Management of Factor Deficiency Disorders

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Cutting Edge
Surgical Medical Group

Disclosures

NONE

Learning Objectives

- Evaluate

- Primary, Secondary, and Tertiary Hyperparathyroidism
- Acute Hypercalcemia
- Hyperthyroidism and Thyroid Storm
- Hypothyroidism and Myxedema Coma
- Hypoparathyroidism

Hypercalcemia and Related Effects

Causes of Hypercalcemia

- PHPT (80–90% of outpatient cases)
- Malignancy (lung, breast, multiple myeloma)
- Thiazide diuretics, granulomatous diseases.

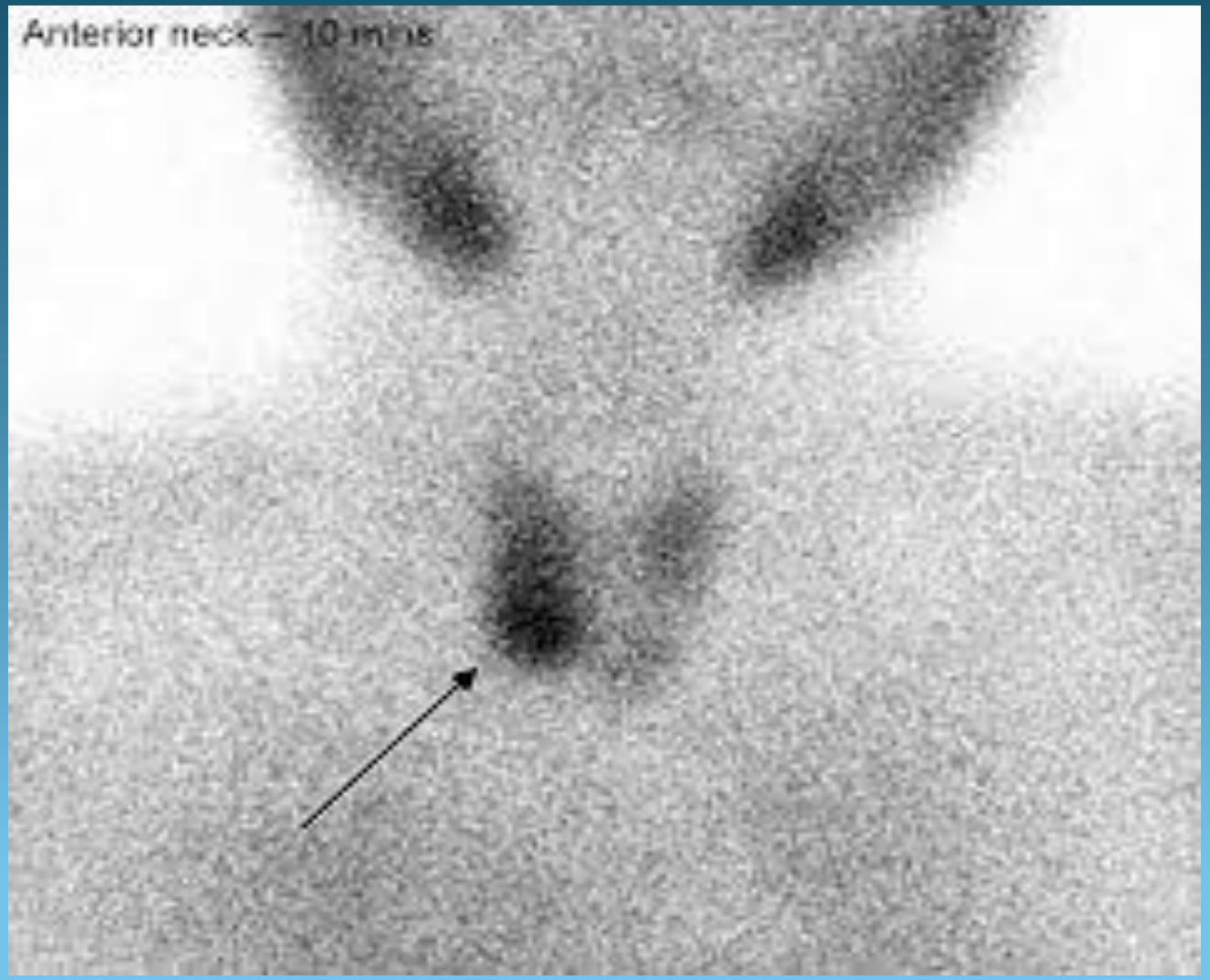
Effects of Hypercalcemia

- Neuropsychiatric: Confusion, lethargy.
- Gastrointestinal: Constipation, nausea.
- Renal: Nephrolithiasis, polyuria.
- Cardiovascular: QT interval shortening, arrhythmias.

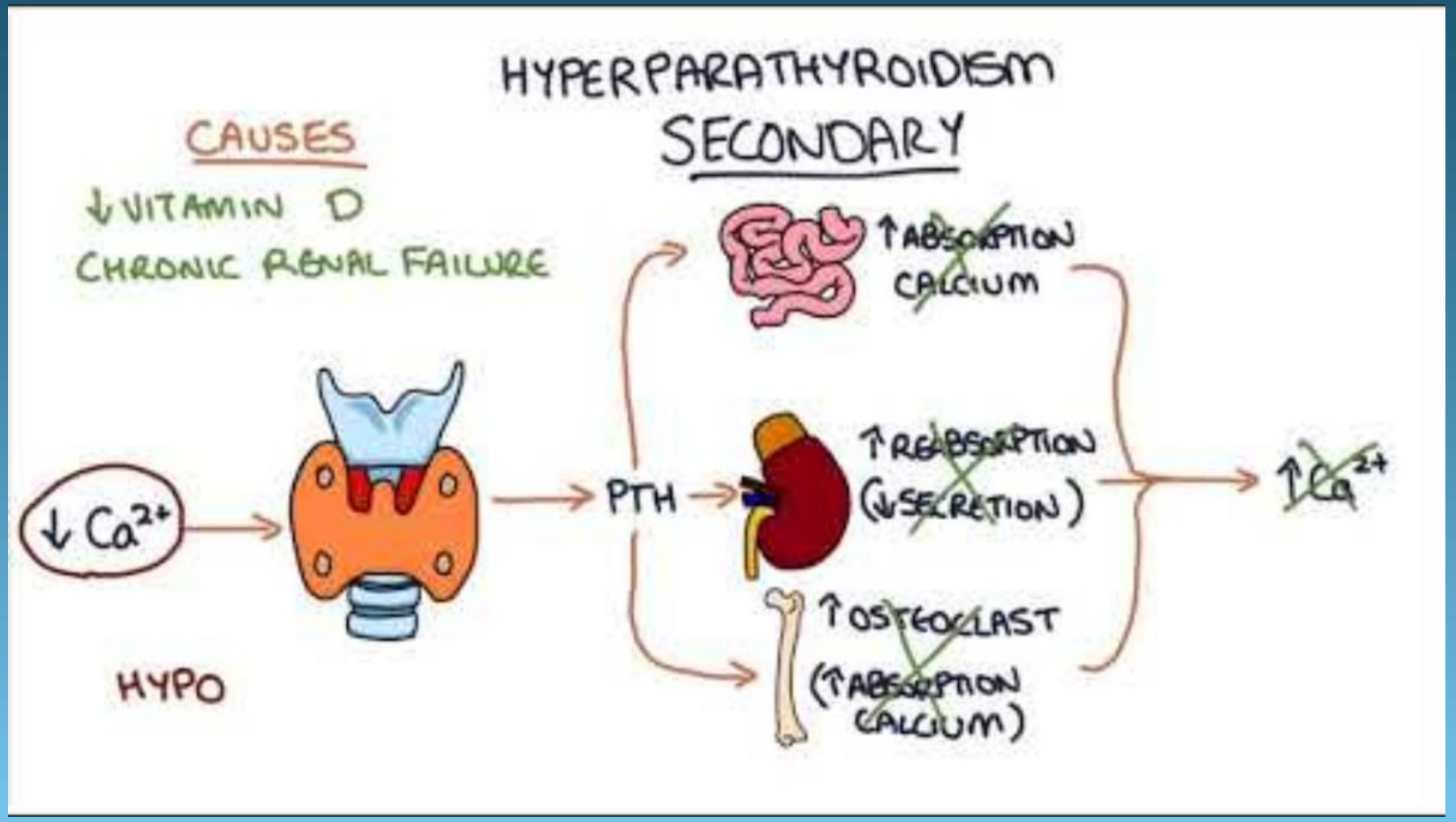
Acute Management of Hypercalcemia

- **Hydration**: Isotonic saline (200–300 mL/h) to restore volume.
- **Bisphosphonates**: Zoledronate 4 mg IV over 15 min (effects in 48–72 hrs).
- **Calcitonin**: 4 IU/kg SC q12h (rapid onset, short duration).
- **Steroids**: Especially for vitamin D-mediated hypercalcemia.
- **Dialysis**: In renal failure or severe hypercalcemia (>18 mg/dL).

Sestamibi scan



Video



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Primary Hyperparathyroidism (PHPT)

- **Etiology:** Autonomous parathyroid hormone (PTH) secretion, most commonly due to a single adenoma (80-85%) (Bilezikian et al., 2021).
- **Symptoms:** Hypercalcemia, nephrolithiasis (15–20%), osteoporosis (30–50%), fatigue, cognitive changes.
- **Diagnosis:**
  - Elevated serum calcium (>10.5 mg/dL) and PTH.
  - 24-hour urinary calcium >200 mg/day.
  - Bone mineral density (BMD) with T-score ≤ -2.5.

Primary Hyperparathyroidism (PHPT)

- **Management:**
  - **Surgical**: Parathyroidectomy indicated in symptomatic patients or asymptomatic with:
    - Serum calcium >1 mg/dL above upper limit (90%)
    - Creatinine clearance <60 mL/min
    - Age <50 years
    - T-score ≤ -2.5 (Keenan et al., 2017)
  - **Medical**:
    - Cinacalcet (a calcimimetic) for non-surgical candidates.
    - Bisphosphonates for bone protection.

Secondary Hyperparathyroidism (SHPT)

- Secondary hyperparathyroidism (SHPT) is a condition where the parathyroid glands produce excessive parathyroid hormone (PTH) in response to low calcium and vitamin D levels in the blood. It's often caused by kidney problems, which can impair vitamin D activation and lead to low calcium and phosphorus levels, triggering the parathyroid glands to overproduce PTH. Symptoms can include bone pain, fatigue, muscle weakness, and even kidney stones
- Vitamin D deficiency is a major contributor to secondary hyperparathyroidism, a condition where the parathyroid glands produce excessive amounts of parathyroid hormone (PTH) in response to low calcium levels. This low calcium is often a result of impaired vitamin D activation, particularly in individuals with chronic kidney disease (CKD).

Secondary Hyperparathyroidism (SHPT)

- Vitamin D's activation in the body, especially related to cell cycle progression and CDKs, involves a two-step process. First, it's hydroxylated in the liver to produce 25-hydroxyvitamin D, which is then further hydroxylated in the kidney to form the active form, calcitriol (1,25(OH)2D3).
- Calciferol, or vitamin D, plays a crucial role in maintaining calcium and phosphate balance, primarily by promoting their absorption in the small intestine and regulating their levels in the bloodstream. Vitamin D, when activated to its hormonal form, calcitriol (1,25-dihydroxyvitamin D), increases calcium and phosphate absorption, elevates serum calcium levels, and facilitates bone mineralization

Secondary Hyperparathyroidism (SHPT)

- Parathyroid hormone (PTH) primarily regulates calcium levels in the blood, with a secondary effect on phosphate. It increases calcium levels by stimulating bone breakdown, increasing calcium absorption in the intestines (via vitamin D activation), and promoting calcium reabsorption in the kidneys. Simultaneously, PTH decreases phosphate reabsorption in the kidneys, leading to increased phosphate excretion in urine.

Secondary Hyperparathyroidism (SHPT)

Secondary Hyperparathyroidism (SHPT)

- **Etiology:** Chronic kidney disease (CKD), leading to hypocalcemia and phosphate retention.
- **Diagnosis:**
  - Elevated PTH, low-normal calcium, elevated phosphate.
- **Management:**
  - **Phosphate Binders**: Sevelamer reduces phosphate and PTH (Block et al., 2004).
  - **Vitamin D Analogs**: Calcitriol or paricalcitol to suppress PTH.
  - **Calcimimetics**: Cinacalcet reduces PTH by 30–50% (EVOLVE trial).
  - Dialysis optimization and renal transplant if indicated.

Tertiary Hyperparathyroidism (THPT)

- **Etiology:** Prolonged SHPT post-kidney transplant; autonomous PTH secretion despite normocalcemia.
- **Management:**
- Surgical parathyroidectomy.
- Cinacalcet if surgery contraindicated (80% PTH reduction in some cases) (Okada et al., 2014).
- Cinacalcet is used to treat hyperparathyroidism in patients with chronic kidney disease who are on dialysis.

TABLE 3

Lab Comparison

Hyperparathyroidism	Calcium	PTH	Vitamin D	Phosphate
Primary	↑	↑ →	↑	↓
Secondary	↓ →	↑	↓	↑ or ↓
Tertiary	↑	↑↑	↓	↑

Key: ↑Elevated, ↓decreased, →normal.

Source: Brashers, *Pathophysiology*, 2015.[6]

Thyroid Disorders

Hyperthyroidism

- **Causes**: Graves' disease (70–80%), toxic multinodular goiter, thyroiditis.
- **Symptoms**: Weight loss, tremor, palpitations, heat intolerance.
- **Diagnosis**:
  - Low TSH, elevated free T4/T3.
  - Radioiodine uptake scan to differentiate cause.
- **Treatment**:
  - **Antithyroid Drugs**: Methimazole (first-line), PTU in pregnancy.
  - **Beta-Blockers**: Propranolol 10–40 mg TID for symptom control.
  - **Radioiodine**: I-131 in toxic nodules or Graves'.
  - **Surgery**: Indicated in large goiters or malignancy suspicion.

Thyroid Storm

- **Life-threatening**: 10–30% mortality if untreated (Angell et al., 2021).
- **Precipitating Factors**: Infection, surgery, trauma.
- **Symptoms**: Fever, tachycardia, delirium, heart failure.
- **Treatment**:
  - **Supportive**: ICU care, cooling, IV fluids.
  - **Medications**:
    - PTU 500–1000 mg load, then 250 mg q4h.
      - Propylthiouracil inhibits the production of new thyroid hormone in the thyroid gland.
    - Methimazole
      - Methimazole exerts its therapeutic effect by inhibiting thyroperoxidase, a crucial enzyme in synthesizing thyroid hormones. This mechanism decreases the synthesis of thyroid hormones, specifically thyroxine (T4) and triiodothyronine (T3), restoring normal thyroid function

Thyroid Storm

- Iodine (SSKI) 1 hour after PTU.
- Lugol's solution typically has a concentration of 5% elemental iodine (I2) and 10% potassium iodide (KI). This translates to a total iodine content of approximately 126.4 mg/mL in a 5% solution. It's an aqueous solution of iodine and potassium iodide, used as a mordant in various applications.
- Lugol's solution, a solution of iodine and potassium iodide, works in thyroid storm by inhibiting the release of thyroid hormones from the thyroid gland. It achieves this by interfering with several steps in thyroid hormone production, including blocking the thyroid from absorbing more iodine, inhibiting iodide oxidation and organification (the process of attaching iodine to thyroglobulin), and directly blocking the release of stored thyroid hormones. This rapid reduction in thyroid hormone levels helps to alleviate the symptoms of thyroid storm

Thyroid Storm

Beta Blockers IV

Beta-blockers help in thyroid storm primarily by managing the adrenergic symptoms and slowing the heart rate, which is a key feature of this condition. They also help by reducing the conversion of T4 to T3, which can contribute to the severity of thyroid storm

Hypothyroidism

Causes: Hashimoto’s thyroiditis, post-thyroidectomy, radiation.

Symptoms: Fatigue, bradycardia, cold intolerance, depression.

Diagnosis:

- **Elevated TSH, low free T4.**
- **Anti-TPO antibodies positive in 90% of Hashimoto’s (Vanderpump, 2011).**

Treatment:

- **Levothyroxine: 1.6 mcg/kg/day in healthy adults.**
- **Monitor TSH every 6–8 weeks after dose adjustment.**

Myxedema Coma

Severe Hypothyroidism Emergency (Mortality: 30–60%).

Symptoms: Hypothermia, bradycardia, altered mental status, hyponatremia.

Treatment:

- **IV levothyroxine 200–400 mcg bolus.**
- **Hydrocortisone 100 mg IV q8h.**
- **Passive rewarming, mechanical ventilation if needed.**

Hypoparathyroidism

Etiology: Post-surgical (75%), autoimmune, genetic.

Symptoms: Tetany, seizures, paresthesias.

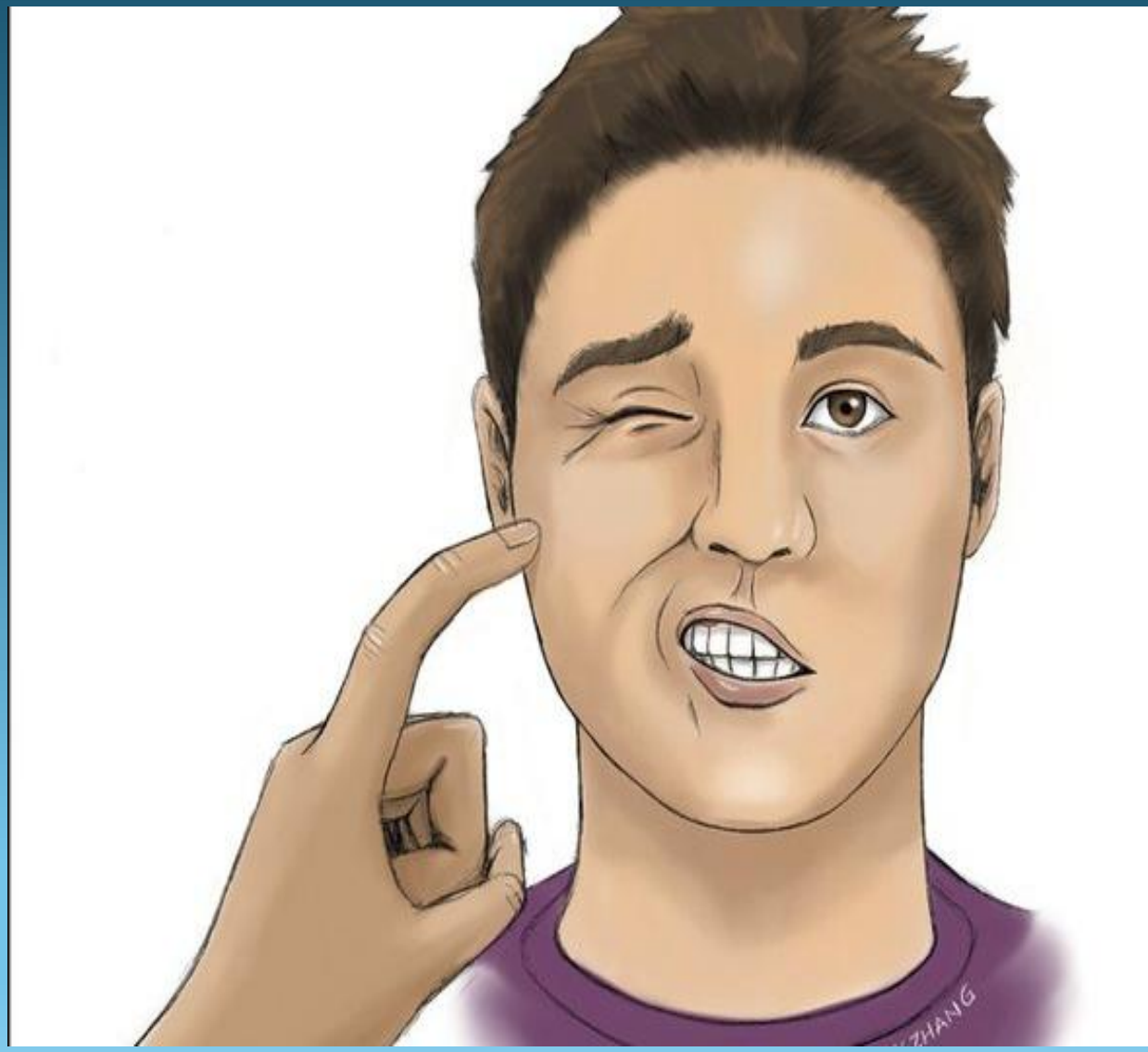
Labs: Low calcium, low PTH, high phosphate.

Treatment:

- **Calcium carbonate 1–2 g elemental/day.**
- **Calcitriol 0.25–2 mcg/day.**
- **Thiazides to reduce urinary calcium excretion.**
- **rhPTH (Natpara) in refractory cases (Winer et al., 2012).**

Chvostek's sign

- Chvostek's sign is a clinical finding associated with hypocalcemia (low blood calcium) where tapping the facial nerve in front of the ear causes a twitch or spasm of the facial muscles on the same side.



Trousseau's sign

- Trousseau's sign is a medical sign, specifically the Trousseau sign of latent tetany, that indicates increased neuromuscular irritability, often associated with hypocalcemia (low blood calcium). (Carpal Pedal spasm)

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References

- sestamibi scan - Google Search
- Chvostek's sign - Google Search
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