

Cardiac, Renal and Hepatic Hypertrophy in Pyridoxine-Deficient Rats.* (22062)

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A statistically significant increase in the weight of the heart and kidneys of the pyridoxine-deficient rat was reported by Agnew (1,2). Olsen and Martindale(3) recently confirmed this work and also reported an increase in the weight of the liver of the pyridoxine-deficient rat.

The present study was undertaken to see: (1) if the increases in weight of the heart, kidneys, and liver could be found after feeding the deficient diet for a much shorter period of time than in previous experiments; and (2) if these organs were truly hypertrophied or merely heavier by virtue of increased tissue fluid content.

Methods. Male Wistar weanling rats, obtained from the Charles River Breeding Laboratories, Boston, were used, and were housed in individual cages with wide wire-screened bases. The synthetic diet used consisted of sucrose 72%, casein (Sheffield "vitamin-free") 18%, corn oil (Mazola) 5%, salt mixture(4) 4%, cod liver oil 1%. Choline chloride (1.5 g/kilo) was added, and then appropriate amounts of the following substances in alcoholic solution or suspension to give the following concentrations (mg/kilo) in the complete diet: calcium pantothenate 20, niacin 20, riboflavin 3, thiamin 3, pyridoxine HCl (controls only) 3, folic acid 1, biotin 0.2. Fresh diet was made up weekly and stored in the refrigerator. The animals were weighed daily, and had unlimited access to water. The design of the experiment was similar to that used in previous work(1), and involved the use of 12 trios of rats, each trio (littermates) being arranged thus: Rat 1 received the experimental diet *ad lib.* with all vitamin supplements; 2 received the diet *ad lib.* with all

vitamin supplements except pyridoxine; No. 3 was paired-weighed with No. 2 but was given pyridoxine; *i.e.* it received the amount of diet required to keep it equal in weight to No. 2. After 55 days the animals were anesthetized with ether, bled by severance of neck vessels, and the livers, kidneys and hearts dissected out; the hearts were sliced open and any blood removed from the chambers. The organs were washed in 0.9% NaCl solution, gently dried between sheets of filter paper, and the wet weights determined on a Roller-Smith Precision balance. The organs were placed on watch glasses, dried at 58°-60°C for 7 days, and the dry weights then determined.

Results. The results are summarized in Table I. The wet and dry weights of the hearts and kidneys of the pyridoxine-deficient animals were significantly heavier (g/100 g bodyweight) than those of the *ad lib.* and paired-weighed controls. The wet and dry weights of the livers of the pyridoxine-deficient rats, although significantly heavier than those of the paired-weighed controls, did not differ significantly from those of the *ad lib.* controls. Thus it would appear that the increase in weight of these organs is a true hypertrophy and not the result of an increased tissue fluid content in them. Increased fat content was not a factor as histological examination of frozen sections of tissues obtained in earlier experiments(1,2) did not reveal the amount of fat that would have been expected if the increase in organ weight had been caused by increased fat; further, when the dried hearts and kidneys referred to in Table I were defatted, those that belonged to pyridoxine-deficient rats were still heavier than those of the *ad lib.* and paired-weighed controls.

The results obtained (Table I) also show that protracted feeding of the pyridoxine-deficient diet is not necessary to induce hypertrophy of the heart, kidneys and liver as

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TABLE I. Wet and Dry Organ Weights (g/100 g Body Weight) of *Ad lib.* Fed, Paired-Weighed, and Pyridoxine-Deficient Rats.

Organ	<i>Ad lib.</i> control (11 animals*)	Paired-weighted control (12 animals)	Pyridoxine-deficient (12 animals)
Body wt	310.9 ± 30.6	124.7 ± 9.6	130.5 ± 10.1
Liver, wet	4.30 ± .66	3.34 ± .27	4.24 ± .45
dry	1.38 ± .08	1.04 ± .09	1.38 ± .18
Kidney, wet	.689 ± .045	.834 ± .069	1.159 ± .138
dry	.166 ± .008	.194 ± .014	.261 ± .030
Dried and defatted	.147 ± .007	.174 ± .012	.234 ± .026
Heart, wet	.307 ± .022	.344 ± .022	.435 ± .068
dry	.069 ± .005	.079 ± .005	.100 ± .017
Dried and defatted	.064 ± .004	.073 ± .005	.092 ± .015

* Originally 12 animals, but one was accidentally killed before experiment ended.

the duration of the experiment was only 55 days. Agnew(1) had previously reported the occurrence of marked cardiac and renal hypertrophy in rats that had been on the deficient diet for periods ranging from 79 to 175 days; and Olsen and Martindale(3) had obtained similar results after 266 days. These latter workers also reported the occurrence of liver hypertrophy in their deficient rats, but in the present experiments the weights of the livers of the pyridoxine-deficient rats, although significantly heavier than those of paired-weighted controls, did not differ significantly from those of *ad lib.* controls.

Discussion. The reason for the significant increase in the weight of such important organs as the heart, kidneys and liver in the pyridoxine-deficient rat is as yet unknown. It is possible that the increased heart weight is secondary to the mild hypertension that has been reported(5) in pyridoxine-deficient rats; also, it may be that the increased kidney weight is the result of the increased excretion of urea that has been described(6) in pyridoxine-deficient rats. Whatever the explanation, pyridoxine deficiency in the rat appears to be another method for inducing cardiac, renal and hepatic hypertrophy, and one that may prove of value in future studies of organ growth and function.

Summary. The wet and dry weights of the heart and kidneys of pyridoxine-deficient rats were significantly heavier (g/100 g body-weight) than those of *ad lib.* and paired-weighted littermate controls. The wet and dry weights of the livers of pyridoxine-deficient rats, although significantly heavier than those of paired-weighted controls, did not differ significantly from those of *ad lib.* controls. The increased weight of these organs is considered to be a true hypertrophy, and was observed after a period of 55 days. It is felt that this relatively rapid method of inducing hypertrophy of these important organs may prove a useful tool in studies of organ growth and function.

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