Magnesium Research (1989) **2**, 3, 211-218 ORIGINAL ARTICLE

Delayed metabolic changes after strenuous exertion in trained young men

G. Stendig-Lindberg[1], Y. Shapira[2], E. Graff[3], E. Schonberger[4], W. E. C. Wacker[5]

[1]Department of Physiology and Pharmacology, The Sackler School of Medicine, Tel Aviv University and Back Rehabilitation Center, Ichilov Hospital, Tel Aviv; [2]The Heller Institute of Medical Research, Sheba Medical Center, Tel Hashomer; [3]Department of Clinical Chemistry, Ichilov Hospital, Tel-Aviv; [4]National Physical Laboratory, Hebrew University, Jerusalem, Israel; [5]Harvard University Health Services, Cambridge, MA, USA.

Summary: Twenty apparently healthy, young male volunteers, aged 18-25 (mean 19.3, SD 1.4) years received a 6 months standardized, graded outdoor physical training and were screened for serum magnesium concentration (S-Mg), serum calcium concentration (S-Ca), serum aspartate amino transferase (S-AST), serum alanine amino transferase (S-ALT), serum creatine kinase activity (S-CK), other laboratory variables, weight, and $\dot{V}O_2$ ml·min^{-1}·kg^{-1} ($\dot{V}O_2$ max), before a 70 km march, as well as at 1, 24 and 72 h and 18 days after. Maximal aerobic power, body weight, haemoglobin, haematocrit, serum creatinine, total protein and albumin remained unchanged throughout. Immediately after the march, S-Mg did not change, S-AST, S-ALT and S-CK rose, but the rise was not statistically significant, while small but significant rises in S-Ca ($P<0.05$, Student's *t*-test) and serum cholesterol ($P<0.01$) normalized at 24 h. At 72 h after the march, a significant fall in S-Mg was found ($P<0.01$), together with a second significant rise in S-Ca ($P<0.05$). After 18 days, with no intervening marches or dietary changes, S-Mg remained significantly lowered ($P<0.05$), mean S-ALT and S-CK became significantly raised for the first time ($P<0.001$ and $P<0.01$ respectively), whereas S-Ca normalized. Concomitantly, for the first time there was now a significant rise in blood sugar ($P<0.001$), serum triglycerides ($P<0.01$), and a second rise of serum cholesterol ($P<0.001$).

This is, to our knowledge, the first study which shows (1) a significant delayed fall in S-Mg, appearing first 3 days after the termination of strenuous effort and persisting 18 days later, indicating the presence of magnesium depletion, and (2) a relative, yet significant, delayed increase in blood sugar and lipids, observed first 18 days after the 70 km march.

Key words: Blood sugar, lipids, magnesium, strenuous exercise.

Introduction

In a previous report[1], we showed that after strenuous exercise (a 120 km brisk hike) there is a profound, biphasic fall in serum magnesium concentration (S-Mg) which peaks at 72 h after completing the exertion. Thereafter, despite resumption of normal physical activity and the ingestion of a diet estimated to contain 300 mg of Mg per day, the S-Mg remained low for at least 3 months after the strenuous exercise. While others have reported a slight decrease in S-Mg immediately after short bouts of intensive exercise[2-6], to our knowledge, no one has carried out serial follow up measurements prior to our study. The lowering in Mg concentration, therefore, was considered to be transient.

The present study was intended to extend our earlier observations in order to see whether following a less intense exertion (a 70 km march) similar changes in S-Mg and other biochemical variables could be observed.

Material and methods

Twenty healthy young male volunteers entered the study, aged 18-25 (mean 19.3, SD 1.4) years, mean body weight 68.5, SD 6.2, kg, and mean $\dot{V}O_2$ max 44.0, SD 4, ml· kg $^{-1}$·min $^{-1}$.

Informed consent was obtained from all the volunteers. The subjects underwent a 6 month period of graded physical standardized outdoor training (modelled on military training), beginning with marches of 1 km a day and increasing gradually over time in lengths and intensity, up to 20 km a day.

Throughout the training period all subjects received a uniform diet. At the end of the training period the subjects undertook a 40 km march, followed 2 weeks later by a 70 km march.

The subjects were screened for serum magnesium concentration (S-Mg), serum calcium concentration (S-Ca), serum aspartate amino transferase (S-AST), serum alanine amino transferase (S-ALT), serum creatine kinase activity (S-CK), serum creatinine, total protein, albumin, globulin, triglycerides, cholesterol, blood sugar, haemoglobin and haematocrit, and their aerobic capacity was measured before the 70 km march, as well as at 1, 24 and 72 h, and 18 days after.

In addition, S-Mg and S-Ca were screened before the start of the training period.

Laboratory amd $\dot{V}O2$ max screening

Blood samples were taken in the sitting position, between 8:00 and 10:00 am, after an overnight fast, using brief stasis. Magnesium was measured in all probands using a Perkin Elmer atomic absorption spectrophotometer No 305 A, according to Stendig-Lindberg *et al.*[7], at the National Physical Laboratory of the Hebrew University, Jerusalem. The remaining laboratory variables were measured in a standard manner at the Clinical Chemistry Laboratory, Ichilov Hospital, and $\dot{V}O_2$ max was estimated from submaximal heart rates according to Astrand[8] at the Heller Institute of Medical Research.

Statistics

The data were evaluated using the paired Student's *t*-test and the χ^2 test.

Results

Maximal aerobic power and body weight remained unchanged throughout (Table 1), as did haemoglobin, haematocrit, serum creatinine, total protein and albumin.

Table 1. Weight and $\dot{V}O_2$ before and after 70 km march. Values are means ± SD, numbers

	Before 70km	*After 1h*	*After 24h*	*After 72h*	*After 18d*
		NS	NS	NS	NS
Weight (kg)	68.5 ± 6.2 (18)	68.5 ± 6.6 (18)	66.5 ± 5.5 (19)	68.0 ± 5.5 (20)	68.1 ± 5.3 (20)
		NS	NS	NS	NS
$\dot{V}O_2$ max ($ml \cdot min^{-1} \cdot kg^{-1}$)	43.8 ± 4.6 (18)	43.8 ± 4.6 (18)	44.8 ± 5.8 (19)	45.4 ± 10.0 (20)	42.4 ± 7.6 (20)

NS = non-significant

The 70 km march

During the 70 km march, the ambient temperature was 27-30.5°C, and the relative humidity 57-75%. The march, which was continuous over a hilly dirt road terrain, began in the evening to minimize heat exposure and lasted 13 h. As a safeguard, a specially trained physician was in attendance and fluid was provided *ad libitum*. The estimated 24 h Mg intake was 270 mg from the food and 226 mg from the water (8 litres), a total of 496 mg.

Mean S-AST and S-CK peaked first at 1 h, reaching respective mean values of 41.0 (SD 17.1) and 327.8 (SD 123.2) IU, and then again at 18 days, reaching 41.4 (SD 23.9) and 280.3 (SD 341.2) IU. The latter rise was statistically significant for S-CK ($P<0.05$). S-ALT rose gradually and reached a mean of 10.5 (SD 6.1) IU at 18 days after the march. This was a highly significant increase ($P<0.001$) in relation to the initial mean of 4.8 (SD 1.0) IU (Figs 1,2,3).

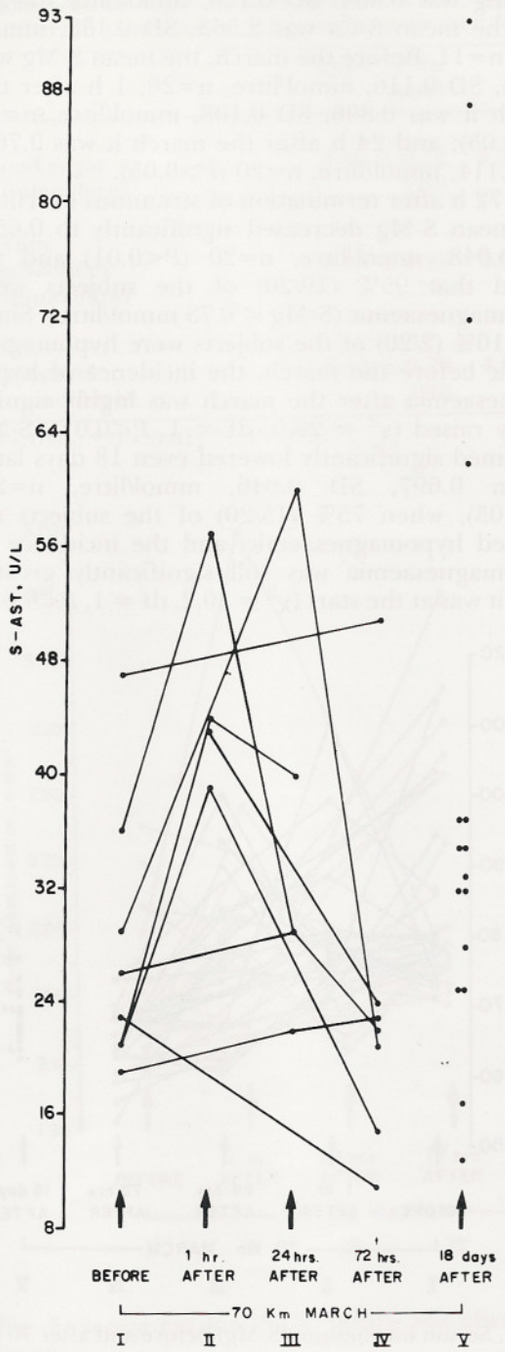

Fig. 1. Serum aspartate amino transferase (S-AST) before and after 70 km march.

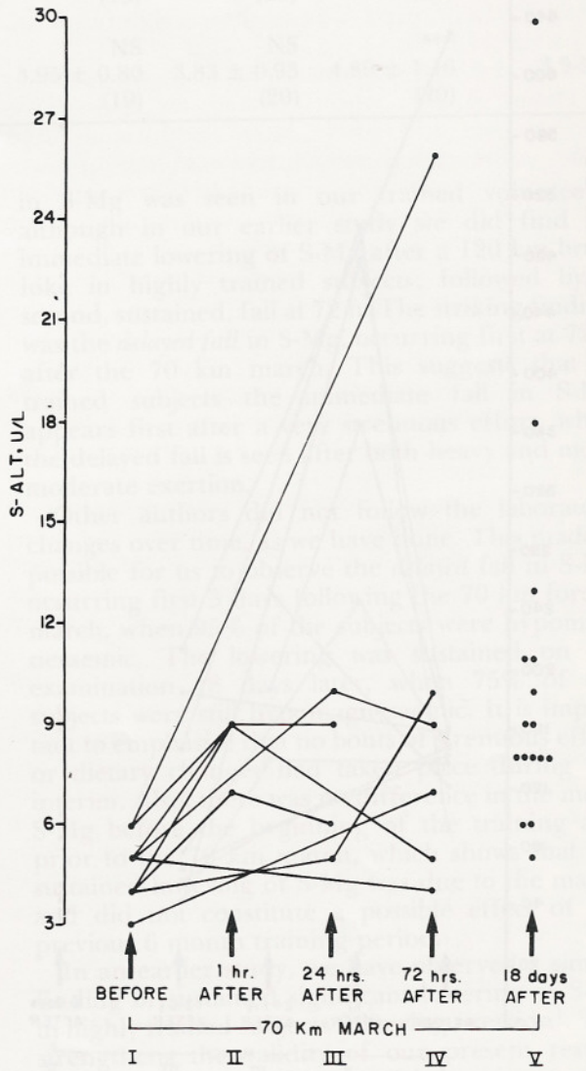

Fig. 2. Serum alanine amino transferase (S-ALT) before and after 70 km march.

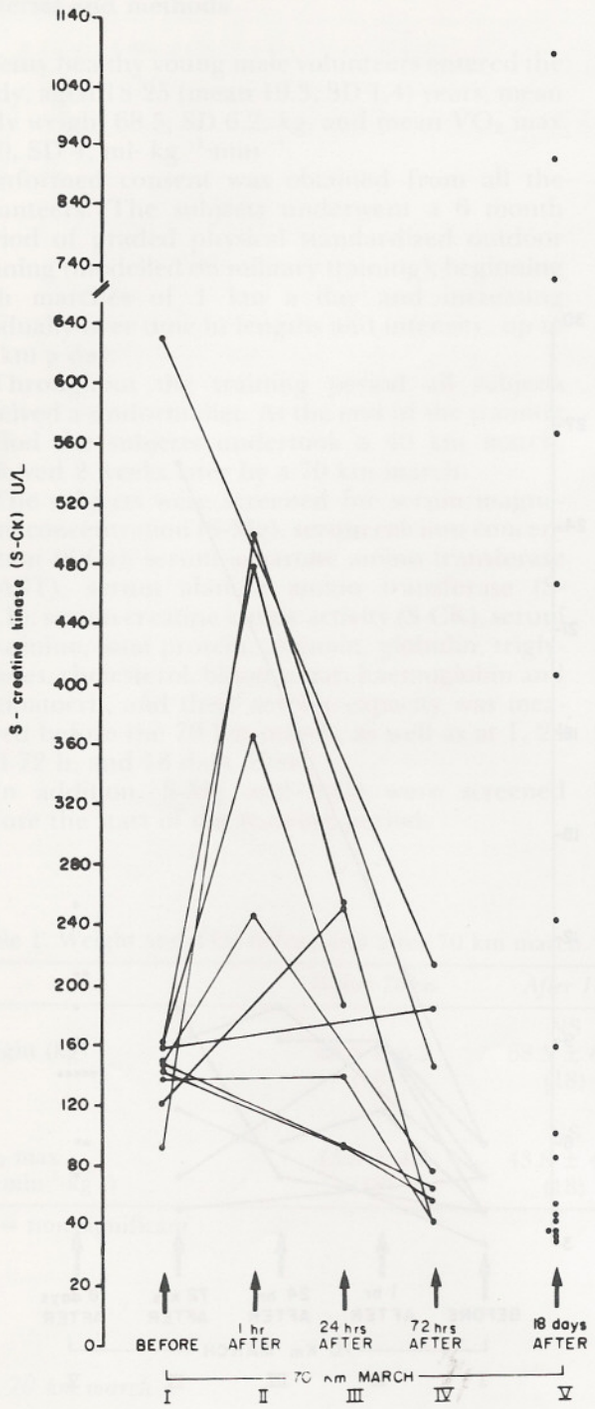

Fig. 3. Serum creatine kinase activity (S-CK) before and after 70 km march.

Serum magnesium concentration, calcium concentration, blood sugar and lipids

The initial mean S-Mg before the start of the training was 0.834, SD 0.116, mmol/litre. n=20, and the mean S-Ca was 2.563, SD 0.138, mmol/litre, n=11. Before the march, the mean S-Mg was 0.834, SD 0.116, mmol/litre, n=20; 1 h after the march it was 0.806, SD 0.108, mmol/litre, n=17 ($P>0.05$); and 24 h after the march it was 0.763, SD 0.114, mmol/litre, n=20 ($P>0.05$).

At 72 h after termination of strenuous exertion, the mean S-Mg decreased significantly to 0.650, SD 0.048, mmol/litre, n=20 ($P<0.01$) and we found that 95% (19/20) of the subjects were hypomagnesaemic (S-Mg < 0.73 mmol/litre). Since only 10% (2/20) of the subjects were hypomagnesaemic before the march, the incidence of hypomagnesaemia after the march was highly significantly raised ($\chi^2 = 29.0$, df = 1, $P<0.01$). S-Mg remained significantly lowered even 18 days later (mean 0.697, SD 0.046, mmol/litre, n=20, $P<0.05$), when 75% (15/20) of the subjects remained hypomagnesaemic, and the incidence of hypomagnesaemia was still significantly greater than it was at the start ($\chi^2 = 10.2$, df = 1, $P<0.01$);

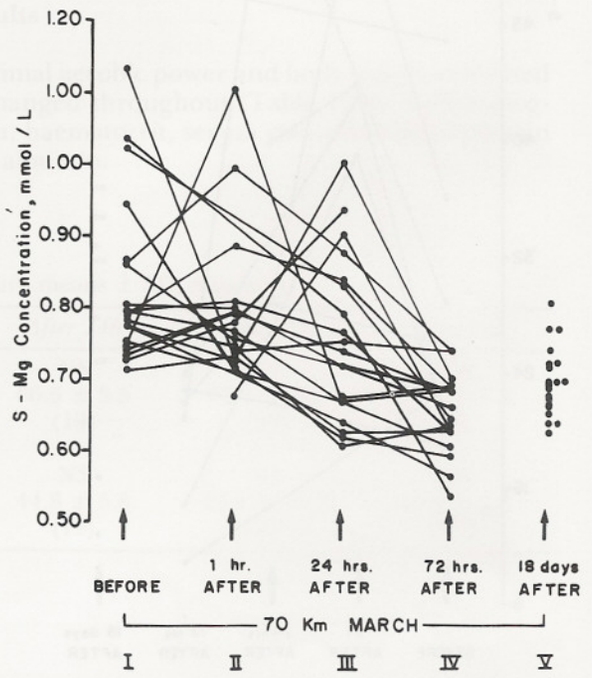

Fig. 4. Serum magnesium (S-Mg) before and after 70 km march.

Fig. 4. A small but significant biphasic rise in S-Ca was found at 1 and 72 h, but 18 days after the march S-Ca no longer differed from the initial value; Fig. 5.

Another important finding was the late yet significant rise in blood sugar and serum triglycerides 18 days after the march, together with a second rise of serum cholesterol (the first rise occurring 1 h after the march); Table 2.

Table 2. Blood sugar, serum triglycerides and cholesterol, before and after the 70 km march. Values are means ± SD, numbers in parentheses. (SI conversion factors: for blood sugar; 18, S-triglycerides; 0.0113, S-cholesterol; 0.0257.)

	Before 70 km march	*1h after*	*24h after*	*72h after*	*18 days after*	*Reference values*
		NS	NS	*	***	
Blood sugar (mmol/litre)	4.49 ± 0.32 (20)	4.52 ± 0.70 (18)	4.72 ± 0.56 (19)	3.77 ± 0.68 (20)	5.17 ± 0.62 (20)	3.9-6.1
		NS	NS	NS	**	
Serum triglycerides (mmol/litre)	0.59 ± 0.25 (20)	0.56 ± 0.20 (18)	0.50 ± 0.12 (19)	0.70 ± 0.28 (20)	1.10 ± 0.76 (20)	<17.4
		**	NS	NS	***	
Serum cholesterol (mmol/litre)	3.61 ± 0.70 (20)	4.05 ± 0.84 (18)	3.95 ± 0.80 (19)	3.83 ± 0.93 (20)	4.89 ± 1.16 (20)	3.9-5.1

*$P<0.05$; **$P<0.01$; ***$P<0.001$

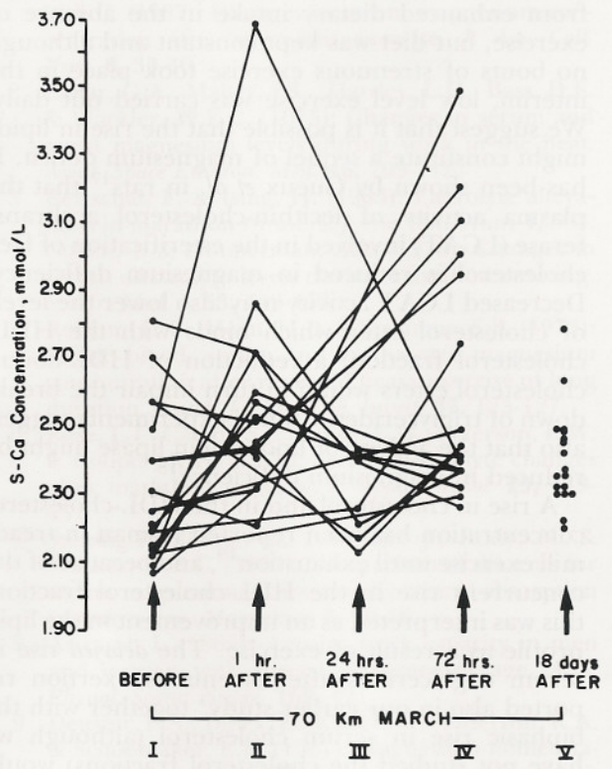

Fig. 5. Serum calcium (S-Ca) before and after 70 km march.

Discussion

Transient lowering of S-Mg has been reported by several authors immediately after marathon runs, skiing events and exercise in a laboratory setting[2-6], and it was assumed to be transient.

Immediately following the 70 km march, no fall in S-Mg was seen in our trained volunteers, although in our earlier study we did find an immediate lowering of S-Mg after a 120 km brisk hike in highly trained subjects, followed by a second, sustained, fall at 72 h. The striking finding was the *delayed fall* in S-Mg, occurring first at 72 h after the 70 km march. This suggests that in trained subjects the immediate fall in S-Mg appears first after a very strenuous effort, while the delayed fall is seen after both heavy and more moderate exertion.

Other authors did not follow the laboratory changes over time, as we have done. This made it possible for us to observe the *delayed* fall in S-Mg occurring first 3 days following the 70 km forced march, when 95% of the subjects were hypomagnesaemic. The lowering was sustained on re-examination 18 days later, when 75% of the subjects were still hypomagnesaemic. It is important to emphasize that no bouts of strenuous effort or dietary changes had taken place during the interim. Also, there was no difference in the mean S-Mg before the beginning of the training and prior to the 70 km march, which shows that the sustained lowering of S-Mg was due to the march and did not constitute a possible effect of the previous 6 month training period.

In an earlier study, we have observed a similar finding of sustained significant lowering of S-Mg in highly trained subjects following exertion[1]. This strengthens the validity of our present results, which show the persistence of hypomagnesaemia over time, following strenuous effort.

In our previous study[1], we interpreted the loss of body magnesium to be due to a number of possible causes, one of which was a leakage of intracellular magnesium into the extracellular pool due to exertional rhabdomyolysis, a view supported in this study by the concomitant peak rise of S-CK at 1 h. Such an efflux could possibly mask the anticipated lowering of S-Mg immediately after

termination of effort[1-6], thus delaying the appearance of hypomagnesaemia.

It can be assumed that the magnesium lost due to exertional rhabdomyolysis would be excreted via kidney. Such magnesium diuresis could constitute one cause of magnesium body loss, manifesting itself, after a delay, as hypomagnesaemia.

The second cause of loss of magnesium could be via sweat[2], a supposition especially relevant to our present study because of the relatively high ambient temperature during the march, even though the subjects did not show a significant loss of weight (Table 1).

Loss through intracellular shift was suggested by Refsum *et al.*[5], who reported an increase in erythrocyte and whole blood magnesium after competitive skiing, and Deuster *et al.*[9], who showed a rise in erythrocyte magnesium after treadmill exercise. Increase of intracellular magnesium could be due to an increase in oxidative phosphorylation, increased breakdown of creatine phosphate and gluconeogenesis caused by strenuous effort, all being magnesium-dependent processes[10]. The intracellular shift would thus constitute an influx in response to increased energy production and energy consumption — i.e., to an increased demand for magnesium inherent in strenuous effort.

Linjen *et al.*[11], who studied 23 runners before and after a marathon race, reported on the other hand that there was a decrease in erythrocyte magnesium and suggested that the latter was released into the extracellular pool and taken up by the adipose cells.

Obviously, there is a need for further studies on the fluxes of magnesium in effort. Nonetheless, we have established that chronic hypomagnesaemia follows strenuous exertion, and since *chronic* hypomagnesaemia is associated with a significant lowering of intracellular magnesium[12], our present results, which validate our earlier finding[2], show that strenuous effort gives rise to magnesium depletion, which the daily food and water magnesium intake of the probands of about 500 mg proved incapable of preventing or alleviating.

A rise in S-Ca after exercise has been reported earlier by Ljunghall *et al*[13] and a biphasic rise in S-Ca following a 120 km brisk hike by Stendig-Lindberg *et al.*[12], and was interpreted as probably due to acidosis[13].

The rise in blood sugar, reported by Naven *et al.*[14] after strenuous exertion and by Stendig-Lindberg *et al.*[1], immediately following a 120 km brisk hike, is first seen in this study 3 days after termination of the 70km march. This *delayed* appearance of the rise of blood sugar (even though the mean remained within the reference value) is striking and may be due to slowing of glycolysis secondary to magnesium deficiency, seven out of 13 steps of glycolysis being magnesium-dependent[15]. In addition, the presumably initially increased glycolysis may aggravate the magnesium depletion by possibly giving rise to magnesuria[16], thus setting up a vicious circle.

The significant rise in serum triglycerides reported earlier by us at 72 h after a brisk 120 km hike[1] was observed here first 18 days after the 70 km march. Lowering of serum cholesterol was reported by several workers, as well as by us following strenuous effort at 72 h after a 120 km brisk hike[1]. In this study, however, serum cholesterol rose significantly immediately after the march and again 18 days later.

The *delayed* rise in triglycerides and cholesterol (in both cases the mean remaining within the reference values) is astonishing. It could result from enhanced dietary intake in the absence of exercise, but diet was kept constant and although no bouts of strenuous exercise took place in the interim, low level exercise was carried out daily. We suggest that it is possible that the rise in lipids might constitute a sequel of magnesium deficit. It has been shown by Gueux *et al.* in rats[17] that the plasma activity of lecithin-cholesterol acyltransferase (LCAT) involved in the esterification of free cholesterol is reduced in magnesium deficiency. Decreased LCAT activity may also lower the levels of cholesterol ester which binds with the HDL-cholesterol fraction; a reduction of HDL-bound cholesterol esters would in turn impair the breakdown of triglycerides. Animal experiments suggest also that the activity of lipoprotein lipase might be reduced in magnesium deficiency[18].

A rise in cholesterol and in the HDL-cholesterol concentration has been reported in man in treadmill exercise until exhaustion[19], and because of the concurrent rise in the HDL-cholesterol fraction, this was interpreted as an improvement in the lipid profile as a result of exercise. The *delayed* rise in serum triglycerides after strenuous exertion reported also in our earlier study[1] together with the biphasic rise in serum cholesterol (although we have not studied the cholesterol fractions) would rather seem to suggest a possible long-term detrimental effect of severe exercise on the lipid profile in men.

Further studies are in progress to define by what route Mg is predominantly lost during strenuous exercise (via sweat, diuresis, or owing to intracellular shift) and to determine the magnitude of magnesium supplement which may be required in subjects undergoing strenuous exertion (especially in the heat) to prevent possible long-term detriment to health.

Conclusion

After moderately strenuous exercise (a forced 70 km march) we found no immediate fall of S-Mg in trained subjects, as reported by others, but instead, a delayed and sustained lowering of S-Mg which indicates the presence of magnesium deficiency secondary to strenuous effort. The late relative rise in blood sugar, triglycerides, and serum cholesterol concurrent with the sustained fall of S-Mg, might constitute a sequel of magnesium deficiency — due to the pivotal role of magnesium in intermediary metabolism.

Acknowledgements

We wish to thank Karen Ehrmann and Nydia Chesler for excellent secretarial help.

References

1 Stendig-Lindberg, G., Shapira, Y., Epstein, Y., Galun, E., Schoenberger, E., Graff, E. & Wacker, W.E.C. (1987): Changes in serum magnesium concentration after strenuous exercise. *J. Am. Coll. Nutr.* **6,** 35-40.

2 Bellar, G.A., Maher, J.T., Hartley, L.H., Bass, D.E. & Wackler, W.E.C. (1075): Changes in serum and sweat magnesium levels during work in the heat. *Aviat. Space Environ. Med.* **46,** 709-712.

3 Bertschat, F. & Ising, H. (1985): Eletrolyte alterations in marathon runners. *J. Am. Coll. Nutr.* **4,** 393.

4 Cohen, I. & Zimmerman, A.L. (1978): Changes in serum electrolyte levels during marathon running. *S. Afr. Med. J.* **53,** 449-453.

5 Refsum, H.E., Meen, H.D. & Stromme, S.B. (1973): Whole blood, serum and erythrocyte magnesium concentration after repeated heavy exercise of long duration. *Scand. J. Clin. Lab. Invest.* **32,** 123-127.

6 Rose, L.I., Carrol, S.L., Lowe, E.W., Peterson, E.W. & Cooper, K.H. (1970): Serum electrolyte changes after marathon running. *J. Appl. Physiol.* **29,** 449-451.

7 Stendig-Lindberg, G., Penciner, J., Rudy, N. & Wacker, W.E.C. (1984): Comparison of diluents for serum magnesium estimation by atomic absorption spectrometry. *Magnesium* **3,** 50-56.

8 Astrand, I. (1960): Aerobic work capacity in men and women with special reference to age. *Acta. Physiol. Scand. Suppl.* **169,** 49.

9 Deuster, P.A., Dolev, E., Kyle, S.B., Anderson, R.A. & Schoomaker, E.B. (1987): Magnesium homeostasis during high-intensity aerobic exercise in men. *J. Appl. Physiol.* **62,** 545-550.

10 Wacker, W.E.C. (1980): *Magnesium and man,* Cambridge, MA: Harvard University Press.

11 Linjen, P., Hespel, P., Fagard, R., Lysens, R., Vauden Eynde, E. & Amery, A. (1988): Erythrocyte plasma and urinary magnesium in men before and after a marathon. *Eur. J. Appl. Physiol.* **58,** 252-256.

12 Stendig-Lindberg, G., Bergstrom, J. & Hultman, E. (1977): Hypomagnesaemia and muscle electrolytes and metabolites. *Acta. Med. Scand.* **201,** 273-280.

13 Ljunghall, S., Joborn, H., Benson, L., Fellstrom, B., Wide, L. & Akerstrom, G. (1984): Effects of physical exercise on serum calcium and parathyroid hormone. *Eur. J. Clin. Invest.* **14,** 469-473.

14 Naven, H., Rehunen, S., Kuopposalmi, K., Tulikoura, I. & Harkonen, M. (1978): Muscle metabolism during and after strenuous intermittent running. *Scand. J. Clin. Lab. Invest.* **38,** 329-336.

15 Heaton, F.W. (1980): Magnesium in intermediary metabolism. In *Magnesium in health and disease,* ed M. Cantin & M.S. Seelig, pp. 43-57. New York, London: SP Medical and Scientific Books.

16 Lindeman, R.D. (1969): Influence on various nutrients and hormones on urinary divalent cation excretion. *Ann. N.Y. Acad. Sci.* **162,** 802-809.

17 Gueux, E., Alcinor, L. & Rayssiguier, Y. (1984): The reduction of plasma lecithin-cholesterol acyltransferase activity by magnesium deficiency in the rat. *J. Nutr.* **114,** 1479-1483.

18 Gueux, E.. & Rayssiguier, Y. (1983): The hypercholesterolemic effect of magnesium deficiency following cholesterol feeding in the rats. *Hormone Metabol. Res.* **15,** 594-597.

19 Durstine, J.L., Miller, W., Farrell, S., Sherman, W.M. & Ivy, J.L. (1983): Increases in HDL-cholesterol and the HDL/LDL cholesterol ratio during prolonged endurance exercise. *Metabolism* **3,** 993-997.

Changements métaboliques tardifs après effort exténuant chez des jeunes gens entrainés

G. Stendig-Lindberg*, Y. Shapira†, E. Graff*, E. Schonberger‡, W.E.C. Wacker§ (*Tel Aviv, †Tel Hashomer, ‡Jerusalem, Israel; §Cambridge, MA, USA).

Resumé: Vingt jeunes hommes, voluntaires, apparement sains, âgés de 18 à 25 ans (m̄: 19.3 ans, DS 1.4) subissent pendant 6 mois un entrainement physique extérieur standardisé et sont soumis aux explorations suivantes: magnésium sérique (S-Mg), calcium sérique (S-Ca), aspartate-amino-transferase sérique (S-Ast), alanine-amino-transferase sérique (S-ALT), activité serique de la créatine-kinase (S/CK), poids, VO_2 ml·min^{1}·kg^{1} (VO_2 max), avant une longue marche de 70 km et 1, 24 et 72 h, et 18 jours après.

Pouvoir aérobique maximum, poids corporel, Hb, hématocrite, créatinine sérique, proteïnes totales et albumine demeurent inchangé. Immédiatement après la marche, S-Mg n'est pas modifié, S-AST, S-ALT et S-CK augmentent mais de façon non significative, tandis que les augmentations modestes mais cependant significatives des S-Ca ($P<0.05$ au test de Student) et cholesterol ($P<0.01$) se normalisent toutes deux après 24 h. Ensuite, 72 h après la marche, c'est d'abord une chute significative du S-Mg qui s'observe ($P<0.01$) suivie d'une augmentation significative du S-Ca ($P<0.05$). Après 18 jours, sans qu'intervienment ni d'autres marches ni des changements alimentaires, S-Mg demeure significativement réduit ($P<0.05$) tandis que S-ALT et S-CK deviennent alors significativement augmenté ($P<0.001$ et $P<0.01$ respectivement) alors que le S-Ca se normalise. Concomitemment, il y a alors pour la première fois une augmentation de la glucémie ($P<0.001$), des triglycérides sériques ($P<0.01$) et une nouvelle augmentation du cholesterol sérique ($P<0.001$).

Cette étude nous semble mettre en évidence pour la première fois (1) une baisse tardive du S-Mg significative n'apparaissment que 3 jours après la fin d'un effort exténuant; persistent après 18 jours, elle traduit la présence d'une dépletion magnésique; (2) la survenue tardive 18 jours après une longue marche de 70 km une hypoglycémie et d'une hyperlipidémie; elles pourraient être secondaire au déficit magnésique qui joue un rôle essentiel dans les processes de glycolyse et de lipolyse.

Mots clés: Effort exténuant, glycémie, lipides, magnésium.

Reprint requests to: Professor G. Stendig-Lindberg, Department of Physiology and Pharmacology, Tel-Aviv University, Ramat Aviv 669978, Israel.