

Life Extension Magazine December 2014

Report

# **Magnesium The Missing Link To A Healthy Heart**

By Jennifer Dawson

Cardiovascular disease remains the leading cause of death in the US.<sup>1</sup>

With nearly half the US population consuming less than the recommended amount of magnesium in their diets,<sup>2</sup> this widespread **magnesium deficiency** is a commonly overlooked risk factor for cardiovascular disease.<sup>3</sup> Studies demonstrate that the lower your intake of magnesium, the greater your risk of succumbing to cardiovascular disease.<sup>4</sup>



Research has shown that magnesium supplementation can be therapeutic for a range of cardiac factors including arrhythmias, hypertension, atherosclerosis, and endothelial dysfunction.<sup>3,5</sup>

Even a *moderate* magnesium deficiency can cause profound changes in how the heart, blood vessels, blood cells, intestinal tract, and other tissues function.<sup>6</sup> This is because magnesium is critical for tissues that have electrical or mechanical activity, such as nerves, muscles (including the heart), and blood vessels.<sup>5,7,8</sup>

Experiencing a heart attack or stroke because of a simple magnesium deficiency does not need to happen. In this article we provide important information to protect yourself from unnecessary cardiac events.

## Are You At Risk Of Magnesium Deficiency?

Nearly half of the US population consumes less than the recommended amount of magnesium in their diet.<sup>2</sup>

Inadequate dietary intake is one reason why magnesium deficit is so prevalent in the elderly. Older people have reduced magnesium absorption in their intestines, reduced stores of magnesium in their bones, and increased magnesium losses in their urine. This correctable deficiency exposes the aging population to an *entirely preventable* cardiovascular risk factor. <sup>10</sup>

Magnesium deficit is also responsible for inflammation, endothelial dysfunction, type II diabetes, excessive platelet "clumping," and other changes that put your heart—and your life—at risk.9

# Magnesium Deficit Increases Cardiovascular Risk

Because magnesium is essential for healthy control of blood vessel function, blood pressure regulation, and normal heart contractions, a deficiency in magnesium increases risk of conditions such as endothelial dysfunction, hypertension, and cardiacarrythmias.<sup>3</sup>

# **Arrhythmias**

Low magnesium levels raise the risk of developing potentially fatal disorders of heart rhythm, known as *cardiac* 



arrhythmias. 4,11-13

There are many different kinds of arrhythmias, but all have one thing in common: They involve abnormal conduction of the electrical impulses that govern heartbeat and heart rate. Such electrical disturbances in turn result in a heart rate that is irregular, or too fast or too slow.<sup>14</sup>

Mild arrhythmias may simply cause discomfort when the heartbeat can be felt in palpitations, while ones that are more serious can cause cardiac arrest or fibrillation, in which the beating chambers of the heart either stop entirely or result in an irregular heartbeat.<sup>14</sup>

The deadliest arrhythmias involve the major pumping chambers of the heart, the ventricles, while milder, more chronic arrhythmias involve the upper chambers, or atria. Atrial arrhythmias can also degenerate into dangerous atrial fibrillation or flutter, in which slow blood flow can produce clots that travel to the brain, lungs, or other vulnerable areas. <sup>14</sup>

Many arrhythmias are managed by drug therapies aimed at restoring normal electrical activity in the heart. These drugs, however, by their very nature can be dangerous and can easily overshoot their goals, resulting in actual increases or changes to more dangerous arrhythmias.<sup>14</sup>

This cause-and-effect can be particularly dangerous in people with congestive heart failure, who may take diuretic drugs ("water pills") that cause them to lose magnesium at a high rate, <sup>15</sup> raising their already high risk for arrhythmias. <sup>12</sup> Similarly, coronary artery bypass surgery, a procedure still used for many people with severe atherosclerosis of the heart's blood vessels, is known to lower magnesium levels and raise the risk of arrhythmias. <sup>16</sup>

In one study, 13 women consumed an experimental diet low in magnesium.<sup>17</sup> Three of the women (23%) developed arrhythmias (atrial fibrillation and atrial flutter), in which the upper pumping chambers of the heart lose their normal beating pattern, and four (31%) had to begin magnesium repletion by supplementation earlier than scheduled.

Fortunately, magnesium supplementation readily corrects drug-induced or other low magnesium-related arrhythmias. Supplementation is now routinely used *before* many kinds of heart surgery that are known to induce postoperative arrhythmias, and is also recommended for people with chronic arrhythmias having known low magnesium levels. 19-22

Research suggests magnesium supplementation can combat that risk by restoring healthy heart cell electrical functions, fighting the development of arrhythmias at its source.<sup>23</sup>

Emergency departments have used intravenous magnesium infusions to reduce dangerously rapid heart rates in patients with a common arrhythmia called **rapid atrial fibrillation**.<sup>24</sup> In addition, giving oral magnesium supplements in the days before surgery has proven to have similar benefits to infusion of magnesium during surgery in preventing dangerous arrhythmias in patients undergoing open heart surgery.<sup>25</sup>

A recent study evaluated the use of oral magnesium supplements in preventing **premature ventricular contractions** (often called PVCs), which have been described as feeling like a "punch in the chest" and have the potential of converting into serious, life-threatening arrhythmias. For the study, patients with known PVCs were randomly assigned to receive a placebo or **3 grams** of magnesium pidolate delivering **260 mg** of magnesium daily. After 30 days, **76.6%** of the supplemented group showed a significant reduction in daily arrhythmia episodes, while only **40%** of placebo recipients showed slight improvement. <sup>26</sup>

These are exciting results for a condition in which the medical establishment has struggled to find adequate treatment.

## Hypertension

Having low blood magnesium levels increases risk for *hypertension*, the dangerous persistent rise in blood pressure that leads to congestive heart failure, strokes, and other catastrophes. <sup>28,29</sup>

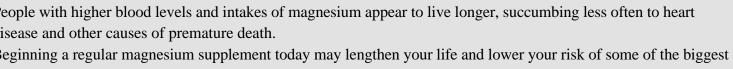
Lower magnesium levels are associated with higher blood pressure readings. 30,31 In fact, you are nearly twice as likely to develop "prehypertension" (blood pressures of 120-139/80-89 mmHg) if your magnesium levels are below the safe lower limit (1.7mg/dL). 32 Epidemiologic research shows that people in areas where drinking water is higher in magnesium tend to have lower blood pressure. 33 Certain common blood pressure medications, paradoxically, can also deplete your body of magnesium.34

Supplementation with magnesium has a beneficial effect on blood pressure. A large meta-analysis demonstrated an average decrease in blood pressure of 3 to 4 mmHg systolic (top number), and 2 to 3 mmHg diastolic, a change that increased further when intake of magnesium topped 370 mg/day. 35 A subsequent meta-analysis of people with existing high blood pressure, with a mean starting systolic pressure of greater than 155 mmHg, reported a highly significant 18.7 mmHg mean reduction in systolic, and a similarly significant 10.9 mmHg mean reduction in diastolic blood pressures.<sup>36</sup> In a group of patients with type II diabetes, a major cardiovascular risk factor, systolic blood pressure fell by an average of 7.4 mmHg after supplementation with **384 mg** magnesium chloride a day.<sup>37</sup>

#### WHAT YOU NEED TO KNOW

### **Magnesium Reduces Heart Disease Risk**

- Your body relies on ample magnesium supplies to maintain normal, healthy function of muscle and nerve tissue, especially those found in the heart and blood vessels.
- Inadequate magnesium intake, or deficiency in total body magnesium, increases the risk of cardiovascular diseases such as heart attacks, strokes, and arrhythmias, as well as metabolic syndrome and type II diabetes.
- Restoring magnesium supplies through supplementation is proven to reduce cardiovascular disease and to potentially reverse many of the troubling signs of metabolic syndrome and diabetes.
- People with higher blood levels and intakes of magnesium appear to live longer, succumbing less often to heart disease and other causes of premature death.
- Beginning a regular magnesium supplement today may lengthen your life and lower your risk of some of the biggest killers of older adults.



## **Enlarged Heart**

Hypertension is also a leading risk factor for the development of dangerous enlargement of the heart, specifically the left ventricle, which is the heart's main pumping chamber. <sup>38</sup> Preclinical and human studies reveal that a deficiency in dietary magnesium and low magnesium levels are associated with such enlargement, producing a condition known as hypertrophic cardiomyopathy, in which the heart muscle becomes so enlarged that it can no longer pump bloodeffectively. 39,40

#### MAGNESIUM IMPACTS LIFE SPAN

Supplementing with magnesium is a simple, inexpensive, and effective way to reduce your unnecessary *risk of* cardiovascular death, and even death from multiple causes. Research shows that the higher the magnesium blood levels, the lower the risk of dying from cardiovascular disease, cancer, and all causes.<sup>62</sup> This is supported by other research showing that those with the highest magnesium intake enjoy a **34%** reduction in mortality risk compared with those having the lowest intake.<sup>63</sup> Another compelling study showed that for each **0.25 mg/dL** increase in plasma magnesium, the risk of sudden cardiac death fell by **41%**.<sup>23</sup>



Preliminary research shows that magnesium is an absolute requirement for maintaining and repairing *telomeres*, the "aging timers" that are found on our DNA strands. <sup>64</sup> Without sufficient magnesium, the aging process itself might be drastically accelerated.

In fact, numerous new studies have appeared demonstrating that low magnesium levels are associated not only with specific diseases, but also with life span. As blood levels of magnesium diminish, the risk of death increases; similar risks arise with diminished magnesium intake. 11,23,65,66

Lower magnesium levels have been associated with the following negative effects:

- 23% higher risk of death from all causes, 11
- 38% higher risk of death from cardiovascular disease, 11
- 18% higher risk of hospitalization for all causes, 11
- 14% higher risk of hospitalization for cardio-vascular disease. 11

Fortunately, higher magnesium levels have been associated with the following beneficial results, demonstrating the benefits of supplementing with magnesium:

- 40% lower risk of death from all causes, <sup>62</sup>
- 50% lower risk of death from cancer, <sup>62</sup>
- 40% lower risk of death from cardiovascular disease, <sup>62</sup>
- 77% lower risk of sudden cardiac death. 23

Raising your blood levels of magnesium, then, appears to have the potential to save your life, especially if you are already at risk for heart disease or stroke.

### Atherosclerosis

Endothelial dysfunction leads to thickening and stiffening of the arterial walls ("hardening of the arteries," or atherosclerosis). While arterial stiffening drives up blood pressure, magnesium supplementation not only lowers blood pressure, but also sharply decreases the resistance against which the heart must pump; this is especially notable in the smaller arteries that provide blood flow to major organs and help improve the amount of nutrient-rich blood they receive. 41

Magnesium supplementation can also improve the quality of life for those suffering from cardiovascular disease. For instance, in people with known coronary artery disease, magnesium supplementation improved exercise tolerance and reduced exercise-induced chest pain. <sup>42</sup> And in a six-month study of patients with known ischemic heart disease (poor blood circulation to heart muscle), magnesium supplementation led to an impressive *decrease* in angina attacks and a *decrease* in the use of antianginal drugs such as nitroglycerin. <sup>43</sup>

In patients on dialysis for kidney failure, thickening of arterial walls occurs much faster than in healthy patients. However, magnesium can provide important reduction of this condition.<sup>44</sup> In one study, supplementation with **440 mg** of magnesium

oxide three times weekly for six months was found to be effective at reducing that thickening among dialysis patients, while placebo recipients had increased thickening over the same period. Another study of dialysis patients observed similar results when supplementing with **610 mg** of magnesium citrate every other day for two months.

#### CAUSES OF MAGNESIUM DEFICIENCY

Low blood levels of magnesium are considered to be one of the most underdiagnosed blood chemical deficiencies in modern medical practice. Many experts now believe that blood magnesium should be checked whenever testing of other electrolytes (chemical ions) in the blood is done. 67,68

Magnesium deficiency has two major common causes: 69,70

- 1. Decreased intake of magnesium, which can occur with alcoholism, starvation, or poor appetite, and in patients with cancer or on chemotherapy. Another growing cause of low magnesium intake is the increased consumption of bottled and filtered water. While some natural mineral waters may contain adequate magnesium, the amounts vary, and many "pure" spring waters contain very little magnesium at all, leading to widespread lack of sufficient magnesium. 71-73
- 2. Increased losses of magnesium, either through the digestive tract or in the urine, can occur with severe diarrhea, gastrointestinal fistulas (surgical or pathological connections between the intestinal tract and the outside world), and especially from drug therapy with diuretics and antibiotics such as *gentamicin*.

The so-called "loop" diuretics such as *furosemide* (**Lasix**<sup>®</sup>) and the thiazide diuretics (e.g., *hydrochlorothiazide*) are especially notorious for producing magnesium losses in the urine; fortunately, magnesium supplementation can prevent or correct low magnesium from these drugs.<sup>74,75</sup>

Since so many people drink bottled or filtered water, have otherwise inadequate magnesium intakes, or are taking magnesium-depleting drugs, it is important to get regular tests of your blood magnesium levels, and to supplement with a good source of this vital mineral.

### **Metabolic Syndrome And Diabetes**

Magnesium is vital for normal metabolic function, including glucose metabolism and insulin action. This is why magnesium supplementation in type II diabetics appears to reverse much of the damage wrought by low levels. Magnesium is an essential "co-factor" for more than 300 enzymes and is vital to the ways your body manages its energy. <sup>46,47</sup>

In one study, a daily dose of **2.5 grams** of magnesium chloride significantly reduced insulin resistance, fasting blood sugar levels, and hemoglobin A1c, a measure of chronic exposure to high sugar. <sup>48</sup> In another study, 12 weeks of supplementation with **360 mg/day** of magnesium produced a **10 mg/dL** drop in fasting glucose levels. <sup>49</sup>

Magnesium supplementation also directly counteracts metabolic syndrome. In a group of type II diabetics, treatment with **600 mg/day** of magnesium oxide produced significant drops in total and LDL ("bad") cholesterol and triglycerides, with a rise in HDL ("good") cholesterol. <sup>50</sup> Similar results were seen in another study when healthy volunteers supplemented with magnesium oxide, enough to deliver **520 mg/day** of elemental magnesium. <sup>51</sup> Magnesium oxide and magnesium citrate have been shown to reduce platelet aggregation, and thereby reduce the risk of a dangerous blood clot. <sup>51</sup>

In a study representative of today's typical middle-aged person (namely, people who were overweight and insulin resistant,

but not yet diabetic), six months of magnesium supplementation significantly improved fasting blood sugar and insulin sensitivity, compared to placebo. <sup>52</sup> Intriguingly, none of the patients had detectably low blood magnesium at the study's outset, suggesting that it's possible to be total-body deficient in magnesium, while still maintaining normal blood levels. According to the authors, this study emphasized "the need for an early optimization of magnesium status to prevent insulin resistance and subsequently type II diabetes." Subsequent preclinical research has confirmed that type II diabetes can be delayed by magnesium supplementation. <sup>53</sup>

People with lower magnesium levels or low magnesium intake may be at an increased risk for developing metabolic syndrome, the combination of central obesity with at least two of the following: hypertension, lipid disorders, impaired glucose tolerance, or diabetes. 33,46,51,52

As is the case with other health problems, the lower your magnesium intake, the greater your risk of obesity, excess body fat percentage, and high triglycerides.<sup>54</sup> In fact, as magnesium levels decrease, the number of metabolic syndrome components increase, as does an important marker of inflammation C-reactive protein (CRP).<sup>46,55,56</sup>

People with existing diabetes, or with "pre-diabetes" (impaired fasting glucose or impaired glucose tolerance) have significantly lower magnesium levels than do those with normal metabolism.<sup>57</sup> In one study, **88.6%** of type II diabetics had magnesium intake less than the dietary recommendations, and **37.1%** had low blood magnesium levels.<sup>54</sup>

Magnesium deficiency is especially dangerous for diabetics. In one study of diabetic patients with heart failure, **73.3%** were found to have low serum magnesium. <sup>58</sup> Low magnesium levels in red blood cells are strongly associated with increased incidence of cardiac events and poor outcomes. <sup>43</sup>

Some of these observations may be explained by the fact that low magnesium levels appear to raise insulin resistance through a variety of biochemical mechanisms.<sup>59,60</sup> In addition, low magnesium levels make platelets "stickier," increasing the risk of a destructive or fatal blood clot forming, and thereby increasing the likelihood of a dangerous heart attack or stroke.<sup>61</sup>

#### TABLE 1

### Health Risks Associated With Magnesium Deficiency In Older Adults<sup>9</sup>

General Physiology	Cardiovascular	Metabolic	Other
<ul> <li>Increased inflammation</li> <li>Increased oxidative stress</li> </ul>	<ul> <li>Stroke</li> <li>Atherosclerosis</li> <li>Ischemic heart disease</li> <li>Cardiac arrhythmias</li> <li>Endothelial dysfunction</li> <li>Abnormal vascular remodeling</li> <li>Alterations in lipid metabolism</li> <li>Increased platelet aggregation and risk of blood clots</li> <li>Hypertension</li> </ul>	<ul> <li>Glucose intolerance</li> <li>Insulin resistance</li> <li>Type II diabetes</li> </ul>	<ul> <li>Asthma</li> <li>Chronic fatigue</li> <li>Depression</li> <li>Neuropsychiatric disorders</li> </ul>

# **Summary**

Magnesium is an element critical to multiple vital functions in the human body, yet even people interested in optimizing their nutritional health frequently ignore it. Low magnesium levels trigger problems in the heart muscle, blood vessel walls, and blood vessel linings that can lead to heart attacks, heart failure, atherosclerosis, and cardiac arrhythmias.

Magnesium deficiency also contributes to metabolic syndrome and type II diabetes, two epidemic conditions that themselves lead to cardiovascular disease and other chronic, age-related conditions.

But nearly half of all Americans (and more than that among the elderly) fail to get enough magnesium in their diets, and therefore have suboptimal blood levels of this vital mineral.

Magnesium supplementation is an easy, inexpensive, and effective way to restore magnesium to your whole body, and studies show that boosting your magnesium levels sooner rather than later offers the best protection. Indeed, people with the highest blood levels of magnesium, and/or the highest dietary intake of magnesium, are at lower risk for dying of both cardiac and noncardiac conditions.

If you are an older adult concerned about the possibility of a premature death from cardiovascular or metabolic diseases, you should begin a regular magnesium supplement today.

If you have any questions on the scientific content of this article, please call a **Life Extension**<sup>®</sup> Health Advisor at 1-866-864-3027.

### References

- 1. Available at: <a href="http://www.cdc.gov/nchs/fastats/leading-causes-of-death.htm">http://www.cdc.gov/nchs/fastats/leading-causes-of-death.htm</a>. Accessed June 23, 2014.
- 2. Rosanoff A, Weaver CM, Rude RK. Suboptimal magnesium status in the United States: are the health consequences underestimated? *Nutr Rev.* 2012 Mar;70(3):153-64.
- 3. Geiger H, Wanner C. Magnesium in disease. Clin Kidney J. 2012; 5(Suppl 1), i25-i38.
- 4. Del Gobbo LC, Imamura F, Wu JH, de Oliveira Otto MC, Chiuve SE, Mozaffarian D. Circulating and dietary magnesium and risk of cardiovascular disease: a systematic review and meta-analysis of prospective studies. *Am J Clin Nutr.* 2013 Jul;98(1):160-73.
- 5. Cunha AR, Umbelino B, Correia ML, Neves MF. Magnesium and vascular changes in hypertension. *Int J Hypertens*. 2012;2012;754250.
- 6. Weglicki WB, Mak Iu T, Chmielinska JJ, Tejero-Taldo MI, Komarov AM, Kramer JH. The role of magnesium deficiency in cardiovascular and intestinal inflammation. *Magnes Res.* 2010 Dec;23(4):S199-206.
- 7. Dominguez LJ, Barbagallo M, Lauretani F, et al. Magnesium and muscle performance in older persons: the InCHIANTI study. *Am J Clin Nutr*. 2006;84(2):419-26.
- 8. Mert T, Gunes Y, Guven M, Gunay I, Ozcengiz D. Effects of calcium and magnesium on peripheral nerve conduction. *Pol J Pharmacol.* 2003 Jan-Feb;55(1):25-30.
- 9. Barbagallo M, Belvedere M, Dominguez LJ. Magnesium homeostasis and aging. Magnes Res. 2009 Dec;22(4):235-46.
- 10. Altura BM, Shah NC, Shah GJ, et al. Short-term Mg deficiency upregulates protein kinase C isoforms in cardiovascular tissues and cells; relation to NF-kB, cytokines, ceramide salvage sphingolipid pathway and PKC-zeta: hypothesis and review. *Int J Clin Exp Med.* 2014;7(1):1-21.
- 11. Adamopoulos C, Pitt B, Sui X, Love TE, Zannad F, Ahmed A. Low serum magnesium and cardiovascular mortality in chronic heart failure: a propensity-matched study. *Int J Cardiol*. 2009 Aug 21;136(3):270-7.
- 12. Gao X, Peng L, Adhikari CM, Lin J, Zuo Z. Spironolactone reduced arrhythmia and maintained magnesium homeostasis in patients with congestive heart failure. *J Card Fail*. 2007 Apr;13(3):170-7.
- 13. Ganga HV, Noyes A, White CM, Kluger J. Magnesium adjunctive therapy in atrial arrhythmias. *Pacing Clin Electrophysiol.* 2013 Oct;36(10):1308-18.
- 14. Available at: <a href="http://www.nhlbi.nih.gov/health/health-topics/topics/arr/">http://www.nhlbi.nih.gov/health/health-topics/topics/arr/</a>. Accessed July 17, 2014.
- 15. Iezhitsa, IN. Potassium and magnesium depletions in congestive heart failure--pathophysiology, consequences and

- replenishment. Clin Calcium. 2005;15(11): 123-33.
- 16. Najafi M, Haghighat B, Tafti HA. Relationship between serum magnesium level and arrythmias following post-coronary artery bypass grafting. *Middle East J Anesthesiol*. 2007 Oct;19(3):661-72.
- 17. Nielsen FH, Milne DB, Klevay LM, Gallagher S, Johnson L. Dietary magnesium deficiency induces heart rhythm changes, impairs glucose tolerance, and decreases serum cholesterol in post menopausal women. *J Am Coll Nutr.* 2007 Apr;26(2):121-32.
- 18. Agus ZS. Hypomagnesemia. *J Am Soc Nephrol*. 1999;10:1616-22.
- 19. Classen HG, Grober U, Kisters K. Drug-induced magnesium deficiency. *Med Monatsschr Pharm.* 2012 Aug;35(8):274-80.
- 20. Shechter M. Magnesium and cardiovascular system. Magnes Res. 2010 Jun;23(2):60-72.
- 21. Lee HY, Ghimire S, Kim EY. Magnesium supplementation reduces postoperative arrhythmias after cardiopulmonary bypass in pediatrics: a metaanalysis of randomized controlled trials. *Pediatr Cardiol.* 2013 Aug;34(6):1396-403.
- 22. Orenes-Pinero E, Montoro-Garcia S, Banerjee A, Valdes M, Lip GY, Marin F. Pre and post-operative treatments for prevention of atrial fibrillation after cardiac surgery. *Mini Rev Med Chem.* 2012 Nov;12(13):1419-31.
- 23. Chiuve SE, Korngold EC, Januzzi JL, Jr., Gantzer ML, Albert CM. Plasma and dietary magnesium and risk of sudden cardiac death in women. *Am J Clin Nutr*. 2011 Feb;93(2):253-60.
- 24. Davey MJ, Teubner D. A randomized controlled trial of magnesium sulfate, in addition to usual care, for rate control in atrial fibrillation. *Ann Emerg Med.* 2005 Apr;45(4):347-53.
- 25. Besogul Y, Aslan R. Oral magnesium prophylaxis provides spontaneous resumption of cardiac rhythm in patients undergoing cardiac surgery. *J Int Med Res*. 2009 Mar-Apr;37(2):318-24.
- 26. Falco CN, Grupi C, Sosa E, et al. Successful improvement of frequency and symptoms of premature complexes after oral magnesium administration. *Arq Bras Cardiol.* 2012 Jun;98(6):480-7.
- 27. Chakko S, de Marchena E, Kessler KM, Myerburg RJ. Ventricular arrhythmias in congestive heart failure. *Clin Cardiol*. 1989 Sep;12(9):525-30.
- 28. Ozono R, Oshima T, Matsuura H, et al. Systemic magnesium deficiency disclosed by magnesium loading test in patients with essential hypertension. *Hypertens Res.* 1995 Mar;18(1):39-42.
- 29. Available at: http://www.nhlbi.nih.gov/health/health-topics/topics/hbp. Accessed on July 17, 2014.
- 30. Joosten MM, Gansevoort RT, Mukamal KJ, et al. Urinary magnesium excretion and risk of hypertension: the prevention of renal and vascular end-stage disease study. *Hypertension*. 2013 Jun;61(6):1161-7.
- 31. Jin K, Kim TH, Kim YH, Kim YW. Additional antihypertensive effect of magnesium supplementation with an angiotensin II receptor blocker in hypomagnesemic rats. *Korean J Intern Med.* 2013 Mar;28(2):197-205.
- 32. Rodriguez-Moran M, Guerrero-Romero F. Hypomagnesemia and prehypertension in otherwise healthy individuals. *Eur J Intern Med.* 2014 Feb;25(2):128-31.
- 33. Rasic-Milutinovic Z, Perunicic-Pekovic G, Jovanovic D, Gluvic Z, Cankovic-Kadijevic M. Association of blood pressure and metabolic syndrome components with magnesium levels in drinking water in some Serbian municipalities. *J Water Health.* 2012 Mar;10(1):161-9.
- 34. Cocco G, Iselin HU, Strozzi C, Cesana B, Baumeler HR. Magnesium depletion in patients on long-term chlorthalidone therapy for essential hypertension. *Eur J Clin Pharmacol*. 1987;32(4):335-8.
- 35. Kass L, Weekes J, Carpenter L. Effect of magnesium supplementation on blood pressure: a meta-analysis. *Eur J Clin Nutr*. 2012 Apr;66(4):411-8.
- 36. Rosanoff A, Plesset MR. Oral magnesium supplements decrease high blood pressure (SBP>155 mmHg) in hypertensive subjects on anti-hypertensive medications: a targeted meta-analysis. *Magnes Res.* 2013 Jul-Sep;26(3):93-9.
- 37. Purvis JR, Cummings DM, Landsman P, et al. Effect of oral magnesium supplementation on selected cardiovascular risk factors in non-insulin-dependent diabetics. *Arch Fam Med.* 1994 Jun;3(6):503-8.
- 38. Available at: <a href="http://www.mayoclinic.org/diseases-conditions/left-ventricular-hypertrophy/basics/causes/con-20026690">http://www.mayoclinic.org/diseases-conditions/left-ventricular-hypertrophy/basics/causes/con-20026690</a>. Accessed July 17, 2014.
- 39. Freeman LM, Brown DJ, Smith FW, Rush JE. Magnesium status and the effect of magnesium supplementation in feline hypertrophic cardiomyopathy. *Can J Vet Res.* 1997 Jul;61(3):227-31.

- 40. Reffelmann T, Ittermann T, Dorr M, et al. Low serum magnesium concentrations predict cardiovascular and all-cause mortality. *Atherosclerosis*. 2011 Nov;219(1):280-4.
- 41. Wu G, Tian H, Han K, Xi Y, Yao Y, Ma A. Potassium magnesium supplementation for four weeks improves small distal artery compliance and reduces blood pressure in patients with essential hypertension. *Clin Exp Hypertens*. 2006 Jul;28(5):489-97.
- 42. Pokan R, Hofmann P, von Duvillard SP, et al. Oral magnesium therapy, exercise heart rate, exercise tolerance, and myocardial function in coronary artery disease patients. *Br J Sports Med.* 2006 Sep;40(9):773-8.
- 43. Lasserre B, Spoerri M, Moullet V, Theubet MP. Should magnesium therapy be considered for the treatment of coronary heart disease? II. Epidemiological evidence in outpatients with and without coronary heart disease. *Magnes Res.* 1994 Jun;7(2):145-53.
- 44. Turgut F, Kanbay M, Metin MR, Uz E, Akcay A, Covic A. Magnesium supplementation helps to improve carotid intima media thickness in patients on hemodialysis. *Int Urol Nephrol*. 2008;40(4):1075-82.
- 45. Mortazavi M, Moeinzadeh F, Saadatnia M, Shahidi S, McGee JC, Minagar A. Effect of magnesium supplementation on carotid intima-media thickness and flow-mediated dilatation among hemodialysis patients: a double-blind, randomized, placebo-controlled trial. *Eur Neurol*. 2013;69(5):309-16.
- 46. Evangelopoulos AA, Vallianou NG, Panagiotakos DB, et al. An inverse relationship between cumulating components of the metabolic syndrome and serum magnesium levels. *Nutr Res.* 2008 Oct;28(10):659-63.
- 47. Kikuchi K, Tanaka H, Gima M, et al. Abnormalities of magnesium (Mg) metabolism and therapeutic significance of Mg administration in patients with metabolic syndrome, type 2 diabetes, heart failure and chronic hemodialysis. *Clin Calcium*. 2012 Aug;22(8):1217-26.
- 48. Rodriguez-Moran M, Guerrero-Romero F. Oral magnesium supplementation improves insulin sensitivity and metabolic control in type 2 diabetic subjects: a randomized double-blind controlled trial. *Diabetes Care*. 2003 Apr;26(4):1147-52.
- 49. Song Y, He K, Levitan EB, Manson JE, Liu S. Effects of oral magnesium supplementation on glycaemic control in Type 2 diabetes: a meta-analysis of randomized double-blind controlled trials. *Diabet Med.* 2006 Oct;23(10):1050-6.
- 50. Lal J, Vasudev K, Kela AK, Jain SK. Effect of oral magnesium supplementation on the lipid profile and blood glucose of patients with type 2 diabetes mellitus. *J Assoc Physicians India*. 2003 Jan;51:37-42.
- 51. Shechter M, Saad T, Shechter A, Koren-Morag N, Silver BB, Matetzky S. Comparison of magnesium status using X-ray dispersion analysis following magnesium oxide and magnesium citrate treatment of healthy subjects. *Magnes Res.* 2012 Mar 1;25(1):28-39.
- 52. Mooren FC, Kruger K, Volker K, Golf SW, Wadepuhl M, Kraus A. Oral magnesium supplementation reduces insulin resistance in non-diabetic subjects a double-blind, placebo-controlled, randomized trial. *Diabetes Obes Metab*. 2011 Mar;13(3):281-4.
- 53. Nagai N, Ito Y. Effect of magnesium ion supplementation on obesity and diabetes mellitus in Otsuka Long-Evans Tokushima Fatty (OLETF) rats under excessive food intake. *J Oleo Sci.* 2013;62(6):403-8.
- 54. Huang JH, Lu YF, Cheng FC, Lee JN, Tsai LC. Correlation of magnesium intake with metabolic parameters, depression and physical activity in elderly type 2 diabetes patients: a cross-sectional study. *Nutr J.* 2012;11:41.
- 55. Rayssiguier Y, Libako P, Nowacki W, Rock E. Magnesium deficiency and metabolic syndrome: stress and inflammation may reflect calcium activation. *Magnes Res.* 2010 Jun;23(2):73-80.
- 56. Weglicki WB. Hypomagnesemia and inflammation: clinical and basic aspects. *Annu Rev Nutr.* 2012 Aug 21;32:55-71.
- 57. Xu J, Xu W, Yao H, Sun W, Zhou Q, Cai L. Associations of serum and urinary magnesium with the pre-diabetes, diabetes and diabetic complications in the Chinese Northeast population. *PLoS One*. 2013;8(2):e56750.
- 58. Shaikh S, Karira KA. Magnesium deficiency in heart failure patients with diabetes mellitus. *J Pak Med Assoc*. 2011 Sep;61(9):901-3.
- 59. Lima Mde L, Cruz T, Rodrigues LE, et al. Serum and intracellular magnesium deficiency in patients with metabolic syndrome-evidences for its relation to insulin resistance. *Diabetes Res Clin Pract*. 2009 Feb;83(2):257-62.
- 60. Takaya J, Iharada A, Okihana H, Kaneko K. Down-regulation of hepatic phosphoenolpyruvate carboxykinase expression in magnesium-deficient rats. *Magnes Res.* 2012 Jul-Sep;25(3):131-9.
- 61. Nadler JL, Malayan S, Luong H, Shaw S, Natarajan RD, Rude RK. Intracellular free magnesium deficiency plays a key

- role in increased platelet reactivity in type II diabetes mellitus. Diabetes Care. 1992 Jul;15(7):835-41.
- 62. Leone N, Courbon D, Ducimetiere P, Zureik M. Zinc, copper, and magnesium and risks for all-cause, cancer, and cardiovascular mortality. *Epidemiology*. 2006 May;17(3):308-14.
- 63. Guasch-Ferre M, Bullo M, Estruch R, et al. Dietary magnesium intake is inversely associated with mortality in adults at high cardiovascular disease risk. *J Nutr.* 2014 Jan;144(1):55-60.
- 64. Rowe WJ. Correcting magnesium deficiencies may prolong life. Clin Interv Aging. 2012;7:51-4.
- 65. Sakaguchi Y, Fujii N, Shoji T, Hayashi T, Rakugi H, Isaka Y. Hypomagnesemia is a significant predictor of cardiovascular and non-cardiovascular mortality in patients undergoing hemodialysis. *Kidney Int.* 2014 Jan;85(1):174-81.
- 66. Ishimura E, Okuno S, Yamakawa T, Inaba M, Nishizawa Y. Serum magnesium concentration is a significant predictor of mortality in maintenance hemodialysis patients. *Magnes Res.* 2007 Dec;20(4):237-44.
- 67. Whang R. Magnesium deficiency: pathogenesis, prevalence, and clinical implications. *Am J Med*. 1987 Mar 20;82(3a):24-9.
- 68. Whang R, Hampton EM, Whang DD. Magnesium homeostasis and clinical disorders of magnesium deficiency. *Ann Pharmacother*. 1994 Feb;28(2):220-6.
- 69. Whang R. Magnesium deficiency. Causes and clinical implications. Drugs. 1984 Oct;28 Suppl 1:143-50.
- 70. Bobkowski W, Nowak A, Durlach J. The importance of magnesium status in the pathophysiology of mitral valve prolapse. *Magnes Res.* 2005 Mar;18(1):35-52.
- 71. Innerarity S. Hypomagnesemia in acute and chronic illness. Crit Care Nurs Q. 2000 Aug;23(2):1-19.
- 72. Martinez-Ferrer A, Peris P, Reyes R, Guanabens N. Intake of calcium, magnesium and sodium through water: health implications. *Med Clin (Barc)*. 2008 Nov 15;131(17):641-6.
- 73. Azoulay A, Garzon P, Eisenberg MJ. Comparison of the mineral content of tap water and bottled waters. *J Gen Intern Med.* 2001 Mar;16(3):168-75.
- 74. Cevette MJ, Franz KB, Brey RH, Robinette MS. Influence of dietary magnesium on the amplitude of wave V of the auditory brainstem response. Otolaryngol Head Neck Surg . 1989 Nov;101(5):537-41.
- 75. Efstratiadis G, Sarigianni M, Gougourelas I. Hypomagnesemia and cardiovascular system. *Hippokratia*. 2006 Oct;10(4):147-52.

These statements have not been evaluated by the Food and Drug Administration.

These products are not intended to diagnose, treat, cure, or prevent any disease.

The information provided on this site is for informational purposes only and is not intended as a substitute for advice from your physician or other health care professional or any information contained on or in any product label or packaging. You should not use the information on this site for diagnosis or treatment of any health problem or for prescription of any medication or other treatment. You should consult with a healthcare professional before starting any diet, exercise or supplementation program, before taking any medication, or if you have or suspect you might have a health problem. You should not stop taking any medication without first consulting your physician.

All Contents Copyright © 1995–2014 Life Extension® All rights reserved

Foundation for Longer Life