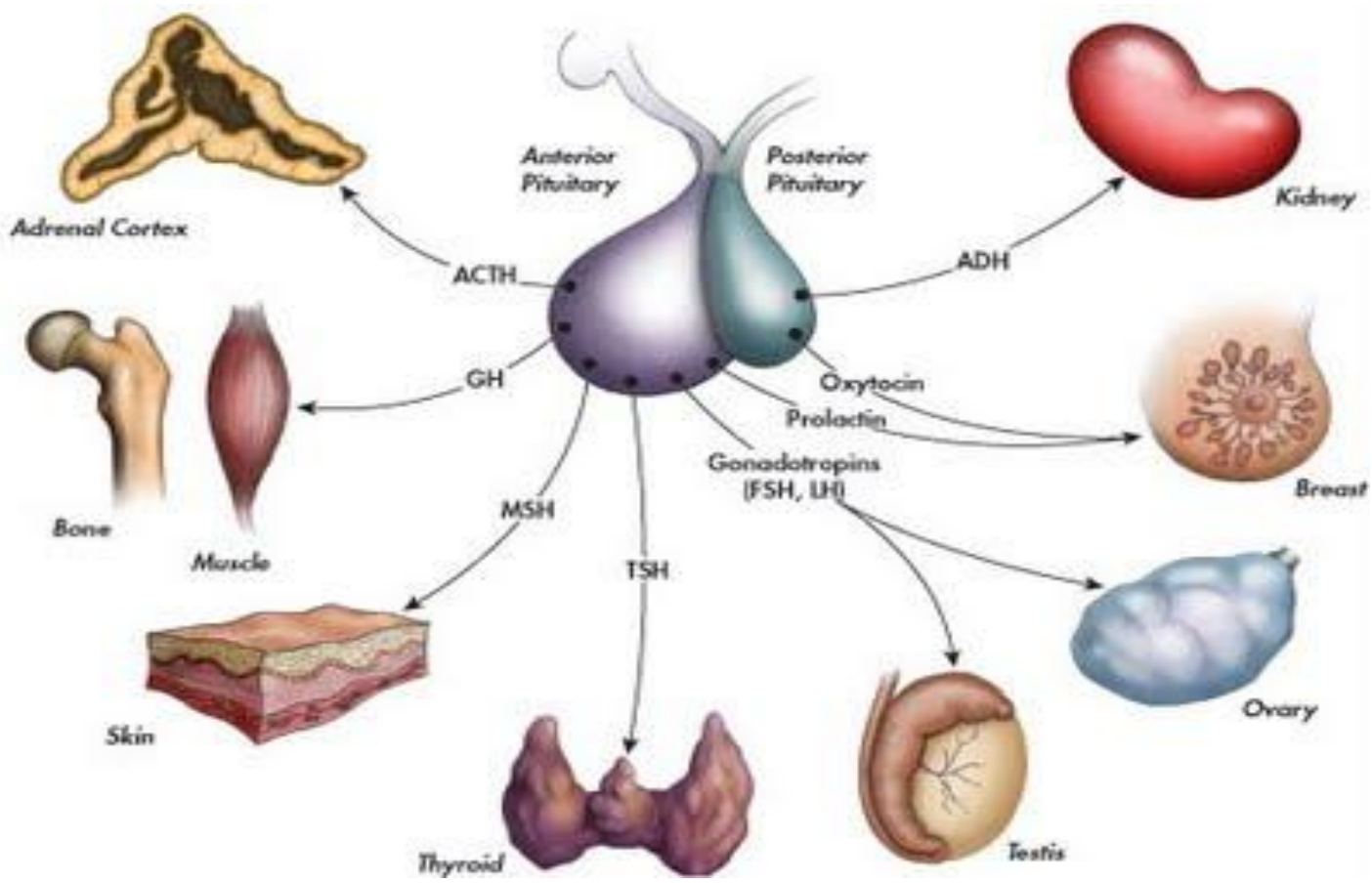
Endocrine Block

9th Lecture

Physiology of Parathyroid gland



PHYSIOLOGY TEAM – 430

Physiology Team Leaders:

Al-Waleed Al-Johar Layan Akkielah

This Lecture is done by:

Ahmad Bogari Sara Al-Hilali

Organized by : Layan Akkielah

Introduction:

- Four glands located on the ***posterior surface*** of the thyroid gland
- Secrete the ***polypeptide hormone PTH.***
- Total weight of parathyroid tissue is about 150mg.
- Parathyroid hormone (PTH) is made by ***Chief Cells*** in these glands.
- ***Decreased blood level of Ca++ stimulates*** the parathyroid glands to secrete PTH:
  - Increase blood Ca++ .
  - Decrease blood Phosphate.

PTH synthesis:

- PTH is translated as a ***pre-prohormone***.
- Cleavage of leader and pro-sequences yield a biologically active peptide of 84 amino acids.
- Cleavage of C-terminal end yields a biologically inactive peptide

Additional information to understand:

- PTH is synthesized as a 115- amino acid polypeptide called pre-pro-PTH, which is cleaved within parathyroid cells at the N-terminal portion first to pro-PTH (90 amino acids) (Pro-sequences) and then to PTH (84 amino acids). The latter is the major storage, secreted, and biologically active form of the hormone.

- The C-terminal portion of PTH is also essential for the PTH secretory process, during hypocalcemia, intracellular degradation of PTH decreases, and mostly PTH 1-84 is secreted; in comparison, during hypercalcemia mostly biologically inactive C-terminal fragments of PTH are secreted.

Regulation of PTH secretion:

- Secretion of PTH is inversely related to plasma [Ca^{2+}] because plasma Ca^{2+} level is the dominant regulator of PTH secretion:
  - Plasma Ca^{2+} level below 3.5 mg/dL stimulates PTH secretion.
  - Plasma Ca^{2+} level more than 5.5 mg/dL inhibits PTH secretion.

- **Stimulators:**
  - ***Low Ca2+:*** dominant regulator of PTH. PTH is inversely related to Ca2+
  - Mild ***decrease in magnesium***.
- **Inhibitors:**
  - ***1,25-(OH)2-D*** inhibits PTH gene expression, providing another level of feedback control of PTH.
  - ***Increased Ca++ level***
  - Despite close connection between Ca2+ and PO4, no direct control of PTH is exerted by phosphate levels.
- A unique calcium receptor within the parathyroid cell plasma membrane senses changes in the extracellular fluid concentration of Ca2+.

Mechanism of PTH action:

- It binds with its receptor ***on the cell*** **membrane of bones & kidney mediated by cAMP**.

Actions of PTH:

- **Stimulates**: renal reabsorption of ***calcium*** , ***bone resorption*** and ***synthesis of calcitriol***.
- **Inhibits:** renal reabsorption of ***phosphate*** and ***bone formation and mineralization***.

Net effect: Increase of serum calcium and decrease in serum phosphate

Hypoparathyroidism:

- **Causes** :

1. Abnormal parathyroid gland causes reduced or absent synthesis of PTH.
2. Inadvertent (Accidental) removal of parathyroid gland during thyroid surgery.
3. Parathyroid surgery.
4. Autoimmune.
5. Congenital hypoparathyroidism.

- **Characteristics:**

- ***Hypocalcemia***
- ***Low circulating PTH.***
- ***Hyperphosphatemia***.

- **Treatment:**
  Oral calcium and active form of vitamin D.

- **Signs and symptoms***:*

- Positive Chvostek's (facial muscle twitch) sign:
  Tapping the facial nerve as it emerges from the parotid gland in front of the ear causes contraction of facial muscles.
- Positive Trousseau's (carpal spasm) sign:
- Arresting (stopping) blood flow to the forearm for few minutes (e.g., by sphygmomanometer) → causes flexion at the wrist, thumb and metacarpophalangeal joints.
- Delayed cardiac repolarization with prolongation of the QT interval.
- Paresthesia.
- Tetany (Overt or latent)

Pseudohypoparathyroidism:

- **Cause:**
  Reduction of activity of Gs protein and failure of PTH to produce normal increase in cAMP.
- **Characteristics**:
  Symptoms of hypoparathyroidism but the ***circulating levels of PTH are normal or elevated.***

Hyperparathyroidism:

Primary hyperparathyroidism:

- **Cause:**
  Due to excess PTH secreted from adenomatous or hyperplastic parathyroid tissue.
- *Hypercalcemia* results from combined effects of PTH-induced bone resorption, intestinal calcium absorption and renal tubular reabsorption.
- Pathophysiology related to both PTH excess and concomitant *excessive production of 1,25-(OH)2-D.*
- *Hypophosphatemia* due to decreased renal phosphate reabsorption and phosphaturia.
- *Hypercalciuria & stone formation.*
- *Increased urinary cAMP*

Secondary hyperparathyroidism:

- Parathyroid glands are stimulated to secrete excess PTH secondary to hypocalcemia caused by:
  - Vitamin D deficiency.
  - Chronic renal failure.

- **Characterized by:**

  - High PTH level.
  - ***Calcium level: hypocalcaemia or normal, never hyper.***

Features of hyperparathyroidism:

- Kidney: Polyuria, polydipsia and renal stones.
- Bones: Rickets or osteomalacia, osteitis fibrosa cystica (soft bones with cyst formation).
- GIT: Nausea, vomiting, indigestion, constipation, peptic ulcer, pancreatitis.
- Musculoskeletal: Proximal muscle weakness.
- CNS: Depression, memory loss, psychosis and coma.