^{28}Mg STUDIES IN MAGNESIUM-DEFICIENT ANIMALS

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The first investigators to succeed in producing magnesium (Mg) deficiency experimentally were Orent and his coworkers,[1] who reported in 1934 that the rats used for their study showed a depletion of bone magnesium. Subsequent investigators[2] have reported that the soft-tissue content of magnesium is not appreciably altered even in severe deficiency. When ^{28}Mg became available several years ago, we made a preliminary study of the dynamics of magnesium transfer in the tissues of rabbits maintained on a Mg-deficient diet for 30 days.[3] The results of this study are reviewed in the present report, which also describes subsequent studies made in rabbits maintained on a diet extremely low in magnesium for four to six weeks. In addition to studying changes in blood constituents in such animals, we have done some preliminary *in vitro* studies on the intestinal transfer of magnesium in Mg-deficient and normal rabbits.

The External Balance and Mg_e Study

Material and Methods

Adult male domestic rabbits were placed in individual stainless steel metabolism cages and were given unrestricted quantities of tap water containing 0.6 milliequivalent (mEq) of magnesium per liter. The basal diet used for rats by Mackenzie and Mackenzie[4] was supplemented by the salt mixture of Hubbell and his coworkers,[5] except that the magnesium salts were omitted. The composition of this diet, which contains 6.6 mEq of magnesium per kilogram, has been described previously.

The ^{28} Mg was received as $MgCl_2$ in concentrated HCl; the specific activity was on the order of 8–10 μc/mEq. The concentration of magnesium in the solution injected was 0.4 mEq/ml, and each injection contained 2 mEq.

The procedures for collecting the samples for the external balance study, for measuring the exchangeable magnesium content (Mg_e), and for assaying radioactivity have been described previously.[3] The magnesium concentration in urine and serum[6] and in tissues[7] was determined by a modification of the molybdivanadate method for phosphate.

In the statistical analyses, the t test[8] was used to determine the significance either of the mean differences or of the differences between group means. A P of <0.01 was considered significant.

This experiment was conducted as follows. During a control period of three days the eight rabbits in the test group were fed a balanced stock diet of compressed pellets, containing 172 mEq of magnesium per kilogram. Base-line data for body weight, serum magnesium concentration, and urinary excretion of

magnesium were obtained daily. On the fourth day each animal's Mg_e was measured.

After an overnight fast, the rabbits were given free access to the Mg-deficient diet for 30 days. The body weight, food consumption, and urinary volume were recorded daily. Mg_e and serum magnesium determinations were made on the eighth, fourteenth, twenty-second, and thirtieth days of the experimental period. On the thirty-first day, 24 hours after the last intravenous dose of ^{28}Mg, the animals were killed by air embolism, and tissues were assayed for radioactivity and magnesium content.

The four rabbits in the control group were maintained on the stock diet for the same period of time. They too were killed by air embolism 24 hours after the administration of ^{28}Mg, and the tissues were assayed.

Results

When the intake of magnesium abruptly decreased to less than 0.3 mEq per day, the renal excretion of magnesium fell below 0.8 mEq per day. The serum magnesium concentration dropped to 1.2 mEq/l by the end of the first week and remained low. The Mg_e decreased to one-third of the control value by the end of the first week and continued to decline progressively; at 30 days it was less than 20% of the control value (FIGURE 1).

The appearance and behavior of the experimental animals remained normal until the fourth week, when two rabbits in the test group began to lose hair from the back, hind legs, and tail. The coat lost its luster and appeared ragged. At no time did any animal become hyperirritable.

A significant decrease in *relative radioactivity* (FIGURE 2) was observed only in the skin and bones of rabbits in the test group. The *magnesium content* was

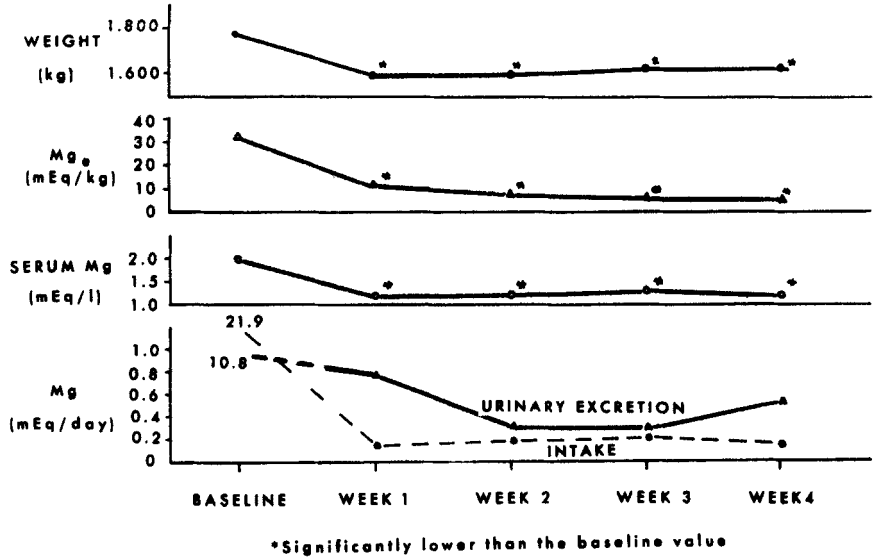

FIGURE 1. Effect of Mg-deficient diet (6.6 mEq/kg) on external balance and exchangeable magnesium in rabbits.

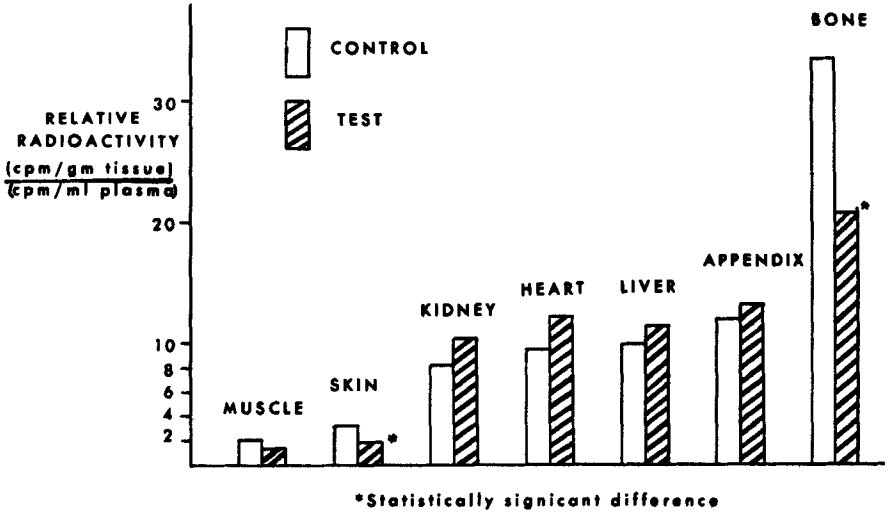

FIGURE 2. Effect of Mg-deficient diet (6.6 mEq/kg) on relative radioactivity of tissues in rabbits.

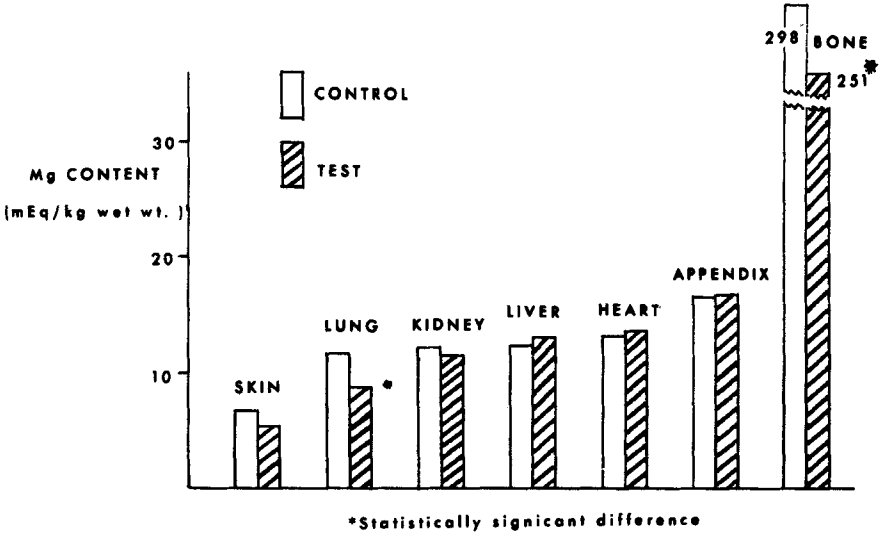

FIGURE 3. Effect of Mg-deficient diet (6.6 mEq/kg) on tissue magnesium content in rabbits.

significantly decreased in the lungs and bones of the experimental animals (FIGURE 3).

Discussion

The results of the external balance study confirmed those previously reported.[1,2,9-11] Although the urinary excretion of magnesium decreased as the intake of this ion was reduced, the net output still exceeded the intake. Consequently, the body store of magnesium was progressively depleted; body weight

decreased. An abrupt decrease in serum magnesium concentration occurred within the first week and persisted throughout the experimental period. Despite the deficient diet, the only significant reduction in the tissue content of magnesium occurred in the bones and lungs. In view of the relative size of these two organs, it appears that the greatest deficiency of magnesium must have occurred in bone.

Measurements of relative radioactivity showed that most of the soft tissues studied continued to accumulate magnesium at or above the usual rate. Relative radioactivity was significantly decreased only in skin and bone. The decrease in the relative radioactivity of the skin may be a factor in producing the edema and hyperemia of the skin associated with magnesium deficiency.

The largest pools of magnesium in the body are in muscle and bone. Since the relative radioactivity and magnesium content of muscle were not significantly altered under the conditions of this experiment, the explanation for the progressive decrease in Mg_e lies primarily in the depletion of the labile exchangeable pool of magnesium in bone. Bone apparently serves as a reservoir from which magnesium is drawn during the ingestion of a Mg-deficient diet.

The absence of vasodilatation and hyperirritability, characteristic clinical manifestations of magnesium deficiency, may be explained by the fact that the diet we used was not as low in magnesium as those employed in some previous studies.[1]

Study of Tissue Magnesium Content and Blood Chemical Changes in Rabbits with Severe Magnesium Deficiency

Because no profound clinical evidence of deficiency was found when rabbits were maintained for 30 days on a diet containing 6.6 mEq of magnesium per kilogram, meticulous care was used in the subsequent studies to reduce the magnesium content of the diet to about 0.8 mEq/kg.

Material and Methods

Six young male rabbits, weighing approximately 1.8 kg each, were placed in individual metabolism cages and given unrestricted quantities of this Mg-deficient diet until they appeared moribund. Water containing 0.19 mEq of magnesium per liter was also given without restriction.

The procedures for collecting blood samples and for assaying radioactivity were the same as those used in the previous study.[3] The magnesium concentration in urine and serum and in tissues was determined by the Perkin-Elmer Model 303 double-beam atomic absorption spectrophotometer.[12] Pooled material similar in type and treatment to that of the experimental samples was used to determine the reproducibility of results obtained by this method. In 30–50 analyses, the coefficient of variation (C.V.) for pooled serum was 5.5% and for pooled gut specimens, 13.0% $\left(\text{C.V.} = \frac{\text{standard deviation}}{\text{mean}} \times 100\right)$.

Results

The average serum magnesium concentration fell 43% within the first week – from a mean base-line value of 1.93 mEq/l to 1.09 mEq/l. Thereafter, the average serum magnesium concentration rose slightly and then dropped to a low of 0.98 mEq/l.

Although the only clinical sign at the end of the first week was hyperexcitabil-

ity, the clinical changes thereafter were pronounced and characteristic. Hyperirritability, tachycardia, vasodilatation, and loss of hair were noted during the second and third weeks. These signs gradually increased in severity, in spite of the fact that the rabbits were eating well and maintaining their base-line weight. Between the fourth and sixth weeks, the animals stopped eating; evidence of malnutrition and of renal failure, and jaundice appeared and gradually increased in severity. One rabbit became moribund at 30 days, five others at 42 to 45 days.

When the rabbits were killed, their average weight was 1.07 kg – 40% lower than the mean base-line value of 1.79 kg. Although the average magnesium concentration in the serum had risen from the low of 0.98 to 1.39 mEq/l, it was still considerably less than the base-line value of 1.93 mEq/l.

Other Changes in the Blood

Because of the small number of samples analyzed in the test and control groups, no attempt was made at statistical analysis of these data. However, certain differences in the blood constituents are obvious (TABLE 1). These include marked elevation in the total bilirubin, as well as in the conjugated portion, and in the cholesterol, lactic dehydrogenase, glutamic oxalacetic transaminase, urea nitrogen, and the total leukocyte count.

TABLE 1

DIFFERENCES IN SELECTED CONSTITUENTS OF THE BLOOD BETWEEN Mg-DEFICIENT AND NORMAL RABBITS

CONSTITUENT	CONTROLS			Mg-DEFICIENT RABBITS		
	n*	Mean	Range	n*	Mean	Range
Bilirubin, mg/100ml, Total	5	<0.2	(0.1 – 0.4)	6	3.4	(1.3 – 5.0)
Conjugated	5	<0.1	(0 – 0.1)	5	1.2	(0.6 – 1.8)
Cholesterol, mg/100 ml	3	95	(50 –155)	4	416	(290 –450)
Creatinine, mg/100 ml	5	1.2	(1.0 – 1.5)	6	1.8	(1.3 – 2.4)
Lactic Dehydrogenase, Sigma	5	164	(100 –320)	6	627	(190 –1,300)
Magnesium, mEq/1	10	1.82	(1.33– 2.57)	5	1.39	(0.92– 1.54)
Transaminase, SGO– Sigma Frankel	5	33	(20 – 52)	6	136	(55 –240)
Urea Nitrogen, mg/100 ml	5	20	(12 – 30)	6	42	(25 – 62)
WBC, 1000/cu mm	3	2.96	(2.7 – 3.5)	5	4.64	(2.5 – 7.6)

* Number of determinations.

Tissue Analyses

The mean *magnesium content* of most tissues was lower in Mg-deficient rabbits than in normal rabbits; the exceptions were skeletal muscle, skin, testis, and lymphoid tissue from the neck. The mean values for the appendix, bone cortex, and large intestine were significantly lower in the Mg-deficient rabbits (TABLE 2); the differences for the bone marrow, brain, and mid-jejunum were of borderline significance at the 2% or 5% level.

The mean *calcium* values for Mg-deficient rabbits were significantly higher in the mid-jejunum, large intestine, liver, and muscle (TABLE 2).

The mean *potassium* values for Mg-deficient rabbits were significantly decreased in bone cortex and kidney and significantly increased in the large intestine (TABLE 2).

The mean *sodium* values for Mg-deficient animals were significantly higher in bone cortex, brain, liver, lung, skin, spleen, stomach, and testis (TABLE 2).

TABLE 2

TISSUES SHOWING SIGNIFICANT DIFFERENCES IN CATION CONTENT BETWEEN Mg-DEFICIENT AND NORMAL RABBITS

CATION	TISSUE	CONTROLS			Mg-DEFICIENT RABBITS			
		n*	Mean†	± S.E.	n*	Mean†	± S.E.	P
MG	Appendix	4	17.59	0.964	5	12.14	1.136	<.01
	Bone Cortex	8	261	2.986	12	208	7.277	<.001
	Intestine, Large	6	21.23	1.990	10	12.71	1.279	<.01
CA	Intestine, Mid-Jejunum	8	7.06	0.728	12	12.41	1.686	<.01
	Intestine, Large	6	32.70	2.434	10	78.69	7.583	<.001
	Liver	8	2.07	0.146	12	4.99	0.426	<.001
	Muscle	8	2.52	0.235	12	15.07	2.632	<.001
K	Bone Cortex	8	13.55	0.791	9	7.03	0.424	<.001
	Intestine, Large	6	71.40	2.898	10	84.57	2.486	<.01
	Kidney	8	64.46	0.948	12	57.72	2.011	<.01
NA	Bone Cortex	8	231	4.919	12	253	3.314	<.01
	Brain	8	55.94	1.329	12	61.20	1.139	<.01
	Liver	8	27.89	1.068	12	50.36	0.888	<.001
	Lung	8	59.43	2.175	12	68.24	1.713	<.01
	Skin	8	59.66	4.987	12	82.69	4.773	<.01
	Spleen	4	34.95	0.723	6	46.34	3.072	<.01
	Stomach	7	44.20	2.210	12	60.41	2.685	<.01
	Testis	8	43.06	1.332	10	59.52	3.643	<.001

* Number of determinations.

† mEq/kg wet weight.

Discussion

The concentration of nonprotein nitrogen was elevated terminally in Mg-deficient dogs,[13] and azotemia has been reported in rats.[14] These results, together with the increased values for urea nitrogen and creatinine found in this study, suggest the presence of renal damage. In rats, the increase in urea nitrogen[14] could not be attributed solely to catabolic processes, since the nitrogen balance and weight of the experimental animals did not differ from those of the controls; it was concluded that deposition of calcium had caused an alteration in renal function. The increased serum creatinine observed in the present study is considered supportive evidence for renal damage; the possibility that this elevation was due to muscle damage was not explored, however.

The increases in the serum concentration of total and conjugated bilirubin, lactic dehydrogenase, and SGO-transaminase are compatible with liver damage. This is the first report of an elevation in serum bilirubin associated with a Mg-deficient diet. While it is impossible, in an experiment not using pair-fed controls, to rule out nutritional failure as the cause of liver damage, it is noteworthy that other investigators[15] visually observed icterus in 6 of 20 sheep that were in excellent nutritional condition after being maintained on a Mg-deficient diet.

Tissue Changes

The data from this study suggest that magnesium deficiency that is extreme enough and prolonged enough to result in severe nutritional failure will cause a depletion of magnesium in most of the soft tissues. We have been unable to confirm the report of some investigators[14,16–18] that the concentration of magnesium is decreased in the muscle of Mg-deficient animals. A striking increase in calcium content was found in the muscle of the Mg-deficient rabbits.

All areas of the small intestine in the Mg-deficient rabbits contained increased amounts of calcium. This observation is of interest in view of the suggestion by some observers[19] that the small intestine has a common absorptive mechanism for calcium and magnesium.

The increase of calcium in the liver of these Mg-deficient rabbits may be associated with the hepatic damage presumably responsible for the increased serum concentration of bilirubin. In a subsequent study of livers from other Mg-deficient rabbits, histologic evidence compatible with biliary cirrhosis was found.[20]

In Vitro Studies of Intestinal Segments From Mg-Deficient Rabbits

The Saltman apparatus[21] was used to determine the transfer of ^{28}Mg and the concentrations of stable magnesium, calcium, sodium, and potassium in segments of the small intestine from rabbits used in the previous experiment. The determinations were made with the following variables: (1) using intestinal segments from both normal and Mg-deficient rabbits, (2) using both proximal and distal segments of the small intestine, and (3) in the aerobic state and in the presence of cyanide. Three to six preparations of intestinal segments were used for each group of observations upon a variable.

In all experiments, the fluid bathing the mucosal (M) and serosal (S) surfaces of the intestinal segments was Ringer's solution, to which was added glucose and stable magnesium. The content of 1 liter was as follows: sodium, 147.5 mEq; potassium, 4.0 mEq; calcium, 4.5 mEq; chloride, 156 mEq, glucose, 1 g; and magnesium, 1.6–1.8 mEq. The pH of all the solutions was adjusted to 7.4, and

the solutions were heated to 37° C before coming into contact with the tissues. All experiments were carried out at this temperature.

In order to study the mucosal-to-serosal ("M to S") transfer of cations, the tissue segments were everted and ^{28}Mg was added to the solution bathing the mucosal surface; for the study of ("S to M") transfer, the segments were not everted and ^{28}Mg was added to the serosal solution.

For aerobic metabolic conditions, a mixture of 95% oxygen and 5% carbon dioxide was bubbled through both solutions; for incubation with cyanide, 0.05 M sodium cyanide was added to the solutions, and pure oxygen was bubbled through them.

Each preparation was observed for seven hours. At the end of that time, the segments were assayed for radioactivity and electrolyte content.

Results

Tissue Electrolyte Content

Effect of magnesium deficiency. Both under aerobic conditions and with exposure to cyanide, the mean concentration of *magnesium* in the everted distal segments of small intestine was higher in Mg-deficient rabbits than in animals on a normal diet; this difference was significant only when cyanide was present in the medium. Under other experimental conditions there was no significant difference in the intestinal concentration of magnesium between Mg-deficient and normal rabbits (TABLE 3).

In the presence of cyanide, the concentration of *calcium* in the everted distal segments was also significantly higher in the Mg-deficient group. Under aerobic conditions, the concentration of calcium in the everted proximal segment was significantly lower in the Mg-deficient group than in the normal group.

The concentration of *sodium* in the everted proximal and distal segments was significantly increased in the Mg-deficient group as compared with the normal rabbits, when the segments were bathed with cyanide.

Magnesium deficiency was associated with an increased concentration of *potassium* in the everted proximal segments treated with cyanide.

Variations according to anatomic site. Both with aerobic incubation and with exposure to cyanide, the concentration of *magnesium* in the everted segments from the Mg-deficient animals was significantly greater in the distal portions than in the proximal portions.

TABLE 3

ELECTROLYTE CONTENT* OF INTESTINAL SEGMENTS

EXPERIMENTAL CONDITIONS†			CONTROLS				Mg-DEFICIENT RABBITS			
1	2	3	MG	CA	NA	K	MG	CA	NA	K
E	P	A	46.4	98.6‡	1451	158	43.3	57.8	1112	140
E	P	C	47.4	81.4	1522	71	40.6	85.7	2528‡	96‡
E	D	A	47.9	50.3	1202	216	57.0	68.8	1392	213
E	D	C	41.2	88.9	1737	78	59.6‡	120.5‡	2668‡	71

* mEq/kg dry weight. Each value is the average of 6–12 replicate determinations on 3–6 segments.

† Conditions: 1. E = everted.
2. P = proximal, D = distal.
3. A = incubated aerobically, C = incubated with cyanide.

‡ Significantly greater than the corresponding value in the other group of animals.

TABLE 4

SPECIFIC ACTIVITY* OF INTESTINAL SEGMENTS

EXPERIMENTAL CONDITIONS†			CONTROLS			Mg-DEFICIENT RABBITS		
1	2	3	cpm/mg Wet Weight‡	mEq Mg/kg Wet Weight§	Specific Activity¶	cpm/mg Wet Weight‡	mEq Mg/kg Wet Weight§	Specific Activity¶
M–S	P	A	9.718	4.64	2.09	13.316	4.33	3.08
M–S	P	C	11.272	3.92	2.88	11.519	4.83	2.38
M–S	D	A	9.883	4.61	2.14	10.358	9.83	1.05
M–S	D	C	10.814	3.85	2.81	14.060	7.10	1.98
S–M	P	A	11.344	3.72	3.05	10.895	3.61	3.02
S–M	P	C	12.388	3.22	3.85	13.661	3.45	3.96
S–M	D	A	11.111	3.48	3.19	10.805	3.53	3.06
S–M	D	C	13.235	3.51	3.77	12.666	3.96	3.20

* Measured after seven hours' incubation.

† Conditions: 1. M–S = ^{28}Mg movement from mucosal to serosal solutions bathing everted gut.
2. P = proximal, D = distal.
3. A = incubated aerobically, C = incubated with cyanide.

‡ Each value is the average of 3–6 observations.

§ Each value is the average of 6–12 observations.

¶ Specific activity = $\frac{\text{cpm/mg wet weight}}{\text{mEq Mg/kg wet weight}}$

Effect of oxygen and cyanide in the incubating media. The presence of oxygen or cyanide in the incubating medium made very little difference in the intestinal concentration of *magnesium.*

Except in the everted proximal segments from normal rabbits, the concentration of *calcium* was increased by the presence of cyanide.

The concentration of *sodium* was higher in all segments incubated with cyanide, and the difference was statistically significant in all experiments except the ones that used proximal segments from normal animals.

Without exception, the concentration of *potassium* was significantly lower in experiments employing cyanide than in those using aerobic incubation.

At the end of the experiment, the intestinal segments incubated in the presence of cyanide contained a higher *concentration* of ^{28}Mg than those incubated aerobically. The one exception occurred in the proximal segments from Mg-deficient rabbits (TABLE 4).

The lowest *specific activities* were found in the distal segments of small intestine from Mg-deficient rabbits (TABLE 4). Except in the proximal segments from Mg-deficient rabbits, tissue specific activity was higher in the presence of cyanide than under aerobic conditions.

Changes in Mucosal and Serosal Solutions

The serosal-mucosal or mucosal-serosal ratio of ^{28}Mg in the solutions increased in proportion to the duration of incubation. When ^{28}Mg was added to the mucosal solution, the serosal-mucosal ratio of ^{28}Mg increased more rapidly when normal distal segments were incubated aerobically and when the Mg-deficient segments were incubated under any condition, than in the other three experiments employing normal segments (FIGURE 4). When ^{28}Mg was added to the

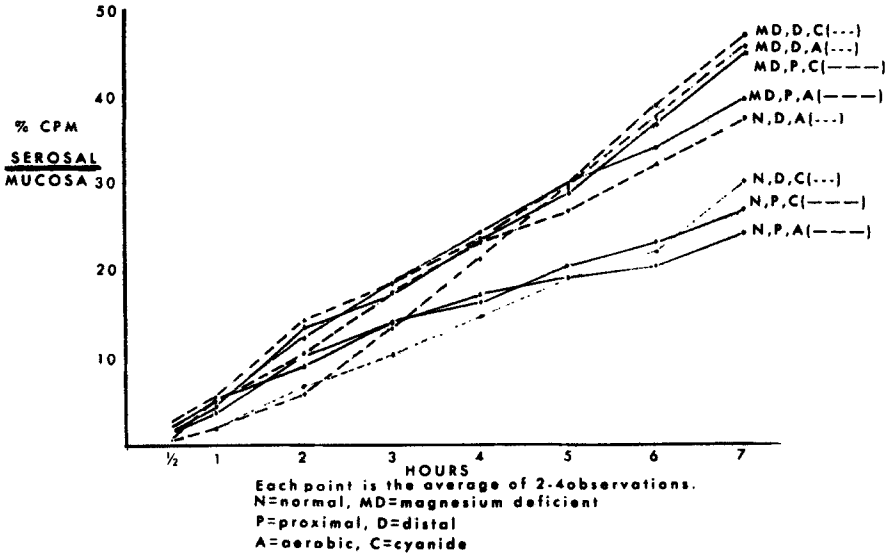

FIGURE 4. Relationship between the duration of incubation and the serosal/mucosal ratio of ^{28} Mg concentration in solutions bathing everted segments.

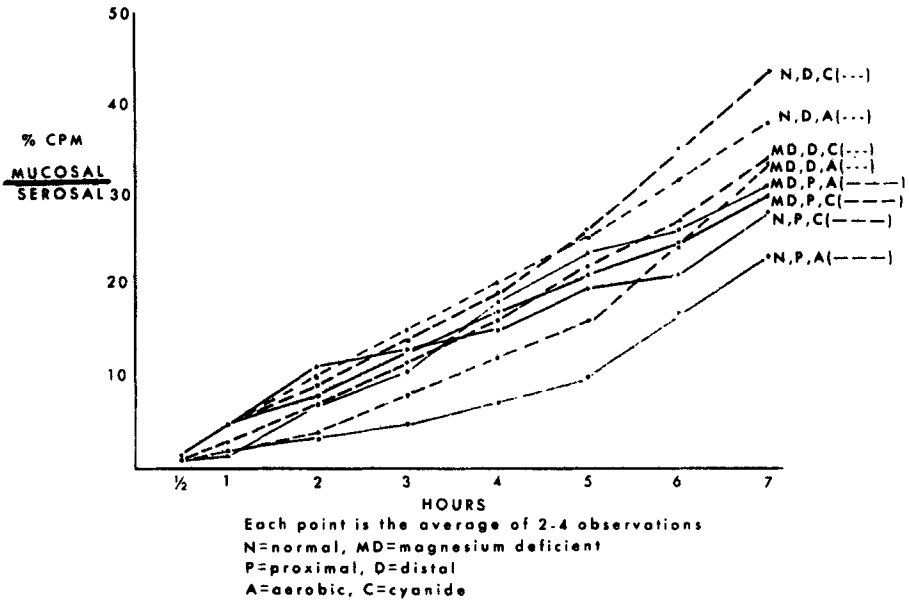

FIGURE 5. Relationship between the duration of incubation and the mucosal/serosal ratio of ^{28}Mg concentration in solutions bathing noneverted segments.

serosal solution, the increase in the mucosal/serosal ratio was greatest across the normal distal segment exposed to cyanide (FIGURE 5).

In general, when all other conditions were comparable, the specific activity of the *receiving solution* increased more in the presence of Mg-deficient gut than in the presence of a normal gut, regardless of the direction of movement (TABLE 5).

Discussion

A Mg-deficient diet appears to enhance the movement of ^{28}Mg across both proximal and distal portions of the small intestine. At the end of the experiments employing everted intestinal segments from either portion and under either metabolic condition, the ^{28}Mg concentration in the serosal solution was greater when the segments came from Mg-deficient rabbits than when they were obtained from rabbits in a normal nutritional state. The specific activity of the serosal solution was also higher in the experiments employing intestinal segments from the Mg-deficient group.

In the normal gut, the net result of movement in the proximal segment is similar to that in all segments of a Mg-deficient gut. If this evidence is extended to an *in vivo* situation, it is possible to conclude that, while magnesium passes from the mucosal to the serosal surface and vice versa in all areas of the small intestine, the net positive gain for the normal rabbit may occur in the proximal area. In the Mg-deficient rabbit, the magnesium-absorbing ability of both the proximal and distal area of the small intestine is enhanced.

The fact that the presence of cyanide did not affect the concentration of ^{28}Mg in the intestinal segments or in the mucosal and serosal solutions suggests that movement of magnesium across the intestinal wall does not require an energy-yielding process.

TABLE 5

SPECIFIC ACTIVITY* OF MUCOSAL AND SEROSAL SOLUTIONS

EXPERIMENTAL CONDITIONS†			CONTROLS				Mg-DEFICIENT RABBITS			
1	2	3	0 hr/7 hr	Difference	0 hr/7 hr	Difference	0 hr/7 hr	Difference	0 hr/7 hr	Difference
M–S	P	A	9.15/7.50	−1.65	0/1.38	+1.38	8.62/9.48	+0.86	0/ 3.16	+3.16
M–S	P	C	8.57/6.15	−2.42	0/1.76	+1.76	8.88/7.54	−1.33	0/ 2.74	+2.74
M–S	D	A	8.77/7.05	−1.72	0/2.78	+2.78	8.52/7.94	−0.58	0/ 3.57	+3.57
M–S	D	C	8.57/6.51	−2.06	0/2.01	+2.01	8.88/8.31	−0.57	0/ 3.01	+3.01
S–M	P	A	0/1.63	+1.63	12.20/8.54	−3.66	0/2.63	+2.63	10.14/ 8.57	−1.57
S–M	P	C	0/2.02	+2.01	9.80/7.04	−2.76	0/2.58	+2.58	9.55/10.10	+0.55
S–M	D	A	0/2.30	+2.30	12.20/7.91	−4.29	0/2.77	+2.77	10.31/ 8.05	−2.26
S–M	D	C	0/3.58	+3.58	9.80/6.23	−3.57	0/2.22	+2.22	10.24/ 8.21	−2.03

*Specific activity $= \frac{\text{cpm}/\mu\text{l}}{\text{mEq Mg/liter}}$

† Conditions: 1. M–S = ^{28}Mg movement from mucosal to serosal solutions bathing everted gut.
2. P = proximal, D = distal.
3. A = incubated aerobically, C = incubated with cyanide.

Summary

In experiments performed several years ago, domestic rabbits were placed on a synthetic diet containing 6.6 mEq of magnesium per kilogram. Using ^{28}Mg, the exchangeable magnesium content (Mg_e) was determined by the radioisotopic dilution technique, 20 to 24 hours being allowed for equilibration. Serum magnesium concentration fell within eight days from a mean base-line value of 2.0 mEq/l to 1.2 mEq/l and remained at this level for 22 days. The mean Mg_e fell progressively from a base-line level of 33.0 mEq/kg to 13.2, 8.2, 6.6, and 6.0 mEq/kg at 8, 14, 22, and 32 days respectively. ^{28}Mg uptake was decreased in skin and bone, and magnesium content was significantly decreased in lung and bone cortex.

In recent experiments, a Mg-deficient diet containing only 0.8 mEq/kg was used. Within two to four weeks the rabbits stopped eating, lost weight, and revealed chemical evidences of renal and hepatic failure, with elevated blood concentrations of total and conjugated bilirubin, cholesterol, lactic dehydrogenase, glutamic oxalacetic transaminase, creatinine, and urea nitrogen. The mean magnesium content of most tissues was lower for the experimental animals than for a control group; in the appendix, bone cortex, and large intestine, the differences were significant.

Segments of small intestine from the deficient and normal animals were placed in the Saltman apparatus and subjected to various experimental conditions. At the end of the experiment employing everted intestinal segments, whether proximal or distal, the concentration of ^{28}Mg in the serosal solution, both under aerobic conditions and in the presence of cyanide, was greater when the segments came from magnesium-deficient rabbits than when segments from normal animals were used. The specific activity of the serosal solution was also higher in the deficient group. These findings suggest that the Mg-absorbing ability of both proximal and distal areas of the small intestine is enhanced by magnesium deficiency and is not energy-dependent.

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