Bull. Environ. Contam. Toxicol. 31, 267–277 (1983)
© 1983 Springer-Verlag New York Inc.

Concentration and Chemical Species of Arsenic in Human Tissue

Hiroshi Yamauchi and Yukio Yamamura

Department of Public Health, St. Marianna University School of Medicine, 2095, Sugao, Miyamae-ku, Kawasaki 213, Japan

There are reports of total arsenic levels in the normal tissue of the Japanese (KADOWAKI 1960; YUKAWA et al. 1980), of the English (LIEBSCHER and SMITH 1968) and of the Italian (GERIN and ZORZI 1961). Man is ingesting a considerable amount of arsenic from the daily diet (NAKAO 1960; SCHROEDER and BALASSA 1966; ISHIZAKI 1979). We investigated into the chemical species of arsenic occurring in the normal foods the Japanese eat, and found that 5 chemical species of arsenic, i.e., arsenite (As(III)), arsenate (As(V)), methylarsonic acid (MAA), dimethylarsinic acid (DMAA) and trimethylarsenic compound (TMA) occurred in 59 kinds of foods we assayed, and that the ratios of TMA, DMAA and As(V) contents were high (YAMAUCHI and YAMAMURA 1980).

The chemical species of arsenic occurring in foods have mostly been got hold of, while those of arsenic retained in the tissue are still unknown. The chemical species of arsenic only in the urine, blood and hair have heretofore been determined (BRAMAN and FOREBACK 1973; CRECELIUS 1977; YAMAMURA and YAMAUCHI 1980).

This paper describes the chemical species and levels of arsenic deposited in the tissues and organs of autopsied cadavers.

MATERIALS AND METHODS

The tissues and organs (the adrenal gland, aorta, cerebellum, cerebrum, kidney, liver, lung, muscle, pancreas, skin and spleen) from the autopsied cadavers of human patients (13 men and 10 women at the age of 36~79) who had died of cerebral bleeding, pneumonia and cancer at the St. Marianna University Medical Center, Kawasaki, Japan were assayed for chemical species of arsenic. None of them had a premortal history of exposure to high concentrations of arsenic due to occupational or environmental contamination in particular. All tissues and organs assayed were those which appeared macroscopically normal. All specimens had been preserved frozen at -20°C before assayed. For the assay for arsenic, 0.5~1.0 g of each tissue or organ was used. The specimen was transferred into a 50-ml glass-stoppered test tube, and after the addition of 2N NaOH, it was heated in a hot water bath for 3 hr for use as the assay sample. To each sample were added 10% oxalate solution and 10% phthalate solution as buffers. The arsenic contained in the mixture was reduced into arsines with 2 ml of 10% $NaBH_4$ in 0.2 N NaOH solution, and the arsines were then fixed with liquid nitrogen. From the fixed arsines were separated the component

arsines, which were determined by arsine-generator flameless atomic absorption spectrophotometry (BRAMAN et al. 1977; YAMAUCHI and YAMAMURA 1979a).

RESULTS

Comparison of total arsenic levels in the assayed tissues and organs showed that the highest mean total arsenic level of 551 ng of As per g occurred in the aorta (pulmonary artery) tissue, followed by the levels in the adrenal gland > pancreas > skin > cerebellum > liver > kidney > muscle > lung > spleen > cerebrum in decreasing sequence of significance (Table 1). Four chemical species of arsenic, i.e., As(III), As(V), MAA and DMAA, were found in the tissues and organs. There was no statistically significant sexual difference in the arsenic level between the 11 kinds of tissues and organs assayed. The As(III) level in the livers from the men tended to be slightly higher than that in the liver from the women, but when the difference was analyzed by SMIRNOV test and THOMPSON test, it was of no statistical significance. Out of the 4 chemical species of arsenic detected in the tissues and organs, As(III) and As(V) was detected in all tissues and organs, the former accounting for 20.4 ± 3.7% and the latter, for 72.0 ± 7.9% of total arsenic: in other words, As(V) was the most predominant of the 4 chemical species of arsenic detected. A trace of MAA was found only in the liver and kidney. MAA accounted for 3% of total arsenic in the liver and 4.6% in the kidney. DMAA was detected in 100% of the samples of adrenal gland, lung, pancreas and aorta, but in 85% of the samples of liver, kidney, spleen, muscle and skin on an average. In all the tissues and organs where DMAA was detected, DMAA accounted for only 10.3 ± 6.4% of total arsenic. Especially, in the skin and aorta, DMAA accounted no more than 2~3% of total arsenic.

In other words, arsenic deposited in human tissues and organs in 4 chemical species, i.e., As(III), As(V), MAA and DMAA, and out of these species, As(V) accounted for the greatest part, followed by As(III), DMAA and MAA in decreasing sequence of significance.

DISCUSSION

There are reports by KADOWAKI (1960), SUMINO et al. (1975) and YUKAWA et al. (1980) of total arsenic levels in the tissues of the Japanese. Our recent findings are mostly consistent with the findings by YUKAWA et al. (1980), but 2~5 times as high as the levels reported by KADOWAKI (1960). This difference presumably has resulted from the difference in assay technology rather than chronological changes in arsenic levels in the tissues.

It is known that man ingests from the daily diet 5 chemical species of arsenic, i.e., As(III), As(V), MAA, DMAA and TMA–among others, TMA, DMAA and As(V) at especially high levels (YAMAUCHI and YAMAMURA 1980). On the other hand, inorganic As(V) was the main chemical species of arsenic detected in the tissues and organs from autopsied cadavers, followed by inorganic As(III). No TMA was detected in human tissues and organs, and only traces of DMAA and MAA were detected. From these findings, we surmised that the methylated arsenic ingested together with foods such as TMA, DMAA or MAA was the species of arsenic which is rapidly excreted and very little retained in the body. It has been shown that inorganic arsenic such as As(III) or As(V), when ingested, is mostly converted into MAA and

DMAA *in vivo* before it is excreted into the urine (CRECELIUS 1977; YAMAUCHI and YAMAMURA 1979a,b; TAM et al. 1979). It is not true to say, however, that the ingested inorganic arsenic is entirely methylated *in vivo*. A part of the inorganic

Table 1. Levels and chemical species of arsenic in the normal tissues and organs of the Japanese

Tissue & organ	Sex	Number	Levels of arsenic (ng of As per g wet weight)									
			As (III)		As(V)		MAA		DMAA		Total	
							%*		%*			
Aorta	♂	8	117	±61.1	335	± 82.3	ND		17.1± 6.5	100	469	±131
	♀	8	131	±74.3	486	±411	ND		15.8± 4.4	100	633	±480
	Total	16	124	±66.1	411	±297			16.4± 5.4	100	551	±350
Adrenal gland	♂	10	33.5	±11.5	134	±135	ND		26.2±10.0	100	194	±140
	♀	9	59.9	±57.3	390	±433	ND		25.4±20.1	100	475	±479
	Total	19	46.0	±41.3	255	±331			25.8±15.2	100	327	±364
Cerebellum	♂	15	28.7	±13.9	99.5	± 60.2	ND		ND		128	± 71.9
	♀	15	31.8	± 9.9	107	± 33.7	ND		ND		138	± 41.5
	Total	30	30.0	±12.2	102	± 50.0					132	± 60.2
Cerebrum	♂	15	20.8	±10.7	56.1	± 38.7	ND		ND		77.3	± 49.0
	♀	15	17.0	±11.9	59.8	± 30.4	ND		ND		75.3	± 39.1
	Total	30	19.0	±11.3	57.8	± 34.5					76.3	± 43.9
Kidney	♂	14	31.2	±15.5	88.2	± 74.8	3.8	±2.7	71 27.2±12.3	71	142	± 89.1
	♀	10	21.9	± 7.5	45.6	± 11.0	3.4	±2.7	80 28.2± 9.2	80	94.8	± 21.4
	Total	24	27.3	±13.4	70.4	± 60.6	3.6	±2.6	76 27.6±10.7	76	129	± 72.3
Liver	♂	12	30.9	±18.0	99.5	± 38.0	6.8	±6.8	75 13.4± 3.8	67	145	± 45.4
	♀	11	17.9	± 5.3	82.3	± 24.3	4.6	±6.2	55 14.7± 7.6	73	112	± 24.3
	Total	23	24.7	±14.8	91.3	± 32.7	5.9	±6.5	65 14.0± 5.7	70	129	± 39.7
Lung	♂	12	17.1	± 7.0	74.2	± 20.1	ND		6.7± 3.8	100	98.0	± 26.1
	♀	10	17.4	± 9.2	87.0	± 32.3	ND		8.9± 5.9	100	113	± 32.9
	Total	22	17.2	± 7.8	79.7	± 26.1			7.6± 4.8	100	104	± 29.5
Muscle	♂	12	24.5	±11.1	65.5	± 34.0	ND		20.2± 8.7	92	109	± 42.7
	♀	10	24.5	± 6.0	61.4	± 13.3	ND		17.7± 9.0	100	104	± 18.2
	Total	22	24.5	± 8.8	63.6	± 25.7			18.9± 8.7	96	106	± 32.7
Pancreas	♂	10	35.3	±18.0	107	± 64.0	ND		13.7± 9.4	100	156	± 82.0
	♀	8	25.0	±10.6	111	± 49.6	ND		16.0± 6.6	100	152	± 60.4
	Total	18	30.7	±15.6	109	± 56.5			14.7± 8.1	100	154	± 71.4
Skin	♂	11	19.6	± 7.3	111	± 45.4	ND		4.5± 5.0	91	134	± 51.9
	♀	11	27.6	±17.7	141	±113	ND		2.9± 4.1	91	172	±129
	Total	22	23.6	±13.9	126	± 85.5			3.7± 4.5	91	153	± 97.7
Spleen	♂	10	24.6	±15.8	66.3	± 41.5	ND		11.8± 7.8	90	101	± 58.7
	♀	10	24.5	± 9.0	67.4	± 34.5	ND		13.7± 3.8	70	101	± 41.2
	Total	20	24.5	±12.5	66.9	± 37.2			12.6± 6.2	80	101	± 49.4

Values denote the mean ± SD. As(III) and As(V) was detected in all tissues. ND: Not detected (the lower detectable limit: 1.0 ng of As per g wet weight). * Ratio of tissue/organ samples where MAA or DMAA was detected.

arsenic excreted in the urine or retained in the body without any change in its chemical species (YAMAUCHI et al. 1980). From the results of this study, inorganic arsenic seems to be more affinitive for tissues and organs than methylated arsenic. There was no statistically significant difference in the chemical species of arsenic in the tissues and organs between humans who had suddenly died (of cerebral bleeding) and those who had died of chronic diseases such as cancer and pneumonia. These findings lead to a speculation that the chemical species of arsenic in the tissues and organs do not change greatly with the premortal nourishing condition.

ACKNOWLEDGEMENTS

This study was aided in part by the Grants for Scientific Research from the Ministry of Education, Japan (1980, 1981).

We are grateful to Profs. K. OIKAWA and S. USHIGOME, Asst. Prof. T. UCHIKOSHI and the staff at the Department of Pathology, St. Marianna University School of Medicine, Kawasaki, for the supply of assay specimens.

REFERENCES

BRAMAN, R.S. and C.C. FOREBACK: Science **182**, 1247 (1973).
BRAMAN, R.S., D.L. JOHNSON, C.D. FOREBACK, J.M. AMMONS, and J.L. BRICKER: Anal. Chem., **49**, 621 (1977).
CRECELIUS, E.A.: Environ. Health Persepct., **19**, 147 (1977).
GERIN, C., and C. de ZORZI: Zacchia, **36**, 1 (1961).
ISHIZAKI, M.: Jap. J. Hyg., **34**, 605 (1979).
KADOWAKI, K.: Osaka City Med. J., **9**, 2083 (1960).
NAKAO, M.: J. Osaka City Med. Center, **9**, 541 (1960).
LIEBSCHER, G., and H. SMITH: Arch. Environ. Health, **19**, 159 (1968).
SCHROEDER, H.A., and J.J. BALASSA: J. Chron. Dis., **19**, 85 (1966).
SUMINO, K., K. HAYAKAWA, T. SHIBATA, and S. KITAMURA: Arch. Environ. Health, **30**, 487 (1975).
TAM, G.K.H., S.M. CHARBONNEAU, F. BRYCE, C. POMROY, and E. SANDI: Toxicol. Appl. Pharmacol., **50**, 319 (1979).
YAMAMURA, Y. and H. YAMAUCHI: Ind. Health, **18**, 203 (1980).
YAMAUCHI, H., and Y. YAMAMURA: Jpn. J. Ind. Health, **12**, 47 (1979a).
YAMAUCHI, H., and Y. YAMAMURA: Ind. Health, **17**, 79 (1979b).
YAMAUCHI, H., and Y. YAMAMURA: Jap. J. Public Health, **27**, 647 (1980).
YAMAUCHI, H., M. IWATA and Y. YAMAMURA: Jap. J. Ind. Health, **22**, 111 (1980).
YUKAWA, M., M. SUZUKI, K. AMANO, and M. TERAI: Arch. Environ. Health, **35**, 36 (1980).
Accepted May 18, 1983