The Effect of Nutritional Deficiency on the Pitressin Inactivating Ability of the Liver*

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THE essential departure from the normal organization of the body water in undernutrition expresses itself by a relative increase in space occupied by the extracellular fluid.[1,2] Visible edema—rare in animals, but common in man suffering from lack of either protein or thiamine—is only one aspect of this change. In our experiments we could show that hormonal factors are—at least partially—responsible for the water retention in deficient animals.[3-5]

In the first series of our experiments, a water load amounting to 8 per cent of the body weight was imposed on rats deficient in either protein or thiamine. Thirty minutes after the administration of the water load, urine collection was begun and continued for three hours. Table I shows that the deficient animals exhibited a delayed diuretic response, an effect which appears to be specific for the lack of the above mentioned nutrients, since caloric deficiency in itself was found to exert no influence. When 50 mU of Pitressin® were injected subcutaneously at the beginning of the urine collection, a more powerful and longer lasting effect was observed on animals deficient in protein or thiamine than on controls receiving a normal diet either *ad libitum* or in restricted amounts. Intrahepatic injection of 50 mU of Pitressin, while having a smaller antidiuretic effect than subcutaneous injection in rats kept on a control diet, caused in the deficient animals a strong antidiuresis, in its extent similar to that observed upon subcutaneous administration.

In a second experiment, 250 mU Pitressin were injected subcutaneously into normal and thiamine-deficient rats. Urine was collected

TABLE I

Excretion of Water by Protein- and Thiamine-Deficient Rats

Diet	No. of tests	Pitressin	Means and standard errors 1 hr	2 hr	3 hr
			per cent	*per cent*	*per cent*
Normal	47	—	39 ± 1.6	67 ± 1.9	76 ± 2.4
Protein-defic.	9	—	19 ± 3.1	55 ± 3.9	82 ± 4.3
Thiamine-defic.	12	—	8 ± 2.0	32 ± 3.5	49 ± 5.0
Calorie-defic.	12	—	34 ± 3.6	59 ± 5.6	78 ± 5.2
Normal	46	Subcutan.	5 ± 0.6	13 ± 1.4	38 ± 2.3
Protein-defic.	9	"	3 ± 1.2	7 ± 3.6	22 ± 4.3
Thiamine-defic.	12	"	5 ± 1.1	10 ± 1.6	12 ± 1.6
Calorie.-defic.	22	"	5 ± 0.9	11 ± 1.4	38 ± 4.2
Normal	44	Intrahep.	6 ± 1.0	25 ± 1.3	55 ± 2.7
Protein-defic.	9	"	2 ± 1.9	7 ± 3.0	27 ± 6.3
Thiamine-defic.	12	"	5 ± 1.6	7 ± 1.9	17 ± 2.0
Calorie-defic.	12	"	8 ± 2.0	26 ± 3.0	53 ± 4.3

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during four hours, filtered and injected into normal, hydrated rats (Table II). It was found that the rats given injections of urine of the thiamine-deficient animals showed a greater antidiuresis than those treated with the urine of the control groups. It follows that thiamine-deficient rats receiving injections of Pitressin inactivate a smaller percentage and excrete a larger amount of the hormone than do animals maintained on a qualitatively full diet, even if it is offered in limited quantities.

The impaired ability of liver tissue from thiamine-deficient rats to inactivate Pitressin was also demonstrated by the following *in vitro* experiments. Aqueous extracts of liver were incubated with Pitressin and subcutaneously injected into hydrated animals (Table III). As can be seen, rats injected with Pitressin that had been incubated with liver extract from thiamine-deficient animals exhibited a much stronger antidiuresis than those treated with Pitressin after incubation with liver extract from control groups. A similar effect was observed with livers of choline-deficient rats—a condition in which water retention has already been described.[6]

It is assumed that this failure to inactivate Pitressin may be one of the causes of the water retention in protein, thiamine, and choline deficiency.

A markedly delayed response to a water load was also observed in pyridoxine and pantothenic acid deficiences, without, however, impairing effect on the ability of the liver to destroy Pitressin (Table IV). Since animals deficient in either pyridoxine or pantothenic acid increase their urine excretion after subcutaneous injection of cortisone (3 mg per rat, 90 min before water load) or corticotropin (ACTH) (4 mg per rat, 90 min before water load), in contrast to well-fed controls, it is concluded that the water retention observed in the former group is due to an inadequate stimulation of the adrenals by the adrenocorticotropic hormone.

TABLE II

Urinary Excretion of Injected Antidiuretic Hormone in Thiamine-Deficient Rats; Excretion of a Water Load by Normal Rats after Injection of Urine from Pitressin-Treated Rats

Diet of experimental rats	No. of tests	Means and standard errors 1 hr	2 hr	3 hr
		per cent	*per cent*	*per cent*
Normal	36	18 ± 2.2	45 ± 2.1	65 ± 2.0
Thiamine-defic.	12	3 ± 1.0	28 ± 3.2	60 ± 2.6
Calorie-defic.	12	18 ± 2.5	51 ± 3.5	67 ± 3.9

TABLE III

In Vitro Inactivation of Pitressin by Liver of Thiamine- and Choline-deficient Rats. Excretion of a Water Load by Normal Rats Following Injection of Pitressin Previously Incubated with Liver Extract

Diet of experimental rats	No. of tests	Means and standard errors 1 hr	2 hr	3 hr
		per cent	*per cent*	*per cent*
Normal	62	7 ± 0.9	37 ± 1.1	62 ± 2.4
Thiamine-defic.	42	6 ± 1.1	25 ± 2.3	48 ± 2.8
Calorie-defic.	24	10 ± 1.9	43 ± 3.0	65 ± 2.1
Choline-defic.	28	6 ± 1.2	29 ± 2.0	49 ± 2.5

TABLE IV

Excretion of Water by Pyridoxine and Pantothenic Acid-deficient Rats

Diet	No. of tests	Treatment	Means and standard errors 1 hr	2 hr	3 hr.
			per cent	*per cent*	*per cent*
Normal	40	—	48 ± 2.0	67 ± 2.0	75 ± 1.9
Pyridoxine-defic.	44	—	24 ± 3.2	41 ± 3.2	46 ± 3.8
Pantothen. acid-defic.	30	—	33 ± 3.1	49 ± 2.7	56 ± 2.9
Normal	18	Cortisone	51 ± 1.9	67 ± 1.8	72 ± 1.9
Pyridoxine-defic.	17	"	63 ± 2.4	71 ± 2.0	73 ± 1.8
Pantothen. acid-defic.	14	"	53 ± 3.9	63 ± 4.1	66 ± 3.8
Normal	12	ACTH	48 ± 3.0	73 ± 3.3	79 ± 3.5
Pyridoxine-defic.	13	"	39 ± 4.4	55 ± 4.1	60 ± 3.7
Pantothen. acid-defic.	13	"	45 ± 4.5	67 ± 4.0	71 ± 4.0

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