HYPOMAGNESEMIA

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INTRODUCTION

- Magnesium is the second most abundant cation in ICF.
- Normal plasma magnesium concentration is 1.7 to 2.1 mg/dl.
- Less than 1% of total body Mg is in plasma.
- Protein-bound (30%), complexed with anions (15%), and free or ionized (around 55%).

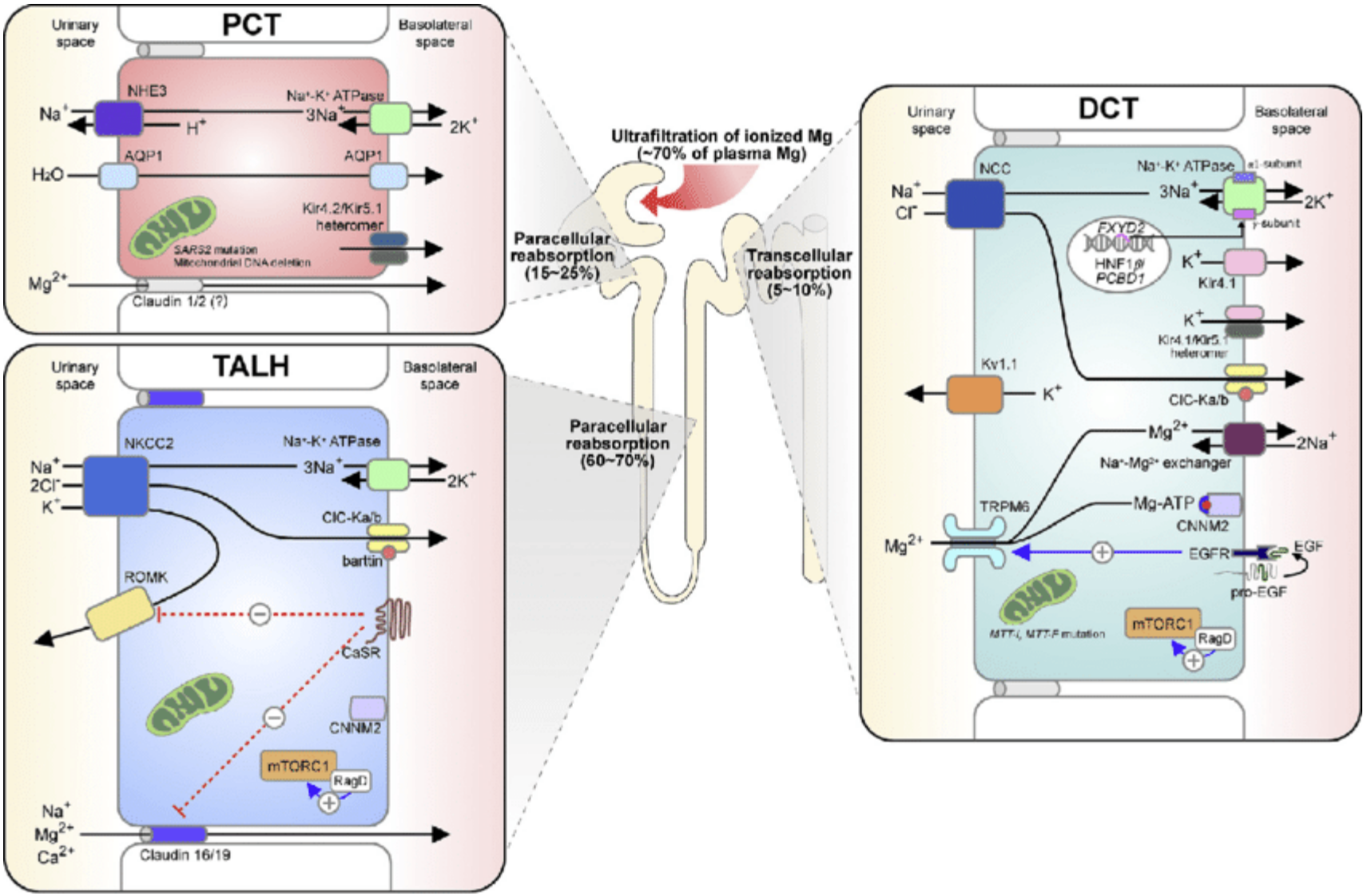
- Cofactor for about 600 enzymes .Activation of ATP , DNA repair, nucleic acid stabilisation.

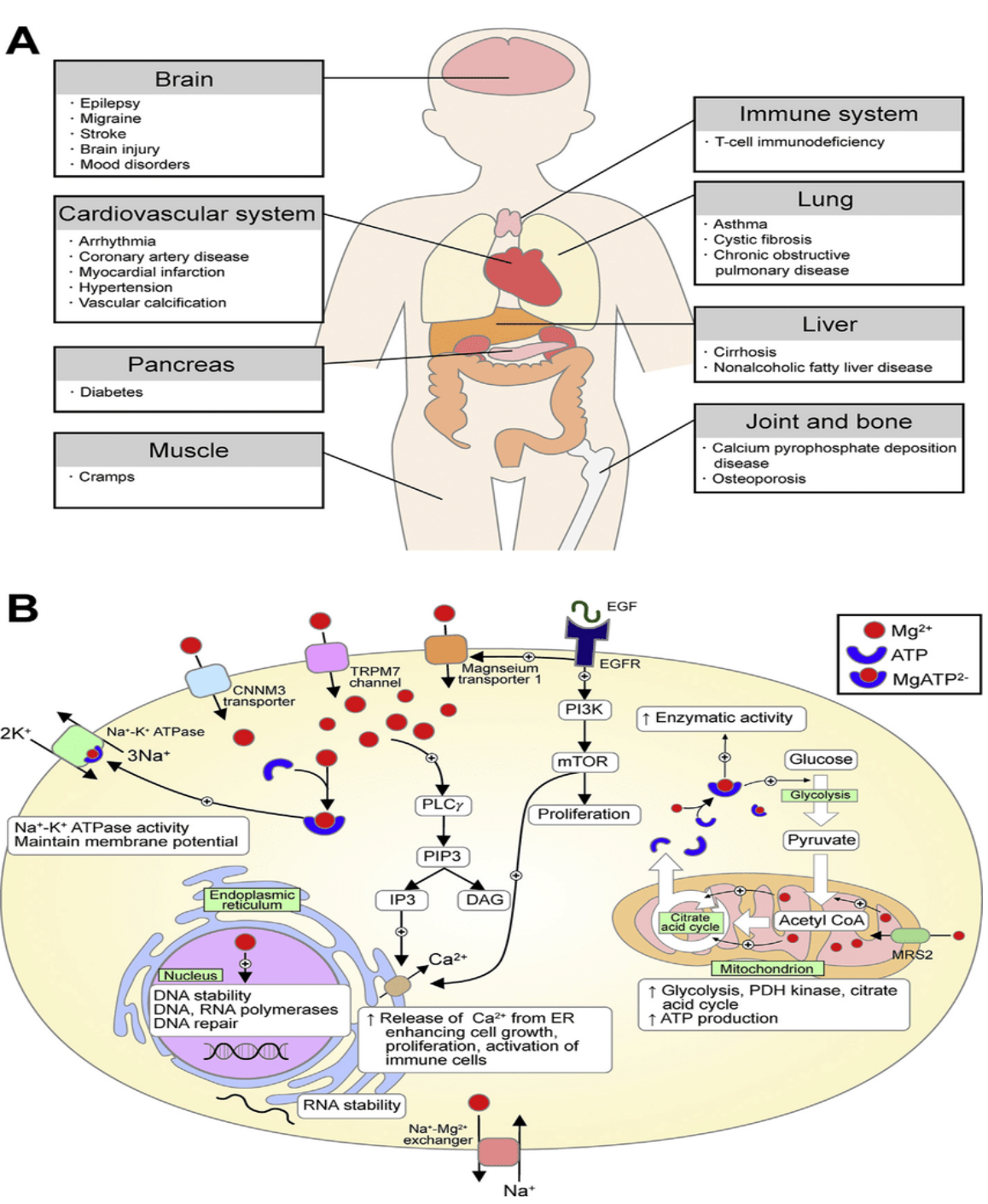
- Magnesium gating is the distal nephron is important for potassium homeostasis.
- Role in regulating parathyroid hormone secretion by its indirect effect on vitamin D metabolism.

MAGNESIUM TRANSPORT

- Magnesium reabsorption happens in proximal convoluted tubule, cortical thick ascending limb of Henle's loop, and distal convoluted tubule.
- Around 25% of filtered Mg 2þ is reabsorbed passively via paracellular pathway (probable claudin 1 and 2) in proximal convoluted tubule.
- The positive luminal voltage generated by apical NKCC2 and ROMK provides the driving force for paracellular reabsorption of 70% filtered Mg 2þ in thick ascending limb of Henle's loop.
- The Mg 2þ is reabsorbed actively through TRPM6 in DCT.
- The Mg 2þ efflux is conducted in Na þ -Mg 2þ exchanger and possibly also in CNNM2.

MAGNESIUM HANDLING PCT /DCT/TALH





Pathophysiology of hypomagnesemia.

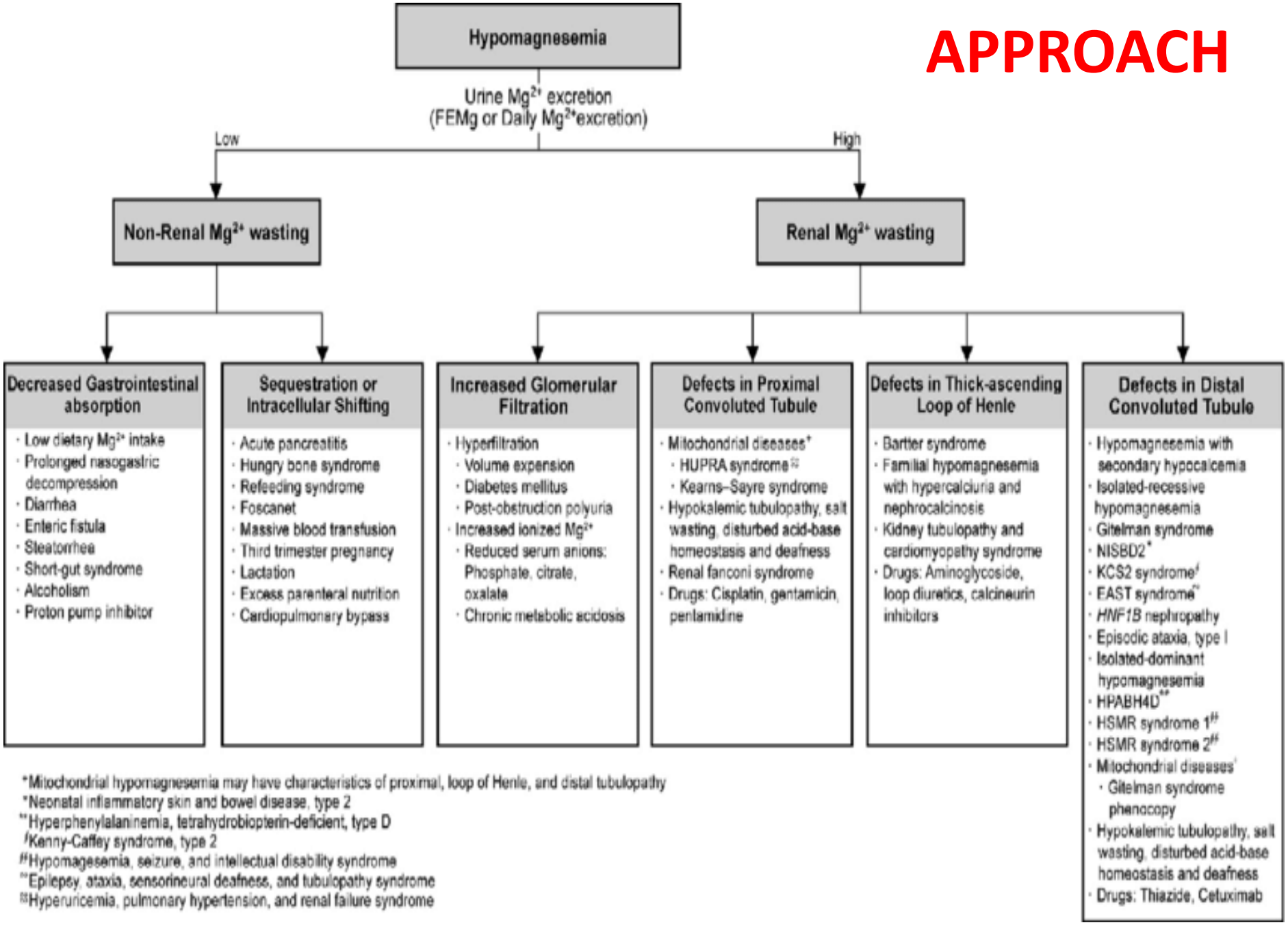
(A) Clinical manifestations and organ-specific consequences of hypomagnesemia.

(B) (B) Cellular physiology of Mg 2þ . Several transporters are responsible for the cellular Mg 2þ homeostasis.

Mg 2þ stabilizes the structures of DNA and RNA, DNA and RNA polymerases, and their repair in the nucleus.

Additionally, Mg 2þ also regulated the cell growth and proliferation. In cytosol, Mg 2þ is involved in many enzymatic reactions and regulates the glycolysis and ATP synthesis.

APPROACH



*Mitochondrial hypomagnesemia may have characteristics of proximal, loop of Henle, and distal tubulopathy
*Neonatal inflammatory skin and bowel disease, type 2
**Hyperphenylalaninemia, tetrahydrobiopterin-deficient, type D
†Kenny-Caffey syndrome, type 2
††Hypomagesemia, seizure, and intellectual disability syndrome
‡Epilepsy, ataxia, sensorineural deafness, and tubulopathy syndrome
☆Hyperuricemia, pulmonary hypertension, and renal failure syndrome

TREATMENT

MAGNESIUM

Goal serum magnesium concentration 2.0 – 2.4 mg/dL

Intravenous Treatment of Hypomagnesemia

Serum magnesium concentration	Intravenous magnesium sulfate dose†	Oral magnesium oxide dose	Recheck serum magnesium concentration
1.6 – 1.9 mg/dL	2 g	800 mg	4 to 6 hours after dose if symptomatic otherwise with next AM lab draw
1.0 – 1.5 mg/dL	4 g	Not recommended	4 to 6 hours after dose if symptomatic otherwise with next AM lab draw
< 1.0 mg/dL	6 g and **notify MD**	Not recommended	4 to 6 hours after dose if symptomatic otherwise with next AM lab draw
Rate of intravenous infusion of magnesium	Recommend infusing 1 g magnesium sulfate/hour (~8 mEq magnesium/hour), up to maximum of 2 g magnesium sulfate/hour (doses of up to 32 mEq magnesium can be given over 4 – 5 minutes in **severe symptomatic hypomagnesemia** (urgent or emergent situation))		

† 1 g magnesium sulfate = 8.1 mEq magnesium

****Consider adding scheduled oral magnesium oxide as indicated****

Reduce the IV Mg dose by 50 % and closely monitoring Mg in CKD patients with eGFR less than 30 ml/min/1,73 m2.

Table 5. Different magnesium formulations.

Magnesium Supplement	Elemental Magnesium (Percent)	Bioavailability (as Fractional Absorption of the Administered Dose)	Bioavailability (Relative Comparison)	Tolerability (Diarrhea)
Magnesium Oxide	60	4%	Extremely low	++
Magnesium Carbonate	45	*	Extremely low	*
Magnesium Hydroxide	42	4%	*	++
Magnesium Citrate	16	12%	Good	++
Magnesium Lactate	12	12%	Excellent	+
Magnesium Chloride	12	12%	Good	+
Magnesium Aspartate	10	*	*	*
Magnesium Sulfate	10	4%	*	++
Magnesium Gluconate	5	*	Good	±

Data obtained from Guerrera et al [46], Firoz M [47], Ranade [48], Epocrates [49], The Schrier Atlas of Diseases of the Kidney [50]. * Data could not be obtained. ++ Indicates higher incidence of diarrhea, + indicates lesser incidence of diarrhea. ± Indicates equivocal incidence of diarrhea.

Typical daily dose in a patient with normal kidney - 240 to 1000 mg of elemental Mg in divided doses.

Patients with hypomagnesemia due to renal magnesium wasting may benefit from the addition of a potassium-sparing diuretic such as amiloride or triamterene.