Health effects of arsenic-contaminated drinking water : final report submitted to the Wisconsin Department of Natural Resources. 2002

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Health Effects of Arsenic-Contaminated Drinking Water

Final Report

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Wisconsin Department of Natural Resources

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Background

Inorganic arsenic is a well-known human poison that causes a wide array of adverse health effects. The World Health Organization[1] and U.S. Environmental Protection Agency[2] classify inorganic arsenic as a human carcinogen. Long-term ingestion of contaminated drinking water has been found to increase the risk of skin cancer and tumors of the bladder, kidney, liver and lung[3-6]. Exposure to inorganic arsenic may also cause thickening and discoloration of the skin[7-9], nausea and diarrhea[10], decreased production of blood cells[11,12], abnormal heart rhythm[13], blood vessel damage[14] and numbness in the hands and feet.[15,16] Recent investigations have also linked arsenic exposure to the development of Type II diabetes[17,18] or "sugar diabetes."

Arsenic concentrations in U.S. drinking water supplies are usually below 3 micrograms per liter (ug/L). Presently the Wisconsin groundwater protection standard for arsenic is set at 50 ug/L, however, the U.S. EPA recently adopted a standard of 10 ug/L. Public water supplies will be required to achieve compliance with this standard in 2006. The World Health Organization also uses a standard of 10 ug/L. This standard is based primarily on epidemiological studies that have found an association between ingestion of water that has an arsenic level greater than 50 ug/L and the incidence of cancers of the lung and bladder. Studies indicating these associations have been conducted in Taiwan, Chile and Bangladesh.

Arsenic occurs naturally in soil and bedrock and can readily enter groundwater. Concentrations above 5 ug/L have been found in approximately 5% of Wisconsin's municipal wells. In 1987, a groundwater study conducted by the Department of Natural Resources identified elevated arsenic in groundwater coincident with a bedrock layer found at the interface of the St. Peter Sandstone and Sinnippee Dolomite. This geologic formation stretches from southern Brown County into Outagamie and Winnebago counties and lies beneath more than 20,000 private water supply wells. Water samples that were collected from 1,943 private wells between 1990 and 1993 contained arsenic concentrations that ranged from 1.0 to 12,000 ug/L. Levels exceeded 5 ug/L in 622 (32%) of these wells, and 68 (3.5%) of the wells had arsenic concentrations that exceeded the federal standard of 50 ug/L.[19] In response to this finding, the Department of Health and Services' Bureau of Environmental Health developed a public education campaign and conducted a family health survey. One component of the education campaign was the development of a fact sheet on the health effects of ingested arsenic that was distributed to private well owners in this area. During 1993, the Bureau of Public Health conducted a drinking water and health study in Outagamie and Winnebago counties. Self-administered surveys were used to collect information about individual water use habits and health status. These surveys were returned by 637 families and provided information for 1,623 individuals of all ages. Comparison of daily arsenic intake levels and illness rates found that people who ingested more than 49 ug of arsenic per day were significantly more likely to report skin cancer, kidney problems, tremors and unexplained hair loss than others.[20]

More recent testing has found that arsenic levels have increased during the past decade. Although the geochemistry is poorly understood, this trend appears to correlate with groundwater withdrawal rates and may involve the introduction of oxygen or chlorine into the aquifer. If arsenic levels continue to rise and the federal standard is reduced, a large percentage of residents in this area may be advised to stop using their water for drinking and cooking.

Families whose drinking water contains arsenic levels above 10 ug/L are advised to seek an alternate supply of water for drinking and cooking. However, since a limited number of studies conducted in experimental animals and humans indicates that inorganic arsenic is poorly absorbed through intact skin, these families are encouraged to continue using their well water to bathe and shower. Several families with infants and pre-school aged children have questioned this advice, and additional research is needed to ensure protection of these age groups since their skin surface area:body weight ratio is significantly higher than an adults, and because their skin may allow more arsenic absorption. Arsenic test results of 10 ug/L or less are deemed acceptable at this time. The US Environmental Protection Agency recently lowered the federal drinking water standard for arsenic from 50 ug/L to 10 ug/L.

Funding for this study was provided by the Department of Natural Resources. The principal objective of this research was to evaluate the health impacts of arsenic-contaminated groundwater on families that use water from private wells that are located within the advisory area that stretches from southern Winnebago to northern Outagamie county. In addition, dermal absorption of arsenic from water during bathing and showering was evaluated.

Methods

Arsenic exposure and health outcome study

Between June 2000 and January 2002, the Outagamie and Winnebago county health departments worked with 19 townships to organize well-water testing programs. Residents were encouraged to submit a sample of their well water for arsenic analysis. Families were also encouraged to complete a family water use and health history questionnaire (Appendix A). Water sample kits and questionnaires were available for pick-up at township offices. Residents paid a small fee to cover the analytical costs. The cost was typically between $15 and $20 and was paid at the time the water test kit was picked up. Residents were instructed to return their water sample along with their health survey to the town hall.

The water samples were then shipped to a certified laboratory for arsenic analysis and the family health surveys were forwarded to the Department of Health and Family Services' central office in Madison. Approximately one month after the water samples were collected, residents were invited to attend an informational meeting at their local town hall. Well owners received their arsenic test report at the meeting. Water quality experts from several state agencies made brief presentations and answered questions on

topics including regional geology, well construction, the health effects of arsenic, and arsenic-removal technology.

Survey data were entered into an electronic database and analyzed using Microsoft Access and Statistical Analysis System (SAS) Version 8.2 software. Standard statistical analyses including frequency analysis, two-by-two tables, odds ratios, and logistic regression were used to evaluate associations between arsenic exposure and health outcomes.

Dermal absorption study

Several families who used arsenic-contaminated water for bathing and household chores, but used bottled water for drinking, were invited to participate in an arsenic absorption study. The purpose of this effort was to determine whether non-consumptive uses of this water was a significant source of arsenic exposure.

Residents who agreed to participate in this portion of the study collected early morning urine specimens which were analyzed for arsenic by the State Laboratory of Hygiene. They were instructed to eliminate fish and seafood from their diets for five days prior to the collection of urine since laboratory analyses cannot distinguish between "fish arsenic" which is heavily methylated and relatively non-toxic, and inorganic froms of arsenic found in groundwater.

Findings

Cohort characteristics

Water use and health surveys were returned by 2,233 families comprising a total of 6,669 individuals. Survey respondents included 522 pre-school aged children and 752 adults over the age of 65 years. Because this study was limited to families living in privately-owned homes, very few respondents were between the ages of 18 and 30 years. People in this age group tend to live in rental housing such as college dormitories and apartments. Respondents lived in 19 different townships (see Table 1).

Table 1. Arsenic Levels and Number of Responses by Township

Township	No. Of Families That Completed Health Surveys	Mean (Max) Arsenic Level In Ug/L	No. Of Wells With Arsenic Levels > 10 Ug/L	% Of Families That Reported A Prior Arsenic Test
Algoma	456	29.4 (3,100)	151	66
Black Creek	101	7.6 (76)	23	20
Black Wolf	12	1.2 (3.5)	0	8
Bovina	36	3.5 (15)	2	8
Center	237	12.8 (233)	70	27
Cicero	51	4.6 (58)	6	4
Clayton	219	11.7 (266)	49	18
Ellington	141	1.5 (18)	4	10
Freedom	167	5.0 (240)	19	14
Grand Chute	138	2.3 (66)	6	17
Greenville	142	4.3 (79)	12	20
Maple Creek	27	4.3 (14)	2	4
Omro	61	6.8 (41)	12	26
Osborn	108	5.6 (142)	10	32
Seymour	93	18.9 (1,300)	16	15
Utica	41	8.7 ( )	9	12
Vinland	88	10.3 (327)	23	24
Winchester	23	2.8 (34)	2	26
Winneconne	92	3.6 (46)	10	14
Total	2,233	12.0 (3,100)	426	28

Well construction vs. arsenic levels

Approximately two-thirds of the well owners who completed surveys provided information on the depth of their wells. According to the information they provided, most of their wells are more than 100 feet deep and have 40 to 60 feet of casing. The lowest arsenic levels were found in very shallow wells (< 50 ft deep) and deep wells that were cased to a depth of at least 200 feet (see Tables 2 and 3). The average arsenic level in wells less than 50 feet deep was 3.6 ug/L. In comparison, the average level in wells 100 to 200 feet deep was 18.4 ug/L. Wells that were more than 50 feet deep were 2 to 3 times more likely to have an arsenic level greater than 10 ug/L than the shallow wells.

Table 2. Well Depth vs. Arsenic Concentration

Depth of well in feet*	Min-Max Arsenic Level in ug/L	% As level > 10 ug/L
< 50 N = 39	0-27	8
50-100 N = 284	0-1,300	18
100-200 N = 867	0-3,100	21
> 200 N = 250	0-174	14
Unknown N = 793	0-327	18
Total N = 2,233	0-3100	19

*Note: This data was self-reported and was not verified.

Table 3. Casing Length vs. Arsenic Concentration

Casing length in feet*	Min-Max Arsenic levels in ug/L	% As levels > 10 ug/L
< 50 N = 465	0-3,100	18
50-100 N = 401	0-490	22
100-200 N = 249	0-266	18
> 200 N = 52	0-71	10
Unknown N = 1,066	0-2389	21
Total N= 2,233	0-3,100	19

*Note: This data was self-reported data and was not verified.

Well age vs. arsenic levels

The age of a given well was not predictive of its arsenic concentration. Wells constructed during the 1990's were just as likely to yield water that was high in arsenic as wells that were constructed before 1960. The age of wells varied among townships. Many of the wells in Algoma, where arsenic levels tend to be highest, were constructed after 1989.

Table 4. Well age vs Arsenic Concentration

Year of installation	Arsenic level in ug/L Min-Max	% As levels > 10 ug/L	% of wells located in Algoma
< 1960 N =123	0-2389	17	15
1960-1974 N = 381	0-662	19	20
1975-1989 N = 588	0-1300	21	18
> 1989 N = 758	0-3100	19	27
Unknown N = 383	0-177	17	14
Total N= 2,233	0-3100	19	20

Correlation of previous test results and current arsenic levels

A previous arsenic analysis was reported by 634 families. The result of the previous test was provided by 383 of these families. Most of the earlier test results were from samples collected during the period between 1992 and 1994 when the Department of Natural Resources was conducting an investigation of water quality in the region. Current and previous arsenic levels were highly correlated (see table 5).

Table 5. Comparison of Previous and Current Test Results

Previous arsenic result	No. wells in category	No. of wells with current test results		
		<10 ug/L	10-50 ug/L	>50
< 10 ug/L	243	204 (84%)	27 (11%)	12 (5%)
10-50 ug/L	110	28 (25%)	69 (63%)	13 (12%)
> 50 ug/L	30	3 (10%)	11 (37%)	16 (53%)

Arsenic Exposure

Many of the families that participated in this study had very little exposure to arsenic-contaminated water and are at low risk for arsenic-related health problems (see table 6). More than forty percent of the wells that were sampled provided water that contained no detectable arsenic. An almost equal percentage had an arsenic level between 1 and 9.9 ug/L. Approximately 20% of the samples had an arsenic level of 10 ug/L or higher. Slightly more than ten percent of families consumed water that had an arsenic level greater than 20 ug/L. This level is twice the current federal standard and poses a significant cancer risk if consumed over a long period of time. Preschool-aged children were twice as likely to consume water that had an arsenic concentration above 20 ug/L than people over the age of 65 years (14.2% vs 6.8%). Because of their rapid growth and developing nervous and endocrine systems, young children are potentially more susceptible to the toxic effects of arsenic than adults.

Approximately half of the participants in this study (2,940 of 6,669) had consumed their well water for at least 10 years (table 7). Only 408 residents over the age of 34 reported more than 9 years of exposure to well water that was high in arsenic ($\geq$ 10 ug/L). The relatively small number of individuals in this high exposure cohort reduced the power of this study to evaluate associations between arsenic exposure and chronic health conditions such as adult onset diabetes, cancer, and neurological disease.

Table 6. Distribution of Drinking Water Levels Among Survey Participants

Arsenic level in ug/L	No. people (%)	No. aged < 6 yrs (%)	No. aged >64 yrs (%)	No. households (%)
< 1.0	2,728 (40.9)	209 (39.6)	335 (44.5)	920 (41.2)
1-4.9	1,565 (23.5)	115 (21.8)	187 (24.9)	544 (24.4)
5-9.9	988 (14.8)	81 (15.3)	97 (12.9)	322 (14.4)
10-19.9	645 (9.7)	42 (8.0)	82 (10.9)	208 (9.3)
>19.9	743 (11.1)	75 (14.2)	51 (6.8)	239 (10.7)
Total	6,669 (100)	528 (100)	752 (100)	2,233 (100)

Table 7. Distribution of Drinking Water Exposure Times Among Respondents

Years of water use	No. people	(%)	No. with As ≥ 10 ug/L	No. with As ≥ 20 ug/L	No. with As ≥ 50 ug/L	No. with As ≥ 100 ug/L
<2	722	10.8	150	82	29	9
2-9	2,999	45.0	655	293	108	30
10-19	1,617	24.2	348	187	47	10
20+	1,323	19.8	230	68	30	8
Total	6,669	100	1,398	650	264	157

Long-term Arsenic Exposure Estimates

Lifetime arsenic exposure categories displayed in Table 8 were developed by multiplying the concentration of arsenic in the well water by the number of years an individual had consumed the water. This method provides an exposure estimate with the unit ug/L-yrs. It is not a quantitative dose estimate, which would be more appropriately expressed in total milligrams of arsenic per kilogram of body weight. The ug/L-yrs estimates are one method that can be used to place research subjects into low, medium and high exposure cohorts based on their long-term exposure potentials.

Table 8. Distribution of Lifetime Arsenic Exposure Estimates

Arsenic Level in ug/L-yrs	No. residents	No. aged < 18 yrs	No. adults
<10	3,415	1,029	2,386
10-100	1,949	572	1,376
>100	1,305	230	1,060
>200	740	117	623
>300	469	74	395
>500	222	33	189
>1,000	89	11	78

Assessment of Dermal Absorption During Bathing and Showering Activities

Six families, including 11 adults and 4 children, who had stopped using arsenic-contaminated wells as a source of drinking water but continued to use it for baths, showers, and household chores submitted first morning urine samples for arsenic analysis. All were advised not to consume fish or seafood products for at least three days prior to urine collection to avoid exposure to "fish arsenic." Arsenic levels in these families' wells ranged from 34 to 3,100 ug/L. All of the urine arsenic levels were within the normal range reported by the laboratory (see Table 9).

Two of the four children had detectable urine arsenic levels, while the majority (7 of 11) of the adults did not. No correlation was seen between the well water and urine arsenic levels. These findings are consistent with earlier reports that arsenic is poorly absorbed through the skin during bathing and showering activities.

Table 9. Urine Arsenic Levels Following Dermal Contact

Family No.	As level in well (ug/L)	Gender	Age	Urine Arsenic Level (ug/L) Normal range (0-30 ug/L)
1	233	M	44	< 10
		F	43	< 10
		F	13	< 10
		F	11	< 10
		M	7	12
2	47	M	60	< 10
		F	57	< 10
3	34	F	54	< 10
4	29	M	47	15
		F	46	10
		M	19	<10
5	71	M	71	< 10
6	3,100	M	49	15
		F	51	16
		M	13	17

Cancer

A diagnosis of cancer was reported by 380 residents who lived in 332 different households. Forty-seven individuals reported multiple cancer diagnoses. Cancers reported included 305 internal cancers and 25 cases of melanoma, and 122 non-melanoma skin cancers. Cancer types reported by survey respondents are listed in the table 10. Ninety-five non-melanoma skin cancers, 19 melanomas and 211 internal cancers were diagnosed while the person was living in their current home. The remaining 45 cancer cases involved diagnoses that were made before the person moved into their current home. Long-term exposure to arsenic has been linked to increased rates of several forms of cancer. The primary sites of interest are non-melanoma skin cancers, bladder cancer, lung cancer, liver cancer and kidney cancer.

Table 10. Summary of Cancers Reported by Survey Participants

Cancer site/type	Total no. of reports	No. diagnosed while living in home	Cancer site/type	Total no. of reports	No. diagnosed while living in home
Amyeloblastic Fibroma	1	1	Oral	2	2
Bladder	11	11	Ovarian	3	2
Bone	1	1	Pancreas	3	3
Brain	6	6	Parathyroid	1	1
Breast	61	51	Parotid Gland	1	1
Cervical	13	5	Prostate	43	41
Colon	23	13	Rectal	10	10
Esophageal	1	1	Sarcoma	1	1
Gall Bladder	1	1	Sinus	2	2
Giant Cell Tumor	1	0	Skin	122	95
Kidney	9	8	Small Intestine	1	1
Laryngeal	4	4	Stomach	3	3
Leukemia	14	10	Testicular	5	4
Liver	1	1	Thyroid	3	2
Lung	13	12	Tongue	2	2
Hodgkin's Disease	7	4	Tonsil	1	1
Non-Hodgkin's Lymphoma	11	9	Tumor Pregnancy	1	0
Mediastinum	1	1	Unknown	6	4
Melanoma	25	19	Unspecified	1	0
Multiple Myeloma	1	1	Uterine	11	11
	205	159		222	186

Crude cancer rates are shown by age group, gender and smoking status in Table 11. As expected, people over the age of 65 were more likely to report a diagnosis of cancer than others. Men and people who smoked cigarettes were also more likely to have been diagnosed with cancer. The higher rate among men is likely related to their higher rate of tobacco use. Although comparable statewide cancer rates are not available for comparison, the cancer rates listed in Table 11 seem in line with cancer incidence data maintained by the Wisconsin Cancer Reporting System (WCRS).

Table 11. Overall Cancer Rate By Age Group, Gender And Smoking Status

Group	Cases/person	Rate per 100
Age in years		
0-18	4/1,834	0.22
19-34	14/1,004	1.39
35-64	195/3,076	6.33
65+	207/753	27.49
Females (all ages)	194/3,266	5.94
Males (all ages)	227/3,403	6.67
Age > 34 years		
Women		
Non-smokers	123/1,439	8.54
Cigarette smokers	60/454	13.21
Men		
Non-smokers	121/1,224	9.88
Cigarette smokers	98/712	13.76

Bladder cancer

Eleven residents reported a past diagnosis of bladder cancer. All of these reports were confirmed by review of the Wisconsin Cancer Registry. Arsenic exposure data for these individuals is summarized in the table 12. As shown, four of these individuals had consumed water that contained more than 5 ug/L of arsenic for more than 10 years prior to their diagnosis. Each had life-time exposure estimates (LEEs) that exceeded 100 ug/L-yrs. The bladder cancer rate among adult residents with LEEs > 100 ug/L-yrs was twice as high as that observed among adults whose LEEs were less than 100 ug/L-yrs. (4/1060 vs 7/3,762; OR 1.80; 95% confidence interval 0.48-6.69). One individual was diagnosed with bladder cancer after drinking water from his private well for 15 years. His well was sampled in1993 and found to have an arsenic concentration of 229 ug/L. The most recent test result was 69 ug/L. Although the number of bladder cancer cases in our cohort is quite small, our findings are consistent with previous reports of a higher incidence of bladder cancer among individuals who have had long-term exposure to inorganic forms of arsenic.

Table 12. Arsenic Exposure Histories For Residents Diagnosed With Bladder Cancer

Case No.	Gender	Age At Diagnosis	Arsenic Level In Ug/L	Years Of Water Use Prior To Diagnosis	Exposure In Ug/L-Yrs
1	M	44	69 (229 in 1993)	15	3,435*
2	F	72	5	48	240
3	M	69	11	17	187
4	F	50	6.2	25	155
5	M	63	3	27	81
6	M	80	1.8	30	54
7	M	55	2.5	3	7.5
8	F	83	2	1	2
9	M	76	0	25	0
10	M	66	0	32	0
11	M	65	0	11	0

*Estimate based on 1993 sample result.

Lung cancer

Twelve residents were diagnosed with lung cancer while living in their current residences. Arsenic exposure data for these individuals is summarized in table 13. As shown, only two of these individuals had consumed water that contained more than 5 ug/L of arsenic for more than 10 years prior to their diagnosis. Only one of them consumed water that had an arsenic level above 10 ug/L. These data should be interpreted cautiously due to the small number of highly exposed individuals in our cohort and the small number of lung cancer cases reported. However, they do not seem to indicate that exposure to arsenic-contaminated drinking water is contributing to a higher incidence of lung cancer in our cohort.

Table 13. Arsenic Exposure Histories For Residents Diagnosed With Lung Cancer

Case No.	Gender	Age At Diagnosis	Arsenic Level In Ug/L	Years Of Water Use Prior To Diagnosis	Exposure In Ug/L-Yrs
1	M	73	12	25	300
2	M	62	4	26	104
3	M	65	4.7	18	89
4	M	73	6	13	78
5	M	59	1.5	24	36
6	M	47	1	22	25
7	F	54	3	2	6
8	M	65	1	2	2
9	M	60	0	12	0
10	F	52	0	17	0
11	M	70	0	33	0
12	M	81	0	14	0

Kidney cancer

Eight residents were diagnosed with kidney cancer while living in their current residences. Arsenic exposure data for these individuals is summarized in table 13. As shown, only one of these individuals had consumed water that contained more than 10 ug/L of arsenic for more than 10 years prior to their diagnosis. These results should be interpreted cautiously due to the small number of highly exposed individuals in our cohort and the small number of kidney cancers reported, but do not seem to suggest a link between exposure to arsenic-contaminated drinking water and the development of kidney cancer.

Table 13. Arsenic Exposure Histories For Residents Diagnosed With Kidney Cancer

Case No.	Gender	Age At Diagnosis	Arsenic Level In Ug/L	Years Of Water Use Prior To Diagnosis	Exposure In Ug/L-Yrs
1	M	58	12	27	324
2	F	60	3	5	15
3	M	40	1	17	17
4	M	50	0	27	0
5	M	56	0	23	0
6	F	56	0	35	0
7	M	70	0	41	0
8	M	70	0	70	0

Liver cancer

One case of liver cancer was reported and it was confirmed by review of the WCRS. This case involved a 49-yr old female who consumed water that was very high in arsenic (112 ug/L) for approximately 3 years prior to her diagnosis. Her cumulative exposure estimate was 336 ug/L-yrs. Due to the short duration of her exposure, it seems unlikely that her exposure to arsenic from her existing well could have contributed to her condition. Her exposure to arsenic during the years before she began drinking water from this well is not known. Thus it is impossible to draw any conclusions regarding the effect of arsenic on liver cancer development from this single case.

Skin cancer

Skin cancer incidence

A previous diagnosis of non-melanoma skin cancer was reported by 115 individuals who ranged in age from 35 to 96 years. The overall skin cancer prevalence rate for residents aged 35 years and over was 3.00 percent. Reporting rates varied within this cohort and were significantly higher among those aged 65 and older, men, and cigarette smokers (see table 15).

Table 15. Skin Cancer Rates Among Adults Aged 35 Years Or More

Group	Cases/pop	Rate per 100	OR (95% CI)	Mean age in years
All adults	115/3828	3.00	NA	53.4
Ages 35-64 yrs	55/3076	1.79	1.00	48.3
Ages ≥ 65 yrs	60/752	7.98	4.74 (3.21-7.01)*	73.4
Women	42/1893	2.22	1.00	53.1
Men	73/1935	3.77	1.73 (1.16-2.59)*	53.6
Non-smokers	64/2662	2.40	1.00	52.7
Cigarette smokers	51/1166	4.37	1.86 (1.26-2.74)*	54.8

*Significant at p<0.05

In an effort to evaluate the effect of chronic arsenic ingestion on skin cancer occurrence, rates were calculated for adults aged 35 years and over who had consumed their well water for 10 years or longer. Because age and cigarette use were strongly associated with the risk of skin cancer, the cohort was subdivided by age group and smoking status.

Table 16. Skin Cancer Rates Versus Well-Water Arsenic Level, Age, And Cigarette Use

Age group	Smoker	As Level	Skin cancer prevalence	Rate per 100	OR (95% CI)
40-64 yrs	No	< 5 ug/L	10/601	1.66	1.00
	No	≥ 5 ug/L	9/354	2.54	1.54 (0.57-4.15)
	Yes	< 5 ug/L	5/284	1.76	1.06 (0.31-3.40)
	Yes	≥ 5 ug/L	4/139	2.88	1.75 (0.46-6.18)
≥ 65 yrs	No	< 5 ug/L	13/283	4.59	1.00
	No	≥ 5 ug/L	10/115	8.69	1.98 (0.78-4.99)
	Yes	< 5 ug/L	10/135	7.41	1.66 (0.66-4.18)
	Yes	≥ 5 ug/L	12/64	18.75	4.79 (1.92-11.96)*

Analysis restricted to residents who had consumed their water for 10 years or longer.
*Significant at p<0.05.

Ages 40-64 years (see table 16)

Non-smokers between the ages of 40 and 64 were 54 percent more likely to report a diagnosis of skin cancer if their water contained at least 5 ug arsenic per liter, however this difference was not statistically significant. Smokers whose water was low in arsenic were not significantly more likely to report a diagnosis of skin cancer than non-smokers. However, smokers who consumed water that contained more than 5 ug arsenic per liter reported the highest rate of skin cancers among this age group. The prevalence among this subgroup was nearly twice the rate reported by non-smokers (2.88 vs 1.66 percent).

Ages 65 years and over (see table 16)

Among residents aged 65 years or more, cigarette use and arsenic-contaminated water were both associated with a higher prevalence of skin cancer. The rate among cigarette users was 22 per 199 (11 percent). This rate was nearly twice as high as the rate among non-smokers (23/398; 5.78%). This effect appeared to synergize the effect of long-term exposure to arsenic-contaminated water among this cohort. Nearly one in five smokers in this age group who had long-term exposure to arsenic-contaminated well

water reported a diagnosis of skin cancer. This prevalence rate was more than five times higher than that observed among age-matched residents with neither risk factor.

In an effort to further evaluate the effects of arsenic exposure on skin cancer prevalence, exposures were estimated using drinking water arsenic concentrations, daily arsenic doses, and cumulative lifetime doses (see Table 17). For the purposes of this analysis the cohort was limited to adults aged 50 and older who had consumed their well water for at least 10 years. Each method of estimation revealed a dose-related increase in skin cancer rates with the effect being strongest among smokers. Regardless of the method used to estimate dose, skin cancer prevalence was greatest among smokers who were exposed to high levels of arsenic.

Table 14. Odds Ratios And 95% Confidence Intervals For Skin Cancer And Arsenic Exposure Among Adults Aged 50 Years And Over Who Had Consumed Their Water For At Least 10 Years

Exposure Estimate	Cigarette Smoker	No. (Rate per 100)	OR	(95% CI)
Conc. of As in Water (ug/L)				
< 1.0	No	12/394 (3.04)	1.00	
1-4.9	No	8/203 (3.94)	1.28	(0.53-3.09)
≥5	No	16/310 (5.16)	1.66	(0.80-3.46)
< 1.0	Yes	8/211 (3.79)	1.25	(0.46-3.36)
1-4.9	Yes	7/119 (5.88)	1.99	(0.69-5.59)
≥5	Yes	15/162 (9.26)	3.25	(1.40-7.60)*
Daily Dose of As (ug/Day)				
< 1.0	No	13/400 (3.25)	1.00	
1-19.9	No	8/195 (4.10)	1.25	(0.53-2.97)
≥20	No	15/312 (4.81)	1.46	(0.84-4.68)
< 1.0	Yes	8/215 (3.72)	1.15	(0.43-3.03)
1-19.9	Yes	8/124 (6.45)	1.99	(0.70-3.02)
≥20	Yes	14/156 (8.97)	2.76	(1.33-5.74)*
Cumulative Dose of As (ug/L-yrs)				
< 1.0	No	12/396 (3.03)	1.00	
1-199	No	13/293 (4.44)	1.46	(0.43-3.05)
≥ 200	No	11/218 (5.04)	1.66	(0.75-3.71)
< 1.0	Yes	8/212 (3.77)	1.16	(0.68-3.16)
1-199	Yes	13/168 (7.74)	2.68	(1.12-6.44)*
≥ 200	Yes	9/112 (8.03)	2.80	(1.05-7.35)*

Analysis restricted to residents who had consumed their water for 10 years or longer.
*Significant at $p<0.05$.

Adult Onset Diabetes

A diagnosis of adult onset diabetes was reported by 122 residents. The effect of chronic arsenic exposure on the development of this condition was evaluated by assessing diabetes rates among adults who had consumed their well water for 10 years or longer. Within this cohort, diabetes was more prevalent among residents whose drinking water contained a detectable level of arsenic, however, a dose response relationship was not

observed (see table 18). These findings are inconclusive, but appear consistent with previous reports of an association between arsenic exposure and the development of adult onset diabetes and suggest the need for additional study.

Table 18. Adult Onset Diabetes Rates vs Arsenic Levels in the Water

Age group	As Level in Water	Diabetes prevalence	Rate per 100	OR (95% CI)
35-64 yrs	< 1.0 ug/L	19/625	3.04	1.00
	1-4.9 ug/L	12/373	3.22	1.06 (0.52-2.16)
	≥ 5 ug/L	21/535	3.92	1.29 (0.70-2.38)
≥ 65 yrs	< 1.0 ug/L	15/283	5.30	1.00
	1-4.9 ug/L	15/135	11.11	2.10 (1.06-4.16)*
	≥ 5 ug/L	14/179	7.82	1.48 (0.73-2.98)
	Cumulative Dose Estimate			
35-64 yrs	< 1.0 ug/L-yrs	19/627	3.0	1.00
	1-199 ug/L-yrs	22/604	3.6	1.21 (0.62-2.36)
	≥ 200 ug/L-yrs	11/302	3.6	1.21 (0.53-2.71)
≥ 65 yrs	< 1.0 ug/L-yrs	15/285	5.3	1.00
	1-199 ug/L-yrs	20/176	11.4	2.31 (1.09-4.90)*
	≥ 200 ug/L-yrs	10/137	7.3	1.42 (0.57-3.46)

Analysis restricted to residents who had lived in their homes for at least 10 years.
*Significant at $p < 0.05$.

Cardiovascular Effects

Several investigators have reported effects of arsenic exposure on the cardiovascular system. In an attempt to evaluate this, arsenic exposure data were compared to rates of hypertension, heart attack, and bypass surgery.

Hypertension rates are shown by age, smoking status and arsenic exposure level in Table 19. Among non-smokers between the ages of 35 and 64, exposure to water that contained arsenic was associated with a modest, non-significant increase in the rate of hypertension. Cigarette smokers in this age group whose water had no detectable arsenic were 40 percent more likely to report a diagnosis of hypertension that non-smokers. Smokers whose well water contained more than 5 ug arsenic per liter were twice as likely to have been diagnosed with hypertension than non-smokers who consumed water that was low in arsenic. The effect of arsenic exposure on hypertension is less clear among older residents, however smoking continues to be associated with higher diagnosis rates.

Table 19. Hypertension Rates vs Arsenic Exposure

Age group	Cigarette smoker	Arsenic level in ug/L	No. cases/person (%)	OR (95% CI)
35-64 years	No	<1.0	42/441 (9.5)	1.00
		1-4.9	27/250 (10.8)	1.15 (0.67-1.97)
		≥ 5	42/388 (10.8)	1.15 (0.72-1.85)
	Yes	<1.0	24/184 (13.0)	1.42 (0.81-2.51)
		1-4.9	14/123 (11.4)	1.22 (0.61-2.41)
		≥ 5	27/147 (18.4)	2.14 (1.22-3.73)*
≥ 65 yrs	No	<1.0	37/189 (19.6)	1.00
		1-4.9	25/95 (26.3)	1.47 (0.79-2.73)
		≥ 5	24/115 (20.9)	1.08 (0.59-2.00)
	Yes	<1.0	26/94 (27.7)	1.57 (0.85-2.91)
		1-4.9	13/41 (31.7)	1.91 (0.84-4.28)
		≥ 5	15/64 (23.4)	1.26 (0.60-2.62)

Analysis restricted to residents who had consumed their water for 10 years or longer.

Sixty-eight residents who had consumed their water for 10 years or longer reported having bypass surgery. As shown in Table 20, the number of bypass procedures reported by people under the age of 65 was too small to support analysis. Among residents over the age of 64, drinking water arsenic levels and cigarette smoking are both associated with higher bypass surgery rates. Although residents who drank water that contained arsenic were more likely to report a history of bypass surgery, a dose-response was not observed.

Table 20. Coronary Bypass Rates vs Arsenic Exposure

Age group	Cigarette smoker	Arsenic level in ug/L	No. cases/person (%)	OR (95% CI)
35-64 years	No	<1.0 1-4.9 ≥ 5	3/441 (0.7) 2/250 (0.4) 3/388 (0.8)	Not calculated due to small numbers
	Yes	<1.0 1-4.9 ≥ 5	1/184 (0.5) 4/123 (3.2) 4/147 (2.7)	Not calculated due to small numbers
≥ 65 yrs	No	<1.0 1-4.9 ≥ 5	6/189 (3.2) 10/95 (10.5) 10/115 (8.7)	1.00 3.59 (1.15-11.53)* 2.90 (0.94-9.28)
	Yes	<1.0 1-4.9 ≥ 5	12/94 (12.8) 6/41 (14.6) 7/64 (10.9)	4.46 (1.49-13.89)* 5.23 (1.39-19.71)* 3.75 (1.08-13.21)*

Analysis restricted to residents who had consumed their water for 10 years or longer.

Eighty-two people reported a diagnosis of heart attack. Sixteen of these individuals had consumed their water for fewer than 10 years, however. As shown in Table 18, too few heart attacks were reported by residents under the age of 64 to support statistical analysis of rates. Among older residents, those who smoked cigarettes or

consumed water that contained more than 5 ug of arsenic per liter were more likely to have suffered a heart attack than others, however this difference was not statistically significant.

Table 21. Heart Attack Rates vs Arsenic Exposure

Age group	Cigarette smoker	Arsenic level in ug/L	No. cases/person (%)	OR (95% CI)
35-64 years	No	< 1.0 1-4.9 ≥ 5	2/441 (0.4) 3/250 (1.2) 3/388 (0.8)	Not calculated due to small numbers
	Yes	< 1.0 1-4.9 ≥ 5	5/184 (2.7) 7/123 (5.7) 3/147 (2.0)	Not calculated due to small numbers
≥ 65 yrs	No	< 1.0 1-4.9 ≥ 5	11/189 (5.8) 5/95 (5.2) 9/115 (7.8)	1.00 Not calculated 1.37 (0.50-3.71)
	Yes	<1.0 1-4.9 ≥ 5	8/94 (8.5) 3/41 (7.3) 7/64 (10.9)	1.51 (0.53-4.22) Not calculated 1.99 (0.66-5.87)

Analysis restricted to residents who had consumed their water for 10 years or longer.

Aneurysms

Fourteen individuals suffered aneurysms while living in their current homes. One of these individuals suffered a fatal intra-cranial bleed shortly after completing our survey. The well water serving her home was very high in arsenic level of 2,389 ug/L. In addition to this woman, four other people who reported aneurysms had lifetime exposure estimates of more than 100 ug/L-years, and six had exposure estimates that were less than 10 ug/L-yrs. Although residents with high arsenic exposure estimates were more likely to report aneurysms than others (5/1,060 vs 4/2,386), the odds ratio of 1.88 was not statistically significant (95 % CI 0.5 – 6.95).

Cerebrovascular

Strokes were reported by 42 survey participants. Thirty-six of these events involved individuals who had lived in their homes for at least 10 years and were used to analyze the effect of long-term arsenic exposure. As shown in the table below, the highest incidence of stroke was reported by people over the age of 65 who were non-smokers and consumed water that was low in arsenic. While these results show no association between arsenic exposure and the risk of stroke, they should be interpreted with caution because of the relatively small numbers of cases involved.

Table 22. Prevalence Of Stroke Versus Arsenic Level And Smoking Status

Age group	Cigarette smoker	Arsenic level in ug/L	No. cases/person (Rate per 100)	OR (95% CI)
35-64 years	No	< 1.0 1-4.9 ≥ 5	3/441 (0.68) 1/250 (0.40) 2/388 (0.52)	Not calculated due to the small number of cases
35-64 years	Yes	< 1.0 1-4.9 ≥ 5	0/184 (0.00) 1/123 (0.81) 0/147 (0.00)	Not calculated due to the small number of cases
≥ 65 yrs	No	< 1.0 1-4.9 ≥ 5	13/189 (6.88) 3/94 (3.19) 7/115 (6.09)	Not calculated due to the small number of cases
≥ 65 yrs	Yes	< 1.0 1-4.9 ≥ 5	4/194 (2.06) 0/41 (0.00) 2/64 (3.12)	Not calculated due to the small number of cases

Keratosis

Fourteen respondents reported keratosis of the skin. All of them were adults and had consumed their water for 6 years or longer. Keratosis is characterized by a thickening and darkening of the skin. It is unclear whether the people who reported this condition had been evaluated by a dermatologist. Three people reporting keratosis were members of a single family whose well water arsenic level was 54 ug/L when tested in 2000. The level had been 94 ug/L when the well was tested approximately 8 years earlier. The family had consumed water from this well for 22 years. A water treatment device was installed following the earlier test for arsenic. In addition to this family, 11 others reported keratosis. Nine of these individuals consumed water that was low in arsenic (<10 ug/L). The remaining two individuals who reported keratosis consumed water that had arsenic levels of 11 and 32 ug/L. Both of these individuals had consumed water from their wells for more than 20 years.

Hairloss

Short-term exposure to high levels of inorganic arsenic has been associated with hair loss. Twenty-four women and nine men experienced unexplained hair loss after moving into their homes. While most of these individuals' water supplies were low in arsenic (23 were below 10 ug/L), 3 individuals developed hair loss while consuming water that was very high in arsenic. A husband and wife, both 38 years old, began to lose their hair shortly after moving into their home in 1992. At water test conducted in 1993 revealed an arsenic concentration of 5,860 ug/L. Following that test, the well was reconstructed and the home was equipped with a reverse osmosis system. The arsenic level was below detection in a water sample taken in May, 2000. In addition to this couple, a 37-yr old woman developed symptoms of hair loss and anemia shortly after she moved into her new home in 1999. A water sample submitted in February 2001 contained an arsenic level of 247 ug/L.

Anemia

Anemia was assessed among women between the ages of 20 and 50 years. This subgroup is much more likely to suffer from anemia than others. Women who consumed water that contained an arsenic level greater than 50 ug/L were almost five times more likely to report a history of anemia than others (3/56 vs 12/1367). However this difference is difficult to interpret due to the extremely small number of individuals who reported this condition.

Neurological Diseases

Parkinson's Disease

Six men and one woman were diagnosed with Parkinson's Disease while living in their current homes. All were over the age of 65 years and only one had an elevated arsenic level of 28 ug/L. Arsenic levels in the other 6 wells ranged from below detection to 3.2 ug/L. Exposure times ranged from 9 to 79 years of water use. Because of the very small number of cases, no statistical analysis was conducted.

Multiple Sclerosis

Five women and two men were diagnosed with Multiple Sclerosis while living in their current homes. These individuals ranged in age from 31 to 67 years. Only one had an elevated drinking water arsenic level of 14 ug/L. Arsenic levels in the remaining wells ranged from below detection to 3.5 ug/L. Statistical analyses were not performed due to the small number of cases of Multiple Sclerosis in this cohort.

Numbness & Tingling

Eighty-nine people reported symptoms of numbness and tingling. Although symptom rates were somewhat higher among residents whose life-time exposure estimates exceeded 100 ug/L-yrs, than among people with estimates below 10 ug/L-yrs, the difference was not statistically significant (OR 1.50; 95% CI 0.50-6.95).

Reproductive outcomes

The female head of each household was asked to complete a reproductive history questionnaire. Data provided by 1,013 women who were under the age of 50 when they completed the survey are summarized in Table 20. Outcome information was available for 1,182 pregnancies. Women whose well water contained more than 5 ug of arsenic per liter were more likely to report a premature birth or stillbirth than others, however the difference was not statistically significant.

Table 23. Pregnancy Outcomes Versus Well Water Arsenic Levels

	Pregnancy Outcome						
As level	**Smoker**	**Full-term**	**Miscarriage**	**Stillbirth**	**Premature**	**No. Pregnancies**	**No. Women**
<1.0 ug/L	Yes	73 (86%)	10 (12%)	1	2	85	82
	No	342 (82%)	50 (12%)	2	12	415	324
	Both	415 (83%)	60 (12%)	3	14 (2.8%)	500	406
1-4.9 ug/L	Yes	39 (80%)	4 (8%)	1	4	49	53
	No	202 (81%)	37 (15%)	0	7	250	183
	Both	251 (80%)	41 (14%)	1	11 (3.7%)	299	236
≥ 5 ug/L	Yes	53 (74%)	10 (12%)	2 (2%)	6	72	82
	No	259 (83%)	38 (13%)	3 (1%)	12	311	289
	Both	312 (81%)	48 (12%)	5 (1%)	18 (4.7%)	383	371

Discussion

This report summarizes arsenic exposure and health outcome information for nearly 7,000 Wisconsin residents who live in an area that is affected by arsenic-contaminated groundwater. All of these residents live in private homes and obtain their drinking water from private wells. Information about well construction, water use, and health outcomes were provided voluntarily by 2,233 families. With the exception of internal cancers and melanomas, this self-reported information was not verified by a review of medical records. Nonetheless, a high degree of confidence in the database is supported by the accuracy of the cancers and well water arsenic data that were reported by study participants.

This research effort has provided a wealth of information regarding arsenic exposure in the Wisconsin's Fox River Valley as well as about the consequent impacts on the health of residents living in the affected communities. The observation of low urine arsenic levels among children and adults who used arsenic-contaminated water for bathing, showering and other household chores is reassuring and supports the current water use recommendations.

Our health findings are consistent with findings from other published studies. Skin cancer rates were highest among people who had had long-term exposure to arsenic-contaminated water and who also smoked cigarettes. This combined effect of arsenic from water and cigarette use was slightly more than additive. This would imply that arsenic was in some way enhancing the dermal carcinogenicity of chemicals present in cigarette smoke. This effect might be due to the ability of inorganic arsenic to inhibit DNA repair enzymes and increase mutation rates.

Adults who were exposed to arsenic-contaminated water for 10 years or more were also more likely to report a history of heart disease or adult onset diabetes. While the numbers of each of these diagnoses was relatively small in our cohort, our findings

are consistent with previous reports associating long-term exposure to inorganic arsenic with cardiovascular disorders and diabetes.

This research study is among the largest epidemiological studies that has ever been conducted in Wisconsin related to contaminated drinking water. It was conducted in cooperation with the county health departments and officials in each local township. The study is unique in that the residents themselves bore much of the cost by paying for the arsenic analyses. Analytical costs paid by families that completed health surveys were in excess of $40,000. Residents were extremely cooperative. More than half of those who submitted a water sample for analysis also completed a health survey.

Major strengths of this study are the large cohort size, the availability of current arsenic measurements on each water supply, and detailed information about exposure times and health outcomes. The major weaknesses are the self-reported aspect of the data and the fact that groundwater in the arsenic-affected region often contains a variety of other minerals that could contribute to the health effects were are attempting to assess, or antagonize the health effects of arsenic. This is a significant problem, in part, because only a few wells in this region have been tested for potential co-contaminants like nickel, lead and cadmium.

Our understanding of the long-term health impact of arsenic could be improved by continuing to follow the health of some of the families who participated in this study. It would be useful to continue to monitor the health of residents who reported long-term exposure to well water that contained more than 20 ug of arsenic per liter. An exposure registry could be established using this database. Families who agreed to participate in the registry would be contacted on a regular basis and asked to provide ongoing health outcome and arsenic exposure information.

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