EMERGENCY MANAGEMENT OF HYPOCALCAEMIA AND HYPERCALCAEMIA

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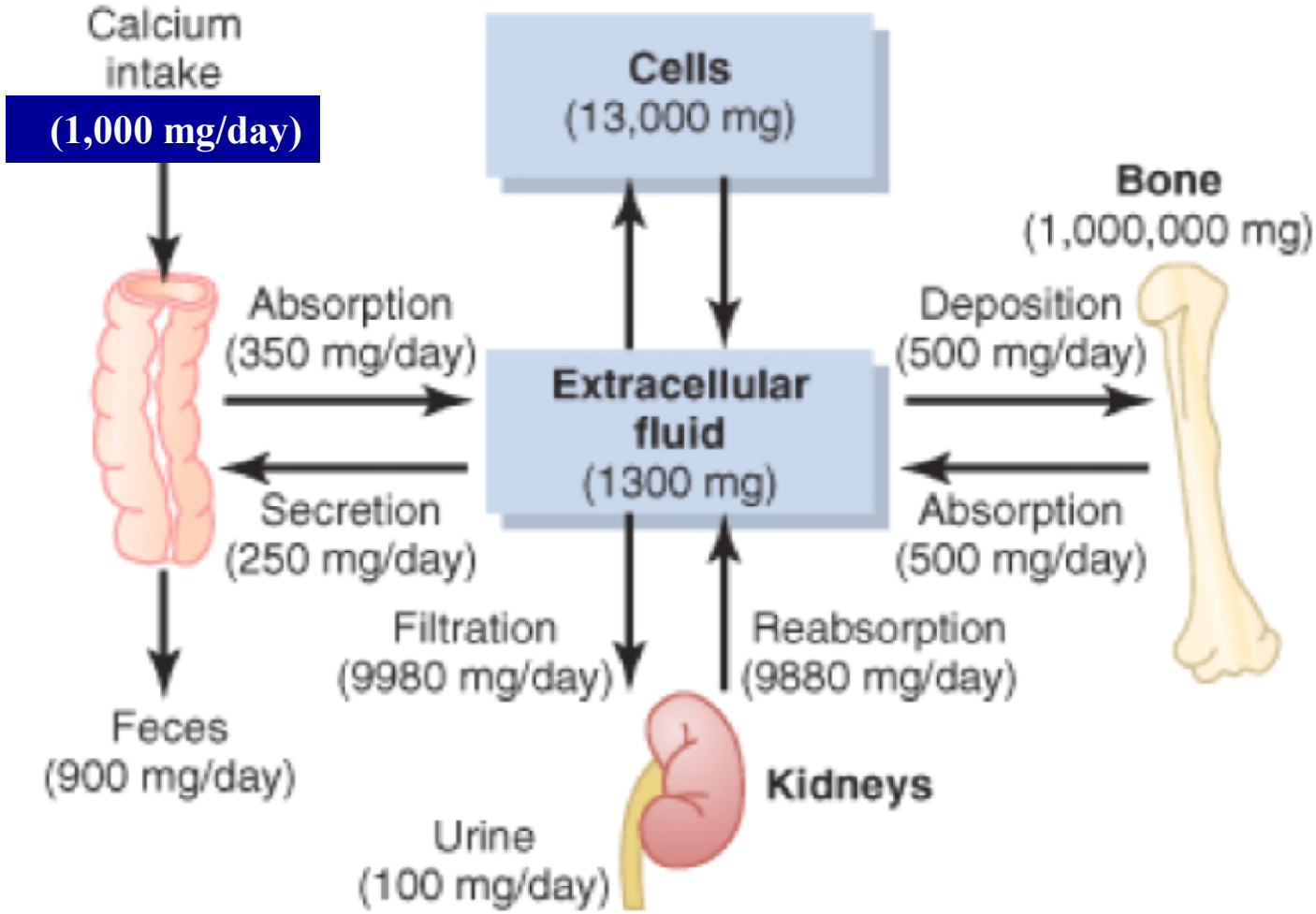
Physiology of Calcium

- 98% of the body calcium is in the skeleton
- Only 2% is circulation and only half of this is free calcium (ionized Ca^{++})
- Free calcium is physiologically active
- The remainder 1% is bound to proteins
- Serum ionized calcium is the free form of calcium

Calcium Homeostasis

Calcium Homeostasis

Calcium Metabolism



Hormonal regulation of Calcium

Hormone	Effect	Bone	Gut	Kidney
PTH	↑ Ca ↓ PO_4	Increases Osteoclasts	Indirect via Vit. D	Ca reab PO_4 exr.
Vitamin D3	↑ Ca ↑ PO_4	No direct action	↑Ca ↑ PO_4 ↑absorption	No direct effect
Calcitonin	↓ Ca ↓ PO_4	Inhibits Osteoclasts	No direct effect	Ca & PO_4 excretion

Corrected Serum Calcium

Corrected total calcium (g/L) =

[(Measured total calcium g/L) +

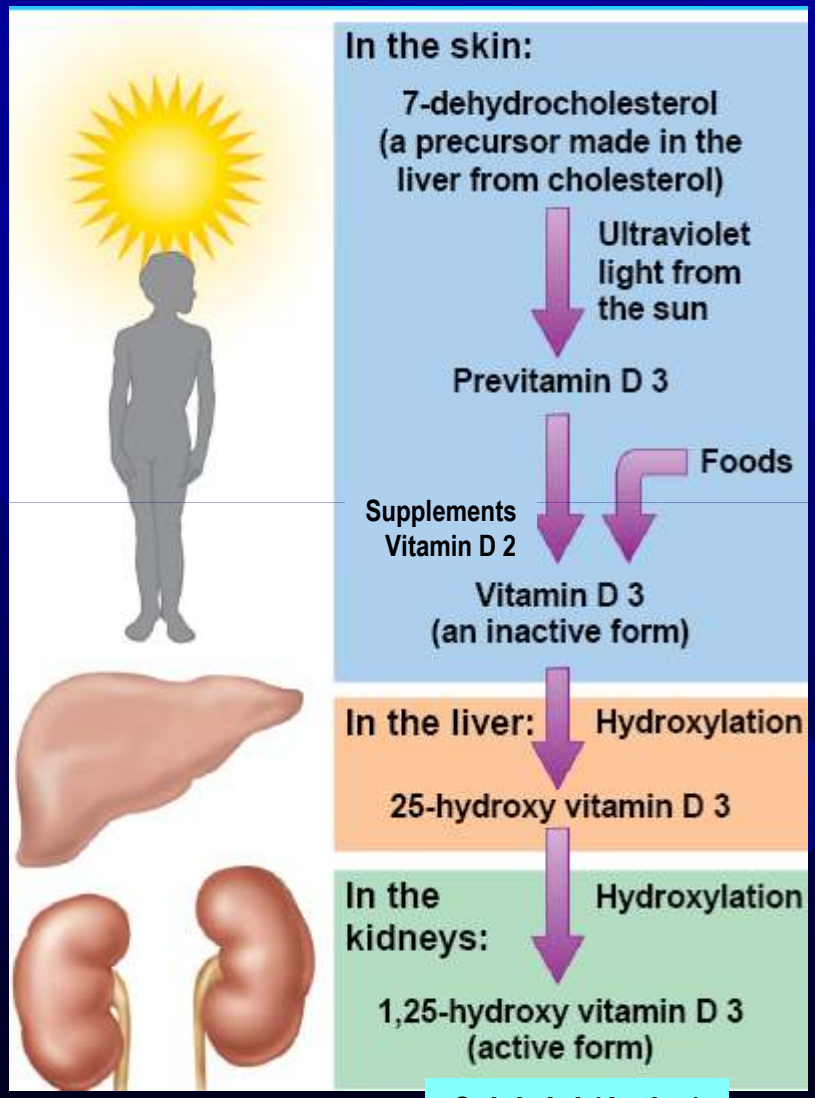
{(40 - measured albumin g/L) x 0.02}]

Example:

[3 + {(40 – 24) x 0.02}] =

[3 + (16 x 0.02)] = 3+ 0.32 = 3.4 mmol/L

Vitamin D Metabolism



Formation of Calcitriol

Vitamin D is a steroid hormone

From dietary sources	Action of Sunlight on skin

Successive hydroxylations of Cholecalciferol

25 hydroxylation in the Liver	25 hydroxy Cholecalciferol

Second hydroxylation in the Kidney at first position

1,25 dihydroxy Cholecalciferol	Active Vitamin D (Calcitriol)

Calcium Homeostasis

PTH

- 4 PT glands
- 84 AA hormone
- Low Calcium stimulates it

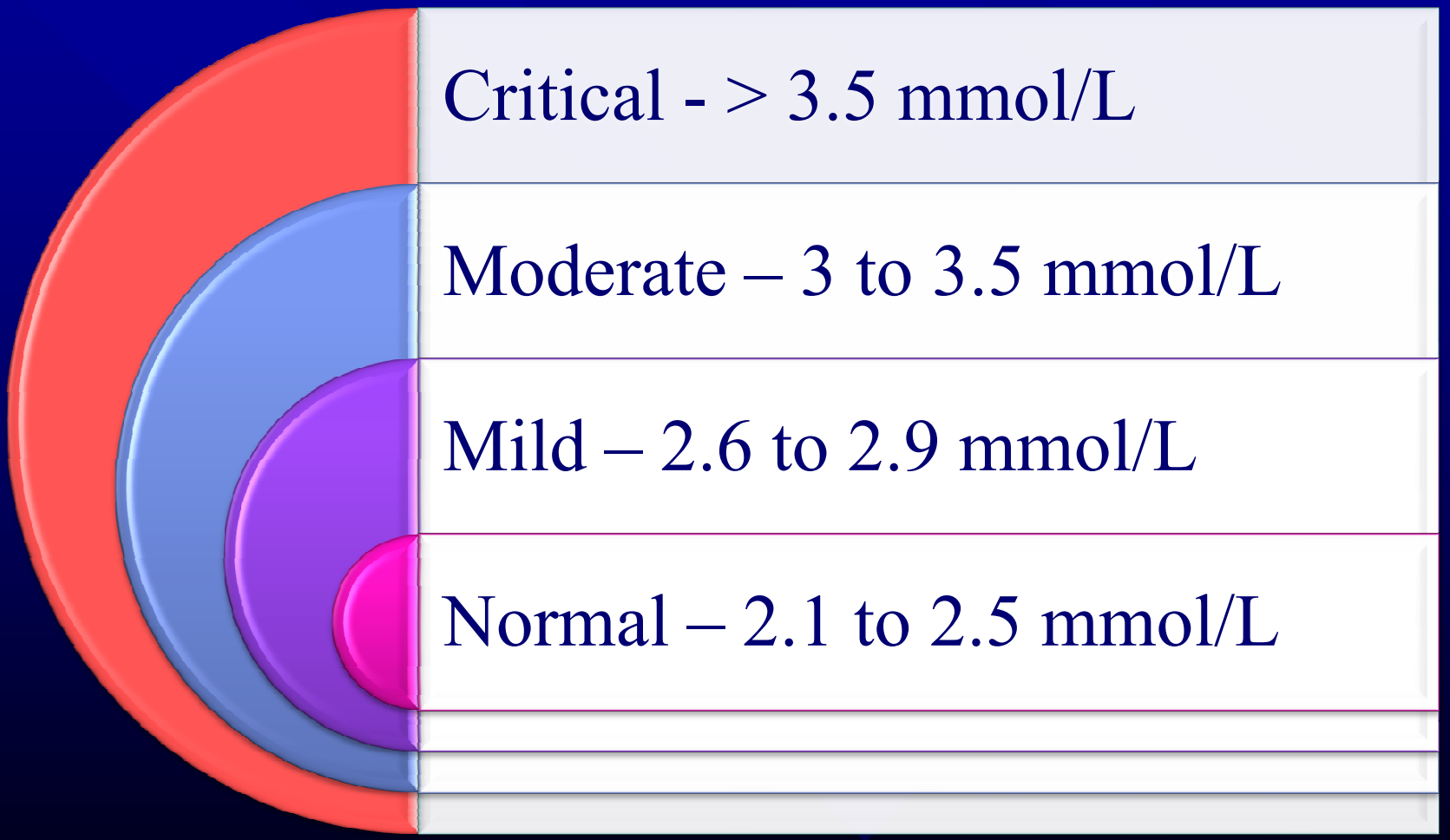
Calcitriol (D)

- Active bone formation
- Main effect is on the Gut
- PTH ↑ Vit. D

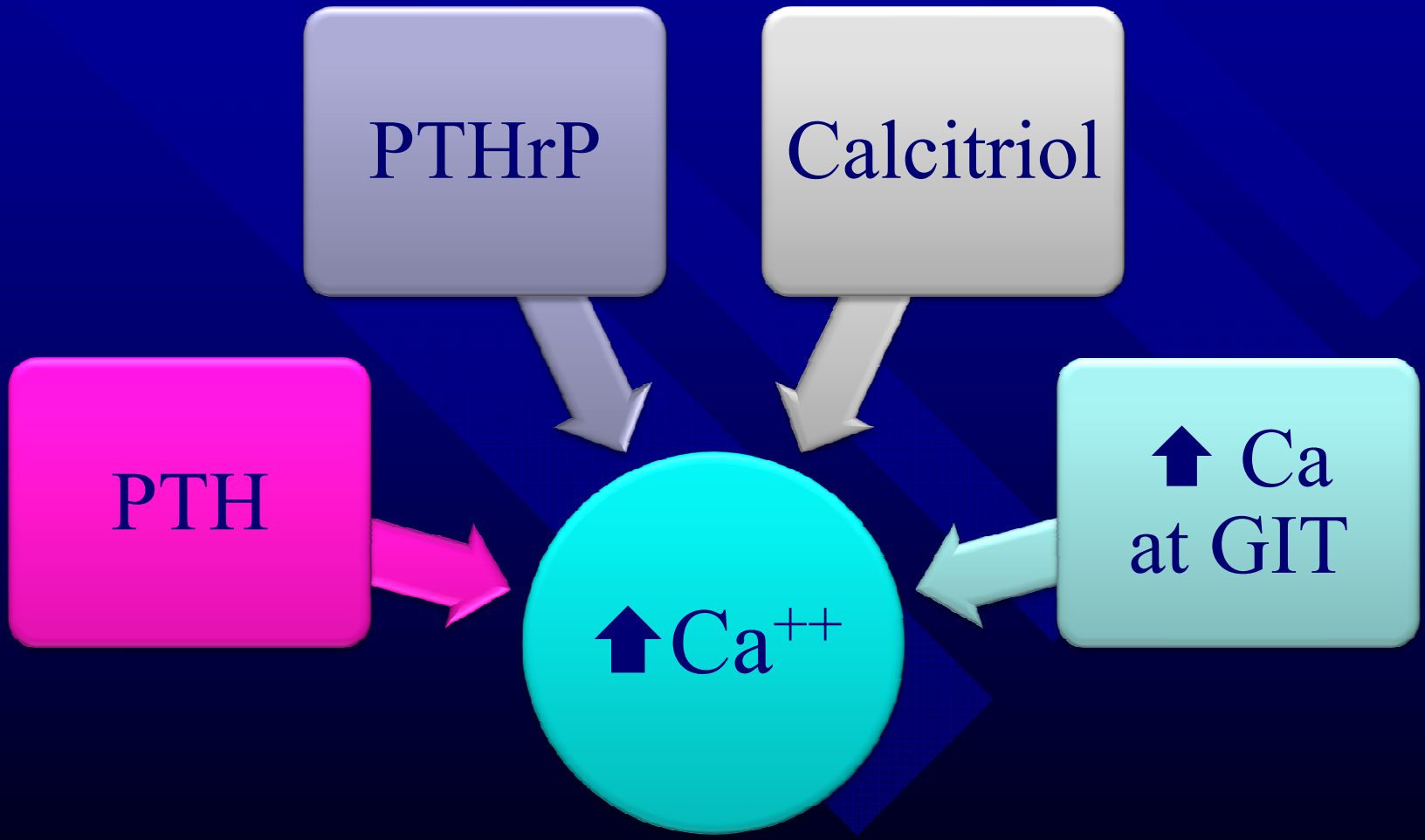
Calcitonin

- Para follicular C of Thyroid
- 34 AA hormone
- On Kidney

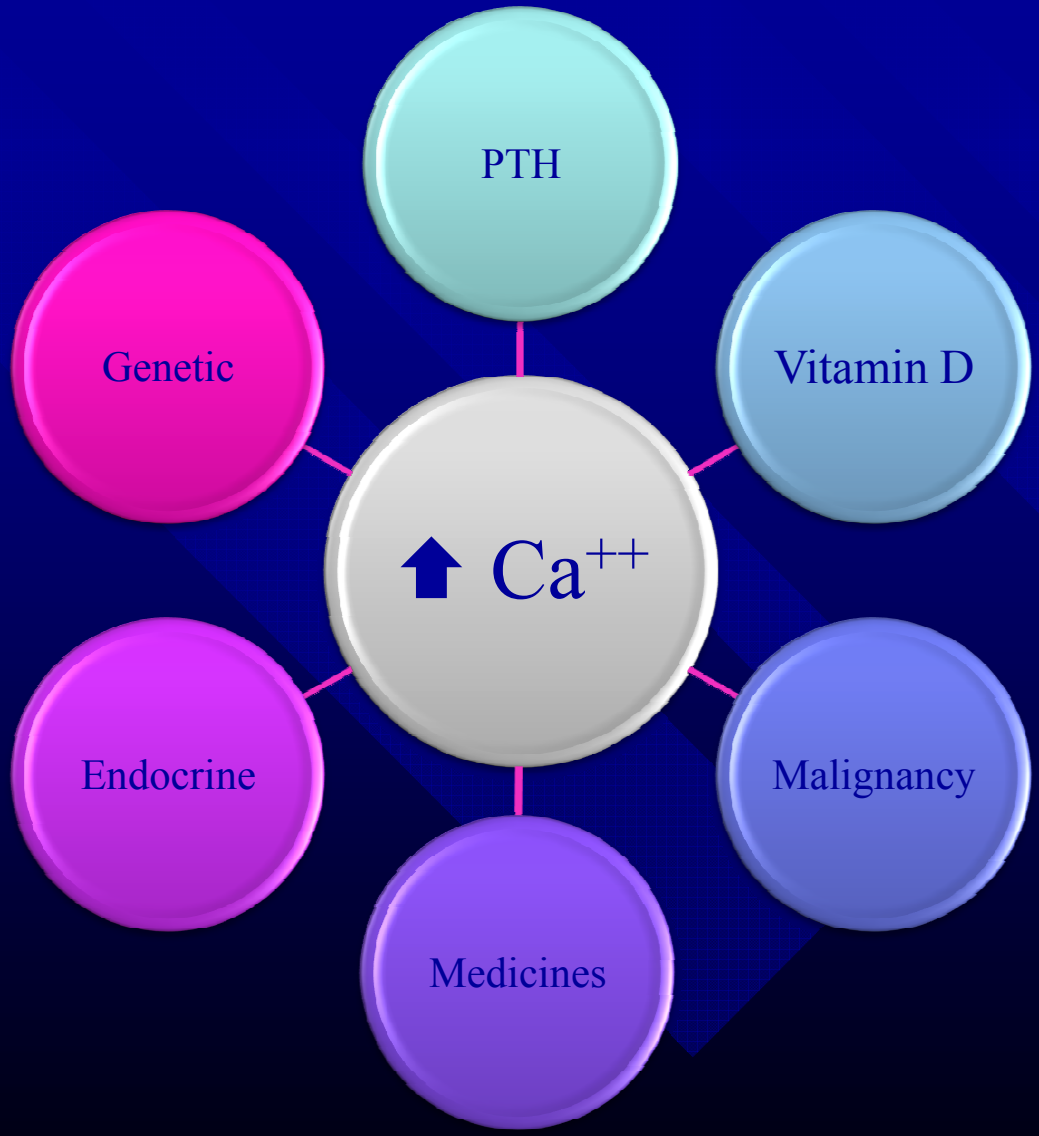
Hypercalcemia Grading



Hypercalcemia



Causes of Hypercalcemia



Hypercalcemia

- Occasionally encountered in Practice
- Diagnosis often is made incidentally
- The most common causes are primary hyperparathyroidism and malignancy
- Diagnostic work-up includes measurement of serum calcium, intact parathyroid hormone history of any medications
- Hypercalcemic crisis is a life-threatening emergency

Investigations

- Plasma calcium and albumin
- Plasma phosphate
- Plasma alkaline phosphate
- Plasma Urea
- Plasma parathyroid hormone
- Vit D
- Plasma HCO_3^-
- Urinary calcium excretion
- Urinary phosphate excretion
- Urinary hydroxyproline
- Urinary cyclic AMP
- Radiology
  - Ultrasound
  - X-ray
  - CT Scan

Important Issues

- Most often asymptomatic – Incidental Diagnosis
- Mild Hypercalcaemia is asymptomatic
- Most important cause is hyperparathyroidism
- Diagnosis is needed to decide the treatment
- Optimal step by step evaluation is a must.

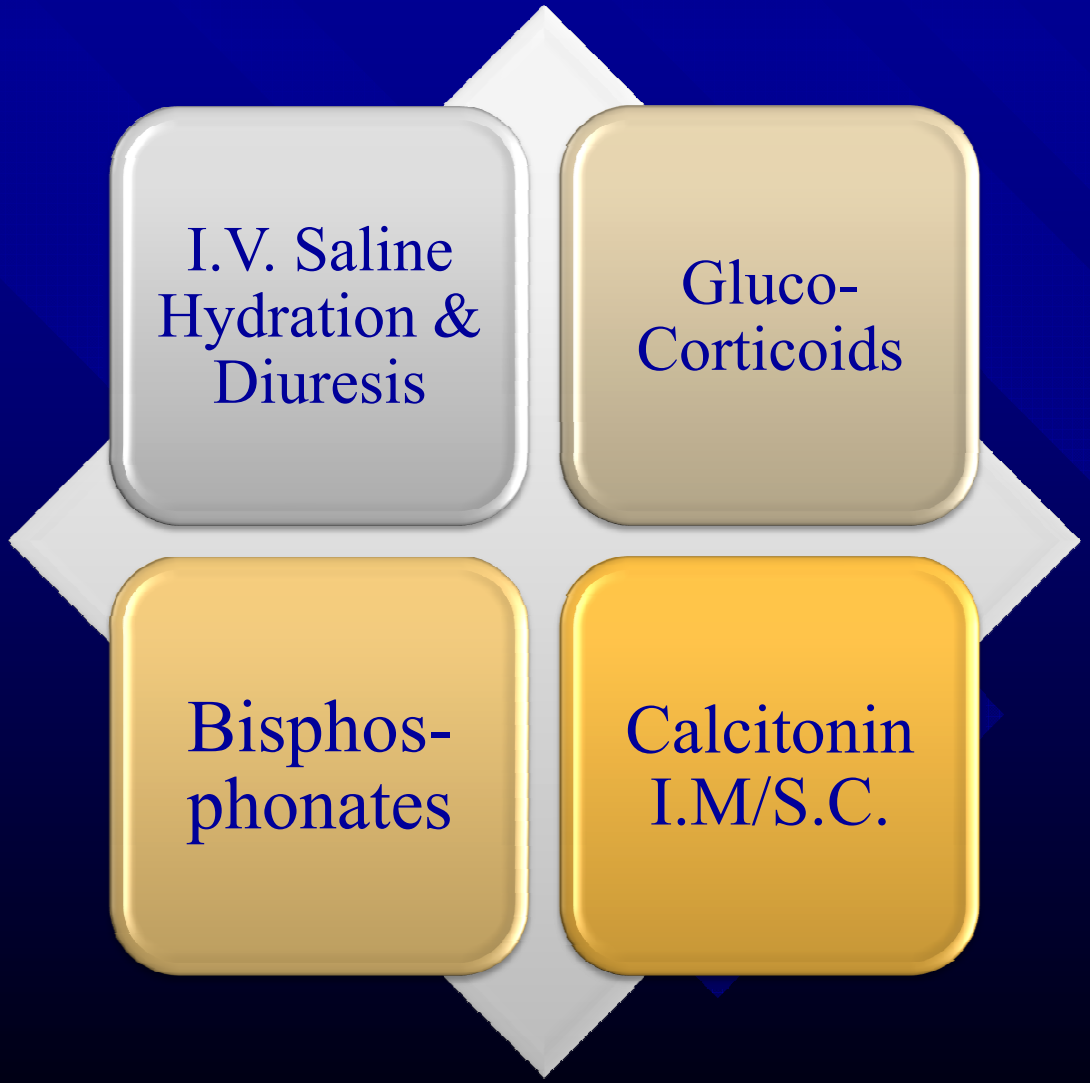
Treatment of Hypercalcaemia

- Volume repletion and diuresis
  - NaCl 0.9% 4 L in first 24 h
  - Loop diuretics (furosemide has calciuretic effects)
- Bisphosphonates IV (Pamidronate)
- Corticosteroids (prednisone 30 – 60 mg daily) are the drugs of choice if granulomatous disease or vit A or D intoxication is the cause

Treatment

- Calcium < 3 but > 2.5 mmol/L – no appreciable clinical benefit – they need evaluation
- Any patient with serum calcium > 3 mmol/L should be aggressively treated
- Calcium > 3.5 mmol/L is Hypercalcemic crisis
- Always correct the calcium value for albumin

The Four Treatment Modalities



Hydration and Diuresis

- Vigorous I.V. NaCl Diuresis – N Saline
- Adequate hydration – urine out put must be maintained 200 ml/hour = 5 L /day
- The safest and most effective treatment of Hypercalcemic crisis is saline rehydration
- Once the urine out put is maintained – give I.V. Furosemide – a loop diuretic in low doses of 10 to 20 mg

Calcitonin

- In severe hypercalcaemia refractory to saline diuresis
- Calcitonin (Zycalcit, Miacalcin) 6 -8 U/kg IM/SC (400 iu) given every six hours.
- This treatment has a rapid onset but short duration of effect
- Patients develop tolerance to the calcium-lowering effect of calcitonin

Bisphosphonates

- Zoledronic acid - 4 mg IV diluted in 100 ml of N Saline - over at least 15min /month
- Pamindronate - 60 mg IV infusion over 4 h initial – repeated after a month
- Etidronate - 7.5 mg/kg IV over 4 h daily for 3-7 d; dilute in at least 250 ml of sterile N Saline
- They inhibit bone resorption, inhibit the Osteoclastic activity.

Other Treatment Options

- Dialysis for refractory Hypercalcemic crisis
- Parathyroidectomy for adenomas
- Treatment of the underlying cause – Eliminate drugs
- Plicamycin (Mithracin) 25 mcg/kg/d IV for 4 d
- Gallium nitrate (Ganite) 100 mg/m^2/d IV for 5 days in 1 L of NS or 5% Dextrose
- Cinacalcet (Sensipar) - 30 mg PO od – (increases sensitivity of calcium sensing receptor)

Take Home Points

- Hypercalcaemia is often asymptomatic
- Screen all suspected by doing Serum Calcium
- If elevated, do I-PTH and follow algorithm
- 90% Hyperparathyroidism and malignancy
- Vitamin D toxicity is an important cause
- Thiazide diuretics common cause, Vitamin A
- Adequate hydration - N Saline + Furosemide
- Calcitonin + Zoledronic acid main stay of treatment.

Acute Hypocalcaemia

HYPOCALCEMIA < 2.1 mmol/L)

- Overview
  - Symptoms usually start developing at level < 2.1mmol/L
  - < 1.6 - Severe hypocalcemia leading to tetany
- Symptoms related to skeletal & muscle contraction
- Etiology
  - Decreased parathyroid hormone
  - Malabsorption of calcium (Pancreatitis, GI diseases)
  - Marked deficiencies of dietary calcium and/or Vit D
- Laboratory = Ca < 2.1 mmol/L

Clinical Picture of Acute Hypocalcaemia

- Symptoms
  - Perioral numbness
  - Tingling parasthesias
  - Muscle cramps
  - Carpopedal spasm
  - Seizures
- Signs
  - Hyperreflexia
  - Chvostek's sign
  - Trousseau's sign
  - Hypotension
  - Bradycardia
  - Prolonged QT interval
  - Arrhythmias

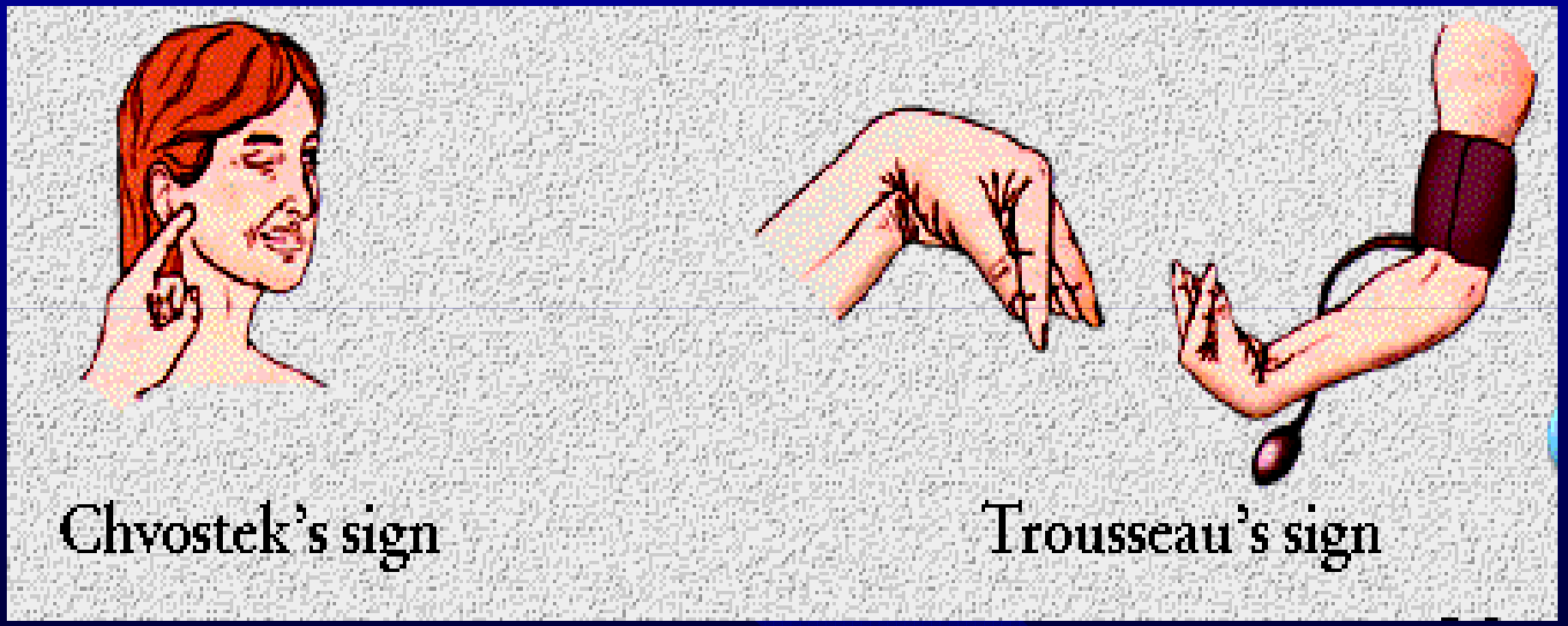
Chvostek's sign

Trousseau's sign

HYPOCALCEMIA:

Physical Assessment/ Clinical Manifestations =

TETANY, paresthesias



•Bronchial muscle spasm, laryngospasm leading to respiratory arrest

Hypocalcemia: Calcium Food Sources (which 2 do not belong?

broccoli

cheese

tofu

yogurt

Cream cheese

Ice cream

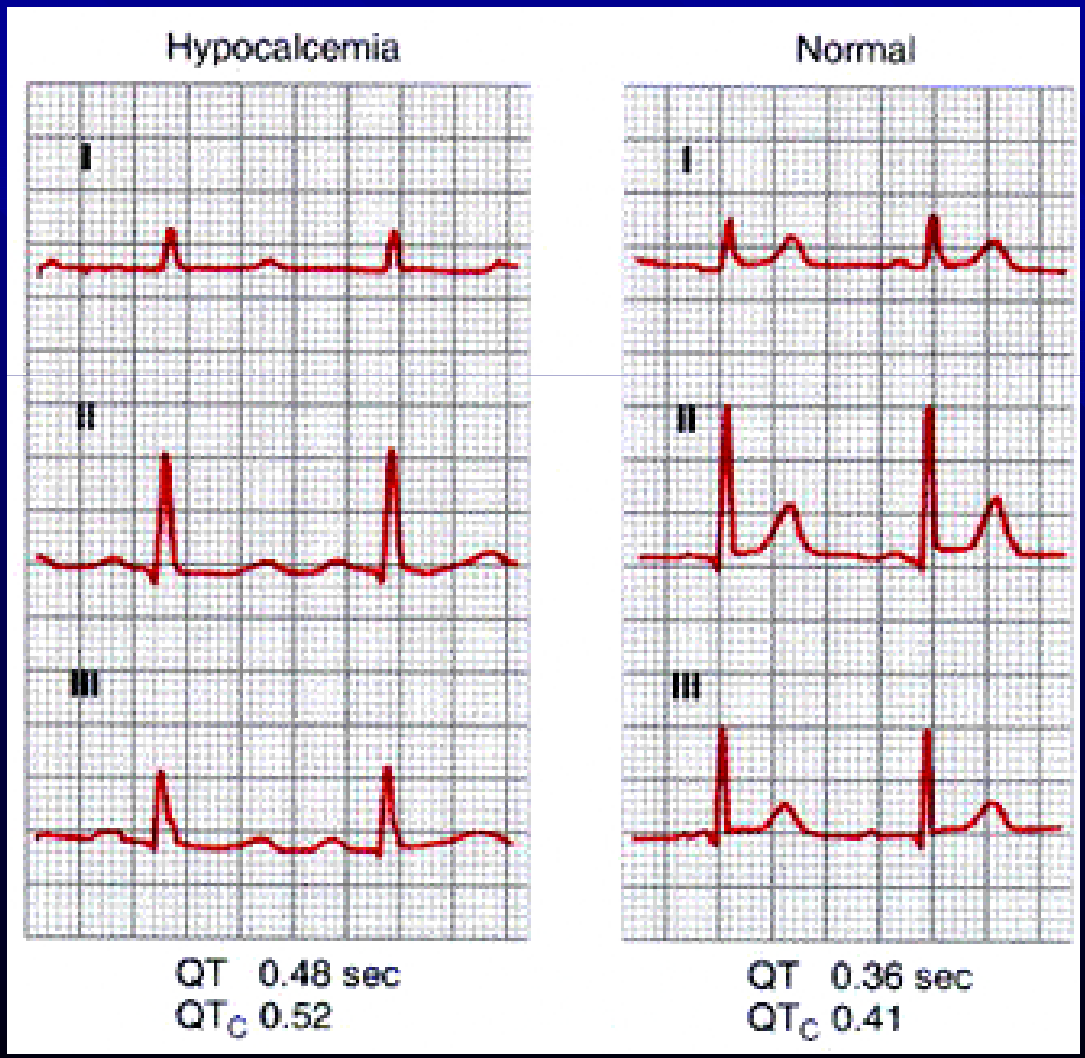
Sardines

Canned salmon

Skim milk

Spinach

ECG in Hypocalcemia



Causes of Acute Hypocalcemia

- Hypoparathyroidism
  - Destruction of parathyroid
    - » Most commonly surgical – parathyroid resection or accidental
  - Acute hypomagnesaemia
- Reduced 1,25(OH) vit D
  - Chronic renal insufficiency
  - Acute systemic illness
  - Drugs: ketoconazole, doxorubicin, cytarabine

Causes of Acute Hypocalcaemia

- Increased uptake of calcium in bone
  - Osteoblastic metastases
  - Hungry bone syndrome
- Complexing of calcium from the circulation
  - ↑ albumin binding in alkalosis
  - Acute pancreatitis with formation of Ca soaps
  - Transfusion related citrate complexing

Biochemical Workup

- S total Ca^{++}, Albumin and Ionized Ca^{++}
- S PO_4^{++}
- S Mg^{++}
- Plasma PTH
  - Low in hypoparathyroidism
  - High in hungry bones syndrome
- 25(OH)D_3 and 1,25 (OH)D_3
- S Amylase and Lipase

HYPOCALCEMIA < 2.1 mmol/L

- Diet Therapy
  - Food sources of Calcium
  - Supplementation
- Drug Therapy
  - Oral calcium
  - IV Calcium (with caution)
  - Vitamin D
- Interventions
  - Protect from injury

Hypocalcemia

- **Treatment of hypocalcaemia**
  - IV calcium chloride : 3~5 ml of 10% solution
  - Calcium gluconate : 10~20ml of 10% solution
  - Precipitation bicarbonate phosphate solution
  - Repeat bolus or continuous infusion(Ca2+ 1~2mg/kg/hr)
  - Serial ionized Ca measurement
  - Chronic
    - » Oral calcium(CaCO3)
    - » Vitamin D replacement

- Correct serum Mg^{++}
- Calcium gluconate 10 ml of 10% solution IV over 5 – 10 min and repeat as necessary in cases with frank generalized tetany
- Slower continuous infusion of Calcium gluconate in less acute cases

Case 1

A 40 year old alcoholic was brought to the Emergency department, he was thought to be confused simply due to intoxication, but was admitted for mild alcoholic hepatitis and marked malnutrition. His mental status cleared up about 8 hours after admission. During morning rounds on hospital day #2, he complained of feeling fatigued and weak. Later that day, the nurses find him seizing. The seizures stop with low dose IV diazepam. Stat labs are sent:

Sodium – 136 meq/L
Potassium – 3.2 meq/L
Calcium (total) – 1.7 mmol/L (normal ~ 2.1-2.5 mmol/L)
Phosphate – 0.17 mmol/L (normal ~ 0.5-1.07 mmol/L)
Albumin – 30 g/L (normal ~ 0.8-1.25 mmol/L)
Creatinine – 0.014 µmol/L
CK – 3500 U/L

Case 2

A 74 year old man with a past history significant for hypertension and COPD from smoking 2 packs per day for the last 40 years. He presented to an urgent pulmonary clinic appointment with 2 months of increased cough and 5 days of "mild" hemoptysis. Upon further obtaining further history, he reports feeling fatigued, nauseous, and chronically thirsty for several weeks. His exam is significant for bilateral rhonchi (no change from baseline lung exam) and absent reflexes. Stat labs are ordered from clinic:

Sodium – 138 meq/L
Potassium – 3.7 meq/L
Magnesium – 0.45 mmol/L
Calcium (total) – 3.2 mmol/L
Phosphate – 0.3 mmol/L
Creatinine – 0.7 mmol/L (baseline creatinine = 1.1)

CBC, PT/PTT – WNL
PTH - 102 ng/L (8-60)
Albumin – 45 g/L

Case 3

65 male with bone pains and known carcinoma prostate.

Hb	10.1 (13.0-18.0)	Calcium	3.2 (2.2-2.6)
WCC	9.7 (4.9-11.0)	Phosphate	0.89 (0.85-1.45)
Plt	222 (150-400)	Albumin	35 (35-50)
ESR	25	Alk Phos	985 (25-96)
Clotting	Normal	Total protein	65 (60-80)
Urea	7.5 (3.0-6.5)	LFTs	normal
Creat	112 (35-120)		