

## Appendix I. A brief history of the beginnings of the Mg Hypothesis of Cardiovascular Disease:

In 1936, Greenberg and colleagues showed that Mg deficiency in animals caused myocardial degeneration with fibrosis. In 1938, L. A. Moore and colleagues reported that Mg deficient calves displayed atherosclerotic lesions with **calcification** in aortas and some hearts. In 1957, researchers at Harvard reported that male rats fed an atherogenic diet for only 24 – 26 days (Vitale et al., 1957; Hellerstein et al., 1957; Vitale et al., 1959) developed a low serum Mg (Mg deficiency) along with **calcium deposition** in kidney tubular lesions that could be wholly prevented by feeding the animals 8 to 16 times their normal requirement of Mg. These animals also developed early atherosclerotic lesions in the heart valves and aortas which could be diminished but not totally abolished with exceedingly high dietary levels of Mg. This atherosclerotic diet was high in cholesterol and fat. Such atherosclerotic lesions had previously been seen in animals fed a severely Mg deficient diet (see review of Bajusz, 1965).

In addition to the above findings, early studies from 1957 through the 1990s also showed low water/soil Mg correlating with high rates of sudden cardiac death rates and ischemic heart disease in several countries. (Kobayashi, J. 1957; Seelig & Rosanoff, 2003 pp 303-307). In confirmation, recent epidemiological studies have inversely related both serum magnesium levels (Leone et al., 2006) and magnesium levels in drinking water to cardiovascular death rates (Catling et al., 2008; Monarca et al., 2003, 2006).

### References

Greenberg, D.M., Anderson, C.E., and Tufts, E.V., J Biol Chem, 1936, 114, xliii.

Moore, L.A., Hallman, E.T., and Sholl, L.B., Arch. Path., 1938, 26, 820.

VITALE JJ, WHITE PL, NAKAMURA M, HEGSTED DM, ZAMCHECK N, HELLERSTEIN EE. Interrelationships between experimental hypercholesteremia, magnesium requirement, and experimental atherosclerosis. J Exp Med. 1957 Nov 1;106(5):757-66. PubMed PMID: 13475629; PubMed Central PMCID: PMC2136817. **for full text of article:** <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2136817/>

HELLERSTEIN EE, VITALE JJ, WHITE PL, HEGSTED DM, ZAMCHECK N, NAKAMURA M. Influence of dietary magnesium on cardiac and renal lesions of young rats fed an atherogenic diet. J Exp Med. 1957 Nov 1;106(5):767-76. PubMed PMID: 13475630; PubMed Central PMCID: PMC2136825. **For full text of article:** <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2136825/>

VITALE JJ, HELLERSTEIN EE, HEGSTED DM, NAKAMURA M, FARBMAN. Studies on the interrelationships between dietary magnesium and calcium in atherogenesis and renal lesions. Am J Clin Nutr. 1959 Jan-Feb;7(1):13-22. PubMed PMID: 13626881. **For full text of article:** <http://ajcn.nutrition.org/content/7/1/13.long>

Bajusz Eors, Nutritional Aspects of Cardiovascular Diseases, 1965. See p 69 of this monograph, available for purchase at

<http://www.cabdirect.org/abstracts/19661403690.html;jsessionid=399828FCEBB2DBC55D488E61EEADA00C>

**Early articles reporting higher rates of cardiovascular mortality in areas of low Mg soil/water:**

Koyayashi, J., "On Geographical Relationship Between the Chemical Nature of River Water and Death Rate from Apoplexy," *Berichte des Ohara Instituts fur Landwirtschaftliche Biologie* 11, 1957: 12-21.

Seelig, M.S. & Rosanoff, A., *The Magnesium Factor*, 2003. Avery Penguin Pubnam. New York. See pp 302 – 307 for bibliography of hard-soft water and heart disease mortality studies (1957 – 1998).

**Confirming recent articles on cardiovascular mortality rates with low Mg water:**

Catling LA, Abubakar I, Lake IR, Swift L, Hunter PR. A systematic review of analytical observational studies investigating the association between cardiovascular disease and drinking water hardness. *J Water Health* 2008;6:433-42.

<http://www.ncbi.nlm.nih.gov/pubmed/18401109>

Monarca S, Donato F, Zerbini I, Calderon RL, Craun GF. Review of epidemiological studies on drinking water hardness and cardiovascular diseases. *Eur J Cardiovasc Prev Rehabil* 2006;13:495-506. <http://www.ncbi.nlm.nih.gov/pubmed/16874137>

Monarca S, Zerbini I, Simonati C, Gelatti U. [Drinking water hardness and chronic degenerative diseases. II. Cardiovascular diseases]. *Ann Ig* 2003;15:41-56.

<http://www.ncbi.nlm.nih.gov/pubmed/12666324>

**[See PDF file for the Vitale et al abstract from the 1957 Fed Proc.](#)**