University Hospitals of Derby and Burton NHS Foundation Trust

# Hypocalcaemia- Full Clinical Guideline

**Reference No: CG-PHARM/2024/004**

## Introduction

Hypocalcaemia is a potentially life threatening biochemical abnormality that carries serious risks if left untreated.

## Aim and Purpose

The aim of the guideline is to ensure that calcium replacement therapy is safe and appropriate for the patient.

## Scope

This guideline is applicable to all adult inpatients except those on ICU. This guideline is suitable for use in the majority of clinical situations but patients with chronic hypocalcaemia, recent head and neck surgery or CKD 4/5 should be discussed with the relevant speciality teams. For patients with end stage renal failure or those in dialysis refer to Renal. Tumour lysis must be considered in all haematology or oncology patients – seek senior advice.

## Definition

Hypocalcaemia is a medical condition that can lead to life-threatening consequences if left untreated. Mild hypocalcaemia is often asymptomatic. The rate and magnitude of calcium depletion often determine the severity of symptoms.

## Calcium Ranges

The normal reference range of albumin-corrected calcium in an adult is 2.2 – 2.6 mmol/L.

**Mild hypocalcaemia – Adjusted calcium 2.0 - 2.20 mmol/L**
**Severe hypocalcaemia – Adjusted calcium ≤1.90 mmol/L**

**Severity also relates to presence of symptoms and ECG changes - severity in patients with Adjusted calcium 1.9 - 2.0 mmol/L is best judged by these factors.**

## Physiology of Calcium

Total calcium and corrected (adjusted for albumin) calcium results are reported on iCM. Caution must be taken when interpreting results. Please refer to adjusted calcium when making clinical decisions.

Approximately 40% of plasma calcium is bound to albumin. However, it is the unbound fraction that plays the significant clinical role. The correction is not valid in acid-base disorders as calcium binding to albumin is affected by pH. For example, acidosis will increase the ionised plasma calcium, whereas alkalosis will have the opposite effect. Therefore a patient with acute respiratory alkalosis may exhibit signs of hypocalcaemia, such as paraesthesia.

Where there is concern that Adjusted Calcium is unreliable due to acid-base disorders and/or any other factors, Ionised Calcium can be assessed via Venous Blood Glucose sample with normal range 1.1-1.3 mmol/l.

**Signs and symptoms of Hypocalcaemia**

Extracellular calcium concentrations are important for the normal functioning of muscles and nerves. Thus, classic symptoms of hypocalcaemia are neuromuscular excitability in the form of muscle twitching, spasms, tingling, and numbness.

Other features of hypocalcaemia include:

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| Neuromuscular | Numbness/Paraesthesia<br>Muscle cramps/tremors<br>Tetany<br>Muscle weakness<br>Laryngospasm/stridor/bronchospasm/wheeze<br>Dysphagia<br>Chvostek and Trousseau signs |
| Neurological | Changes in mental state - e.g. confusion, irritability, anxiety<br>Seizures<br>Fatigue<br>Depression<br>Personality changes |
| Cardiac | Prolonged QT interval, leading to heart block or VF<br>Cardiac arrhythmias<br>Hypotension |

**Causes**

The cause of hypocalcaemia should be determined and if possible, measures should be taken to correct the underlying cause alongside any calcium treatments.

It should be recognised that a major cause in hospital inpatients is post-operative hypoparathyroidism following total parathyroidectomy (usually in the context of advanced Chronic Kidney Disease) or total thyroidectomy. If total thyroidectomy has recently occurred, see Chart 3 to guide required assessment and initial treatment. Refer to Endocrinology for further advice.

In more general terms, hypocalcaemia is normally caused by parathyroid hormone disturbances or low vitamin D levels. This can be due to the following causes:

- Low dietary intake of vitamin D/reduced exposure to sunlight
- Calcium malabsorption
- Reduced vitamin D synthesis hydroxylation (e.g. in renal failure, liver disease or anticonvulsant therapy)
- Hypomagnesaemia (reduces PTH secretion and action) – Please refer to hypomagnesaemia guideline for further guidance
- Autoimmune hypoparathyroidism
- Pseudohypoparathyroidism (failure of target tissues to respond to hormone)
- Surgical removal of parathyroid glands/post-operative dysfunction after thyroidectomy
- Hyperphosphataemia
- Others- Acute pancreatitis, Septic shock, Rhabdomyolysis, Massive blood transfusion
- Drug-induced – e.g. some anticonvulsants, bisphosphonates, calcitonin, phosphate, colchicine overdose, foscarnet, radio contrast dye, ketoconazole and some antineoplastic agents.

## Investigation and Treatment

The initial priority is to assess for severity of the problem and treat with IV calcium if indicated. Due to the potential for severe soft tissue damage from extravasation it is important not to treat patients unnecessarily with IV calcium. Please see Chart 1 below which outlines the steps required to assess severity and tailor immediate action to that assessment.

It is ***essential*** that the underlying cause of hypocalcaemia is identified and addressed regardless of extent of hypocalcaemia. Failure to do this in patients with mild hypocalcaemia will risk severe hypocalcaemia. Failure to do this in patients treated with IV calcium will lead to an extended (potentially hazardous) IV treatment and/or recurrence upon cessation of IV calcium. Tests to identify causes always include Adjusted Calcium, PTH, Vitamin D, U&E, phosphate and Magnesium levels. The initial interpretation of these tests is described in Chart 2, but in inpatients with recent complex/severe illness, advice from relevant speciality teams will be needed if the cause is not derived from Chart 2.

## Further information on Specific Cause

**Post total (or 'completion') thyroidectomy** Onset typically within 72 hours of operation and due to hypoparathyroidism which can be temporary or permanent. See Chart 3 for further details of management. Involve Endocrinology at the earliest opportunity.

**Post total parathyroidectomy** This can be in the context of advanced Chronic Kidney disease - involve Nephrology team. Endocrinology patients also occasionally have a total parathyroidectomy (as opposed to the more frequent partial parathyroidectomy)- these patients should be proactively managed with alfacalcidol and calcium supplements immediately post-operatively. Hypocalcaemia after partial parathyroidectomy is much rarer; if it does occur it could indicate Hungry Bone Syndrome- refer to Endocrinology and manage as per Chart 1 whilst awaiting further advice.

**Chronic Kidney Disease** Hypocalcaemia is due to the reduction in the renal activation of vitamin D, which normally increases circulating calcium by increasing intestinal absorption.

**Hypomagnesaemia** Hypomagnesaemia is a common cause of hypocalcaemia, both by inducing resistance to parathyroid hormone (PTH) and by diminishing its secretion. If patient is asymptomatic, correct the hypomagnesaemia first before giving calcium, as this may lead to a spontaneous normalisation of calcium concentrations (see hypomagnesaemia guidelines).

**Hypoparathyroidism** Parathyroid hormone increases vitamin D activity via hydroxylation, increases bone resorption and decreases renal calcium excretion. Most patients with hypoparathyroidism require lifelong calcium and vitamin D supplementation. An exception is the occurrence of transient hypoparathyroidism after thyroidectomy or parathyroidectomy as detailed above.

**Shared care guidelines** The following guidelines are available for primary and secondary care. They refer to the management of hypocalcaemia detected in Primary Care and the management of associated conditions.

Shared care guidelines are available from:
http://www.derbyhospitals.nhs.uk/primary/pathology/shared-care-pathology-guidelines/

**Chart 1- Management of Hypocalcaemia in Inpatients**

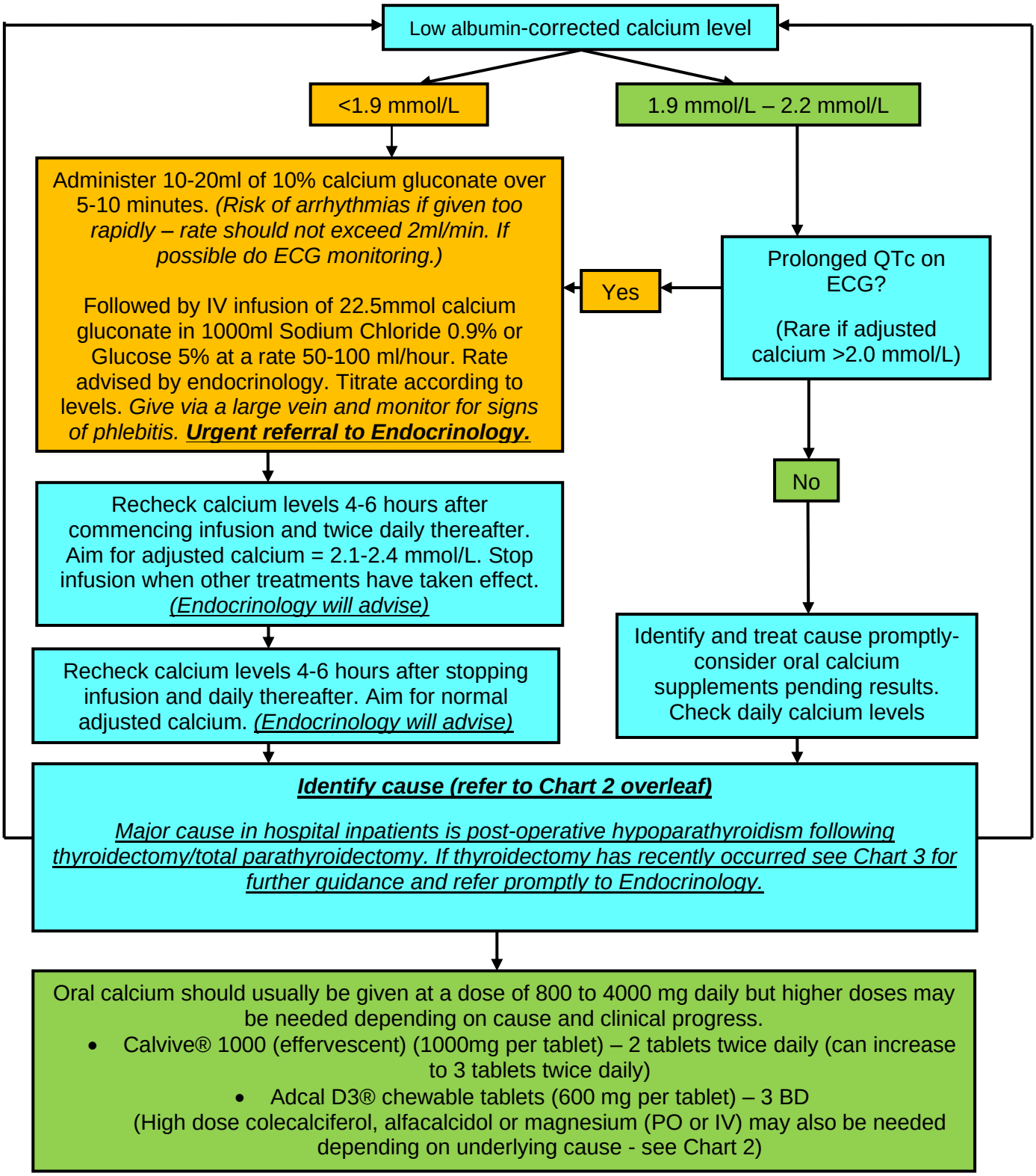
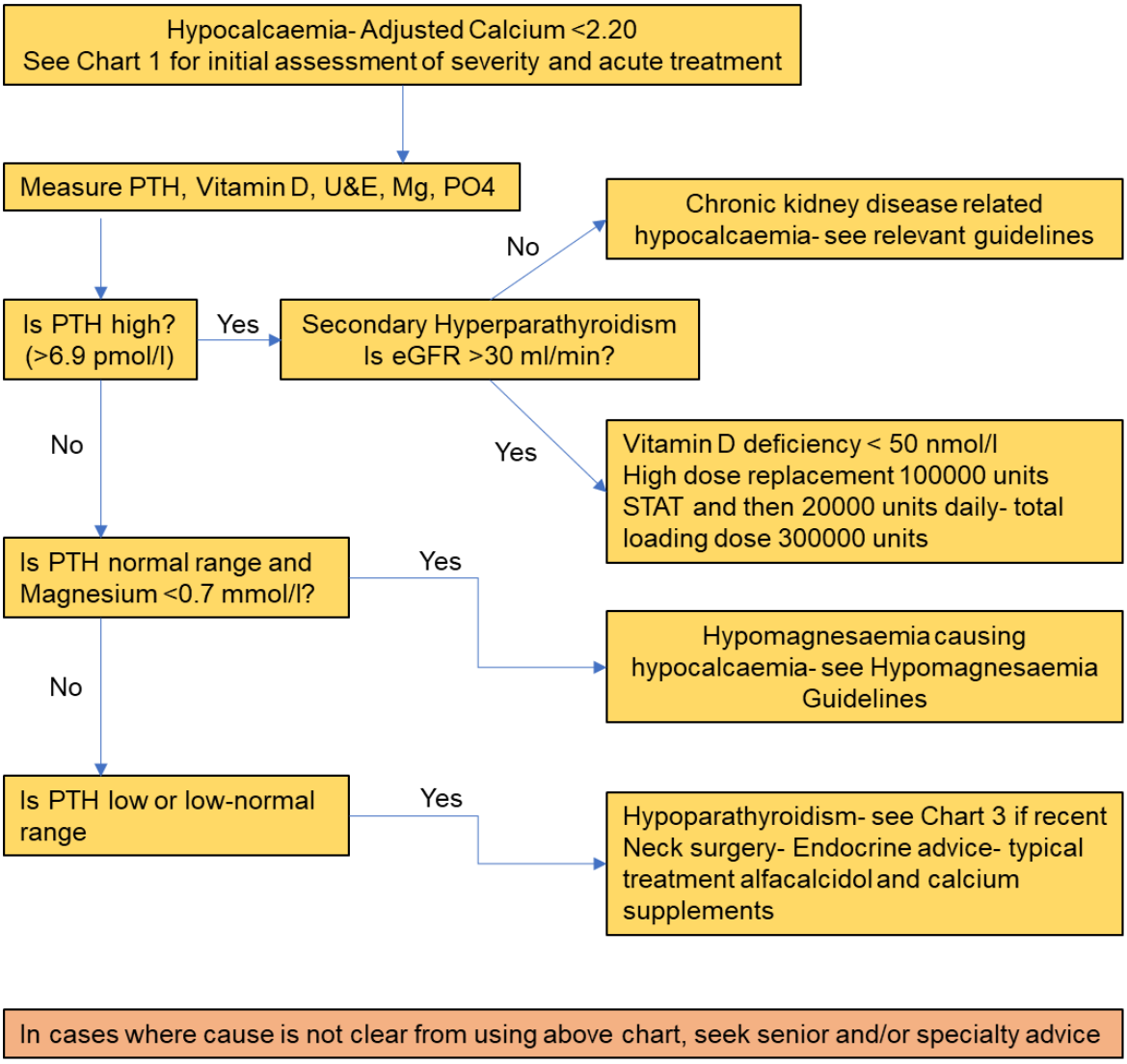


**Chart 2 - Initial investigations**




**Notes on Treatments and Prescribing;**

**iv Calcium Gluconate** – 10ml of 10% calcium gluconate contains 2.25mmol of calcium. Some centres use 20ml as a bolus over 10 minutes without apparent problem. This is the preferred calcium preparation for any patient with peripheral access. Intravenous calcium in presence of high phosphate can precipitate calciphylaxis and renal advice should be taken.

**iv Calcium chloride** – is an option if using central access - it may offer more stable IV levels during infusion compared with calcium gluconate but concerns about severe tissue injury with peripheral use mean it is not appropriate for peripheral vein use. For ICU use only.

**Prescribing iv calcium** - iv Calcium is prescribed as an intravenous infusion on our electronic systems. The decision to stop the infusion should be an active one that reflects that the

treatment is no longer necessary due to other treatments having taken effect. It is important to ensure that treatment does not stop in error at the time a prescribed infusion is complete. A further prescription for iv calcium should be planned in advance of completion of the previous prescription.

**Oral calcium supplements** – Annotate chart with *'short term for hypocalcaemia – review ongoing need'* in the additional information box on EPMA prescription.

**Available Oral Calcium supplements** from UHDB Pharmacy Stocks are as follows;

Calvive 1000: (1000mg/tab)
Calcichew: (500mg/tab)
Adcal D3 chewable: (600mg/tab)
Calcium carbonate 1.25g effervescent tablet: (500mg/tab)

**Interactions –** Oral calcium supplements reduce the absorption of a number of other drugs, and should not be taken at the same time of day. These include tetracyclines, ciprofloxacin and bisphosphonates.

**Oral calcium carbonate** preparations (eg. Adcal D3) can cause GI symptoms and are unreliably absorbed if taken alongside PPIs. Please contact pharmacy for advice on management.

**Cautions and contraindications** – Calcium administration is contraindicated in those with ventricular fibrillation and patients with hypercalcaemia.

**Patients on digoxin –** These patients should be monitored closely as calcium may precipitate digitalis toxicity.

**Adverse effects of calcium therapy** – Hypercalcaemia – refer to Chart 1 and monitor levels. GI side effects including constipation. Rapid IV administration may result in venous irritation, hot flushes and peripheral vasodilation. Rapid administration may also result in hypotension, bradycardia, arrhythmias, syncope and cardiac arrest.

## Appendix

## Prevention and Management of Post-Operative Hypocalcaemia following Total Thyroidectomy

### Introduction

Post-operative hypocalcaemia following Total Thyroidectomy is a common event.

- -30% incidence of temporary hypocalcaemia (BAETS Audit data)
- -permanent hypoparathyroidism is less common- typically 1-2%

Certain groups of patient may be more at risk;

- Thyroid cancer patients- especially in the context of level VI neck dissection
- Young females with Graves disease

### 1. Pre-operative loading of vitamin D

Pre-operative vitamin-D deficiency has been shown to increase the chance of post-thyroidectomy hypocalcaemia.

Check serum calcium, phosphate and vitamin D
If calcium not raised and 25OH-vitamin D <50 nmol/l give Colecalciferol 20000 units/day for 14 days and then maintenance dose of 800 units/day (eg Fultium D3)

### 2. Identification of hypocalcaemia post-thyroidectomy (Total Thyroidectomy/Completion Thyroidectomy)

Check calcium 4 hours post-operative AND on first morning post-op.
Patients with normal and stable calcium levels on both tests can be considered for early discharge from hospital
Overall Interpretation and Action as per Chart 3

### 3. Treatment of Post-operative hypoparathyroidism

Chart 3 outlines the suggested interpretation and actions for differing levels of calcium result following parathyroidectomy.
If hypocalcaemia is present it is important that further blood tests (including PTH) are sent to confirm the cause.
Early referral and/or discussion with Endocrinology is advised for all patients with hypocalcaemia in this context.
Patients should only be discharged from hospital when calcium levels are stable on consecutive days.

### 4. Subsequent progress

**Patients sent home on calcium supplements alone**

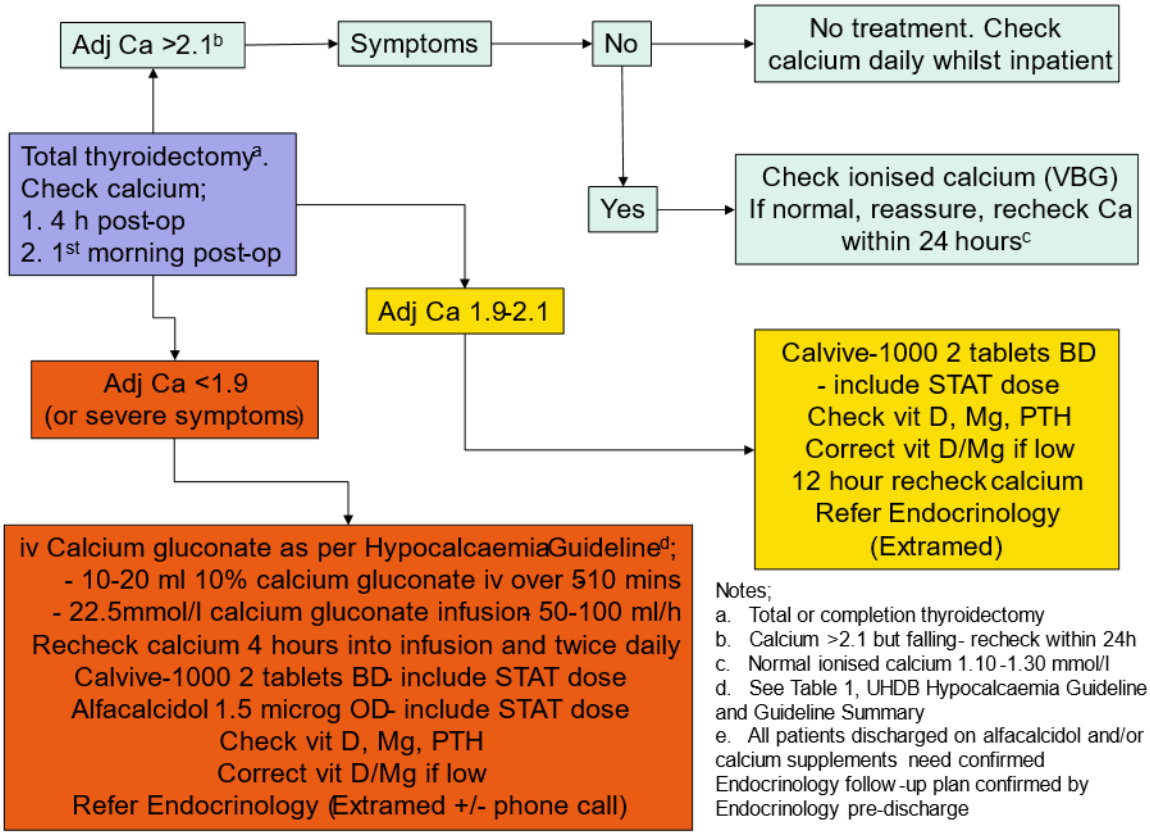
Calcium supplements should continue until outpatient review from the Endocrine team.
This may be with Endocrine Consultant or Nurse team depending on the patient. Please refer to Endocrinology via ExtraMed when commenced on Calcium supplements- expected response will include clarification of required follow-up

**Patients sent home on calcium supplements *and* alfacalcidol**

These patients will require close Endocrine follow-up post-discharge involvement (risk of treatment related hypercalcaemia in addition to monitoring for hypocalcaemia). Please refer to the endocrine team via ExtraMed at the time of commencing alfacalcidol.

At discharge please give patient three request forms for calcium and PTH (marked 'urgent') The first blood test to take place 2-3 days post discharge- plan for this sample should be in place when discharged (eg booked via Swiftqueue or arranged as ward re-attender) Agreed Endocrine Follow-up must be in place pre-discharge.

**Chart 3 Assessment of Calcium levels Post Thyroidectomy Hypoparathyroidism**




Notes;
a. Total or completion thyroidectomy
b. Calcium >2.1 but falling- recheck within 24h
c. Normal ionised calcium 1.10-1.30 mmol/l
d. See Table 1, UHDB Hypocalcaemia Guideline and Guideline Summary
e. All patients discharged on alfacalcidol and/or calcium supplements need confirmed Endocrinology follow-up plan confirmed by Endocrinology pre-discharge

## References


1. Cooper M, Gittoes N (2008) Diagnosis and management of hypocalcaemia. BMJ 336: 1298-1302
2. Joint Formulary Committee (2018) British National Formulary [Ed]. London: British Medical Association and the Royal Pharmaceutical Society of Great Britain; [July, 2018]. Available online: https://www.new.medicinescomplete.com/#/browse/bnf [accessed: 01/08/2018]
3. Adcal $D_3$ chewable tablets (2017) Summary of product characteristics. Available online: https://www.medicines.org.uk/emc/product/1356/smpc [accessed: 01/08/2018]
4. Sandocal® 1000 (2016) Summary of product characteristics. Available online: https://www.medicines.org.uk/emc/product/1191 [accessed: 01/08/2018]
5. Calcium gluconate injection BP (2015) Summary of product characteristics. Available online: https://www.medicines.org.uk/emc/product/6264/smpc [accessed: 01/08/2018]
6. Calcium chloride injection 10 millimoles in 10 ml (2018) Summary of product characteristics. Available online: https://www.medicines.org.uk/emc/product/3585/smpc [accessed: 01/08/2018]
7. Medusa (2016) Calcium chloride monograph. Available online: http://medusa.wales.nhs.uk/IVGuideDisplay.asp [accessed: 01/08/2018]
8. Medusa (2017) Calcium gluconate monograph. Available online: http://medusa.wales.nhs.uk/IVGuideDisplay.asp [accessed: 01/08/2018]
9. UpToDate (2015) Treatment of hypocalcaemia. Available online: http://www.uptodate.com/hypocalcaemia [accessed: 23/06/2016]
10. UKMI Medicines Q&As: *How is acute hypocalcaemia treated in adults?* [June, 2017]
11. Nottingham University Hospitals (2013) Guidelines for the treatment of hypocalcaemia in adults [May, 2013]
12. Southern Derbyshire Shared Care Pathology Guidelines (2016) Hypocalcaemia in Adults [March, 2016]
13. (2016) Society for Endocrinology Endocrine Emergency Guidance: Emergency management of Acute Hypocalcaemia in Adult Patients. Available online: http://www.endocrineconnections.com/content/5/5/G7.full [accessed: 01/08/2018]
14. BAETS 4th National Audit (2012)
15. Kirkby-Bott, J., Markogiannakis, H. et al (2011) Preoperative Vitamin D Deficiency Predicts Postoperative Hypocalcaemia After Total Thyroidectomy. *World Journal of Surgery* 35; 324-330

Documentation Controls

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