CALIUM HOMEOSTASIS

- Normal adult = 1-2 kg of calcium
- 99% is in bone
- Remaining 1% is in ICF, ECF and cell membranes

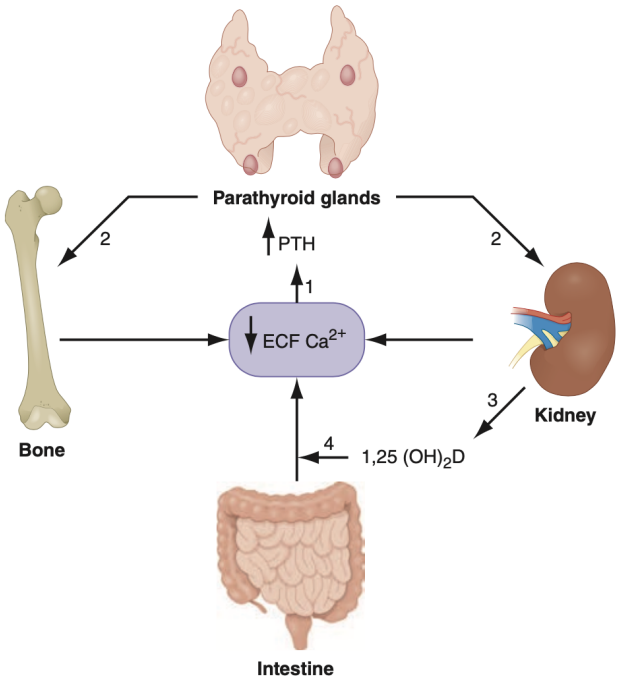
- Total calcium concentration in blood = 8.5-10.5 mg/dl
- Almost 50% is ionized (Free calcium)
- Bound calcium ---> Albumin, globulins, phosphate, citrate, sulfate

Corrected calcium in hypoalbuminemia

- Corrected calcium = Measured calcium + 0.8 x (4 - serum albumin)

eg : Serum calcium = 7.5mg/dl. Serum albumin = 2g/dl

- Calcium binding to albumin is dependent on the serum pH
- As pH decreases, H^+ displaces Ca^{2+} from binding sites and the amount of iCa^{2+} increases. Conversely, as the blood pH increases, albumin and the globulins become more negatively charged and bind more calcium, causing the amount of iCa^{2+} circulating to decrease.



- CaSR senses ECF ionized Ca^{2+}
- High serum Ca^{2+}, CaSR is activated
- Inhibits PTH secretion
- Increase in renal calcium excretion

Opposite effect when serum Ca^{2+} is low

Low Parathyroid Hormone Levels (Hypoparathyroidism)
Parathyroid agenesis
Isolated
DiGeorge's syndrome
Parathyroid destruction
Surgical
Radiation
Infiltration by metastases or systemic diseases
Autoimmune
Reduced parathyroid function
Hypomagnesemia
Autosomal dominant hypocalcemia
High Parathyroid Hormone Levels (Secondary Hyperparathyroidism)
Vitamin D deficiency or impaired $1,25(OH)_2D$ production/action
Nutritional vitamin D deficiency (poor intake or absorption)
Renal insufficiency with impaired $1,25(OH)_2D$ production
Vitamin D resistance, including receptor defects
Parathyroid hormone resistance syndromes
PTH receptor mutations
Pseudohypoparathyroidism (G protein mutations)
Drugs
Calcium chelators
Inhibitors of bone resorption (bisphosphonates, plicamycin)
Altered vitamin D metabolism (phenytoin, ketoconazole)
Miscellaneous causes
Acute pancreatitis
Acute rhabdomyolysis
Hungry bone syndrome after parathyroidectomy
Osteoblastic metastases with marked stimulation of bone formation (prostate cancer)

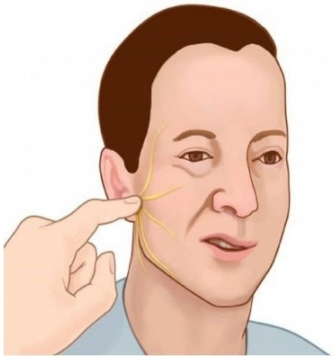
- Magnesium deficiency - Decreased cAMP in parathyroid

  Impaired PTH secretion

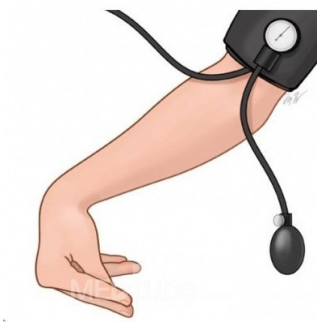
CLINICAL FEATURES

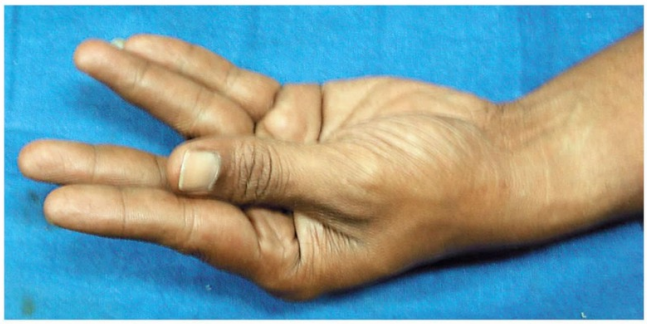
- Increased excitability of nerves and muscles - tetany
- Paraesthesias - circumoral regions, fingers, toes
- Chvostek's sign
- Carpopedal spasm

- Twitching of the circumoral muscles on gentle tapping of facial nerve just anterior to the ear



- Inflation of BP cuff 20 mm Hg above SBP for 3 minutes
- Flexion of the metacarpophalangeal joints of the fingers and adduction of the thumb





- Severe cases - Seizures, bronchospasm, laryngospasm, prolongation of QT interval

INVESTIGATIONS

	Total serum calcium	Ionised serum calcium	Serum phosphate	Serum PTH
Hypoalbuminaemia	↓	↔	↔	↔
Alkalosis	↔	↓	↔	↔ or ↑
Vitamin D deficiency	↓	↓	↓	↑
Chronic renal failure	↓	↓	↑	↑
Hypoparathyroidism	↓	↓	↑	↓
Pseudohypoparathyroidism	↓	↓	↑	↑

TREATMENT

- Depends on the severity

  & rapidity with which it develops

ACUTE SYMPTOMATIC HYPOCALCEMIA

- IV Calcium gluconate

  10 ml 10% diluted in 50 ml NS given over 5 minutes

  followed by continuous iv infusion
  (10 ampoules of calcium gluconate or 900 mg of calcium in 1 L of 5% dextrose or 0.9% sodium chloride administered over 24 h)

- Treat accompanying hypomagnesemia (if any)

CHRONIC HYPOCALCEMIA

- Oral calcium tablets
- VitaminD2/Vitamin D3/Calcitriol
- Injection Recombinant human PTH

  Refractory hypoparathyroidism

HYPERCALCEMIA- CAUSES

Excessive PTH production
Primary hyperparathyroidism (adenoma, hyperplasia, rarely carcinoma)
Tertiary hyperparathyroidism (long-term stimulation of PTH secretion in renal insufficiency)
Ectopic PTH secretion (very rare)
FHH
Alterations in CaSR function (lithium therapy)
Hypercalcemia of malignancy
Overproduction of PTHrP (many solid tumors)
Lytic skeletal metastases (breast, myeloma)
Excessive $1,25(OH)_2D$ production
Granulomatous diseases (sarcoidosis, tuberculosis, silicosis)
Lymphomas
Vitamin D intoxication

CLINICAL FEATURES

- GI, Kidney, Nervous system
- GI - nausea, anorexia, constipation, pancreatitis, peptic ulcer disease
- Kidney - polyuria (and dehydration), Nephrolithiasis
- Nervous system - Depression ---> Lethargy & stupor

  Short QT interval

INVESTIGATIONS

- iPTH : PTH mediated or non PTH mediated
- Activated Vitamin D
- PTHrP
- 24 hour urinary calcium/spot urine calcium creatinine ratio

TREATMENT

- Correct dehydration

  Normal saline 4 litres/day

- Salmon Calcitonin injection (i.m or subcutaneous) given 6-12 hourly

  - decreases bone resorption

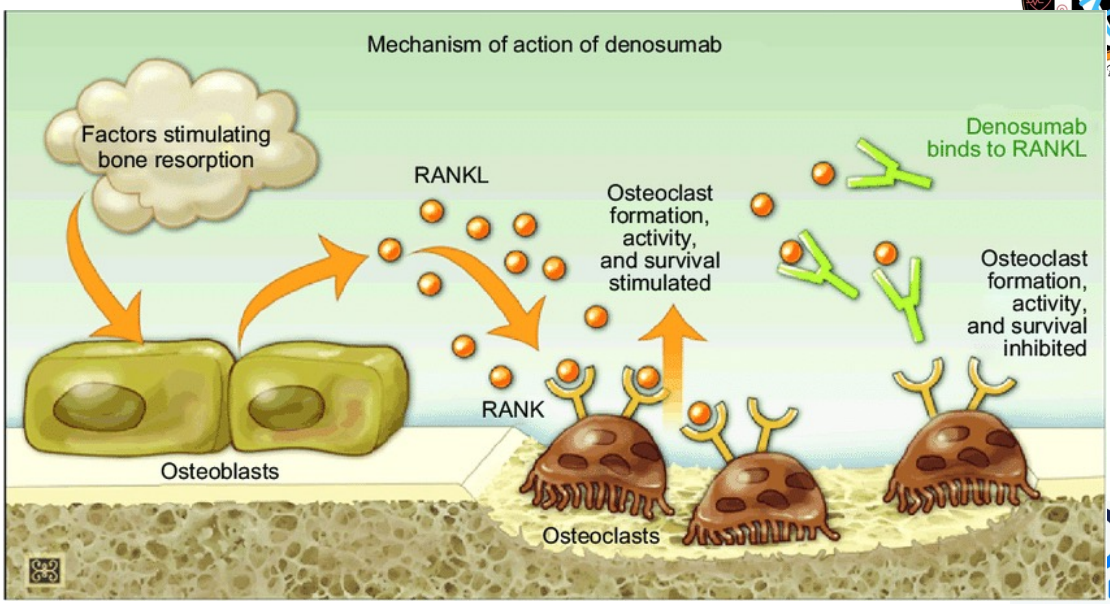
  - enhances renal excretion

- Bisphosphonates : potent inhibitors of bone resorption

  - Zoledronate, Pamidronate

- Refractory to bisphosphonates : Denosumab subcutaneously

  - antibody to RANKL



- Prednisone : Hypercalcemia due to overproduction of Vitamin D3
- Cinacalcet : oral calcimimetic agent
  - calcium sensing receptor agonist
- Hemodialysis using low calcium dialysate