pertensive rats subjected to either nephrectomy or ureteral ligation.

Discussion. There are a number of changes in electrolyte content of the various tissues of the experimental rats. It is apparent that most of them are probably the result of urinary retention since they were induced either by nephrectomy or ureteral ligation. For the purpose of this presentation, there seems little need to discuss them in detail.

There is a distinct difference between the effect of nephrectomy and ureteral ligation on aorta potassium content of the hypertensive rats. Following removal of the ischemic kidney, potassium content of the aorta falls promptly to normal values along with the marked decline in blood pressure. Hypertensive rats with the ureteral ligature show neither a change in aorta potassium content nor blood pressure. The effect of nephrectomy on loss of potassium from the aorta appears to be a specific response since in the same animal there is an increase in skeletal muscle potassium content.

It would appear therefore that removal of the ischemic kidney eliminates a substance elaborated by this organ which induces an elevation in aorta potassium content in association with hypertension. It remains to be demonstrated whether or not this is a pressor substance. These results add to the evidence that potassium content of arterial tissues has a positive correlation with blood pressure levels. As has been previously discussed, this cation may influence blood pressure level through altering arterial tone(1).

The evidence pertaining to the role of potassium in regulation of blood pressure is quite scanty in comparison to that of sodium. The relationship of arterial tissue electrolytes to blood pressure was recently reviewed extensively by Tobian(6), who stated "the level of potassium correlates somewhat better with blood pressure than the level of sodium."

Summary. Removal of the ischemic kidney of hypertensive rats but not ureteral ligation, induces a marked fall in blood pressure and a significant decrease in aorta potassium content. It is suggested that the ischemic kidney elaborates a substance which induces hypertension and also increases potassium content of arterial tissue.

1. Freed, S. C., St. George, S., Rosenman, R. H., *Ciculation Research,* 1959, v7, 219.

2. Tobian, L., Binion, J., *J. Clin. Invest.,* 1954, v33, 1407.

3. Freed, S. C., PROC. SOC. EXP. BIOL. AND MED., 1960, v104, 136.

4. Friedman, M., Freed, S. C., *ibid.,* 1949, v70, 670.

5. St. George, S., Freed, S. C., Rosenman, R. H., Winderman, S., *Am. J. Physiol.,* 1955, v181, 550.

6. Tobian, L., *Physiol. Rev.,* 1960, v40, 280.

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Differences in Thyroid Function of Several Strains of Mice.*† (26230)

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The reaction of the thyroid to an antithyroid drug differs in intensity in different strains of the same animal species. Thiouracil administration increases thyroid weight in some strains of mice more than in others (1,2). Wilson(3), using increase of thyroid epithelium and depletion of colloid as criteria, found considerable differences in degree of histological reaction between different strains of mice after feeding a semisynthetic diet with 0.5% sulfadiazine. The strongest reaction was found in the C_3H/Wi and BUB/Wi mice, a less strong reaction in

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the YBR/HeWi strain, a still smaller reaction in the BUC/Wi strain, and the least reaction in the C_{57}BL/Fn strain.

The secretion rate of thyroid hormone differs also in different strains of mice. Hurst and Turner(4), using Dempsey and Astwood's goitrogen technic, found a higher secretion rate in Schwing albino mice than in Rockland mice. By measuring the retention of a tracer dose of radioactive iodine, Chai, Amin and Reineke(5) found consistent differences in thyroid hormone output rate between the inbred mouse strains A/Jax, BALB/c, C_{57}BR/cd and C_{57}BL/6.

The present knowledge of the action of antithyroid drugs might imply that the strains which normally have the highest thyroid hormone output rate are also most affected by administration of an antithyroid drug and thus will show the strongest histological reaction. To test this hypothesis, in the same strains as in the above mentioned experiments of Wilson, I^{131} uptake and retention were measured in the present experiments.

Materials and methods. Male mice, 60 to 90 days of age, of the following strains were used: BUB/Wi, BUC/Wi, C_3H/AnWi, C_3H/StWi, C_{57}BL/Fn and YBR/HeWi. In the YBR/HeWi strain only the yellow mice, heterozygous for the A^y gene were used. The mice were raised on Purina Laboratory Chow, and kept at constant temperature (78°F). Fifteen days before experiment, 12 mice of each strain were transferred to a basal diet consisting of 20% Crisco, 30% Vitamin test casein (G.B.I.), 29% Argo corn starch, 8% powdered brewer's yeast (G.B.I.), 7% salt mixture U.S.P. XII #2 (G.B.I.), 4% Mazola corn oil and 2% cod liver oil (Squibb). In each experiment the mice were injected intraperitoneally with ca. 4 μc of a carrier-free NaI^{131} solution. A standard solution was prepared containing 1/50 of the dose injected into a mouse. Each mouse was counted externally at 10, 16, and 22 hours after injection, and on the following days once or twice a day. For this *in vivo* counting, the thyroid region of the mouse was held in front of the slit-formed aperture in the lead shielding of the counter.‡ In order to compensate for the extrathyroidal background and to enable the comparison between *in vivo* counts and counts of the standard solution, the geometric conversion ration, R, was determined by the method of Fish, Carlin and Hickey(6) for each strain of mice. The fractional uptake, F, is calculated as follows:

$$F = \frac{\text{Counts/min. of mouse } \textit{in vivo}}{\text{Counts/min. of standard solution}} \times R \times 0.02$$

The logarithm of the fractional uptake is plotted against the time after dose administration in hours. The point at which output of I^{131} surpasses uptake of I^{131} is referred to as maximum uptake. This peak is usually reached by 22 hours after injection. After the peak a straight regression line is fitted by the method of least squares. The regression coefficient measures the slope of the retention line and thus represents the rate of loss of I^{131} from the thyroid. Since the organic binding of iodine is a rapid process and since eventually most, if not all, of an injected tracerdose I^{131} is incorporated into thyroid hormone, this slope is considered to reflect the secretion rate of I^{131} labeled hormone.

Results. The maximum uptake and the regression coefficient of 7 identical experiments are averaged for each strain and summarized in Table I.§ Maximum uptake for BUB/Wi, BUC/Wi and C_3H/Wi mice is around 19% (18.8%, 20.4% and 19.2% respectively), whereas the C_{57}BL/Fn and YBR/HeWi strains have a lower maximum uptake (12.3% and 13.0% respectively). The retention line is steepest in the C_{57}BL/Fn mice (–0.0039) and thus this strain is concluded to have the fastest output of thyroid hormone. The BUB/Wi strain has the second highest rate of output (–0.0025), followed by the C_3H/Wi strain (–0.0023), the YBR/HeWi strain (–0.0021) and the BUC/

‡ Grateful acknowledgement is made to Dr. F. C. Hickey, O.P., for lending this part of the counting equipment and for his help in this investigation. For description, see reference (6).

§ C_3H/Wi refers to the 2 sublines C_3H/AnWi and C_3H/StWi, the results of which have been combined, because they were in good agreement.

TABLE I. Average Uptake and Retention of Radioiodine in Different Mouse Strains.

Strain	No. of experiments*	Avg maximum uptake† (%)	Avg regression coefficient†	Reaction to 0.5% sulfadiazine (Wilson, 3)
C_{57}BL/Fn	2	12.3 ± 1.8	−.0039 ± .00037	+
BUB/Wi	7	18.8 ± 2.3	−.0025 ± .00008	++++
C_3H/Wi	3	19.2 ± 1.4	−.0023 ± .00010	++++
YBR/HeWi	2	13.0 ± 2.7	−.0021 ± .00042	+++
BUC/Wi	3½	20.4 ± 3.6	−.0019 ± .00014	++

* Each experiment represents 12 mice/strain.
† Values are given with their stand. error of the mean.

Wi strain (−0.0019). In spite of considerable variation between experiments, this order is generally observed in each individual experiment.‖ Analysis of variance showed that the variance attributable to strains is highly significant ($P<0.005$).

Discussion. The order in which the strains in the present experiments have been found to rank in their normal thyroid hormone output rate does not parallel the order of degree of histological reaction after sulfadiazine feeding (Wilson,3). This does not support the hypothesis that the strain which normally has the highest thyroid hormone output rate would be most affected after administration of sulfadiazine, and thus show the strongest histological reaction. Degree of reaction following sulfadiazine treatment is thus not directly dependent upon the normal rate of thyroid hormone output. The order in which the strains in the present experiments can be arranged according to their maximum uptake also does not coincide with the order of the reaction to sulfadiazine. The maximum uptake is an index for the function of the thyroid in so far as it is dependent upon the iodide concentrating ability of the thyroid, but the value found for the maximum uptake is also influenced by rate of output of iodine by the thyroid. In the present experiments no inverse relationship was found between the order of output rate and maximum uptake of the strains. Therefore, the differences in maximum uptake among the strains reflect true differences in rate of I^{131} uptake.

It was expected that differences in thyroid function between strains could be explained by the assumption that in one mouse strain the pituitary-thyroid axis operates at a higher level than in another strain. D'Angelo (7) and coworkers found that the pituitary-thyroid axis functions at a much higher level in the rat than in the guinea pig. In the rat the thyrotropin content of blood and adenohypophysis is high, the thyroid takes up a large percentage of injected I^{131} and secretes I^{131} relatively fast; whereas in the guinea pig thyrotropin content is low and rate of I^{131} uptake and output is slow. If in one mouse strain the pituitary-thyroid axis operates at a higher level than in another, the strain with the highest thyrotropin content should have the highest uptake of I^{131}, the largest output rate, and the most hypertrophied thyroid in case of intervention with the normal thyroxine production by sulfadiazine. This was not found in the present experiments. The thyrotropin content of the pituitary is not known, but a strain with a high maximum uptake did not necessarily have a fast output rate, nor a strong reaction to sulfadiazine. This lack of correlation between the 3 indices of thyroid function measured leads to the conclusion that in these strains each index reflects the pituitary-thyroid interaction in its own way, independent of each other.

Summary. I^{131} uptake and retention by the thyroid of several strains of mice was measured with an *in vivo* technic and compared with the histological reaction of the thyroid to sulfadiazine administration. The order in which the strains of mice rank in their thyroid hormone output rate was found not to parallel the order in which the strains rank in their histological reaction to sulfadiazine. Degree of reaction to sulfadiazine is thus not directly dependent upon the nor-

‖ Detailed results are listed in Ph.D. thesis of the author, University Microfilms, Ann Arbor, Mich.

mal rate of thyroid hormone output, but they represent 2 separate independent aspects of the pituitary-thyroid axis.

1. Dickie, M. M., Woolley, G. W., *Genetics,* 1948, v33, 102.
2. Smith, F. W., Gardner, W. U., *Anat. Rec.,* 1949, v103, 506.
3. Wilson, J. W., *ibid.,* 1952, v113, 565.
4. Hurst, V., Turner, C. W., *Mo. Agr. Exp. Sta. Res. Bull.,* 1948, v417.
5. Chai, C. K., Amin, A., Reineke, E. P., *Am. J. Physiol.,* 1957, v188, 499.
6. Fish, W. A., Carlin, H., Hickey, F. C., *Endocrinology,* 1952, v51, 282.
7. D'Angelo, S. A., *Symp. Brookhaven Nat. Lab.,* 1954, v7, 9.

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Comparative Efficacy of Intravenous and Intraperitoneal Administration of Antiserum in Passive Anaphylaxis.* (26231)

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Early workers(1) observed that the latent period in passive anaphylactic sensitization in guinea pigs varied with different routes of administration of the antiserum and was shortest following intravenous injection. For example, after intraperitoneal administration of antiserum, Doerr and Russ(2) obtained the best results by permitting 24 hours to elapse before challenging. This interval was shortened to 4 hours by injecting the antiserum intravenously. From these and similar observations, the natural deduction was made that the intravenous route of passive sensitization was more uniformly effective than other routes (3, cf4, p143). In their quantitative studies of passive anaphylaxis, Kabat and coworkers injected antiserum by the intravenous method and challenged after an interval of 48 hours. Under these conditions, they showed that about 0.03 mg of antibody nitrogen from either rabbit or guinea pig antiserum produced uniformly fatal sensitization when the animals were challenged with adequate doses of antigen (cf4, p144). However, because of its greater convenience, many contemporary investigators continue to use the intraperitoneal route for passive sensitization with the interval between injection of antiserum and challenge ranging between 24 to 48 hours(5,6,7). The present communication deals with a quantitative comparison of the effectiveness of the intravenous and intraperitoneal routes of passive sensitization when the interval between sensitization and challenge was maintained at 48 hours.

Comparison of effectiveness of the 2 routes of sensitization was accomplished by determining the median sensitizing dose (SD_{50}) of antibody nitrogen by the 2 methods and by determining the median lethal dose (LD_{50}) of antigen in animals passively sensitized with uniform doses of antibody by both routes.

Materials and methods. Rabbit antibodies to dextran were used to produce passive anaphylaxis in guinea pigs. The antiserum was produced by injecting rabbits with saline suspensions of formalin-killed *Leuconostoc mesenteroides*† (Strain NRRL B-1424(8)) that had been cultured in sucrose broth. Such antiserums give strong precipitin reactions to purified dextrans prepared from sucrose broth cultures(9). The serum was analyzed by the quantitative precipitin method of Heidelberg and Kendall (cf 4, p59) and found to contain 1.45 mg of antibody-N per ml.

For determination of the SD_{50} of antibody-N, 2 groups of 60 guinea pigs each, weighing between 280 and 320 g, were sensi-

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