Non-Creatinine Chromogen and Creatinine Clearance in the Rat. (20711)

RICHARD W. LIPPMAN.*

From the Institute for Medical Research, Cedars of Lebanon Hospital, Los Angeles.

A controversy concerning the significance of renal creatinine clearances in the rat has resulted from conflicting observations. Lippman(1) reported that the exogenous creatinine clearance is much greater than the endogenous clearance. Fingl(2) reported that the creatinine/inulin clearance ratio is depressed toward 1 as the plasma creatinine concentration is raised or after administration of para-aminohippurate or probenecid. Martel, Wang, and Gingras(3) have also suggested that creatinine is secreted by the renal tubule of the rat. On the other hand Friedman(4) has reported the identity of creatinine and inulin clearances in the rat. Recently Muntwyler and Griffin(5) performed "true creatinine" clearances (utilizing adsorption on Lloyd's reagent) and state that the endogenous and exogenous clearances of "true creatinine" approximate each other in the rat. The earlier reports mentioned above were all based upon total chromogen determinations.

In the experiments reported here endogenous creatinine determinations were performed upon the serum and urine obtained from 6 male and 6 female rats of the Slonaker-Addis strain, taken from stock, where they had received a diet which contained 17% protein. Creatinine determinations were performed upon serum and urine samples both by the total chromogen method of Bonsnes and Taussky(6) and by the method of Miller and Miller(7) which utilizes adsorption on Lloyd's reagent to obtain a value for "true creatinine". The results are given in Table I.

In spite of the relatively small number of observations, it is clear without statistical analysis that non-creatinine chromogen constitutes about one-third of the total chromogen in rat *serum*, while it constitutes not more than one-tenth of the total chromogen in rat urine. These values are similar to, but less striking than, those obtained in *plasma* and urine by Muntwyler and Griffin, who used Wistar strain rats, which have a common genetic ancestry with those of the Slonaker-Addis strain. Although Muntwyler and Griffin obtained endogenous and exogenous "true creatinine" clearances that approximated each other, neither their values nor ours account completely for the four-fold difference in endogenous and exogenous total chromogen clearances previously reported(1). It is necessary to mention that determinations of the endogenous chromogen, which depend on the Jaffé reaction, are performed at a level which is

TABLE I. Proportion of Non-Creatinine Jaffé Chromogen in Rat Serum and Urine.

Sex	Total chromogen, Serum conc.	Total chromogen, Urine conc.	"True creatinine," Serum conc.	"True creatinine," Urine conc.	Non-creatinine chromogen (% of total chromogen) Serum	Non-creatinine chromogen (% of total chromogen) Urine
	mg/100 ml		mg/100 ml			
♂	.655	5.02	.480	5.16	27	−2
	.678	19.11	.457	17.08	33	11
	.742	14.05	.352	12.28	53	13
	.699	11.20	.374	10.20	46	9
	.723	8.20	.417	7.95	42	3
	.588	14.92	.460	12.80	22	14
♀	.588	11.42	.290	11.42	51	0
	.588	10.52	.374	9.01	36	14
	.480	7.12	.226	6.80	53	4
	.655	9.56	.458	8.99	30	5
	.458	10.11	.331	9.50	28	6
	.458	10.99	.417	10.07	9	8

* Present address: 414 N. Camden Drive, Beverly Hills, Calif.

barely within the sensitivity of those methods which have been used. If a more precise measurement were devised for plasma or serum chromogen levels less than 1.0 mg/100 ml the difference between the reported non-creatinine chromogen proportions might be reconciled.

The presence of non-creatinine chromogen would have a negligible influence upon the creatinine/inulin ratios obtained at high plasma creatinine concentrations. Work which has not been reported previously (because we could not offer a reasonable explanation), but which is based upon 92 animals, resulted in a creatinine/inulin clearance ratio of 1.26 ± .09 within the serum creatinine concentration range of 9.5 to 15.0 mg/100 ml.

1. Lippman, R. W., *Am. J. Physiol.*, 1947, v151, 211.

2. Fingl, E., *Am. J. Physiol.*, 1952, v169, 357.

3. Martel, F., Wang, M., and Gingras, R., *Renal Function Studies in the Rat*, Quebec: Les Presses Universitaires, Laval, 1951.

4. Friedman, M., *Am. J. Physiol.*, 1947, v146, 387.

5. Muntwyler, E., and Griffin, G. E., *Am. J. Physiol.*, 1953, v173, 145.

6. Bonsnes, R. W., and Taussky, H. H., *J. Biol. Chem.*, 1945, v158, 581.

7. Miller, Z., and Miller, B. F., PROC. SOC. EXP. BIOL. AND MED., 1951, v78, 471.

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Effects of Cortisone, Ascorbic Acid and Piromen on Phagocytosis in Mice.*† (20712)

STANLEY MARCUS, DON W. ESPLIN, AND GILBERT A. HILL.

From the Department of Bacteriology, College of Medicine, University of Utah, Salt Lake City, Utah.

In considering the role of host mechanisms in resistance to experimentally induced infection, attention was drawn to certain compounds which might augment phagocytic activity. In the experiments described, cortisone, ascorbic acid and Piromen administered parenterally in critical amounts have been shown to alter significantly functional activity of mouse phagocytes *in vivo*.

Methods. Animals. Adult albino (*Mus musculus*) mice of mixed sexes were used in all experiments. The weight range was 24 ± 4 g. *Thorium dioxide analysis.* The ThO_2 uptake by mouse spleens after intravenous injection of Thorotrast‡ was determined by the technic described by Gordon and Katsh(1). Details of technic and precision of the analytical procedure with mouse tissues have been described previously(2). *Peritoneal phagocytosis technic.* The intraperitoneal phagocytosis of *Micrococcus pyogenes* var. *aureus* (FDA 209 P) by phagocytic leukocytes was studied. The organism was grown in (Difco) brain heart infusion broth at 37°C for 18 hours. After 4 hours at refrigerator temperature the culture was diluted with broth to contain approximately 4 x 10^9 organisms/ml which gave a turbidity reading of 650 nephelos in a photonephelometer (Coleman, Model 7). Mice (6 for each determination) were injected intraperitoneally with 0.25 ml of this suspension and sacrificed after 2 hours. Several drops of the peritoneal exudate from each mouse were smeared on a slide and stained with Wright's stain. Exactly 200 phagocytic cells were examined on each slide making a total of 1200 cells for each determination. Activity of these cells was estimated by noting the number of cells containing bacteria (active) or no bacteria (nonactive)(3). In each category the values obtained for the 6 animals were added to give one series of numbers for each determination. Substances tested for effect on

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‡ Thorotrast is a stabilized colloidal solution of ThO_2 (24-26% by vol.), generously supplied by the Heyden Chemical Corp., New York.