# Urine Arsenic Concentrations and Species Excretion Patterns in American Indian Communities Over a 10-year Period: The Strong Heart Study

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**Background:** Arsenic exposure in drinking water disproportionately affects small communities in some U.S. regions, including American Indian communities. In U.S. adults with no seafood intake, median total urine arsenic is 3.4 μg/L.

**Objective:** We evaluated arsenic exposure and excretion patterns using urine samples collected over 10 years in a random sample of American Indians from Arizona, Oklahoma, and North and South Dakota who participated in a cohort study from 1989 to 1999.

**Methods:** We measured total urine arsenic and arsenic species [inorganic arsenic (arsenite and arsenate), methylarsonate (MA), dimethylarsinate (DMA), and arsenobetaine] concentrations in 60 participants (three urine samples each, for a total of 180 urine samples) using inductively coupled plasma/mass spectrometry (ICPMS) and high-performance liquid chromatography/ICPMS, respectively.

**Results:** Median (10th, 90th percentiles) urine concentration for the sum of inorganic arsenic, MA, and DMA at baseline was 7.2 (3.1, 16.9) μg/g creatinine; the median was higher in Arizona (12.5 μg/g), intermediate in the Dakotas (9.1 μg/g), and lower in Oklahoma (4.4 μg/g). The mean percentage distribution of arsenic species over the sum of inorganic and methylated species was 10.6% for inorganic arsenic, 18.4% for MA, and 70.9% for DMA. The intraclass correlation coefficient for three repeated arsenic measurements over a 10-year period was 0.80 for the sum of inorganic and methylated species and 0.64, 0.80, and 0.77 for percent inorganic arsenic, percent MA, and percent DMA, respectively.

**Conclusions:** This study found low to moderate inorganic arsenic exposure and confirmed long-term constancy in arsenic exposure and urine excretion patterns in American Indians from three U.S. regions over a 10-year period. Our findings support the feasibility of analyzing arsenic species in large population-based studies with stored urine samples.

**Key words:** American Indians, analytical chemistry, arsenic, arsenic species, arsenobetaine, exposure assessment, metabolism, mixed-effects models, multilevel analysis, Strong Heart Study. *Environ Health Perspect* 117:1428–1433 (2009). doi:10.1289/ehp.0800509 available via *http://dx.doi.org/* [Online 7 May 2009]

Inorganic arsenic (arsenite, arsenate) is a naturally occurring toxicant and carcinogen (International Agency for Research on Cancer 2004; National Toxicology Program 2002) that contaminates groundwater supply systems in countries around the world (Smedley and Kinniburgh 2002). In the United States, arsenic levels in drinking water > 10 μg/L—the U.S. Environmental Protection Agency (EPA) maximum contaminant level—disproportionately affect small communities in the West, Midwest, and Northeast regions (Focazio et al. 2000; U.S. EPA 2001). Flour and rice also contain inorganic arsenic, particularly if grown or cooked in areas with arsenic contamination in soil and water (Del Razo et al. 2002). The metabolism of inorganic arsenic in the human body results in methylarsonate (MA) and dimethylarsinate (DMA), which are excreted in urine together with unchanged inorganic arsenic (Aposhian and Aposhian 2006; Cullen and Reimer 1989). Seafood is a source of organic arsenic compounds (arsenobetaine, arsenosugars, arsenolipids) that have no or low toxicity compared with inorganic arsenic (Francesconi and Kuehnelt 2004).

In populations with low seafood intake, total urine arsenic and the sum of inorganic arsenic and methylated (MA and DMA) urine arsenic species are established biomarkers that integrate inorganic arsenic exposure from multiple sources (Calderon et al. 1999; Francesconi and Kuehnelt 2004; Hughes 2006; National Research Council 1999). The proportion of arsenic species that is excreted as inorganic arsenic, MA, or DMA also provides information on the metabolism of inorganic arsenic in the human body. The arsenic species excretion pattern in human urine is approximately 10–20% inorganic arsenic, 10–20% MA, and 60–80% DMA, with substantial variation among individuals (Chiou et al. 1997; Del Razo et al. 1997; Hopenhayn-Rich et al. 1996b; Vahter 2000). Individual arsenic excretion patterns, on the other hand, were fairly constant over time in studies of up to 1 year of follow-up (Concha et al. 2002; Steinmaus et al. 2005b). Because a higher proportion of MA in urine has been associated with an increased risk of cancer (Chen et al. 2003a, 2003b, 2005; Hsueh et al. 1997; Maki-Paakkanen et al. 1998; Steinmaus et al. 2006; Yu et al. 2000) and cardiovascular (Tseng et al. 2005; Wu et al. 2006) outcomes, there is substantial interest in characterizing the long-term arsenic species excretion patterns, especially for MA.

The objective of this study was to conduct an initial assessment of arsenic exposure and excretion pattern, as measured by total urine arsenic and urine arsenic species, in American Indians from Arizona, Oklahoma, and North and South Dakota who participated in the Strong Heart Study, a population-based prospective cohort study funded by the National Heart, Lung, and Blood Institute (Lee et al. 1990; Strong Heart Study 2008). On the basis of arsenic concentrations measured in public drinking water systems in the Strong Heart Study communities, we expected arsenic exposure levels to be higher in Arizona, intermediate in the Dakotas, and lower in Oklahoma. Given dietary patterns in the study communities (Stang et al. 2005), we expected arsenobetaine concentrations, a marker of seafood arsenicals, to be very low. Using three urine samples for each participant, we also assessed arsenic exposure and excretion patterns over a 10-year period and the feasibility of measuring arsenic

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