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Neurologic Evaluation of a Population Exposed to Arsenic in Alaskan Well Water

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ABSTRACT. One hundred forty-seven persons exposed to arsenic from well water were evaluated by neurologic examination and nerve conduction studies. Total arsenic concentrations in well water ranged from 1 to 4781 μg/L and from 6 to 4964 μg/L in urine; a calculated index of arsenic ingestion ranged from 1 to 4521 μg/day. No dose-response relationship existed between arsenic ingestion and symptoms or physical findings compatible with peripheral neuropathy. Five of six persons with symptoms or physical findings suggestive of sensory neuropathy had normal nerve conduction velocities. Thirteen persons with elevated arsenic ingestion but no signs or symptoms of neuropathy had one or more abnormal nerve conduction velocities. No dose-response relationship, however, existed between arsenic ingestion and nerve conduction velocities. The authors concluded that arsenic ingestion from well water at the concentrations found in this Alaskan community did not result in clinical or subclinical neuropathy.

INORGANIC ARSENIC is one of several metallic elements which can cause peripheral neuropathy.[1-4] It occurs naturally in ground water in many areas of the world. In high concentrations, it has resulted in dermatologic signs of arsenicalism in persons ingesting the water.[5,6] Only one study[7] has assessed neurologic findings in such a population.

High levels of arsenic in well water and in biologic samples were found for residents in Ester Dome, Alaska, a residential area just outside of Fairbanks.[8] No

differences in neurologic symptoms or in overt clinical findings were demonstrated among the exposure groups. Nerve conduction tests of workers with industrial exposure to arsenic, however, have shown subclinical neuropathy.[9] A test which detects neurologic dysfunction at a subclinical stage would have wide applications in screening persons with exposure to neurotoxins at work or in communities with toxic chemical dumps. This study reports the results of nerve conduction test screening for persons living in Ester Dome who ingested well water with arsenic concentrations above or below the maximum level of 50 μg/L recommended by the U.S. Environmental Protection Agency.

METHODS

Ester Dome residents were contacted on the basis of well water arsenic concentrations which were obtained from the State Department of Environmental Conservation. Adults less than 60 yr of age who had lived in their residences for at least 2 yr were invited to participate in the study. Two persons who had a well water arsenic level of 2655 μg/L were asked to participate despite only 13 months' residency. After giving written informed consent, participants were interviewed regarding demographic information; water consumption from home wells, hauled, or other water sources; occupational sources of arsenic exposure; and medical history. Nonfasting blood samples were collected for hematocrit, blood urea nitrogen, and glucose determinations.

One of two neurologists, without knowledge of the interview data, examined each participant for peripheral motor and sensory neuropathy and for other neurologic abnormalities. One of two other neurologists, without knowledge of interview or physical examination results, performed nerve conduction tests on the peroneal motor nerve, sural sensory nerve, and ulnar sensory and motor nerves by using TECA4 (White Plains, NY) electromyographs. A supramaximal stimulus (100–300 V) of 0.1–0.2 msec duration was used. Sensory antidromic evoked potentials were averaged 32 times with a digital ensemble averager. Skin temperature of the limbs was monitored by telethermometers (Yellow Springs Instrument Company, Yellow Springs, OH). For data analysis, we used 4 of the 13 measurements obtained for which paired t tests had shown a probability of >0.5 that repeat measurements on a subset of 39 participants did not differ from the first measurement. The four test results were the ulnar motor velocities from wrist to elbow to axilla, the sural sensory velocity, and the peroneal motor velocity.

Participants were supplied acid-washed plastic bottles for collecting urine (first void in the morning) and household water. Portions (100 ml) of urine specimens were acidified with 10 drops of concentrated nitric acid and refrigerated for transfer to the laboratory. Specific gravity was measured on the remaining urine. Water samples (100 ml) were taken after 60 sec flow from the tap, acidified in the laboratory, and then frozen. Quality assurance for the analytic method for total arsenic[10] was maintained by daily analyzing a National Bureau of Standards Reference Material and a pooled urine specimen, and by including duplicate specimens unknown to the analyst. For statistical analysis, urine arsenic levels were corrected to a specific gravity of 1.024[11]; where specific gravity was unknown (7 samples), the mean urine specific gravity of the remaining samples (1.0197) was assumed.

Statistical methods used in analysis of questionnaire and laboratory data included Student's t test for paired and independent samples, one-way analysis of variance, simple and multiple linear regression, and chi-square tests of independence.[12,13] A probability of $<.05$ was considered statistically significant. Because of the positive skewness in the distributions of some variables, logarithmic transformations were used to reduce skewness and to stabilize their variances.

RESULTS

Population characteristics. A total of 149 persons participated in the study; 2 were excluded from data analysis because they were over 60 yr of age. The remaining 147 had a mean age of 36.3 yr (range = 17–57 yr); 64 (43.5%) were male. The study group had lived an average of 74 months (median 60 months; maximum 336 months) in their current residences. None had significant occupational exposure to arsenic.

In the study group 132 persons had a home well, although 5 denied ever drinking well water, and many more hauled-in a portion of their drinking water from other sources. Well water arsenic concentrations ranged from 1 to 4781 μg/L, with a mean of 347.3 and a median of 41 μg/L. Arsenic concentrations in water hauled or available from piped sources ranged from 0 to 32 μg/L, with a mean of 4.8 and a median of 1.4 μg/L. To account for the variability in amounts and sources of water consumed, we calculated an index of arsenic ingestion by adding the arsenic present in the usual quantity of well water consumed to that present in the usual quantity of other water consumed. This index of arsenic ingestion ranged from 0.0 to 4521.0 μg/day (with one outlying value of 14,479 μg/day) and correlated closely with urine arsenic concentration (Pearson correlation coefficient for log values = 0.730; $P < 10^{-5}$). Urine arsenic concentrations ranged from 6 to 4964 μg/L with a median of 50.9 μg/L. Males and females had similar geometric mean urine arsenic levels (61.6 vs 71.0 μg/L, $P = .5333$).

Neurologic findings. Of the 147 persons receiving neurologic examinations, 6 had symptoms or physical findings compatible with mild sensory peripheral neuropathy (Table 1). Two of the 6 had conditions associated with neuropathy—diabetes mellitus and Raynaud's disease, respectively. Of the 4 remaining persons, 1 had a calculated daily arsenic ingestion of 3437 μg, and the other 3 were in the lowest arsenic exposure group (Table 2), which was a control group. Of the 6 persons, only the diabetic and 1 in the control group met rigorous criteria of neuropathy: impairment of two sensory modalities and reduced deep tendon reflexes. The remaining persons had either subjective

Table 1.—Persons with Symptoms or Physical Findings of Sensory Neuropathy, Alaska, 1978

Age	Well Water Arsenic (μg/L)	Calculated Arsenic Intake from Water (μg/day)	Urine Arsenic (μg/L)	Nerve Conduction Test (m/sec)				Clinical Evaluation
				Ulnar Motor Velocity				
				Wrist-Elbow	Elbow-Axilla	Sural Sensory Velocity	Peronal Motor Velocity	
36	2436	3457	1090	56.7	71.4	46.7	54.5	Hyperpathia of soles
51†	28	40	14	54.7	68.2	43.8	49.7	Patchy hypalgesia of hands
44	4	4	6	49.3	69.0	46.7	52.9	Hyperpathia of soles
49‡	203	480	610	44.3*	65.2	42.2	37.1*	↓pain, ↓vibration in all extremities ↓tendon reflexes
34	23	22	103	56.8	62.5	50.0	59.0	↓pain, ↓touch in all extremities ↓tendon reflexes
18	5	9	14	51.0	83.3	48.3	52.5	↓pain in lower extremities

* Abnormal.

† This patient had Raynaud's disease antedating residence in Ester Dome.

‡ This person had diabetes and residua of a cerebrovascular accident.

complaints, such as hyperpathia of the soles of the feet, or single abnormalities on neurologic examination, such as decreased pinprick sensation on hands or feet.

None of the four nerve velocity measurements were associated with daily arsenic ingestion, urine arsenic concentration, or well water arsenic concentration. The lower limit of normal for each of these velocity measurements was defined as the fifth percentile value for the 95 control persons whose estimated arsenic ingestion was ≤ 100 μg/day (Table 3). The four persons in this low-exposure group with symptoms or physical findings compatible with peripheral neuropathy had normal nerve conduction velocities; their exclusion made no difference in the fifth percentile value used as the criteria of normality. The only person for whom abnormal nerve conduction velocities corroborated the physical examination was the diabetic (Table 4). The other person who met rigorous criteria of neuropathy had normal nerve conduction velocities.

The proportion of persons having abnormal nerve conduction velocities did not differ significantly among the different arsenic exposure groups. Among persons ingesting more than 100 μg arsenic/day, those with abnormal nerve conduction velocities did not have

Table 2.—Characteristics of Arsenic Exposure Groups, Alaska, 1978

Characteristic	Calculated Daily Arsenic Ingestion from Drinking Water			
	0–100 μg	101–1,000 μg	1,001–15,000 μg	*P* Value
Number	95	39	13	. . .
Geometric mean arsenic ingestion (μg/day)	12.3	235.1	2072.0	<0.0001
Geometric mean urine arsenic (μg/L)	34.9	143.2	741.7	<0.0001
Geometric mean well water arsenic (μg/L)	9.1	222.4	1475.0	<0.0001
Mean age (yr)	35.7	37.9	36.6	0.428
Mean duration of residence (months)	78.2	71.4	52.3	0.323
Number (%) with neuropathy by examination	4 (4.2)	1 (2.6)	1 (7.7)	0.171
Number (%) below 5th percentile value:				
Any conduction velocity	13 (13.7)	12 (30.8)	2 (15.4)	0.065
Ulnar motor nerve velocity: wrist-elbow	4 (4.2)	3 (7.7)	1 (7.7)	0.683
Sural sensory nerve velocity	4 (4.2)	3 (7.7)	1 (7.7)	0.476
Ulnar motor nerve velocity: elbow-axilla	4 (4.2)	3 (7.7)	0 (0)	0.489
Peroneal motor nerve velocity	4 (4.2)	6 (15.4)	0 (0)	0.041
Number (%) with abnormal exam or velocity	17 (17.9)	12 (30.8)	3 (23.1)	0.259

Table 3.—Nerve Conduction Measurements (m/sec) for Arsenic Exposure Groups, Alaska, 1978

Nerve Conduction Measurement	Calculated Daily Arsenic Ingestion from Drinking Water		
	0–100 μg (N = 95)	101–1,000 μg (N = 39)	1,001–15,000 μg (N = 13)
Ulnar motor velocity: wrist-elbow			
$X \pm SD$*	54.9 ± 4.1	55.8 ± 4.9	53.9 ± 4.7
Range	45.1 – 63.0	44.3 – 66.7	45.3 – 62.8
Fifth percentile	48.9	44.4	. . .
Sural sensory nerve velocity			
$X \pm SD$	45.9 ± 4.1	45.1 ± 4.9	46.5 ± 4.5
Range	32.6 – 56.0	30.4 – 56.5	39.2 – 56.0
Fifth percentile	40.0	37.8	. . .
Ulnar motor velocity: elbow-axilla			
$X \pm SD$	64.8 ± 7.3	64.5 ± 7.3	67.8 ± 8.6
Range	50.0 ± 83.3	51.8 – 83.3	53.6 – 81.6
Fifth percentile	53.5	52.0	. . .
Peroneal motor nerve velocity			
$X \pm SD$	49.4 ± 4.6	48.7 ± 5.9	50.1 ± 3.7
Range	41.6 ± 66.9	31.8 – 63.0	45.7 – 55.6
Fifth percentile	43.7	37.1	. . .

* Mean ± standard deviation.

higher urine arsenic levels or higher arsenic ingestion than the rest (geometric mean urine arsenic: 186.7 vs 228.0 μg/L, P = .598; geometric mean arsenic ingestion: 370.3 vs 418.8 μg/L, P = .741).

DISCUSSION

Although inorganic arsenic can produce peripheral neuropathy, neurologic symptoms have not been reported in response to chronic exposure to naturally occurring arsenic in ground water. With the exception of one case report,[14] neuropathy is not mentioned in reports of investigations of arsenical skin cancer or vascular disease in Taiwan,[5,15] Chile,[6] Argentina,[16] and Oregon.[17] Only in Nova Scotia[7] have electromyographic studies of a population been related to arsenic levels in hair and well water. The results of neurologic examination of that population were not reported. For 7 of 14 persons with well water arsenic concentrations ranging from 100 to 1400 μg/L, abnormal electromyographic or nerve conduction results were obtained. However, only 1 of those persons had an abnormal velocity measurement; the remainder had abnormal amplitudes, distal latencies, or absent response to sural nerve stimulation. Without data on reproducibility of those measurements, that Canadian experience may be consistent with our finding of no increased prevalence of nerve velocity abnormalities in a larger Alaskan population exposed to much higher mean well water arsenic concentrations.

The literature on nerve conduction abnormalities in clinical arsenic neuropathy is meager.[1,2,18–20] Velocity slowing—which may result from demyelination, failure of the most rapidly conducting fibers, or slowing of individual fibers—is a late finding in axonal neuropathies, such as that caused by arsenic. Thus, it is not surprising that five of six patients with mild sensory changes by history or on physical examination had normal conduction velocities. These findings suggest that nerve conduction velocities were insensitive in screening for subclinical neuropathy in persons exposed to inorganic arsenic in this study. Decreases in amplitude may result from alterations in the connective tissue associated with age or trauma or from changes in the nerve, such as axonal degeneration, conduction block, or unequal slowing of conduction in individual fibers. Amplitude decreases would be an earlier finding than velocity slowing in axonal neuropathies, but lack of reproducibility in this measurement may preclude its use in cross-sectional population studies. Sources of variability of amplitude measurements taken at the skin surface, such as electrode placement and tissue resistance, may be subject to better control. Alternatively, estimating the distribution of conduction velocities making up a compound action potential might prove useful for detecting subclinical neuropathies of smaller and slower nerve fiber groups.[21]

Table 4.—Persons with Elevated Arsenic Consumption and Abnormal Nerve Conduction Tests, Alaska, 1978

Age	Well Water Arsenic (μg/L)	Calculated Arsenic Intake from Drinking Water (μg/day)	Urine Arsenic (μg/L)	Nerve Conduction Test (m/sec)			
				Ulnar Motor Velocity			
				Wrist-Elbow	Elbow-Axilla	Sural Sensory Velocity	Peroneal Motor Velocity
42	474	228	33	55.7	62.5	37.8*	51.4
39	4781	4521	979	55.6	60.4	39.2*	46.1
38	867	830	153	52.4	60.4	30.4*	46.9
20	744	1055	187	45.3*	75.0	41.2	46.5
38	2436	602	221	44.4*	71.4	45.2	50.8
52	203	768	562	51.6	65.2	45.2	42.9*
49†	203	480	610	44.3*	65.2	42.2	37.1*
43‡	626	592	307	48.4*	58.7	42.4	46.8
50§	53	125	74	51.9	61.4	45.2	31.8*
47	82	116	80	56.7	62.5	46.7	42.4*
35	55	106	147	51.9	52.0*	46.5	53.2
44	216	205	167	58.4	51.9*	51.7	40.5*
47	101	120	108	60.6	53.6	37.8*	42.0*
21	142	201	185	60.4	53.4*	41.0	44.2

* Abnormal.

† Diabetes and residua of a cerebrovascular accident.

‡ Blood urea nitrogen 27 mg/100 ml.

§ Right parietal dysfunction.

Thirteen persons in the study who consumed more than 100 μg arsenic/day had one or more abnormal nerve conduction velocities, but no peripheral neuropathy on physical examination (Table 4). The meaning of these abnormalities is unclear, since conduction velocities did not confirm the clinical impression, even for one person meeting rigorous criteria of neuropathy. Since arsenic exposure is not correlated with nerve conduction velocities, we cannot argue that those persons with abnormal velocities have subclinical neuropathy due to arsenic.

Acute arsenic intoxication produces peripheral neuropathy, which is clinically evident within 10 days to 3 wk of a single large dose. A recent report[20] of two patients with acute exposure to arsenic showed the typical clinical neuropathy, electrophysiologic correlates, and elevated arsenic levels. These two patients developed paraesthesiae; loss of perception of touch, pain, and vibration; and weakness. In the first patient, a 24-hr urine specimen for arsenic contained 1260 μg/L approximately 2 wk after arsenic ingestion. In the second patient, a 24-hr urine specimen contained 732 μg/L approximately 19 days after arsenic ingestion. Motor and sensory nerve conduction velocities were recorded 3 and 4 wk after the arsenic exposures of the respective cases and were repeated serially. Slowing of motor conduction velocities in median, ulnar, tibial, and peroneal nerves was maximal 3 months after exposure, after which the velocities increased. Of motor nerves, tibial and peroneal nerves were most severely affected, and the median nerve was affected to a greater degree than the ulnar nerve. Sensory nerve action potentials in median, ulnar, and sural nerves could not be detected for either case during the 28- and 22-month periods of follow-up after their respective exposures.

The prevalences of sensory neuropathy and of nerve conduction velocity abnormalities in the study for persons with arsenic intake greater than 100 μg/day are much lower than the prevalences found for a group of smelter workers with arsenic exposure.[9,22] Mean urine arsenic concentration for the smelter workers, who had a 43% prevalence of abnormal peroneal velocity, was 98 μg/L, a concentration considerably lower than the geometric mean urine arsenic concentrations for our two arsenic-exposed groups. The historical mean urine arsenic concentration for this smelter group was 235 μg/L.[22] As in the Alaskan group, there was poor correlation, at best, between persons with clinical neuropathy on physical examination and persons with abnormal nerve conduction tests,[22] although the latter group was interpreted to have subclinical neuropathy.

Comparison of findings for different populations is hindered by different sensitivities of analytic methods for total arsenic in water and biologic specimens. In addition, speciation of arsenic is rarely reported in

epidemiologic studies, although trivalent arsenic is more toxic than pentavalent arsenic.[23] In the Ester Dome area, the percent of total arsenic in the trivalent form varied from 3% to 64% (mean 34%) on five well water samples.[8] Other workers have found a much higher proportion in the trivalent form (Daniel B. Hawkins, Ph.D., Institute of Water Resources, University of Alaska, written communication, October 27, 1980). Duration, route of arsenic exposure, and nutritional status could also contribute to discrepancies in findings among different populations. These reservations aside, however, consumption of naturally occurring arsenic in ground water has not been associated with increased prevalence of peripheral neuropathy on physical examination, and no evidence of subclinical neuropathy associated with arsenic existed in our study of this Alaskan population.

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REFERENCES

1. Goldstein, N. P.; McCall, J. T.; and Dyck, P. J. 1975. Metal neuropathy. In *Peripheral Neuropathy*, P. J. Dyck, P. K. Thomas, and E. H. Lambert, Eds., Vol. II, pp. 1227–62. Philadelphia, PA: W. B. Saunders.
2. Jenkins, R. B. 1966. Inorganic arsenic and the nervous system. *Brain* 89: 479–98.
3. Chhuttani, P. M.; Chawla, L. S.; and Sharma, T. D. 1967. Arsenical neuropathy. *Neurology* 17: 269–74.
4. Heyman, A.; Pfeiffer, J. B.; Willett, R. W.; and Taylor, H. M. 1956. Peripheral neuropathy caused by arsenical intoxication. *N Engl J Med* 254: 401–09.
5. I'Cheng, CH'I, and Blackwell, R. Q. 1968. A controlled retrospective study of Blackfoot disease: An epidemic peripheral gangrene disease in Taiwan. *Am J Epidemiol* 88: 7–24.
6. Zaldivar, R. 1974. Arsenic contamination of drinking water and food stuffs causing epidemic chronic poisoning. *Beitrag Pathol* 151: 384–400.
7. Hindmarsh, J. T.; McLetchie, O. R.; Heffernan, L. P. M.; Hayne, O. A.; Ellenberger, H. A.; McCurdy, R. F.; and Thiebaux, H. J. 1977. Electromyographic abnormalities in chronic environmental arsenicalism. *J Anal Toxicol* 1: 270–76.
8. Harrington, J. M.; Middaugh, J. P.; Morse, D. L.; and Housworth, J. 1978. A survey of a population exposed to high concentrations of arsenic in well water in Fairbanks, Alaska. *Am J Epidemiol* 108: 377–85.
9. Feldman, R. G.; Niles, C. A.; Kelly-Hayes, M.; Sax, D. S.; Dison, W. J.; Thompson, D. J.; and Landau, E. 1979. Peripheral neuropathy in arsenic smelter workers. *Neurology* 29: 939–44.
10. Cox, D. H. 1980. Arsine evolution-electrothermal atomic absorption method for the determination of nanogram levels of total arsenic in urine and water. *J Anal Toxicol* 4: 207–21.
11. Elkins, H. B.; Pagnotto, L. D.; and Smith, H. L. 1974. Concentration adjustments in urinalysis. *Am Ind Hygiene Assoc J* 35: 559–65.
12. Dixon, W. J., and Massey, F. R., Jr. 1969. *Introduction to Statistical Analysis,* Third ed. New York: McGraw-Hill.
13. Nie, N. H.; Hull, C. H.; Jenkins, J. G.; Steinbrenner, K.; and Bent, D. H. 1975. *Statistical Package for the Social Sciences*, Second ed. New York: McGraw-Hill.
14. Wagner, S. L.; Maliner, J. S.; Morton, W. E.; and Braman, R. S. 1979. Skin cancer and arsenical intoxication from well water. *Arch Dermatol* 115: 1205–07.
15. Tseng, W. P.; Chu, H. M.; How, S. W.; Fong, J. M.; Lin, C. S.; and Yeh, S. 1968. Prevalence of skin cancer in an epidemic area of chronic arsenicalism in Taiwan. *J Natl Cancer Inst* 40: 453–63.
16. Bergoglio, R. M. 1964. Mortalidad por cancer en zonas de aguas arsenicales de la Provincia de Cordoba. Republica Argentina. *Prensa Med Argent* 51: 994–98.
17. Morton, W.; Starr, G.; Pohl, D.; Stoner, J.; Wagner, S.; and Weswig, A. 1976. Skin cancer and water arsenic in Lane County, Orgeon. *Cancer* 31: 2523–32.
18. Ohta, M. 1970. Ultrastructure of sural nerve in a case of arsenical neuropathy. *Acta Neuropathol* (Berlin) 167: 233–42.
19. LeQuesne, P. M., and McLeod, J. G. 1977. Peripheral neuropathy following a single exposure to arsenic. *J Neurol Sci* 32: 437–51.
20. Murphy, M. J.; Lyon, L. W.; and Taylor, J. W. 1981. Subacute arsenic neuropathy: Clinical and electrophysiological observations. *J Neurol Neurosurg Psychiatry* 44: 896–900.
21. Sax, D. S.; Kovacs, Z. L.; Johnson, T. L.; and Feldman, R. G. 1981. Clinical applications of the estimation of nerve conduction velocity distributions. In *Conduction Velocity Distributions: A Population Approach to Electrophysiology of Nerve*, L. J. Dorfman, K. L. Cummins, W. Liefer, Eds., pp. 113–136. New York: Alan R Liss.
22. Landau, E.; Thompson, D. J.; Feldman, R. G.; Gable, G. J.; and Dixon, W. J. 1977. *Selected Noncarcinogeic Effects of Industrial Exposure to Inorganic Arsenic.* Final Report on EPA Contract No. 560/6-77-018. Washington, D.C., U.S. Environmental Protection Agency, Office of Toxic Substances.
23. Committee on Medical and Biologic Effects of Environmental Pollutants. 1977. *Arsenic.* Washington, D.C.: National Academy of Sciences.