SNS COLLEGE OF ALLIED HEALTH SCIENCES

SNS Kalvi Nagar, Coimbatore - 35

Affiliated to Dr MGR Medical University, Chennai

DEPARTMENT OF CARDIO PULMONARY PERFUSION CARE TECHNOLOGY

COURSE NAME : Pharmacology Pathology and Clinical Microbiology

II nd YEAR

TOPIC : CALCIUM AND MAGNESIUM

CALCIUM

OVERVIEW..

- Calcium definition and requirement .
- Calcium metabolism regulators : Vitamin D , PTH and calcitonin.
- Functions of calcium
- Calcium metabolism disorders.

what IS CALCIUM !!!!!

- Most Abundant Mineral In The Body
- Its about 1-2 kg ,of which 99% in bones and teeth
- Rest of it is present in ECF
- Normal level of calcium is 9-11 mg/dl of blood

Calcium in the plasma:

45% in ionized form (the physiologically active form)
45% bound to proteins (predominantly albumin)
10% complexed with anions (citrate, sulfate, phosphate)

Dietary sources

- Milk and milk products-good source
- Boned fish, green leafy veg , beans

Body requirement

- Adult – 700 mg/day
- Children-1.2gm/day
- Pregnancy and lactation-1.5 gm/day

Calcium homeostasis

Blood calcium level is maintained by various factors. They ARE

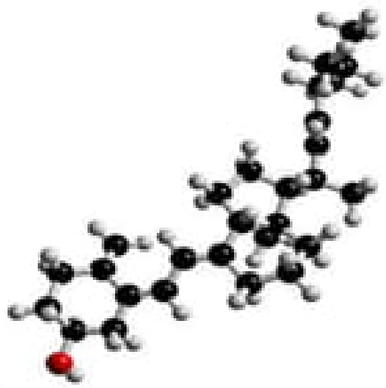
- VITAMIN D
- PTH
- CACITONIN

Vitamin D metabolism

- The active form of vitamin D is 1,25-dihydroxycholecalcififerol. Its production in the kidney is catalyzed by 1 a-hydroxylase .

1 a-hydroxylase activity is increased by :

- Decreased serum Ca2+
- Increased PTH level
- Decreased serum phosphate

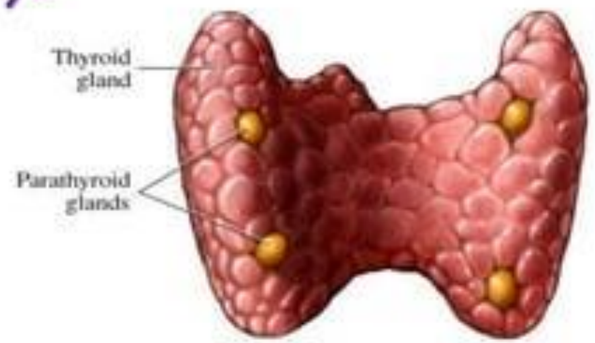


Action of 1,25-dihydroxycholecalcififerol(Calcitriol)

- Increases intestinal Ca^{2+} absorption
- Increases intestinal phosphate absorption
- Increase renal reabsorption of Ca^{2+} and phosphate
- Increases resorption of bone

Parathyroid hormone (PTH):

- it is an 84-amino-acid hormone.



Secretion:

- from the chief cells of the
- parathyroid glands.

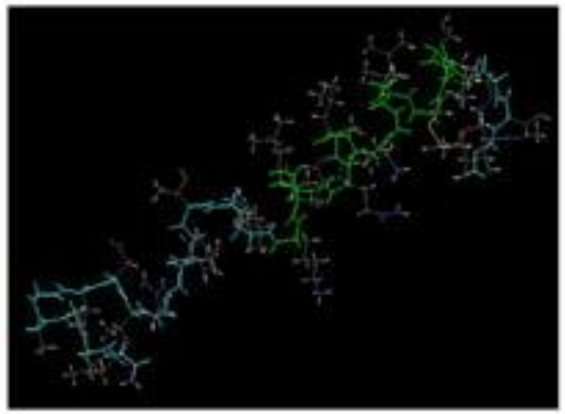
Function:

- increase renal phosphate excretion , and increases plasma calcium by:
- Increasing osteoclastic resorption of bone (occurring rapidly).
- Increasing intestinal absorption of calcium (a slower response).
- Increasing synthesis of 1,25-(OH)2D3 (stimulating GIT absorption).
- Increasing renal tubular reabsorption of calcium

Regulation of PTH

- Low serum [Ca+2] → Increased PTH secretion
- High serum [Ca+2] → Decreased PTH secretion

Calcitonin



Produced by :

- thyroid C cell.

Function:

- Inhibition of osteoclastic bone resorption .
- Increasing the renal excretion of calcium and phosphate.

Metabolism

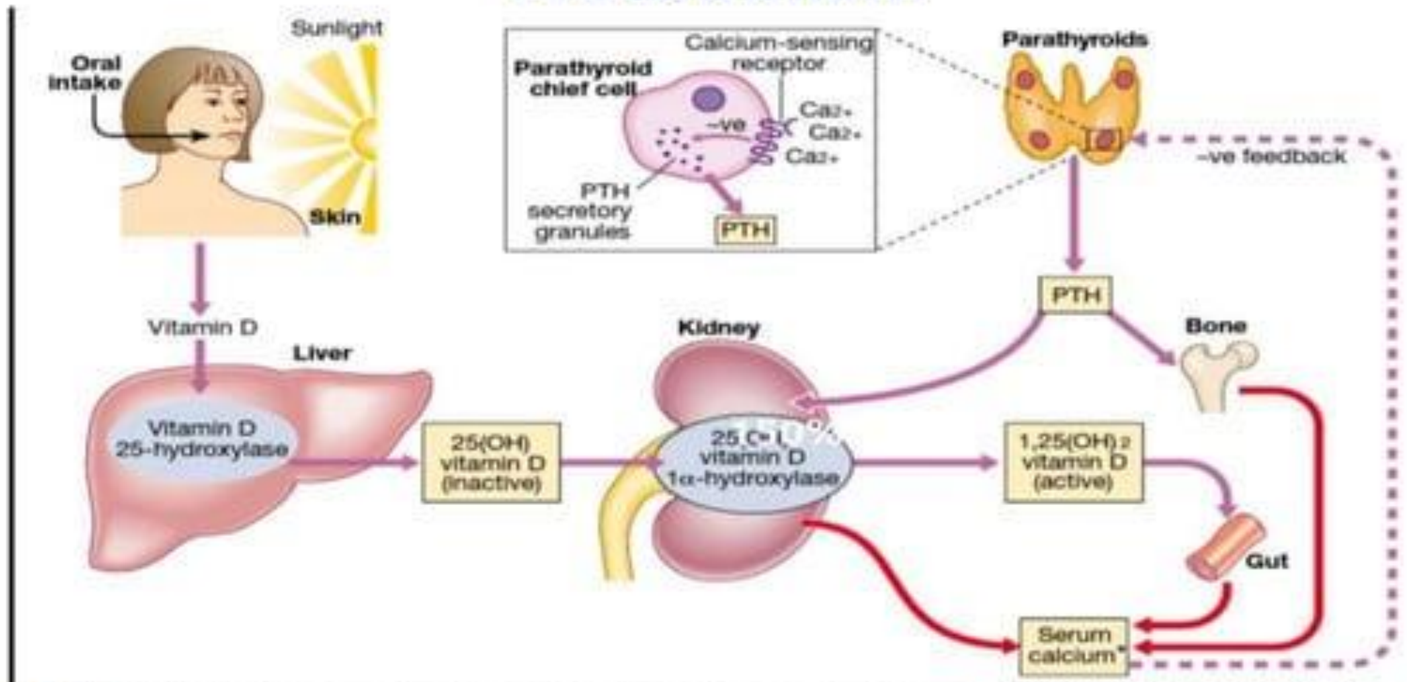


Fig. 20.17 Outline of calcium homeostasis showing interactions between parathyroid hormone (PTH), vitamin D and calcium. *Calcium in serum exists as 50% ionised (Ca^{2+}), 10% non-ionised or complexed with organic ions such as citrate and phosphate, and 40% protein-bound, mainly to albumin. It is the ionised calcium concentration which regulates PTH production.

Absorption of calcium

facilitators

Calcitriol , PTH,lactose,gastric acidity

inhibitors

Phytate, oxalate, fatty acids,highphosphate,alkaline condition

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Functions

- Muscle contraction
- Signal transmission
- Bone and teeth formation
- Blood coagulation
- Transmission of nerve impulse
- Release of hormones
- Activation of enzymes

CALCIUM DISORDERS

Calcium metabolism disorders:

- Hypercalcemia
- Hypocalcemia

Hypercalcemia

- Is condition in which the calcium level in the body is above the normal.
- The main cause is over activity of the parathyroid gland.
- cancer and some medication may cause over activity of the calcium level.

Etiology of hypercalcemia

Increased GI Absorption:

- Vitamin D excess
- Elevated PTH
- **Decreased Urinary Excretion:**

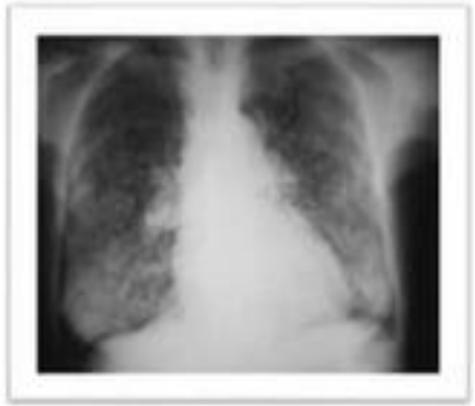
  Thiazide diuretics

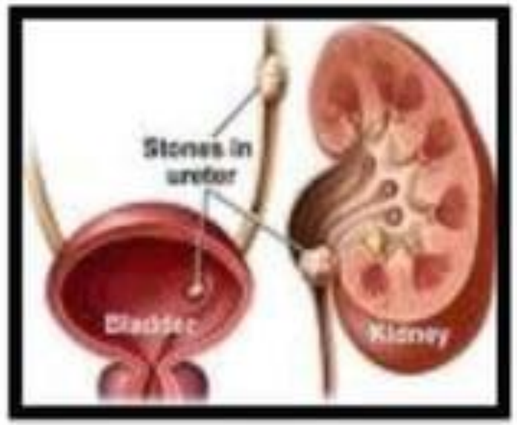
Increased Loss From Bone:

- Elevated PTH
- Hyperparathyroidism
- Malignancy
- Osteolytic metastases

Complication:

- Metastatic calcification
- Renal stones





Symptoms and sign

- Often non specific and may mimic those of malignancy
- Drowsiness , confusion , nausea , vomiting
- Polyuria , polydipsia
- dehydration

Hypercalcemia: presentations

Chronic, mild-moderate

- Often asymptomatic
- Cause: primary hyperparathyroidism
- Issues: parathyroidectomy or not

Acute, severe

- Symptomatic
- Cause: malignant hypercalcemia (rarely others)
- Issues: treat hypercalcemia, find & treat cause

diagnosis

- By measuring serum total calcium by adjusting albumin level
- Measurement of PTH
  - ✓ If PTH is elevated with hypercalcemia , primary hyperPTH is likely diagnosis
  - ✓ High plasma po_4+alkaline phosphatase + renal impairement , suggest tertiary hyperparathyroidism

Management

11.13 Medical management of severe hypercalcaemia

- I.v. 0.9% saline 2–4 L/day
- I.v. bisphosphonate
- Zoledronic acid 4 mg i.v.

or

- Pamidronate 60–90 mg i.v.

or

- Clodronate 300 mg i.v. daily over 5 days
- I.m./s.c. calcitonin 100 U 8-hourly for first 24–48 hours in life-threatening hypercalcaemia

Hypocalcaemia

- Is a condition in which the calcium level below the normal.

- Is caused by low level of PTH , low level of magnesium, deficiency of vitamin D

- The kidney dysfunction play role in hypocalcaemia

Etiology of the hypocalcemia

- Decreased GI Absorption
- Poor dietary intake of calcium, impair absorption
- Increased Urinary Excretion
- Decreased Bone Resorption/Increased Mineralization
- Low PTH
- PTH resistance
- Vitamin D deficiency
- Magnesium depletion
- Accidental removal of parathyroid gland

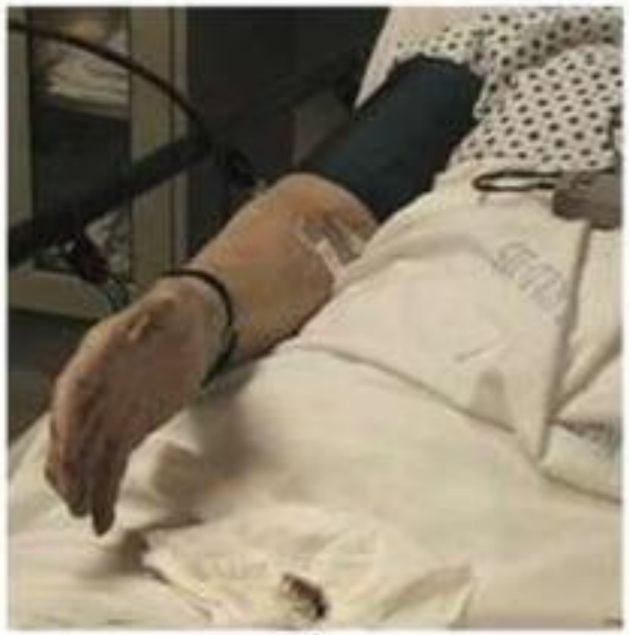
Complication

- **Tetany:** condition of mineral imbalance in the body that results in severe muscle spasms. **usually** occurs when the concentration of calcium ions (Ca++) in extracellular fluids below normal

Symptoms and signs

- Paresthesias
- Tetany (carpopedal spasm)
- Trousseau's, Chvostek's signs
- Seizures
- Chronic: cataracts, basal ganglia Calcification

Trousseau's sign



A

B

Management

20.36 Management of severe hypocalcaemia

Immediate management

- 10–20 mL 10% calcium gluconate i.v. over 10–20 minutes
- Continuous i.v. infusion may be required for several hours (equivalent of 10 mL 10% calcium gluconate/hr)
- Cardiac monitoring is recommended

If associated hypomagnesaemia

- 50 mmol magnesium chloride i.v. over 24 hours
- Most parenteral magnesium will be excreted in the urine, so further doses may be required to replenish body stores

MAGNESIUM

- Magnesium is the fourth most abundant cation in the body
- Magnesium is mainly seen in intracellular fluid
- And it is the second most prevalent intracellular cation
- **Body distribution:**
- The human body contains about 25g of magnesium
- About 60% of which is complexed with calcium and phosphorous in bones
- About 1% is in ECF and remainder in soft tissues

Sources

- Magnesium is widely distributed in vegetables & also found in almost all animal tissues
- Other important sources are cereals, beans, green vegetables, potatoes, almonds, and dairy products, e.g. cheese
- ***RDA:***
- Adult man : 350 mg/day
- Women : 300 mg/day
- During pregnancy and lactation : 450 mg/day

Biochemical functions

- **Co-factor:**
- Magnesium acts as a co-factor
- More than 300 enzymes requires magnesium as a cofactor
- Magnesium is an allosteric activators of many enzyme systems
- It is essential for peptidases, ribonucleases, glycolytic enzymes etc
- Magnesium influences the secretion of PTH by the parathyroid glands & hypomagnesaemia may cause hypoparathyroidism

- Magnesium exerts an effect on neuromuscular irritability similar to that of Ca^{2+}, high levels depress nerve conduction & low levels may produce tetany (Hypomagnesemia tetany)
- About 70% of body magnesium is present as apatite's in bones, dental enamel and dentin
- Insulin-dependent uptake of glucose is reduced in Mg^{2+} deficiency, magnesium supplementation improves glucose tolerance
- Magnesium is required for DNA replication process (DNA Polymerase III

- **Normal plasma levels:**
- Normal range of serum magnesium is 1 to 3.5 mg/dl
- About 70% of magnesium exists in free state and remaining 30% is protein bound (primarily albumin)
- Small amount is complexed with anions like phosphate & citrate
- **Absorption:**
- About 1/3 of dietary magnesium is absorbed
- It occurs primarily in the small intestine.
- Remaining is passively excreted in faeces.

Factors affecting absorption

- **Size of Mg load:**
- Absorption is doubled when normal dietary Mg requirement is doubled and vice versa.
- **Dietary calcium:**
- Calcium levels in the diet is low, Mg absorption is increased
- Decreased absorption occurs in presence of excess of Ca
- Vitamin D helps in increased absorption
- Para hormone and growth hormone increases absorption

- High protein intake increases absorption
- Fatty acids, phytates and phosphates decreases Mg absorption
- **Excretion:**
- Magnesium is lost from the body in faeces, sweat and urine.
- 60 to 80% of orally taken Mg is lost in faeces
- **Urine:**
- Regulation of Mg balance is dependent on renal mechanisms
- Mg is reabsorbed from loop of henle & not from proximal tubules
- 3 to 17 mEq of Mg is excreted daily in normal person

Hypermagnesaemia

- Increase in serum magnesium than the normal levels is called as hypermagnesaemia
- It is uncommon but is occasionally seen in renal failure
- It is rarely be caused by intravenous injection of magnesium salts and adrenocortical hypofunction
- **Symptoms:**
- Depression of the neuromuscular system is the most common manifestation in Hypermagnesaemia

Clinical feature

- Bradycardia
- Hypotension
- Reduced consciousness
- Respiratory depression

Management

- Cease all Mg intake
- Promote urinary Mg excretion by loop diuretic
- Calcium gluconate, to reverse overt cardiac effects
- If renal function is minimal ,dialysis is necessary to remove Mg load.

Hypomagnesaemia

- Decrease in serum magnesium levels than the normal range is called as hypomagnesaemia
- Magnesium is present in most common food stuffs, low dietary intakes of magnesium are associated with nutritional insufficiency, accompanied by intestinal malabsorption, severe vomiting, diarrhea or other causes of intestinal loss
- Symptoms are impaired neuromuscular function, tetany, hyper irritability, tremor, convulsions and muscle weakness

MAGNESIUM DEFICIENCY

- Hypomagnesemia is reported in as many as 65% of patients in ICU's.

- magnesium depletion has been described as :
- "the most underdiagnosed electrolyte abnormality in current medical practice"

Predisposing Conditions

Predisposing Conditions	Clinical Findings
Drug Therapy:* Furosemide (50%) Aminoglycosides (30%) Amphotericin, pentamidine Digitalis (20%) Cisplatin, cyclosporine	Electrolyte abnormalities: Hypokalemia (40%) Hypophosphatemia (30%) Hyponatremia (27%) Hypocalcemia (22%)
Diarrhea (secretory)	Cardiac manifestations: Ischemia Arrhythmias Digitalis toxicity
Alcohol abuse (chronic)	
Diabetes mellitus	
Acute MI	Hyperactive CNS Syndrome

*Numbers in parentheses indicate incidence of associated hypomagnesemia.

Diuretic Therapy

- Diuretics are the leading cause of Mg deficiency.
- Urinary Mg excretion is most pronounced with the loop diuretics (furosemide and ethacrynic acid).
- reported in 50% of patients receiving chronic therapy with furosemide.
- thiazide diuretics show a similar tendency for magnesium depletion, but only in elderly patients .
- Mg depletion does not occur with "potassium-sparing" diuretics

Antibiotic Therapy

- Aminoglycosides, amphotericin and pentamidine.

- The aminoglycosides block Mg reabsorption in the ascending loop of Henley.

- Hypomagnesemia has been reported in 30% of patients receiving aminoglycosides therapy

Alcohol

- Hypomagnesemia is reported in 30% of hospital admissions for alcohol abuse, and in 85% of admissions for delirium tremens.

- There is an association between magnesium deficiency and thiamine deficiency
- (required for the transformation of thiamine into thiamine pyrophosphate)

Acute Myocardial Infarction

- Hypomagnesemia is reported in as many as 80% of patients with acute myocardial infarction.

- The mechanism is unclear.

Clinical Manifestations

- no specific clinical manifestations of magnesium deficiency
- often accompanied by depletion of potassium, phosphate, and calcium.
- **HYPOKALEMIA:** Hypokalemia is reported in 40% of cases of magnesium depletion.
- hypokalemia that accompanies magnesium depletion can be refractory to potassium replacement therapy.
- magnesium replacement is often necessary before the hypokalemia can be corrected

CONTD...

- **HYPOCALCEMIA:** can cause hypocalcemia as a result of impaired parathormone release.
- Hypocalcemia from magnesium depletion is difficult to correct unless magnesium deficits are corrected.

- **HYPOPHOSPHATEMIA:** Phosphate depletion is a cause rather than effect of magnesium depletion.
- The mechanism is enhanced renal magnesium excretion.

CONTD...

- One of the serious arrhythmias associated with magnesium depletion is torsade de pointes

- Hypomagnesemia is associated with an increased incidence of atrial fibrillation.

Diagnosis

- serum Mg level is an insensitive marker of magnesium depletion.

- When magnesium depletion is due to nonrenal factors (e.g., diarrhea), the urinary magnesium excretion is a more sensitive test for magnesium depletion.

Management

- Oral Mg salt have limited effectiveness
- iv Mg chloride <0.5mmol/kg in the first 24 hr.
- If iv not available , Mg sulphate im can be given
- If hypomagnesemia is due to diuretic treatment adjunctive use of potassium sparing diuretic will reduce Mg loss in the urine.

THANK YOU