

tex, the medulla remaining intact (in others the medulla shared in extensive degeneration and necrosis) and zones of regenerated cortical cells were present, presenting a picture (Fig. 1) comparable, if not identical, with that seen in so-called "cytotoxic atrophy" associated with Addison's disease.

In a few experiments it was possible to create pathological changes in the adrenals leading to purulent infiltration or areas of purulent necrosis, by superposing infection on the degenerative processes induced by sub-total ligation. Frequently, this procedure leads to total acute purulent necrosis of the gland.

In some experiments the glands were removed for examination during periods of good health, in others when clinical symptoms were present. These and other observations are still in progress. The experiments thus far performed constitute a foundation for studies which may lead to a better understanding of Addison's disease and of the function of the adrenal cortex.

It is a pleasure to acknowledge my gratitude to Doctors D. P. Seecof and H. Goldblatt for valuable aid in preparation and interpretation of much of my experimental and human pathological material.

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Studies in Hypertension. I. Injection of Various Substances, Especially Amino-Acids, upon Blood Pressure of Rabbits.*

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(With the technical assistance of Dorothy Davis.)

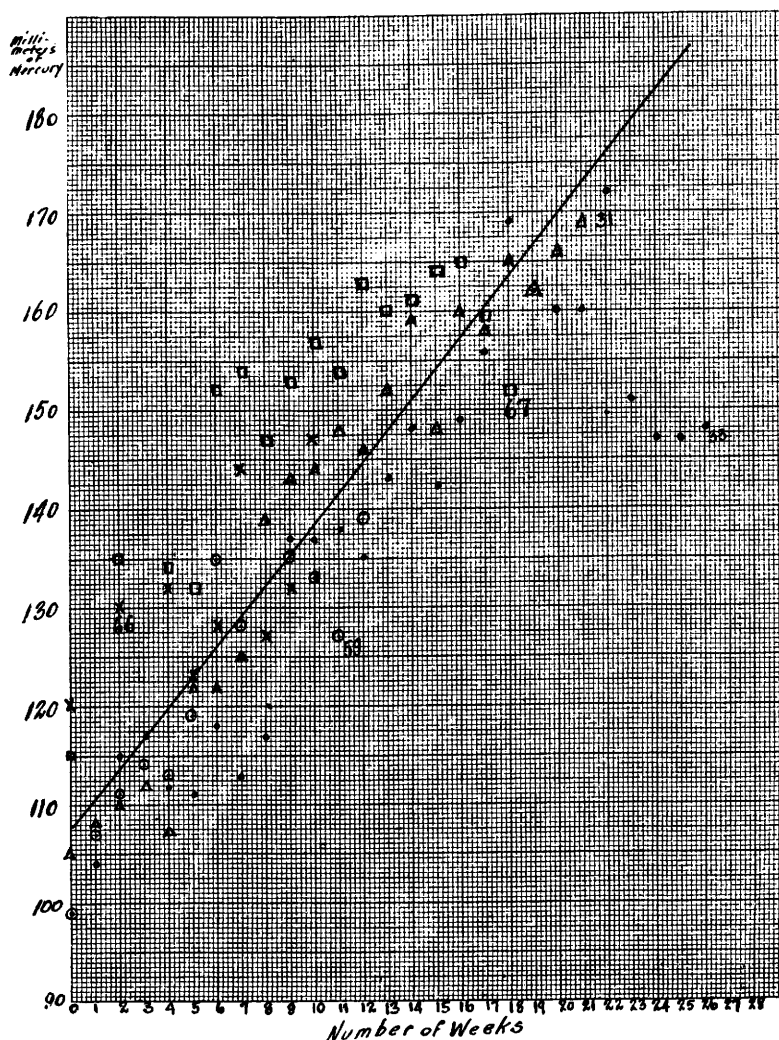
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The smallest dose of the selected substances which would produce histological changes in the kidneys of rabbits was first determined. Doses approximately one-half this amount were then injected daily intramuscularly and the effect upon the blood pressure studied. Uranium nitrate, lead acetate, phosphorus, ergot, viosterol, cholesterol, lecithin, putrescin, tyramine, arginine carbonate, asparagine, glutamic acid, histidine, tyrosine, tryptophane, succinic acid, aspartic acid, and guanidine carbonate were used. Of this entire group aspartic acid and guanidine alone produced progressive increase in systolic blood pressure.

* Aided by a grant from The W. C. Durant Fund for the Study of Hypertension.

The animals were kept in the laboratory for at least one week before blood pressures were taken. Then daily blood pressures were recorded for at least one week before the animals were used. The animals received the same diet of oats, greens, and carrots. The control animals were observed for the same length of time as treated ones. Only the systolic pressure was taken and the procedure of McGregor¹ used. The blood pressure was taken at first daily, and

AVERAGE WEEKLY BLOOD PRESSURE. ASPARTIC ACID GROUP



¹ McGregor, L., *Arch. Path.*, 1928, 5, 630.

then 3 times weekly, the longer period being found sufficient for statistical purposes. The pressures for each week were averaged and the rise or fall recorded. Increases of 20 mm. of mercury or greater were considered as significant.

Fourteen animals injected with neutralized aspartic acid (doses varying between 20 and 250 mg. per kilo of body weight) all showed a rise in systolic blood pressure, the maximum rise being 25 mm. after 6 weeks and 73 mm. after 22 weeks. (See chart 1). The minimum dose of aspartic acid to produce an elevation of blood pressure was 40 mg. per kilo. Further increases of aspartic acid did not cause a more rapid or higher elevation of blood pressure. Blood urea and creatinin were within normal limits. The urine showed albumin and casts in 4 animals. Newburgh and Marsh² report that aspartic acid is mildly nephrotoxic when injected intravenously into rabbits. They also state that the smallest dose that produced renal injury was 0.5 gm. per kilo. Our dosage was considerably less. The histological changes observed were thickening of the elastic tissues of the aorta, congestion of the glomeruli of the kidney, and in a few instances tubular degeneration.

Two rabbits injected with guanidine carbonate, neutralized with HCl, showed a maximum rise of 42 and 46 mm. in systolic blood pressure after 5 weeks. No abnormal changes in the blood urea or creatinin or in the urine were noted. No histological change in the kidney was observed in one animal after 7 weeks of injection.

Rabbits injected with glutamic acid and succinic acid showed no definite rise in blood pressure.

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Studies in Hypertension. II. Changes in Blood Proteins in Experimental Hypertension.

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It has been shown¹ that in rabbits the daily injection of aspartic acid and guanidine produces a definite rise in blood pressure. The blood proteins of these animals were analyzed both before and after

² Newburgh, L. H., and Marsh, P. L., *Arch. Int. Med.*, 1925, **36**, 682.

¹ Rafsky, H. A., Bernhard, A., and Rohdenburg, G. L., *PROC. SOC. EXP. BIOL. AND MED.*, 1932, **29**, 1243.