Blackfoot Disease in Taiwan: A 30-Year Follow-up Study

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Abstract

Blackfoot disease is an endemic peripheral vascular disease found among the inhabitants of a limited area on the southwest coast of Taiwan, where artesian well water with a high concentration of arsenic has been used for more than eighty years. The natural history of blackfoot disease, based on a prospective study of 1,300 patients, is presented. The overall male/female ratio was 1.5:1. Although the clinical onset was usually insidious, it may be quite sudden and almost always begins with numbness or coldness in one or more extremities, usually the feet. Ultimately, rest pain develops and progresses to gangrene.

In this series, 68% of the patients underwent spontaneous or operative amputation, and the reamputation rate was 23.3%. Lower extremity involvement in
Black Foot Diseases

Blackfoot disease was observed in 97.7% of the cases. The average annual rate for major amputation was 3.81 per 100 patient-years. The factors influencing the prognosis, such as amputation in relation to age and disease onset, are analyzed.

The case fatality rate was 66.5% during thirty years; 44% of these were cardiovascular deaths. The annual death rate was 4.84 per 100 patient-years. Other reported case fatality rates for vascular insufficiency are reviewed. A dose-response relationship between blackfoot disease and the duration of water intake was also noted. The survival rates after the onset of blackfoot disease were: five years, 76.0%; ten years, 59.5%; twenty years, 38.2%; thirty years, 28.6%. The 50% survival point was 13.5 years after onset of the disease.

Water-related diseases
Arsenosis

Drinking water rich in arsenic over a long period leads to arsenic poisoning or arsenicosis. Many waters contain some arsenic and excessive concentrations are known to naturally occur in some areas. The health effects are generally delayed and the most effective preventive measure is supply of drinking water low in arsenic concentration.

The disease and how it affects people

Arsenosis is the effect of arsenic poisoning, usually over a long period such as from 5 to 20 years. Drinking arsenic-rich water over a long period results in various health effects including skin problems (such as colour changes on the skin, and hard patches on the palms and soles of the feet), skin cancer, cancers of the bladder, kidney and lung, and diseases of the blood vessels of the legs and feet, and possibly also diabetes, high blood pressure and reproductive disorders.

Absorption of arsenic through the skin is minimal and thus hand-washing, bathing, laundry, etc. with water containing arsenic do not pose human health risks.

In China (Province of Taiwan) exposure to arsenic via drinking-water has been shown to cause a severe disease of the blood vessels, which leads to gangrene, known as ‘black foot disease’. This disease has not been observed in other parts of the world, and it is possible that malnutrition contributes to its development. However, studies in several countries have
demonstrated that arsenic causes other, less severe forms of peripheral vascular disease.

**The cause**

Arsenicsosis is caused by the chemical arsenic. Arsenic is a toxic element that has no apparent beneficial health effects for humans.

Natural arsenic salts are present in all waters but usually in only very small amounts. Most waters in the world have natural arsenic concentrations of less than 0.01 mg/litre.

Arsenicsosis is caused by exposure over a period of time to arsenic in drinking water. It may also be due to intake of arsenic via food or air. The multiple routes of exposure contribute to chronic poisoning. Arsenic contamination in water may also be due to industrial processes such as those involved in mining, metal refining, and timber treatment. Malnutrition may aggravate the effects of arsenic in blood vessels.

WHO's Guideline Value for arsenic in drinking water is 0.01 mg/litre. This figure is limited by the ability to analyse low concentrations of arsenic in water.

**Distribution**

Natural arsenic contamination is a cause for concern in many countries of the world including Argentina, Bangladesh, Chile, China, India, Mexico, Thailand and the United States of America.

**Scope of the Problem**

Because of the delayed health effects, poor reporting, and low levels of awareness in some communities, the extent of the adverse health problems caused by arsenic in drinking-water is unclear and not well documented. As a result there is no reliable estimate of the extent of the problem worldwide. WHO is presently collecting information in order to make such an estimate.

Case reports on the situation in various countries have been compiled and the arsenic problem in Bangladesh in particular has prompted more intensive monitoring in many other countries. In Bangladesh, 27% of shallow tube-wells have been shown to have high levels of arsenic (above 0.05 mg/l). It has been estimated that 35 - 77 million of the total population of 125 million
Black Foot Diseases

of Bangladesh are at risk of drinking contaminated water (WHO bulletin, volume 78, (9):page 1096). Approximately 1 in 100 people who drink water containing 0.05 mg arsenic per litre or more for a long period may eventually die from arsenic related cancers.

**Interventions**

The most important action in affected communities is the prevention of further exposure to arsenic by provision of safe drinking-water. Arsenic-rich water can be used for other purposes such as washing and laundry. In the early stages of arsenicosis, drinking arsenic-free water can reverse some of the effects. Long term solutions for prevention of arsenicosis include:

For provision of safe drinking-water:

- Deeper wells are often less likely to be contaminated.
- Rain water harvesting in areas of high rainfall such as in Bangladesh. Care must be taken that collection systems are adequate and do not present risk of infection or provide breeding sites for mosquitoes.
- Use of arsenic removal systems in households (generally for shorter periods) and before water distribution in piped systems.
- Testing of water for levels of arsenic and informing users.

In order to effectively promote the health of people the following issues should be taken into account:

- Monitoring by health workers - people need to be checked for early signs of arsenicosis - usually skin problems in areas where arsenic is known to occur.
- Health education regarding harmful effects of arsenicosis and how to avoid them.

"The blackfoot disease (BFD), which was endemic peripheral vascular disease in southwestern Taiwan before the 1990s, has known to be caused by drinking arsenic-contaminated groundwater. Although arsenic has been regarded as the most important determinant BFD, several compounds are found in the high arsenic well water, including ergotamine, organic chloride, and fluorescent humic substances. In addition, trace elements
such as molybdenum, mercury, copper, and cadmium, were reported to be higher in the serum and/or urine of BFD patients and in the groundwater. The etiological agent of the BFD is rather complicate and remains unclear up to present. Intriguingly, the symptoms for the patients that drank groundwater from the artesian well water in the southwestern coast of Taiwan (Chia-Nan plain) were significantly different from those in the northeastern coast of Taiwan (Ilan plain) due to the differences in the constituents and biochemical structures of potential etiological agents. The symptoms for the patients in the Chia-Nan plain was characterized particularly by BFD, skin diseases (e.g., hyperkeratosis, skin cancer, etc.) and internal cancers (e.g., lung, bladder, prostate, etc.) that were caused by arsenic and lesser amounts of fluorescent humic substances in the groundwater, while those in the Ilan plain was characterized particularly by skin diseases and internal cancers but not BFD that were caused by arsenic and considerable amounts of fluorescent humic substances in the groundwater. The humic substances having a benzene rings could possess polymers of many ions (COOH group, C=O group, and OH group) presenting chelating ability, thereby easily combining with arsenic and other metal groups (e.g., iron, manganese, strontium, lead, zinc, nickel, etc.), fatty acids, phthalate esters, some unknowns, and free radicals to form an organometallic complex. The health effects in the Chia-Nan and Ilan plains were serious with water from artesian wells that tapped groundwater under reducing conditions, and they were absent with water from shallow wells that tapped groundwater under phreatic conditions. In general, in the blackfoot disease-endemic area in Taiwan, artesian wells contained higher arsenic and fluorescent humic substances relative to shallow wells.

Water-related diseases - Arsenicosis

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Blackfoot Disease and Arsenic: A Never-Ending Story
Chin-Hsiao Tseng.
"Black foot disease (BFD) is an endemic peripheral vascular disease confined to the southwestern coast of Taiwan. This article reviews the epidemiology, clinical manifestations and diagnosis, pathology, etiology and pathogenesis of this disease. Sporadic cases of BFD occurred as early as in the early 20th century, and peak incidence was noted between 1956 and 1960, with prevalence rates ranging from 6.51 to 18.85 per 1,000 population in different villages. Typical clinical symptoms and signs of progressive arterial occlusion mainly found in the lower extremities, but in rare cases, the upper extremities might also be involved. Ulceration, gangrene and spontaneous or surgical amputation were typical fate. An extensive pathological study concluded that 30% of the BFD patients had histologic lesions compatible with thrombangiitis obliterans and 70% showed changes of arteriosclerosis obliterans. Epidemiologic studies carried out since mid-20th century revealed that BFD was associated with the consumption of inorganic arsenic from the artesian wells. Recent studies confirmed the existence of preclinical peripheral vascular disease, subclinical arterial insufficiency and defects in cutaneous microcirculation in the residents of the endemic villages. A more recent study suggested that the methylation capacity of arsenic can interact with arsenic exposure in the development of peripheral vascular disease among residents of BFD-endemic areas. The incidence of BFD decreased dramatically after the implementation of tap water in these villages over the past 2-3 decades. The atherogenicity of arsenic could be associated with its effects of hypercoagulability, endothelial injury, smooth muscle cell proliferation, somatic mutation, oxidative stress, and apoptosis. However, its interaction with some trace elements and its association with hypertension and diabetes mellitus could also explain part of its higher risk of developing atherosclerosis. Although humic substances have also been suggested as a possible cause of BFD, epidemiologic studies are required to confirm its etiologic role."

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