Appendix VII – highlighted abstracts for references

Elin, R. J. (2010). "Assessment of magnesium status for diagnosis and therapy." Magnes Res **23**(4): 194-198.

Magnesium is an essential element needed for health. Even though only 1% of the total body magnesium is present in blood, the serum magnesium concentration (SMC) is the predominant test used by medicine to assess magnesium status in patients. The traditional method to establish a reference interval for the SMC is flawed by the large number of "normal" individuals who have a subtle chronic negative magnesium balance due to a significant decrease in magnesium intake over the past century. Evidence-based medicine should be used to establish the appropriate lower limit of the reference interval for health and I recommend 0.85 mmol/L based on current literature. The decrease in magnesium in the diet has led to chronic latent magnesium deficiency in a large number of people since their SMC is still within the reference interval due to primarily the bone magnesium supplementing the SMC. These individuals need adjustment of their diet or magnesium supplementation to achieve a normal magnesium status for health.

Rosanoff, A., et al. (2012). "Suboptimal magnesium status in the United States: are the health consequences underestimated?" Nutr Rev **70**(3): 153-164. (See full text)

In comparison with calcium, magnesium is an "orphan nutrient" that has been studied considerably less heavily. Low magnesium intakes and blood levels have been associated with type 2 diabetes, metabolic syndrome, elevated C-reactive protein, hypertension, atherosclerotic vascular disease, sudden cardiac death, osteoporosis, migraine headache, asthma, and colon cancer. Almost half (48%) of the US population consumed less than the required amount of magnesium from food in 2005-2006, and the figure was down from 56% in 2001-2002. Surveys conducted over 30 years indicate rising calcium-to-magnesium food-intake ratios among adults and the elderly in the United States, excluding intake from supplements, which favor calcium over magnesium. The prevalence and incidence of type 2 diabetes in the United States increased sharply between 1994 and 2001 as the ratio of calcium-to-magnesium intake from food rose from <3.0 to >3.0. Dietary Reference Intakes determined by balance studies may be misleading if subjects have chronic latent magnesium deficiency but are assumed to be healthy. Cellular magnesium deficit, perhaps involving TRPM6/7 channels, elicits calcium-activated inflammatory cascades independent of injury or pathogens. Refining the magnesium requirements and understanding how low magnesium status and rising calcium-to-magnesium ratios influence the incidence of type 2 diabetes, metabolic syndrome, osteoporosis, and other inflammation-related disorders are research priorities.

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

Comprehensive analytical review of 44 human studies in 43 publications of oral Magnesium (Mg) therapy for hypertension (HT) shows Mg supplements may enhance the blood-pressure (BP) lowering effect of anti-hypertensive medications (medications) in Stage 1 HT subjects. 9 studies conducted on subjects treated with medications continuously >/= 6 months (with </= 2-wk washout) resulted in significant decreases in both SBP and DBP with oral Mg supplements as low as 230 mg (10 mmol) per day. Twice this oral Mg dose, i.e. 460 mg/day, was required to significantly lower both SBP and DBP in 18 of 22 studies conducted on Stage 1 HT subjects either treatment-naive or with their medication use interrupted >/= 4 weeks within 6 months pre-study. Of the 4 remaining studies showing no BP change at these high Mg doses, two had large placebo effect, a third one had significant baseline discrepancies between Mg-test and placebo groups, and the fourth showed a significant decrease in DBP but not SBP. Thirteen studies on normotensive subjects, both treated and untreated with medications, showed no significant BP lowering effect with oral Mg therapy up to 25 mmol/day (607 mg). Conclusions: Mg supplements above RDA may be necessary to significantly lower high blood pressure in Stage I HT unless subjects have been continuously treated with anti-HT medications >/= 6 months. Such medication use may lower by half the oral Mg dose needed to significantly decrease high blood pressure. Oral Mg therapy may have no effect in studies with normotensive subjects. Study of oral Mg therapy for severe or complicated hypertension has been neglected. Often the first cardiovascular risk factor to present, high blood pressure may be an early opportunity to correct poor Mg status and its possible complications including cardiovascular disease, respiratory diseases, and type 2 diabetes. Such preventive potential encourages quantification of these findings and testing of these hypotheses with a meta-analysis using categories elucidated by this preliminary study and finally would warrant a call for a prospective study.

Klevay, L. M. (1975). "Coronary heart disease: the zinc/copper hypothesis." Am J Clin Nutr **28**(7): 764-774.

Epidemiologic and metabolic data are consonant with the hypothesis that a metabolic imbalance in regard to zinc and copper is a major factor in the etiology of coronary heart disease. This metabolic imbalance is either a relative or an absolute deficiency of copper characterized by a high ratio of zinc to copper. The imbalance results in hypercholesterolemia and increased mortality due to coronary heart disease. The imbalance can occur due to the amounts of zinc and copper in human food, to lack of protective substances in food or drinking water and to alterations in physiological status that produce adverse changes in the distribution of zinc and copper in certain important organs. Because no other agent, with the possible exception of cholesterol, has been related so closely to risk, the ratio of zinc to copper may be the preponderant factor in the etiology of coronary heart disease.

Fan, M.-S., et al. (2008). "Evidence of decreasing mineral density in wheat grain over the last 160 years " Journal of Trace Elements in Medicine and Biology **22**(4): 315-324.

Wheat is an important source of minerals such as iron, zinc, copper and magnesium in the UK diet. The dietary intake of these nutrients has fallen in recent years because of a combination of reduced energy requirements associated with sedentary lifestyles and changes in dietary patterns associated with lower micronutrient density in the diet. Recent publications using data from food composition tables indicate a downward trend in the mineral content of foods and it has been suggested that intensive farming practices may result in soil depletion of minerals. The aim of our study was to evaluate changes in the mineral concentration of wheat using a robust approach to establish whether trends are due to plant factors (e.g. cultivar, yield) or changes in soil nutrient concentration. The mineral concentration of archived wheat grain and soil samples from the Broadbalk Wheat Experiment (established in 1843 at Rothamsted, UK) was determined and trends over time examined in relation to cultivar, yield, and harvest index. The concentrations of zinc, iron, copper and magnesium remained stable between 1845 and the mid 1960s, but since then have decreased significantly, which coincided with the introduction of semi-dwarf, high-yielding cultivars. In comparison, the concentrations in soil have either increased or remained stable. Similarly decreasing trends were observed in different treatments receiving no fertilizers, inorganic fertilizers or organic manure. Multiple regression analysis showed that both increasing yield and harvest index were highly significant factors that explained the downward trend in grain mineral concentration.