ceived little attention from the laboratories engaged in these studies. The results of the present work focus attention on this particular group of degradation products.

Summary. Studies on the metabolism of the 8-aminoquinolines, pamaquine, isopentaquine, primaquine, pentaquine, SN 13,058, and CN 1100, have been carried out in the rhesus monkey. As shown by differential analyses of the 8-aminoquinoline contents of plasma, each of the above compounds is degraded to alkali-soluble, ethylene dichloride-insoluble derivatives. This degradation follows either oral or intramuscular administration of the drugs. The extent of degradation of the different compounds varies markedly, being greatest with CN 1100 and least with SN 13,058. Preliminary studies on CN 1100 have indicated that the degradation products of this compound are present in the urine in considerable quantity.

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Distribution of Mercury in Rats Following Oral and Intravenous Administration of Mercuric Acetate and Phenylmercuric Acetate.* (17752)

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(Introduced by A. J. Lehman.)

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Chronic toxicity investigations in rats over a 2-year period have shown that mercury in the form of the phenylmercuric acetate salt is far more toxic than mercury in the form of the mercuric acetate salt(1). The following experiments were undertaken in an effort to trace the fate of the 2 mercurials following oral and intravenous introduction into the rat.

Method. Young adult male rats, ranging from 250 to 300 g body weight were used in these experiments. Equivalent quantities of mercury, in the form of aqueous solutions of phenylmercuric acetate and mercuric acetate were administered under very light ether anesthesia, either by the femoral vein or by stomach tube. In all but a few preliminary experiments, the dose of mercury was 120 μg per animal. For the intravenous injection the dose was contained in 0.25 ml volume, for the oral, in 2.0 ml volume. The animals were sacrificed at intervals of 2, 6, 24, 48 and 96 hours after treatment; tissues, blood, and excreta were analyzed for mercury. In the case of the excreta, urine and feces were collected separately, and the contents of the bladder and of the cecum and large intestine at the time of sacrifice were considered part of the respective voided samples. Mercury analyses were made by the method of Laug and Nelson(2).

Results. Table I shows the tissue distribution of mercury 24 hours after intravenous injection of the metal in the form of the 2 salts under investigation. It can be seen that the kidney is the most important storage depot for mercury and that the amounts found in this tissue are fairly well graded to the quantities of mercury injected. This storage response of the kidney after intravenous injection of mercury is, as might be expected, similar to that obtained when the metal is introduced by other routes, such as the dermal(3), vaginal(4), and oral(1).

* A part of these data was presented at the meetings of the Federation of American Societies for Experimental Biology, March, 1949.

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TABLE I.
Distribution of Mercury in the Rat 24 Hours After Intravenous Injection of Mercury as Mercuric Acetate and Phenylmercuric Acetate.

Dose, μg mercury	μg mercury per g of tissue						
	Kidney	Liver	Blood	Spleen	Muscle	Bone	Brain
			Phenylmercuric acetate*				
120	13	.93	0	0	0	0	0
60	9.1	.52	.22	.66	0	.17	.51
30	5.4	.44	.16	0	0	0	0
10	2.2	.14	0	0	0	0	0
			Mercuric acetate*				
120	19	.69	0	0	0	0	0
60	7.0	.17	.07	0	0	0	0
30	2.6	.10	.19	0	0	0	0
10	2.4	.06	0	0	0	0	0
			Control*				
0	.30	.06	0	0	0	0	Tr

* Represents the average of 4 animals at each dosage level. Tr = Trace.

Reference to Table I also shows that other tissues, such as spleen, muscle, bone, and brain, are of relatively minor importance as storage depots for mercury. Fig. 1 shows that the storage of mercury in the kidney is markedly different for the 2 compounds within the first 24 hours. Thus, 2 hours after the intravenous injection of 120 μg of mercury as mercuric acetate, there is approximately 4 times as much mercury within this organ than after phenylmercuric acetate. With time, the mercuric acetate storage curve tends to fall, while the phenylmercuric acetate storage curve tends to rise, so that after 48 hours, they have converged to approximately the same value. With the exception of the 48 and 96-hour values, all storage differences between compounds are statistically signifi-

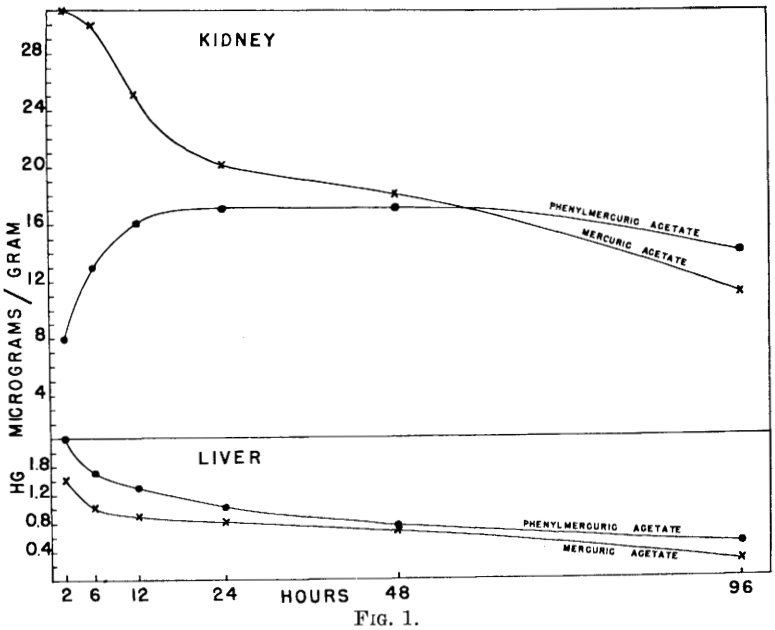

FIG. 1.

The storage response of the kidney and the liver of the rat to the intravenous injection of 120 μg of mercury in the form of mercuric acetate and phenylmercuric acetate. Each point represents average of 8 animals.

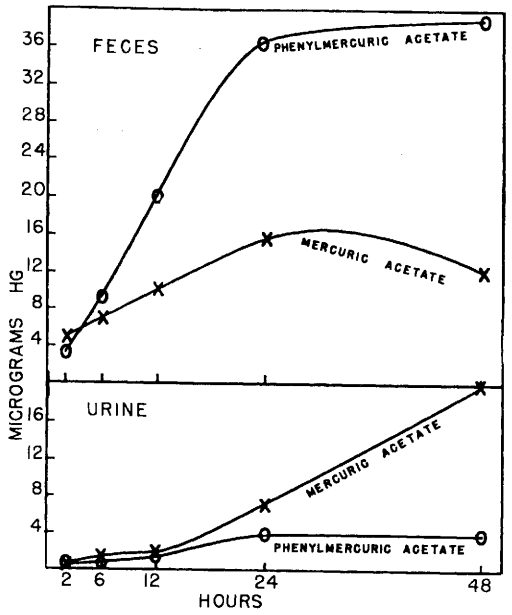

FIG. 2.

The excretion of mercury in the urine and feces following intravenous injection of 120 μg of mercury in the form of mercuric acetate and phenylmercuric acetate. Each point represents average of 3 animals.

cant. It is interesting to note that the storage response of the liver for the 2 compounds is reversed, that is to say, the initial storage of mercury after phenylmercuric acetate is significantly higher than after mercuric acetate. It should be noted that except for the first 24 hours, the subsequent loss in stored mercury from kidney and liver is relatively slow.

Fig. 2 describes the urinary and fecal excretion of mercury following intravenous injection of phenylmercuric acetate and mercuric acetate. It can be seen that urinary excretion of mercury is significantly greater after mercuric acetate than after phenylmercuric acetate, the differences being most marked in the second 24-hour period. In the feces, however, the situation is reversed, the largest amount of mercury being found after phenylmercuric acetate, with virtual completion of excretion within the first 24 hours.

Table II shows that the larger amounts of mercury in the feces after phenylmercuric acetate appear to originate in the small intestine, where it can be seen that the mercury content after phenylmercuric acetate is significantly higher than after mercuric acetate. Secretion of mercury into the stomach does not appear to offer an explanation for this observation, for a number of analyses of gastric contents indicate a small mercuric concentration of about the same order for both compounds.

Table III shows the distribution of mercury in kidney, liver, blood, urine and feces at various periods following oral and intravenous administration of mercuric acetate and phenylmercuric acetate. With mercuric acetate, the difference between intravenous and oral administration is very well marked, especially in the mercury content of the kidney. In contrast, the differences between the amounts of mercury found after oral and intravenous injection are not nearly as marked with phenylmercuric acetate. These observations, together with the fact that only about half as much mercury is found in the feces within the first 24 hours after phenylmercuric acetate as that after mercuric acetate would indicate far greater absorption of the former salt. This is further pointed up by the difference in the blood levels after oral administration. In this connection one interesting observation may be made of the blood mercury levels 2, 6 and 12 hours after intravenous injection of either salt. It can be seen that while progressive changes in kidney and liver mercury are occurring during this period, the blood mercury remains practically fixed.

Discussion. Two salient facts may be noted from the above results. 1. Phenylmercuric acetate is much more readily absorbed from the intestinal tract than mercuric

TABLE II.

Total Mercury Content of the Small Intestine Following Intravenous Injection of 120 μg of Mercury as Mercuric Acetate and Phenylmercuric Acetate.

Hr after inj.	Mercuric acetate	Phenylmercuric acetate
	μg mercury in total contents	
2	5.5	9.4
6	4.7	12
12	4.5	8.1
24	2.4	3.7
48	2.0	2.4

Each value represents the average of 3 animals.

TABLE III.
Comparative Tissue Distribution of Mercury Following Oral and Intravenous Administration of 120 μg of Mercury as Mercuric Acetate and Phenylmercuric Acetate.

		Mercuric acetate					Phenylmercuric acetate				
Hr		Kidney, μg/g	Liver, μg/g	Blood, μg/g	Urine total, μg	Feces total, μg	Kidney, μg/g	Liver, μg/g	Blood, μg/g	Urine total, μg	Feces total, μg
2	(I)	28	.95	.60	.39	5.4	4.2	1.8	1.9	.43	1.7
	(O)	0.79	.13	.03	.12	22	5.3	1.2	0.33	.64	9.0
6	(I)	28	.73	.63	1.3	7.1	11	1.1	1.8	.74	9.3
	(O)	1.5	.13	.14	.48	75	7.1	1.1	.52	2.7	24
12	(I)	26	.54	.60	1.8	10	14	.85	1.9	1.4	19
	(O)	1.5	.16	.09	.18	80	10	.81	.46	2.3	37
24	(I)	22	.56		7.0	16	16	.78		3.9	37
	(O)	1.4	.24		.15	82	7.9	.74		2.8	45
48	(I)	19	.53		20	12	14	.48		3.9	40
	(O)	1.6	.10		1.5	95	9.5	.58		5.3	78

(I) Intravenous. (O) Oral. Each value represents avg of 3 animals.

acetate. This is reflected in greater storage of mercury in the liver and kidney after phenylmercuric acetate than after mercuric acetate, and confirmed also in the chronic feeding tests conducted in this laboratory(1); 2. There are important differences in the behavior of the two salts when they are injected intravenously. For example, 2 hours after mercuric acetate (Table III), the mercury concentration in the kidney rose to 28 μg per gram. This is equivalent to a total mercury content of 56 μg, based on an average weight of 2 grams for both kidneys. Thus within 2 hours the kidneys account for about half of the dose of mercuric acetate; in contrast, less than 1/10 of the dose after phenylmercuric acetate. It seems likely that part of the initial high concentration of mercury in the kidney after mercuric acetate is metal "in transit". This is confirmed by the subsequent rise in urinary excretion which eliminates about 17% of the dose in 48 hours; in contrast only 3% after phenylmercuric acetate. It would appear, therefore, that the urinary tract is the favored route for excretion of mercuric acetate. For phenylmercuric acetate the evidence points to the liver as the favored route of excretion of mercury. Thus the initial concentration in this organ is higher after phenylmercuric acetate than after mercuric acetate, resulting, perhaps, in a higher concentration in the bile, which in turn would account for the elevated intestinal and subsequent fecal concentrations of mercury. Roughly, one third of the dose of phenylmercuric acetate is excreted in the feces in 48 hours, but only 10% of the mercuric acetate.

Summary. 1. Phenylmercuric acetate is more readily absorbed from the gastrointestinal tract than mercuric acetate.

2. The favored route for the excretion of mercury after phenylmercuric acetate is via the intestinal tract.

3. The favored route for the excretion of mercury after mercuric acetate is via the urine.

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