Elimination Pattern of Methyl Mercury From Blood and Brain of Rats (Dams and Offspring) after Delivery, Following Oral Administration of Its Chloride Salt During Gestation

by JAMES L. CASTERLINE, JR. and CLARA H. WILLIAMS*
Bureau of Foods
Food and Drug Administration
U.S. Department of Health, Education, and Welfare
Washington, D.C. 20204

Methyl mercury has become widely dispersed in the environment. This has become a problem since inorganic mercury from industrial and agricultural chemical wastes is converted into organic mercury by microorganisms in fresh and marine waters (1). The organic compound eventually finds its way into food and thence into humans and animals. There are considerable differences in distribution patterns of this compound among different species, but sensitivity to methyl mercury is more pronounced in the fetal stage of brain development (2). Methyl mercury has been shown to cause irreversible neurological damage (3), and there is little information on the biotransmission of mercury to the unborn infant. The present study was undertaken to determine the pattern by which methyl mercury is eliminated from the blood and brains of dams and young rats following delivery, after administration of methyl mercury chloride to the dams during the period of organogenesis.

Method and Materials

Three groups of pregnant Charles River rats were given oral doses of methyl mercury chloride (in corn oil) at 0.1, 0.5, or 2.5 mg/kg daily from day 6 through day 15 of gestation. Another group of pregnant rats was given only corn oil. Each rat was caged individually and fed ad libitum. The dams were allowed to litter normally and the young were weaned at 28 days. Three dams and 10 female offspring of each group were killed at intervals of 30, 60, and 90 days after birth of the offspring. Sex difference was not studied; the male offspring were separated at weaning and used in neurological experiments. In a second experiment, only the 2.5 mg/kg dose was used; 5 dams and 20 offspring were killed at each of days 6, 13, and 20 after delivery. The offspring in this group of rats were still nursing.

Rats were killed by decapitation and blood was collected in heparinized tubes and centrifuged. Brains were removed and stored along with red blood cells and plasma at -30°C until assayed. Depending upon concentrations of methyl mercury, 0.5 to 6 g of these samples were used for analysis. In some cases where methyl mercury content was low or where the amount of sample was not large enough, pooling was necessary; this resulted in too few test samples for significance statistics.

*Present address: Office of Pesticides, Pesticides Tolerances Division, Environmental Protection Agency, Washington, D.C. 21250

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Methyl mercury was extracted into benzene and determined by the gas-liquid chromatographic methods of Westöö (4) and Kamps and McMahon (5) with a Barber-Colman Model 5360 gas-liquid chromatograph. A 10-coil glass column, 6' x 4 mm, was filled with Chromosorb W(HP) as the solid support and the liquid phase, 5% HIEFF-10B (Applied Science Laboratories, State College, Pa.), was used as recommended. The temperature was set at 170°C for the column and the flow rate of carrier gas, N_2, was 120 ml/min. The injector and detector (electron-capture, tritium foil) were heated to 200°C. Sensitivity and voltage were set so that 1.6 ng of a methyl mercury chloride standard caused approximately 80% full scale deflection.

Results and Discussion

No overt toxic signs were noted at any time in either the dams or their offspring, except for a slight but statistically significant ($P \leq 0.05$) growth retardation only in the young that were the offspring of dams given 2.5 mg/kg and maintained until the 60 and 90 day sacrifice period. At the end of 60 days, the affected offspring weighed 130 $\pm$ 1.9 g, whereas the control offspring weighed 160 $\pm$ 4.9 g. At the end of 90 days, affected rats weighed 152 $\pm$ 1.7 g while the controls weighed 183 $\pm$ 2.3 g.

The data (Table 1) indicate that the orally administered methyl mercury chloride in the mother rats had been transferred to the young. Whether this transfer was placental or through the mother's milk after birth has not been determined. Analysis of samples revealed that the storage of methyl mercury was highest in the red blood cells, less high in the brain, and of a very low order in the plasma. In the dams there was a steady decrease with time of the methyl mercury content. In Experiment 1, at 90 days after delivery, the methyl mercury level in the red blood cells of adult rats given the 2.5 mg/kg dose had decreased to 0.4 ppm from the 5.4 ppm level present at 30 days; similarly, in Experiment 2, it had decreased to 8.8 ppm at 20 days from the 60 ppm level present at 6 days. At 20 days the methyl mercury had disappeared from the plasma and at 60 days it had cleared from the brain. At the lower doses the amount of methyl mercury was proportionally lower. At 6 days after delivery, the methyl mercury content in the offspring was equal to that in the red blood cells, brain, and plasma of the dams. The clearance rates of methyl mercury, however, were more rapid in the young than in the dams in both the blood components and brain, possibly due to growth factors. This lessened ability of young rats to retain methyl mercury may reflect a lower capacity to bind this compound.

TABLE 1

Blood and Brain Methyl Mercury Levels[a] in Rats After Methyl Mercury Chloride Exposure

Source	Methyl Mercury Chloride (mg/kg)[b]	Days After Delivery: Experiment 2 — 6	13	20	Experiment 1 — 30	60	90
				Mother			
RBC	2.5*	59.91 ± 8.98	23.50 ± 3.23	8.80 ± 0.36	5.40 ± 0.53	1.64[c]	0.41[c]
	0.5				0.88	0.25[c]	0.10[c]
	0.1				0.06[c]	0.09[c]	
Plasma	2.5*	0.31 ± 0.05	0.13 ± 0.03	0.04 ± 0.004	trace[c]		
Brain	2.5*	5.41 ± 0.95	2.21 ± 0.19	0.99 ± 0.01	0.34[c]	0.07[c]	trace[c]
	0.5				0.09[c]	trace[c]	
				Offspring			
RBC	2.5*	59.73 ± 0.95	11.03 ± 0.88	2.28 ± 0.20	0.51 ± 0.05	0.11 ± 0.00	trace[c]
	0.5				0.10[c]	0.04[c]	
	0.1				0.03[c]		
Plasma	2.5	0.27[c]	0.06[c]	trace[c]			
Brain	2.5*	4.74 ± 0.23	1.20 ± 0.03	0.31 ± 0.03	0.04 ± 0.00	trace[c]	
	0.5				trace[c]	not detectable	

[a] Values are expressed as ppm ± standard error of the mean of 3 or 5 mother rats and 10 or 20 offspring rats (see text). Asterisks indicate that the change in methyl mercury content with the time was significant when tested by the Student's *t* test at the 2% level of significance for difference between two means.

[b] Pregnant rats were orally given methyl mercury chloride daily from days 6 to 15 of gestation. Samples were removed from mother and offspring rats after delivery.

[c] Samples were pooled.

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