WGH normal range of total calcium is 2.1-2.6 nmol/l. Correct for albumin by adding 0.02 mmol/l for every g albumin is below 40 g/l.

**Causes of Hypercalcaemia**: 1-2 below account for ≥80%.

- **Primary Hyperparathyroidism** (prevalence 0.05-0.1 % F:M=4:1), caused by a single adenoma (85%), hyperplasia (10-15%), carcinoma <2%, or MEN 1/2. This is associated with low plasma phosphate unless renal impairment is present. Often raised Cl⁻.
- **Malignancy**: i) solid tumours with metastasis to bones, ii) Humoral Hypercalcaemia of Malignancy (HHM - due to secretion of PTHrP; Suva et al. Science 1987;237:893), iii) haematological malignancy.
- Familial Hypocalciuric Hypercalcaemia (FHH), which is a loss of function mutation in the Ca++ sensing receptor gene in the parathyroid gland & kidney (Pollak et al. Cell 1993;75: 1297). Neonatal Severe Hyperparathyroidism is probably a homozygous variant.
- Sarcoidosis & other granulomatous diseases
- Endocrine causes such as thyrotoxicosis, Addison's disease (crises), pheochromocytoma (PTHrP).
- Other causes: Milk-Alkali Syndrome, Idiopathic Infantile Hypercalcaemia, Immobilisation (age usually <16y), Medication: Vit-D/A and analogues, oestrogens/antioestrogens, lithium, theophylline, thiazides.

**Clinical Features**

Vary by patient, level (emergency if corrected Ca >3.5 mmol/l), speed of change, but include dehydration with polyuria and thirst, anorexia, nausea, vomiting, abdominal pain, peptic ulceration, constipation, pancreatitis, headache, pruritus, confusion, muscle weakness, hyporeflexia, psychosis, drowsiness, coma. Also specific signs of underlying disease, corneal calcification (Band Keratopathy: usually primary hyperparathyroidism) and short QT on ECG.
Investigations
FBC, ESR, Na+, K+, Cl-, Ca PO4; Mg, ionised Ca++, albumin, ALP, LFTs, PTH
ECG, CXR, and depending on Hx consider bone scintigraphy, myeloma screen - incl.
skeletal survey, TFTs, s-ACE, 24h urine for calcium and creatinine, hand x-ray.

Specific Emergency Treatment
Emergency treatment is required if corrected calcium >3.5 mmol/l or ionized calcium
greater than 1.8 mmol/l.

Fluids
- Urgent fluid replacement with 0.9% saline (add KCl as required) will lower
calcium and enhance renal clearance.
- Check U&E’s and calcium twice daily.

Diuretics
- Loop diuretics (e.g. frusemide 40 mg IV bd) will enhance calcium loss in the
  urine. DO NOT start until fluid deficits have been rectified.
- NEVER use thiazides as they cause calcium retention.

Bisphosphonates
- A single infusion of pamidronate (see dose table below) will lower calcium levels
  within 2-4 days.
- Maximal effect is at about 1 week.
- Recurrent hypercalcaemia may be treated with oral clodronate or repeated IV
  infusions of pamidronate.

Other Measures
- If patient is on digoxin, discontinue.
- In most cases glucocorticoids are no longer needed. They may still be helpful in
e.g. sarcoidosis, myeloma and hypervitaminosis-D (Prednisolone 60-80mg/d).
- Calcitonin may be considered if the above fails.
<table>
<thead>
<tr>
<th>Serum Calcium (mmol/l)</th>
<th>Pamidronate Dose (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;3.0</td>
<td>15</td>
</tr>
<tr>
<td>3.0-3.5</td>
<td>30</td>
</tr>
<tr>
<td>3.6-4.0</td>
<td>60</td>
</tr>
<tr>
<td>&gt;4.0</td>
<td>90</td>
</tr>
</tbody>
</table>

Notes: For PTH, the blood needs to be taken to Clinical Chemistry within 30 minutes of venepuncture and Clinical Chemistry notified beforehand; 6-8ml in a clear top serum tube is sufficient. For ionised calcium, also contact Clinical Chemistry beforehand to obtain the correct syringe for collection and deliver to Clinical Chemistry within 30 minutes.

Protocol prepared by Rafn Benediktsson, 1996
Revised, October 2002