- Calcium homeostasis is maintained by 3 hormones : PTH, Calcitonin, Vit D:

1. **PTH**: secreted from the parathyroid gland in response to hypocalcemia, **increases** the **Ca** level and **decreases** the **PO4** (Phosphate) level in the blood, by acting **directly** on the **Bones & Kidneys**[1] and **indirectly** on the **Intestines**.
2. **Calcitonin:** secreted from C-Cells of the thyroid gland, In response to Hypercalcemia, Decreases the Ca and Increases the PO4. Acts on Bones and kidneys. In short it is the physiological antagonist to PTH.
3. **Vit D :** Increases Renal and intestinal **calcium** and **Phosphate** **absorption**.

[1]The primary response to parathyroid hormone (PTH) by the kidney is to increase renal calcium resorption and phosphate excretion. And Synthesis of calcitriol — PTH stimulates the synthesis of 1-alpha hydroxylase in the proximal tubules and thus conversion of calcidiol to calcitriol, thereby stimulating intestinal calcium absorption.

❖ Hyperparathyroidism:

- Primary hyperparathyroidism (PHPT) is the unregulated overproduction of PTH resulting in abnormal calcium homeostasis[2].
- Most common cause of hypercalcemia in hospitals → malignancy.
- Most common cause in community → primary hyperparathyroidism.
- More common in females.
- Etiology[3]: Single adenoma (90%), 4 glands hyperplasia (10%), cancer (rare).

- Dx:
  - Patients most common presentation is asymptomatic hypercalcemia(routine biochemical screening).
  - Hx:
    - Classical Sx of PHPT "bones, stones, abdominal moans and psychic groans".
    - General Sx: Fatigue, muscle weakness or pain, arthralgia, depression and restlessness.
    - Advanced disease: Abdominal pain, Peptic ulcer (increased gastrin secretion), Pancreatitis, Renal stones and nephrocalcinosis (diffuse deposition of Po4 & Ca in parenchyma) and may lead to renal failure, Bone pain and osteoporosis.
    - Others: polydipsia and polyuria, anemia (downregulation of erythropoietin receptors in bone marrow by PTH-normocytic normochromic anemia), HTN (effect of PTH on endothelium), shortened QT interval.
  - PEx[4]: No specific physical findings of PHPT.
  - Labs:
    - High Ca + high PTH → diagnostic.
    - Usually phosphate level is low and chloride is high.
  - X-ray: Hands (subperiosteal bone resorption, cysts formation and generalized osteopenia), skull (Moth eaten appearance).

[2] The parathyroid gland secretes PTH. In normal subjects, a decrease in serum ionized calcium results in a large increase in serum PTH concentration within minutes; (immediately, less than 5 minutes); conversely, when serum ionized calcium is normalized; PTH concentration rapidly falls back to normal (also within minutes) because of the feedback inhibition of parathyroid hormone (PTH).
[3] When the negative feedback is abnormal, the parathyroid hormone increases regardless of the calcium level. In primary hyperparathyroidism due to adenomas, the normal feedback on parathyroid hormone production by extracellular calcium seems to be lost, resulting in a change in the set point. However, this is not the case in primary hyperparathyroidism from parathyroid hyperplasia. An increase in the cell numbers is probably the cause.
[4] Parathyroid adenomas are rarely palpable, and if a neck mass is palpated in a patient with PHPT, the diagnosis is more likely to be thyroid nodule or parathyroid carcinoma.

Treatment[5]

- Asymptomatic: inform the patient and follow up.
- Surgical treatment (hyperparathyroidectomy):
  - Adenoma: Removal of the single adenoma.
  - Hyperplasia: In the case of 4 gland hyperplasia, a 3.5 gland (subtotal) parathyroidectomy is performed.
- Surgery indications:
  1. Serum calcium is more than >12 mg/dL.
  2. Low bone density on bone densitometry.
  3. Symptomatic.
- Preoperative localization:
  - Adenoma:
    - Sestamibi scintigraphy/MIBI [6]: Parathyroid adenoma (uptake).
    - US: Sensitivity for detecting parathyroid adenoma ranges from 70-80 %.
    - ★ Doctor recommended doing both, but if u have to choose one then go for US.
  - Hyperplasia: Sestamibi scanning and ultrasound are often unrevealing.
- How to differentiate b/w adenoma & hyperplasia ?
  - Hyperplasia & adenoma can NOT be differentiated by pathological examination.However, by taking a biopsy if only one gland is diseased then it is adenoma, and if all are diseased then it is a hyperplasia.
  - Intraoperatively:
    - PTH level measurement post excision (after 5, 10 and 15 minutes). If decreased it is adenoma, if not it is hyperplasia u have to remove the rest.
    - Tissue to pathology → to confirm that what u excised is parathyroid not a lymph node.

Secondary Hyperparathyroidism[7]	Tertiary hyperparathyroidism[8]
• Low Ca + high Po4 + High PTH.	• Normal Ca at beginning + High PTH, thus Ca increase eventually.

- Secondary and Tertiary are caused by hyperplasia of the parathyroid gland. Adenoma ONLY causes primary. [9]
- Rx:
  - Secondary: Treat the underlying cause.
  - Tertiary: 1 year after the kidney transplantation if the PTH does not go back to normal, then surgery[10] is indicated.

---

[5] Medical : Hydration (saline+diuretics → get rid of excess ca). And prevent bone resorption by estrogen (postmenopausal), calcitonin (inhibits osteoclast), bisphosphonates, phosphate (antihypercalcemic).

[6] Technetium-99m-methoxyisobutylisonitrile (99mTc-sestamibi or MIBI) /Subtraction scan: (injecting a substance that is absorbed by the thyroid and the parathyroid and the image is recorded. Then injecting another substance that is absorbed only by the thyroid and the image is recorded. The thyroid image is subtracted from the combined thyroid-parathyroid image, and what remains is potentially a parathyroid adenoma.)
SPECT: Sestamibi-single photon emission computed tomography (SPECT or MIBI-SPECT) is a three-dimensional sestamibi scan that provides higher resolution imaging and improves the performance of sestamibi scanning.

[7] One of the commonest causes of secondary hyperparathyroidism is renal failure. In renal failure Ca level low and Po4 high. As a normal response the parathyroid gland will secrete PTH, but because of the chronicity of the disease the PTH level is very high compared to PHPT.

[8] A state of excessive secretion of parathyroid hormone after long standing secondary hyperparathyroidism and resulting in hypercalcemia.

[9] Example: A patient, who was known to have renal failure on dialysis and had a secondary hyperparathyroidism was received a kidney transplant. In secondary hyperparathyroidism, PTH level goes back to the normal level after the transplantation. In tertiary hyperparathyroidism, PTH levels remain high after renal transplantation.

[10] Total parathyroidectomy and implantation of parathyroid tissue (1/ 2 gland or less than 1/ 2) into the non-dominant forearm.

★ Parathyroidectomy

- You have to provide an informed consent of the following: (Included in objectives)
  - The variable position of the glands.
  - Function of the glands.
  - Results of hyperfunction: renal effects, bone disease and systemic effects.
  - That only one gland is likely to be diseased and overactive, and that this is very rarely malignant (< 1%).
  - That surgery will attempt to remove the abnormal gland but may fail to locate it because it is in an ectopic position.
  - That there may be a need for calcium and vitamin D supplements after surgery.

Hypoparathyroidism[11]:

- Causes:
  - Surgical (excision of thyroid, parathyroid, head & neck surgery).
  - Functional: Hypomagnesemia (Mg helps PTH to be released and helps in it's peripheral action).
  - Idiopathic.

- **Dx**:
  - S&Sx[12]:
    - Paraesthesia, Lethargy, Stridor (laryngeal muscles spasm), Chovstek's sign, Trousseau sign, carpopedal spasm, prolonged QT interval.
  - Labs: Low Ca + Low PTH + High PO4 = hypoparathyroidism.
  - Hypocalcemia W/O Hypoparathyroidism :
    - Acute pancreatitis.
    - Chronic renal failure (loss of vit D3, Hyperphosphatemia decreases the Ca conc.)

- **Rx**:
  - Acute: IV calcium gluconate (20 mL of a 10% solution given intravenously diluted in 100 mL of saline) 4-hourly until calcium levels rise.
  - Definitive: Oral calcium and, if required, vitamin D (must be active becuz it's normally activated by PTH whi is deficient) is prescribed according to serial blood calcium levels. Po4 restriction in diet.

Good luck :)
Adel Alshihri.

[11] Deficient PTH leading to decreased Ca and increased PO4. may occur temporarily after parathyroidectomy (until the suppressed residual glands assume normal function).
[12] All r generally related to hyperactivity (low Ca lowers the threshold of excitability in nerves). **Paresthesia** → Affecting perioral region and hands and feet (early symptoms). **Chovstek's sign** → Twitching of the facial muscles on tapping of the facial (VII) nerve over the angle of the jaw. **Trousseau** → Spasm of hand and forearm muscles after applying a tourniquet to occlude the pulse.