

**SUDDEN DEATH OF ATHLETES:
IS IT DUE TO LONG-TERM CHANGES IN SERUM
MAGNESIUM, LIPIDS AND BLOOD SUGAR?**

Gustawa Stendig-Lindberg

*Department of Physiology and Pharmacology
Sackler Faculty of Medicine, Tel Aviv University
and Back Rehabilitation Unit
Ichilov Hospital, Tel Aviv Sourasky Medical Center
Tel Aviv, Israel*

ABSTRACT

In young, apparently healthy, trained Israeli men, strenuous effort was reported to give rise to persistent magnesium (Mg) deficiency and a parallel long-term increase of cholesterol, triglycerides and blood sugar /1-3/.

The relationship of Mg deficiency to the pathogenesis of cardiovascular disease has been increasingly documented during the last decade. Several authors have highlighted the phenomenon of sudden deaths in sport and have suggested that it is associated with cardiovascular disease.

The association is discussed between Mg deficiency and increase of blood lipids and sugar, found as a sequel to strenuous effort, and cardiovascular morbidity and mortality risk reported in athletes.

It is postulated that sudden death of athletes and other intensely training individuals during exertion, is mediated by the deleterious cardiovascular effects of persistent magnesium deficiency and the resultant hyperlipaemia and hyperglycaemia, which, as we have documented, follows strenuous effort.

KEY WORDS

magnesium deficiency, exertion, athletes, sudden death

Accepted 1 July 1992

INTRODUCTION

A number of studies showed that in young, trained, apparently healthy, Israeli men, as a sequel of strenuous effort, there was a persistent decrease of serum magnesium concentration (S-Mg) /1-4; Stendig-Lindberg, this issue/. A delayed 30% increase of triglycerides ($p < 0.001$) was observed in parallel, 3 days after the termination of strenuous effort (a 120 km brisk hike). This increase coincided with the peak decrease of S-Mg /1/. In addition, a significant increase of blood sugar ($p < 0.001$) was seen, immediately after the termination of the strenuous effort, which coincided with the first peak of the biphasic decrease of S-Mg.

The only previous report of an increase of triglycerides following effort was that of Sutherland *et al.* /5/ in 20-55 year-old men after four months of training culminating in a marathon run.

As regards the increase of blood sugar, Naven *et al.* /6/ reported a rise of blood sugar after strenuous intermittent running. However, it has been generally accepted that blood sugar and lipids decrease after effort. For this reason, further studies were undertaken to examine the long-term effect of strenuous effort on intermediary metabolism in young, trained, apparently healthy, Israeli men. The results are briefly summarized, to form an experimental basis for the proposed hypothesis. The relevant methodology is detailed in /1-3/.

In the first study, twenty men were examined (mean age 19.3, S.D. 1.4) following a 70 km brisk hike /2/. The results are shown in Figs. 1, 2 and 3. Serum triglycerides began to rise 24 h after termination of strenuous effort and were significantly raised 17 days later. Blood sugar, which decreased at 24 h after the hike, was significantly increased at day 18. Mean serum cholesterol, which was seen to decrease gradually, reaching the lower border of the reference value at 72 h after termination of the 70 km march, was also highly significantly raised on day 18. No bouts of strenuous effort took place within the 18 days after the termination of the march. Since the increase was *delayed*, it is possible that the generally accepted impression of a decrease of blood sugar and lipids occurring as a result of strenuous effort, may have been due to an insufficiently long follow-up.

In the second study, 15 volunteer soldiers (mean age 18.6, S.D. 1.3 years) were examined 6 and 10 months after a 120 km brisk march

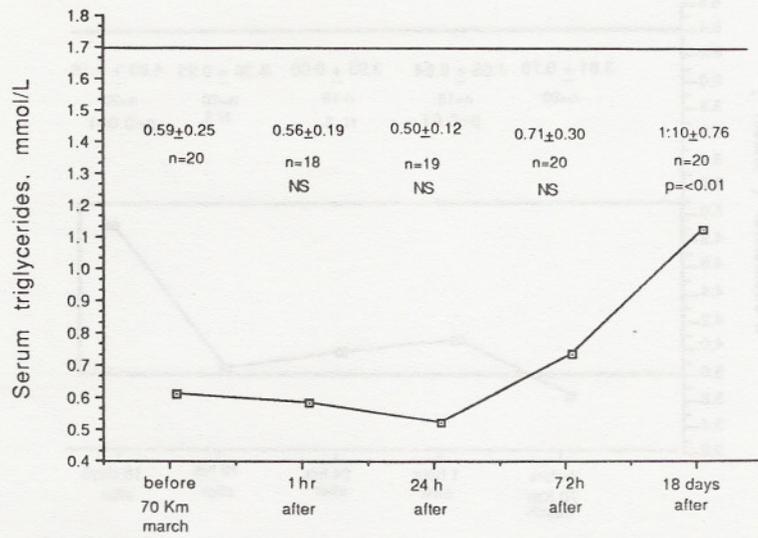


Fig. 1: Serum triglycerides before and after 70 km brisk hike. The horizontal upper line represents the upper border of the reference range. p values represent the probability in comparison with the baseline value. NS = Non-significant.

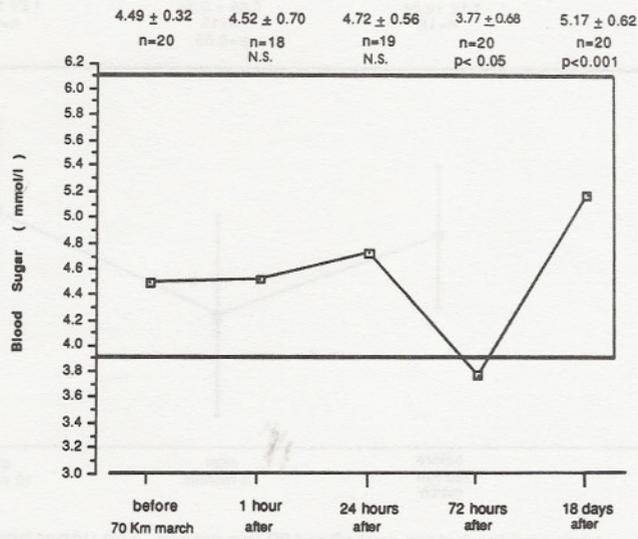


Fig. 2: Blood sugar before and after 70 km march. The shaded area represents the reference range. p values represent the probability in comparison with the baseline value. NS = Non-significant.

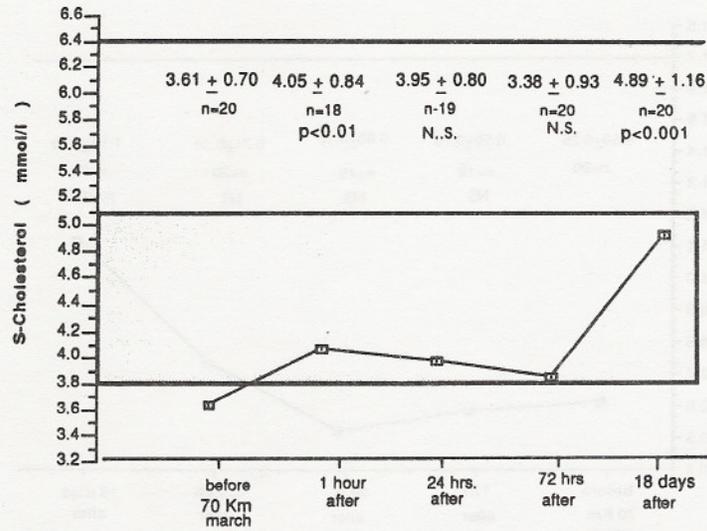


Fig. 3: Serum cholesterol before and after 70 km brisk hike. The shadowed area represents the reference range. p values represent the probability in comparison with the baseline value. NS = Non-significant.

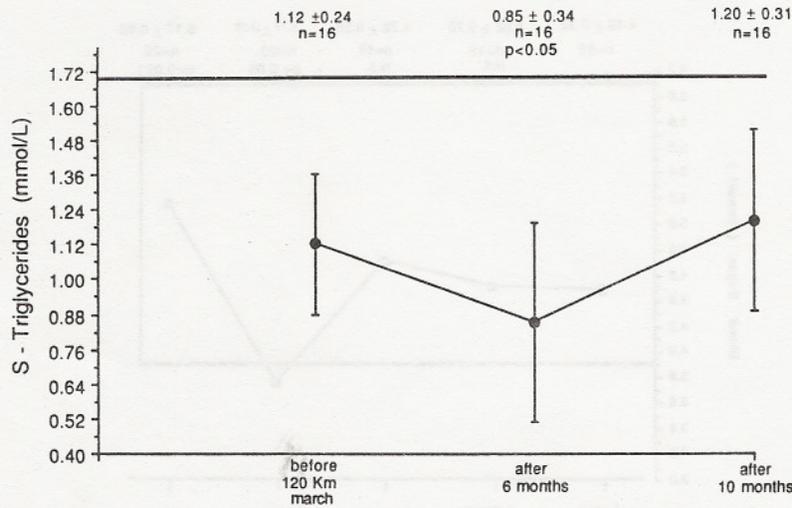


Fig. 4: Serum triglycerides before and after 120 km march. The upper horizontal line represents the upper border of the reference range. p represents the probability in comparison with the baseline value. NS = Non-significant.

/3/. Figs. 4, 5 and 6 show a gradual, although non-significant, rise of blood sugar and lipids over time. In the cases of blood sugar and triglycerides, this was preceded by a decrease, a phenomenon which may have been the cause of the usually reported decrease of the latter following exertion.

Although the subjects carried out daily training (not exceeding 4000 kcal [16.7 mJ] energy expenditure), no bouts of comparable strenuous effort took place between the termination of the forced marches and the end of the observation period, in either study.

In the third and last study, 16 volunteer soldiers (mean age 18.7, S.D. 0.6 years) were followed for 11 months after a 120 km brisk march (with no further bouts of comparable strenuous effort in the interim period) /3/. The results are shown in Figs. 7-9. Serum triglycerides show a biphasic rise; at 11 months after the effort, the mean lies at the upper border of the reference range. Serum cholesterol rises, beginning 9 months after the effort, to become significantly raised 11 months afterwards, while blood sugar decreases after a significant rise at 9 months.

A rise in cholesterol and the HDL-cholesterol fraction has been reported in man in treadmill exercise until exhaustion /7/. This was, nevertheless, interpreted as a beneficial effect of effort on the lipid profile, due to the increase in the HDL-cholesterol fraction.

We did not carry out lipoprotein electrophoresis, but nonetheless the findings in the three studies show a consistent trend of increase in lipid levels. This suggests a deleterious effect of strenuous effort on the lipid profile which, together with the tendency to an increase in blood sugar, could pose a health hazard to large sections of populations engaged in strenuous effort (e.g. manual workers, soldiers). This hazard will be increased further by exertion at high temperatures (hot climate, factory conditions, etc.) due to the additional loss of magnesium in sweat /1, 2, 8, 9/.

THE CONTRIBUTION OF Mg DEFICIENCY TO LONG-TERM CHANGES IN INTERMEDIARY METABOLISM AFTER EXERTION

Mg is essential for intermediary metabolism /10-14/. In the glycolytic pathway, 7 out of 13 steps are Mg-dependent and in the tricarboxylic acid cycle (Krebs' cycle) 3 out of 9 steps are Mg-dependent, including the initial conversion of pyruvate to acetyl-CoA through activation by Mg^{2+} of pyruvate dehydrogenase /8/.

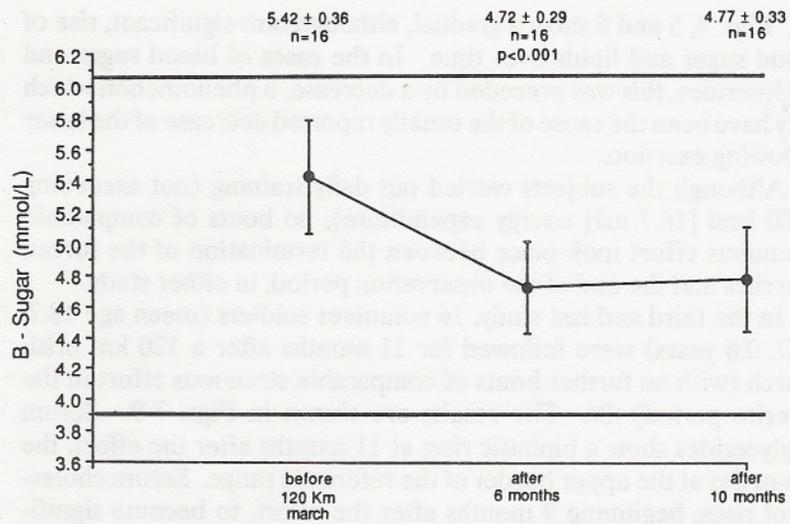


Fig. 5: Blood sugar before and after 120 km march. The horizontal lines represent the reference interval. p represents the probability in comparison with the baseline value. NS = Non-significant.

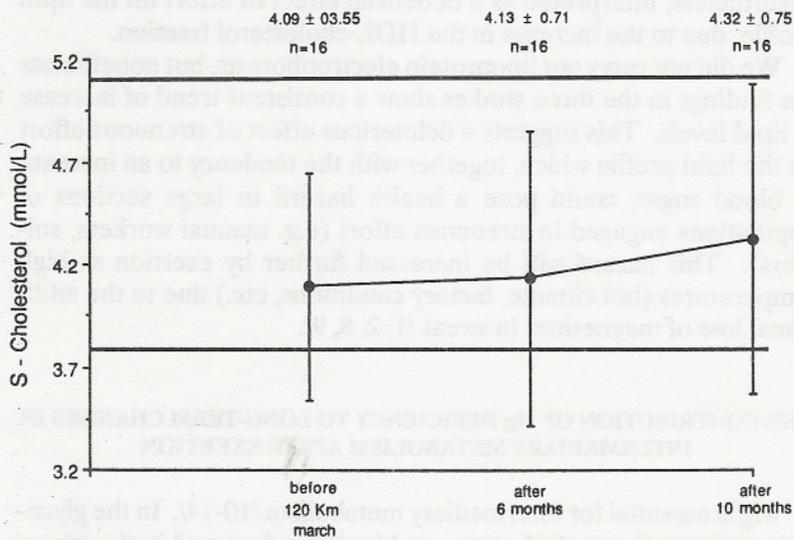


Fig. 6: Serum cholesterol before and after 120 km march. The horizontal lines represent the reference interval. p represents the probability in comparison with the baseline. NS = Non-significant.

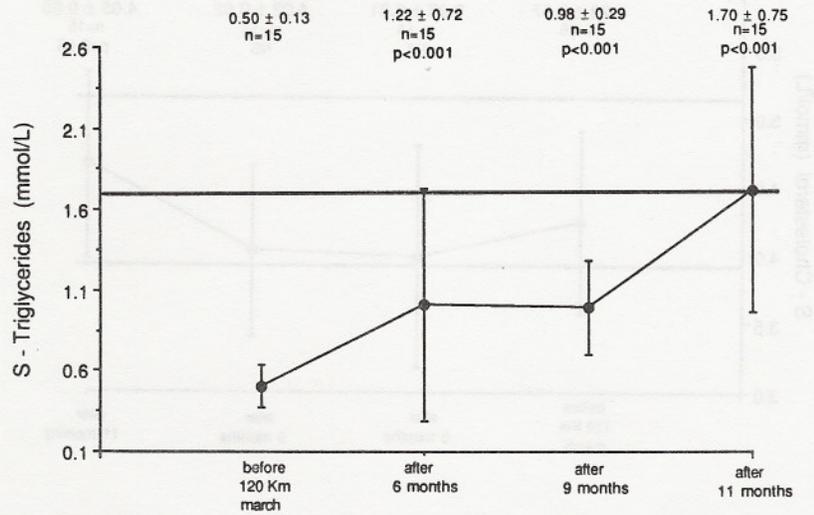


Fig. 7: Serum triglycerides before and after 120 km march. The upper horizontal line represents the upper border of the reference range. p represents the probability in comparison with the baseline. NS = Non-significant.

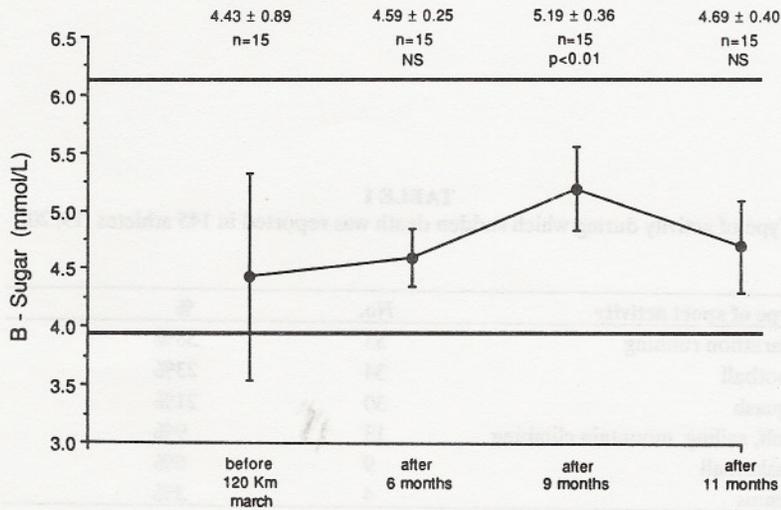


Fig. 8: Blood sugar before and after 120 km march. The horizontal lines represent the reference interval. p represents the probability in comparison with the baseline. NS = Non-significant.

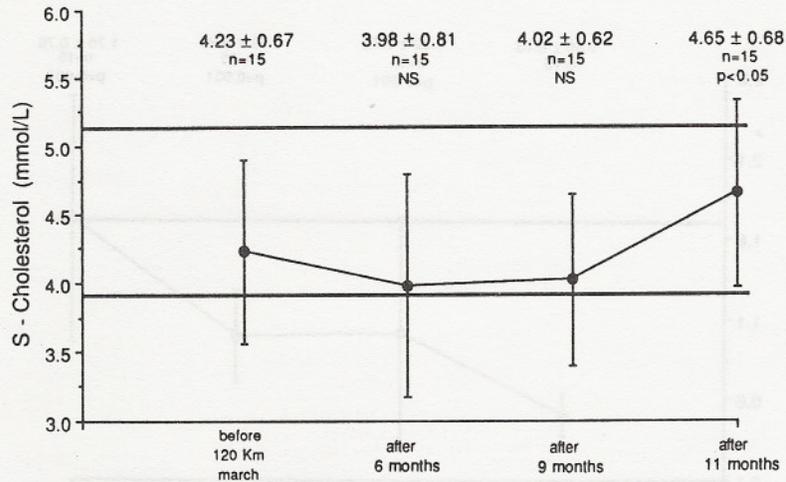


Fig. 9: Serum cholesterol before and after 120 km march. The horizontal lines represent the reference interval. p represents the probability in comparison with baseline. NS = Non-significant.

TABLE 1
Type of activity during which sudden death was reported in 145 athletes /19, 20/

Type of sport activity	No.	%
Marathon running	55	38%
Football	34	23%
Squash	30	21%
Golf, sailing, mountain climbing	13	9%
Basketball	9	6%
Tennis	4	3%

Animal experiments show that the plasma activity of lecithin-cholesterol acetyltransferase (LCAT), which is needed to esterify cholesterol, is decreased in magnesium deficiency /15/. This decrease may cause the lowering of cholesterol esters, which bind to the HDL-cholesterol fraction. The resultant decrease would impair the breakdown of triglycerides. In addition, lipoprotein lipase activity may be impaired in magnesium deficiency causing hypercholesterolaemia /16/. Although research on the effect of Mg deficiency on glucose and lipid metabolism has been scanty hitherto in man, evidence derived from animal experiments allows us to extrapolate that Mg deficiency due to strenuous effort would impair the breakdown of blood glucose and lipids. Hormonal changes seen during exercise, including a rise of catecholamines, thyroid stimulating hormone, glucagon, and corticosteroids and a decrease of plasma insulin, which favour mobilization of fatty acids and hepatic glucose /17/, may enhance the demand for Mg during strenuous effort, resulting in a vicious circle. This is even more likely to occur when dietary Mg intake is inadequate, as, e.g., found in Israel /18/.

SUDDEN DEATH IN ATHLETES

Northcote and Ballantyne analysed the type of activity during which death occurred in 145 reported cases of sudden death in athletes /19, 20/; see Table 1.

According to the literature, the most common cause of sudden death in sport is cardiac arrest. According to Northcote and Ballantyne /19/, 14% of cases are due to structural abnormalities such as hypertrophic myopathy or congenital anomaly, 7% are due to myocarditis, 2% to fatal arrhythmias and 73% to coronary artery disease. The latter is the most frequent cause of sudden death in sport. In the study of Thompson *et al.* /22/, all deaths while jogging in Rhode Island during 1975-1980 were due to coronary artery disease.

Mg DEFICIENCY, HYPERGLYCAEMIA AND HYPERLIPIAEMIA IN STRENUOUS EFFORT AND SUDDEN DEATH IN ATHLETES

Mg regulates smooth muscle contraction /23/ and its deficiency favours vasoconstriction. The latter, occurring in the coronary vessels, predisposes to coronary disease /24/. The relationship between

Mg, mineral content of drinking water and cardiovascular morbidity was first reviewed by Marier *et al.* /25/. Since then, an increasing body of literature has dealt with the role of magnesium in the pathogenesis of ischaemic heart disease.

Coronary disease was reported to be the most frequent cause of sudden death in sports /21/. In 33% of the cases of sudden death in sport, the prodromal complaints were chest pain of anginal type and fatigue /21, 26/. Fatal ventricular fibrillation was reported as one of the causes of death in strenuous exercise /21/. The association of Mg deficiency and cardiac arrhythmia was first documented in man by Chadda *et al.* /27/, and experimental animal research has shown that Mg facilitates defibrillation /28/. Finally, in experimental animals, Mg deficiency has recently been shown to be implicated in the pathogenesis of arteriosclerosis /29/.

In subjects engaged in strenuous effort, therefore, the deleterious effect of Mg deficiency will compound the already extensively documented negative effects of hyperlipaemia and hyperglycaemia on the cardiovascular system; together, they will enhance the risk of cardiovascular morbidity and potential mortality.

The increased cardiovascular morbidity of exertion, mediated by Mg deficiency and raised blood lipids and sugar, may give rise both to the "burn out" of athletes, as well as to an increased risk of occurrence of coronary disease, myocardial infarction and cardiac arrhythmias, which, in turn, predispose to the risk of sudden death /21/. The dramatic decrease of S-Mg found to follow strenuous exertion /1, 2/, together with a pre-existing Mg deficiency and the accompanying metabolic changes /1, 2, 3/, may at one point in time serve as a trigger for cardiovascular sudden death in exposed individuals, e.g. athletes or elite soldiers during strenuous effort.

REFERENCES

1. Stendig-Lindberg G, Shapira Y, Epstein Y, Galun E, Schonberger E, Graff E, Wacker WEC. Changes in serum magnesium concentration after strenuous exercise. *J Am Coll Nutr* 1987; 5: 35-40.
2. Stendig-Lindberg G, Shapira Y, Graff E, Shonberger E, Wacker WEC. Delayed metabolic changes after strenuous exertion in trained young men. *Magnesium Res* 1989; 2: 211-218.
3. Stendig-Lindberg G, Wacker WEC, Shapira Y. Long term effects of peak strenuous effort on serum magnesium, lipids, blood sugar in apparently healthy young men. *Magnesium Res* 1991; 4.

4. Stendig-Lindberg G, Bergström J, Hultman E. Hypomagnesaemia and muscle electrolytes and metabolites. *Acta Med Scand* 1977; 201: 273-280.
5. Sutherland WHF, Woodhouse SP, Williamson S, Smith B. Decreased and continued physical activity and plasma lipoprotein lipids in previously trained men. *Atherosclerosis* 1981; 39: 307-311.
6. Naven H, Rehunen S, Kuopposalmi K, Tulkiouta I, Harkonen M. Muscle metabolism during and after strenuous intermittent running. *Scand J Clin Lab Invest* 1978; 38: 329-336.
7. Durstein JL, Miller W, Farrell S, Sherman WM, Ivy JL. Increase in HDL-cholesterol and the HDL-LDL cholesterol ratio during prolonged endurance exercise. *Metabolism* 1983; 3: 973-987.
8. Epstein Y, Stendig-Lindberg G, Shapira Y, Rosenbaum J, Galun E, Schonberg E, Graff E, Wacker WEC. The effect of exercise under severe heat load on serum magnesium. 1st Joint Congress of Israeli Association of Life Sciences. *Isr Acad Sci* 1983.
9. Bellar GA, Moher JT, Hartley LH, Bass DE, Wacker WEC. Changes in serum and sweat magnesium levels during work in the heat. *Aviat Space Environ Med* 1975; 46: 709-715.
10. Heaton F. Magnesium in intermediary metabolism. In: Catin M, Seelig M, eds, *Magnesium in Health and Disease*. New York, London: Spectrum Books, 1980.
11. Wacker WEC. *Magnesium and Man*. Cambridge, MA: Harvard University Press, 1980.
12. Durlach J, Rayssiguier Y. Données nouvelles sur les relations entre magnésium et hydrates de carbone. I. Données physiologiques. *Magnesium* 1983; 2: 174-191.
13. Durlach J, Rayssiguier Y. Données nouvelles sur les relations entre magnésium et hydrates de carbone. II. Données clinique et thérapeutiques. *Magnesium* 1983; 2: 192-224.
14. Durlach J. *Magnesium in Clinical Practice*. London: John Libbey, 1988.
15. Gueux E, Alcinor L, Rayssiguier Y. The reduction of plasma lecithin-cholesterol acyl-transferase activity by magnesium deficiency in the rat. *J Nutr* 1984; 114: 1479-1483.
16. Gueux E, Rayssiguier Y. The hypercholesterolemic effect of magnesium deficiency following cholesterol feedings in the rat. *Hormone Metab Res* 1983; 15: 595-597.
17. Galbo H, Richter A, Hilstead J, Holst JJ, Christiansen NJ, Henriksson J. Hormonal regulation during prolonged exercise. *Ann NY Acad Sci* 1977; 301: 72-80.
18. Stendig-Lindberg G, Rudy N, Penciner J, Chayne M, Katcharow O. Serum magnesium pattern in apparently healthy Israeli population. *Magnesium* 1983; 2: 26-35.
19. Northcote RJ, Ballantyne D. Sudden death and sport. *Sports Med* 1981; 1: 181.
20. Northcote RJ, Ballantyne D. Cardiovascular implications of strenuous exercise. *Int J Cardiol* 1985; 8: 3.
21. Northcote RJ, Ballantyne D. Sudden cardiac death in sport. *Br Med J* 1983; 287: 1357-1359.

22. Thompson PD, Funk EJ, Carleton RA, Sturner WQ. Incidence of death during jogging in Rhode Island from 1975 through 1980. *JAMA* 1982; 247: 2535-2538.
23. Altura BM, Altura BT. Magnesium ions and contraction of smooth muscles: relationship to some vascular diseases. *Fed Proc* 1981; 40: 2672-2679.
24. Altura BM, Altura BT. Mg, Na and K interaction and coronary heart diseases. *Magnesium* 1982; 1: 241-265.
25. Marier JR, Neri LC, Anderson TW. Water hardness, human health, and the importance of magnesium. National Research Council of Canada, NRC Associate Committee on Scientific Criteria for Environmental Quality. Publ No NRCC 17581, Environmental Secretariat, Publications, NRCC/CNRC, Ottawa, Canada KIA OR6, 1979.
26. Alonzo AA, Simon AB, Feinlab M. Prodromata of myocardial infarction and sudden death. *Circulation* 1975; 52: 1056-1062.
27. Chadda KD, Gupta PK, Lichstein E. Magnesium in cardiac arrhythmias. *New Engl J Med* 1972; 287: 1102.
28. Stendig-Lindberg G, Varon D, Graff E, Schonberger E, Manoch M. Magnesium fluxes in ventricular fibrillation and defibrillation in untreated and dibenzepine HCl® pretreated cats. *Magnesium Res* 1988; 1: 45-50.
29. Rayssiguier Y. Role of magnesium and potassium in the pathogenesis of arteriosclerosis. *Magnesium* 1984; 3: 226-238.