



Welcome to the CLU-IN Internet Seminar

Arsenic - Health and Remediation Applications, Session 1

Sponsored by: NIEHS Superfund Research Program

Delivered: October 19, 2012, 2:00 PM - 4:00 PM, EDT (18:00-20:00 GMT)

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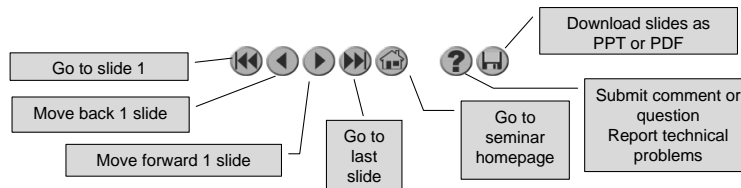
Moderator:

Joseph H. Graziano, Ph.D., program director Columbia University SRP Center (jg24@columbia.edu)

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Although I'm sure that some of you have these rules memorized from previous CLU-IN events, let's run through them quickly for our new participants.

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With that, please move to slide 3.



Emerging Issues: Arsenic Exposure

Joseph H. Graziano, Ph.D.

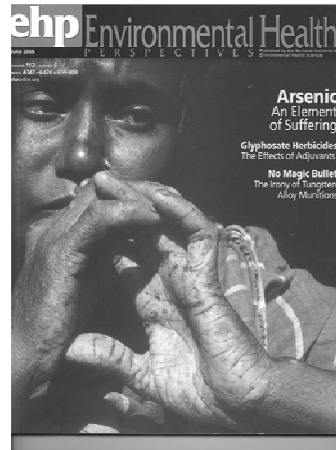
Program Director

Columbia University Superfund Research Program



Arsenic Presents a Major Public Health Problem

- Known carcinogen
 - Lung, liver, skin, bladder, kidney, and more
 - Early life exposure → increased risk as adults
- Multiple potential health effects on essentially every bodily system
 - Skin
 - Respiratory system
 - Cardiovascular system
 - Endocrine system (e.g., diabetes)
 - Immune system
 - Nervous system
 - And more...
- Arsenic rated #1 on the ATSDR 2011 Substance Priority List as the top chemical of concern as a public health hazard



History of SRP Arsenic Research

- SRP has been committed to arsenic research since the inception of SRP in 1987
- SRP takes a “soup-to-nuts” approach to arsenic research and development
 - Detection systems
 - Remediation
 - Identifying and reducing exposures
 - Health effects
 - Training and education of scientists and community partners
 - Community and government engagement
 - Transdisciplinary partnerships to solve problems in communities



History of SRP Arsenic Research

- Started funding arsenic research from SRP's inception in 1987
- Currently funding numerous arsenic-related projects at 19 university SRP research centers
- SRP researchers have published over 150 arsenic-related scientific papers since 2006



SRP Activities to Address Arsenic Challenges

- Identifying sources of contamination
- Characterizing toxic arsenic species and biomarkers of exposure in humans
- Identifying arsenic-related health effects and mechanisms of toxicity
- Exploring ways to mitigate health effects
- Engaging communities, government, and stakeholders as partners in solving real-life problems related to arsenic
- Training scientists in arsenic research



Variable Toxicity of Arsenic Metabolites

| | | LD ₅₀ |
|------------------------------|-------------------------|-----------------------------------|
| Inorganic Arsenic | | <u>LD₅₀ (Toxicity)</u> |
| •As ⁺³ | Arsenite | 8 mg/kg |
| •As ⁺⁵ | Arsenate | 22 mg/kg |
| Mammalian Metabolites | | |
| •MMA ⁺³ | Monomethylarsonous Acid | 2 mg/kg |
| •MMA ⁺⁵ | Monomethylarsonic Acid | 916 mg/kg |
| •DMA ⁺⁵ | Dimethylarsinic Acid | 648 mg/kg |
| Fish Metabolites | | |
| •AsB | Arsenobetaine | ~10,000 mg/kg |
| •AsC | Arsenocholine | |

What We Have Learned: Arsenic Exposure

- Naturally occurring element in Earth's crust
- Industrial sources (e.g., former smelters)
- Some types of chemically treated wood
- Some homeopathic remedies

- Drinking water
- Diet (e.g., rice)
- Soil and dust

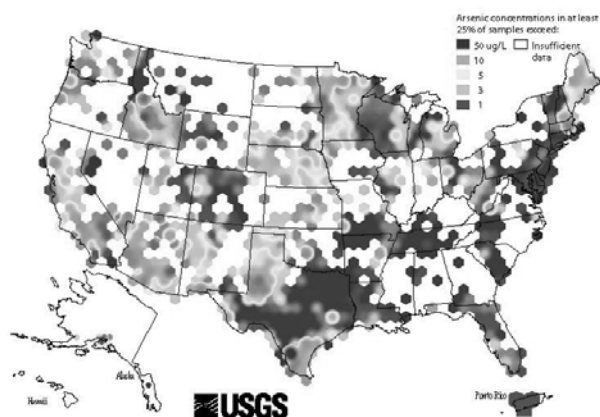
Arsenic in Groundwater: An International Problem

- Taiwan
- China
- Chile
- Argentina
- Mexico
- United States
- India
- Bangladesh
- Nepal
- Vietnam
- Cambodia
- Mongolia

U.S. EPA Maximum Contaminant Level for arsenic: 10 µg/L.
Concentrations reported in some regions of many of these countries reached over 3,000 µg/L.



Arsenic in Groundwater in the U.S.



Global and U.S. Activities Funded by NIEHS SRP

- **Large cohort studies**
 - Bangladesh
 - Chile
- **Global/U.S. studies of exposures and health effects**
 - Identify and reduce exposures
 - Identify health effects
 - Identify mechanisms of toxicity
 - Explore approaches to mitigating toxicity
- **Taking action at the local level**
 - Outreach to encourage private well testing
 - Helping provide safe water sources



SRP-funded Cohort Studies

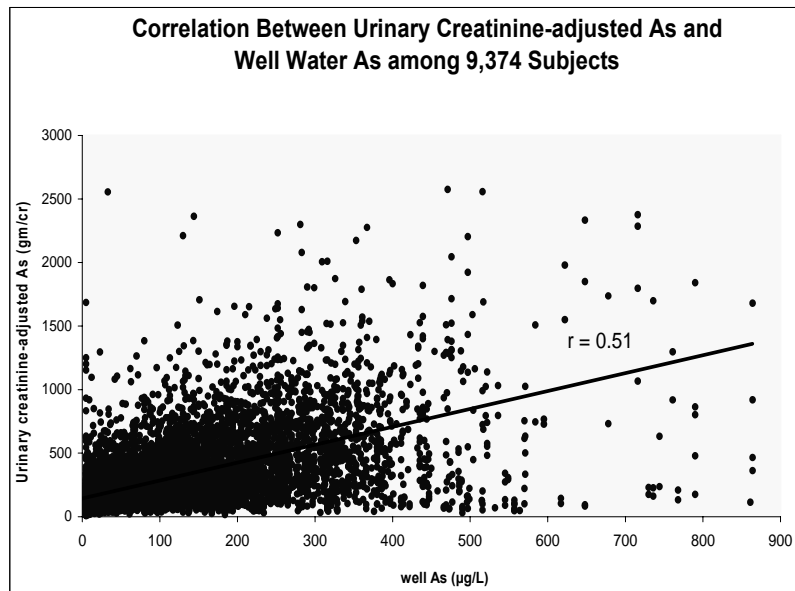
Health Effects and Longitudinal Study (HEALS) in Bangladesh

- Population exposed via tube wells
 - Revealing information about exposure, health effects, susceptibilities, and nutritional factors
-

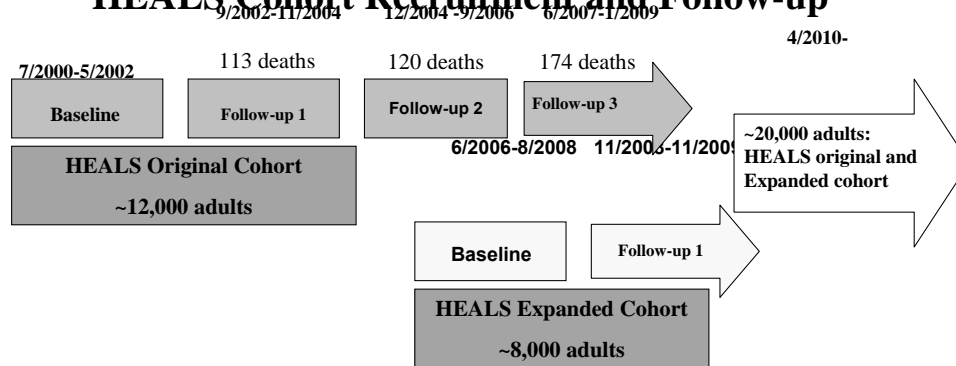
Chilean Cohort

- Population exposed for a defined period of time
- Population followed for >50 years
- Revealing information about health effects and latency





HEALS Cohort Recruitment and Follow-up



A validated verbal autopsy was used to classify deaths using WHO's ICD-10

All-cause and Chronic Disease Mortality

Table 2. Hazard ratio for mortality of HEALS participants in relation to baseline arsenic exposure, Bangladesh

| Arsenic exposure | No. of deaths | All-cause mortality* | | No. of deaths | Chronic disease mortality* | |
|---------------------------------|---------------|----------------------|------------|---------------|----------------------------|------------|
| | | HR | 95% CI | | HR | 95% CI |
| Well water arsenic (µg/L) | | | | | | |
| 0.1–10 | 74 | 1.00 | Referent | 58 | 1.00 | Referent |
| 10.1–50 | 90 | 1.34 | 0.99, 1.82 | 69 | 1.33 | 0.94, 1.87 |
| 50.1–150 | 98 | 1.09 | 0.81, 1.47 | 83 | 1.22 | 0.87, 1.70 |
| 150.1–854 | 131 | 1.68 | 1.26, 2.23 | 101 | 1.68 | 1.21, 2.33 |
| P for trend | | 0.003 | | | 0.005 | |
| Daily arsenic dose (µg/day) | | | | | | |
| 0.041–35.0 | 87 | 1.00 | Referent | 66 | 1.00 | Referent |
| 35.1–163.0 | 97 | 1.10 | 0.83, 1.47 | 80 | 1.21 | 0.88, 1.67 |
| 163.1–401.0 | 91 | 1.09 | 0.81, 1.46 | 76 | 1.22 | 0.88, 1.71 |
| 401.1–4898.0 | 118 | 1.54 | 1.17, 2.04 | 89 | 1.58 | 1.15, 2.18 |
| P for trend | | 0.004 | | | 0.007 | |
| Urinary total arsenic (µg/g Cr) | | | | | | |
| 7.0–105.0 | 83 | 1.00 | Referent | 64 | 1.00 | Referent |
| 105.1–199.0 | 96 | 1.07 | 0.80, 1.43 | 80 | 1.17 | 0.84, 1.62 |
| 199.1–352.0 | 100 | 1.22 | 0.91, 1.63 | 83 | 1.37 | 0.98, 1.90 |
| 352.1–5000.0 | 105 | 1.45 | 1.09, 1.94 | 77 | 1.47 | 1.05, 2.06 |
| P for trend | | 0.008 | | | 0.01 | |

HR=hazard ratio; CI=confidence interval; Cr=creatinine.

* Multivariate estimates adjusted for age, sex, body mass index, systolic blood pressure, education, and smoking status.

Early Life Exposure Can Have Effects into Adulthood



- Increased infant mortality
- Reduced birthweight
- Increased infections during infancy and childhood
- Neurological and motor impairments in children
- Increased cancer risks as children (liver cancer)
- Increased cancer risks as adults (lung, bladder, and kidney cancer)

Vahter 2008.
Basic Clin Pharmacol Toxicol 102(2):204.



Early Life Exposure Can Have Life-long Effects

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,² Yan Yuan,¹ Catterina Ferreccio,² Jane Liaw,¹ Ondine von Ehrenstein,¹ Craig Steinmaus,^{1,3} Michael N. Bates,⁴ and Steve Selvin⁴

¹Arsenic Health Effects Research Program, University of California, Berkeley, California, USA; ²Pontificia Universidad Católica de Chile, Santiago, Chile; ³Office of Environmental Health Hazard Assessment, California Environmental Protection Agency, Oakland, California, USA; ⁴School of Public Health, University of California, Berkeley, California, USA

Environ Health Perspect 114:1293–1296 (2006).
doi:10.1289/ehp.8832 available via <http://dx.doi.org/>



SRP: Making a Difference in the Community

Columbia University SRP in Bangladesh

- Installation of >150 deep community wells that provide low-arsenic water to thousands of residents
- Providing primary medical care to the >20,000 HEALS participants





Inter-School Art Contest

School-Based Educational Intervention in Araihaaz, Bangladesh

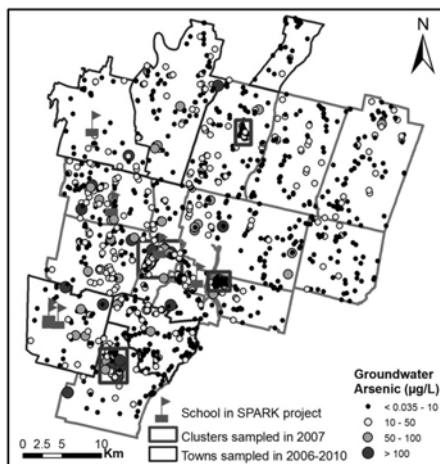


SRP: Making a Difference in the Community

Columbia University SRP in Maine

- Established a Community Engagement Core
- Disseminating knowledge about the hazards of local well water arsenic contamination
- Disseminating technologies to filter arsenic

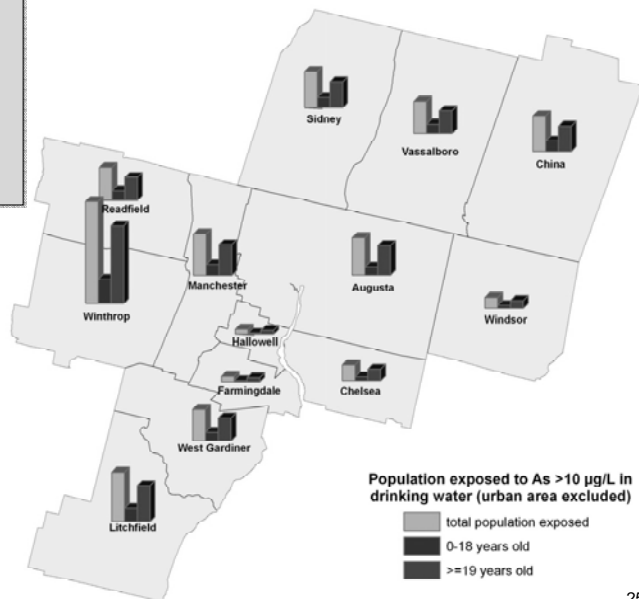
Community Engagement in Maine



- Arsenic concentrations in 1,428 domestic wells from 17 towns central Maine
- 31% of the wells contain >10 ug/L arsenic (source: Yang 2010).
- Columbia Community Engagement Core aims to double the testing and treatment rate for arsenic in these towns. A survey is underway to determine the current rates.

Assessment of Exposures to High Concentrations of Arsenic in Well Water in Maine

[As] >10 ug/L in Maine
Total Exposed = 12,458
0-18 yr olds = 3272
(2000 Census)

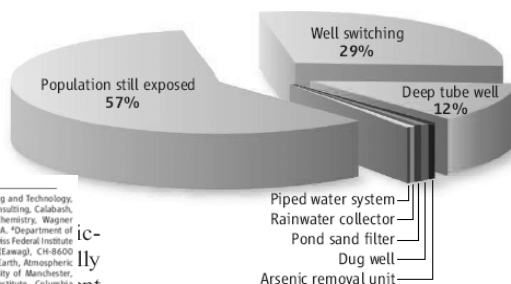


EPIDEMIOLOGY

Ensuring Safe Drinking Water in Bangladesh

M. F. Ahmed,¹ S. Ahuja,² M. Alauddin,³ S. J. Hug,⁴ J. R. Lloyd,⁵ A. Pfalt,⁶ T. Pichler,⁷ C. Salnikov,⁸ M. Stute,^{1,10} A. van Geen^{10*}

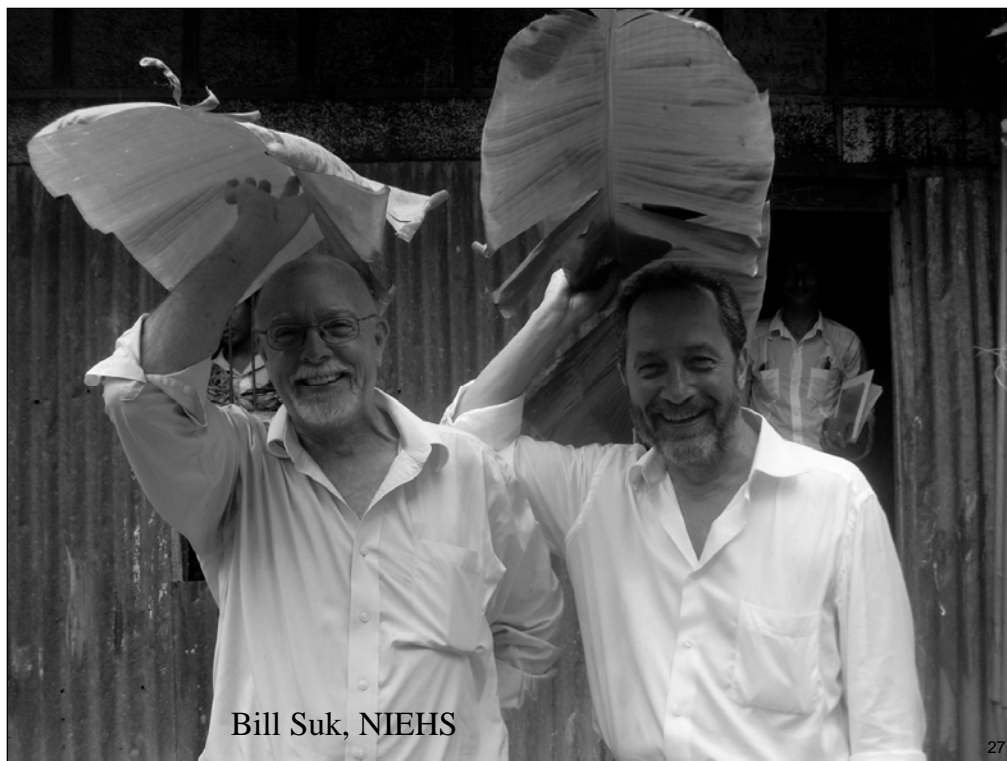
Excessive levels of arsenic in drinking water is a vast health problem in Southeast Asia. Several viable approaches to mitigation could drastically reduce arsenic exposure, but they all require periodic testing.



¹Bangladesh University of Engineering and Technology, Dhaka-1000, Bangladesh. ²Ahuja Consulting, Calabash, NC 28467, USA. ³Department of Chemistry, Wagner College, Staten Island, NY 10301, USA. ⁴Department of Water Resources and Drinking Water, Swiss Federal Institute of Aquatic Science and Technology (Eawag), CH-8600 Dübendorf, Switzerland. ⁵School of Earth, Atmospheric and Environmental Sciences, University of Manchester, Manchester M13 9PL, UK. ⁶Earth Institute, Columbia University, New York, NY 10027, USA. ⁷Department of Geology, University of South Florida, Tampa, FL 33620, USA. ⁸Environmental Toxicology, University of California, Santa Cruz, Santa Cruz, CA 95064, USA. ⁹Department of Environmental Sciences, Barnard College, Columbia University, New York, NY 10027, USA. ¹⁰Lamont-Doherty Earth Observatory of Columbia University, Palisades, NY 10964, USA.

*Correspondence to: avangeen@ldeo.columbia.edu

Impact of arsenic mitigation in Bangladesh (SOM Text). The initially exposed population has been estimated at 28 to 35 million relative to the local standard of 50 µg per liter arsenic in drinking water (3).



Atmospheric transport of metal and metalloid contaminants by dust and aerosol from mining operations

E.A. Betterton, J.C. Csavina, O. Felix, K. Rine, J. Field, M. Russell, M. Stovern, P. Saliba, M.P. Taylor, Scott White, Juliana Gil, Raina Meier, A.E. Sáez

Risk e-Learning Seminar, 19 October 2012



Mt. Isa, Australia



Hayden , AZ



Iron King tailings, Dewey-Humboldt, AZ



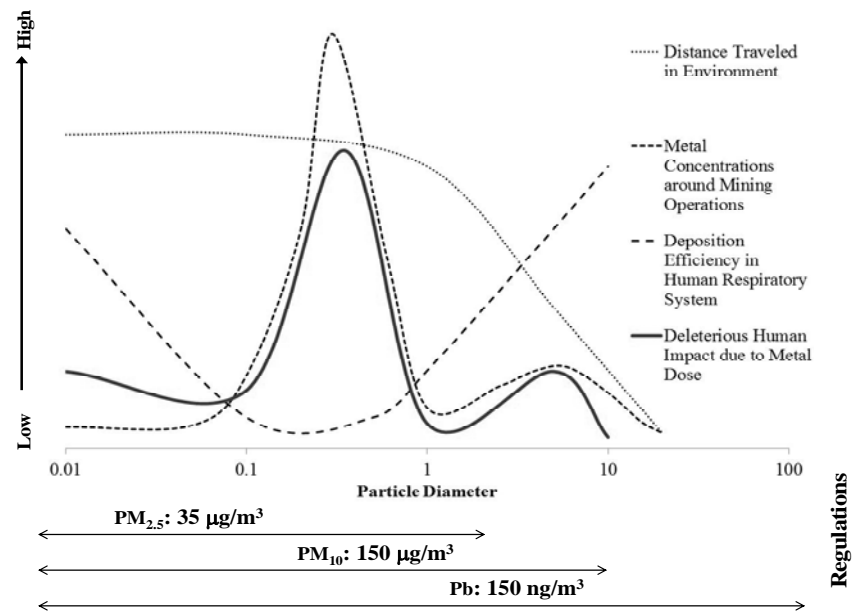
Mining operations that generate dust and aerosol

- Crushing, grinding, mine tailings management
 - Coarse particles $>2.5 \mu\text{m}$
mechanical action
 $\tau \approx \text{min to hours}$
- Smelting, Refining
 - Ultra-fine $<0.1 \mu\text{m}$
gas - particle conversion
 $\tau \approx \text{sec to min}$
 - Accumulation $0.1\text{-}2.5 \mu\text{m}$
coagulation of ultrafine and condensation growth
 $\tau \approx 10 \text{ days}$



Emissions from mining activities

Why do we care about mining operation particles?



Methods

TSP (Total Suspended Particulate)

- Mass concentration for all ambient particulate

MOUDI (Micro-Orifice Uniform Deposit Impactor)

- Size fractionated aerosols in 11 different sizes ranging from 18 to 0.056 μm

Dustrak Aerosol Monitor

- Optical mass measurements of aerosols

SMPS (Scanning Mobility Particle Sizer)

- Number concentration of aerosols $<1 \mu\text{m}$

Weather Station

- Wind speed/direction, temperature, relative humidity

Metal and metalloid content: ICP-MS after extraction with *aqua regia*



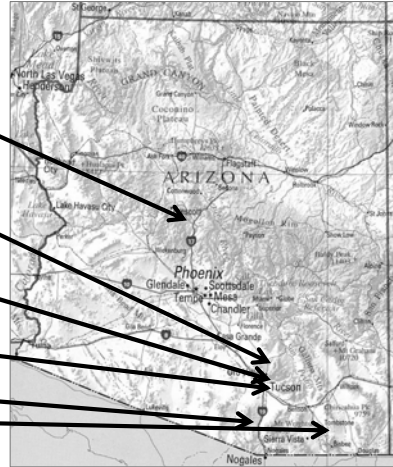
Arizona Field Sites

■ Contaminated Sites

- **Iron King** - Inactive copper mine and smelter; now a Superfund site (arsenic, lead contaminated tailings)
- **Hayden & Winkelman** - ASARCO active copper mine with smelter (arsenic, lead contaminated soil; airborne lead)

■ Comparison Sites

- **Mount Lemmon** - Remote background
- **Tucson** - Urban
- **Green Valley** - Active copper mine; "clean" tailings
- **Wilcox Playa** - Natural dust source

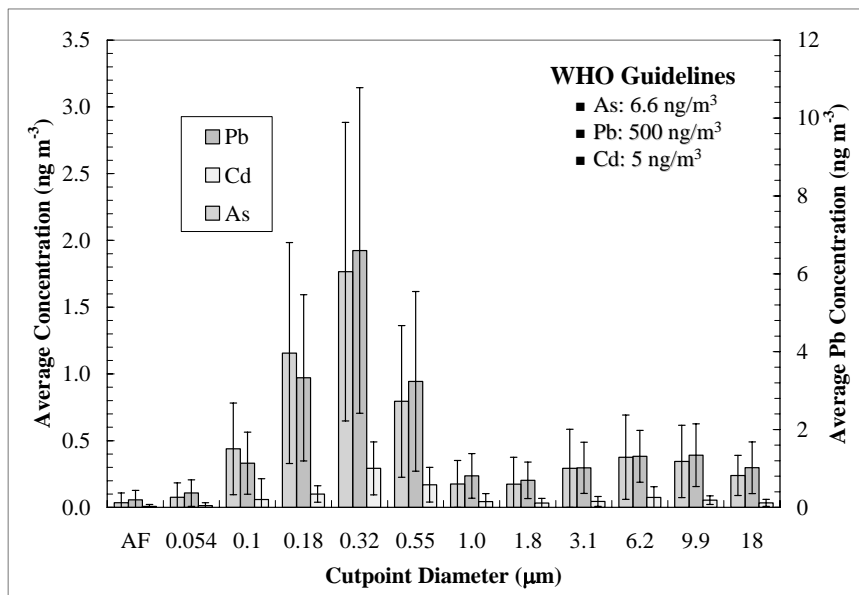


Australia Field Sites

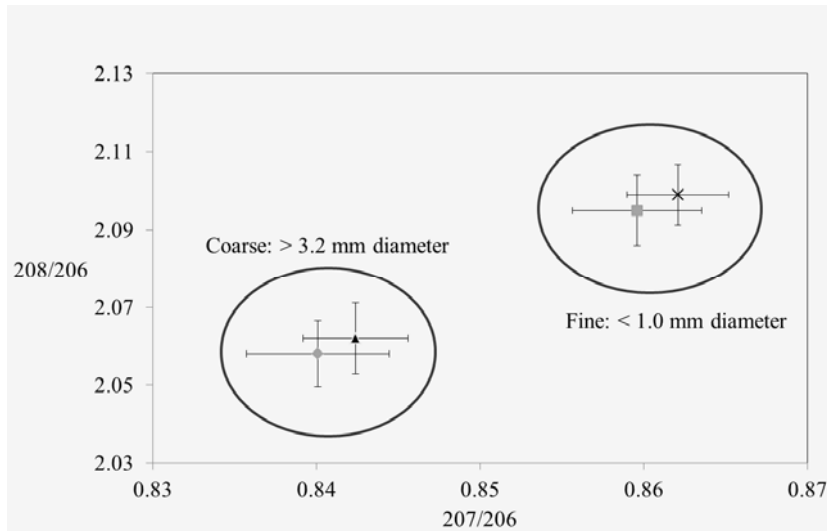
- **Mount Isa, Qld Australia**
XSTRATA Cu, Zn, Pb, and Ag
mine with smelter
2010/2011 airborne emissions:
As =44,000 kg and Pb =160,000 kg
- **Port Pirie, SA Australia**
Nystar Pb smelter
2010/2011 airborne emissions:
As =1,100 kg and Pb =44,000 kg
- **Sydney, NSW Australia**
urban reference site



Hayden - MOUDI Results 2009 Annual Average



Hayden Pb Isotopes by Size Fraction All Wind Directions



35

This graph shows that the isotope ratios are different for fine and coarse particles, it is known that smaller particles are related with process involving high temperatures, also in the literature was found that higher ratios are related with mining and smelting activities. From this graph we can conclude that the source of lead in fine and coarse particles is different, we have at least two sources.

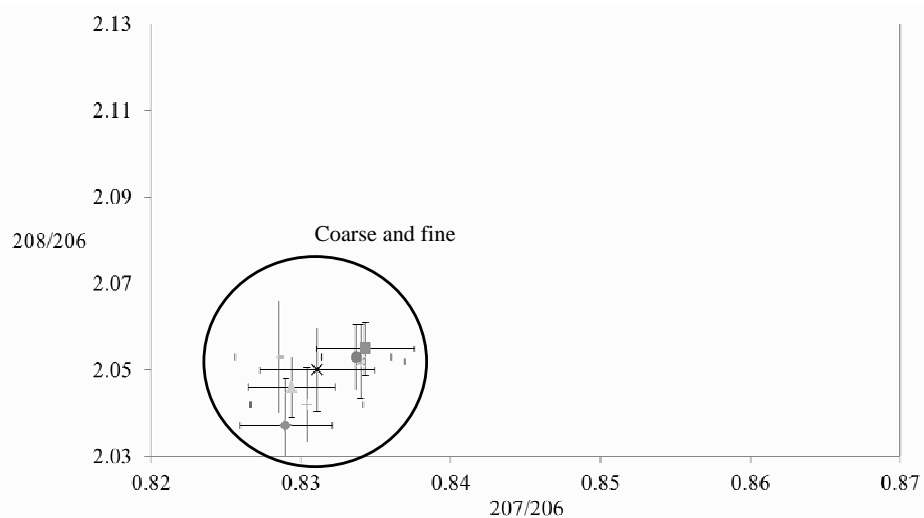
Hayden Pb Isotopes by Size Fraction

Wind from Smelter

The plot shows the relationship between the $^{208}\text{Pb}/^{206}\text{Pb}$ ratio (Y-axis) and the $^{207}\text{Pb}/^{206}\text{Pb}$ ratio (X-axis). The Y-axis ranges from 2.03 to 2.13, and the X-axis ranges from 0.83 to 0.87. Data points are plotted with error bars, and a large ellipse labeled "Coarse and fine" encompasses the main cluster of points.

| $^{207}\text{Pb}/^{206}\text{Pb}$ | $^{208}\text{Pb}/^{206}\text{Pb}$ |
|-----------------------------------|-----------------------------------|
| 0.848 | 2.092 |
| 0.853 | 2.090 |
| 0.855 | 2.098 |
| 0.858 | 2.107 |

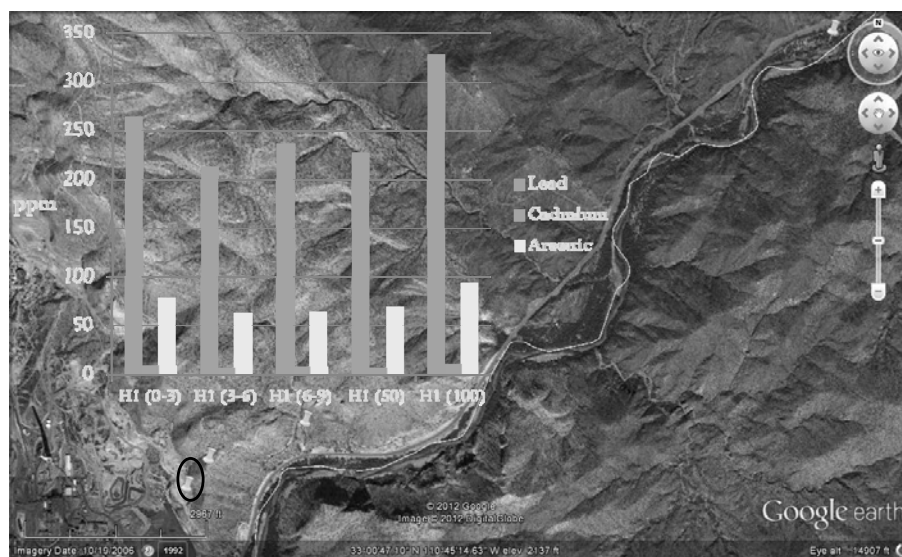
Tucson Pb Isotopes by Size Fraction



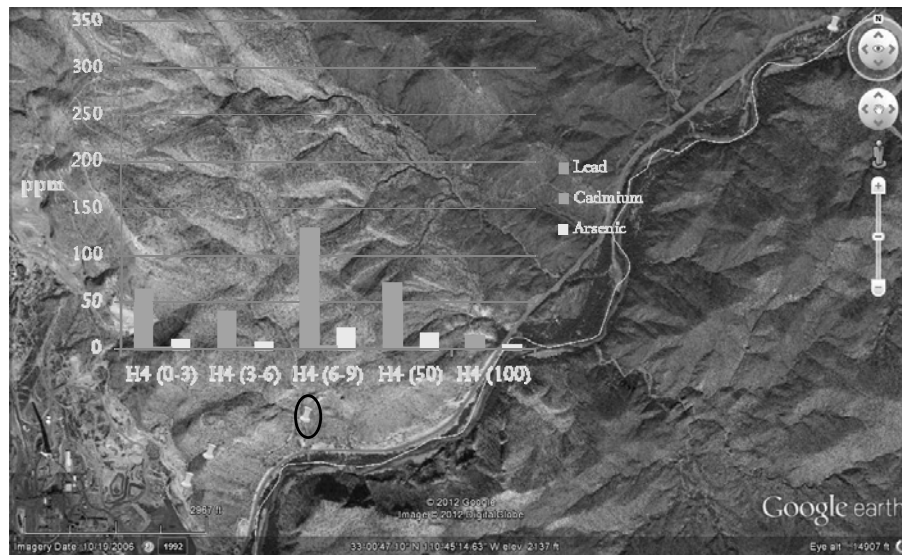
Contaminants in Soil - Hayden Site



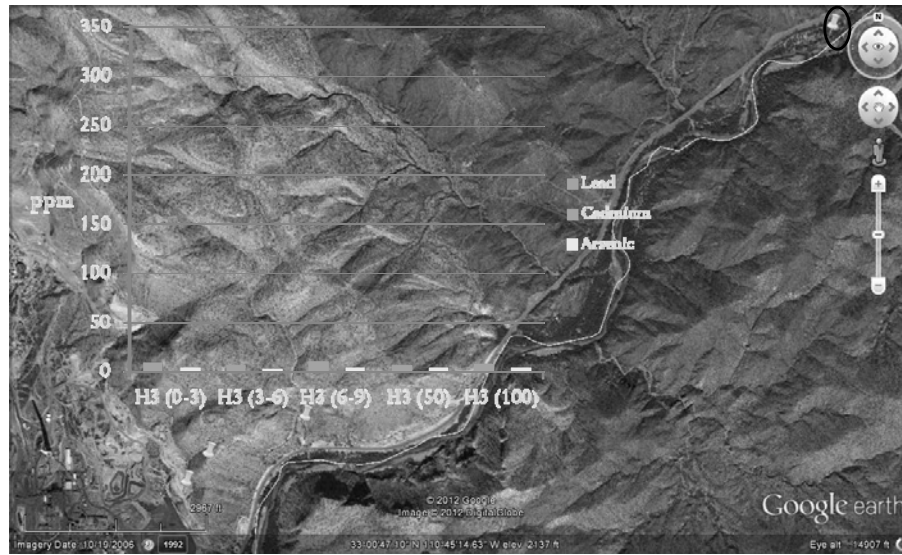
Soil Concentrations 0.2 mi from smelter



Soil Concentrations 0.8 mi from Smelter

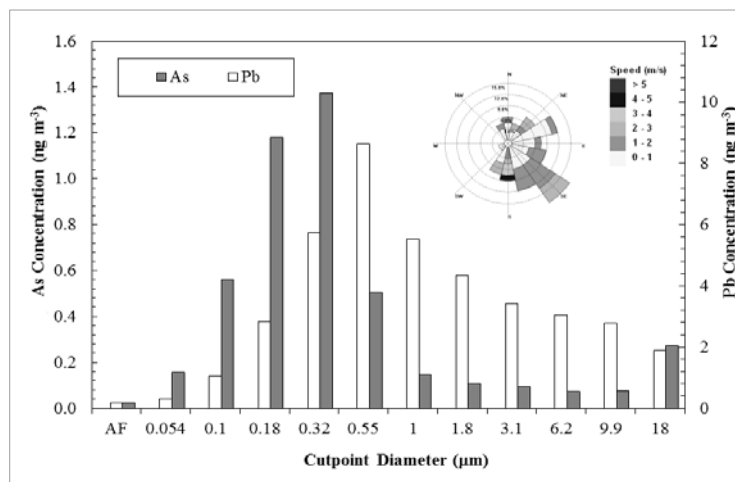


Soil Concentrations 2.5 mi from Smelter



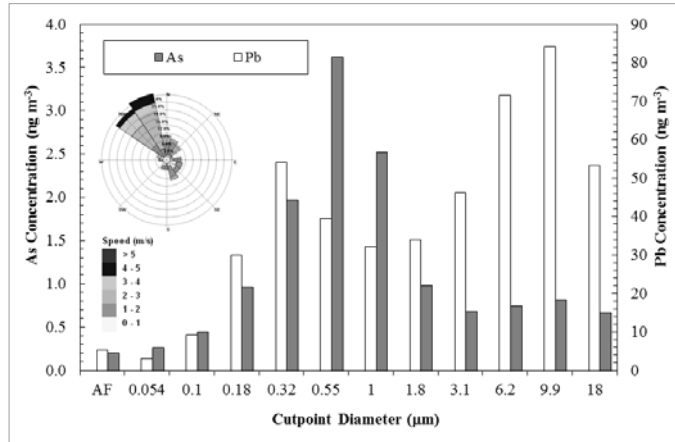
Mount Isa, Qld Australia MOUDI Results

- 2 different maxima at 0.32 and 0.55 μm for As and Pb, respectively.
- Again majority of contaminants in fine size fraction. (average 75% $<1 \mu\text{m}$)



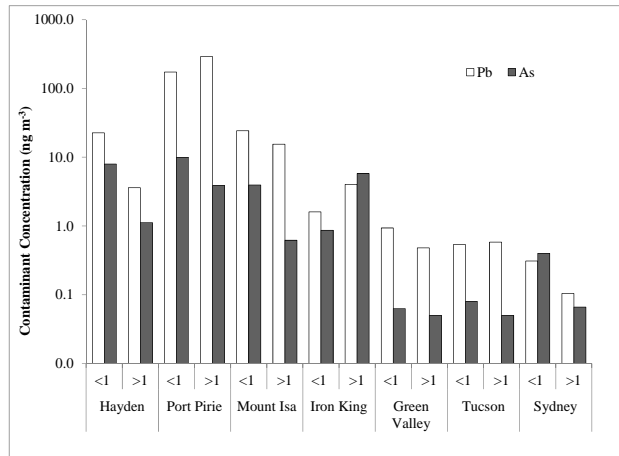
Port Pirie, SA Australia MOUDI Results

- Both As and Pb follow bimodal distributions.
- Majority of As in fine size fraction.
- Particles have significant concentrations of Pb in the coarse size fraction likely due to crushing grinding operations of Pb ore.



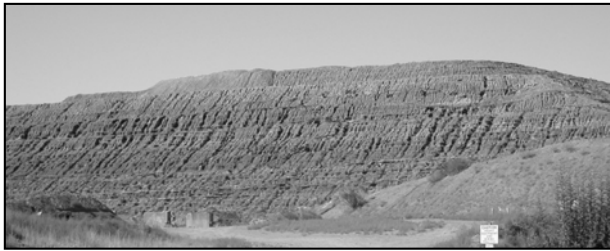
MOUDI Field Site Comparison

- Concentrations summed over fraction with particles sizes <1 and $>1 \mu\text{m}$.
- Concentrations for As and Pb enriched in the fine size fraction around smelting operations except Port Pirie Pb concentrations.
- With windblown contaminated mine tailings as source, Iron King is more heavily impacted in the coarser size fraction.



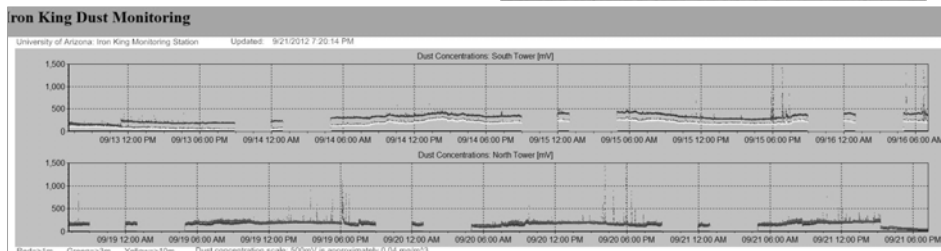
The Iron King Mine Humboldt Smelter Superfund Site

- Sulfide ore body discovered in 1880
- Operated 1904-1969; 3250 ft deep and 40 miles of shafts
- Lead, gold, silver, zinc, and copper mined
- Closed 1967
- Tailings pH = 2 to 4
- Tailings contain up to 4000 mg/kg arsenic
up to 4000 mg/kg lead
- Listed as an NPL site in Sept. 2008



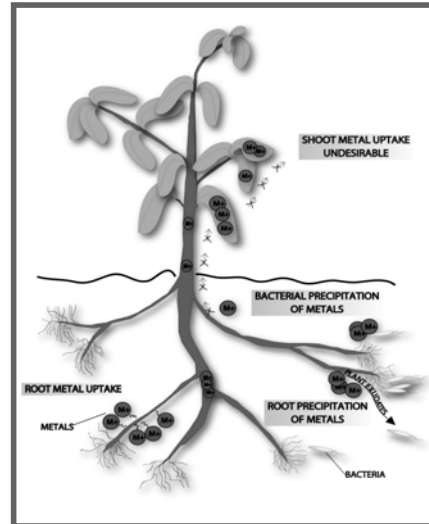
Iron King Dust Flux Monitors

- Two 10-m dust flux towers
- PM_{10} , $PM_{2.5}$, $PM_{1.0}$
- Passive dust samplers
- Meteorological stations
- 3-D wind anemometer

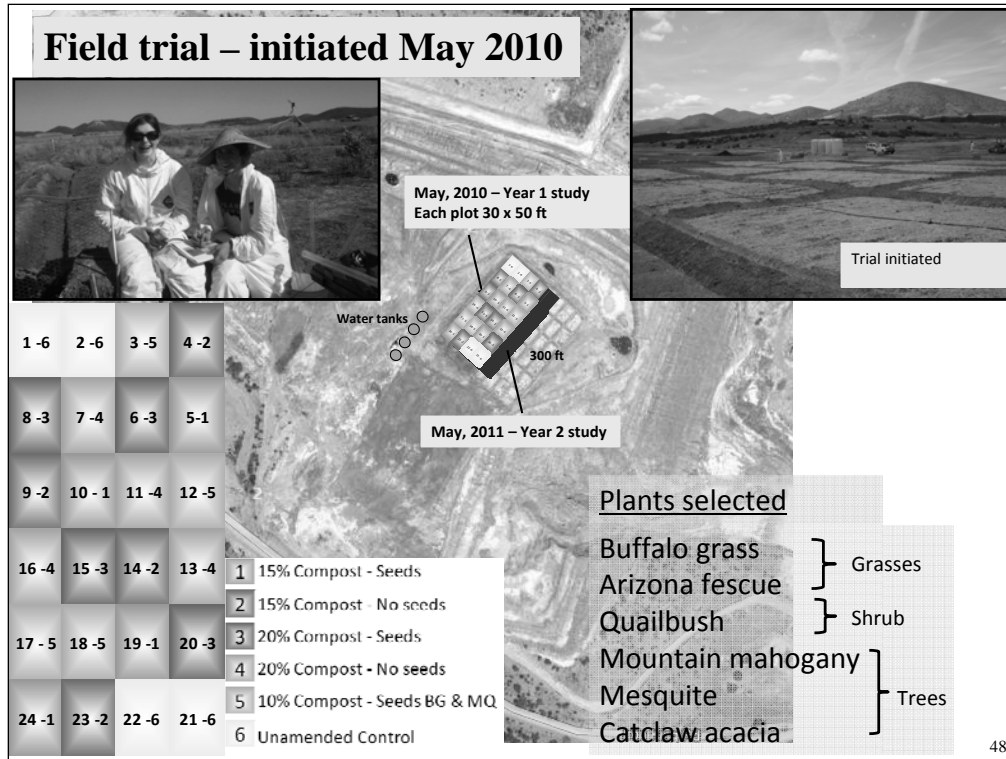


Direct Assisted Phytostabilization

- Stabilization of tailings by direct amendment (e.g., compost, lime) to allow establishment of drought-, salt-, and metal-tolerant plants.
- No soil cap used.
- Plants should not shoot-accumulate metals.
- Metal bioavailability (and hence toxicity) decreases as plants facilitate the precipitation of metals to less soluble forms, for example, metal sulfides or metal carbonates.



Mendez and Maier, 2008. Environ. Health Perspec.



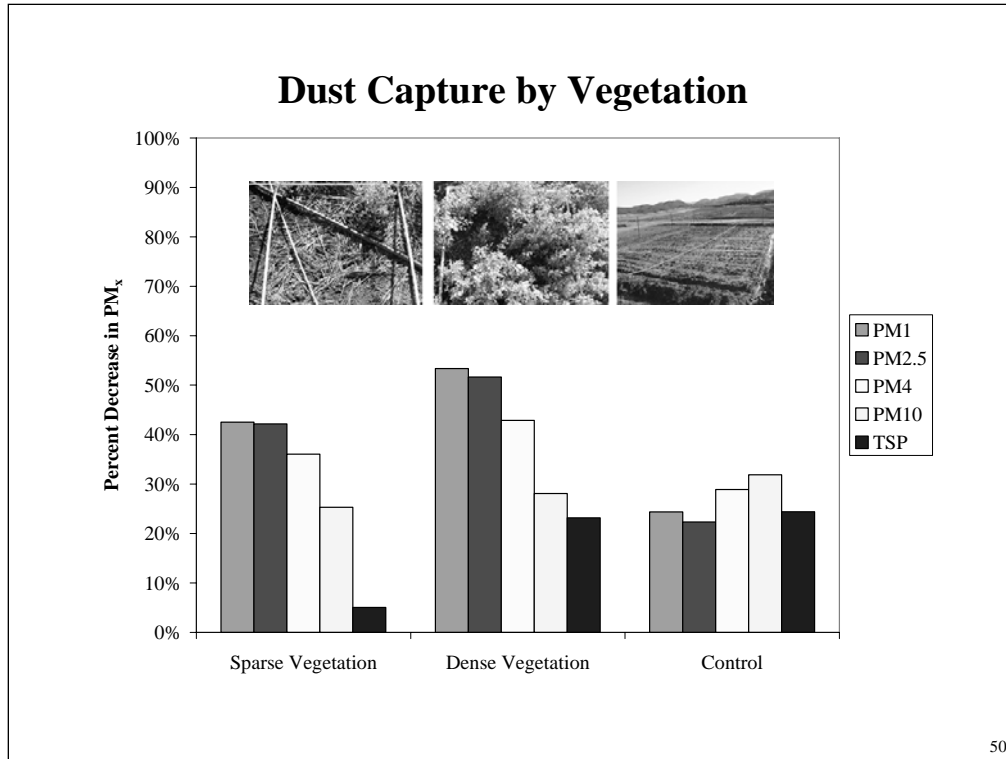
This figure explains the studies we are doing with TSPs and Dusttrak around the phytoremediation plots. We set the instruments up on either side of the plots as described above in the numbers. The windrose coincides with the sampling results in the following plot. The instruments were run for 4 hours. The Dusttrak samples continuously with optical measurements of mass concentrations of the different size fractions of particulate matter. TSP collects the ambient particulate on a filter which I have yet to get the metals results back. Future work includes duplicate studies like this and the passive samplers which are located throughout the plots to characterize horizontal dust flux.

Canopy Cover (measured at 5 and 16 months)



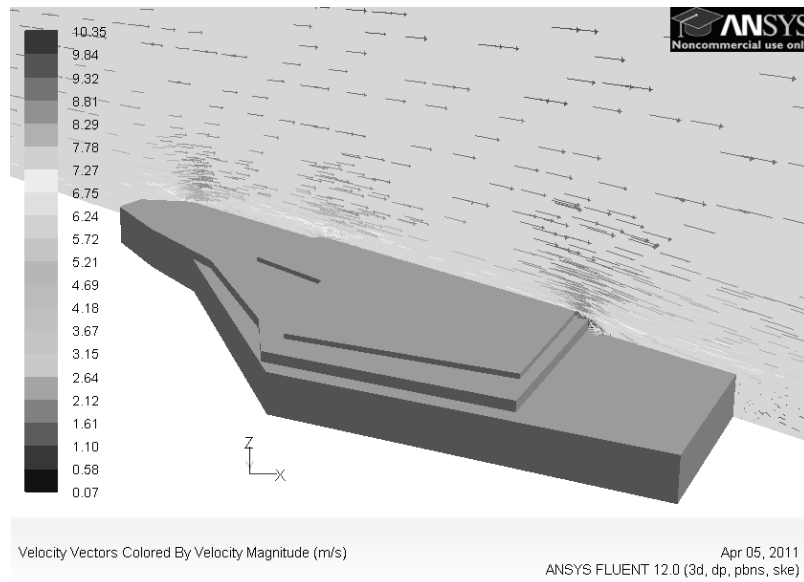
| Treatments | ----- % Canopy Cover ----- | | T-test | Irrigation | |
|-------------------|----------------------------|----------------|--------|--|-----------------------------|
| | 5 Months | 16 Months | | <u>0 - 5 mo</u> | <u>5 - 16 mo</u> |
| 20% - Seeds | 33.8 ± 5.4 a | 32.8 ± 14.5 a | NS | 37.8 cm | 61.1 cm |
| 15% - Seeds | 38.7 ± 6.6 a | 23.3 ± 19.5 ab | NS | Rainfall <u>0 - 5 mo</u> 32.8 cm | <u>5 - 16 mo</u> 21.7 cm |
| 10% - BG/MQ | 29.9 ± 10.0 a | 29.7 ± 18.6 ab | NS | Total <u>0 - 5 mo</u> 70.6 cm | <u>5 - 16 mo</u> 82.8 cm |
| Unamended control | 0 b | 0 b | NS | | |

~ 30% canopy cover is equivalent to off-site vegetation



Dusttrak results for the percent decrease of PMx crossed the plots. This is one sampling period on 5/24/11. What might be happening with the coarser particles is that the plants are trapping them and then high winds are resuspending them. The finer particles are affect more by diffusive forces than wind force. So this is what we would expect to see.

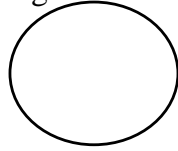
CFD Modeling: IK Mine Tailings



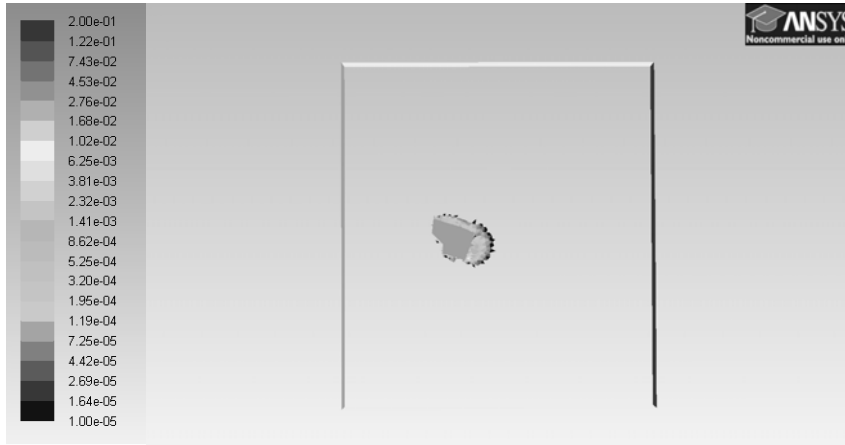
Simulated wind speeds over tailings

Mine tailings

Humboldt

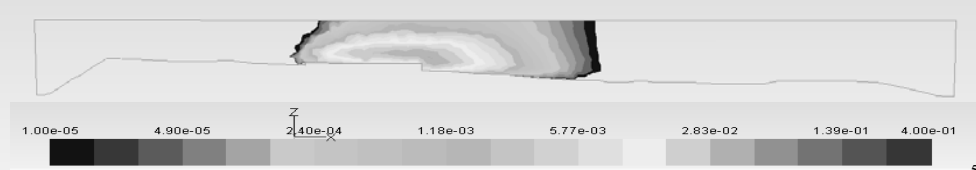


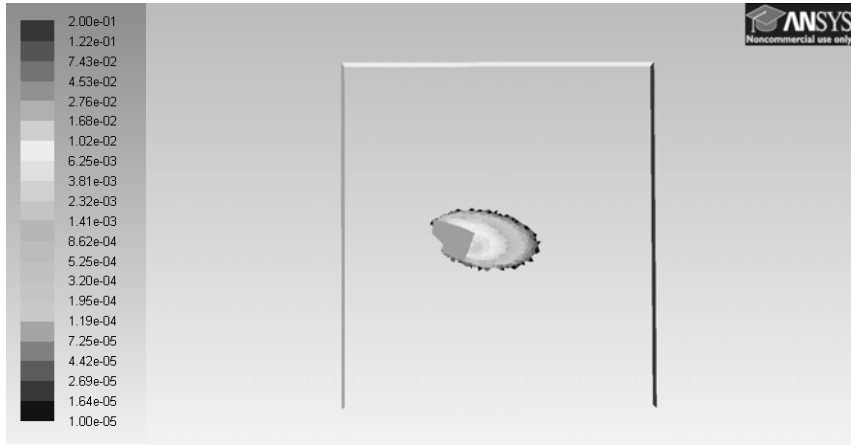
Simulation of conservative tracer plume



Contours of Mass fraction of ash3 (Time=3.5000e+01)

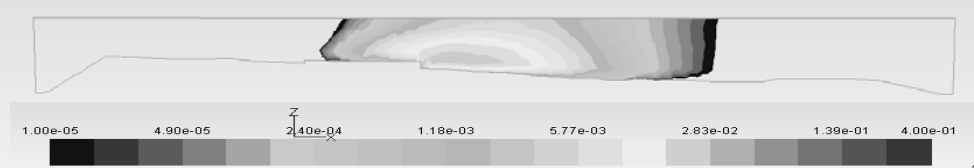
Jul 23, 2012

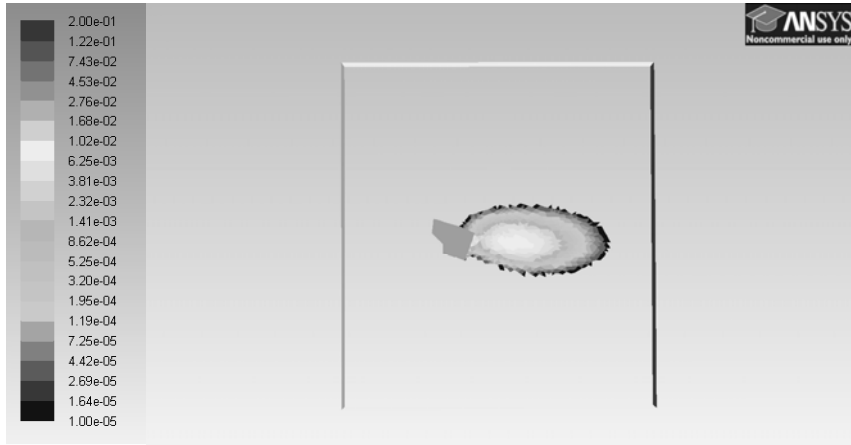




Contours of Mass fraction of ash3 (Time=7.0000e+01)

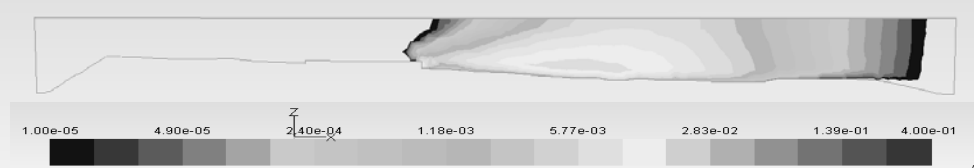
Jul 23, 2012

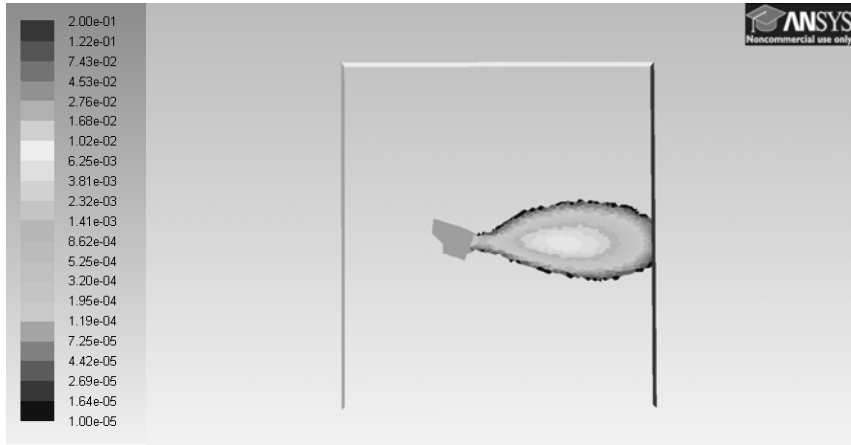




Contours of Mass fraction of ash3 (Time=1.4500e+02)

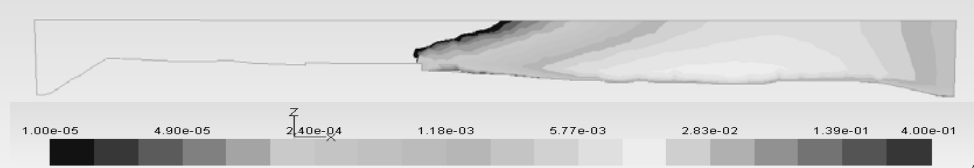
Jul 23, 2012

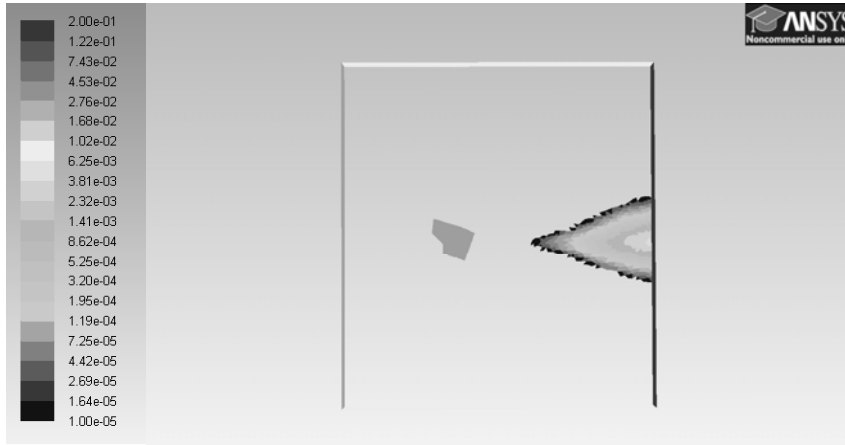




Contours of Mass fraction of ash3 (Time=2.2500e+02)

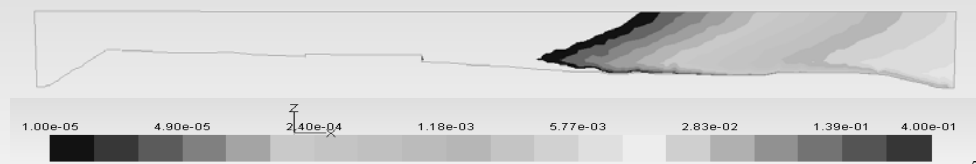
Jul 23, 2012





Contours of Mass fraction of ash3 (Time=3.7500e+02)

Jul 23, 2012



Summary

- Concentrations of As and Pb near smelter sites peak in the fine particle size fraction ($0.3\ \mu\text{m}$). These particles penetrate deep into the lungs. They are, in principle, collected at small efficiency (20%) but can grow due to their hygroscopic nature.
- Windblown dust from mine tailings leads to concentration of contaminants in coarse particle size range.
- Pb isotope analysis provides a “fingerprint” that may be used to provide source apportionment of contaminants.
- Preliminary results suggest that phytoremediation may lead to net decrease in contaminated dust concentrations.
- CFD can be used to assess contaminant transport from mining sources to populated areas.

Questions?



Phoenix July 5, 2011

Epidemiologic approaches to tracking human health effects of low-level arsenic exposure

Margaret Rita Karagas
Dartmouth College, Geisel School of Medicine



Arsenic Drinking Water Standards

World Health Organization

- 1958 – 200 $\mu\text{g/L}$
- 1963 – 50 $\mu\text{g/L}$
- 1993 – 10 $\mu\text{g/L}$

US EPA

- 2001 – 10 $\mu\text{g/L}$

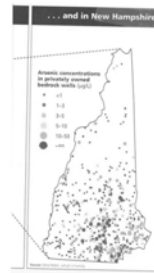
Some states

- 5 $\mu\text{g/L}$



Private Wells Not Regulated

Arsenic in Private Wells in the US...New Hampshire



~40% use **private water systems**

>10% private well **As >MCL**


Largely attributed to **bedrock geology**



Overview

- Biomarker approach to studying arsenic exposure and cancer risk in a US population (>7000 participants, >3000 wells)
 - exposure biomarkers & cancer
 - gene-environment interactions
- Extending this work to examine health impacts of *in utero* and early life exposures (1000 maternal/infant pairs projected)

Skin Lesions & Cancer

- **Dermal lesions**, including pre-cancers: early manifestation of chronic arsenic exposure in highly exposed populations
 - **Skin cancer**, especially SCC: malignancy noted in 1887 from Fowler's solution; SW Taiwan 1968
 - **What about lower levels of exposure?**
- 
- © Elsevier 2004. Habit. Clinical Dermatology
- Often occur near vital structures, capable of metastasizing, can be difficult to treat
 - Challenge to study in US because they not monitored

US Population-Based Skin Cancer Case-Control Study

Design:

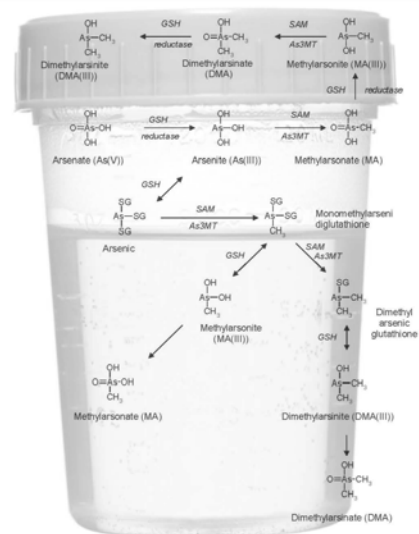
- Cases: state-wide surveillance
- Controls: population lists

Elevated odds ratio for SCC in highest category of toenail arsenic OR = 2.1, and evidence of a dose-related increase at higher levels of exposure



Data Collection

- Interview
- Samples
 - Water
 - Blood/buccal
 - Toenails
 - Tumor

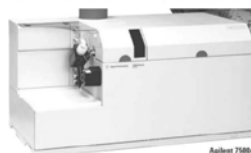


Urinary Arsenic Metabolism

iAs3 \rightarrow iAs5 \rightarrow MA \rightarrow DMA

Total* = Σ

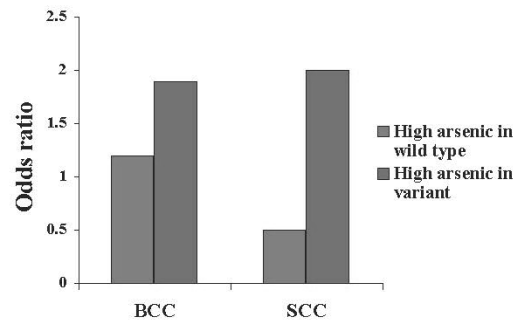
*excludes arsenobetaine



ICP-MS sensitive approach
0.10 to 0.15 ug/L for individual species

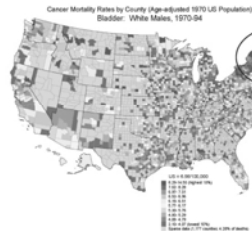
Individual Susceptibility

Greater risks of BCC and SCC among those with high arsenic & variant XPD 751 genotype



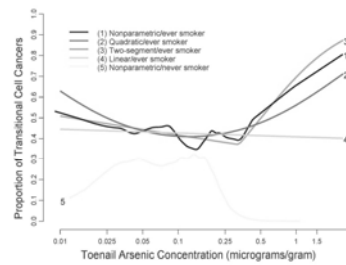
Applebaum, Nelson et al., 2007 EHP

Bladder Cancer



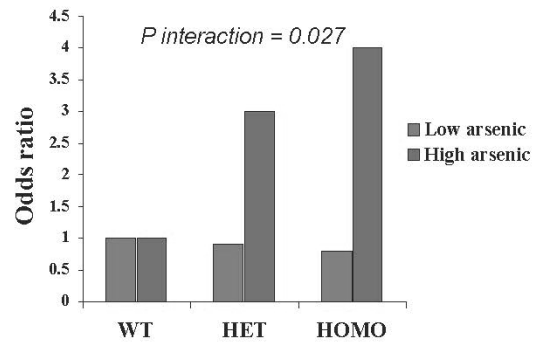
High bladder cancer mortality rates
in NH

Dose-response: relation with
toenail As among smokers



Genome-Wide Study, Validated in Bladder Cancer Case-Control Study

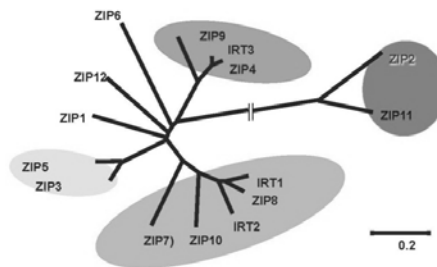
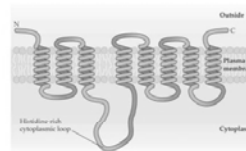
As-SLC39A2 interaction, especially among smokers



Karagas et al., Human Genetics, 2012

SLC39A: ZIP2 - ZIP family of metal transporters

- ZIP family members are metal transporters found in a wide range of organisms
- ZRT - IRT related Proteins
 - ZRTs – zinc regulated transporters
 - IRTs, major iron transporters
- Not known to transport As
- As replaces zinc in protein motifs i.e., tumor suppressors



Susceptible Populations



Arsenic passes through the placenta

Concordance between maternal-cord blood concentrations

- In an Andean population: median arsenic levels in maternal blood (11 ug/L) were nearly as high in infant cord blood (9 ug/L); placental tissue also elevated (Concha et al, 1998)
- In Bangladesh, maternal-cord blood highly correlated for total arsenic ($r=0.93$), MMA ($r=0.80$), DMA ($r=0.94$), As+3 ($r=0.80$), As+5 ($r=0.89$) (Hall et al., 2007)



In Utero/early life exposures and cancer risk

- Animal experiments found maternal arsenic exposure during pregnancy led to cancers in the offspring (*Waalkes et al., 2004*)
- Antofagasta Chile found increased mortality risks of lung and liver cancer among those with born around the time of peak exposure (*Smith et al., 2006*; *Liaw et al., 2008*)

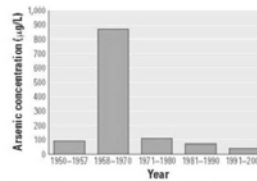


Figure 1. Arsenic concentrations in Antofagasta/Mejillones water by year. An arsenic removal plant was installed in 1971.

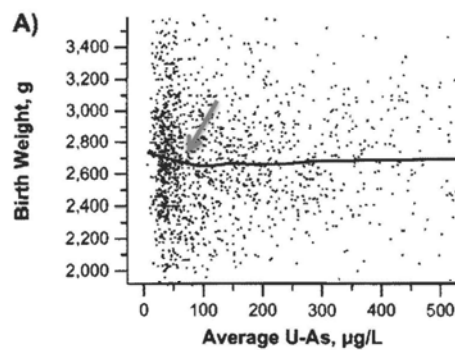
Thailand Study



- Women receiving prenatal care in an area with arsenic-containing drinking water (n=32 maternal/infant pairs)
- Microarray analysis of cord blood samples & toenail arsenic ($\leq 0.5 \mu\text{g/g}$)
- Identified altered gene expression in
 - Tumor promoter, progression
 - Immune response pathways.

Fry et al., PLoS Genetics, 2007

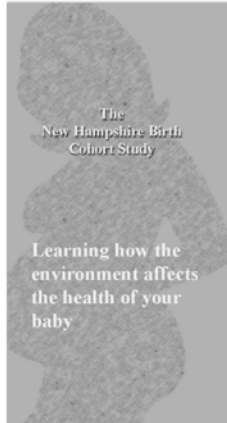
Arsenic & Birth weight



Decreased birth weight
< 100 $\mu\text{g/L}$ urinary As
of 1.7 g per $\mu\text{g/L}$

*No data on these
outcomes in a US
population*

Rahman et al., 2009



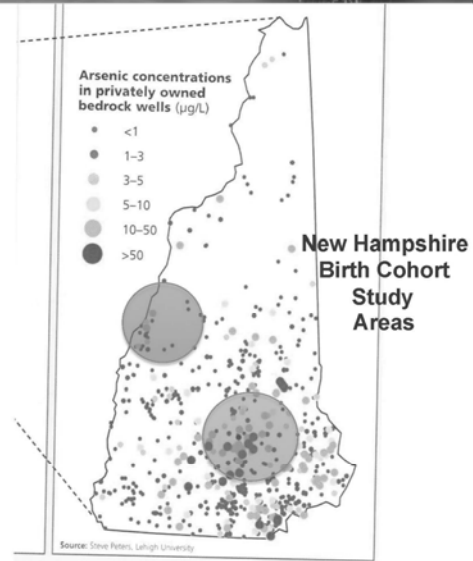
Study Goals

To test the hypothesis that prenatal exposure to arsenic is associated with reduced birth weight, fetal growth and gestational age (i.e., premature births) in New Hampshire.

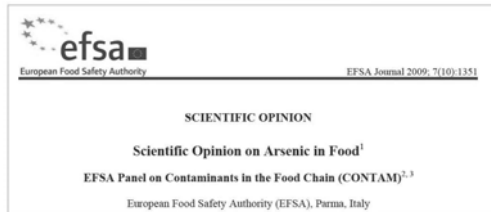
Water: an important exposure route



15-20% of pregnant
women enrolled in
our study – tap
water exceeds the
MCL of 10 $\mu\text{g/L}$ As



Dietary Sources of Arsenic



Conclusions:

Adult intake 0.13 – 0.56 ug/kg of body weight

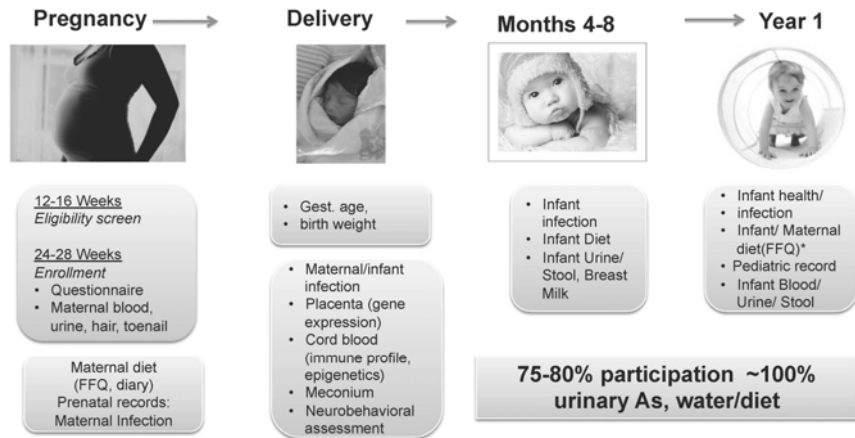
Children < 3 yrs is 2-3 x higher than adults

Diet is the main source of exposure

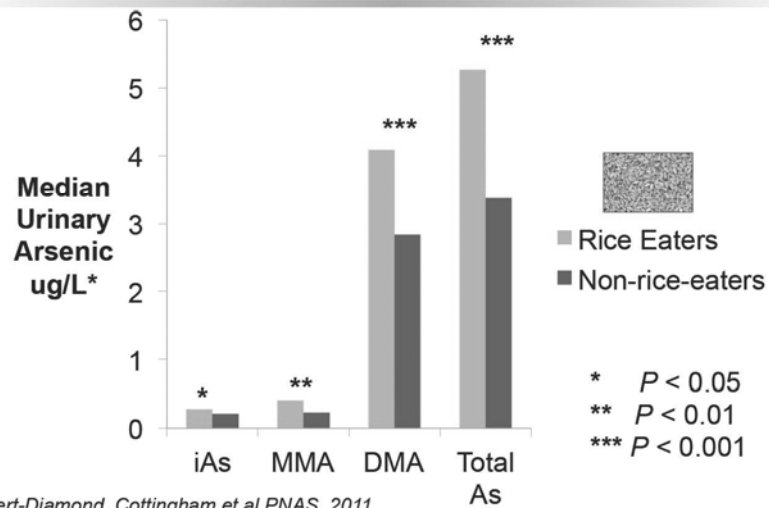
BMD01 0.3 – 8 ug/kg of body weight

“Dietary exposure to arsenic should be reduced”

New Hampshire Birth Cohort Study

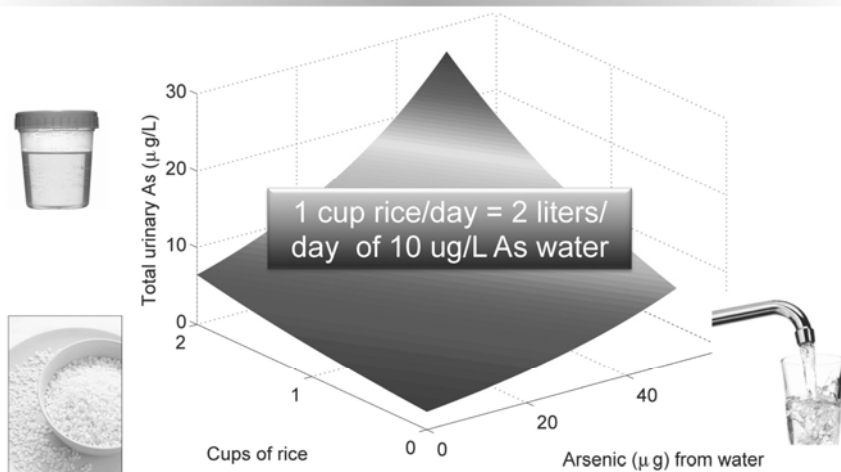


Urinary arsenic higher in rice eaters (n=229)



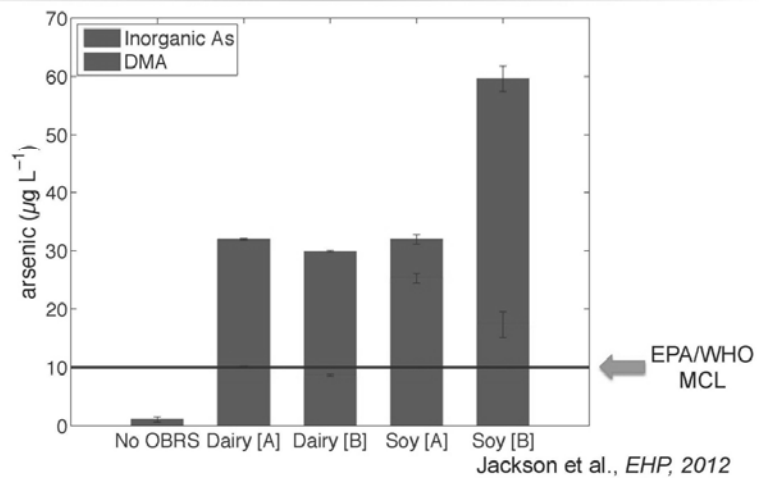
Gilbert-Diamond, Cottingham et al PNAS, 2011

Water Arsenic & Rice Intake Contribute to Urinary Arsenic

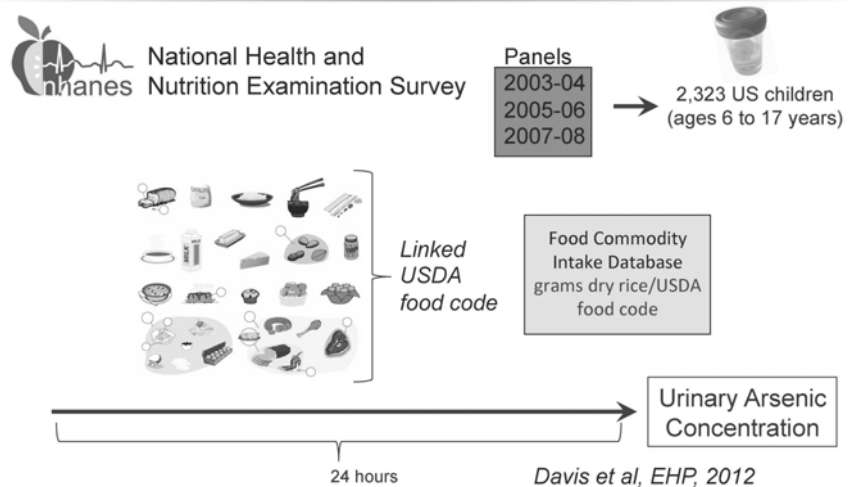


Gilbert-Diamond, Cottingham et al PNAS, 2011

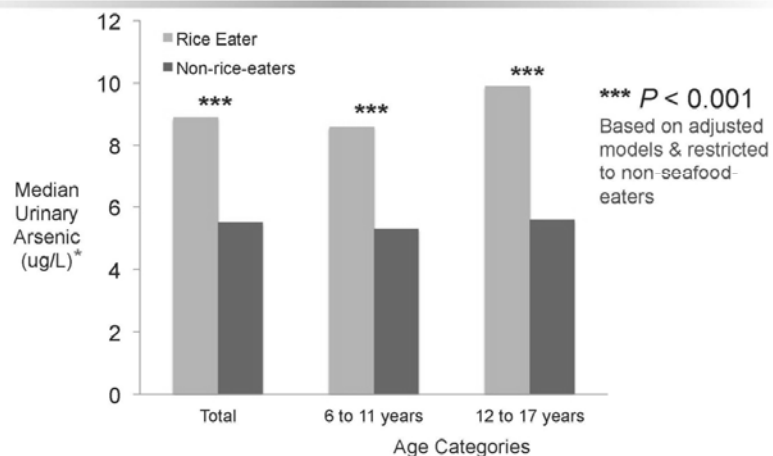
**Formulas with organic brown rice syrup contained As when
reconstituted with As-free water**



Rice Consumption and Urinary Arsenic Concentration in US Children



Rice Consumption and Urinary Arsenic Concentration in US Children



*excludes arsenobetaine & arsenocholine

Davis et al, EHP, 2012



Studies characterizing dose-response at low level arsenic exposures

| Endpoint | Population | Reference point µg/L water | Reference point µg/kg b.w. per day |
|----------------|---|---|---|
| Dermal lesions | Bangladesh (Ahsan et al., 2006) | BMCL ₀₁ : 23 ^(a) | BMDL ₀₁ : 2.2-5.7 ^(b) |
| Dermal lesions | Bangladesh (Rahman et al., 2006a) | BMCL ₀₁ : 5 ^(a) | BMDL ₀₁ : 1.2-4.1 ^(b) |
| Dermal lesions | Mongolia (Xia et al., 2009) | BMCL ₀₁ : 0.3 ^(a) | BMDL ₀₁ : 0.93-3.7 ^(b) |
| Lung cancer | Chile (Ferreccio et al., 2000) | BMCL ₀₁ : 14 (NRC, 2001) | BMDL ₀₁ : 0.34-0.69 ^(c) |
| Bladder cancer | North East Taiwan (Chiou et al., 2001) | BMCL ₀₁ : 42 (NRC, 2001) | BMDL ₀₁ : 3.2-7.5 ^(b) |
| Skin cancer | USA (New Hampshire) (Karagas et al., 2002) | Change point ^(d) : 1-2 | Change point: 0.16-0.31 ^(c) |
| Bladder cancer | USA (New Hampshire) (Karagas et al., 2004) | Change point: <i>ca.</i> 50 | Change point: 0.9-1.7 ^(c) |

**Benchmark response of 1% excess risk, lower 95% confidence interval per ug/kg body weight
0.3 to 8 ug/kw body weight, EFSA 2009**



Future Directions

“... infectious diseases remain a significant cause of mortality worldwide, and indeed prompted the installation of the wells in Bangladesh as a means of supplying pathogen-free drinking water. Recent evidence suggests that environmental toxins, such as arsenic, might affect immune response. Thus far, the repercussions of arsenic exposure on the occurrence and virulence of infectious diseases have not been realised entirely.”

Karagas MR. Lancet 2010

Dartmouth Toxic Metals
Superfund Research Program

Dartmouth

Angeline Andrew, Brock Christensen,
Kathy Cottingham, Matt Davis,
Diane Gilbert-Diamond,
Eugene Demidenko,
Mary Lou Guerinot,
John Heaney, Brian Jackson,
Zhongze Li, Carmen Marsit,
Jason Moore, Ann Perry,
Tracy Punshon, Vicki Sayarath,
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Steve Spencer, Anna Tyler,
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Jay Gandolfi

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David Robbins

THE CHILDREN'S ENVIRONMENTAL HEALTH AND DISEASE PREVENTION CENTER AT DARTMOUTH



DARTMOUTH COLLEGE. HANOVER. NEW HAMPSHIRE

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- To view a complete list of resources for this seminar, please visit the **Additional Resources**
- Please complete the **Feedback Form** to help ensure events like this are offered in the future

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