Bull. Environ. Contam. Toxicol. (1988) 40:633–640

Bulletin of Environmental Contamination and Toxicology

Concentrations and Chemical Species of Arsenic in Human Urine and Hair

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Because marine products are rich in arsenic, the concentration of arsenic in the human urine varies greatly with the state of ingestion of marine products. It has been reported that the analysis of foods for chemical species of arsenic detects 4 chemical species: inorganic arsenic, methylarsonic acid (MAA), dimethylarsinic acid (DMAA) and trimethylarsenic compound (TMA) (Yamauchi and Yamamura 1980). It has also been reported that TMA occurs as arsenobetaine in fishes and shellfishes (Edmonds et al. 1977) and that a trace of arsenocholine also occurs in some fishes and shellfishes (Norin and Christakopoulos 1982). On the other hand, it has been revealed that inorganic arsenic is methylated in the human body to form MAA and DMAA (Yamauchi and Yamamura 1979; Tam et al. 1979; Buchet et al. 1981). It appears therefore that the arsenic present in the human urine is a mixture of the arsenic originating from marine products and the arsenic metabolized *in vivo.*

Arsenic is found in all human tissues, and it is known that arsenic binds tightly to the SH groups in the hair in particular. Because the arsenic detected in the hair is composed of the endogenous arsenic and the arsenic adhering to the external surface of the hair, the assay of the hair for arsenic does not provide the primary biological value of arsenic.

Recent studies have shown that inorganic arsenic and methylarsenic compounds are quite different in toxicity and effect on the living body due to their difference in chemical species. Finding the chemical species of arsenic in the urine and hair of normal subjects will

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therefore provide valuable basal data for the biological monitoring of arsenic exposure and for toxicological studies of arsenic.

MATERIALS AND METHODS

Urine samples were taken from 102 students (94 male and 8 female) of St. Marianna University School of Medicine, Kawasaki, Japan, who were in the age range from 20~23, and not on any dietary restrictions. Hair samples were taken from 100 teaching staff (87 male and 13 female) of St. Marianna University School of Medicine, Kawasaki, aged 19~70. The hair samples were not washed before assay. The urine and the hair samples were thus taken from different populations.

Two milliliters of each urine sample or 0.5 g of each hair sample was used for the assay for arsenic. Each sample was placed in a 10-ml polymethylpentene test tubes, and after the addition of 5 ml of 2 N NaOH, the mixture was heated at 95°C for 3 hours. The mixture was stirred once every 30 minutes during the heating. The heated mixture was diluted to 50 ml with distilled water for use as an assay sample. MAA, DMAA and TMA, even when heated in 2 N NaOH, are not decomposed to form inorganic arsenic and/or any other methylarsenic compounds. The assay of the samples for the chemical species of arsenic, i.e., inorganic arsenic, MAA, DMAA and TMA, was performed by liquid nitrogen trapping-arsine generation-atomic absorptiometry. The detectable limit of each of the 4 chemical species of arsenic by this method was 0.5 ng, with a coefficient of variation of less than 5% (Yamauchi and Yamamura 1984a).

RESULTS AND DISCUSSION

As shown in Table 1, 4 chemical species of arsenic were detected in the human urine samples: inorganic arsenic, MAA, DMAA and TMA. The specific gravity of urine samples from the 102 students was 1.026 ± 0.005. The mean total arsenic concentration in the urine samples, corrected with the mean urine specific gravity of 1.024 for the Japanese, was 121 (25.9~668) µg As/l: the total arsenic concentration in the urine samples, when corrected with specific gravity, was slightly lower. Of the 4 chemical species, inorganic arsenic accounted for 9.4%; MAA, for 3.0%; DMAA, for 28.9%, and TMA, 58.2% of the total arsenic concentration in the urine samples: in other words, methylarsenic compounds made up about 90% of the arsenic in the urine. There are only a few published studies of the ratio of inorganic arsenic to methylarsenic compounds in the urine. When compared with

Table 1. Concentrations and chemical species of arsenic in the human urine and hair

Sample	Concentration of arsenic				
	InAs	MAA	DMAA	TMA	Total
Urine[1,2]					
Mean	12.7	4.07	38.5	75.4	131
S.D.	7.08	2.98	25.1	97.6	106
Min	2.62	0.96	6.1	2.50	21.8
Max	22.7	22.6	130	558	585
Urine[1,2,3]					
Mean	11.9	3.66	35.1	70.6	121
S.D.	6.46	2.79	20.8	95.8	102
Min	0.89	0.82	8.61	2.40	25.9
Max	32.9	24.6	111	638	667
Hair[4,5]					
Mean	0.056	–	0.020	–	0.075
S.D.	0.033		0.021		0.043
Min	0.018		0.003		0.008
Max	0.264		0.108		0.329

1) Urine, n = 102; 2) μg As/l; 3) Urinary values adjusted with S.G. 1.024; 4) Hair, n = 100; 5)μg As/g; InAs: Inorganic arsenic; –, Not detected.

the results of a study by Foa et al. (1984) in the Italians, the total arsenic concentration in the urine of the Japanese was about 5 times higher, while the inorganic arsenic—methylarsenic compound ratios in the respective urines were similar to each other. Foa et al. (1984), however, described the urinary TMA as an unidentified methylarsenic compound.

Fig. 1 depicts the frequency distribution of each chemical species of arsenic in the urine. Inorganic arsenic was distributed in concentrations up to 20 μg As/l; MAA, up to 10 μg As/l, and DMAA, up to 120 μg As/l in most urine samples, respectively. The total arsenic concentration in the urine was basically similar to the distribution pattern of the TMA concentration, and there was a statistically significant correlation between them (r = 0.972; p = 0.01). On the other hand, there was no significant difference between the total arsenic concentration and the inorganic arsenic, MAA or DMAA concentration in the urine.

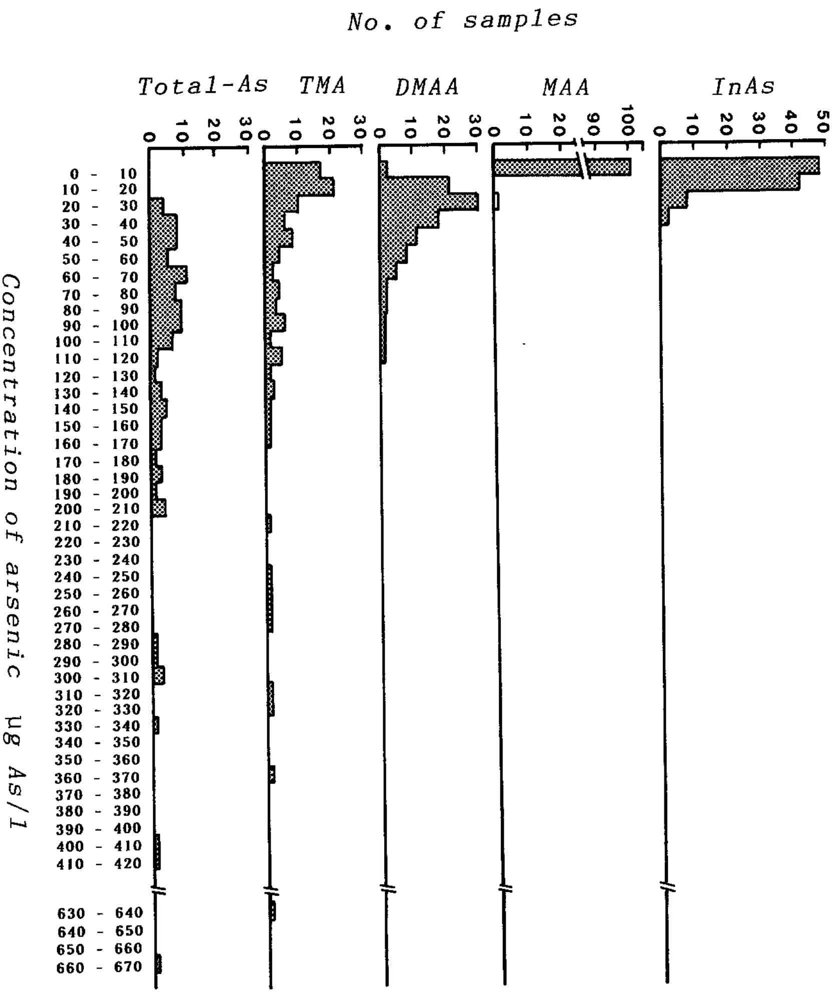

Figure 1. Frequency distribution of the concentrations of arsenic compounds in the human urine

The following may be speculated for the 4 chemical species of arsenic detected in the urine. It has been revealed in studies in humans and animals that MAA (Yamauchi et al., unpublished data), DMAA (Buchet et al 1981; Yamauchi and Yamamura 1984a; Vahter et al. 1984) and TMA (Vahter et al 1983; Yamauchi and Yamamura 1984b; Yamauchi et al. 1986) are stable *in vivo,* and not decomposed to form inorganic arsenic. From the findings, it may be surmised that the inorganic

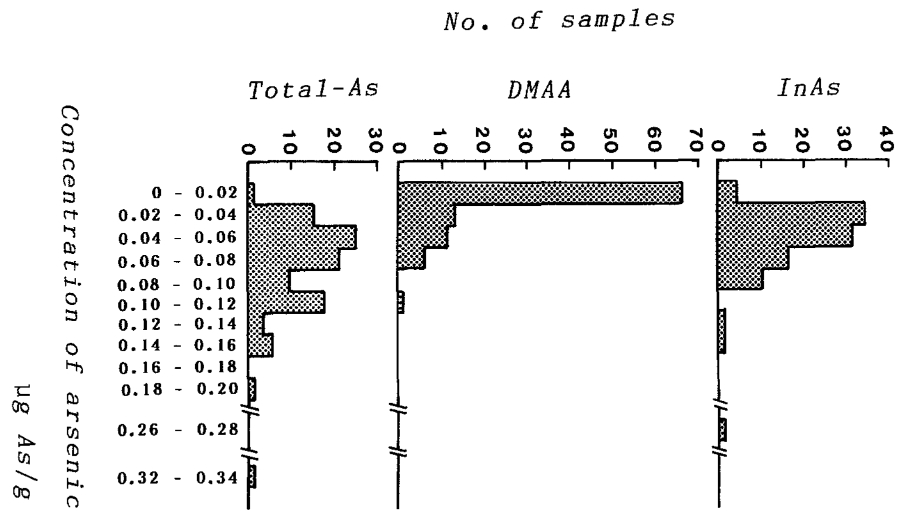

Figure 2. Frequency distribution of the concentrations of arsenic compounds in the human hair

arsenic detected in the urine derives from a portion of the dietary inorganic arsenic being excreted in unchanged form in the urine. The finding in the present study that the inorganic arsenic concentration in the urine of humans on normal diet is about 20 µg As/l, is very effective and important in using the inorganic arsenic concentration in the urine as an indicator in the biological monitoring for occupational exposure to inorganic arsenic. The MAA concentration was the lowest of the 4 chemical species of arsenic in the urine, and this low ratio may have derived from the fact that only a very fine amount of MAA is contained in foods (Yamauchi and Yamamura 1980) and that MAA is not produced from inorganic arsenic *in vivo* as much as DMAA. From the fact that humans do not ingest so much inorganic arsenic, however, the most portion of DMAA found in the urine seems to originate from seafoods and seaweeds. The results of recent studies suggest that little TMA may be produced *in vivo* if any (Yamauchi and Yamamura 1984a; Yamauchi and Yamamura 1985), and as predicted by Cannon et al. (1981), it may be estimated that the most portion of TMA in the human urine originates from marine products. From the results of the present study, it may be surmised that the arsenic in the urine closely represents the chemical species of arsenic in foods, and that the arsenic concentration in the urine of the Japanese tends to be very high, compared with that in the urine of inhabitants in Europe and

America. This difference most probably derives from the difference in the ingested amount of TMA occurring in fishes and shellfishes.

Because arsenic as an external contaminant of the hair cannot be completely removed by washing with any detergent, distilled water or alcohol, the hair samples were used without washing in the present study. As shown in Table 1, no MAA or TMA but only inorganic arsenic and DMAA were detected in the hair samples. The mean total arsenic concentration in the hair samples from the 100 subjects was 0.075 (0.042~0.329) µg As/g. Since this total arsenic concentration in the hair was mostly consistent with the mean total arsenic concentration in the washed hair samples of the Japanese subjects reported by Fukushima et al (1983), there seems to be no heavy arsenic contamination in general environments. There was no significant difference in the total arsenic concentration in the hair between the present series of subjects by age.

Inorganic arsenic accounted for 73%, and DMAA, for 27% of the total arsenic in the hair. Fig. 2 depicts the distribution of inorganic arsenic and DMAA concentrations in the hair. There was a significant correlation between the total arsenic concentration and the inorganic arsenic or DMAA concentration in the hair (InAs, $r = 0.841$; DMAA, $r = 0.651$; $p = 0.01$, respectively). Also in the present study, the inorganic arsenic in the hair could not be classified into the external contaminant and the endogenous arsenic. On the other hand, because DMAA or dimethylated arsenic compounds rarely occur in the ambient air, the DMAA in the hair was judged to be the endogenous arsenic. Furthermore, it has already been shown that DMAA, when administered orally to hamsters once only, deposits in the hair (Yamauchi and Yamamura 1984a).

It is obvious from the excretion of TMA in the urine that humans ingest large amounts of TMA from seafoods, while it has been contradictory that no TMA is detected in the hair. In connection with this problem, it has been reported that TMA, when orally ingested by humans, is rapidly eliminated from the body, compared with other arsenic compounds (Luten et al 1982; Yamauchi and Yamamura 1984). The results of animal experiments also indicate that TMA is not likely to deposit in the hair (Vahter et al. 1983; Yamauchi et al. 1986). The findings of TMA in the human hair in the present study was consistent with the results of such published studies in humans and experimental animals. Inorganic arsenic accounts for the most part, and MAA and DMAA, for a small portion, respectively, of the arsenic detected in humans organs and tissues, while no TMA was detected (Yamauchi and Yamamura 1983). It was revealed in the present study that the chemical species of arsenic in the hair are similar to those in tissues.

The finding in the present study that the chemical species of arsenic in the human urine were converse to those in the hair seems to derive form the properties of TMA (trimethylarsenic compound, namely, arsenobetaine).

Acknowledgments. The author is grateful to Prof. Y. Yamamura and Dr. H. Yamauchi at the Department of Public Health, St. Marianna University School of Medicine, Kawasaki, Japan, for their advice in the present study.

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Received October 19, 1987; accepted October 19, 1987.