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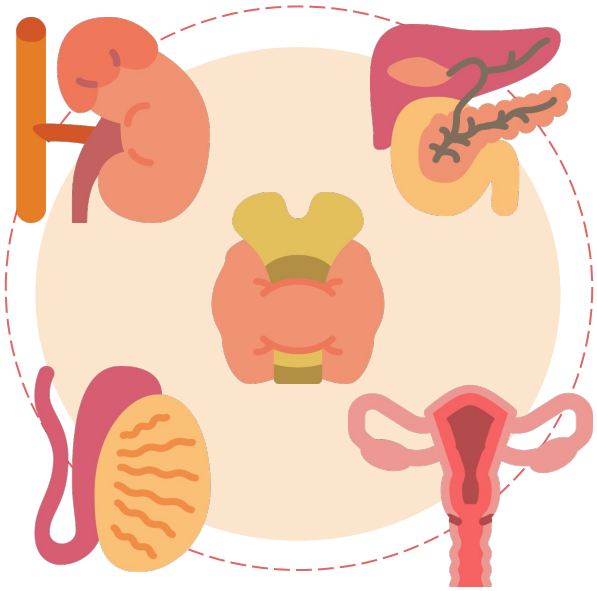

Hypo & Hyperparathyroidism

Objectives:

- Understand the causes and consequences of over-secretion, and under-secretion of parathyroid hormone
- Describe the consequences of vitamin D deficiency and vitamin D excess.

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Colour index:
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Common causes of hypercalcemia

*Red coloured represent main cause of hypercalcemia

1) PTH mediated	Primary hyperparathyroidism
2) Non-PTH mediated	• Parathyroid hormone related peptide **(PTHrP)**: certain tumors secrete high levels of PTHrP, which causes **hypercalcemia of malignancy.** • Vitamin D intoxication, granulomatous disorders, osteolytic bone metastases, malignancy.
3) Medications	Thiazide diuretics — Increase Ca reabsorption

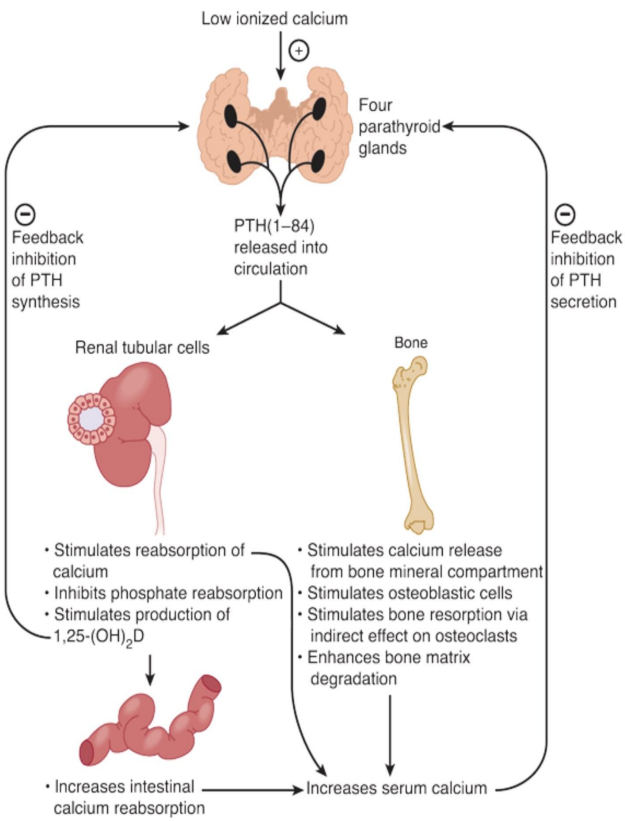
Work also on PTH receptors

Wolff's Law

- States that bone in a healthy person or animal will adapt to the loads under which it is placed. If loading on a particular bone increases, the bone will remodel itself over time to become stronger to resist that sort of loading.
- The remodeling of bone in response to loading is achieved via mechanical stress.
- Prolonged immobilization might lead to bone resorption and increased calcium plasma levels.

Bedridden people will have hypercalcemia because there will be less stress on the bone.

Hyperparathyroidism



Hyperparathyroidism

What is it?

Is a disorder characterized by hypercalcemia, hypercalciuria, hypophosphatemia and hyperphosphaturia.

Investigation results?

- Parathyroid hormone causes phosphaturia and a decrease in serum phosphate.
- Calcium rises and it is also secreted in the urine.

Complications?

- Most common complication are renal stones made of calcium phosphate.
  ➔ Stone chemistries: calcium,phosphate, urate.
- **Most serious complication** is the deposition of calcium in the kidney tubules resulting in impaired renal function.

Causes Of Hyperparathyroidism

Primary

➔ Adenoma (90%).
➔ Multiple gland enlargement (10%).
➔ Familial hyperparathyroidism:
1) Carcinoma (<1%).
2)Familial benign hypercalcemia (FBH).
Ca- sensing receptor mutation

Secondary (normo- or hypocalcemic)

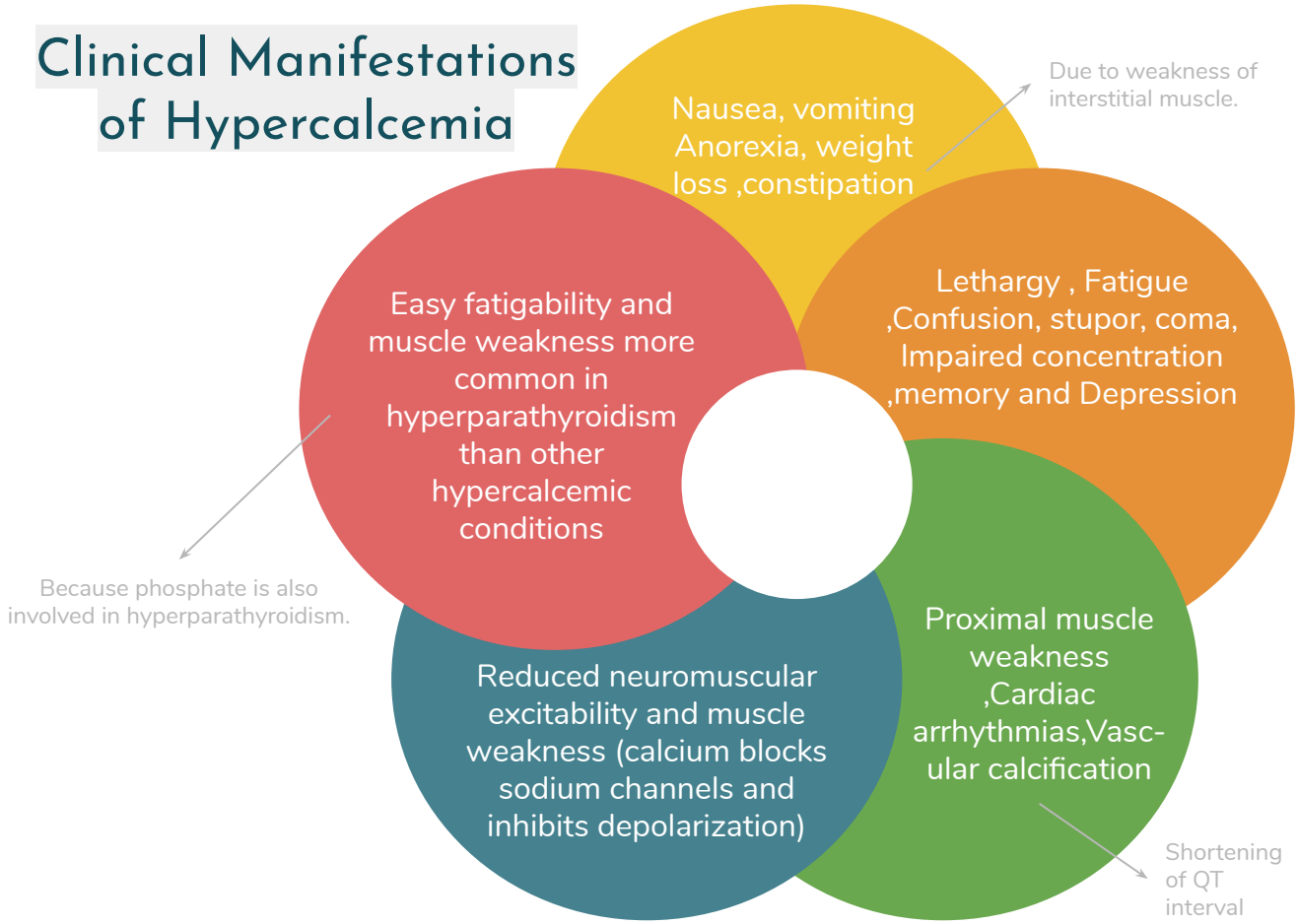
➔ Due to ↓ Ca^{++} in ECF
➔ Causes:
1. Low calcium diet
2. Pregnancy
3. Lactation
4. Rickets
5. Osteomalacia
6. Chronic renal failure
   ↓ 1,25(OH) D3 synthesis (VIT D deficiency)

By two ways:
1- there will be missing of vitamin D action so hypocalcemia persist.
2-missing of negative feedback of vitamin D on parathyroid hormone.

Primary Hyperparathyroidism

- Affects approximately 100,000 patients a year (in the US).
- Prevalence: 0.1 to 0.3% of the general population.
- More common in women (1:500) than in men (1:2000).
- Patients with single adenoma (~90%): minimally invasive surgery.

Clinical Manifestations of Hypercalcemia



Treatment Of Hypercalcemia

1-Indications for therapy
- Symptoms of hypercalcemia.
- Plasma [Ca] >14 mg/dl.

2-Principles of therapy
- Expand ECF volume. (By normal saline .)
- Increase urinary calcium excretion.
- Decrease bone resorption.

➔ NS (normal saline) bolus to restore volume; then 100 200ml/hr.
➔ Bisphosphonates (onset 24-48 hrs). (Increase calcitonin, Suppress osteoclast)
➔ Calcitonin 4 8 IU q6-8 hrs (onset immediate,resistance develops in 24-48 hrs).
➔ Surgery for adenoma.

Hypoparathyroidism

What does it cause?

hypocalcemia, hyperphosphatemia, neuromuscular irritability, numbness, cramps, anxiety, tetany, and carpopedal spasms.

Severe hypocalcemia is followed by convulsions, stridor, dystonia, and depression.

Hypocalcemia

Caused by

1. **Hypoparathyroidism**
2. **Surgical** (thyroid, parathyroid surgery)
3. Autoimmune
4. Magnesium deficiency — Mg is important to parathyroid to produce PTH.
5. PTH resistance (pseudohypoparathyroidism)
6. Normal PTH levels but deficient receptors
7. Vitamin D deficiency
8. Vitamin D resistance
9. Lack of 1α hydroxylase, no vit D3 activation
10. Other: renal failure, pancreatitis, tumor lysis

-Renal failure causes increase Ca excretion and decrease the level of active vitamin D.
-Pancreatitis physiologically causes hypocalcemia, because Ca increase cell damage.

Two common signs of hypocalcemia are:

Chvostek's sign

It refers to an abnormal reaction to the stimulation of the facial nerve. When the facial nerve is tapped at the angle of the jaw (i.e. masseter muscle), the facial muscles on the same side of the face will contract momentarily (typically a twitch of the nose or lips) because of hypocalcemia.

Trousseau's sign

To elicit the sign, a blood pressure cuff is placed around the arm and inflated to a pressure greater than the systolic blood pressure and held in place for 3 minutes. This will occlude the brachial artery. In the absence of blood flow, the patient's hypocalcemia and subsequent neuromuscular irritability will induce spasm of the muscles of the hand and forearm. The wrist and metacarpophalangeal joints flex.

*(This is due to enhanced neuromuscular excitability)

*A prolonged QT interval on an ECG can also be seen.

Clinical signs of hypocalcemia include:

- Neuromuscular excitability
- Paraesthesia (tingling sensation) around mouth, fingers, and toes
- Muscle cramps, carpopedal spasms
- Tetany
- Seizures - focal or generalised
- Laryngospasm, stridor, and apneas (neonates)
- Cardiac rhythm disturbances (prolonged QT interval)
- Chvostek's and Trousseau's signs - latent hypocalcemia

Major Symptoms
CATS =
Convulsions
Arrhythmia
Tetany
Spasm
Stridor

- Tetany: Normally Ca causing partial blocking of Na receptor to decrease action potential frequency. In hypocalcemia this blockage is absent and we will have Tetany.

Treatment:

Calcium carbonate and vitamin D supplements

Vitamin D Deficiency

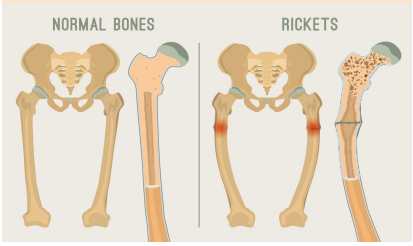
Rickets

Rickets occurs when there is normal formation of the collagen matrix but incomplete mineralization (poor calcification) which leads to soft bones. Clinically, bone deformity is seen (rickets).

*Bones have collagen but not enough calcium
-The body weight on the legs leads to Bowing of the legs

Tetany in Rickets

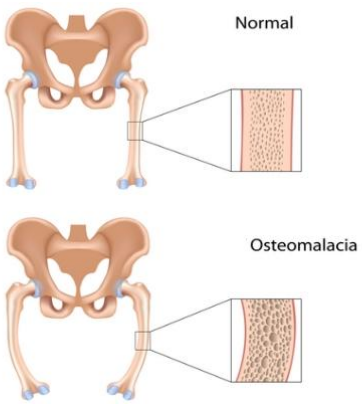
Early stages	When the bones finally become exhausted of calcium	Blood level of calcium falls below 7 mg/dl
• No tetany • PTH stimulate osteoclastic absorption of bone. • ECF calcium level is normal	• Calcium level falls rapidly	• Signs of tetany: positive Chvostek's sign • Death: tetanic respiratory spasm



Osteomalacia "Adult rickets"

Occur as a result of **steatorrhea** (failure to absorb fat and vitamin D)

Osteomalacia: demineralization (poor calcification) of preexisting bones which leads to more susceptibility to fractures.



Renal rickets

- It is a type of Osteomalacia due to prolonged kidney disease

Osteoporosis

- Inadequate bone matrix and minerals.
- Osteoporosis is the most common of all bone diseases in adults, especially in old age.
- Results from equal loss of both organic bone matrix and minerals resulting in loss of total bone mass and strength.

The cause of the diminished bone:

- ❏ The osteoblastic activity in the bone is usually less than normal so the rate of bone osteoid deposition is depressed.

In elderly the resorption is more than the synthesis.

- ❏ Excess osteoclastic activity.
- ❏ Lack of physical stress.
- ❏ Malnutrition (lack of vitamin C)
- ❏ Postmenopausal lack of estrogen
- ❏ Old age. Estrogen inhibits the osteoclasts.
- ❏ Cushing's syndrome

Summary

Hypercalcemia Vs Hypocalcemia

Causes:
1- PTH mediated --- primary hyperparathyroidism
2- non-PTH mediated --- PTHrP
3- medications --- Thiazide diuretics ss

Causes:
1. **Hypoparathyroidism**
2. **Surgical** (thyroid, parathyroid surgery)
3. Autoimmune
4. Magnesium deficiency
5. PTH resistance (pseudohypoparathyroidism)
6. Normal PTH levels but deficient receptors
7. Vitamin D deficiency/resistance
8. Lack of 1α hydroxylase, no vit D3 activation

Clinical signs

1-Reduced neuromuscular excitability and muscle weakness
2-- GIT disturbances
3- Cardiac arrhythmias,Vascular calcification

Clinical signs:

1- Chvostek's sign
2-Trousseau's sign
3- Prolonged QT interval on an ECG
4 - Cardiac rhythm disturbance
5- Seizure
6- Tetany

Treatment:

- Expand ECF volume.
- Increase urinary calcium excretion.
- Decrease bone resorption.

Treatment:

Calcium carbonate and vitamin D supplements

Hyperparathyroidism Vs Hypoparathyroidism

Characterized by:
1- hypercalcemia
2-hypercalciuria
3-hypophosphatemia
4-hyperphosphaturia
Most <u>common</u> complication:
Is renal stones made of calcium phosphate.
Most <u>serious</u> complication:
Is impaired renal function.
Causes:
1- Primary: Mostly Adenoma
2-Secondary: Due to ↓ Ca2+ in ECF

Characterized by:
1- Hypocalcemia
2- Hyperphosphatemia

Vitamin D deficiency

Rickets
Normal formation of the collagen matrix but incomplete mineralization

Osteomalacia
Normal formation of the collagen matrix but incomplete mineralization

Osteoporosis
Inadequate bone matrix and minerals.

MCQs

1 - A patient came with hypercalcemia, hypophosphatemia and renal stones the diagnosis would be

a. hyperparathyroidism

b. hypoparathyroidism

c. thyroid gland tumor

2 -regarding hypoparathyroidism choose the incorrect statement

A.lead to hyperreflexia

B.can trigger Chvostek's sign

c.lead to renal stones

3 - In Surgical Hypoparathyroidism :

a · Serum Ca2+ is increase

B. Serum phosphate is decrease

C. Urinary cAMP decrease

4- In secondary hyperparathyroidism, circulating levels of PTH are elevated and blood levels of Ca2+ are

a. Low or normal

b. Normal or high

c. high

5 - which one of the following is refers to an abnormal reaction to the stimulation of the facial nerve

A - Chvostek's sign

B - Trousseau's sign

c) None of above

6 - which one of the following is a symptom of hypercalcemia

a. shortened QT interval

b. Irritability

c. weight gain

7 - Hypoparathyroidism characterized by which signs

A. osteitis fibrosa cystica

B. Chvostek and Trousseau

C. shortened QT interval

Answers

1- a
2- c
3- c
4- a
5- a
6- a
7- b