used as quick measure of erythropoiesis in Swiss male mice. In normal nonirradiated mice, iron uptake is not affected by intravenous injection of isologous, homologous and heterologous bone marrow cells except for inocula greater than 40 x 10^6 cells. Injection of these cell types after 900 R whole body x-radiation increases Fe_{59} uptake rates in the order: heterologous, homologous, isologous. Protection against lethal radiation effect as measured by survival and Fe_{59} uptake depended on genetic relationship between bone marrow donor and recipient.

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Effects of Pyridoxine and Desoxypyridoxine on Magnesium Metabolism in the Rabbit.* (25873)

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Factors regulating metabolism of magnesium are obscure. Development of a relatively simple and reliable chemical method for determination of magnesium in biological material, and availability of radioactive isotope of magnesium, Mg^{28}, have made possible a restudy of the entire problem of magnesium metabolism. Studies of plasma clearance and tissue uptake of Mg^{28} in experimental animals (1) and in human beings(2) have been reported. Changes in carbohydrate metabolism alter rate of uptake of Mg^{28} by various tissues(3). The effects of cortisone acetate have also been determined (unpublished). These studies suggested that tissue uptake of Mg^{28} was considerably slower than that of another intracellular ion, potassium, and that cellular uptake of magnesium might be associated with anabolic activities of cells. If this hypothesis is correct, then any factor altering metabolism of protein might affect that of magnesium. Pyridoxine deficiency alters protein metabolism and produces changes in enzymatic reactions(4); pyridoxine also influences magnesium metabolism(5). Our experiments were undertaken to determine effects of pyridoxine and its antagonist, desoxypyridoxine, on magnesium metabolism in the rabbit. Mg^{28} was used to measure exchangeable body content of this ion and its relative tissue uptake.

Material and methods. Forty-seven normal adult male rabbits weighing between 1.6 and 2.5 kg were kept in individual stainless steel metabolism cages and fed a stock diet of compressed pellets. Tap water was given *ad lib. Pyridoxine* hydrochloride and *desoxypyridoxine* hydrochloride were dissolved in distilled water, neutralized with 1 N NaOH, and made to concentration of 40 mg/ml. *Exp. I and II.* External balance studies for magnesium were performed daily at least 11 days in 2 groups of 8 rabbits each. During first 2 days, baseline studies were done. Starting on third day and continuing 8 days, each animal in

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Exp. I received daily dose of *pyridoxine* (100 mg), given intravenously into marginal ear vein. Starting on third day and continuing 6 days, each animal in *Exp. II* received daily dose of *desoxypyridoxine* (40 mg kg) given by same route. *External balance of magnesium* and *exchangeable magnesium content* (Mg_e) were determined as previously described(1). Magnesium concentrations in urine and serum were determined by modification of the molybdivanadate method for phosphate(6). *Exp. III and IV.* The remaining 31 animals were divided into 3 groups. Each of 8 rabbits in *Exp. III* received intravenous dose of *pyridoxine* (100 mg). Twenty-four hours later, a second dose of pyridoxine and 5 ml of Mg^{28} solution, used in Exp. I and II, were given intravenously. Animals were killed by air embolism exactly 4 hours after injection of Mg^{28}, and samples of tissues obtained. Tissue relative activity was determined as previously described(1). Each of 15 rabbits in *Exp. IV* received 7 daily doses of *desoxypyridoxine* (40 mg/kg) given intravenously. The seventh injection of desoxypyridoxine was accompanied by injection of 5 ml of Mg^{28} solution. Animals were then killed by air embolism at 4 hours, and tissues obtained as described previously(1). Eight animals in the *control group* were not given pyridoxine or desoxypyridoxine, but were otherwise treated identically with those in test groups. *Exp. I and II.* Each animal served as its own control. After the difference between baseline values and values at end of treatment period had been calculated for each animal, mean differences for the whole group were obtained. The significance of mean differences was determined by use of "t" test(7), a "P" value of less than 0.01 being considered significant. *Exp. III and IV.* Mean relative activity of each type of tissue was determined for both test groups and for control group, and the significance of differences between group means was tested(7).

Results. Exp. I and II. Baseline values for serum magnesium, exchangeable magnesium, Mg^{28} excretion, food intake, urinary magnesium excretion, urine volume and magnesium balance were similar to those previously reported in other similar experiments (3). *Exp. I.* Clinically, animals injected with *pyridoxine* appeared healthy throughout experiment. With administration of pyridoxine, a significant increase in mean body weight (2.195 to 2.272 kg) occurred. No other significant changes were noted in this external balance study. Exchangeable magnesium content was not altered. *Exp. II.* After third injection of *desoxypyridoxine,* rabbits became hyperirritable. About 2 hours after fifth and sixth injections of the drug, generalized convulsions occurred, lasting several minutes. No significant changes were noted in mean body weight or in other parameters studied.

Exp. III and IV (Table I). In rabbits given *pyridoxine,* a significant increase was observed in relative tissue activity of appendix and heart. Rabbits given *desoxypyridoxine* showed a significant increase in serum magnesium concentration and a significant de-

TABLE I. Effect of Pyridoxine, 100 mg Daily for 2 Days, and Desoxypyridoxine, 40 mg/kg Daily for 7 Days, on Relative Radioactivity* of Tissues in Rabbits.

Tissue	Control group[1]	Pyridoxine group[2]	Desoxy-pyridoxine group[3]
	Relative radioactivity*		
Muscle	.50 ± .10†	.78 ± .12	.58 ± .06
Skin	1.25 ± .14	1.83 ± .25	1.43 ± .12
Appendix	3.90 ± .23	8.26 ± .61‡	5.57 ± .30
Lung	4.25 ± .26	4.52 ± .29	3.19 ± .12‡
Liver	5.10 ± .42	7.10 ± .61	4.65 ± .28
Heart	5.90 ± .99	10.37 ±1.03‡	6.85 ± .35
Kidney	11.00 ± .60	11.42 ± .63	8.65 ± .48‡
Bone	12.90 ±1.13	16.54 ±1.25	9.29 ± .50‡
	Mg concentration		
Serum (meq/l)	2.06 ± .14	1.93 ± .03	2.80 ± .28‡
	Blood glucose (mg %)		
	91.4 ±5.27	102.8 ±6.22	92.9 ±4.01

* Relative radioactivity $= \frac{\text{cpm/g tissue}}{\text{cpm/ml serum}}$ at time of death.

† Stand. error.

‡ Statistically significant difference when compared with control group.

[1] Mean value in 8 rabbits not inj.

[2] Mean value in 8 rabbits receiving 2 daily inj. of pyridoxine.

[3] Mean value in 15 rabbits receiving 7 daily inj. of desoxypyridoxine.

crease in relative tissue activity of kidney, lung and bone.

Comment. In previous experiments with rabbits, administration of insulin and glucose increased relative tissue activity of all tissues studied(3). Cortisone increased exchangeable magnesium content of body and uptake of Mg^{28} in muscle, appendix and heart. The increase in exchangeable magnesium was attributed primarily to increased uptake of Mg^{28} in muscle, since the relative mass of appendix and heart is too small to have an appreciable influence on exchangeable magnesium content of the body.

Under our conditions, pyridoxine did not alter clinical behavior of rabbits, although it may have accelerated body growth. It did not affect the external balance of magnesium, and exchangeable body pool of magnesium was not altered. Relative tissue uptake of Mg^{28} was increased in appendix and heart only, and not in muscle. These observations are consonant with the impression that exchangeable magnesium content of body is increased by conditions which increase uptake of Mg^{28} by muscle and bone, the body's largest reservoirs of magnesium.

The dose of desoxypyridoxine administered was sufficient to produce typical convulsions of pyridoxine deficiency. Animals receiving desoxypyridoxine, however, showed no significant changes in external balance of magnesium, and the body's pool of exchangeable magnesium was not altered. Uptake of Mg^{28} in kidney, lung, and bone was suppressed, and serum magnesium concentrations were elevated. Elevation of serum magnesium, in presence of unaltered urinary excretion of magnesium, suggests that renal excretion of magnesium was not suppressed by desoxypyridoxine; it further suggests that pyridoxine deficiency might alter distribution of magnesium between intra- and extra-cellular compartments.

Summary. External balance studies for magnesium and isotopic determinations of exchangeable magnesium content of body were made in 8 adult male rabbits before and after 8 daily injections of pyridoxine (100 mg), and in another group of 8 rabbits before and after 6 daily injections of desoxypyridoxine, 40 mg/kg. Except for increase in mean body weight in the group receiving pyridoxine, no significant changes were observed. In 8 animals given 2 intravenous injections of pyridoxine (100 mg) 24 hours apart, relative tissue activity of Mg^{28} was increased in appendix and heart. In 15 rabbits given desoxypyridoxine, 40 mg/kg, daily for 7 days, there was a significant decrease in relative activity of kidney, lung, and bone, and a significant increase in serum magnesium concentration. The results suggest that excess or deficiency of pyridoxine alters rate of uptake of Mg^{28} by various tissues.

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