Elevated Urine Arsenic: Un-Speciated Results Lead to Unnecessary Concern and Further Evaluations

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Abstract

The consumption of seafood within two to three days of testing can increase total urine arsenic concentrations. Few clinicians are familiar with this fact and often misinterpret elevated results. A retrospective chart review of all cases with arsenic testing seen between 1991 and 2004 at an occupational and environmental medicine referral clinic was performed. Urine arsenic results were classified as follows: total arsenic levels; speciated results (inorganic, ionic arsenic); and whether the patient abstained from seafood prior to the collection. Laboratory detection limits for total and for ionic arsenic were ≤ 2 µg/L. Fifty-four patients with urine arsenic testing were identified. The total urine arsenic concentration exceeded 40 µg/L for 28 patients. On paired, speciated testing (n = 21), mean total arsenic was 122 ± 227 µg/L, and ionic arsenic was not detected in any of these same samples (p = 0.023). On paired testing, before and after seafood abstention (n = 12), total urine arsenic without abstention was 291 ± 267 µg/L, and it was only 9 ± 12 µg/L after seafood abstention (p = 0.004). The total urine arsenic elevations observed in our series were due to benign organic arsenic compounds commonly found in seafood. Laboratories should reflexively perform speciation on most samples with elevated total arsenic concentrations prior to reporting the results. Reflexive speciation could reduce unnecessary referrals, further testing, and patient anxiety.

Introduction

With public concern about environmental exposures, testing for arsenic exposure is often requested by patients and provided by health care providers. It is well-known among specialists in toxicology, occupational, and laboratory medicine that the co-incidental consumption of seafood within several days of testing can yield unexpectedly elevated total urine arsenic concentrations (1–7). On the other hand, few primary care physicians and neurologists who order heavy metal screening panels or specific arsenic tests are familiar with this fact. Many laboratories communicate urine arsenic results as total arsenic concentrations accompanied by reference intervals that represent toxicity thresholds for inorganic arsenic. As a result, clinicians and patients can easily misinterpret elevated total arsenic results as indicative of inorganic arsenic toxicity when, in fact, more often than not they reflect benign dietary forms of arsenic. Therefore, laboratories could prevent unnecessary psychological stress on the patient, further examinations, and inappropriate treatment by utilizing testing protocols that specifically assess inorganic arsenic exposure.

Naturally occurring organic arsenic compounds, including arsenobetaine, arsenocholine, and arsenosugars, are found in high levels in fish, shellfish, and seaweed and are nontoxic (4,8). Toxic inorganic arsenic compounds may occur naturally in rocks and soil; synthetically in preserved wood, insecticides, herbicides, glass manufacturing, smelting, semiconductors, circuits, and laser technology; and as adulterants in some traditional Chinese and Indian medicines (9,10). Worldwide, the most important exposures occur in discrete geographic areas with high levels of inorganic arsenic in groundwater (11–14). Chronic arsenic-related health effects are endemic in these populations.

Inorganic arsenic exposure occurs most frequently through ingestion and inhalation. Once absorbed, arsenic is distributed primarily to the kidneys and liver and can accumulate in skin, hair, and nails (1,15,16). Arsenic is cleared rapidly from the blood, not significantly stored in internal organs, and excreted mainly by the kidneys. Therefore, urine testing is the best means of assessing ongoing or recent arsenic exposure. Most arsenic is eliminated within 96 h after exposure cessation (17). Most inorganic arsenic is excreted in methylated forms [monomethylarsonic acid (MMA) and dimethylarsinic acid (DMA)], and the remaining 20–40% as unchanged ionic arsenite (As^{III}) and arsenate (As^{V}) (5,18).

Inorganic arsenic toxicity can result in neurologic, dermatologic, gastrointestinal, hematopoietic, and other pathology

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(9,11,13,14). Not surprisingly, physicians often test patients with unexplained neurologic, dermatologic, gastrointestinal or multi-system complaints for urine arsenic, either alone or as part of a heavy metal screening panel. Standard arsenic testing by most laboratories measures total urine arsenic. These tests measure As^{III}, As^{V}, MMA, and DMA, as well as organic seafood arsenic and do not distinguish among these forms.

In this study, we describe patients seen at an occupational and environmental medicine clinic who received arsenic testing. These included patients referred for the evaluation of possible or presumed arsenic toxicity, usually on the basis of elevated total urine arsenic concentrations. In particular, we evaluated the relative contributions of inorganic arsenic exposure and dietary seafood arsenic to elevated urine arsenic results.

Methods

Study sample

Retrospective analysis of medical records from the Occupational and Environmental Medicine Clinic at The Cambridge Hospital in Cambridge, Massachusetts from August 1991 to June 2004 was performed. All cases with a blood or urine arsenic test performed through our clinic or an outside institution were included. The study of these records for research purposes was approved by the Cambridge Health Alliance's Institutional Review Board.

Data collection

Demographic and epidemiologic information included age,

Table I. Patients Tested for Arsenic

	All Patients Tested for As (*N* = 63)	Patients Referred for Possible As Toxicity (*N* = 30) Group A	Patients Referred for Other Reasons but Tested for As (*N* = 33) Group B	P Value for Comparison of Means or Proportions between Groups A and B
Highest total urine As range (μg/L)	0–907 (*n* = 54)	0–907 (*n* = 29)	0–140 (*n* = 25)	
Mean	110 ± 174	179 ± 212	31 ± 42	0.001
25th percentile	9	39	0	
Median	45	106	11	
75th percentile	142	221	46	
Age range (years)	17–82	17–82	19–71	
Mean	46 ± 13	47 ± 15	45 ± 10	0.575
Gender (% women)	36 (57%)	18 (60%)	18 (54%)	0.662
Source of referral				0.134
Health care provider	45 (71%)	20 (67%)	25 (76%)	0.578*
Government agency	4 (6%)	3 (10%)	1 (3%)	
Self	10 (16%)	3 (10%)	7 (21%)	
Lawyer	2 (3%)	2 (7%)	0	
Not indicated	2 (3%)	2 (7%)	0	
Current smoker	13/60 (22%)	2 (7%)	11/30 (37%)	0.005
Reason for initial As test				0.028
Screen for cause of illness	43 (68%)	16 (53%)	27 (82%)	
Screen for possible exposure	17 (27%)	11 (37%)	6 (18%)	
Confirm result of other form of testing	3 (5%)	3 (10%)	0	
Documented source of potential exposure to Inorganic As				0.139
None	56 (89%)	26 (87%)	30 (91%)	
Occupation	5 (8%)	4 (13%)	1 (3%)	
Asian folk medication	2 (3%)	0	2 (6%)	
Predominant symptom				0.118
Neurologic	24 (38%)	10 (33%)	14 (42%)	0.604†
Gastrointestinal	10 (16%)	8 (27%)	2 (6%)	
Musculoskeletal	7 (11%)	2 (7%)	5 (15%)	
ENT	4 (6%)	1 (3%)	3 (9%)	
Dermatologic	5 (8%)	1 (3%)	4 (12%)	
Other	3 (5%)	1 (3%)	2 (6%)	
None	10 (16%)	7 (23%)	3 (9%)	

* The second P-value for "source of referral" was determined by merging the data into two categories: "healthcare provider" and "non-healthcare provider and using Fisher's exact test".
† The second P-value for "predominant symptoms" was determined by merging the data into two categories: "neurologic" and "non-neurologic and using Fisher's exact test".

geographic location of residence, smoking history, recent seafood consumption, occupation, and reported and identified routes of exposure. The presenting complaint, types of arsenic testing, and urine, blood, and hair arsenic results were also entered into the database.

Urine arsenic results were further classified as total arsenic (unspeciated results representing the sum of all arsenic present in the urine regardless of form) or speciated inorganic arsenic (ionic As^{III} and As^{V}). Whether the patient abstained from all fish and other seafood for 48–72 h prior to the urine collection was also recorded. All results whether random or 24-h collections were entered in the database and reported in micrograms per liter.

Further evaluation of patients with arsenic exposure

Among patients evaluated for arsenic toxicity and those found incidentally to have elevated total urine arsenic excretion, further testing was done to rule out exposure to inorganic arsenic. One or more of the following methods were used: urine arsenic speciation (determination of inorganic, ionic arsenic, as well as total urine arsenic), repeated urine arsenic testing after abstention from all seafood for 48–72 h, or analysis of scalp hair for arsenic.

Arsenic analyses

When specimens were collected at our clinic, they were sent to an experienced reference laboratory. This laboratory performs all urine arsenic analyses at a single facility. The presence and concentration of total arsenic was determined by inductively coupled plasma-mass spectroscopy (ICP-MS). If a sample's total arsenic concentration exceeded 10 µg/L, then inorganic, ionic forms (As^{III}, As^{V}) were reflexively determined by flow-injected atomic absorption spectrophotometry (FIAS). The detection limits for both total and for inorganic arsenic were ≤ 2 µg/L. Quality control procedures at the reference laboratory included the following. Every batch of samples for either ICP-MS and FIAS contained reference arsenic samples (Biorad) at approximately 10% of the total samples in each run. Both negative and positive control samples are used. Positive control samples consist of primarily inorganic arsenic and are present in each run at various concentrations (personal communications with Dr. Richard Earley, January and February 2005 and Ray Gegen, August 2005). The laboratory assesses both the accuracy and precision of all results using computerized control algorithms based on Westgard rules (19,20) to identify any significant outliers from the actual reference concentrations. If an outlier is detected, no results are released from that run unless the control problem is reconciled or the analyses have been satisfactorily repeated (personal communication with Ray Gegen, August 2005).

Statistical analyses

We performed statistical analyses with SPSS software (21). Urine arsenic values that were obtained in response to provocative chelation were not included in data analyses. Non-detected results were treated numerically as 0 µg/L. Total urine concentrations exceeding 40 µg/L were considered elevated. This value was set conservatively at 20% below the upper limit of the reference interval of 50 µg/L intended for total arsenic concentration. Because the laboratory's speciation method determined ionic As^{III} and As^{V}, but not their methylated metabolites, we estimated conservatively that ionic As represented 20% of the sum of all inorganic As and associated metabolites. T-tests were used to compare mean values. Chi-square tests were used to compare proportions. The level of statistical significance was $p < 0.05$ for all analyses and two-tailed.

Results

Sixty-three patients were identified who had been tested for arsenic by blood, hair, or urine. Fifty-four patients (86%) had urine arsenic results available, including 97% of those referred to the clinic for arsenic toxicity. Mean urine arsenic, urine arsenic ranges, and demographics stratified by referral type, are presented in Table I. Urine values in Table I are based on each patient's highest observed urine arsenic concentration. Thirty patients (48%) were referred for possible or presumed arsenic

Table II. Patients with Peak Urine Total Arsenic > 40 µg/L and Speciated Arsenic Results

Patient	Highest Total Urine As (µg/L) (Speciated or Non-speciated Test)	Speciated Urine As Testing		
		Total As (µg/L)	Inorganic As (µg/L)	Seafood abstention prior to speciated test
1	44	Non-detected	Non-detected	Yes
2	46	46	Non-detected	Unknown
3	53	Non-detected	Non-detected	Unknown
4	76	16	Non-detected	Yes
5	79	Non-detected	Non-detected	Unknown
6	80	80	Non-detected	No
7	83	83	Non-detected	No
8	92	92	Non-detected	Unknown
9	94	Non-detected	Non-detected	Yes
10	106	Non-detected	Non-detected	Yes
11	148	11	Non-detected	Unknown
12	162	33	Non-detected	No
13	165	Non-detected	Non-detected	Unknown
14	168	86	Non-detected	No
15	170	170	Non-detected	No
16	190	54	Non-detected	No
17	272	272	Non-detected	No
18	472	472	Non-detected	No
19	481	481	Non-detected	No
20	578	Non-detected	Non-detected	Yes
21	907	907	Non-detected	No

toxicity. The remaining 33 cases were referred for other reasons, but tested for arsenic based on symptoms, suspected exposures, or as part of a heavy metal screen. Among those evaluated for arsenic toxicity, 67% were referred primarily because of previous testing by another healthcare provider suggesting arsenic toxicity, and 22 (73%) had urine arsenic results exceeding 40 µg/L.

Urine arsenic concentrations were significantly higher among patients who were referred for arsenic toxicity compared to those referred for other reasons. The referral groups did not differ significantly with respect to mean age, gender, referral source, identified exposure sources to inorganic arsenic, or predominant symptoms. Smoking was more common among those patients referred for reasons other than possible arsenic toxicity, and it was not associated with higher urine arsenic concentrations.

Speciated results were available for 21 of the 28 patients (75%) whose peak urine arsenic exceeded 40 µg/L (Table II). On paired testing from the same urine sample, the mean total arsenic was 122 ± 227 µg/L, whereas inorganic arsenic was not detected in any of these samples ($p = 0.023$). For those patients who reported abstaining from seafood prior to the speciated test, mean total arsenic values were also negligible (range: not detected to 16 µg/L) and much lower than initial testing.

Table III compares paired results for total arsenic excretion before and after abstention from seafood ($n = 12$). Before seafood abstention, mean total urine arsenic was 291 ± 267 µg/L, compared to 9 ± 12 µg/L after abstention ($p = 0.004$).

Additionally, four patients who were referred based on elevated urine arsenic excretion (range of peak results: 148–467 µg/L) underwent arsenic-specific hair analysis. Three of them had been documented as having unexplained neuropathies by neurologists. In all four cases, arsenic was not detected in hair.

Discussion

Among patients referred to our specialty center for possible or presumed arsenic toxicity, more than 85% lacked a potential source of exposure to inorganic arsenic on thorough review of their occupational and environmental histories. We also found no laboratory evidence of inorganic arsenic exposure in any of the patients. First, among patients with elevated urine arsenic, none of the speciated tests detected inorganic arsenic. Second, we documented total urine arsenic excretions as high as 272 to 907 µg/L that contained no inorganic arsenic, and after seafood abstention, these patients' total urine arsenic excretion also became negligible. Third, in selected cases where possible chronic toxicity was a concern, we also performed hair testing. Inorganic arsenic accumulates in hair, but organic seafood forms of arsenic do not (1,16,22–24). In those hair tests, arsenic was non-detected. Irrespective of referral source and testing rationale, our results strongly suggest that most, if not all, of the observed elevations in total urine arsenic were due to benign, seafood-derived, organoarsenic compounds.

Importantly, most of the patients referred for further evaluation of elevated urine arsenic excretion suffered varying amounts of psychological distress and concern about the possibility they had arsenic intoxication. In some cases, they had incurred additional unnecessary financial expenses. Many had undergone several blood or urine tests for arsenic prior to coming to our clinic, and some had consulted multiple healthcare providers. In several cases, the initial test results led the patients to test their drinking water or other family members for the presence of arsenic. Anecdotally, some of these elevated total urine arsenic results had triggered telephone consultations with Poison Control Centers or community environmental investigations by public health officials. In our opinion, most of these undesirable consequences can be prevented if laboratories adopt two practices. First, they should reflexively speciate most urine specimens with elevated total arsenic concentrations for the presence of inorganic arsenic and its metabolites. (Exceptions might include cases involving a known inorganic arsenic exposure and/or follow-up of an identified inorganic exposure.) Direct determination of the remaining arsenic as seafood-derived would provide additional reassurance that an elevated total arsenic did not represent the presence of toxic substances. Second, they should provide an explanatory statement along with numerical results regarding recent seafood consumption and its potential to influence urine arsenic.

Although it is ideal for subjects to abstain from seafood for 72–96 h before the collection of urine for arsenic testing, it is not as convenient or efficient as speciation of the sample. Also, reports of seafood abstention are not always accurate. When asked, some patients initially do not recall recent seafood consumption (2,6). Those who eat seafood infrequently seem most likely to report no consumption. However, because of the rapid excretion of arsenic from the body, the frequency of fish meals has less influence on urine arsenic results than the timing relative to the urine collection.

Our results and conclusions are supported by previous reports of patients tested for arsenic for various clinical purposes (2,6). Nixon and Moyer (6) analyzed urine samples from all 220 patients tested for arsenic during a 3-month period at the Mayo Clinic. Ten specimens yielded elevated results, which ranged between 149 and 1054 µg/L. Of these, eight had

Table III. Results Before and After Seafood Abstention for Patients with Peak Urine Arsenic > 40 µg/L

Patient	Highest Urine As Total (µg/L)	Urine As after Seafood Abstention Total (µg/L)
1	44	Non-detected
2	52	Non-detected
3	76	16
4	94	Non-detected
5	106	Non-detected
6	162	12
7	251	40
8	272	4
9	472	13
10	481	19
11	578	Non-detected
12	907	Non-detected

no source of exposure to inorganic arsenic, contained no detectable inorganic arsenic, and had negative hair analyses. In these patients, organic forms of arsenic were directly measured and accounted for the elevated total results. The other two patients had demonstrable exposure sources, significantly elevated inorganic arsenic concentrations, and positive hair analyses. Similarly, Wisconsin public health authorities investigated four adults with elevated urine arsenic levels between 340 and 1485 µg/L (2). None had an identifiable source of inorganic arsenic exposure, and in retrospect, interviews revealed that all four persons had consumed at least one fish meal within 36 h of the original urine collection. In all four cases, repeat testing after seafood abstention demonstrated non-detected to background arsenic concentrations. In two cases, hair analyses failed to detect arsenic, and additionally, elevated urine arsenic was reproducible after a planned fish meal. Other controlled dietary experiments also demonstrate that seafood consumption can significantly elevated total urine arsenic concentrations (3,25,26).

Our study does have some limitations. First, we used retrospective methods and a population limited to patients seen at a specialty clinic. Referral bias at an occupational and environmental medicine clinic, however, should have favored finding patients with true inorganic arsenic exposure. Second, the speciated analyses we obtained determined only ionic, inorganic forms, but not their methylated metabolites. None of the speciated results in our sample contained detectable inorganic As, which should account for 20–40% of excretion after exposure to inorganic arsenic. Given the detection limit of ≤ 2 µg/L, any significant exposure to inorganic arsenic would have resulted in some detectable ionic As. Third, whereas most organic arsenic found in seafood is thought to be excreted unchanged within 48 to 72 h after ingestion (27), several recent studies suggest that a fraction in certain seafood is converted to DMA prior to excretion (3,25,26,28). Our study could not assess this because our reference laboratory did not assess DMA; however, the possibility that small amounts of seafood arsenic may be metabolically transformed to DMA would not affect our findings that the total arsenic elevations observed were due to seafood consumption.

Strengths of our study included the availability of two types of paired data. Both total and inorganic arsenic were measured from the same urine samples, and pre- and post-seafood abstention urine samples were collected from the same patients.

Given the financial and psychological impact of receiving a diagnosis of possible arsenic toxicity, we recommend that laboratories analyzing urine arsenic reflexively perform speciation of samples with elevated total arsenic concentrations prior to reporting the results. Consideration should also be given to directly determining the seafood-derived As forms in samples with elevated total arsenic, as well as ionic As and its methylated metabolites. Additionally, laboratories should include a statement regarding recent seafood consumption as a benign and common cause of high total urine arsenic. If further testing is still indicated or judged necessary in order to further reassure the patient, consideration should be given to repeat speciated testing 48 to 72 h after strict abstention from seafood with or without arsenic-specific hair testing.

References

1. R.R. Lauwerys and P. Hoet. *Industrial Chemical Exposure: Guidelines for Biological Monitoring.* Lewis Publishers, Boca Raton, FL, 2001.
2. L. Knobeloch, S. Korthof, and H. Anderson. Never on a Saturday (or a Sunday): the case against using weekend urine specimens to assess arsenic exposure. *Wisc. Med. J.* **97(9):** 46–48 (1998).
3. J.P. Buchet, D. Lison, M. Ruggeri, V. Foa, and G. Elia. Assessment of exposure to inorganic arsenic, a human carcinogen, due to the consumption of seafood. *Arch. Toxicol.* **70(11):** 773–778 (1996).
4. L. Benramdane, F. Bressolle, and J.J. Vallon. Arsenic speciation in humans and food products: a review. *J. Chromatogr. Sci.* **37(9):** 330–344 (1999).
5. Y.M. Hsueh, M.K. Hsu, H.Y. Chiou, M.H. Yang, C.C. Huang, and C.J. Chen. Urinary arsenic speciation in subjects with or without restriction from seafood dietary intake. *Toxicol. Lett.* **133(1):** 83–91 (2002).
6. D.E. Nixon and T.P. Moyer. Arsenic analysis II: rapid separation and quantification of inorganic arsenic plus metabolites and arsenobetaine from urine. *Clin. Chem.* **38(12):** 2479–2483 (1992).
7. P. Apostoli, D. Bartoli, L. Alessio, and J.P. Buchet. Biological monitoring of occupational exposure to inorganic arsenic. *Occup. Environ. Med.* **56(12):** 825–832 (1999).
8. W. Li, C. Wei, C. Zhang, M. van Hulle, R. Cornelis, and X. Zhang. A survey of arsenic species in Chinese seafood. *Food Chem. Toxicol.* **41(8):** 1103–1110 (2003).
9. T.G. Rossman. Arsenic. In *Environmental and Occupational Medicine*, 3rd ed., W.N. Rom, Ed. Lippincott-Raven, Philadelphia, PA, 1998, pp 1011–1017
10. R.H. Goldman. Arsenic exposure and poisoning. http://patients.uptodate.com.
11. M.M. Rahman, U.K. Chowdhury, S.C. Mukherjee, B.K. Mondal, K. Paul, D. Lodh, B.K. Biswas, C.R. Chanda, G.K. Basu, K.C. Saha, S. Roy, R. Das, S.K. Palit, Q. Quamruzzaman, and D. Chakraborti. Chronic arsenic toxicity in Bangladesh and West Bengal, India—a review and commentary. *J. Toxicol. Clin. Toxicol.* **39(7):** 683–700 (2001).
12. K. Chandra Sekhar, N.S. Chary, C.T. Kamala, J. Venkateswara Rao, V. Balaram, and Y. Anjaneyulu. Risk assessment and pathway study of arsenic in industrially contaminated sites of Hyderabad: a case study. *Environ. Int.* **29(5):** 601–611 (2003).
13. T.H. Lin, Y.L. Huang, and M.Y. Wang. Arsenic species in drinking water, hair, fingernails, and urine of patients with blackfoot disease. *J. Toxicol. Environ. Health A* **53(2):** 85–93 (1998).
14. Y.C. Chen, Y.L. Guo, H.J. Su, Y.M. Hsueh, T.J. Smith, L.M. Ryan, M.S. Lee, S.C. Chao, J.Y. Lee, and D.C. Christiani. Arsenic methylation and skin cancer risk in southwestern Taiwan. *J. Occup. Environ. Med.* **45(3):** 241–247 (2003).
15. M. Ford. Arsenic. In *Toxicologic Emergencies*, 7th ed., L.R. Goldfrank, N.E. Flomenbaum, and N.A. Lewin, Eds. McGraw-Hill, New York, 2002, pp 1183–1195.
16. J.T. Hindmarsh. Caveats in hair analysis in chronic arsenic poisoning. *Clin. Biochem.* **35(1):** 1–11 (2002).
17. T.P. Moyer. Testing for arsenic. *Mayo Clin. Proc.* **68(12):** 1210–1211 (1993).
18. J.P. Buchet, R. Lauwerys, and H. Roels. Comparison of the urinary excretion of arsenic metabolites after a single oral dose of sodium arsenite, monomethylarsonate, or dimethylarsinate in man. *Int. Arch. Occup. Environ. Health* **48(1):** 71–79 (1981).
19. J.O. Westgard, P.L. Barry, M.R. Hunt, and T. Groth. A multi-rule Shewhart chart for quality control in clinical chemistry. *Clin. Chem.* **27(3):** 493–501 (1981).
20. The Quality process. Laboratory Corporation of America. http://www.labcorp.com/pdf/quality_process_brochure.pdf (accessed August 13, 2005).
21. SPSS 12.0: SPSS 12.0 Brief Guide. SPSS Inc., Chicago, IL 2003.
22. M. Vahter, E. Marafante, and L. Dencker. Metabolism of arseno-

betaine in mice, rats and rabbits. *Sci. Total Environ.* **30:** 197–211 (1983).
23. E. Marafante, M. Vahter, and L. Dencker. Metabolism of arsenocholine in mice, rats and rabbits. *Sci. Total Environ.* **34(3):** 223–240 (1984)
24. B.K. Mandal, Y. Ogra and K.T. Suzuki. Speciation of arsenic in human nail and hair from arsenic-affected area by HPLC-inductively coupled argon plasma mass spectrometry. *Toxicol. Appl. Pharmacol.* **189(2):** 73–83 (2003)
25. M.W. Arbouine and H.K. Wilson. The effect of seafood consumption on the assessment of occupational exposure to arsenic by urinary arsenic speciation measurements. *J. Trace Elem. Electrolytes Health Dis.* **6(3):** 153–160 (1992)
26. J.P. Buchet, J. Pauwels, and R. Lauwerys. Assessment of exposure to inorganic arsenic following ingestion of marine organisms by volunteers. *Environ. Res.* **66(1):** 44–51 (1994).
27. E.A. Crecelius. Changes in the chemical speciation of arsenic following ingestion by man. *Environ. Health Perspect.* **19:** 147–150 (1977).
28. R. Heinrich-Ramm, S. Mindt-Prufert, and D. Szadkowski. Arsenic species excretion after controlled seafood consumption. *J. Chromatogr. B* **778(1-2):** 263–273 (2002).

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