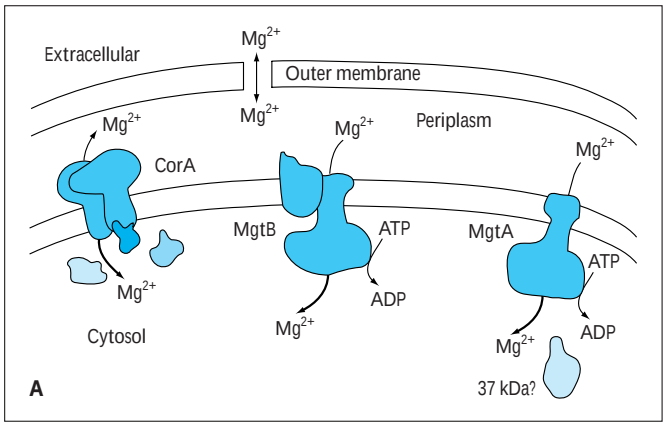
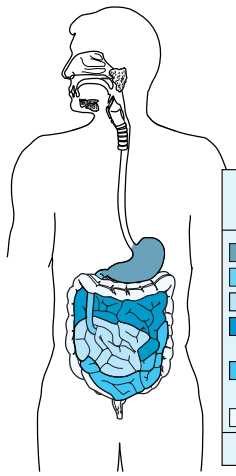


FIGURE 4-4

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].

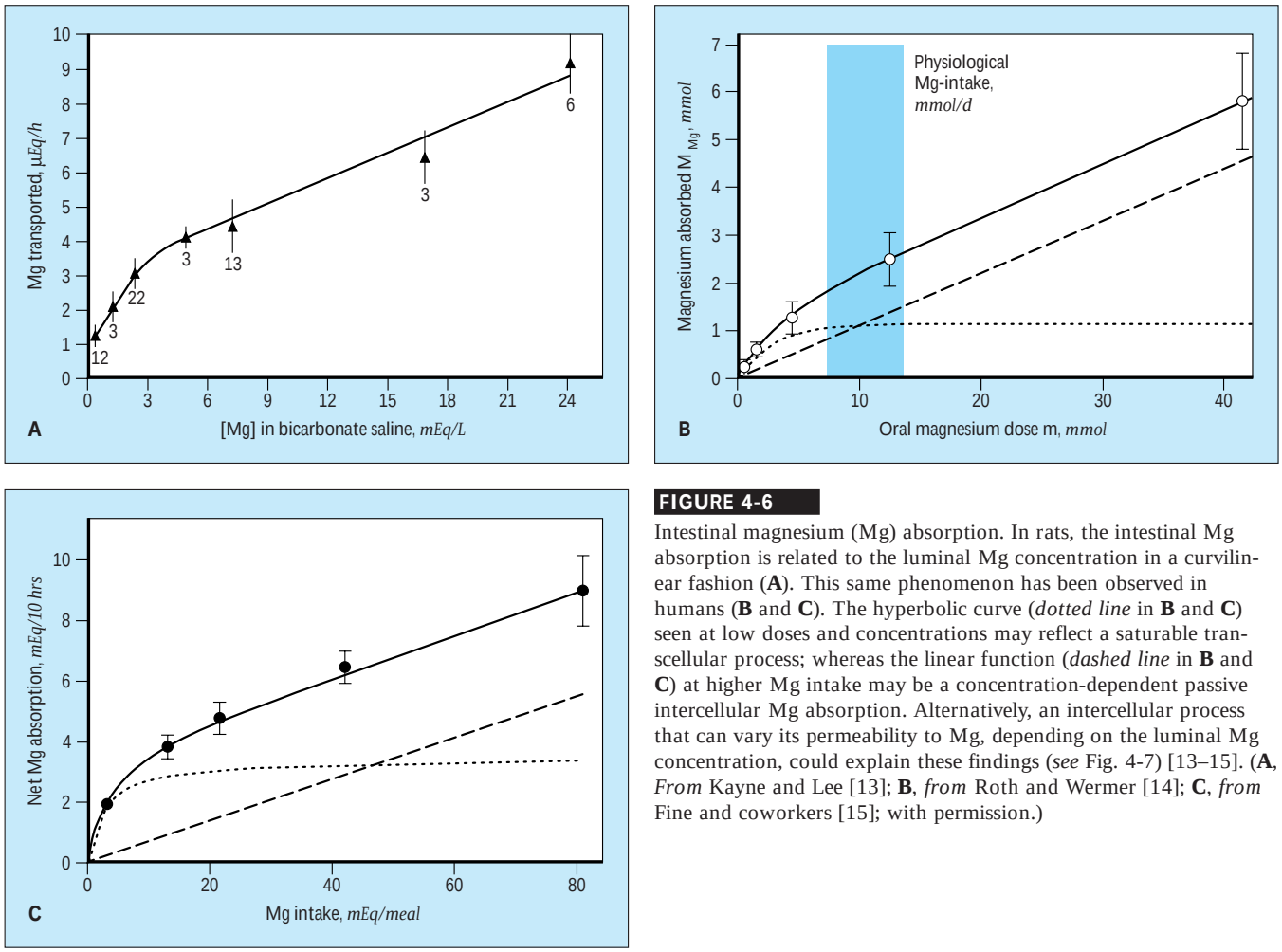


FIGURE 4-6

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.)

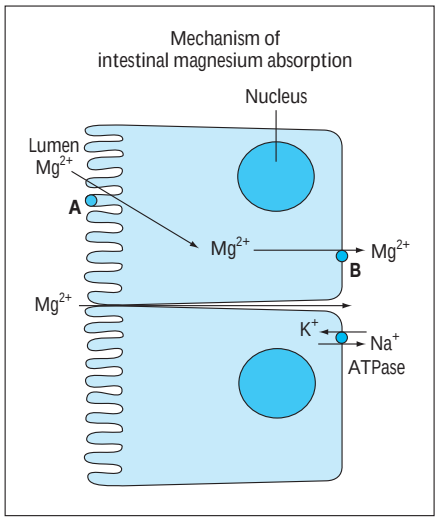


FIGURE 4-7

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

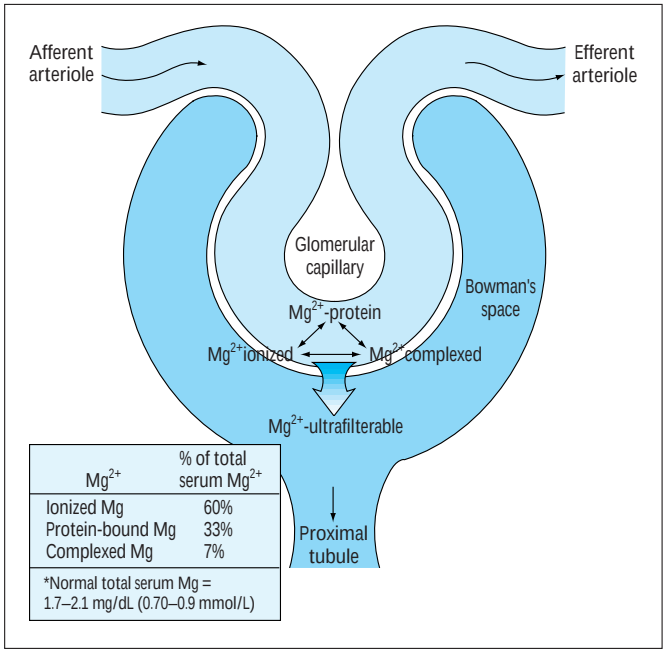


FIGURE 4-8

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].

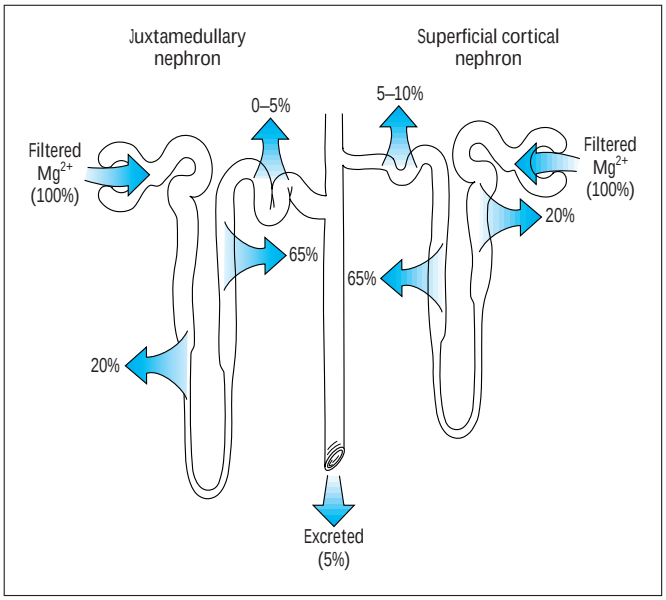


FIGURE 4-9

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].