### Health Effects of Arsenic Exposure

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# Arsenic in Groundwater: An International Problem

- Taiwan
- China
- Chile
- Argentina
- Mexico
- United States

- India
- Bangladesh
- Nepal
- Vietnam
- Cambodia
- Mongolia
- Myanmar

### **Targets of Arsenic Toxicity**



# **Known Health Effects of Arsenic**

- "Early/Intermediate""
  - Skin Lesions:
    - Melanosis
    - Keratosis
- Other Conditions
  - Diabetes mellitus
  - Non-malignant respiratory disease
  - Cognitive deficits
  - Black-foot Disease

- "Late"
  - Cancers:
    - Skin
    - Bladder
    - Lung
    - Liver
  - Cardiovascular:
    - Hypertension
    - Ischemic Heart Disease







Arsenic in 5,966 wells

## Cohort Recruitment and Follow-up: The HEALS Cohort



### **Cohort Recruitment and Follow-up**



### RESEARCH

# BMJ

# Arsenic exposure from drinking water and mortality from cardiovascular disease in Bangladesh: prospective cohort study

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#### ABSTRACT

**Objective** To evaluate the association between arsenic exposure and mortality from cardiovascular disease and to assess whether cigarette smoking influences the association.

**Design** Prospective cohort study with arsenic exposure measured in drinking water from wells and urine.

Setting General population in Araihazar, Bangladesh.

Participants 11 746 men and women who provided urine samples in 2000 and were followed up for an average of 6. 6 years.

Main outcome measure Death from cardiovascular disease.

other heart disease. In particular, the hazard ratio for the joint effect of a moderate level of arsenic exposure (middle third of well arsenic concentration 25.3-114.0  $\mu$ g/L, mean 63.5  $\mu$ g/L) and cigarette smoking on mortality from heart disease was greater than the sum of the hazard ratios associated with their individual effect (relative excess risk for interaction 1.56, 0.05 to 3.14; P=0.010).

Conclusions Exposure to arsenic in drinking water is adversely associated with mortality from heart dise especially among smokers.



#### INTRODUCTION

### **Arsenic Exposure and Impaired Lung Function** Findings from a Large Population-based Prospective Cohort Study



Faruque Parvez<sup>1</sup>, Yu Chen<sup>2</sup>, Mahbub Yunus<sup>3</sup>, Christopher Olopade<sup>4,5,6,7</sup>, Stephanie Segers<sup>2</sup>, Vesna Slavkovich<sup>1</sup>, Maria Argos<sup>4,5,6,7</sup>, Rabiul Hasan<sup>3</sup>, Alauddin Ahmed<sup>3</sup>, Tariqul Islam<sup>3</sup>, Mahmud M. Akter<sup>8</sup>, Joseph H. Graziano<sup>1</sup>, and Habibul Ahsan<sup>4,5,6,7</sup>

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*Rationale*: Exposure to arsenic through drinking water has been linked to respiratory symptoms, obstructive lung diseases, and mortality from respiratory diseases. Limited evidence for the deleterious effects on lung function exists among individuals exposed to a high dose of arsenic.

*Objectives*: To determine the deleterious effects on lung function that exist among individuals exposed to a high dose of arsenic.

Methods: In 950 individuals who presented with any respiratory symptom among a population-based cohort of 20,033 adults, we evaluated the association between arsenic exposure, measured by well water and urinary arsenic concentrations measured at baseline, and post-bronchodilator-administered pulmonary function assessed during follow-up.

Measurements and Main Results: For every one SD increase in baseline water arsenic exposure, we observed a lower level of FEV<sub>1</sub> (-46.5 ml; P < 0.0005) and FVC (-53.1 ml; P < 0.01) in regression models adjusted for age, sex, body mass index, smoking, socioeconomic status, betel nut use, and arsenical skin lesions status. Similar inverse relationships were observed between baseline urinary arsenic and FEV<sub>1</sub> (-48.3 ml; P < 0.005) and FVC (-55.2 ml; P < 0.01) in adjusted models. Our analyses also demonstrated a dose-related decrease in lung function with increasing levels of baseline water and urinary arsenic.

#### Am J Respir Crit Care Med. 2013

#### AT A GLANCE COMMENTARY

#### Scientific Knowledge on the Subject

Nonmalignant respiratory effects of low- to moderate-dose arsenic exposure are currently unknown.

#### What This Study Adds to the Field

This study documents, for the first time, that low- to moderatedose arsenic exposure may have deleterious nonmalignant respiratory effects.

has also been linked to nonmalignant respiratory effects including respiratory symptoms, chronic obstructive pulmonary disease, and respiratory disease mortality (9–12). However, the evidence of the effect of arsenic exposure on lung function is limited, especially at the low- to moderate-dose ranges. Several studies from arsenic-endemic areas of South Asia reported lower FEV<sub>1</sub>

### Fifty-Year Study of Lung and Bladder Cancer Mortality in Chile Related to Arsenic in Drinking Water

Guillermo Marshall, Catterina Ferreccio, Yan Yuan, Michael N. Bates, Craig Steinmaus, Steve Selvin, Jane Liaw, Allan H. Smith



Fig. 1. Map of Chile, showing regions II and V. The country is administratively divided into regions that are numbered from north to south.



Fig. 2. Lung and bladder cancer mortality rate ratios comparing region II with region V for men and women aged 30 and above, separately, as estimated by Poisson regression with smoothing. The shading represents the 95% confidence bands. The circles represent the mortality rate ratios plotted at the midpoint of each successive 3-year period. Histograms (gray lines) of the population-weighted average arsenic water concentrations for region II, from 1950 to 1994 in 5-year increments, are also presented (vertical axes at right).







Available online at www.sciencedirect.com



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### Transplacental carcinogenicity of inorganic arsenic in the drinking water: induction of hepatic, ovarian, pulmonary, and adrenal tumors in mice

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### Unusual Cancer Excess After Neonatal Arsenic Exposure From Contaminated Milk Powder <u>Takashi Yorifuji</u>, <u>Toshihide Tsuda</u> and <u>Philippe Grandjean</u>

"During the summer of 1955, mass arsenic poisoning of bottle-fed infants occurred in the western part of Japan because of contaminated milk powder (2). Although the milk powder was distributed countrywide, Okayama was the most severely affected prefecture, with a consumption of at least 33 500 one-pound cans of milk powder (3)..."

Mortality data in the survivors later in life: Excess skin and liver cancer, as well as pancreatic cancer and leukemia.

J. Natl. Cancer Inst. 102, 360-361.

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

#### Allan H. Smith,<sup>1</sup> Guillermo Marshall,<sup>2</sup> Yan Yuan,<sup>1</sup> Catterina Ferreccio,<sup>2</sup> Jane Liaw,<sup>1</sup> Ondine von Ehrenstein,<sup>1</sup> Craig Steinmaus,<sup>1,3</sup> Michael N. Bates,<sup>4</sup> and Steve Selvin<sup>4</sup>

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### Relationship Between Water Arsenic Concentrations and Intellectual Function



Wasserman et al, EHP, 2004



Wasserman et al, EHP 2004

### **Elevated groundwater arsenic from natural sources**



# A cross-sectional study of well water arsenic and child IQ in Maine schoolchildren

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#### Abstract

**Background:** In recent studies in Bangladesh and elsewhere, exposure to arsenic (As) via drinking water is negatively associated with performance-related aspects of child intelligence (e.g., Perceptual Reasoning, Working Memory) after adjustment for social factors. Because findings are not easily generalizable to the US, we examine this relation in a US population.

**Methods:** In 272 children in grades 3–5 from three Maine school districts, we examine associations between drinking water As (WAs) and intelligence (WISC-IV).

**Results:** On average, children had resided in their current home for 7.3 years (approximately 75% of their lives). In unadjusted analyses, household well WAs is associated with decreased scores on most WISC-IV Indices. With adjustment for maternal IQ and education, HOME environment, school district and number of siblings, WAs remains significantly negatively associated with Full Scale IQ and Perceptual Reasoning, Working Memory and Verbal Comprehension scores. Compared to those with WAs < 5  $\mu$ g/L, exposure to WAs ≥ 5  $\mu$ g/L was associated with reductions of approximately 5–6 points in both Full Scale IQ (p < 0.01) and most Index scores (Perceptual Reasoning, Working Memory, Verbal Comprehension, all *p*'s < 0.05). Both maternal IQ and education were associated with lower levels of WAs, possibly reflecting behaviors (e.g., water filters, residential choice) limiting exposure. Both WAs and maternal measures were associated with school district.

**Conclusions:** The magnitude of the association between WAs and child IQ raises the possibility that levels of WAs  $\geq$  5 µg/L, levels that are not uncommon in the United States, pose a threat to child development.

Keywords: Arsenic, Child intelligence, Well water, WISC-IV, Working Memory

Estimating IQ Points Lost Attributable to Water Arsenic (Maine): WAs > 5 ppb vs WAs <5ppb

Full Scale IQ was 4 points lower (p<0.01) in those children whose water arsenic was > 5 ppb!

Adjusted for HOME, number of children in the home, mother's IQ

Wasserman et al, Environ Health, 2014

## So what to do...?

## Test, Test, Test!



