Interpreting Hypercalcaemia and Hypocalcaemia in Primary Care

Medscape UK X Guidelines
Primary Care Hacks

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Background[1–6]

- PTH is the main regulator of calcium homeostasis and is secreted by the parathyroid glands in response to low calcium levels
- PTH increases calcium reabsorption in the kidneys, stimulates conversion of vitamin D to its active form (promoting calcium uptake in the bowel), and stimulates osteoclasts to release calcium from bone
- Normal serum calcium ranges from 2.15 to 2.6 mmol/l
- Raised calcium levels of <3.0 mmol/l are usually asymptomatic and do not require urgent correction; levels >3.0 mmol/l typically cause symptoms (see below) but may be well tolerated if they rise slowly
- The symptoms of hypocalcaemia typically develop when adjusted calcium levels are <1.9 mmol/l, but this threshold is affected by the rate of change and can vary greatly
- Abnormal calcium levels can be a medical emergency. If calcium levels are >3.5 mmol/l or <1.9 mmol/l, or severe symptoms are present, consider hospital admission
  - hypercalcaemia >3.0 mmol/l can potentiate cardiac arrhythmias and is often associated with malignancy
- A recent observational audit[6] found that serum calcium was checked in around 10% of the population per year in primary care. In the 2.4% with a raised calcium on initial testing, nearly half normalised on repeat testing. Of those who remained persistently hypercalcaemic, only half had a PTH measured and the majority were in keeping with PHPT being the most common cause of hypercalcaemia.

Hypercalcaemia[1–3,5,7–12]

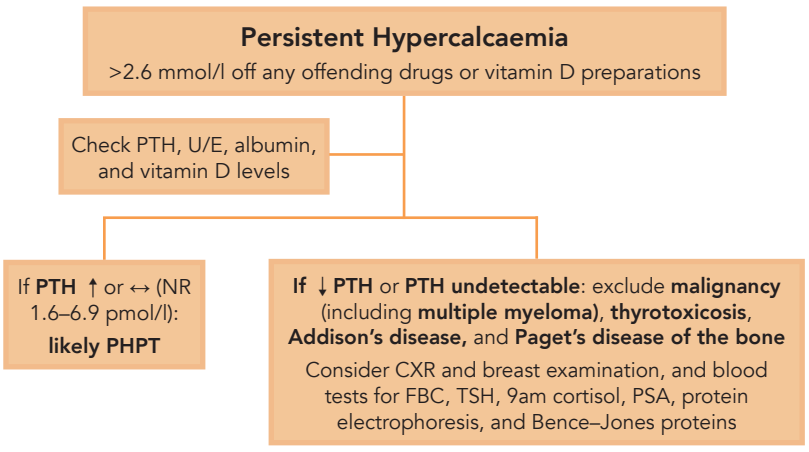
Hypercalcaemia is common in primary care—the well-known adage, **'bones, stones, moans, and groans'** summarises the classical signs and symptoms of hypercalcaemia:

- **Bones**: vague muscle, bone, and joint pains or rarely fractures associated with underlying bone disorder
- **Stones**: kidney stones, polyuria, and polydipsia
- **Moans**: fatigue, low mood, muscle weakness, confusion, ataxia, and coma
- **Groans:** constipation, dyspepsia, nausea and vomiting, and pancreatitis.

Causes of Hypercalcaemia

- **PHPT and malignancy account for around 90% of all cases**[1]
  - PHPT is more common in women, with an estimated prevalence of 2.1% in postmenopausal women. It can also be part of familial syndromes such as MEN
  - a recent cohort study[10] suggested >25% of patients had a significant delay between first presentation of hypercalcaemia and subsequent diagnosis of PHPT, with >10% waiting >5 years before PTH was checked
  - hypercalcaemia of malignancy can be due to ectopic PTH production or lytic bone lesions. Common cancers causing hypercalcaemia include **multiple myeloma** (around 30% have high calcium levels at first diagnosis), **breast**, **lung**, **kidney**, and **prostate**
- **Endocrine disorders**, e.g. thyrotoxicosis, adrenal insufficiency/Addison's disease, phaeochromocytoma
- **Granulomatous disease**, e.g. sarcoidosis, TB, IBD
- **Certain drugs**, e.g. thiazide diuretics, lithium, and calcium/vitamin D supplements (including OTC)
- **Vitamin D intoxication**, e.g. in renal patients
- **Familial hypocalciuric hypercalcaemia** (benign autosomal dominant condition)
- **CKD** and **tertiary hyperparathyroidism**.

Investigation of Hypercalcaemia[2–5,7,8,13]



Hypocalcaemia[4,5,13,14]

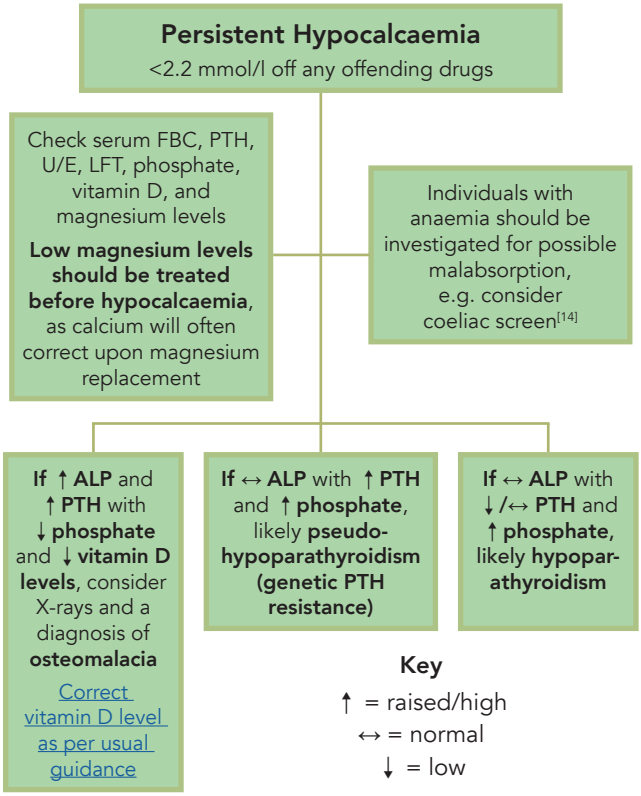
Mild hypocalcaemia (1.9–2.15 mmol/l) is often an incidental finding in an asymptomatic patient.

Corrected calcium levels <1.9 mmol/l can cause mood change, muscle spasm (e.g. carpo-pedal spasm), tingling and numbness, and in severe cases, seizures.

Causes of Hypocalcaemia

- **Vitamin D deficiency or osteomalacia**
- **Alcohol excess**
- **Hypomagnesaemia**, e.g. secondary to long-term PPI use
- **Hypoparathyroidism**, e.g. following neck surgery, radiotherapy, or autoimmune disease
- **Certain medications**, e.g. bisphosphonates or denosumab
- **CKD**
- **Malabsorption**, e.g. coeliac disease.

Investigation of Hypocalcaemia[2,4,5,13–15]



ALP=alkaline phosphatase; **CKD**=chronic kidney disease; **CXR**=chest X-ray; **FBC**=full blood count; **IBD**=inflammatory bowel disease; **LFT**=liver function test; **MEN**=multiple endocrine neoplasia; **NR**=normal range; **OTC**=over the counter; **PPI**=proton pump inhibitor; **PHPT**=primary hyperparathyroidism; **PSA**=prostate-specific antigen; **PTH**=parathyroid hormone; **TB**=tuberculosis; **TSH**=thyroid-stimulating hormone; **U/E**=urea and electrolytes