Divalent Cation Metabolism: Magnesium

James T. McCarthy
Rajiv Kumar

Magnesium is an essential intracellular cation. Nearly 99% of the total body magnesium is located in bone or the intracellular space. Magnesium is a critical cation and cofactor in numerous intracellular processes. It is a cofactor for adenosine triphosphate; an important membrane stabilizing agent; required for the structural integrity of numerous intracellular proteins and nucleic acids; a substrate or cofactor for important enzymes such as adenosine triphosphatase, guanosine triphosphatase, phospholipase C, adenylate cyclase, and guanylate cyclase; a required cofactor for the activity of over 300 other enzymes; a regulator of ion channels; an important intracellular signaling molecule; and a modulator of oxidative phosphorylation. Finally, magnesium is intimately involved in nerve conduction, muscle contraction, potassium transport, and calcium channels. Because turnover of magnesium in bone is so low, the short-term body requirements are met by a balance of gastrointestinal absorption and renal excretion. Therefore, the kidney occupies a central role in magnesium balance. Factors that modulate and affect renal magnesium excretion can have profound effects on magnesium balance. In turn, magnesium balance affects numerous intracellular and systemic processes [1–12].

In the presence of normal renal function, magnesium retention and hypermagnesemia are relatively uncommon. Hypermagnesemia inhibits magnesium reabsorption in both the proximal tubule and the loop of Henle. This inhibition of reabsorption leads to an increase in magnesium excretion and prevents the development of dangerous levels of serum magnesium, even in the presence of above-normal intake. However, in familial hypocalciuric hypercalcemia, there appears to be an abnormality of the thick ascending limb of the loop of Henle that prevents excretion of calcium. This abnormality may also extend to Mg. In familial hypocalciuric hypercalcemia, mild hypermagnesemia does not increase the renal excretion of magnesium. A similar abnormality may be caused by lithium [1,2,6,10]. The renal excretion of magnesium also is below normal in states of hypomagnesemia, decreased dietary magnesium, dehydration and volume depletion, hypocalcemia, hypothyroidism, and hyperparathyroidism [1,2,6,10].

CHAPTER 4

Magnesium Distribution

TOTAL BODY MAGNESIUM (MG) DISTRIBUTION

Location	Percent of Total	Mg Content, mmol*	Mg Content, mg*
Bone	53	530	12720
Muscle	27	270	6480
Soft tissue	19.2	192	4608
Erythrocyte	0.5	5	120
Serum	0.3	3	72
Total		1000	24000

*data typical for a 70 kg adult

FIGURE 4-1

Total distribution of magnesium (Mg) in the body. Mg (molecular weight, 24.305 D) is predominantly distributed in bone, muscle, and soft tissue. Total body Mg content is about 24 g (1 mol) per 70 kg. Mg in bone is adsorbed to the surface of hydroxyapatite crystals, and only about one third is readily available as an exchangeable pool. Only about 1% of the total body Mg is in the serum and interstitial fluid [1,2,8,9,11,12].

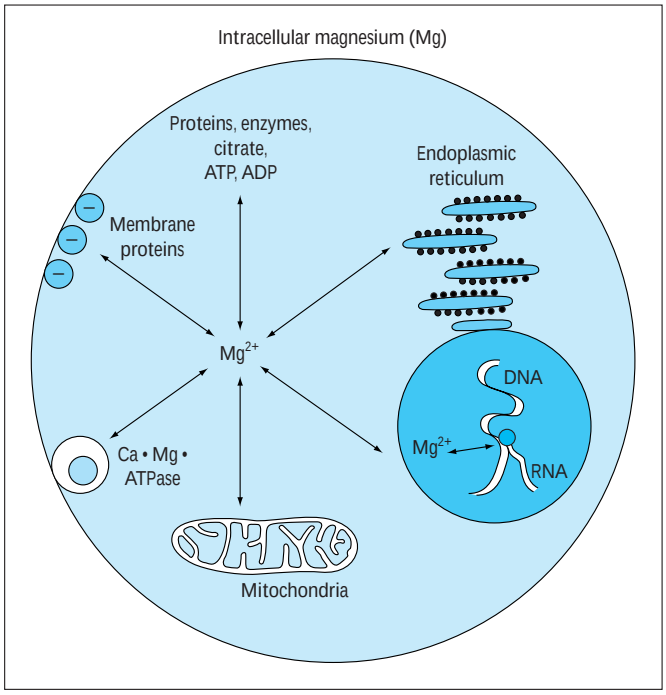


FIGURE 4-2

Intracellular distribution of magnesium (Mg). Only 1% to 3% of the total intracellular Mg exists as the free ionized form of Mg, which has a closely regulated concentration of 0.5 to 1.0 mmol. Total cellular Mg concentration can vary from 5 to 20 mmol, depending on the type of tissue studied, with the highest Mg concentrations being found in skeletal and cardiac muscle cells. Our understanding of the concentration and distribution of intracellular Mg has been facilitated by the development of electron microprobe analysis techniques and fluorescent dyes using microfluorescence spectrometry. Intracellular Mg is predominantly complexed to organic molecules (*eg*, adenosine triphosphatase [ATPase], cell and nuclear membrane-associated proteins, DNA and RNA, enzymes, proteins, and citrates) or sequestered within subcellular organelles (mitochondria and endoplasmic reticulum). A heterogeneous distribution of Mg occurs within cells, with the highest concentrations being found in the perinuclear areas, which is the predominant site of endoplasmic reticulum. The concentration of intracellular free ionized Mg is tightly regulated by intracellular sequestration and complexation. Very little change occurs in the concentration of intracellular free Mg, even with large variations in the concentrations of total intracellular or extracellular Mg [1,3,11]. ADP—adenosine diphosphate; ATP—adenosine triphosphate; Ca^{+}—ionized calcium.

Intracellular Magnesium Metabolism

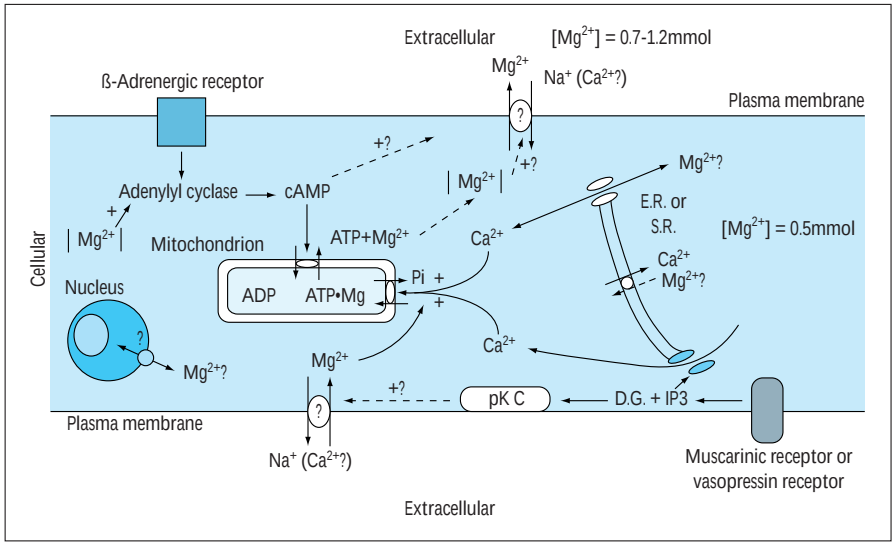


FIGURE 4-3

Regulation of intracellular magnesium (Mg^{2+}) in the mammalian cell. Shown is an example of Mg^{2+} movement between intracellular and extracellular spaces and within intracellular compartments. The stimulation of adenylate cyclase activity (*eg*, through stimulation of β-adrenergic receptors) increases cyclic adenosine monophosphate (cAMP). The increase in cAMP induces extrusion of Mg from mitochondria by way of mitochondrial adenine nucleotide translocase, which exchanges 1 Mg^{2+}-adenosine triphosphate (ATP) for adenosine diphosphate (ADP). This slight increase in cytosolic Mg^{2+} can then be extruded through the plasma membrane by way of a Mg-cation exchange mechanism, which may be activated by either cAMP or Mg. Activation of other cell receptors (*eg*, muscarinic receptor or vasopressin receptor) may alter cAMP levels or produce diacylglycerol (DAG). DAG activates Mg influx by way of protein kinase C (pK C) activity. Mitochondria may accumulate Mg by the exchange of a cytosolic Mg^{2+}-ATP for a mitochondrial matrix Pi molecule. This exchange mechanism is Ca^{2+}-activated and bidirectional, depending on the concentrations of Mg^{2+}-ATP and Pi in the cytosol and mitochondria. Inositol 1,4,5-trisphosphate (IP3) may also increase the release of Mg from endoplasmic reticulum or sarcoplasmic reticulum (ER or SR, respectively), which also has a positive effect on this Mg^{2+}-ATP-Pi exchanger. Other potential mechanisms affecting cytosolic Mg include a hypothetical Ca^{2+}-Mg^{2+} exchanger located in the ER and transport proteins that can allow the accumulation of Mg within the nucleus or ER. A balance must exist between passive entry of Mg into the cell and an active efflux mechanism because the concentration gradient favors the movement of extracellular Mg (0.7–1.2 mmol) into the cell (free Mg, 0.5 mmol). This Mg extrusion process may be energy-requiring or may be coupled to the movement of other cations. The cellular movement of Mg generally is not involved in the transepithelial transport of Mg, which is primarily passive and occurs between cells [1–3,7]. (*From* Romani and coworkers [3]; with permission.)

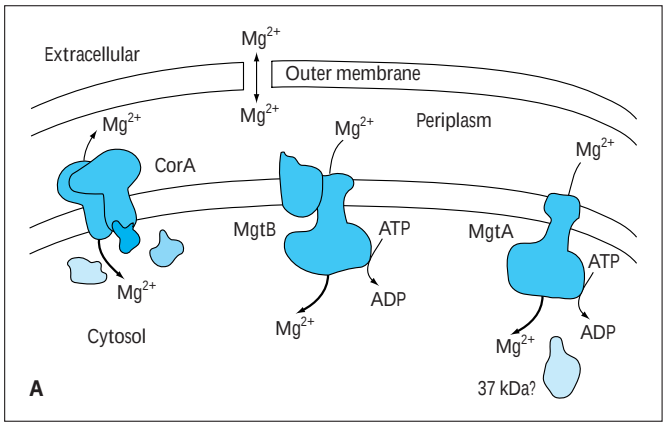
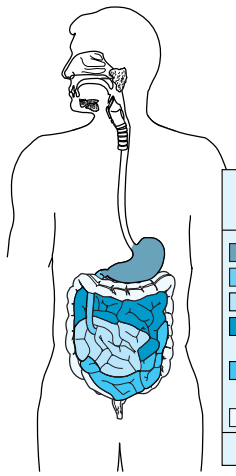


FIGURE 4-4

A, Transport systems of magnesium (Mg). Specific membrane-associated Mg transport proteins only have been described in bacteria such as *Salmonella*. Although similar transport proteins are believed to be present in mammalian cells based on nucleotide sequence analysis, they have not yet been demonstrated. Both MgtA and MgtB (molecular weight, 91 and 101 kDa, respectively) are members of the adenosine triphosphatase (ATPase) family of transport proteins. **B**, Both of these transport proteins have six C-terminal and four N-terminal membrane-spanning segments, with both the N- and C-terminals within the cytoplasm. Both proteins transport Mg with its electrochemical gradient, in contrast to other known ATPase proteins that usually transport ions against their chemical gradient. Low levels of extracellular Mg are capable of increasing transcription of these transport proteins, which increases transport of Mg into *Salmonella*. The CorA system has three membrane-spanning segments. This system mediates Mg influx; however, at extremely high extracellular Mg concentrations, this protein can also mediate Mg efflux. Another cell membrane Mg transport protein exists in erythrocytes (RBCs). This RBC Na^+-Mg^{2+} antiporter (not shown here) facilitates the outward movement of Mg from erythrocytes in the presence of extracellular Na^+ and intracellular adenosine triphosphate (ATP) [4,5]. ADP—adenosine diphosphate; C—carbon; N—nitrogen. (*From* Smith and Maguire [4]).

Gastrointestinal Absorption of Magnesium



Gastrointestinal absorption of dietary magnesium (Mg)

Site	Mg absorption mmol/day	Mg absorption mg/day	% of intake absorption
Stomach	0	0	0
Duodenum	0.63	15	5
Jejunum	1.25	30	10
Proximal Ileum	1.88	45	15
Distal Ileum	1.25	30	10
Colon	0.63	15	5
Total*	5.6	135	45

*Normal dietary Mg intake = 300 mg (12.5 mmol) per day

FIGURE 4-5

Gastrointestinal absorption of dietary intake of magnesium (Mg). The normal adult dietary intake of Mg is 300 to 360 mg/d (12.5–15 mmol/d). A Mg intake of about 3.6 mg/kg/d is necessary to maintain Mg balance. Foods high in Mg content include green leafy vegetables (rich in Mg-containing chlorophyll), legumes, nuts, seafoods, and meats. Hard water contains about 30 mg/L of Mg. Dietary intake is the only source by which the body can replete Mg stores. Net intestinal Mg absorption is affected by the fractional Mg absorption within a specific segment of intestine, the length of that intestinal segment, and transit time of the food bolus. Approximately 40% to 50% of dietary Mg is absorbed. Both the duodenum and jejunum have a high fractional absorption of Mg. These segments of intestine are relatively short, however, and the transit time is rapid. Therefore, their relative contribution to total Mg absorption is less than that of the ileum. In the intact animal, most of the Mg absorption occurs in the ileum and colon. 1,25-dihydroxy-vitamin D_3 may mildly increase the intestinal absorption of Mg; however, this effect may be an indirect result of increased calcium absorption induced by the vitamin. Secretions of the upper intestinal tract contain approximately 1 mEq/L of Mg, whereas secretions from the lower intestinal tract contain 15 mEq/L of Mg. In states of nausea, vomiting, or nasogastric suction, mild to moderate losses of Mg occur. In diarrheal states, Mg depletion can occur rapidly owing to both high intestinal secretion and lack of Mg absorption [2,6,8–13].

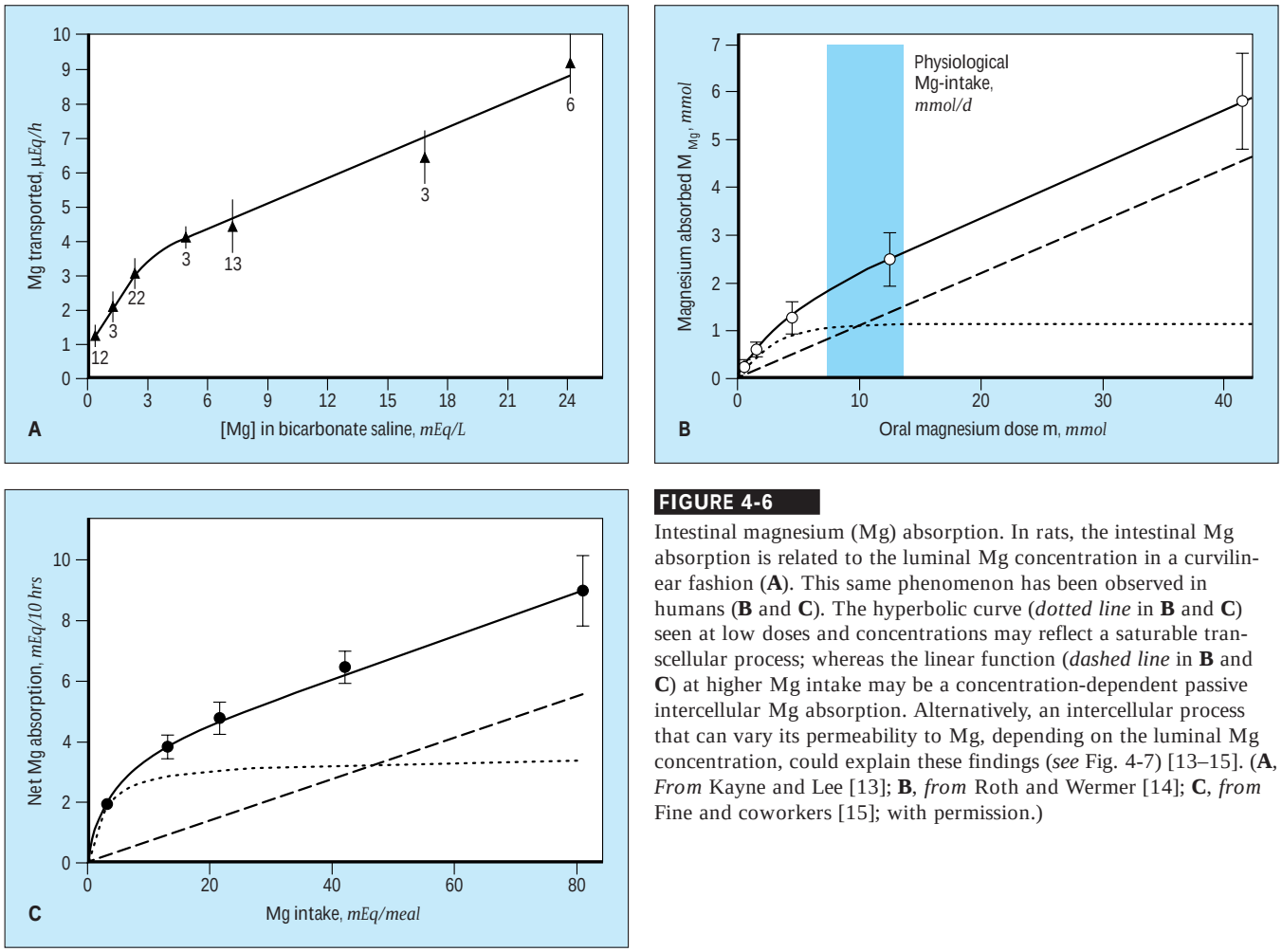


FIGURE 4-6

Intestinal magnesium (Mg) absorption. In rats, the intestinal Mg absorption is related to the luminal Mg concentration in a curvilinear fashion (**A**). This same phenomenon has been observed in humans (**B** and **C**). The hyperbolic curve (*dotted line* in **B** and **C**) seen at low doses and concentrations may reflect a saturable transcellular process; whereas the linear function (*dashed line* in **B** and **C**) at higher Mg intake may be a concentration-dependent passive intercellular Mg absorption. Alternatively, an intercellular process that can vary its permeability to Mg, depending on the luminal Mg concentration, could explain these findings (*see* Fig. 4-7) [13–15]. (**A**, *From* Kayne and Lee [13]; **B**, *from* Roth and Wermer [14]; **C**, *from* Fine and coworkers [15]; with permission.)

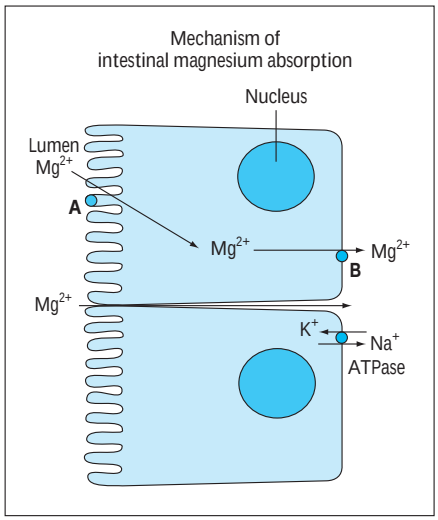


FIGURE 4-7

Proposed pathways for movement of magnesium (Mg) across the intestinal epithelium. Two possible routes exist for the absorption of Mg across intestinal epithelial cells: the transcellular route and the intercellular pathway. Although a transcellular route has not yet been demonstrated, its existence is inferred from several observations. No large chemical gradient exists for Mg movement across the cell membrane; however, a significant uphill electrical gradient exists for the exit of Mg from cells. This finding suggests the existence and participation of an energy-dependent mechanism for extrusion of Mg from intestinal cells. If such a system exists, it is believed it would consist of two stages. 1) Mg would enter the apical membrane of intestinal cells by way of a passive carrier or facilitated diffusion. 2) An active Mg pump in the basolateral section of the cell would extrude Mg. The intercellular movement of Mg has been demonstrated to occur by both gradient-driven and solvent-drag mechanisms. This intercellular path may be the only means by which Mg moves across the intestinal epithelium. The change in transport rates at low Mg concentrations would reflect changes in the "openness" of this pathway. High concentrations of luminal Mg (*eg*, after a meal) are capable of altering the morphology of the tight junction complex. High local Mg concentrations near the intercellular junction also can affect the activities of local membrane-associated proteins (*eg*, sodium-potassium adenosine triphosphate [Na-K ATPase]) near the tight junction and affect its permeability (*see* Fig. 4-6) [13–15].

Renal Handling of Magnesium

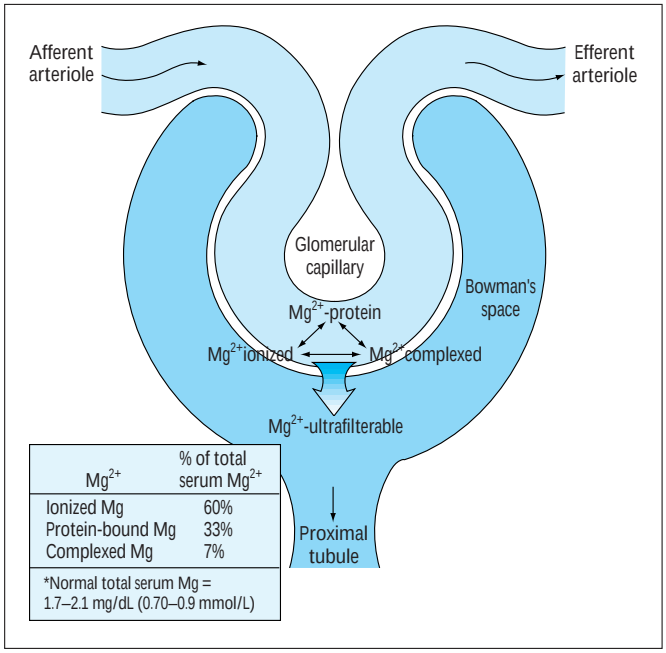


FIGURE 4-8

The glomerular filtration of magnesium (Mg). Total serum Mg consists of ionized, complexed, and protein bound fractions, 60%, 7%, and 33% of total, respectively. The complexed Mg is bound to molecules such as citrate, oxalate, and phosphate. The ultrafilterable Mg is the total of the ionized and complexed fractions. Normal total serum Mg is approximately 1.7 to 2.1 mg/dL (about 0.70–0.90 mmol/L) [1,2,7–9,11,12].

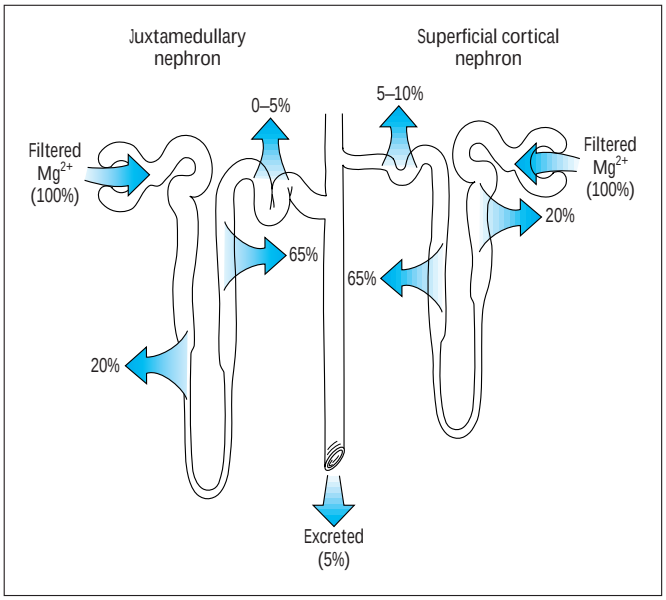


FIGURE 4-9

The renal handling of magnesium (Mg^{2+}). Mg is filtered at the glomerulus, with the ultrafilterable fraction of plasma Mg entering the proximal convoluted tubule (PCT). At the end of the PCT, the Mg concentration is approximately 1.7 times the initial concentration of Mg and about 20% of the filtered Mg has been reabsorbed. Mg reabsorption occurs passively through paracellular pathways. Hydrated Mg has a very large radius that decreases its intercellular permeability in the PCT when compared with sodium. The smaller hydrated radius of sodium is 50% to 60% reabsorbed in the PCT. No clear evidence exists of transcellular reabsorption or secretion of Mg within the mammalian PCT. In the pars recta of the proximal straight tubule (PST), Mg reabsorption can continue to occur by way of passive forces in the concentrating kidney. In states of normal hydration, however, very little Mg reabsorption occurs in the PST. Within the thin descending limb of the loop of Henle, juxtamedullary nephrons are capable of a small amount of Mg reabsorption in a state of antidiuresis or Mg depletion. This reabsorption does not occur in superficial cortical nephrons. No data exist regarding Mg reabsorption in the thin ascending limb of the loop of Henle. No Mg reabsorption occurs in the medullary portion of the thick ascending limb of the loop of Henle; whereas nearly 65% of the filtered load is absorbed in the cortical thick ascending limb of the loop of Henle in both juxtamedullary and superficial cortical nephrons. A small amount of Mg is absorbed in the distal convoluted tubule. Mg transport in the connecting tubule has not been well quantified. Little reabsorption occurs and no evidence exists of Mg secretion within the collecting duct. Normally, 95% of the filtered Mg is reabsorbed by the nephron. In states of Mg depletion the fractional excretion of Mg can decrease to less than 1%; whereas Mg excretion can increase in states of above-normal Mg intake, provided no evidence of renal failure exists [1,2,6–9,11,12].

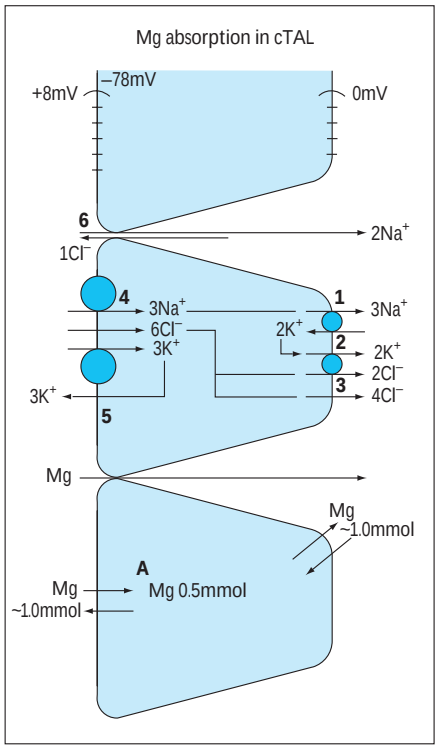


FIGURE 4-10

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].)

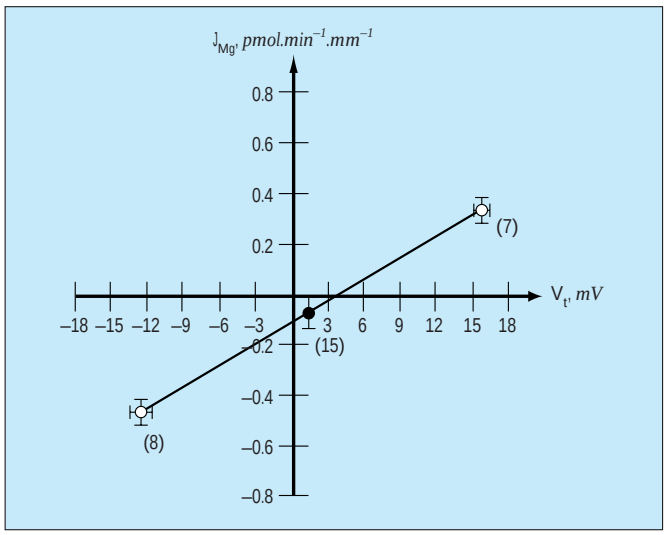


FIGURE 4-11

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]).

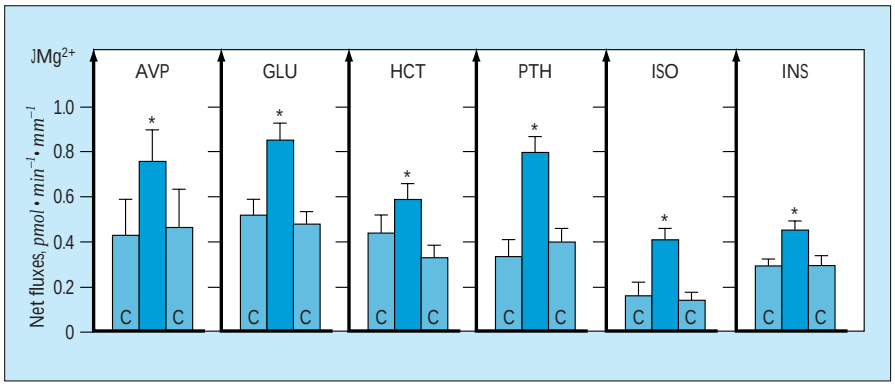


FIGURE 4-12
Effect of hormones on magnesium (Mg) transport in the cortical thick ascending limb (cTAL). In the presence of arginine vasopressin (AVP), glucagon (GLU), human calcitonin (HCT), parathyroid hormone (PTH), 1,4,5-isoproteronol (ISO), and insulin (INS), increases occur in Mg reabsorption from 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
- Starvation
- Anorexia
- Protein calorie malnutrition
- 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

Other
- Lactation
- Extensive burns
- Exchange transfusions

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].

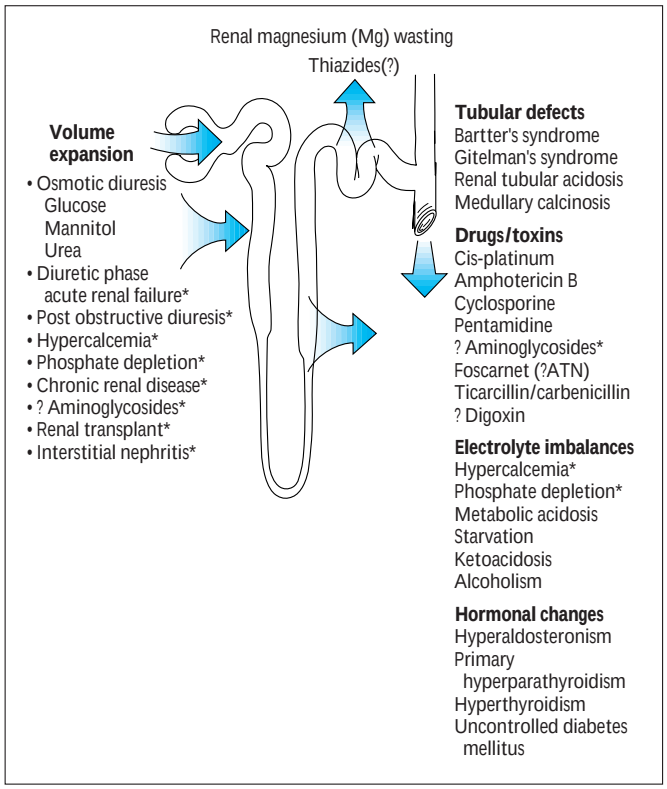


FIGURE 4-14

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

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 D_3 into 1,25-dihydroxy-vitamin D_3, 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].

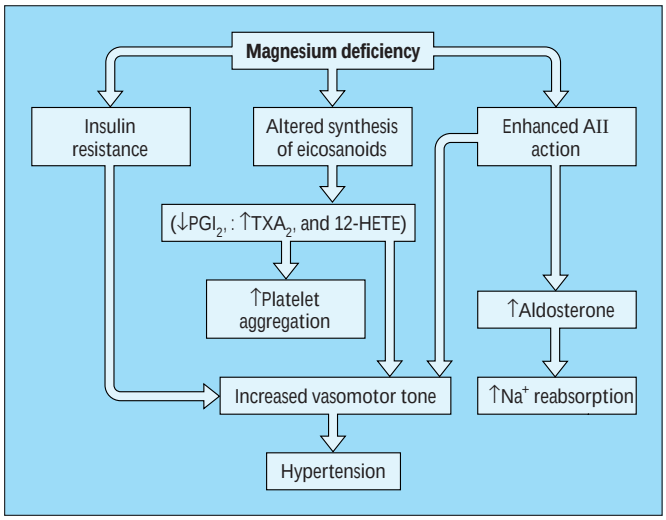


FIGURE 4-16

Mechanism whereby magnesium (Mg) deficiency could lead to hypertension. Mg deficiency does the following: increases angiotensin II (AII) action, decreases levels of vasodilatory prostaglandins (PGs), increases levels of vasoconstrictive PGs and growth factors, increases vascular smooth muscle cytosolic calcium, impairs insulin release, produces insulin resistance, and alters lipid profile. All of these results of Mg deficiency favor the development of hypertension and atherosclerosis [10,11]. Na^+—ionized sodium; 12-HETE—hydroxy-eicosatetraenoic [acid]; TXA_2—thromboxane A2. (*From* Nadler and coworkers [17].)

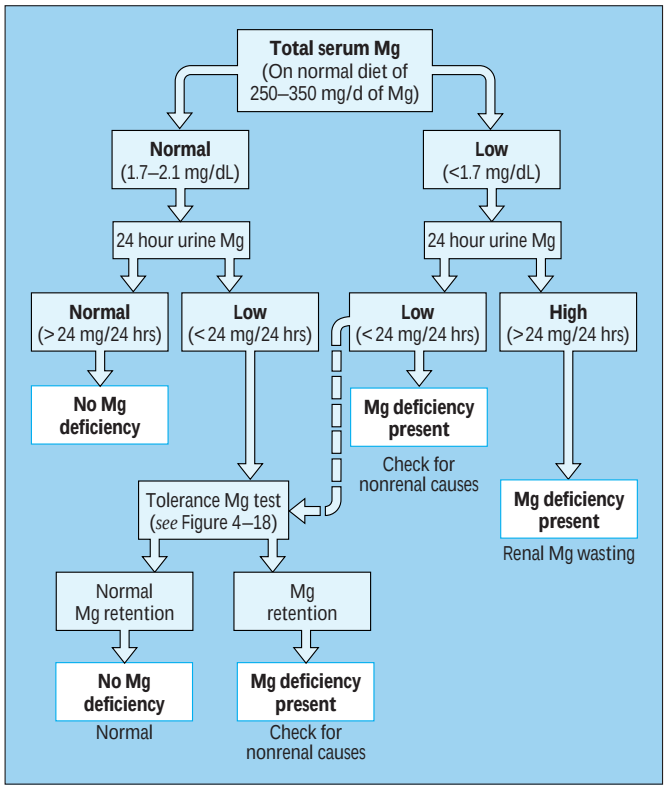


FIGURE 4-17

Evaluation in suspected magnesium (Mg) deficiency. Serum Mg levels may not always indicate total body stores. More refined tools used to assess the status of Mg in erythrocytes, muscle, lymphocytes, bone, isotope studies, and indicators of intracellular Mg, are not routinely available. Screening for Mg deficiency relies on the fact that urinary Mg decreases rapidly in the face of Mg depletion in the presence of normal renal function [2,6,8–15,18]. (*Adapted from* Al-Ghamdi and coworkers [11].)

MAGNESIUM (Mg) TOLERANCE TEST FOR PATIENTS WITH NORMAL SERUM MAGNESIUM

Time	Action
0 (baseline)	Urine (spot or timed) for molar Mg:Cr ratio
0–4 h	IV infusion of 2.4 mg (0.1 mmol) of Mg/kg lean body wt in 50 mL of 50% dextrose
0–24 h	Collect urine (staring with Mg infusion) for Mg and Cr
End	Calculate % Mg retained (%M)

$$\%\,M = 1 - \frac{(\text{24-h urine Mg}) - ([\text{Preinfusion urine Mg:Cr}] \times [\text{24-h urine Cr}])}{\text{Total Mg infused}} \times 100$$

Mg retained, %	Mg deficiency
>50	Definite
20–50	Probable
<20	None

Cr—creatinine; IV—intravenous; Mg—magnesium.

FIGURE 4-18

The magnesium (Mg) tolerance test, in various forms [2,6,8–12,18], has been advocated to diagnose Mg depletion in patients with normal or near-normal serum Mg levels. All such tests are predicated on the fact that patients with normal Mg status rapidly excrete over 50% of an acute Mg load; whereas patients with depleted Mg retain Mg in an effort to replenish Mg stores. (*From* Ryzen and coworkers [18].)

MAGNESIUM SALTS USED IN MAGNESIUM REPLACEMENT THERAPY

Magnesium salt	Chemical formula	Mg content, mg/g	Examples*	Mg content	Diarrhea
Gluconate	$Cl_2H_{22}MgO_{14}$	58	Magonate®	27-mg tablet 54 mg/5 mL	±
Chloride	$MgCl_2 . (H_2O)_6$	120	Mag-L-100	100-mg capsule	+
Lactate	$C_6H_{10}MgO_6$	120	MagTab SR*	84-mg caplet	+
Citrate	$C_{12}H_{10}Mg_3O_{14}$	53	Multiple	47–56 mg/5 mL	++
Hydroxide	$Mg(OH)_2$	410	Maalox®, Mylanta®, Gelusil® Riopan®	83 mg/ 5 mL and 63-mg tablet 96 mg/5 mL	++
Oxide	MgO	600	Mag-Ox 400® Uro-Mag® Beelith®	241-mg tablet 84.5-mg tablet 362-mg tablet	++
Sulfate	$MgSO_4 . (H_2O)_7$	100	IV IV Oral epsom salt	10%—9.9 mg/mL 50%—49.3 mg/mL 97 mg/g	++ ++
Milk of Magnesia			Phillips' Milk of Magnesia®	168 mg/ 5 mL	++

Data from McLean [9], Al-Ghamdi and coworkers [11], Oster and Epstein [19], and Physicians' Desk Reference [20].

*Magonate®, Fleming & Co, Fenton, MD; MagTab Sr®, Niche Pharmaceuticals, Roanoke, TX; Maalox®, Rhone-Poulenc Rorer Pharmaceutical, Collegeville, PA; Mylanta®, J & J-Merck Consumer Pharm, Ft Washinton, PA; Riopan®, Whitehall Robbins Laboratories, Madison, NJ; Mag-Ox 400® and Uro-Mag®, Blaine, Erlanger, KY; Beelith®, Beach Pharmaceuticals, Conestee, SC; Phillips' Milk of Magnesia, Bayer Corp, Parsippany, NJ.

FIGURE 4-19

Magnesium (Mg) salts that may be used in Mg replacement therapy.

GUIDELINES FOR MAGNESIUM (Mg) REPLACEMENT

Life-threatening event, eg, seizures and cardiac arrhythmia

I. 2–4 g $MgSO_4$ IV or IM stat
(2–4 vials [2 mL each] of 50% $MgSO_4$)
Provides 200–400 mg of Mg (8.3–16.7 mmol Mg)
Closely monitor:
- Deep tendon reflexes
- Heart rate
- Blood pressure
- Respiratory rate
- Serum Mg (<2.5 mmol/L [6.0 mg/dL])
- Serum K

II. IV drip over first 24 h to provide no more than 1200 mg (50 mmol) Mg/24 h

Subacute and chronic Mg replacement

I. 400–600 mg (16.7–25 mmol Mg daily for 2–5 d)
IV: continuous infusion
IM: painful
Oral: use divided doses to minimize diarrhea

FIGURE 4-20

Acute Mg replacement for life-threatening events such as seizures or potentially lethal cardiac arrhythmias has been described [8–12,19]. Acute increases in the level of serum Mg can cause nausea, vomiting, cutaneous flushing, muscular weakness, and hyporeflexia. As Mg levels increase above 6 mg/dL (2.5 mmol/L), electrocardiographic changes are followed, in sequence, by hyporeflexia, respiratory paralysis, and cardiac arrest. Mg should be administered with caution in patients with renal failure. In the event of an emergency the acute Mg load should be followed by an intravenous (IV) infusion, providing no more than 1200 mg (50 mmol) of Mg on the first day. This treatment can be followed by another 2 to 5 days of Mg repletion in the same dosage, which is used in less urgent situations. Continuous IV infusion of Mg is preferred to both intramuscular (which is painful) and oral (which causes diarrhea) administration. A continuous infusion avoids the higher urinary fractional excretion of Mg seen with intermittent administration of Mg. Patients with mild Mg deficiency may be treated with oral Mg salts rather than parenteral Mg and may be equally efficacious [8]. Administration of Mg sulfate may cause kaliuresis owing to excretion of the nonreabsorbable sulfate anion; Mg oxide administration has been reported to cause significant acidosis and hyperkalemia [19]. Parenteral Mg also is administered (often in a manner different from that shown here) to patients with preeclampsia, asthma, acute myocardial infarction, and congestive heart failure.

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