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THE EFFECTS OF DITHIOLS ON THE DISTRIBUTION OF MERCURY IN RABBITS

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The efficiency of dimercaprol as an antidote in poisoning by mercuric chloride has been established by both experimental (Gilman, Allen, Philips, and St. John, 1946; Stocken, 1947; etc.) and clinical (Longcope and Luetscher, 1946, 1949) investigations. Gilman *et al.* (1946) also reported that the glucoside of dimercaprol (BAL-Intrav) was more active. The following observations were made in order to discover the fate of mercury in poisoned animals after treatment with these substances. A short report has been published recently by Fitzsimmons and Kozelka (1950) of similar investigations on rats and Rhesus monkeys.

Materials and Methods

Materials.—The dimercaprol was a water-purified sample, and was stored in a refrigerator when not in use. Solutions in 66 per cent (v/v) aqueous propylene glycol were made up freshly as required.

Dimercaprol glucoside was received as the barium salt, contained in nitrogen-filled ampoules. Solutions of the free dithiol were prepared as described by Weatherall and Weatherall (1949). The impurity of the preparations of dimercaprol glucoside necessitated estimations of the thiol content of each solution, by means of iodine titration; this procedure is probably more satisfactory than calculating the dosage from the weight of barium salt used (Weatherall, 1949).

The radioactive isotope of mercury (Hg^{203}) was obtained by neutron irradiation of mercuric chloride at A.E.R.E., Harwell. Radioactive chloride (Cl^{36}) was removed by reducing the salt to metallic mercury with stannous chloride. The metal was dissolved in aqua regia, and the solution gently heated almost to dryness. Drying was completed in a vacuum desiccator. The low specific activity (4mC. per g.) of the mercury necessitated the quantitative transfer of the mercuric chloride to the injection solutions, which finally consisted of 1.35 mg. mercuric chloride, incorporating 3–5 μC. of Hg^{203}, per ml., dissolved in 4 per cent (w/v) dextrose. A dose of 1.0 ml. per kg. body weight was injected intravenously over a period of 2–3 minutes.

Method.—The treatment of the animals, sampling and ashing of tissues, estimation of radioactivity, and calculation of results followed the procedures reported previously in studies of the distribution of lead (Ginsburg and Weatherall, 1948; Adam, Ginsburg, and Weatherall, 1949). The mercury isotope used (Hg^{203}) emitted β-radiation of only moderate energy (0.2 MeV) and counts in the fluid counter were consequently appreciably affected by the densities of the media. A graph was constructed relating the decrease in count to the density; the density of each sample was measured, using simple

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hydrometers, and the counts corrected by reference to the graph. On the range of densities encountered, the decreases in count were never greater than 10 per cent.

Preliminary recovery experiments indicated that up to 15 per cent of the mercury could be lost during the ashing process, but that this was reduced to 5 per cent or so by avoiding vigorous boiling. As urine and bile were not ashed, mercury was not lost from these fluids in this way. Duplicate samples of liver and kidney were taken routinely, and from these the standard error of the estimations of mercury was found to be ± 14 per cent. The counting-rate was low, and the time of counting was prolonged only sufficiently to give an error of up to ± 10 per cent. The fractions of the dose accounted for by adding together the calculated amounts in all the organs sampled ranged from 70–90 per cent.

RESULTS

Results are presented for the distribution and excretion of mercury in 19 rabbits, all of which received a single intravenous dose of 5 μM (1.0 mg. Hg) mercuric chloride per kg. body weight. This dose usually caused some damage to the kidneys, as shown by the presence of albumin and casts in the urine. No other toxic effects, apart from general apathy, were noted in the poisoned animals. Some of the animals were treated with dimercaprol, and some with dimercaprol glucoside, at different times after the injection of mercuric chloride. Signs of poisoning appeared less definite in the urines of the treated animals, but this impression may be biased.

The results obtained from the control animals are shown in Table I as the concentrations of mercury in μg. per g. tissue and as the percentage of the dose found in various organs and tissues. Although considerable variation was always found between animals receiving the same treatment, certain general trends can be seen. One hour after the injection of mercury a small quantity of the element remained in the plasma ; but within six hours the amounts had fallen and were generally below the detectable level. Of all the organs and tissues sampled, the kidneys contained by far the highest concentration of mercury, and, after 24 hours, accounted for 20–30 per cent of the mercury absorbed. The liver generally contained about 2 μg. mercury per g., and this concentration did not alter significantly during 14 days after the injection of mercury. The next highest concentrations usually occurred in the lungs, while heart, spleen, and brain contained only very small quantities. A high concentration of mercury was found in bone marrow after one hour, but this fell to below the detectable level later ; similarly, the concentrations in bone decreased, and only very small amounts of mercury were found in this site after 24 hours. Skin usually held a few per cent of the dose, but skeletal muscle contained only small quantities. The amount of mercury in the gastro-intestinal tract rose during the first few hours as excretion increased, then maintained a fairly steady concentration for a few days. Very small amounts occurred in the stomach, but the stomach contents usually showed a much higher concentration of mercury, perhaps because of the excretion of the metal in the saliva. After 24 hours the small intestine, caecum, and colon contained small and similar concentrations, but again higher concentrations of mercury were generally found in the respective contents. A high concentration was found in the bile after one hour, but thereafter the quantities of mercury in this fluid were below the level of detection.

About 4 per cent of the dose was excreted in the urine within an hour, but this rate slowed considerably, and after 24 hours the urine contained 6–15 per cent

TABLE I

The concentrations and the percentages of the dose of mercury in the tissues of rabbits after the intravenous injection of 5 μM/kg. of mercuric chloride

Time after injecting mercury:	1 hr.		6 hr.		24 hr.						5 days		14 days	
Rabbit No.:	367 ♂		371 ♂		361 ♀		365 ♂		369 ♂		363 ♂		359 ♂	
Weight, kg.:	1.50		1.55		2.55		1.80		1.33		1.87		2.25	
	μg. Hg/g. tissue	% of dose	μg. Hg/g. tissue	% of dose	μg. Hg/g. tissue	% of dose	μg. Hg/g. tissue	% of dose	μg. Hg/g. tissue	% of dose	μg. Hg/g. tissue	% of dose	μg. Hg/g. tissue	% of dose
Plasma	0.97	3.5	<0.24	<1.7	<0.04	<0.2	<0.09	<0.3	0.26	1.4	<0.11	<0.3	<0.06	<0.3
Blood cells	0.12	0.4	<0.33	<1.7	0.66	1.3	<0.11	<0.3	<0.30	<0.5	<0.09	<0.3	<0.09	<0.3
Lungs	0.76	0.4	1.63	0.5	0.46	0.2	0.49	0.2	2.10	1.0	1.23	0.6	<0.04	<0.02
Heart	<0.12	<0.03	<0.52	<0.08	<0.04	<0.01	0.03	0.01	<0.20	<0.05	—	—	—	—
Stomach	<0.02	<0.03	<0.08	<0.08	0.10	0.1	<0.02	<0.03	0.30	0.4	0.04	0.02	0.29	0.3
,, contents	<0.03	<0.11	0.20	0.6	0.41	1.2	0.85	3.2	1.10	4.6	0.97	2.1	0.18	1.2
Small intestine	0.08	0.2	1.18	1.9	0.29	0.6	0.51	1.0	0.61	1.6	0.40	0.1	0.35	0.4
,, contents	<0.01	<0.03	1.04	0.6	0.34	0.7	0.53	0.5	1.09	0.8	0.16	0.1	<0.02	<0.02
Caecum	—	—	—	—	0.65	0.6	0.43	0.4	0.67	0.9	0.88	0.7	—	—
,, contents	—	—	—	—	<0.04	<0.1	0.89	3.2	<0.11	<0.6	2.22	5.1	—	—
Colon	—	—	0.29	0.1	0.20	0.1	0.36	0.2	0.66	0.4	<0.09	<0.02	<0.03	<0.02
,, contents	<0.03	<0.03	0.57	0.3	1.08	0.7	1.81	0.5	<0.23	<0.1	1.85	0.5	0.05	0.04
Kidneys	35.62	22.6	47.75	20.6	28.31	19.8	23.06	13.2	31.92	22.3	17.41	18.4	15.36	10.2
Liver	1.84	7.3	2.91	10.6	0.76	2.9	2.03	6.3	2.90	9.2	1.96	4.3	1.84	5.3
Bile	10.32	—	<2.01	—	<0.34	—	<1.71	—	—	—	<0.45	—	<0.81	—
Spleen	<0.80	<0.03	<1.22	<0.08	1.35	0.04	<0.65	<0.03	<0.16	<0.05	<1.01	<0.06	<0.33	<0.02
Skin	0.92	11.1	0.32	3.9	1.25	15.1	0.10	1.2	0.51	6.2	0.24	2.9	0.22	2.6
Brain	<0.05	<0.03	—	—	<0.03	<0.01	<0.05	<0.03	<0.13	<0.08	—	—	—	—
Bone marrow	2.58	5.2	<1.18	<2.3	<0.24	<0.5	<0.36	<0.7	<0.51	<1.0	<0.45	<0.9	<0.13	<0.3
Skull vault	—	—	—	—	<0.14		<0.31		<0.28		<0.21		<0.17	
Epiphyses	0.50	2.9	0.42	1.5	0.11	0.2	<0.05	<0.5	<0.09	<1.1	<0.05	0.7	<0.03	<0.2
Diaphyses	0.45		<0.23		0.13		<0.09		<0.20		0.32		<0.05	
Skeletal muscle	<0.04	<2.0	0.13	6.8	<0.03	<1.7	0.12	6.6	<0.07	<3.9	<0.04	<2.4	<0.03	<1.9
Excreted, urine	—	3.9	—	7.6	—	5.9	—	12.4	—	15.1	—	33.0	—	38.6
,, faeces	—	—	—	—	—	1.0	—	1.1	—	0.6	—	8.5	—	26.7
Injection site	—	18.8	—	26.2	—	36.4	—	32.4	—	16.6	—	3.3	—	7.8
Total accounted		76.3%		81.2%		85.8%		82.4%		81.1%		80.3%		93.1%

of the dose or 8–18 per cent of the mercury absorbed. Only about two-fifths of the dose was excreted in the urine in 14 days. About 1 per cent of the dose was found in the faeces after 24 hours, but this rate of excretion increased and nearly 27 per cent was excreted in this way in 14 days.

The results obtained from animals treated with dimercaprol are shown in Table II. The doses of dimercaprol, and the times after the injection of mercury at which they were given, are set out in this Table. The concentrations of mercury found in most of the tissues investigated were not significantly different from those occurring in the tissues of the control animals. The concentrations of mercury in the kidneys, however, fell profoundly after treatment. After 24 hours, these organs contained 1–5 per cent of the dose of mercury as compared with 13–22 per cent in the control rabbits. This loss of mercury was paralleled by a greatly increased excretion of mercury in the urine. These actions of dimercaprol were found, though on a smaller scale, when treatment was delayed until nine days after the administration of mercury. The two rabbits killed after five days showed similar amounts of mercury in the urine, but it should be noted that the rabbit (No. 364) treated with dimercaprol retained about 30 per cent of the dose at the site of injection. When dimercaprol was administered three days after the mercury, an increase occurred in the concentration of mercury in the urine, as shown in Fig. 1. Treatment begun nine days after the mercury had a similar effect, but this disappeared rapidly in spite of continued treatment (Fig. 2).

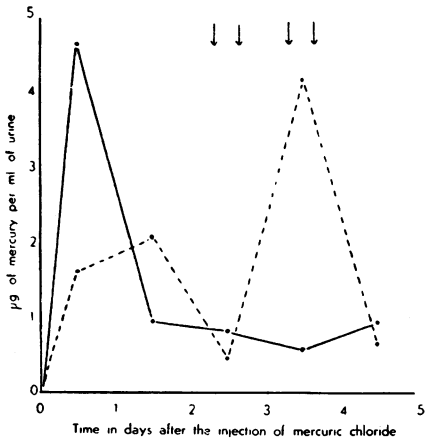

FIG. 1.—The concentrations of mercury found in samples of urine after the intravenous injection of 5 μM/kg. of mercuric chloride. Each arrow represents the injection of propylene glycol or of 25 mg./kg. of dimercaprol. ●———● Rabbit 363 (control). ● - - - - ● Rabbit 364 (treated with dimercaprol).

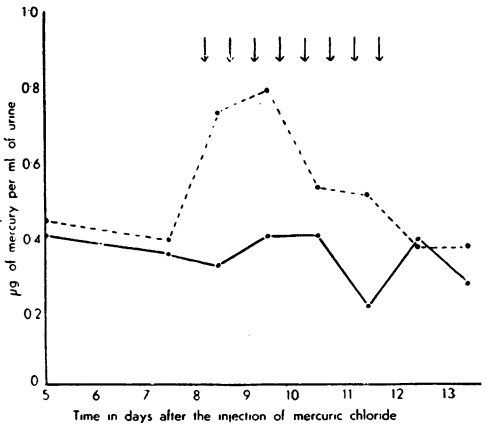

FIG. 2.—The concentrations of mercury found in samples of urine after the intravenous injection of 5 μM/kg. of mercuric chloride. Each arrow represents the injection of propylene glycol or of 12.5 mg./kg. of dimercaprol. ●———● Rabbit 359 (control). ● - - - - ● Rabbit 360 (treated witn dimercaprol).

TABLE II

The concentrations and the percentages of the dose of mercury found in the tissues of rabbits after the intravenous injection of 5 μM/kg. of mercuric chloride, and subsequent treatment with dimercaprol. (50 mg. dimercaprol = 0.4 mM, approximately)

Time after injecting mercury:	1 hr.		6 hr.		24 hr.				5 days		14 days	
Treatment with dimercaprol:	50 mg./kg. immediately		50 mg./kg. at 1 hr., 12.5 mg. kg. at 5 hr.		50 mg./kg. at 1 hr., 12.5 mg./kg. at 5 hr.		50 mg./kg. at 19 hr., and 12.5 mg./kg. at 23 hr.		25 mg./kg. twice daily on days 3 and 4		12.5 mg./kg. twice daily on days 9–12 and once on day 13	
Rabbit No.: Weight, kg.:	368 ♂ 1.40		372 ♀ 1.86		370 ♀ 2.05		362 ♂ 1.72		366 ♂ 2.37		364 ♂ 1.78		360 ♂ 1.54	
	μg. Hg/g. tissue	% of dose	μg. Hg/g tissue	% of dose	μg. Hg/g. tissue	% of dose	μg. Hg/g. tissue	% of dose	μg. Hg/g. tissue	% of dose	μg. Hg/g. tissue	% of dose	μg. Hg/g. tissue	% of dose
Plasma	1.66	7.1	<0.19	<0.9	<0.10	<0.5	<0.07	<0.3	<0.13	<0.5	<0.08	<0.3	<0.06	<0.3
Blood cells	2.82	7.8	1.24	2.8	2.42	5.8	<0.07	<0.3	<0.15	<0.5	<0.10	<0.3	<0.11	<0.3
Lungs	2.41	0.9	<0.18	<0.07	<0.08	<0.03	<0.04	<0.02	0.53	0.2	<0.06	<0.02	<0.05	<0.02
Heart	0.34	0.07	<0.27	<0.07	<0.14	<0.03	<0.06	<0.02	<0.08	<0.02	—	—	—	—
Stomach	0.71	0.8	0.20	0.2	<0.03	<0.03	0.16	0.2	<0.03	<0.02	<0.03	<0.02	<0.06	<0.06
,, contents	0.26	1.4	<0.11	<0.4	0.49	2.8	<0.01	<0.05	0.34	0.7	0.22	0.9	<0.02	<0.2
Small intestine	1.43	2.9	0.95	1.6	0.12	0.2	0.24	0.6	0.17	0.2	0.21	0.3	0.38	0.5
,, ,, contents	2.65	4.1	<0.12	<0.07	0.96	0.5	1.02	0.8	<0.04	<0.02	0.13	0.2	0.21	0.3
Caecum	—	—	—	—	<0.36	<0.4	<0.01	<0.02	<0.03	<0.02	0.01	0.01	—	—
,, contents	—	—	—	—	<0.12	<0.6	0.46	2.0	0.59	1.7	0.13	0.6	—	—
Colon	0.64	0.3	0.58	0.3	<0.07	<0.03	<0.02	<0.02	<0.06	<0.02	<0.07	<0.02	<0.03	<0.02
,, contents	<0.05	<0.03	0.61	0.2	<0.06	<0.06	0.26	0.3	1.00	0.06	0.16	0.1	0.07	0.06
Kidneys	8.79	5.8	1.83	1.4	6.65	4.6	3.30	2.5	1.78	1.0	1.95	1.5	1.43	1.2
Liver	1.11	3.3	1.19	3.9	1.23	4.7	0.41	2.0	0.64	2.1	0.50	1.4	1.13	3.3
Bile	2.30	—	<2.22	—	1.51	—	<1.36	—	<0.85	—	<1.33	—	—	—
Spleen	<0.81	<0.03	<1.64	<0.07	2.99	0.3	<0.64	<0.04	<0.83	<0.02	<0.40	<0.06	<0.42	<0.03
Skin	0.52	6.3	<0.29	<3.4	<0.15	<1.8	<0.04	<0.5	0.33	4.0	<0.09	<0.11	0.05	0.7
Brain	<0.07	<0.03	—	—	<0.09	<0.03	<0.03	<0·02	<0.06	<0.02	—	—	—	—
Bone marrow	<0.30	<0.6	<0.63	<1.2	<0.45	<0.9	<0.35	<0.7	<0.32	<0.6	<0.32	<0.6	<0.20	<0.4
Skull vault	—	—	—	—	<0.46		<0.21		<0.27		<0.30		—	—
Epiphyses	<0.05	<0.4	<0.18	<1.2	<0.09	<0.9	0.03	0.05	<0.04	0.8	<0.06	<0.6	<0.05	<0.3
Diaphyses	<0.09		<0.22		<0.12		<0.06		0.37		<0.08		<0.06	
Skeletal muscle	0.32	16.7	0.50	26.3	<0.07	<3.9	0.08	4.4	0.11	5.6	0.07	3.9	0.18	9.4
Excreted, urine	—	12.8	—	34.1	—	56.1	—	32.1	—	33.8	—	34.2	—	45.7
,, faeces	—	—	—	—	—	0.7	—	3.7	—	0.9	—	4.2	—	22.9
Injection site	—	11.7	—	19.2	—	10.6	—	32.4	—	36.2	—	29.6	—	5.6
Total accounted		82.0%		90.0%		86.7%		81.0%		87.3%		76.9%		89.7%

The results of treatment with dimercaprol glucoside are presented in Table III. Considerable differences from the actions of dimercaprol were found. The mercury content of the plasma was consistently raised, and in rabbits, Nos. 400 and 402, the content of the blood cells was also increased. Large increases in the concentration of mercury in the bile occurred, but the amounts of mercury contained in the small intestine, colon, and their contents were generally similar to those found in untreated animals. No definite change in the concentration of mercury in the liver was observed, but the mercury content of the kidneys was diminished to an extent

TABLE III

The concentrations and the percentages of the dose of mercury found in the tissues of rabbits after the intravenous injection of 5 μM/kg. of mercuric chloride, and subsequent treatment with dimercaprol glucoside. (175 mg. dimercaprol glucoside = 0.6 mM, approximately)

Time after injecting mercury:	1 hr.		24 hr.							
Treatment with dimercaprol glucoside:	175 mg./kg. immediately		175 mg./kg. at 1 hr., and 55 mg./kg. at 5 hr.				175 mg./kg. at 19 hr., and 55 mg./kg. at 23 hr.			
Rabbit No.:	410 ♂		400 ♀		402 ♀		406 ♀		401 ♀	
Weight, kg.:	1.85		1.75		1.75		1.75		1.72	
	μg. Hg/g. tissue	% of dose	μg. Hg/g. tissue	% of dose	μg. Hg/g. tissue	% of dose	μg. Hg/g. tissue	% of dose	μg. Hg/g. tissue	% of dose
Plasma	3.67	12.8	1.64	6.7	1.25	4.8	2.02	8.5	1.07	4.5
Blood cells	<0.23	<0.8	2.57	7.5	5.35	16.7	<0.07	<0.2	0.90	2.5
Lungs	1.66	0.7	0.87	0.3	1.63	0.5	0.53	0.2	1.30	0.6
Small intestine	—	—	<0.01	<0.02	1.12	1.9	—	—	0.69	1.5
,, ,, contents	—	—	1.10	0.5	1.25	0.4	—	—	1.37	0.4
Colon	—	—	0.66	0.3	1.14	0.5	0.75	0.4	0.80	0.4
,, contents	—	—	1.84	1.3	7.30	1.1	0.55	0.1	—	—
Kidneys	3.32	2.2	4.76	2.8	6.25	4.7	1.93	1.5	4.82	3.9
Liver	4.72	13.3	2.27	8.3	2.48	7.3	1.58	6.1	1.46	5.6
Bile	3.59	—	6.29	—	2.56	—	6.19	—	14.62	—
Skin	1.42	17.0	0.66	11.4	1.80	21.6	0.47	8.8	—	—
Skeletal muscle	<0.07	<3.9	0.08	4.9	<0.02	<1.3	0.05	3.5	0.09	6.9
Excreted, urine	—	17.4	—	24.5	—	20.2	—	29.2	—	20.6
,, faeces	—	—	—	2.5	—	1.5	—	0.2	—	0.9
Injection site	—	8.1	—	0.5	—	1.8	—	15.3	—	23.8
Total accounted		71.5%		71.5%		83.0%		73.8%		71.6%

similar to that occurring in dimercaprol-treated animals. The urinary excretion of mercury was increased, though to a smaller extent than by dimercaprol. Two additional rabbits (not shown in the Table) were treated with 175 mg./kg. of the glucoside at one hour, and with 55 mg./kg. at five hours, after the injection of mercury: these animals excreted 32.5 and 42.2 per cent of the dose in the urine in 24 hours. At the same time, another rabbit was treated with 50 mg./kg. of dimercaprol at one hour, and 12.5 mg./kg. at five hours, after the injection of mercury ; this animal excreted 56.9 per cent of the dose in its urine during 24 hours. The mean quantities of mercury excreted in the urine in 24 hours, calculated as percentages of the mercury absorbed, were for the control animals 14 per cent, for

the animals treated with dimercaprol 53 per cent, and for those treated with dimercaprol glucoside 30 per cent. All these differences were significant ($P<0.01$).

A summary of the mean percentages of the absorbed mercury found in various tissues after 24 hours, for the three groups of animals, is given in Table IV. The results thus presented tend to be over-simplified, but this may be justified by the more immediate comprehensibility of the data.

TABLE IV

Summary table of the distribution of mercury in rabbits, without and with treatment with dimercaprol or dimercaprol glucoside. The figures given are the mean percentages of the absorbed mercury found in each group of tissues twenty-four hours after the intravenous administration of 5 μM/kg. of mercuric chloride. Details of treatment are as shown in Tables I, II, and III

Treatment:	None	Dimercaprol	Dimercaprol glucoside
No. of rabbits:	3	3	4
Blood	1.2	2.1	13.7
Small intestine plus contents, Colon plus contents, Faeces	4.6	3.7	4.1
Kidneys	25.8	3.5	3.6
Liver	8.0	3.8	7.5
Skin, Skeletal muscle	14.2	7.2	19.0
Urine	15.1	54.1	26.5

DISCUSSION

The literature describing the distribution of mercury in animals is small in quantity and meagre in information. Very small amounts of the soluble inorganic compounds of mercury kill animals within a short period of time, and hence a sensitive analytical method is necessary for such studies.

The results obtained in the present investigations are in accord with those found by Lomholt (1924) after intramuscular injection of various compounds of mercury into rabbits ; and with those obtained by Sollmann and Schreiber (1936) by analysis of the tissues of human cadavers after death from mercuric chloride poisoning. They are not consistent with the observations of Young, Taylor, and Merritt (1930) who reported that considerable amounts of mercury were deposited in the bones of rabbits. The paucity of the latter authors' data prevents any attempt to explain this discrepancy.

The striking decreases in the concentrations of mercury in the kidneys which occurred after treatment with dimercaprol have also been reported recently by Fitzsimmons and Kozelka (1950), using rats and Rhesus monkeys. These authors state that the mercury content of other tissues was raised after dimercaprol, but they do not give any details. They also found that rats excreted more mercury in the urine after treatment with dimercaprol, but that the faecal excretion was unchanged. This increased urinary excretion of mercury was found in the present work, and it occurred even when treatment was delayed until nine days after the administration of mercuric chloride. Evidence was also obtained that the increase in the excretion of mercury was transient in spite of continued treatment with dimercaprol.

The decreased amounts of mercury in the kidneys after treatment correspond with the diminished renal injuries noted in rabbits by Ginzler (1946) and by Gilman *et al.* (1946). These authors found that delay in treatment greatly decreased the protection of the kidneys by dimercaprol. It should be noted that the quantities of mercury in the kidneys are still diminished by treatment begun several days after poisoning.

Continued treatment did not maintain a supra-normal excretion of mercury, although a considerable amount of the metal remained in the body. This may be due to part of the mercury being bound more firmly to tissue constituents; or, conceivably, to an increasing ability of the body to detoxicate dimercaprol, but so far no evidence in favour of this is known.

The results reported here support to some extent the hypothesis of an extracellular distribution of dimercaprol glucoside (Danielli, Danielli, Fraser, Mitchell, Owen, and Shaw, 1947). The mercury level in the plasma was consistently raised after treatment with the glucoside, but not after dimercaprol therapy. Considering the size of the dose, and the water-solubility, of dimercaprol glucoside, it is surprising that the excretion of mercury in the urine after treatment with this substance was less than that obtained after dimercaprol therapy. It should be noted that when the glucoside was administered immediately after the mercuric chloride, the quantity of metal in the urine after one hour was similar to that obtained after dimercaprol treatment at a corresponding time. Possibly some type of renal damage occurs within an hour after the administration of mercury, and can be alleviated by treatment with dimercaprol, but not with dimercaprol glucoside. Nevertheless, Gilman *et al.* (1946) found dimercaprol glucoside to be as effective an antidote in mercury poisoning as dimercaprol, in equimolecular doses. As even larger doses of mercury were administered in their experiments, it must be assumed that the mercury retained in the plasma by dimercaprol glucoside is as effectively non-toxic as if it had been excreted in the urine. Possibly this plasma mercury would have been found to diminish, and the metal excreted in the urine increased, had the observations been prolonged beyond 24 hours. In any case, the plasma mercury was maintained at a considerably higher level than that found in the control animals, suggesting either that the dithiol-mercury complex was attached to plasma proteins or that the renal tubules tended to reabsorb it.

Summary

1. Studies have been made of the distribution and excretion of mercury, using a radioactive isotope, in rabbits, without and with treatment with dimercaprol or dimercaprol glucoside.

2. After the intravenous injection of 5 μM/kg. of mercuric chloride, the highest concentrations of mercury were found in the kidneys. Of the other tissues sampled, only the liver contained more than 1 μg. Hg per g. consistently. The excretion of mercury was slow and accounted for only two-thirds of the dose after two weeks, occurring mainly in the urine.

3. After treatment with dimercaprol, much smaller amounts of mercury were found in the kidneys. The excretion of mercury in the urine was greatly enhanced, but the faecal excretion was unaffected. These changes were found even when treatment was delayed until nine days after poisoning.

4. Similar changes occurred after the administration of dimercaprol glucoside, except that the concentrations of mercury in the plasma, and the biliary excretion, increased. The urinary excretion of mercury was less than that obtained after treatment with dimercaprol.

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