

# CALCIUM [Ca<sup>2+</sup>]

The most abundant mineral in the human body.

- 99% bound in bone. Remainder in ECF compartment.
- Homeostasis maintained by parathyroid hormone, vitamin D & calcitonin.

## PTH.

- Released from parathyroid glands in response to ↓ Ca<sup>2+</sup> levels.
- Stimulates osteoclasts to ↑ bone resorption.
- ↑ Ca<sup>2+</sup> resorption [and PO<sub>4</sub> excretion] by kidney.
- ↑ Ca<sup>2+</sup> intestinal absorption (w/ calcitriol).

## Calcitriol.

- Influenced by ↑ Ca<sup>2+</sup> levels (plus adrenaline, glucagon & gastrin).
- Inhibits osteoclasts & potentiates Ca<sup>2+</sup> loss through the kidney.

### Note.

- Calcium is protein-bound (albumin), free active ion or non-ionised.
- The *ionised-fraction* is physiologically active.

## HYPOCALCAEMIA.

Defined as an ionised Ca<sup>2+</sup> level < 1.0 mmol/L. [Normal 1.05-1.30 mmol/L].

### Pathophysiology.

Many causes of hypocalcaemia including shock, sepsis, ARF & pancreatitis. The tables below have a larger list of DDx.

- *Cellular dysfunction.*
  - Any interference to cell-metabolism will ↓ iCa<sup>2+</sup> levels.
  - Allows Ca<sup>2+</sup> movement into cytoplasm of poor-functioning cells.
- *Pancreatitis.*
  - Lipase breaks down fat into fatty-acids & glycerol.
  - Fatty acids combine with Ca<sup>2+</sup> → *saponification*.
- *Drugs.*
  - as in Table 21-15.
- *Post-operative Hypocalcaemia.*
  - ~10% of parathyroidectomy patients will develop hypoparathyroidism & subsequent hypocalcaemia.
- *Renal Failure.*
  - ?due to hyperphosphataemia + ↓ vitamin D production.
- *Phosphate Overload.*
  - eg. rhabdomyolysis.

**Table 21-14 Some Causes of Hypocalcemia**

|                              |
|------------------------------|
| Decreased calcium absorption |
| Vitamin D deficiency         |
| Malabsorption syndromes      |
| Increased calcium excretion  |
| Alcoholism                   |
| Chronic renal insufficiency  |
| Diuretics                    |
| Endocrine disorders          |
| Hypoparathyroidism           |
| Pseudohypoparathyroidism     |
| Drugs ( <b>Table 21-15</b> ) |
| Miscellaneous                |
| Sepsis                       |
| Acute pancreatitis           |
| Massive transfusions         |
| Hypomagnesemia               |
| Rhabdomyolysis               |

**Table 21-15 Drugs that Can Cause Hypocalcemia**

|                                      |
|--------------------------------------|
| Phosphates (e.g., enemas, laxatives) |
| Phenytoin, phenobarbital             |
| Gentamicin, tobramycin, actinomycin  |
| Cisplatin                            |
| Heparin                              |
| Theophylline                         |
| Protamine                            |
| Glucagon                             |
| Norepinephrine                       |
| Citrate                              |
| Loop diuretics                       |
| Glucocorticoids                      |
| Magnesium sulfate                    |
| Sodium nitroprusside                 |

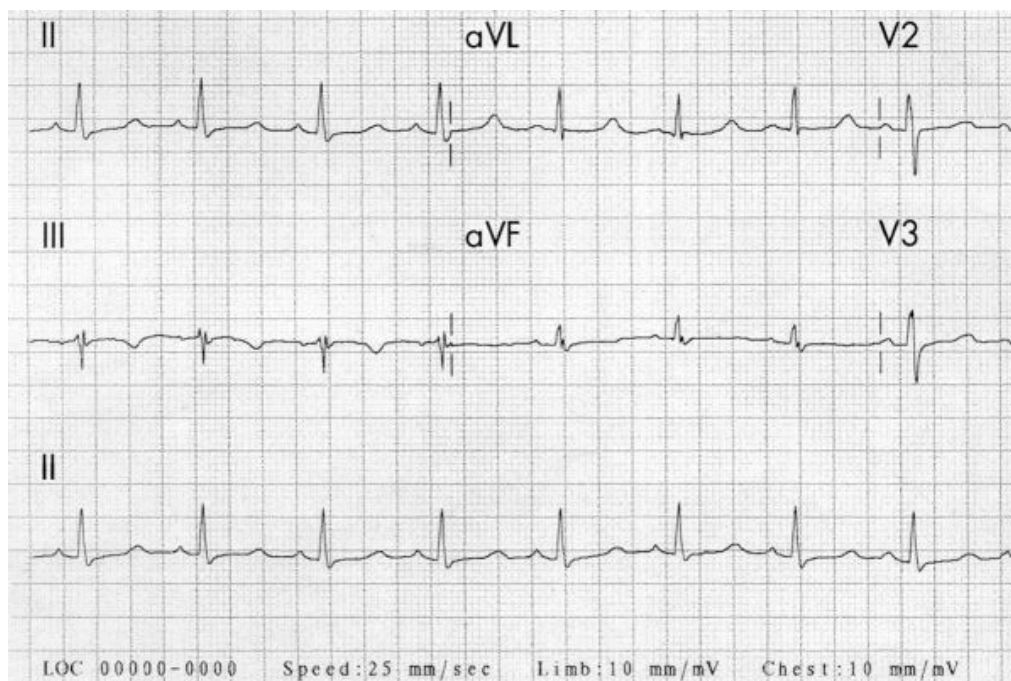
### **Symptoms & Signs.**

Serious physiologic changes do not occur until  $iCa^{2+}$  levels are  $< 0.7-0.8$  mmol/L.

- ↓ myocardial contraction (2\* to inhibiting relaxation)
  - Bradycardia, hypotension.
  - QTc prolongation
- Paraesthesias (mouth & fingertips).
  - Muscle weakness & spasm.
  - Hyperactive deep-tendon reflexes.
- Chvostek sign:
  - Tapping facial nerve → facial twitching.
- Trousseau sign: carpal spasm produced by elevated BP-cuff  $> 3$  mins.
  - Most reliable indicator.
- Anxiety, irritability, confusion, psychosis.

#### Hypocalcaemia & the ECG...

- Most characteristic finding is *prolonged QT interval* (typically the ST-segment).
- T-wave is normal.



## **Management.**

Tailored to the individual presentation & directed towards the underlying cause.

- Prolonged symptom duration (& asymptomatic patient) can be treated with oral replacement (with or without Vitamin D).
- IV replacement recommended for symptomatic cases ( $iCa^{2+} < 0.65$  mmol/l).
  - 10mL of 10% CaCl (or 10-30mL 10% Ca-gluconate) over 10-20mins.
  - Infusion to follow.

**Caution:** Do not give if patient is on *digoxin*.

Empirically given IV Calcium during massive transfusion.

- 10mL 10% CaCl per 4-6 units of pRBC.

Replace *OTHER* electrolytes also (esp. magnesium).

## **HYPERCALCAEMIA.**

Common. ~90% assoc. w/ hyperparathyroidism or malignancy.

Defined as an  $iCa^{2+} > 1.35$ mmol/L.

### **BOX 123-9 CAUSES OF HYPERCALCEMIA**

Primary hyperparathyroidism  
Malignant disease  
Parathyroid hormone-related protein  
Ectopic production of 1,25-dihydroxyvitamin D  
Other bone-resorbing substances  
Osteolytic bone metastasis  
Medications  
Thiazide diuretics  
Lithium  
Estrogens  
Vitamin D toxicity  
Vitamin A toxicity  
Calcium ingestion  
Granulomatous disorders  
Sarcoidosis  
Tuberculosis  
Coccidioidomycosis  
Berylliosis  
Histoplasmosis  
Leprosy  
Nonparathyroid endocrine disorders  
Hyperthyroidism  
Adrenal insufficiency  
Pheochromocytoma  
Acromegaly  
Vasoactive intestinal polypeptide-producing tumor  
Miscellaneous  
Milk-alkali syndrome  
Immobilization  
Idiopathic hypocalcemia of infancy  
Physiologic (in the newborn)

### **BOX 123-10 CLINICAL FEATURES OF HYPERCALCEMIA**

#### **Neurologic**

Fatigue, weakness  
Confusion, lethargy  
Ataxia  
Coma  
Hypotonia, diminished deep tendon reflexes

#### **Cardiovascular**

Hypertension  
Sinus bradycardia, atrioventricular block  
ECG abnormalities (short QT, bundle branch block)  
Ventricular dysrhythmias  
Potentiation of digoxin toxicity

#### **Renal**

Polyuria, polydipsia  
Dehydration  
Loss of electrolyte  
Prerenal azotemia  
Nephrolithiasis  
Nephrocalcinosis

#### **Gastrointestinal**

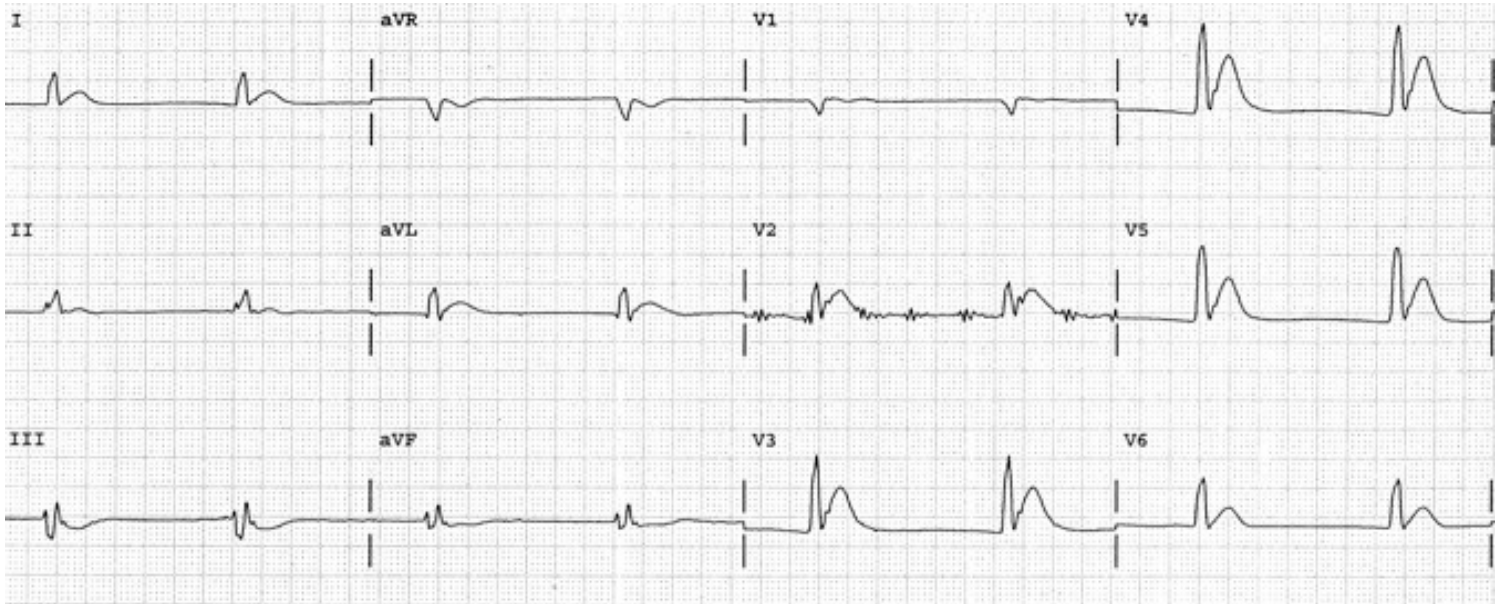
Nausea, vomiting  
Anorexia  
Peptic ulcer disease  
Pancreatitis  
Constipation, ileus

stones (renal calculi), bones (osteolysis),  
moans (psychiatric disorders), groans:  
(peptic ulcer disease, pancreatitis, and  
constipation)

## Hypercalcaemia & the ECG...

- Shortening of QT-interval
- (severe) Osborn J-waves
- Ventricular irritability → cardiac arrest.

Hypercalcaemia causing marked shortening of the QT interval (260ms).



### Management.

Initiated immediately with evidence of severe dehydration, altered LOC or symptomatic dysrhythmias. Consists of;

- Volume replacement
- Decreasing mobilisation of  $\text{Ca}^{2+}$  from bone.
- Correcting the underlying disorder.
- Up to  $\frac{1}{3}$  of patients will have *hypokalaemia* also. Check other electrolytes !!
  - Hypomagnesaemia is also common.

#### 1. IV Fluids.

- Normal saline.
- Targeting UO > 100-150mL/hr
- Modest ↓ in  $\text{Ca}^{2+}$
- Correct electrolyte abnormalities



Restores GFR, also presents ↑  $\text{Na}^{+}$  to renal tubule (↑  $\text{Ca}^{2+}$  excretion)

#### 2. Bisphosphonates

- Usually under advisement of in-patient specialist !!
- Pamidronate 90mg is most commonly used.
- Calcitonin can also be used.

#### 3. Loop diuretics

- Inhibit  $\text{Ca}^{2+}$  reabsorption.
- Must be adequately volume-resuscitated prior to its use.
- **NO** thiazides.
- Its use remains controversial & possibly no longer recommended.

#### 4. Underlying cause.

- Further investigation required.
  - PTH & Vitamin D levels.
  - Myeloma screen
  - Withhold offending medications.