Levels of Urinary Total and Speciated Arsenic in the US Population: National Health and Nutrition Examination Survey 2003-2004

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The findings and conclusions in this report are those of the authors and do not necessarily represent the views of the Centers for Disease Control and Prevention.

Abstract

Objective: To provide levels of total and speciated urinary arsenic in a representative sample of the US population.

Methods: For the first time, total arsenic and seven inorganic and organic arsenic species were measured in the urine of participants (n = 2557) for the 2003-2004 National Health and Nutrition Examination Survey (NHANES). Data were compiled as geometric means and selected percentiles of urinary arsenic concentrations (ug/L) and creatinine corrected urinary arsenic (ug/g creatinine) for total arsenic, dimethylarsinic acid, arsenobetaine, and a sum of the inorganic related species.

Results: Arsenic acid, arsenous acid, arsenocholine, and trimethylarsine oxide were detected in 7.6, 4.6, 1.8, and 0.3% of the participants, respectively (limits of detection of 0.6-1.2 μg/L). Monomethylarsonic acid was detected in 35% of the overall population. For all participants aged ≥6 years, dimethylarsinic acid (geometric mean of 3.71 μg/L) and arsenobetaine (geometric mean of 1.55 μg/L) had the greatest contribution to the total urinary arsenic levels. A relatively greater percentage contribution from arsenobetaine is seen at higher total urinary arsenic levels and from dimethylarsinic acid at lower total urinary arsenic levels. For all participants aged ≥6 years, the 95th percentiles for total urinary arsenic and the sum of inorganic-related arsenic (arsenic acid, arsenous acid, dimethylarsinic acid, and monomethylarsonic acid) were 65.4 μg/L and 18.9 μg/L, respectively. For total arsenic and dimethylarsinic acid, covariate adjusted geometric means demonstrated several slight differences due to age, gender, and race/ethnicity.
Conclusions: The data reflect relative background contributions of inorganic and seafood-related arsenic exposures in the US population. Arsenobetaine and dimethylarsinic acid are the major arsenic species present with arsenobetaine accounting for a greater proportion of total arsenic as total arsenic levels increase.

Introduction

Arsenic is an element that is widely distributed in the earth's surface in small amounts, primarily in its inorganic forms. Anthropomorphic sources of arsenic have included the smelting of mined metals. Inorganic arsenic is used currently as an outdoor wood preservative, in some pesticides, as semiconductor dopant materials, and in certain medicines. General human exposure to inorganic arsenic results from natural amounts consumed in drinking water. However, dietary arsenic may be an important source (NRC, 2002) when drinking water levels are low. Arsenic also forms organic compounds through biological action on inorganic arsenic. These organic forms are found in fish, shellfish, seaweed, and aquatic sediments and are generally much less toxic.. These dietary arsenic species are commonly represented by arsenobetaine and to a lesser extent, arsenocholine and the arsenosugars (Heinrich-Ramm et. al., 2002). In addition to the arsenical forms found in marine organisms, mono- and dimethylated pentavalent and trivalent arsenicals are formed from inorganic arsenic in mammals. Historically this metabolic pathway was viewed as a detoxification mechanism. The trivalent methylated metabolites are believed to be highly toxic and have been recently detected in human urine (Cohen et al, 2006; Vahter, 2002). Exposure to inorganic arsenic or metabolites of inorganic arsenic, above typical environmental levels can result in a variety of adverse health effects, such as skin disorders, neuropathy, and cancer of the lung, bladder, and skin (ATSDR, 2007; NRC, 2001; WHO, 2001).

Urinary levels of arsenic are generally regarded as a good measure of exposure (WHO, 2001). In this article, we provide the first urinary arsenic data in a representative sample of the US population reported in 2003-2004 National Health and Nutrition Examination

Survey (NHANES). Total urinary arsenic was measured by inductively coupled plasma-dynamic reaction cell-mass spectrometry (ICP-DRC-MS), a technique that minimizes or eliminates many argon-based polyatomic interferences (Jarrett et al., 2007). Seven urinary inorganic and organic forms of arsenic were measured separately by high performance liquid chromatography (HPLC) coupled to ICP-DRC-MS.

Methods

Study Design

NHANES is conducted by the National Center for Health Statistics (NCHS) of the Centers for Disease Control and Prevention (CDC). This survey is designed to assess the health and nutrition status of the civilian, noninstitutionalized US population by using a complex multistage probability sample design as previously described (NCHS, 2007). For NHANES 2003-2004, urine was collected for arsenic measurements in a random one-third subset of persons aged ≥6 years representing the civilian, noninstitutionalized population of the United States by age, gender, and self-reported race-ethnicity categories. Race-ethnicity categories were non-Hispanic white, non-Hispanic black, and Mexican Americans. Remaining race-ethnic groups, though not categorized separately, were included in total population calculations. Age categories were children 6-11 years, adolescents 12-19 years, and adults ≥20 years. The survey incorporates sample population weights to account for the unequal selection probabilities caused by the cluster design, nonresponse, and planned oversampling of certain subgroups. The overall NHANES unweighted interview response rate was 79%. Each subsample involves

separate sample weights. For analysis of subsample data, appropriate subsample weights must be used.

Laboratory Methods

During the physical examinations, spot urine specimens were collected in arsenic-free containers, stored at ≤4ºC, and then shipped on dry ice to the CDC's National Center for Environmental Health. Urine samples were stored frozen (≤-70ºC) and typically analyzed within three weeks of collection. Total urinary arsenic concentrations are stable at -70ºC for >3 years). Total urinary arsenic was analyzed using ICP-DRC-MS (Jarrett et al., 2007). Briefly, 0.25 mL urine was diluted with 2.25 mL of diluent (2% v/v nitric acid and 10 µg/L gallium internal standard). Matrix-matched calibrators were prepared by adding 0.1 mL of a calibration standard into 0.9 mL of pooled urine (tested to be <5 µg/L As) and 9 mL of diluent. Analysis was performed on a ELAN® DRC^{Plus} or ELAN® DRC™ II ICP-MS (PerkinElmer SCIEX, Concord, Ontario, Canada) equipped with a Meinhard quartz nebulizer (Type TQ-30-A3), a DRC quartz cyclonic spray chamber, a 2.0 mm I.D. quartz injector, and nickel sampler and skimmer cones. Total urinary arsenic was quantified based on the ratio of analyte to that of the internal standard in peak hopping mode. Argon chloride polyatomic interferences were eliminated by operating the ICP-MS in DRC mode using 10% hydrogen in a balance of argon with a flow rate of 0.2 -0.6 sccm (standard cubic centimeters per minute) and a bandpass rejection parameter (RPq) of 0.65- 0.75. During urinalyses conducted for NHANES, we analyzed two bench quality control pools along with blind quality control pools interspersed among the participant samples. The bench QC (n = 272) had an inter-day precision of 10.05% relative standard deviation (RSD) at 8.2 µg/L and RSD of 3.03% at 179.7 µg/L. Limit of detection for

urinary arsenic was 0.74 µg/L. Accuracy was verified by analyzing standard reference material (SRM 2670) from the National Institute of Standards Technology (NIST) and reference materials from the Centre de toxicologie du Québec (CTQ).

Seven arsenic species in urine were separated by high performance liquid chromatography (HPLC) using an anion exchange column (PRP-X100® 4.6 x 150 mm, 5 µ, PEEK hardware, Hamilton Company, Reno, NV, USA) (Verdon et al., 2004). Urine was diluted 1:4 in 0.1 M ammonium acetate, pH 5, centrifuged at 10,000 g for 10 min, then 20 µL of the supernatant was injected onto the column. Arsenic species were eluted using a linear gradient with a starting mobile phase of 10 mM ammonium carbonate, 10 mM TRIS buffer, pH 8.6 that switched to 10 mM ammonium carbonate, 5 mM ammonium sulfate, and pH 8 pumped at 1.0 mL/min. Column effluent was directed to a Meinhard quartz nebulizer (Type TQ-30-A3) in a quartz cyclonic spray chamber attached to an ELAN DRC II ICP-MS (PerkinElmer SCIEX, Concord, Ontario, Canada) that was equipped with a 2 mm i.d. quartz injector, platinum sampler and skimmer cones. The ICP-MS was operated in DRC mode using 10% hydrogen in a balance of argon with a flow rate of 0.2 sccm, RPQ of 0.4. ^{75}As was monitored in single ion mode as described previously (Jarrett et al., 2007). Signal data was collected and analyzed using TotalChrom chromatography data processing software (PerkinElmer) and Microsoft Excel 2003 (Microsoft Corporation, Richmond, WA, USA). An electronically activated 6-port switching valve with a 200 µL sample loop installed between the column and the ICP-MS was programmatically switched to the inject position at 30 s following the autosampler's sample injection. This introduced an arsenic internal standard peak that appeared on the chromatogram before the column void volume. Figure one illustrates a typical patient sample and one of our bench quality control samples containing all seven arsenic species. The integrated peak area ratios (analyte areas divided by internal

standard area) were used to calculate the concentration of each arsenic species against calibration curves constructed using the human urine-based calibrators that contained arsenocholine, arsenobetaine, trimethylarsine oxide, dimethylarsinic acid, monomethylarsonic acid, arsenic acid, and arsenous acid. The limits of detection were as follows: arsenic acid 1.0 μg/L, arsenous acid 1.2 μg/L, arsenobetaine 0.4 μg/L, arsenocholine 0.6 μg/L, dimethylarsinic acid 1.7 μg/L, monomethylarsonic acid 0.9 μg/L, and trimethylarsine oxide 1.0 μg/L. Quality-control samples consisting of previously characterized urine spiked with known amounts of arsenic species were co-analyzed with each run. The RSD for all bench QC (n = 95) were <10% for bi-level QC concentrations of each arsenic species in the range from 4.9 to 22.1 μg/L.

We assessed arsenic contamination by screening all reagents, collection containers, storage containers, and sample vials and analyzed blanks with each batch of unknowns. Reported results met the accuracy and precision specification of the quality-control/quality-assurance program of the Division of Laboratory Sciences, National Center for Environmental Health, CDC (similar to rules outlined by Westgard et al., 1981).

Urinary creatinine concentrations were determined using an automated colorimetric method on a Beckman Synchron As/ASTR clinical analyzer (Beckman Instruments Inc. Brea, CA, USA) at the Coulston Foundation (Alamogordo, NM, USA) in 2003-2004 (CDC, 2004). Arsenic concentrations in both the total and species methods were adjusted using creatinine concentrations to correct for variable water excretion rates at the time of spot urine specimen collection (Barr et al., 2005).

Statistical Analysis

Urinary arsenic measurements were log transformed prior to data analysis. Geometric means and percentiles were calculated using SUDAAN version 9.0 (Research Triangle Institute, Research Triangle Park, NC, USA). Ninety-five percent confidence limits (CI) for geometric means were estimated based on the Taylor series linearization method (SUDAAN user's manual, 2001) and CIs for percentiles were adapted from the methods of Korn and Graubard (1998) and Woodruff (1952). SUDAAN uses sample weights and calculates variance estimates that account for the complex survey design. Geometric means were computed when >60% of the samples had detectable values. The limit of detection (LOD) divided by the square root of 2 was used for imputation of values lower than the LOD. For each of total urinary arsenic and dimethylarsinic acid, sufficient data were available for comparing the covariate-adjusted geometric means of demographic groups by least squares multiple regression using the covariates of age, gender, race/ethnicity, and urinary creatinine. All two-way interactions were tested. Significant differences were considered at an alpha of 0.05. Arsenic concentrations in urine were also characterized into three groups: <20 ug/L, 20-49 ug/L and ≥50 ug/L; medians and confidence intervals were calculated.

Results

For total urinary arsenic, arsenobetaine, and dimethylarsinic acid, Tables 1-3 present the geometric means and percentiles in μg/L and Tables 4-6 present the data in μg/g of creatinine, respectively. Arsenic acid, arsenous acid, arsenocholine, and trimethylarsine oxide were detected in only 7.6, 4.6, 1.8, and 0.3% of the population, respectively (limits of detection of 0.6-1.2 μg/L), therefore geometric means and percentiles could not be calculated, except the 95th percentile of urinary arsenic acid in participants aged 6 years

and older was 1.10 (95%CI: <LOD-1.20) µg/L or 3.04 (<LOD-3.50) µg/g of creatinine. Monomethylarsonic acid was detected in 35% of participants for all participants aged 6 years and older; the 75th percentile was 1.2 (1.00-1.30) µg/L or 1.33 (1.18-1.54) µg/g creatinine and 95th percentile was 2.4 (2.00-2.80) µg/L or 2.86 (2.40-3.33) µg/g creatinine, respectively. Arsenobetaine and dimethylarsinic acid were the major contributors to the total urinary arsenic level. For subjects aged 6 years and older (n = 2557), the geometric mean levels of total urinary arsenic, arsenobetaine, and dimethylarsinic acid were 8.3 (7.19-9.57), 1.55 (1.31-1.83), and 3.71 (3.21-4.05) µg/L, respectively.

At higher percentiles, arsenobetaine levels appeared to reflect a relatively larger proportion of the total urinary arsenic than at lower percentiles. In a separate analysis (Table 7), the median percentage of the total arsenic from either arsenobetaine or dimethylarsinic acid for three categories of total urinary arsenic (<20, 20-50, >50 µg/L) was determined. Arsenobetaine, usually due to seafood ingestion (Heinrich-Ramm et. al., 2002), comprised a greater portion of the total urinary arsenic as levels increased and dimethylarsinic acid was the major contributor at lower levels of total urinary arsenic.

Inorganic-related arsenic species (arsenic acid, arsenous acid, dimethylarsinic acid, and monomethylarsonic acid) were summed for each participant and percentiles were computed. The 95th and 50th percentiles for all participants aged ≥6 years were 18.9 (15.8-22.9) µg/L and 6.0 (5.4-6.1) µg/L, respectively, with dimethylarsinic acid accounting for most of the inorganic sum. Due to the high proportion of non-detection for three of these arsenic species, the influence of imputed values (below LOD) may slightly

bias the ≤50th percentiles. Table 8 gives the 95th and 50th percentiles and confidence limits for the three age groups.

The covariate-adjusted geometric mean of total urinary arsenic levels in the 12-19 year-old group (6.06 μg/L [5.22-7.05]) was lower than either the 6-11 year-old group (7.29 μg/L [CI: 6.23-8.54], p = 0.006) or the ≥20 years group (8.16 μg/L [7.11-9.37], p <0.001). There was an interaction between race/ethnicity and gender. The covariate-adjusted geometric mean of total urinary arsenic levels in Mexican American males (9.67 μg/L [8.34-11.2]) was higher than the mean in non-Hispanic white males (7.52 μg/L [6.29-8.99], p = 0.034), non-Hispanic black males (7.79 μg/L [6.88-8.81], p = 0.038), and Mexican American females (8.21 μg/L [6.74-9.98], p = 0.005). Non-Hispanic black females (9.96 μg/L [7.87-12.6]) also had higher means than did non-Hispanic black males (p = 0.038). All other possible comparisons were not significant.

The covariate-adjusted geometric mean of urinary dimethylarsinic acid levels in the 12-19 year-old group (2.99 μg/L [2.64-3.39]) was lower than that in either the 6-11 (3.68 μg/L [3.21-4.21], p = 0.002) or ≥20 years (3.58 μg/L [3.23-3.97], p <0.001) groups. Mexican American males had a higher geometric mean (4.46 μg/L [4.04-5.15]) than did either non-Hispanic whites (3.39 μg/L [2.99-3.85], p = 0.004) or non-Hispanic blacks (3.52 μg/L [3.08-4.03], p = 0.008). All other possible comparisons were not significant.

Discussion

We report the total and speciated urinary arsenic levels collected from a representative sample of 2,557 US residents aged ≥6. Human exposure to inorganic arsenic occurs predominately through drinking water and less frequently from other sources, including

contact from wood treated with chromated copper arsenic preservatives and certain pesticides. Exposure to organic forms of arsenic primarily occurs from seafood. Measuring total arsenic in human urine assesses the combined exposure from all routes of exposure and all species of arsenic. The individual species of arsenic measured in this study were the common inorganic and organic forms; some rarer types of arsenic, such as 3-nitro-4-hydroxyphenyarsonic acid (a chicken feed additive, roxarsone), were not measurable by our speciation method.

The levels of total urinary arsenic in the NHANES 2003-2004 subsample were similar to levels reported in National Human Exposure Assessment Survey 1995-1996 (NHEXAS) for about 80 children residing in the Great Lakes region (Pellizzari and Clayton, 2006). In the German Environmental Survey III of 1998, median urinary total arsenic levels in 4,052 adults varied with seafood intake and were approximately twofold lower than those for NHANES 2003-2004 (Schulz et al., 2007). Higher mean or median levels of total urinary arsenic than in NHANES 2003-2004 have been reported for people in western areas of North America (Rubin et al., 2007; Meza et al., 2004; Calderon et al., 1999; Josyula et al., 2006; Valenzuela et al., 2005), as well as other areas of the world (Sun et al., 2007; Ahsan et al., 2000; Aposhian et al., 2000; Caceres et al., 2005), that were known to have higher levels of arsenic in their drinking water. Median and mean total urinary arsenic levels for residents in some districts in Bangladesh have been reported to be about 50-fold higher than respective levels in NHANES 2003-2004 (Ahsan et al., 2000; Chowdhury et al., 2003) and geometric mean levels were about 70-fold higher for residents of Inner Mongolia, China (Sun et al., 2007). In the NHANES 2003-2004 subsample, only small differences in total urinary arsenic levels (and also dimethylarsinic

acid) were observed among the various demographic groups. Whether these reflect differences in exposure or pharmacokinetic factors is unknown.

Total urinary arsenic values can occasionally rise to several thousands of μg/L after seafood ingestion due to the contribution of the organic forms of arsenic (arsenobetaine, arsenocholine, and trimethylarsine oxide) to the total urinary arsenic measurement. Most arsenochloline and some trimethylarsine oxide are converted to arsenobetaine in environmental biosystems so that the main seafood exposure is from arsenobetaine; the NHANES 2003-2004 data show little arsenocholine and trimethylarsine oxide in human urine compared with arsenobetaine. After ingestion, organic forms of arsenic are excreted quickly in the urine. Our analysis shows that as total urinary arsenic levels rise from <20 to 20-50 μg/L and to >50 μg/L, the percentage of the total urinary arsenic is increasingly due to arsenobetaine, with median percentages being 62.7% for total urinary arsenic levels >50 μg/L. The cutpoint of 50 μg/L was chosen because some studies suggest that slight health risks may be associated above this level (Tseng et al., 2005; Valenzuela et al., 2005; ACGIH, 2001; WHO, 2001) and also because this value has been used as an upper reference range. The cutpoint of 20 μg/L was chosen to correspond roughly to the 95th percentile of the sum of inorganic species; thus, a urine <20 μg/L is likely to have little contribution from organic arsenic species. Hence, the higher relative contribution from dimethylarsinic acid is found at lower levels (median percent contribution from dimethylarsinic acid for a urine <20 μg/L is 53.4%).

In NHANES 2003-2004 and most human studies, dimethylarsinic acid is the predominant metabolite composing the majority of measurable inorganic-related arsenic in the urine. Levels of dimethylarsinic and monomethylarsonic acids will increase in approximate

proportion to the intake of inorganic arsenic. In the late 1980s, a control population of 696 Tacoma residents demonstrated a median urinary dimethylarsinic acid level similar to those reported in NHANES 2003-2004 (Kalman et al., 1990). In the residents of a Chilean town who consumed water with high levels of arsenic, median levels of urinary dimethylarsinic acid were about 40-fold higher than the adult median levels in NHANES 2003-2004, and urinary dimethylarsinic acid represented about 67% of the total urinary arsenic (Hopenhayn-Rich et al., 1996). Levels of monomethylarsonic acid reported in NHANES 20003-2004 were characterized only at the upper percentiles and, as with dimethylarsinic acid, these levels were much lower than those found in other studies where environmental exposures were highly elevated (Chowdhury et al., 2003; Sun et al., 2007).

Because arsenic acid, arsenous acid, arsenocholine, and trimethylarsine oxide were detected in only 7.6, 4.6, 1.8, and 0.3%, respectively, of specimens, each species made only a small contribution to the total urinary arsenic level. Arsenic acid and arsenous acid are often the primary forms of arsenic to which people are exposed to in drinking water; however, these are metabolized in the body with arsenic acid being reduced to arsenous acid and then methylated to monomethylarsonic acids and dimethylarsinic (WHO, 2001). The sum of the inorganic-related species provided estimates at the 95th percentiles; this level is an important upper benchmark for the US population because the sum of these species represents a dose of the more toxic inorganic arsenic likely incurred from drinking water. Also, in recent years, occupational monitoring and research studies have focused on the sum of inorganic-related species as a measure of inorganic arsenic intake. Studies of small groups of metal smelter and sulfuric acid workers with varying industrial hygiene conditions have reported urinary inorganic arsenic levels ranging up to several

hundreds of μg/L during or following work exposure (Vahter et al., 1986; Offergelt et al., 1992; Jakubowski et al., 1998; WHO, 2001). Timber treatment workers had median urinary dimethylarsinic acid levels (a surrogate marker for inorganic arsenic exposure) that were about 15-fold higher than adult median levels reported elsewhere (Morton et al., 2006). The American Conference of Governmental Industrial Hygienists (ACGIH) provided an occupational biologic effect index (BEI) for urinary inorganic arsenic plus metabolites of 35 μg/L (ACGIH, 2001). The 95th percentile of the NHANES 2003-2004 subsample for the sum of inorganic-related species was 18.9 μg/L and below the ACGIH BEI. Also, about 95% of the adult US population is likely to be below the US EPA reference dose (USEPA, 2001) for inorganic arsenic intake (0.3 μg /kg/d), if 18.9 μg is considered an approximated daily exposure (assumes about one liter of urine is produced per day, steady state conditions, and all ingested arsenic appears in urine), then 18.9 μg/70 kg = 0.27 μg/kg/d. CDC began monitoring urinary arsenic in the US population starting with the NHANES 2003-2004 survey and will collect future survey data. This may allow assessment of the current maximum contaminant level on human exposure to arsenic.

Conclusion

The data reflect relative background contributions of inorganic and seafood-related arsenic exposures in the US population. Arsenobetaine and dimethylarsinic acid are the major arsenic species present with arsenobetaine accounting for a greater proportion of total arsenic as total arsenic levels increase.

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References

Agency for Toxic Substances and Disease Registry (ATSDR). Toxicological Profile for Arsenic. August 2007. http://www.atsdr.cdc.gov/toxprofiles/tp2.html.2/4/2008

Ahsan H, Perrin M, Rahman A, Parvez F, Stute M, Zheng Y, et al. Associations between drinking water and urinary arsenic levels and skin lesions in Bangladesh. *J Occup Environ Med* 2000: 42(12):1195-201.

American Conference of Government Industrial Hygienists (ACGIH). Documentation of biological exposure indices. 7th edition. Cincinnati (OH): ACGIH Worldwide; 2001.

Aposhian HV, Gurzau ES, Le XC, Gurzau A., Healy S.M., Lu X., et al. Occurrence of monomethylarsonous acid in urine of humans exposed to inorganic arsenic. *Chem Res Toxicol* 2000: 13(8):693-697.

Barr DB, Wilder LC, Caudill SP, Gonzalez AJ, Needham L., Pirkle JL. Urinary creatinine concentrations in the U.S. population: implications for urinary biologic monitoring measurements. *Environ Health Perspect* 2005: 113:192-200.

Caceres DD, Pino P, Montesinos N, Atalah E, Amigo H, Loomis D. Exposure to inorganic arsenic in drinking water and total urinary arsenic concentration in a Chilean population. *Environ Res* 2005: 98(2):151-159.

Calderon RL, Hudgens E., Le XC, Schreinemachers D., Thomas DJ. Excretion of arsenic in urine as a function of exposure to arsenic in drinking water. *Environ Health Perspect* 1999: 107(8):663-667.

Centers for Disease Control and Prevention (CDC). National Health and Nutrition Examination Survey 2004. www.cdc.gov/nchs/nhanes.htm accessed 2/4/2008]

Chowdhury UK, Rahman MM, Sengupta MK, Lodh D, Chanda CR, Roy S, et al. Pattern of excretion of arsenic compounds [arsenite, arsenate, MMA(V), DMA(V)] in urine of children compared to adults from an arsenic exposed area in Bangladesh. *J Environ Sci Health A Tox Hazard Subst Environ Eng* 2003 Jan;38(1):87-113.

Cohen SM, Arnold LL, Eldan M, Lewis AS, Beck BD Methylated arsenicals: the implications of metabolism and carcinogenicity studies in rodents to human risk assessment. *Crit Rev Toxicol* 2006 Feb; 36(2):99-133

Heinrich-Ramm R., Mindt-Prufert S, Szadkowsk D Arsenic species excretion after controlled seafood consumption. *J Chromatogr B Analyt Technol Biomed Life Sci* **2002**, *778*, 263-73.

Hopenhayn-Rich C, Biggs ML, Kalman DA, Moore LE, Smith AH. Arsenic methylation patterns before and after changing from high to lower concentrations of arsenic in drinking water. *Environ Health Perspect*. 1996 Nov;104(11):1200-7.

Jakubowski M, Trzcinka-Ochocka M, Razniewska G, Matczak W. Biological monitoring of occupational exposure to arsenic by determining urinary content of inorganic arsenic and its methylated metabolites. *Int Arch Occup Environ Health* 1998 Sep;71 Suppl:S29-32.

Jarrett JM, Jones RL, Caldwell KL, Verdon CV. Total Urine Arsenic Measurements Using Inductively Coupled Plasma Mass Spectrometry With a Dynamic Reaction Cell, *Atomic Spectroscopy* 2007; 28(4): 113-122.

Josyula AB, McClellen H, Hysong TA, Kurzius-Spencer M, Poplin GS, Sturup S, et al. Reduction in urinary arsenic with bottled-water intervention. *J Health Popul Nutr* 2006 Sep;24(3):298-304.

Kalman DA, Hughes J, van Belle G, Burbacher T, Bolgiano D, Coble K, et al. The effect of variable environmental arsenic contamination on urinary concentrations of arsenic species. *Environ Health Perspect* 1990 Nov;89:145-51.

Korn EL, Graubard BI. Confidence intervals for proportions with small expected number of positive counts estimated from survey data. *Survey Method* 1998: 24: 193-201.

Morton J, Mason H. Speciation of arsenic compounds in urine from occupationally unexposed and exposed persons in the U.K. using a routine LC-ICP-MS method. J *Anal Toxicol* 2006 Jun;30(5):293-301.

Meza MM, Kopplin MJ, Burgess JL, Gandolfi AJ. Arsenic drinking water exposure and urinary excretion among adults in the Yaqui Valley, Sonora, Mexico. *Environ Res* 2004 Oct;96(2):119-26.

National Center for Health Statistics. National Health and Nutrition Examination Survey. Hyattsville, MD: U.S. Departmetn of Health and Himan Services, CDC. Available at http://www.cdc.gov/nchs/about/major/nhanes/nhanes01-02.htm last accessed on Feb 4, 2008.

National Research Council (NRC). Arsenic in Drinking Water-2001 Update. National Academy Press, 2001, Washington, DC.

Offergelt JA, Roels H, Buchet JP, Boeckx M, Lauwerys R. Relation between airborne arsenic trioxide and urinary excretion of inorganic arsenic and its methylated metabolites. *Br J Ind Med* 1992 Jun;49(6):387-93.

Pellizzari ED, Clayton CA. Assessing the measurement precision of various arsenic forms and arsenic exposure in the National Human Exposure Assessment Survey (NHEXAS). Environ Health Perspect 2006 Feb;114(2):220-7.

Rubin CS, Holmes AK, Belson MG, Jones RL, Flanders WD, Kieszak SM, et al. Investigating childhood leukemia in Churchill County, Nevada. *Environ Health Perspect* 2007 Jan;115(1):151-7.

Schulz C, Conrad A, Becker K, Kolossa-Gehring M, Seiwert M, Seifert B. Twenty years of the German Environmental Survey (GerES): human biomonitoring--temporal and spatial (West Germany/East Germany) differences in population exposure. *Int J Hyg Environ Health* 2007 May;210(3-4):271-97.

Sun G, Xu Y, Li X, Jin Y, Li B, Sun X. Urinary arsenic metabolites in children and adults exposed to arsenic in drinking water in Inner Mongolia, China. *Environ Health Perspect* 2007 Apr;115(4):648-52.

Tanner S D, Baranov VI. Theory, design and operation of a DRC™ for ICP-MS. *Atomic Spectroscopy* 1999; 20(2):45-52.

Tseng CH, Huang YK, Huang YL, Chung CJ, Yang MH, Chen CJ, et al. Arsenic exposure, urinary arsenic speciation, and peripheral vascular disease in blackfoot disease-hyperendemic villages in Taiwan. Toxicol *Appl Pharmacol* 2005 Aug 15;206(3):299-308. Erratum in: Toxicol Appl Pharmacol 2006 Mar 1;211(2):175.

US Environmental Protection Agency, *National Primary Drinking Water Regulations; Arsenic and Clarifications to Compliance and New Source Contaminants Monitoring. Final Rule*. 2001 Jan 22. p. 6976-7066.

Vahter M, Friberg L, Rahnster B, Nygren A, Nolinder P. Airborne arsenic and urinary excretion of metabolites of inorganic arsenic among smelter workers. *Int Arch Occup Environ Health* 1986;57(2):79-91.

Vahter M Mechanisms of arsenic biotransformation. Toxicology 181-182, 2002:211-217

Valenzuela OL, Borja-Aburto VH, Garcia-Vargas GG, Cruz-Gonzalez MB, Garcia-Montalvo EA, Calderon-Aranda ES, et al. Urinary trivalent methylated arsenic species in a population chronically exposed to inorganic arsenic. *Environ Health Perspect* 2005 Mar;113(3):250-4.

Verdon CP, Caldwell KL, Jones RL Urine arsenic speciation by High Performance Liquid Chromatography Inductively Coupled Plasma Dynamic Reaction Cell Mass Spectrometry (HPLC-ICP-DRC0MS) Centers for Disease Control and Prevention (2004).

Westgard JO, Barry PL, Hunt MR, Groth T. A multi-rule Shewhart chart for quality control in clinical chemistry. *Clin Chem* 1981;27:493-501.

Woodruff RS. Confidence intervals for medians and other position measures. *J Am Stat Assoc* 1952;47:635-647.

World Health Organization (WHO). Arsenic and Arsenic Compounds. 2nd ed. Environmental Health Criteria 224. Geneva 2001. Available at URL: http://www.inchem.org/documents/ehc/ehc/ehc224.htm. Accessed 2/4/2008

Table 1. Urinary total arsenic
Geometric mean and selected percentiles of urine concentrations (in µg/L) for the US population, NHANES 2003-2004

	Geometric mean	Selected percentile (95% confidence interval)						Sample
	(95% confidence limit)	10th	25th	50th	75th	90th	95th	size
Total	**8.30** (7.19-9.57)	**2.10** (1.60-2.60)	**4.10** (3.30-4.80)	**7.70** (6.70-8.70)	**16.0** (13.9-18.4)	**37.4** (31.6-43.5)	**65.4** (48.7-83.3)	2557
Age group								
6-11 years	**7.08** (5.66-8.84)	**2.40** (1.50-2.80)	**4.40** (3.20-4.90)	**6.70** (5.90-7.50)	**10.7** (8.70-13.9)	**23.3** (13.8-61.8)	**46.9** (17.5-178)	290
12-19 years	**8.55** (7.34-9.97)	**2.70** (2.20-3.00)	**4.60** (3.80-5.40)	**8.10** (6.60-9.30)	**15.1** (12.2-17.3)	**30.5** (23.1-40.4)	**46.1** (32.5-56.5)	725
≥20 years	**8.41** (7.25-9.77)	**1.90** (1.40-2.50)	**3.90** (3.20-4.80)	**7.90** (7.00-9.10)	**17.0** (14.9-19.6)	**40.5** (34.9-46.2)	**66.1** (51.2-93.1)	1542
Gender								
Female	**7.30** (6.02-8.84)	**1.70** (1.30-2.40)	**3.20** (2.60-4.20)	**6.80** (5.80-8.30)	**15.0** (11.3-19.5)	**32.9** (26.5-41.7)	**60.5** (40.8-77.1)	1276
Male	**9.50** (8.34-10.8)	**2.70** (2.20-3.20)	**4.80** (4.30-5.60)	**8.90** (7.70-9.70)	**17.5** (15.0-20.1)	**41.6** (32.5-52.8)	**64.6** (48.7-95.4)	1281
Race/ethnicity								
Non-Hispanic white	**7.12** (6.13-8.27)	**1.70** (1.50-2.30)	**3.50** (3.00-4.20)	**7.00** (6.10-7.90)	**13.7** (11.3-15.8)	**28.7** (22.6-35.9)	**53.1** (38.4-65.6)	1074
Mexican American	**9.29** (8.12-10.6)	**2.60** (1.70-3.90)	**5.00** (4.50-5.70)	**9.20** (7.90-10.1)	**16.1** (13.5-19.9)	**34.4** (24.0-60.5)	**67.1** (41.3-111)	618
Non-Hispanic black	**11.6** (9.50-14.1)	**3.70** (2.50-4.50)	**5.70** (5.00-6.30)	**10.3** (7.90-11.8)	**21.5** (14.9-34.4)	**43.5** (36.2-61.8)	**76.0** (43.6-141)	722

Table 2. Urinary arsenobetaine
Geometric mean and selected percentiles of urine concentrations (in µg/L) for the US population, NHANES 2003-2004

	Geometric mean	Selected percentile (95% confidence interval)						Sample
	(95% confidence limit)	10th	25th	50th	75th	90th	95th	size
Total	**1.55** (1.31-1.83)	**< LOD**	**< LOD**	**1.00** (.700-1.30)	**5.10** (4.00-6.50)	**16.6** (12.7-22.3)	**35.0** (27.6-44.6)	2568
Age group								
6-11 years	*	**< LOD**	**< LOD**	**< LOD**	**1.70** (.800-4.00)	**8.80** (3.90-29.9)	**29.7** (6.20-190)	292
12-19 years	*	**< LOD**	**< LOD**	**.600** (<LOD-.800)	**3.10** (2.00-4.60)	**13.4** (7.20-23.7)	**29.7** (17.2-35.8)	728
≥20 years	**1.74** (1.48-2.05)	**< LOD**	**< LOD**	**1.30** (1.00-1.50)	**6.10** (4.90-7.10)	**18.5** (14.0-23.3)	**35.2** (26.8-50.5)	1548
Gender								
Female	**1.45** (1.17-1.80)	**< LOD**	**< LOD**	**.900** (.700-1.30)	**4.70** (3.40-6.20)	**15.6** (11.1-25.3)	**32.7** (21.1-51.3)	1284
Male	**1.66** (1.43-1.93)	**< LOD**	**< LOD**	**1.20** (.900-1.40)	**5.80** (4.40-7.10)	**18.6** (13.9-23.7)	**34.9** (26.8-40.5)	1284
Race/ethnicity								
Non-Hispanic white	**1.37** (1.11-1.68)	**< LOD**	**< LOD**	**.700** (.700-1.00)	**4.20** (2.50-6.30)	**13.2** (9.70-21.4)	**29.0** (21.4-35.5)	1078
Mexican American	**1.19** (.871-1.62)	**< LOD**	**< LOD**	**.800** (.400-1.30)	**3.10** (1.80-5.20)	**9.80** (6.70-21.4)	**31.4** (16.3-39.1)	621
Non-Hispanic black	**2.29** (1.60-3.28)	**< LOD**	**.500** (<LOD-.700)	**1.90** (1.20-3.40)	**7.70** (5.00-11.9)	**23.7** (13.2-38.7)	**45.6** (25.1-94.0)	725

< LOD means less than the limit of detection.
* Not calculated. Proportion of results below limit of detection was too high to provide a valid result.

Table 3. Urinary dimethylarsinic acid
Geometric mean and selected percentiles of urine concentrations (in µg/L) for the US population, NHANES 2003-2004

	Geometric mean	Selected percentile (95% confidence interval)						Sample
	(95% confidence limit)	10th	25th	50th	75th	90th	95th	size
Total	**3.71** (3.33-4.14)	**< LOD**	**2.00** (<LOD-2.00)	**3.90** (3.00-4.00)	**6.00** (5.00-6.00)	**11.0** (9.20-12.0)	**16.0** (13.0-17.8)	2568
Age group								
6-11 years	**3.73** (3.12-4.45)	**< LOD**	**1.90** (<LOD-2.00)	**3.90** (3.00-4.00)	**5.90** (5.00-7.00)	**8.70** (7.00-12.0)	**12.0** (7.30-18.4)	292
12-19 years	**3.85** (3.34-4.42)	**< LOD**	**2.30** (2.00-3.00)	**4.00** (3.00-4.00)	**5.80** (5.00-7.00)	**9.30** (7.70-12.0)	**13.0** (10.0-16.0)	728
≥20 years	**3.69** (3.31-4.11)	**< LOD**	**2.00** (<LOD-2.00)	**3.70** (3.00-4.00)	**6.00** (5.00-6.00)	**10.5** (9.20-12.0)	**15.8** (13.0-18.0)	1548
Gender								
Female	**3.37** (3.00-3.78)	**< LOD**	**2.00** (<LOD-2.00)	**2.90** (2.00-3.00)	**5.50** (4.80-6.10)	**10.0** (8.00-11.0)	**13.6** (11.0-17.0)	1284
Male	**4.12** (3.60-4.71)	**< LOD**	**2.20** (2.00-3.00)	**3.90** (3.00-4.00)	**6.00** (5.00-6.00)	**11.0** (9.00-13.0)	**17.0** (12.1-22.0)	1284
Race/ethnicity								
Non-Hispanic white	**3.27** (2.95-3.62)	**< LOD**	**2.00** (<LOD-2.00)	**3.00** (2.00-3.00)	**4.90** (4.00-5.00)	**9.00** (7.00-10.0)	**11.0** (9.50-15.0)	1078
Mexican American	**4.72** (4.27-5.22)	**1.90** (<LOD-2.00)	**3.00** (2.00-3.00)	**4.70** (4.00-5.00)	**6.80** (6.00-7.80)	**11.9** (9.30-15.0)	**16.0** (12.0-25.0)	621
Non-Hispanic black	**4.27** (3.71-4.92)	**1.90** (<LOD-2.00)	**2.60** (2.00-3.00)	**3.90** (3.00-4.10)	**6.90** (6.00-7.90)	**11.4** (9.00-15.0)	**15.9** (13.0-18.4)	725

< LOD means less than the limit of detection.

Table 4. Urinary total arsenic (creatinine corrected)
Geometric mean and selected percentiles of urine concentrations (µg/g creatinine) for the US population, NHANES 2003-2004

	Geometric mean	Selected percentile (95% confidence interval)						Sample
	(95% confidence limit)	10th	25th	50th	75th	90th	95th	size
Total	**8.24** (7.07-9.59)	**2.86** (2.36-3.36)	**4.22** (3.67-4.77)	**7.04** (5.93-8.51)	**14.1** (11.6-17.2)	**30.4** (26.0-38.7)	**50.2** (40.3-64.5)	2557
Age group								
6-11 years	**8.25** (6.58-10.3)	**3.21** (3.01-3.57)	**5.00** (3.90-6.15)	**7.14** (5.93-9.45)	**11.6** (9.10-16.3)	**22.0** (12.0-69.5)	**38.2** (14.7-188)	290
12-19 years	**6.11** (5.23-7.13)	**2.75** (2.11-3.01)	**3.62** (3.20-4.11)	**5.06** (4.47-6.04)	**9.66** (7.44-11.2)	**17.7** (12.0-26.0)	**27.7** (20.7-35.9)	725
≥20 years	**8.64** (7.38-10.1)	**2.82** (2.32-3.47)	**4.26** (3.69-4.89)	**7.46** (6.20-8.99)	**15.4** (12.7-18.8)	**33.7** (27.3-41.2)	**53.9** (45.4-64.5)	1542
Gender								
Male	**8.00** (6.81-9.40)	**2.83** (2.49-3.28)	**4.06** (3.51-4.71)	**6.73** (5.66-8.35)	**13.7** (11.0-18.0)	**28.7** (25.1-36.4)	**45.6** (35.3-62.1)	1281
Female	**8.47** (7.12-10.1)	**2.87** (2.26-3.60)	**4.31** (3.75-4.93)	**7.33** (6.10-8.75)	**14.4** (11.7-17.7)	**32.3** (24.2-46.6)	**58.4** (42.8-75.0)	1276
Race/ethnicity								
Non-Hispanic white	**7.50** (6.25-9.01)	**2.63** (2.07-3.28)	**3.97** (3.43-4.58)	**6.32** (5.27-7.95)	**12.4** (9.86-17.1)	**26.8** (21.8-32.0)	**40.0** (31.3-53.9)	1074
Mexican American	**8.61** (7.33-10.1)	**3.77** (3.06-4.44)	**5.05** (4.01-6.31)	**7.74** (6.30-9.44)	**12.6** (10.2-15.9)	**24.0** (17.7-34.8)	**42.3** (24.8-62.4)	618
Non-Hispanic black	**8.31** (6.99-9.88)	**2.98** (2.72-3.37)	**4.21** (3.78-4.67)	**6.88** (5.66-8.41)	**13.8** (11.5-17.0)	**27.6** (17.9-56.0)	**53.8** (27.5-120)	722

Table 5. Urinary arsenobetaine (creatinine corrected)
Geometric mean and selected percentiles of urine concentrations (in µg/g creatinine) for the US population, NHANES 2003-2004

	Geometric mean	Selected percentile (95% confidence interval)						Sample
	(95% confidence limit)	10th	25th	50th	75th	90th	95th	size
Total	**1.54** (1.30-1.82)	**< LOD**	**< LOD**	**1.15** (.959-1.43)	**5.00** (3.61-6.80)	**16.2** (12.5-20.3)	**29.4** (24.0-36.4)	2568
Age group								
6-11 years	*	**< LOD**	**< LOD**	**< LOD**	**1.98** (1.15-4.83)	**11.7** (4.13-39.7)	**28.8** (6.80-153)	292
12-19 years	*	**< LOD**	**< LOD**	**.531** (<LOD-.638)	**2.13** (1.39-3.51)	**9.29** (4.29-14.7)	**17.1** (10.4-28.7)	728
≥20 years	**1.79** (1.51-2.12)	**< LOD**	**< LOD**	**1.47** (1.15-1.88)	**5.91** (4.32-7.72)	**17.1** (13.4-21.8)	**30.0** (26.1-36.4)	1548
Gender								
Male	**1.40** (1.18-1.67)	**< LOD**	**< LOD**	**1.10** (.866-1.26)	**4.78** (3.61-6.70)	**14.4** (11.1-18.5)	**26.5** (18.6-29.9)	1284
Female	**1.68** (1.37-2.05)	**< LOD**	**< LOD**	**1.24** (.938-1.67)	**5.58** (3.50-7.43)	**16.9** (12.3-24.5)	**32.9** (25.6-46.3)	1284
Race/ethnicity								
Non-Hispanic white	**1.44** (1.15-1.80)	**< LOD**	**< LOD**	**1.05** (.833-1.36)	**4.44** (2.73-6.83)	**14.3** (10.9-18.6)	**26.5** (18.6-32.0)	1078
Mexican American	**1.10** (.786-1.55)	**< LOD**	**< LOD**	**.877** (.612-1.40)	**2.93** (1.78-5.21)	**8.88** (5.50-15.4)	**19.0** (9.64-29.4)	621
Non-Hispanic black	**1.65** (1.19-2.30)	**< LOD**	**.395** (<LOD-.545)	**1.53** (.901-2.45)	**5.81** (4.25-7.82)	**13.6** (9.76-27.9)	**32.9** (13.4-82.1)	725

< LOD means less than the limit of detection for the uncorrected urine values.
* Not calculated. Proportion of results below limit of detection was too high to provide a valid result.

Table 6. Urinary dimethylarsinic acid (creatinine corrected)
Geometric mean and selected percentiles of urine concentrations (in µg/g creatinine) for the US population, NHANES 2003-2004

	Geometric mean	Selected percentile (95% confidence interval)						Sample
	(95% confidence limit)	10th	25th	50th	75th	90th	95th	size
Total	**3.69** (3.24-4.19)	**< LOD**	**2.24** (<LOD-2.46)	**3.37** (2.94-3.91)	**5.69** (4.62-6.67)	**9.09** (7.61-11.5)	**13.0** (10.7-16.0)	2568
Age group								
6-11 years	**4.34** (3.57-5.28)	**< LOD**	**2.81** (<LOD-3.43)	**4.00** (3.20-4.80)	**6.25** (4.62-8.33)	**10.3** (7.00-13.9)	**13.9** (7.86-21.8)	292
12-19 years	**2.74** (2.39-3.14)	**< LOD**	**1.83** (1.62-2.08)	**2.55** (2.27-2.94)	**3.77** (3.16-4.44)	**5.88** (4.65-6.67)	**7.18** (6.16-11.7)	728
≥20 years	**3.79** (3.34-4.31)	**< LOD**	**2.26** (<LOD-2.47)	**3.48** (3.00-4.00)	**5.95** (4.86-7.05)	**9.45** (8.00-12.0)	**13.5** (11.1-18.6)	1548
Gender								
Male	**3.48** (2.95-4.10)	**< LOD**	**2.07** (1.84-2.36)	**3.16** (2.69-3.79)	**5.45** (4.14-6.90)	**8.57** (6.91-12.0)	**12.0** (8.84-18.9)	1284
Female	**3.89** (3.49-4.34)	**< LOD**	**2.42** (<LOD-2.63)	**3.57** (3.13-4.06)	**5.78** (4.95-6.67)	**9.28** (8.00-11.5)	**13.5** (10.6-18.6)	1284
Race/ethnicity								
Non-Hispanic white	**3.44** (2.97-3.98)	**< LOD**	**2.16** (<LOD-2.35)	**3.16** (2.80-3.73)	**5.16** (4.03-6.49)	**7.94** (6.25-10.6)	**11.1** (8.00-15.0)	1078
Mexican American	**4.38** (3.80-5.05)	**2.24** (<LOD-2.55)	**2.80** (2.57-3.17)	**4.11** (3.28-4.90)	**6.19** (4.84-8.15)	**10.3** (8.00-11.8)	**12.9** (11.1-15.2)	621
Non-Hispanic black	**3.08** (2.69-3.52)	**1.41** (<LOD-1.60)	**1.96** (1.74-2.14)	**2.86** (2.60-3.24)	**4.34** (3.82-5.05)	**7.80** (5.81-9.28)	**10.4** (7.61-16.9)	725

< LOD means less than the limit of detection for the uncorrected urine values.

Table 7. Contribution of arsenobetaine and dimethylarsinic acid to total urinary arsenic

Total urinary arsenic (µg/L)	n	Median % contribution to total urinary arsenic* (25th, 75th percentiles) Arsenobetaine	Dimethylarsinic acid
<20	2038	16.2 (7.9, 34.2)	53.8 (41.4, 66.7)
20-49	360	43.4 (24.8, 59.8)	29.8 (19.2, 44.8)
50+	156	62.7 (45.7, 72.7)	13.6 (6.8, 24.8)

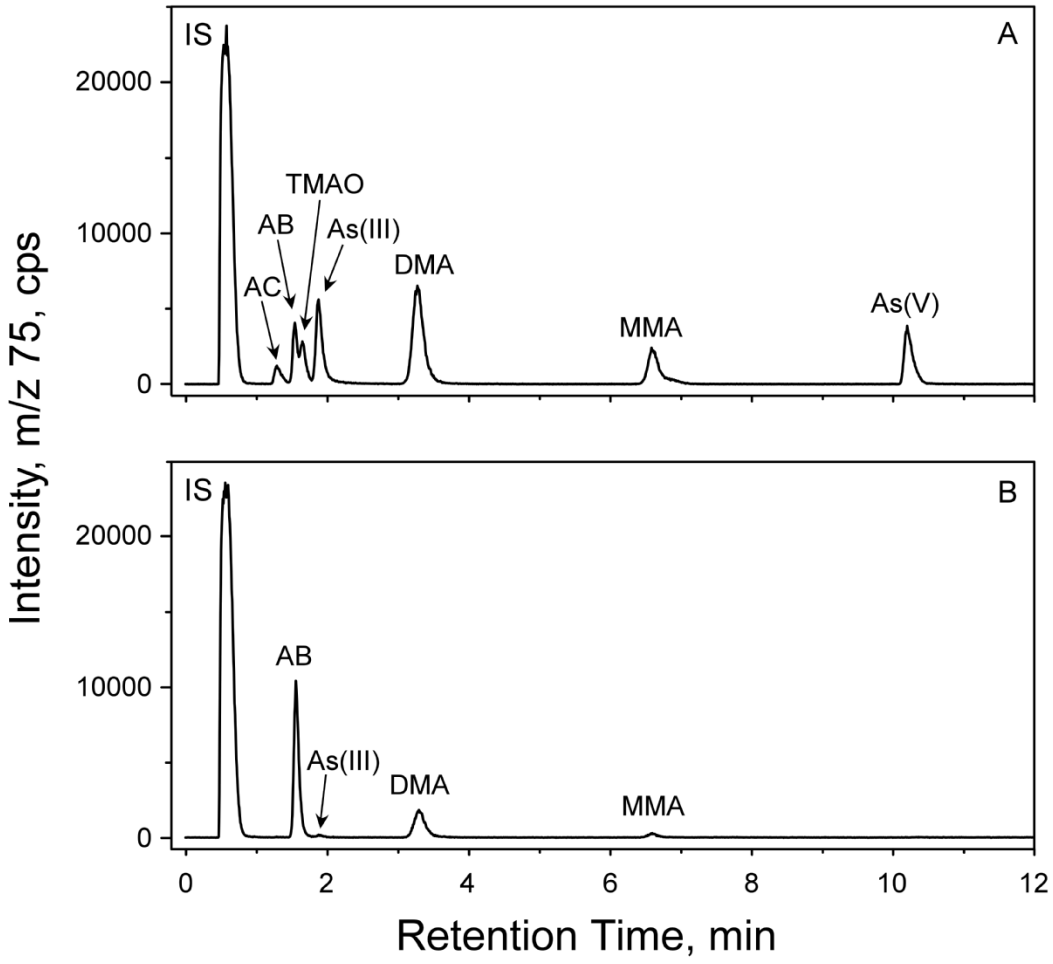
* Median % in each category for all participants aged ≥6 years

Table 8. Percentiles (95% confidence interval) for the sum of urinary inorganic-related arsenic species (μg/L) *

Group (age)	95th Percentile	50th Percentile†
6-11 yrs	14.7	6.0
	(10.7-26.3)	(5.1-6.1)
12-19 yrs	16.7	6.1
	(14.5-20.3)	(5.1-6.3)
≥20 yrs	19.4	5.9
	(16.8-24.6)	(5.1-6.1)
All	18.9	6.0
	(15.8-22.9)	(5.4-6.1)

* Sum of arsenic acid, arsenous acid, dimethylarsinic acid, and monomethylarsonic acid.
† For 50th and lower percentiles, the sum of imputed values may slightly bias the estimate. For 25th and lower percentiles (not shown), the estimate is below the summed LOD.

Figure 1


IS
A
20000
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TMAO
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As(III)
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MMA
As(V)
IS
B
20000
10000
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AB
As(III)
DMA
MMA
0
2
4
6
8
10
12
Intensity, m/z 75, cps
Retention Time, min

Figure 1
Chromatographic profile of seven arsenic species acquired form HPLC-ICP-DRC-MS analysis of human urine. IS internal standard; AC arsenocholine (3.4µg/L); AB arsenobetaine (5.9µg/L); TMAO trimethylarsine oxide (6.6µg/L); DMA dimethylarsinic acid (27.4 µg/L); MMA monomethylarsonic acid (11.9 µ/L); As(V) arsenic acid (11.2 µg/L); As (III) arsenous acid (16.5 µg/L). (A) Quality Control Sample routinely run at the beginning and end of each analytical run. (B) Typical patient sample showing AB (15.5µg/L) as the main species also DMA (7.5µg/L); MMA(1.0µg/L); AS(III) <LOD (LOD=1.2µg/L).