

FIGURE 4-10

Magnesium (Mg) reabsorption in the cortical thick ascending limb (cTAL) of the loop of Henle. Most Mg reabsorption within the nephron occurs in the cTAL owing primarily to voltage-dependent Mg flux through the intercellular tight junction. Transcellular Mg movement occurs only in response to cellular metabolic needs. The sequence of events necessary to generate the lumen-positive electrochemical gradient that drives Mg reabsorption is as follows: 1) A basolateral sodium-potassium-adenosine triphosphatase (Na⁺-K⁺-ATPase) decreases intracellular sodium, generating an inside-negative electrical potential difference; 2) Intracellular K is extruded by an electroneutral K-Cl (chloride) cotransporter; 3) Cl is extruded by way of conductive pathways in the basolateral membrane; 4) The apical-luminal Na-2Cl-K (furosemide-sensitive) cotransport mechanism is driven by the inside-negative potential difference and decrease in intracellular Na; 5) Potassium is recycled back into the lumen by way of an apical K conductive channel; 6) Passage of approximately 2 Na molecules for every Cl molecule is allowed by the paracellular pathway (intercellular tight junction), which is cation permselective; 7) Mg reabsorption occurs passively, by way of intercellular channels, as it moves down its electrical gradient [1,2,6,7]. (Adapted from de Rouffignac and Quamme [1].)

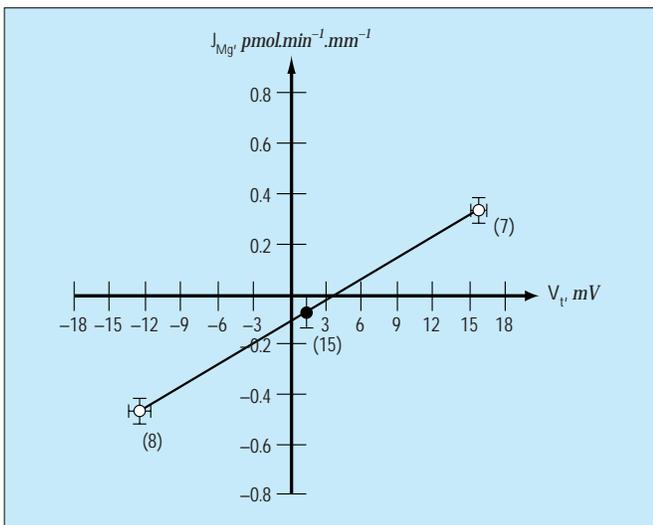
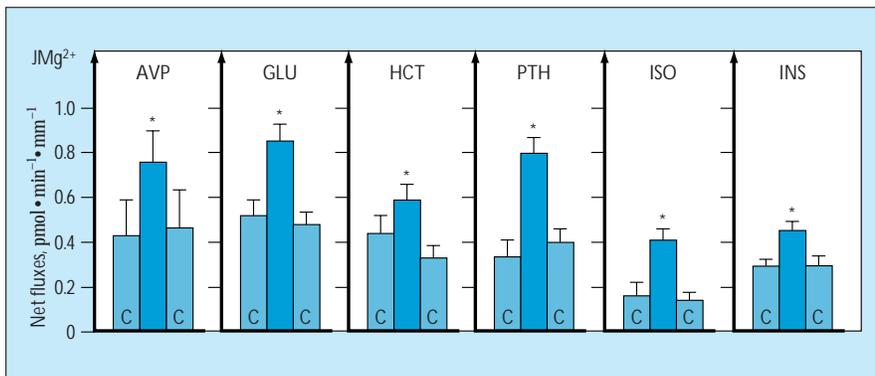


FIGURE 4-11

Voltage-dependent net magnesium (Mg) flux in the cortical thick ascending limb (cTAL). Within the isolated mouse cTAL, Mg flux (J_{Mg}) occurs in response to voltage-dependent mechanisms. With a relative lumen-positive transepithelial potential difference (V_t), Mg reabsorption increases (positive J_{Mg}). Mg reabsorption equals zero when no voltage-dependent difference exists, and Mg is capable of moving into the tubular lumen (negative J_{Mg}) when a lumen-negative voltage difference exists [1,16]. (From di Stefano and coworkers [16]).

**FIGURE 4-12**

Effect of hormones on magnesium (Mg) transport in the cortical thick ascending limb (cTAL). In the presence of arginine vasopressin (AVP), glucagon (GLU), human calcitonin (HCT), parathyroid hormone (PTH), 1,4,5-isoproterenol (ISO), and insulin (INS), increases occur in Mg reabsorption from isolated segments of mouse cTALs. These hormones have no effect on medullary TAL segments. As already has been shown in Figure 4-3, these hormones affect intracellular “second messengers” and cellular Mg movement. These hormone-induced alterations can affect the paracellular permeability of the intercellular tight junction. These changes may also affect the transepithelial voltage across the cTAL. Both of these forces favor net Mg reabsorption in the cTAL [1,2,7,8]. Asterisk—significant change from preceding period; J_{Mg} —Mg flux; C—control, absence of hormone. (*Adapted from de Rouffignac and Quamme [1].*)

Magnesium Depletion

CAUSES OF MAGNESIUM (Mg) DEPLETION

Poor Mg intake	Other
Starvation	Lactation
Anorexia	Extensive burns
Protein calorie malnutrition	Exchange transfusions
No Mg in intravenous fluids	
Renal losses	
see Fig. 4-14	
Increased gastrointestinal Mg losses	
Nasogastric suction	
Vomiting	
Intestinal bypass for obesity	
Short-bowel syndrome	
Inflammatory bowel disease	
Pancreatitis	
Diarrhea	
Laxative abuse	
Villous adenoma	

FIGURE 4-13

The causes of magnesium (Mg) depletion. Depletion of Mg can develop as a result of low intake or increased losses by way of the gastrointestinal tract, the kidneys, or other routes [1,2,8–13].

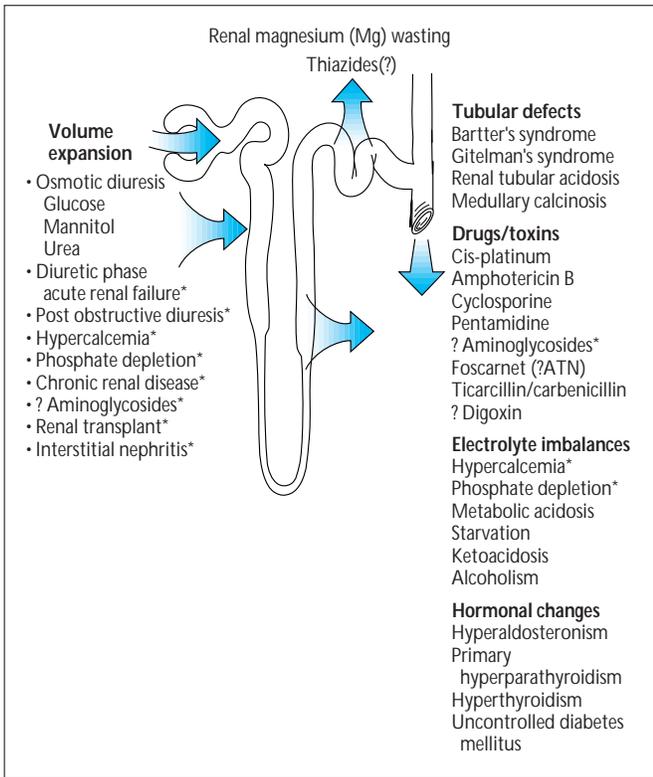


FIGURE 4-14

Renal magnesium (Mg) wasting. Mg is normally reabsorbed in the proximal tubule (PT), cortical thick ascending limb (cTAL), and distal convoluted tubule (DCT) (see Fig. 4-9). Volume expansion and osmotic diuretics inhibit PT reabsorption of Mg. Several renal diseases and electrolyte disturbances (asterisks) inhibit Mg reabsorption in both the PT and cTAL owing to damage to the epithelial cells and the intercellular tight junctions, plus disruption of the electrochemical forces that normally favor Mg reabsorption. Many drugs and toxins directly damage the cTAL. Thiazides have little direct effect on Mg reabsorption; however, the secondary hyperaldosteronism and hypercalcemia effect Mg reabsorption in CD and/or cTAL. Aminoglycosides accumulate in the PT, which affects sodium reabsorption, also leading to an increase in aldosterone. Aldosterone leads to volume expansion, decreasing Mg reabsorption. Parathyroid hormone has the direct effect of increasing Mg reabsorption in cTAL; however, hypercalcemia offsets this tendency. Thyroid hormone increases Mg loss. Diabetes mellitus increases Mg loss by way of both hyperglycemic osmotic diuresis and insulin abnormalities (deficiency and resistance), which decrease Mg reabsorption in the proximal convoluted tubule and cTAL, respectively. Cisplatin causes a Gitelman-like syndrome, which often can be permanent [1,2,8–12].

SIGNS AND SYMPTOMS OF HYPOMAGNESEMIA

Cardiovascular	Muscular
Electrocardiographic results	Cramps
Prolonged P-R and Q-T intervals,	Weakness
U waves	Carpopedal spasm
Angina pectoris	Chvostek's sign
?Congestive heart failure	Trousseau's sign
Atrial and ventricular arrhythmias	Fasciculations
?Hypertension	Tremulous
Digoxin toxicity	Hyperactive reflexes
Atherogenesis	Myoclonus
Neuromuscular	Dysphagia
Central nervous system	Skeletal
Seizures	Osteoporosis
Obtundation	Osteomalacia
Depression	
Psychosis	
Coma	
Ataxia	
Nystagmus	
Choreiform and athetoid movements	

FIGURE 4-15

Signs and symptoms of hypomagnesemia. Symptoms of hypomagnesemia can develop when the serum magnesium (Mg) level falls below 1.2 mg/dL. Mg is a critical cation in nerves and muscles and is intimately involved with potassium and calcium. Therefore, neuromuscular symptoms predominate and are similar to those seen in hypocalcemia and hypokalemia. Electrocardiographic changes of hypomagnesemia include an increased P-R interval, increased Q-T duration, and development of U waves. Mg deficiency increases the mortality of patients with acute myocardial infarction and congestive heart failure. Mg depletion hastens atherogenesis by increasing total cholesterol and triglyceride levels and by decreasing high-density lipoprotein cholesterol levels. Hypomagnesemia also increases hypertensive tendencies and impairs insulin release, which favor atherogenesis. Low levels of Mg impair parathyroid hormone (PTH) release, block PTH action on bone, and decrease the activity of renal 1- α -hydroxylase, which converts 25-hydroxy-vitamin D₃ into 1,25-dihydroxy-vitamin D₃, all of which contribute to hypocalcemia. Mg is an integral cofactor in cellular sodium-potassium-adenosine triphosphatase activity, and a deficiency of Mg impairs the intracellular transport of K and contributes to renal wasting of K, causing hypokalemia [6,8–12].