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Adrenalectomy in Experimental Hypertension from Kaolin.

W. A. JEFFERS, M. A. LINDAUER AND F. D. W. LUKENS. (Introduced by J. H. Austin.)

From the Robinette Foundation, the George S. Cox Medical Research Institute, and the Pepper Laboratory of the Hospital of the University of Pennsylvania.

A possible rôle of the adrenal glands in the maintenance of arterial hypertension has been the subject of recent clinical and animal investigation. Goldblatt[1] has suggested that the adrenal cortex is concerned in the maintenance of blood pressure in dogs made hypertensive by constriction of the renal artery.

In our experiments dogs were made hypertensive by intracisternal kaolin injection by the method of Dixon and Heller.[2] There is evidence that this type of arterial hypertension is not affected by denervation of the adrenal glands.[3] Because denervation is presumed to affect only the medullary secretion, it was felt that complete adrenalectomy might yield evidence concerning the importance of the adrenal cortex to this type of hypertension.

Blood pressure measurements were made daily, using the method of Allen, as modified by Collins.[4] After a control period of 7 to 14 days the right adrenal gland was removed. About 10 days later kaolin was injected into the cisterna magna. After 7 to 10 days of arterial hypertension (160-300 mm. of Hg systolic) left adrenalectomy was performed. The dogs were then maintained free from cortical insufficiency by the use of an adrenalin-free cortical extract (Upjohn) (1-3 cc. per day), and salt (sodium chloride, 4 to 6 gm. per day, or a mixture of 6 gm. sodium chloride and 5 gm. sodium citrate).

Four hypertensive animals survived the removal of both adrenal glands. One of them showed a gradual fall in blood pressure to the range of 90-140 mm. of Hg following the second adrenalectomy, without any signs of cortical insufficiency. The other 3 exhibited persistent arterial hypertension (160-250 mm. of Hg) after the second adrenalectomy, as long as they were well maintained by the use of cortical extract and salt. We attempted to keep 2 of the hypertensive animals using only salt. These efforts were unsuccessful.

1 Goldblatt, H., *Ann. Int. Med.*, 1937, **11**, 69.

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3 Hogler, F., Uberrack, K., Zell, F., and Falta, W., *Klin. Wchnschr.*, 1934, **13**, 255.

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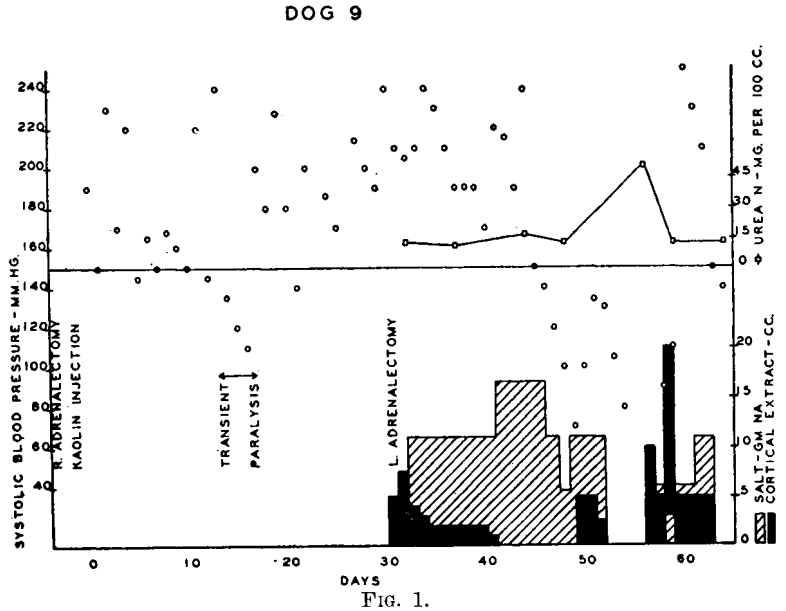

FIG. 1.

Effect of adrenalectomy upon hypertension which has been induced by an intracisternal injection of kaolin. Circles show systolic blood pressure.

Signs of cortical insufficiency soon appeared and the blood pressure fell to the range of 80-100 mm. of Hg. Upon resumption of adequate doses of cortical extract there was evidence of recovery, and a coincident return of blood pressure to the previous hypertensive range.

The results confirm the contention of Hogler, Uberrack, Zell, and Falta[3] that the adrenal medulla is not necessary for this type of hypertension.

It appears that the adrenal cortex, or an extract of it, is necessary for the maintenance of both normal and hypertensive blood pressure levels. It may be pointed out, however, that whereas three times the usual maintenance dose of cortical extract fails to replace the action of the normal adrenal cortex in an adrenalectomized depancreatized animal,[5] no increase above the maintenance dose is needed to support this type of hypertension. The significance of the amount of cortical hormone required under varying conditions is not yet understood.

Summary. Three out of 4 dogs made hypertensive by intracisternal injections of kaolin showed a persistent elevation of arterial blood pressure following bilateral adrenalectomy, as long as they were adequately maintained by the use of salt and of a non-pressor

[5] Long, C. N. H., and Lukens, F. D. W., *J. Exp. Med.*, 1936, **63**, 465.

extract of the adrenal cortex. The fall in blood pressure of the fourth animal was attributed to the spontaneous remission of the experimental hypertension.

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Influence of Ergotamine Tartrate Upon Peripheral Blood-Flow in Subjects with Liver Disease.

DAVID I. ABRAMSON* AND S. S. LICHTMAN.† (Introduced by B. S. Oppenheimer.)

From the Medical Department, The Mount Sinai Hospital, New York.

It has been established in animals[1-5] and in man[6] that ergotamine tartrate in therapeutic doses generally constricts peripheral arteries with a consequent decrease in blood flow. The recent reports of the occurrence of peripheral gangrene following the use of this drug[7, 8] for the relief of pruritus associated with jaundice[9, 10] raises the question as to whether the presence of liver insufficiency might not influence quantitatively this response of the blood vessels. Accordingly, the effect of a single subcutaneous injection of ergotamine tartrate (0.5 mg.) upon the rate of blood-flow was determined in a series of patients with liver disease and compared with that in a control group.

The principles and details of the method of determining blood-flow outlined by Brodie,[11] and Hewlett and Van Zweluwenburg[12] were

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† Mr. J. Marrus rendered expert technical assistance.

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