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Effect of magnesium deficiency on the uptake of ^{28}Mg by the tissues in mature rats

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An animal's ability to withdraw magnesium from its soft tissues during Mg deficiency is very limited. For example, in both young and mature rats given a Mg-deficient diet for periods up to 10 weeks, no Mg depletion of soft tissue, except from muscle, was demonstrable (Tufts & Greenberg, 1937–8; MacIntyre & Davidsson, 1958). It would appear, therefore, that if any depletion occurs it must be within the normal variation in the concentration of Mg in soft tissue from animal to animal.

Radioactive Mg may provide a means of detecting depletion resulting from a deficiency. McAleese, Bell & Forbes (1961) using lambs found, for instance, that after Mg-deficient and control lambs were dosed intravenously with ^{28}Mg the soft tissues from the deficient animals had higher concentrations of isotope than those of the controls. It may have been due to the tissues of the Mg-deficient lambs taking up ^{28}Mg to replace Mg lost during depletion or to increased rates of exchange of ^{28}Mg between plasma and soft tissues. The rate of exchange of a radioactive isotope between plasma and a tissue depends, *inter alia*, on the difference between their specific activities. Since no determinations of sp. ac. were made in the experiments on lambs it is not possible to ascertain the exact cause of the increased concentration of ^{28}Mg in the tissues of deficient animals. For this reason we considered that a more detailed investigation of the effects of Mg deficiency on the uptake of ^{28}Mg when related to sp. ac. would be valuable. It was carried out with rats as experimental animals.

EXPERIMENTAL

The adult rats, their management and the Mg-deficient and control diets were the same as described in the previous paper (Smith & Field, 1963).

On the 19th day after the Mg-deficient diet was introduced, each rat was injected intraperitoneally with a solution containing both stable Mg and ^{28}Mg. Groups of four rats, two from each dietary régime, were killed at 10, 20, 30 and 45 min and 1, 2, 3, 4, 5, 6, 12, and 22 h after dosing. For technical reasons, injection of the groups was spread over 12 h, the groups with the longest period between dosing and killing being injected first. Before being killed by decapitation, each animal was anaesthetized with ether and bled by cardiac puncture with a $0{\cdot}8 \times 15$ mm stainless-steel needle attached to a heparinized syringe (Burhoe, 1940). The samples of whole blood were immediately centrifuged and the plasma was removed. The following tissues were quickly removed: brain, heart, liver, both kidneys, muscle (inner thigh), left half of mandible and left

femur. Similar tissues, except liver and plasma, from the two rats with common killing times and dietary history were pooled. The samples of soft tissue were finely chopped, transferred to 16 × 125 mm Pyrex glass tubes, pressed down firmly to exclude air and, when possible, the tubes were filled to a 4 cm mark. Bones were freed from adhering tissue and transferred whole to the Pyrex tubes. The heights of all samples which did not fill the tubes to the 4 cm mark were measured to the nearest 0·5 cm.

For injection, the carrier-free ^{28}Mg solution (supplied by UKAEA, Harwell) was diluted to 100 ml with $MgCl_2$ solution containing 0·5 mg stable Mg/ml and 1 % was removed for counting standard. The stable Mg was included because, with the small amount of Mg in carrier-free ^{28}Mg, there is, particularly in the Mg-deficient animals, a great danger with an intraperitoneal injection that local uptake may prevent the general dissemination of ^{28}Mg in the body through the blood stream. Preliminary experiments showed that 1 mg was sufficient to raise the plasma Mg of a deficient rat throughout the experimental period. Since the counting efficiency was not known, it was not possible to determine the absolute activity injected into each animal. An estimate was, however, made from the stated activity at the time of dispatch from Harwell. The rats injected at the commencement of the experiment received about 0·25 μc (10000 counts/sec), whereas the last rats received only 0·15 μc (6200 counts/sec) because of the physical decay of the isotope during the period of injection.

The radioactivity of the samples was determined in a well-type scintillation counter (Ekco Type 550) and scaler (Panax A.C. 300/6) and at least 3000 counts were recorded. Since the half life of Mg is sufficiently short (21·3 h) for appreciable decay to occur during the period of the experiment, all counts were corrected to a fixed point in time, the commencement of the injections, by means of a decay curve. A correction for differences in the geometrical efficiency of the counter due to differences in the height of the sample in the tubes was required: it was obtained by diluting the counting standard successively from 1 to 5 ml in increments of 1 ml and recording the heights and the counts. All counts of samples were adjusted to a fixed height of 4 cm and expressed as a percentage of the total activity administered to each rat. All radioactivity determinations were completed within 1 h of collection.

Since the samples of ^{28}Mg may have contained ^{7}Be, the standard was recounted after an interval of 1 week, when the activity due to ^{28}Mg had disappeared, but no correction for the contaminant was found necessary.

Measurement of Mg in plasma and tissue was by the method previously described (Smith & Field, 1963).

RESULTS

Plasma

The carrier dose of 1 mg stable Mg increased the concentration of Mg in the plasma of the rats in both groups. The maximum values, which occurred 0·33 h after dosing, were 1·69 and 3·08 mg/100 ml plasma for the deficient and control animals, respectively. The values for the plasma Mg of the deficient rats were all higher than the mean value of 0·49 mg/100 ml found on the previous day (Smith & Field, 1963).

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The mean values for the concentration of ^{28}Mg in the plasma from the two rats of the same group killed at each interval after dosing are given in Table 1. After reaching a maximum 0·33 h after dosing, the concentration of ^{28}Mg in the plasma from the Mg-deficient rats fell with the interval after dosing. The changes in the corresponding values for the control group were similar but they showed no maximum apart from the observation at 0·17 h. The values at each interval were always higher for the control group than for the deficient group.

Table 1. *Mean concentrations of stable Mg (mg/100 ml) and of ^{28}Mg (% dose/ml) in, and specific activity (sp. ac.)* of, the plasma of pairs of rats in the deficient (Def.) and control (Cont.) groups*

Interval after dosing (h)	Concentration: Stable Mg		Concentration: ^{28}Mg		Sp. ac.	
	Def.	Cont.	Def.	Cont.	Def.	Cont.
0·17	1·16	2·55	0·179	0·368	15	14
0·33	1·69	3·08	0·331	0·367	19	12
0·50	1·11	2·43	0·182	0·224	16	11
0·75	1·22	2·43	0·164	0·231	13	10
1·0	1·11	2·28	0·0874	0·163	7·8	7·1
2·0	1·03	2·21	0·0456	0·0950	4·4	4·3
3·0	1·11	2·16	0·0303	0·0593	2·7	2·7
4·0	1·01	2·00	0·0269	0·0461	2·6	2·3
5·0	1·11	2·08	0·0282	0·0397	2·5	1·9
6·0	0·84	2·03	0·0196	0·0388	2·3	1·9
12·0	1·02	1·92	0·0210	0·0239	2·0	1·2
22·0	0·88	2·11	0·0161	0·0211	1·8	1·0

* Sp. ac. = percentage of total radioactivity injected into each rat in sample divided by the quantity of stable Mg (in mg) in sample.

The values for the sp. ac. corresponding to those for the concentration of ^{28}Mg in the plasma are given also in Table 1. The sp. ac. is expressed as the percentage of the total radioactivity injected into each rat in the sample, divided by the quantity of stable Mg in mg in the sample. The variations in sp. ac. with the period between dosing and killing were similar to those described for concentrations of ^{28}Mg in plasma, except that the difference between the dietary groups was reversed; the sp. ac. of the plasma of the deficient animals was always higher than the corresponding control values, owing to the lower concentration of stable Mg in the plasma of the deficient group. Graphical logarithmic analysis showed that the fall in sp. ac. with interval after dosing could be described by the sum of two exponentials. The equation for each group was:

$$\text{(Deficient)}\ S(T) = 25e^{-1\cdot5t} + 0\cdot85e^{-0\cdot074t} + 1\cdot81,$$

$$\text{(Control)}\ S(T) = 17e^{-1\cdot5t} + 0\cdot70e^{-0\cdot079t} + 1\cdot0,$$

where $S(T)$ is the plasma sp. ac. at time t after intraperitoneal injection of ^{28}Mg.

Tissues

The values for the concentration of ^{28}Mg found in the selected tissues at each interval after dosing are given in Table 2. The values for the liver in this and subsequent tables are the mean for two rats from the same group killed at the same time. The

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Table 2. *Mean concentration of* ^{28}*Mg (percentage of total radioactivity injected into each rat/g dry tissue) in selected tissues of pairs of rats in the deficient (Def.) and control (Cont.) groups*

Interval after dosing (h)	Kidney		Heart		Liver		Brain		Muscle		Femur		Mandible	
	Def.	Cont.	Def.	Cont.	Def.	Cont.	Def.	Cont.	Def.	Cont.	Def.	Cont.	Def.	Cont.
0·17	1·5	2·7	0·95	1·0	0·38	0·47	0·062	0·049	—	—	0·36	0·21	0·11	0·19
0·33	4·7	3·4	2·4	1·7	2·1	0·60	0·22	0·11	—	—	0·28	0·32	0·49	0·38
0·50	4·0	3·0	2·7	1·7	1·4	0·59	0·24	0·11	—	—	0·29	0·34	0·31	0·35
0·75	6·3	—	3·5	1·8	2·0	0·62	0·35	0·13	—	—	0·44	0·45	0·45	0·45
1·0	3·5	3·4	4·1	2·7	2·4	0·96	0·44	0·17	0·58	0·36	0·42	0·65	0·49	0·66
2·0	5·0	3·7	5·4	3·5	3·5	0·83	0·61	0·25	0·25	0·27	0·35	0·53	0·47	0·61
3·0	4·6	3·1	6·4	3·4	3·3	1·2	0·69	0·31	0·29	0·20	0·48	0·49	0·49	0·53
4·0	5·4	2·9	5·0	3·3	3·6	1·6	0·70	0·33	0·25	0·24	0·42	0·52	0·48	0·65
5·0	3·3	2·5	3·7	3·2	2·8	1·5	0·63	0·31	0·25	0·27	0·39	0·41	0·41	0·59
6·0	3·4	2·2	3·5	2·9	4·1	1·6	0·79	0·33	0·27	0·26	0·38	0·46	0·37	0·59
12·0	3·1	1·3	3·9	2·2	3·9	1·4	0·90	0·43	0·35	0·33	0·45	0·42	0·42	0·55
22·0	2·8	1·2	3·5	1·7	3·3	1·4	1·2	0·48	0·36	0·30	0·50	0·41	0·48	0·66

Table 3. *Mean specific activity of selected tissues from pairs of rats in the deficient (Def.) and control (Cont.) groups*

Interval after dosing (h)	Kidney		Heart		Liver		Brain		Muscle		Femur		Mandible	
	Def.	Cont.	Def.	Cont.	Def.	Cont.	Def.	Cont.	Def.	Cont.	Def.	Cont.	Def.	Cont.
0·17	2·2	3·6	1·2	1·3	0·43	0·50	0·086	0·076	—	—	0·091	0·051	0·019	0·028
0·33	7·0	4·7	3·8	2·1	2·3	0·64	0·30	0·17	—	—	0·080	0·076	0·097	0·055
0·50	6·1	4·0	4·6	2·7	1·5	0·65	0·36	0·14	—	—	0·069	0·084	0·055	0·068
0·75	9·8	—	6·1	3·7	2·2	0·69	0·52	0·20	—	—	0·10	0·10	0·075	0·065
1·0	6·6	5·3	5·5	3·4	2·5	0·98	0·65	0·22	0·55	0·39	0·12	0·15	0·085	0·094
2·0	8·6	5·1	6·8	4·7	3·4	0·81	0·96	0·38	0·23	0·27	0·089	0·13	0·088	0·080
3·0	8·0	4·8	6·8	4·1	3·4	1·1	0·91	0·48	0·33	0·29	0·14	0·12	0·085	0·079
4·0	8·5	4·5	8·2	5·1	3·5	1·5	1·1	0·44	0·24	0·24	0·12	0·12	0·075	0·090
5·0	4·5	3·7	6·7	3·9	2·7	1·4	0·87	0·46	0·28	0·27	0·10	0·097	0·070	0·092
6·0	5·9	3·3	7·2	4·0	4·2	1·8	1·1	0·46	0·29	0·25	0·10	0·12	0·060	0·085
12·0	4·7	2·4	5·1	2·8	4·3	1·6	1·3	0·62	0·39	0·36	0·13	0·091	0·061	0·071
22·0	3·9	1·7	6·2	1·9	4·0	1·5	1·7	0·68	0·47	0·33	0·13	0·10	0·072	0·094

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abnormally high values found for muscle for periods of up to 1 h between dosing and killing have been discarded, since they indicate contamination of the samples with unabsorbed ^{28}Mg from the peritoneal cavity.

The uptake of ^{28}Mg by all tissues examined was linear for short periods after injection. The rates for the different tissues in order of magnitude were kidney, heart, liver, mandible, femur and brain. The length of time for which the initial rate of increase remained constant varied with the tissue. The periods were: femur and mandible 1 h; kidney, heart and brain 2–3 h and liver 4 h.

After this first phase the concentration of ^{28}Mg increased in the brain, fell in the kidney and heart and remained relatively constant in the femur, mandible, liver and muscle.

The pattern of uptake of ^{28}Mg by each tissue was the same irrespective of whether the tissue came from Mg-deficient or control rats. There were, however, quantitative differences: kidney, liver, heart and brain from Mg-deficient rats took up more ^{28}Mg than the corresponding tissues from control rats; mandible took up less and femur and muscle were about equal.

The values obtained for the sp. ac. of the selected tissues are given in Table 3. As the concentration of stable Mg in each tissue was constant throughout the experimental period of 22 h, the changes in sp. ac. in a tissue were a simple reflection of the changes in the concentration of ^{28}Mg. On the other hand, the differences between tissues in rate of increase in sp. ac. are dependent in part on the differences between tissues in the concentration of stable Mg. Thus, although the uptake of ^{28}Mg was fast, the higher concentration of stable Mg in bone as compared with soft tissue made the increase in sp. ac. relatively slow. In the first phase, the rates in order of magnitude were kidney, heart, liver, brain, femur and mandible.

The differences in sp. ac. between the same tissues from the Mg-deficient and from the corresponding control rats were as follows: values for kidney, liver, heart and brain were higher in the deficient, and muscle, femur and mandible showed little difference between the two groups.

The values for the relative sp. ac. of the selected tissues are given in Table 4. Relative sp. ac. is the ratio of the sp. ac. of the tissue to that of the plasma and is a measure of the proportion of stable Mg that has exchanged during the interval between the administration of ^{28}Mg and the death of the rat. At 2 h after injection the values for the kidney and heart were >1 and from 3 h to the end of the experimental period they remained relatively constant despite the fact that the sp. ac. of both the plasma and tissues decreased. The values for the liver from the Mg-deficient and from the control rats were >1 at 3 and 12 h after injection respectively and they continued to increase up to the end of the period of observation. For the remaining tissues, the values never reached 1, and at the last observation the tissues in decreasing order of relative sp. ac. were brain, muscle, femur and mandible. The values for the kidney, liver, heart and brain from the Mg-deficient rats were greater than those for the corresponding tissues from the control rats. The opposite obtained with muscle, femur and mandible.

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Table 4. *Mean relative specific activity of selected tissues from pairs of rats in the deficient (Def.) and control (Cont.) groups*

Interval after dosing (h)	Kidney		Heart		Liver		Brain		Muscle		Femur		Mandible	
	Def.	Cont.	Def.	Cont.	Def.	Cont.	Def.	Cont.	Def.	Cont.	Def.	Cont.	Def.	Cont.
0·17	0·14	0·25	0·080	0·093	0·029	0·036	0·0055	0·0053	—	—	0·0059	0·0035	0·0012	0·0019
0·33	0·36	0·40	0·20	0·17	0·12	0·053	0·015	0·014	—	—	0·0042	0·0064	0·0051	0·0047
0·50	0·37	0·35	0·29	0·25	0·094	0·059	0·022	0·012	—	—	0·0042	0·0073	0·0034	0·0059
0·75	0·74	—	0·47	0·37	0·17	0·069	0·039	0·021	—	—	0·0079	0·011	0·0056	0·0067
1·0	0·85	0·74	0·71	0·48	0·32	0·14	0·083	0·031	0·070	0·055	0·015	0·020	0·011	0·013
2·0	1·9	1·2	1·5	1·1	0·77	0·19	0·22	0·088	0·053	0·062	0·020	0·030	0·020	0·019
3·0	3·0	1·6	2·5	1·5	1·3	0·42	0·34	0·17	0·12	0·10	0·051	0·041	0·031	0·031
4·0	3·1	2·0	3·2	2·2	1·3	0·65	0·39	0·19	0·088	0·10	0·046	0·054	0·028	0·039
5·0	1·7	2·0	2·7	2·1	1·1	0·76	0·33	0·24	0·11	0·14	0·039	0·051	0·027	0·048
6·0	2·6	1·8	3·1	2·1	1·8	0·93	0·50	0·24	0·12	0·13	0·043	0·061	0·026	0·045
12·0	2·3	2·0	2·5	2·3	2·1	1·3	0·64	0·52	0·19	0·30	0·067	0·076	0·030	0·059
22·0	2·2	1·7	3·4	1·9	2·2	1·5	0·94	0·68	0·26	0·33	0·071	0·10	0·040	0·094

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DISCUSSION

Our finding that tissues differ markedly in the ability to take up ^{28}Mg from the plasma agrees with the results of previous workers using dogs (Brandt, Glaser & Jones, 1958), lambs (McAleese *et al.* 1961), sheep (Field, 1961), rabbits (Aikawa, 1958) and rats (Rogers & Mahan, 1959). Of the soft tissues it is generally agreed that kidney, liver and heart show the greatest uptake and muscle the smallest, brain occupying an intermediate position. The uptake by bone varies with the type of bone (Brandt *et al.* 1958), the age and the species. Aikawa (1960), for example, found that the bones of young rabbits took up ^{28}Mg faster than any other tissue studied, whereas the uptake by bones of older rabbits was much slower (Aikawa & Bruns, 1960). The uptake of ^{28}Mg by the bones of men and dogs (Glaser, Jones & Brandt, 1958), sheep (Field, 1961) and rats is relatively slow. It should be noted that the quantity of trapped plasma and red cells in liver is likely to be much greater than in muscle, brain or bone, for example, which will increase the apparent uptake of ^{28}Mg, especially in those samples taken from rats killed at a short interval after injection.

McAleese *et al.* (1961) have studied the concentration of ^{28}Mg in the tissue of Mg-deficient and normal lambs after intravenous administration of a single dose of ^{28}Mg. They found that the soft tissues from the deficient lambs had a higher concentration of ^{28}Mg than did the corresponding tissues from the control lambs, whereas for plasma and for the shaft of long bones the difference was reversed. The results obtained by us with rats are in complete agreement with these findings.

A system with a single central compartment represented by the plasma exchanging with multiple peripheral compartments and with no direct transfer between peripheral compartments may be used as a model in discussion of Mg distribution. In such systems, called mamillary, the exchange rate between the central compartment and any particular peripheral compartment can be determined from observations on the two compartments only. Before discussing the factors controlling the uptake of ^{28}Mg by a tissue, it is necessary to identify the compartments in the plasma and tissues.

There is evidence in our study of a multicompartmental distribution for plasma Mg. The sp. ac. of the kidney, liver and heart was greater than that of the plasma. This finding is in agreement with those of MacIntyre (1959) for rats, and Field (1961) for sheep. MacIntyre (1959) found, for example, that the relative sp. ac. for liver 24 h after dosing was about 1·6, which agrees closely with the value of 1·5 found by us for the control rats 22 h after dosing. A value for the sp. ac. of tissue greater than that of plasma could only arise in three ways: firstly, ^{28}Mg could reach the tissues from the injection site by a route other than the plasma; secondly, there could be a delay in the equalization of the sp. ac. of the plasma and of the tissues, and thirdly the plasma Mg could exist in more than one compartment. The word compartment is used here to mean that Mg in plasma exists in different physico-chemical states and that in each state it has a different mobility. Since the first was thought very unlikely, only the last two possibilities will be discussed further.

The delay in the equalization of the sp. ac. of the plasma and of a particular tissue is dependent upon the rate of exchange of ^{28}Mg between plasma and that tissue and the

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rate of change of the sp. ac. of the plasma. With heart, liver and kidney, exchange is rapid, equilibration being achieved 3–4 h after dosing. Further, there is only a slow fall in the sp. ac. of the plasma from 4 h onwards, so that only a small delay would be expected with heart, liver and kidney, certainly not as large as that observed. The values for sp. ac. of these tissues at 22 h after dosing were equal respectively to the sp. ac. of the samples of plasma taken about 20 h previously from the deficient rats and about 10 h previously from the control rats. From 3 h after dosing onwards, the values obtained for the relative sp. ac. of both the kidney and the heart were relatively constant and averaged about 3 for the deficient and 2 for the control rats. These findings are consistent with, firstly, a multicompartmental distribution for plasma Mg and, secondly, the presence in the fast compartment, i.e. the plasma compartment which is in equilibrium with the tissue, of 33 and 50% of the Mg in the plasma of deficient and control rats, respectively. Further, the constancy of the relative sp. ac. of the tissues suggests that there is no appreciable exchange between the fast and slow compartments of the plasma during the period of observation. It is tempting to think of these compartments as ionic and bound Mg, but there is no evidence at present for this assumption. In fact, recent studies on the distribution of ^{45}Ca in the plasma of dogs suggest that ^{45}Ca labels ionic and protein-bound Ca preferentially and complexed Ca containing compounds only secondarily (Wiester, Whitla & Goldsmith, 1963).

The interpretation of recent findings from studies on the dynamics of Mg excretion by the kidney in terms of a multi-compartmental distribution of plasma Mg presents difficulties. With such a distribution, the sp. ac. of the urine would be higher than that of the plasma, the difference being inversely proportional to the size of the fast compartment. This situation arises because the glomerular filtrate contains the plasma ionic Mg, a part of the fast compartment, and because there is no Mg excretion in the nephron. Both Bronner & Thompson (1961) with dogs, and Raynaud (1962) with rabbits, found instead that the sp. ac. of the urine approached that of the plasma, the lag phase being a matter of minutes; this result is consistent with a single compartmental distribution of plasma Mg. Unfortunately the size of the fast compartment in the plasma of the dog and the rabbit is unknown, as is the increase in the size of this compartment due to the ionic stable Mg given with the ^{28}Mg in the above renal studies.

Because of these conflicting results on the number of plasma Mg compartments, the calculations of the accretion rates and the exchangeable pools in bone have been carried out in two ways. The distribution of Mg in the plasma has been assumed to be, first, in one compartment only and, secondly, in more than one compartment, the compartment which is in equilibrium with the tissue Mg containing 33 and 50% of the Mg in the plasma of Mg-deficient and control rats respectively. Studies on the uptake of ^{45}Ca by the bone in rats have shown that bone Ca consists of two main fractions, one which exchanges rapidly with the plasma Ca, the exchangeable fraction, and the other the non-exchangeable fraction, which incorporates Ca atoms by accretion (Norris & Kisieleski, 1948). Since there is a close similarity in the behaviour of bone Ca and Mg, the equation developed for determining accretion rates and the size of the

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exchangeable pool of Ca in bone by Bauer, Carlsson & Lindquist (1961) has been used for bone Mg. The appropriate values found at 4, 12 and 22 h after dosing have been substituted in this equation and the values for the accretion rate and exchangeable pool so obtained have been pooled and their means are given in Table 5. There was little difference between the Mg-deficient and control rats in the size of the exchangeable pool in both femur and mandible, but the rate of accretion was much greater for both bones from the control than from the deficient rats. In the femur and mandible, only 1–5 %, depending upon the method of calculation, existed in the exchangeable fraction, a value which is of the same order as that found for the exchangeable fraction of bone Ca (3 % for tibia, Bauer *et al.* 1961). Further, the accretion rate for bone Mg from control rats, as expected, was much smaller than that for bone Ca, the order approaching that of the ratio Mg: Ca in bone.

Table 5. *Exchangeable pool and accretion rate of Mg in the femur and mandible of Mg-deficient and control rats*

		Mg-deficient rats			Control rats		
			Exchangeable pool			Exchangeable pool	
Bone	No. of plasma compartments	Accretion rate (mg/h)	mg	% of bone Mg	Accretion rate (mg/h)	mg	% of bone Mg
Femur	1	0·0012	0·14	4·3	0·0042	0·13	3·5
	2+	0·00040	0·046	1·4	0·0021	0·066	1·7
Mandible	1	0·0013	0·17	2·7	0·0092	0·16	2·2
	2+	0·00044	0·056	0·9	0·0046	0·079	1·1

The uptake of ^{28}Mg by a tissue is dependent upon the differences in sp. ac. and in the rates of flux between tissue and plasma. For example, if the rate of flux of Mg from plasma to tissue is greater than the reverse process there is a net uptake of Mg.

If the uptake of ^{28}Mg by a tissue from the control group is equal to or greater than that by the tissue from the deficient group, this observation can only be due to one cause. The flux between plasma and tissue must be greater for the control animal, since the sp. ac. of the plasma from the deficient was always higher than the corresponding control value, irrespective of the distribution of Mg in plasma. Such a tissue is bone. Thus the deficient rats with the smaller accretion rates had also the smaller fluxes of Mg. Histopathological examination of the femur from similar rats after 3 weeks on the Mg-deficient diet showed a marked reduction in the size of the trabeculae owing to osteoporosis (D. I. Nisbet, private communication). This observation suggests that the difference in the rate of flux is due to a decrease in the surface area of bone in contact with extracellular fluids.

On the other hand, if there is a greater uptake by a tissue from a deficient than from a control rat, this difference may be due to three causes: the higher sp. ac. of the plasma from the deficient animals, a net uptake of ^{28}Mg by the tissues of the Mg-deficient rat and a greater flux of Mg between plasma and tissue in the deficient animals. With our present knowledge, it is impossible to ascertain the true cause of the

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increased uptake of ^{28}Mg by the liver, heart, kidney and brain from the deficient rat, and consequently the use of ^{28}Mg has given no evidence for depletion of the soft tissues in Mg deficiency.

SUMMARY

1. Two groups of twenty-four rats were given a semi-synthetic diet free of Mg or the same diet supplemented with Mg for 18 days. On the last day each rat was given an intraperitoneal injection containing 1 mg stable Mg and approximately 0·15–0·25 μc ^{28}Mg. The rats were bled and killed at intervals up to 22 h after dosing. The contents of ^{28}Mg and stable Mg were determined in plasma and selected tissues.

2. The concentration of ^{28}Mg in the plasma of the Mg-deficient rats showed a maximum at 0·33 h after dosing and thereafter fell exponentially. The values for the control were greater than the corresponding values for the deficient rats and they fell exponentially with time between dosing and killing. The changes in specific activity of the plasma were similar to those for concentration of ^{28}Mg except that the values for the control were less than those for the deficient rats at any given interval after dosing.

3. Corresponding tissues of the Mg-deficient rats and of the control rats, killed at the same interval after dosing, showed differences in uptake of ^{28}Mg. Of the tissues of the Mg-deficient rats, the kidney, heart, liver and brain took up more, and the mandible took up less, than the corresponding tissues of the control rats.

4. Sp. ac. of corresponding tissues from the two groups differed only in the values for liver, heart, kidney and brain, which were higher in the deficient animals.

5. Tissues from the same rat differed markedly in their concentration of ^{28}Mg and sp. ac.: the liver, heart and kidney had relatively high values, the brain an intermediate value, and muscle, femur and mandible low values.

6. The relative sp. ac. of the kidney and heart were greater than 1 in both groups 2 h after dosing. That of the liver was greater than 1 at 3 and 12 h after injection in the deficient and control groups respectively.

7. There was little difference between the Mg-deficient and control rats in the size of the exchangeable pool (1–5 %) of Mg in both femur and mandible, but the flux of Mg between plasma and bone and the rates of accretion were much greater for both bones from the control than from the deficient rats.

8. The factors controlling the uptake of ^{28}Mg by tissue are discussed, and it is concluded that the greater uptake by the heart, kidney, liver and brain from deficient rats could arise in ways other than by the replacement of Mg lost in deficiency.

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