

## Effect of Adrenal Cortical Hormone on Renal Excretion of Electrolytes in Normal Subjects.

GEORGE W. THORN.\* (Introduced by G. A. Harrop.)  
(With the technical assistance of Irving Miller.)

*From the Chemical Division, Medical Clinic, Johns Hopkins University and Hospital.*

The effect of the adrenal cortical hormone on the renal excretion of electrolytes in normal human subjects has been described.<sup>1</sup> A marked alteration in the renal excretion of sodium and potassium was noted during a 5-hour period in which the subjects received adrenal cortical hormone intravenously; little or no effect was observed on the subsequent 24-hour excretion. Subcutaneous injections of hormone in a quantity sufficient to produce a change in the sodium and potassium balance of patients with Addison's disease did not affect the balance of electrolytes in normal subjects. It seemed probable that repeated injections of larger quantities of hormone might produce a significant alteration in the 24-hour renal excretion.

In the present study the effect of repeated intravenous injections of hormone† on the 24-hour renal excretion of 3 normal subjects has been observed.

Three subjects (F. D., female, 14 years of age; D. W., female, 29 years of age; G. W., male, 31 years of age) were provided with a diet of constant mineral composition and a constant fluid intake. The subjects had been maintained on a constant metabolic regime for other purposes during a period of 3 to 4 weeks immediately preceding this investigation.

The 24-hour urine collection was completed at 7 A. M. The subjects were injected intravenously with adrenal cortical hormone (500 dog units) at 8 A. M., 12 M., 6 P. M., and 11 P. M. An amount of normal saline solution equivalent to the sodium chloride content of the extract was injected during the 24-hour control period.

The preparation of the diet and the methods used for determining the sodium, chloride, phosphate and total nitrogen content

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\* Rockefeller Fellow in Medicine.

<sup>1</sup> Thorn, G. W., Garbutt, H. R., Hitchcock, F. A., and Hartman, F. A., *PROC. SOC. EXP. BIOL. AND MED.*, 1936, **35**, 247.

† Adrenal cortical hormone used in this study was generously supplied by Doctor David Klein of the Wilson Laboratories, Chicago, Illinois, and by Doctor George F. Cartland of the Upjohn Company, Kalamazoo, Michigan.

of both diet and urine specimens have been described.<sup>2</sup> Potassium determinations were made according to the method of Shohl and Bennett<sup>3</sup> on specimens ashed with thorium nitrate.<sup>4</sup> Calcium was analyzed according to the method of Tisdall and Kramer.<sup>5</sup> The method of Briggs<sup>6</sup> was used for the determination of magnesium. Total base was calculated as the sum of the individual cations, determined separately.

The injection of adrenal cortical hormone resulted in a marked decrease in the excretion of sodium in all subjects. Diminished urine volume and chloride excretion were associated with the reduced output of sodium. During the period of hormone administration the concentration of sodium in the urine was actually reduced; the concentration of chloride was not altered significantly. In contrast to the decreased sodium, chloride and urine output, the excretion of potassium was increased during the period of hormone injection. No consistent alteration occurred in the renal excretion of either calcium or magnesium.

The total base content of the urine decreased during the period of hormone injection. As a result of the diminished urine volume and the increase in the excretion of potassium, however, the concentration of total base was increased.

The excretion of inorganic phosphate was increased in 2 subjects during the period of hormone administration. Total nitrogen excretion was not altered significantly.

On the day following injection of the hormone, excretion of sodium was greatly increased in all subjects. Potassium excretion was reduced during the same period. This complete alteration in the sodium and potassium excretion on the day following hormone injection has been observed to occur in normal dogs injected with adrenal cortical hormone.<sup>7</sup> The change might be described as a "rebound" phenomenon.

The injection of hormone was accompanied by a slight gain in body weight (0.1 to 0.3 kg.) in all subjects. A comparable weight loss occurred on the day subsequent to hormone administration. The hormone had no demonstrable effect on the loss of insensible water†

<sup>2</sup> Thorn, G. W., Garbutt, H. R., Hitchcock, F. A., and Hartman, F. A., *Endocrinology*, 1937, **21**, 202, 213.

<sup>3</sup> Shohl, A. T., and Bennett, H. B., *J. Biol. Chem.*, 1928, **78**, 643.

<sup>4</sup> Strauss, M., *J. Biol. Chem.*, 1937, **118**, 331.

<sup>5</sup> Tisdall, F. F., and Kramer, B. J., *J. Biol. Chem.*, 1921, **48**, 1.

<sup>6</sup> Briggs, A. P., *J. Biol. Chem.*, 1924, **59**, 255.

<sup>7</sup> Harrop, G. A., and Thorn, G. W., *J. Exp. Med.*, 1937. (In press.)

† The loss of insensible water has been approximated by measuring the reduction in body weight which occurred during a 10-hour period (9 P.M. to 7 A.M.), correction being made for the weight of ingesta and excreta.

TABLE I.  
Effect of Repeated Intravenous Injections of Adrenal Cortical Hormone\* on the Twenty-four Hour Renal Excretion of Electrolytes in 3 Normal Subjects.

Subjects and Body wt., kg.	Urine vol., cc.	Na, m. eq.	K, m. eq.	Ca, m. eq.	Mg, m. eq.	Total base, m. eq.	Conc. of base, m. eq./liter	Chloride, m. eq.	Inorganic phosphate, mg.	Total N, gm.	Insensible water loss, gm./hour	Mean atmospheric temp., °F.	Relative humidity, % noon	Day	Injection
F. D.															
39.8	1720	94.6	56.6	4.7	2.4	158.3	92.0	110.0	679	6.79	30	34	47	1	Control Saline
39.9	1240	52.9	59.0	4.6	1.8	118.3	95.4	76.4	638	6.38	30	28	44	2	Hormone
39.6	1540	103.5	47.8	5.5	2.2	159.0	103.2	99.5	677	6.77	40	42	31	3	Control Saline
D. W.															
50.5	1360	109.0	48.8	1.8	0.9	160.5	118.0	108.0	588	7.46		46	59	1	Control Saline
50.7	1150	85.8	57.0	1.5	0.9	145.2	126.2	102.5	614	7.56		35	48	2	Hormone
50.6	1150	103.0	29.8	1.6	0.9	135.3	117.6	92.0	495	6.90		40	92	3	Control Saline
G. W.															
75.2	590	83.5	48.5	1.0	0.4	133.4	226.1	85.2	635	7.84		41	72	1	Control Saline
75.5	500	64.9	59.4	2.1	0.4	126.8	253.6	72.6	735	7.66		46	59	2	Hormone
75.2	700	122.0	31.6	2.5	0.5	156.6	223.7	112.0	592	8.06		35	48	3	Control Saline

The values expressed for urine volume, sodium, potassium, calcium, magnesium, chloride, phosphate, total base, and total nitrogen refer to the total 24-hour renal excretion.

\*Adrenal Cortical Hormone (500 dog units) was injected intravenously at 8 A.M., 12 M., 6 P.M., and 11 P.M.

in subject F. D. (Table I). The greater loss which was observed during the control period following hormone injection was within previously noted daily variation.

No untoward reaction has been observed during the intravenous injection of quantities of hormone as large as 30 cc. (3,000 dog units). In experimental studies on human subjects the hormone has been injected intravenously since the subcutaneous injection of large quantities of extract is painful. The transitory action of the hormone following its intravenous administration necessitates repeated injections throughout the 24 hours to produce a continued effect.

It is particularly significant that sodium was the only substance studied which was reduced both in total amount and concentration during the period of hormone injection. Chloride excretion was reduced but the concentration of chloride in the urine was not altered significantly. The injection of hormone was associated with an increased excretion of potassium. The increase in potassium excretion in the normal subjects was not nearly so great as that noted in patients with Addison's disease.<sup>2</sup> It is probable that in Addison's disease other factors such as loss of base from extra-cellular compartments, increased water content of cells, destruction of cells and nitrogen retention, may modify the action of the adrenal cortical hormone.<sup>8</sup>

*Summary.* Repeated intravenous injections of adrenal cortical hormone under controlled conditions in 3 normal subjects resulted in a decreased renal excretion of sodium, chloride and water. During the same period inorganic phosphate excretion was increased in 2 of the subjects. The excretion of calcium, magnesium and total nitrogen was not significantly affected. The retention of sodium, chloride and water was reflected in a slight increase in body weight in all of the subjects. Withdrawal of hormone was accompanied by a marked increase in the excretion of sodium, a reduction in potassium excretion, and a loss of weight. Repeated intravenous injections of adequate quantities of adrenal cortical hormone, therefore, appear to influence the 24-hour renal excretion of electrolytes in normal subjects. The nature of the change produced by the hormone is similar to that which has been noted in patients with Addison's disease but is quantitatively less marked. §

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<sup>8</sup> Harrop, G. A., Nicholson, W. M., Soffer, L. J., and Strauss, M., *Proc. Soc. Exp. Biol. and Med.*, 1935, **32**, 1312.

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