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Concentrations of Cadmium, Manganese, Lead, Copper and Zinc in the Blood of Hokkaido Residents

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北海道住民の血液中カドミウム，マンガン，鉛，銅，亜鉛濃度

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Introduction

In Japan, there are many problems to be solved in relation to diseases caused by environmental pollution such as Minamata disease, Itai itai disease and pulmonary disease. The mass media have called our country an environmentally polluted island. However, Hokkaido, located in the northern part of the country, is still the least populated and least polluted area in Japan. Its natural environment is characterized by snowfall and cold weather for about half the year.

This paper is concerned with (1) the establishment of background values and distributions of blood metal contents in inhabitants of Hokkaido, and (2) comparisons of metal contents in blood by sex and age in subjects from rural and urban districts in a few areas of central and eastern Hokkaido.

Materials and Methods

One hundred and forty male and 163 female subjects aged from 20 to 65 years living in the Hidaka, Sarabetsu and Sapporo areas of Hokkaido had blood drawn from the Vena mediana cubiti by a heparinized vacuum syringe. These samples were diluted with 15 times or 450 times the volume of 0.1 N HCl respectively, prior to measuring copper (Cu), manganese (Mn), lead (Pb) and cadmium

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Table 1. Analytical conditions for Zeeman type flameless spectrophotometry.

		Copper	Zinc	Manganese	Lead	Cadmium
Wavelength	(nm)	324.7	213.8	279.4	283.3	228.8
Lamp current	(mA)	7.5	5	7.5	10	5
Slit width in nm		2.2	1.1	1.1	1.1	1.1
Cuvette type		cup	cup	cup	cup	cup
Flow gas	(Ar)					
Sheath	(ℓ/min)	3.3	3.0	3.0	3.0	3.0
Carrier	(ℓ/min)	—	0.5	—	—	—
Drying current	(A)	16–18	16–18	16–18	16–18	16–18
Time	(sec)	120–	60	120–	120–	120–
Ashing current*	(A)	100	80	100	80	80
Atomize current	(A)	300	240	260	220	220
Temperature	(°C)	2500	2000	2200	1900	1900
Range	(mV)	10	10	10	10	10
Expansion		3	1	3	3	2.5
Response		1	1	1	1	1
Detective sense $g\times10^{-12}$ in 10 $\mu\ell$		30	1	30	8	0.6

* ramp mode; the rate of increase in electric current one Amp. per sec.

(Cd) or zinc (Zn).

These diluted blood samples were directly analyzed by the method of standard additions using 10 $\mu\ell$ of sample with a Zeeman type flameless atomic absorption spectrophotometer[1] (Hitachi Model 170-70 type). Analytical conditions by the Zeeman type flameless atomic absorption spectrophotometry are shown in Table 1.

Results

The mean concentrations in males from the three locations in Hokkaido were in μg/100 mℓ : 0.36 Cd, 1.70 Mn, 7.5 Pb, 95.0 Cu and 854 Zn, and of females were in μg/100 mℓ : 0.32 Cd, 1.85 Mn, 6.6 Pb, 96.9 Cu and 815 Zn. Significant differences between male and female subjects were recognized in Cd, Mn and Pb (Table 2).

Table 2. Concentrations of metal in blood of inhabitants from the three locations of Hokkaido (as μg/100 mℓ).

	Male (N=145)			Female (N=163)		
	Median	Mean±S.E.	Range	Median	Mean±S.E.	Range
Cd	0.32	0.36±0.01	0.09–0.94	0.27	0.32±0.01	0.08–1.08
Mn	1.6	1.7±0.05	0.6–6.5	1.8	1.8±0.04	0.8–3.6
Pb	7.0	7.5±0.3	2.7–34.6	5.9	6.6±0.3	2.3–38.2
Cu	97	95± 1	58–130	97	97±1	68–135
Zn*	843	854±10	619–1135	795	815±14	425–1837

* N=112 (Male) N=138 (Female)

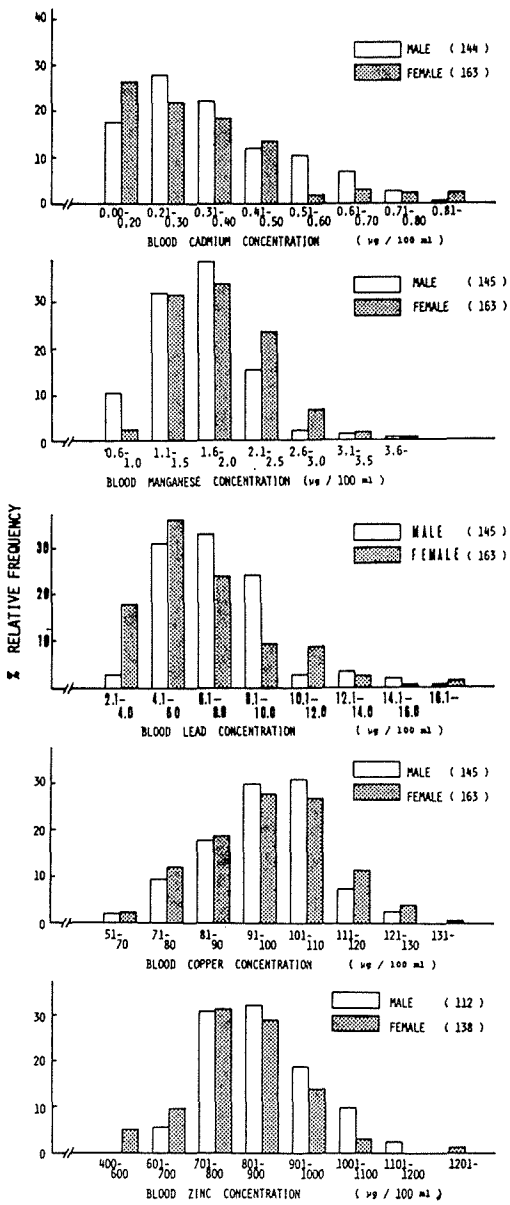

Fig. 1. Distribution of blood concentration. Numbers in parenthesis mean number of subjects.

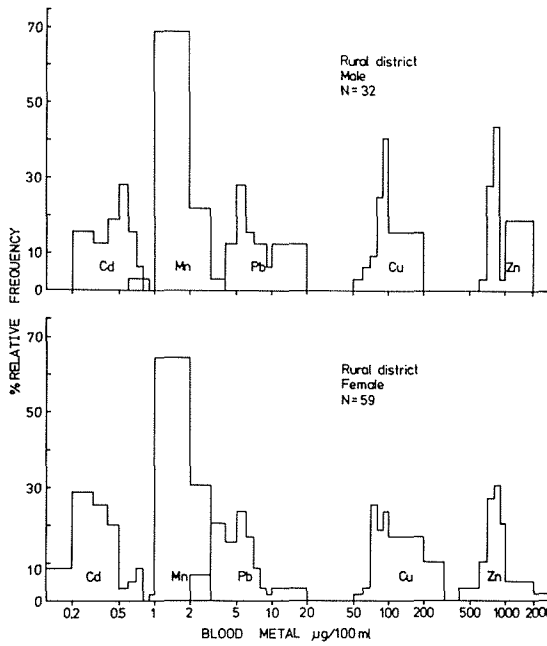

Fig. 2. Pattern of blood metal concentration in rural district of Hidaka. Horizontal axis shows logarithmic scale in μg/100 mℓ of blood.

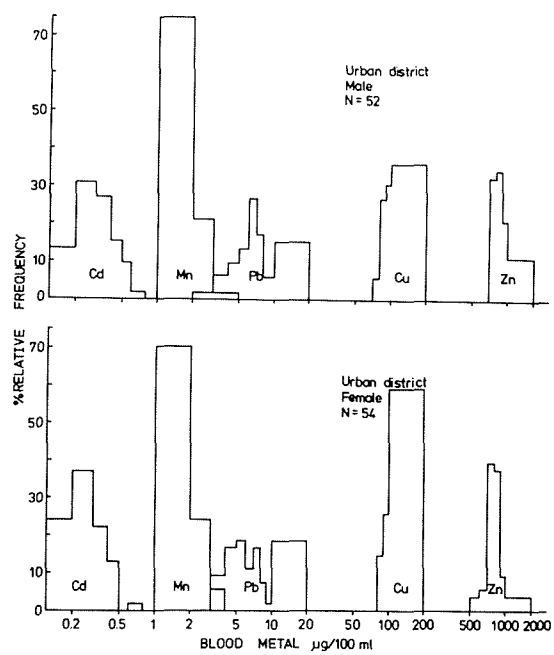

Fig. 3. Pattern of blood metal concentration in urban district of Hidaka. Horizontal axis shows logarithmic scale in μg/100 mℓ of blood.

Table 3. Comparison of cadmium, manganese, lead, copper and zinc concentration (Mean±S.E. μg/100 mℓ) in blood between rural and urban districts in Hidaka area.

	Male			Female		
	Rural (32)	Urban (52)	Signif.	Rural (59)	Urban (54)	Signif.
Cd	0.48±0.03	0.33±0.02	P<0.01	0.39±0.02	0.28±0.20	P<0.01
Mn	1.7±0.1	1.8±0.0	N.S.	1.9±0.1	1.8±0.1	N.S.
Pb	7.2±0.5	7.3±0.4	N.S.	5.4±0.3	6.8±0.4	P<0.01
Cu	90±3	96±2	P<0.01	90±2	101±2	P<0.01
Zn	852±20	856±14	N.S.	832±24	821±21	N.S.

These average values, as μg/100 mℓ, in the three locations were distributed from 0.24 to 0.48 Cd, 1.4 to 2.2 Mn, 5.4 to 9.7 Pb, 89.7 to 101 Cu and 757 to 859 Zn.

The distributions of blood Cd and Pb levels showed a logarithmically normal distribution. Those of Cu and Zn showed normal distributions and Mn showed a medium distribution (Fig. 1). Figure 2 and 3 show the distribution of blood metal concentrations of male and female residents in rural and urban districts of the Hidaka area. These figures show that the concentrations of Cd, Mn, Pb, Cu and Zn in blood distribute independently of each other metals.

In a comparison of metal concentrations in blood between rural and urban districts, Cd showed a significantly higher level in both male and female subjects in the rural districts. Lead concentration showed a significant increase in female subjects of the urban district and Cu concentration showed the significantly lower levels in both male and female subjects in the rural district (Table 3).

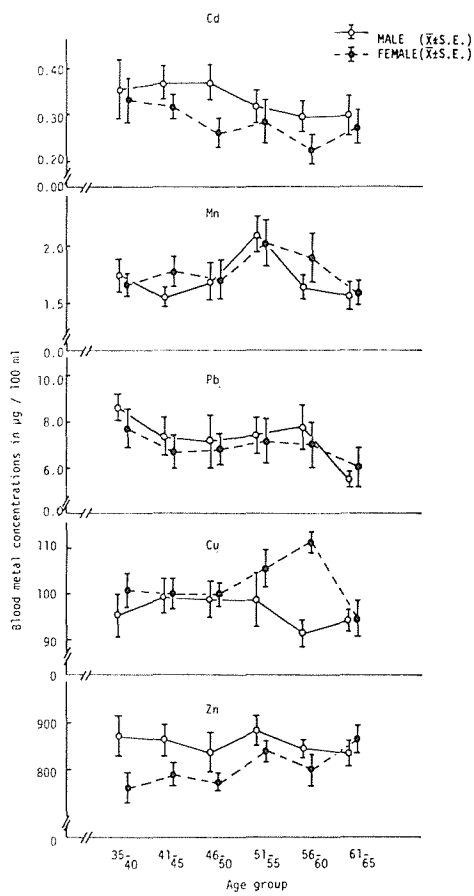

Fig. 4. Changes in blood metal level by sex and age in Hidaka area. Subjects are 52 male and 54 female.

Blood Cd concentration by age showed a peak value in the late forties and tended to decrease at fifty years and over. Manganese concentration in blood of the 51-55 age group showed a peak level. Any significant changes in Pb and Zn levels in blood of each age group from 35 to 65 years were not recognized except for the differences between male and female.

Copper concentration in blood showed a remarkable peak level in the late fifties of female. This level of Cu was significant in comparison with any of the other age group (Fig. 4).

Discussion

Although many investigations on signal metal concentrations for sample of Pb, Cd, Hg in human blood have been carried out from the viewpoint of environmental pollution. There have been few reports on the normal values of each metal in Japanese human blood. Blood trace metal levels many change due to many environmental factors caused by urbanization and industrialization.

The mean blood Cd level reported by Kubota, *et al.*[2] for 243 individuals from 19 locations in the U. S. A. was 0.94 μg/100 mℓ which were calculated by Hecker, *et al.*[3] They showed also 1.71 μg/100 ℓ for 47 people in Ann Arbor, Mich. and 0.57 μg/100 mℓ for 90 Yanomanö Indians in Venezuela.

Patients with Itai itai disease and residents in the same area as these patients in Japan were determined to have 2.13 μg/100 ml on the average[4].

The values of blood Cd levels in this report were 0.36 μg/100 mℓ for 145 male subjects and 0.32 μg for 63 female subjects.

Blood Mn levels of nonindustrially exposed populations have been reported to range from 1.0 to 5.28 μg/100 mℓ[5,6,7] compared with 1.70 μg for male subjects and 1.85 μg for female subjects in this report. It seems that microanalysis of blood Mn determined by the direct method of standard additions with a Zeeman type flameless atomic absorption spectrophotometer is better than the extraction method with an organic solvent. The values of our report are similar to the values of Kaneko, *et al.*[6] and Tasalev[7] who used a direct atomic absorption spectrometric method. And, perhaps, the peak in Mn values for the 51-55 age group in this report is worth a mention.

Regional differences in blood Pb level are remarkable as shown by Goldwater and Hoover[8] in 16 countries, Kubota, *et al.*[2] in the U. S. A., Haeger-Aronsen, *et al.*[9] in Sweden, Nakagawa, *et al.*[10], Hasegawa[11], Taira and Miura[12] and Saito, *et al.*[13] in Japan, Hecker, *et al.*[3] in the U. S. A. and Venezuela, Nay and Ramachandran[14] in Thailand, Auermann, *et al.*[15] in Germany and Wibowo, *et al.*[16] in Holland; average values range from 0.83 to 32 μg/100 mℓ of blood. Our levels of 7.5 μg/100 mℓ for males and 6.6 μg/100 mℓ for female subjects in Hokkaido were less than the other values except for those of Venezuela.

Blood Cu levels which have been reported by Hecker, *et al.*[3] show an almost similar level in both acculturated and unacculturated populations, that is both peoples in Ann Arbor, Mich. and in southern Venezuela, with consideration for analytical methods. However, in our results a significantly higher level of blood Cu concentration was observed in urban districts. The values were similar to those of Hecker, *et al.*[3] in Michigan and Venezuela. An interesting fact in our investigation is that a high blood Cu level was observed in the late fifties of female, depending perhaps on the hormonal specificity caused by the age. Significant cor-

relation of the blood Cu level to carbonic anhydrase isozyme B, catalase, delta aminolevulinic acid dehydratase, pyrimidine 5′ nucleotidase and super oxide dismutase in erythrocytes were recognized in our other study[17].

Significantly lower levels of blood Zn concentrations were observed in female subjects compared with male subjects in those under fifty years old, and a significant correlation with hemoglobin level was recognized in rural districts.

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Summary

Background values for the concentrations of cadmium, manganese, lead, copper and zinc were determined in samples of blood from 308 residents in rural and urban areas of Hokkaido, which is characteristic of northern regions. The mean blood cadmium and lead concentrations were markedly lower than published values. Significant differences were observed in the mean values of cadmium, manganese and lead by sex, and in cadmium, lead and copper by districts. A markedly high blood copper level was observed for females in the 56–60 age group. Manganese concentration in blood of the 51–55 age group showed a peak level. The blood zinc level in females was lower in those below fifty years of age. These results are important for judging pollution levels in the human body and environmental conditions in the future.