Hypocalcaemia is a serum (albumen-adjusted) total calcium, (s[Ca]) <2.20mmol/L (normal range 2.2–2.6mmol/L)[1–4]. Severe hypocalcaemia, if untreated, can lead to serious neurological and cardiovascular complications[1–4].

**Causes: (commonly caused by Hypothyroidism and VD deficiency)[1–8]**

| iPTH: Inappropriately low or normal <1.5pmol/L | **Hypoparathyroidism** (the commonest in-patient cause)[1–3]:  
  - **Post-surgery** is the commonest cause[5,6]; usually secondary to total thyroidectomy[5]. Hypocalcaemia is transient or permanent[4].  
  - **Auto-immune**[1,2,4].  
  - **Genetic** (rare)[1,2,4,6].  
  - Irradiation, storage or infiltrative diseases of the PTG (rare)  
  - Hypomagnesaemia (can cause PTH end organ-resistance and impaired PTH secretion)[1,4,8], see hypomagnesaemia chapter |
|---|---|
| iPTH: High >1.5pmol/L | **Vitamin D deficiency** (VD) (The commonest community cause[1–4])  
  - Reduced intake + reduced exposure to UVL, malabsorption[1,4,6].  
  - Functional VD deficiency: decreased 25:- (liver) or 1-hydroxylation (kidney)[1,3,4,6].  
  **[Severe VD deficiency can cause rickets and osteomalacia]**  
  - PTH resistance[1–4,8]; target organs (kidney/bone) resistance to PTH: (Pseudohypoparathyroidism, hypomagnesaemia)  
  - Renal disease (low calcitriol and hyperphosphatemia)[1,8]. |
**Extravascular deposition:**
- Hyperphosphatemia: Ca-Po4 is deposited mostly in bone, but also in extra-skeletal tissues,[4] as in TLS, Rhabdomyolysis and CKD.[3,4,8]
- Acute pancreatitis.[3–5,8]
- Sepsis or severe illness: impaired PTH secretion/end organ resistance and reduced calcitriol production.[5–7,8]
- Widespread osteoblastic metastasis: possible in carcinoma prostrate; breast.[3,4,8]

**PTH:**
- Normal
- Drugs[1–4]
  - Inhibitors of bone resorption (OCIs): (bisphosphonates, calcitonin, denosumab), especially if VD deficient.[2–4]
  - Cinacalcet[4], consider PPI-associated hypomagnesaemia.[5]
  - Ca Chelation: Citrate in massive blood transfusion.[2–5,7]. It reduces sCa but not s[Ca].[4]

### Symptoms and Signs[1–9]
Asymptomatic or non-specific if mild and/or chronic. Prominent when the decrease in s[Ca] occurs rapidly or is large.[1–5,8,9]
- **Neuromuscular Excitability:** paresthesia, carpopedal spasm, severe cases can progress to tetany, seizures
- **Neuropsychiatric Symptoms:** depression, cognitive impairment
- **Bone:** pain and fractures (if osteomalacia present)
- **CVS:** Prolonged QT and ventricular fibrillation or heart block in severe cases.
- **Other:** dry skin, cataract.

### Investigations (the diagnosis is often clear from the history and physical examination)[4]
- Do all necessary tests before starting treatment[1,3].
- s[Ca] (adjusted for albumin), ALP, UEs, s[PO4], s[Mg]
- iPTH: the single most important diagnostic test[1–4].
- **Selective tests[1–4],** based on history and physical examination, to determine the cause:
  a. Low or normal iPTH: indicates hypoparathyroidism.
  b. High iPTH: UEs deranged (CKD); if UEs normal check:
    1. 25HCC – VD deficiency if low; if normal: suggest pseudohypoparathyroidism.[3–12].
    2. High ALP/low PO4 suggest VD deficiency/osteomalacia.[1,4].

Poor correlation between the ionised (free) serum calcium (sCa++) and s[Ca], especially in states of low albumin or acid/base imbalances:
- **Pseudohypocalcaemia:** in hypoalbuminaemic states the s[Ca] is low but the sCa++ is normal.[12,4]
  - Hence, the albumin-correction equation[1,2,4,8].
- **The adjusted calcium calculation is not valid in acidosis or alkalosis:** the affinity of calcium to albumin is increased in alkalosis; acute respiratory alkalosis can be associated with reduced sCa++, but not s[Ca] and development of symptoms – paraesthesia. Consider checking sCa++.[1,2,4,8].

**Abbreviations:** iPTH=Intact PTH; PTG=Parathyroid Gland, UVL=Ultra-Violet Light, TLS=Tumour Lysis Syndrome, OCIs=Osteoclast Inhibitors.
Management of Hypocalcaemia

Treatment choice depends on the biochemical severity and rate of onset of hypocalcaemia, in addition to the symptoms and the underlying cause. Managing hypocalcaemia is based mainly on clinical experience and accepted practice rather than controlled trials\(^1,2,4\).

<table>
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<tr>
<th>s[Ca] (mmol/L)</th>
<th>Treatment (^{1-10})</th>
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| (Chronic) Mild, asymptomatic s[Ca] 2.0–2.2 | ● Prompt identification and treatment of the underlying cause  
● **Oral calcium:** give 25–50mmol (2000mg) elemental Ca/day\(^{2-5}\) (e.g. Ca carbonate 1250mg 2 tab BD\(^{3}\), alternatively Sandocal 1000mg bd\(^{6}\)), before meals\(^{8}\). Monitor s[Ca] as per monitoring section below  
**Add: Cause-specific treatment**  
**Hypoparathyroidism**  
● **Hypoparathyroidism:** give Calcitriol 0.5\(\mu\)g or alfacalcidol 1\(\mu\)g od – increase dose every 4–7 days to achieve a s[Ca] in the lower end of the reference range to avoid hypercalc iuria\(^{1,2,5,6,8}\).  
● **Post-thyroidectomy, repeat calcium 24hrs later, if s[Ca]\(^{5}\):**  
  ○ >2.1: discharge and re-check s[Ca] within one week  
  ○ 1.9–2.1: increase Sandocal\(^{TM}\) 1000 to three BD –  
  ○ 1.9–2.1 for >72hrs post-operatively despite Ca supplementation: start 1-alfaalcaldiol 0.25\(\mu\)g/day (or calcitriol) with close monitoring  
● **Post-parathyroidectomy:** judicious pre-operative preparation will avoid the development of hungry bone syndrome\(^{5,8}\). Close monitoring, treat hypocalcaemia as per its severity, see guidance.  
● Ergocalciferol (VD2) and cholecalciferol (VD3) are ineffective, as PTH is needed for the 1\(\alpha\)-hydroxylation\(^{1,4}\). This is also true in advanced CKD because of 1\(\alpha\)-hydroxylase deficiency\(^{4}\).  
● Recombinant PTH is not a standard care measure because of its cost, subcutaneous use, and long term safety is not established\(^{4}\). |
| | **Vitamin D deficiency** |
| | ● Give VD, either VD2 or VD3 at 1000–2000u daily. Combined Ca-VD 2tab (800u) od\(^{1}\).  
● Symptomatic VD deficiency or non-responders can be treated with VD (D2 or D3) 50 000 IU orally once a week for eight weeks\(^{3}\).  
● Long-term maintenance is usually 1000iu/VD3/day. |
| | **Monitoring** |
| | ● Initially, s[Ca] levels should be monitored weekly, until deficiency is corrected and then monthly while optimal dose is determined, thereafter:  
  ○ Monitor s[Ca]: every 3–6 months\(^{5,6,3}\).  
  ○ Monitor urine [Ca] annually. Hypercalciuria is the main side effect, if detected reduce VD dose to avoid nephrocalcinosis\(^{1,2,8}\).  
**Refer to endocrine, renal, or other teams as appropriate** |
**ABC of Intravenous Fluids**

### Acute severe hypocalcaemia:
- **S[Ca] ≤ 1.9**, and/or symptomatic:
  - CPS, tetany, seizures
  - Prolonged QT/CCF

#### Treatment:
- **IV Ca + oral VD**

1. Hospital admission/ECG monitoring – too rapid Ca infusion can induce hypotension and serious dysrhythmias.
2. Secure proper IV access – a large vein or CV line if access poor.
3. **IV Calcium gluconate** is the preferred form for peripheral IV calcium. 10–20ml of 10% calcium gluconate (2.25–4.5mmol), diluted in 50–100ml of 5% dextrose and infused slowly over 10–20 minutes. Its effect lasts for only 2–3 hours.
4. Repeat treatment until symptoms clear.

   Follow by slow, continuous IV infusion of a dilute solution of Ca to prevent recurrence of hypocalcaemia. Use infusion pump.

5. **Dilute** 100ml of calcium gluconate 10% (10 ampules) in 1 litre 5% D or 0.9% NS and infuse at 50ml/hour.
   - Monitor S[Ca], titrate rate of infusion to achieve S[Ca] at the lower end of the reference range. An infusion of 10ml/kg of this solution is estimated to increase S[Ca] by 0.3–0.5mmol/l.
   - The usual maximum total daily dose is 15 ampoules of 10ml of 10% calcium gluconate (i.e. 33.75mmol Ca).
6. Phosphate and bicarbonate should not be infused with calcium to avoid precipitation of Ca salts.
7. NB. CaCl2 is more likely to cause phlebitis and tissue necrosis if extravasated; should be given via central vein.
8. Oral Ca supplements, as above, should be given concurrently.
9. If PTH is deficient or non-functional calcitriol (preferred more potent + rapid onset of action) should be given at 1μg/day.

#### Further Management

- **Give disease-specific treatment as per treatment of mild, asymptomatic cases box above**
- **Hypomagnesaemia-associated hypocalcaemia**: the association frequently co-exist due to malabsorption or poor dietary intake. HoM causes PTH deficiency and PTH resistance. Correct hypomagnesaemia first, unless the patient presents with severe symptoms. Give IV MgSO4, 24mmol/24 hours in 500ml 0.9% NS or 5% D, to achieve normal S[Mg] level. Monitor S[Mg] S[Ca].
  - **Hyperphosphataemia-related hypocalcaemia**: the increased Ca×PO4 product induces precipitation of Ca-PO4 in soft tissues resulting in hypocalcaemia. Thus, acute hypocalcaemia in TLS or Rhabdomyolysis should not be treated with Ca, unless symptomatic from hypocalcaemia (e.g. tetany or cardiac arrhythmia), until the hyperphosphatemia is corrected. This is to avoid further calcium-phosphate precipitation in vasculature and soft tissue. Hemodialysis is often indicated in such patients.
Management of Hypocalcaemia

- CKD-associated hypocalcaemia: correction of hyperphosphataemia and calcitriol deficiency (secondary to reduced renal mass/increased FGF-23) is the primary goal.
- Metabolic acidosis: replace s[Ca] to near normal range first, before correcting the acidosis[3,8]. Failure to do this may result in convulsions or cardiac arrest[3,8].
- Digoxin: IV calcium must be used cautiously as it may precipitate digitalis intoxication; calcium enhances the effects of digoxin on the heart[1–3,8].

Hungry Bone Syndrome (HBS): It follows parathyroidectomy. The sudden drop in PTH level results in acute mineralisation of osteoid. This causes a rapid drop in serum calcium (Ca), magnesium and phosphate. HBS can result in seizures and tetany. Associated hypomagnesaemia can be severe, prolonged and symptomatic; accompanied by hypophosphatemia[8,9]. It may require high doses IV Calcitriol (0.25-1mcg) and prolonged periods of high doses of Ca supplementation[8]. Good preparation and giving Ca and calcitriol supplementation for several days pre-operatively prevents HBS[8].

REFERENCES