

able to effect an approximately 40-fold concentration of the toxic material by absorption on a cation-exchange resin, from which the toxicant could be eluted by 2-4% hydrochloric acid. In view of the interest in lathyrism, experimental and clinical, we are reporting these observations, since there is no prospect that we can extend our investigations of this subject in the immediate future.

Summary. A comparison of the toxicity of the seed of 5 species of *Lathyrus* for the rat has been made. Intoxication with *L. sylvestris Wagneri* has also been studied in the

white mouse, rabbit, and guinea pig. A partial purification of the toxic principle of *L. sylvestris Wagneri* which has concentrated the factor about 40 times is described.

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Received July 21, 1952. P.S.E.B.M., 1952, v81.

Renal Transport of Para-Aminohippurate in the Hypophysectomized Rat.* (19786)

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A number of investigators have shown that the clearance of inulin, diodrast and para-aminohippurate as well as the tubular transport maximum (Tm) of para-aminohippurate and glucose are reduced in hypophysectomized animals(1-5). The reduction in Tm as determined with para-aminohippurate (PAH Tm) could be due to a reduction in the renal blood flow or due to a defect in the tubular transport of para-aminohippurate. The latter point can be readily studied by the para-aminohippurate concentration technic of Cross and Taggart(6) in kidney slices.

Methods. Male, Sprague Dawley rats, 30-36 days following hypophysectomy† were used in this study; litter mates were used as controls. The hypophysectomized rats weighed 89 to 97 g while the control litter mates weighed 110 to 230 g. A series of hypophysectomized rats were injected with the equivalent of 1 mg of growth hormone‡ (Armour standard) per 100 g of body weight twice daily for 5 days. Two growth hormone preparations

(Armour & Co.)† prepared by the method of Wilhelmi, *et al.*(7) were administered to each of 2 groups of hypophysectomized rats. Kidney slices were prepared by conventional methods and incubated in a buffer similar to that of Cross and Taggart(6). The PAH concentration used was 0.0013 molar. The weight of the incubated slices varied between 55 to 80 mg. One set of vessels contained no substrate while the other set contained 0.01 molar sodium acetate. The vessels were incubated for 2 hours at 25°C in an oxygen atmosphere in a Dubnoff metabolic shaking incubator. PAH determinations in the slice and medium were determined by the same methods as those used by Cross and Taggart(6).

Results. Cross and Taggart have expressed the PAH concentrating ability of kidney slices as the slice medium PAH concentration ratio (SM ratio). In the present series of experiments, the SM ratio will be used as an index of activity of the renal slices.

Table I summarizes our results obtained so far and it is clear that the kidney slices from hypophysectomized rats have a much lower SM ratio than slices from control rats. The administration of growth hormone for 5 days increased the body weight of the rats by about 24 grams and the para-aminohippurate SM

* Supported by a grant-in-aid from the Hendricks Research Fund, Syracuse, N. Y.

† Hypophysectomized rats were supplied by Hormone Assay Laboratory, Chicago, Ill.

‡ Kindly supplied by Mr. Irby Bunding, Armour and Co., Chicago, Ill.

TABLE I. Effect of Hypophysectomy and Growth Hormone Treatment on Para-aminohippurate Slice Medium Ratio of Rat Kidney Slices. Values are slice medium ratio of para-aminohippurate, and standard deviation. Substrate when used was .01 molar sodium acetate.

Rats	No. of rats	Wt of rats, g	S/M ratio for PAH	
			No substrate	With substrate
Normal control	6	218-230	9.71 ± 1.00	14.48 ± 1.36
" "	6	110-120	9.16 ± 1.58	12.45 ± 1.36
Hypophysectomized	6	90-97	5.36 ± 1.17	6.38 ± 2.26
Hypophysectomized, treated with growth hormone*	6	92-96	10.68 ± 1.69	14.07 ± 1.33
Hypophysectomized, treated with growth hormone†	9	89-96	9.98 ± 2.11	15.76 ± 3.62
Normal, treated with growth hormone†	6	215-239	9.50 ± 1.98	13.54 ± 3.47

* Growth hormone, Armour & Co., Lot No. K40805R.

† R377237.

ratio of the kidney slices to normal levels. Furthermore, it can be seen that with normal kidney slices the addition of acetate increased the SM ratio by about 40-50%; with kidney slices from hypophysectomized animals the stimulating effect of acetate is very small. Growth hormone administration increased the SM ratio in the absence of substrate and also restored the ability of the kidney slices to respond to acetate. The administration of growth hormone to normal rats weighing 200 to 250 g in the same dosage as that used in the hypophysectomized rats did not have any significant effects on the SM ratio of the kidney slices.

Discussion and conclusion. The reduction in the SM ratio of kidney slices from hypophysectomized animals may be due to the reduction of some rate limiting factor in the kidney. Cross and Taggart(6) and Mudge and Taggart(8) have postulated that acetate or the hypothetical two carbon fragment may be a rate limiting factor. However, our results clearly indicate that in the present instance this is not the case since addition of acetate did not restore the ability of kidney slices from hypophysectomized rats to concentrate para-aminohippurate. In hypophysectomized rats, QO_2 , as well as alkaline phosphatase activity of the kidney are less than normal(9). It is possible that this enzyme may be important for kidney function and the probable defect may be a reduced concentration of this enzyme or some other rate limiting enzyme system essential for PAH transport. Growth

hormone which produces nitrogen retention may well stimulate the production of the enzyme or enzyme systems necessary for PAH transport. The above findings may in part explain the restorative effects of growth hormone on the PAH Tm of the hypophysectomized animals. Although the restoration of the SM ratio was produced by growth hormone, the possibility remains that this restorative action may have been produced by some contaminant of the hormone preparations used.

Summary. The uptake of para-aminohippurate of rat kidney slices was determined. Kidney slices from hypophysectomized rats show a lower ability to concentrate para-aminohippurate than normal rat kidney slices. This defect is corrected by the prior administration of growth hormone to the hypophysectomized rats.

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Received July 21, 1952. P.S.E.B.M., 1952, v81.