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Strain Differences in Excretion of Methylmercury in Mice

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Marked strain differences were found in the distribution and biological half-time of methylmercury (MeHg) in various strains of mice (Doi and Kobayashi 1982). The strain difference in MeHg distribution in the blood was explained clearly by the difference in the molecular structure and chemical affinity of hemoglobins for MeHg (Doi and Tagawa 1983;Doi et al. 1983). Strain difference in the biological half-time, however, could not be explained by these chemical properties of hemoglobins.

In the present study, excretion of MeHg was examined with 3 strains of mice under a supposition that the strain difference in MeHg excretion was one of the important causes of the strain difference in biological half time of MeHg in mice.

MATERIALS AND METHODS

Male mice of 2 inbred strains, C3H/HeN and C57BL/6N, and 1 random-bred strain, ICR, were used in the experiment at the 6th week after birth. These mice were supplied by Charles River Tokyo, Inc. at the 5th week after birth and were kept in the Animal Experiment Center of Asahikawa Medical College before use. Each mouse was kept in a specially made separate cage of 7 x 18 x 10 (H) cm and open bottom which was covered with a sheet of filter paper and a sheet of stainless steel wire netting on it.

Feces and urine of mouse were discharged on the filter paper. Evaporation of MeHg was minimized by spraying 0.4% solution of dithizone in chloroform on the paper. Ten mice of each strain were injected ip with ^{203}Hg-CH_3HgCl (20 μCi/mg Hg) at a dose of 1 mg CH_3HgCl/kg. Radioactivity in feces and urine was measured individu-

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ally every day with LKB Wallac 1280 Ultrogamma. Radioactivity in urine was estimated by measuring levels in the filter paper.

Methylmercury content in feces and urine was determined by benzene extraction from feces and urine which were acidified with HCl and by measuring the radioactivity in the benzene extracts.

RESULTS AND DISCUSSION

Fecal excretion of ^{203}Hg from the mice after a single ip injection of ^{203}Hg-CH_3HgCl is shown in Fig. 1-A. C3H mice excreted the largest amount of ^{203}Hg through feces as compared to the other 2 strains. The amount of ^{203}Hg excreted into feces was approximately 43% of total amount of administered dose in C3H, 37% in C57BL and 28% in ICR by the 20th day after MeHg injection.

Urinary excretion of ^{203}Hg is shown in Fig. 1-B. ICR mice excreted the largest amount of ^{203}Hg through urine as compared to other strains. Total amount of ^{203}Hg excreted in urine was approximately 46% in ICR, 26% in C3H and 29% in C57BL by the 20th day after MeHg injection. The amount of ^{203}Hg excreted into the urine was nearly twice the amount in the feces of ICR, while that into the feces of ICR was considerably lower than that in the feces of the other 2 strains.

Whole body retention and whole body half-time of ^{203}Hg in the mice are shown in Fig. 1-C. ICR mice excreted approximately 74% of the administered dose of ^{203}Hg within 20 days of MeHg administration, 69% in C3H and 66% in C57BL. These results were proportional to the results obtained in the previous study (Doi and Kobayashi 1982).

The chemical form of the mercury was largely inorganic in feces excreted from 1 to 7 days after MeHg administration and mostly organic in urine during the same period as shown in Table 1. The proportion of organic form decreased in both feces and urine in the course of time.

Excretion of MeHg has been investigated extensively with various species of animals including human volunteers. Feces was the predominant route of excretion of mercury after MeHg administration in rats (Friberg 1959 Norseth and Clarkson 1971;Cikrt and Tichy 1974), mice (Östlund 1969), cats (Hollins et al. 1975), pigs (Gyrd-Hansen 1981), Squirrel monkey (Berlin et al. 1975) and man (Aberg et al. 1969;Miettinen et al. 1971).

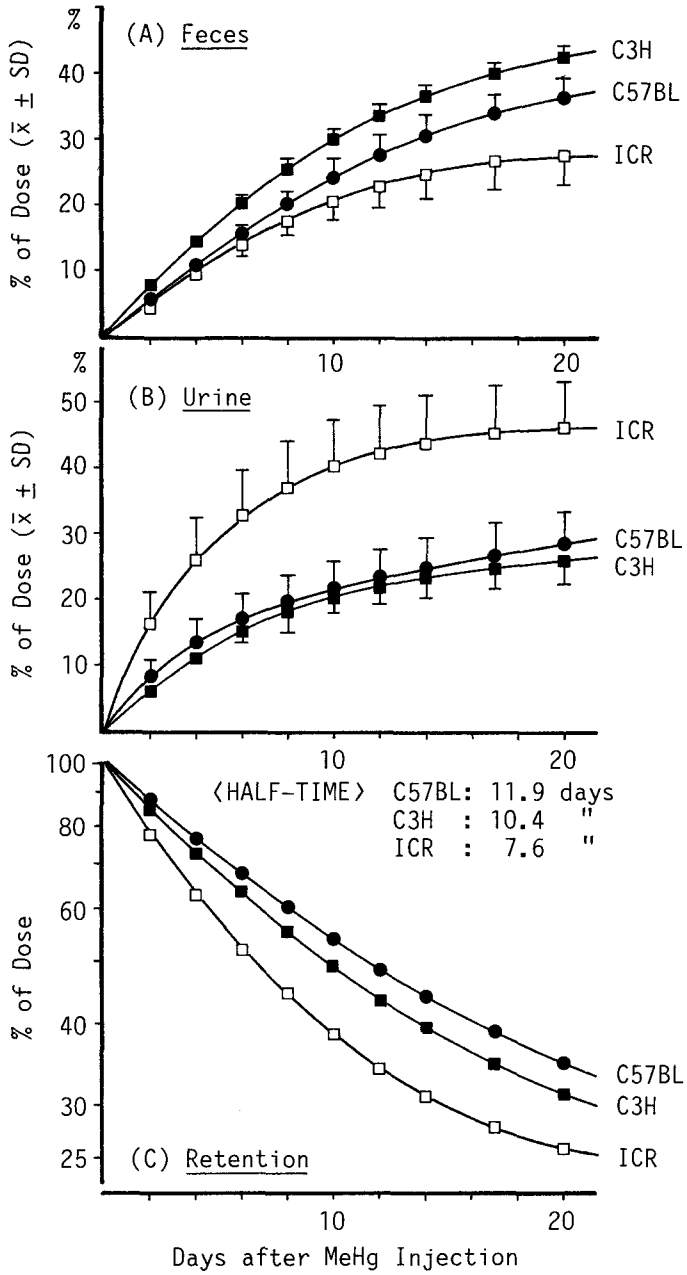

Figure 1. Excretion of ^{203}Hg via feces (A) and via urine (B), and whole body retention of ^{203}Hg in mice (C) after a single ip injection of ^{203}Hg-CH_3HgCl at a dose of 1 mg/kg.

Table 1. Proportion of Organic/Total Mercury in the Feces or Urine of Mice after a Single ip Injection of MeHg (%)*

Strain	Days after MeHg Injection					
	1	4	7	1	4	7
	Feces			Urine		
C3H	35.5	22.9	24.5	90.2	89.3	77.8
C57BL	47.0	32.1	29.4	94.3	88.8	80.3
ICR	47.5	14.0	10.6	95.5	83.3	75.6

*: Benzene extraction of organic mercury was carried out with the feces or urine collected from 3 mice of each strain.

In the present study, inbred mice of the C3H and C57BL strains excreted mercury predominantly into feces rather than urine, though random-bred mice of ICR strain excreted nearly twice as much mercury into urine as into feces. Similar results had been obtained using 2 strains of inbred mice, CBA/J and CFW (Kostyniak 1980). Following single non-toxic dose of ^{203}Hg-CH_3HgCl the urinary excretion rate of ^{203}Hg was 5-fold higher in CFW than in CBA/J, whereas fecal excretion rate was the same for both strains.

It is well known that the urinary excretion of mercury is enhanced by coadministration of the chemicals containing sulfhydryl groups such as mercaptodextran and N-acetylhomocysteine to mice (Aaseth and Norseth 1974) dimercaptosuccinic acid to rats and mice (Magos 1976) and sodium-2,3-dimercaptopropane-1-sulfonate to rats (Gabard 1976). ICR strain used in the present study and CFW in Kostyniak's study were considered to be the extraordinary strains that excrete the largest part of mercury in the body through urine after MeHg administration without coadministration of any thiol-containing chemicals, though the causes were not revealed by either of the present author and Kostyniak (1980).

The short half-time of mercury in the organs of ICR (Doi and Kobayashi 1982) and CFW (Kostyniak 1980) might result from the large urinary excretion of mercury.

The chemical form of mercury in feces was inorganic in nearly half of total mercury content in rats (Norseth and Clarkson 1970;Magos and Butler 1976) and in mice (Norseth 1971), while it was mostly organic in urine. In the present study, more than half of the total mer-

cury was inorganic in the feces of all strains of mice, though the proportion of inorganic form to total mercury was a little larger in the present study than that reported previously (Norseth 1971). This difference in the proportion of inorganic to total mercury might be caused by various factors including the liver and kidney functions, demethylation of methylmercury by intestinal flora and experimental conditions. In the present study, most part of the total mercury in the urine was also organic.

Further studies on the strain differences of mice in distribution and excretion of methylmercury will bring much informations on the metabolis of methylmercury in animals.

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REFERENCES

Aaseth J, Norseth T (1974) The effect of mercaptodextran and N-acetylhomocysteine on the excretion of mercury in mice after exposure to methyl mercury chloride. Acta Pharmacol Toxicol 35:23-32

Aberg B, Ekman L, Falk R, Greitz U, Persson G, Snihs J-O (1969) Metabolism of methyl mercury (^{203}Hg) compounds in man. Arch Environ Health 19:478-484

Berlin M, Carlson J, Norseth T (1975) Dose-dependence of methylmercury metabolism. Arch Environ Health 30: 307-313

Cikrt M, Tichy M (1974) Biliary excretion of phenyl and methyl mercury chlorides and their enterohepatic circulation in rats. Environ Res 8:71-81

Doi R, Kobayashi T (1982) Organ distribution and biological half-time of methylmercury in four strains of mice. Japan J Exp Med 52:307-314

Doi R, Tagawa M (1983) A study on the biochemical and biological behavior of methylmercury. Toxicol Appl Pharmacol 69:407-416

Doi R, Tagawa M, Tanaka H, Nakaya K (1983) Hereditary analysis of the strain difference of methylmercury distribution in mice. Toxicol Appl Pharmacol 69:400-406

Friberg L (1959) Studies on the metabolism of mercuric chloride and methyl mercury dicyandiamide. A.M.A. Arch Ind Health 20:42-49

Gabard B (1976) Improvement of oral chelation treatment of mercury poisoning in rats. Acta Pharmacol Toxicol 39:250-255

Gyrd-Hansen N (1981) Toxicokinetics of methyl mercury

in pigs. Arch Toxicol 48:173-181
Hollins JG, Willes RF, Bryce FR, Charbonneau SM, Munro IC (1975) The whole body retention and tissue distribution of ^{203}Hg methylmercury in adult cats. Toxicol Appl Pharmacol 33:438-449
Kostyniak PJ (1980) Differences in elimination rates of methylmercury between two genetic variant strains of mice. Toxicol Letters 6:405-415
Magos L (1976) The effects of dimercaptosuccinic acid on the excretion and distribution of mercury in rats and mice treated with mercuric chloride and methylmercury chloride. Br J Pharmacol 56:479-484
Magos L, Butler WH (1976) The kinetics of methylmercury administered repeatedly to rats. Arch Toxicol 35:25-39
Miettinen JK, Rahola T, Hattula T, Rissanen K, Tillander M (1971) Elimination of ^{203}Hg-methylmercury in man. Ann Clin Res 3:116-122
Norseth T (1971) Biotransformation of methyl mercuric salts in the mouse studied by specific determination of inorganic mercury. Acta Pharmacol Toxicol 29:375-384
Norseth T, Clarkson TW (1970) Studies on the biotransformation of ^{203}Hg-labeled methyl mercury chloride in rats. Arch Environ Health 21:717-727
Norseth T, Clarkson TW (1971) Intestinal transport of ^{203}Hg-labeled methyl mercury chloride. Arch Environ Health 22:568-577
Östlund K (1969) Studies on the metabolism of methyl mercury and dimethyl mercury in mice. Acta Pharmacol Toxicol 27(Suppl 1):1-132

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