SODIUM AND CHLORIDE RETENTION IN ADDISON'S DISEASE TREATED WITH DESOXYCORTICOSTERONE ACETATE

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The new synthetic adrenal cortical hormone, desoxycorticosterone acetate, promises to be of great assistance in the clinical management of Addison's disease. It was produced by Reichstein[1] and is made from stigmasterol. Its clinical value has not yet been established although the investigation of it is progressing in various parts of this country and abroad. Levy Simpson[2] reported its use over a short period in two cases of Addison's disease with encouraging although not conclusive results.

At present, we do not feel justified in attempting to draw conclusions regarding its value in the cases of Addison's disease we have treated. Some observations presented here indicate that the material causes a rather marked diminution in excretion of sodium and chloride. In this respect, it duplicates the metabolic effect which has been proved for adrenal cortical extract[3].

It should be noted that other steroids are known to produce a similar result. For example, Kenyon[4] has shown that urinary sodium and chlorides are retained in the body in cases of testicular deficiency treated with testosterone propionate and our own observations in one case confirm this. The fact that corticosterone causes sodium and chloride retention is therefore not to be considered as[3] evidence that it will duplicate other effects of cortical extracts.

The material has been tested in the following manner on two patients who had clinical Addison's disease. Both were subjected to the salt deprivation test described by Cutler, Power, and Wilder[5]. This test may be briefly described as follows: A diet is supplied which is calculated to yield a daily intake of 0.95 gm. of chlorides, 0.59 gm. of sodium, and 4.1 gm. of potassium. On the evening of the first and the morning of the second day, additional potassium citrate is given in the amount of 0.92 gm. per kilogram of body weight. Free drinking of water is encouraged on the first day. On the second day 40 cc. per kilogram are given and on the third, 20 cc. per kilogram are given before 11 a. m.

The urine is collected in three specimens, two during 12 hour periods and one in a 4 hour period. The first specimen is from 8 a. m. to 8 p. m. of the second day, the second from 8 p. m. the second day to 8 a. m. of the third day, and the last specimen is from 8 a. m. to 12 noon of the third day. Blood sodium and potassium levels are estimated, fasting the second day of the test and at 10 a. m. on the morning of the third day.

It is unnecessary to describe the results of the test in detail here. It is sufficient to say that the most striking changes are observed in the sodium and chloride excretion on the morning of the third day in cases of adrenal deficiency. The results are shown to greatest advantage as milligrams per 100 cc. of urine, and the chloride excretion shows a wider deviation from normal than the sodium. The potassium excretion is not changed in any way to make it of clinical value.

In seven cases of Addison's disease in Cutler's report, the sodium excretion on the third day of the test varied from 165 to 282 mg. per 100 cc. while in 28 control cases the excretion was between 6 and 85 mg. per 100 cc. at the same period. The chloride excretion during this period in the cases of Addison's disease was 229 to 356 mg. per 100 cc. while in those not having Addison's disease, it varied between 17 and 141 mg. per 100 cc.

The first of our two cases is that of a woman, 35 years of age, who had symptoms typical of Addison's disease. She had no abnormal pigmentation but she did have calcification of the right adrenal. Previously she had shown a typical clinical response to eschatin* and sodium chloride therapy.

TABLE 1

	Blood (*mg. per 100 cc.*)			*Urine* (*mg. per 100 cc.*)			
Date	*Sod.*	*Pot.*	*Chlor.*	*Sod.*	*Pot.*	*Chlor.*	*Remarks*
Nov. 29	371″	19″		114	137	220	Test 12 hrs.
30	371′	17′	544′	22	86	180	Test 4 hrs.
Dec. 12							C.S. 10 mg.
13	352″	17″					C.S. 10 mg.
14				24	105	20	Test 12 hrs. C.S. 15 mg.
15	362′	17′		14	85	17	Test 4 hrs. C.S. 5 mg.

″—fasting
′—mid a.m.

Table 1 shows the results of a test similar in all respects to the one described above except that only the second twelve hour specimen of

* Eschatin is adrenal cortical extract, Parke, Davis & Co.

urine was examined in each test. She had had no eschatin or extra sodium chloride for more than one month.

It will be seen that the chloride excretion levels are within the range described above for Addison's disease but the urinary sodium is not.

Between the time of the first and the second test, the diet was calculated to contain between 0.8 and 1.9 grams of potassium daily and from 0.7 to 1.5 grams of sodium. No sodium chloride or adrenal extract was used in treatment during this period but a potassium tolerance test, using 3.9 grams of potassium citrate on December 5 and 5.4 grams on December 6, was used. She was also given 8 grams of potassium citrate daily on December 9, 10, and 11, which precipitated marked evidence of Addison's disease.

Desoxycorticosterone marked C.S. in the table was given as shown. The striking fall in sodium and chloride excretion is evident during the second test period.

The second case is that of a man, 38 years of age, who had typical Addison's disease of moderate severity with weakness, gastro-intestinal symptoms, arterial hypotension, and mucosal hyperpigmentation.

TABLE 2

	Blood (*mg. per 100 cc.*)			*Urine* (*mg. per 100 cc.*)			
Date	*Sod.*	*Pot.*	*Chlor.*	*Sod.*	*Pot.*	*Chlor.*	*Remarks*
Jan. 4	356″	18.9″		178	293	465	12 hr. test
4				113	372	400	12 hr. test
5	347′	16.7′	495′	55	272	425	4 hr. test
5	Injections begun at 1 p. m.						C.S. 10 mg.
6							C.S. 20 mg.
7	357″	22.9″	511″	34	259	120	C.S. 15 mg. 12 hr. test
7				23	228	75	12 hr. test
8	344′	19.1′		17	86	50	4 hr. test

″—fasting
′—mid a.m.

Table 2 indicates the results of the salt restriction test before and after the administration of desoxycorticosterone acetate.

Summary

In two cases of Addison's disease, administration of desoxycorticosterone acetate caused a striking fall in sodium and chloride excretion similar to that known to result from adrenal cortical extracts.

References

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