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Quantitative Factors Regarding Magnesium Status in the Modern-Day World

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Abstract. This brief review examines the quantitative aspects concerning the inadequate dietary intake of magnesium in the modern-day world. The importance of magnesium is discussed in relation to myocardial seizures and urolithiasis, along with intake of magnesium from drinking water and other forms of oral magnesium supplementation.

The importance of magnesium in the modern-day world has been the subject of previous reviews by the present author [52–55]. The following paragraphs present a brief summarization of some aspects that seem to require particular emphasis or elaboration, especially with regard to recent developments in the magnesium field.

Magnesium Status

Mankind's ever-increasing reliance on refined food staples has meant a gradually decreasing intake of magnesium in the modern-day world [54]. Thus, instead of the 410 mg/day intake estimated for the year 1910, the current intake of magnesium now averages less than 300 mg/day. This contemporary situation is illustrated in table I, which presents a compendium of recent surveys conducted in Britain, Canada, France, West Germany, and the USA. Note that, when expressed in relation to the 'Recommended Dietary Allowance' (RDA) proposed by the US National Academy of Sciences [59], the contemporary magnesium intake ranges all the way from minimal adequacy to as low as 50% suboptimal.

Aside from the data shown in table I, it has recently been reported that magnesium intake among young women in the Seattle region averages 'less than 2/3 of the RDA' [67]. Also, an identical trend prevails among both men and women in central Kentucky, where 'the wide distribution of low magnesium intakes ... should be recognized by nutritionists' [48]. It is therefore not surprising

Table I. Surveys of dietary magnesium intake in the modern-day world

Reference	Locality	Subjects	Age years	Magnesium, mg/day			Intake % of RDA
				intake	RDA	shortfall	
Leverton et al., 1961 [50]	central USA	30 women	19–24	av. = 279 low = 174	300 300	21 126	93.0 54.0
Schroeder et al., 1969 [70]	USA institutions hospitals	 men men	 – –	 av. = 220 av. = 198	 350 350	 130 152	 62.7 56.6
Brown et al., 1970 [10]	Boston	955 men	20–> 60	av. = 262	350	88	74.9
Holtmeier and Kuhn, 1972 [40]	FRG	1,852 adults	–	av. = 235	325	90	72.3
Hamilton and Minski, 1972/3 [32]	UK	adults	–	av. = 250	325	75	76.9
Greger, 1977 [29]	Indiana institutions	34 women 31 men	> 70 > 70	av. = 283 low = 162 av. = 251 low = 190	300 300 350 350	17 138 99 160	94.3 54.0 71.7 54.3
Fodor et al., 1978 [27]	Newfoundland	105 women 83 men	– –	av. = 143 av. = 189	300 350	157 161	47.7 53.4
Srivastava et al., 1978 [75]	Montreal	15 women 15 men	students students	av. = 224 av. = 247	300 350	76 103	74.7 70.6
Seelig, 1978 [73]	USA	pregnant women	–	av. = 204	450	246	45.3
Ashe et al., 1979 [6]	USA	pregnant women	19–29	av. = 270	450	180	60.0
Greger et al., 1979a [30]	Indiana	11 girls	12–14	av. = 270	300	30	90.0
Greger et al., 1979b [31]	Ind. 1976 Ind. 1977	80 girls 76 girls 25 girls	12–14 12–14 12–14	av. = 238 av. = 231 av. = < 200	300 300 300	62 69 > 100	79.3 77.0 < 66.0
Vir and Love, 1979 [78]	Belfast institutions	90 women 36 men	> 64 > 64	av. = 169 av. = 198	300 350	131 152	56.3 56.6
Huber et al., 1980 [41]	Tennessee	60 girls	9–11	white = 200–300 black = lower	300 300	up to 100	66–100 lower
Durlach et al., 1980 [23]	France	adults (5 surveys)	–	260–325	325	up to 65	80–100

that recent allusion has been made to 'magnesium malnutrition' in the modern-day world [21, 57].

It could be argued that the currently reported dietary magnesium inadequacy is illusory because the RDA [59] was set too high. However, as discussed in a previous review [53], even though metabolic balance studies have indicated that humans can maintain a positive magnesium balance at intakes representing only 60% of the currently proposed RDA, such low magnesium intakes probably represent a mere 'subsistence' level. It must not be forgotten that metabolic balance studies are conducted under conditions of relative serenity which do not represent the stresses or excesses of contemporary life. The importance of the stress factor has been revealed in studies with various animal species. Thus, in studies with pigs, magnesium supplementation increased cardiac function and survival during hemorrhagic stress [20] and also increased survival during 'transportation stress' [62]. Also, after a long-term study with cold-stressed rats, it was concluded that: 'Although chronic suboptimal intake of magnesium may not result in overt signs of magnesium deficiency, it severely reduces stress resistance' [38].

A previous calculation [see pp. 80–82 in ref. 54] had indicated that 170 mg/day of supplementary magnesium would probably alleviate magnesium insufficiency in a modern-day population. This is corroborated in the 'shortfall' column of table I, where it can be seen that a 170 mg/day magnesium supplement would indeed rectify any inadequacy in dietary intake (with the sole exception of pregnancy cases, for whom the RDA is considerably higher than normal). Also, *Durlach* [22] has reported that, for patients with a suboptimal magnesium status, an oral magnesium supplement of at least 150 mg/day (as Mg) is required to alleviate the symptoms of intracellular magnesium deficiency.

Here, it must be emphasized that the suboptimal intakes listed in table I do not necessarily lead to *acute* magnesium deficiency (involving hypomagnesemia and obvious clinical symptoms), but rather, represent a more subtle form of what might be termed 'long-term marginal magnesium insufficiency' [53, 54] with the attendant risk of increased vulnerability to several disease processes [8, 12, 22, 26, 45, 47]. It is also important to remember that body stores of magnesium can be depleted by chronic digitalis usage or long-term diuretic therapy, as mentioned in recent reports [8, 26, 66]. Moreover, it has long been known that habitual alcohol intake can lead to magnesium depletion [26]. Therefore, when these various factors are superimposed on the pattern of suboptimal magnesium intake listed in table I, they reinforce the concern that was expressed by *Seelig* [71] as long ago as 1964.

Some Metabolic Considerations

One of the ongoing problems concerning a suboptimal magnesium status is that it can easily elude diagnosis. The fact that depletion of intracellular magnesium can occur without detectable change in serum magnesium concentration has been previously reviewed [53, 54] and has received emphasis in recent reports [8, 47]. Also, *Caddell* [12] has commented on the shortcomings of the magnesium loading test, which 'serves as a guide to the adequacy of the magnesium stores in a patient, but does not quantitate the deficiency'. Recently, it has been suggested [47] that electrocardiographic monitoring might pro-

vide an accurate index of intracellular cardiac magnesium status.

The emphasis on intracellular myocardial magnesium is understandable when it is realized that the heart can become selectively depleted of magnesium, whereas the magnesium content of other muscles remains unchanged [2, 4, 7, 37, 72]. In consequence, it has been suggested that myocardial magnesium loss is a factor that could predispose such hearts to fatal arrhythmias, calcification, necrosis, and infarction [5, 11, 37, 39, 49, 72, 76].

Table II illustrates the extent of myocardial magnesium depletion in humans who have succumbed to a fatal cardiac seizure. Note that there is a 42–50% loss of myocardial magnesium in necrosed tissue, but only a 19–27% loss in 'non necrosed' tissue of the same hearts. It can be seen that the latter range is close to the 12–22% magnesium loss found in non necrosed myocardial tissue of cardiac-ischemia fatalities and sudden death cardiac cases.

Elwood and Beasley [25] have recently discussed the pitfalls of using postmortem tissue to interpret an in vivo status, and one of the factors they emphasize is that variable myocardial magnesium loss can occur in 'lingering' or chronic heart disease fatalities, i.e., the apparent magnesium loss can range from 17% [24] all the way down to 2% [7]. It is therefore likely that the data listed in table II represents 'uncomplicated' heart seizures of the 'sudden death' type. In the longer term cardiac fatalities, it is possible that the 'chronic stress' nature of the trauma has induced a depletion of myocardial ATP [see Discussion in ref. 36]. Because myocardial ATP (in the form of a Mg:ATP complex) is vital for cardiac energetics, it can be suggested that future studies of the myocardial magnesium status should include concomitant analysis of the myocardial ATP status.

Table II. Myocardial magnesium loss in humans with fatal heart seizures

Type of situation studied	% depletion of myocardial Mg (vs. controls)	Country	Reported by
Infarcted hearts			
Necrosed tissue	42	Canada	*Heggtveit* et al., 1969 [37]
	50	France	*Speich* et al., 1979 [74]
Non necrosed tissue	19	Canada	*Heggtveit* et al., 1969 [37]
	20–27	France	*Speich* et al., 1979 [74]
Cardiac-ischemia fatalities	22	Canada	*Anderson* et al., 1975 [4]
	12	USA	*Johnson* et al., 1979 [43]
Sudden death cardiac cases	16	England	*Chipperfield and Chipperfield,* 1973 [13]
	12	England	*Behr and Burton,* 1973 [7]
	12	England and Wales	*Elwood* et al., 1980 [24]

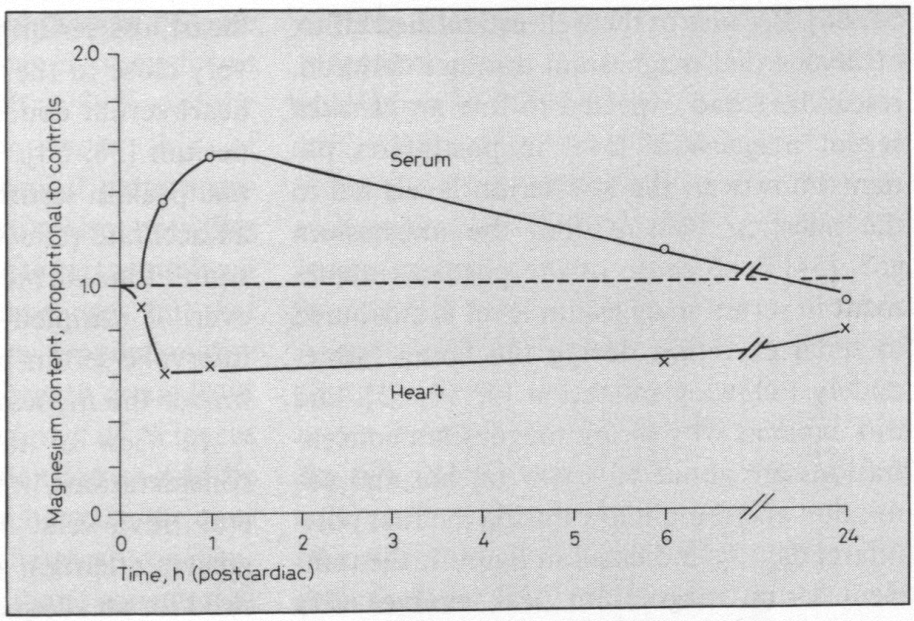

Fig. 1. Magnesium flux during myocardial infarction (plotted from the data in ref. 2).

Here, it is relevant to note that an adequate (or supernormal) dietary magnesium intake prevents the fall of soft tissue ATP that otherwise occurs in phosphate-deficient rats [9].

The interpretation of what myocardial magnesium loss actually means, especially in non necrosed tissue, poses a dilemma, i.e., is magnesium loss merely a consequence of infarction, or can prior magnesium depletion predispose the heart to a subsequent infarctus process? *Lehr* [49] has recently presented a comprehensive treatise on the various magnesium-related mechanisms involved in myocardial necrosis; among the points discussed are: (1) in cardiac trauma, loss of myocardial magnesium is the earliest electrolyte disturbance to occur; (2) loss of myocardial magnesium can occur in normal-appearing cells, and does not necessarily require obvious morphological lesions that can be seen under the light microscope; (3) myocardial magnesium loss represents an early prenecrotic stage of aberrant intracellular processes.

Thus, the initial loss of myocardial magnesium is a *pre*-necrotic phenomenon, although magnesium leakage is a continuing process that can extend into the necrotic stage of cardiac infarction; this is fully compatible with the data presented in table II.

A visual representation of the magnesium flux during cardiac infarction is shown in figure 1. Note the precipitous drop in myocardial magnesium which becomes obvious within minutes. Also, note that the efflux of myocardial magnesium is reflected by a transient increase in serum magnesium which peaks at about 1 h postinfarct, but which then subsides until the serum magnesium level is about 10% subnormal after 24 h.

The experimentally derived pattern shown in figure 1 helps to explain a seeming anomaly concerning the magnesium status of postinfarct patients. As discussed in a previous review [54], the serum magnesium in cardiac patients is about 10% lower than normal on hospital admission and also on the first postinfarct day; this phenomenon has also been reported in recent publications [28,

51, 66]. Because of the well-established efflux of myocardial magnesium during infarction, researchers had expected to find an *elevated* serum magnesium level in postinfarct patients; however, the low serum levels led to the question 'Where does the magnesium go?' [54]. The cause of the postpeak abatement in serum magnesium level is attributed to renal excretion during the hours immediately following infarction [2, 54, 63], and this explains why serum magnesium concentrations are about 10% low on hospital admission and remain low during the first postinfarct day. As indicated in figure 1, the transient serum magnesium peak evolves very rapidly during the infarction process. The rapidity of this pattern had been anticipated by *Lehr* [49]: 'It is conceivable that ... initial hypermagnesemia is not routinely detected because patients do not usually come to the attention of clinical investigators during the very early phase of infarctation.'

In a discussion of cardiac arrhythmias, *Bigg and Chia* [8] have sounded a more somber note: 'The magnesium-depleted (patients) may be less likely to reach hospital.'

It must be added that the lower than normal serum magnesium levels (i.e., seen on admission and on the first postinfarct day) tend to return to normal during subsequent days [54]. The rapidity with which normal magnesium levels are restored is thought to be a function of the magnesium intake provided by the patients' food-beverage chain [66, 77].

One final comment can be made about the reciprocal trends shown in figure 1. From the original data [2], it can be calculated that the maximum myocardial magnesium loss was 19.6 mg/100 g tissue (*note:* the entire heart was analyzed); in serum, the maximum magnesium increase was 1.2 mg/100 g. Thus, the 'heart loss/serum gain' ratio is 16.3, which is very close to the 17.3 ratio reported for the heart/serum concentration gradient of magnesium [36, 64]. Therefore, the early maximal peak in serum magnesium appears to be an accurate reflection of myocardial magnesium efflux *at the time of infarctation;* however, if sampled at subsequent postinfarct intervals, serum magnesium is less likely to mirror the myocardial magnesium efflux.

In view of the several aforementioned considerations, it is not surprising that several reviewers have recommended that greater attention should be devoted to the need for an adequate dietary magnesium status, as a means of lessening the likelihood of cardiac arrhythmias and/or infarction [3, 5, 8, 15, 43, 45, 47, 49]. In particular, it appears likely that an adequate dietary magnesium status could serve as a safeguard against stress-induced efflux of myocardial magnesium.

Drinking Water

Although this aspect has been previously reviewed [52–55], a few factors seem to warrant additional emphasis [see ref. 33, 56]. Many studies of the so-called 'water factor' have only considered the softness-hardness distinction between drinking waters and have therefore assessed the epidemiological consequences solely on a 'total hardness' basis. This can only be done if there is a consistent Ca vs. Mg proportionality in the various waters being intercompared; however, the data in table III illustrates that waters of very similar total hardness can differ enormously in their respective calcium and magnesium contents.

In the extreme right-hand column of table III, note that magnesium can account for as little as 10% – and as much as 89% – of the total hardness designation (*note:* this, of course, means that a reciprocal pattern applies for waterborne calcium). Also, note that the data in table III is compartmentalized into 4 distinct total hardness ranges, but that the variation in magnesium proportionality applies throughout. Therefore, to quote from a 1979 US National Academy of Sciences report [60]: 'Additional attention should be directed toward the relation between the concentration of individual chemical constituents in water ... rather than considering "lumped" parameters such as Hardness.'

The probable importance of waterborne magnesium was demonstrated by *Anderson* et al. [4], who showed that the hearts of 'control' fatalities (i.e., noncardiac deaths) in soft water regions contained about 6% less magnesium than similar controls from hard water localities; furthermore, the same 6% debit in myocardial magnesium content was seen in nonnecrosed heart tissue of cardiac fatalities from the same comparison of soft vs. hard water districts. It must be emphasized that the 6% debit in myocardial magnesium of soft water residents is a significant proportion of the 12–27% range found in non necrosed tissue of cardiac fatalities (as previously shown in table II).

Table III. Illustration of how total hardness of drinking water can be an unreliable index of waterborne magnesium content (adapted from Marier et al. [54])

Reference	Region	Total hardness	Ca mg/l	Mg mg/l	Mg intake via 2 liters water mg/day	% of total hardness attributable to Mg
Schroeder, 1960 [68]	USA (163 cities)	118	31.1	9.75	19.5	34
Schroeder, 1966 [69]	USA (25 cities)	125	22.5	16.5	33.0	55
Crawford et al., 1968 [17]	UK (6 localities)	295	102.0	9.25	18.5	13
Hankin et al., 1970 [34]	California (18 localities)	312	58.8	40.0	80.0	53
Anderson et al., 1975 [4]	Ontario (3 cities)	421	119.4	29.4	58.8	29
Dawson et al., 1978 [18]	Texas (1 locality)	470	21.0	100.0	200.0	89
DeFulvio and Olori, 1975 [19]	France (1 city)	661	238.0	16.0	32.0	10
DeFulvio and Olori, 1975 [19]	Italy (1 city)	676	133.9	79.1	158.2	49

In the study by *Anderson* et al. [4], the waterborne magnesium concentration averaged 29.4 mg/l in the hard water regions, and 2.8 mg/l in the soft water localities. The difference is therefore 26.6 mg/l. Assuming a daily ingestion of 2 liters of drinking water in all forms (e.g., coffee, tea, soups, reconstituted beverages, etc.), residents in these hard water regions would thereby receive about 53 mg/day of additional magnesium, in comparison with soft water residents. The possibility that this amount of supplementary magnesium can make a 6% difference in the magnesium status of the heart is something that warrants serious consideration [see also ref. 60]. However, it must be stipulated that, although these results illustrate that waterborne magnesium can indeed have a demonstrable effect on the myocardial magnesium status, this can only be demonstrated when the hard water magnesium concentration is sufficient to provide a significant proportion of the daily magnesium requirement.

In the case of the study by *Anderson* et al. [4], it can be calculated that waterborne magnesium provided about 18% of the daily magnesium requirement in hard water regions, but only about one-tenth as much in soft water localities. *Hankin* et al. [34] have reported that California hard waters provide from 9 to 27% of the daily magnesium requirement. In contrast, British hard waters are preponderantly calcic and can contain no more than 5 mg/l of magnesium, whereas the soft waters contain about 2 mg/l of magnesium [14]; therefore, intake of magnesium from these British waters would account for only 3 and 1%, respectively, of the daily magnesium requirement. It is therefore not surprising that British researchers have encountered difficulties in their efforts to confirm an association between myocardial status and waterborne magnesium [15].

In table I, it was shown that the shortfall in contemporary magnesium intake can range from 17 to 161 mg/day (not including pregnancy cases). In table III, the second column from the right shows that some very hard waters would provide barely enough magnesium to rectify only the lowest end of the shortfall range; similarly, very few hard waters can provide sufficient magnesium to compensate for the highest end of the shortfall range. Overall, this illustrates the fact that the suitability of a particular hard water can only be assessed if there is knowledge concerning the *dietary* magnesium among the region's inhabitants. As stated by *Neri and Hewitt* [61]: 'Eventually, the water story will have to be understood in the context of a more general food and drink story.'

Supplementation

As emphasized by *Durlach* [22], it is difficult to supplement the magnesium intake by recourse to currently available dietary staples because very few modern-day food items contain high levels of magnesium [see also ref. 54, 55]. Furthermore, high magnesium substances such as nuts and chocolate do not lend themselves to incorporation into a long-term dietary regimen. It has been reported that vegetarian diets provide more magnesium than refined food regimens [1], and that the magnesium content of typical vegetarian diets is 'adequate' [46], although no quantitative data was included with these comments.

In view of the suboptimal dietary magnesium intake in the modern-day world (table I), and considering the fact that the magne-

sium content of drinking water may not always be sufficient to compensate for the magnesium shortfall (table III), it is not surprising that alternate means of magnesium supplementation have been sought. Thus, the addition of magnesium to bread is being considered in the USA [65]. Magnesium supplementation has already begun in Finland, where a specially formulated table salt contains 65% sodium, 25% potassium, and 10% magnesium [44]. This 'new salt' has the double purpose of increasing magnesium intake with a concomitant reduction in sodium intake. Ingestion of 10 g of this salt per day would provide 100 mg of supplementary magnesium.

Oral magnesium supplementation has long been used to increase the urinary Mg/Ca ratio and thereby prevent urolithiasis in stone-forming patients [cf. 54]. For this purpose, magnesium oxide has been the preferred form of magnesium supplement, and successful results have been obtained at dosages providing from 120 to 250 mg magnesium/day. It has been reported that, in contrast with magnesium oxide, neither magnesium carbonate or magnesium citrate is effective for the prevention of kidney stones [cf. 54]. Paradoxically, recent studies with horses have shown [35] that both magnesium carbonate and magnesium sulfate are as well absorbed as magnesium oxide (which had previously been used as a supplement for the successful prevention of myocardial and aortic lesions in magnesium-deficient horses). The successful clinical use of magnesium hydroxide in Sweden has recently been reviewed [42]; formation of kidney stones was inhibited by an oral supplement that provided 400 mg magnesium/day. This dosage is about two times greater than used in previous successful urolithiasis therapy, but is very close to the 450–500 mg/day oral supplement recommended for magnesium-depleted patients [26]. In the latter case, the oral magnesium supplement can be given as magnesium hydroxide or magnesium acetate.

Durlach [22] has stated that any form of readily absorbable magnesium salt can be used for oral supplementation; aside from the chloride and other forms of inorganic salt, these include organo-forms such as acetate, ascorbate, lactate, etc. In assessing the effectiveness of various orally administered magnesium salts, *Classen* et al. [16] have made a distinction between deficiency and nondeficiency status. Thus, in magnesium deficiency, the chloride, aspartate, aspartate hydrochloride, and sulfate salts of magnesium were all effective for the prevention of experimentally induced adrenergic cardiopathy. However, in the absence of magnesium deficiency, only the chloride-containing magnesium salts were maximally effective, with aspartate hydrochloride being less toxic than the chloride form at high dosages. *Lehr* [49] has recently discussed what he terms 'the beneficial magnesium-sparing and sodium-depleting effect of the chloride ion' in the prevention of myocardial necrosis.

It would therefore seem that, for oral supplementation, a chloride-containing magnesium salt may provide maximum cardioprotection; in comparison, either the oxide or hydroxide forms appear adequate for the prevention of urolithiasis. It is possible that the cardiac-related importance of the chloride factor is due to the fact that cardioprotection involves an *intra*cellular phenomenon, whereas prevention of uroliths is mediated by increasing the Mg/Ca ratio in urine. Here, it is interesting to note that *Lehr* [49] has recently reviewed the role of magnesium as a 'calcium antagonist'; this role of magnesium

would be meaningful, not only at the cardiac site, but also with regard to nephrocalcinosis [54]. Both *Lehr* [49] and *Altura* [3] have emphasized the Mg:Ca competition at membranal sites, and how an adequate magnesium status prevents excessive influx of calcium; therefore, in this mechanism, magnesium adequacy is essential to maintain the functional integrity of cells and tissues.

One final comment can be made regarding oral magnesium supplementation, and this involves what can be termed 'the bulk factor'. Table IV illustrates that magnesium oxide is the most 'compact' form of oral supplementation, because it contains 60% as magnesium. In comparison, oral intake of other magnesium salts requires the ingestion of larger amounts to provide the same magnesium dosage.

In clinical practice, intravenous infusion of magnesium (as the sulfate) has long been used to stabilize cardiac arrhythmias and to treat various snydromes associated with magnesium depletion [cf. 26, 54]. Recently, there is evidence that prompt postinfarct recourse to magnesium infusion can reduce infarct size [58], and this provides substantiation for a statement made by *Lehr* [49]: 'In the early phases of myocardial infarction ... the judicious administration of magnesium ... may be the decisive factor in the survival of critically injured myocardial cells.' However, the various aspects summarized in the present review suggest the possible need for an *earlier* 'preventive' use of magnesium, in the form of daily oral supplementation.

Table IV. Some physical characteristics of various magnesium salts that might be used for supplementation

Magnesium salt	% Mg	Approx. mg salt needed to supply 100 mg magnesium
MgO	60.3	165
$Mg(OH)_2$	41.5	240
$MgCl_2$	25.5	390
$MgCO_3 \cdot CaCO_3$ (dolomite)	13.2	760
$Mg(acetate)_2 \cdot 4H_20$	11.3	900
$MgSO_4 \cdot 7H_2O$	9.9	1,000
Mg aspartate $\cdot HCl \cdot 3H_2O$	9.9	1,000
$Mg(lactate)_2 \cdot 3H_2O$	9.5	1,050
$Mg(aspartate)_2 \cdot 3H_2O$	8.4	1,200

Résumé

Cette brève revue examine les aspects quantitatifs de l'apport alimentaire insuffisant en magnésium dans le monde moderne. L'importance du magnésium est discutée en relation avec les attaques myocardiques et la formation de calculs urinaires, l'apport de magnésium par l'eau de boisson et les autres formes de supplémentation en magnésium du régime.

References

1 Abdulla, M.: Clinical signs of magnesium deficiency. Nutr. Rev. *38:* 99–100 (1980).

2 Abraham, A.S.; Baron, E.; Eylath, U.: Changes in the magnesium content of tissues following myocardial damage in rats. Med. Biol. *59:* 99–102 (1981).

3 Altura, B.M.: Sudden-death ischemic heart disease and dietary magnesium intake – is the target-site coronary vascular smooth muscle? Med. Hypoth. *5:* 843–848 (1979).

4 Anderson, T.W.; Neri, L.C.; Schreiber, G.; Talbot, F.D.F.; Zdrejewski, A.: Ischemic heart disease, water hardness, and myocardial magnesium. Can. med. Ass. J. *113:* 199–203 (1975).

5 Anderson, T.W.: Water hardness, magnesium, and ischemic heart disease. Nova Scotia med. Bull. *1977:* 58–61.

6 Ashe, J.R.; Schofield, F.A.; Gram, M.R.: The re-

tention of calcium, iron, phosphorus, and magnesium during pregnancy. Am. J. clin. Nutr. *32:* 286–291 (1979).

7 Behr, G.; Burton, P.: Heart muscle magnesium. Lancet *ii:* 450 (1973).

8 Bigg, R.P.C.; Chia, R.: Magnesium deficiency – role in arrhythmias complicating acute myocardial infarction. Med. J. Aust. *ii:* 346–348 (1981).

9 Brautbar, N.; Lee, D.B.N.; Coburn, J.W.; Montcalm, A.; Kleeman, C.R.: Role of dietary magnesium in the soft tissue, phosphorus, ATP, and bone mineral changes of phosphate depletion. Mineral Electrolyte Metab. *2:* 212 (1979).

10 Brown, J., et al.: Nutritional and epidemiological factors related to heart disease. Wld Rev. Nutr. Diet., vol. 12, pp. 1–42 (Karger, Basel 1970).

11 Burch, G.E.; Giles, T.D.: The importance of magnesium deficiency in cardiovascular diseases. Am. Heart J. *94:* 649–657 (1977).

12 Caddell, J.: Clinical signs of magnesium deficiency. Nutr. Rev. *38:* 100–102 (1980).

13 Chipperfield, B.; Chipperfield, J.R.: Heart muscle magnesium, potassium, and zinc concentrations after sudden death from heart disease. Lancet *ii:* 293–296 (1973).

14 Chipperfield, B.; Chipperfield, J.R.; Behr, G.; Burton, P.: Magnesium in heart muscle. Lancet *i:* 1354–1355 (1976).

15 Chipperfield, B.; Chipperfield, J.R.: Magnesium and the heart. Am. Heart J. *93:* 679–682 (1977).

16 Classen, H.G.; Marquardt, P.; Spath, M.; Ebel, H.; Schumacher, K.A.: Improvement by chlorine of the intestinal absorption of inorganic and organic Mg compounds and of their protective effect against adrenergic cardiopathy; in Fleckenstein, Rone, Recent advances in studies on cardiac structure and metabolism, vol. 6: Pathophysiology and morphology of myocardial cell alterations, pp. 111–119 (University Park Press, Baltimore 1975).

17 Crawford, M.D.; Gardner, M.J.; Morris, J.N.: Mortality and hardness of local water supplies. Lancet *i:* 827–831 (1968).

18 Dawson, E.B.; Frey, M.J.; Moore, T.D.; McGanity, W.J.: Relationship of metal metabolism to vascular disease mortality in Texas. Am. J. clin. Nutr. *31:* 1188–1197 (1978).

19 DeFulvio, S.; Olori, L.: Definitions and classification of naturally soft and naturally hard waters. Proc. Symp. Hardness of drinking water and public health, Luxembourg 1975, pp. 95–122 (Pergamon Press, Oxford 1975).

20 DiStazio, J.; Maley, W.; Thompson, B.; Thomas, R.; Sembrat, R.; Stremple, J.: Effect of ATP-$MgCl_2$-glucose administration during hemorrhagic shock on cardiac metabolism, function, and survival. Cir. Shock *6:* 184 (1979).

21 Drews, L.M.; Kies, C.; Fox, H.M.: Effect of dietary fiber on copper, zinc, and magnesium utilization by adolescent boys. Am. J. clin. Nutr. *32:* 1893–1897 (1979).

22 Durlach, J.: Intérêt du magnésium en médecine. Gaz. méd. Fr. *79:* 1179–1191 (1972).

23 Durlach, J.; Rayssiguier, Y.; Laguitton, A.: Le besoin en magnésium et son apport dans la ration. Méd. Nutr. *16:* 15–21 (1980).

24 Elwood, P.C.; Sweetnam, P.M.; Beasley, W.H.; Jones, D.: Magnesium and calcium in the myocardium – cause of death and area differences. Lancet *ii:* 720–722 (1980).

25 Elwood, P.C.; Beasley, W.H.: Myocardial magnesium and ischaemic heart disease. Artery *9:* 200–204 (1981).

26 Flink, E.B.: Nutritional aspects of magnesium metabolism. West. J. Med. *133:* 304–312 (1980).

27 Fodor, G.: Personal communication (Memorial University, St. Johns, Newfoundland 1978).

28 Forster, A.; Stalder, R.; Bloch, A.; Suter, P.: The value of serum magnesium estimations in the diagnosis of acute perioperative myocardial infarction after coronary artery surgery. J. cardiovasc. Surg. *22:* 163–165 (1981).

29 Greger, J.L.: Dietary intake and nutritional status in regard to zinc of institutionalized aged. J. Geront. *32:* 549–553 (1977).

30 Greger, J.L.; Huffman, J.; Abernathy, R.P.; Bennett, O.A.; Resneck, S.E.: Phosphorus and magnesium balance of adolescent females fed two levels of zinc. J. Food Sci. *44:* 1765–1766 (1979a).

31 Greger, J.L.; Gruner, S.M.; Ethyre, G.M.; Abernathy, R.P.; Sickles, V.: Dietary intake and nutritional status in regard to magnesium of adolescent females. Nutr. Rep. int. *20:* 235–243 (1979b).

32 Hamilton, E.I.; Minski, M.J.: Abundance of the chemical elements in man's diet and possible relations with environmental factors. Sci. Tot. Environ. *1:* 375–394 (1972/73).

33 Hammer, D.I.; Heyden, S.: Water hardness and cardiovascular mortality. J. Am. med. Ass. *243:* 2399–2400 (1980).

34 Hankin, J.H.; Margen, S.; Goldsmith, N.F.: Contribution of hard water to calcium and magnesium intakes of adults. J. Am. Diet. Ass. *56:* 212–224 (1970).
35 Harrington, D.D.; Walsh, J.J.: Equine magnesium supplements – evaluation of magnesium oxide, magnesium sulfate, and magnesium carbonate in foals fed purified rations. Equine Vet. J. *12:* 32–33 (1980).
36 Hearse, D.J.; Stewart, D.A.; Braimbridge, M.V.: Myocardial protection during ischemic cardiac arrest. J. thorac. cardiovasc. Surg. *75:* 877–885 (1978).
37 Heggtveit, H.A.; Tanser, P.; Hunt, B.: Magnesium content of normal and ischemic human hearts. Proc. 7th Int. Congr. Clin. Pathol., Montreal 1969, p. 53.
38 Heroux, O.; Peter, D.; Heggtveit, H.A.: Long-term effect of suboptimal dietary magnesium. J. Nutr. *107:* 1640–1652 (1977).
39 Holtmeier, H.J.: Magnesiumstoffwechselstörungen und Herzinfarkt. Proc. Symp. Herzinfarkt und Schock, Freiburg 1968, pp. 110–142 (Thieme, Stuttgart 1969).
40 Holtmeier, H.J.; Kuhn, M.: Zink- und Magnesium-Mangel beim Menschen. Therapiewoche *22:* 4536–4546 (1972).
41 Huber, H.G.; Disney, G.M.; Mason, R.L.: Dietary intake and urinary excretion of magnesium in black or white preadolescent girls. Fed. Proc. *39:* 546 (1980).
42 Johansson, G.; Backman, U.; Danielson, B.G.; Fellstrom, B.; Ljunghall, S.; Wikstrom, B.: Biochemical and clinical effects of the prophylactic treatment of renal calcium stones with magnesium hydroxide. J. Urol. *124:* 770–774 (1980).
43 Johnson, C.J.; Peterson, D.R.; Smith, E.K.: Myocardial tissue concentration of magnesium and potassium in men dying suddenly from ischemic heart disease. Am. J. clin. Nutr. *32:* 967–970 (1979).
44 Karppanen, H.: Rationale of 'new salt' mineral salt, pp. 1–4 (Pharmacology Department, University of Helsinki 1979).
45 Karppanen, H.: Epidemiological studies on the relationship between magnesium intake and cardiovascular diseases. Artery *9:* 190–199 (1981).
46 Kramer, L.; Coffey, J.; Osis, D.; DeBartolo, M.; Spencer, H.: Mineral and trace element content of vegetarian diets. Fed. Proc. *40:* 882 (1981).
47 Krasner, B.S.; Girdwood, R.; Smith, H.: The effect of slow-releasing oral magnesium chloride on the QT interval of the electrocardiogram during open-heart surgery. Can. Anaesth. Soc. J. *28:* 329–333 (1981).
48 Lee, C.J.; Lawler, G.S.: Nutrient intakes of elderly in relation to age. Fed. Proc. *39:* 347 (1980).
49 Lehr, D.: Magnesium and cardiac necrosis. Magnesium Bull. *1a:* 178–191 (1981).
50 Leverton, R.M.; Leichsenring, J.M.; Linkswiler, H.; Meyer, F.: Magnesium requirement of young women receiving controlled intakes. J. Nutr. *74:* 33–38 (1961).
51 Manthey, J.; Stoeppler, M.; Morgenstern, W.; Nussel, E.; Opherk, D.; Weintraut, A.; Wesch, H.; Kubler, W.: Magnesium and trace metals – risk factors for coronary heart disease. Circulation *64:* 722–729 (1981).
52 Marier, J.R.: The importance of dietary magnesium with particular reference to humans. Z. Vitalstoffe Zivilisationskrankh. *13:* 144–149 (1968).
53 Marier, J.R.: Cardio-protective contribution of hard waters to magnesium intake. Rev. can. Biol. *37:* 115–125 (1978).
54 Marier, J.R.; Neri, L.C.; Anderson, T.W.: Water hardness, human health, and the importance of magnesium, pp. 1–119 (National Research Council of Canada Report NRCC-17581, 1979).
55 Marier, J.R.: Nutritional and myocardial aspects of magnesium in drinking-water. Magnesium Bull. *1a:* 48–54 (1981).
56 Marier, J.R.: Water hardness and heart disease. J. Am. med. Ass. *245:* 1315–1316 (1981).
57 McHale, M.; Kies, C.; Fox, H.M.: Calcium and magnesium nutritional status of adolescent humans fed cellulose or hemicellulose supplements. J. Food Sci. *44:* 1412–1417 (1979).
58 Morton, B.C.; Smith, F.M.; McKibbon, T.J.; Nair, R.C.; Poznanski, W.J.: Magnesium therapy in acute myocardial infarction. Magnesium Bull. *1a:* 192–194 (1981).
59 National Academy of Sciences: 'Recommended Dietary Allowances'; 8th ed. (National Academy of Sciences, Washington 1974).
60 National Academy of Sciences: Geochemistry of water in relation to cardiovascular disease (National Academy of Sciences, Washington 1979).
61 Neri, L.C.; Hewitt, D.: Review and implications of ongoing and projected research outside the European Community. Proc. Symp. Hardness of drink-

ing water and public health, Luxembourg, 1975, pp. 443–466 (Pergamon Press, Oxford 1975).
62 Niemack, E.A.; Stockli, F.; Husmann, F.; Sonderegger, J.; Classen, H.G.; Helbig, J.: Einfluss von Magnesium-Aspartat-Hydrochlorid auf Transportstress und den Elektrolytgehalt im Herzen von Schweinen. Krankenhausarzt *52:* 354–357 (1979).
63 Nuoranne, P.: On the reliability of the magnesium serum value as an indicator of body magnesium status. Nord. VetMed. *39:* 71–73 (1978).
64 Polimeni, P.I.; Page, E.: Magnesium in heart muscle. Circulation Res. *33:* 367–374 (1973).
65 Ranhotra, G.S.; Lee, C.; Gelroth, J.A.: Expanded cereal fortification – bioavailability and functionality of magnesium in bread. J. Food Sci. *45:* 915–917 (1980).
66 Rector, W.G.; DeWood, M.A.; Williams, R.V.; Sullivan, J.F.: Serum magnesium and copper levels in myocardial infarction. Am. J. med. Sci. *281:* 25–29 (1981).
67 Schaffer, M.D.; Roberts, B.W.; Little, R.E.: Dietary, life-style, and anthropometric characteristics of young female clients at a detoxification facility. Fed. Proc. *40:* 803 (1981).
68 Schroeder, H.A.: Relation between mortality from cardiovascular disease and treated water supplies. J. Am. med. Ass. *172:* 98/1902–104/1908 (1960).
69 Schroeder, H.A.: Municipal drinking-water and cardiovascular death rates. J. Am. med. Ass. *195:* 81/125-85/129 (1966).
70 Schroeder, H.A.; Nason, A.P.; Tipton, I.H.: Essential metals in man – magnesium. J. chron. Dis. *21:* 815–841 (1969).
71 Seelig, M.S.: The requirements of magnesium by the normal adult. Am. J. clin. Nutr. *14:* 342–390 (1964).
72 Seelig, M.S.; Heggtveit, H.A.: Magnesium interrelationships in ischemic heart disease. Am. J. clin. Nutr. *27:* 59–79 (1974).
73 Seelig, M.S.: Magnesium deficiency with phosphate and vitamin D excesses. Cardiovasc. Med. *3:* 637–650 (1978).
74 Speich, M.; Bosquet, B.; Nicolas, G.; DeLajartre, A.Y.: Incidences de l'infarctus du myocarde sur les teneurs en magnésium plasmatique, érythrocytaire et cardiaque. Revue fr. Endocr. clin. *20:* 159–163 (1979).
75 Srivastava, U.S.; Nadeau, M.H.; Gueneau, L.: Mineral intakes of university students – magnesium content. Nutr. Rep. int. *18:* 235–242 (1978).
76 Szelenyi, I.: Magnesium and its significance in cardiovascular and gastrointestinal disorders. Wld Rev. Nutr. Diet., vol. 17, pp. 189–224 (Karger, Basel 1973).
77 Vejlsted, H.; Eliasen, P.: Post-operative serum levels and urinary excretion of magnesium following heart surgery. Scand. J. thorac. cardiovasc. Surg. *12:* 91–94 (1978).
78 Vir, S.C.; Love, A.H.G.: Nutritional status of institutionalized and non-institutionalized aged in Belfast. Am. J. clin. Nutr. *32:* 1934–1947 (1979).

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