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HEALTH EFFECTS OF ARSENIC INGESTION FROM DRINKING WATER

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I would like to take this opportunity to acknowledge and thank my mentor, Floyd Frost, who unfortunately could not be here. Floyd has been a source of real inspiration for me over the last year, and I am truly indebted to him for the time and help he has freely given me. In fact, I am repaying a large part of that debt today because Floyd is the one who volunteered me to give this presentation. I know that he is sorry that he could not be here (but not quite as sorry as I am). It does, however, provide me with an opportunity to talk about one of my most favorite topics, and that is the health risks associated with arsenic ingestion.

Arsenic through the Years

Arsenic has a long and distinguished history. It has been used for at least the last 3,400 years, initially by the ancient Greeks and Romans. The results of the intake of arsenic have ranged from gross malevolence to perhaps overenthusiastic benefits.

Perhaps our greatest concern today with arsenic is the exposure of populations to environmental arsenic.

Arsenic has long been a popular poison. It has been known as the "Inheritance Powder," the means by which some heirs acquired their inheritance. Its popularity also is due to its ready availability, its low cost and the fact that it is tasteless and odorless. However, the drawback is that death is slow and painful rather than instantaneous. For this reason it is usually combined with other poisons. Many of you are probably familiar with Joseph Kesselring's classic, *Arsenic and Old Lace*. This work could just as easily have been called *Cyanide and Old Lace* or *Strychnine and Old Lace* since the little old ladies who so deftly disposed of their gentlemen callers were careful to include cyanide and strychnine with their arsenic because they knew arsenic may not do the trick.

If you feel that politics is a dirty business these days you are right, but probably it is not as bad as it used to be. In 55 A.D. we have records of Nero using arsenic to poison his political rival to secure his position in the Roman Empire. Arsenic was the favorite poison in France in the 1800s—we have documentation by an early forensic toxicologist named Blythe who listed arsenic at the top of the list of frequently used poisons.

By the early 1900s due to the development of reliable detection techniques, arsenic's popularity as a poison declined. These techniques involved the acidification of body tissues and body fluids. If arsenic were present, arson gas was generated and this could readily be detected.

Large-scale accidental poisonings have occurred in the past and I will note some of these. It obviously is extremely regrettable that they occurred, but they did provide toxicologists the opportunity to observe populations exposed to arsenic. They also illustrate some of the diverse conditions under which arsenic exposure has occurred. In the early 1900s there was an epidemic in which at least 6,000 beer drinkers were poisoned by beer contaminated with arsenic. The contamination was due to iron pyrite used in the fermentation of beer. In 1955 an incident occurred in which 4,000 infants were poisoned in Japan. The poisonings resulted in 130 deaths due to contamination of the stabilizer used in the infants' formula. Close to home, in 1973, on a smaller scale but nonetheless relevant, was the Minnesota well-water incident. In this case, 11 cases of poisoning were caused by contamination of well water by arsenic insecticide storage dumps.

Uses of Arsenic

Arsenic has long been considered a panacea for almost every ailment. It has been available in a number of tonics; for example, Fowler's Solution consisted of 1% potassium arsenite. It was introduced in 1786, and was used in the "cure of argues, remitting fevers, and periodic headaches." Arsenic has been used in a number of ailments ranging from anorexia to diabetes to malaria. Before the 1940s it was perhaps the most popular drug used to treat syphilis; perhaps the only drug available to treat the disease. It was replaced by penicillin in the 1940s. Today it is used as a veterinary medicine in the treatment of heartworm and haemobartonella.

Arsenic causes cutaneous capillary flush resulting in the "milk and roses" complexion that many fashion conscious women find desirable. It has been used by the notorious Austrian arsenic eaters, a group of mountaineers who consumed large amounts of arsenical ores believing that they improved their endurance at high altitudes, increased their weight, strength and appetite and cleared their complexion.

Sources and Manifestations of Arsenic Exposure

Populations can be exposed to arsenic from various industrial sources. It is used as a coloring agent in glass production and wood preservative, used in the manufacturing of electrical semiconductors, and as a food additive for poultry and livestock.

The clinical manifestations of arsenic poisoning fall into two categories: acute toxicity and chronic toxicity. It has been estimated that a fatal dose of arsenic toxin ranges from 200 to 300 milligrams, although this is extremely variable. In some individuals 20 milligrams is life threatening and other individuals have been reported to recover after ingestion of 10 grams of arsenic.

With acute toxicity the symptoms occur within 30 minutes of ingestion. For those of us who suspect that perhaps our friends and relatives value our assets more than our company, this is what you should look out for: metallic taste, garlicky odor to the breath, dry mouth, difficulty swallowing, severe nausea and vomiting, colicky abdominal pain, profuse diarrhea with rice-water stools, capillary damage, generalized vasodilation, transudation of plasma resulting in shock, sloughing of intestinal fragments, drowsiness, confusion, paranoid delusions, hallucinations and delirium. This all culminates in seizures, trauma and death. If your constitution is strong enough to survive the first onslaught, it is unfortunate that you probably will not survive the second. Death usually results over the next several days due to multiple organ failure.

The insidiousness and diversity of clinical manifestations have probably led to the diagnosis of only about 50 percent of cases of chronic poisoning. The adverse health effects reported due to chronic poisoning have been inconsistent. Taiwanese studies, conducted in the 1980s, predicted that the lifetime risk of dying from cancer of the

Health Effects of Arsenic Ingestion from Drinking Water

liver, lung, kidney or bladder from drinking one liter of water per day containing only 50 parts-per-billion of arsenic may be as high as one in 100. The current U.S. Environmental Protection Agency's minimum contaminant level is 50 parts-per-billion. However, the predicted incidence of cancers in the United States is very different from the observed incidence in the U.S. Studies of U.S. communities served by drinking water supplies with high arsenic levels have failed to show any excess skin disorders. A retrospective cohort study of internal cancers in Fowler's Solution patients in Lancaster, England, showed that with the exception of bladder cancer, none of the risk estimates were noticeably elevated; and there was a weak dose response trend for respiratory cancer risk with increasing cumulative arsenic dose.

Problems in Predicting the Effects of Arsenic

There are numerous problems in predicting the effects of arsenic in U.S. populations. Some problems have to do with the use of inconsistent data showing inconsistent results from the same population observed in different studies. This may be due to problems of interpretation of epidemiological data, confounding factors, selection bias, or low statistical power. Also, in the U.S., we have a very mobile population with alternative water supplies available, making longitudinal studies difficult to conduct. Another problem is that no animal model is available to predict the effects of arsenic. And lastly, the mechanism of action is not known; that is, arsenic does not cause point mutations, but it does induce chromosomal aberrations and sister chromatid exchange. It may interfere with DNA repair enzymes by binding to sulfhydryl groups, or it may amplify human oncogenes.

Sources of Inconsistencies

Why do arsenic's effects differ from population to population? There are a number of possible reasons including: genetic factors such as metabolic differences and oncogene suppression; dietary factors such as malnutrition, methionine deficiency, or antioxidant deficiencies of vitamins A, C or E; zinc deficiency; smoking; alcohol; Hepatitis B virus; aflatoxin; fluorescent humic substances; and low intake of selenium, an arsenic antagonist, which may have anticarcinogenic effects.

Effects of Arsenic

Hepatic effects of arsenic exposure are important and I would like to draw your attention specifically to angiosarcoma. This is a very rare cancer that is associated specifically with polyvinyl chloride exposure and also with arsenic exposure. Renal failure may occur and dialysis may be necessary. Cardiovascular effects are diverse and can be fatal. Neurological effects include parasthesia (which is pins and needles) weakness, and possible paralysis.

Possibly some of the most controversial and also the most worrisome effects of arsenic are the carcinogenic effects. Although controversial, there appears to be a strong association between cancer of the skin and cancer of the respiratory tract, specifically lung cancer. However, an increase in arsenic exposure does appear to be associated with an increase in bladder, renal, liver and colon cancers. The incidence of these cancers varies from population to population and there is no definitive data on these cancers.

Further Research Needed

We are not sure by what mechanism arsenic induces a wide array of adverse health effects. We think it may be genotoxic and may cause chromosomal aberrations. Unfortunately, no animal model is available to predict arsenic's adverse health effects on humans being. It is important that we develop appropriate models that will predict the exposure effects of arsenic. We need to perfect the cell cultures and tissue cultures that are being used now in order to better understand and predict the effects of arsenic on humans and understand its methods of action. We must develop standardized procedures to evaluate populations exposed to arsenic. And we need to investigate further the interaction between arsenic with other common environmental contaminants, including carcinogens, co-carcinogens and promoters.