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Comparative Biochemical Studies on the Histamine Metabolism in Acute Magnesium-Deficient Mice and Rats

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Introduction

Formerly, Kruse *et al.*[23] observed the erythema, hyperemia and edema resulting from the vasodilation of peripheral blood vessels as a part of symptoms caused by the magnesium deficiency in the rat. Thereafter many investigators including the authors[1,7,10,12-14,19,29] have recognized the same symptoms. Furthermore, the following phenomena have been elucidated, *i.e.*, the decrease of dermal mast cell population and intracellular granules[6,9], the increase of plasma and urine histamine contents[10,12,13], the elevation of eosinophil counts[12], the appearance of polynuclear leucocyte and basophil etc.[13] in magnesium deficient rats, besides the increase of serum IgE level in magnesium deficient mice[32].

In our preliminary experiments, the acute symptoms in magnesium deficiency in mice differed fairly from those in rats. Inflammatory symptoms, such as erythema and hyperemia, were not found in the mouse, and vigorous tonic convulsion was observed in the animal having normal appearance. Similar results have been recognized by Alcock and Shils[1].

Accordingly, it is expected that some relations may exist between the magnesium deficiency and histamine metabolism in both species of the animals, the extent differing considerably between the two. Thus, the short-term effects of magnesium deficiency on the histamine metabolism were investigated in rats and mice.

Materials and Methods

Young female ICR–JCL mice weighing about 11 g, and male and female Wistar rats weighing about 50 g, were used. After given the synthetic control diet (Mg: 0.07%, Table 1) and deionized water ad libitum for 7 days, they were divided into 3 groups: control, deficient (Mg: 0.001%) and recovery groups. The former two groups were maintained on the respective diets for 8 days, excepting for the sub-divided groups in which plasma or urine histamine was determined. The animals of the sub-divided groups were fed on the respective diets for 12 to 14 days. Animals of the recovery groups were given magnesium-deficient diet for the first 6 days and were switched over to the high magnesium diet (Mg: 0.21%) for the following 2 days. All the animals were housed similarly and kept under constant temperature and light-cycles.

Plasma magnesium, calcium, sodium and potassium were determined by flame atomic absorption spectroscopy.

Histamine contents in various tissues, blood and urine were measured by a modification of fluorometric assay by Shore *et al.*[36]. For collecting urine the rats were kept in metabolism cages.

Table 1. Composition of experimental diets

Mg Concentration (%)	0.07	0.001	0.21
Group	Control	Deficiency	Recovery
Vitamine-free Casein	20	20	20
Glucose	35	35	35
Sucrose	27.2839	27.39833	27.0518
Cellulose	5	5	5
Liver Oil	8	8	8
Choline Chloride	0.15	0.15	0.15
Vitamine Mixture*	0.85	0.85	0.85
Mineral Mixture*	3.6	3.6	3.6
Magnesium Oxide	0.1161	0.00167	0.3482

* Haper, A. E.; J. Nutr. 68, 405–418 (1958)

The 24-hour samples were collected in flasks containing 5 ml of 6 N HCl, filtered through filter papers, adjusted to pH 7.5 with 10 N NaOH and were diluted to about 40 ml with 0.25 M Na–P buffer. The histamine in this material was absorbed on a colum of IRC–50, washed with 15 ml of 0.5 M Na–P buffer and eluted with 1 N HCl. The histamine was assayed on the first 5 ml eluate.

The enzyme activities were measured on the supernatant fluid after the tissues were homogenized with 0.1 M Na–K–P buffer and centrifuged (14,000 rpm) for 30 minutes at 4°C. The protein concentration in this fluid was determined by the Lowry method. Histidine decarboxylase (HDC) activity was assayed by a modification of the procedure of Kobayashi[22], using an apparatus of Fukui *et al.*[18]. L-[carboxyl-^{14}C]-histamine (55 mCi/mM) was obtained from the Radiochemical Center. The activity was expressed as dpm/mg protein/60 min. Diamine oxidase (DAO) activity was assayed by a modification of the method of Beaven and Shaff[5], based upon that of Okuyama and Kobayashi[31]. [1, 4-^{14}C]-putrescine dihydrochloride (122 mCi/mM) was obtained from the avove Co.. The activity was expressed as dpm/mg protein/30 min. Histamine methyltransferase (HMT) activity was assayed by a modification of the methods of Snyder and Axelrod[37], and Tayler and Snyder[39]. S-adenocyl-L-[methyl-^{14}C]-methionine (58 mCi/mM) was obtained from the above Co., the unit of activity being the same as DAO.

Results

Body-weight-gain and food consumption

The average body weights after a preliminary feeding were 18.2 ± 1.2 g in mice and 52.0 ± 7.0 g in rats. The growth-rates of the control and the deficient animals after this fixed time were shown in Fig. 1. The weight-gain came to be depressed in both the deficient animals nearly on the first or the 4th day on diet. In the recovery groups fed with the high magnesium diet, the body weight began to increase in both the deficient animals and appeared to approach that of the control.

The food consumption in the control and the deficient groups was represented as the difference from the initial consumption (mouse 4.3 g, rat 7.5 g) (Fig. 2). It increased smoothly in both the control animals but depressed in the deficient ones. This depression was recovered quickly by the high magnesium regimen.

Symptoms

The deficient rats developed the pinnal hyperemia nearly on the 4th day and the extent of

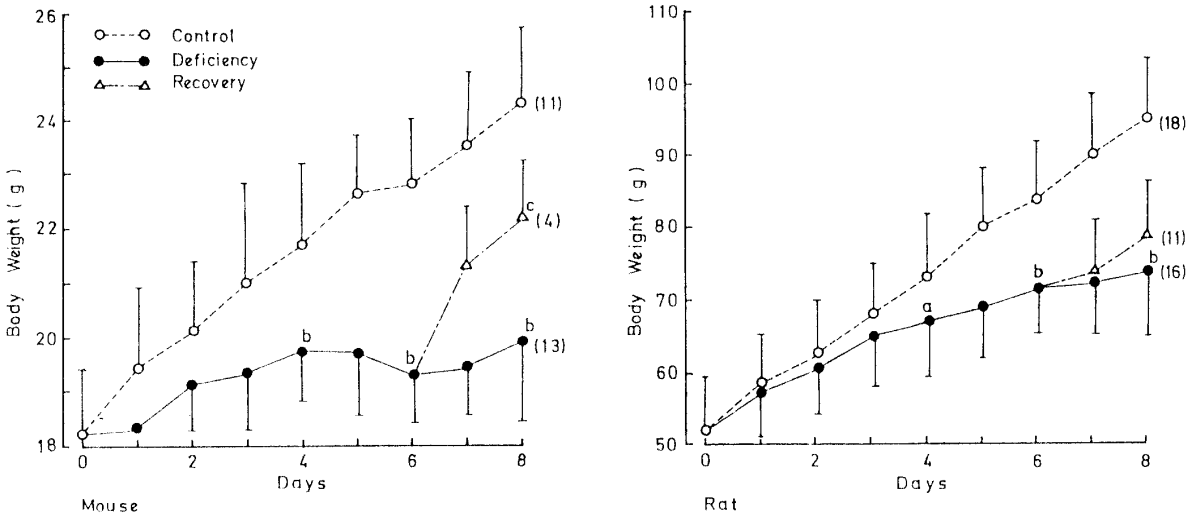

Fig. 1. Effects of magnesium deficiency on the growth in mice and rats. Each point represents the mean±S. D. of samples. (Number of animals)

a) Significantly different from control animals. $0.025<P<0.05$

b) Significantly different from control animals. $P<0.005$

c) Significantly different from magnesium deficient animals. $0.01<P<0.025$

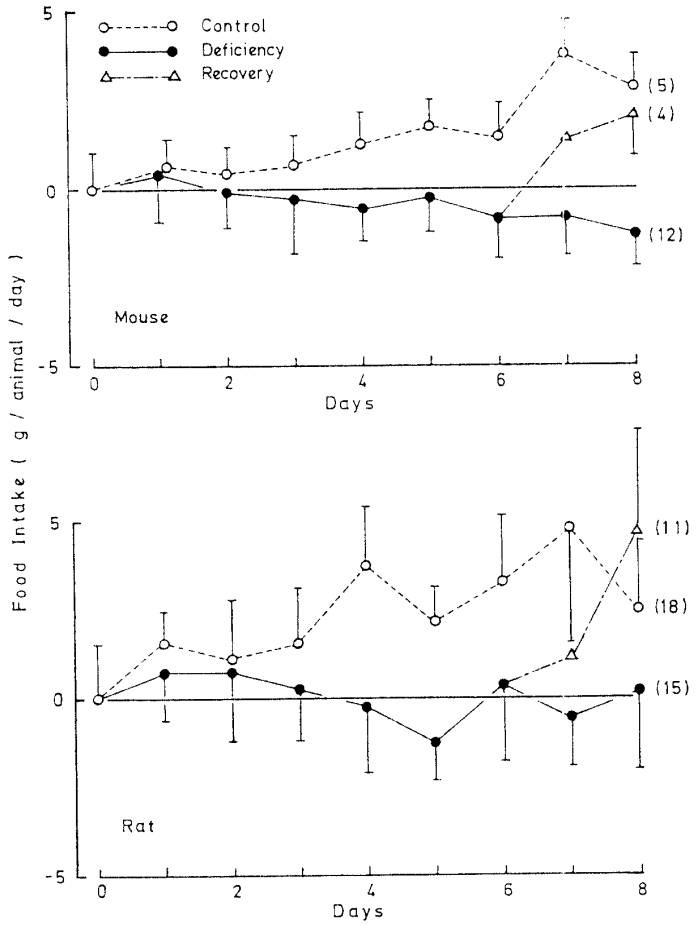

Fig. 2. Food intakes of control or magnesium deficient mice and rats. Each point represents the mean±S. D. of samples. (Number of animals) First intakes (0 day) are 4.3 g (mouse) and 7.5 g (rat).

hyperemia became more intense with the lapse of day. The surface of the whole body also came to be tinted more reddish in the deficient rats than in the control ones. The other deficient symptoms were not observed until the 8th day.

The deficient mice showed rude hair with the depression of weight-gain and no hyperemia. Some mice stretched their limbs, and developed the tonic convulsion fatal in many cases nearly on the 4th day. A convulsive seizure occurred suddenly with the external stimulations, such as the noise resulting from opening the gate of cage and touching of the body for weighing. No convulsion was observed in the mice switched over to the high magnesium diet.

Plasma electrolyte level

Plasma magnesium levels were significantly lower in both the deficient animals (Fig. 3). This decrease in plasma magnesium concentration accorded well with the occurrence of hyperemic symptom in the deficient rats or of convulsion in the deficient mice, and appeared to play some roles in the development of deficient symptoms. When the plasma magnesium concentration was rapidly restored by the high magnesium regimen, disappearance of this symptom or convusion was brought forth.

The change in plasma calcium concentration showed a large difference between both species of the deficient animals. The plasma calcium level in rats fluctuated at each period after being got into magnesium deficiency, but there was no difference among the control, the deficient and recovery groups. In mice, however, the plasma calcium concentration decreased gradually after the supply of deficient diet. This hypocalcemia in mice was rapidly recovered by supplementation of magnesium (Fig. 4).

Plasma sodium and potassium concentrations were noted to be unaffected by magnesium depletion in both the animals (Figs. are abbreviated).

Histamine contents in various tissues

Histamine contents were determined in tissues of the skin, stomach, duodenum, heart, brain,

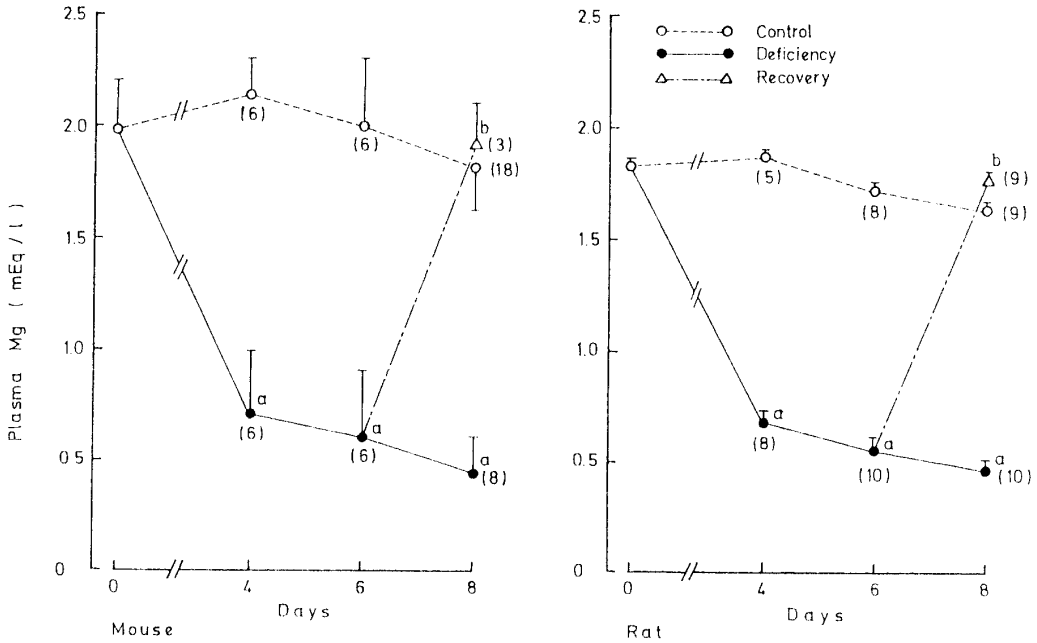

Fig. 3. Effects of magnesium deficiency on plasma magnesium levels in mice and rats. Each point represents the mean±S. D. of samples. (Number of samples)
a) Significantly different from control animals. $P<0.005$
b) Significantly different from magnesium deficient animals. $P<0.005$

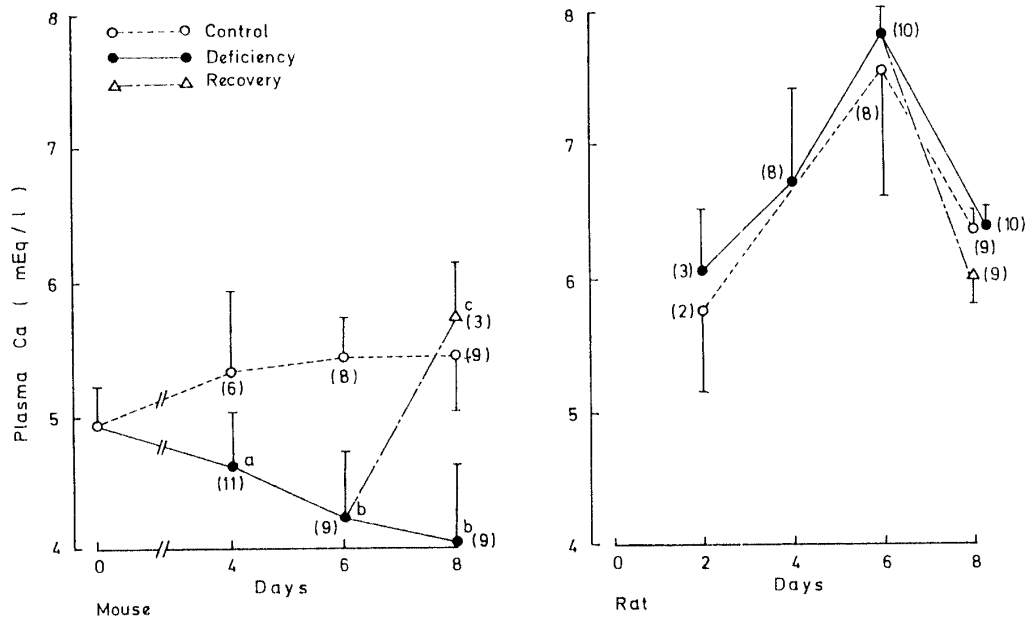

Fig. 4. Effects of magnesium deficiency on plasma calcium levels in mice and rats.
Each point represents the mean±S. D. of samples. (Number of samples)
a) Significantly different from control animals. $0.01<P<0.025$
b) Significantly different from control animals. $P<0.005$
c) Significantly different from magnesium deficient animals. $0.005<P<0.01$

liver, lung, kidney and spleen of both species of the animals on the 4th, 6th, 8th and 12th or 14th days after feeding on the magnesium-deficient diet (Tables 2 and 3). The normal values obtained

Table 2. Histamine contents in some tissues of control and magnesium-deficient mice

Tissue	Days on diet	4	6	8	14
	Group	Histamine (μg/g wet tissue)			
Skin	Control	30.7 ±7.6 (2)	NT	19.6 ±8.9 (2)	NT
	Deficiency	48.9 ±2.1 (2)	NT	19.0 ±1.7 (2)	NT
Stomach	C.	7.95 ±0.07 (2)	8.1	7.13 ±0.35 (4)	4.6
	D.	8.15 ±0.35 (2)	6.9	7.40 ±1.08 (4)	3.4
Duodenum	C.	0.30 ±0.07 (3)	0.32	0.32 ±0.05 (7)	0.34 ±0.05 (2)
	D.	0.48 ±0.08 (3)	0.34	0.26 ±0.08 (7)	0.39 ±0.09 (2)
Heart	C.	0.70	NT	0.55 ±0.07 (4)	0.60
	D.	0.98 ±0.16 (2)	NT	0.84 ±0.12 (4)[a]	1.07
Brain	C.	0.14 ±0.01 (2)	0.11	0.16 ±0.05 (6)	NT
	D.	0.13 ±0.01 (2)	0.15	0.17 ±0.02 (6)	NT
Liver	C.	0.063±0.002 (2)	0.065±0.004 (2)	0.074±0.011 (6)	0.054±0.020 (2)
	D.	0.071±0.001 (2)	0.075±0.060 (2)	0.125±0.079 (6)	0.088±0.016 (2)
Lung	C.	0.57 ±0.01 (2)	0.50	0.44 ±0.06 (6)	0.51
	D.	0.55 ±0.01 (2)	0.48	0.39 ±0.08 (6)	0.50
Kidney	C.	5.35 ±3.4 (2)	4.7	6.82 ±3.62 (4)	NT
	D.	3.25 ±1.0	5.5	3.17 ±0.40 (4)	NT
Spleen	C.	0.29 ±0.01 (3)	0.25 ±0.01 (2)	0.33 ±0.10 (7)	0.33 ±0.09 (2)
	D.	0.21 ±0.15 (3)	0.23 ±0.17 (2)	0.81 ±0.07 (7)[a]	1.05 ±0.02 (2)[a]

Each value is the mean±S.D. of samples. Single estimations on pooled tissues of three mice. (Number of samples) NT: Not tested.
a) Significantly different from control animals. $P<0.05$

Table 3. Histamine contents in some tissues of control and magnesium-deficient rats

Tissue	Days on diet	4	6	8	12
	Group	Histamine (μg/g wet tissue)			
Skin	Control	32.58±1.37	35.00±2.01	20.08±6.73	32.50±5.50
	Deficiency	30.54±4.99	35.66±2.36	29.70±6.24	25.00±9.54
Stomach	C.	NT	13.53±0.42	7.41±2.17	12.15±0.87
	D.	12.10±1.95	14.20±2.89	11.46±5.12	9.88±1.36
Duodenum	C.	NT	12.36±2.77	10.79±3.38	9.02±2.48
	D.	11.86±0.83	10.40±2.65	36.54±5.77[a]	33.80±0.26[a]
Heart	C.	NT	3.64±0.96	3.44±0.44	2.33±1.04
	D.	8.86±0.93	3.16±0.51	6.87±0.96[a]	1.75±0.86
Brain	C.	NT	0.15±0.09	0.16±0.02	0.06±0.03
	D.	0.16±0.01	0.32±0.16	0.19±0.06	0.04±0.01
Liver	C.	NT	0.22±0.06	0.58±0.07	0.26±0.04
	D.	NT	0.34±0.07	2.81±1.24[a]	1.42±0.57[a]
Lung	C.	3.73±0.42	3.16±1.07	7.43±2.45	5.50±0.51
	D.	3.24±1.01	4.57±1.69	14.55±2.76[a]	9.03±2.66
Kidney	C.	NT	0.23±0.08	0.24±0.03	0.51±0.03
	D.	NT	0.33±0.10	1.50±0.60[a]	0.56±0.16
Spleen	C.	0.57±0.25	1.26±0.49	0.69±0.23	0.45±0.18
	D.	0.77±0.05	3.54±0.43[a]	15.79±1.53[a]	25.26±12.25[3]

Each value is the mean±S.D. of samples (n=6). NT: Not tested.
a) Significantly different from control animals. $P<0.05$

were similar to those reported by the other investigators[2, 4, 25, 36] excepting for the mouse spleen. Histamine contents were approximately increased at various periods after the depletion, excepting for the mouse kidney. On the 8th day, histamine contents in the spleen increased markedly in both species of the deficient animals, but the degree of increment was extreme in rats. Namely, histamine contents increased about 2.5 times in deficient mice but about 31 times in deficient rats over the respective control animals. This increase in the spleen of rats got nearly 60 times on the 12th day. In the other tissues the increased histamine contents associated with magnesium deficiency were observed in the heart of mice and in the liver, duodenum and kidney of rats. The extent of increment in these organs was larger in rats than in mice. All other tissues examined were unaffected by magnesium depletion. The spleen weight increased in the deficient rats while it rather decreased in the deficient mice (The table is abbreviated).

Plasma histamine level and urinary histamine excretion

The plasma histamine level began to increase on the 4th day, showing the highest value on the 8th day in the deficient rats, but no elevation of plasma histamine level was found in the deficient mice (Fig. 5).

The urinary histamine excretion increased significantly on the 4th to 12th day in deficient rats (Fig. 6). Although the urinary histamine excretion in the mouse was examined by ^{3}H-histamine formation from ^{3}H-histidine, no remarkable difference was found between the control and the magnesium-deficient mice (Table 4). The ratio of ^{3}H-histamine to total ^{3}H was rather less by the depletion. Accordingly, the increase in the urinary histamine excretion does not appear to be induced by the magnesium deficiency.

HDC and DAO activities

HDC and DAO activities in both the animals were examined on tissues in which some changes of histamine contents were observed in magnesium depletion. The HDC activity was elevated in

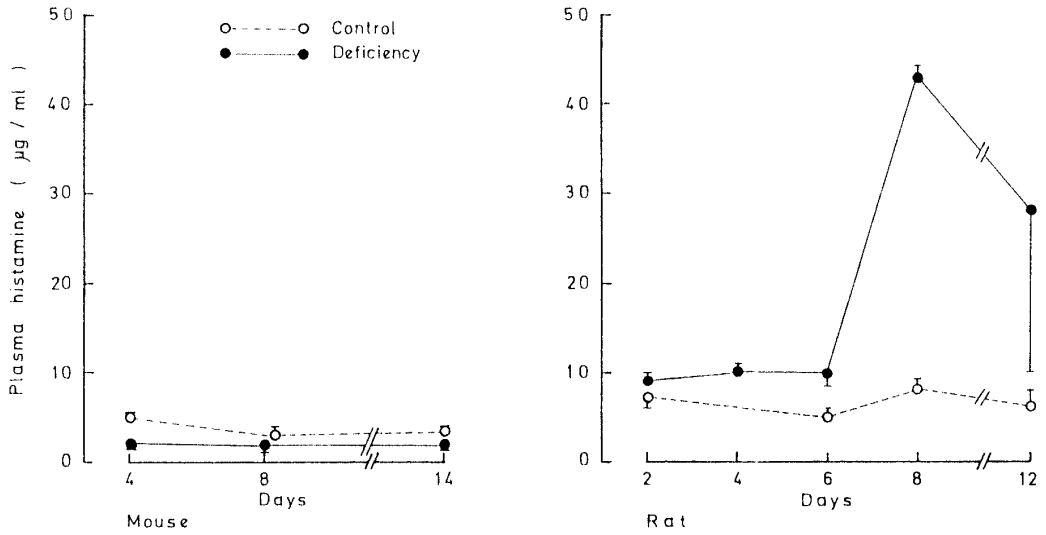

Fig. 5. Effects of magnesium deficiency on plasma histamine levels in mice and rats. Each point represents the mean±S. D. of samples.

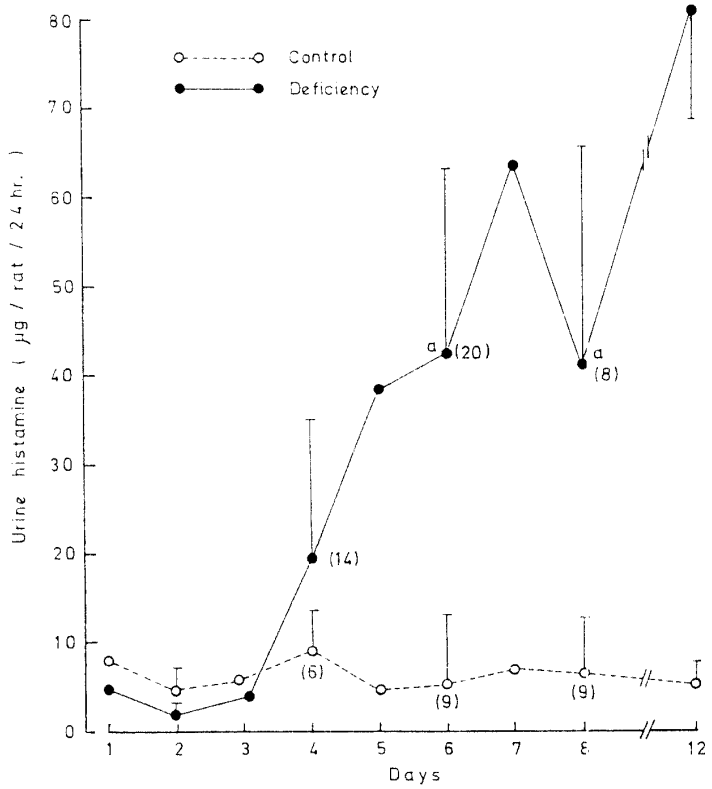

Fig. 6. Effects of magnesium deficiency on urine histamine contents in rats. Each point represents the mean±S. D. of samples
a) Significantly different from control animals. $P<0.01$

Table 4. ^{3}H-histamine and total ^{3}H in urine of magnesium-deficient mice at 1 hr. after intravenous injection with free ^{3}H-L-histidine

Experiment No.	Group	(A) ^{3}H-histamine $\times 10^3$ dpm/g urine	(B) Total ^{3}H $\times 10^5$ dpm/g urine	$\frac{(A)}{(B)} \times 100$ (%)
1	Control	513.4	250.5	2.0
	Deficiency	276.4	272.8	1.0
2	C.	291.7	216.8	1.3
	D.	46.1	86.1	0.5
3	C.	115.8	115.4	1.0
	D.	83.3	251.0	0.3
4	C.	1025.4	920.0	1.1
	D.	179.1	242.9	0.7

Single estimations on pooled tissues of three mice.
8 days after magnesium deficiency.

the spleen, lung, liver and skin of the deficient rats (Fig. 8), while DAO activity was rather depressed in the two examined tissues (duodenum and spleen) of rats (Fig. 10). These changes seemed to be corresponding to the increase of histamine contents in those tissues of the deficient rats. HDC and DAO activities in mice were determined respectively, in the kidney and duodenum of the tissues examined. Both activities of HDC in the kidney and DAO in the duodenum were significantly unaffected by magnesium depletion (Figs. 7 and 9).

HMT activity

The methylating pathway of histamine by HMT is said to be a main pathway for histamine catabolism in the mouse, cat and dog[33]. This enzyme is distributed widely in the body of mammals, exhibiting a high degree of substrate specificity. In this respect, HMT activities were examined in the various tissues from both species of the deficient animals. In the mouse, the HMT activity was recognized in all the 7 tissues examined (Fig. 11). However, no signigicant difference was

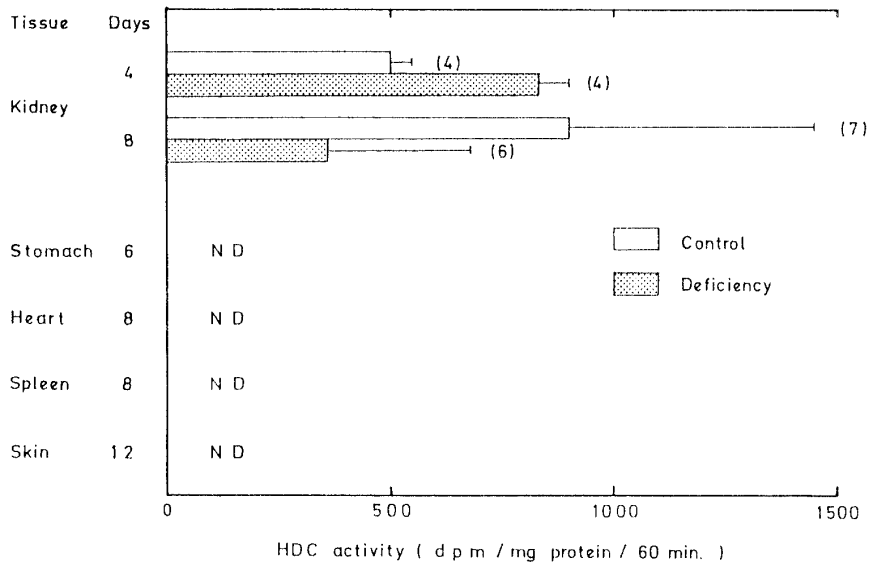

Fig. 7. Effects of magnesium deficiency on histidine decarboxylase (HDC) activity in some tissues of mice.

Each value is the mean ± S. D. of samples. Single estimations on pooled tissues of three mice. (Number of samples) ND: Not detected.

found between the control and the deficient groups. In the rat, the activity was assayed in 6 tissues of the kidney, liver, spleen, stomach, lung and skin, but it was detectable only in the liver and kidney (Fig. 12). The activity in both tissues seemed to be unaffected by the magnesium depletion.

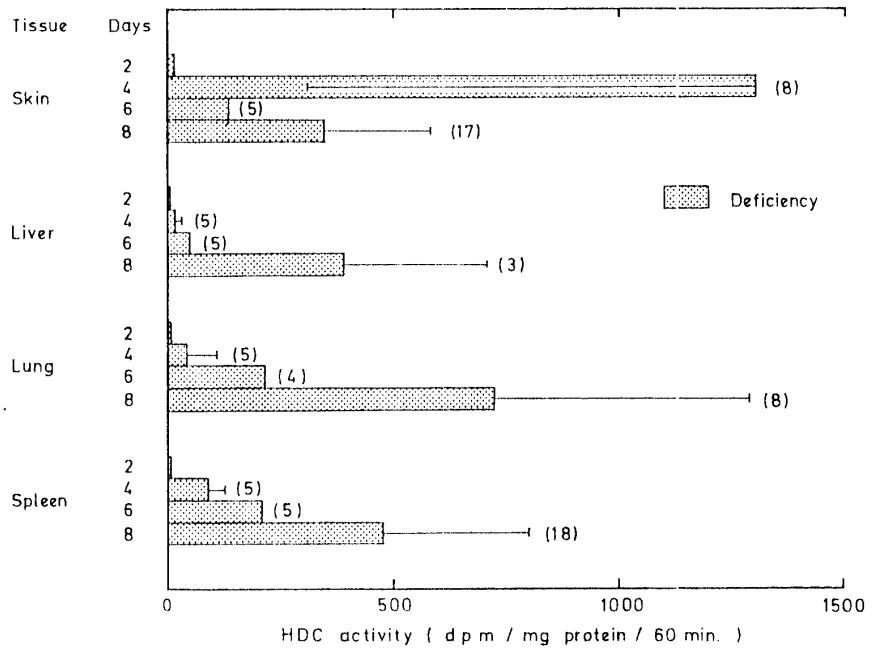

Fig. 8. Effect of magnesium deficiency on histidine decarboxylase (HDC) activity in some tissues of rats.

Each value is the mean±S. D. of samples. (Number of samples)

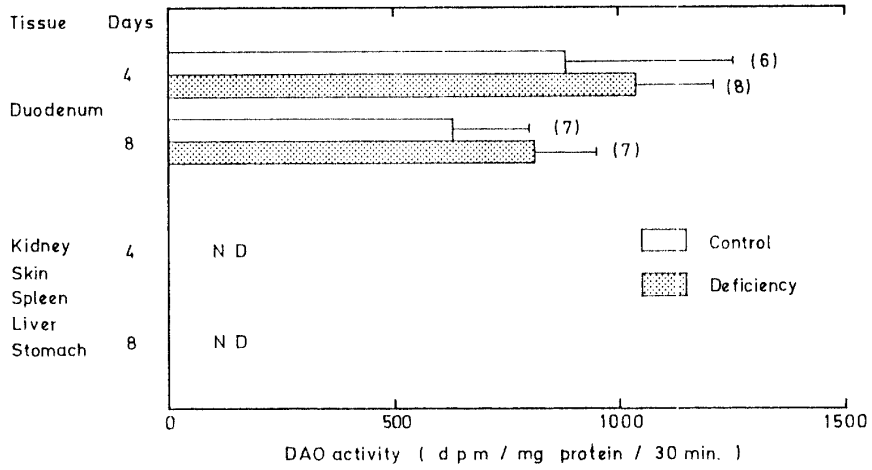

Fig. 9. Effects of magnesium deficiency on diamine oxidase (DAO) activity in some tissues of mice.

Each value is the mean±S. D. of samples. Single estimations on pooled tissues of three mice. (Number of samples) ND: Not detected

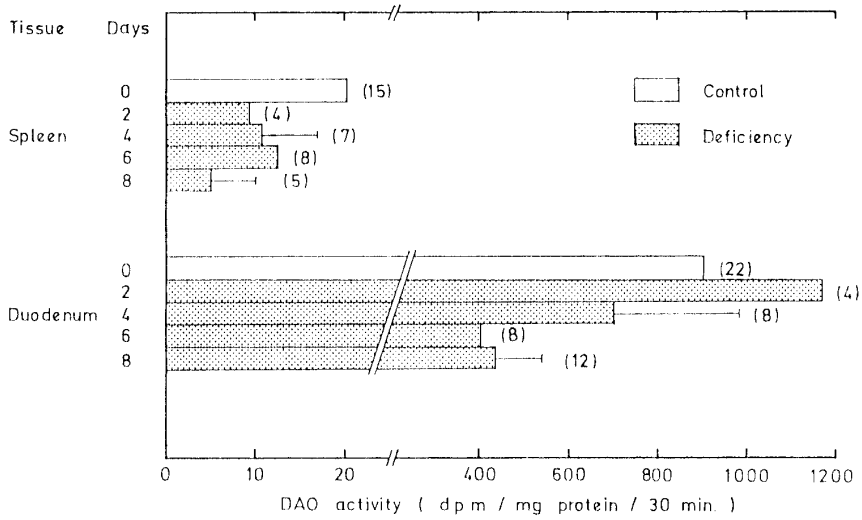

Fig. 10. Effects of magnesium deficiency on diamine oxidase (DAO) activity in some tissues of rats.

Each value is the mean ± S. D. of samples. (Number of samples)

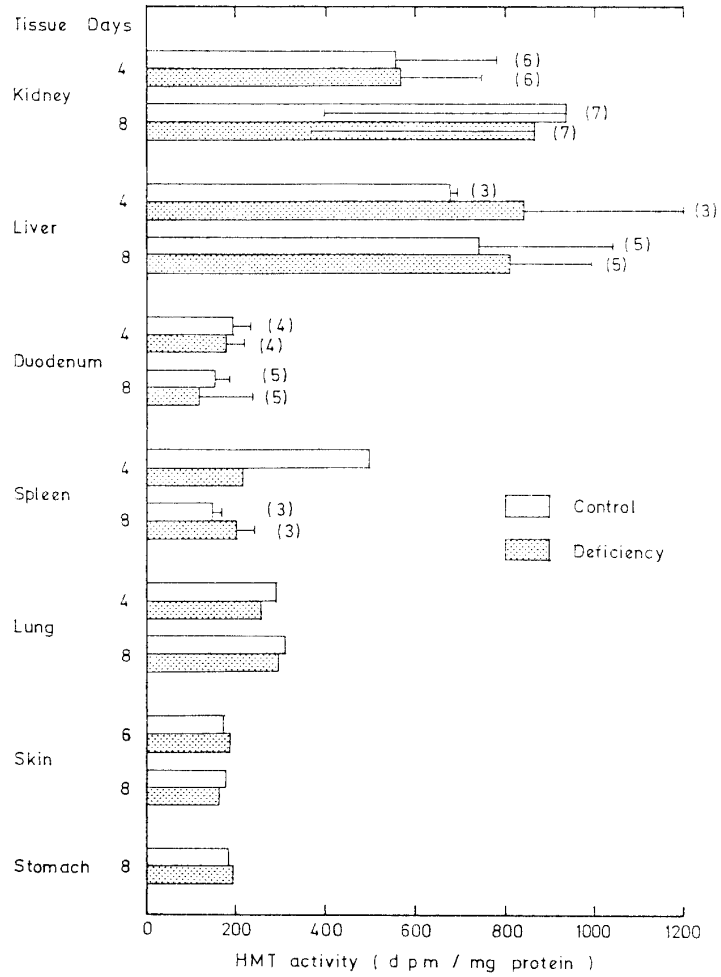

Fig. 11. Effects of magnesium deficiency on histamine methyltransferase (HMT) activity in some tissues of mice.

Each value is the mean ± S. D. of samples. Single estimations on pooled tissues of three mice. (Number of samples)

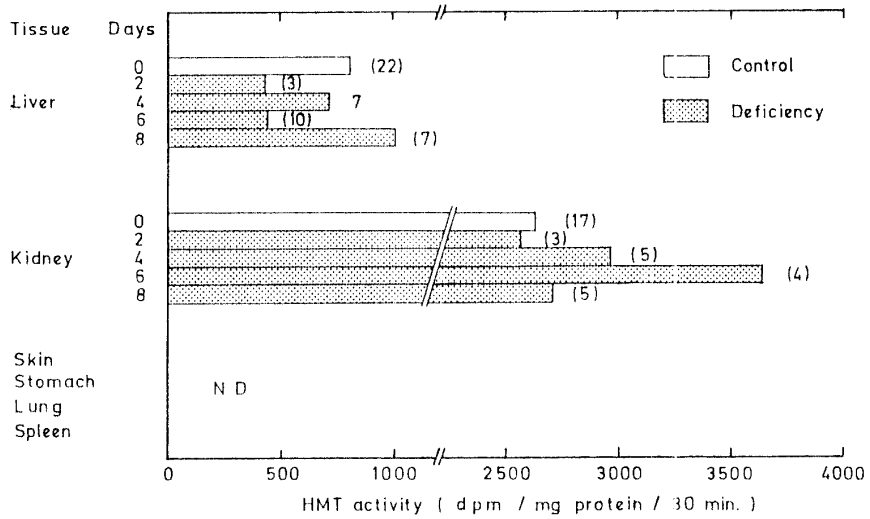

Fig. 12. Effects of magnesium deficiency on histamine methyltransferase (HMT) activity in some tissues of rats.
Each value is the mean. (Number of samples) ND: Not detected.

Discussion

The magnesium deficiency depressed remakably the body-weight-gain in the both animals (Fig. 1). As this depression was improved by the high magnesium regimen, and the food consumption also was elevated with the recovery of body-weight-gain (Fig. 2), it appeared that the depression of body-weight-gain after magnesium deficiency was due to a lowering of food consumption, resulting from an aggravation of general conditions.

The inflammatory symptoms such as erythema and hyperemia began to appear on nearly the 4th day on deficient diet in the rat, but not in the mouse, in which some animals died of tonic convulsion on nearly the 4th day. Bac[3] and Modak *et al.*[28] also observed audiogenic seizures and changeable relations between brain acetylcholine and motor activity in deficient mice, respectively. Accordingly, it was assumed that the metabolic system influenced strongly by magnesium depletion in the mouse might be different from that in the rat. The fact that the deficient symptoms were improved in recovery groups of both species suggests the possibility of contribution of magnesium depletion to the development of deficient symptoms.

The hypomagnesemia and its rapid restoration by the high magnesium regimen agreed well with the appearance and disappearance of deficient symptoms in both the species. The deficient rats were normocalcemic but the mice were hypocalcemic. The existence of hypocalcemia in the deficient mice and that of normocalcemia in the rats agreed with Alcock and Shils[1]. The qestion which was more participated in the development of convulsion in the mice deficient acutely in magnesium, the hypocalcemia or the hypomagnesemia, should be further studied with the change of serum ionized calcium and magnesium, since the fall of serum ionized calcium was suggested in the hypomagnesemia caused by magnesium depletion[43].

Although decrease of intracellular potassium was suggested in magnesium depletion[26,40,41] and enlargement of histamine sensititvity was observed in the mice under the high potassium regimen[27], no significant change was found in plasma potassium and sodium concentration in this study. This might be owing to a short-term magnesium depletion.

Histamine contents in the spleen increased markedly in both species of the deficient animals,

but the degree of increment was extreme in rats (Tables 2 and 3). The spleen weight itself also increased in the deficient rats. However, on account of the fact that histamine contents are represented in units per g of wet weight of tissues, this increase appears not to be directly related with the spleen hypertrophy. The remarkable increase of histamine contents and hypertrophy in the spleen in deficient rats agreed well with the observation of Claverie-Benureau *et al.*[12,13]. Elin[15,16] also observed the spleen hypertropy and anemia in deficient rats. Judging from the fact that histamine contents increased about 2.5 times but the spleen weight itself decreased in the deficient mice, as well as the fact that no increase of spleen HDC activity was noted in the deficient mice, the effect of magnesium deficiency on the spleen appeared to be different considerably between both the species.

The cause of the elevation of plasma histamine level is considered to be derived from either one of the stimulation of histmaine anabolic capacity, the elevation of histamine release from its reservoir and the depression of histamine catabolic capacity or the combination of these. From the fact that the histaminase activity was in a normal range and HDC activity was slightly increased in the deficient rats, Bois[8] suggested that the elevation of plasma histamine level in the deficient rats might be due to the lack of obstruction of the enzymatic histamine releasing system. In this study, although no remarkable change was seen in the oxidizing or methylating pathway of histmaine between the normal and deficient rats, HDC activities were noted to be significantly elevated in the skin, liver, lung and spleen of the deficient rats (Fig. 8). This notice differs markedly from Bois[8]. If the enhancement of histamine release causes this elevation of plasma histamine level, it is to be considered that some changes may be observed in histamine content of the skin rich in mast cells. However, as no change was recognized in histamine content in the skin, the elevation of plasma histamine level in the rat was suggested to be due to the enlargement of histamine anabolic capacity.

Itokawa *et al.*[21] observed that the plasma serotonin level increased in the magnesium-deficient rats and the injection of histamine (10 mg/kg) caused no vasodilation of peripheral blood vessels, but the same dose of serotonin caused the oto- and rhino-erythema. From these results, they suggested that the hyperemia in the deficient rats was due to serotonin and that thiamine might be related to this phenomenon. Further, they observed a lowering of liver monoamine oxidase in the deficient rats[20]. Gaudin-Harding *et al.*[19] found no difference among serotonin derivatives in the liver of the normal and deficient rats, whereas they observed that the administration of serotonin caused acute and vigorous hyperemia in both the normal and deficient rats. Furthermore, Bois *et al.*[9] observed the disappearance of the vasodilation of peripheral blood vessels and erythema in the magnesium-deficient rats pretreated with compound 48/80. Accordingly, although the existence of mast cells appears to be essential to the development of hyperemic symptom, which is more responsible for its development, histamine or serotonin, comes to be of interest. It has been suggested that the rabbit devoid of mast cells does not develop any hyperemic symptom by magnesium depletion[24]. It is also interesting that the mouse having them showed no hyperemic symptom in this study.

According to the observation of Itokawa *et al.*[20], the plasma serotonin increased only twice in 4 weeks in the deficient rats, but in this experiment, the plasma histamine increased about 5 times in 8 days of the deficiency. Bois *et al.*[10] and Gaudin-Harding *et al.*[13,19] have observed about 4- and 8-fold increases of plasma histamine in 10 and 14 days after the depletion, respectively. In the subsequent study in this laboratory, the pinnal hyperemia in the rat was partly depressed by diphenhydramine, H_1-blocker, or cimetidine, H_2-blocker; and completely by the simultaneous use of the both drugs[30]. Consequently, histamine appears to be more responsible for the development

of this hyperemic symptom than serotonin.

In the mouse, HDC activity, which was appreciable in the kidney alone, was rather depressed by the magnesium deficiency (Fig. 7). DAO activity in the kidney was almost unappreciable (Fig. 9), but HMT activity was considerably detected (Fig. 11). As the latter activity was almost the same between the control and the deficient groups, the decrease of histamine content in the kidney was considered to be chiefly due to the fall of HDC activity there. Schayer and Reilly[34] have shown that administration of thyroxine to mice significantly increases HDC activity and decreases HMT activity in the kidney. Since the hyperthyroidism is assumed to be one of the causes of hypomagnesemia, it was expected that the change of these activities might agree with their results, but it did not happen so. The reason of this difference remains obscure.

In the rat, HDC activity was unappreciable in the kidney and tended to be increasing in the skin, liver, lung and spleen after the magnesium deficiency (Fig. 8). The increase of histamine content in the spleen seems to be too significant to be attributed to the elevation of HDC activity alone and may be due to the fact that the uptake of histamine into the spleen was also increased as observed in the mouse[38]. The cause of this phenomenon is now under study in this laboratory.

DAO activity is said to be localized in the alimentary canal, kidney, thymus and decidual placenta[42]. Fogel *et al.*[17] observed a high DAO activity in the duodenum and a lower activity in the kidney (about one sixth of the former). The high DAO activity was shown in the duodenum alone among the examined organs in this study, too. The organ in which DAO is implicated in the histamine metabolism, therefore, appears to be only the duodenum in both the species. Furthermore, it is considered that DAO activity as the histamine decomposition-system is not so responsible for the elevation of plasma and urine histamine contents in the magnesium-deficient rats.

HMT activity seems not be much influenced by magnesium in both species of the rat and the mouse in which a methylating pathway of histamine is said to be main.

The present results suggest that the acute magnesium deficiency significantly influences the histamine metabolism, which was responsible for the development of acute symptom of magnesium deficiency, in the rat; while it did not affect so much in the mouse. Furthermore, it was concluded that the effects of magnesium deficiency on histamine metabolism were remarkable in the rat but slight in the mouse.

Summary

Effects of the acute magnesium deficiency on the histamine metabolism were compared in young mice and rats.

Plamsa magnesium levels were rapidly lowered in both species of the deficient animals, and were recovered quickly by the high magnesium regimen.

In the mice the hypocalcemia was developed with hypomagnesemia but in the rat it was otherwise. The hypocalcemia in the mice was rapidly restored by the high magnesium regimen.

The deficient rats developed the pinnal hyperemia on nearly the 4th day. This symptom also was improved by supplementation of magnesium. However, no hyperemic symptom was found in the deficient mice, some of which died of tonic convulsion.

The plasma and urine histamine increased significantly in the deficient rats, but did not in the mice.

Histamine contents in the spleen increased markedly in both the deficient animals, but the degree of increment was extreme in rats.

The spleen weight increased in the deficient rats, while it rather decreased in the deficient mice.

In deficient rats, the HDC activity was elevated in the spleen, lung, liver and skin, while DAO activity was depressed in the two examined tissues (duodenum and spleen). HDC and DAO activities in mice were detected only in the kidney and duodenum, respectively, among the tissues examined. Both the activities of HDC in the kidney and DAO in the duodenum were noted to unaffected by magnesium depletion.

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