17127. Xanthine and Mercurial Diuretics and Renal Tubular Transport of Glucose and P-aminohippurate in the Dog.*

CARROLL A. HANDLEY, JANE TELFORD, AND MARGUERITE LA FORGE.
From Department of Pharmacology, Baylor University College of Medicine, Houston, Texas.

Mercurial and probably xanthine diuretics[1] inhibit certain enzyme systems in the kidney. It is probable that the diuretic action of these agents is due to their selective accumulation in the kidney in concentrations sufficient to inhibit the systems concerned with the reabsorption of water and sodium chloride. The action of these compounds on other renal transport mechanisms has not received much attention. It has been reported[2,3] that mersalyl (Salyrgan) depresses the maximal rate of transfer of diodrast and p-aminohippurate

TABLE I.
Effects of Salyrgan and Mercuhydrin on Transfer Maxima of Glucose and PAH.

Dog No.	Wt (kg)	Date	Control GF* cc/min.	Control TmG* mg/min.	Control TmPAH* mg/min.	During diuresis GF* cc/min.	During diuresis TmG* mg/min.	During diuresis TmPAH* mg/min.
Tm-1	17	7- 2-48	53	212		62	228	
1	17	11-23-	65	245		79	254	
1	17	12-17-	54		11	61		14
1	17	1-13-49	61		10	70		13
2	17	-20-	63		14	68		15
3	15	10-22-48	65	215		63	198	
3	15	11- 1-	52		9	44		10
3	15	12- 3-	56	196		64	220	
3	15	-29-	53		10	63		10
4	15	11-18-	67	232		61	220	
6	14	7-16-	47	233		42	228	
6	14	-22-	42		10	45		9
7	16	- 9-	60	225		47	205	
7	16	8-18-	55	200		48	172	
7-F	15	4-29-	52	193		49	180	

* Average of three 10-minute periods.

TABLE II.
Effects of Theophylline on Transfer Maxima of Glucose and PAH.

Dog No.	Wt (kg)	Date	Control GF* cc/min.	Control TmG* mg/min.	Control TmPAH* mg/min.	During diuresis GF* cc/min.	During diuresis TmG* mg/min.	During diuresis TmPAH* mg/min.
Tm-1	15	7- 2-48	66		10	58		11
1	15	- 7-	53	212		60	230	
1	15	12-17-	50		11	57		14
3	15	9- 9-	53		11	57		12
3	15	-16-	51	187		47	173	
6	14	7-16-	47	232		42	225	
6	14	-23-	52		11	58		10
7	17	6-23-	71	261		64	242	
6-F	16	11-13-	60	252		62	270	

* Average of three 10-minute periods.

* This investigation was supported in part by a research grant from the Division of Research Grants and Fellowships of the National Institute of Health, United States Public Health Service.

1 Handley, C. A., unpublished data.

2 Brun, C., Hilden, T., and Raaschow, F., *Acta Pharmacol. Toxicol.*, 1947, **3**, 1.

3 Berliner, R. W., Kennedy, T. J., and Hilton, J. G., *Am. J. Physiol.*, 1948, **154**, 537.

(PAH) in man although the TmPAH in the dog is not influenced by mersalyl.[3] The following data concerns the measurement of glucose and PAH Tm's in normal dogs and during the period of maximal diuresis by mercurial diuretics and theophylline.

Methods. Trained, unanesthetized, female dogs weighing 14-17 kg were used. Glomerular filtration rate (GF) was measured by creatinine. Glucose and p-aminohippurate Tm's were measured in independent experiments because of the reported mutual interference in the tubular transfer of these substances.[4,5]

Creatinine was determined by the method of Folin and Wu,[6] p-aminohippurate by the method of Bratton and Marshall[7] and glucose by Hanes' modification of Hagedom and Jensen's method.[8] The dose of meralluride (Mercuhydrin) and mersalyl, the two mercurials used, was 0.1 cc per kg (4 mg per kg of combined mercury) and 10-20 mg per kg of theophylline was employed.

Results. The results recorded in Tables I and II show that neither theophylline nor the mercurial diuretics studied interfere with the renal tubular transfer mechanisms for glucose or p-aminohippurate. These results indicate that the energy yielding mechanism concerned with the reabsorption of water and sodium chloride in the dog is distinct from the mechanisms concerned in the transfer of glucose and PAH. During this investigation it was observed that it is possible to reduce the TmG and TmPAH indirectly by diuretics.[1] This effect is due to dehydration and may be produced by the saline diuretics as well as the mercurial and xanthine groups, if sufficient urine output is produced to cause dehydration.

Summary. Mercuhydrin, salyrgan and theophylline, in diuretic doses, do not interfere with the renal tubular transfer of glucose or p-aminohippurate in the dog.

Received April 22, 1949. P.S.E.B.M., 1949, **71**.

[4] Klopp, C., Young, N. F., and Taylor, H. D., *J. Clin. Invest.*, 1945, **24**, 117.

[5] Houck, C. R., PROC. SOC. EXP. BIOL. AND MED., 1946, **63**, 398.

[6] Folin, O., and Wu, H. J., *J. Biol. Chem.*, 1919, **38**, 81.

[7] Bratton, A. C., and Marshall, E. K., *J. Biol. Chem.*, 1939, **128**, 537.

[8] Hanes, C. S., *Biochem. J.*, 1929, **23**, 99.

17128. Absorption of Manganese by the Thyroid Gland of the Guinea Pig.

L. J. DEYSACH AND T. W. RAY.

From the Departments of Physiology and Biochemistry, Marquette University School of Medicine, Milwaukee, Wis.

Ray and Deysach[1] found that subcutaneous injection of manganese chloride into guinea pigs resulted in the accumulation of manganese in varying amounts in all organs tested, but that the accumulation was especially great in the thyroid gland where deposition was in direct proportion to the dose administered. Injections of large doses of the salt depressed the oxygen consumption of the animal and small doses augmented it. Noticeable effects within a few minutes after administration suggested early absorption by the thyroid gland. The purposes of the present study were to find the exact time interval for the appearance of manganese in the thyroid following its subcutaneous injection, to determine the rate at which it is deposited in this organ during a 24 hour period, and finally to obtain information on its rate of elimination.

Experimental. Each of 27 guinea pigs was given one subcutaneous injection of 10.0 mg of manganese chloride per kg of body weight. The animals were sacrificed 3 at a time, at intervals ranging from 15 minutes to 4 days following the injection, and the manganese

[1] Ray, T. W., and Deysach, L. J., PROC. SOC. EXP. BIOL. AND MED., 1942, **51**, 228.