

SERUM SODIUM, POTASSIUM AND CHLORIDE AFTER SUPRARENALECTOMY IN CATS WITH DIABETES INSIPIDUS

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Many investigators (1-11) have shown that changes occur in the concentration of serum electrolytes during suprarenal insufficiency. There is evidence that these changes are due to shifts of such ions within the body fluids, and some workers (2, 3) have suggested that the kidney may be one of the sites of action of the suprarenal cortical hormone regulating serum electrolytes. Animals with diabetes insipidus show a relatively unrestrained loss of fluids *via* the kidney due to lack of the antidiuretic hormone of the posterior lobe of the pituitary. It has been maintained by certain clinical investigators that patients with this disease also show disturbances in the metabolism and excretion of sodium and chloride, and it is well known that administration of posterior pituitary substance promotes the excretion of salt. It is, therefore, of interest to observe the changes in serum sodium, potassium and chloride following removal of the suprarenals in cats with diabetes insipidus.

Methods

Adult cats were used, without regard to sex. The general feeding and care of the animals have been described elsewhere (12). Diabetes insipidus was produced by interruption of the supraoptico-hypophyseal tract, using the Horsley-Clarke stereotaxic instrument; the lesions so produced involve a portion of the hypothalamus and result in atrophy of the pars nervosa of the pituitary (12). Suprarenals were removed in two stages, using a dorsal approach. It was early found that the survival time following suprarenalectomy was considerably shorter in the cats with diabetes insipidus than in control animals; therefore, some of the animals were maintained for a short time following the second suprarenal operation

with active extracts of the suprarenal cortex¹ to insure complete recovery from the effects of the operation itself.

Blood for analysis was obtained from the unanesthetized animal by puncture of the left ventricle. Chlorides were determined by the method of Wilson and Ball (16), potassium by Shohl and Bennett's procedure (17) and sodium by the Butler and Tuthill method (18). The control blood specimens (called insufficiency none in Table I) were usually obtained just before the removal of the second suprarenal; those called insufficiency pronounced in Table I were obtained within a few hours of death, when the animal was obviously *in extremis*.

RESULTS

The results are summarized in Table I. There are two groups of controls: one in which the animals were left intact except for suprarenalectomy (called normal controls in Table I), and the other group (two animals) which received a hypothalamic lesion, but did not develop the polyuria and polydipsia of diabetes insipidus. Histological sections show the supraoptico-hypophyseal tracts and posterior lobes of the latter two cats to be normal, while in those cats which developed polyuria, the tracts are interrupted and the posterior lobes atrophic. The daily urine output of our normal cats is about 100 to 125 cc.; the polyuric cats excrete from 300 to 600 cc. a day on the average, except DI-23, which averaged only about 200 cc. The urine volume in both the control and the polyuric cats was somewhat reduced following the removal of the second suprarenal.

Although the data on chloride are more complete than on sodium or potassium, Table I clearly shows that the only change in serum electrolytes consistently shown in all groups of animals following suprarenal removal is an increase in the concentration of serum potassium. The average serum potassium value found for all cats before bilateral suprarenalectomy was 24.8 mg. per cent. Control cats after the development of symptoms of suprarenal insufficiency showed an average serum potassium figure of 36.0 while the polyuric cats in suprarenal insufficiency have a mean serum potassium of 34.0.

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TABLE I

Cat No.	Date	Gross symptoms of suprarenal insufficiency	Serum electrolytes			Remarks
			Potas- sium	Sodium	Chloride	
			<i>mg. per cent</i>	<i>mg. per cent</i>	<i>mg. per cent</i>	
NA	June 24	None	22.9	—	—	Normal control
NA-2	" 21	"	27.9	350	424	" "
NA-1	" 8	"	—	—	419	" "
	" 21	Moderate	34.7	280	346	
	" 26	Slight (on inadequate extract)	26.2	297	352	
	" 30	Pronounced	30.5	273	344	
NA-3	Sept. 8	None	26.4	363	417	Normal control
	" 16	Pronounced	34.4	303	390	
DI-29	Aug. 16	None	24.7	338	441	Control cat with hypothalamic lesion, but no polyuria
	" 27	Pronounced	39.3	240	381	
DI-31	" 17	None	22.9	349	415	" "
	" 21	Moderate	26.1	313	387	
	" 23	Pronounced	41.0	300	368	
DI-11	May 6	None	—	—	404	Marked polyuria
DI-7	" 6	"	—	—	409	" "
	" 9	Pronounced	—	—	442	
DI-8	" 28	None	—	—	406	Marked polyuria
	" 31	Slight	—	—	403	
	June 1	Pronounced	—	—	409	
DI-14	" 3	None	—	—	414	Marked polyuria; cortin June 3 to 11 in gradually reduced doses
	" 9	"	—	—	415	
	" 13	Pronounced	34.4	328	423	
DI-26	Aug. 11	None	22.9	340	427	Marked polyuria; cortin Aug. 11 to 15 in gradually reduced doses
	" 18	Pronounced	34.4	337	397	
DI-32	Sept. 8	None	27.6	334	419	Marked polyuria; cortin Sept. 8 to 12
	" 15	Pronounced	38.5	316	417	
DI-23	Aug. 10	None	23.4	325	423	Slight polyuria; cortin Aug. 8 to 16
	" 20	Moderate	28.7	310	400	

Both groups of control cats present the typical picture of suprarenal insufficiency, the increased serum potassium being accompanied by a decrease in serum sodium and chloride, but in the polyuric animals these changes are slight or absent. The average serum sodium value for all animals before suprarenalectomy is 343 mg. per cent; during suprarenal insufficiency, the average figures are 279 mg. per cent for the control cats and 323 mg. per cent for the polyuric animals. For the three control cats for which the sodium figures both before and after suprarenalectomy are available, the change in serum sodium level ranges from -49 to -98 mg. per cent, while in the polyuric animals the range is from -3 to -18 mg. per cent. The average serum chloride value before suprarenalectomy is 418 mg. per cent, and during suprarenal insufficiency the average for the control animals is 366 mg. per cent and for the polyuric animals 415 mg. per cent. The change in chloride levels during suprarenal insufficiency as compared to the concentration before suprarenal removal ranges from -27 to -67 mg. per cent for the control animals, and from -30 to $+33$ for the polyuric cats. From these figures, it is evident that the behavior of serum electrolytes following bilateral suprarenalectomy is markedly different in cats with diabetes insipidus than in the control animals.

DISCUSSION

Since the work of Loeb (1, 2) and Harrop (3), the view has been widely held that the vital hormone of the suprarenal cortex is primarily a regulatory mechanism for sodium. The beneficial effect of sodium therapy in suprarenal insufficiency (1-6) supports this view. Much recent work, however, indicates that such an explanation for suprarenal insufficiency may be inadequate. Truszkowski and Zwemer (7) suggest that the primary defect may be in potassium metabolism. Swingle and coworkers have shown (8, 9) that in dogs on a sodium- and chloride-free diet, withdrawal of cortical extract leads to symptoms of suprarenal insufficiency without significant change in serum sodium or chloride. Swingle (9) considered the changes in serum potassium in these animals to be insignificant, but his data show an increase of about the same order of magnitude which we find. In suprarenalectomized-nephrectomized rats, Ingle, Nilson

and Kendall (10) found the concentrations of sodium and chloride in the serum normal, but the potassium increased. Nilson (11) reported that acute symptoms of suprarenal insufficiency may be produced in suprarenalectomized dogs either by a low intake of sodium and chloride or by a high intake of potassium; in such animals, changes in blood urea, sugar, sodium, chloride and hematocrit value may be found, but only an increased potassium content was found to be characteristic. In the opossum and marmot, suprarenal insufficiency is not accompanied by lowered values for sodium or chloride, but rather by an increase, according to Silvette and Britton (13, 14); these authors have not reported on potassium changes.

The survival time following suprarenalectomy is shorter for the polyuric than for the non-polyuric cats. It might therefore be argued that the usual decrease in serum sodium and chloride does not appear in the animals with diabetes insipidus simply because there has not been time enough for such a change. To meet such possible objection, we have prolonged the survival time of several of the polyuric animals to a week to 10 days with extract, and in two of the animals (DI-14 and DI-26) the extract dosage was gradually tapered off so that the suprarenal insufficiency would develop gradually, as it does in non-polyuric animals. Furthermore, cat DI-23 survived 4 days after complete withdrawal of extract, and cat DI-8 survived the operation 4 days although no extract was administered. In all cases, the external symptoms were the same in the polyuric suprarenalectomized animals as in those with uncomplicated suprarenal insufficiency; there was lack of appetite, loss of skeletal muscle tone, ataxia (especially in the hind limbs), gradual loss of interest in the surroundings, and in the terminal stages occasional mild convulsions. At autopsy, hyperemic or hemorrhagic areas were often found in the stomach and intestinal wall. The only difference noted between the two groups of animals was the rapidity with which the symptoms developed; the onset of suprarenal insufficiency was unquestionably hastened by the presence of diabetes insipidus.

Our data indicate that an increase in concentration of potassium in the serum is a more consistent characteristic of suprarenal insufficiency than a decrease of sodium, and that in the absence of normal functioning of the posterior lobe of the pituitary the usual

decrease in serum sodium and chloride does not occur. They do not, however, show that a disturbance in potassium metabolism or distribution is the sole or the primary disturbance in suprarenal insufficiency. MacKay, Bergman and MacKay (15) have recently shown that nephrectomized rats survive much longer than nephrectomized-suprarenalectomized rats, although the potassium content of the serum reaches a much higher level in the former than it attains in the terminal stages of the latter.

Our results suggest the possibility of some sort of interrelationship between the suprarenal cortex and the posterior lobe of the pituitary, so far as salt metabolism or distribution is concerned. Karlson and Norberg (19) and Debré, Marie, Nachmansohn and Bernard (20) have reported tests performed on patients with diabetes insipidus which indicate that in this condition there is diminished ability to concentrate sodium chloride in the urine. When unusual amounts of sodium chloride were added to the diet, the ability to concentrate the salt was improved after administration of pituitrin. The results of Smith and MacKay (21) are somewhat at variance with these. The latter report that while pituitrin increased the sodium and chloride output of normal persons so that the balance became negative, equivalent doses given to a subject with diabetes insipidus caused no increase in sodium chloride excretion nor did the sodium balance become negative; salt feeding was not attempted in these experiments, however. The observations of the two groups of workers first mentioned might lead to the suggestion that serum sodium and chloride remained normal in our animals because the kidneys of the cats with diabetes insipidus failed to respond to lack of suprarenal cortical hormone by increased clearance of these substances. Silvette (22) has found that pituitrin facilitates salt excretion in suprarenalectomized opossums receiving extra salt in the diet. Our animals, however, did not receive unusual amounts of salt, and appear, under ordinary circumstances, to run quite constant chloride balances. It appears that the suprarenal cortex and the posterior lobe interact in such a way that serum sodium and chloride remain unaffected in the absence of both principles. However, as we have only two control animals with hypothalamic lesions without diabetes insipidus, the possibility is not excluded that the effect which we observe may be due to the

hypothalamic lesion itself rather than to the diabetes insipidus. Further work along these lines is indicated. Nevertheless, it is clear that the level of sodium and chloride in the serum is not necessarily a measure of suprarenal insufficiency.

SUMMARY

The external symptoms of suprarenal insufficiency in cats with diabetes insipidus are the same as in those animals with only the suprarenals removed, except that the symptoms develop more rapidly in the former. The serum electrolyte changes, however, are different; there is no consistent or marked decrease in the concentration of sodium or chloride following suprarenalectomy in cats with diabetes insipidus, but there is the usual increase in the concentration of potassium. It is suggested that this indicates that changes in sodium are less characteristic of suprarenal insufficiency than are disturbances of potassium metabolism or distribution. A possible inter-relationship between the suprarenal cortex and the posterior lobe of the pituitary as salt-regulating mechanisms is discussed.

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