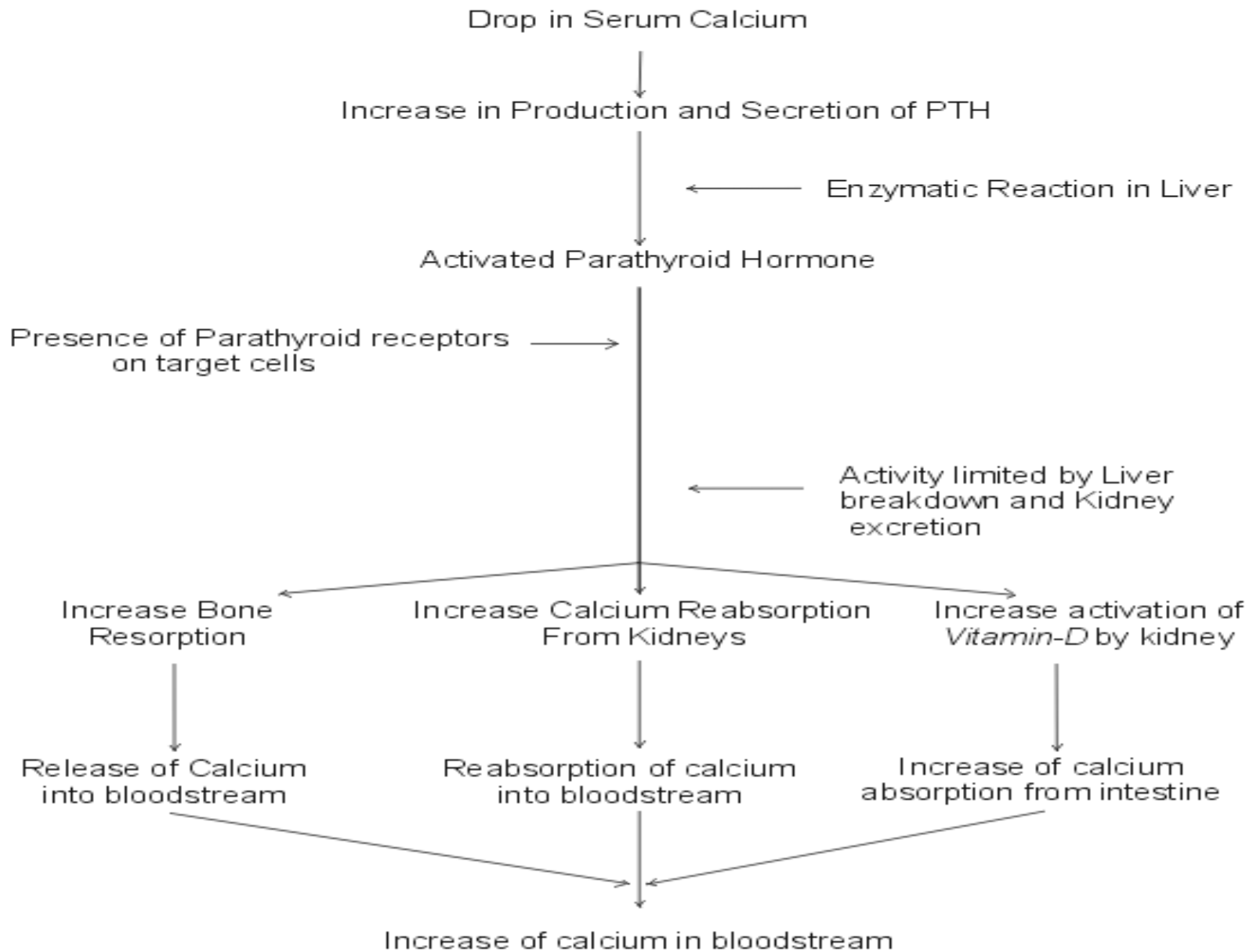
➤ **Bone**

- **Increases bone turnover**
- **Causes loss of calcium from bone → ↑ osteoclast**
- **Anabolic actions in bone**

➤ **Stimulus for PTH secretion : Hypocalcemia⁴**



Parathyroid Hormone (PTH)



Calcium ion sensor (CaSR)

- **Transmembrane**
 - **G protein-linked receptor**
 - **Regulates PTH secretion via intra-cellular second messenger systems**
 - **Inactivating and activating mutations of CaSR**
 - **Hypercalcemic and hypocalcemic disorders**
 - **Mineral ion homeostasis**
 - **The receptor is involved in regulation :**
 - **Cellular proliferation and differentiation, secretion, membrane polarization, and apoptosis tissues and cells**
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Hypocalcemia



Parathyroid gland



**Release preformed PTH
From intracellular granules**

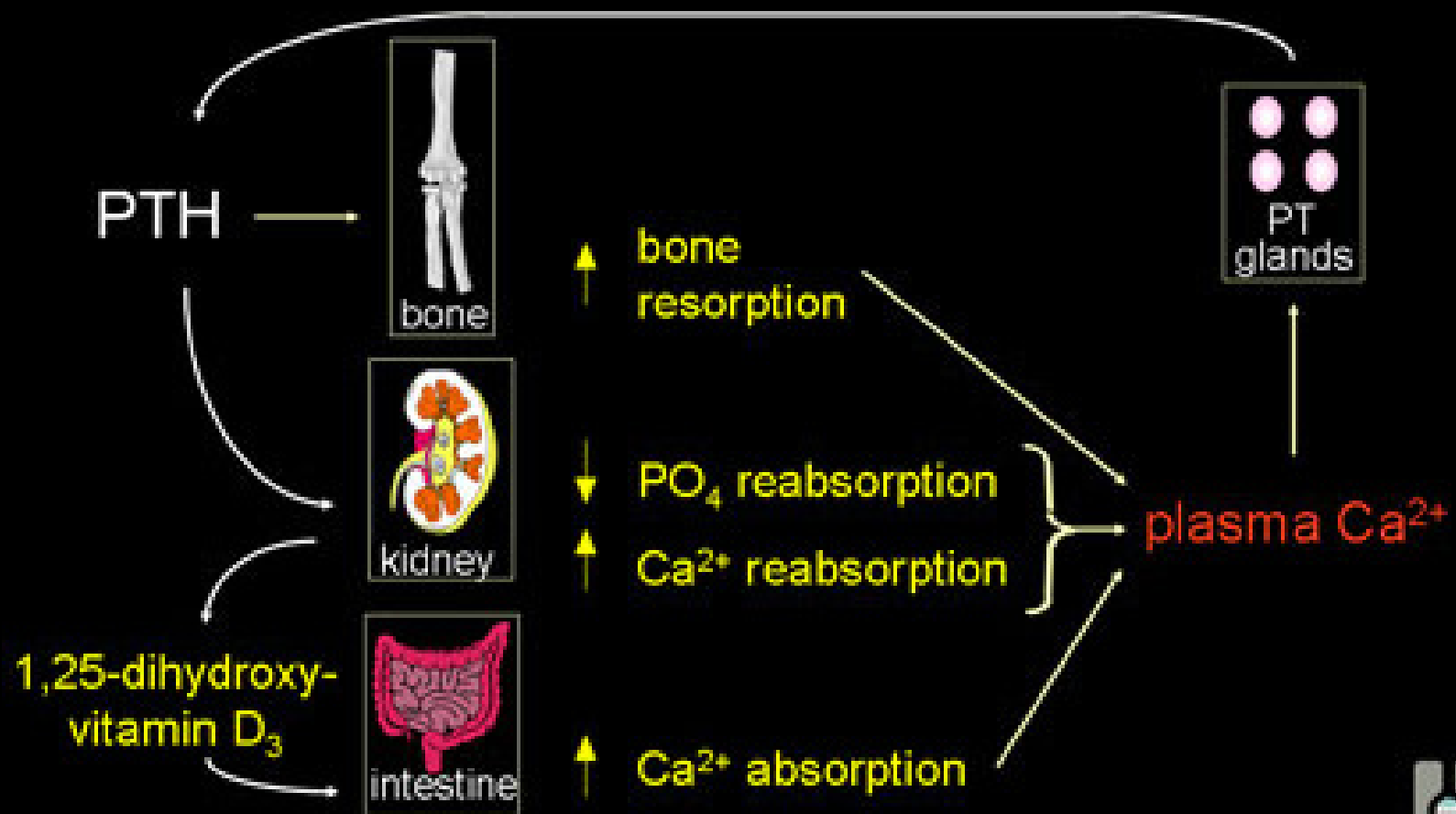


Synthesis PTH

➔ **Parathyroid hormone messenger RNA (mRNA)**

- ➔ **Regulated by calcium, phosphate, and 1,25-dihydroxyvitamin D₃**
- ➔ **Dietary-induced hypocalcemia increases and hypophosphatemia decreases parathyroid hormone mRNA level transcriptionally**
- ➔ **Half life circulating PTH : 2-4 minutes**
- ➔ **Predominantly cleared by kidney and liver**

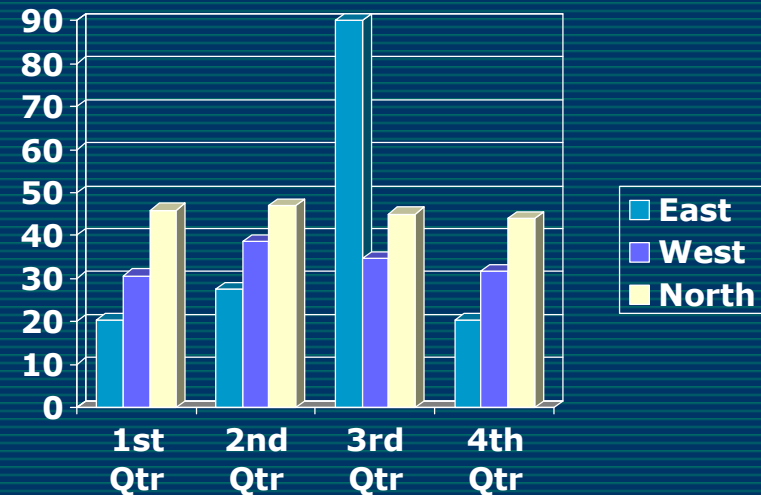
Regulation of Systemic Calcium Homeostasis



HYPOPARATHYROIDISM

Hypoparathyroidism

- **Characterized by hypocalcemia and hyperphosphatemia**
- **Manifest when : PTH secreted is **insufficient** to maintain normal extracellular fluid calcium concentrations, **or** when PTH is **unable to function optimally** in target tissue, despite adequate circulating levels**



Etiology

- ➔ **Ageneis or dysgenesis parathyroid glands**
 - Di George syndrome, hypoparathyroidism-retardation-dysmorphism (HRD) syndrome, Kenny Cafey syndrome, The Kearns-Sayre Syndrome.
- ➔ **Destruction of Parathyroid glands**
 - Autoimmune, parathyroid surgery, after radioactive iodine therapy of the thyroid gland, after irradiation, infiltrative disease, Wilson disease, granulomatous diseases

- ➔ **Impaired Parathyroid secretion**
 - ➔ **Maternal hypoparathyroidism**
 - ➔ **Hypomagnesemia**
 - ➔ **PTH mutations**

- ➔ **Clinical manifestation**
 - ➔ **Sign and symptoms of hypocalcemia**
 - **Neuromuscular irritability : perioral paresthesias, tingling of the fingers and toes, tetany**
 - **Carpopedal spasm**
 - **Laryngeal spasm**
 - **Seizure**
 - **Prolongation of QTc interval in ECG**
 - **Cardiac arrhythmias → *Torsades de pointes***

➔ **Laboratory finding**

- **Low serum calcium**
- **Raised serum phosphorus**
- **Normal renal function**
- **Serum PTH low or undetectable**
- **Circulating level 1,25 (OH)₂D low or normal**
- **24-hour urinary excretion of calcium is decreased**

Management

- MAINTAINING AN ADEQUATE SERUM CALCIUM
 - CALCIUM AND CALCITRIOL SUPPLEMENTATION
- RISK OF NEPHROCALCINOSIS DURING TREATMENT
 - MAINTAIN THE SERUM CALCIUM IN THE LOW NORMAL RANGE
- MONITORING OF URINARY CALCIUM-TO-CREATININE RATIO
- ~~INTERMITTENT RENAL SONOGRAPHY~~₁₇

PSEUDOHYPOPARATHYROIDISM (PHP)

Hypoparathyroidism

- ➔ **Disorders that have typical biochemical features of hypoparathyroidism (hypocalcemia and hyperphosphatemia) associated with elevated PTH levels.**
- ➔ **Pathophysiology : end-organ resistance to PTH**
- ➔ **First described by Albright**

Type of PHP

1. PHP type 1 a

- **Skeletal and developmental abnormalities : round face, short stature, obesity, brachydactyly, heterotopic calcification, mental retardation**
→ **Albright's hereditary osteodystrophy (AHO)**
- **Hypothyroidism and hypogonadism**
- **Caused by mutation in gene (GNAS 1)**

2. PHP type 1 b

- **Resistance to PTH**
- **Hypocalcemia and hyperphosphatemia**
- **Without phenotypic features of AHO**
- **Normal Gs α activity**
- **Etiology : post-PTH receptor pathway**

3. PHP type 1 c

- ➔ Phenotypic similar to AHO
- ➔ Resistant to multiple hormones
- ➔ Normal GNAS 1 activity

4. PHP type 2

- ➔ Similar to PHP type 1 b
- ➔ Hypocalcemia and hyperphosphatemia
- ➔ Normal increase in urinary cAMP but have an impaired phosphaturic response

Management

- ➔ **Administration of calcium and calcitriol to maintain low-normal serum calcium concentrations**
- ➔ **This patient are at less risk for nephrocalcinosis**

Thank You