Associations Between Drinking Water and Urinary Arsenic Levels and Skin Lesions in Bangladesh

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The present study examined the associations between drinking water and urinary arsenic levels and skin lesions among 167 residents of three contiguous villages in Bangladesh. Thirty-six (21.6%) had skin lesions (melanosis, hyperkeratosis, or both), of which 13 (36.1%) occurred in subjects who were currently drinking water containing concentrations of arsenic <50 μg/L. The risk for skin lesions in relation to the exposure estimates based on urinary arsenic was elevated more than 3-fold, with the odds ratios for the highest versus the lowest quartiles being 3.6 (95% confidence interval, 1.2 to 12.1) for urinary total arsenic and 3.2 (95% confidence interval, 1.1 to 10.0) for urinary creatinine-adjusted total arsenic. The risks for skin lesions in relation to the exposure estimates based on arsenic in drinking water were less strongly elevated, with the odds ratios for the highest versus the lowest quartiles of exposure being 1.7 (95% confidence interval, 0.6 to 5.1) for drinking-water arsenic and 2.3 for cumulative arsenic index. The study suggests that arsenic exposure is associated with skin lesions in the Bangladesh population and that urinary arsenic may be a stronger predictor of skin lesions than arsenic in drinking water in this population. (J Occup Environ Med. *2000;42:1195–1201*)

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Human health effects of arsenic exposure from drinking water have been a major public health problem in many countries, including Taiwan, Chile, Argentina, and the United States.[1–5] Recently, groundwater in some regions of Bangladesh has been found to be contaminated with high levels of arsenic.[6] During the 1960s and 1970s, the United Nations International Children's Emergency Fund (UNICEF), with the help of the government at that time, installed about 4 million tube-wells in Bangladesh to ensure safe drinking water for the Bangladesh population, primarily to prevent the waterborne diseases that had been the major causes of morbidity and mortality.[7] Subsequently, another 4 to 6 million tube-wells were installed through private initiatives. Tube-well water has since been the major source of drinking water for 97% of the country's population.[8] Since the late 1980s, previously unknown skin lesions have emerged in the Bangladeshi population,[6,9,10] and a high arsenic level has been detected in tube-well water in different parts of the country.[6,10] It has been estimated that between 25 and 40 million people in Bangladesh have been exposed to arsenic (range, <10 μg/L to >2500 μg/L) from drinking water since at least the 1970s.[11,12]

On the basis of studies conducted in Taiwan[1] and South America,[5] exposure to inorganic arsenic has been linked to a variety of illnesses, including cancers and dermatologic, cardiovascular, neurologic, and neurodevelopmental disorders. Of the

many arsenic-related disorders, skin lesions (both malignant and non-malignant lesions) are considered to be the most common adverse health effect associated with arsenic exposure in humans.[13,14] Non-malignant skin lesions are far more common than skin cancers among subjects exposed to arsenic from drinking water.[14] Unlike skin cancer, which takes decades to appear, arsenic-related lesions appear within a few years after chronic exposure begins.[14] The skin lesions most commonly involve alterations in skin pigmentation (known as melanosis) and/or thickening of skin (known as keratosis).[14] Melanosis starts with hyperpigmentation of the skin of the upper chest, other parts of the trunk, arms, and legs, followed by the development of rounded hypopigmented maculae (usually 2 to 4 mm in diameter) against the hyperpigmented background.[14] Keratosis involves a characteristic bilateral thickening of the palms and soles (palmar-planter hyperkeratosis), which in early stages is felt on palpation.[14] Although not all skin lesions turn into malignant lesions, the majority of the basal and squamous cell skin cancers among arsenic-exposed subjects develop from these lesions.[15] The skin lesions thus may be considered precursors of skin cancers.[15]

The extent and nature of the health effects of arsenic in Bangladesh are largely unknown.[12] Although ecologic studies have linked the occurrences of skin lesions to populations with high concentration of arsenic in water,[15] there have been no systematic analyses of the relation between skin lesions and an individual's arsenic exposure (eg, urinary arsenic, a putative indicator of body burden of arsenic exposure).[16,17] This is the first systematic study in Bangladesh to examine the association between drinking water and urinary arsenic and the independent associations of each with skin lesions.

Methods

Study Design and Data Collection

A cross-sectional study was designed to examine the association between arsenic exposure and skin lesions among the Bangladesh population. The study focused only on skin lesions because the induction period of arsenic-induced carcinogenesis for internal organs is considered to be several decades, and many of the exposed population in Bangladesh probably have not yet been exposed for such a long duration. After discussion with arsenic researchers at National Institute of Preventive and Social Medicine and Dhaka Community Hospital in Bangladesh, and with guidance from the first comprehensive Bangladesh Government/British Geological Survey report,[18] we chose Sonargaon, a rural area northeast of the capital Dhaka, as the study area. Residents in three contiguous villages of Sonargaon, where well water has not been tested before, were targeted for this study. With assistance from the local leaders, a house-to-house survey was performed to recruit study participants by field research teams consisting of physicians and field interviewers. Attempts were made to recruit at least one subject from every cluster of houses in the three villages. Within a given cluster, no attempts were made to cover all of the households. Thus, the study included subjects who were (1) available at the time of the visit, and (2) willing to participate. Although efforts were made to select study subjects independent of study personnel's knowledge of well-water arsenic concentration, it was difficult to keep the personnel blinded to the presence or absence of the skin lesions because some of the subjects had clearly visible skin lesions. Moreover, because the villagers were aware that the research project was about arsenic in drinking water, it is likely that subjects with skin lesions or other symptoms were more likely to have participated in the study. Thus, the prevalence estimates of skin lesions in this study might be overestimated.

Subjects were enrolled after providing informed consent and receiving an explanation of the broad purpose of the study. Once all clusters of houses in a village were visited at least once (some larger clusters required more than one visit), the next contiguous village was included. In this manner, 167 subjects were recruited over a 4-week period from 83 household clusters of the three study villages. The total population of these three study villages was 3000.

The study obtained interview data, spot-urine, and drinking-water samples from the study participants. We collected water samples both directly from the tube-wells (one tube-well served each cluster) and from the household water pitchers (which villagers use for storing drinking water in the house); however, we used arsenic contents in the pitcher-water samples for examining the association between arsenic exposure and skin lesions because arsenic concentrations may change (eg, by precipitation or evaporation) during storage. Structured in-person interviews were completed with all 167 subjects regarding demographics, socioeconomic status, occupation, drinking-water sources, and patterns of well water use. In addition, every participant underwent a thorough physical examination by one of the study physicians, and clinical data, including the presence of melanosis, keratosis, or skin cancers, were collected. A detailed and structured method was used to examine the skin lesions. For each subject, the examination of skin lesions and their grading for severity were conducted by two independent study physicians. There were only a few instances when disagreements between examiners occurred. In such cases, a consensus diagnosis was made through discussion between the two examiners. In addition to collection of samples and

interview data, every participant was counseled about the arsenic problem in drinking water, the use of alternative sources of drinking water, the possible health effects of arsenic exposure, and their signs and symptoms.

Collection of Drinking Water and Urine Samples

The urine, tube-well, and pitcher-water samples were collected in 50-cc acid-washed plastic tubes. All samples were kept in portable coolers (carried with the research team) immediately after collection. Four microliters of 1% ultrapurified hydrochloric acid were added to each water tube. The urine and water samples were kept in a refrigerator in the field until they were shipped to New York in dry ice.

Laboratory Analyses

Measurements of arsenic in pitcher-water and tube-well water samples were conducted by graphite furnace atomic absorption spectrometry methods on a Hitachi Z-8200 system in the Geochemistry Laboratory at Lamont Doherty Earth Institute of Columbia University under the direction of one of the authors (A. van Geen). All water samples were diluted to between 30 to 60 μg/L in a matrix of 2% HNO_3 and 50-ppm nickel. The addition of nickel has been found to increase the sensitivity, expand the linear range, and improve reproducibility.[19] The 10- to 20-μL samples were dried in a graphite tube, ashed at 600°C for 20 seconds, and atomized at 2400°C. An electrode-less discharge lamp and a time constant (filter) of 0.5 second was used. With 20-μL injections, sensitivity was about 0.0023 absorbance units per microgram per liter. The response was linear to at least 0.2300 absorbance units (about 90 μg/L). Relative standard deviations of replicate injections were generally less than 5%. Blank values averaged about 0.0025 absorbance units. Most or all of the blank signal was due to electronic noise in the lamp or elsewhere and not to trace amounts of arsenic in the solutions. The detection limit (3 × SD of the blank) was about 0.0030, or about 1 μg/L. For quantification, selected samples were run with standard additions. Other samples were determined by using the slope of the standard addition set. Matrix effects seemed to be minimal, because for all sample types, slopes of standard additions generally agree with standard curves to within 10%. The arsenic concentration between the pitcher and well water correlated closely (correlation coefficient, 0.64).

The urinary arsenic concentration assays were performed by graphite furnace atomic absorption spectometry methods using the Analyst 600 graphite furnace system in the Division of Environmental Health Sciences of Columbia University under the direction of one of the authors (J.G.), essentially as described.[19] Arsenic levels in urine were estimated with or without adjustment for urinary creatinine levels, which was analyzed by a colorimetric Sigma Diagnostics Kit (Sigma, St. Louis, MO).[20]

Exposure Assessment

We used three different approaches to measure arsenic exposure among study subjects. The first measure of exposure was the pitcher-water arsenic concentration. Because arsenic concentrations may be altered by storage of water in the home, we examined the arsenic levels in the pitcher water obtained directly from the household pitchers as a measure of exposure. It should be noted that the arsenic levels in the pitcher water were strongly correlated (with a correlation coefficient 0.64) with tube-well water. The second measure of exposure was the urinary total arsenic concentration, which is considered to be a reliable indicator of arsenic exposure.[16,17] The third measure of exposure used in this study was the Cumulative Arsenic Index (CAI), which was calculated by multiplying arsenic concentration in pitcher water times the estimated amount of water consumed per year times the estimated number of years that the current tube-well had been used for drinking. Because the tube-well water in this village had never been tested for arsenic before the initiation of this study, the CAI was calculated by assuming a constant arsenic concentration in each tube-well during the time of its use for each subject. Therefore, the CAI is not a refined index of exposure that takes into consideration the variations over time but rather one that may potentially reflect a measure of cumulative exposure in the absence of data on repeated measures of exposure.

Statistical Analyses

Mean and median arsenic concentrations in urine and pitcher water were calculated for subjects with and without skin lesions of other variables. Mean arsenic levels were compared between the two groups by *t* tests. For further analyses, subjects were categorized within quartiles of arsenic levels according to the distribution among controls. Logistic regression models were fit to examine the associations between different levels of arsenic exposures (arsenic levels in drinking water and urine and the CAI) and skin lesions adjusted for age, sex, and body mass index. Proxies for socioeconomic status, ie, household income and education level, did not confound the associations between measures of arsenic exposure and skin lesions in this study. Because this information was missing for some subjects, the income and education variables were not included in the final model to secure the largest possible sample size in estimating effect measures.

Standard logistic regression models assume statistical independence of study subjects. Subjects from the same households or clusters of

TABLE 1
Description of Study Subjects According to Demographic Characteristics and Different Arsenic Exposure Measures

Characteristics of Study Population	Any Skin Lesion				Keratosis				Melanosis			
	Yes		No		Yes		No		Yes		No	
	n	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%
Age (*n* = 167)												
Q1 <=25	11	30.6	35	26.7	8	29.63	38	27.9	11	32.35	36	26.3
Q2 > 26–35	16	44.4	29	22.1	12	44.44	33	23.6	14	41.18	31	23.3
Q3 > 36–50	7	19.4	32	24.4	6	22.22	33	23.6	7	20.59	32	24.1
Q4 > 51	2	5.6	35	26.7	1	3.70	36	25.7	2	5.88	35	26.3
Sex (*n* = 167)												
Men	18	50.0	69	52.7	14	51.85	73	52.1	16	47.06	71	53.4
Women	18	50.0	62	47.3	13	48.15	67	47.9	18	52.94	62	46.6
Body mass index (kg/m^2) (*n* = 167)												
Q1 <=17.51	4	11.1	36	27.5	3	11.1	37	26.4	4	11.8	36	27.1
Q2 > 17.51–18.43	8	22.2	35	26.7	6	22.2	37	26.4	8	23.5	35	26.3
Q3 > 18.43–20.64	11	30.6	33	25.2	7	25.9	37	26.4	10	29.4	34	25.6
Q4 > 20.64–27.00	13	36.1	27	20.6	11	40.7	29	20.7	12	35.3	28	21.1
Arsenic concentration in urine (μg/L) (*n* = 167)												
Q1 <=122	6	16.7	36	27.5	5	18.5	37	26.4	6	17.7	36	27.1
Q2 > 122–244	6	16.7	36	27.5	3	11.1	39	27.9	6	17.7	36	27.1
Q3 > 244–471	10	27.8	32	24.4	6	22.2	36	25.7	9	26.5	33	24.8
Q4 > 471–1840	14	38.9	27	20.6	13	48.2	28	20.0	13	38.2	28	21.1
Arsenic concentration in urine (μg/g creatinine) (*n* = 166)												
Q1 <=242	8	22.2	34	26.2	6	22.2	36	25.9	8	23.5	34	25.8
Q2 > 242–440	6	16.7	35	26.9	3	11.1	38	27.3	6	17.7	35	26.5
Q3 > 440–766	6	16.7	36	27.7	3	11.1	39	28.1	5	14.7	37	28.0
Q4 > 766–5727	14	44.4	25	19.2	15	55.6	26	18.7	15	44.1	26	19.7
Arsenic concentration in drinking water (μg/L) (*n* = 164)												
Q1 <=29	10	27.8	31	24.2	7	25.9	34	24.8	10	29.4	31	23.9
Q2 > 29–90	8	22.2	33	25.8	5	18.5	36	26.3	8	23.5	33	25.4
Q3 > 90–278	5	13.9	36	28.1	4	14.8	37	27.0	3	8.8	38	29.2
Q4 > 278–991	13	36.1	28	21.9	10	40.7	30	21.9	13	38.2	28	21.5
AI* (mg) (*n* = 156)												
Q1 <=116.4	7	19.4	31	25.8	5	18.5	33	25.6	7	20.6	31	25.4
Q2 > 116.4–474.9	10	27.8	30	25.0	7	25.9	33	25.6	9	26.5	31	25.4
Q3 > 474.9–1279.9	5	13.8	34	28.3	4	14.8	35	27.1	5	14.7	34	27.9
Q4 > 1279.9–22147.1	14	38.9	25	20.8	11	40.7	28	21.7	13	38.2	26	21.3

* Cumulative Arsenic Index calculated as follows: yearly drinking water consumption × arsenic concentration in water × years of well use.

houses obtain water from a common tube-well. Thus, our use of well-water arsenic concentrations would yield the same value for all subjects who use a particular well. Therefore, to avoid the problem of colinearity in the regression models, pitcher-water arsenic level (with a unique value for each participant) was used in place of well-water arsenic concentrations. As mentioned above, arsenic levels in pitcher water are strongly correlated with the arsenic levels in the well water.

Results

Of the total of 167 study participants, 27 (16.2%) had keratosis, 34 (20.4%) had melanosis, and 36 (21.6%) had "any" skin lesions (ie, either melanosis and/or keratosis) at the time of the survey. Among those subjects with "any" skin lesion, 25 presented with both keratosis and melanosis, 9 presented only with melanosis, and 2 presented with only keratosis. Two subjects had histologically confirmed skin cancer, and three had lesions suggestive of malignancy that were not histologically confirmed.

We classified the study subjects according to their skin lesion status and cross-sectionally examined the associations between water and urinary arsenic and skin lesions. Table 1 shows the distribution of study subjects with or without skin lesions with respect to water and urinary arsenic levels and the demographic characteristics. Subjects with skin lesions were younger than those with-

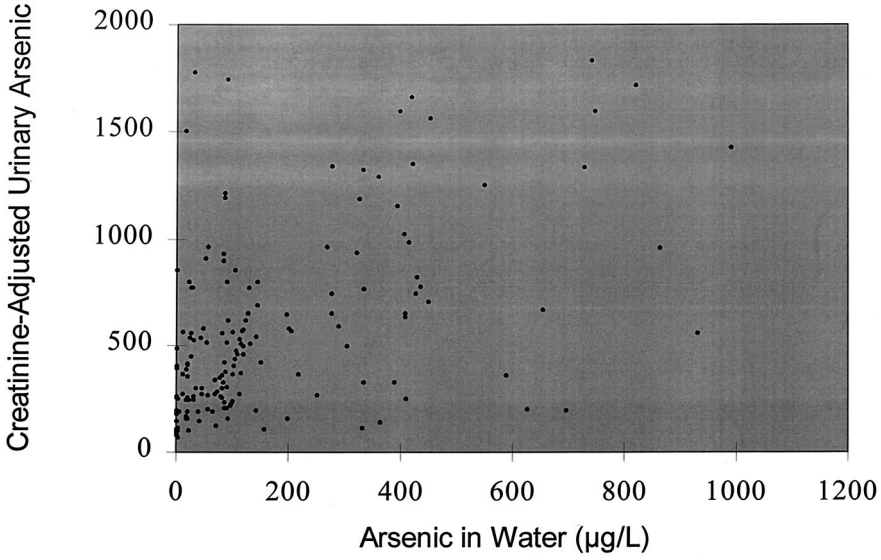

Fig. 1. Association between drinking water and creatinine-adjusted urinary arsenic.

TABLE 2
Associations Between Different Measures of Arsenic Exposure and Skin Lesions*

	Any Skin Lesion		Keratosis		Melanosis	
Level of Arsenic	**OR†**	**95% CI**	**OR†**	**95% CI**	**OR†**	**95% CI**
In urine (μg/L) (n = 167)						
Q1 <=122	1.0		1.0		1.0	
Q2 > 122–244	1.0	0.3, 3.6	0.5	0.1, 2.4	1.0	0.3, 3.6
Q3 > 244–471	2.1	0.6, 7.4	1.2	0.3, 4.7	1.8	0.6, 6.5
Q4 > 471–1840	3.6	1.2, 12.1	3.9	1.2, 14.7	3.1	1.0, 10.6
In urine (μg/g of creatinine) (n = 166)						
Q1 <=242	1.0		1.0		1.0	
Q2 > 242–440	0.83	0.2, 2.9	0.52	0.1, 2.3	0.8	0.2, 2.8
Q3 > 440–766	0.88	0.2, 3.1	0.61	0.1, 2.7	0.7	0.2, 2.5
Q4 > 766–5727	3.22	1.1, 10.1	4.41	1.4, 15.7	2.7	0.9, 8.1
In pitcher-water (μg/L) (n = 164)						
Q1 <=29	1.0		1.0		1.0	
Q2 > 29–90	0.90	0.3, 2.9	0.88	0.2, 3.4	0.9	0.3, 2.8
Q3 > 90–278	0.36	0.1, 1.2	0.48	0.1, 1.9	0.2	0.0, 0.8
Q4 > 278–991	1.67	0.6, 5.1	2.14	0.7, 7.4	1.6	0.6, 5.0
CAI‡ (mg) (n = 156)						
Q1 <=116.4	1.0		1.0		1.0	
Q2 > 116.4–474.9	1.3	0.4, 4.4	1.3	0.3, 5.0	1.1	0.3, 3.6
Q3 > 474.9–1279.9	0.6	0.15, 2.2	0.7	0.2, 3.1	0.6	0.2, 2.2
Q4 > 1279.9–22147.1	2.3	0.7, 7.6	2.6	0.8, 9.9	2.0	0.6, 6.3

* OR, odds ratio; CI, confidence interval.
† OR adjusted for body mass index, sex, and age.
‡ Cumulative Arsenic Index calculated as follows: yearly drinking water consumption × arsenic concentration in well × years of well use.

out lesions, with about 75% of subjects with lesions under 35 years of age. On average, subjects with skin lesions were of a greater body size than subjects without lesions. The sex distribution, however, was similar among subjects with or without skin lesions, with each group consisting of about half male and half female subjects.

As expected, subjects with skin lesions were more likely to have a higher level of water and urinary arsenic (with or without creatinine adjustment). Similarly, subjects with skin lesions were more likely to have a higher CAI value. Importantly, a sizable proportion of subjects with skin lesions was observed at the lowest levels of these measures; ie, 13 (36.1%) of the 36 subjects with skin lesions had been drinking water with arsenic concentrations less than 50 μg/L, and 5 (or 13.9%) of the 36 subjects with skin lesions had been drinking water with arsenic levels less than 10 μg/L.

Figure 1 illustrates the relationship between urinary arsenic concentration (μg/creatinine) and water-arsenic concentration (μg/L). The two measures were positively correlated (correlation coefficient, 0.50). For both water and urinary arsenic, we examined the ranges of values for one measure within each quartile of the other (results not shown). In general, a larger variability was observed in the urinary arsenic levels within each quartile of water arsenic levels than the water-arsenic variability observed within categories of urinary arsenic levels, suggesting possible interindividual variation in arsenic metabolism.

Table 2 shows adjusted odds ratios and 95% confidence intervals for the associations between different measures of arsenic exposure and skin lesions. Subjects with skin lesions (melanosis and/or keratosis) were 3 times more likely to have the highest level of urinary arsenic (odds ratios, 3.6 and 3.2 for total urinary arsenic and creatinine-adjusted total urinary arsenic, respectively). These associations were, in general, stronger for keratosis than for melanosis. Although subjects with skin lesions were also more likely to have been drinking water with a higher arsenic concentration (odds ratio, 1.7 for the highest vs the lowest quartile) the association was not statistically significant (95% confidence interval, 0.6 to 5.1). Similarly, subjects with skin lesions were also more likely to be in the highest CAI quartile (odds

ratio, 2.3 for the highest vs the lowest quartile and 95% confidence interval, 0.8 to 7.6).

Discussion

Inorganic arsenic is a naturally occurring constituent of drinking water in many parts of the world. Although arsenic has been considered a massive public health problem in Bangladesh, relatively little systematic research has been conducted to examine the health effects of arsenic exposure among the Bangladesh population. One recent study examined the prevalence of skin lesions among Bangladesh population and assessed the prevalence in association with arsenic levels in tube-well water.[10] The study found a dose-response relationship between arsenic level in drinking water and skin lesions (melanosis and keratosis). The same authors have also previously shown associations of hypertension[21] and diabetes mellitus[22] with arsenic exposure from drinking water. Another recently published study examined the association between prevalences of non-malignant skin lesions (melanosis and keratosis) and arsenic exposure from drinking water. This cross-sectional study from West Bengal, India, examined 7683 subjects and found a dose response relationship between prevalence of hyperpigmentation and keratosis and doses of arsenic concentrations in the drinking water. The authors found a higher prevalence of both conditions in male subjects compared with female subjects at every dose level, and they reported that these skin conditions may occur even among those who consume water with arsenic levels <50 μg/L.[23]

The present study is the first in Bangladesh to systematically examine the associations between urinary and drinking water arsenic levels and skin lesions. The study used a cross-sectional design and found 36 (21.6%) of the total 167 study participants to have detectable skin lesions (melanosis and/or keratosis). This prevalence estimate was likely an overestimate among the population in the study villages because people with skin lesions (or with family members with skin lesions) were probably more likely to have volunteered to participate in the study. After age-adjustment to the World Standard Population, the prevalence estimate was 19.4%, which is somewhat lower than the reported prevalence estimate found in a recently published study.[10] Unlike the previous report,[10] the current study did not find a higher prevalence of skin lesions among men compared with women.

This study found a sizable number of skin lesions among subjects who were currently drinking water containing an arsenic level <50 μg/L, the allowable limit for both Bangladesh and the United States. In fact, about 13.9% of all subjects with skin lesions were currently drinking water with an arsenic level of <10 μg/L. Another study also reported the occurrence of skin lesions among subjects with very low level of arsenic exposure from drinking water in West Bengal.[23] This finding may indicate a wide inter-individual variability in susceptibility to the effects of arsenic exposure from drinking water, a finding supported by an examination of mean urinary arsenic levels within categories of pitcher-water arsenic. There was a wide variability in urinary arsenic levels within a narrow range of water-arsenic concentration within each category.

We found a more than 3-fold elevated risk of skin lesions for the subjects who had the highest level of urinary arsenic levels. Adjustment for urinary creatinine did not markedly alter the finding. The risk was also elevated, but not significantly so, when arsenic exposure was measured from the current arsenic level in drinking water, or as the CAI value. The finding that skin lesions are more strongly associated with urinary arsenic levels rather than drinking-water arsenic (including the CAI) is interesting and certainly requires further examination in future studies. It is possible that water-arsenic concentration may vary over time and, therefore, current water arsenic level may represent recent exposure rather than cumulative exposure. Although 75% of the villagers reported that they had used the same tube-well for more than 5 years and, 50% of the subjects reported that they had used the same tube-well for more than 10 years, the study could not validate whether there have been changes in the exposure over time. In contrast, urinary arsenic, which receives the inputs from external sources as well as tissue stores, may reflect more closely the actual body burden of arsenic and, possibly, interindividual variability in the metabolism of arsenic.[15]

Studies in Taiwan and Argentina have reported associations between urinary arsenic metabolites and skin and other cancers.[17,18] Urinary arsenic has also been shown to be correlated with chromosomal aberrations and breakage[24,25] and has been suggested to be the best indicator of arsenic exposure in humans.[24] Most prior epidemiologic studies assessed arsenic exposure from drinking water concentrations coupled with the history (frequency and duration) of that water use. It is possible that the information on water arsenic concentration may or may not accurately reflect the body's internal exposure.

A limitation is that the study used the total urinary arsenic as a measure of arsenic exposure and did not examine specific urinary arsenic metabolites. After absorption, arsenic is methylated to monomethyl arsonate and dimethyl arsinate, both of which bind less strongly with tissues, are less reactive, and are excreted more rapidly in urine than arsenic. Estimation of arsenic exposure is thus complicated by the presence of different metabolites of arsenic and by remarkable interindividual variability in metabolism in humans.[17] Given the individual variability in the con-

centrations of arsenic, monomethyl arsonate, and dimethyl arsinate in urine, and the differences in the deleterious effects of these different compounds, it will be important to study these metabolites in relation to arsenic exposure and health effects.

In conclusion, this study found a high prevalence of skin lesions among Bangladesh population, particularly among young adults. The study found more than 3-fold elevated risk of skin lesions in relation to the highest quartile of urinary arsenic levels, indicating a potential role of urinary arsenic measurements in the assessment of the health effects of arsenic exposure.

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