Hypocalcemia & Hypomagnesemia

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Calcium

- Crucial component -many physiologic processes - nerve conduction, blood coagulation, hormone secretion
- Total body calcium -1000 -1200 g
  - 99% store: skeletal calcium phosphate complexes/hydroxyapatite (serves -dynamic rapidly exchangeable pool to maintain serum calcium levels)
  - 1% : intra& extracellular fluid: half in active ionized form; remaining inactive(bound): to proteins (mostly albumin) /complexed with anions including phosphate, bicarbonate, lactate
- S.Ca : 8.8 -10.4 mg/dL
- S. Ca ionized : 4.4 - 5.4 mg/dL
- Hyper & hypocalcemia - physiologically important electrolyte derangement - short- and long-term sequela for children

Calcium

- Calcium homeostasis by hormonal & physiological factors - coordination with intestine, kidney, bone
- Serum ionized calcium : Tightly regulated processes- monitored by
  - Calcium sensing receptor (CaSR) – Chief cells - parathyroid glands
  - Actions - calciotropic hormones
    - Parathyroid hormone (PTH)
    - Active vitamin D (1,25(OH)2D)
    - Calcitriol

Calcium and kidney

- PCT resorbs 60–70% of filtered calcium – passive diffusion and solvent drag
  - Active transport accounts –small portion of PCT reabsorption - tightly regulated by PTH and calcitonin
- Thick ascending limb - 20% reabsorption - paracellular & transcellular pathways
  - paracellular pathway - by a transtubular electrochemical gradient established by apical Na-K-Cl2 co-transporter (NKCC2) & renal outer medullary potassium K (ROMK) channel
  - NKCC2 transports 1 Na+, 1 K+, 2 Cl− into cell while 1 K+ diffuses back into urinary lumen through ROMK channel.
  - Sodium and chloride moved out of cell into blood stream through basolateral Na+ K+ ATPase & Cl- channels - net result is positive transepithelial potential which provides gradient for passive paracellular calcium transport
- Distal convoluted tubule - 5–10% reabsorption - active transport and transcellular pathway

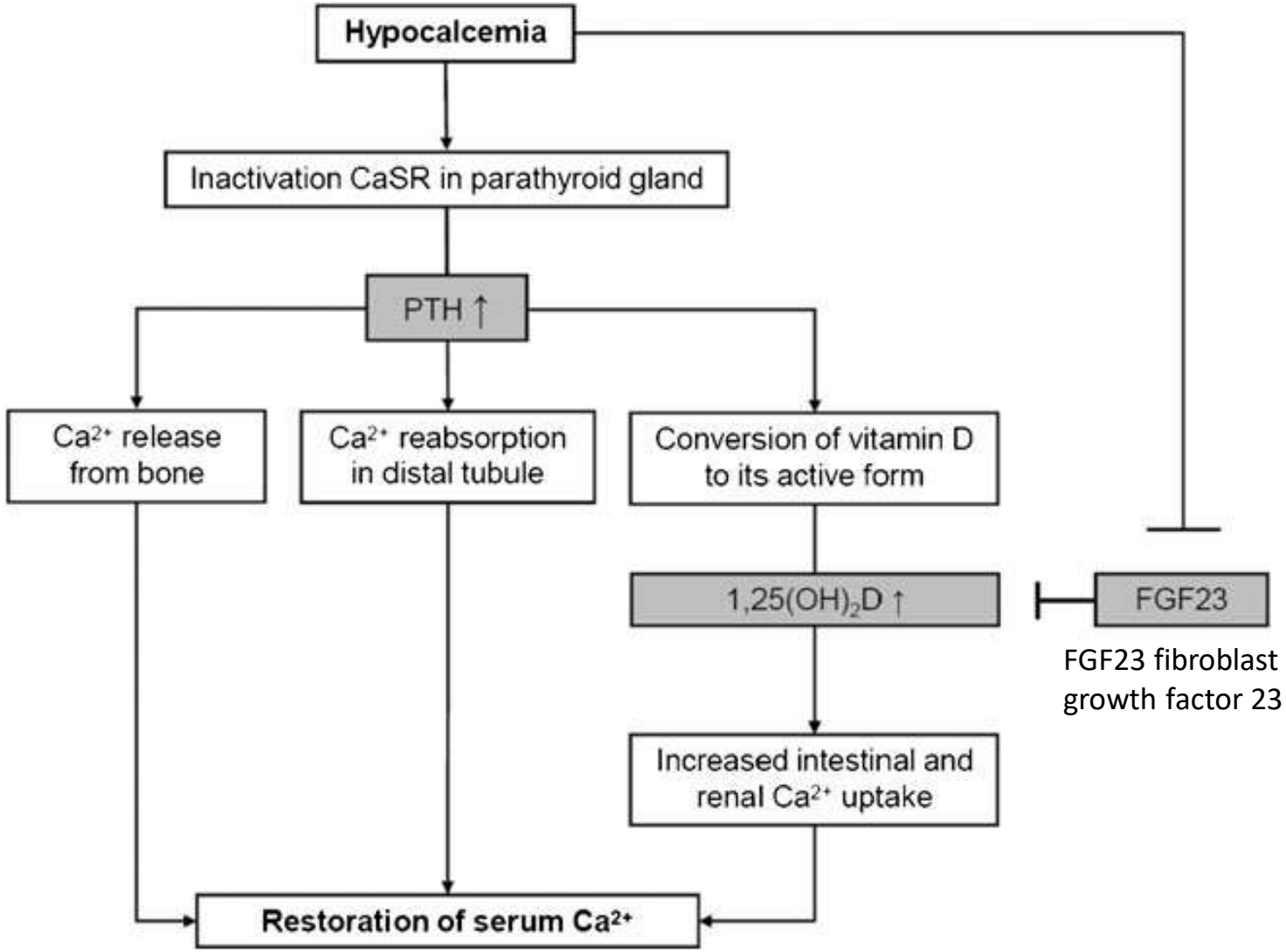
Calcium sensing receptor(CaSR) located at cell surface of Chief cells - binds calcium in extracellular domain

Hypercalcemia

- conformational change within CaSR –alters intracellular signaling -reducing cAMP levels
- Activates MAP kinases & phospholipases – rapidly inhibit preformed PTH release

Hypocalcemia

- Inactivation -CaSR
- PTH secretion stimulated



FGF23 fibroblast growth factor 23

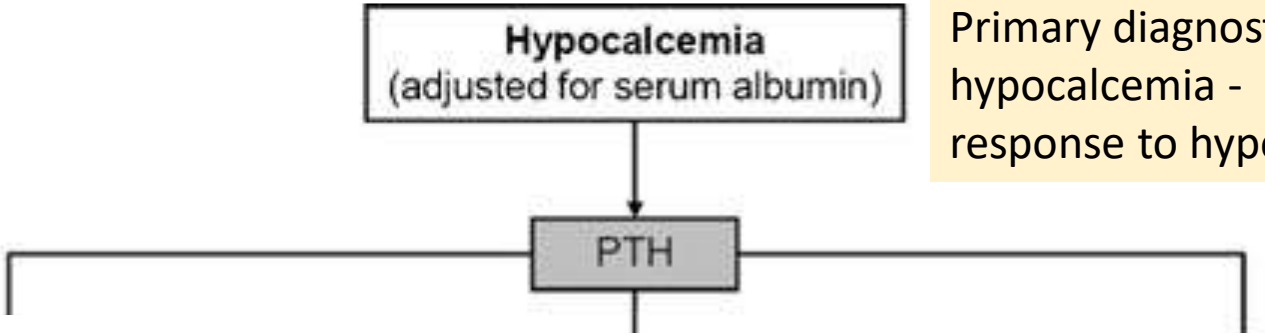
Hypocalcemia

- Low total serum calcium levels below age specific normative values
  - Pre-term newborn < 7.0 mg/dl
  - Term newborn < 8.0mg/dl
  - Children < 8.8 mg/dl
- Hypocalcemia - often nonspecific symptoms-
  - in young : poor feeding, lethargy
  - in older patients : irritability, muscle twitching, jitteriness, tremors
- More severe symptoms: tetany, seizure, cardiac arrhythmia
- Chronic low serum calcium levels: short stature, rickets, brittle nails, dry skin & hair

Suspected hypocalcemia- child or infant - Clinical approach

- True calcium derangement +/-
- Corrected serum Ca = [Ca mg/dL]+{0.8×(4−[Alb g/dL])

- Acid-base status affect ionized calcium level (H^+ & Ca^+ bound to S. albumin)
- If alkalosis: H^+ ions - dissociate from albumin – allow albumin to bind additional Ca^+
  - For every 0.1 change in pH - ionized calcium changes by 0.12 mg/dL (decrease amount of active ionized calcium)



Primary diagnostic test - differentiate etiology of hypocalcemia - PTH assessment -Normal physiologic response to hypocalcemia - increase in PTH

Kusumi K, Narla D, Mahan JD. Evaluation and Treatment of Pediatric Calcium Disorders. Current Treatment Options in Pediatrics. 2021 Jun;7(2):60-81.

Immediate management – severity of clinical symptoms

- Seizures, broncho/laryngospasm, tetany, mental status changes, impaired cardiac contractility, and/or QT interval prolongation
- Initial treatment - IV calcium administration till symptoms resolve & oral replacement can be initiated
- No specific universal protocol for IV calcium : Infusion - 20 mg/kg elemental Calcium -10 to 20 min (equivalent approximately 0.7 mL/kg of 10% Ca chloride / 2mL/kg of 10% Ca gluconate)
- Other dosing regimens :
  - IV Calcium chloride:
    - for cardiac arrest : 20 mg/kg/dose (maximum dose: 2000 mg)
    - for tetany : 10 mg/kg/dose over 5–10 min
  - IV Calcium gluconate
    - for symptomatic children: 100 to 200 mg/kg/dose over 5–10 min followed by continuous infusion of 200 to 800 mg/kg/day

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- IV Calcium- Rapid infusion - precipitate bradycardia & cardiac arrest
- IV Calcium gluconate rates - not exceed 100mg/min - Close monitoring - cardiac arrhythmia
- Calcium gluconate preferred over calcium chloride - peripheral lines used - less tissue necrosis if extravasation
- Care - to avoid fluids with phosphorous/ bicarbonate - to avoid precipitation of parenteral calcium
- Oral calcium and active vitamin D therapy - initiated as soon as possible

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Oral management

- Elemental calcium 50–100 mg/kg of in 3–4 divided doses
- Severe vitamin D–deficient rickets: Vitamin D3 at 150,000–600,000 units by IM once
- Multiple Oral vitamin D replacement regimens
- Recheck Vit D levels after 3 months of therapy - if normal - conversion to maintenance doses (400– 1200 units/day depending on age)
- In addition -magnesium deficiency if present -should be corrected
  - success of treatment of hypocalcemia - limited in cases of coexisting hypomagnesemia

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Hypomagnesemia

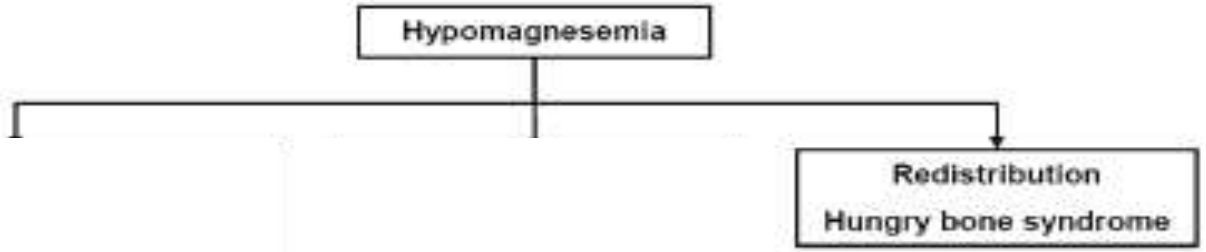
Magnesium

- Fourth most abundant mineral in body
- Second most common intracellular cation after potassium
- Normal :1.46 - 2.68 mg/dl
- Hypomagnesemia: asymptomatic till serum levels < below 0.5 mmol/L (1.2 mg/dl)
- Magnesium plasma levels :primarily regulated by kidneys
- Hormone regulation of magnesium excretion in kidneys -not been fully understood

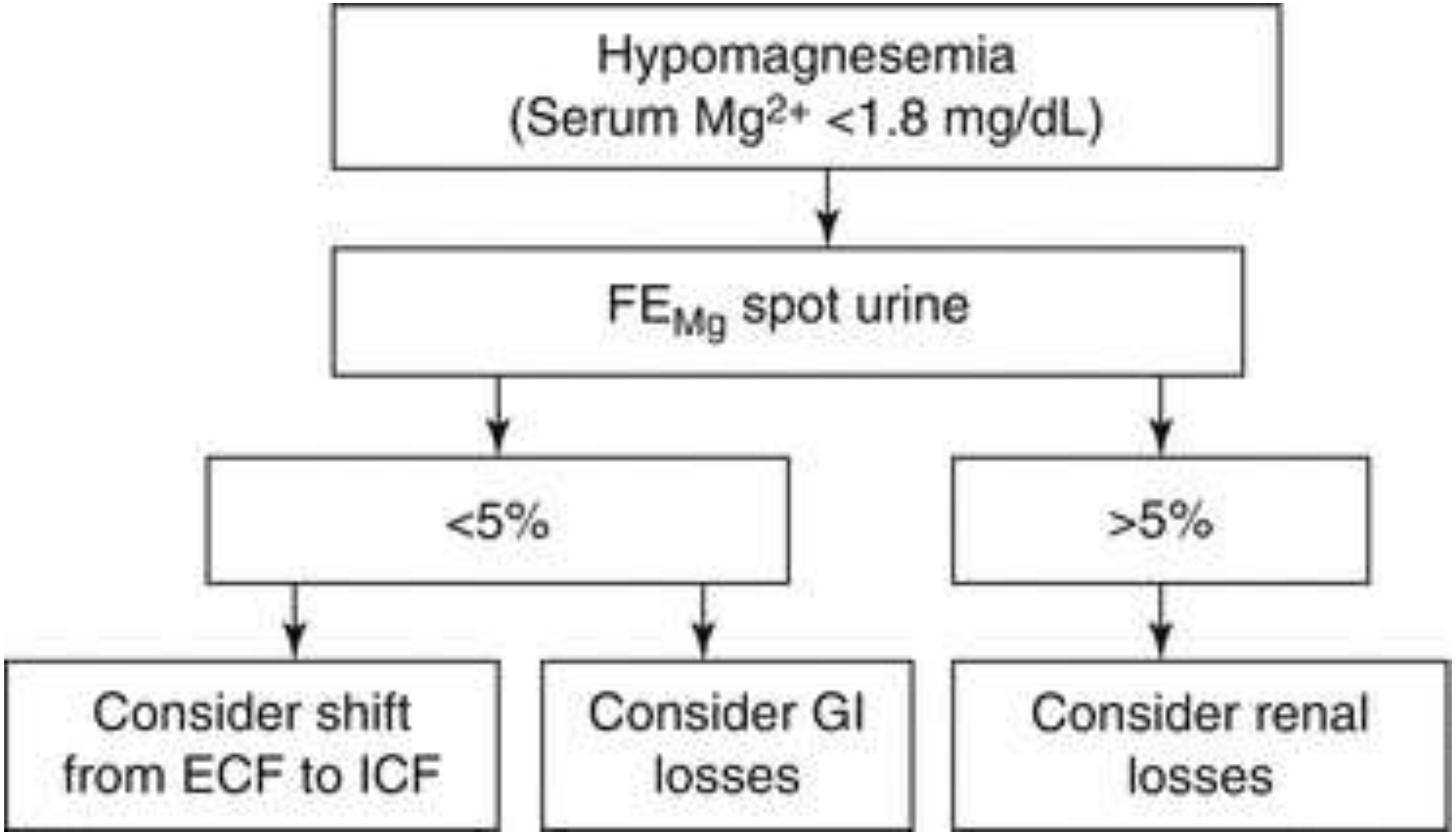
Hypomagnesemia - features

Cardiac
- Tachycardia
- Premature ventricular beats
- VT, VF
- Torsade de pointes

Neuromuscular	Muscular cramps, twitches, tremor of any or all muscles
	Muscles wasting, muscle weakness
	Numbness and tingling
	Carpopedal spasm or tetany
	Positive Chvostek sign
	Athetoid and choreiform movements
	Vertigo, ataxia, and nystagmus
	Apathy, depression and poor memory, psychosis
	Mild to severe delirium (confusion, disorientation, hallucinations, paranoia)
	Seizures, coma, death



FHHNC familial hypomagnesemia with hypercalciuria and nephrocalcinosis,
IDH isolated dominant hypomagnesemia
FHSH: Familial hypomagnesemia with secondary hypocalcemia


Hypomagnesemia
(Serum Mg^{2+} <1.8 mg/dL)
FE_{Mg} spot urine
<5%
>5%
Consider shift from ECF to ICF
Consider GI losses
Consider renal losses

Treatment

Oral/enteral dosing: Asymptomatic children with mild hypomagnesemia [unless significant gastrointestinal intolerance (eg diarrhoea) which oral magnesium will exacerbate]

- Dose: 2.5 - 5 mg/kg (0.1 - 0.2 mmol/kg) 3 times daily orally
- Increase to 10 - 20 mg/kg (0.4 - 0.8 mmol/kg) up to 4 times daily orally if required
- Tolerance better with smaller, more frequent dosing

Intravenous dosing : Children with severe symptoms (eg tetany, arrythmia, seizures)

- **Dose :** IV magnesium 0.1 - 0.2 mmol/kg up to 0.4 mmol/kg (max dose 8 mmol)- administer over 2-4 hours (reduces risk of adverse effects, improves cellular uptake of administered dose)
- In children with severe symptoms - given over shorter period of time

Hoorn, E.J., Zietse, R. Disorders of calcium and magnesium balance: a physiology-based approach. *Pediatr Nephrol* **28**, 1195–1206 (2013)
Kaplinsky C, Alon US. Magnesium homeostasis and hypomagnesemia in children with malignancy. Pediatric Blood & Cancer. 2013 May;60(5):734-40

Thank you