Investigation of Hypocalcaemia in Primary Care (Adults)

1: DEFINITION

Hypocalcaemia is defined as a serum adjusted calcium concentration of 2.20mmol/L or lower, on two occasions. Adjusted calcium is calcium corrected for changes in albumin concentration.

Mild Hypocalcaemia	= 1.90 – 2.19 mmol/L, asymptomatic
Severe Hypocalcaemia	= <1.90 mmol/L and / or symptomatic at any level below reference range

2: CLINICAL PRESENTATION

Mild to moderate hypocalcaemia is usually asymptomatic. Severe hypocalcaemia, particularly of acute onset, results in increased excitability of neuromuscular tissue. Typical features include:

Acute	Chronic
Neuromuscular irritability (Tetany): Paraesthesias (usually fingers, toes, around mouth); Muscle twitching; Carpopedal spasm; Trousseau's sign; Chvostek's sign; Seizures; Laryngospasm; Bronchospasm; Weakness	Ectopic calcification (Basal ganglia) Extrapyramidal signs Parkinsonism Dementia Subcapsular cataracts Abnormal dentition Dry skin
Cardiac: Prolonged QT interval; Hypotension; Heart failure; Arrhythmia	
Papilloedema	

3: CAUSES

Mechanism	PTH (1.6 - 6.9 pmol/L)	Causes
Factitious	1.6 – 6.9 pmol/L	• K^+-EDTA contamination - Look for any laboratory comments, raised K, unusually low ALP, low Mg^{++} • Low albumin (low total calcium but normal adjusted calcium)

Inadequate PTH	<6.9 pmol/L	**HYPOPARATHYROIDISM**
		• **Post neck surgery, post-neck irradiation**
		• **Hypomagnasaemia**
		  ○ Malabsorption, chronic diarrhoea
		  ○ Chronic alcohol excess
		  ○ Drugs – PPI, diuretics, aminoglycosides
		• Cinacalcet
		• Autoimmune
		• Infiltrative
		  ○ β-thalassaemia, haemochromatosis (iron), Wilson disease (copper)
		  ○ Malignancy
		  ○ Granulomas
		• Genetic e.g. DiGeorge syndrome, Fanconi syndrome
		• Idiopathic hypoparathyroidism

Inadequate Vitamin D	>6.9 pmol/L	**VITAMIN D DEFICIENCY** • Severe vitamin D deficiency • Deficient 1α-hydroxylation ○ CKD (eGFR <15mL/min/1.73m^2) • Vitamin D resistance

Other causes	>6.9 pmol/L	• CKD / AKI
		• Low dietary intake, malabsorption (usually other co-existing deficiencies)
		• Drugs, e.g. (not exhaustive):
		  ○ Bisphosphonates, Denosomab
		  ○ Chemotherapy (cisplatin)
		  ○ Foscarnet
		  ○ Calcitonin (rare)
		  ○ Glucocorticoids
		  ○ Anticonvulsants
		• Acute pancreatitis
		• Hyperphosphataemia
		• Rhabdomyolysis
		• Severe acute illness (e.g. toxic shock syndrome, Gram-negative sepsis)
		• Osteoblastic metastases (e.g. prostate, breast)
		• Abrupt inhibition of bone resorption (hungry bone syndrome)
		• Pseudohypoparathyroidism (PTH resistance)

4: INVESTIGATION

Diagnostic approach involves confirming the presence of hypocalcaemia by repeat measurement. Diagnosis may be obvious from the patient history e.g. CKD, post-surgical hypoparathyroidism. Where the cause remains unknown or suspected cause needs to be confirmed, investigations should include:

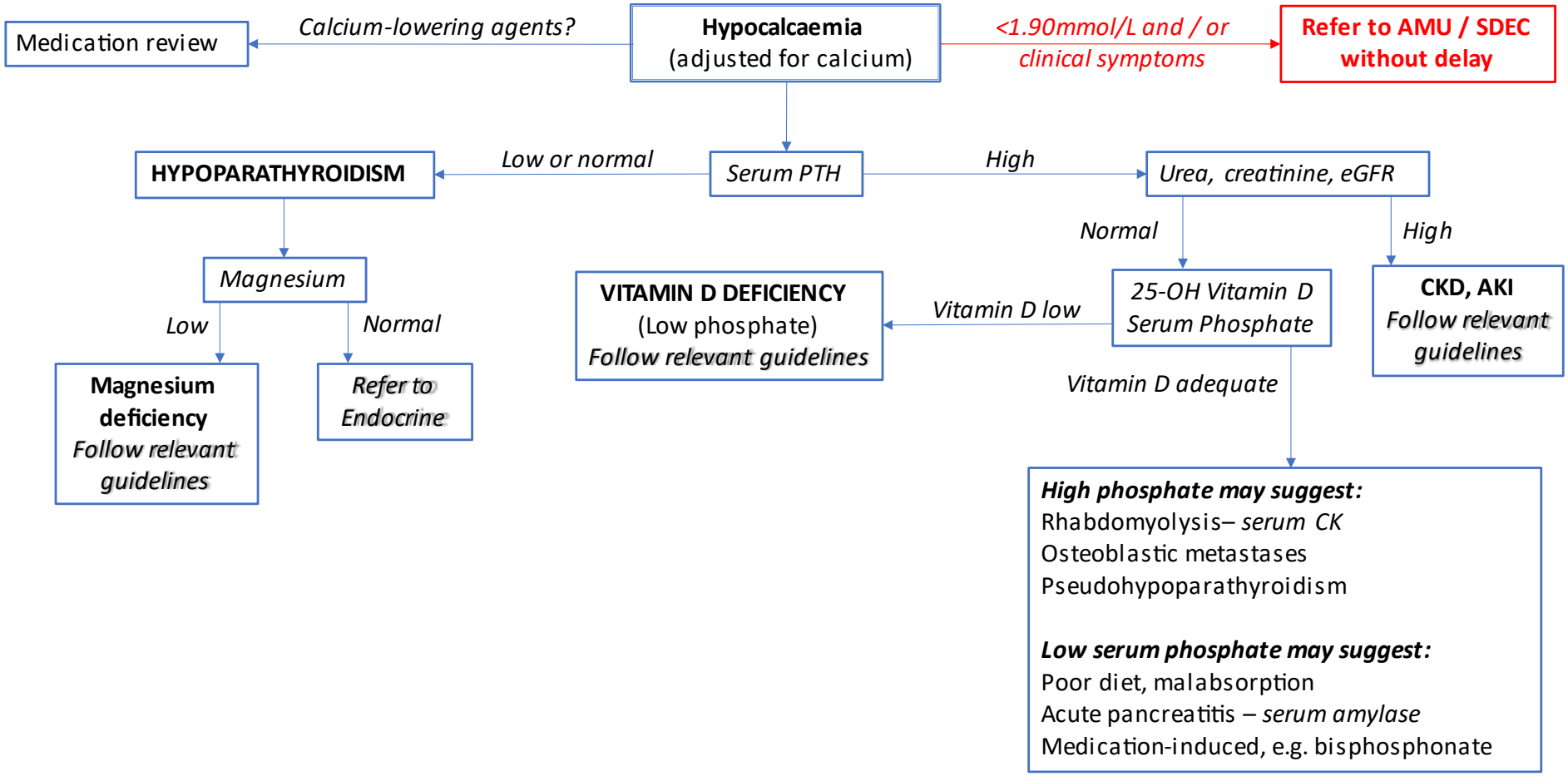
- Serum calcium (adjusted for albumin)
- PTH (requires separate EDTA sample)
- Magnesium
- U&E
- Vitamin D
- Phosphate
- Amylase, CK (based on patient history)

These tests should be performed selectively based on the patient's history and physical examination.

The flow chart on the next page summarises the approach to differential diagnosis of hypocalcaemia.

6: REFERENCE SOURCES

- Turner, J, et al. Emergency management of acute hypocalcaemia in adult patients. *Society for Endocrinology Endocrine Emergency Guidance*, 2016;5:G7.
- UpToDate - Diagnostic approach to hypocalcemia - UpToDate – Accessed 14/08/2023
- Hannan F, et al. Investigating hypocalcaemia. BMJ, 2013; 346: 2213


Medication review
Calcium-lowering agents?
Hypocalcaemia
(adjusted for calcium)
<1.90mmol/L and / or
clinical symptoms
Refer to AMU / SDEC
without delay
HYPOPARATHYROIDISM
Low or normal
Serum PTH
High
Urea, creatinine, eGFR
Normal
High
Magnesium
Low
Normal
Magnesium
deficiency
Follow relevant
guidelines
Refer to
Endocrine
VITAMIN D DEFICIENCY
(Low phosphate)
Follow relevant guidelines
Vitamin D low
25-OH Vitamin D
Serum Phosphate
CKD, AKI
Follow relevant
guidelines
Vitamin D adequate
High phosphate may suggest:
Rhabdomyolysis– serum CK
Osteoblastic metastases
Pseudohypoparathyroidism
Low serum phosphate may suggest:
Poor diet, malabsorption
Acute pancreatitis – serum amylase
Medication-induced, e.g. bisphosphonate