Heavy Metals in Normal Japanese Tissues

Amounts of 15 Heavy Metals in 30 Subjects

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• To obtain the usual values of arsenic, beryllium, bismuth, cadmium, chromium, cobalt, copper, mercury, methyl mercury, manganese, molybdenum, nickel, lead, antimony, vanadium, and zinc in the normal human body, the amounts of 15 metals were determined in 15 male and 15 female Japanese cadavers (average weight, 55 kg [121 lb]). The content of metals found ranged as follows: Zn, 1,800 mg; Cu, 65 mg; Cd, 35 mg; Pb, 25 mg; Mn, 8 mg; Ni, 6 mg; Cr, 4 mg; Hg, 3 mg; Sb, 0.7 mg; MeHg, 0.4 mg.

Cadmium and mercury were higher in Japanese blood than in blood of other people. Cadmium and mercury were absorbed by the metabolic tissues; Cr, Ni, and Pb showed higher concentration in tissue exposed to the environment. Concentrations of Cd, Pb, and Hg tended to be higher in females, and Cr, Cu, MeHg, and Mn concentrations tended to be higher in males.

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After World War II, Japan underwent rapid economic recovery and industrial growth, resulting in the release of many pollutants, such as mercury, cadmium, sulfur oxide, and arsenic. Therefore, it seemed worthwhile to measure the concentration of a number of metals in the tissues of normal Japanese people. Four public hazard diseases that were caused by the four pollutants mentioned above have been recognized by the Japanese government. Among these four diseases, the three caused by heavy metals are as follows: Minamata disease was caused by mercury in waste water from factories; "Itai-Itai" was apparently caused by cadmium in water and rice from refineries (some questions still remain); and arsine intoxication arose from arsenic in air and plants, produced by mines. Environmental pollution from these and other heavy metals has been a major problem in Japan.

It has previously been reported[1,2] that Japanese or Far Eastern people had a higher level of cadmium, chromium, and other metals in their tissues than did white and black people. The difference in these levels might be due to eating habits, types of food, geographical conditions, or man-made pollution. This report presents usual values of arsenic, beryllium, bismuth, cadmium, cobalt, chromium, copper, mercury, manganese, molybdenum, nickel, lead, antimony, vanadium, and zinc in normal body tissues of Japanese people as of 1972. It provides values against which future effects may be measured, both in Japan and elsewhere.

MATERIALS AND METHODS

The human tissues analyzed were obtained from 30 cadavers examined at the Department of Legal Medicine of Kobe University School of Medicine from November 1971 to May 1972. All subjects had lived in Hyogo Prefecture, in the central part of Japan. It was not always possible to know how much of these heavy metals the subjects had taken in through foods, water, and smoking.

The causes of death of the subjects were as follows: four died due to internal hemorrhage in the brain by trauma; four had fractured skulls and brain injury; 12 died because of blood loss; two were poisoned by sleeping pills; six died of suffocation; and two died of CO intoxication.

The age and sex distributions for the subjects are shown in Table 1. The average age was approximately 39 years. Twenty different types of tissue were removed from different subjects, but not all of these were removed from every subject. The tissue specimens that were removed were rinsed free of blood with distilled water, placed in polyethylene bags or glass bottles, and stored until analysis at a temperature below −10 C.

The following fifteen elements were studied: As, Be, Bi, Cd, Cr, Co, Cu, Hg, Mn, Mo, Ni, Pb, Sb, V, and Zn. Total mercury (T Hg) and methyl-mercury (MeHg) were treated separately. Among the above elements, Cd, Cr, Cu, Hg, Mn, Mo, Ni, Pb, and Zn were found in almost all tissues of all bodies. Cobalt and Sb were found in about half of the samples. Beryllium, Bi, and V were analyzed in only a few samples due to their high detection limits. Arsenic was detected in only five cadavers.

The total Hg and MeHg analyses were carried out by flameless atomic absorption[3] and gas chromatography,[4] but were reported separately.[5]

For As, Cd, Cu, Mn, Pb, Sb, and Zn, pretreatment consisted of the ashing method. The ashed solutions then underwent wet digestion. A definite wet weight sample (20 gm as standard) was placed in a flask, 2 ml

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of hydrogen sulfate was added, along with moderate amounts of nitric acid, and the sample was then digested. For analysis of Sb, a part of the ashed solution was digested with perchloric acid.

For Be, Bi, Cr, Mo, Ni, and V, pretreatment again consisted of the ashing method, with the solutions undergoing dry digestion. Five to twenty grams of the major tissues, such as brain, lung, liver, kidney, spleen, intestine, and bone was put on a glass boat. The tissue was then ashed by low-temperature apparatus at 300 to 400 w of forward power (50 to 70 w per chamber), with 300 to 400 ml/min oxygen flow, for approximately 48 hours. The ashed samples were transferred to a glass test tube with 2% HNO_3 and exactly 15 or 20 ml distilled water.

The extraction method was employed for Cd, Pb, Cu, Mn, and Ni. After digestion, 5 ml of solution was adjusted to pH 4 with diluted NH_4OH, and extracted with 1 ml of 2% sodium diethyl-dithiocarbamate and 5 ml isopropylacetone, saturated with water.

Measurement for Cd, Cu, Mn, Ni, Pb, and Zn was estimated by flame atomic absorption spectroscopy. Sample solutions were analyzed directly or in the form of extract by spectrometers with background correctors.

Measurement for Be, Bi, Cr, Mn, Mo, Ni, and V was estimated by flameless atomic absorption. Measurement by flameless atomizer was not yet in general use, but the authors succeeded in developing it. The detailed method has been reported separately in Japanese.

The spectrophotometric (silver carbamine) method was employed for As. The digested solution was made acid with HCl, and stannous chloride was added. After adding Zn powder, H_3As gas was caught in silver diethyl-dithiocarbamate, and then its solution was determined at 525 mμ.

The rhodamine B method was used for Sb.[6] The solution was completely digested, and 5 ml of 6N HCl and 13 ml of distilled water were added. It was extracted into 5 ml of an isopropyl ether layer, shaken, and determined at 545 mμ.

Table 1.—Age and Sex of Subjects

Group	Age, yr	Male		Female	
	0-9				
Young	10-19	2	4		4
	20-29	2		4	
Middle	30-39	4	7	6	7
	40-49	3		1	
Old	50-59	1	4	3	4
	Over 60	3		1	

RESULTS

In Tables 2 through 8, the concentration of each metal in each tissue is shown as the average in each sex, the overall average range in both sexes, the overall average, and the median. The amount of metal in each of the tissues and the

Table 2.—Arsenic and Cadmium Concentration in Japanese Human Tissues*

Organ or Part	Arsenic Sex	No.	Average	Range	Mean ± SD	Median	Cadmium Sex	No.	Average	Range	Mean ± SD	Median
Cerebrum	F	1	0.025		†	†	M F	10 11	0.084 0.15	0.020-0.23	0.12 ± 0.063	0.11
Cerebellum	F	1	0.065		†	†	M F	9 11	0.11 0.13	0.030-0.23	0.12 ± 0.057	0.10
Trachea	F	1	0.12		†	†	M F	12 4	0.32 0.47	0.11-0.74	0.36 ±0.22	0.32
Lung	F	3	0.052	0.044-0.065	†	†	M F	15 15	0.58 0.86	0.15-2.3	0.72 ± 0.52	0.57
Heart	M F	1 4	0.033 0.041	0.017-0.060	0.040 ± 0.018	0.033	M F	14 13	0.16 0.17	0.060-0.33	0.16 ± 0.69	0.14
Liver	F	4	0.053	0.033-0.070	†	†	M F	15 15	3.2 8.1	1.1-23.0	5.7 ± 4.6	4.6
Pancreas	F	3	0.058	0.033-0.085	†	†	M F	15 15	2.2 3.2	0.74-8.0	2.7 ± 1.7	2.10
Spleen	F	2	0.040	0.015-0.065	†	†	M F	10 12	0.40 1.1	0.20-2.4	0.81 ± 0.69	0.52
Kidney	M F	1 3	0.068 0.077	0.045-0.095	0.074 ± 0.023	0.079	M F	15 15	36 58	10-94	47 ± 24	40
Adrenal gland			‡	‡	†	†	M F	13 13	0.97 2.0	0.40-4.1	1.5 ± 1.0	1.2
Small intestine	M F	2 1	0.095 0.11	0.090-0.11	0.10 ± 0.010	0.10	M F	13 14	0.88 1.2	0.39-1.9	1.1 ± 0.44	1.0
Large intestine	F	2	0.081	0.032-0.13	†	†	M F	14 13	0.38 0.49	0.13-0.98	0.43 ± 0.22	0.38
Testicles Ovary		†	‡	‡	†	†	M F	12 12	0.52 0.75	0.14-0.90 0.21-1.9	0.52 ± 0.24 0.75 ± 0.51	0.44 0.66
Muscle	F	3	0.062	0.043-0.095	†	†	M F	11 14	0.23 0.34	0.075-1.1	0.29 ±0.24	0.20
Skin	F	1	0.043		†	†	M F	14 12	0.30 0.35	0.045-0.94	0.32 ± 0.28	0.22
Blood	F	3	0.056	0.050-0.060	†	†	M F	13 12	0.16 0.21	0.05-0.58	0.17 ± 0.11	0.15
Rib (bone)		†	‡	‡	†	†	M F	6 6	0.11 0.089	0.04-0.21	0.097 ± 0.056	0.085
Fat	F	3	0.055	0.045-0.065	†	†	F	3	0.068	0.035-0.13	†	†

* Expressed as micrograms per gram wet tissue.
† Not calculated because less than five samples were available or because there was no mean (testicles and ovary).
‡ Not measured.

Table 3.—Chromium and Copper Concentration in Japanese Human Tissues*

Organ or Part	Chromium Sex	No.	Average	Range	Mean ± SD	Median	Copper Sex	No.	Average	Range	Mean ± SD	Median
Cerebrum	M	10	0.079	<0.01-0.18	0.056 ± 0.052	0.030	M	9	5.2	2.9-8.4	5.1 ± 1.4	4.7
	F	9	0.030				F	11	5.0			
Cerebellum	M	10	0.054	0.013-0.18	0.050 ± 0.051	0.023	M	7	5.9	2.7-8.0	6.2 ± 1.2	5.9
	F	10	0.045				F	10	6.4			
Trachea	M	8	0.088	0.025-0.15	0.090 ± 0.036	0.10	M	11	0.83	0.37-1.2	0.85 ± 0.21	0.86
	F	5	0.093				F	5	0.89			
Lung	M	14	0.38	0.051-0.81	0.26 ± 0.21	0.17	M	15	1.4	0.81-1.9	1.3 ± 0.24	1.3
	F	15	0.15				F	15	1.2			
Heart	M	12	0.10	0.020-0.36	0.080 ± 0.080	0.058	M	15	3.6	2.2-4.6	3.3 ± 0.67	3.4
	F	11	0.073				F	14	3.1			
Liver	M	14	0.078	0.015-0.23	0.066 ± 0.053	0.053	M	15	10.0	2.1-23	9.9 ± 5.5	8.0
	F	15	0.054				F	15	9.7			
Pancreas	M	14	0.11	0.01-0.30	0.10 ± 0.081	0.092	M	15	1.6	0.83-2.1	1.5 ± 0.31	1.6
	F	14	0.090				F	15	1.5			
Spleen	M	5	†	<0.01-0.020	†	†	M	10	1.2	0.83-1.7	1.2 ± 0.23	1.1
	F	3					F	10	1.1			
Kidney	M	15	0.083	0.015-0.22	0.076 ± 0.059	0.053	M	15	2.7	1.8-3.4	2.6 ± 0.38	2.6
	F	15	0.070				F	14	2.5			
Adrenal gland	M	5	<0.01-0.3	†	†	†	M	12	2.4	1.4-4.4	2.1 ± 0.62	2.1
	F	2					F	12	2.0			
Small intestine	M	11	0.15	0.013-0.48	0.12 ± 0.099	0.093	M	12	2.1	1.3-3.2	2.1 ± 0.48	2.1
	F	12	0.084				F	14	2.1			
Large intestine	M	12	0.24	0.022-0.83	0.16 ± 0.18	0.10	M	15	1.8	1.0-2.6	1.7 ± 0.40	1.7
	F	13	0.093				F	13	1.7			
Testicles	M	5	†	<0.01-0.040	†	†	M	11	0.94	0.61-1.2	0.94 ± 0.17	0.93
Ovary	F	3					F	13	0.97	0.41-1.3	0.97 ± 0.28	1.10
Muscle	M	12	0.12	0.015-0.37	0.10 ± 0.10	0.060	M	12	1.1	0.41-1.7	0.92 ± 0.29	0.85
	F	9	0.077				F	15	0.81			
Skin	M	10	0.075	0.015-0.25	0.095 ± 0.072	0.10	M	15	0.72	0.27-1.5	0.71 ± 0.29	0.66
	F	9	0.12				F	11	0.70			
Blood	M	7	0.036	0.016-0.080	0.045 ± 0.018	0.046	M	13	1.1	0.79-1.7	1.1 ± 0.24	1.1
	F	8	0.052				F	13	1.1			
Rib (bone)	M	6	0.020	<0.01-0.16	0.062 ± 0.051	0.052	M	7	0.48	0.23-0.79	0.52 ± 0.21	0.50
	F	7	0.098				F	1				
Fat	F	3	†	<0.01-0.035	†	†	F	3	0.26	0.24-0.28	†	†

* Expressed as micrograms per gram wet tissue.
† Not calculated because less than five samples were available or because there was no mean (testicles and ovary).
‡ Not measured.

total body burden of each metal are calculated by multiplication of tissue concentration and tissue weight (Table 9). The statistical calculations were carried out by tissue concentration, sex, and the age groups in each organ, separately. Results from some metals are given below. The numeral indicates micrograms per gram, based on wet weight.

Cadmium

The highest value for cadmium (Table 2) was found in kidney (47 ± 24). There was a significant difference at $P=.01$ between liver (5.7 ± 4.6) and pancreas (2.7 ± 1.7), and at $P=.05$ between pancreas and adrenal glands (1.5 ± 1.0) and between adrenal glands and small intestine (1.1 ± 0.44). Blood contained 0.17 ± 0.11. Brain, bone, and fat contained less. The levels for females in all age groups were substantially higher, especially in liver and kidney. The kidney concentrations increased with age in both sexes. Generally, cadmium levels were higher as age increased in women (in tissues other than kidney) and in men (only in the testicles). Total body burden was higher than 35 mg. Of this amount, the kidney contained 11.7 mg and the liver contained 8.5 mg. Approximately two thirds of the total was in these two organs. Cadmium accumulation was higher in females, even when tissue weights were calculated.

Chromium

There was a decreasing tendency for chromium concentration (Table 3) in the following order: lung (0.26 ± 0.21), large intestine (0.16 ± 0.18), small intestine (0.12 ± 0.099), muscle (0.10 ± 0.10), and spleen. There was a significant difference at $P=.05$ between lung and large intestine. Hepatic content was low at 0.066, and brain and blood contents were even lower. Concentrations in the organs of males were generally higher than those of females, except in trachea, bone, and skin. Higher values were found in the lung ($P=.05$) and large intestine ($P=.01$) of the male in particular. The average contents in the large intestine and muscle of the male tended to decrease with age. Total body burden was more than 4 mg, and half of it was in muscle.

Copper

Copper concentration (Table 3) ranged downward from liver

Table 4.—Total Mercury and Methyl Mercury Concentration in Japanese Human Tissues*

Organ or Part	Total Mercury: Sex	No.	Average	Range	Mean ± SD	Median	Methyl Mercury: Sex	No.	Average	Range	Mean ± SD	Median
Cerebrum	M	10	0.11	0.039-0.17	0.10 ± 0.042	0.097	M	9	0.022	0.0015-0.069	0.016 ± 0.014	0.012
	F	10	0.099				F	11	0.010			
Cerebellum	M	10	0.11	0.048-0.23	0.10 ± 0.045	0.093	M	9	0.028	0.0015-0.096	0.019 ± 0.020	0.014
	F	11	0.089				F	11	0.012			
Trachea	M	12	0.036	0.015-0.11	0.047 ± 0.029	0.036		†	‡	‡	†	†
	F	4	0.079									
Lung	M	15	0.081	0.015-0.30	0.080 ± 0.054	0.070	M	5	0.0083	0.0023-0.015	0.0065 ± 0.0034	0.0060
	F	13	0.078				F	6	0.0050			
Heart	M	15	0.054	0.023-0.13	0.069 ± 0.028	0.069	M	7	0.011	0.0030-0.027	0.0092 ± 0.0066	0.0070
	F	14	0.085				F	6	0.0067			
Liver	M	15	0.42	0.16-1.3	0.47 ± 0.26	0.42	M	15	0.058	0.012-0.080	0.044 ± 0.019	0.042
	F	15	0.52				F	15	0.041			
Pancreas	M	15	0.077	0.023-0.29	0.083 ± 0.048	0.077	M	14	0.010	0.0013-0.033	0.010 ± 0.0078	0.0083
	F	15	0.09				F	15	0.010			
Spleen	M	13	0.073	0.021-0.14	0.068 ± 0.028	0.062		†	‡	‡	†	†
	F	15	0.064									
Kidney	M	15	0.97	0.18-2.6	1.1 ± 0.67	0.98	M	15	0.029	0.010-0.080	0.023 ± 0.015	0.019
	F	15	1.24				F	14	0.018			
Adrenal gland	M	12	0.12	0.03-0.33	0.14 ± 0.073	0.15		†	‡	‡	†	†
	F	12	0.16									
Small intestine	M	12	0.057	0.024-0.19	0.069 ± 0.037	0.064	M	12	0.016	0.0030-0.069	0.014 ± 0.017	0.0082
	F	13	0.08				F	12	0.012			
Large intestine	M	14	0.078	0.032-0.16	0.083 ± 0.037	0.075	M	9	0.0086	0.0018-0.026	0.0065 ± 0.0061	0.0044
	F	13	0.09				F	11	0.0047			
Testicles	M	14	0.067	0.029-0.12	0.067 ± 0.029	0.070		†	‡	‡	†	†
Ovary	F	14	0.069	0.028-0.13	0.069 ± 0.028	0.070						
Muscle	M	13	0.056	0.018-0.15	0.060 ± 0.027	0.057	M	6	0.0090	0.0041-0.019	0.0078 ± 0.0043	0.0064
	F	14	0.064				F	6	0.0065			
Skin	M	15	0.051	0.017-0.15	0.059 ± 0.034	0.048		†	‡	‡	†	†
	F	12	0.066									
Blood	M	9	0.054	0.016-0.11	0.059 ± 0.026	0.058	M	6	0.012	0.0036-0.026	0.011 ± 0.0073	0.0092
	F	10	0.064				F	6	0.010			
Hair	M	14	5.4	1.4-15.0	4.1 ± 2.6	3.4	M	14	3.4	0.63-10.4	2.6 ± 2.1	2.0
	F	15	3.0				F	14	1.8			

* Expressed as micrograms per gram wet tissue.
† Not calculated because there were less than five samples available or there was no mean (testicles and ovary).
‡ Not measured.

(9.9 ± 5.5), cerebellum (6.2 ± 1.2), cerebrum (5.1 ± 1.4), heart (3.3 ± 0.67), and kidney (2.6 ± 1.2). There was a significant difference at $P = .01$ between liver and cerebellum and between cerebrum and heart. Higher concentrations of Cu than of any other metals were found in both portions of the brain. The values in organs of males were generally higher than those in females, except for the cerebellum. The concentrations in the lung, heart, and muscle of the male were significantly higher ($P = .05$). In the older groups, the levels tended to be a little lower than in the young or middle-aged groups. About 70 mg of Cu was estimated for the whole body, with one third in the liver and brain together, and another third in the muscle. The rest was dispersed in other tissues.

Total Mercury

The results of analysis for T Hg and MeHg have been reported in detail separately.[5,7] Contents of T Hg (Table 4) tended to decrease in order of kidney (1.1 ± 0.67), liver (0.47 ± 0.26), adrenal glands (0.14 ± 0.073), cerebellum (0.10 ± 0.045), and cerebrum (0.10 ± 0.042). There was a significant difference at $P = .01$ between kidney and liver and between liver and adrenal glands. There was also a significant difference at $P = .05$ between adrenal glands and cerebellum. Individual averages in the lung, cerebrum, spleen, and hair in particular tended to be higher in the male, but the average in all other tissues tended to be higher in the female. No difference with age was found. Normal Japanese people had more than 3 to 4 mg total mercury in their whole bodies, and about two thirds of this amount was present in the muscle (1.4 mg), liver (0.7 mg), and brain (0.13 mg).

Methyl Mercury

The range of MeHg (Table 4) in the tissues was from liver (0.044 ± 0.019), kidney (0.023 ± 0.015), cerebellum (0.019 ± 0.020), cerebrum (0.016 ± 0.014), and blood (0.011 ± 0.073) to less than 0.01 in the other tissues. There was a significant difference at $P = .01$ between liver and kidney. The concentration in hair was 2.6 ± 2.1, and only three female subjects among 14 showed less than 1.0. The level in all viscera tended to be higher in the male (in contrast to the level of T Hg), and the difference in the kidney level was statistically significant

Table 5.—Manganese and Molybdenum Concentration in Japanese Human Tissues*

Organ or Part	Manganese Sex	No.	Average	Range	Mean ± SD	Median	Molybdenum Sex	No.	Average	Range	Mean ± SD	Median
Cerebrum	M	10	0.28	0.11-0.46	0.25 ± 0.098	0.25	M	5	<0.03		†	†
	F	10	0.34				F	4				
Cerebellum	M	10	0.39	0.12-0.53	0.36 ± 0.11	0.39	M	2	<0.03		†	†
	F	10	0.34				F	6				
Trachea	M	11	0.19	0.083-0.34	0.20 ± 0.092	0.22	M	5	<0.02		†	†
	F	3	0.24				F	1				
Lung	M	13	0.28	0.067-0.38	0.22 ± 0.091	0.21	M	14	†	<0.02-0.05	†	†
	F	15	0.17				F	11				
Heart	M	12	0.24	0.083-0.83	0.21 ± 0.084	0.19	M	13	†	<0.02-0.04	†	†
	F	13	0.19				F	9				
Liver	M	15	1.2	0.45-2.1	1.2 ± 0.36	1.2	M	15	0.52	0.20-1.2	0.57 ± 0.25	0.50
	F	15	1.2				F	15	0.61			
Pancreas	M	15	0.73	0.26-1.3	0.77 ± 0.24	0.74	M	7	†	<0.02-0.025	†	†
	F	15	0.81				F	11				
Spleen	M	8	0.082	0.010-0.13	0.080 ± 0.032	0.076	M	8	<0.03		†	†
	F	9	0.078				F	9				
Kidney	M	15	0.59	0.11-1.0	0.56 ± 0.22	0.58	M	14	0.18	0.075-0.30	0.16 ± 0.060	0.15
	F	15	0.54				F	15	0.16			
Adrenal gland	M	2	0.80	0.22-1.25	0.69 ± 0.34	0.67	M	1	<0.02		†	†
	F	7	0.66				F	1				
Small intestine	M	14	0.69	0.12-2.3	0.86 ± 0.051	0.77	M	8	<0.03		†	†
	F	14	1.02				F	9				
Large intestine	M	14	1.3	0.23-4.0	1.2 ± 0.93	0.83	M	8	<0.02		†	†
	F	13	1.1				F	9				
Testicles	M	13	0.20	0.08-0.33	0.20 ± 0.069	0.21	M	2	<0.02			
Ovary	F	6	0.19	0.78-0.40	0.19 ± 0.12	0.15	F	1				
Muscle	M	9	0.11	0.014-0.24	0.090 ± 0.052	0.080	M	5	<0.03		†	†
	F	10	0.076				F	3				
Skin	M	8	0.10	0.030-0.46	0.14 ± 0.11	0.11	M	6	<0.02		†	†
	F	10	0.17				F	3				
Blood	M	13	0.082	0.012-0.27	0.064 ± 0.053	0.047	M	2	<0.02		†	†
	F	14	0.048				F	1				
Rib (bone)	M	7	0.022	<0.01-0.17	0.074 ± 0.056	0.070	M	3	<0.01		†	†
	F	9	0.11									
Fat	F	3	0.054	0.041-0.065	0.054 ± 0.012	0.055	†		†	†	†	†

* Expressed as micrograms per gram wet tissue.
† Not measured.
‡ Not calculated because testicles and ovary had no mean.

($P=.05$). This was not remarkable in older groups, but the middle-aged group of males had higher MeHg levels in the kidney, small intestine, muscle, and hair than did females. More than 400μg MeHg was present in the whole body, and about 50% of all MeHg was contained in the muscle.

Methyl Mercury-Total Mercury Ratio

From the facts mentioned above, it is obvious that the ratio of MeHg to T Hg is higher in the male. In both sexes, the MeHg/T Hg ratio was high in the hair (59.9% in the male, 56.1% in the female), in the blood (20.7%, 15.4%), and small intestine (19.7%, 14.2%).

The ratio was low in the kidney (3.6%, 1.9%) and colon (10.6%, 6.2%). Aside from hair, the MeHg/T Hg ratio was not more than 40% in any tissue of any subject, and the ratio of MeHg/T Hg in the whole body was less than 10% to 15%.

Manganese

Manganese occurred (Table 5) in the tissues in order of liver (1.2 ± 0.36), large intestine (1.2 ± 0.93), small intestine (0.86 ± 0.51), pancreas (0.77 ± 0.24), and adrenal glands (0.69 ± 0.34). There was a significant difference between the large intestine and small intestine at $P=.05$. Contents of blood (0.064 ± 0.053) and spleen (0.080 ± 0.032) were low, but Mn was almost uniformly distributed to most of the tissues, with little difference. The values for skin and small intestine in the female were higher than in the male, and only in lung were the male values higher ($P=.01$). Other tissues had almost the same values. In lung and small and large intestine of the female, an increasing tendency was found with age. Total body burden was about 8 mg in the average Japanese. Muscle had approximately 30% of this amount, liver had approximately 20%, and the digestive canal had approximately 15%.

Nickel

The results for Ni (Table 6) were as follows: bone (0.23 ± 0.068), lung (0.16 ± 0.094), large intestine (0.14 ± 0.099), small intestine (0.13 ± 0.067), and skin (0.10 ± 0.083). There was a significant difference at $P=.05$ between bone and lung. Other organs contained less than 0.1. The value in liver was 0.078 ± 0.046. The metabolic organs generally had low contents of

Table 6.—Nickel and Lead Concentration in Japanese Human Tissues*

Organ or Part	Nickel: Sex	No.	Average	Range	Mean ± SD	Median	Lead: Sex	No.	Average	Range	Mean ± SD	Median
Cerebrum	M	2	0.062	0.015-0.11	0.050 ± 0.11	0.025	M	6	0.18	0.11-0.62	0.26 ± 0.16	0.19
	F	1	0.025				F	9	0.31			
Cerebellum	M	1	<0.03		†	†	M	7	0.16	0.08-0.63	0.27 ± 0.17	0.22
	F	1					F	9	0.35			
Trachea	M	3	0.086	0.060-0.11	0.092 ± 0.022	0.098	M	8	1.1	0.15-3.2	0.94 ± 1.04	0.58
	F	1	0.11				F	4	0.57			
Lung	M	15	0.21	0.038-0.44	0.16 ± 0.094	0.16	M	14	0.20	0.098-0.81	0.30 ± 0.20	0.24
	F	15	<0.10				F	15	0.39			
Heart			‡	‡	†	†	M	15	0.30	0.065-0.98	0.32 ± 0.25	0.24
							F	14	0.34			
Liver	M	14	0.10	0.028-0.22	0.078 ± 0.046	0.068	M	15	0.55	0.16-1.0	0.46 ± 0.24	0.44
	F	13	0.053				F	15	0.37			
Pancreas	M	6	<0.1	†	†	†	M	15	0.47	0.16-1.5	0.50 ± 0.37	0.37
	F	2					F	15	0.52			
Spleen	M	1	<0.3	†	†	†	M	4	0.12	0.080-0.33	0.20 ± 0.084	0.19
							F	8	0.24			
Kidney	M	14	0.095	0.012-0.30	0.098 ± 0.070	0.081	M	14	0.42	0.16-1.2	0.47 ± 0.23	0.44
	F	14	0.10				F	14	0.52			
Adrenal gland	M	1	<0.1	†	†	†	M	8	0.88	0.24-2.5	1.2 ± 0.79	0.87
							F	6	1.7			
Small intestine	M	5	0.11	0.05-0.29	0.13 ± 0.067	0.12	M	11	0.34	0.16-1.3	0.55 ± 0.36	0.49
	F	5	0.15				F	12	0.74			
Large intestine	M	5	0.14	0.040-0.30	0.14 ± 0.099	0.11	M	15	0.72	0.20-2.5	0.84 ± 0.57	0.65
	F	5	0.15				F	13	0.98			
Testicles	M	1	0.05	†	†	†	M	8	0.35	0.11-0.75	0.35 ± 0.23	0.28
Ovary							F	6	1.2	0.34-3.2	1.2 ± 1.1	0.82
Muscle	M	5	0.11	0.020-0.27	0.099 ± 0.083	0.076	M	8	0.22	0.09-0.52	0.26 ± 0.16	0.18
	F	5	0.090				F	5	0.31			
Skin	M	4	0.086	0.023-0.22	0.10 ± 0.083	0.072	M	14	0.75	0.23-20	0.88 ± 0.49	0.72
	F	2	0.14				F	10	1.1			
Blood	M	3	0.055	0.040-0.12	0.069 ± 0.028	0.066	M	10	0.26	0.10-0.53	0.29 ± 0.13	0.25
	F	3	0.084				F	10	0.32			
Rib (bone)	M	6	0.19	0.13-0.35	0.23 ± 0.068	0.23	M	4	0.34	0.13-0.82	0.35 ± 0.18	0.34
	F	6	0.27				F	8	0.35			
Fat	F	3	<0.01		†	†	F	3	0.84	0.18-2.0	0.84 ± 1.0	0.34

* Expressed as micrograms per gram wet tissue.
† Not measured.
‡ Not calculated because there were less than five samples available or there was no mean (testicles and ovary).

Ni. The liver of the male had a higher concentration than that of the female, but the kidneys had almost the same concentration in both sexes. Differences among age groups were not remarkable. More than 6 mg of Ni was calculated for the whole body.

Lead

The highest value for Pb (Table 6) was found in the adrenal glands (1.2 ± 0.79), and the next highest values were in trachea (0.94 ± 1.04), skin (0.88 ± 0.49), large intestine (0.84 ± 0.57), small intestine (0.55 ± 0.36), and pancreas (0.50 ± 0.37). Two males had 3.0 in trachea, but in other organs the range of values was primarily between 0.2 to 1.0. Blood contained 0.29 ± 0.13 (29μg ± 13μg/deciliter), and rib, which has been thought to have the highest value, contained 0.35 ± 0.18. A few fatty tissues had comparably higher value at 0.84. The average content of the female tissue was higher than the male, except in the liver. Significant differences were found in small intestine ($P=.01$), lung, brain, adrenal glands, and spleen ($P=.05$). No difference with age was found. The whole body contained more than 22 mg of Pb, an amount less than reported by other researchers, possibly because of the low value of bone, which was not tubular, but flat.

Antimony

All averages of Sb (Table 7) in each organ were less than 0.1, and sometimes below detection limit (0.01). The skin (0.096 ± 0.10), adrenal glands (0.073 ± 0.14), and lung (0.062 ± 0.056) generally had higher values, but metabolic organs, such as liver, kidney, or pancreas, were lower. No differences were found in values between sexes and age groups. About 1 mg of Sb was present in the average Japanese body, and it was characteristic to find a great amount of Sb in the skin.

Zinc

The highest level of Zn (Table 7) was found in the muscle (60 ± 10.2), liver (56 ± 16), and kidney (55 ± 17). Also high were the levels in the pancreas (35 ± 8.8), adrenal glands (28 ± 8.2), heart (25 ± 5.7), and small intestine (24 ± 4.5). There was a significant difference at $P=.05$ between the pancreas and adrenal glands and

Table 7.—Antimony and Zinc Concentration in Japanese Human Tissues*

Organ or Part	Antimony Sex	No.	Average	Range	Mean ± SD	Median	Zinc Sex	No.	Average	Range	Mean ± SD	Median
Cerebrum	M F	4 5	0.016	<0.01-0.07	0.017 ± 0.024	<0.01	M F	5 9	16 16	10-22	16 ± 3.6	16
Cerebellum	M F	3 7	0.043	<0.01-0.10	0.030 ± 0.032	0.03	M F	5 9	15 15	12-20	15 ± 2.1	15
Trachea	M	4	0.045	0.02-0.09	0.045 ± 0.031	0.035	M F	5 1	15.00	11-21	15 ± 4.4	13
Lung	M F	11 11	0.066 0.057	<0.01-0.20	0.062 ± 0.056	0.05	M F	13 15	15 16	8.9-25	16 ± 4.4	15
Heart	M F	8 7	0.033 0.032	<0.01-0.12	0.032 ± 0.038	0.025	M F	12 10	24 25	11-37	25 ± 5.7	24
Liver	M F	 11	0.025 0.020	<0.01-0.07	0.023 ± 0.026	0.01	M F	15 14	53 58	21-82	56 ± 16	53
Pancreas	M F	12 12	0.027 0.034	<0.01-0.10	0.030 ± 0.029	0.03	M F	15 15	35 36	21-52	35 ± 8.8	36
Spleen	M F	3 5	0.017 0.036	<0.01-0.07	0.029 ± 0.025	0.025	M F	4 7	24 19	14-33	21 ± 5.8	21
Kidney	M F	13 10	0.046 0.039	<0.01-0.14	0.043 ± 0.041	0.03	M F	14 15	56 55	27-95	55 ± 17	53
Adrenal gland	M F	5 4	0.11	<0.01-0.43	0.073 ± 0.14	<0.01	M F	4 5	26 30	15-43	28 ± 8.2	27
Small intestine	M F	11 10	0.039 0.039	<0.01-0.15	0.039 ± 0.044	0.03	M F	12 14	23 24	17-37	24 ± 4.5	23
Large intestine	M F	13 8	0.046 0.049	<0.01-0.21	0.047 ± 0.062	0.03	M F	15 11	22 24	11-33	23 ± 5.8	23
Testicles Ovary	M F	6 4	0.017 0.021	†	†	†	M F	6 6	15 16	12-19 7.0-26	15 ± 3.0 16 ± 6.9	16 16
Muscle	M	3	†	<0.01-0.10	†	†	M F	4 6	68 55	47-72	60 ± 10.2	57
Skin	M F	14 9	0.085 0.11	<0.01-0.35	0.096 ± 0.10	0.05	M F	14 10	10 11	5.2-17	11 ± 4.0	10
Blood	M F	3 4	0.013	<0.01-0.06	0.016 ± 0.022	<0.01	M F	7 11	13 11	7.8-16	12 ± 3.2	11
Rib (bone)			‡	‡	†	†			‡	‡	†	†
Fat							F	3	2.7	1.6-3.7	2.7 ± 1.1	2.7

* Expressed as micrograms per gram wet tissue.
† Not calculated because there were less than five samples available or because there was no mean (testicles and ovary).

the adrenal glands and the heart. Cerebellum (.05 ± 2.1) and blood (12 ± 3.2) levels were both low. All tissue analyzed contained more than 10μg, except for fat. Each organ had almost the same concentration, irrespective of age and sex. The whole body burden was more than 1,800 mg, and 70% of it existed in muscle.

The concentrations of Be, Bi, Co, and V are shown in Table 8. The amount of metal in each of the tissues and the total body burden appear in Table 9.

Table 8.—Beryllium, Bismuth, Cobalt, and Vanadium Concentration in Japanese Human Tissues*

Organ or Part	Sex	No.	Average	Range	Mean ± SD	Median
				Beryllium		
Lung	M F	6 6	†	0.01-0.03	†	†
				Bismuth		
Liver	M F	5 2	0.023	0.012-0.056	0.030 ± 0.020	†
Kidney	M F	3 2	†	0.01-0.09	0.038 ± 0.031	†
				Cobalt		
Liver	M F	14 15	0.029 0.026	0.013-0.062	0.028 ± 0.011	0.025
Kidney	M F	8 8	0.016 0.013	0.01-0.035	0.015 ± 0.0098	0.012
				Vanadium		
Lung	M F	10 3	0.1 0.1	0.1-0.33	0.1	0.1
Rib (bone)	M F	3 3	†	0.1-0.20	†	†

* Expressed as micrograms per gram wet tissue.
† Not calculated because there were less than five samples available.

COMMENT

Most of the analytic values fell within the ranges reported earlier. The values of Bi, Co, Cr, Mo, Ni, and Zn in the liver and kidney accord well with the observations of far Eastern people made by Tipton et al.[1] The values of Cd, Cu, Mn, and Pb in our anal-

Tissues	Average Weight	Cd	Cr	Cu	Total Hg	Me Hg	Mn	Ni	Pb	Sb	Zn
Muscle	24,000 gm	7.0	2.4	22	1.4	0.19	2.2	2.4	6.2	*	1,440.00
Bone	8,500	0.82	0.53	4.4	*	*	0.63	2.4	3.0	*	*
Fat	6,600	0.45	*	1.7	*	*	0.36	<0.66	5.5	*	18
Blood	4,500	0.76	0.20	5.1	0.27	0.050	0.29	0.31	1.3	0.072	54
Skin	4,200	1.3	0.40	3.0	0.25	*	0.59	0.42	3.7	0.40	45
Connective tissue	1,800	*	*	*	*	*	*	*	*	*	*
Liver	1,500	8.5	0.099	15	0.71	0.066	1.8	0.12	0.69	0.034	84
Brain	1,300	0.16	0.073	6.7	0.13	0.023	0.32	0.065	0.34	0.022	21
Digestive tract	1,000	0.75	0.14	1.9	0.076	0.010	1.0	0.14	0.70	0.043	23
Lung	900	0.65	0.23	1.1	0.072	0.0058	0.20	0.14	0.27	0.056	14
Heart	300	0.048	0.027	1.0	0.021	0.0028	0.063	*	0.096	0.0096	7.4
Kidney	250	12	0.019	0.64	0.28	0.0058	0.14	0.024	0.12	0.011	14
Spleen	150	0.12	*	0.17	0.010	*	0.012	*	0.030	0.0044	3.1
Pancreas	100	0.27	0.010	0.15	0.0083	0.0010	0.077	<0.01	0.050	0.0030	3.5
Total	55 kg	>33	>4.1	>63	>3.3	>0.35	>7.7	>5.7	>22	>0.66	>1,800
Values as determined by Schroeder[11]	70 kg	30	<6	100	*	*	20	<10	80	*	2,300

Table 9.—Contents of Heavy Metals in Organs and Whole Body, mg

* Not calculated because there were less than five samples available.

Table 10.—Statistically Significant Correlation Coefficients Between Pairs of Elements

Pairs of Elements	Correlation Coefficients
T Hg—Cd	.96
MeHg—Cu	.88
T Hg—Zn	.62
T Hg—MeHg	.56
Ni—Sb	.53
Cd—Zn	.52
Mn—Ni	.52
Cu—Mn	.51

ysis were lower than those of Tipton et al. However, Cd concentrations in liver and kidney in Japanese people were clearly higher than Curry and Knott's[8] findings in England, or Hammer and co-workers'[9] values in the United States. The biggest difference between our study and that of Tipton and colleagues was regarding the range of tissue concentrations. In our analysis, the maximum concentration was usually not over ten times the minimum, and was never over 20 times. In their data, the concentration was from several hundred to several thousand times over the minimum, even in essential metals.

Only a few data have been reported about the normal Hg concentration, but our values coincided fairly well with the report by Joselow et al.[10] There have been few previous analytic studies of the concentration of Be, MeHg, and Sb in the human body, and there are few data for comparison.

Table 10 shows the correlation coefficients (above $r=.50$) between the average concentrations of various pairs of metals in all tissues. Extremely high correlations are found between T Hg and Cd, and MeHg and Cu. The correlation coefficient between T Hg and MeHg was .56, but became .95 when the kidney was excluded. The correlation between Cd and Zn is .52 (significant, $P=.05$). Zinc, Cd, and Hg belong to the Be group, and the higher correlations with each other may be based on this fact.

From the behaviors of heavy metals in the order of accumulation in the tissues, Cd, T Hg, MeHg, and Zn were found in large quantities in the metabolic organs, whereas concentrations of Cr, Ni, and Pb were greatest in the tissues exposed to the exterior. As for Cu and Mn, a relatively constant distribution was observed throughout the whole body.

As to the difference between sexes, the concentration of toxic metals, such as Cd, Hg, and Pb (except MeHg), tended to be higher in the female, but that of essential metals, such as Cr, Cu, and Mn, tended to be higher in the male. This may reflect a difference in general metabolism.

Japanese people had relatively higher concentrations of Cd and Hg in their blood than did American and European people, but they also had a much higher concentration of Cd and Hg in other tissues of their bodies. This may indicate the extent of present environmental pollution caused by Cd and Hg in Japan.

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