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Adrenal Ascorbic Acid Depletion by ACTH in Nephrectomized and in Subtotally Hepatectomized Rats.* (19487)

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The specificity of the adrenal ascorbic acid depletion test for pituitary adrenocorticotrophic hormone (ACTH) originally devised by Sayers *et al.*(1) is generally accepted, and the method has been widely used in assaying this hormone. In a recent communication it has been reported that when rat ACTH is injected into intact rats, large quantities are found in the kidneys(2). At the same time it cannot be detected in liver or urine(2). Absence from the liver could result from rapid hepatic inactivation. Its presence in the kidneys might reflect the importance of these organs in removing the hormone from general circulation. In view of the rapid disappearance of ACTH from the circulation(3) and the importance of the kidneys and liver in hormonal inactivation in general, it was felt that a study of the effect of these organs upon injected ACTH was warranted. This was tested by determining whether total nephrectomy or subtotal hepatectomy rendered a small quantity of ACTH, in itself sufficient to produce a moderate drop in adrenal ascorbic acid, more effective in this respect.

Materials and methods. Rats of the Holtzman strain were utilized in the present study. In a preliminary assay, designed to suggest a dosage meeting the requirements of the study to be made, a commercial ACTH powder (Armour, standardized against LA-1A) was obtained and from it 4 solutions in physiologic saline containing 4, 2, 1, and 0.5 μg/cc respectively were prepared. Thirteen female rats hypophysectomized 24 hours previously were divided into 4 groups. The left adrenal was removed in each animal under nembutal anesthesia, weighed on a Roller-Smith balance, placed in 6% trichloracetic acid, homogenized and the ascorbic acid determined by the method of Roe and Kuether(4). Each of the 4 concentrations of hormone was administered to a group of animals, each animal receiving 0.5 ml/100 g of the solution to be assayed by tail vein injection. One hour later the animals were sacrificed and the right adrenals re-

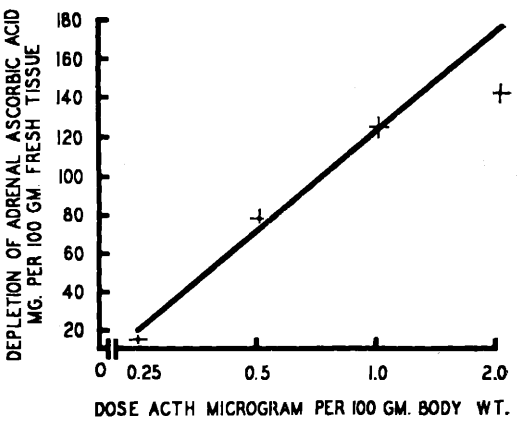

FIG. 1. Adrenal ascorbic acid depletion following intravenous ACTH.

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TABLE I. Effect of Nephrectomy and of Subtotal Hepatectomy on Adrenal Ascorbic Acid Depletion in Hypophysectomized Rats Following Intravenous ACTH.

Group	No. rats	Dose ACTH, μg/100 g	Ascorbic acid depletion*
Nephrectomized	17	.5	82 ± 11†
Subtotally hepatectomized	16	.5	57 ± 6
Control	22	.5	81 ± 8

* Conc. in left adrenal minus conc. in right.
† Mean ± stand. error.

moved, weighed and analyzed for ascorbic acid. The results, summarized graphically in Fig. 1, compared favorably with other results reported for similar preparations(5,6), and a dosage of 0.5 μg/100 g was selected as fulfilling the requirements of producing a moderate ascorbic acid depletion of 77 mg. Fifty-five female rats were hypophysectomized and divided into 3 groups 24 hours postoperatively. In Group 1, 17 animals were bilaterally nephrectomized and then each received 0.5 μg ACTH in 0.25 ml physiologic saline per 100 g body weight by tail-vein injection. In Group 2, 16 animals each received ACTH in the same amount and manner, following subtotal hepatectomy (70% removed) by the method of Waelsch and Selye(7). Group 3, consisting of 22 animals, received the same hormone treatment without further surgical intervention, and thus served as controls. In each case the left adrenal was removed prior to hormone injection, and in the case of hepatectomized or nephrectomized animals at the time of operation, and the right adrenal extirpated one hour after the injection.

Results and conclusions. The results are summarized in Table I. It is evident that the low dosage of hormone was not rendered more effective by removal of the kidneys. The adrenal ascorbic acid-depletion was identical in animals with and those without kidneys. The inference to be drawn is that the kidneys are not preferentially endowed with the property of inactivating ACTH or withdrawing it from the circulation. Similarly the removal of 70% of the liver was without influence on the ascorbic acid depletion produced by the dosage of ACTH employed. The depletion was actually slightly less in subtotally hepatectomized animals. Although the difference was not statistically significant it invites speculation as to whether total hepatectomy would have produced a more conclusive result.

These experiments, utilizing porcine ACTH, indicate that neither renal nor hepatic tissue is endowed with a prepotent ability to inactivate ACTH or remove it from the circulation.

Summary. Neither total nephrectomy nor subtotal hepatectomy have any effect on the moderate decline in adrenal ascorbic acid which results from the intravenous injection of 0.5 μg/100 g ACTH. It is concluded that ACTH is not preferentially inactivated or withdrawn from the circulation by either liver or kidneys.

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