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— **Minireview** —

Current Hair Mercury Levels in Japanese for Estimation of Methylmercury Exposure

Akira Yasutake,*[,a] Miyuki Matsumoto,[b] Masako Yamaguchi,[c] and Noriyuki Hachiya[d]

[a]Biochemistry Section, [b]Rehabilitation Section, Department of Clinical Medicine, [c]Survey Section, Department of Epidemiology, [d]Social Science Section, Department of International Affairs and Environmental Sciences, National Institute for Minamata Disease, 4058–18 Hama, Minamata, Kumamoto 867–0008, Japan

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Methylmercury (MeHg) is an environmental pollutant with neurotoxic effects on the central nervous system. The major exposure route of MeHg to humans is *via* consumption of fish and shellfish which accumulate the chemical through the food web in an aquatic environment. We have been conducting a survey on hair mercury contents among general populations from different districts to estimate the current Japanese MeHg exposure level. In Japan, a provisional regulatory standard of mercury and MeHg in fish and shellfish was determined in 1973 based on the assumption of a safe intake limit of 0.17 mg/person/week (0.48 μg/kg/day). On the other hand, the US EPA issued a revised reference dose based on a cohort study conducted in the Faroe Islands. Recently, a provisional tolerable weekly intake (PTWI) of MeHg was revised to 1.6 μg/kg/week in 61st Joint FAO/WHO Expert Committee on Food Additives (JECFA), which was about half that of the Japanese standard. The distribution of hair mercury levels in Japanese populations currently obtained from 10 districts indicated that 25% of the Japanese females of child-bearing age were estimated to be exposed to MeHg over the PTWI level. This would reflect the high Japanese consumption of marine products. Not only mercury contamination, but also the nutritional benefit may have to be considered when discussing the risk involved in the current level of fish and shellfish consumption in Japan.

Key words —— hair mercury, Japanese population, methylmercury exposure, provisional tolerable weekly intake, fish consumption

Methylmercury (MeHg) is formed by saprophyte microorganisms from inorganic mercury compounds in the aquatic environment.[1] It is accumulated in fish and shellfish through the marine food web. Since the MeHg accumulation increases with the food web, carnivorous fish such as tuna, swordfish and shark often exhibit high levels of mercury. Furthermore, due to the long biological half-life of MeHg, the chemical tends to accumulate throughout the life of fish.[2] Marine mammals such as whales and dolphins also show high concentrations of mercury. Accordingly, the major route of human exposure to MeHg is the ordinary consumption of fish and shellfish. MeHg is readily absorbed from the gastrointestinal tract and distributed among various tissues including the brain. The permeability of the chemical at the blood-brain barrier is responsible for its hazardousness neurotoxic effect.

A WHO report[3] concluded that the no observed adversary effect level (NOAEL) for adults is 50 μg/g of the hair mercury level based on the analytical data of MeHg pollution in the past. Since the developing nervous system of the fetus has been considered highly susceptible to the effect of MeHg,[4] the report also mentioned a possible association with an increased risk to the neurodevelopment of the fetus when maternal hair levels rise above 10 μg/g. Accordingly, recent studies on the health effects of MeHg have focused on the exposure risk to pregnant women and the neuropsychological outcomes in newborns.

In Japan, the provisional regulatory standards of mercury and MeHg in fish and shellfish were determined in 1973 to be 0.4 and 0.3 μg/g, respectively, based on the assumption of a safe intake limit of

*To whom correspondence should be addressed: Biochemistry Section, National Institute for Minamata Disease, 4058–18 Hama, Minamata, Kumamoto 867–0008, Japan. Tel.: +81-966-63-3111; Fax: +81-966-61-1145; E-mail: yasutake@nimd.go.jp

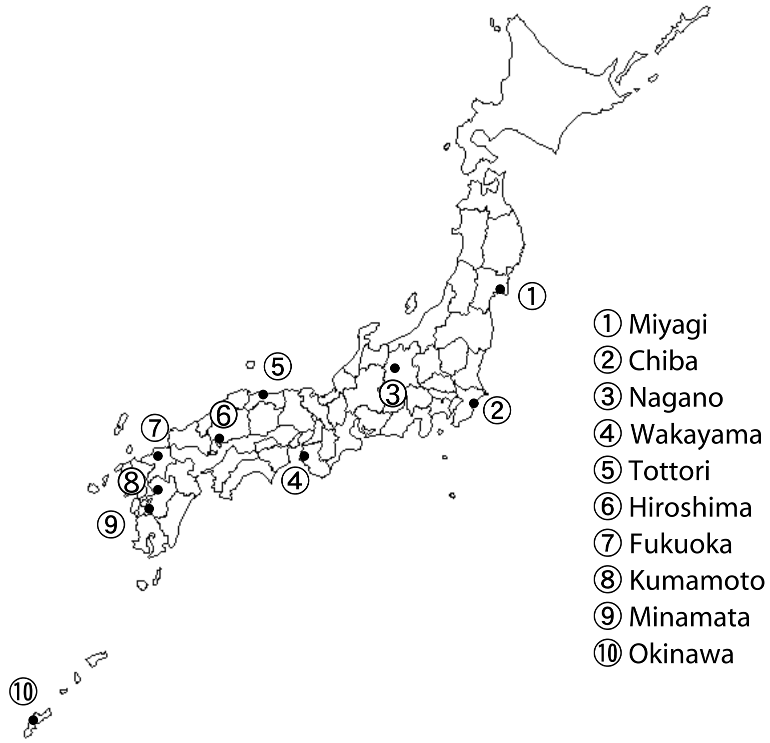

Fig. 1. Hair Sampling Locations

0.17 mg mercury/person/week (0.48 μg/kg bw/day). On the other hand, the revised reference dose (RfD) of the US Environmental Protection Agency (EPA)[5] set the safe exposure limit to MeHg of 0.1 μg mercury/kg bw/day in 1997. This RfD is aimed at the protection of the developing fetus from neurological deficits induced by MeHg in utero, and has been calculated as 1/10 of the benchmark dose obtained in a study of the Iraq incident of 1971–1972. However, since the manner of MeHg exposure in that incident was quite different from the ordinary exposure risk incurred through fish consumption, the Committee on Toxicological Effects of Methylmercury convened by the United States National Research Council (NRC) reevaluated the RfD.[6] Although the committee scientifically verified the EPA's RfD level, it recommended that its calculation should instead be based on the data obtained in a cohort study conducted in the Faroe Islands.[7] On the other hand, a provisional tolerable weekly intake (PTWI) of MeHg was determined to be 1.6 μg mercury/kg/week at the 61st meeting of the Joint FAO/WHO Expert Committee on Food Additives (JECFA).[8] However, a considerable segment of the Japanese population is thought to be exposed to MeHg in excess of the above levels due to their habitually high consumption of marine products. Here we reported on a survey of the hair mercury levels in a cross section of representative Japanese sub-populations to estimate the current MeHg exposure levels in Japan.

Current Hair Mercury Levels in Japanese

To estimate the current hair mercury levels in a cross section of Japanese sub-populations hair samples from 8665 individuals were collected from 1999 to 2002 at beauty parlors, barbershops, and primary schools in nine prefectures: Miyagi, Chiba, Nagano, Wakayama, Tottori, Hiroshima, Fukuoka, Kumamoto (Kumamoto and Minamata Cities), and Okinawa (Fig. 1). Using a questionnaire, we gathered information from each individual on age, sex, amount and species of fish consumed, and artificial waving and coloring of hair. Total mercury levels of all hair samples thus collected were analyzed by the oxygen combustion-gold amalgamation method using an atomic absorption mercury detector. Since the mercury levels analyzed were distributed in a log-normal manner (Figs. 2A and 2B), a geometric rather than an arithmetic mean was used as representative of hair mercury levels. Multiple regression analysis revealed that mercury levels were significantly correlated with several covariates including sex, age, the amount of daily intake of total fish/shellfish, a

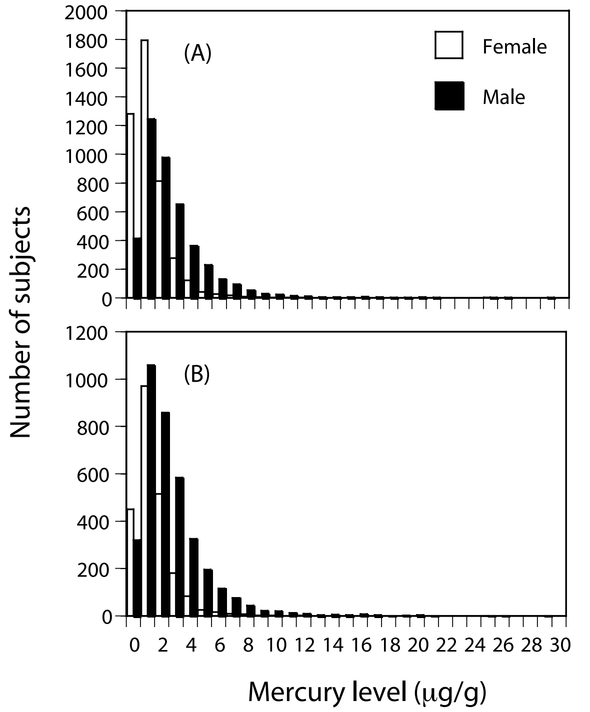

Fig. 2. Distribution of Hair Mercury Content among the Total Study Population (A) and the Population without Artificial Waving (B)

Open bar and solid bar indicate female and male populations, respectively.

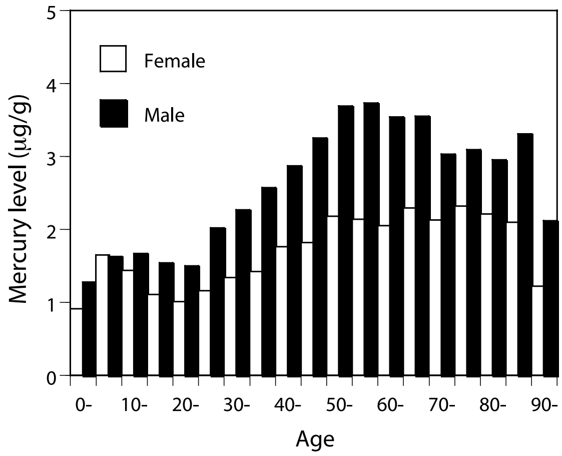

Fig. 3. Age-Dependent Distribution of the Geometric Mean of Hair Mercury Content among the Population without Artificial Waving

Open bar and solid bar indicate female and male populations, respectively.

preference for certain fish such as tuna or bonito, and artificial waving ($p < 0.001$). Some detailed results are given below.

Sex Differences

The mercury levels of 8665 hair samples collected from 10 districts showed a significant sex difference, with females distributed at lower levels than males (Fig. 2A). Geometric means of the levels for males and females in the total population were 2.42 ($n = 4274$) and 1.37 μg/g ($n = 4391$), respectively. These levels were somewhat higher than those estimated from mercury concentrations in blood or toenails recently reported in western countries.[9–11] Since thioglycolate used in the lotion for artificial waving effectively removed some of the hair mercury,[12,13] the lower value for females might, at least partly, be due to the high incidence of artificial waving among women. In fact, the frequencies of participants without waving were 52 and 90% for females and males, respectively. Figure 2B showed the distribution of hair mercury concentrations obtained from the nonwaved population. It was evident that female mercury levels were lower than for males. The geometric means for the population without waving were 2.46 and 1.63 μg/g for males ($n = 3668$) and females ($n = 2265$), respectively. Even after excluding the contribution from artificial waving, males still showed a higher level than females. Other factors such as the amount of fish consumed might be responsible for the higher male mercury levels, and hormonal control might also be a possible factor as discussed below.

Age-Dependent Variations

Hair mercury levels varied with age as shown in Fig. 3. Such variations were more significant in males. Following a transient decline around the 20s, male levels increased into their 50s and 60s, and declined thereafter. The highest levels in the 50s and 60s were mostly twice those in childhood. On the other hand, the age-dependent variations in females were less significant. Although the difference between sexes was not evident at younger ages, the significant increase with age in male mercury levels accounted for a notable sex difference beyond the 20s. Since a marked sex difference subject to modification by hormone treatment has been reported in the tissue uptake and elimination of mercury in MeHg-treated animals,[14] some hormonal control might also be involved in the mercury uptake by human hair.

Regional Differences

The average mercury levels in our hair samples varied from 1.67 to 4.75 μg/g for males and from 1.07 to 2.29 μg/g for females among the sampling

Table 1. Geometric Mean and Range of Hair Mercury Content in Ten Geographic Populations

Prefecture (city)	Sex	N	Hair mercury content (μg/g)		
			Geometric mean	Min	Max
Miyagi	F	624	1.77	0.05	10.14
	M	561	3.31	0.25	26.57
	Total	1185	2.38	0.05	26.57
Chiba	F	232	2.29	0.14	25.75
	M	253	4.75	0.26	26.76
	Total	485	3.35	0.14	26.76
Nagano	F	311	1.76	0.10	7.05
	M	342	2.97	0.28	21.36
	Total	653	2.32	0.10	21.36
Wakayama	F	299	1.46	0.09	8.09
	M	413	2.37	0.10	20.66
	Total	712	1.93	0.09	20.66
Tottori	F	207	1.40	0.26	12.52
	M	611	2.30	0.28	10.21
	Total	818	2.04	0.26	12.52
Hiroshima	F	561	1.07	0.07	7.47
	M	440	2.02	0.34	29.37
	Total	1001	1.41	0.07	29.37
Fukuoka	F	570	1.09	0.02	8.67
	M	474	1.67	0.17	10.35
	Total	1044	1.33	0.02	10.35
Kumamoto	F	326	1.33	0.14	6.20
(Kumamoto)	M	385	2.23	0.20	19.18
	Total	711	1.76	0.14	19.18
Kumamoto	F	648	1.24	0.09	7.33
(Minamata)	M	389	2.17	0.22	10.56
	Total	1037	1.53	0.09	10.56
Okinawa	F	613	1.29	0.08	7.16
	M	406	2.14	0.26	15.50
	Total	1019	1.58	0.08	15.50
Total	F	4391	1.37	0.02	25.75
	M	4274	2.42	0.10	29.37
	Total	8665	1.82	0.02	29.37

districts (Table 1). Such variations seemed to depend on the total amount of the daily intake of fish/shellfish and on the preference for consuming certain fish. Table 2 showed average amounts of the daily intake of fish/shellfish and the rate of preference for tuna consumption. The average consumption of fish/shellfish varied from 43 to 95 g/day for males and from 40 to 98 g/day for females among the districts. On the whole, males (64 g/day) consumed higher amounts than females (56 g/day), which would partly account for the sex difference in the hair mercury levels mentioned above. Tuna is a major carnivorous fish with high mercury accumulations that is often consumed in Japan. The highest rate of tuna consumption was found in Okinawa and Chiba, while Tottori and Minamata had the lowest rate. The highest hair mercury level found in Chiba among all the districts was probably due to the high consumption of tuna there. Although Okinawa also showed a marked tendency to consume tuna, their lower levels of fish/shellfish consumption would tended to depress their hair mercury levels. In contrast, the two districts with the lowest hair mercury levels, Fukuoka and Hiroshima, showed both lower amounts of fish consumption and a lower preference for tuna among all the districts. Thus, the amount of fish consumption and the preference rate for tuna would appear to be responsible for the regional varia-

Table 2. Average Amount of Fish Consumption and Tuna Preference Rate

Residence	Amount of fish consumption (g/person/day)			Frequency of tuna consumption (%)[a]
	Female	Male	Total	
Miyagi	98	95	96	69.0
Chiba	50	89	70	75.5
Nagano	56	59	57	60.5
Wakayama	53	57	55	52.5
Tottori	47	76	69	16.6
Hiroshima	43	55	48	30.6
Fukuoka	51	46	48	23.1
Kumamoto	46	54	50	38.8
Minamata	56	64	59	20.0
Okinawa	40	43	42	77.5

a) Frequency of persons who often eat tuna.

Table 3. Cumulative Frequency of Individual Hair Mercury Content

Sex	Age	Mercury concentration (μg/g)					
		≤ 1	≤ 2	≤ 2.2	≤ 5	≤ 10	Total
Female	All	461	1426	1570	2200	2260	2265
		(20.4%)	(63.0%)	(69.3%)	(97.1%)	(99.8%)	(100%)
	15–49	214	576	611	800	813	814
		(26.3%)	(70.8%)	(75.1%)	(98.3%)	(99.9%)	(100%)
Male	All	325	1388	1577	3149	3595	3668
		(8.9%)	(37.8%)	(43.0%)	(85.9%)	(98.0%)	(100%)
Total	All	786	2814	3147	5349	5855	5933
		(13.2%)	(47.4%)	(53.0%)	(90.2%)	(98.7%)	(100%)

tion in hair mercury levels in Japan.

Safe MeHg Exposure Levels

The exposure level to MeHg can be estimated from hair mercury levels using the following formula:[6)]

$$d = \frac{C \times b \times V}{A \times f \times bw}$$

where

C = mercury concentration in blood (μg/l) = hair level (μg/g) $\times$ 1000/250

b = elimination rate constant (0.014/day)

V = blood volume (9% of body weight)

A = fraction of the dose absorbed (0.95)

f = absorbed fraction distributed to the blood (0.05)

bw = body weight (kg)

d = dose (μg/kg bw/day).

Various levels has been recommended as a safe exposure limit to MeHg in several countries and by international committees. In Japan 0.17 mg mercury/person/week (3.4 μg mercury/kg bw/week) was suggested as a safe exposure limit in 1973. This is almost equal to the former PTWI (3.3 μg mercury/kg bw/week) reaffirmed at the 53rd JECFA meeting,[15)] and corresponds to a hair mercury level of about 5 μg/g. On the other hand, 0.1 μg mercury/kg bw/day, which was suggested as an RfD by the EPA[5)] and reevaluated by the NRC,[6)] is the lowest level, and corresponds to a hair level of 1.0 μg/g. However, EPA's fish advisories announced that their RfD level had been applied exclusively to recreationally caught fish. The more recently determined PTWI,[8)] 1.6 μg mercury/kg bw/week, corresponds to a hair mercury level of 2.2 μg/g.

The cumulative frequency of hair mercury levels in our survey was shown in Table 3. The districts that exceeded the 5 μg/g which was recommended in Japan and by the former PTWI[15)] were less than 10% of the total population surveyed. When restricted to females of child-bearing age, 1.7% of the sub-population had hair mercury concentrations exceeding that level. However, the majority (87% of the total, 80% of females, 74% of females child-bearing age from 15 to 49 years, and 91% of males) exceeded 1 μg/g. On the other hand, the average hair mercury levels of all Japanese females (1.63 μg/g, without waving) and females of child-bearing age (1.43 μg/g, without waving) were lower than the new PTWI level.[8)] However, considerable population segments (31% of all females and 25% of females of child-bearing age) exceeded the PTWI level, which was determined using NOEL/BMD for maternal hair mercury levels reported in the Faroes (12 μg/g) and Seychelles (15.3 μg/g) with an uncertainty factor of 6.4.[8)] Although it is difficult to assess the risk level for females of child-bearing age, they may not be urgently at risk, since none of them exceeded the NOEL/BMD levels obtained in the Faroes and Seychelles.

For pregnant women and those who may become pregnant, the Japanese Government[16)] recently announced a program to regulate the consumption of several kinds of fishes and whales that showed high concentrations of mercury. Such a program may be sufficiently effective to bring about some reduction in fish consumption in Japan. However, not only the risk of mercury contamination, but also food habits and nutritional benefits may have to be considered when determining a regulatory standard of fish and shellfish. Sufficient and accurate information must be provided to reach an appropriate decision on fish consumption. Hair analysis may, at least in part, contribute to such decisions by providing information on the MeHg exposure levels of each individual.

REFERENCES

1) Agency for Toxic Substances and Disease Registry (1992) Mercury toxicity. *Am. Fam. Physician.*, **46**, 1731–1741.
2) Clarkson, T. W. (1992) Mercury: major issues in environmental health. *Environ. Health Perspect.*, **100**, 31–38.
3) World Health Organization (1990) *IPCS Environmental Health Criteria 101 Methylmercury*, WHO, Geneva.
4) Cox, C., Clarkson, T. W., Marsh, D. O., Amin-Zaki, L., Tikriti, S. and Myers, G. G. (1989) Dose–response analysis of infants prenatally exposed to methylmercury. An application of a single compartment model to single-strand hair analysis. *Environ. Res.*, **49**, 318–332.
5) United States Environmental Protection Agency (1997) *Mercury Study Report to Congress*, Washington, DC., EPA.
6) National Research Council. Committee on the Toxicology Effects of Methylmercury (2000) *Toxicological Effects of Methylmercury*, National Academy Press, Washington DC.
7) Grandjean, P., Weihe, P., White, R. F., Debes, F., Araki, S., Yokoyama, K., Murata, K., Sørensen, N., Dahl, R. and Jørgensen, P. J. (1997) Cognitive deficit in 7-year-old children prenatally exposed to methylmercury. *Neurotoxicology*, **19**, 417–428.
8) Joint FAO/WHO Expert Committee on Food Additives (2003) JECFA 61st Meeting, Rome, 10-19 June 2003, http://www.who.int./pcs/jecfa/jecfa.htm.
9) Sanzo, J. M., Dorronsoro, M., Amiano, P., Aguinagalde, F. X. and Azpiri, M. A. (2001) Estimation and validation of mercury intake associated with fish consumption in an EPIC cohort of Spain. *Public Health Nutr.*, **4**, 981–988.
10) Guallar, E., Sanz-Gallardo, M. I., van't Veer, P., Bode, P., Aro, A., Gomez-Aracena, J., Kark, J. D., Riemersma, R. A., Martin-Moreno, J. M. and Kok, F. J. (2002) Mercury, fish oils, and the risk of myocardial infarction. *N. Engl. J. Med.*, **347**, 1747–1754.
11) The Centers for Disease Control and Prevention, United States (2003) *Second National Report on Human Exposure to Environmental Chemicals*, National Center for Environmental Health, http//:www.cdc.gov/exposurereport/.
12) Yamamoto, R. and Suzuki, T. (1978) Effects of artificial hair-waving on hair mercury values. *Int. Arch. Occup. Environ. Health*, **42**, 1–9.
13) Yasutake, A., Matsumoto, M., Yamaguchi, M. and Hachiya, N. (2003) Current hair mercury levels in Japanese: survey in five districts. *Tohoku J. Exp. Med.*, **199**, 161–169.
14) Hirayama, K., Yasutake, A. and Inoue, M. (1987) Effect of sex hormones on the fate of methylmercury and glutathione metabolism in mice. *Biochem. Pharmacol.*, **36**, 1919–1924.
15) Joint FAO/WHO Expert Committee on Food Additives (1999) JECFA 53rd Meeting, Rome, 1-10 June 1999, http://www.who.int./pcs/jecfa/jecfa.htm.
16) The Ministry of Health, Labor and Welfare (2003) http://www.mhlw.go.jp/shinngi/2003/06/s0603-3.html.