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Biological and behavioral factors modify biomarkers of arsenic exposure in a U.S. population

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ABSTRACT

Although consumption of drinking water contaminated with inorganic arsenic is usually considered the primary exposure route, aggregate exposure to arsenic depends on direct consumption of water, use of water in food preparation, and the presence in arsenicals in foods. To gain insight into the effects of biological and behavioral factors on arsenic exposure, we determined arsenic concentrations in urine and toenails in a U.S. population that uses public or private water supplies containing inorganic arsenic. Study participants were 904 adult residents of Churchill County, Nevada, whose home tap water supplies contained <3 to about 1200 μg of arsenic per liter. Biomarkers of exposure for this study were summed urinary concentrations of inorganic arsenic and its methylated metabolites (speciated arsenical), of all urinary arsenicals (total arsenical), and of all toenail arsenicals (total arsenical). Increased tap water arsenic concentration and consumption were associated with significant upward trends for urinary speciated and total and toenail total arsenical concentrations. Significant gender differences in concentrations of speciated and total arsenicals in urine and toenails reflected male-female difference in water intake. Both recent and higher habitual seafood consumption significantly increased urinary total but not speciated arsenical concentration. In a stepwise general linear model, seafood consumption significantly predicted urinary total arsenical but not urinary speciated or toenail total arsenical concentrations. Smoking behavior significantly predicted urinary speciated or total arsenical concentration. Gender, tap water arsenic concentration, and primary drinking water source significantly predicted urinary speciated and total concentrations and toenail total arsenical concentrations. These findings confirm the primacy of home tap water as a determinant of arsenic concentration in urine and toenails. However, biological and behavioral factors can modify exposure–response relations for these biomarkers. Refining estimates of the influence of these factors will permit better models of dose–response relations for this important environmental contaminant.

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1. Introduction

Chronic exposure of humans to inorganic arsenic (iAs) in non-occupational settings has been conclusively linked to increased cancer risk (Cantor and Lubin, 2007; Straif et al., 2009) and increased risk of diseases of the peripheral vascular (Tseng, 2005), cardiovascular (Navas-Acien et al., 2005; Balakumar and Kaur, 2009), and cerebrovascular (Meliker et al., 2007) systems. To elucidate dose–response relations for these adverse effects of chronic iAs exposure, the magnitude, pattern, and duration of exposure to iAs must be determined. Many epidemiological studies have used concentrations of iAs in drinking water and

Abbreviations: iAs, (in order of occurrence)—Inorganic arsenic; TAs, total arsenic; UTAs, total arsenic in urine; NTAs, total arsenic in toenails; MCL, maximum contaminant level; FMV, first morning void; NTU, nephelometric turbidity unit; ICP–MS, inductively coupled plasma–mass spectrometry; iAs^{III}, arsenite; MAs^{V}, methylarsonic acid; iAs^{V}, arsenate; $DMAs^{V}$, dimethylarsinic acid; USAs, urinary speciated arsenic; NAA, neutron activation analysis; ANOVA, analysis of variance; IQR, interquartile range.

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consumption histories to estimate exposure. However, reconstruction of long-term exposure to iAs from these data can be complicated by temporal changes in iAs concentrations and changes in patterns of water consumption (Greschonig and Irgolic, 1997). Concentrations of arsenic in urine or toenails are commonly used in epidemiological studies as biomarkers of exposure to arsenic. Concentrations of total arsenic (TAs) in urine (UTAs) or toenails (NTAs) reflect aggregate exposure to arsenicals from all sources, including food, which contains inorganic, methylated, and other organic arsenicals, and from drinking water in which iAs is the predominant arsenical (Kile et al., 2007). Notably, UTAs and NTAs concentrations reflect exposures to arsenicals over different timescales. UTAs concentrations reflect exposure over a few days because it is strongly influenced by recent changes in exposure to arsenicals (Karim, 2000; Mandal et al., 2004). Nails are a continuously elaborated biomaterial that act as a long-term integrator of arsenic exposure (Karagas et al., 2001; Slotnick et al., 2008; Button et al., 2009). Thus, NTAs concentrations reflect the equilibrium distribution of arsenic between blood and nail during nail formation and extrusion (Hinwood et al., 2003; Pearce et al., 2010) and recapitulate exposure over a period of months before sampling (Slotnick and Nriagu, 2006; Slotnick et al., 2008).

The current study examined relations among concentrations of iAs in tap water and concentrations of arsenic in urine and toenails in a cohort of adults (>45 years old) who were long-term residents of Churchill County, Nevada. Age-dependent reduction in residential mobility (Hurley et al., 2005) suggested that older residents of this northwestern Nevada county would be a good source population to evaluate biomarkers of arsenic exposure in individuals with relatively stable patterns for use of residential drinking water sources. In particular, this study examined the effects of biological factors (age and gender) and behavioral factors (patterns of water use, seafood consumption, smoking, and alcohol use) on biomarker responses. The results demonstrated that arsenic concentration in the home tap water source was an important determinant of exposure to iAs. However, gender and smoking behavior also affected the response of biomarkers. Identifying and assessing biological and behavioral factors that influence aggregate exposure to iAs are critical factors to developing a dose metric for population-based studies of the effects of chronic exposure to this metalloid.

2. Materials and methods

2.1. Site selection

Field work was conducted in August and September 2002, in Churchill County, NV. In 2000, the population of this northwestern Nevada county was 23,982 with 7536 residing in Fallon, the county's largest city (U.S. Census Bureau, http://factfinder2.census.gov). Agriculture is the county's main industry with some mining, smelting, and manufacturing activities. In Churchill County, surface water is used exclusively for crop irrigation; drinking water is supplied by public and private wells. The State of Nevada has documented iAs concentrations in drinking water wells in Churchill County for several decades. For many years, the City of Fallon had a variance to exceed the existing maximum contaminant level (MCL) of 50 μg of arsenic per liter. At the time of this study, the concentration of arsenic in the city's water supply was 89 ± 6 μg (mean and standard deviation) per liter. After fieldwork for this study was completed, the City of Fallon built a new water treatment plant; tap water levels of arsenic are now below the current MCL (10 μg/l).

2.2. Participant selection

Participants were residents of Churchill County who were at least 45 years of age at the time of enrollment and who had resided continuously in the county for 5 years. In addition, participants were required to have attained cumulative residence of at least 20 years in Churchill County. About one-third of participants were residents of Fallon. Other participants were recruited elsewhere in Churchill County where arsenic concentrations in drinking water ranged from below the limit of detection (3 μg/l) to greater than 1200 μg/l. Participants who resided outside the city limits of Fallon provided samples of home tap water. Participants who used an in-home water treatment device for removal of arsenic from drinking water provided a sample of untreated tap water. Hence, efficacies of different in-home water treatment systems were not examined in this study. For verification, one-third of the participants who resided in Fallon also provided samples of home tap water. Demographic characteristics of the source population and study participants are summarized in Supplemental Information Table 1.

The study protocol was approved by the Institutional Review Board of the University of North Carolina at Chapel Hill and reviewed by the Human Subjects Protection Office of the U.S. EPA. All participants provided written consent.

2.3. Collection of medical and exposure histories

At the initial clinic visit, each participant provided a spot urine sample and a blood sample. Height, weight, and blood pressure were also measured and participants completed a computer administered exposure assessment and medical history questionnaire that requested demographic information, medical history, information on recent and habitual seafood consumption, and the length of residence in their present home. All participants estimated their drug, alcohol, or tobacco usage, and daily drinking water consumption and provided information on potential exposure to arsenic from other environmental or occupational sources. At the end of the clinic visit, participants were given a home collection kit for toenails and a container for collection of a sample of untreated tap water from their home. A container for collection of a first morning void (FMV) urine sample was provided to participants who did not provide a urine sample during the initial clinic visit.

2.4. Sample collection and processing

On the day after their initial clinic visit, study participants returned to the clinic between 7:00 and 8:30 a.m. with a sample of home tap water, a FMV urine sample (if needed), and toenails. Based on a volume of urine required for analyses, either the spot urine sample or the FMV urine sample was processed to provide samples for arsenic and cotinine analysis. These samples were stored at 4 °C until shipped to North Carolina on dry ice. Samples were thereafter stored at −80 °C until analyzed.

2.5. Analytical methods

2.5.1. Total arsenic (TAs) in drinking water

Home tap water samples were collected by study participants in acid-washed containers provided by the State Health Laboratory, Bureau of Health Protection

Table 1
Sources and magnitude of exposure to arsenic for study participants.

Exposure variable	*N*	Percentage
Primary source of drinking water		
Untreated home tap water	446	49
Treated home tap water	207	23
Commercially bottled water	251	28
Primary source of water used for cooking		
Untreated tap water	661	73
Treated tap water	172	19
Commercially bottled water	71	8
Primary source of water used for cooking		
Untreated tap water	661	73
Treated tap water	172	19
Commercially bottled water	71	8
Untreated home tap water consumption (oz./day)		
0	198	22
>0 to ≤70	393	43
>70	313	35
Arsenic concentration (ppb) in untreated tap water		
≤10	145	16
11–50	289	32
51–100	336	37
101–300	89	10
≥301	45	5
Seafood consumption		
Within 48 h	258	29
Monthly seafood consumption		
<1 time	301	33
1–5 times	483	53
>5 times	120	13