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Arsenic-induced skin conditions identified in southwest dermatology practices: an epidemiologic tool?

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Abstract

Populations living in the Southwest United States are more likely to be exposed to elevated drinking water arsenic levels compared to other areas of the country. Skin changes, including hyperpigmentation and generalized hyperkeratosis, are the most common signs of chronic arsenic ingestion from drinking water. The purpose of this study was to determine the feasibility of using dermatology practices in New Mexico, Arizona, and western Texas as a surveillance system for arsenical skin disorders related to drinking water. Postcard questionnaires were mailed to practicing dermatologists. The number of cases of arsenical hyperpigmentation/keratoses seen by these dermatologists during the past 10 years and the past year were estimated. Of 240 dermatologists who were mailed questionnaires, 37 reported seeing 237 patients with arsenical hyperpigmentation/keratoses in the past 10 years and 35 patients in the past year. Since approximately one-eighth of dermatologists practicing in the Southwest saw at least one patient with arsenical hyperpigmentation/keratoses during one year, it appears feasible to complete a population-based study of these conditions.

1. Introduction

Arsenic is a naturally-occurring element found in many types of rocks, especially ores that contain copper, lead, or gold. In the United States, large areas of the desert Southwest are affected by alkaline brines trapped in closed basins. These alkaline waters, which are in contact with arsenic containing rocks, can accumulate high levels of inorganic arsenic. Numerous closed basins in the deserts of New Mexico, Utah, Nevada, and California have elevated groundwater arsenic levels. Arsenic also occurs in isolated locations in the Midwest, New England, and in the coastal ranges of Washington, Oregon, and California. Several national surveys have found arsenic levels in drinking water that range from 0 to 100 $\mu g\ l^{-1}$. In general, though, the US average arsenic level for tap water is 2.4 ppb (Life Systems Inc., 1993). A recent study by the United States Geological Survey estimated that 8 and 14% of public water-supply systems exceeded arsenic concentrations of 10 and 5 $\mu g\ l^{-1}$, respectively (Focazio *et al.* 2000). The populations living in these areas

are more likely to be exposed to elevated levels of arsenic in the drinking water compared to other areas of the United States.

Some of the most common effects of arsenic ingestion are non-cancerous changes to the skin that can lead to arsenic-induced non-melanoma skin cancers (Neubauer 1946). Skin changes, including hyperpigmentation, hypopigmentation, generalized hyperkeratosis and formation of hyperkeratotic warts on the palms and soles, and skin cancer are the most characteristic signs of chronic arsenic ingestion from drinking water (Yeh 1973; Shannon and Strayer 1989). Arsenic-induced keratoses may become malignant, most frequently transforming from a benign lesion to a squamous cell carcinoma. Arsenic exposure may also induce Bowen's disease (*in situ* squamous cell carcinoma) and multiple basal cell carcinomas. The development of hyperpigmentation and arsenical keratosis occurs at a lower dose than malignant lesions. Thus, they serve as potential precursors for invasive carcinoma and may also be important markers for health effects from exposure to low levels of waterborne arsenic.

Characteristic arsenical skin lesions have served as markers of high drinking water arsenic exposure in human populations. Both non-cancerous dermatological changes and skin cancers have been found in populations exposed to drinking water arsenic in Taiwan, Bangladesh, India, South America, and Mexico (Tseng 1977; Zaldivar *et al.* 1981; Cebrian *et al.* 1983; Guo *et al.* 1998; Mazumder *et al.* 1998; Tondel *et al.* 1999; Chowdhury *et al.* 2000). In most of these studies, the waterborne arsenic levels were between 200 and 1000 $\mu g\ l^{-1}$. In the studies in Taiwan, hyperpigmentation was the most frequently encountered skin change resulting from chronic ingestion of arsenic contaminated drinking water (Yeh 1973). Despite the common occurrence of hyperpigmentation and keratoses following arsenic exposure in populations in Taiwan, India, Chile and northern Mexico, there have been relatively few studies of the occurrence of hyperpigmentation and keratosis in US populations. Studies of US communities served by drinking water with arsenic levels above 50 $\mu g\ l^{-1}$. have failed to show any excess skin disorders or cancers (Morton *et al.* 1976; Harrington *et al.* 1978; Southwick *et al.* 1983; Shannon and Strayer, 1989; Valentine *et al.* 1992).

The 1996 amendments to the Safe Drinking Water Act require the US Environmental Protection Agency (EPA) to set the maximum contaminant levels for arsenic in drinking water. Recently, the EPA proposed reduction in the maximum contaminant level for arsenic from 50 $\mu g\ l^{-1}$. to 10 $\mu g\ l^{-1}$. A major concern with this lower arsenic standard is the uncertainty of the health effects at low arsenic doses. The National Research Council (1999) recently noted that there are important limitations in the scientific data for the relationship between low drinking water arsenic exposures and cancer in US. Results of recent studies on arsenic-related health risks in US and European populations exposed to waterborne arsenic levels less than 50 $\mu g\ l^{-1}$ are not consistent with the elevated risks predicted from the studies conducted in Taiwan and South America (Bates *et al.* 1995; Kurttio *et al.* 1999; Lewis *et al.* 1999). Thus, it is important to determine whether there are signs of arsenic exposure which can be detected before cancers occur.

The purpose of this study was to determine the feasibility of using dermatology practices in New Mexico, Arizona, and western Texas as a surveillance system for arsenic-induced skin conditions related to drinking water. Dermatology practices in the Southwest were selected since there are numerous areas in New Mexico, Arizona, and western Texas with elevated groundwater arsenic levels. Information was also collected by postcard questionnaires on cases of arsenical hyperpigmentation or keratosis seen by dermatologists in this geographic area during two time periods (the past 10 years and the past year).

2. Methods

2.1. *Initial survey*

Names and addresses of practicing dermatologists and dermatology clinics in the states of New Mexico and Arizona, and the city of El Paso, Texas, were identified from lists of members of the American Academy of Dermatology on its web site, listings of dermatologists on the USwestdex Yellow Pages web site, and lists in the Official BAMS Directory of Board Certified Medical Specialists in Dermatology. Each participant was sent a letter describing the study, as well as a

stamped, self-addressed postcard questionnaire asking about any cases of arsenical hyperpigmentation or keratoses he/she had observed during the past 10 years. The letter was signed by the chair of the Department of Dermatology at the University of New Mexico. Information collected included the number of cases seen during the past 10 years, as well as the number of new cases in the past year. Several practicing dermatologists at the major health centers in Albuquerque were consulted about the ability of a dermatologist to identify arsenical hyperpigmentation/keratoses. Based on their recommendations, we relied upon each dermatologist's experience to identify a case in his/her practice. In addition, the respondent was asked whether he/she could be re-contacted for additional information on the cases. Telephone follow-up was completed for those dermatologists not responding within a month to the initial mail-out. If necessary, a second questionnaire was sent by fax to the dermatologist and, often, the information was collected over the telephone. Updated addresses were obtained if the letter was returned by the postal service.

2.2. *Followup survey*

Dermatologists who had seen a patient with arsenical hyperpigmentation/keratoses and agreed to be re-contacted were sent a second self-addressed stamped postcard survey for each patient they reported seeing in the past year. Questions included age and gender of the patient, as well as the physician's 'best' guess of the likely source of exposure to arsenic.

3. Results

A total of 240 dermatologists were identified from the web-sites and directory (Table 1). Overall, 149 (62.1%) responded to the initial postcard survey. This included three who had relocated their practices to another state; one was deceased. They were removed from further analysis. The response rate was highest for New Mexico (69.1%) and lowest for El Paso, Texas (50.0%).

Overall, approximately one-fourth of the dermatologists (37) reported that he/she had seen patients with arsenical hyperpigmentation/keratoses in the past 10 years (Table 2). In El Paso, two of the six dermatologists had seen such patients. In the past year, only 18 (12.4%) of the respondents had seen patients with arsenical keratoses/hyperpigmentation. Higher percentages of dermatologists in New Mexico and El Paso reported seeing patients with arsenical hyperpigmentation/keratoses, although this was not significant. The 37 dermatologists reported seeing a total of 237 patients with arsenical hyperpigmentation/keratoses in the past 10 years and 35 patients in the past year.

Table 1. Response rates for initial post-card survey to dermatologists in the Southwest.

Geographic area	Number of dermatologists sent questionnaire	Responded to survey	
		Number	Percentage
Arizona	173	105	60.7
New Mexico	55	38	69.0
El Paso, Texas	12	6	50.0
Total	240	149	62.1

The number of patients with arsenical hyperpigmentation/keratoses seen by an individual dermatologist ranged from 1 to 50 in the past 10 years and from 1 to 10 in the past year (Table 3). Although the majority of dermatologists reported seeing 1–2 patients in the past 10 years, four dermatologists reported seeing between 20–50 patients, accounting for over half of the total patients.

Eighteen dermatologists were mailed follow-up questionnaires for the 35 patients they had seen in the past year. Eight of the dermatologists returned the follow-up questionnaires for 11 patients. Three of the patients were from two dermatology practices in New Mexico, and eight of the patients were from six dermatology practices in Arizona. The characteristics of these patients are shown in Table 4. The ages of the cases ranged from 40 to 80 years. The most frequently noted possible source of arsenic exposure was well water (9 of the 11 cases). One older male reported using Fowler's solution for asthma.

4. Discussion

The purpose of this study was to determine the feasibility of using dermatology practices as a

Table 2. Percentage of dermatologists who have seen patients with arsenical hyperpigmentation/keratoses in the Southwest and number of patients with these conditions.

	Arizona (n = 101)	New Mexico (n = 38)	El Paso, TX (n = 6)	All areas (n = 145)[a]
Have seen patients with arsenical hyperpigmentation/keratoses in the past 10 years.	23.8%	29.0%	33.3%	25.5%
Number of patients with arsenical hyperpigmentation/keratoses in the past 10 years.	113	72	52	237
Have seen patients with arsenical hyperpigmentation/keratoses in the past year.	10.9%	15.8%	16.7%	12.4%
Number of patients with arsenical hyperpigmentation/keratoses in the past year.	14	11	10	35

[a] Excludes three dermatologists who had relocated to another state and one who was deceased.

Table 3. Number of patients with arsenical keratoses/hyperpigmentation each dermatologist reported seeing in the past 10 years and the past year.

	Arizona (n = 101)	New Mexico (n = 38)	El Paso, TX (n = 6)	All areas (n = 145)
In past 10 years:				
None	77	27	6	108
1 patient	10	4	0	14
2 patients	5	4	1	10
3–5 patients	4	2	0	6
6–10 patients	3	0	0	3
10+ patients	2	1	1	4
In past year:				
None	90	32	5	127
1 patient	9	4	0	13
2 patients	1	1	0	2
3–5 patients	1	1	0	2
6–10 patients	0	0	1	1

Table 4. Summary of ages, gender, and possible source of arsenic exposure in patients with arsenical hyperpigmentation/keratoses seen by a Southwest dermatologist in the past year.

Location	Age	Gender	Possible source of exposure
New Mexico	Unknown[a]	Unknown[a]	Well water
New Mexico	64	Male	Worked in lab
New Mexico	44	Male	Ground/well water
Arizona	60	Female	Well water in area of heavy mining
Arizona	70	Female	Well water
Arizona	72	Male	Fowler's solution for asthma
Arizona	65	Male	Well water
Arizona	40	Female	Farm well
Arizona	40	Female	Family well
Arizona	65	Female	Well water or fertilizer on farm
Arizona	80	Male	Ground water

[a] Physician did not complete this item on the follow-up questionnaire.

surveillance system for arsenic-induced skin conditions related to drinking water. For this study purpose, feasibility was considered to be determined by a relatively high response rate to the initial survey. Response rates to mailed surveys typically range from 60 to 75% (Aday 1996; Dillman 1978). The overall response rate for all three geographic locations was 62.1%. Thus, we consider it feasible to use dermatology practices.

This study did not attempt to estimate the prevalence of arsenical skin disorders related to drinking water, although demographic information was collected on recent cases. Hyperpigmentation and arsenical keratosis have been observed in many studies of populations chronically exposed to arsenic in drinking water in Taiwan, India, Chile and northern Mexico (Tseng *et al.* 1968; Yeh, 1973; Tseng, 1977; Zaldivar *et al.* 1981; Cebrian *et al.* 1983; Guo *et al.* 1998; Mazumder *et al.* 1998; Tondel *et al.* 1999; Chowdhury *et al.* 2000), but there have been few studies in US populations. Valentine *et al.* (1992) compared the health status of residents of four communities in California and Nevada exposed to arsenic drinking water levels ranging from 100–390 $\mu g\ l^{-1}$ to residents of a Wyoming community with levels less than 1 $\mu g\ l^{-1}$. They found no differences in the prevalence of skin disorders. Two earlier epidemiologic studies of populations in Utah and Oregon exposed to drinking water arsenic levels exceeding the current drinking water standard (50 $\mu g\ l^{-1}$) focused on the occurrence of skin cancer (Harrington *et al.* 1978; Southwick *et al.* 1983). These studies noted very low prevalences of arsenical hyperpigmentation and keratoses. In Utah, eight cases were observed in 250 people exposed to 180–210 $\mu g\ l^{-1}$ of arsenic, and in an Oregon population representing 190,871 people, arsenical keratoses were observed in 3 out of 3257 cases of skin cancer.

There is a need in the US for surveillance of populations that may be exposed to drinking water arsenic levels that exceed the standard such as private wells or larger systems that may be out of compliance. Use of dermatologists to identify arsenical skin conditions has also been suggested by Stohrer who reported that dermatologists in the United States recall small numbers of arsenical cancer cases in their practices and will diagnose this cancer when it occurs (Stohrer 1991). We viewed this study as the first step in identifying a practical method to identify potential cases of arsenical skin lesions. Thus, we relied upon the experience and ability of each participating dermatologist to diagnose these conditions and did not use a detailed case definition. We did not want to burden the participating dermatologists with a strict case definition that would require collecting additional exposure information from individual patients.

Additional work should include the development of a strict case definition that is applicable to populations in the United States and readily used by dermatologists. For example, Yeh (1973) provides a detailed description of the pathology of skin lesions in chronic arsenicism based on cases from the southwest coast of Taiwan. He describes the hyperpigmentation as occurring 'everywhere on the body, often showing a raindrop-like appearance or a diffuse dappling of dark brown, especially marked in unexposed parts of the body, such as the trunk, buttock, and upper thigh... Arsenical keratosis is marked characteristically by small, horny, corn-like elevations, usually 0.4–1 cm. in diameter ad nodular in form. They are encountered most frequently on the thenar and lateral borders of the palms, on the roots, and lateral surfaces of the fingers, and on the soles, heels, and toes of feet. Such small nodules may coalesce to form a large verrucous growth... The keratotic areas of the palms and soles are usually symmetrically distributed, but sometimes only the palms or soles are affected'. A panel of dermatologists who are familiar with arsenical lesions could review existing case definitions and develop one that could be readily used for surveillance.

The findings of our study suggest it is feasible to develop a study using dermatologists to identify cases of arsenical hyperpigmentation and keratosis and that dermatologists will participate in such surveillance. It also appears that many potential cases of hyperkeratosis/hyperpigmentation are likely to be referred to a dermatologist for treatment. In our study, as many as one-eighth of dermatologists practicing in the Southwest may see at least one patient with arsenical hyperpigmentation/keratoses in a 1 year time period. If the time period is extended to 10 years, the percentage doubles. Since patients with arsenic-induced skin conditions may not visit a dermatologist, especially in the Southwest where health care access is poor, or the dermatologist may not

diagnose it correctly, our estimates are conservative.

EPA has recently lowered the standard for arsenic in drinking water. This has elicited interest in monitoring the effects of exposure to low levels of arsenic in drinking water in populations in the United States. Our study suggests that it may be possible to monitor arsenical skin changes by developing a sentinel health network using key dermatology practices in areas with higher levels of drinking water arsenic. Arsenic-induced skin conditions could also be reported as 'sentinel health events' to the state health department which would collect exposure information. By using such a reporting system to identify cases and then, collecting additional exposure information for each case, it may be possible to determine if there is clustering in communities with high levels of waterborne arsenic. In addition, identification of private wells with arsenic contaminated drinking water often occurs only after acute health effects have been observed. By identifying individuals with arsenic-related skin lesions, the exposure may be prevented at an earlier stage of disease. Dermatologists are in the position to participate in public health surveillance that will yield many public health benefits at minimal cost.

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