Comparative Study of Uptake and Distribution of Hg^{203} Given as Labelled Chlormerodrin (Neohydrin).*† (23937)

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It is well established that organic mercurial compounds are preferentially concentrated in renal tissue of fish(1), rat(2), rabbit(3), dog (2) and man(4). The present investigation provides quantitative information as to uptake and distribution of organic mercurial diuretic by a variety of tissues in poikilothermic animals such as amphibia, reptiles and fish, and a comparison is made with higher homoiothermic forms including chicken, rat and dog. As far as renal uptake was concerned, attention was particularly directed to site of preferential mercury uptake within the nephron and to species differences regarding time course of mercury binding and maximum concentration attained.

Methods. A total of 40 experiments was performed on specimens of mudpuppies (*Necturus maculosus*), bullfrogs (*Rana catesbiana*), turtles (*Terrapene carolina*), carp (*Cypria carpio*), chickens and mongrel dogs. Each animal was injected intramuscularly with a neutralized solution of Hg^{203}-labelled chlormerodrin (3 - chloromercuri-2-methoxypropylurea, Neohydrin). In mudpuppies, frogs, turtles, fish and chickens, a site was chosen for injection which was not predominantly within the drainage area of the portal circulation. At time intervals ranging from 2-70 hrs after injection, the animals were anaesthetized as follows: 30 mg Nembutal/kg (dogs), 1.5% Urethan (Necturi), pithed (bullfrogs) or stunned (carp, chicken). Blood was obtained either from the heart (turtle, bullfrog), aorta (mudpuppies), carotids (chicken), postcaval vein (carp) or femoral artery (dogs). Samples of kidney, liver, spleen, heart muscle, gut, abdominal wall muscle, lung and gills were removed immediately following collection of blood, and adherent connective tissue removed by dissection. In Necturus separation of kidney into a medial and lateral section was undertaken since anatomical evidence(5,6,7) indicates that the lateral part of kidney of Necturus is made up predominantly of proximal convoluted tubules and collecting ducts (ureteral tissue having been removed by dissection) while the medial strip of kidney contains the following parts of the nephron: glomerulus, distal tubular segment, neck, intermediate tubule and nephrostome. Separation into medial and lateral strip of tissue was done by saggital dissection about 1 mm lateral to the visible row of glomeruli. Samples of tissues were blotted, weighed on torsion-balance, transferred to standard test tubes and counted in well-type scintillation counter. Plasma and tissue concentration of the organic mercurial compound are expressed in terms of μg mercury/g wet tissue.

Results. In Table I data obtained in Necturus are summarized. It is evident that, with one exception, the concentration of radiomercury in renal tissue exceeds that of plasma. Furthermore, a comparison of the respective tissue/plasma concentration ratios (T/P ratios) shows that concentration of Hg^{203}, given as radiochlormerodrin, in lateral kidney tissue was always higher than that taken up by medial strips of the kidney. Accordingly, tissue/plasma concentration ratios were consistently higher for that part of kidney which constitutes predominantly proximal convoluted tubules. It can also be seen that, while there is some scatter, there is a trend toward increased uptake of mercury with time elapsed after administration. Thus a comparison of Exp. No. 2 and 9, or 3 and 8 shows considerably higher concentrations of radiomercury within the renal tissue, for a comparable dose, 26 hrs or later after radiochlormerodrin had been given.

Tissue/plasma ratios for Hg^{203} exceeded one in only liver, gut and, occasionally, spleen (range of T/P ratios: liver 1.13-21.6, gut: 0.33-4.17, spleen: 0.40-2.15). Of these tis-

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TABLE I. Plasma and Kidney Concentration and Tissue/Plasma Concentration Ratios of Mercury[203] Given as Radiochlormerodrin.

Exp. No.	Dose of Hg^{203}, mg/kg	Time after inj., hr	Hg conc. (γ/g)			T/P ratio	
			Plasma	Kidney			
				Lateral	Medial	Lateral	Medial
2	12.7	2	8.4	13.2	7.3	1.6	.9
3	9.2	2	4.1	8.0	2.2	2.0	.6
1	15.0	3	17.7	10.7	8.7	.6	.5
4	9.7	8	10.2	86.2	44.4	8.4	4.3
5	5.8	16	12.2	106.0	52.5	8.7	4.3
6	5.0	16	4.2	50.2	36.1	12.0	8.6
12	1.0	19	.9	8.3	.6	9.2	.7
13	1.0	19	.6	7.1	3.6	11.8	6.0
7	6.3	26	8.6	106.8	62.6	12.4	7.3
8	8.8	26	7.3	251.4	115.6	34.5	15.9
10	2.8	46	6.9	261.2	40.0	38.2	5.9
11	2.5	46	1.67	36.7	13.8	22.0	8.3
9	12.1	70	5.3	153.0	87.0	29.0	16.4

sues, liver consistently bound more mercury than did gut or spleen. All other specimens studied (heart muscle, skeletal muscle and gills) showed T/P ratios below one, and skeletal muscle always exhibited the lowest mercury concentration.

Table II shows that in all other species studied a considerable degree of Hg^{203} concentration occurred in the kidney. In both poikilothermic and homoiothermic animals mercury storage occurred in the kidney, for a high mercury content is sustained despite a progressive fall in plasma concentration with time. In our series of poikilothermic animals, the turtle had both the highest T/P ratios and the highest mercury content in renal tissue.

No preferential binding of mercury by liver, gut and spleen was observed in turtle and frog (range of T/P ratios: frog: liver 0.14-0.42, gut 0.02-0.62, spleen 0.17-0.92; turtle: liver 0.30-1.04, spleen 0.17-0.38, gut 0.06-0.48). In contrast these concentration

TABLE II. Plasma and Kidney Concentrations and Tissue/Plasma Concentration Ratios of Mercury[203] Given as Radiochlormerodrin in Poikilothermic and Homoiothermic Animals. Data for rats and 2 dogs are taken from Borghgraef, R. R. M. and Pitts, R. F.(2).

Time after inj., hr	Hg^{203} concentration								
	Kidney γ/g	Plasma γ/g	T/P ratio	Kidney γ/g	Plasma γ/g	T/P ratio	Kidney γ/g	Plasma γ/g	T/P ratio
	Carp			Bullfrog			Turtle		
5	32.4	1.6	20.8	111.6	9.7	11.5	80.0	6.2	12.9
5	10.5	.2	52.5	138.0	11.9	11.6	111.0	6.1	18.2
18–24	24.9	1.4	17.8	100.0	5.6	17.9	129.0	2.7	47.8
"	32.3	4.1	7.9	121.4	7.9	15.4	203.0	3.9	52.1
46–48	18.6	.3	62.0	75.0	3.6	20.8	233.0	2.7	86.3
"	16.0	.6	26.7	136.9	6.4	21.4	265.0	3.4	78.0
	Chicken			Rat			†	Dog*	
1–2				55.6	4.2	13.3	163.0	.9	181.0
"				75.2	.8	94.2	131.0	1.0	131.0
3–6	32.8	.4	82.0	97.7	.6	163.0	74.5	.8	93.2
4–6	34.2	.2	171.0	108.0	.2	540.0	83.3	.22	378.
12				94.0	.2	470.0			
18–24	16.2	.2	81.0	97.5	.1	975.0	13.3	.01	1330.
"	19.2	.2	96.0						
46–48	4.2	.06	70.0						
"	23.9	.1	239.0						

Dose of Hg in all cases from 1.0 to 2.0 mg/kg body wt.

* Hg administered intrav. † Kidney cortex only.

ratios were often above one in carp (range of T/P ratios: liver 0.76-5.0, spleen 0.76-5.14, gut 0.26-1.84). In all animals skeletal muscle again contained the least mercury.

The lower section of Table II contains results on renal mercury uptake in the group of homoiothermic animals studied. Data obtained on rats and 2 dogs by other authors(2), using the same mercurial compound, have been included for comparison. It is evident that in all animals tissue plasma concentration ratios exceeded those obtained in the poikilothermic group. This, however, is a reflection of low plasma concentration ratios rather than an increased accumulation of Hg^{203} in the kidney. With the exception of the dog, in all animals there was a slow fall in kidney radiomercury content over the time period studied.

Discussion. The results presented indicate that radiochlormerodrin is bound to a considerable degree by kidney tissue in a variety of animals other than mammals. While in general renal storage of mercury is sustained up to 46-70 hrs, our findings show significant species differences as to absolute amount of mercury bound and time course of renal mercury accumulation. Thus in Necturus and turtle, maximum concentration was reached more slowly. The delay in reaching a high concentration of radiomercury in the kidney of Necturus may account for failure to obtain a significant diuresis in short-term experiments(8). Since the nature of binding of mercury in renal tissue is poorly understood, nothing can be said about the cause of the observed species differences. Our results on regional distribution of Hg^{203} within the kidney indicate that it is the proximal tubule which preferentially binds mercury. This region is most likely also the site of secretion into urine since in the aglomerular toadfish whose nephron consists of proximal tubules only, radiomercury has been found in urine in concentrations higher than in plasma(1).

Summary. The uptake and distribution of Hg^{203} given as labelled chlormerodrin (Neohydrin) has been studied in the mudpuppy, carp, bullfrog, turtle, chicken and dog. Preferential binding of radiomercury by renal tissue was found in all animals with most tissue/plasma ratios of Hg^{203} well above one. For a given dose poikilothermic animals showed a slower accumulation and loss of radiomercury than did homoiothermic specimens. With the exception of the dog, in all animals there was only a slow fall in renal content of radiomercury over a time period of 46 to 70 hrs. In Necturus maximum mercury uptake was found in a part of the kidney made up predominantly of proximal tubules.

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