Chronic Arsenic Poisoning from Burning High-Arsenic-Containing Coal in Guizhou, China

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Arsenic is an environmental hazard and the reduction of drinking water arsenic levels is under consideration. People are exposed to arsenic not only through drinking water but also through arsenic-contaminated air and food. Here we report the health effects of arsenic exposure from burning high arsenic-containing coal in Guizhou, China. Coal in this region has undergone mineralization and thus produces high concentrations of arsenic. Coal is burned inside the home in open pits for daily cooking and crop drying, producing a high concentration of arsenic in indoor air. Arsenic in the air coats and permeates food being dried producing high concentrations in food; however, arsenic concentrations in the drinking water are in the normal range. The estimated sources of total arsenic exposure in this area are from arsenic-contaminated food (50–80%), air (10–20%), water (1–5%), and direct contact in coal-mining workers (1%). At least 3,000 patients with arsenic poisoning were found in the Southwest Prefecture of Guizhou, and approximately 200,000 people are at risk for such overexposures. Skin lesions are common, including keratosis of the hands and feet, pigmentation on the trunk, skin ulceration, and skin cancers. Toxicities to internal organs, including lung dysfunction, neuropathy, and nephrotoxicity, are clinically evident. The prevalence of hepatomegaly was 20%, and cirrhosis, ascites, and liver cancer are the most serious outcomes of arsenic poisoning. The Chinese government and international organizations are attempting to improve the house conditions and the coal source, and thereby protect human health in this area. *Key words*: arsenic, ascites, cirrhosis, coal, food contamination, hepatomegaly, liver cancer, skin cancer. *Environ Health Perspect* 110:119–122 (2002). [Online 10 January 2002]
http://ehpnet1.niehs.nih.gov/docs/2002/110p119-122liu/abstract.html

Inorganic arsenic is considered one of the most significant hazards to the population of the United States and in the world, largely because of its carcinogenic potential. The establishment of safe levels of arsenic in drinking water is currently a contentious issue in the United States. People are exposed to arsenic in various forms through air, water, and food. Occupational exposure to arsenic through inhalation of arsenic dust and environmental exposure through arsenic-contaminated drinking water have been extensively documented and are primary routes of exposure with typical patterns of toxic lesions, including cancer (*1–5*). Arsenicals can also be emitted to the air by coal combustion (*1–3*), and some coals are unusually high in arsenic because of geologic factors (*6–9*). However, little is known about the health effect from domestic use of arsenic-containing coal. In this article we briefly describe chronic arsenic intoxication in Guizhou, China, where burning high-arsenic coal in unventilated stoves is a common practice for heating and drying various foods. This practice expels high levels of arsenic into indoor air and food, which become major sources of exposure. In addition, drinking water stored indoors may be contaminated, adding another source of exposure. This population is thus important in that it is exposed through all major routes (ingestion of food and drinking water and inhalation). People in many developing and undeveloped countries use coal in a similar way and may suffer from similar health problems (*6*). Various current attempts are under way to alleviate this situation (*10,11*). Information gained from studying the toxicity resulting from this complex chronic exposure to arsenic could help us understand the mechanisms of arsenic poisoning and carcinogenesis and develop tactics to prevent or intervene in such poisonings.

Exposure of Arsenic from Burning Coal Containing High Arsenic

Guizhou Province, located in southwest China, is rich in coal and metal deposits. In some areas the coals have undergone a geologic process called epigenetic mineralization resulting in extraordinarily high concentrations of arsenic (100–9,000 ppm) within the coal (*6–9*)—much higher than the arsenic levels in coal in the United States and other countries (about 10 ppm) (*7–9*). Arsenic concentrations in certain coal deposits even reach 35,000 ppm, a truly astounding level (*9*). The distribution of arsenic-containing coal in Guizhou province coincides with several chronic arsenic poisoning endemics (Figure 1).

The affected regions are located in a high mountainous plateau that has a damp, generally cool autumn climate. Coal became the main source of energy for domestic cooking and heating in the 1960s, when wood became scarce with the depletion of the local natural forest. The residents frequently bring foods indoors and place them above their coal-burning stoves to dry. Coal is burned inside the home in open pits for daily cooking and crop drying over nonvented ovens (Figure 2). As a result, the indoor air arsenic concentrations are 5–100 times higher than China's Air Quality Permission Standard (standard, 3 μg As/m^3; measured, 20–400 μg As/m^3) (*6,10,12–16*). Arsenic in the air coats and permeates the food being dried. Chili peppers, used to flavor food, and corn are commonly dried in this manner and thereby become highly concentrated in arsenic (*6,9,10,12–16*). We recently used graphite furnace atomic absorption spectrometry to assay arsenic, chromium, antimony, and cadmium concentrations in these arsenic-smoked foods, collected in 1998, in comparison to similar foods collected from areas with low-arsenic coal (Table 1).

Arsenic concentrations in chili peppers and corn dried in this way are 30–70 times higher than those in normal food (both from China and U.S. markets), but are lower than those for foods reported previously (*6,8,12–16*), probably because the domestic environment has improved. These values are close to those reported in a recent survey (*10*), indicating that the residents in this region are still exposed to a significant

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We thank H. Chen, J. Wachsman, Y. Xie, and L. Keefer for critical internal review and comments on this commentary.

This work was supported in part by China Bridge Fellowship (J.L); NIH Public Health Grant ES-06694 (V.A.); Chinese National Science Fund 49873007 (B.Z.), 49271389 (Y.Z.), 49775201 (A.Z.); and Guizhou Science Fund (M-L.C).

Received 19 April 2001; accepted 13 June 2001.

amount of arsenic in their domestic environments. The geologic localization of high arsenic-coal varies among villages, and a clear dose–response relationship exists between local arsenic content in coal in a given village, arsenic content in major foods commonly dried over nonventilated stoves (chili peppers and corn), and arsenic concentration in the urine of village residents (Figure 3).

Other elements contained in coal, such as chromium, antimony, cadmium, and fluorine (*6–9,12–15*), also concentrate in these dried foods, and this likely exposes the population to a complex metal mixture in this Guizhou region. In this region, arsenic exposure is often accompanied by fluorosis (*9,12,13*), which likely complicates toxic response. Coexposure of arsenic with chromium, cadmium, lead, and other metals exacerbates arsenic toxicity in laboratory animals and in cultured cells (*17–19*) and could be responsible for some of the exaggerated health effects, such as liver and kidney lesions, observed in this region. Although arsenic is clearly the main inorganic toxicant in this exposure setting, other metals are also common and likely add to the poisoning.

It is important to consider total exposure (i.e., exposure through air, food, and water) when evaluating adverse health effects of arsenic. In this region of China, arsenic concentrations in the drinking water are in the normal range except for few villages close to the coal mine (*6,9,10*). The various sources of arsenic in this endemic arsenic poisoning area are therefore food (50–80%), air (10–20%), water (1–5%), and direct skin contact (< 1%) (*6,8,10,14*). In an experiment, normal coal (< 45 ppm arsenic) and arsenic-containing coal (3,200 ppm arsenic) were used to dry corn for one week, and the smoked corn was then fed to mice. All the mice survived and grew normally when fed on normal coal-dried corn, but all the mice fed on corn dried over arsenic-rich coal died within 15 days, with apparent intestinal, hepatic, and renal lesions (*20*). Thus, in contrast to arsenic poisoning through drinking water or occupational exposure through inhalation of arsenic dust, the exposures in this region are unique in that arsenic-contaminated food is clearly an important source of environmental arsenic exposure. This exposure, of course, is added to inhalation exposure from the unventilated burning of coal containing arsenic.

Figure 1. Geographic localization of high arsenic coal-containing areas in Guizhou, in southwest China.

Clinical Symptoms of Patients Chronically Exposed to Arsenic in Guizhou

At least 3,000 patients with chronic arsenic poisoning have been diagnosed since 1976 in the Southwest Prefecture of Guizhou (*9,10,16*), with Xingren County alone having approximately 2,000 cases (*14,15*). Approximately 70,000–200,000 people from six counties are considered at risk via the use of high-arsenic coal (*10,21*). As is common in other types of endemic arsenic poisoning, skin lesions are predominant, and approximately 17% of the residents in the region have obvious dermal lesions. Hyperkeratosis of palms of the hands and soles of the feet and pigmentation and hypopigmentation on the trunk are common clinical symptoms and were used as diagnostic criteria for defining an arsenic patient. Two unique features in arsenic-induced skin lesions in this region must be pointed out: Some skin lesions are severe enough to progress to skin ulceration (Figure 4), leading to skin cancers (*6,10,13–16*); and the arsenic-induced skin lesions are persistent. In this regard, a 20-year retrospective study indicates that even after stopping the use of coal containing high arsenic or after receiving chelation therapy with 2,3-dimercapto-1-propanesulfonic acid (DMPS) or meso-2,3,-dimercaptosuccinic acid (DMSA), most the other clinical symptoms show remarkable improvement, but there is little or no improvement in dermal pathology (*16*). Thus, the use of skin lesions to reflect the therapeutic effect of chelation therapy or ameliorative effects of improved domestic environment is dubious at best (*16*).

Figure 2. Traditional crop drying over nonvented open-pit stove.

An important aspect of endemic arsenic poisoning is the prevalence of liver injury (*6,10,13–16*). The incidence of liver injury is, in fact, higher in this area where exposure comes from high-arsenic coal than in areas where arsenic poisoning is caused by contaminated drinking water, such as in Xinjiang and Inner Mongolia (*22,23*), or in West Bengal, India (*24*). The liver injury is clinically manifested as liver enlargement (hepatomegaly), abdominal pain, loss of appetite, chronic indigestion with portal hypertension, with or without elevations in serum aminotransferases (indicative of hepatocellular death) (*6,10,14–16*). The incidence of hepatomegaly (Figure 5) in areas with high-arsenic coal was 37% by physical examination in 1992 (*14*) and approximately 21% by ultrasound examination in 1998 (*10*). The most serious outcomes of arsenic-induced liver injury are cirrhosis and ascites. Patients usually die approximately 6–12 months after the onset of significant ascites (*6,12,13*). According to the available records, cirrhosis with ascites has caused more than 60 deaths of confirmed arsenic poisoning patients in this area (*6,10,12–14,16*), accounting for more than 80% of the mortality in the arsenic patients of Jiao-Le village, Xingren County (*6,14*). However, whether the cause of death is from ascites or from hepatocellular carcinoma is not always known, as autopsy is frequently refused by the victim's family, but hepatocellular carcinoma cells are found in ascites fluid (*6,13*),

Table 1. Arsenic and other metal concentrations in chili peppers and corn.

Groups	Arsenic (ppm)	Chromium (ppm)	Antimony (ppb)	Cadmium (ppb)
Chili peppers				
Normal (n = 3)	0.04 ± 0.01	0.77 ± 0.11	57.2 ± 5.1	48 ± 4.5
As-smoked (n = 6)	70.5 ± 40.3	6.18 ± 3.43	171 ± 20	230 ± 85
Corn				
Normal (n = 3)	0.01 ± 0.00	0.99 ± 0.05	19 ± 1.1	5.1 ± 0.01
As-smoked (n = 5)	3.40 ± 0.95	1.78 ± 0.21	26 ± 0.9	20 ± 1.11

and arsenic-induced liver cancers have been reported (*6,14*).

Because chelation therapy with DMSA and DMPS in this set of patients was not as effective as expected, efforts were directed at using alternative Chinese herbal medicine preparations to treat chronic arsenic-induced diseases. For example, Han-Dan-Gan-Le, a Chinese medicine preparation, improved arsenic-induced liver lesions, as assessed by clinical symptoms and by histology from liver biopsy samples before and after treatment (*25*). With liver biopsy samples available before this treatment, we used cDNA microarray analysis to profile the expression of genes associated with chronic arsenic-induced liver diseases. The results revealed the aberrant expression of genes encoding oxidative stress, DNA damage and repair, and cell proliferation (*26*). These findings are consistent with those observed in livers of animals chronically fed arsenic-containing water for 48 weeks and longer (*27,28*), and in livers of mice receiving repeated arsenic injections (*28,29*). These lesions and aberrant gene expressions could potentially progress to neoplastic changes as seen in chronic arsenic-transformed rat liver cells (*30*) as well as in mice given repeated arsenic injections where hepatic proliferative and pre-neoplastic lesions have recently been observed (*29*).

Other arsenic-induced toxicities are also common. For example, inhalation of arsenic in the indoor air can cause respiratory symptoms including persistent cough, chronic bronchitis, reduced residual volume and vital capacity, and X-ray abnormalities (*6,10,13*). Neurotoxicity, manifested as loss of hearing, loss of taste, blurred vision, and tingling and numbness of the limbs frequently occurs (*6,13*). Corneal inflammation, tearing eyes, and blurred vision become more frequent and severe as exposure levels to arsenic in the indoor air increase (*6,10,13*). In contrast to widely known bladder and kidney cancers caused by arsenic, no bladder and kidney cancers have been reported in these arsenic patients. The reasons for this are not entirely clear, but mortality from other causes may counteract long-term effects of arsenic poisoning. However, clouded urine is frequently seen in most severely arsenic-intoxicated patients, and kidney injury was evidenced by increased urinary protein content (*6,13*) and by aberrant urinary excretion of trace elements (*21*). We have begun a more detailed survey to detect bladder and kidney cancer incidence in this population.

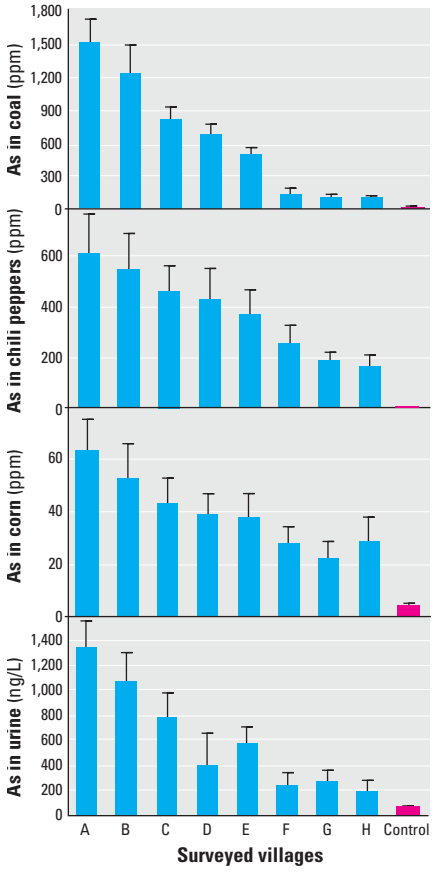

Figure 3. The relationship between arsenic concentration in coal, in main food (corn and chili), and in urine among 8 selected villages using arsenic-containing coal (A–H) and control village using normal coal [adapted from Zhou et al. (*14,15*)].

Efforts to Improve the Environment and Relieve Arsenic Poisoning

Efforts have been made since 1976 to improve public health in this arsenic-endemic area. For arsenic poisoning in Guizhou province, the best way to improve human health is to alter the domestic environment by reducing the use of high-arsenic coal, thereby reducing arsenic exposure through indoor air (*10,16*). Such efforts have included prohibition of the use of coal containing high levels of arsenic, the purchase of coal containing low levels of arsenic for affected residents' use, and provision of free chimneys for ventilation. Unfortunately, these efforts have not proven entirely successful, and affected residents frequently bypass or defeat the environmental improvements because of local economics, among other factors. Because this region is considered an underdeveloped part of China, the most urgent need is for financial support to improve general living conditions of the residents, through either the Chinese government or international organizations. Health education of the local population is critical to the success of any program. A recent plan suggested that the problem in Guizhou could be fixed by buying 3,000 stoves to reduce indoor air arsenic contamination, and this would decrease the risk of cancer for children (*11*).

To treat these chronic arsenic-intoxicated patients, the Chinese government has also provided free chelation therapy. The arsenic-chelating agents, DMSA and DMPS, have been distributed several times on a large-scale basis since the 1980s. However,

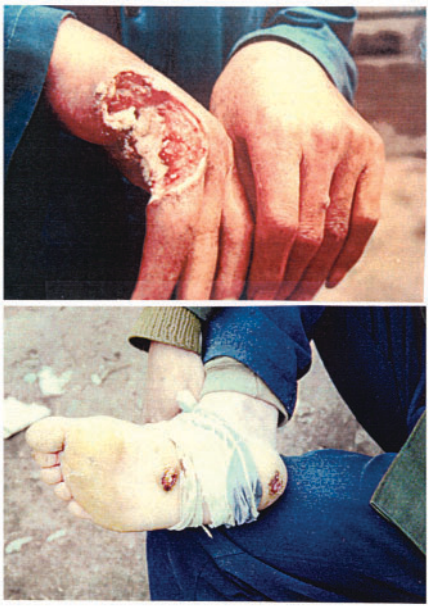

Figure 4. Arsenic-induced hyperkeratosis causing skin ulceration, which leads to skin cancer

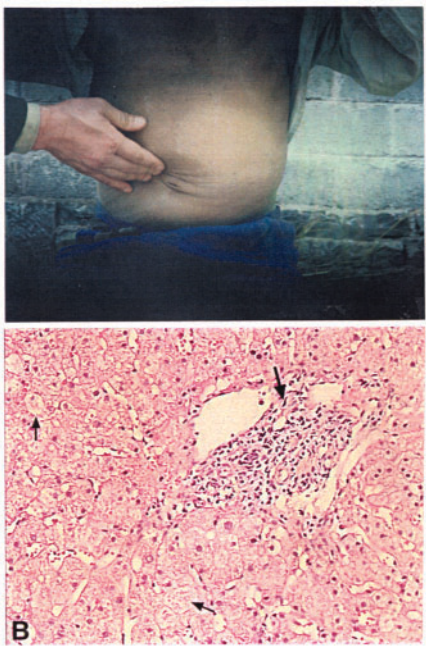

Figure 5. Arsenic-induced hepatomegaly by physical examination (*A*) and liver lesions from liver biopsy samples (*B*). Small arrows indicate hepatocellular degenerative lesions; the large arrow indicates inflammatory cells infiltration in the periportal area [hemoxylin and eosin; magnification × 175; adapted from Lu et al. (*26*)].

the effect of chelating therapy does not last long and its efficacy for improving disease states, including liver and dermal lesions, is not appreciable (*10,16*). Similar situations were also noted in Bangladesh and West Bengal, India, where the use of medications for chronic arsenic toxicity showed only limited success (*31*). To understand the mechanism of arsenic toxicity and carcinogenesis, efforts have been made to increase basic research and to treat various arsenic-related diseases. The Chinese government has recently encouraged international collaboration to help these arsenic patients. However, chronic arsenic poisoning remains an important issue in areas that use high-arsenic coal. Persistent international efforts on many levels will be required to solve this problem. Resolution of these environmental health issues should involve collaborative scientific research on both the basic toxicologic mechanisms and clinical aspects of chronic arsenic poisoning. Special efforts should also be made to protect the health of children (*11*) and to provide a livable environment for children of future generations.

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