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# The Effect of Variable Environmental Arsenic Contamination on Urinary Concentrations of Arsenic Species

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**Urinary arsenic species have been determined for approximately 3000 urine samples obtained from residents of a community surrounding an arsenic-emitting copper smelter. Levels of inorganic, monomethylated and dimethylated arsenic species ranged from less than 1 μg/L (the instrumental detection limit) to 180 μg/L seen for dimethyl arsenic. Comparison of a subsample of this population that had the least environmental contamination with the subsample having highest environmental arsenic concentrations showed small but statistically significant differences in urinary arsenic levels for all species except dimethylated arsenic. However, for children under 7 years of age living in areas with increased environmental arsenic contamination, there was a larger and equally significant ($p < 0.001$) increase in all urinary species. This effect was more pronounced in males (5-fold increase in median sum of species concentration over control group) than in females (2-fold increase in median sum of species concentration over control group) and was observed as a weaker effect in the next higher age group (7-13 years of age). Reported consumption of seafood also was significantly related to increased urinary dimethyl arsenic, but changes in distribution among the urinary arsenic species detected was not a sensitive indicator of recent seafood consumption.**

## Introduction

Urinary arsenic levels are indicative of recent (previous 1–2 days) exposures to arsenic (*1*). When total urinary arsenic is measured, intake of all forms of arsenic is detected. Urinary arsenic species that are metabolically related to inorganic arsenic intake have been recommended for use as biological indicators of exposures to inorganic arsenic rather than total urinary arsenic because of the latter's potential for dietary artifacts associated with seafoods containing high levels of organoarsenic compounds (*2,3*). These organoarsenic compounds are not thought to be toxic but compose the majority of total urinary arsenic for persons consuming some types of seafood (*4*). Since some forms of seafood-derived organoarsenic such as arsenobetaine are excreted without metabolic transformation and are not detectable in an arsine generation assay, it has been generally believed that such assays exclude the influence of all seafood arsenic on urinary arsenic levels. While this approach is well documented for groups with occupational exposure (*2,5*), urinary arsenic speciation data reflective of more general populations and background levels of exposure do not exist. We have applied an arsine generation method for the speciation of urinary arsenic to be a population living in an area of significant environmental arsenic contamination in order to assess exposures.

Tacoma, WA is the location of a former primary copper smelter that has been designated as a hazardous waste site under CERCLA (Superfund). The smelter was converted from lead production in the period 1912–1921, and continued to smelt copper until 1985. As a facility specializing in the smelting of high arsenic copper ores, the smelter also produced arsenic trioxide until 1986. Numerous studies have documented arsenic contamination of air, soil, and dusts in the vicinity of the smelter (*6*). Elevated urinary arsenic in schoolchildren living near the smelter has been reported since the early 1970s (*7*). The Ruston-Vashon Island Exposure Pathways study was initiated in 1984 by the Centers for Disease Control under Superfund to address the following questions: *a*) What degree of exposure(s) were occurring in communities surrounding the smelter? *b*) What pathways were contributing most to exposure? *c*) What was the relative impact of current emissions versus environmental arsenic accumulated from historical releases? The overall findings of this study have been reported previously (*8*). In this report, we present urinary arsenic species results for both exposed and relatively unexposed populations.

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The influence of dietary seafood on urinary arsenic has recently been shown to include elevations (exceeding 10-fold in some cases) of dimethyl arsenic following consumption of specific seafoods such as clams and mussels (*9*), resulting in shifts in the distribution of arsine-forming species. In reporting the distribution of arsenic species observed for groups with and without reported seafood consumption, we will consider the potential usefulness of urinary arsenic species distributions in distinguishing seafood arsenic sources from exposures resulting from environmental contamination with inorganic arsenic.

From this data set, we were interested in the following questions: *a*) Are there significant differences in urinary arsenic levels (arsenate, arsenite, monomethylarsonate, dimethylarsinate, or sum of these species) between the cases and controls for any of the age/sex subgroups after eliminating samples collected following reported seafood consumption, and *b*) Are changes in the relative amounts of urinary arsenic species useful in distinguishing between environmental and seafood arsenic exposures? This second question was addressed by considering whether the ratio of dimethylarsinate to sum of urinary arsenic species was different between the cases and controls for any of the age/sex/seafood subgroups.

## Methods

The Ruston-Vashon Island Exposure Pathways study was a longitudinal study conducted over 1 year, with quarterly sample collection from 121 study households (435 individuals) in the general vicinity of the smelter. A small comparison population of 10 homes (31 persons) located in Bellingham, WA, 105 miles north of Tacoma, was sampled once during the study. The study population was divided among five census tracts, of which one (735, the incorporated town of Ruston) was within 0.5 miles of the smelter. Other households in the general Tacoma area ranged from 0.5 to 12 miles in distance from the smelter. Homes were selected with a design that weighted the population by proximity to the smelter and emphasized children as a target population.

Quarterly sampling visits consisted of information gathering by questionnaire and interview, collection of environmental samples (personal, indoor, and outdoor ambient air particulates in 0–2.5 and 2.5–10 $\mu$m size ranges; soil, housedust and road dust samples, drinking water and homegrown fruit/vegetable samples); and personal samples (urine, hair, and handwash samples). Urine samples were self-collected as first-morning void grab samples for each of the 2 days following environmental sampling. An abbreviated questionnaire was collected with each sample to provide information about dietary sources of arsenic.

Urine samples were assayed for arsenic species that are metabolically related to exposures to inorganic arsenic: the inorganic arsenic species arsenate and arsenite (INA), monomethylarsonate (MMA), and dimethylarsinate (DMA), using a previously-described method (*10*) based on arsine generation, chromatographic separation, and atomic absorption spectrophotometric detection. Rigorous quality control procedures included daily replicate analyses of a benchmark sample pool, use of NBS-traceable standards, analysis of NBS-SRM 2670 (toxic elements in freeze-dried urine), replicate analysis of 10% of the actual samples, and analysis of blind submissions of replicate samples (*11*). External audit samples provided by the U.S. Environmental Protection Agency (Contract Lab QC Program, Las Vegas, NV) and by the Centers for Disease Control (Atlanta, GA) were assayed and reported successfully during the analysis period as well. Overall method precision for actual study samples, expressed as a coefficient of variation based on 251 pairs of replicates, was 6.5%. This assay was also used for handwash and drinking water arsenic determination.

Other chemical assays were neutron activation analysis for total arsenic (applied to hair, soil, and bulk dust samples) and X-ray fluorescence analysis for arsenic and other elements (applied to air samples collected on filters and to resuspended dust and soil samples). Questionnaires were coded for diet according to three categories: no seafood consumption reported, (any amount of) finfish consumption reported, and (any amount of) shellfish/crustacean consumption reported.

Descriptive statistical methods (e.g., means, median values, and standard deviations broken down by subgroups of interest) are used to characterize the data. For these analyses, results of less than the method quantitation limit were included as quantitation limit results (0.7 ppb). More formal tests of hypotheses use the random effects regression of Laird and Ware (*19*). This method explicitly accounts for the correlation between multiple observations from the same individual, a condition that violates the independence assumption of the ordinary regression model. To fit the models reported, a stepwise backward elimination strategy was used. All model terms with $p > 0.10$ (two-tailed) were successively eliminated until the final model was obtained.

## Results

Approximately 3000 urine samples were assayed in this study. Spot urinary arsenic species concentrations ranged from $< 1$ to 30 $\mu$g/L for INA and MMA, and from $< 1$ to 180 $\mu$g/L for DMA. Census tract average urinary arsenic expressed as the sum of INA, MMA, and DMA ranged from 19.6 (Ruston) to 9.4 $\mu$g/L (Census Tract 609.01), revealing relatively less variation between census tracts than within census tracts when all age and sex categories were combined. Environmental arsenic levels showed a stronger geographic variation, with census tract average soil varying by a factor of 12 within the contiguous area of the study, and by a factor of more than 50 when the Bellingham control area was included.

Although a control area was selected and some sample types obtained, these data are few compared with the main location of the study. Comparison of the urinary arsenic results from the control area with urinary arsenic from those census tracts most remote from the smelter showed equivalently low levels in the latter regions. The urinary species data taken from the study area (within 10 miles of the smelter) were therefore grouped into three pools: Ruston,

the census tract surrounding the smelter; a low-exposure reference group selected from homes/sampling episodes that had uniformly low associated environmental arsenic levels; and the rest of the study homes. The second-mentioned group (designated "Tacoma/control") was selected from those homes 1.5 miles or more from the smelter by expressing the values for soil, indoor (fine and coarse) and outdoor (fine and coarse) airborne arsenic as log-transformed standardized values, and requiring that the average of these five measures be below the geometric mean of all values collected in the study. Figure 1 shows this index of environmental arsenic versus distance from the smelter for Ruston, Tacoma/control, and the rest of the Pathways study homes.

Table 1 compares the environmental arsenic levels for Ruston, Bellingham (control group), and Tacoma/control households. These data are skewed toward high values, so the median is a preferred value for comparison purposes. The soil arsenic values for the Ruston group are well elevated compared to the other groups and are in the range of values reported for arsenic-contaminated soils (*12*). The Tacoma/control group shows soil arsenic that is elevated above the Bellingham control group, but within the range reported for uncontaminated soils of 40 ppm or less. The (outdoor) airborne arsenic levels are well above ambient background for the Ruston group but nearly equivalent and lower than reported background values from the other two groups. Arsenic levels in indoor air and on hands (children) were slightly elevated in the Tacoma/control group compared with Bellingham, but were significantly higher in the Ruston group. Hair arsenic values were not obtained for the control group and were much lower in the Tacoma/control group than in Ruston. Based on these environmental levels, it appears that the Tacoma/control population is more comparable to the Bellingham control group than to the Ruston exposed group.

Group urinary arsenic species levels are compared in Table 2. Because preliminary experiments indicated that the analytical methods used might not entirely exclude the effects of dietary seafood, samples identified as following seafood consumption in questionnaires were excluded from group statistics and summarized separately (groups B and E). Tables 1 and 2 indicate that while some differences exist between the background/Tacoma and the Bellingham group in terms of soil arsenic level and, to a lesser extent, air levels and hand loadings, these two groups (C and D) are similar to each other and each is distinct from Ruston, the most

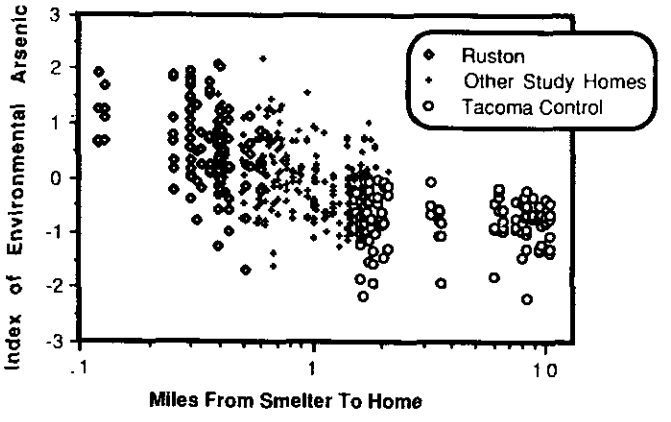


FIGURE 1. Environmental arsenic contamination by distance from smelter. The index of environmental arsenic is the average of log-transformed, standardized values of soil, air, and house dust arsenic levels.

**Table 1. Characteristics of study subgroups.**

| Variable | Ruston | Tacoma/ control | Bellingham |
|---|---|---|---|
| Number of homes | 28 | 42 | 10 |
| Distance, miles | | | |
| Mean | 0.35 | 4.1 | 105 |
| Range | 0.12–0.60 | 1.5–10.4 | — |
| Arsenic levels | | | |
| Soil, μg/g dry weight | | | |
| Median | 215 | 30.9 | 7.3 |
| Mean | 353 | 57.2 | 6.6 |
| SD | 411 | 74.5 | 2.7 |
| *n* | 28 | 42 | 10 |
| Airborne, median values, ng/m³ | | | |
| Indoor, coarse[a] | 9.0 | 0.19 | 0.13 |
| Indoor, fine[b] | 15.8 | 2.77 | 0.23 |
| Outdoor, coarse | 41.9 | 0.39 | 0.41 |
| Outdoor, fine | 17.2 | 1.48 | 2.08 |
| Hair, μg/g dry weight | | | |
| Median | 3.7 | 0.5 | — |
| Mean | 15.2 | 6.8 | — |
| SD | 35.0 | 27.7 | — |
| *n* | 40 | 32 | 0 |
| Hand loadings, μg/hand | | | |
| Median | 2.2 | 0.3 | 0.1 |
| Mean | 5.1 | 0.7 | 0.3 |
| SD | 6.8 | 1.4 | 0.5 |
| *n* | 148 | 165 | 16 |

[a] Coarse = 2.5–10 μm.
[b] Fine = <2.5 μm.

**Table 2. Group concentrations of urinary arsenic species.**

| Study group | Concentration, ng/mL[a] | | | |
|---|---|---|---|---|
| | INA | MMA | DMA | Sum |
| A: Ruston[b] (*n* = 557) | | | | |
| Median | 1.5 | 1.9 | 7.1 | 11.1 |
| Mean | 2.6 | 3.3 | 13.8 | 19.6 |
| SD | 3.1 | 4.4 | 19.6 | 26.5 |
| B: Ruston[c] (*n* = 92) | | | | |
| Median | 1.5 | 1.7 | 8.9 | 11.6 |
| Mean | 1.9 | 2.3 | 14.2 | 18.4 |
| SD | 1.8 | 2.3 | 15.0 | 18.0 |
| C: Bellingham[b] (*n* = 53) | | | | |
| Median | 1.2 | 1.2 | 6.2 | 9.4 |
| Mean | 1.4 | 1.2 | 7.0 | 9.6 |
| SD | 0.9 | 0.6 | 4.7 | 5.4 |
| D: Tacoma/control[b] (*n* = 696) | | | | |
| Median | 1.1 | 1.3 | 4.8 | 7.5 |
| Mean | 1.3 | 1.6 | 6.4 | 9.2 |
| SD | 1.1 | 1.3 | 5.8 | 7.5 |
| E: Tacoma/control[c] (*n* = 140) | | | | |
| Median | 1.2 | 1.4 | 8.3 | 10.8 |
| Mean | 1.5 | 1.7 | 11.3 | 14.5 |
| SD | 1.2 | 1.4 | 9.4 | 11.2 |

[a] INA, arsenite; MMA, monomethylarsonate; DMA, dimethylarsinate.
[b] Samples with reported seafood consumption excluded.
[c] Samples with reported seafood consumption only.

**Table 3. Urinary arsenic species by age, sex, and exposure group.**

| Age and sex group | Concentration, ng/mL[a] | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Ruston | | | | Tacoma/control + Bellingham | | | |
| | INA | MMA | DMA | Sum | INA | MMA | DMA | Sum |
| 0–6 Years | | | | | | | | |
| Males | | | | | | | | |
| Median | 6.2 | 7.7 | 37.8 | 50.1 | 1.1 | 1.7 | 7.6 | 10.1 |
| Mean | 7.2 | 10.6 | 47.5 | 65.2 | 1.1 | 1.8 | 8.4 | 11.3 |
| SD | 5.5 | 8.0 | 35.8 | 48.1 | 0.7 | 1.2 | 5.9 | 7.1 |
| *n* | 70 | | | | 64 | | | |
| Females | | | | | | | | |
| Median | 2.8 | 3.7 | 18.8 | 25.1 | 1.1 | 1.5 | 8.0 | 12.4 |
| Mean | 3.9 | 4.9 | 21.3 | 30.1 | 1.4 | 1.8 | 9.8 | 13.0 |
| SD | 3.4 | 3.8 | 14.0 | 30.7 | 1.0 | 1.1 | 6.6 | 8.2 |
| *n* | 38 | | | | 23 | | | |
| 7–13 Years | | | | | | | | |
| Males | | | | | | | | |
| Median | 1.4 | 1.6 | 7.3 | 10.7 | 1.2 | 1.3 | 5.2 | 8.2 |
| Mean | 2.2 | 2.4 | 11.2 | 15.8 | 1.2 | 1.4 | 6.7 | 9.4 |
| SD | 2.0 | 2.1 | 9.2 | 12.9 | 0.7 | 4.7 | 5.5 | |
| *n* | 32 | | | | 49 | | | |
| Females | | | | | | | | |
| Median | 2.0 | 2.0 | 8.8 | 13.6 | 1.0 | 1.2 | 3.8 | 6.0 |
| Mean | 2.1 | 2.2 | 9.9 | 14.3 | 1.2 | 1.3 | 4.8 | 7.3 |
| SD | 0.9 | 1.0 | 5.4 | 6.7 | 0.8 | 0.8 | 3.3 | 4.4 |
| *n* | 18 | | | | 84 | | | |
| 14–20 years | | | | | | | | |
| Males | | | | | | | | |
| Median | 1.4 | 1.8 | 5.0 | 8.5 | 1.3 | 1.5 | 4.9 | 7.8 |
| Mean | 1.6 | 2.0 | 5.9 | 9.5 | 1.5 | 1.6 | 5.8 | 8.9 |
| SD | 0.9 | 1.3 | 3.4 | 5.1 | 1.0 | 0.6 | 4.2 | 4.9 |
| *n* | 48 | | | | 46 | | | |
| Females | | | | | | | | |
| Median | 1.6 | 1.5 | 10.5 | 13.7 | 1.0 | 1.3 | 4.9 | 7.8 |
| Mean | 1.8 | 1.7 | 11.7 | 15.1 | 1.2 | 1.5 | 5.1 | 7.8 |
| SD | 0.8 | 0.6 | 8.6 | 9.6 | 0.9 | 0.9 | 4.2 | 5.4 |
| *n* | 14 | | | | 27 | | | |
| 20+ Years | | | | | | | | |
| Males | | | | | | | | |
| Median | 1.7 | 1.8 | 8.6 | 10.2 | 1.2 | 1.4 | 4.8 | 7.9 |
| Mean | 2.1 | 2.3 | 6.4 | 13.0 | 1.6 | 1.9 | 6.7 | 10.2 |
| SD | 1.5 | 1.8 | 7.8 | 10.2 | 1.6 | 1.9 | 7.0 | 10.1 |
| *n* | 174 | | | | 195 | | | |
| Females | | | | | | | | |
| Median | 1.0 | 1.3 | 5.5 | 8.1 | 1.0 | 1.2 | 4.0 | 6.4 |
| Mean | 1.2 | 1.7 | 6.4 | 9.3 | 1.1 | 1.4 | 5.9 | 8.4 |
| SD | 0.8 | 1.3 | 5.1 | 6.5 | 0.8 | 1.0 | 5.6 | 6.6 |
| *n* | 163 | | | | 208 | | | |

[a]INA, arsenite; MMA, monomethylarsonate; DMA, dimethylarsinate.

exposed group. The magnitude of the dietary effect was small in the Ruston group (A versus B) and larger in the Tacoma/control group (D versus E). Based on comparison of group urinary arsenic values among groups, the differences in environmental arsenic shown in Table 1 would not seem to produce large differences in exposures.

Table 3 compares the combined Bellingham and Tacoma control groups urinary arsenic species results with those from Ruston by age and sex subgroups. An age effect is seen within each population, and clear differences between Ruston and control are seen for the youngest subgroups (0–6-year-old males, 5-fold increase for Ruston over controls; 0–6-year-old females, 2-fold increase).

## Discussion

These control group data are the first reported general U.S. population urinary arsenic species results, while the Ruston data indicate the effects of modest arsenic exposures resulting from discernable environmental contamination. Total arsenic values from previous studies of urinary arsenic levels or estimates based on dietary total arsenic intake are not comparable because of the influence of those organoarsenic compounds excluded by the speciation assay. Buchet (*3*) has estimated that the sum of species detected would be below 20 $\mu$g/g urinary creatinine in persons without either occupational exposures to arsenic or significant levels of

geological arsenic in drinking water. Total arsenic levels below 100 μg/g creatinine are expected for individuals without occupational or (seafood) dietary exposures (*2*). Total urinary arsenic in unexposed individuals has been suggested to range from 10 to 300 μg/L (*13*). In the 1984 final Health Assessment Document for Inorganic Arsenic (*14*), the Environmental Protection Agency estimated that a national population average bioavailable arsenic intake for nonsmokers was ≤ 60 μg/day (based on adult ventilation and intake rates for food and water). Of this, 40 μg/day was food-derived [based on the 1974 FDA Market Basket survey (*15*)] and was discounted in the EPA discussion on the basis that most or all of the arsenic would be in organic rather than inorganic chemical forms. Based on the observation that dietary (seafood) organoarsenic is excreted in urine without transformation to inorganic or methylated arsenic (*4,14,16*), this analysis would suggest that total urinary arsenic might be as much as three times higher than the sum of arsine-forming species for a U.S. mean arsenic intake model. Using the EPA bioavailable intake estimate (20 μg/day; excluding diet) and assuming 70% urinary excretion (*17*), 1.4 L/day urine volume (*18*), and steady state, one would estimate an average level of summed urinary arsine-forming species of 10 ng arsenic/mL. This compares reasonably well with the mean and median values seen in Tables 2 and 4 for the least-exposed group (Tacoma-Control and Bellingham, excluding seafood consumers).

The results shown in Table 4 address the question of whether significant differences in urinary arsenic species exist between cases and controls for any of the age/sex subgroups after exclusion of samples collected following reported seafood consumption. For each outcome variable (log-transformed INA, MMA, DMA, and sum of species), the magnitude and significance of the effects of several explanatory variables are given. These models were obtained by starting with a completely saturated model that included age (4 levels: 0–6, 7–13, 14–19, 20+), sex, and status (case, control), and all interactions. Terms were successively eliminated until only factors with significance levels of 0.10 or less (two-tailed) were retained in the model. The regression coefficients may be interpreted as representing the average increase (decrease if negative) in log urinary arsenic species for a person in that population category over the baseline (intercept) level. Thus, from Table 4, the effect of being male is to increase the logarithm of the sum of urinary arsenic species (expressed in μg/mL) by 0.171 over females ($p < 0.01$). A 5-year-old male in Ruston would be predicted to have a long increase of 1.931 [0.171 (male) + 0.181 (case) + 1.13 (case × age) + 0.449 (case × age × male)] over baseline.

Significant main effects include sex (males, on average have higher levels than females) and case/control status (cases have higher arsenic levels than controls, although the effect is not significant for DMA). The magnitude of these effects is relatively small compared to that of the interactions, however. The interactions reflect the differences between cases and controls in a particular age, sex, or age/sex subgroup. The results show a highly significant status by age interaction that indicates higher arsenic levels in 0- to 6-year-old cases for all arsenic species and sum of species; 7- to 13-year-old cases for DMA, sum, and (to a lesser extent) INA; and 14- to 19-year-old cases for DMA only. There is also a significant status × age × sex interaction for MMA and sum, which indicates that, among 0- to 6-year-old cases, males have higher arsenic levels than females. The magnitude of this effect is relatively large (for instance, it is about twice as large as the overall case effect), but the significance is only marginal ($p < 0.10$) because the estimate is based on a comparatively small number of samples.

The fact that the magnitudes of the interactions are much larger than those of the main effects suggests that the differences in urinary arsenic levels are not determined by environmental arsenic levels alone, but may reflect age- and/or sex-related behavioral or physiological differences. Relatively little information on possible physiological differences between age and sex categories that might affect efficiency and time course for arsenic excretion is available. The differences in arsenic concentration observed between age/sex categories within a single exposure group might in fact have a physiological explanation rather than a behavior-related cause. The strong distinction between cases and controls for some age- and sex-matched groups does suggest that environmental contamination is a key factor. The possible confounding roles of behavior and/or physiological effects

**Table 4. Random-effects analysis of variance for urinary arsenic species.**

| | Coefficient[a] | | | |
|---|---|---|---|---|
| | Outcome variable | | | |
| Effect | log (sum As) | log (DMA) | log (MMA) | log (INA) |
| Intercept | 1.91 | 1.46 | 0.092 | −0.021 |
| Sex (male) | 0.171‡ | 0.213‡ | 0.233§ | 0.240§ |
| Status (case) | 0.181‡ | —* | 0.244§ | 0.203§ |
| Status × age 0–6 | 1.13* | 1.70 | 1.03§ | 1.12§ |
| Status × age 7–13 | 0.363‡ | 0.553‡ | —* | 0.261 |
| Status × age 14–19 | —* | 0.783† | —* | —* |
| Status × sex × age 0–6 | 0.449 | —* | 0.418 | —* |
| Status × sex × age 14–19 | —* | −0.817 | —* | —* |
| Percent variation explained by: | | | | |
| Covariates | 29.0 | 23.0 | 28.6 | 24.3 |
| Between-person variability | 28.4 | 32.5 | 29.8 | 21.2 |
| Within-person variability | 42.6 | 44.5 | 41.6 | 54.5 |

[a]All results are two-tailed. *, $0.05<p<0.10$; †, $0.01<p<0.05$; ‡, $0.001<p<0.01$; §, $p<0.01$.

underscore the importance of using matched control groups when attempting to infer exposure patterns from small increases in urinary arsenic species concentrations.

Table 4 also shows the amount of variation that can be explained by the various components of the model. In the usual regression model, the square of the multiple correlation coefficient, $R^2$, is used to apportion the total variation into that part explainable by the regression and that part due to random error. In the random-effects models used here, the total variation is divided into three components: the portion that can be explained by the covariates listed in Table 4, the portion due to unexplained variations between persons (even among individuals within a single age/sex/case subgroup), and that portion that is due to unexplained variation within a person. For the sum of species, for instance, 42.6% of the total variation is due to unexplained variations in repeated observations on the same individual; 29% can be explained by the age/sex/case and interaction effects model; and the remaining 28.4% is attributable to unexplained variations between individuals. Previously reported results (*8*) lead us to believe that variations in behavior leading to greater or lesser exposure are a major source of unexplained variability. Physiological differences between individuals and even within individuals over time are also likely to account for a large share of the unexplained variation in urinary arsenic.

To address the question of whether ratios among arsenic species can be used as an indicator of seafood consumption versus environmental arsenic exposure, the ratio DMA/sum is first corrected for the differential effects of age, sex, case status, and interactions using a (random-effects) regression model. The overall mean of the uncorrected ratios is 0.665. After correcting for age, sex, case status, and interactions, the mean ratio of samples not associated with reported seafood consumption is 0.645 (uncorrected mean + residual from regression). The mean associated with consumption of finfish is 0.733, and the mean associated with shellfish consumption is 0.767. The standard deviation of an individual observation is 0.142 (the sum of the between-person and within-person variance components). While the means for finfish and shellfish consumption are highly significantly different from the nonseafood mean ($p < 0.001$), there is still substantial overlap between the three distributions. For this reason, the ratio DMA/sum does not seem very useful as an indicator of dietary effects in urinary arsenic for individual samples, at least for the amounts of dietary intake seen in this population.

## Conclusions

The sum of concentrations of inorganic and methylated arsenic species detected in nominally unexposed individuals were lower than previous reports of total arsenic in unexposed populations. Although this difference may be largely attributable to dietary arsenic from seafood (detected in total arsenic assays but at least partially excluded in the arsenic species assay), seafood consumption and diet also appeared to influence the levels of arsenic species detected. Relationships among species concentrations were too variable to be diagnostic of seafood intake.

While urinary arsenic species did increase with increasing environmental arsenic contamination for the populations studied, this effect was highly variable and was statistically significant only for children living in the most highly contaminated area. The potential importance of behavior as a factor influencing the relationship between environmental arsenic contamination and arsenic exposures was suggested by the strong age and sex dependence of the correlation between urinary arsenic and environmental arsenic level.

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