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Can Humans Metabolize Arsenic Compounds to Arsenobetaine?

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Arsenic compounds were determined in 21 urine samples collected from a male volunteer. The volunteer was exposed to arsenic through either consumption of codfish or inhalation of small amounts of $(CH_3)_3As$ present in the laboratory air. The arsenic compounds in the urine were separated and quantified with an HPLC–ICP–MS system equipped with a hydraulic high-pressure nebulizer. This method has a determination limit of 0.5 μg As dm^{-3} urine. To eliminate the influence of the density of the urine, creatinine was determined and all concentrations of arsenic compounds were expressed in μg As g^{-1} creatinine. The concentrations of arsenite, arsenate and methylarsonic acid in the urine were not influenced by the consumption of seafood. Exposure to trimethylarsine doubled the concentration of arsenate and increased the concentration of methylarsonic acid drastically (0.5 to 5 μg As g^{-1} creatinine). The concentration of dimethylarsinic acid was elevated after the first consumption of fish (2.8 to 4.3 μg As g^{-1} creatinine), after the second consumption of fish (4.9 to 26.5 μg As g^{-1} creatinine) and after exposure to trimethylarsine (2.9 to 9.6 μg As g^{-1} creatinine). As expected, the concentration of arsenobetaine in the urine increased 30- to 50-fold after the first consumption of codfish. Surprisingly, the concentration of arsenobetaine also increased after exposure to trimethylarsine, from a background of approximately 1 μg As g^{-1} creatinine up to 33.1 μg As g^{-1} creatinine. Arsenobetaine was detected in all the urine samples investigated. The arsenobetaine in the urine not ascribable to consumed seafood could come from food items of terrestrial origin that—unknown to us—contain arsenobetaine. The possibility that the human body is capable of metabolizing trimethylarsine to arsenobetaine must be considered.

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INTRODUCTION

Most of the arsenic that humans ingest under normal circumstances comes from food. Ingested and resorbed inorganic arsenic compounds are detoxified in the body by methylation to methylarsonic acid and dimethylarsinic acid. These metabolites are excreted with the urine.[1] Approximately 10% of the arsenic in the average urine is inorganic, 70% is dimethylarsinic acid, and about 20% is methylarsonic acid. Because most of an ingested dose of arsenic leaves the body with the urine within a few days of ingestion, urinary arsenic is indicative of recent exposure to arsenic.[2]

The arsenic compounds identified and quantified in urine may provide information about the detoxifying capacity, metabolic pathways and foods delivering special arsenic compounds. Seafood, for instance, may be rich in arsenobetaine or arsenic-containing riboses and may be the source of much of the ingested arsenic.[3–6] Consumption of seafood increases not only the concentration of arsenobetaine in the urine, but also the concentrations of dimethylarsinic acid and inorganic arsenic.[7]

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Generally, the concentration of total arsenic in the urine does not measure the risk associated with ingestion of arsenic. Exposure to inorganic arsenic compounds that may cause cancer[8] brings higher risks than exposure to arsenobetaine, which appears to be not toxic at all.[9] Risks are reduced by detoxifying, metabolic reactions. A realistic estimate of risks from ingested arsenic can be obtained only when the types and doses of arsenic compounds that are ingested and subsequently excreted in the urine are known.

A male volunteer at our institute, who is occupied intermittently with the synthesis of organic arsenic compounds, provided the opportunity to explore the influence of exposure to normal arsenic compounds ingested with the food, and of exposure to unusual arsenic compounds inhaled during synthetic work, on the urinary excretion of arsenic compounds. The results of the determination of arsenic compounds in the urine voided by this volunteer over a three-week period are reported in this paper.

EXPERIMENTAL

Instrumentation

For the separation of the arsenic compounds a Hewlett Packard 1050 solvent delivery unit and the 100-mm^3 injection loop of a Rheodyne 9125 six-port injection valve were used. The arsenic compounds were separated at a flow rate of 1.5 cm^3 min^{-1} on a Supelcosil LC-SAX anion-exchange column (250 mm × 4.6 mm i.d.; spherical, 5-μm particles of silica with quaternary aminopropyl exchange sites) with a 30 mM aqueous ammonium phosphate buffer at pH 3.75 as the mobile phase or on a Hamilton PRP™-X100 (Hamilton, Reno, NV, USA) anion-exchange column with a 30 mM aqueous ammonium phosphate buffer at pH 6.0 as the mobile phase. The exit of the column was connected to a hydraulic high-pressure nebulizer (HHPN; Knauer, Berlin, Germany) via 300-mm 1/16 in (1.6 mm) PEEK (polyether ether ketone) capillary tubing (0.25 mm i.d.). A VG PlasmaQuad 2 Turbo Plus (VG Elemental, Winsford, UK) inductively coupled plasma mass spectrometer (ICP–MS) served as arsenic-specific detector. The elbow that normally ties the spray chamber to the torch was replaced by a 40-mm long, 5-mm i.d. quartz tube tapered at one end and carrying a female ball-joint at the other end. The outlet of the HHPN was connected with 600-mm long Tygon tubing (10-mm i.d.) to the tapered end of the quartz tube, which in turn provided the connection to the plasma torch via the ball-joint. The operating conditions for the HHPN and the ICP-MS are summarized in Table 1. The ion intensities at *m/z* 75 (^{75}As) and *m/z* 77 (^{40}Ar^{37}Cl) were recorded with the time-resolved analysis software© Version 1a (Fisons Scientific Equipment Division, Middlesex, UK). Prior to each HPLC–ICP–MS run, the ion intensity at *m/z* 87 (^{87}Rb) was checked on the rate meter, aspirating the mobile phase with rubidium at a concentration of 50 ng cm^{-3}. The lens settings were adjusted as needed for optimal response of the instrument (typically 8×10^5 Hz for 50 ng dm^{-3} Rb). For quantification the chromatograms were exported, peak areas determined, and the concentrations calculated with external calibration curves using software written in-house.[10]

Creatinine was determined in all urine samples with a Synchron CX® Systems creatinine kit P/N

Table 1 Operating conditions for the hydraulic high-pressure nebulizer and the inductively coupled argon plasma mass spectrometer

Hydraulic high-pressure nebulizer	
Desolvation	
Heating	150 °C
Cooling	7 °C
Nebulizer gas flow rate	1.00 dm^3 min^{-1}
Back-pressure	~200 bar
Inductively coupled plasma mass spectrometer	
Plasma	
Radiofrequency power	
Forward	1.4 kW
Reflected	<1 W
Argon gas flow rate	
Cooling gas	13.5 dm^3 min^{-1}
Auxiliary gas	1.1 dm^3 min^{-1}
Vacuum	
Expansion	1.6 mbar
Intermediate	1.0×10^{-4} mbar
Analyzer	2.1×10^{-6} mbar
Ion sampling	
Sample cone	Nickel orifice, 1.00 mm diameter
Skimmer cone	Nickel orifice, 0.75 mm diameter
Measuring parameters	
Monitored signal	^{75}As, ^{40}Ar^{37}Cl
Time/slice	0.51 s
No. of slices	700
Total analysis time	~360 s

443340 (Beckman Instruments, Galway, Ireland) based on the Jaffé rate method.

Chemicals

$NaAsO_2$ [As(III)], $Na_2HAsO_4 \cdot 7H_2O$ [As(V)], $NH_4H_2PO_4$ and H_3PO_4 (all p.a. quality) were purchased from Merck. Methylarsonic acid (MA; m.p. 156 °C) and dimethylarsinic acid (DMA; m.p. 190 °C) were gifts from Vineland Chemical Co. (Vineland, NJ, USA). Arsenobetaine bromide[11, 12] (AB, m.p. 225 °C) was prepared according to published procedures. The water used for analytical work was purified to 18.2 MΩ cm resistivity.

Stock solutions of the arsenic compounds containing 100 mg As dm^{-3} were prepared by dissolving 86.7 mg $NaAsO_2$, 208.2 mg $Na_2HAsO_4 \cdot 7H_2O$, 93.4 mg methylarsonic acid and 92.1 mg dimethylarsinic acid to 500 cm^3, or 86.3 mg arsenobetaine bromide to 250 cm^3. These stock solutions were diluted with NANOpure water to the desired concentrations just before use.

The mobile phase for chromatography was prepared by dissolving $NH_4H_2PO_4$ (3.45 g, 0.03 mol) in NANOpure water to 1000 cm^3. To the stirred $NH_4H_2PO_4$ solution H_3PO_4 (conc.) or NH_3 (conc.) was added until the pH of 3.75 or 6.0 had been reached. Methanol (10 g) was added to each liter of these solutions, which were then spiked with 50 mm^3 of a solution containing 1000 mg Rb dm^{-3}. The mobile phase at pH 6.0 was used to separate methylarsonic acid and arsenate on the PRP-X100 column, when high chloride concentrations in the urine interfered with the separation of these arsenic compounds on the Supelco LC-SAX column.

Urine samples

The urine samples were collected daily during the period 2 to 23 October 1995 with the exception of 18 October 1995. About 50 cm^3 of urine was voided each morning between 6 and 7 a.m. into clean polyethylene bottles. The samples were immediately frozen at −20 °C and stored at this temperature. Before analysis the samples were warmed to room temperature. The precipitate that had formed was removed by centrifugation for 15 min at 2500 rpm. Immediately before the chromatography the supernatants were filtered through 0.2-μm cellulose nitrate filters (Sartorius, Goettingen, Germany). Aliquots (100 mm^3) of the undiluted supernatants were chromatographed.

RESULTS AND DISCUSSION

The concentration of total arsenic in the urine of persons who do not consume food or water with higher-than-normal arsenic concentrations[14] is in the range of 10–20 μg dm^{-3}. Therefore, the 3σ-detection limit of a method for the determination of total arsenic in undiluted urine must not be higher than 1 μg dm^{-3} and preferably should be at 0.1 μg dm^{-3}. When the urine has to be diluted, for instance during the process of mineralization, the detection limits must be lower (inversely proportional to the dilution factor) than needed for the analysis of undiluted urine.

Urine may contain inorganic and organic arsenic compounds (arsenite, arsenate, methylarsonic acid, and dimethylarsinic acid, arsenobetaine). Because the concentration of each of these compounds will only be a fraction of the total arsenic concentration, the detection and the determination limits for the quantification of arsenic compounds must be considerably lower than required for the determination of total arsenic. Methods described in the literature during the past decade for the determination of arsenic compounds are summarized in Table 2. Hydride generation applicable to the determination of arsenic compounds reducible to volatile arsines (arsenite, arsenate, methylarsonic acid and dimethylarsinic acid) has detection limits uncomfortably close to the concentrations of the arsenic compounds in normal urine. Currently, the best method for the separation and quantification of arsenic compounds present in urine is high-performance liquid chromatography with anion-exchange columns coupled to an inductively coupled argon plasma mass spectrometer as arsenic-specific detector. Replacement of the conventional nebulizer with a hydraulic high-pressure nebulizer reduces the determination limit for each arsenic compound to 0.5 μg As dm^{-3} and the 3σ-detection limit to approximately 0.05 μg As dm^{-3}.[13] Inductively coupled optical emission spectrometers have detection limits much too high for the quantification of arsenic compounds in normal urine samples.

Arsenic compounds in the urine of a volunteer intermittently exposed to arsenic derivatives in the laboratory

A volunteer of the academic staff of the institute, who from time to time synthesizes organic arsenic compounds that are needed for research, agreed to provide daily—during a three-week period—first morning urine, to eat seafood only on designated days, and to keep records of food consumption and of synthetic work with arsenic compounds. Four days before the first urine sample was collected on 2 October 1995, the volunteer did not eat any seafood. Approximately 170 g of codfish was ingested by the volunteer for lunch on 6 October and again on 19 October. On 10 to 11 October a Ph.D. (graduate) student synthesized trimethylarsine from arsenic trichloride and methylmagnesium iodide in a well-ventilated hood in the laboratory, through which the volunteer had to walk to reach his office. The door to his office opens into the laboratory and is kept open most of the time. On 12 and 13 October the volunteer synthesized trimethylarsine.

The centrifuged and filtered undiluted urine samples were chromatographed on a Supelcosil LC-SAX anion-exchange column.[13] Arsenite, dimethylarsinic acid, arsenobetaine, methylarsonic acid and arsenate are cleanly separated on this column with a 30 mM ammonium phosphate solution at pH 3.75 within 6 min at a flow rate of 1.5 $cm^3\,min^{-1}$. When high chloride concentrations in the urine interfered with the separation of methylarsonic acid and arsenate, a Hamilton PRP-X100 column with the same mobile phase at pH 6 was used to quantify these species. An example of a chromatogram using the Supelcosil LC-SAX column is presented in Fig. 1. Background arsenic levels in urine are sometimes near or even below the determination limit of the HPLC–HHPN–ICP–MS but still above the 3σ detection limit.

To eliminate the influence of the water con-

Table 2 Summary of methods used for the identification and determination of arsenic compounds in human urine

Method	Species[a]	Detection limit ($\mu g\,dm^{-3}$)[b]	Ref.
HPLC–HG–AAS	As(III), DMA, MA, As(V)	5 all	6
LC–FI–HG–AAS	As_i, DMA, MA	2 all	15
HPLC–HG–AAS	As(III), DMA, MA, As(V)	2 all	16
LC–HG–AAS	As(III), DMA, MA, As(V)	0.5 all	17
LC–HG–AAS	As_i, DMA, MA	0.5 all	18
HPLC–HG–AAS	As(III), DMA, MA, As(V)	1.0; 4.7; 1.2; 1.6	19
HG–AAS	As_i, DMA, MA	1 all	5
FI–HG–AAS	As(III), DMA, MA, As(V)	nr	4
HPLC–HG–ICP–OES	As(III), DMA, MA, As(V)	5; 10; 6; 12	20
HPLC–ICP–OES	As(III), DMA, MA, As(V), AB	102 all	3
HPLC–ICP–MS	As_i, DMA, MA, AB	5 all	24
HPLC–ICP–MS	As(III), DMA, MA, As(V)	0.2; 0.1; 0.2; 0.5	21
HPLC–ICP–MS	AB, As(III), DMA, MA, As(V)	1–5	27
HPLC–ICP–MS	AB, As(III), DMA, MA, TMAO	0.22; 0.39; 0.28; 0.44; 0.25[c]	22
HPLC–ICP–MS	AB, As(III), DMA, MA, As(V), TMAO, AsC, Tetra	6.0; 9.2; 6.5; 8.0; 10.4; 2.8; 3.2; 2.7	28
HPLC–HG–ICP–MS	As(III), DMA, MA, As(V)	0.46 all	23
HPLC–HHPN–ICP–MS	As(III), DMA, MA, As(V), AC, AB	0.5[d] all	13
HPLC–ICP–MS	As(III), As(V), DMA	0.17; 0.35; 0.21	25
HPLC–ICP–MS	As(III), As(V), DMA, MA	4.9; 6.0; 1.2; 3.6	26

[a] Abbreviations: As(III), arsenite; As(V), arsenate; MA, methylarsonic acid; DMA, dimethylarsinic acid; As_i, inorganic arsenic; AB, arsenobetaine; TMAO, trimethylarsine oxide; AC, arsenocholine; Tetra, tetramethylarsonium cation; nr, not reported; FI, flow injection; LC, liquid chromatography; HG, hydride generation.

[b] 2σ or 3σ detection limits.

[c] Ten times square root (SQRT) of the blank.

[d] Determination limit (five replicate injections give results with 20% RSD).

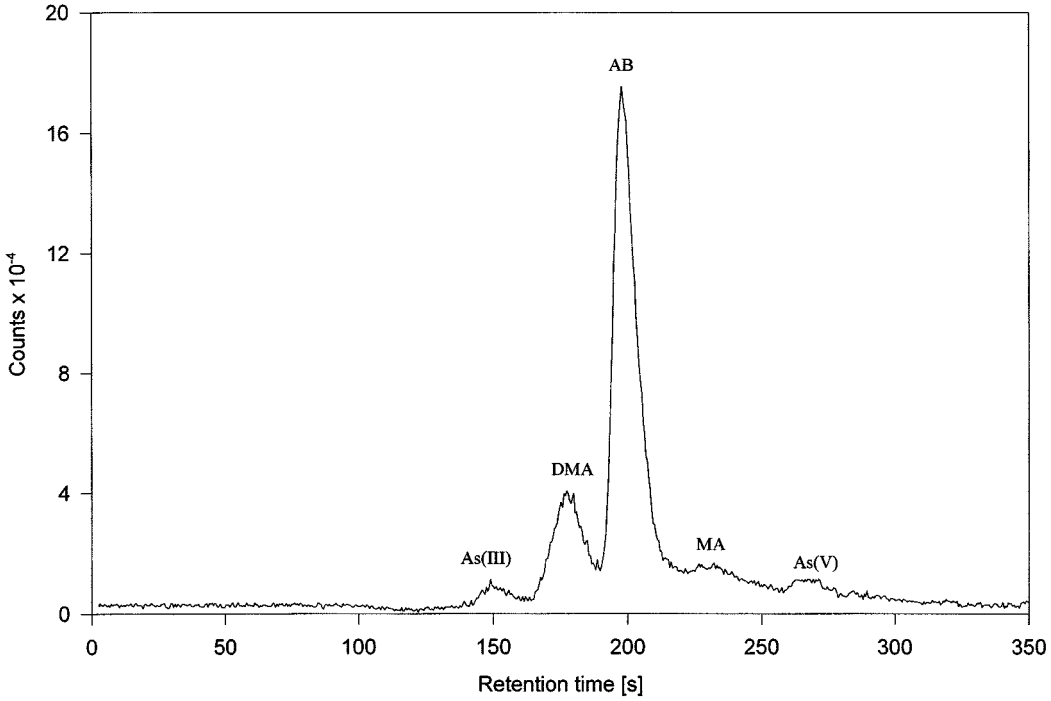

Figure 1 Chromatogram of the urine sample from 13 October 1995 (Supelco, LC-SAX column, 0.03 mol dm^{-3} $NH_4H_2PO_4$ at pH 3.75, 100 mm^3 undiluted urine injected, flow rate 1.5 cm^3 min^{-1}; As-specific detection at *m/z* 75 by ICP–MS).

Table 3 Results of the determination of arsenic compounds in urine

Date, October 1995	Concentration of creatinine (g dm^{-3})	Concentration (μg As g^{-1} creatinine)					
		Arsenite	DMA	AB	MA	Arsenate	Sum
02	1.36	1.5	1.9	1.1	0.6	0.8	5.9
03	1.59	1.1	1.9	1.3	0.5	0.5	5.3
04	2.84	0.6	2.0	0.4	0.8	0.3	4.1
05	2.03	0.5	1.8	0.5	0.7	0.3	3.8
06	1.32	1.0	2.8	0.5	0.8	0.7	5.8
07	1.68	0.9	4.3	28.5	1.0	0.7	35.4
08	2.15	0.4	2.8	9.1	0.7	0.5	13.5
09	2.09	0.8	1.5	4.9	0.5	0.5	8.2
10	2.65	0.8	2.9	4.4	1.1	0.6	9.8
11	1.98	0.6	4.0	1.5	2.0	1.0	9.1
12	2.01	0.9	7.5	1.1	5.3	1.8	16.6
13	1.57	1.8	9.6	33.1	4.9	1.9	51.3
14	2.14	1.1	7.5	13.1	2.0	1.6	25.3
15	1.55	0.8	6.6	6.3	3.1	0.6	17.4
16	0.75	1.1	3.4	4.6	0.6	1.0	10.7
17	2.90	0.4	3.6	3.0	0.4	0.4	7.8
18							
19	0.96	0.8	4.9	1.4	0.9	0.9	8.9
20	1.31	0.9	7.0	49.6	0.6	0.4	58.7
21	2.12	1.1	26.5	51.4	0.4	0.4	79.8
22	1.46	1.1	6.7	21.1	0.7	1.1	30.7
23	1.19	0.6	4.1	8.5	0.5	0.6	14.3

sumption and of the rate of urine accumulation in the bladder on the arsenic concentrations (μg As dm^{-3} urine) obtained over a three-week period, creatinine was determined in each urine sample and the arsenic concentrations were expressed in μg As g^{-1} creatinine. The concentration of creatinine in the urine samples ranged from 0.75 to 2.90 g dm^{-3} (average 1.8 ± 0.6 g dm^{-3}) during the three-week period (Table 3). Creatinine concentrations between 0.1 and 4.0 g dm^{-3} are considered to be normal. The pattern of the arsenic concentrations in the urine over three weeks is not appreciably influenced by the manner of expressing the arsenic concentrations (μg As dm^{-3} or μg As g^{-1} creatinine). Arsenite, arsenate, methylarsonic acid, dimethylarsinic acid and arsenobetaine were present in all the urine samples.

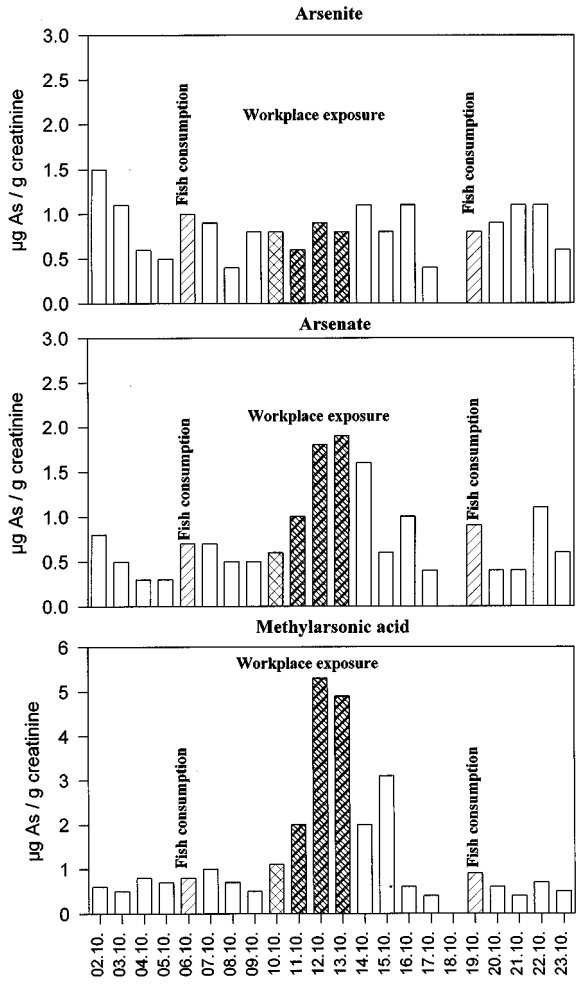

Figure 2 Concentration of arsenite, arsenate, and methylarsonic acid in first morning urine expressed as μg As g^{-1} creatinine during the three-week period.

The concentrations of arsenite and arsenate in the first morning urine are not much higher on the days after the fish consumption than on the days before. The highest concentrations of arsenite and arsenate were observed during the period during which the volunteer had synthesized trimethylarsine (Fig. 2, Table 3). The concentration of methylarsonic acid is not influenced at all by codfish consumption, but is increased to approximately ten times the background level through exposure during synthetic work. The concentration of dimethylarsinic acid is increased slightly by the first consumption of fish, appreciably by the exposure during synthesis, and drastically by the second consumption of fish (Fig. 3, Table 3). The concentration of arsenobetaine is low (0.4–1.3 μg As g^{-1} creatinine) on the days preceding the first consumption of fish and—as expected—very high (28 and 51 μg As g^{-1} creatinine) on the days after fish consumption. The high concentration of arsenobetaine (33 μg As g^{-1} creatinine) after exposure to trimethylarsine is surprising (Fig. 3, Table 3).

Trend in the concentration of total arsenic in the urine

The sum of the concentrations of arsenite, arsenate, methylarsonic acid, dimethylarsinic acid and arsenobetaine is in the range from 3.8 to 80 μg As g^{-1} creatinine, corresponding to 7.7–170 μg As dm^{-3} urine. The maxima in the time-dependent trend of the total arsenic concentrations are caused by arsenobetaine from codfish (maximum on 7 October), by the increase of the concentration of all five arsenic species, but particularly by arsenobetaine following exposure to trimethylarsine (maximum on 13 October), and by the increase of the concentration of dimethylarsinic acid and arsenobetaine after the second codfish meal (maximum on 21 October) (Fig. 4, Table 3). The consumption of fish and the exposure during synthetic work raised the concentrations of total arsenic considerably above the levels of 10–20 μg As dm^{-3} considered to be normal. Comparison of the data presented in Figs 2–4 and in Table 3 clearly demonstrates the inadequacy of total arsenic concentrations in urine as indicators of risk through exposure to arsenic compounds.

Attempt to explain the appearance of arsenic compounds in urine

Arsenite, arsenate, methylarsonic acid and dimethylarsinic acid are known to be trace constituents of food of terrestrial origin. The human body is capable of reducing arsenate to arsenite, methylating arsenite to methylarsonic acid, reducing methylarsonic acid to a compound with trivalent arsenic, and methylating this trivalent methylarsenic derivative to dimethylarsinic acid. Therefore, exposure to arsenite and arsenate in the food will lead to excretion of methylarsenic acids. In addition to these metabolites, dimethylarsinic acid present in the food will be excreted unchanged, and methylarsonic acid may partially be excreted unchanged and partially metabolized to dimethylarsinic acid. The low concentrations of arsenic compounds in most terrestrial food items and the metabolic reactions in the body produce the low concentrations of arsenite, arsenate, methylarsonic acid, and dimethylarsinic acid in the urine samples collected on the four days (2–5 October) preceding the first codfish meal. The low concentration of arsenobetaine (0.4–1.3 μg As g^{-1} creatinine) during this period is not so easy to explain. With the exception of mushrooms,[29] terrestrial food items are not known to contain arsenobetaine. Further investigations will probably show arsenobetaine to be as ubiquitous in terrestrial as in marine organisms. The small amount of arsenobetaine could also come from residual arsenobetaine from prior seafood consumption, perhaps stored in the body.

The arsenic compounds found in the urine after consumption of codfish, particularly dimethylarsinic acid and arsenobetaine (Fig. 3), come from the fish. Fish are known to contain inorganic and organic arsenic compounds,[30] fre-

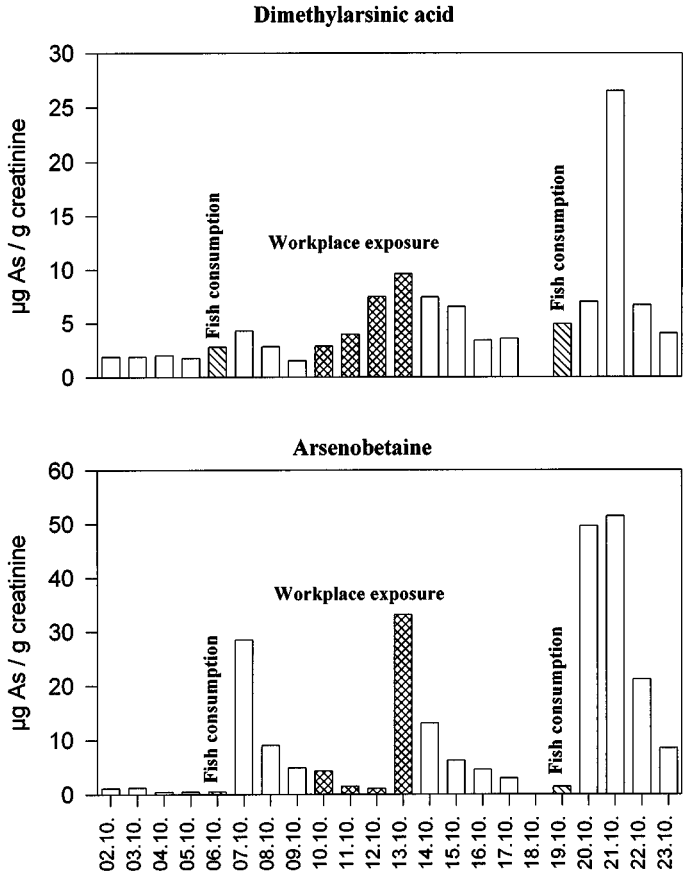

Figure 3 Concentration of dimethylarsinic acid and arsenobetaine in first morining urine expresed as μg As g^{-1} creatinine during the three-week period.

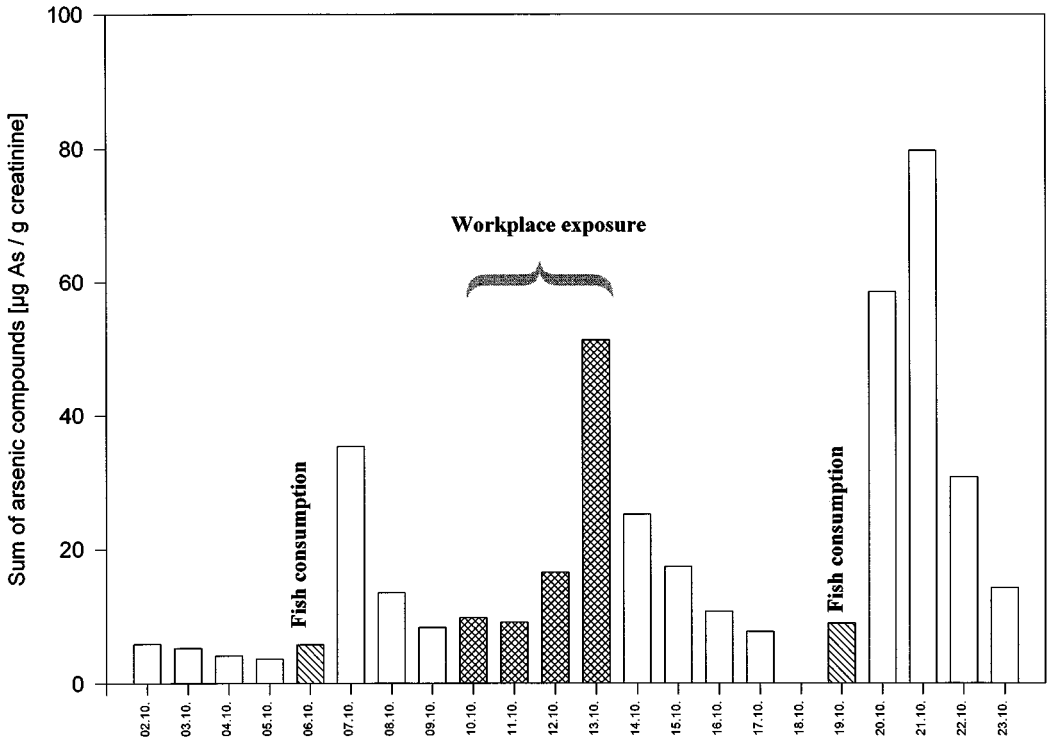

Figure 4 Concentration of excreted arsenic compounds (sum of arsenite, dimethylarsinic acid, arsenobetaine, methylarsonic acid and arsenate) in first morning urine expressed as μg As g^{-1} creatinine during the three-week period.

quently at high concentrations and in species-dependent concentration ratios. The fish with which the second meal (19 October) was prepared must have had higher concentrations of dimethylarsinic acid and arsenobetaine than the fish used for the first meal (6 October).

The high concentration of arsenobetaine (33 μg As g^{-1} creatinine) and the elevated concentrations of arsenite, arsenate, methylarsonic acid and dimethylarsinic acid during the period during which the volunteer synthesized trimethylarsine came as a surprise. The synthesis involved the reaction of arsenic trichloride in dibutyl ether with methylmagnesium iodide at 0 °C under nitrogen, refluxing the reaction mixture for 12 h, distilling trimethylarsine (b.p. 52 °C) and some dibutyl ether until the temperature of the condensing distillate had reached 140 °C, and redistilling the product. All these operations were carried out in a well-ventilated hood. Although some exposure to arsenic trichloride (b.p. 132 °C) could have occurred, the much more volatile trimethylarsine, to which the volunteer was exposed during the distillation for a longer period than to arsenic trichloride, delivered most of the arsenic detected in the urine. The trimethylarsine present at traces in the laboratory air must have entered the body via the lung. Because during the days trimethylarsine was synthesized, seafood containing arsenobetaine was not consumed, no other food known to contain arsenobetaine was eaten and the arsenobetaine consumed with codfish on 6 October had already been excreted (Fig. 3), the novel hypothesis that humans are capable of synthesizing arsenobetaine when challenged with trimethylarsine must be seriously considered. Under the assumption that the decrease of the concentration of arsenobetaine in urine is proportional to decreasing amounts of this compound in the body and follows first-order kinetics, the half-life of arsenobetaine in the body is calculated to be approximately 30 h. Additional experiments must be carried out to verify the generality of the formation of arsenobetaine from inhaled trimethylarsine and to establish whether other arsenic compounds can also be precursors of arsenobetaine in the human body.

The concentration of arsenic in the human urine during the time of exposure to trimethyl-

arsine is increased to twice the background level for arsenite, to four times that level for arsenate (Fig. 2), and to approximately five times that level for methylarsonic acid and dimethylarsinic acid (Fig. 3). These increases suggest that trimethylarsine, or one of its metabolites with three methyl groups, was demethylated stepwise to inorganic arsenite and arsenate in the human body. Another possibility that should be considered is the depletion of storage sites for these arsenic compounds in the body, induced by the exposure to trimethylarsine.

These unexpected results must be verified by additional experiments under carefully controlled conditions, with reliable analytical methods for the determination of the arsenic compounds. The results indicate strongly that the human body can do more than form methylarsonic acid and dimethylarsinic acid. It most probably can demethylate organic arsenic compounds and can synthesize arsenobetaine when appropriately challenged.

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