



# Management of Hypocalcaemia

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# Where Will we be Going?



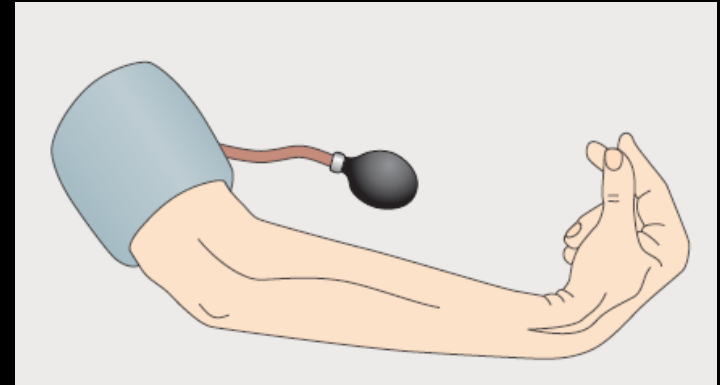
- Physiology
- Vitamin D deficiency
  - Management
- Acute hypocalcaemia
  - Post neck surgery
  - ED management
- Clinical cases of hypocalcaemia
  - Individualised management

# Hypocalcaemia - Principles

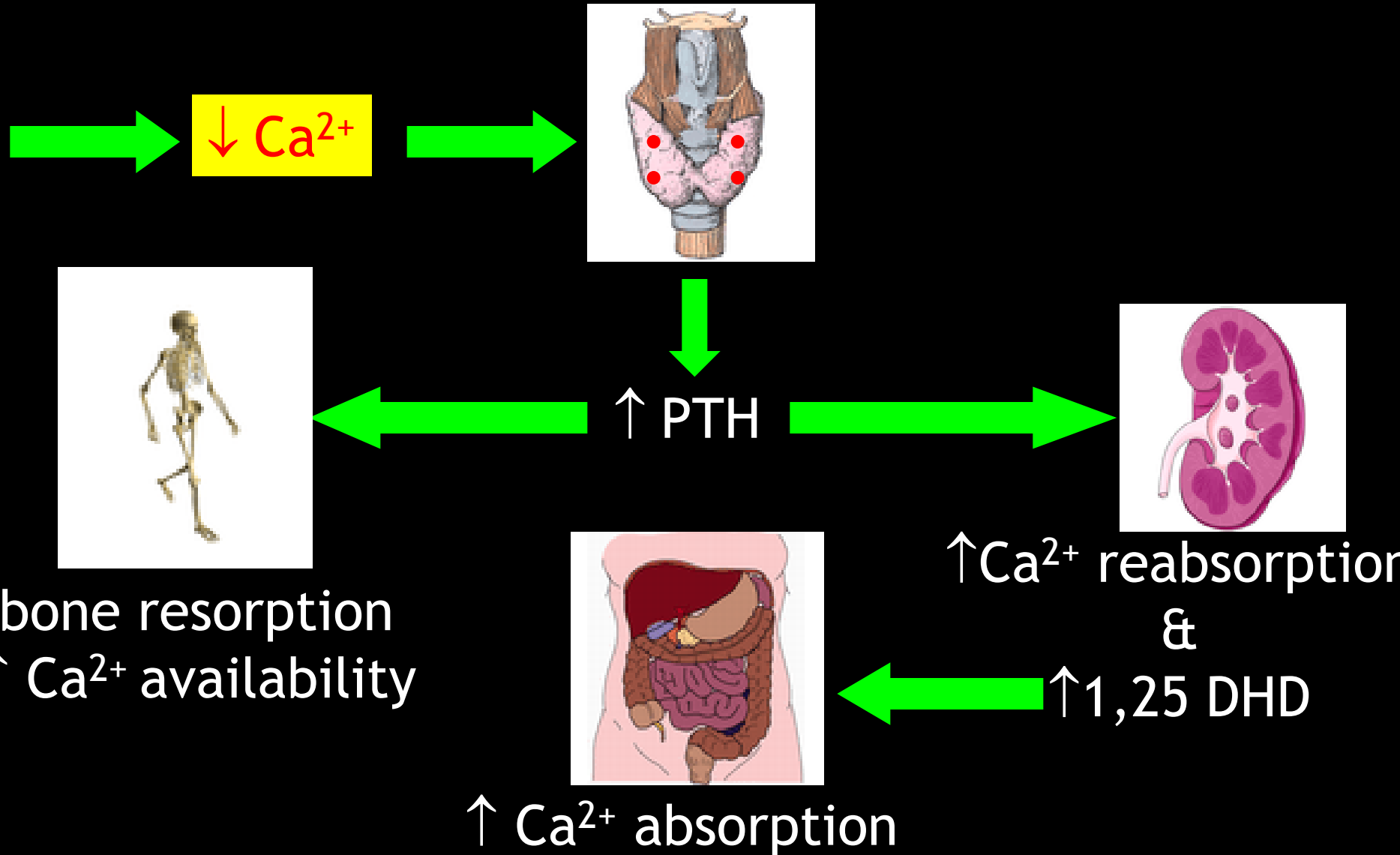
- Adjusted serum Ca < RR (2.10 - 2.60 mmol/L)
  - $\pm(40 - [\text{ALB}]) \times 0.02$
- Clinical presentations
  - Asymptomatic laboratory finding
  - Life threatening metabolic disturbance
- Rate of change of [Ca] important in defining clinical context
  - Slow (even if quantitatively severe)
    - Few/no clinical features
  - Rapid
    - Severe and emergency care

# Clinical Presentations

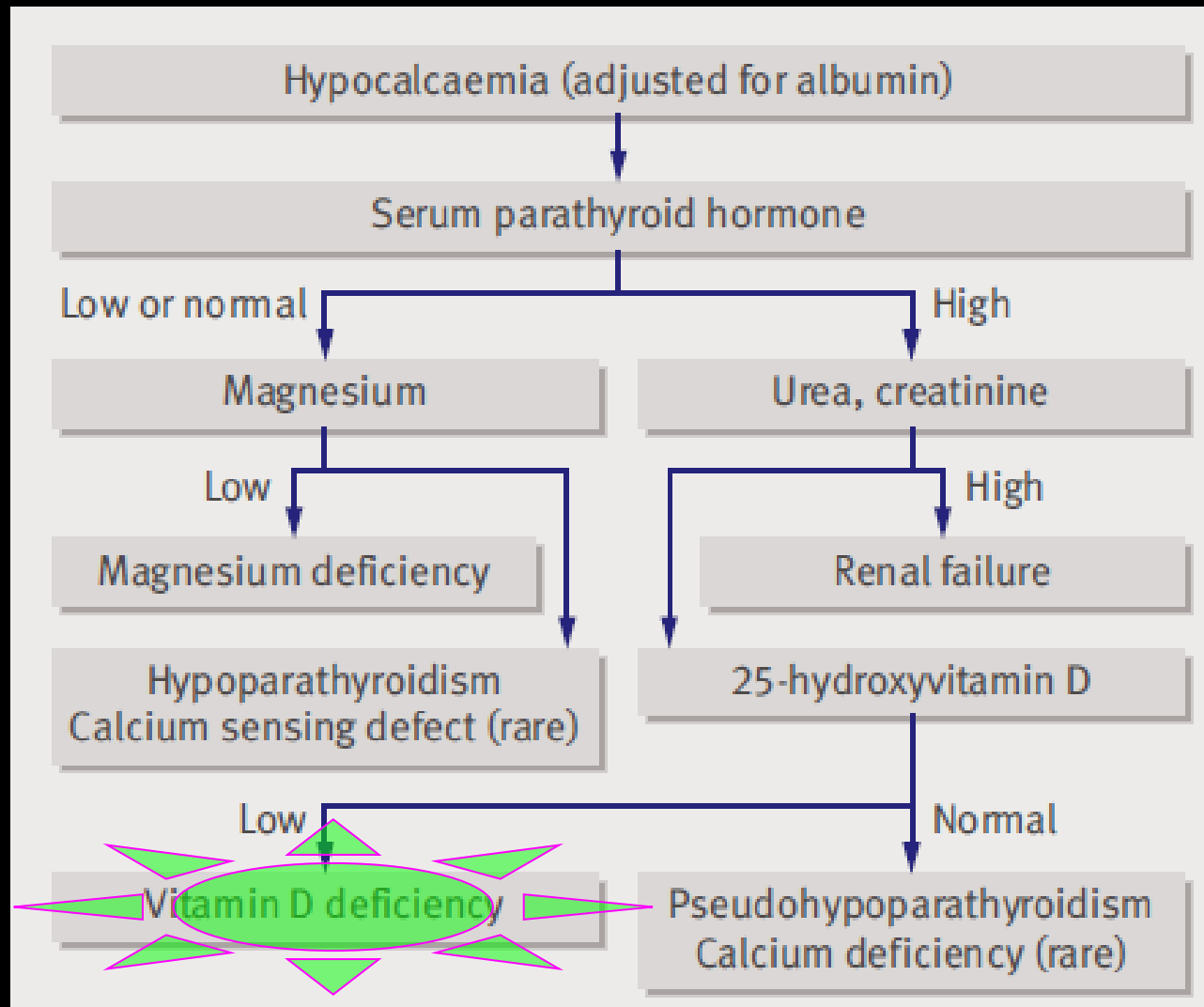
- Neuromuscular hyperexcitability
  - Paraesthesiae (peripheral & circumoral)
  - Cramps & twitching
  - Carpopedal spasm & tetany
  - Seizures
  - Arrhythmias
- Features of underlying cause



# Overview of Calcium Homeostasis



# Approach to Investigating Hypocalcaemia



# Rickets



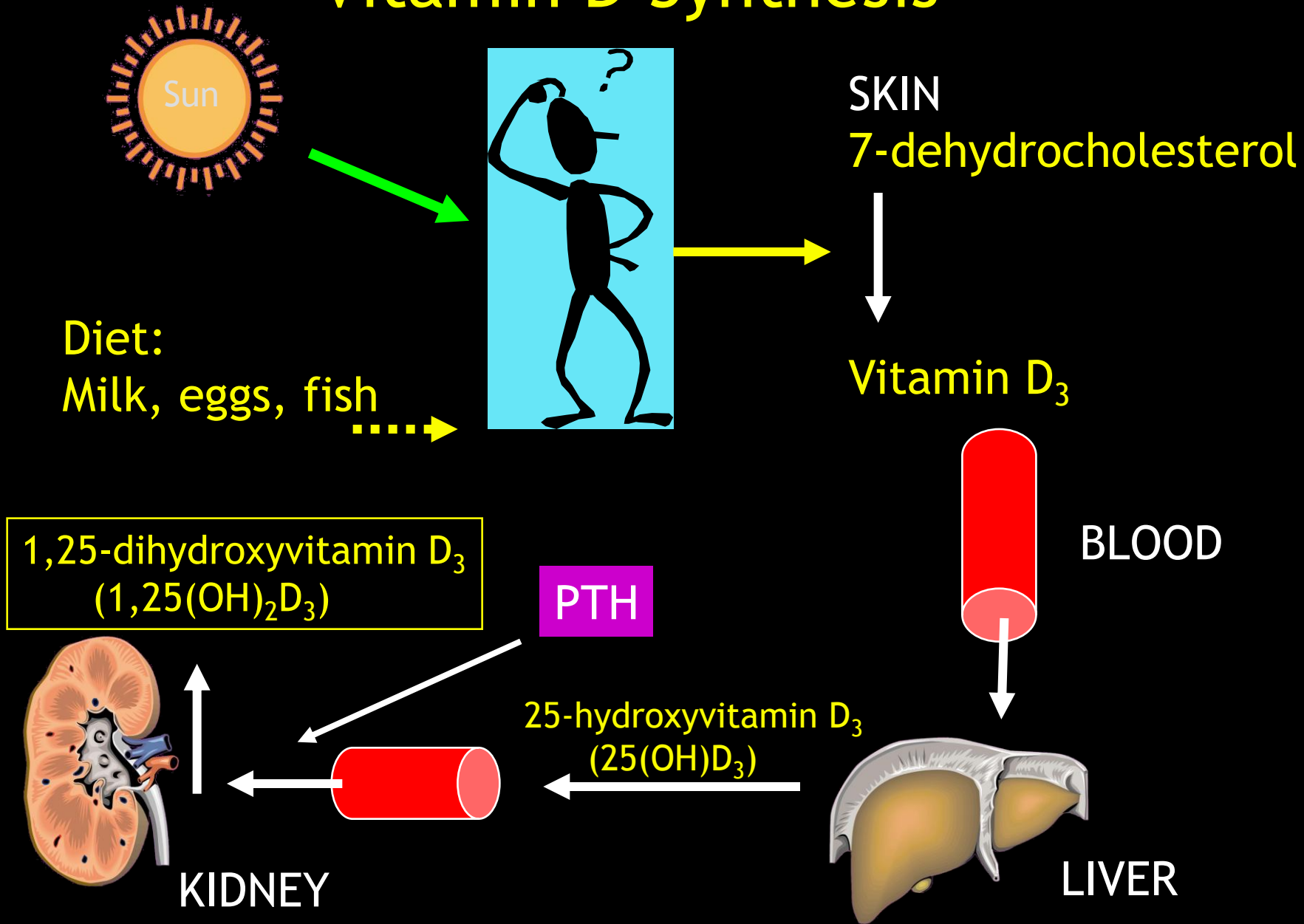
# Osteomalacia



- Bone pain
- Myopathy
  
- Increased fracture risk
- Increased falls risk
  
- Low serum Ca
- High ALP
- High PTH
- Low vitamin D levels



# Vitamin D Synthesis



# Vitamin D Deficiency

- Incidence of both rickets and osteomalacia is increasing
- Importance of UV >> diet
- Demands during/after pregnancy
  - Implications for breast fed children
- Care with use of IV bisphosphonates
- 25(OH) vit D is best measure of vit D stores
- ‘Reference range’
  - 25-170 nmol/L
  - nmol/L (UK) = 2.5 x ng/ml (US)

# Vit D Deficiency in Birmingham Circa 1870



Courtesy of Dr Megan Brickley, Department of Archaeology, University of Birmingham

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# 25(OH) D Levels in WM (median nmol/L)

## City Hospital

	Summer	Winter
Asian female	24.7	12.5
Asian male	34.5	12.1
Non-asian female	50.7	48.9
Non-asian male	63.2	47

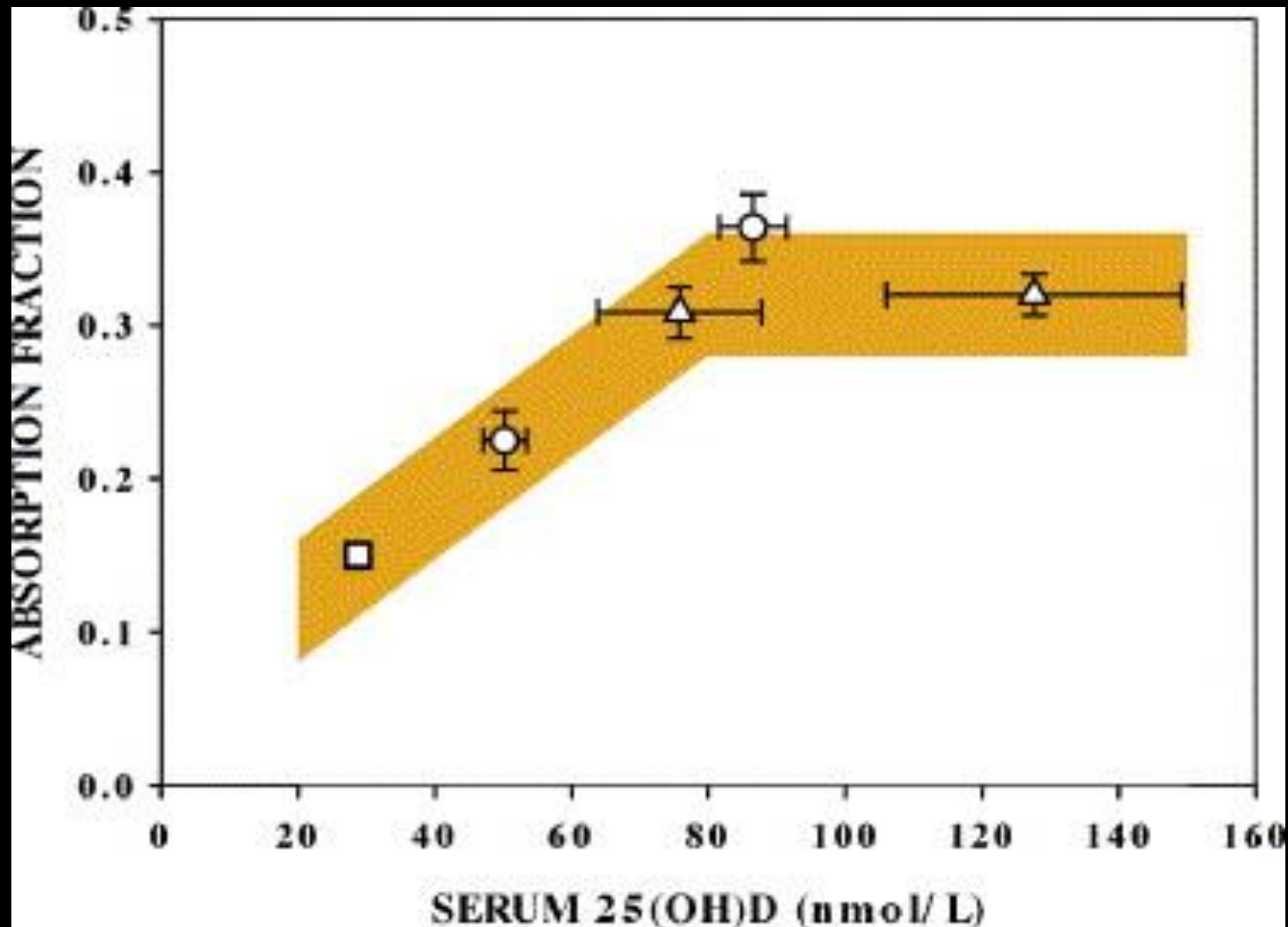
*(Pal et al, J Endo 2003)*

## New Cross Hospital

	Spring/summer
Asian patients	16.5
Asian controls	20.5

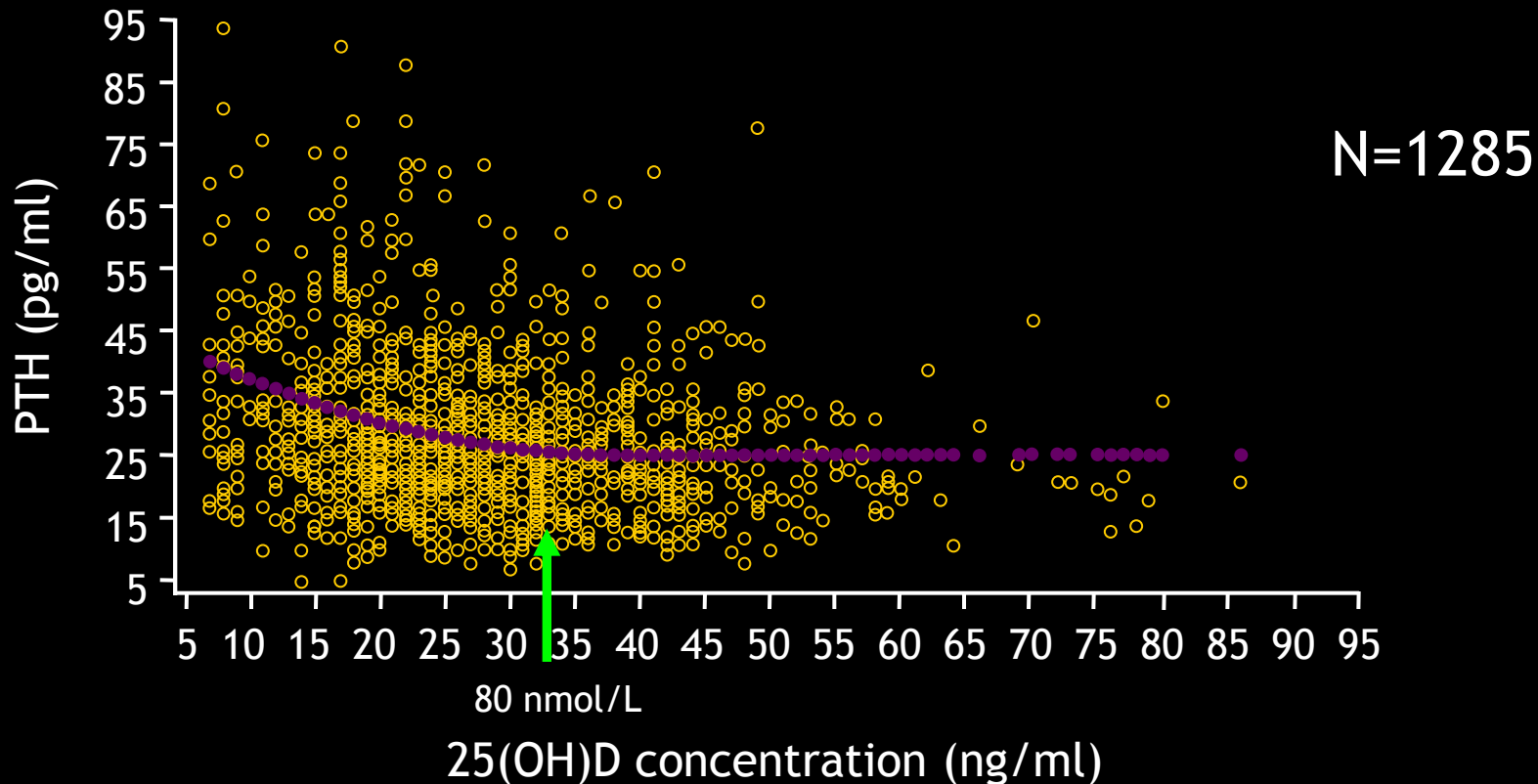
*(Serhan et al, Bone 1999)*

# 25(OH) D Levels and Ca absorption



# 25(OH)D Levels and PTH Secretion

*Post-menopausal women with osteoporosis (worldwide)*



PTH=parathyroid hormone

Study Design: Observational, cross-sectional study of 1285 community-dwelling women with osteoporosis from 18 countries to evaluate serum 25(OH)D distribution.

Adapted from Lim S-K et al. Poster presented at ISCD, February 16-19, 2005, New Orleans, Louisiana, USA.

# How Can Vit D Levels be Increased?

- Main source of vit D is from synthesis in skin
- Minimal total body erythema generates 10-25000 IU per day
- Small area of exposure 3 times per week for 10-15 min should be sufficient during summer (but not winter)
- Skin synthesis greatly reduced in pigmented skin and with ageing
- Difficult to obtain increase through diet alone



# Pharmacological Management of Vitamin D Deficiency

- Low dose PO vitamin D2 or D3 supplements
  - Most include Ca
  - Supplement 800 iU vitamin D per day
  - Slow and variable response
- Pharmacological PO doses of D2 or D3
  - 50,000 iU once weekly 6-8/52
  - 50,000 iU monthly maintenance
  - Rapid reliable response
- High dose parenteral D2
  - Variability in absorption



# Secondary Care Hypocalcaemia

- Acute iatrogenic hypoparathyroidism
  - Neck surgery
    - Who becomes hypocalcaemic?
- Managing degrees of acute hypocalcaemia
  - Evidence free zone
  - Pragmatism
- Cases
  - Specific situations
  - Individualised management

# Incidence of Hypocalcaemia Following TTx National

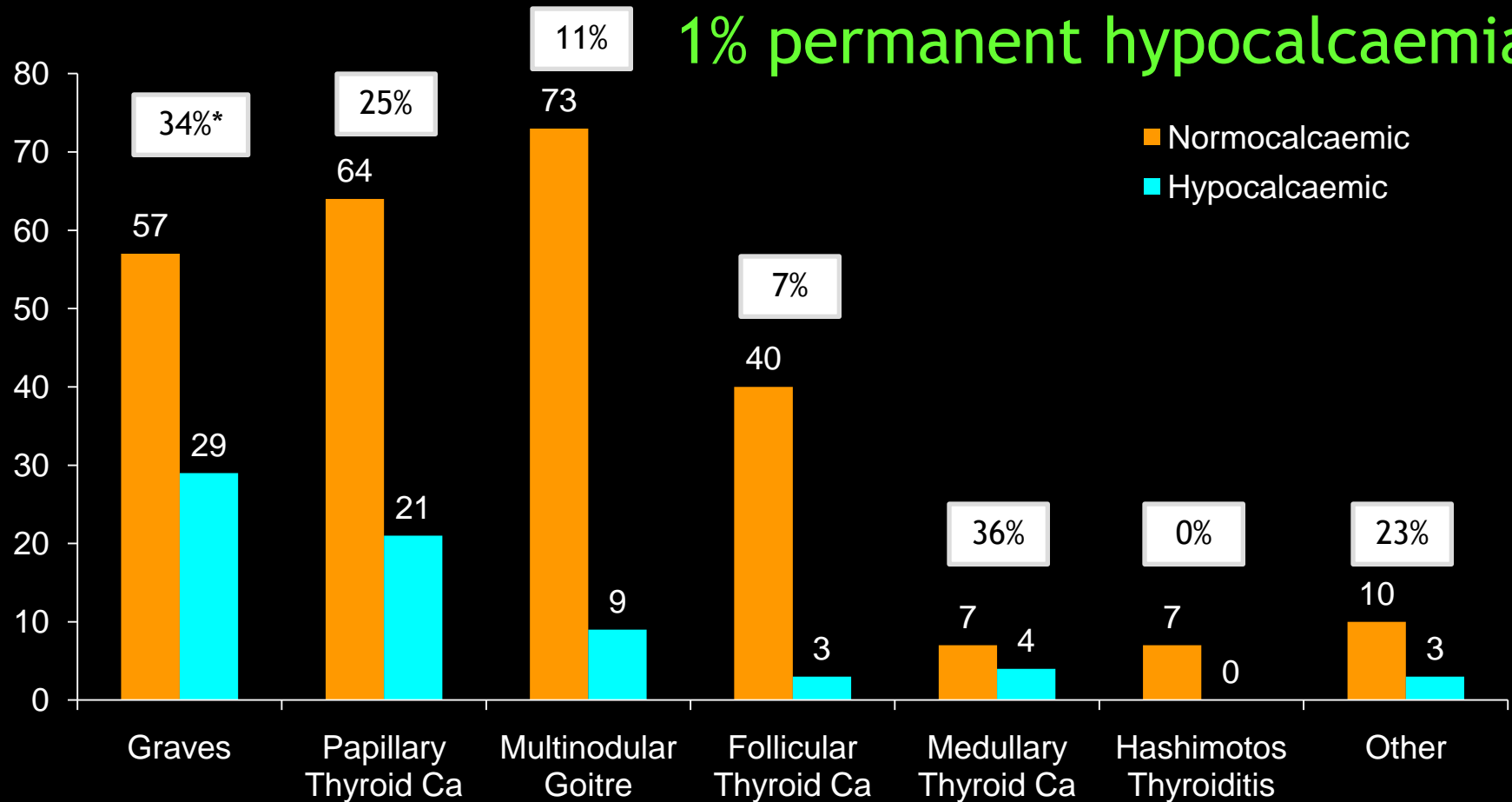
- All pathologies
  - Overall - 33%
  - Primary Tx - 32%
  - Completion Tx - 35%
- Grave's disease
  - Overall -33%
- No correlation between rate of hypocalcaemia and Tx workload

# Incidence of Temporary Hypocalcaemia

- 69 patients (21%)

QEH

1% permanent hypocalcaemia



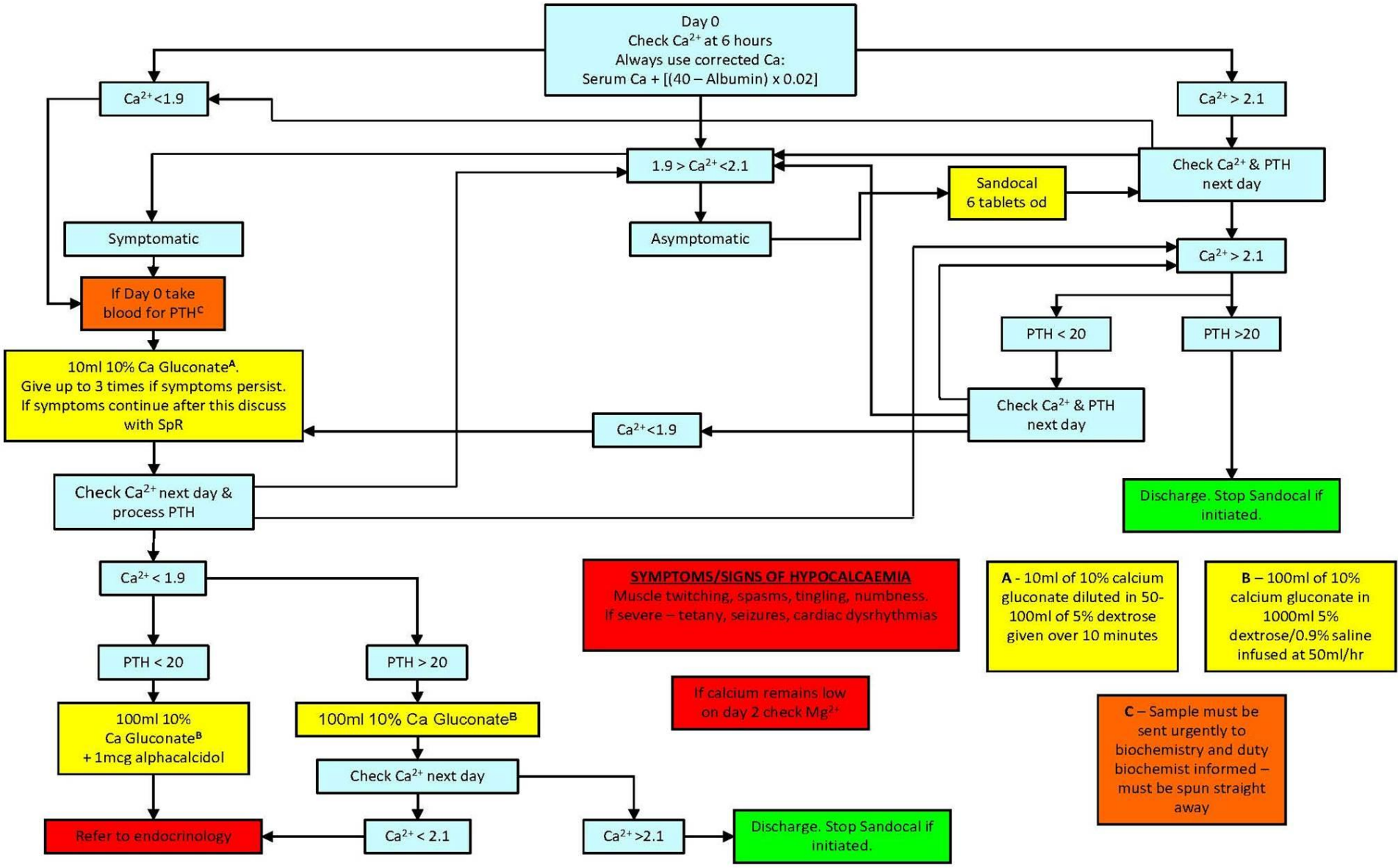
# Pre-operative Prediction of High Risk Patients (TTx & PTx)

- Untreated pre-operative vitamin D deficiency
  - Vitamin D treatment
    - Approach in PHPT
- More elevated PTH and elevated ALP predict post-operative hypocalcaemia in PHPT
  - Close monitoring/empirical treatment
- Active bone disease in thyrotoxicosis
  - Effective pre-operative medical management of thyrotoxicosis

# Post-operative Prediction of Hypocalcaemia

- Strong correlation between postoperative PTH and hypocalcaemia
- Early & sequential PTH measurements required
- Study results and conclusions discrepant
  - PTH and  $\text{Ca}^{2+}$  at 6 hrs identify 'all' patients not at risk of hypocalcaemia (Payne et al, 2004, 2005)
  - PTH at 4 (or 24 hrs) do not reliably identify patients safe for early discharge (Del Rio et al, 2005)
- 5-10% patients with normal PTH may develop hypocalcaemia

# Management of Post-Thyroidectomy Hypocalcaemia



# Practical Management of Post-Operative Hypocalcaemia

## Oral calcium

### Calcium elemental

- 2-3 g

### Threshold

- Empirical
- Asymptomatic mild

## IV calcium

### Calcium gluconate

- 10-20 ml 10% 10 mins
- 10x10 ml 10% in 1 litre at initially 50 ml/hour
- Infusion 10 ml/kg over 4-6 hrs increases  $\text{Ca}^{2+}$  0.3-0.5 mmol/l

### Threshold

- Severe  $<1.8$  mmol/L
- Symptomatic

## Vitamin D

### Alfacalcidol

- Initial 0.5-1  $\mu\text{g}$  bd

### Calcitriol

- Initial 0.5  $\mu\text{g}$  bd

### Threshold

- 2/7 requirement for IV
- (Low PTH)



# Hungry Bone Syndrome

- Rapid reversal of chronic catabolic state in skeleton
  - PTH mediated
  - Thyroid hormone mediated
- Hypocalcaemia driven by rapid remineralisation of mineral-depleted matrix
- May last for weeks
- Requires large doses of  $\text{Ca}^{2+}$  and vitamin D metabolites

# Case 1 -Think Beyond Calcium

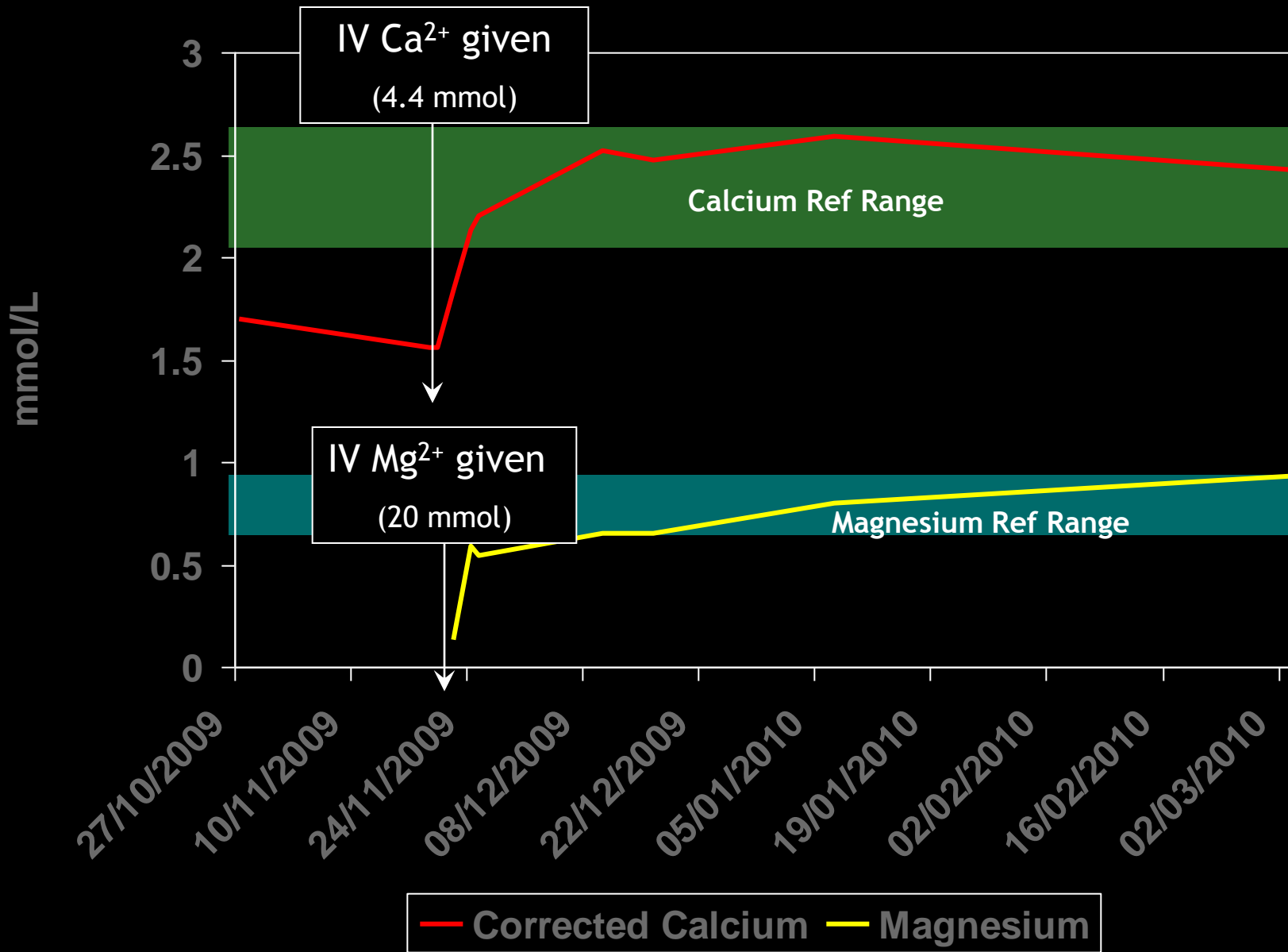
- 77 female
- Presented via ED
  - Unsteadiness and confusion, muscle cramps
  - Few days of diarrhoea, no vomiting
- PHx
  - Diverticulosis, hypertension, recent TIA, reflux
- Medication
  - Diltiazem MR
  - Amitriptyline
  - Aspirin
  - Omeprazole
  - Atorvastatin
  - Doxazosin
  - Dipyridamole MR
  - Gaviscon

# Investigations

- Adjusted calcium
  - 1.56 mmol/L (2.10-2.60)
  - 1.70 mmol/L 3/52 prior to admission
  - 2.00 mmol/L in 2007
- Serum magnesium 0.13 mmol/L (0.70-0.95)
- PTH 27 ng/L (12-60)

# Management

- Intravenous calcium and magnesium
  - Oral magnesium supplements
- Withdrawal of proton-pump inhibitor
- Symptomatic and biochemical resolution



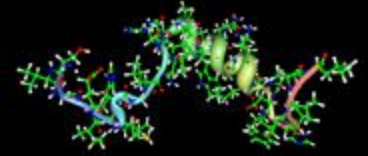
# Treating hypomagnesaemia (-induced hypocalcaemia)

- Extent of total body deficiency is difficult to predict
- Parenteral (IM painful) Mg deficiency usually required
  - 4-12g  $\text{MgSO}_4$  (16-48 mmol Mg) over 24hrs
- Rapid normalisation of Mg
- Calcium may take 3-7/7
  - May reflect slow restoration of intracellular Mg concentration
- If very rapid correction required
  - 8-16 mmol Mg IV injection over 5-10 mins followed by infusion
- If chronic therapy required
  - 300-600mg elemental Mg in divided doses

# Learning points

- Hypocalcaemia - measure Mg
- Resistant hypocalcaemia - consider empirical Mg even if serum Mg normal
- PPI prevalence is high
- Very low Mg - consider PPI-induced hypomagnesaemia
- 'Avoid' further PPI if hypomagnesaemia

# Case 2 - Post TTx Hypoparathyroidism



- 32 Female with Graves' disease
- TTx
  - Hypoparathyroid
- Huge doses of (in)active D + thiazide + Ca/Mg
- Intractable hypocalcaemia
  - ED/in-patient most of time
  - Young twins
- Teriparatide - escalating doses poor control
- Preotact - bd/tds
  - 3 years no hospital admissions



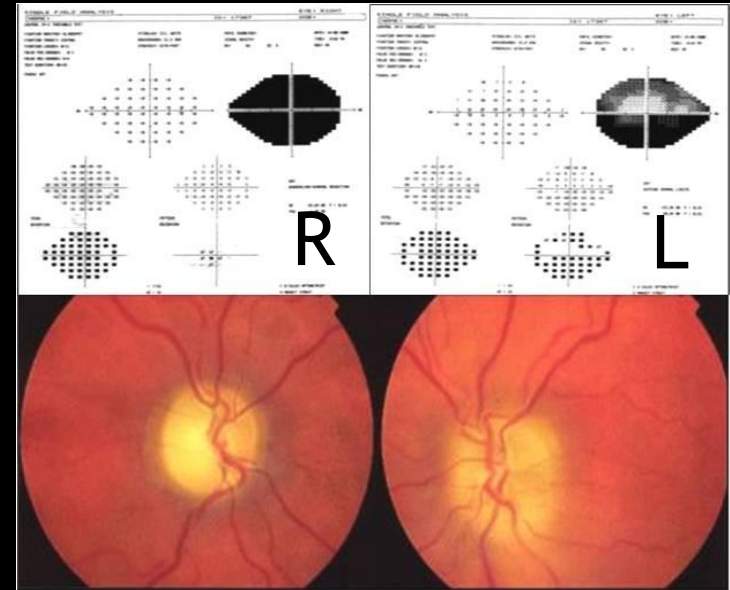
# Case 3 - Post TTx Hypoparathyroidism



- 45 female Graves' disease
- TTx
  - Hypoparathyroid
- Huge doses of active D + thiazide + Ca/Mg
- Intractable hypocalcaemia
  - Couldn't get home
  - Refused PTH Rx
- Tunnelled line - overnight calcium infusions
  - Line sepsis
  - 13/12 out of hospital
  - Reasonable QOL

# Case 4 - It Doesn't Always Look Like Hypocalcaemia

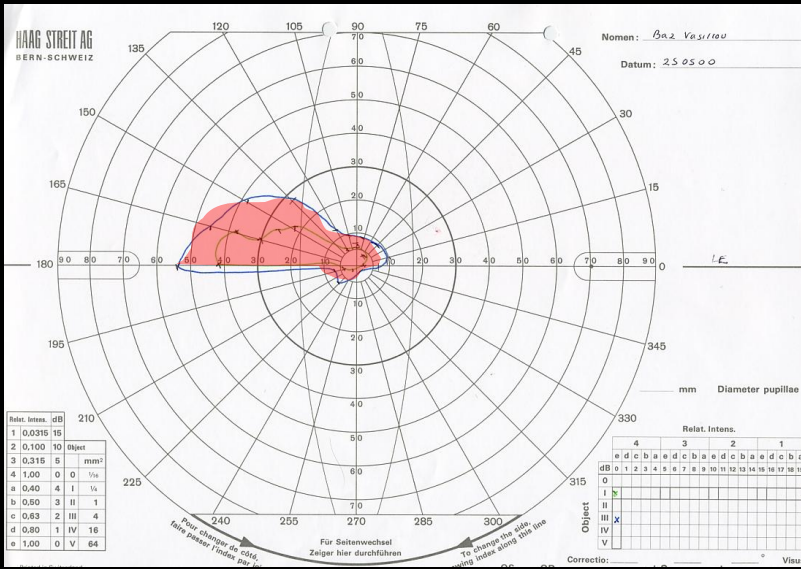
- 49 female
- Visual failure & depression
- Ca 1.27 mmol/L (2.1-2.6)
- PTH 11 ng/L (10-69)
- Primary hypoparathyroidism
- Rx - calcitriol + Ca
- Improved vision ++



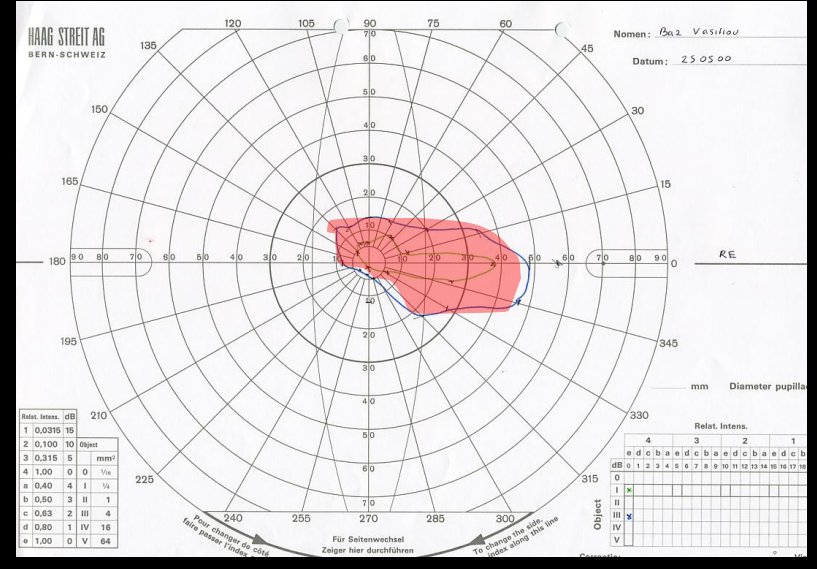
# Case 5 - It Doesn't Always Look Like Hypocalcaemia

- 42 male
- Changed personality/psychiatric problems
- Visual failure
  
- Ca 1.33 mmol/L (2.1-2.6)
- PTH 2 ng/L (10-69)
  
- Primary hypoparathyroidism
- Rx - alfacalcidol + Ca
- Improved vision ++
- Normalisation of psychiatric status

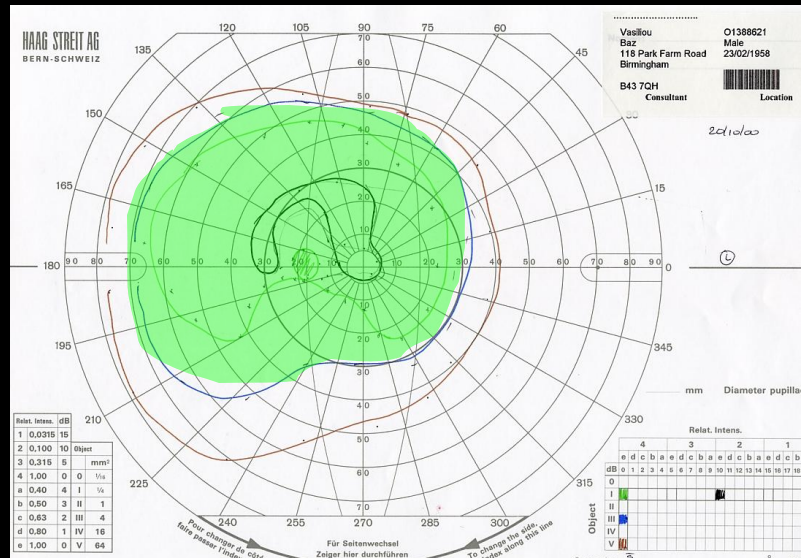
# R



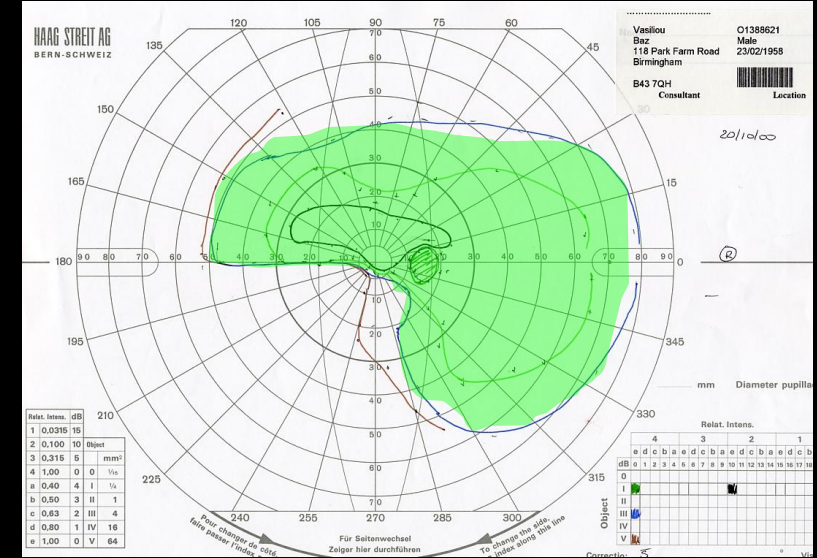
# L



## Baseline



## +5/12 alfalcidol + Ca

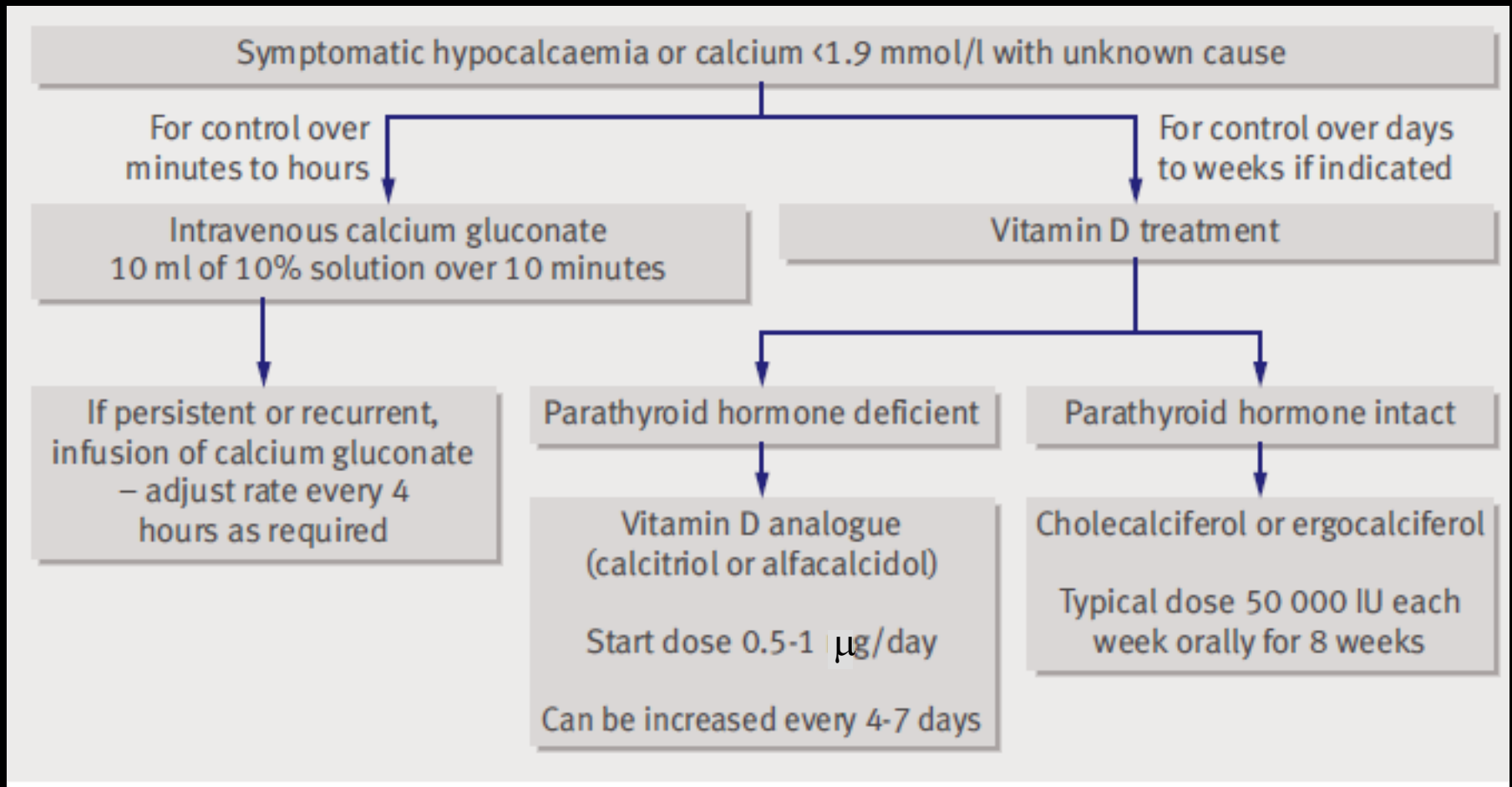


# Case 6 - If it Doesn't Fit, Consider Another Diagnosis

- 28 female
- Difficult to control epilepsy + vitamin D deficiency
- Ca 1.48 mmol/L (2.1-2.6)
- P 1.77 mmol/L (0.8-1.4)
- Mg 0.89 mmol/L (0.67-0.95)
- Vit D 42 nmol/L (25-170)
- PTH 242 ng/L (12-65)
- Pseudohypoparathyroidism
- Rx - alfacalcidol 4 $\mu$ g
  - Ca 2.17 mmol/L (2.1-2.6)
  - No seizures



# Management of Hypocalcaemia



# Summary

- Hypocalcaemia is common
  - Primary and secondary care
- Presentation
  - Asymptomatic
  - Bizarre
  - Life threatening
  - Rate of change important & not just [Ca]
- No universally applicable algorithms to manage
  - Chronic stable
  - Acute
- Decipher the underlying cause and treat
  - PTH

