Health Effects from Drinking Water Contaminants
Arsenic
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Graduate School of Public Health
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A question of hierarchy of water health risks
The Safe Drinking Water Act (SDWA) was originally passed by Congress in 1974 to protect public health by regulating the nation's public drinking water supply. The law was amended in 1986 and 1996 and requires many actions to protect drinking water and its sources: rivers, lakes, reservoirs, springs, and ground water wells. (SDWA does not regulate private wells which serve fewer than 25 individuals.)

SDWA authorizes the United States Environmental Protection Agency (US EPA) to set national health-based standards for drinking water to protect against both naturally-occurring and man-made contaminants that may be found in drinking water. US EPA, states, and water systems then work together to make sure that these standards are met.

EPA seeks public comment on possible drinking water contaminants

Release date: 02/20/2008

(Washington, D.C. - Feb. 20, 2008) EPA is asking for public comment on a list of 104 possible drinking water contaminants that may need to be regulated in the future to ensure the continued protection of drinking water. Under the Safe Drinking Water Act, EPA includes on the draft Contaminant Candidate List (CCL) currently unregulated contaminants that are known or anticipated to occur in public water systems and which may require regulation. This draft CCL, which is the third such listing, lists 93 chemical contaminants or groups and 11 microbes, and describes the process and basis for selecting these contaminants.

“EPA is casting a broader scientific net for potential regulation of chemicals and microbes in drinking water,” said Assistant Administrator for Water Benjamin H. Grumbles. “EPA’s proposed list of priority contaminants will advance sound science and public health by targeting research on certain chemicals and microbes and informing regulators on how best to reduce risk.”

The CCL process was established by the 1996 Amendments to the Safe Drinking Water Act as a mechanism to determine if new regulations are needed to protect drinking water. Under this process EPA conducts extensive research into the occurrence and health effects of the listed contaminants before issuing new regulations or standards. In developing the draft CCL 3, the agency implemented a new approach for selecting contaminants which builds upon evaluations used for previous lists and is based on substantial expert input early in the process and recommendations from a larger number of different groups including stakeholders, the National Research Council and the National Drinking Water Advisory Council.

The draft list includes chemicals used in commerce, pesticides, biological toxins, disinfection byproducts, and waterborne pathogens. The agency evaluated approximately 7,500 chemicals and microbes and selected 104 candidates for the final draft list based on their potential to pose health risks through drinking water exposure. The comment period is open for 90 days beginning the day of publication in the Federal Register.
EPA revisits water contaminant standards every six years to evaluate whether the public is protected.

**Lead and Copper Rule: A Quick Reference Guide**

**Overview of the Rule**

<table>
<thead>
<tr>
<th>Title</th>
<th>Lead and Copper Rule (LCR), 58 FR 26480 - 26486, June 7, 1991</th>
</tr>
</thead>
<tbody>
<tr>
<td>Purpose</td>
<td>Protect public health by mitigating lead (Pb) and copper (Cu) levels in drinking water, primarily by reducing water corrosivity. Pb and Cu enter drinking water mostly from corrosion of Pb and Cu-containing plumbing materials.</td>
</tr>
<tr>
<td>General Description</td>
<td>Establishes action level (AL) of 0.015 mg/L for Pb and 1.3 mg/L for Cu, based on 98th percentile level of tap water samples. An AL exceedance is not a violation but can trigger other requirements that include water quality parameter (WQP) monitoring, lead service line replacement (LSLR), public education, and lead service line replacement (LSLR).</td>
</tr>
<tr>
<td>Utilities Cured</td>
<td>All community water systems (CWSs) and non-transient, non-community water systems (NTNCWSs) are subject to the LCR requirements.</td>
</tr>
</tbody>
</table>

**Public Health Benefits**

Reduction in risk of exposure to Pb that can cause damage to brain, red blood cells, and kidneys, especially for young children and pregnant women. Interferes with development, liver or kidney damage, and complications of Wilson's disease in genetically predisposed people.

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**Risk Assessment in the Federal Government:**

1. **Hazard Identification**
   - What health problems are caused by the pollutant?

2. **Dose-Response Assessment**
   - What are the different health problems at different levels of exposure?

3. **Exposure Assessment**
   - How much of the pollutant do people take in during a time period?

4. **Risk Characterization**
   - What is the extra risk of health problems in the exposed population?
Risk of arsenic in drinking water

Arsenic regulations in the United States

Compliance date for 10 ppb arsenic standard (MCL) was January 2006

Compliance has put a great deal of pressure on municipalities to implement sophisticated removal systems.

This Standard only applies to sources of drinking water that serve 25 or more people.
II.B.1. Summary of Risk Estimates

Oral Slope Factor — 1.5E+0 per (mg/kg)/day
Drinking Water Unit Risk — 5E-5 per (ug/L)
Extrapolation Method — Time- and dose-related formulation of the multistage model (U.S. EPA, 1988)

Drinking Water Concentrations at Specified Risk Levels:

<table>
<thead>
<tr>
<th>Risk Level</th>
<th>Concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td>E-4 (1 in 10,000)</td>
<td>2E+0 ug/L</td>
</tr>
<tr>
<td>E-5 (1 in 100,000)</td>
<td>2E-1 ug/L</td>
</tr>
<tr>
<td>E-6 (1 in 1,000,000)</td>
<td>2E-2 ug/L</td>
</tr>
</tbody>
</table>

II.B.2. Dose-Response Data (Carcinogenicity, Oral Exposure)

The Risk Assessment Forum has completed a reassessment of the carcinogenicity risk associated with ingestion of inorganic arsenic (U.S. EPA, 1988). The data provided in Tseng et al., 1968 and Tseng, 1977 on about 40,000 persons exposed to arsenic in drinking water and 7500 relatively unexposed controls were used to develop dose-response data. The number of persons at risk over three dose intervals and four exposure durations, for males and females separately, were estimated from the reported prevalence rates as percentages. It was assumed that the Taiwanese persons had a constant exposure from birth, and that males consumed 3.5 L drinking water/day and females consumed 2.0 L/day. Doses were converted to equivalent doses for U.S. males and females based on differences in body weights and differences in water consumption and it was assumed that skin cancer risk in the U.S. population would be similar to the Taiwanese population. The multistage model with time was used to predict dose-specific and age-specific skin cancer prevalence rates associated with ingestion of inorganic arsenic; both linear and quadratic model fitting of the data were conducted. The maximum likelihood estimate (MLE) of skin cancer risk for a 70 kg person drinking 2 L of water per day ranged from 1E-3 to 2E-3 for an arsenic intake of 1 ug/kg/day. Expressed as a single value, the cancer unit risk for drinking water is 5E-5 per (ug/L). Details of the assessment are in U.S. EPA (1988).

Diseases caused by chronic arsenic exposures

- Hyperkeratosis
- Skin cancer
- Lung cancer
- Bladder cancer
- Cardiovascular disease
- Liver disease
- Liver cancer
- Lung disease
- Reproductive Dysfunction
- Neurological disease
- Epigenetic disease
Arsenic regulations in the United States

The Main Questions that require good environmental epidemiological and risk assessment studies to answer are:

- Is the standard that is based on 25-30 year old studies in a single population adequate to protect health in the USA?
- What health endpoints are protected by the standards?
- Has the reduction in the standard from 50 to 10 ppb improved health?

This Standard only applies to sources of drinking water that serve 25 or more people.

Are there adequate data to determine risk in the USA.

Environmental Health
Use of NHANES (or other large data bases) versus prospective population studies.

- Routes of exposures
- Individual Exposures
- Individual characteristics
- Tracking
- Numbers of exposed individuals

Arsenic in drinking water worldwide

<table>
<thead>
<tr>
<th>Arsenic levels</th>
<th>2004 or latest available data</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elevated levels of arsenic (over 50 µg/l) reported in water</td>
<td>★-health has been reported due to arsenic-contaminated water</td>
</tr>
</tbody>
</table>

![Map of Arsenic in Drinking Water Worldwide]
The global human health impact of arsenic in drinking water is probably underestimated.

Arsenic in Bangladesh drinking water: A WHO generated environmental health problem
Geological causes of UNICEF generated arsenic exposures

- Naturally high levels of arsenic in granite due to tectonic plate collisions.
- Source of commercial arsenic in 1800’s and early 1900’s.
- Approximately 40% of the population uses private unregulated wells as a water source.
- 10-20% of wells tested are in excess of 10 ppb standard.
- Increased cancer rates for certain skin and lung cancers associated with arsenic consumption.
- Increased bladder cancer risk in ever smokers and smokers associated with arsenic consumption.

New Hampshire: the arsenic state
Could Pennsylvania’s rural communities be at greater risk for arsenic induced diseases?

Reconnaissance of Arsenic Concentrations in Ground Water From Bedrock and Unconsolidated Aquifers in Eight Northern-Tier Counties of Pennsylvania

By Christian J. Lee and Dawn D. Rhodes

http://pubs.usgs.gov/of/2006/1376/

Arsenic in Bangladesh drinking and agricultural water

British Geological Survey and the Department of Public Health Engineering
Arsenic accumulates in rice and grains

Arsenic and new rice. Cotton pesticides still contaminate fields now used for food crops
Environmental Health Perspectives Volume 115, Number 6, June 2007

Rice Not So Nice for Babies?
Environmental Pollution volume 152, 2008

Breast-feeding Protects against Arsenic Exposure in Bangladeshi Infants
Britta Keidingt, Sophie Moore, et al.
Environmental Health Perspectives • volume 116 • number 7 • July 2008
**Arsenic: water to waste to cooking fuel to inhalation**

In some Indian villages dried cow dung is used as fuel in domestic ovens.

<table>
<thead>
<tr>
<th>Media</th>
<th>Contaminated (75 ppb)</th>
<th>Non-contaminated (&lt;3 ppb)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cow dung</td>
<td>6073 mg/kg</td>
<td>1604 mg/kg</td>
</tr>
<tr>
<td>Ash</td>
<td>3887 mg/kg</td>
<td>148 mg/kg</td>
</tr>
<tr>
<td>particulate</td>
<td>0.32 mg/m³</td>
<td>0.012 mg/m³</td>
</tr>
<tr>
<td>Cow urine</td>
<td>2084 mg/L</td>
<td>53 mg/L</td>
</tr>
</tbody>
</table>

*J. Environmental Monitoring 9:1067-1070, 2007*

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**Solutions to arsenic exposure in Bangladesh and India**

Arsenic cannot be removed by charcoal filtering. It must be removed following anion exchange and affinity filtration.

Abul Hussam
2007 Grainger prize
Unfortunately, it takes resources to sustain prevention and remediation.

Defunct. Numerous arsenic-removal units installed by the West Bengal government no longer work due to lack of maintenance.
One Village provides complete dose response: need for exposure assessment

Monitoring for Arsenic Exposure

- Toenails (Mees lines) and hair: digestion then NAA, AA, AF or ICP-MS
  - Advantage: long term exposure history
  - Disadvantage: no information regarding recent exposures, no speciation.
- Blood: ICP-MS
  - Advantage: measure of current exposure, accurate speciation of bioavailable forms.
  - Disadvantage: no long term history, invasive.
- Urine: AA, AF, ICP-MS
  - Advantage: measure of recent or current exposure, abundant sample.
  - Disadvantage: no long term history, metabolites change in bladder.
- Speciation is essential for determining disease risk.
  - iAs(III), iAs(V), MMA(III), MMA(V), DMA(III), DMA(V), TMA
  - Column or HPLC separation and then AF or ICP-MS
Risk of skin lesions from arsenic in drinking water

Correlation Between Urinary Creatinine-adjusted As and Well Water As among 9,374 Subjects

Joseph Graziano, Mailman School of Public Health, Columbia University
Humans convert inorganic arsenic to methylated metabolites.

Ingestion of water containing 200 µg As\textsuperscript{V} leads to excretion of As\textsuperscript{V}, As\textsuperscript{III}, methyl As and dimethyl As in urine.

Methylation genotype and disease prevalence?

David J. Thomas, Ph.D.
Experimental Toxicology Division, NHEERL
U.S. Environmental Protection Agency
Workshop on Arsenic Research and Risk Assessment
NCTC, Shepherdstown, WV
June 1, 2006
What is the toxicological significance of the methylation of inorganic arsenic?

- The effects of total arsenic do not always appear to be dose responsive.
- As\text{III} is more cytotoxic than As\text{V}, since As\text{III} enters cells more freely. Once inside, both forms can have effects; however, all trivalent arsenicals are more potent than corresponding pentavalent forms.
- Because MAs\text{V} and DMAs\text{V} are less acutely toxic than is inorganic As\text{III}, methylation of inorganic As has been commonly considered a mode of detoxification.
- However, at the cellular level, MAs\text{III} and DMAs\text{III} are more potent toxicants than iAs\text{III}.
- Current epidemiological studies suggest that those with higher levels of MAs\text{III} have the highest risk for disease or worse disease outcome.

Gastronomical Delight
Micronutrients Protect against Arsenic Lesions

A diet rich in B vitamins and antioxidants may counter some of the effects of chronic arsenic ingestion

Effect of nutrition on arsenic biomarkers

Folate, Homocysteine, and Arsenic Metabolism in Arsenic-Exposed Individuals in Bangladesh

Mary V. Gambhir, Xinrui Liu, Shehaf Almon, J. Richard Prince, Vincent B. Evers, Paul F. Wark, Joseph E. Levy, Shehaf Almon, Maunul Islam, Fereshe Parvez, Hamidul Islam, and Joseph B. Cucuzzella

Department of Environmental Health Sciences, Department of Nutrition, and Department of Epidemiology, Mailman School of Public Health, Columbia University, New York, NY; Columbia University of Pharmacology, College of Physicians and Surgeons, Columbia University, New York, NY, USA.

Environmental Health Perspectives • Volume 113 Issue 12 (December 2005)

Arsenic Metabolism

Genetic variants in As3MT (arsenite methyltransferase) may account for differences in risk.


Folic acid supplementation lowers blood arsenic

Mary V. Gambhir, Xinrui Liu, Vincent B. Evers, Paul F. Wark, Joseph E. Levy, Shehaf Almon, Maunul Islam, Fereshe Parvez, Hamidul Islam, and Joseph B. Cucuzzella

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Folate Metabolism

Genetic variants in As3MT (arsenite methyltransferase) may account for differences in risk.
### Blood Selenium Level and Risk of Skin Lesions

<table>
<thead>
<tr>
<th>Blood Selenium Level (µg/L)</th>
<th>Total N</th>
<th>Adjusted Hazard Ratios (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 131.8</td>
<td>222</td>
<td>1.0</td>
</tr>
<tr>
<td>131.9-144.3</td>
<td>222</td>
<td>0.71 (0.42-1.21)</td>
</tr>
<tr>
<td>144.5-156.3</td>
<td>221</td>
<td>0.54 (0.32-0.91)</td>
</tr>
<tr>
<td>156.4-169.8</td>
<td>222</td>
<td>0.54 (0.31-0.93)</td>
</tr>
<tr>
<td>169.9-262.6</td>
<td>221</td>
<td>0.53 (0.31-0.90)</td>
</tr>
</tbody>
</table>

*RRs were controlled for age, gender, BMI, and smoking status.

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### Determinants of Arsenic Metabolism: Blood Arsenic Metabolites, Plasma Polypeptide, Cobalamin, and Homocysteine Concentrations in Maternal-Newborn Pairs

**Mimi Kim,† Mary Beban,‡ Vivian Blackwood,† Yosheta Liu,‡ Brian Levy,‡ Zhengyi Cheung,‡ Alice Brown,§ Green,§ Mohammad Ferez,* Rehmat Ramzan,* Richard Wood,* and Joseph Graziano,** Columbia University

![Graphs showing correlations between variables](image-url)

- **Figure 1:** Correlations between and under-reduced blood arsenic (µg/L) total blood arsenic (µg/L), blood arsenic (µg/L), and adjusted blood arsenic (µg/L) and the adjusted sum of blood arsenic metabolites (BMAs) (µg/L) and BAs (µg/L).
- **Figure 2:** Correlations between and under-reduced blood arsenic (µg/L) and the adjusted sum of blood arsenic metabolites (BMAs) (µg/L) and BAs (µg/L).

Environmental Health Perspectives - volume 115 issue 10 December 2007
Arsenic in water supply
Risk of Acute myocardial infarction
In males

Increased Mortality from Lung Cancer and Bronchiectasis in Young Adults after Exposure to Arsenic in Utero and in Early Childhood

Allan H. Smith,1 Guillermo Marshall,1 Yan Yuan,1 Caterina Ferreccio,1 Jane Liao,1 Michael N. Bates,1,3 and Steve Selvin2

Environmental Health Perspectives • volume 114 number 8 August 2006

Figure 2. COPD SMRs for Antofagasta/Majillones for individuals 30–49 years of age, pooled.
Water Arsenic Exposure and Children’s Intellectual Function in Arailhazar, Bangladesh

Gail A. Wiesner 1,2, Xiaohua Liu 1,2, Faresqo Parvez 2, Habibul Ahsan 2, Pam Fuster-Litvak 2, Alexander van Gien 2, Vincent Silverstein 3, Henry J. Lubenow 4, Dengyi Chang 2, Rehmat Hussain 5, Hazrira Morshed 2, and Joseph H. Grizzle 4

Environmental Health Perspectives • volume 114 number 11 January 2006

Research | Children’s Health

Water Manganese Exposure and Children’s Intellectual Function in Arailhazar, Bangladesh

Gail A. Wiesner 1,2, Xiaohua Liu 1,2, Faresqo Parvez 2, Habibul Ahsan 2, Pam Fuster-Litvak 2, Alexander van Gien 2, Vincent Silverstein 3, Henry J. Lubenow 4, Dengyi Chang 2, Rehmat Hussain 5, and Joseph H. Grizzle 4

Environmental Health Perspectives • volume 114 number 11 January 2006

Arsenic and intelligence scores

200 children, 10.5 years old, 196 different wells

Water Arsenic Exposure and Children’s Intellectual Function in Arailhazar, Bangladesh

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Environmental Health Perspectives • volume 114 number 11 January 2006

Figure 1. Adjusted scores by quartiles of water As for Full-Scale, Performance, and Verbal raw scores. In each case, adjustments were made for maternal education and intelligence, type of housing, child height and head circumference, and access to television.

Figure 2. Continuous relationship between water As and Full-Scale raw score, adjusted as in Figure 1. The dotted perpendicular lines illustrate the loss in Full-Scale raw score associated with water As concentrations of 10 and 30 μg/L.
Neurological effects of metals in 10 year olds

Relationship Between Water Arsenic Concentrations and Intellectual Function

Relationship Between Water Manganese Concentrations and Intellectual Function

Could Pennsylvania's rural communities be at greater risk for arsenic induced diseases?

Reconnaissance of Arsenic Concentrations in Ground Water From Bedrock and Unconsolidated Aquifers in Eight Northern-Tier Counties of Pennsylvania

http://pubs.usgs.gov/of/2006/1376/
Summary

- There is a clear hierarchy of water contaminants that both contribute to and degrade public health.
- The EPA is the main regulatory body overseeing safe drinking water from public sources. Private sources that serve less than 25 individuals are not regulated.
- Environmental exposures to contaminants in drinking water do not cause disease equally in everyone exposed.
  - Differences due to age, genetics, life style (nutrition), etc.
- There is a great need for understanding the health effects and risks of low level contaminants and their interactions with other environmental factors to protect public health.
  - To accomplish adequate prospective studies of the true risks of contaminants like arsenic, the levels of active forms of the contaminant and its metabolites must be measured in exposed individuals and in the water they are drinking.

A question of hierarchy of water health risks