

Appendix III: Both old and new peer-reviewed studies show that CVD risk factors are related to Mg status

Discussed below are a few of the most commonly known CVD risk factors with some of the peer-reviewed science that relates them to Mg status.

See references of *The Magnesium Factor* by Mildred Seelig and Andrea Rosanoff.

See also “The Mg Hypothesis of Cardiovascular Disease: A Bibliography” <http://www.magnesiumeducation.com/the-mg-hypothesis-of-cardiovascular-disease-a-bibliography>

High Blood Pressure — Mg normalizes blood pressure, perhaps the most predictive and certainly the oldest cardiovascular risk factor. Mg supplementation also enhances the action of antihypertension medications (Rosanoff, 2010; Houston, 2011). Three meta-analyses on Mg therapy for blood pressure (Dickinson et al., 2006; Jee et al., 2001; Kass et al., 2012) have all reported that Mg supplements do have a small but significant effect on blood pressure, which appears so small as to be clinically insignificant. However, a recent study shows how these meta-analyses failed to include high-responder studies that demonstrate Mg therapy has a highly significant and profound effect on high blood pressure in *some* subjects—that Mg therapy in some hypertensive individuals can consistently lower SBP by 19 mm Hg and DBP by about 8 mm Hg; but other hypertensive subjects as well as normotensive subjects show a much lower or even zero response to Mg therapy. When meta-analyses and studies “average” all these various subjects together, they get the erroneous conclusion that Mg therapy has only a small albeit significant effect on human blood pressure. Not having reliable methods to ascertain Mg status hinders these studies and the interpretation of their results.

Rosanoff A. 2010. Magnesium supplements may enhance the effect of antihypertensive medications in stage 1 hypertensive subjects. *Magnes Res* 23:27–40.

Houston M. 2011. The role of magnesium in hypertension and cardiovascular disease. *J Clin Hypertens* (Greenwich) 13:843–47.

Dickinson HO, Nicolson DJ, Campbell F, Cook JV, Beyer FR, Ford GA, and Mason J. 2006. Magnesium supplementation for the management of essential hypertension in adults. *Cochrane Database Syst Rev* 3, CD004640.

Jee SH, Miller ER, III, Guallar E, Singh VK, Appel LJ, and Klag MJ. 2002. The effect of magnesium supplementation on blood pressure: a meta-analysis of randomized clinical trials. *Am J Hypertens* 15:691–96.

Kass L, Weekes J, and Carpenter L. 2012. Effect of magnesium supplementation on blood pressure: a meta-analysis. *Eur J Clin Nutr*.

Rosanoff A and Plessset M. 2012. Successful treatment of hypertension with Mg—a targeted approach. In XIII International Magnesium Symposium. Ed. F Guerrero-Romero, Merida, Yuc., Mexico.

Cholesterol — Several studies have shown that adequate Mg or Mg therapy will lower LDL (bad) cholesterol and raise HDL (good) cholesterol (see Seelig & Rosanoff, 2003: 330–42). Mg is an essential cofactor for the rate-limiting enzyme in the cholesterol biosynthesis sequence, HMG-CoA-Reductase, the enzyme targeted by the statins (Rosanoff & Seelig, 2004). High cholesterol in rats was an early aspect of atherosclerotic disease that was tightly tied to Mg status (see appendix I). There is ample evidence to consider a high-LDL and/or low-HDL cholesterol as an aspect of Mg deficit warranting Mg therapy.

Seelig MS and Rosanoff A. 2003. *The Magnesium Factor*. New York: Avery Penguin Group. See pp. 330–42 for cholesterol and Mg references.

Rosanoff A and Seelig MS. 2004. Comparison of mechanism and functional effects of magnesium and statin pharmaceuticals. *J Am Coll Nutr* 23:501S–505S.

The following references are selected from the Mg Hypothesis Bibliography cited above.

Mg can correct Low HDL Cholesterol (Low “good” cholesterol)

Davis WH, Leary WP, Reyes AJ, and Olhaberry JV. 1984. Monotherapy with magnesium increases abnormally low high density lipoprotein cholesterol: a clinical assay. *Curr Therap Res* 36:341–44.

Rasmussen HS, Aurup P, Goldstein K, McNair P, Mortensen PB, Larsen OG, and Lawaetz H. 1989. Influence of magnesium substitution therapy on blood lipid composition in patients with ischemic heart disease. A double-blind, placebo controlled study. *Arch Intern Med* 149:1050–53.

Singh RB, Rastogi SS, Sharma VK, Saharia RB, and Kulshretha SK. 1990. Can dietary magnesium modulate lipoprotein metabolism? *Magnes Trace Elem* 9:255–64.

Corica F, Allegra A, Di Benedetto A, Giacobbe MS, Romano G, Cucinotta D, Buemi M, and Ceruso D. 1994. Effects of oral magnesium supplementation on plasma lipid concentrations in patients with non-insulin-dependent diabetes mellitus. *Magnes Res* 7:43–47.

Sowers JR and Draznin B. 1998. Insulin, cation metabolism and insulin resistance. *J Basic Clin Physiol Pharmacol* 9:223–33.

Djurhuus MS, Henriksen JE, Klitgaard NA, Blaabjerg O, Thye-Ronn P, Altura BM, Altura BT, and Beck-Nielsen H. 1999. Effect of moderate improvement in metabolic control on magnesium and lipid concentrations in patients with type 1 diabetes. *Diabetes Care* 22:546–54.

Guerrero-Romero F and Rodriguez-Moran M. 2000. Hypomagnesemia is linked to low serum HDL-cholesterol irrespective of serum glucose values. *Journal of Diabetes and Its Complications* 14:272–76.

Olatunji LA and Soladoye AO. 2007. Effect of increased magnesium intake on plasma cholesterol, triglyceride and oxidative stress in alloxan-diabetic rats. *Afr J Med Med Sci* 36:155–61.

Diabetes — More and more medical science is accepting the strong link between Mg status and the onset of type 2 diabetes (Barbagallo et al., 2007). Diabetes is a risk factor for CVD, and the low Mg status of both is part of the Mg Hypothesis of CVD. Type 1 diabetics have long been known to be at high risk for CVD. These people need insulin to keep their blood glucose from becoming too high; a high blood glucose enhances Mg excretion by the kidneys—often leading to a low magnesium status and its risk of CVD.

Barbagallo M, Dominguez LJ, and Resnick LM. 2007. Magnesium metabolism in hypertension and type 2 diabetes mellitus. *Am J Ther* 14:375–85.

The following references are from the Mg Hypothesis bibliography cited above.

Mg and High Fasting Glucose

Olatunji LA and Soladoye AO. 2007. Effect of increased magnesium intake on plasma cholesterol, triglyceride and oxidative stress in alloxan-diabetic rats. *Afr J Med Med Sci* 36:155–61.

Johansson HE, Zethelius B, Ohrvall M, Sundbom M, and Haenni A. 2009. Serum magnesium status after gastric bypass surgery in obesity. *Obes Surg* 19:1250–55.

Mg and Impaired Glucose Tolerance

Sowers JR and Draznin B. 1998. Insulin, cation metabolism and insulin resistance. *J Basic Clin Physiol Pharmacol* 9:223–33.

Barbagallo M and Dominguez LJ. 2007. Magnesium metabolism in type 2 diabetes mellitus, metabolic syndrome and insulin resistance. *Arch Biochem Biophys* 458:40–47.

Pham PC, Pham PM, Pham SV, Miller JM, and Pham PT. 2007. Hypomagnesemia in patients with type 2 diabetes. *Clin J Am Soc Nephrol* 2:366–73.

Nielsen FH, Milne DB, Klevay LM, Gallagher S, and Johnson L. 2007. Dietary magnesium deficiency induces heart rhythm changes, impairs glucose tolerance, and decreases serum cholesterol in post menopausal women. *J Am Coll Nutr* 26:121–32.

Mg and Diabetes

Anetor JI, Senjobi A, Ajose OA, and Agbedana EO. 2002. Decreased serum magnesium and zinc levels: atherogenic implications in type-2 diabetes mellitus in Nigerians. *Nutrition and Health* (Berkhamsted, Hertfordshire) 16:291–300.

Pham PC, Pham PM, Pham SV, Miller JM, and Pham PT. 2007. Hypomagnesemia in patients with type 2 diabetes. *Clin J Am Soc Nephrol* 2:366–73.

Barbagallo M and Dominguez LJ. 2007. Magnesium metabolism in type 2 diabetes mellitus, metabolic syndrome and insulin resistance. *Arch Biochem Biophys* 458:40–47.

Barbagallo M, Dominguez LJ, and Resnick LM. 2007. Magnesium metabolism in hypertension and type 2 diabetes mellitus. *Am J Ther* 14:375–85.

Larsson SC and Wolk A. 2007. Magnesium intake and risk of type 2 diabetes: a meta-analysis. *J Intern Med* 262:208–14.

Champagne CM. 2008. Magnesium in hypertension, cardiovascular disease, metabolic syndrome, and other conditions: a review. *Nutr Clin Pract* 23:142–51.

Curiel-Garcia JA, Rodriguez-Moran M, and Guerrero-Romero F. 2008. Hypomagnesemia and mortality in patients with type 2 diabetes. *Magnes Res* 21:163–66.

Volpe SL. 2008. Magnesium, the metabolic syndrome, insulin resistance, and type 2 diabetes mellitus. *Critical Reviews in Food Science and Nutrition* 48:293–300.

Ohira T, Peacock JM, Iso H, Chambless LE, Rosamond WD, and Folsom AR. 2009. Serum and dietary magnesium and risk of ischemic stroke: the Atherosclerosis Risk in Communities Study. *Am J Epidemiol* 169:1437–44.

Kim DJ, Xun P, Liu K, Loria C, Yokota K, Jacobs DR, Jr, and He K. 2010. Magnesium intake in relation to systemic inflammation, insulin resistance, and the incidence of diabetes. *Diabetes Care*.

Rosanoff A. 2010. Rising Ca:Mg intake ratio from food in USA adults: a concern? *Magnes Res* 23:181–93.

Mg and Insulin Resistance

Resnick LM. 1992. Cellular calcium and magnesium metabolism in the pathophysiology and treatment of hypertension and related metabolic disorders. *Am J Med* 93:11S–20S.

Laires MJ, Moreira H, Monteiro CP, Sardinha L, Limao F, Veiga L, Goncalves A, Ferreira A, and Bicho M. 2004. Magnesium, insulin resistance and body composition in healthy postmenopausal women. *J Am Coll Nutr* 23:510S–513S.

Barbagallo M and Dominguez LJ. 2007. Magnesium metabolism in type 2 diabetes mellitus, metabolic syndrome and insulin resistance. *Arch Biochem Biophys* 458:40–47.

Barbagallo M, Dominguez LJ, and Resnick LM. 2007. Magnesium metabolism in hypertension and type 2 diabetes mellitus. *Am J Ther* 14:375–85.

Volpe SL. 2008. Magnesium, the metabolic syndrome, insulin resistance, and type 2 diabetes mellitus. *Critical Reviews in Food Science and Nutrition* 48:293–300.

Wells IC. 2008. Evidence that the etiology of the syndrome containing type 2 diabetes mellitus results from abnormal magnesium metabolism. *Can J Physiol Pharmacol* 86:16–24.

Kim DJ, Xun P, Liu K, Loria C, Yokota K, Jacobs DR, Jr, and He K. 2010. Magnesium intake in relation to systemic inflammation, insulin resistance, and the incidence of diabetes. *Diabetes Care*.

Liu ZM and Ho SC. 2011. The association of serum C-reactive protein, uric acid and magnesium with insulin resistance in Chinese postmenopausal women with prediabetes or early untreated diabetes. *Maturitas* 70:176–81.

Mg and Elevated Plasma Insulin

He K, Liu K, Daviglus ML, Morris SJ, Loria CM, Van Horn L, Jacobs DR, Jr, and Savage PJ. 2006. Magnesium intake and incidence of metabolic syndrome among young adults. *Circulation* 113:1675–82.

Smoking — This habit has long been associated with a higher risk of CVD than for nonsmokers. Smoking a tobacco cigarette raises the basal metabolic rate, undoubtedly raising the Mg requirement in smokers. With a higher requirement than the general nonsmoking population, the Mg Hypothesis predicts that smokers will show a higher degree of CVD than nonsmokers, taken as a whole.

C-Reactive Protein and Inflammation — A high C-reactive protein in the serum is a newer predictor of CVD (Albert & Ridker, 1999) and is highly inversely related to Mg status (Almonznino-Sarafian et al., 2007). The first symptom of Mg deficiency in mice is biochemical inflammation reactions (Weglicki et al., 2010).

Albert MA and Ridker PM. 1999. The role of C-reactive protein in cardiovascular disease risk. *Curr Cardiol Rep* 1:99–104.

Almonznino-Sarafian D, Berman S, Mor A, Shteinshnaider M, Gorelik O, Tzur I, Alon I, Modai D, and Cohen N. 2007. Magnesium and C-reactive protein in heart failure: an anti-inflammatory effect of magnesium administration? *Eur J Nutr* 46:230–37.

Weglicki WB, Mak IuT, Chmielinska JJ, Tejero-Taldo MI, Komarov AM, and Kramer JH. 2010. The role of magnesium deficiency in cardiovascular and intestinal inflammation. *Magnes Res* 23:199–206.

The following references are from the Mg Hypothesis bibliography cited above.

Ca:Mg and the Metabolic Syndrome

Resnick LM. 1992. Cellular ions in hypertension, insulin resistance, obesity, and diabetes: a unifying theme. *J Am Soc Nephrol* 3:S78–85.

Resnick LM. 1993. Ionic basis of hypertension, insulin resistance, vascular disease, and related disorders. The mechanism of “syndrome X.” *Am J Hypertens* 6:123S–134S.

Mg and the Metabolic Syndrome

Song Y, Ridker PM, Manson JE, Cook NR, Buring JE, and Liu S. 2005. Magnesium intake, C-reactive protein, and the prevalence of metabolic syndrome in middle-aged and older U.S. women. *Diabetes Care* 28:1438–44.

He K, Song Y, Belin RJ, and Chen Y. 2006. Magnesium intake and the metabolic syndrome: epidemiologic evidence to date. *J Cardiometab Syndr* 1:351–55.

Barbagallo M and Dominguez LJ. 2007. Magnesium metabolism in type 2 diabetes mellitus, metabolic syndrome and insulin resistance. *Arch Biochem Biophys* 458:40–47.

Evangelopoulos AA, Vallianou NG, Panagiotakos DB, Georgiou A, Zacharias GA, Alevra AN, Zalokosta GJ, Vogiatzakis ED, and Avgerinos PC. 2008. An inverse relationship between cumulating components of the metabolic syndrome and serum magnesium levels. *Nutrition Research* 28:659–63.

Volpe SL. 2008. Magnesium, the metabolic syndrome, insulin resistance, and type 2 diabetes mellitus. *Critical Reviews in Food Science and Nutrition* 48:293–300.

Champagne CM. 2008. Magnesium in hypertension, cardiovascular disease, metabolic syndrome, and other conditions: a review. *Nutr Clin Pract* 23:142–51.

Mg and Obesity

Resnick LM. 1992. Cellular ions in hypertension, insulin resistance, obesity, and diabetes: a unifying theme. *J Am Soc Nephrol* 3:S78–85.

Izmozherova NV, Popov AA, Fominykh MI, Andreev AN, Striukova O, Tagil'tseva NV, and Gavrilova EI. 2007. [Magnesium deficit in climacteric women]. *Klin Med (Mosk)* 85:62–64.

Champagne CM. 2008. Magnesium in hypertension, cardiovascular disease, metabolic syndrome, and other conditions: a review. *Nutr Clin Pract* 23:142–51.

Johansson HE, Zethelius B, Ohrvall M, Sundbom M, and Haenni A. 2009. Serum magnesium status after gastric bypass surgery in obesity. *Obes Surg* 19:1250–55.

Mg and Central (Abdominal) Obesity

Sowers JR and Draznin B. 1998. Insulin, cation metabolism and insulin resistance. *J Basic Clin Physiol Pharmacol* 9:223–33.

Corica F, Corsonello A, Lentile R, Cucinotta D, Di Benedetto A, Perticone F, Dominguez LJ, and Barbagallo M. 2006. Serum ionized magnesium levels in relation to metabolic syndrome in type 2 diabetic patients. *J Am Coll Nutr* 25:210–15.

Katcher HI, Legro RS, Kunselman AR, Gillies PJ, Demers LM, Bagshaw DM, and Kris-Etherton PM. 2008. The effects of a whole-grain-enriched hypocaloric diet on cardiovascular disease risk factors in men and women with metabolic syndrome. *Am J Clin Nutr* 87:79–90.

Johansson HE, Zethelius B, Ohrvall M, Sundbom M, and Haenni A. 2009. Serum magnesium status after gastric bypass surgery in obesity. *Obes Surg* 19:1250–55.

Mg and High Blood Triglycerides

Rasmussen HS. 1989 Clinical intervention studies on magnesium in myocardial infarction. *Magnesium* 8:316–25.

Djurhuus MS, Henriksen JE, Klitgaard NA, Blaabjerg O, Thye-Ronn P, Altura BM, Altura BT, and Beck-Nielsen H. 1999. Effect of moderate improvement in metabolic control on magnesium and lipid concentrations in patients with type 1 diabetes. *Diabetes Care* 22:546–54.

Singh RB, Rastogi SS, Sharma VK, Saharia RB, and Kulshretha SK. 1990. Can dietary magnesium modulate lipoprotein metabolism? *Magn Trace Elem* 9:255–64.

Corica F, Corsonello A, Lentile R, Cucinotta D, Di Benedetto A, Perticone F, Dominguez LJ, and Barbagallo M. 2006. Serum ionized magnesium levels in relation to metabolic syndrome in type 2 diabetic patients. *J Am Coll Nutr* 25:210–15.

Olatunji LA and Soladoye AO. 2007. Effect of increased magnesium intake on plasma cholesterol, triglyceride and oxidative stress in alloxan-diabetic rats. *Afr J Med Med Sci* 36:155–61.

Other CVD Risk Factors Linked to Mg status — depression, microalbuminuria, polycystic ovary syndrome, hemodynamic changes, renal sodium retention, prothrombic factors, fibrinogen and other inflammation markers, C-Reactive Protein, endothelial-dependent vasodilation. References available upon request.