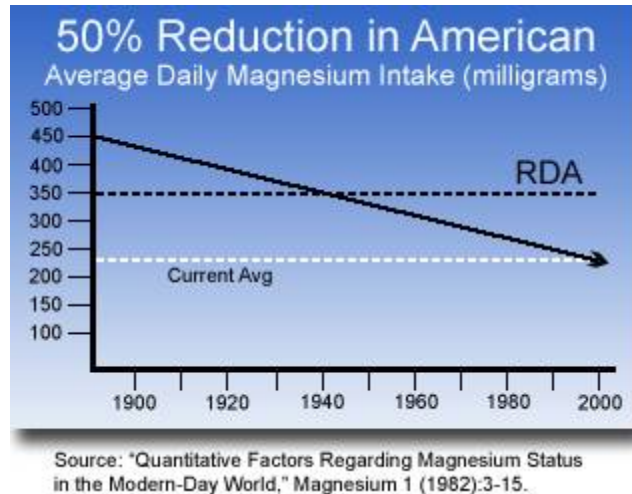


In 2006, the World Health Organization reached consensus that a majority of the world's population is magnesium deficient. Likewise, in 1995, the Gallop Organization conducted a survey and found that 72% of adult Americans consume less than the Recommended Daily Allowance for Magnesium.



Magnesium: What is it?

Magnesium is the fourth most abundant mineral in the body and is essential to good health. Approximately 50% of total body magnesium is found in bone. The other half is found predominantly inside cells of body tissues and organs. Only 1% of magnesium is found in blood, but the body works very hard to keep blood levels of magnesium constant [1].

Magnesium is needed for more than 300 biochemical reactions in the body. It helps maintain normal muscle and nerve function, keeps heart rhythm steady, supports a healthy immune system, and keeps bones strong. Magnesium also helps regulate blood sugar levels, promotes normal blood pressure, and is known to be involved in energy metabolism and protein synthesis [2-3]. There is an increased interest in the role of magnesium in preventing and managing disorders such as hypertension, cardiovascular disease, and diabetes. Dietary magnesium is absorbed in the small intestines. Magnesium is excreted through the kidneys [1-3,4].

What foods provide magnesium?

Green vegetables such as spinach are good sources of magnesium because the center of the chlorophyll molecule (which gives green vegetables their color) contains magnesium. Some legumes (beans and peas), nuts and seeds, and whole, unrefined grains are also good sources of magnesium [5]. Refined grains are generally low in magnesium [4-5]. When white flour is refined and processed, the magnesium-rich germ and bran are removed. Bread made from whole grain wheat flour provides more magnesium than bread made from white refined flour. Tap water can be a source of magnesium, but the amount varies according to the water

supply. Water that naturally contains more minerals is described as "hard". "Hard" water contains more magnesium than "soft" water.

Data from the 1999-2000 National Health and Nutrition Examination Survey suggest that substantial numbers of adults in the United States (US) fail to get recommended amounts of magnesium in their diets. Among adult men and women, the diets of Caucasians have significantly more magnesium than do those of African-Americans. Magnesium intake is lower among older adults in every racial and ethnic group. Among African-American men and Caucasian men and women who take dietary supplements, the intake of magnesium is significantly higher than in those who do not [6].

When can magnesium deficiency occur?

Even though dietary surveys suggest that many Americans do not get recommended amounts of magnesium, symptoms of magnesium deficiency are rarely seen in the US. However, there is concern that many people may not have enough body stores of magnesium because dietary intake may not be high enough. Having enough body stores of magnesium may be protective against disorders such as cardiovascular disease and immune dysfunction [7-8].

The health status of the digestive system and the kidneys significantly influence magnesium status. Magnesium is absorbed in the intestines and then transported through the blood to cells and tissues. Approximately one-third to one-half of dietary magnesium is absorbed into the body [9-10]. Gastrointestinal disorders that impair absorption such as Crohn's disease can limit the body's ability to absorb magnesium. These disorders can deplete the body's stores of magnesium and in extreme cases may result in magnesium deficiency. Chronic or excessive vomiting and diarrhea may also result in magnesium depletion [1,10].

Healthy kidneys are able to limit urinary excretion of magnesium to make up for low dietary intake. However, excessive loss of magnesium in urine can be a side effect of some medications and can also occur in cases of poorly-controlled diabetes and alcohol abuse [11-18].

Early **signs of magnesium deficiency** include loss of appetite, nausea, vomiting, fatigue, and weakness. As magnesium deficiency worsens, numbness, tingling, muscle contractions and cramps, seizures (sudden changes in behaviors caused by excessive electrical activity in the brain), personality changes, abnormal heart rhythms, and coronary spasms can occur [1,3-4]. Severe magnesium deficiency can result in low levels of calcium in the blood (hypocalcemia). Magnesium deficiency is also associated with low levels of potassium in the blood (hypokalemia) [1,19-20].

Many of these symptoms are general and can result from a variety of medical conditions other than magnesium deficiency. It is important to have a physician evaluate health complaints and problems so that appropriate care can be given.

Who may need extra magnesium?

Magnesium supplementation may be indicated when a specific health problem or condition causes an excessive loss of magnesium or limits magnesium absorption [2,7,9-11].

- Some medicines may result in magnesium deficiency, including certain diuretics, antibiotics, and medications used to treat cancer (anti-neoplastic medication) [12,14,19]. Examples of these medications are:
 - Diuretics: Lasix, Bumex, Edecrin, and hydrochlorothiazide
 - Antibiotics: Gentamicin, and Amphotericin
 - Anti-neoplastic medication: Cisplatin
- Individuals with poorly-controlled diabetes may benefit from magnesium supplements because of increased magnesium loss in urine associated with hyperglycemia [21].
- Magnesium supplementation may be indicated for persons with alcoholism. Low blood levels of magnesium occur in 30% to 60% of alcoholics, and in nearly 90% of patients experiencing alcohol withdrawal [17-18]. Anyone who substitutes alcohol for food will usually have significantly lower magnesium intakes.
- Individuals with chronic malabsorptive problems such as Crohn's disease, gluten sensitive enteropathy, regional enteritis, and intestinal surgery may lose magnesium through diarrhea and fat malabsorption [22]. Individuals with these conditions may need supplemental magnesium.
- Individuals with chronically low blood levels of potassium and calcium may have an underlying problem with magnesium deficiency. Magnesium supplements may help correct the potassium and calcium deficiencies [19].
- Older adults are at increased risk for magnesium deficiency. The 1999-2000 and 1998-94 National Health and Nutrition Examination Surveys suggest that older adults have lower dietary intakes of magnesium than younger adults [6,23]. In addition, magnesium absorption decreases and renal excretion of magnesium increases in older adults [4]. Seniors are also more likely to be taking drugs that interact with magnesium. This combination of factors places older adults at risk for magnesium deficiency [4]. It is very important for older adults to get recommended amounts of dietary magnesium.

Magnesium and blood pressure

"Epidemiologic evidence suggests that magnesium may play an important role in regulating blood pressure [4]." Diets that provide plenty of fruits and vegetables, which are good sources of potassium and magnesium, are consistently associated with lower blood pressure [31-33]. The DASH study (Dietary Approaches to Stop Hypertension), a human clinical trial, suggested that high blood pressure could be significantly lowered by a diet that emphasizes fruits, vegetables, and low fat dairy foods. Such a diet will be high in magnesium, potassium, and calcium, and low in sodium and fat [34-36].

An observational study examined the effect of various nutritional factors on incidence of high blood pressure in over 30,000 US male health professionals. After four years of follow-up, it was found that a lower risk of hypertension was associated with dietary patterns that provided more magnesium, potassium, and dietary fiber [37]. For 6 years, the Atherosclerosis Risk in Communities (ARIC) Study followed approximately 8,000 men

and women who were initially free of hypertension. In this study, the risk of developing hypertension decreased as dietary magnesium intake increased in women, but not in men [38].

Foods high in magnesium are frequently high in potassium and dietary fiber. This makes it difficult to evaluate the independent effect of magnesium on blood pressure. However, newer scientific evidence from DASH clinical trials is strong enough that the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure states that diets that provide plenty of magnesium are positive lifestyle modifications for individuals with hypertension. This group recommends the DASH diet as a beneficial eating plan for people with hypertension and for those with "prehypertension" who desire to prevent high blood pressure <http://www.nhlbi.nih.gov/health/public/heart/hbp/dash/> [39-41].

Magnesium and diabetes

Diabetes is a disease resulting in insufficient production and/or inefficient use of insulin. Insulin is a hormone made by the pancreas. Insulin helps convert sugar and starches in food into energy to sustain life. There are two types of diabetes: type 1 and type 2. Type 1 diabetes is most often diagnosed in children and adolescents, and results from the body's inability to make insulin. Type 2 diabetes, which is sometimes referred to as adult-onset diabetes, is the most common form of diabetes. It is usually seen in adults and is most often associated with an inability to use the insulin made by the pancreas. Obesity is a risk factor for developing type 2 diabetes. In recent years, rates of type 2 diabetes have increased along with the rising rates of obesity.

Magnesium plays an important role in carbohydrate metabolism. It may influence the release and activity of insulin, the hormone that helps control blood glucose (sugar) levels [13]. Low blood levels of magnesium (hypomagnesemia) are frequently seen in individuals with type 2 diabetes. Hypomagnesemia may worsen insulin resistance, a condition that often precedes diabetes, or may be a consequence of insulin resistance. Individuals with insulin resistance do not use insulin efficiently and require greater amounts of insulin to maintain blood sugar within normal levels. The kidneys possibly lose their ability to retain magnesium during periods of severe hyperglycemia (significantly elevated blood glucose). The increased loss of magnesium in urine may then result in lower blood levels of magnesium [4]. In older adults, correcting magnesium depletion may improve insulin response and action [42].

The Nurses' Health Study (NHS) and the Health Professionals' Follow-up Study (HFS) follow more than 170,000 health professionals through questionnaires the participants complete every 2 years. Diet was first evaluated in 1980 in the NHS and in 1986 in the HFS, and dietary assessments have been completed every 2 to 4 years since. Information on the use of dietary supplements, including multivitamins, is also collected. As part of these studies, over 127,000 participants (85,060 women and 42,872 men) with no history of diabetes, cardiovascular disease, or cancer at baseline were

followed to examine risk factors for developing type 2 diabetes. Women were followed for 18 years; men were followed for 12 years. Over time, the risk for developing type 2 diabetes was greater in men and women with a lower magnesium intake. This study supports the dietary recommendation to increase consumption of major food sources of magnesium, such as whole grains, nuts, and green leafy vegetables [43].

The Iowa Women's Health Study has followed a group of older women since 1986. Researchers from this study examined the association between women's risk of developing type 2 diabetes and intake of carbohydrates, dietary fiber, and dietary magnesium. Dietary intake was estimated by a food frequency questionnaire, and incidence of diabetes throughout 6 years of follow-up was determined by asking participants if they had been diagnosed by a doctor as having diabetes. Based on baseline dietary intake assessment only, researchers' findings suggested that a greater intake of whole grains, dietary fiber, and magnesium decreased the risk of developing diabetes in older women [44].

The Women's Health Study was originally designed to evaluate the benefits versus risks of low-dose aspirin and vitamin E supplementation in the primary prevention of cardiovascular disease and cancer in women 45 years of age and older. In an examination of almost 40,000 women participating in this study, researchers also examined the association between magnesium intake and incidence of type 2 diabetes over an average of 6 years. Among women who were overweight, the risk of developing type 2 diabetes was significantly greater among those with lower magnesium intake [45]. This study also supports the dietary recommendation to increase consumption of major food sources of magnesium, such as whole grains, nuts, and green leafy vegetables.

On the other hand, the Atherosclerosis Risk in Communities (ARIC) study did not find any association between dietary magnesium intake and the risk for type 2 diabetes. During 6 years of follow-up, ARIC researchers examined the risk for type 2 diabetes in over 12,000 middle-aged adults without diabetes at baseline examination. In this study, there was no association between dietary magnesium intake and incidence of type 2 diabetes in either black or white participants [46]. It can be confusing to read about studies that examine the same issue but have different results. Before reaching a conclusion on a health issue, scientists conduct and evaluate many studies. Over time, they determine when results are consistent enough to suggest a conclusion. They want to be sure they are providing correct recommendations to the public.

Several clinical studies have examined the potential benefit of supplemental magnesium on control of type 2 diabetes. In one such study, 63 subjects with below normal serum magnesium levels received either 2.5 grams of oral magnesium chloride daily "in liquid form" (providing 300 mg elemental magnesium per day) or a placebo. At the end of the 16-week study period, those who received the magnesium supplement had higher blood levels of magnesium and improved control of diabetes, as suggested by lower

hemoglobin A1C levels, than those who received a placebo [47]. Hemoglobin A1C is a test that measures overall control of blood glucose over the previous 2 to 3 months, and is considered by many doctors to be the single most important blood test for diabetics.

In another study, 128 patients with poorly controlled type 2 diabetes were randomized to receive a placebo or a supplement with either 500 mg or 1000 mg of magnesium oxide (MgO) for 30 days. All patients were also treated with diet or diet plus oral medication to control blood glucose levels. Magnesium levels increased in the group receiving 1000 mg magnesium oxide per day (equal to 600 mg elemental magnesium per day) but did not significantly change in the placebo group or the group receiving 500 mg of magnesium oxide per day (equal to 300 mg elemental magnesium per day). However, neither level of magnesium supplementation significantly improved blood glucose control [48].

These studies provide intriguing results but also suggest that additional research is needed to better explain the association between blood magnesium levels, dietary magnesium intake, and type 2 diabetes. In 1999, the American Diabetes Association (ADA) issued nutrition recommendations for diabetics stating that "routine evaluation of blood magnesium level is recommended only in patients at high risk for magnesium deficiency. Levels of magnesium should be [replaced] only if hypomagnesemia can be demonstrated" [21].

Magnesium and cardiovascular disease

Magnesium metabolism is very important to insulin sensitivity and blood pressure regulation, and magnesium deficiency is common in individuals with diabetes. The observed associations between magnesium metabolism, diabetes, and high blood pressure increase the likelihood that magnesium metabolism may influence cardiovascular disease [49].

Some observational surveys have associated higher blood levels of magnesium with lower risk of coronary heart disease [50-51]. In addition, some dietary surveys have suggested that a higher magnesium intake may reduce the risk of having a stroke [52]. There is also evidence that low body stores of magnesium increase the risk of abnormal heart rhythms, which may increase the risk of complications after a heart attack [4]. These studies suggest that consuming recommended amounts of magnesium may be beneficial to the cardiovascular system. They have also prompted interest in clinical trials to determine the effect of magnesium supplements on cardiovascular disease.

Several small studies suggest that magnesium supplementation may improve clinical outcomes in individuals with coronary disease. In one of these studies, the effect of magnesium supplementation on exercise tolerance (the ability to walk on a treadmill or ride a bicycle), chest pain caused by exercise, and quality of life was examined in 187 patients. Patients received either a placebo or a supplement providing 365 milligrams of magnesium citrate twice daily for 6 months. At the end of the study period researchers

found that magnesium therapy significantly increased magnesium levels. Patients receiving magnesium had a 14 percent improvement in exercise duration as compared to no change in the placebo group. Those receiving magnesium were also less likely to experience chest pain caused by exercise [53].

In another study, 50 men and women with stable coronary disease were randomized to receive either a placebo or a magnesium supplement that provided 342 mg magnesium oxide twice daily. After 6 months, those who received the oral magnesium supplement were found to have improved exercise tolerance [54].

In a third study, researchers examined whether magnesium supplementation would add to the anti-thrombotic (anti-clotting) effects of aspirin in 42 coronary patients [55]. For three months, each patient received either a placebo or a supplement with 400 mg of magnesium oxide two to three times daily. After a four-week break without any treatment, treatment groups were reversed so that each person in the study then received the alternate treatment for three months. Researchers found that supplemental magnesium did provide an additional anti-thrombotic effect.

These studies are encouraging, but involved small numbers. Additional studies are needed to better understand the complex relationships between magnesium intake, indicators of magnesium status, and heart disease. Doctors can evaluate magnesium status when above-mentioned medical problems occur, and determine the need for magnesium supplementation.

Magnesium and osteoporosis

Bone health is supported by many factors, most notably calcium and vitamin D. However, some evidence suggests that magnesium deficiency may be an additional risk factor for postmenopausal osteoporosis [4]. This may be due to the fact that magnesium deficiency alters calcium metabolism and the hormones that regulate calcium (20). Several human studies have suggested that magnesium supplementation may improve bone mineral density [4]. In a study of older adults, a greater magnesium intake maintained bone mineral density to a greater degree than a lower magnesium intake [56]. Diets that provide recommended levels of magnesium are beneficial for bone health, but further investigation on the role of magnesium in bone metabolism and osteoporosis is needed.

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