REDUCTION IN THE BLOOD PRESSURES OF RENAL HYPERTENSIVE DOGS WITH HOG RENIN[1]

A NUMBER of attempts to reduce the blood pressure of renal ischemic hypertensive dogs have been reported recently. Most of these have been unsuccessful, although a few investigators have obtained results showing some promise. Several months ago we reported the production of an antiserum for renin and stated that we purposed to determine the value of "antirenin" actively produced in the therapy of experimental renal hypertension.[2] At this time therefore preliminary results obtained by the treatment of hypertensive dogs with hog renin are presented.

Four dogs rendered hypertensive by the Goldblatt technique were treated for four months with daily intramuscular injections of hog renin representing 1 gram of kidney equivalent per Kg of body weight. Blood serums were examined for antirenin before treatment and subsequently at two-week intervals by a technique previously described.[2]

The history of the first dog is typical of the striking reductions in blood pressure observed in the four animals.

This hypertensive dog showed an average femoral blood pressure of 164 mm of Hg with a maximum of 184 mm and a minimum of 146 mm, during the three months preceding treatment. The blood pressure of the animal fell more or less steadily throughout the period of hog renin injections until the normal or prehypertensive range was reached in the fourth month of treatment. During the two months following renin therapy, the blood pressure dropped to an average of 114 mm of Hg or somewhat below the original normotensive level. In the succeeding five months the pressure slowly increased, so that it has now reached the pretreatment hypertensive range.

At no time during treatment or subsequently was there any evidence of untoward effects. The appetites of the four dogs remained excellent, their weights constant and their blood urea nitrogens and urinalyses normal throughout the periods of observation.

Typical of the four dogs, antirenin to hog and dog renin was demonstrable in the serum of the dog cited above by the end of the first month of treatment and in the third month reached a maximum which was maintained with fluctuations during the observation period of seven months following therapy.

Probably the mechanism of these reductions in blood pressure involves an immune (antihormone?) response to the heterologous hog renin, inasmuch as dog renin and heat-inactivated hog renin were shown to be without effect on the blood pressure of other renal hypertensive dogs. However, the failure of the antirenin titres (especially to dog renin) to fall as the blood pressures of the four dogs increased during the months following renin treatment is difficult to explain on this basis. Conceivably the immune response may be due to some other heat labile constituent of the renal cortex present in the hog renin solution.

Without much question the antihypertensive action of the hog renin injections was not due to the coincidental presence of the antipressor substance under investigation by Harrison and coworkers[3] and by Page and associates.[4] Thus the amounts of kidney equivalent used by them were much larger than those employed by us, the blood pressure increases following cessation of therapy were more prompt in their animals than in ours, and frequently signs of toxicity accompanied their reductions in blood pressure. Moreover, Harrison *et al.*[5] have shown that their principle inhibits the acute pressor effect of renin and that it is extractable from dog kidney and presumably when so obtained effective in the hypertensive dog.

If the promise of our preliminary findings is substantiated by further work now in progress this type of treatment will be studied in essential hypertension in man.

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[2] C. A. Johnson and G. E. Wakerlin, *Proc. Soc. Exp. Biol. Med.*, 44: 277, 1940.

[3] A. Grollman, J. R. Williams, Jr., and T. R. Harrison, *Jour. Am. Med. Asn.*, 115: 1169, 1940.

[4] I. H. Page, O. M. Helmer, K. G. Kohlstaedt, P. J. Fouts and G. F. Kempf, *Proc. Cent. Soc. Clin. Res.*, pp. 8, 1940.

[5] A. Grollman, J. R. Williams, Jr., and T. R. Harrison, *Jour. Biol. Chem.*, 134: 115, 1940.

THE CYANIDE STABLE RESPIRATION OF THE SEA URCHIN EGG

BARRON and Hamburger[1] claim complete inhibition of the respiration of the fertilized sea urchin egg by cyanide. This can not be confirmed by others.[2,3] The observation,[4] that the inhibition is complete just after the addition of cyanide, but soon decreases until about 90 minutes after the admixture, when a constant value is reached, explains this discrepancy. Later stages of development behave similarly, though here the inhibition decreases much faster.[5] Further the cyanide resistant respiration of the sea urchin egg, as in some strains of yeast,[6] turned out to be dependent on the oxygen pressure. Owing to these facts Lindahl con-

[1] *Jour. Biol. Chem.*, 96: 299, 1932.

[2] J. Runnström, *Acta Zool.*, 9: 445, 1928; *Protoplasma*, 10: 106, 1930; *Biol. Bull.*, 68: 327, 1935.

[3] I. Korr, *Jour. Cell. Comp. Physiol.*, 10: 461, 1937.

[4] *Zeitschr. vergl. Physiol.*, 27: 136, 1939.

[5] All experiments performed according to Krebs (*Biol. Jour.*, 29: 1920, 1935) to avoid escape of HCN from the medium.

[6] Tamiya and Kubo, *Acta phytochim.*, 10: 317, 1938.