Magnesium and the Kidney: Overview

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Normal human serum magnesium concentration is about 0.7 to 0.85 mmol/L. About 20% to 30% of serum magnesium is protein bound; this leaves 70% to 80% that is ultrafiltrable, which in turn is made up of 55% ionized magnesium and 15% magnesium complexed with anions such as phosphate and citrate. About 100 to 120 mmol per day is filtered, and about 4 to 6 mmol is excreted, so that about 95% of the glomerular filtrate is re-absorbed.

The renal handling of magnesium in humans is a filtration–resorption process; there is no tubular secretion of magnesium. About 15% to 20% of the filtered magnesium is re-absorbed in the proximal convoluted tubule. Then approximately 65% to 75% of filtered magnesium is re-absorbed in the thick cortical ascending loop of Henle. Another 5% to 10% is re-absorbed in the distal convoluted tubule. Finally the collecting duct is only a minor site for magnesium re-absorption.

Magnesium re-absorption in the proximal tubule appears to be passive. It follows changes in salt and water re-absorption and is associated with the rate of fluid flow. In the loop of Henle, there appears to be an additional active transport system; a decrease in magnesium re-absorption in this segment is independent of sodium chloride transport in either hypermagnesemia or hypercalcemia. Recently, a protein, claudin 16, has been identified in the thick ascending loop of Henle (TALH) that forms a tight junction of the paracellular pathway. Magnesium is re-absorbed in the distal convoluted tubule (DCT) through a transcellular, active transport process. In the DCT, magnesium transport into the cytosol is through selective channels and extrusion into the interstitium and is apparently mediated by a sodium/magnesium cotransporter. In vivo studies in animals and humans have demonstrated a tubular maximum for magnesium that reflects a composite of these tubular re-absorptive processes.

The role of the kidney in conserving magnesium during chronic mild magnesium deficiency is controversial. During acute experimental magnesium depletion in humans, urinary magnesium decreases to very low levels, less than 1 mmol/day within 3 to 4 days. However, the effects of long-term low dietary magnesium intake on renal conservation have been little studied. The few studies available are reviewed in the Dietary Reference Intakes.
Despite the tight regulation of magnesium by the kidney, no one has described a dominant hormone or factor that is responsible for renal magnesium homeostasis. Because patients with either primary hyper- or hypoparathyroidism usually have normal serum magnesium concentrations and a normal tubular maximum for magnesium, it is unlikely that parathyroid hormone (PTH) is an important regulator of magnesium homeostasis. Although PTH increases magnesium re-absorption, the PTH-induced hypercalcemia opposes this increase in re-absorption. Glucagon, calcitonin, vasopressin, aldosterone, prostaglandins, insulin, and vitamin D also affect magnesium transport in the loop of Henle, but their physiological relevance is uncertain.²

The calcium-sensing receptor is also sensitive to magnesium, so an elevated serum magnesium concentration will decrease potassium movement into the lumen of the TALH, leading to a decreased lumen-positive voltage and a decrease in magnesium re-absorption.²

**Diet and Drugs Affect Urinary Magnesium Excretion**

Any changes in the cotransport of sodium, chloride, and potassium, as well as active sodium re-absorption, results in changes in the transepithelial voltages in the loop of Henle, which will affect magnesium re-absorption. Although acutely increased dietary sodium chloride increases magnesium excretion, the chronic effects are largely unstudied.

Caffeine acutely increases urinary magnesium excretion relative to creatinine excretion for 9 h after its consumption.⁶ Night time compensatory conservation was insufficient to offset these losses, resulting in a net 24-h urinary increase of 0.16 mm of magnesium Adaptation of magnesium homeostasis to chronic consumption of caffeine is unstudied.

Diuretic therapy affects magnesium renal handling. Loop diuretics, such as furosemide, decrease magnesium absorption in the TALH by inhibiting sodium–potassium–chlorine movement into the cell, resulting in a diminished transepithelial voltage that leads to a decrease in both calcium and magnesium re-absorption. Whereas amiloride and tramterene increase magnesium transport in the DCT, chronic chlorothiazide use may result in renal magnesium wasting. These diuretics, which are used commonly in the treatment of hypertension, heart failure, and other edematous states, may cause hypermagnesuria, leading to possible hypomagnesemia and tissue magnesium deficiency.⁷

**Diseases Impacted by Abnormal Urinary Magnesium**

Magnesium depletion is a common feature of diabetes mellitus, apparently related to glycemic control. Djurhuss and colleagues⁸ directly showed the hypermagnesuric effect of elevated blood glucose by infusing 200% glucose into 10 patients with type 1 diabetes. Blood glucose increased from 5.3 to