TABLE III. Storage of Serum at Temperatures between −30° and −26°C, −5° and 0°C, and 0° and +4°C. Serum concentration in mg %.

		Avg for 3 sera s.f.—storage—s.th.								
		−30° and −26°C			−5° and 0°C			0° and +4°C		
Days of storage→	Orig.	7	28	128	7	28	178	7	78	178
$S^{\circ}_{f\,(1.06)}$ 100-400	250	235	187	98	258	267	151	253	230	108
20-100	356	137	124	87	363	350	140	348	301	208
12- 20	41	24	25	24	39	41	32	42	44	40
0- 12	270	232	247	227	272	284	230	278	272	233
Total LDL	917	628	583	436	932	942	553	921	847	589
HDL	232	236	237	199	227	224	166	257	216	195
Total lipoprotein	1149	864	820	635	1159	1166	719	1178	1063	784

tween −30° and −26°C, between −5° and 0°C, and between 0° and +4°C. Adequate preservation of lipoproteins stored as serum at a temperature between −5° and 0°C was maintained for 4 weeks, between 0°C and + 4°C for 2 weeks, and between −30° and −26°C for a few days.

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Changes in Renal Tissue Composition Induced in Rabbits by Various Intravenous Doses of Mercaptomerin Sodium.* (24832)

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Previous studies(1,2) have shown that the organic mercurial diuretic agent, mercaptomerin sodium, localizes in kidneys when administered parenterally to animals or human subjects. The renal histopathologic effects of the organic mercurials are well known, but the nature of the changes in tissue composition is still obscure. The purpose of the present study in normal rabbits was to determine what changes in water, sodium and potassium contents of renal tissue were produced by intravenous injection of various doses of mercaptomerin sodium.

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Material and methods. Forty-four normal albino male rabbits were kept in individual metabolism cages and fed a stock diet of compressed pellets. Tap water was given without restriction. Six control animals were not injected. Six animals received intravenous injection of mercury of 0.5 mg/kg of body weight; 9 animals were given 1 mg/kg; 5 were given 5 mg/kg and 6 each were given 10, 15 and 20 mg/kg. The mercury was given as commercial lyophilized mercaptomerin sodium (Thiomerin), dissolved in 1 or 2 ml of water immediately prior to injection. All test animals were killed by air embolism 48 hours after administration of the mercurial. Both kidneys were removed and weighed, and the cortices were then separated from the medul-

TABLE I. Renal Water, Sodium and Potassium Content in Rabbits Given Various Intravenous Doses of Mercaptomerin Sodium.

I.V. dose of mercaptomerin (mg Hg/kg)	No. of rabbits in group		Cortex Na (meq/kg wet tiss.)	Cortex K (meq/kg wet tiss.)	Cortex H_2O (%)	Medulla Na (meq/kg wet tiss.)	Medulla K (meq/kg wet tiss.)	Medulla H_2O (%)
0	6	Mean	68.92	60.62	78.93	103.11*	57.29	81.46*
		S.D.	9.30	5.70	1.20	14.40	6.80	3.10
		No.†	20	20	20	16	16	16
.5	6	Mean	70.45	66.96*	77.20*	85.89*	66.04*	80.05
		S.D.	5.42	6.87	1.17	13.05	4.91	1.63
		No.†	22	22	22	22	22	22
1.0	9	Mean	65.16	62.29	79.28	99.48	60.71	81.81
		S.D.	7.62	3.48	1.89	25.34	5.78	2.55
		No.†	30	22	30	30	22	30
5.0	5	Mean	64.69	56.01	80.04*	83.20*	56.49	80.93
		S.D.	4.92	5.21	1.00	23.10	6.02	1.60
		No.†	16	16	16	16	16	16
10.0	6	Mean	77.45*	42.55*	82.60*	71.55*	48.12*	80.02
		S.D.	3.40	2.78	1.56	8.02	5.36	3.03
		No.†	22	22	22	20	20	20
15.0	6	Mean	76.58*	42.55*	82.65*	66.36*	47.33*	82.55
		S.D.	5.66	6.82	1.71	5.22	4.37	1.10
		No.†	22	22	22	19	19	19
20.0	6	Mean	76.29*	42.64*	83.35*	67.17*	50.78*	83.10
		S.D.	4.65	4.65	.90	4.40	4.70	.86
		No.†	20	20	20	20	20	20

* Significant difference when compared with respective mean control values. P = less than 0.01.

† No. of specimens analyzed.

las by gross dissection. In most instances, 2 samples from the medulla and 2 from the cortex of each kidney were placed in test tubes of known weight. The samples weighed approximately 1 g each. The test tubes were then dried at 110°C until constant weights were reached. After dry tissues had been pulverized with glass rod, 10 ml of demineralized distilled water was added to each tube. The tubes were shaken, stoppered, and stored in refrigerator 6 days, then centrifuged. Sodium and potassium contents of supernatant fluid were determined by lithium internal standard method of flame photometry. *Statistical analysis.* The significance of difference between mean values was tested by the formula for comparing 2 groups with a different number of observations in each group(3).

Results. (Table I). In 6 normal rabbits used as controls, the mean concentration of sodium in the medulla (103.1 meq/kg wet wt of tissue) was considerably higher than that found in the cortex (68.9 meq/kg). Water content of medulla (81.5%) was significantly higher than that of the cortex (78.9%).

Administration of mercury 0.5 mg/kg produced the following significant changes: increase in potassium content and decrease in water content in the cortex, decrease in sodium and water content and increase in potassium content in the medulla. Tissue changes at 1 and 5 mg/kg of mercury were not striking except for the decrease in medullary sodium content. Injection of mercury in doses of 10, 15 or 20 mg/kg resulted in a significant increase in cortical sodium concentration and water content and a decrease in cortical potassium concentration. Medullary concentrations of sodium and potassium were significantly and strikingly decreased following injection of mercury in doses of 10, 15 or 20 mg/kg. Water content of the medulla was not significantly altered by these doses of mercury.

Comments. Ullrich and Jarausch(4) have previously shown in dogs that the tissue sodium concentration in thirsted animals increases progressively from the cortex to the

outer zone of the medulla and to the tip of the papilla. The rather high concentration of sodium in the medulla of our control animals given water without restriction as compared with that in the cortex, with very little difference in potassium concentration or water content, may be attributed theoretically to one or more of the following factors: 1) a higher proportion of extracellular fluid in medulla than in cortex, 2) presence of tubular fluid and urine, or 3) a high intracellular concentration of sodium within medullary cells. Since concentration of sodium in serum of normal rabbits is 131.9 ± 7.2 meq/l(5), and since not more than 55% of the medulla is thought to be composed of interstitial tissue (6), it is difficult to account for high concentration of sodium in the medulla on the basis of extracellular fluid alone. It cannot be determined from the present study whether the high medullary concentration of sodium is due to tubular fluid or to intracellular accumulation. Ljungsberg(6) has previously concluded from a histotopochemical study in rats, that chloride is located within the cells of the collecting tubules. Although he attributed this concentration to active chloride reabsorption, Smith(7) has stated that active sodium reabsorption is more probable. Radioautographic studies with Na^{22} in rats(8) have shown that maximal concentration of radioactivity occurs in cells of the renal collecting duct. Data from our study in rabbits are compatible with the interpretation that tubular cells may concentrate sodium.

Diuretic doses of mercury (below 10 mg/kg) appear to have produced dehydration and concentration of potassium in both cortex and medulla, with a decrease in sodium concentration in the medullary tissue. Previous studies with Na^{22}(8) have shown that diuretic doses of an organic mercurial produce autographic changes in the cortex, attributed to alterations in the proximal convoluted tubules, and in the medulla, thought to be due to functional changes in cells of the collecting ducts.

A single intravenous dose of 10 mg of mercury or more/kg body weight is nephrotoxic. In our study on rabbits, doses of 10, 15 and 20 mg/kg produced in the cortical tissue electrolyte changes compatible with cellular damage —a decrease in potassium and an increase in sodium concentration and water content. In the medulla, these dosages caused a decrease in sodium and potassium contents, changes which might be due to a less severe degree of cellular damage than that incurred in the cortex. The relatively greater damage to cortical tissue is compatible with the previous observation in rabbits(2) that concentration of mercury in the cortex is approximately twice that in the medulla.

Summary. Sodium, potassium and water content of the renal cortex and medulla were determined in normal rabbits and in rabbits given intravenous injections of mercury, as mercaptomerin sodium, in doses of 0.5 to 20 mg/kg of body weight. Concentration of sodium in the normal medulla (103.1) meq/kg wet tissue) was considerably higher than that in the normal cortex (68.9 meq/kg). With administration of mercury in doses of 10 mg or more/kg, cortical sodium concentration and water content increased and potassium concentration decreased; medullary sodium and potassium concentrations both decreased.

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