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of the

ANNUAL MEETING

COUNCIL FOR HIGH BLOOD PRESSURE RESEARCH AMERICAN HEART ASSOCIATION

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Cleveland, Ohio
November 30-December 1, 1956

Volume V

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Lecturers

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Scientific Reports

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H. L. WHITE, M.D.—Department of Physiology, Washington University School of Medicine, St. Louis, Mo.

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G. E. WAKERLIN, M.D., Ph.D.—Department of Physiology, University of Illinois College of Medicine, Chicago, Ill.—*(Recent Advances in Hypertension)*

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EDWARD WEISS, M.D.—Department of Medicine, Temple University College of Medicine, Philadelphia, Pa.—*(The Emotional Problems of Coronary Occlusion)*

* The following reports are not included in this volume.

STUDIES ON THE HYPERTENSIVE ACTION OF ADRENAL STEROIDS

ABBIE I. KNOWLTON, M.D., *Assistant Professor of Medicine, Department of Medicine, Columbia University College of Physicians and Surgeons, and the Presbyterian Hospital, New York, N.Y.*

For a number of years Dr. Emily N. Loeb, Dr. Herbert C. Stoerk and myself have been interested in the relationship between the adrenal steroids and hypertension, and we have all shared in the work that I shall report. In earlier studies, Dr. Beatrice C. Seegal joined us, and along the way we have had considerable assistance from medical students who spent the elective period of their third year in our laboratory, and who made many valuable contributions to our work.

I shall not attempt to summarize the literature on the subject of the adrenals and hypertension, for you are perhaps better acquainted with this than I am; I shall confine myself to reviewing our own studies.

A basic question which remains in considering this problem is whether hypertension of *any* type can exist in the absence of the adrenal glands or its hormones. This question has been answered variously in the literature, but in our experience the answer is Yes, at least in the rat(1). Such a hypertensive animal is shown in Figure 1. This rat, representative of a series, developed a significant rise in tension after renal damage had been produced by the intravenous injection of an antirat kidney serum. In the upper portion of the chart, the weekly blood-pressure readings on this animal are plotted. In these and earlier studies, the plethysmographic apparatus, described by Williams, Harrison and Grollman(2), was used in making the determinations. After Friedman and Freed(3) described their method, involving the use of the microphonic manometer, we shifted to this technique, but did not curarize the animals. In the lower part of the chart is plotted the weight of the rat from week to week. The antikidney serum was injected 18 days after bilateral adrenalectomy and a high-sodium regimen was instituted, i.e., a diet made up of 1.7 per cent sodium chloride and normal saline provided in place of tap water. Following the injection of the renal damaging agent, hypertension developed. In order to confirm the completeness of the adrenalectomy the animal was subsequently, at the point indicated by the arrow, placed upon a sodium-restricted regimen. The rapid weight loss, dramatic fall in blood pressure and death which ensued, afforded convincing evidence of a lack of residual adrenal tissue.

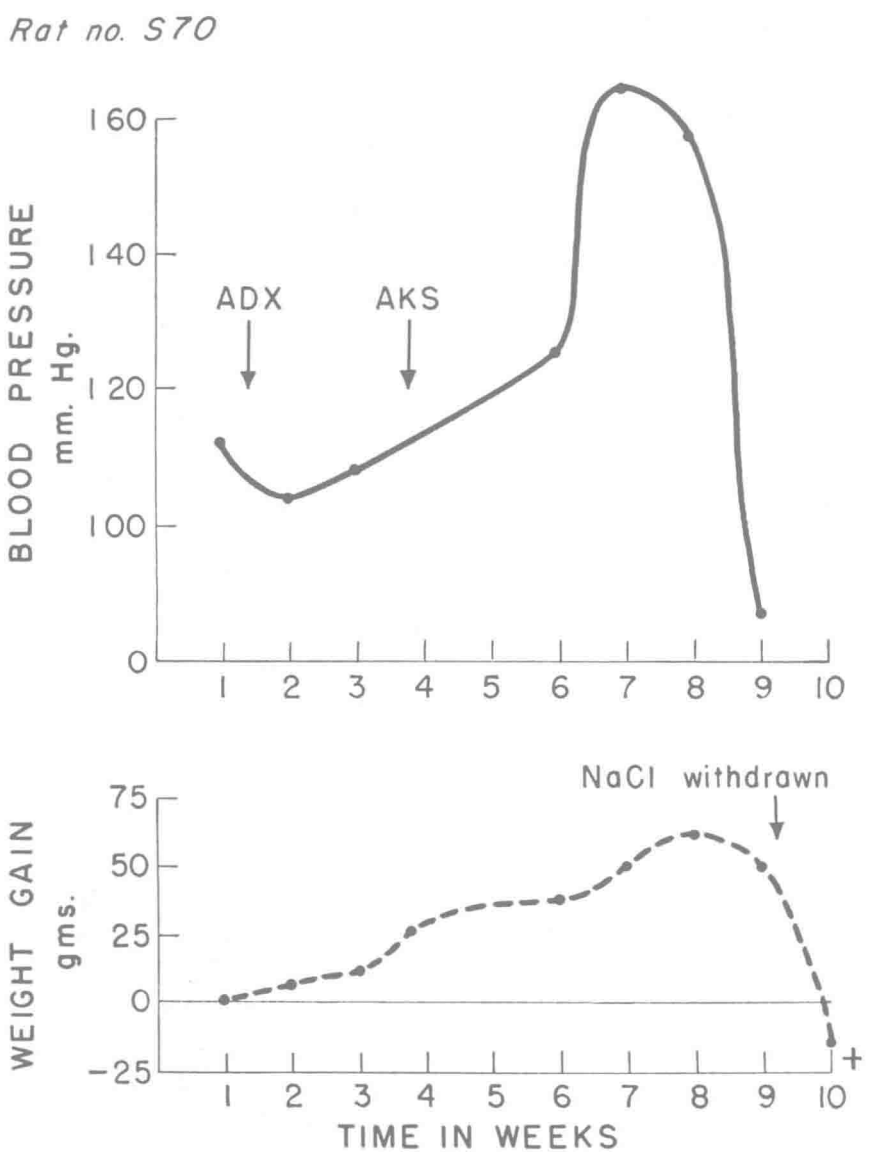

FIGURE 1. Changes in blood pressure and weight in an adrenalectomized rat given antikidney serum. Reprinted from Knowlton, A. I., Loeb, E. N., Seegal, B. C, Stoerk, H. C., and Berg, J. L.: Development of hypertension in adrenalectomized nephritic rat maintained on NaCl. Proc. Soc. Exper. Biol. and Med. 74:661, 1950.

It would seem, therefore, that hypertension, at least of certain types, can develop in the adrenalectomized rat given no steroid replacement therapy.

A second and quite separate question is whether the individual adrenal steroids may, under certain conditions, be hypertensive agents. The answer to this is again Yes. This was first demonstrated for the steroid desoxycorticosterone (DCA) by Kuhlmann, et al. (4). Subsequently, Selye (5) pointed out that an experimental animal could be "sensitized" to the hypertensive action of this compound if the renal mass were reduced, if the kidneys were damaged, or if a high-sodium intake were furnished.

The relationship between the sodium ion and DCA is a particularly interesting one, since the so-called DCA hypertension can develop only when sufficient quantities of this ion are available. In other words, this form of hypertension can be wholly prevented by rigid restriction of the intake of this electrolyte even in animals "sensitized" by renal damage(6).

Figure 2 shows graphically some data which illustrate this point. This experiment was designed so that the sodium intake, which constituted 1.5 per cent of the diet as sodium chloride, did not significantly alter the blood pressure either by itself (see the fourth group on the upper line), or in combination with DCA in a dosage of 2.5 mg. daily (second group on upper line), or with the renal damaging agent which was a rabbit antirat kidney serum (last group in lower line). However, a combination of these three factors, as anticipated, led to a striking rise in arterial tension (second group on lower line). Of particular interest is the first group on the lower line, in which the omission of sodium entirely prevented the hypertension which marked the group provided with liberal quantities of this cation. In addition to averting the appearance of hypertension, the rats on this low-sodium intake failed to develop other characteristic signs of excess DCA action, i.e., they showed no renal or cardiac hypertrophy, and even the histological evidences of DCA activity were minimized.

The group shown third from the left in the upper line, and also the group in a similar position in the lower line, were included in this experiment to determine whether the addition of a potassium chloride supplement would prevent the appearance of DCA hypertension. This possibility was considered since it was known that such a supplement could prevent the abnormal increase in skeletal muscle sodium noted in DCA dogs. It seemed possible that DCA hypertension was in some way related to the accompanying electrolyte shifts. However, the data here indicate that the addition of potassium in no way minimized the rise in blood pressure, although the serum electrolytes in the potassium-treated groups were less abnormal than in the DCA groups receiving only sodium chloride. Subsequently, Rosenman, Freed and Friedman(7) have reported that a liberal intake of potassium permits the prolonged main-