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VARIATION IN THE CONCENTRATION OF CADMIUM IN HUMAN KIDNEY AS A FUNCTION OF AGE AND GEOGRAPHIC ORIGIN

H. MITCHELL PERRY, JR., M.D.,*
ISABEL H. TIPTON, PH.D.,**
HENRY A. SCHROEDER, M.D.,***
ROBERT L. STEINER, M.S.,****
AND MARY JANE COOK, M.S.*****

From the Hypertension Division, Department of Internal Medicine, Washington University School of Medicine, St. Louis, Mo.; Department of Physics, University of Tennessee, Knoxville, Tenn.; and Health Physics Division, Oak Ridge National Laboratory, Oak Ridge, Tenn.

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WHILE analyzing human organs for trace metals, one of us (Tipton) observed surprisingly large amounts of cadmium in the kidney.[1] This unexpected observation prompted a search for factors correlated with the concentration of renal cadmium. In order to explore the effect of age, kidneys of children from St. Louis were compared with kidneys of adults from St. Louis. In order to explore the effect of geographic origin, kidneys of adults from various parts of the world were compared with kidneys of adults from St. Louis.

Liver was the only other organ which consistently contained measurable concentrations of cadmium by the spectrographic technique used.[1] Therefore both hepatic and renal concentrations were studied. Cadmium lies directly below zinc in the periodic table and the two metals are chemically similar; moreover, cadmium is quite different from any other metal commonly found in the human body. The concentration of cadmium, which has no known biologic function, was therefore compared with that of zinc, which is essential to man. Accordingly, both renal and hepatic concentrations of both cadmium and zinc have been presented.

The ideal source of tissues for analysis would seem to be healthy subjects who died suddenly and traumatically. Even in the United States, however, children meeting this criterion were difficult to find; while in places like the non-industrialized areas of Africa, no such subjects were available. It was therefore necessary to use hospitalized patients who had died of various illnesses. Any disease known to produce hepatic or renal abnormalities was excluded; moreover, only grossly normal tissues were assayed.

*Established Investigator of the American Heart Association, Hypertension Division, Department of Internal Medicine, Washington University School of Medicine, St. Louis, Mo.
**Department of Physics, The University of Tennessee, Knoxville, Tenn.
***Formerly with the Hypertension Division at Washington University School of Medicine. Now with the Department of Physiology, Dartmouth Medical School, Hanover, N.H.
****Formerly with the Department of Physics at The University of Tennessee. Now with the Research Laboratories of the Aluminum Company of America, New Kensington, Pa.
*****Health Physics Division, Oak Ridge National Laboratory, Oak Ridge, Tenn.

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Human Subjects Project

Since freezing seems to be the ideal method of preserving tissues, samples collected in the United States were frozen. Unfixed human tissue cannot be imported; therefore formalin was added to the foreign samples. The addition of any substance to a tissue raised the possibility of contamination, and the immersion of a tissue in any liquid raised the possibility of eluting trace constituents. Falsely high analytical values from contamination were excluded by demonstrating the purity of the preservative. Losses from elution were excluded by analysis of the preserving fluid together with each tissue. Moreover, comparisons were limited to tissues that had been similarly handled. Thus assays were performed on two aliquots of each tissue from the American adults. Frozen aliquots were compared with frozen tissues from American children, and formalin-preserved aliquots were compared with formalin-preserved tissues from foreign adults.

MATERIAL

The kidneys and livers of 157 subjects were analyzed for cadmium and zinc. Organs with gross pathologic abnormalities were excluded. No subject was known to have had any industrial or other unusual exposure to metal. The subjects belonged to three categories: American adults, American children, and foreign adults.* The American children were divided into three age groups and the foreign adults were divided into eight national groups.

The 24 American adults ranged in age from 46 to 77 years. The 38 American children were 12 years of age or less, and 7 were stillborn. All American subjects died in St. Louis and the autopsies were performed by the members of the Department of Pathology of the Washington University School of Medicine. Table I presents information about sex, age, race, and cause of death.

The 95 foreign adults came from ten cities in eight different political units of Europe, Africa, and Asia. Their ages ranged from 20 to 79 years. The cultural pattern of the 9 Swiss subjects resembled that of the Americans. The subjects from Ruanda-Urundi came from primitive farming communities with little exposure to industrial civilization; in addition their diets were unusually poor in protein. The Nigerian subjects died in the city of Lagos, but many had spent time in the interior. The Asiatic subjects belonged to relatively nonindustrialized cultures; all except the Indians came from coastal areas and may have consumed considerable seafood. Autopsies were performed within 12 hours of death by the pathologists whose help is subsequently acknowledged.

COLLECTION AND PREPARATION OF TISSUES

At the time of autopsy, an aliquot of renal tissue from each American subject, both adult and child, was sealed in an individual polyethylene bag and immediately quick frozen. Hepatic tissue was sealed in a separate bag and frozen. The samples remained frozen until just before drying and ashing at the Oak

*The term "American" designates subjects from the United States and the term "foreign" subjects from the Eastern Hemisphere.

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TABLE I. DESCRIPTION OF SUBJECTS

GROUP	NO. OF SUBJECTS	PERSONAL DATA			CAUSES OF DEATH						PER CENT ASH*	
		NO. OF MALES	MEAN AGE (YEARS)	RACE	INFECTIOUS	NEOPLASTIC	CARDIOVASCULAR	CONGENITAL ANOMALY	TRAUMATIC	MISCELLANEOUS	KIDNEY	LIVER
American Children.—												
0–45 days	17	11	.003	10 Caucasoid†	1			8	1	7	1.16	1.17
45–450 days	10	5	.55	7 Caucasoid†	3	1		5		1	1.06	1.11
450–4500 days	11	8	4.5	8 Caucasoid†	2	4		3	1	1	1.19	1.41
American Adults.—												
Frozen tissue	24	14	62	23 Caucasoid†		3	16			5	1.02	1.23
Formalin tissue	24										4.0	4.1
Foreign Adults.—												
Ruanda-Urundi	11	7	32	Negroid	3		2		4	2	5.2	5.0
Nigeria	13	8	40	Negroid	6	1	1		3	2	5.3	5.3
Switzerland	9	5	54	Caucasoid		4	4		1		4.4	4.7
India	16	14	38	Caucasoid	1		1		12	2	5.3	5.3
Formosa	9	9	40	Mongoloid	1	5	1		2		4.2	3.9
Thailand	10	5	32	Mongoloid	1	3	1		2	3	4.6	4.5
Hong Kong	10	9	51	Mongoloid	4		4		1	1	5.1	4.9
Japan	17	12	42	Mongoloid	2	2	6		6	1	4.4	4.5

The autopsies from Ruanda-Urundi were performed in Usumbura, those from Nigeria in Lagos, those from Switzerland in Bern, 8 of those from India in Bombay and 8 in New Delhi, those from Formosa in Taipei, those from Thailand in Bangkok, and 8 of those from Japan in Kyoto and 9 in Tokyo. The miscellaneous causes of death included asthma, emphysema, diabetes mellitus, myasthenia gravis, beri beri, ectopic pregnancy, barbiturate poisoning, fibrinous pneumonitis, disseminated lupus erythematosus, and "unknown."

*Per cent ash of the frozen (American) tissue is the mean percentage of the *wet* weight of the tissue which remained after ashing. Per cent ash of the formalin-preserved (adult) tissue is the mean percentage of the *dry* weight of the tissue which remained as ash.

†The other subjects in these four groups were Negroid.

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Ridge National Laboratory when they were thawed, trimmed of fat and connective tissue, and cut into cubes approximately 1 cm. on a side. Each sample was then placed in a tared silica dish, weighed, and dried at 110° C. for 24 to 48 hours. Thereafter the dried sample was reweighed, ashed at 450° C. for 24 hours or longer if necessary, and reweighed again. The gray ash was then transferred to a 15 ml. polyethylene bottle where it was thoroughly ground and mixed by shaking with platinum beads in a pipette shaker for 30 minutes. After the beads had been removed, the ash remained in the bottle until analysis. Table I indicates the percentages of kidney and liver which were ash.

At the time of autopsy, an aliquot of renal tissue from each adult subject, both American and foreign, was trimmed of fat and connective tissue, placed in an individual polyethylene bottle, and preserved in an approximately equal volume of formalin. Similar amounts of hepatic tissue and preservative were placed in a separate bottle. Each sample and all of the formalin in which it had been preserved were removed from the bottle at Oak Ridge and dried at 110° C. for 24 to 48 hours in a tared silica dish. Thereafter the dried formalin-preserved sample was handled in the same manner as the dried frozen tissue.

Except for stainless steel scalpels, nothing but polyethylene, fused silica, and platinum touched frozen samples from the time of collection until they were mixed with graphite and internal standard just prior to analysis. Before use, all polyethylene bottles and silica dishes were washed in five parts of concentrated nitric acid and one part of concentrated sulfuric acid; thereafter they were rinsed in metal-free water, soaked for 24 hours in a solution of ethylenediaminetetraacetate at pH 11, and rerinsed five times in metal-free water. All water used in the procedure was distilled in glass and then passed slowly through an ion exchange resin before being stored in polyethylene bottles.

Except for the addition of formalin, the other samples were similarly handled. Metal-free formalin was specially prepared by E. I. du Pont de Nemours & Co. Aliquots, equal to at least thrice the volume added to any one tissue, were stored for several months in bottles of the type used for tissue collection and then analyzed for zinc and cadmium. For the analysis 100 mg. of spectroscopically pure sodium chloride was added to the formalin and the mixture was dried, ashed in a muffle furnace at 450°C. for 24 hours, and then handled like tissue ash. No cadmium or zinc was detected in the formalin.

SPECTROGRAPHIC PROCEDURE

The spectrographic analyses were performed at the University of Tennessee. Five milligrams of ash from each tissue was mixed with an equal amount of spectroscopically pure graphite to which indium oxide had been added as an internal standard. Each sample was then placed in a crater 5 mm. deep and 1/16 inch in diameter in a *spec. pure* 1/8 inch graphite electrode. The electrode was made the cathode in a 10 ampere direct current arc and burned for 10 seconds, after which all the cadmium and zinc were gone from the sample. The region of the arc 1 mm. above the cathode, "the cathode layer," was focused on the collimator of a Bausch & Lomb Littrow spectrograph with a slit width of 20μ. The spectrum

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from 2,400 to 3,400 Å was photographed on Eastman SA-2 plates which were developed for 3 minutes in D-19 developer, fixed for 16 minutes in F-5 fixer, and washed for 30 minutes in running water. The intensities of the 3,345.0 Å zinc, 3,261.1 Å cadmium, and 3,039.4 Å indium lines were read on a densitometer which had been modified to read intensities directly.

Working curves were made by burning, under identical conditions, standard samples which had been prepared by adding known quantities of trace elements, including cadmium and zinc, to a synthetic tissue ash. The synthetic ash was composed of 56.2 per cent KPO_3, 38.2 per cent NaCl, 2.5 per cent $CaCO_3$, 1.7 per cent MgO, and 1.4 per cent $FeCl_3$. Spectra of standards were included on every plate of unknowns.

To estimate the precision of the spectrographic method and the recovery of cadmium and zinc at the concentrations in which they occur in tissues, samples were prepared by adding known quantities of the two metals, both alone and in combination with known quantities of other trace elements, to a well-mixed composite of several different tissue ashes. The observed cadmium and zinc concentrations for 32 analyses of such samples during four months are shown in Table II. The minimum measurable amount of cadmium approximated 50 γ per gram of tissue ash. No check of the spectrographic method was made by colorimetry or wet chemistry. A complete description of the method has been published.[2]

TABLE II. RECOVERY AND REPRODUCIBILITY OF METHOD (32 ASSAYS)

	COMPOSITE TISSUE ASH	COMPOSITE ASH + 100 γ Cd/GM.	RECOVERY	COMPOSITE ASH + 1,000 Cd/GM. AND 2,000 γ Zn/GM.	RECOVERY
Cadmium	159	257	98	1,150	991
Standard error	±4	±7		±40	
Zinc	5,000			7,400	2,400
Standard error	±160			±240	

All tabulated values are average concentrations of metals found, or their standard errors, expressed as γ per gram of ash. The amount of metal recovered is obtained by subtracting the experimentally determined value for the composite tissue ash from the experimentally determined value for the composite ash plus added metal.

RESULTS

The Effect of Age (Frozen Tissues From American Subjects).—Each of the 24 adults from St. Louis had measurable concentrations of both cadmium and zinc in the frozen aliquots of both liver and kidney. The concentrations of cadmium in kidney ranged from 560 to 4,300 γ per gram of ash, and the median concentration was 2,075 γ. The median concentration of renal zinc was 3,700 γ per gram of ash. The median concentration of cadmium in the liver was a sixth as much as in the kidney, while the median concentration of hepatic zinc

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exceeded that of renal zinc. The first part of Table III includes the medians and ranges of renal and hepatic cadmium and zinc for the American subjects, and the second part includes the means and their standard errors.

Among the adults, no apparent relationship was observed between sex and renal or hepatic cadmium or zinc; moreover, figures for the single adult Negroid subject approximated the average of the entire group in all four parameters. Specifically, the 10 females had a median concentration of 1,950 γ and a mean concentration of 2,010 γ cadmium per gram of renal ash; the Negroid subject had 2,000 γ of cadmium per gram of renal ash.

TABLE III. CADMIUM AND ZINC CONTENT OF 62 AMERICAN KIDNEYS AND LIVERS (FROZEN TISSUE)

AGE GROUPS	NO. OF SUBJECTS	KIDNEY		LIVER	
		CADMIUM	ZINC	CADMIUM	ZINC
Medians and Ranges.—					
0–45 days	17	0 (0–0)	3,000 (1,450–8,200)	0 (0–0)	9,000 (3,600–21,000)
45–450 days	10	0 (0–780)	2,950 (1,750–5,500)	0 (0–0)	3,950 (1,950–5,100)
450–4,500 days	11	360 (0–2,200)	3,700 (1,100–4,900)	50 (0–2,000)	3,700 (1,400–8,400)
>45 years	24	2,075 (560–4,300)	3,700 (2,150–6,000)	360 (50–1,200)	5,400 (2,450–13,500)
Means and Their Standard Errors.—					
0–45 days	17	0	3,850 ± 490	0	9,800 ± 1,235
45–450 days	10	86 ± 74	3,150 ± 318	0	3,875 ± 399
450–4,500 days	11	631 ± 192	3,465 ± 292	178 ± 76	4,760 ± 694
>45 years	24	2,150 ± 170	3,810 ± 194	335 ± 62	5,735 ± 498

The metal concentrations are expressed as γ per gram of ash.

None of 17 infants less than 45 days old, and only 2 of 10 infants between 45 and 450 days old had detectable renal or hepatic cadmium. In contrast, renal cadmium was found in 9, and hepatic cadmium in 6, of 11 older children; moreover, each of 4 children 6 or more years old had cadmium in both organs. Renal zinc varied less with age, as did hepatic zinc after the first few days of life, when nearly twice the adult concentration was present (Table III).

The Effect of Geographic Origin (Formalin-Preserved Tissues From Adults).— The metal concentrations in the formalin-preserved and frozen aliquots of the tissues from American adults were very similar. The figure presents individual concentrations of cadmium and zinc as cumulative frequency graphs for the formalin-preserved kidneys of the adult Americans and the eight foreign national groups. The graphs define ranges of values for both metals and cite median values. Table IV indicates the means and their standard errors for renal and hepatic cadmium and zinc in the formalin-preserved tissues. The same table includes the ratios of renal cadmium to both renal zinc and hepatic cadmium.

The total range of cadmium concentrations in the kidney extended from 150

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to 17,000 γ per gram of ash for the 95 foreign adults; thus there was more than a hundred fold difference between the maximum and minimum values. Within the individual national groups, however, variation was less; in fact, for each of them a factor of 10 encompassed 90 per cent of the concentrations. The median renal cadmium concentrations of the national groups ranged from 720 to 5,300 γ per gram of ash. The large intergroup differences suggested several distinct populations; for example, exclusion of the single relatively high concentration among the subjects from Ruanda-Urundi eliminated all overlap between that group and the groups from Japan and Hong Kong. In general the foreign Negroid subjects tended to have less renal cadmium than the American Caucasoid, while the foreign Caucasoid subjects had similar amounts and the foreign Mongoloid had more (Fig. 1).

TABLE IV. MEAN CADMIUM AND ZINC CONTENT OF 119 ADULT KIDNEYS AND LIVERS (FORMALIN-PRESERVED TISSUE)

COUNTRY OF DEMISE	NO. OF SUB-JECTS	KIDNEY		LIVER		RATIOS	
		CADMIUM	ZINC	CADMIUM	ZINC	RENAL Cd / RENAL Zn	RENAL Cd / HEPATIC Cd
Ruanda-Urundi	11	710 ± 150	4,150 ± 710	70 ± 40	4,680 ± 620	0.24	14.7*
Nigeria	13	1,700 ± 400	4,290 ± 570	100 ± 30	6,950 ± 1,150	0.40	24.9*
United States	24	2,120 ± 172	4,110 ± 279	360 ± 54	5,580 ± 502	0.55	12.6
India	16	2,120 ± 310	3,290 ± 330	200 ± 40	3,540 ± 200	0.76	15.3*
Switzerland	9	2,260 ± 480	4,330 ± 840	190 ± 30	5,660 ± 780	0.59	12.0
Formosa	9	4,150 ± 1,160	19,400 ± 4,270	710 ± 170	18,600 ± 3,000	0.27	7.0
Thailand	10	4,910 ± 1,470	8,190 ± 1,360	470 ± 240	7,990 ± 1,980	0.64	13.7
Hong Kong	10	5,620 ± 950	5,470 ± 400	670 ± 150	5,900 ± 570	0.99	9.0
Japan	17	6,030 ± 800	6,200 ± 670	540 ± 90	7,640 ± 1,450	0.94	15.1

The metal concentrations are means, expressed as γ per gram of ash ± one standard error of the mean. The tabulated ratios are the averages of the individual ratios.

*Five patients from Ruanda-Urundi, 3 from Nigeria, and 2 from India had no measurable hepatic cadmium; hence they were omitted from the calculation of renal to hepatic cadmium ratios.

For the five groups of Negroid and Caucasoid subjects, the concentrations of renal zinc were relatively constant in comparison with the corresponding cadmium concentrations. This constancy was manifested by median concentrations which varied only from 3,100 to 4,200 γ per gram of ash, and by a total range of concentrations which varied only from 1,600 to 9,000 γ per gram of ash. On the other hand the Mongoloid subjects tended to have larger and more variable concentrations of renal zinc (Fig. 1). The highest mean concentration of zinc was the approximately 19,000 γ per gram of ash found in the Formosan kidneys and livers. The highest mean concentration of cadmium was the more than 6,000 γ per gram of ash found in the Japanese kidneys, with three of 17 samples having twice that amount. For the subjects from Hong Kong and Japan, the ratio of renal cadmium to renal zinc averaged 0.96; half of them had ratios greater than unity, but only one had twice as much cadmium as zinc.

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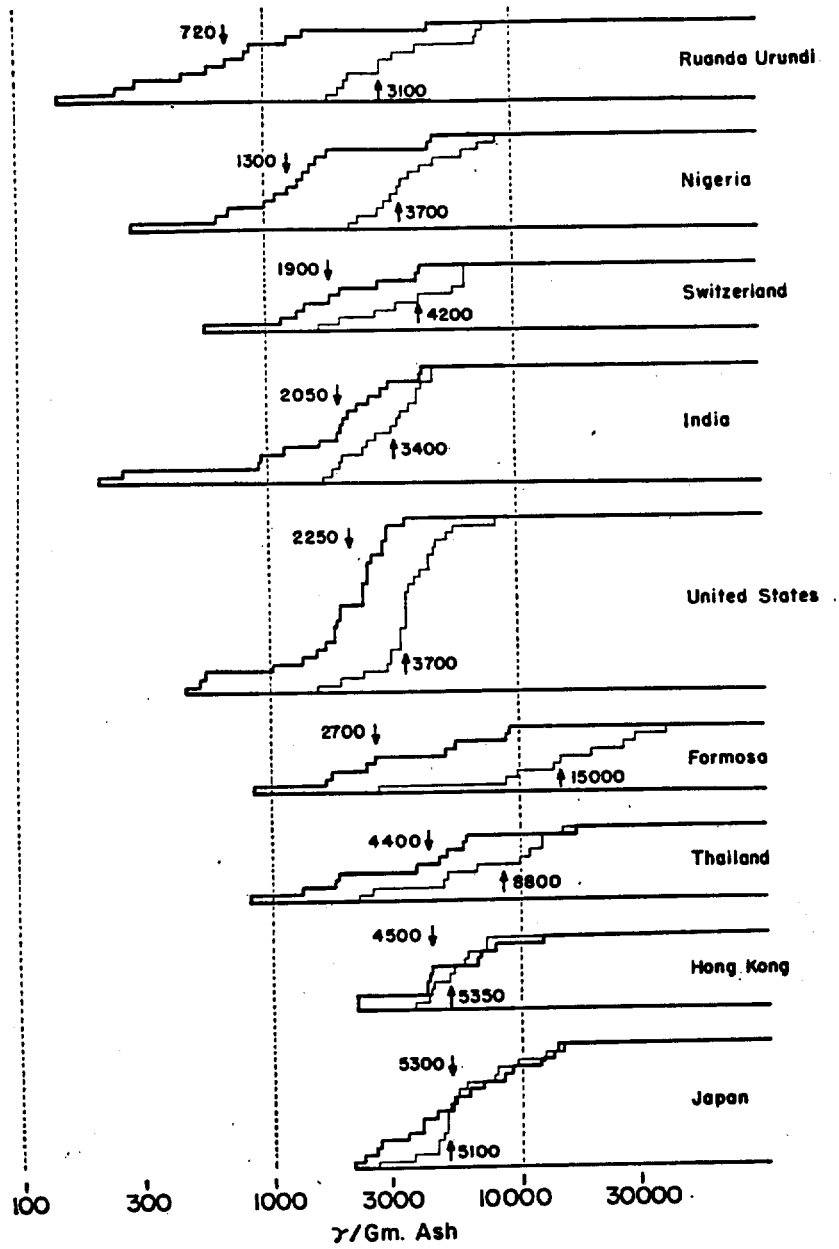

Fig. 1.—Cumulative frequency graphs of the renal concentrations of cadmium and zinc for each of the nine national groups comprising 119 adult subjects (formalin-preserved tissues). The distribution of the individual concentrations is shown for cadmium by heavy lines and for zinc by fine lines. Figures cite and arrows point to median values. The vertical scale indicates the number of patients. For instance, in the top graph each of the 11 subjects from Ruanda-Urundi is represented by one of the steps. The horizontal scale is logarithmic.

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STATISTICAL ANALYSIS

The comparison of the American children and American adults with respect to renal cadmium concentration needs no statistical analysis to demonstrate its significance. Not only is there no overlap between the youngest children and the adults, but the gap which separates them is great. On the other hand, the comparison of the renal cadmium concentrations of the nine national groups of adults has been analyzed statistically in an attempt to indicate which of the observed differences are likely to be significant.

The 119 adult subjects were divided into nine national groups. The distributions of their renal cadmium concentrations were found to be skewed. Transformation of the actual concentrations to their logarithms reduced the skewness and produced homogeneous variances for each of the nine groups (Bartlett's chi-square test: $\chi^2 = 8.59$, DF = 8, $P > 0.25$). Analysis of variance of the logarithms revealed highly significant differences among the means of the nine groups ($P < 0.001$).

Below, the means of the logarithms of the individual renal cadmium concentrations are ranked in order for each of the nine groups:

RUANDA-URUNDI	NIGERIA	INDIA	UNITED STATES	SWITZERLAND	THAILAND	FORMOSA	HONG KONG	JAPAN
2.84	3.14	3.21	3.27	3.28	3.54	3.66	3.69	3.72

The multiple comparison procedure described by Kramer[3] indicates that any two means which are underscored by the same line are not different at the 1 per cent level of significance. Similarly any two means which are not underscored by the same line are significantly different at that level. At least three different populations seem to be present. Subjects from Ruanda-Urundi differ from each of the other eight groups of subjects. In contrast the groups from Nigeria, India, the United States, and Switzerland apparently do not differ among themselves. Similarly the four groups of Mongoloid subjects do not seem to differ among themselves. As indicated in the diagram above, at the 1 per cent level of significance there is some overlap between the second and third populations, possibly due to the small sample sizes. At the 5 per cent level of significance, however, there is a distinct difference between the Caucasoid and the Negroid subjects on the one hand and the Mongoloid subjects on the other.

An attempt was also made to determine whether the nine national groups differed significantly with respect to renal zinc. The distributions of zinc concentrations within these groups were highly skewed, particularly among the Formosans. The use of logarithms reduced the skewness but did not completely

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remove the significant heterogeneity of the variances. When the Formosans, who had a much higher mean zinc concentration than the other groups as well as the largest variance, were excluded, the variances of the remaining groups were homogeneous ($P > 0.05$ by Bartlett's chi-square test). Analysis of variance based on the eight remaining groups revealed highly significant differences among the means ($P < 0.001$). The means for the Formosans and the Thai, who had the highest zinc concentrations of the remaining eight groups, differed significantly ($P < 0.01$) when considered alone. It was therefore presumed that the Formosans differed significantly from all other groups.

Multiple comparisons among the remaining eight groups were performed as before with the results presented below:

INDIA	RUANDA-URUNDI	SWITZERLAND	UNITED STATES	NIGERIA	HONG KONG	JAPAN	THAILAND
3.49	3.56	3.59	3.59	3.62	3.73	3.77	3.84

The lines underscore any means which do not differ at the 1 per cent level of significance. At least two populations are indicated. One includes the Caucasoid and Negroid subjects and the other includes the Mongoloid. The Formosans, of course, comprise a third population.

COMMENT

There are few published data on renal and hepatic cadmium and zinc with which to compare our results. The mean concentrations reported here for the 24 American adults with various diseases approximate the highest concentrations observed by Koch, Smith, Shimp, and Conner,[4] who found considerable variation in 8 normal American subjects. Our data are similar to those reported for 3 normal British subjects by Smith and co-workers,[5] and for many sick American subjects by Butt and associates[6]; however, comparisons are difficult because of differences in the manner of reporting. Finally, there is no evident conflict with the semi-quantitative results of Stitch.[7]

The greatest difficulty in interpreting the data just presented stems from the possible effects which various illnesses might have on tissue metals. Our preliminary investigation, like that of Tietz and his collaborators,[8] has so far failed to reveal abnormal amounts of cadmium or zinc in the kidneys or livers of patients with infections, neoplasia, cardiovascular diseases, or the miscellaneous causes of death involved here. On the other hand, decreased hepatic zinc has been described in cirrhosis of the liver,[9] and further differences in the tissue content of metals are likely to be discovered in specific pathologic conditions.

Since renal cadmium is a function of age among adults, with the maximum concentration occurring during the fifth decade,[10] the difference in age between

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American and foreign subjects might have some significance. Very small amounts of cadmium have been reported in infants[11]; our failure to find it may merely reflect the insensitivity of the spectrographic method. The high concentration of hepatic zinc which was reported here for newborn infants is in agreement with prior observations.[12]

The chemical similarity between cadmium and zinc and the reported biologic competition between them[13,14] suggested that cadmium-to-zinc ratios might be significant. Low ratios of renal to hepatic cadmium in experimental animals after cadmium administration,[15-17] even in small doses over long periods,[18] prompted tabulation of the relatively high human ratios.

SUMMARY AND CONCLUSIONS

Renal cadmium apparently accumulated during childhood. Whereas the kidneys of American infants had no demonstrable cadmium, the kidneys of American adults always contained more than ten times the minimum measurable concentration. The concentration of renal zinc varied less with age.

The concentration of renal cadmium depended on an individual's geographic origin. One group of African adults averaged about a third as much renal cadmium as their American counterparts, the difference being statistically significant; yet the two groups were similar with respect to renal zinc. Whereas individual Caucasoid and Negroid subjects had a more than thirty fold variation in their concentrations of renal cadmium, the invariant presence of considerable amounts of renal zinc limited them to less than a sixfold variation in the concentrations of that metal. Mongoloid subjects from several different areas had considerably higher levels of both renal cadmium and zinc than did their American counterparts, with the Japanese averaging more than twice as much renal cadmium and the Formosans more than four times as much renal zinc.

Drs. Perry and Schroeder were responsible for collecting the tissues. We should like to acknowledge with gratitude the help of the following physicians who actually collected the foreign samples: Francois C. Reubi of Bern, Switzerland; Andre Piraux of Usumbura, Ruanda-Urundi; S. G. Cowper of Lagos, Nigeria; V. R. Khanolkar of Bombay and G. S. Mitel of New Delhi, India; Nong Ting of Taipei, Formosa: Pradit Tansurat of Bangkok, Thailand; Hou Pao-Chang and C. C. Lin of Hong Kong; Tetsuro Yokoyama and K. Sugai of Tokyo and Hisato Yoshimura and M. Araki of Kyoto, Japan. The collection of tissues from Africa was made possible by a grant-in-aid from the National Heart Institute of the United States Public Health Service (H-2577). The collection of tissues from Europe and Asia was made possible by a grant-in-aid from the Lasdon Foundation of Yonkers, New York. The ashing of the tissues was done at the Health Physics Division of the Oak Ridge National Laboratory at Oak Ridge, Tennessee, by K. K. McDaniel under the supervision of Miss Cook. The spectrographic analysis of tissue was done at the Department of Physics of the University of Tennessee at Knoxville, Tennessee, by Dr. Tipton and Mr. Steiner with the technical assistance of Johanna Foland, Johanna Rittner, and Sira Fentress. Dr. Allyn W. Kimball, formerly of the Mathematics Panel at Oak Ridge National Laboratory and now Professor of Biomathematics of the School of Medicine and Professor of Biostatistics of the School of Public Health at Johns Hopkins University, advised us as to the statistical section of the manuscript. The actual statistical analyses were performed by Barbara Bartels Hixon, Lecturer in Biostatistics, Department of Preventive Medicine and Public Health, Washington University School of Medicine. The metal-free formalin was prepared through the courtesy of Dr. Paul Austin of E. I. du Pont de Nemours & Co., Wilmington, Delaware.

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Addendum.—The data presented in the table below became available after completion of the report. The methods of collection, preparation, and analysis were those described for foreign tissues. Although these data are few and their explanation and significance remain unknown, they substantiate the findings in the body of the report, namely, that African Negroids have less and Asiatic Mongoloids have more renal cadmium than American, European, or Asiatic Caucasoids. The renal cadmium concentrations of subjects from South Africa, Uganda, and Ethiopia were low and resembled those found in subjects from Ruanda-Urundi. The concentrations of subjects belonging to a primitive society in Gabon were higher and resembled those of Nigerians. Mongoloid Filipinos had much renal cadmium and resembled the Japanese.

RENAL CADMIUM CONCENTRATIONS (Medians and Ranges)

COUNTRY OF DEMISE	NO. OF PATIENTS	RENAL CADMIUM* MEDIAN	RANGE
Part I: 18 Additional African Negroids			
Union of South Africa	4	500	380–960
Uganda	4	755	380–1,300
Ethiopia	5	760	265–1,400
Gabon	5	1,850	1,200–5,300
Part II: 4 Additional Asiatic Mongoloids			
Philippines	4	6,450	2,100–14,000

*All concentrations are γ of cadmium per milligram of tissue ash.

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