Adrenal Insufficiency in Dogs with Normal Serum Na and Cl.* (19774)

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During the past few years the writers have studied an extensive series of adrenalectomized dogs through cycles of insufficiency and recovery while they were receiving various kinds of replacement therapy and fed a diet low in Na and Cl. During this study an opportunity arose to observe 5 animals which exhibited mild to very severe symptoms of adrenal insufficiency despite the fact their serum Na and Cl levels were well within the normal range. One other dog was also studied in which the serum Na and Cl remained unchanged from normal until a few hours before collapse, when, following the sudden onset of a moderate diuresis, the electrolytes decreased to low levels and severe symptoms appeared. Attention has been called to the ease with which adrenalectomized dogs can be maintained for long intervals free from signs and symptoms of insufficiency, but with serum Na and Cl concentrations characteristic of animals prostrate from adrenal insufficiency(1-3). The situation in which the animal may display marked symptoms and yet exhibit a normal serum electrolyte pattern is, insofar as the dog is concerned, an uncommon occurrence. Nicholson and Soffer(4) observed several such cases and attributed absence of decline in serum electrolytes to hemoconcentration and dehydration. Thus according to these authors "when hemoconcentration has become so marked that insufficient water is available for the excretion of electrolytes, the sodium and chloride of the plasma may be increased, and this fact may explain the apparent paradox occasionally observed of typical suprarenal insufficiency with high plasma sodium and chloride values."

Although the adrenalectomized dog rarely displays insufficiency symptoms with normal serum Na and Cl concentrations, certain other animal species commonly do so. For example, it has been reported that the opossum and marmot show increased plasma concentrations of Na and Cl even when the animals are practically moribund from adrenal insufficiency (5,6). This finding has been confirmed for the opossum(7). Hartman *et al.*(8) found that extirpation of the interrenal gland of elasmobranchs failed to induce changes in the serum Na and Cl. This author, together with Spoor(9), has described the separation of a Na retaining factor from adrenal cortical extracts which elevates the plasma Na of adrenalectomized animals but does not prevent the onset of insufficiency symptoms. The chemical nature of this factor remains undetermined. Finally, it seems not improbable that the Addisonian patient may occasionally succumb without exhibiting undue distortion of the plasma electrolyte pattern(10).

Results. Dogs 1-5, listed in Table I, although showing symptoms of insufficiency, nevertheless had normal or low normal serum Na and Cl. These animals had received various types of therapy while maintained on a low sodium and potassium diet and had been employed in bioassay studies involving use of various esters of desoxycorticosterone or concentrates of beef adrenal extract. The symptoms varied from mild (dogs 4-5) to severe (dogs 1-3, Table I). The dogs refused all food, showed marked depression and lassitude, were spastic and showed signs of weakness. The essential data regarding weight changes, arterial pressure and serum electrolytes are summarized in Table I. Only the control and terminal figures are tabulated. The methods used for all determinations and the diet employed have been referred to elsewhere(11).

Adrenalectomized dogs exhibiting insufficiency and with normal serum Na and Cl arouse suspicion that hypoglycemia might be present and thus account for some of the

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TABLE I. Adrenal Insufficiency in Dogs Exhibiting Minor Changes in Serum Na and Cl.

Dog No.			Body wt, kg	B.P., mm Hg	Blood urea N, mg %	Hb, g %	Blood glucose, mg %	Serum Na, mEq/l	Serum Cl, mEq/l	Serum K, mEq/l	Remarks
1	*		9.6	113	9	10.1	78.5	139	112.6	4.5	§
	†		8.3	68	‡	‡	‡	137	109.6	5.4	Spastic, lethargic, weak, refused rations
2	*		18.8	118	9.7	9.7	76	141.4	115	6.1	§
	†		18.1	52	120	21.4	85	144	114.5	10.2	Severe symptoms, spastic, weak, refused rations.
3	*		10.1	100	15	13.4	82	139.3	114.4	6	§
	†		9.2	52	48	17.5	67	136.4	110.2	8.3	Severe symptoms, spastic, weak, refused rations
4	*		16.1	112	14	15	75	145.4	118	4	§
	†		17	78	57.6	17.8	76	148	116	—	Refused rations, lethargic, weakness in hind limbs
5	*		17.5	130	13.5	15	70	148	112	4.2	§
	†		17.9	78	59.2	19.5	76.5	147	120	5.7	Fall in arterial pressure, marked hemoconcentration, rise in blood urea N
6	*		17.7	96	15.6	10.9	78.5	140	111.8	4.2	§
		11 a.m.	17.3	93	23	12	67.5	140	109.4	5.6	No symptoms
	†	11 p.m.	17.3	59	44.5	12.6	67.5	130.6	98.4	5.4	Refused rations, weakness in hind limbs, spastic

* Control. † Insufficiency. ‡ Not determined. § Normal.

symptoms. However, it seems unlikely that the blood glucose changes which occurred in the dogs (Table I) were of sufficient magnitude to be responsible for the observed symptoms of insufficiency. The changes were not marked and are above the hypoglycemic range. While it is true, as Thorn *et al.*(12) have pointed out, that the Addisonian patient and the adrenalectomized dog may show hypoglycemic symptoms at higher levels of blood glucose than does the patient or dog with intact glands, nevertheless the blood glucose figures for the animals listed are above the critical level even for adrenalectomized dogs.

Three of the animals listed in Table I (dogs 2, 3, and 5) showed severe hemoconcentration as indicated by the striking increase in hemoglobin concentration. The hemoglobin of dog 2 rose approximately 12 g % and the serum K was elevated to 10.2 mEq/1. The blood urea nitrogen registered 120 mg %. The hemoglobin concentration of dog 3 increased 4.1 g % and that of dog 5 by 4.5 g %. The evident dehydration and probable reduction in renal function could well account for the lack of the usual sodium and chloride diuresis in these animals and hence the maintenance of normal values for these ions in the serum. Dog 2 showed an extreme hyperkaliemia which was of sufficient degree to induce collapse owing to cardiac failure. We have repeatedly observed that serum K values in adrenalectomized dogs in excess of 8 mEq/1 may produce serious cardiac disturbances culminating in prostration of the animal. Thus, it seems evident that even in the dog, a species in which adrenal insufficiency is normally characterized by a sodium and chloride diuresis and drastic alterations in the serum concentrations of these electrolytes, it is possible in rare cases to have the onset of mild to severe symptoms with little or no apparent deviation from normal of the serum Na and Cl. Moderate renal retention of K was evident in all cases and was especially prominent in 2 animals (Nos. 2 and 3, Table I).

Dog 6 is an interesting case since the Na and Cl changes given in Table I occurred within a 12-hour period. The animal had been maintained for 3 days on 0.25 mg of the water soluble glucoside of desoxycorticosterone, and during this interval the serum electrolytes had shown no deviation from the normal pattern. At 11 A.M. on the day he developed symptoms of insufficiency, the blood

pressure and blood constituents were normal and the dog appeared free from symptoms. However, by 11 P.M. marked symptoms had appeared: he had refused all food, was depressed, spastic and weak in the hind limbs. The activity and vigor which were so pronounced 12 hours earlier had disappeared. Blood samples were taken at this time and the results of the analyses are given in Table I. During the 12-hour interval (11 A.M. to 11 P.M.), the serum Na and Cl declined to 130.6 and 98.4 mEq/1, respectively. The sharp drop in serum electrolytes was accompanied by a moderate diuresis after which symptoms appeared.

Summary. A group of 5 adrenalectomized dogs of a large series studied, developed typical signs and symptoms of adrenal insufficiency in the absence of noteworthy alterations in the serum Na and Cl values. Hypoglycemia was not present in any of the animals but during insufficiency dehydration and hemoconcentration were evident in 3 of them as indicated by marked increases in hemoglobin. In view of the inspissation of the blood in these dogs it seemed probable that sufficient water was not available for elimination of the electrolytes. This is the interpretation originally given by Nicholson and Soffer(4) to account for the death of their salt-injected dogs. However, a comparison of the hemoglobin concentrations of 8 adrenalectomized dogs exhibiting insufficiency with hyponatriemia (avg. 128 mEq/1) with the hemoglobin increases shown by the 5 animals discussed here, reveals that the hemoconcentration as gauged by hemoglobin changes was not more severe in the latter group. It is unfortunate that plasma volume determinations were not made. However, the drastic decline in arterial pressure and evident weakness of the animals indicated that defective functioning of the vasomotor system was probably the immediate cause of the symptoms. The hyperkaliemia of one dog was of sufficient magnitude to induce cardiac symptoms. The retention of a normal serum electrolyte pattern during insufficiency in these few exceptional dogs is reminiscent of the condition normally occurring in adrenal insufficiency in such animals as the opossum, marmot hamster (13) and certain elasmobranchs.

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