433 Teams

MEDICINE

7 | Parathyroid Disorders

433medicine.team@gmail.com

جامعة الملك سعود
King Saud University

COLOR INDEX

Slides - Step-Up medicine - Kaplan Notes - Extre explanation - Doctor Notes

Objectives:

1.Understand Calcium and related hormones physiology
2. Understand hyperparatyroidism
3. Understand hypoparathyroidism

Normal Physiology

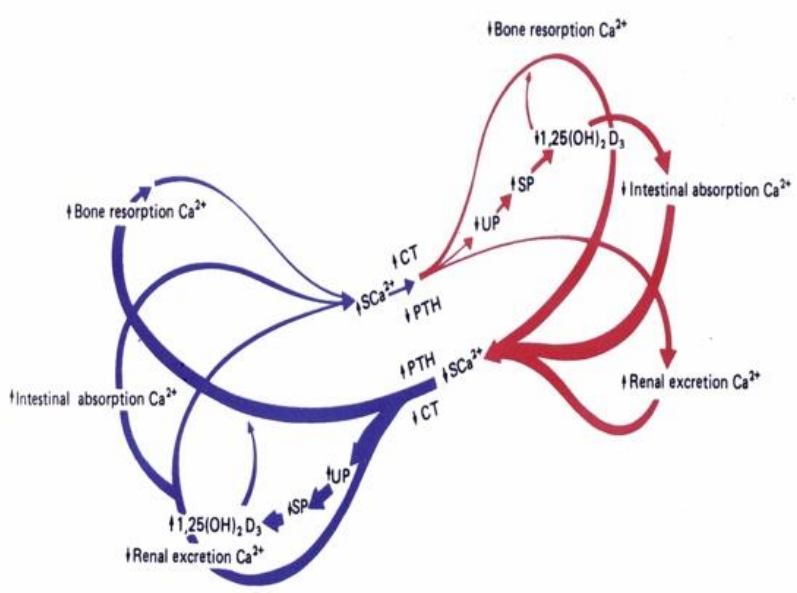
Maintenance of calcium, phosphate and magnesium homeostasis is under the influence of two polypeptide hormones; parathyroid hormone(PTH), and calcitonin (CT), as well as a sterol hormone, 1,25 dihydroxy cholecalciferol (1,25 $(OH)_2D_3$.

These hormones regulate the flow of minerals in and out of the extracellular fluid compartments through their actions on intestine, kidneys, and bones.
The PTH acts directly on the bones and kidneys and indirectly on the intestine through its effect on the synthesis of 1,25 $(OH)_2D_3$.

Its production is regulated by the concentration of serum ionized calcium. Lowering of the serum calcium levels will induce an increased rate of parathyroid hormone secretion.

Calcitonin is released by the "C" cells (Para-follicular cells in the thyroid gland) in response to small increases in plasma ionic calcium. It acts on the kidney and bones to restore the level of calcium to just below a normal set point which in turn inhibits secretion of the hormone.

Calcitonin is therefore the physiological antagonist of PTH. The two hormones act in concert to maintain normal concentration of calcium ion in the extracellular fluid.



$1,25\ (OH)_2D_3$:

Calcitriol also called **1,25-dihydroxycholecalciferol** or **1,25-dihydroxyvitamin D_3**

Hypoparathyroidism:

Deficient secretion of PTH which manifests itself biochemically by hypocalcemia, hyperphosphatemia diminished or absent circulating iPTH (immunoreactive parathyroid hormone) and clinically the symptoms of neuromuscular hyperactivity.

❖ Causes:

Surgical hypoparathyroidism: **(the commonest cause)** Head and neck surgery account for the majority of cases– 1.thyroidectomy 2. para- thyroidectomy 3. Radical surgery for head and neck malignancies. It could be due to the removal of the parathyroid glands or due to interruption of blood supply to the glands.	Idiopathic hypoparathyroidism: - A form occurring at an early age (genetic origin) with autosomal recessive mode of transmission 1.multiple endocrine deficiency - autoimmune-candidiasis (MEDAC) syndrome, 2.Juvenile familial endocrinopathy, 3.Hypoparathyroidism , Addisson's disease, mucocutaneous candidiasis (HAM) syndrome. Circulating antibodies for the parathyroid glands and the adrenals are frequently present. -The late onset form occurs sporadically without circulating glandular autoantibodies.	Functional hypoparathyroidism In patients who has chronic hypomagnesaemia of various causes. Magnesium is necessary for the PTH release from the glands and also for the peripheral action of the PTH.

Major causes of chronic hypocalcemia other than hypoparathyroidism:

Hypomagnesemia: Magnesium is necessary for PTH to be released from the gland. Low magnesium levels also lead to increased urinary loss of calcium.

• Renal failure: This leads to hypocalcemia. The kidney converts 25 hydroxy-D to the more active 1,25 hydroxy-D.

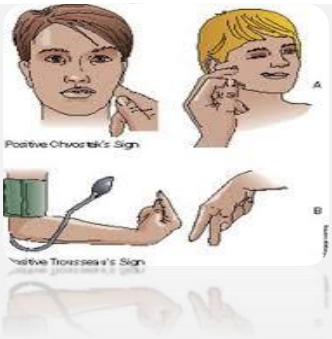
Other causes include vitamin D deficiency, genetic disorders, fat malabsorption, and low albumin states.

Decreased intestinal absorption of vitamin D or calcium due to primary small bowel disease, short bowel syndrome, and post-gastrectomy syndrome.

Drugs that cause rickets or osteomalacia such as phenytoin, phenobarbital, cholestyramine, and laxative

❖ Clinical features:

The rate of decrease in serum calcium is the major determinant for the development of neuromuscular complications.When nerves are exposed to low levels of calcium they show abnormal neuronal function which may include decrease threshold of excitation, repetitive response to a single stimulus and rarely continuous activity.

NUMBNESS/TINGLING	circumoral, fingers, toes (Parathesia)
TETANY	Signs of latent tetany: 1-Hyperactive deep tendon reflexes 2-Chvostek's sign—Tapping the facial nerve elicits contraction of facial muscles. 3-Trousseau's sign—Inflating the BP cuff to a pressure higher than the patient's systolic BP for 3 minutes elicits carpal spasms.
GRAND MAL SEIZURES	
HYPERVENTILATION	
ADRENERGIC SYMPTOMS	
CONVULSION	More common in young people and it can take the form of either generalized tetany followed by prolonged tonic spasms or the typical epileptiform seizures.

❖ Diagnosis:

1. Low serum calcium.
2. High serum phosphate.
3. Serum PTH inappropriately low.
4. Low urine cAMP.

NOTE that both vitamin D and calcium replacement can increase urinary calcium excretion, precipitating kidney stones. Therefore, administer with caution to avoid hypercalciuria

❖ Treatment

Replace calcium and vit D. This is done orally if symptoms are mild or absent and intravenously if symptoms are severe

❖ Primary hyperparathyroidism:

General characteristics:

One or more glands produce inappropriately high amounts of PTH relative to the serum calcium level → This leads to hypercalcemia which fails to inhibit the gland activity in the normal manner.

Causes:

- Adenoma (80% of cases)—majority involve only one gland
- Hyperplasia (15% to 20% of cases)—all four glands usually affected
- Carcinoma (<1% of cases)

1-The cause of primary hyperparathyroidism is unknown

2- The incidence of the disease increases dramatically after the age of 50 and it is 2-4 folds more common in women

❖ Clinical features:

Stones	❖ Nephrolithiasis (renal stones) ❖ Nephrocalcinosiscrine (diffuse deposition of calcium-phosphate complexes in the parenchyma) ❖ Metabolic Diseases e.g. hypomagnesia, pancreatitis, gout or pseudogout (not common)
Bones	❖ Bone aches and pains. ❖ Osteoporosis. ❖ Osteitis fibrosa cystica (brown tumor) "salt and pepper" appearance of the skull as well as bone cysts and brown tumors of the long bones.
Muscle pain and weakness.	Other signs : HTN, shortened QT interval.
Pancreatitis (ca stimulates gastrin)	
Peptic ulcer disease	
Gout and pseudo gout	
Constipation	
Psychiatric overtones	❖ depression, fatigue, anorexia, sleep disturbances, anxiety, lethargy.

❖ Causes of Hypercalcemia: (DDX)

Parathyroid - related	Vitamin D – related
1. Primary hyperparathyroidism A. Solitary adenomas B. Multiple endocrine neoplasia 2. Lithium therapy 3. Familial hypocalciuric hypercalcemia	1. Vitamin D intoxication 2. 1,25(OH)2D; sarcoidosis and other granulomatous diseases 3. Idiopathic hypercalcemia of infancy
Malignancy – related	Associated with high bone turnover
1. Solid tumor with metastases(breast) 2. Solid tumor with humoral mediation of hypercalcemia (lung kidney) 3. Hematologic malignancies (multiple myeloma, lymphoma, leukemia)	1. Hyperthyroidism 2.Immobilization 3.Thiazides 4.Vitamin A intoxication
Associated with Renal Failure:	
1. Severe secondary hyperparathyroidism 2. Aluminum intoxication 3. Milk alkali syndrome	

❖ Diagnosis:

- Besides high calcium and PTH levels, you will also find a low phosphate level, high chloride level, EKG with a short QT, and sometimes an elevated BUN and creatinine

. Alkaline phosphatase may be elevated from the effect of PTH on bone.

- ❖ Preoperative imaging of the neck with sonography or nuclear scanning maybe helpful in determining the surgical approach

- Radiographs

Plain X-ray of hands can be diagnostic showing subperiosteal bone resorption usually on the radial surface of the distal phalanx with distal phalangeal tufting as well as cysts formation and generalized osteopenia.

Bone x-ray is not a good test for bone effects of high PTH. DEXA densitometry is better.

❖ Treatment:

Surgical removal of the involved parathyroid glands is the standard of care. When surgery is not possible, give Cinacalcet.

NOTE

Low calcium = twitchy and hyperexcitable
High calcium = lethargic and slow

❖ Medical Treatment of the hypercalcemia:

Acute hypercalcemia is treated with:
1. Saline hydration at high volume
2. Bisphosphonates: pamidronate, zoledronic acid

If you treat the patient with these two and ca level still high give him Calcitonin

❖ Secondary hyperparathyroidism:

An increase in PTH secretion which is adaptive and unrelated to intrinsic disease of the parathyroid glands is called secondary hyperparathyroidism.
This is due to chronic stimulation of the parathyroid glands by a chronic decrease in the ionic calcium level in the blood.

Hungry bone syndrome:

In patients with hyperparathyroidism and severe bone disease who undergo successful parathyroidectomy hypocalcaemia may be severe and parenteral calcium infusion with later supplementation with oral calcium and vitamin D.

METABOLIC BONE DISEASES

Bone has three major functions:

Provide rigid support to extremities and body cavities containing vital organs.	Provide efficient levers and sites of attachment of muscles which are all crucial to locomotion	Provide a large reservoir of ions such as calcium, phosphorus, magnesium and sodium which are critical for life and can be mobilized when the external environment fails to provide them.

Types of bones:

1.Cortical Bone:

The compact bone of Haversian systems such as in the shaft of long bones.

2.Trabecular Bone:

The lattice – like network of bone found in the vertebrae and the ends of long bones.

Types of bone cells:

I. Osteoblasts:

The bone forming cells

II. Osteocytes:

They are believed to act as a cellular syncytium that permits translocation of mineral in and out of regions of bone removed from surfaces.

III. Osteoclasts:

The bone resorption cells.

.

The difference pattern of bone loss affecting trabecular and cortical bone results in two different fracture syndrome.

Disorders in which cortical bone is defective or scanty lead to fractures of long bones whereas disorders in which trabecular bone is defective or scanty lead to vertebral fractures and also may help in fractures of lone bones because of the loss of reinforcement.

Osteomalacia:

Failure of organic matrix (osteoid) of bone to mineralize normally.

Etiology of Osteomalacia

Vitamin D deficiency: The most common cause of osteomalacia

1-Inadequate sunlight exposure without dietary supplementation.
2-Gastrointestinal diseases that interrupts the normal enterohepatic recycling of vit. D & its metabolites, resulting in their fecal loss.
3-Impaired synthesis of 1,25(OH)2D3 by the kidney.
Target cell resistance to 1,25(OH)2D3 e.g. absent, or diminished number of 1,25(OH)2D3 receptors, as in vit.D-dependency rickets.

Phosphate deficiency:
A. Dietary:
B. Impaired renal tubular reabsorption of phosphate.
C. Tumor-associated hypophosphatemia.
D.Systemic Acidosis:
- Chronic renal failure.
- Distal renal tubular acidosis.

E.Drug induced Osteomalacia.

Osteomalacia in children is known as rickets

Laboratory & Radiological Findings:

Low serum vit D ,Low phosphate , Low serum and urinary calcium
high alkaline phosphatase, high PTH

❖ Clinical Features:

- ❖ Diffuse joint and bone pain (especially of spine, pelvis, and legs)
- ❖ Muscle weakness
- ❖ Difficulty walking, often with waddling gait
- ❖ Hypocalcemia (positive Chvostek sign)

❖ Treatment:

sunlight exposure
calcium and vitamin D supplements

Osteoporosis:

Decrease in bone mass and strength associated with an increased tendency to fractures and It is usually an asymptomatic disease until fractures occur

Etiology of Osteoporosis

- Menopause
- Old age
- Calcium and vitamin D deficiency
- Estrogen deficiency in women and androgen deficiency in men
- Use of steroids

.

Mechanism of steroid:
Renal Ca loss, Inhibition of intestinal Ca absorption
increase osteoclast and inhibition of osteoblast activity
Suppression of gonadotropin secretion (high dose)

❖ Diagnosis:

- The most accurate test is bone densitometry (DEXA) scanning.
- X-rays of skeleton not very sensitive because it doesn't show a decrease in osseous density until at least 30% of bone mass has been lost.

❖ Treatment:

- Prevention
- Public awareness
- Vitamin D and calcium are the best initial therapy.
- Bisphosphonates (alendronate, risendronate, ibandronate) reducing bone breakdown

Recommend the following to all patients with osteoporosis:

- Daily calcium.
- Daily vitamin D.
- Weight-bearing exercise.
- Smoking cessation.

MSQs

1. A 65-year-old white woman presents for an annual examination. She feels well except for occasional nocturnal leg cramp and mild abdominal bloating. She takes a multivitamin and a supplement containing 600 mg calcium carbonate and 200 international units of vitamin D twice daily. She takes no prescription medications. Physical examination is unremarkable for her age. In completing the appropriate screening tests, you order a dual x-ray absorptiometry (DXA) to evaluate whether the patient has osteoporosis. DXA results reveal a T-score of −3.0 at the total hip and −2.7 at the femoral neck (osteoporosis: less than −2.5). Since her Z-score is −2.0, you proceed with an evaluation of secondary osteoporosis. Laboratory evaluation reveals

-Calcium: 8.2 mg/dL Cr: 1.0 mg/dL.	Bun: 19 mg/dL Glucose: 98 mg/dL.
25,OH vitamin D: 12 ng/mL (optimal > 25).	Liver enzymes including alkaline phosphatase: normal.
WBC: 7700/µL Hg: 10.3 g/dL.	HCT: 32 g/dL.
MCV 68 PLT: 255,000/µL.	

What is the likely cause of her osteoporosis?

a. Hypoparathyroidism	b. Estrogen deficiency
c. Renal leak hypercalciuria	d. Primary biliary cirrhosis
e. Celiac sprue	

2. A 58-year-old postmenopausal woman presents to your office on suggestion from a urologist. She has passed three kidney stones within the past 3 years. She is taking no medications. Her basic laboratory work shows the following:

Na: 139 mEq/L	K: 4.2 mEq/L
HCO3: 25 mEq/L	Cl: 101 mEq/L
BUN: 19 mg/dL	Creatinine: 1.1 mg/dL
Ca: 11.2 mg/dL	

A repeat calcium level is 11.4 mg/dL; PO4 is 2.3 mmol/L (normal above 2.5).

Which of the following tests will confirm the most likely diagnosis?

a. Serum ionized calcium	b. Thyroid function profile
c. Intact parathormone (iPTH) level	d. Liver function tests
e. 24-hour urine calcium.	

1	2
e	c

1. The GI symptoms and the iron deficiency anemia suggest that her hypovitaminosis D is due to intestinal malabsorption. Celiac sprue is relatively common and often presents with mild symptoms. A tissue transglutaminase or antiendomysial antibody test will provide important diagnostic information.

Hypoparathyroidism causes hypocalcemia but is not associated with vitamin D deficiency or osteoporosis. Estrogen deficiency is an important contributing factor to the skeletal loss of calcium in the menopause, but is associated with normal calcium and vitamin D levels and not to the iron deficiency. Hypercalciuria of any cause will lead to kidney stones but does not cause hypocalcemia or hypovitaminosis D. primary biliary cirrhosis may present with mild symptoms (usually pruritus) and vitamin D deficiency, the alkaline phosphatase is always elevated (often three to five times upper normal) in this disease.

2. 90% of hypercalcemia is attributed either to hyperparathyroidism or to malignancy. In this otherwise healthy patient, confirmed hypercalcemia should lead to measurement of intact parathyroid hormone (iPTH). Urine calcium excretion is assessed before parathyroidectomy to rule out familial hypocalciuric hypercalcemia, which can otherwise mimic hyperparathyroidism. Osteoporosis should be considered in this postmenopausal woman with hyperparathyroidism and appropriate screening for osteoporosis performed with central dual x-ray absorptiometry (DXA).

Done By:

Felwa Alharthi	Waleed Alrajban
Noha Almandeel	Arwa Alnaseeb
Faroq Abdulfattah	Areej Alwahaib