Calcium Disorders
Calcium balance

BONE (1 kg)

500 mg  500 mg

GUT → Net 175 mg → ECF CALCIUM → Net 175 mg → KIDNEY

1000 mg
Hypercalcemia: clinical signs

- GI:
  - Nausea, vomiting, abdominal pain & Constipation
  - Acute pancreatitis and gastric ulcer

- Renal:
  Polyuria, dehydration, renal calcification & Renal failure

- Neurological
  Fatigue, Confusion, Stupor, coma
  Increased neuromuscular excitability & muscle weakness

- Heart
  Characteristic ECG, and in severe cases cardiac arrest
Hypercalcemia: major causes

- Primary hyperparathyroidism (PHPT), and Tertiary hyperparathyroidism (THPT)
- Malignancy
- Others
Hyperparathyroidism: causes

- **Primary PHPT**
  - Adenoma (90%)
  - Multiple gland enlargement (10%)
    - MEN 1
    - MEN 2A
    - Familial hyperparathyroidism
  - Carcinoma (<1%)
  - Familial benign hypercalcemia (FBH)

- **Tertiary THPT**
  It occurred as a result of secondary HPT
In PHPT, there is autonomous inappropriate secretion of PTH from the gland (mainly because of tumor) and this secretion is not subjected to negative feedback of hypercalcemia. In THPT, the autonomous secretion of PTH is due to sustained and prolonged stimulation of the parathyroid gland by previous hypocalcemia that caused by either renal failure and/or vitamin D deficiency.
In Renal failure and vitamin D deficiency, the resulted hypocalcemia is not corrected even by stimulated secretion of PTH, this referred to secondary HPT, which characterized by ↓ S.Ca, normal PO4 - - , and ↑ S.PTH. The continues stimulation of PTH gland leads to hypertrophy of it with resultant autonomous secretion of PTH which unable to correct hypocalcemia because of renal damage or deficiency vitamin D.
Only after correction of underlying cause of hypocalcemia by kidney transplantation or vitamin D supplementation, the serum levels of Ca will be corrected and increased because of gland hypertrophy, and this state referred to THPT in which $\uparrow \text{S.Ca}$, $\downarrow \text{S.PO4}$ - -, $\uparrow \text{S.PTH}$ and the differentiating parameter between the PHPT and THPT is the marked increased of S.ALP in THPT, but normal in THPT, and the history of previous hypocalcemia in THPT.
Malignant hypercalcemia: major causes

- **PTHrP - mediated**
  - Breast carcinoma
  - Squamous carcinoma (lung, head & neck, esophagus)
  - Renal carcinoma

- **Cytokine - mediated**
  - Myeloma (lymphoma, leukemia)
Hypercalcemia: other causes

- **Drugs:**
  - Vitamin D
  - Calcium carbonate (milk alkali syndrome)
  - Lithium
  - PTH
  - Vitamin A

- Sarcoidosis, other granulomatous disorders

- Hyperthyroidism
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
Primary hyperparathyroidism

- F:M 3:1
- Usually > 50 y/o
- Presentation:
  - Asymptomatic hypercalcemia (>50%)
  - Renal stones (20%)
  - Decreased bone density
  - Symptoms of hypercalcemia (<5%)
Hypercalcemia: evaluation

- Duration >6 months or renal stones: PHPT
- Signs of malignancy, other rare causes

- Plasma PTH
  - Normal or elevated: primary hyperparathyroidism
  - Low: other causes
Parathyroid Localization

Sestamibi scans

Left lower parathyroid adenoma

Mediastinal parathyroid adenoma
Biochemical evaluation:

1. In primary hyperparathyroidism:
   PTH ↑, S.Ca ↑, S.PO4 – – ↓, with normal renal function, the S.Urea and S.Creatinine are normal.
2. In malignancies:

a. Bony tumor; primary or metastasis

S.Ca ↑, S.PO4 - - ↑, S.PTH ↓ and S.ALP ↑. These are due to bone broken down by tumor

b. Humoral hypercalcemia of malignancy: S.Ca ↑, S.PO4 - - ↓ and S. PTHrP (PTH related protein) is detected and increased. This PTHrP
produced by malignant tumors of breast, bronchus, neck, head ... etc and has the biological activity of PTH in rising the serum levels of Ca and decreasing serum PO4 - - levels.
Nonparathyroid hypercalcemia

- Repeat history (especially drugs)
- Vitamin D toxicity suspected: 25 (OH) vitamin D
- Sarcoidosis suspected: 1,25 (OH)$_2$ vitamin D

In vit. D toxicity:
S.Ca $\uparrow$, S.PO4 - - $\uparrow$, S.PTH $\downarrow$ and S. D3 is $\uparrow$. 
Severe hypercalcemia:

- Indications for therapy
  - Symptoms of hypercalcemia
  - Plasma [Ca] > 12 mg/dl
Hypocalcemia: clinical signs

- Paresthesias
- Tetany (carpopedal spasm)
- Trousseau’s, Chvostek’s signs
- Seizures
- Chronic: cataracts, basal ganglia Ca
Trousseau’s sign
Hypocalcemia: causes

- Primary Hypoparathyroidism
  - Surgical, total or partial thyroidectomy and or parathyroidectomy
  - Autoimmune
  - Magnesium deficiency; it is important for PTH secretion

- PTH resistance (pseudohypoparathyroidism)

- Vitamin D deficiency

- Vitamin D resistance

- Other: renal failure, pancreatitis
Hypocalcemia: evaluation

- Confirm low corrected (change in protein bound) & ionized calcium (Free Ca)

History:
- Neck surgery
- Other autoimmune endocrine disorders
- Causes of Mg deficiency
- Malabsorption
- Family history
Hypocalcemia: evaluation

- Physical exam:
  - Signs of tetany

- Lab
  - PTH
  - Creatinine, Mg, P, alkaline phosphatase
  - 25-OH vitamin D
### Hypocalcemia: evaluation

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<thead>
<tr>
<th>Cause</th>
<th>Phosphate</th>
<th>Alk phos</th>
<th>Other</th>
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<tbody>
<tr>
<td>Hypoparathyroidism</td>
<td>High</td>
<td>Normal</td>
<td>PTH low</td>
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<tr>
<td>PTH resistance</td>
<td>High</td>
<td>Normal</td>
<td>PTH high</td>
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<tr>
<td>Vitamin D deficiency</td>
<td>Low</td>
<td>High</td>
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<td>25-OHDDHigh</td>
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In renal failure: ↓ S.Ca, ↑ S.P, ↑ S. Urea and S.Creatinine, with expected increased S.PTH.
Ricket in children and Osteomalacia in adult (demineralized bone dis.) occur due to deficiency of vitamin D and P. In these bone disorder serum Ca & P are decreased due to:
1. low intake of these element
2. low intake in vit. D
3. malabsorption of vitamin D (GIT disorder)
4. defect in normal pathway of vitamin D metabolism
5. hereditary hypophosphatemia
Hypocalcemia: acute therapy

- IV calcium infusion
  - 1-2 gm Ca gluconate (10-20 ml) IV over 10 min
  - 6 gm Ca gluconate/500 cc D5W over 6 hr
  - Follow plasma Ca & P Q 4-6 hr & adjust rate

- IV or oral calcitriol 0.25-2 mcg/day

- Oral calcium carbonate 1-2 gm BID-TID
Hypocalcemia: chronic therapy

- Oral calcitriol 0.25-2 mcg/day
- Calcium carbonate 1-2 gm BID-TID
Hypophosphataemia

Serum or plasma PO4- may be associated with widespread cell dysfunction and cell death. Muscle pain and weakness (↑CPK), urgent phosphate supplementation is required. Dietary deficiency of PO4 is uncommon. ↓PO4 may occur due to; antacids, respiratory and metabolic (Diabetic ketoacidosis DKA & lactic acidosis). Insulin in treatment of DKA aggravate hypophosphataemia (movement to IC).
Magnesium

It is an essential IC cation. It found mainly in skel. eton, a small proportion in ECF. Mg deficiency rarely occurs as an isolated phenomenon, it usually accompanied by Ca, K, and PO4. However, tetany, cardiac arrhythmias, and CNS abnormalities may occur due to Mg deficiency but not Ca. Hypomagnesaemia should be suspected in case of hypocalcaemia and/ or hypokalaemia. Mg may be due to GIT, and renal disorders, and reduced intake