Interrelationship between the Concentration of Toxic and Essential Elements in Korean Tissues

Young Chan Yoo,[a] Sang Ki Lee,[a] Ja Yeol Yang,[a] Ki Wook Kim,[a] Soo-Yeun Lee,[a] Seung Min Oh,[b] and Kyu Hyuck Chung*,[b]

[a]National Institute of Scientific Investigation, 331–1 Shinwol-7 dong, Yangchon-Ku, Seoul 158–707, Korea and [b]College of Pharmacy, Sungkyunkwan University, 300 Chunchun-dong, Jangan-Ku, Suwon, Kyunggi-do 440–746, Korea

(Received September 13, 2001; Accepted October 26, 2001)

In the past a few decades, particular interest has been focused on the distribution and interaction between toxic and essential elements in animals and humans, since such interactions might have adaptive implications to environmental pollution. The current study was performed to assess the correlation of elemental concentration with age and the correlation between toxic and essential elements in Koreans. Toxic elements, such as Cd, Pb, Hg, and essential elements such as Se and Zn, were analyzed in internal organs (liver, kidney cortex, kidney medulla, heart, lung, spleen, cerebrum, testis and bone) of 162 Korean cadavers. The tissues were digested with a microwave digestion system and the 5 elements were determined by inductively coupled plasma atomic emission spectrometry. Positive correlation with age was observed in the following cases: Cd in the liver, kidney cortex, kidney medulla, heart and testis; Pb in testis and bone. The concentration of Hg, Se and Zn was not correlated with age in any of the tissues tested. A significantly high correlation between Hg and Se, Pb and Se was observed in liver, kidney cortex, kidney medulla, heart, lung, spleen, cerebrum, testis and bone. The correlation between Cd and Zn was significant in the liver, kidney cortex, kidney medulla, heart, lung, cerebrum, testis and bone. These results indicate that the distribution of toxic elements is similar to that of essential elements in all tissues.

Key words —— Korean, tissue, heavy metal, interrelationship, distribution

*To whom correspondence should be addressed: College of Pharmacy, Sungkyunkwan University, 300 Chunchun-dong, Jangan-Ku, Suwon, Kyunggi-do 440–746, Korea. Tel.: +82-31-290-7714, Fax: +82-31-292-8800, E-mail: khchung@skku.ac.kr

INTRODUCTION

Trace elements in the body may be divided into two classes depending on whether levels are maintained by some biological process. Where levels are maintained, the elements are essential. The others, due to contamination from food or environment, are termed nonessential.[1)] Because heavy metal concentrations in human body may vary with food or environment, it is very difficult to establish standard values or a range of standard values for heavy metals in human tissues. Tissue concentration of heavy metals, and the interaction between essential and other metals, have been studied extensively in many countries.[1–9)] Selenium (Se) is an essential trace element for human and is well known as a modifying factor in the toxicity of metal compound. Many studies support the close correlation between Se and cadmium (Cd) or mercury (Hg).[10–16)] Animal experiments have also indicated an interaction between Se and Cd. These experiments show that Se prevents the acute damaging effect of Cd on rat tissues.[17–19)] However, there is no information on the interaction between toxic and essential elements in Korean. The purpose of this study is to measure the levels of Cd, Hg, lead (Pb), Se and zinc (Zn) in the internal organs and to determine any correlation with age and interrelationship between toxic and essential elements in Korean humans who lived in Seoul or its satellite cities.

MATERIALS AND METHODS

Preparation of Samples —— The human tissues analyzed were obtained from autopsied cadavers, og forwho had lived in Seoul or its satellite cities and whose ages ranged from 13 to 87 years. They were subject to undergoing forensic medical examinations at the National Institute of Scientific Investigation of Korea, from December 1998 to November 2000. The numbers of male and female cadavers were 102 and 60, respectively (Table 1). All cadavers were selected randomly. Nine organs (liver, kidney cortex, kidney medulla, cerebrum, heart, lung, spleen, bone and testis) were removed from different subjects. The tissue samples were stored at a temperature below –30°C before analysis.

Analytical Methods ——Analytical steps were performed according to the procedure described earlier.[20)] A 1.0–2.0 g portion of sample was digested with 6 ml of concentrated nitric acid and 1 ml of

Table 1. Distribution of Age and Gender of Individual Subjects

Age group	Female	Male	Total
Teens	10	3	13
Twenties	7	10	17
Thirties	26	28	54
Forties	12	30	42
Fifties	4	20	24
Sixties		9	9
Over seventies	1	2	3
Total	60	102	162

Table 2. Analytical Conditions of ICP-AES

Gas flow rate
Torch gas: High flow
Auxiliary gas: Medium (1.0 l/min)
Nebulizer gas: On (PSI): 30.1
Approximate RF power (w): 1350
Slit height (mm): 3
Observation height (mm): 14.9
Peristaltic pump parameters
Pump rate (RPM): 100
Relaxation time (sec): 10
Pump tubing type: EP-19
Wavelength (nm): Cd (228.802), Hg (184.950), Pb (220.353), Se (196.090), Zn (213.856)

hydrogen peroxide in a sealed teflon vessel (Milestone s. r. l., mls 1200 mega, Italy) and diluted with distilled water. Cd, Pb, Hg, Se and Zn were determined by inductively coupled plasma atomic emission spectrometry (ICP-AES, Thermo Jarrell Ash Co., Atomscan25, U.S.A., Table 2). The reagent blanks and standard solutions were treated in a manner identical to that for the samples.

Statistical Methods —— Students *t*-test and calculation of Pearson's correlation coefficients were conducted using the SPSS program.

RESULTS AND DISCUSSION

Table 3 shows the arithmetic mean of the elemental concentration of Korean liver, kidney cortex, kidney medulla, cerebrum, heart, lung, spleen, bone and testis expressed in micrograms per gram wet weight. When the concentration was below the detection limit, the value of zero was substituted to calculate the mean. The highest concentration of Cd was found in the kidney cortex and medulla, which was ten fold higher than in the liver. These values determined in kidney and liver were higher than those in Chinese or European people reported in the literature,[5,21] but lower than in Japanese people.[2,3,7] Large amounts of Hg and Pb were found in the bone. Mercury had a tendency to decrease in the following order: kidney cortex, kidney medulla, liver, lung, spleen, heart, cerebrum and testis. The highest concentration of selenium was found in kidney cortex. Considerable amounts of Zn were detected in all organs. Higher concentrations of zinc were found in bone, kidney cortex, kidney medulla and liver. The concentrations of selenium and zinc in organs were generally in good agreement with the values previously reported for Japanese.[7] In the kidney, elemental concentrations were higher in the cortex than in the medulla.

Table 4 shows the age-related variations in the elemental concentrations in the organs. Positive correlation with age was observed in the following cases: Cd in the kidney cortex, kidney medulla (Fig. 1), liver, heart and testis; Pb in testis and bone.

Table 5 summarizes the correlation coefficients between toxic and essential elements in Korean tissues. In the case of Cd, this element correlated strongly with Zn in most fo the organs tested. The significantly positive correlations between Cd and Zn, particularly those in kidney cortex and medulla (Fig. 2), may indicate the involvement of metallothionein in the accumulation of Cd in the kidney, as has been previously reported.[7,22] Mercury and selenium were also significantly correlated in most organs tested. Correlations between the concentration of Hg and Se in the kidney cortex and medulla are shown in Fig. 3. The correlation between Hg and Se has been reported in human and animals.[7–9,23–26] Lead and selenium were also significantly correlated in all organs tested.

From the present study, high correlations between essential elements, such as Se, Zn, and toxic elements, such as Cd, Hg and Pb, were observed in Korean organs. These results might be a reflection of the protective effects of essential elements against toxic elements.

In conclusion, The amounts of Cd, Hg, Pb, Se and Zn in the internal organs were determined by ICP-AES in 162 Korean cadavers of former residents of Seoul or its satellite cities. The highest concentration of Cd was found in the kidney cortex and medulla. Mercury and lead were found in large quantities in the bone. The highest concentration of Se was found in the kidney cortex, and considerable amounts of Zn were detected in all organs. Positive

Table 3. Elemental Concentrations in Internal Organs of Koreans (μg/g·wet weight)

Element	Liver		Kidney cortex		Kidney medulla	
	N	Mean (S.D.)	N	Mean (S.D.)	N	Mean (S.D.)
Cd	159	2.7 (2.0)	159	37 (18)	154	28 (15)
Hg	159	0.18 (0.18)	158	0.27 (0.25)	154	0.24 (0.25)
Pb	161	0.15 (0.28)	159	0.17 (0.26)	155	0.13 (0.22)
Se	157	0.82 (0.81)	157	1.2 (0.49)	150	1.0 (0.45)
Zn	157	48 (17)	156	49 (15)	154	41 (15)
Element	Heart		Lung		Spleen	
	N	Mean (S.D.)	N	Mean (S.D.)	N	Mean (S.D.)
Cd	160	0.34 (0.38)	154	0.46 (0.53)	155	0.42 (0.35)
Hg	162	0.11 (0.21)	158	0.15 (0.18)	157	0.15 (0.16)
Pb	162	0.17 (0.27)	159	0.23 (0.31)	158	0.13 (0.24)
Se	158	0.54 (0.44)	156	0.79 (0.76)	149	0.86 (0.58)
Zn	151	26 (6.0)	154	12 (4.0)	157	17 (4.8)
Element	Cerebrum		Testis		Bone	
	N	Mean (S.D.)	N	Mean (S.D.)	N	Mean (S.D.)
Cd	158	0.20 (0.29)	85	0.30 (0.23)	154	0.09 (0.10)
Hg	156	0.09 (0.11)	86	0.07 (0.11)	161	2.3 (2.0)
Pb	159	0.07 (0.17)	86	0.14 (0.23)	160	1.5 (1.4)
Se	158	0.40 (0.36)	86	0.48 (0.40)	156	0.36 (0.62)
Zn	159	12 (4.0)	84	12 (3.7)	158	56 (17)

N: Number of specimens, S.D.: Standard deviation

Table 4. Correlation Coefficient of Elemental Concentrations with Age

	Liver	Kidney cortex	Kidney medulla	Heart	Lung	Spleen	Cerebrum	Testis	Bone
Cd	0.184*	0.329**	0.291**	0.197*	0.084	0.151	0.094	0.242*	0.097
Hg	0.060	−0.123	−0.129	−0.012	−0.035	0.016	−0.039	0.112	−0.063
Pb	−0.002	−0.051	0.000	0.019	−0.072	−0.133	−0.014	0.220*	0.252**
Se	0.150	−0.058	−0.038	0.022	0.079	0.106	0.076	0.041	−0.031
Zn	−0.009	0.089	0.107	0.047	−0.002	0.038	0.086	0.029	0.125

Figures in the table are coefficients between elemental concentration and age which are significant at 5% (*) and 1% (**), respectively.

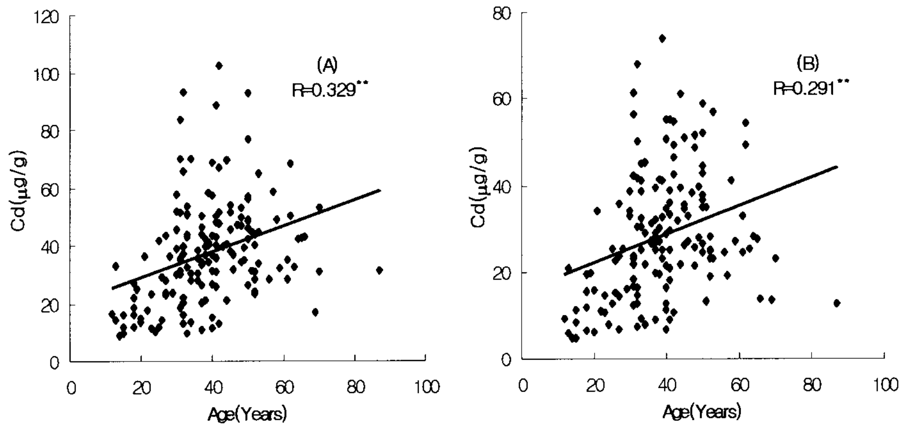

Fig. 1. Correlation between Age and Cd Concentration in Kidney Cortex (A) and Kidney Medulla (B)
All correlations are significant at 1%.

Table 5. Correlation Coefficient between Toxic and Essential Elements in Korean Tissues

Correlation	Tissue				
	Liver	Kidney cortex	Kidney medulla	Heart	Lung
Cd/Zn	0.534**	0.577**	0.682**	0.227**	0.344**
Cd/Se	−0.090	0.079	0.009	0.118	−0.059
Hg/Zn	0.232**	0.037	0.125	0.148	0.204*
Hg/Se	0.070	0.265**	0.219**	0.455**	0.335**
Pb/Zn	0.175*	0.088	0.136	0.295**	0.179*
Pb/Se	0.158*	0.358**	0.283**	0.556**	0.423**

Correlation	Tissue			
	Spleen	Cerebrum	Testis	Bone
Cd/Zn	0.146	0.390**	0.321**	0.170*
Cd/Se	−0.005	0.113	0.031	0.270**
Hg/Zn	0.306**	0.007	0.087	−0.091
Hg/Se	0.454**	0.513**	0.590**	0.268**
Pb/Zn	0.123	0.148	0.198	0.153
Pb/Se	0.347**	0.246**	0.536**	0.465**

Figures in the table are correlation coefficients between toxic and essential elemental concentration which are significant at 5% (*) and 1% (**), respectively.

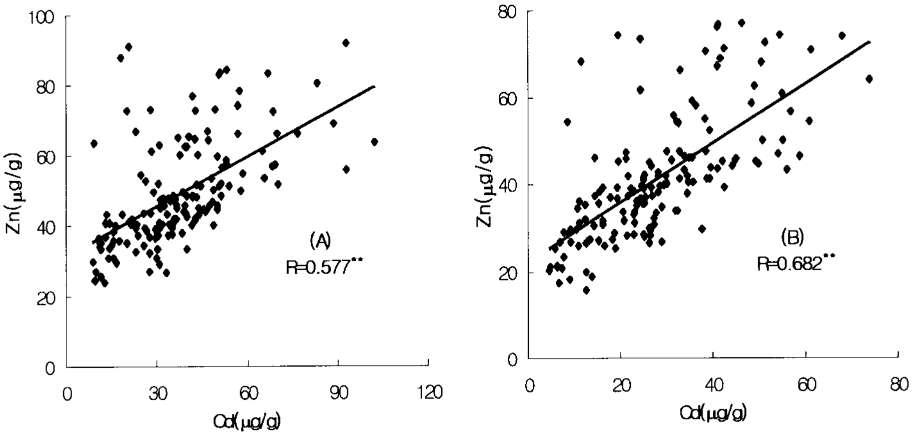

Fig. 2. Correlation between the Concentration of Cd and Zn in Kidney Cortex (A) and Kidney Medulla (B)
All correlations are significant at 1%.

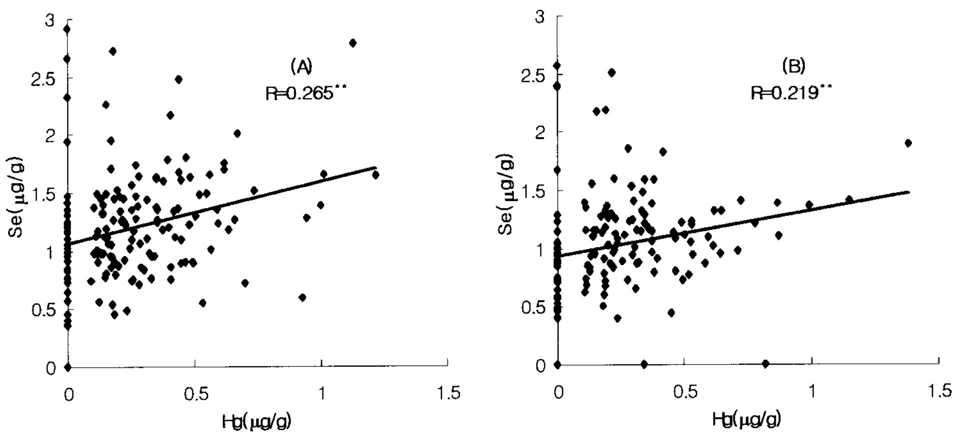

Fig. 3. Correlation between the Concentration of Hg and Se in Kidney Cortex (A) and Kidney Medulla (B)
All correlations are significant at 1%.

correlation with age was observed in the following cases: Cd in kidney cortex, kidney medulla, liver, heart and testis; Pb in testis and bone. Significantly positive correlations were observed between Hg and Se, Pb and Se, Cd and Zn in most tissues. These results reflect the protective effects of essential elements against toxic elements in human organs.

Acknowledgements This study was supported by a Grant-in Aid from the Ministry of Environment of Korea.

REFERENCES

1) Liebscher, K. and Smith, H. (1968) Essential and nonessential trace elements. A method of determining whether an element is essential or nonessential in human tissue. *Arch. Environ. Health*, **17**, 881–890.
2) Sumino, K., Hayakawa, K., Shibata, T. and Kitamura, S. (1975) Heavy metals in normal Japanese tissues. *Arch. Environ. Health*, **30**, 487–494.
3) Yukawa, M., Amano, K., Yasumoto, M. S. and Terai, M. (1980) Distribution of Trace Elements in the Human Body Determined by Neutron Activation Analysis. *Arch. Environ. Health*, **35**, 36–44.
4) Yamamoto, Y., Ushiyama, I. and Nishi, K. (1997) Neutron Activation Analysis of trace elements in human organs. *Current Topic in Forensic Science*, **1**, 73–76.
5) Drasch, G., Müller, R. K., Grasemann, F., Adang, M., Roider, G. and Wowra, D. (1994) Comparison of the burden of the population in the region of Leipzig and Munich with the heavy metals cadmium, lead and mercury — an investigation of human tissues. *Gesundheitswesen*, **56**, 263–267.
6) Oldereid, N. B., Thomassen, Y., Attramadal, A., Olaisen, B. and Purvis, K. (1993) Concentrations of lead, cadmium and zinc in the tissues of reproductive organs of men. *J. Reprod. Fertil.*, **99**, 421–425.
7) Yoshinaga, J., Matsuo, N., Imai, H., Nakazawa, M., Suzuki, T., Morita, M. and Akagi, H. (1990) Interrelationship between the concentrations of some elements in the organs of Japanese with special reference to selenium-heavy metal relationships. *Sci. Total Environ.*, **91**, 127–140.
8) Weiner, J. A. and Nylander, M. (1993) The relationship between mercury concentration in human organs and different predictor variables. *Sci. Total Environ.*, **138**, 101–115.
9) Schmidt, R. and Wilber, C. G. (1978) Mercury and lead content of human body tissues from an elected population. *Med. Sci. Law*, **18**, 155–158.
10) Högberg, J. and Alexander, J. (1986) Selenium. In *Handbook on the toxicology of Metals*, vol. 2 (Friberg, L., Nordberg, G. F. and Vouk, V. B., Eds.), Elsevier, Amsterdam, pp. 482–520.
11) Nordberg, G. F., Fowler, B. A., Friberg, L., Jernelöv, A., Nelson, N., Piscator, M., Sandstead, H. H., Vostal, J. and Vouk, V. B. (1978) Factors influencing metabolism and toxicity of metals: A concensus report by the task group on metal interaction. *Environ. Health Perspect.*, **25**, 3–41.
12) Magos, L. and Webb, M. (1980) The interaction of selenium with cadmium and mercury. *CRC Crit. Rev. Toxicol.*, **8**, 1–42.
13) Ganther, H. E., Groudie, C., Sunde, M. L., Kopecky, M. J., Whanger, P. A., Oh, S. H. and Hockstra, W. G. (1972) Selenium: Relation to decreased toxicity of methylmercury added to diets containing tuna. *Science*, **175**, 1122–1124.
14) Ohi, G., Nishigaki, S., Seki, H., Tamura, Y., Maki, T., Maeda, H., Ochiai, S., Yamada, H., Shimamura, Y. and Yaggu, H. (1975) Interaction of dietary methylmercury and selenium on accumulation and retention of these substances in rat organs. *Toxicol. Appl. Pharmacol.*, **32**, 527–533.
15) Nordberg, G. F., Parizek, J., Pershagen, G. and Gerhardsson, L. (1986) Factors influencing metal toxicity. In *Handbook on the Toxicology of Metals*, vol. 1 (Friberg, L., Nordberg, G. F. and Vouk, V. B., Eds.), Elsevier, Amsterdam, pp. 175–205.
16) Kido, T., Tsuritani, I., Honda, R., Yamaya, H., Ishizaki, M., Yamada, Y. and Nagawa, K. (1988) Selenium, zinc, copper and cadmium concentration in livers and kidneys of people exposed to environmental cadmium. *J. Trace Elem. Electrolytes Health Dis.*, **2**, 101–104.
17) Kar, A. B., Das, R. P. and Mukerji, B. (1960) Prevention of cadmium induced changes in the gonads of rat by zinc and selenium — A study in antagonism between metals in the biological system. *Proc. Nat. Inst. Sci. India B26*, Suppl., 40–50.
18) Gunn, S. A., Gould, T. C. and Anderson, W. A. D. (1968) Mechanisms of zinc, cysteine and selenium protection against cadmium-induced vascular injury to mouse testis. *J. Reprod. Fertil.*, **15**, 65–70.
19) Meyer, S. A., Hous, W. A. and Welch, R. M. (1982) Some metabolic interrelationships between toxic levels of cadmium and non-toxic levels of selenium fed to rats. *J. Nutr.*, **112**, 954–961.
20) Yoo, Y. C. (1998) Rapid determination of toxic elements in human tissue. *Annual Report of NISI.*, **30**, 33–42.
21) Zhuang, G. S., Wang, Y. S., Tan, M. G., Zhi, M., Pan, W. Q. and Cheng, Y. D. (1990) Preliminary study of the distribution of the toxic elements As,

Cd, and Hg in human hair and tissues by RNAA. *Biol. Trace Elem. Res.*, **26–27**, 729–736.

22) Chung, J., Nartey, N. O. and Cherian, M. G. (1986) Metallothionein levels in liver and kidney of Canadians — A potential indicator of environmental exposure to cadmium. *Arch. Environ. Health*, **41**, 319–323.
23) Koeman, J. H., Peeters, W. H. M., Koudstaal-Hol, C. H. M., Tjioe, P. S. and de Goeji, J. J. M. (1973) Mercury-selenium correlations in marine mammals. *Nature*, **245**, 385–386.
24) Koeman, J. H., van de Ven, W. S. M., de Goeji, J. J. M., Tjioe, P. S. and van Haaften, J. L. (1975) Mercury and selenium in marine mammals and birds. *Sci. Total Environ.*, **3**, 279–287.
25) Norstrom, R. J., Schweinberg, R. E. and Collins, B. T. (1986) Heavy metals and essential elements in livers of the polar bear (Ursus maritimus) in the Canadian Arctic. *Sci. Total Environ.*, **48**, 195–212.
26) Kari, T. and Kauranen, P. (1978) Mercury and selenium content of seals from fresh and brackish waters in Finland. *Bull. Environ. Contam. Toxicol.*, **19**, 273–280.