HEALTH EFFECTS OF ARSENIC **October 4, 2001**
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Presented by:

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BACKGROUND

The Baltimore District of the U.S. Army Corp of Engineers requested the services of Dr. Lamm and CEOH to present information on the health effects of arsenic to the residents of Spring Valley in Washington, DC on August 7, 2001. The presentation focused on information that relates potential arsenic-associated health risks and their corresponding doses. The purpose of this lecture was to give residents information so that they could assess their own risks from the arsenic concentrations measured in the soils of their Spring Valley sites.

Dr. Lamm is a physician-epidemiologist in Washington, DC who has studied the health effects of arsenic for over twenty years. He is on faculty at Johns Hopkins University School of Public Health, Georgetown University School of Medicine (Pediatrics), and the Uniformed Services University for the Health Sciences School of Medicine (Preventive Medicine and Biometrics). He has examined both workers exposed to arsenic in Montana and residents exposed to arsenic in drinking water in Inner Mongolia. He has done risk analyses for the risks associated with the clean-up on an arsenic-contaminated industrial site. He has published many articles on the health effects of arsenic and continues to conduct studies and analyses in that field.

The following summarizes and synthesizes the information from his presentation.

Arsenic and its Health Risks

Arsenic is one of the more common elements naturally present in soil. Its toxicity and carcinogenicity have been known for a long time. Arsenic is unusual as a carcinogen since long-term rodent studies have been negative, and only human epidemiological studies can describe the conditions under which arsenic is carcinogenic. Most studies of arsenic and lung cancer have come from studies of smelter workers who have inhaled dusts containing arsenic. Most studies of arsenic and skin or bladder cancers have come from studies of persons who have ingested water containing arsenic, usually under natural conditions. Most of these studies are from Asia (Taiwan and Inner Mongolia) or Latin American (Mexico, Chile, and Argentina). The arsenic in these waters is generally from the bedrock of the water table. Studies in the US have not demonstrated a cancer risk from exposure to arsenic in drinking water. The arsenic situation in Bangladesh and West Bengal has not so far been shown to have a carcinogenic effect, although severe dermal and internal effects have been widely reported. Spring Valley is rather unusual in that its contamination is from man-made activities not associated with the metal mining or smelting industry.

Arsenic is a known toxin and carcinogen, but it is the magnitude of the dose – the amount and the route of administration (inhalation, ingestion, contact, etc.) - and the frequency of exposure that determines what health effects may occur. Classically, Paracelsus has been summarized as saying "The Dose makes the Poison". That was true five hundred years ago, and is still true today.

Arsenic has historically been found to be useful in the treatment of various diseases (e.g., Syphilis, eczema), and today is an effective treatment for acute pro-myelocytic leukemia.

For convenience sake, we will refer to dosages as daily ingestion of arsenic measured in grams, milligrams, or micrograms. Let us define these terms. For comparison, it takes 456 grams to make one pound (lb). A milligram is one thousandth (1/1,000) of a gram, and a microgram is one thousandths (1/1,000) of a milligram. Most medications are written in terms of milligrams.

1 gram (gm) = 1,000 milligrams (mg) = 1,000,000 micrograms (ug)

or

1 microgram = 0.001 milligram = 0.000001 gram

In terms of exposures and health effects, we are referring to the magnitude (amount and duration) of exposure. This discussion will center on the effects of exposure levels in the range of grams, milligrams, and micrograms per day.

For purposes of discussion, we will use the following broad categories of exposure.

KNOWN HEALTH EFFECTS AT DIFFERENT EXPOSURE LEVELS

The exposure levels at which specific health effects are first observed with arsenic exposure are shown below.

Exposure	Dosage	Effect
Very High Exposure – grams (gm)	0.1 – 10 gm	Death from Gastric Bleeding, Circulatory

At this dose, ingestion of arsenic is fatal. It would be difficult to inhale a fatal dose of arsenic. Ingestion in these amounts would be intentional – suicidal or homicidal.

Exposure	Dosage	Effect
High Exposure – milligrams (mg)	0.1 – 10 mg/day	Cancer: Skin, Bladder, Lung, Liver

Exposure at the milligram dosage level is well studied in environmental health. This is the exposure level at which arsenic demonstrates its carcinogenicity. Although arsenic has been proven to cause human cancers including skin, lung, and bladder cancers, it is an infrequent cause of these cancers.

The studies of lung cancer from the inhalation of arsenic are of smelter workers (e.g., copper, cadmium, lead, etc.) who are occupationally exposed to arsenic from the oxidation of the sulfides in the metal ores. Arsenic has been shown to be the cause of lung cancers in studies in which workers have also been exposed to other metals. Some analysis has shown that the lung cancer risk is proportional to the cumulative arsenic dose for those workers who have had very high exposures to arsenic but not for those workers who have not had very high exposures to arsenic. Other studies relate the risk to the measure of arsenic excreted in the urine. This excretion demonstrates that the arsenic is indeed absorbed by the body. There are some recent studies that relate lung cancer to arsenic absorbed from the ingestion of arsenic-containing water.

The studies of skin cancer from the ingestion of arsenic all relate to persons who drank water containing arsenic either for medicinal purposes or inadvertently from the consumption of local drinking water. The classic study was reported from Taiwan in the 1960s and concerned an area with a previously unknown disease – Blackfoot Disease. It was the investigation of Blackfoot Disease and its associated skin cancer that led to the identification of arsenic as the probable or possible cause of both diseases. Extension of this study over the past thirty years has been the major basis for assessing the risk of human cancer from the ingestion of arsenic. The National Academy of Sciences/National Research Council (NAS/NRC) has based both its 1999 assessment and its 2001 assessment the cancer risk from arsenic ingestion on these studies carried out by Dr. C. J. Chen of the National University of Taiwan. Most of the studies of arsenic ingestion deal with water containing about ½ milligram arsenic per liter with daily water

consumptions of 2 – 4 liters per days. These result in daily dosages measured in milligrams per day. [1/2 mg/L x 2 L/day = 1 mg/day; ½ mg/L x 4 L/day = 2 mg/day].

Similarly with bladder cancer, most of the associated arsenic exposures are with water containing one-half to one milligram of arsenic per liter and daily dosages measured in milligrams.

Exposure	Dosage	Effect
Low Exposure – micrograms (ug)	0.1 – 10 ug	No known human adverse health effects

The Inner Mongolia study found no cases of skin cancer where the drinking water had an arsenic level of less than 150 micrograms per liter. The risk of skin cancer at exposures above 150 ug/l was about fifty times greater than for persons with exposures below that level. Thus, skin cancer was not found among persons with exposures in the hundreds of micrograms per day and is, therefore, not expected at levels much lower than that. US studies found no evidence of an association between bladder cancer or lung cancer and drinking waters with arsenic levels between 3 and 60 ppb (ug/L). Neither the studies from Asia nor the studies from Latin America have separated out the low arsenic exposure areas for the assessment of the risk for internal cancers (bladder or lung cancer).

ARSENIC METABOLISM

Arsenic is absorbed from the lung, from the mucous membranes of the nose, and from the gut. It passes through the body and is partially metabolized in the liver. It is excreted in the urine, the sweat, and in the keratin of the skin, the hair, and the nails. Its disappearance rate from the blood is very rapid with a biological half-life of one hour and from the body into the urine with a biological half-life of four days.

Compartment	Time	Pathway of elimination
50% from the blood	1 hour	The body excretes through the urine, sweat, skin, hair.
50% from the body	4 days	

Because of its rapid elimination, arsenic dosages do not build up over time. The measurement of arsenic in the urine will indicate the level of exposure over the past few days, and the measurement of arsenic in the hair will indicate exposure over the past few months. There is no known special sensitivity of children to arsenic. It is known that children eliminate arsenic from their system more rapidly than adults. A study of about 400 children from the Anaconda smelter site in Montana found no evidence of an increase in urinary arsenic level correlating with the general contamination level for the area.

ARSENIC EXPOSURE

Whether from drinking water, or from fruits and vegetables in which it is naturally present, or some other source, we are exposed to arsenic daily. However, most exposures fall well below acceptable daily intakes of inorganic arsenic and are naturally excreted by the body. A number of US regulatory agencies have determined acceptable levels of arsenic intake for the areas they regulate.

The FDA permits a maximum acceptable daily level of inorganic arsenic in the diet at 130 micrograms per day. They estimate the typical US diet contains 20-35 micrograms daily. OSHA permits the inhalation of 100 micrograms per day. The EPA currently permits 50 micrograms per liter (which at up to two liters per day is 100 micrograms per day) and is proposing permitting only 10 micrograms per day (which at up to two liters per day is 20 micrograms arsenic per day). EPA has stated in its integrated risk information system (IRIS) assessment that it will permit (i.e., no greater than a 10^{-4} risk level) the equivalent of 2 ug/liter (or four microgram per day) from other environmental sources.

Type of Exposure	**Acceptable Daily Levels**	**Current Daily Levels**
Dietary Inorganic Arsenic	130 ug/day	25-30 ug/day
Drinking Water Inorganic Arsenic	20-100 ug/day	up to 10 ug/day
Environmental Inorganic Arsenic	4 ug/day	< 4 ug/day

How do these numbers compare with actual exposures. The diet contains about 25-30 micrograms per day. The drinking water in the District of Columbia contains up to five micrograms per liter for a daily intake up to 10 micrograms per day. The actual levels of arsenic in the drinking water are 2 – 4 micrograms per liter. I will show below that the other environmental absorption of arsenic in Spring Valley is unlikely to exceed four micrograms arsenic per day.

CONVERSION OF SOIL CONCENTRATION TO DAILY DOSAGE EQUIVALENT

What does ppm Arsenic in soil mean?

ppm = parts per million = 1 part arsenic per one million parts of soil.

1ppm Arsenic in soil = 1 ug Arsenic per 1 gm soil
10 ppm Arsenic in soil = 10 ug Arsenic per 1 gm soil
40 ppm Arsenic in Soil = 40 ug Arsenic per 1 gm soil

The EPA assumes that adults ingest 100 milligrams of soil per day, which is equivalent to a tenth of a gram of soil a day, and that children ingest twice as much. If the soil contained 10 ppm arsenic (10 ug arsenic/gm soil), then 100 mg of soil would contain 1 ug Arsenic and soil containing 40 ppm arsenic would yield an ingestion rate for adults of 4 ug/day. For most soils,

only about 20 % of the arsenic is absorbed. The rest remains bound to the soil and is processed and eliminated by the body. Thus, the absorbed dose is only one-fifth of the ingested dosage. Thus, an exposure to soil of 200 ppm would be necessary under general circumstances to reach an absorbed dosage of 4 microgram per day for adults or 8 micrograms per day for children. At Anaconda, Montana, the most intensely studied arsenic environment in the world, EPA determined a clean-up level of 250 ppm arsenic for the residential areas and higher for the non-residential areas. Superfund arsenic clean-up goals are often between five and 65 ppm.

Spring Valley Health Concerns

A number of health concerns with respect to arsenic exposure have been raised by members of the Spring Valley community. The tables below present the dosage at which the literature indicates an association. One table is for cancer effects, and the other is for non-cancer effects. Their bases are discussed in greater detail below.

Cancer	**Dosage**
Brain Cancer	No known association
Breast Cancer	No known association
Bone Cancer	No known association
Lung Cancer	> 2.5 mg/day
Bladder Cancer	>1.5 mg/day
Skin Cancer	> 0.6 mg/day
Leukemia	Not indicated
Lymphoma	Not indicated
Multiple Myeloma	Not indicated

Non-Cancer	Dosage
Anemia	3 mg/day (yes) 0.5 mg/day (no)
Myelofibrosis	
Rash	10 mg/day
Respiratory	0.5 mg/day
Allergy/Asthma	No known association
Autoimmune	No known association
Neurologic	>0.3 mg/day
Birth Defects	No known association

Cancer:

The scientific literature does not identify an association between arsenic exposure and cancers of the brain, breast and bone. Although there is an association between arsenic and lung, bladder, and skin cancers, the daily exposure levels at which these are attributed to arsenic are well below the levels found in Spring Valley.

The reports of individual cases of leukemia, lymphoma, or multiple myeloma do not indicate the exposure level, so a quantitative comparison to Spring Valley is not possible.

Non-Cancer:

With regard to anemia and other non-cancer effects on the blood, a study from China found anemia in those with ingestion levels of 3 milligrams per day, but no cases of anemia was found in those ingesting half a milligram per day. In the U.S. and Canada, environmental exposure between 100-200 micrograms did not find any effects.

An ingestion of 10 milligrams of arsenic is known to cause a skin condition called chronic arsenicism, which is a severe condition characterized by the thickening of the palms of the hands and soles of the feet and marked changes in the pigmentation on the trunk. Currently, no cases of Spring Valley residents show symptoms of this nature.

Data from a Chinese environmental study found an association between half a milligram or 500 micrograms of arsenic and an increase in cough, sputum production and other respiratory symptoms. No association with any other respiratory issues was found in dosages below that level.

No evidence of association between arsenic and allergies, asthma or autoimmune conditions has been reported.

An association between arsenic and peripheral neuropathy is found in dosages greater than 0.3 milligrams or 300 micrograms per day.

The issue of arsenic and birth defects has been well studied, and no association with environmental arsenic exposure has been found. Some studies have indicated reproductive effects (spontaneous abortions, stillbirths, and premature births) among women consuming water containing high levels of arsenic (240 ug/L or up to 800 ug/L), levels far above the potential exposures at Spring Valley.

If others are aware of findings I have not mentioned, I would appreciate receiving copies of such studies (Steve@CEOH.com).

SUMMARY

The dose related health effects of arsenic exposure can be summarized as below.

Dosage	**Effect**
> 0.1 grams/day	poisonous
> 0.6 milligrams/day	cancerous
<100 micrograms/day	no known effects

Arsenic is a known toxin and carcinogen. A review of the available literature indicates that the levels of arsenic to which residents of Spring Valley are exposed are not at the levels associated with the known effects of arsenic. There may be some unique sites or soils not readily available for contact that might need special consideration. A number of Agency reviews on health effects of arsenic are listed below and were presented at the meeting.

References:

EPA IRIS (Integrated Risk Information System) on Inorganic Arsenic (4/10/98)

EPA Exposure Factors Handbook (Feb 1999)

ATSDR Toxicological Profile on Arsenic (Sept 2000)

EPA Arsenic Standard (January 22, 2001)

THANK YOU