Fetal risks from arsenic – exposure biomarkers and risk reduction

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Arsenic

- Recognized as a toxic chemical of concern
- Known health effects in the highly exposed
- Emerging evidence of adverse health effects at lower exposure levels, particularly in certain subgroups of the population

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  - Is a susceptible subgroup the fetus or children?

Arsenic crosses the placenta

Among Andean women exposed to 200 mg/L arsenic in drinking water:

- [Arsenic] maternal blood ~ cord blood
  - –maternal blood = 11 µg/L
  - –infant cord blood = 9 µg/L
- –Placental arsenic elevated.

Concha et al, 1998

Developing fetuses may be especially vulnerable to arsenic exposure

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  - Abrogated growth
  - Infant mortality

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- Humans, highly exposed
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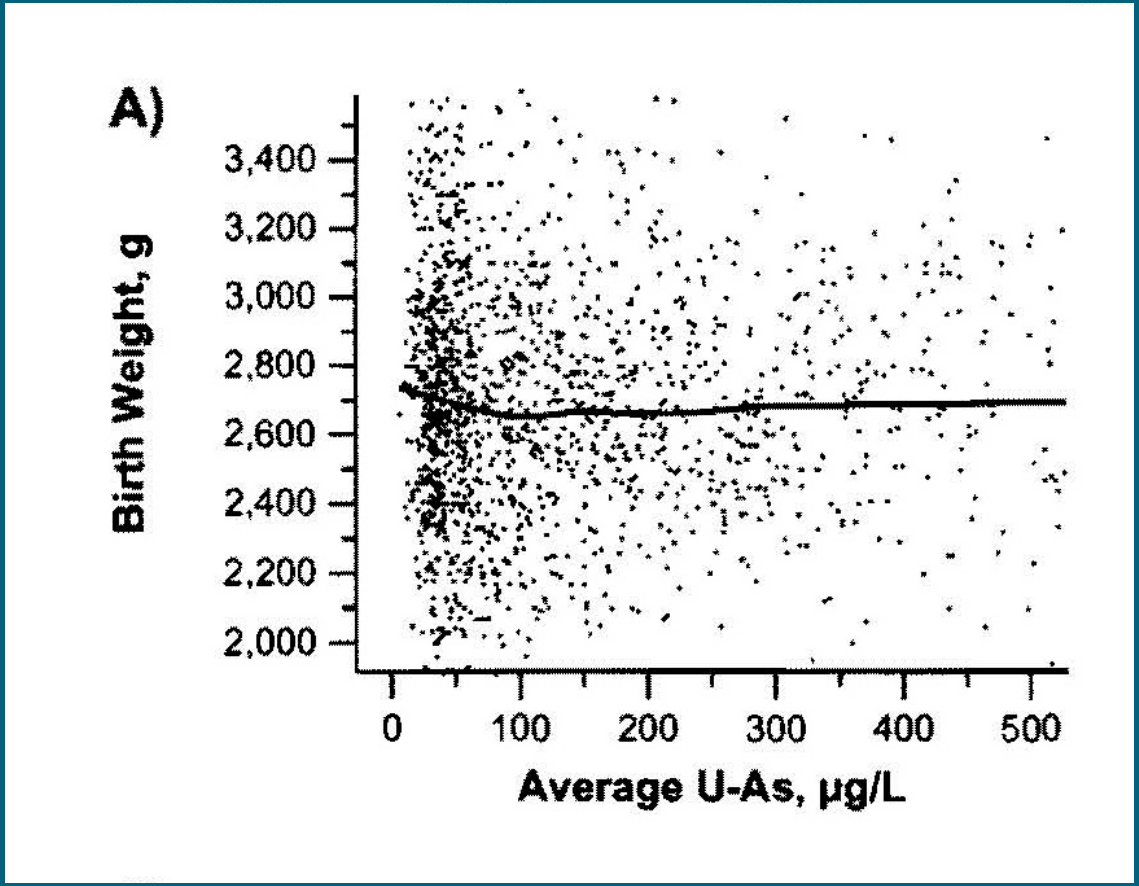
  - Low birth weight, prematurity
  - Cognitive, immune effects, later cancers
- Little is known about effects at lower levels

Increased urinary arsenic associated with lower birth weight



Rahman et al., 2009

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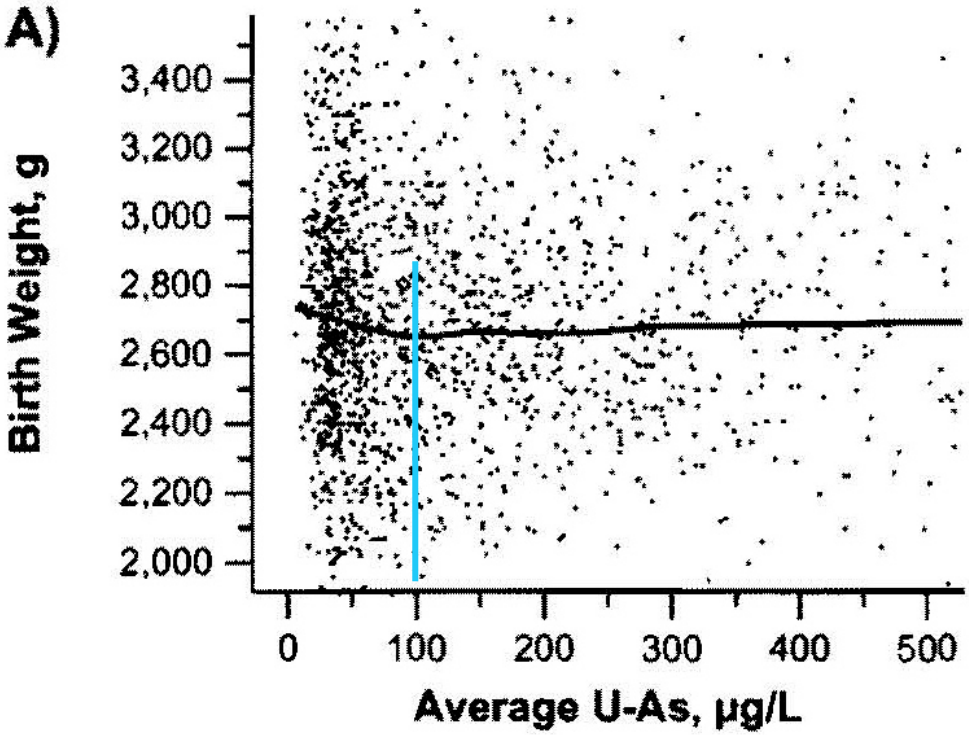

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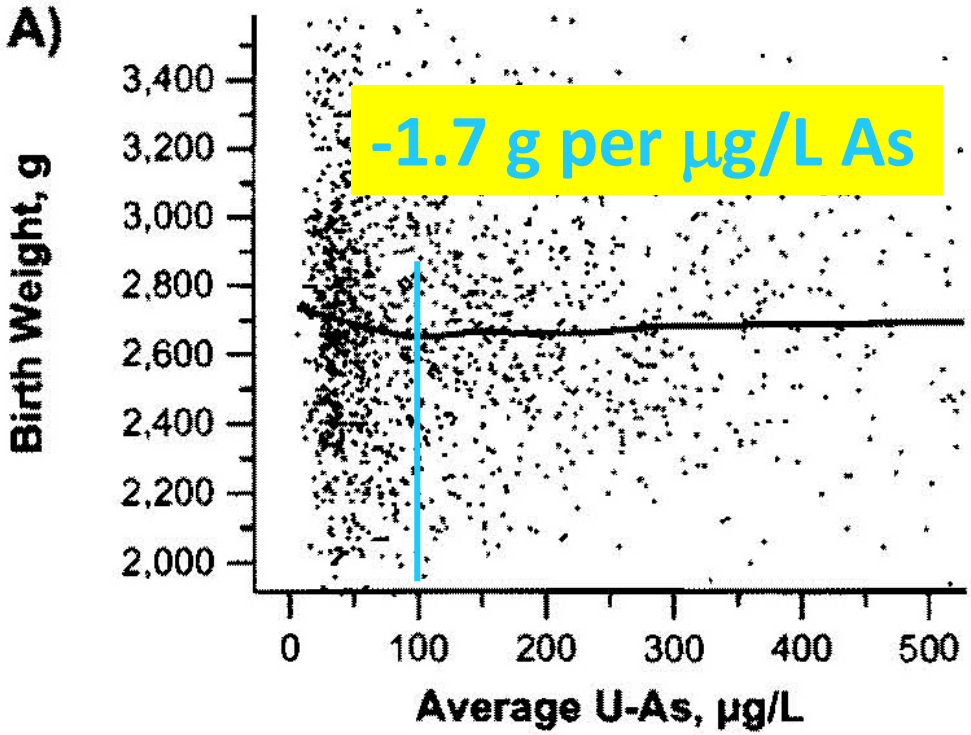

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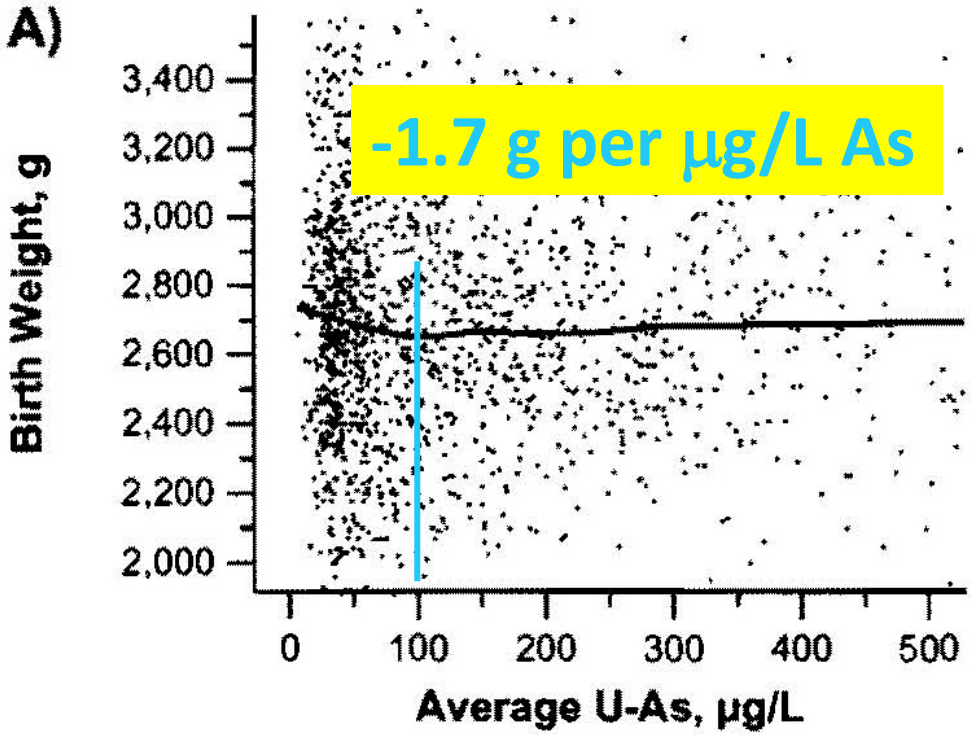
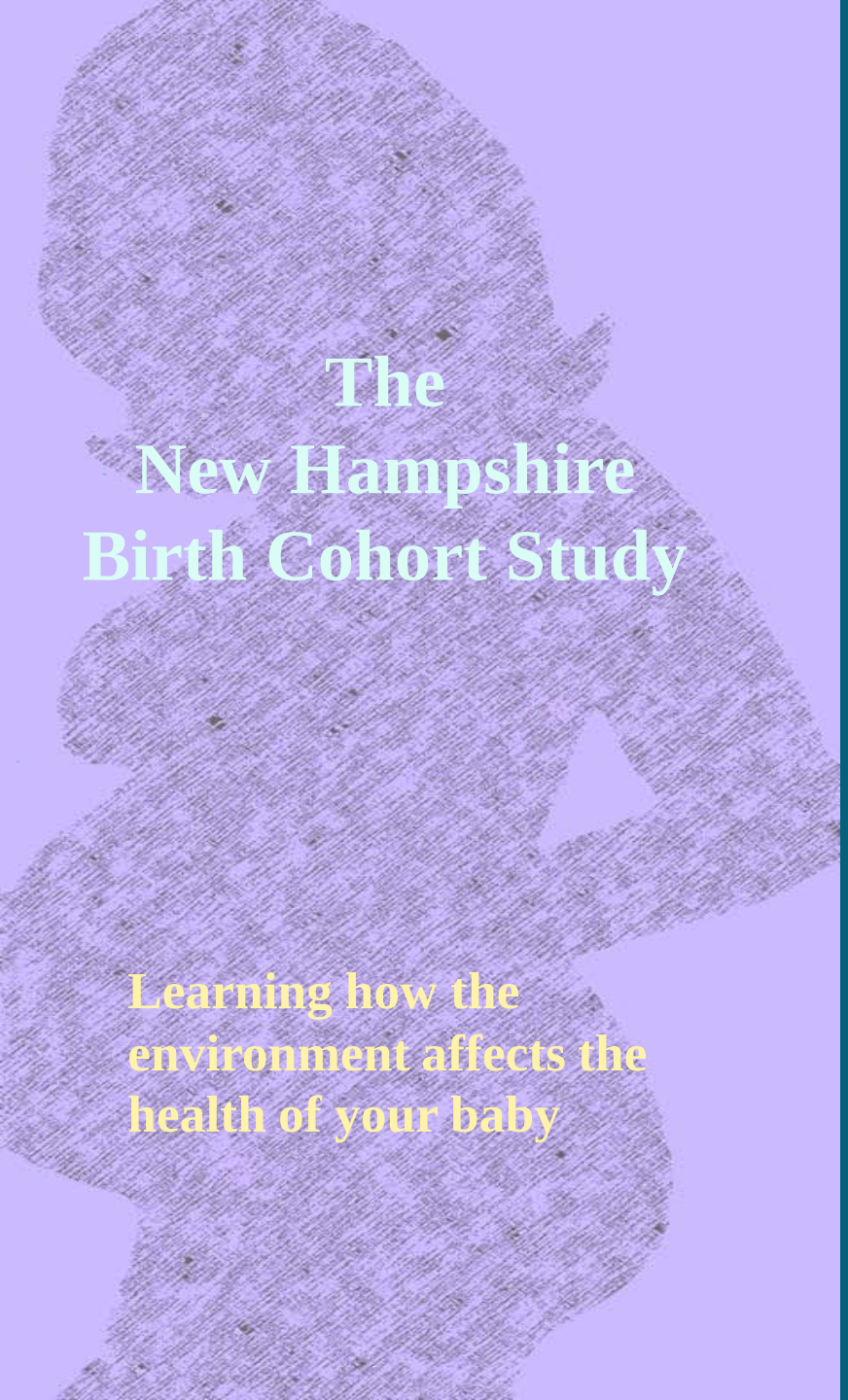


These outcomes not studied in US populations

Rahman et al., 2009

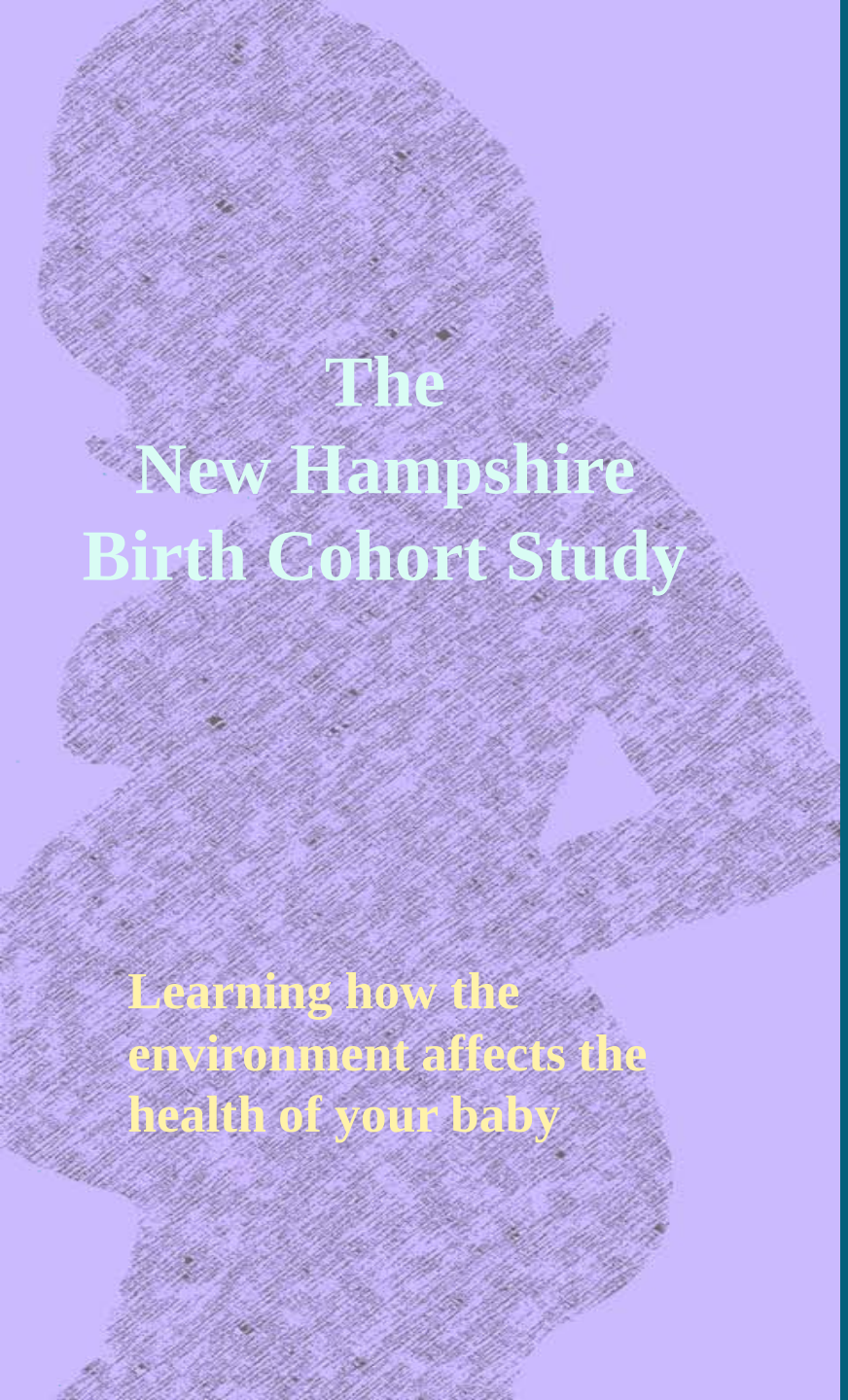
The New Hampshire Birth Cohort Study

Learning how the environment affects the health of your baby



Designed to test:

Whether prenatal exposure to arsenic is associated with reduced birth weight, fetal growth, and gestational age.



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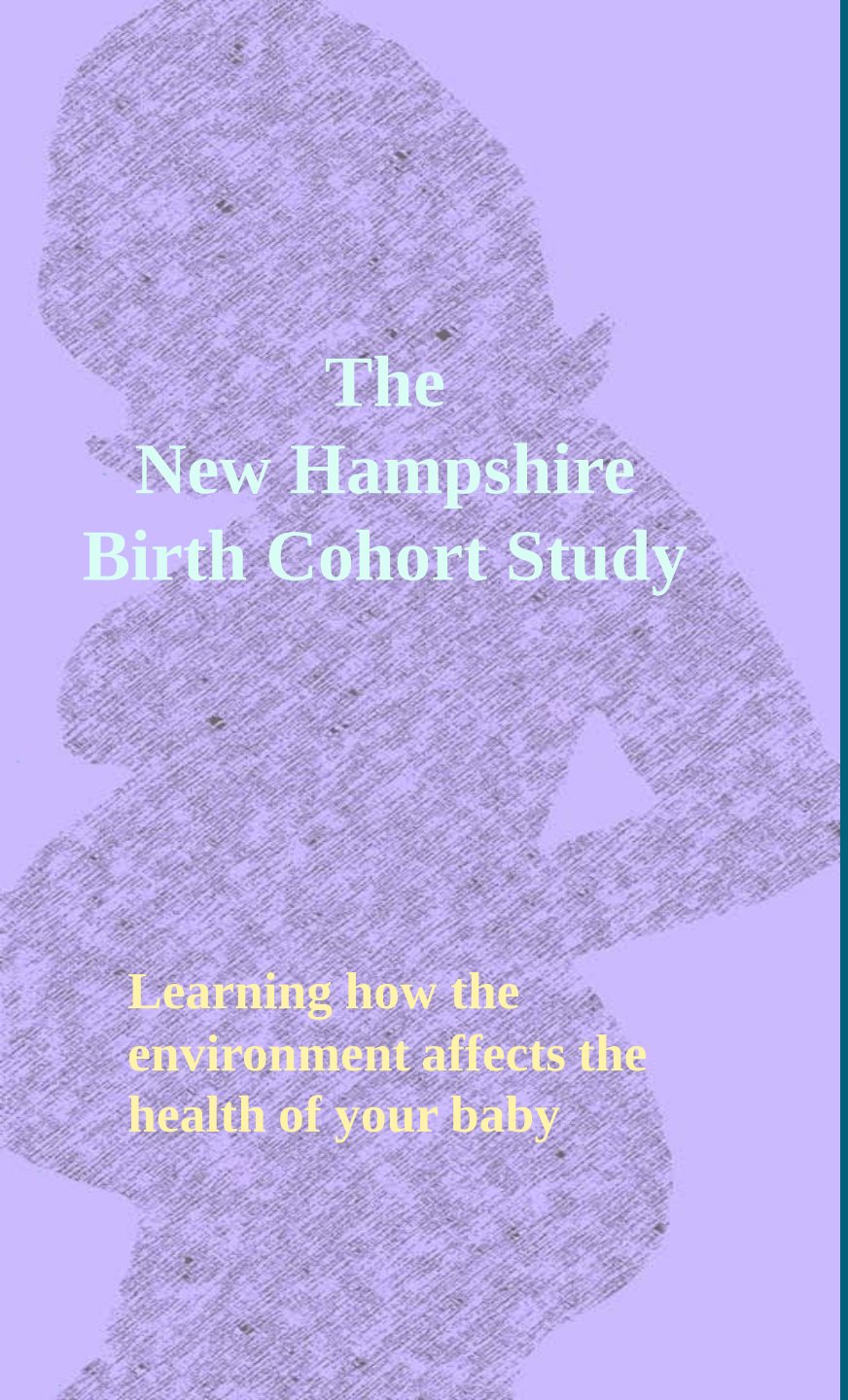
Potential modification of risk by nutritional or genetic factors



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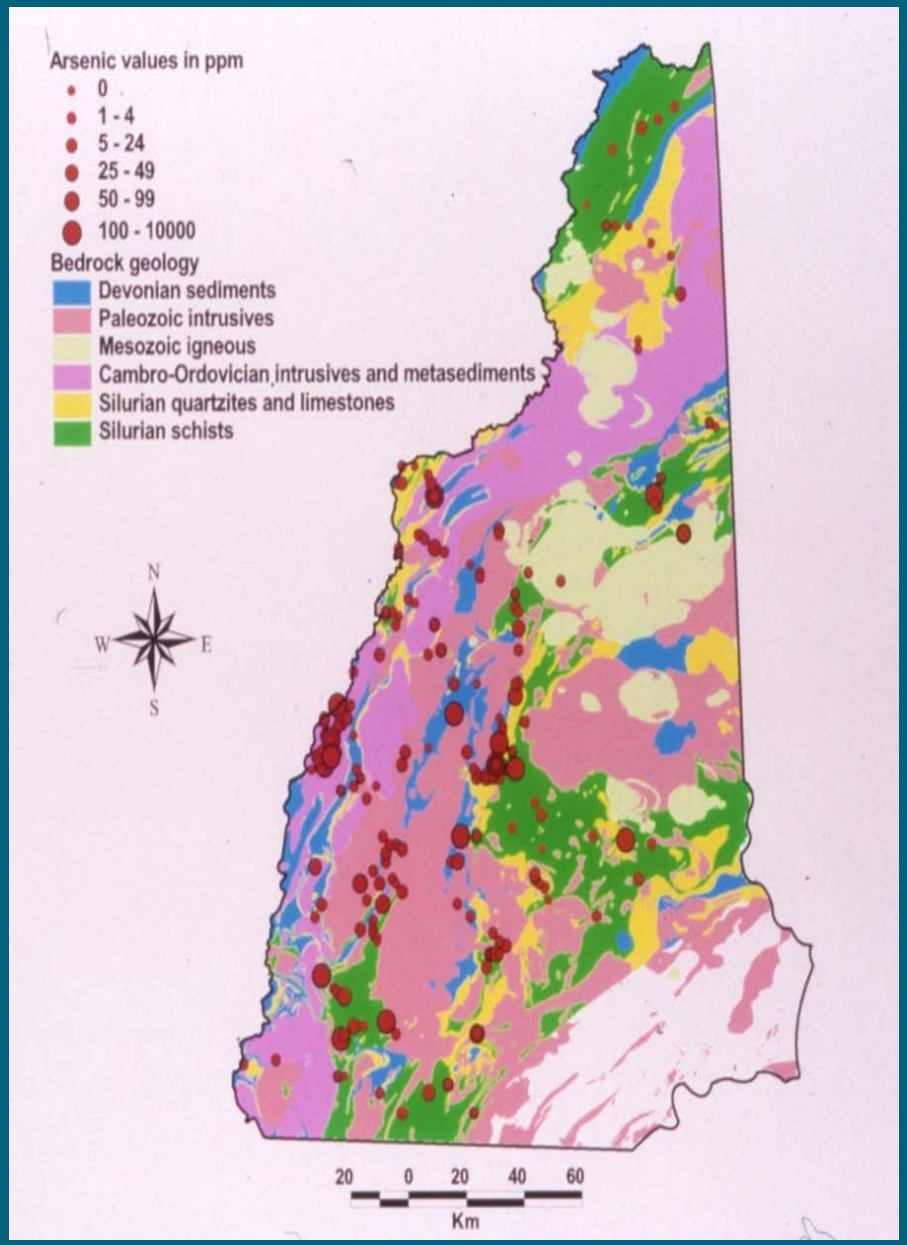
Biomarkers of maternal/fetal arsenic metabolism.

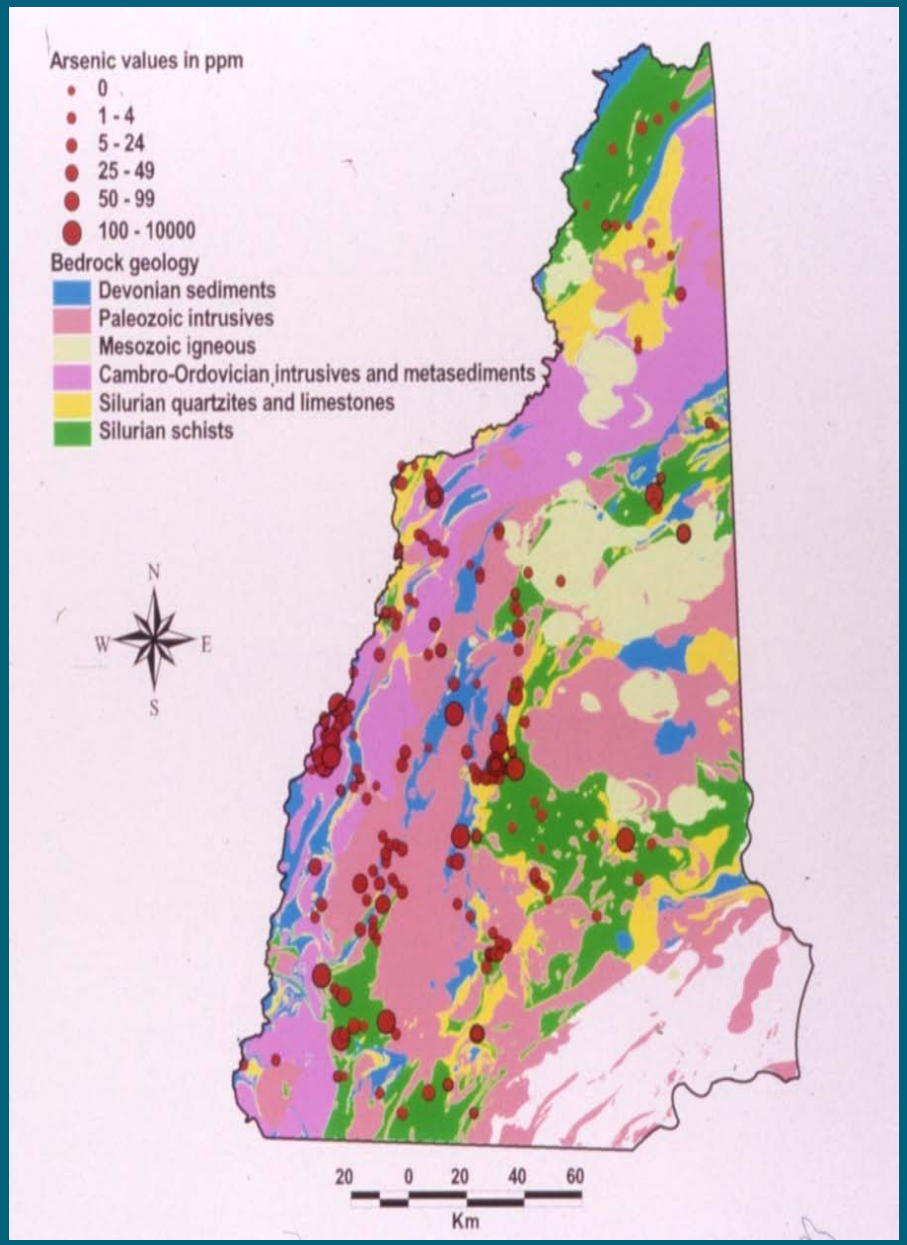
New Hampshire Arsenic State



New Hampshire Arsenic State

>40% of residents use private water systems

>10% wells have [As] greater than10 ug/L



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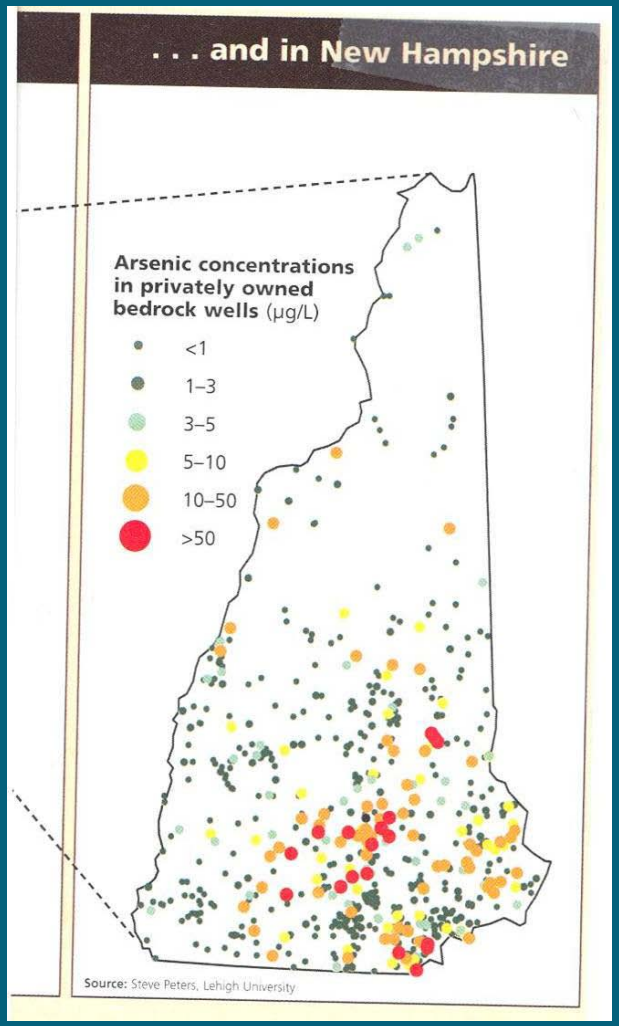
Site Selection

Clinics in regions of New Hampshire with reportedly **high levels of arsenic in the well water** in GIS analysis



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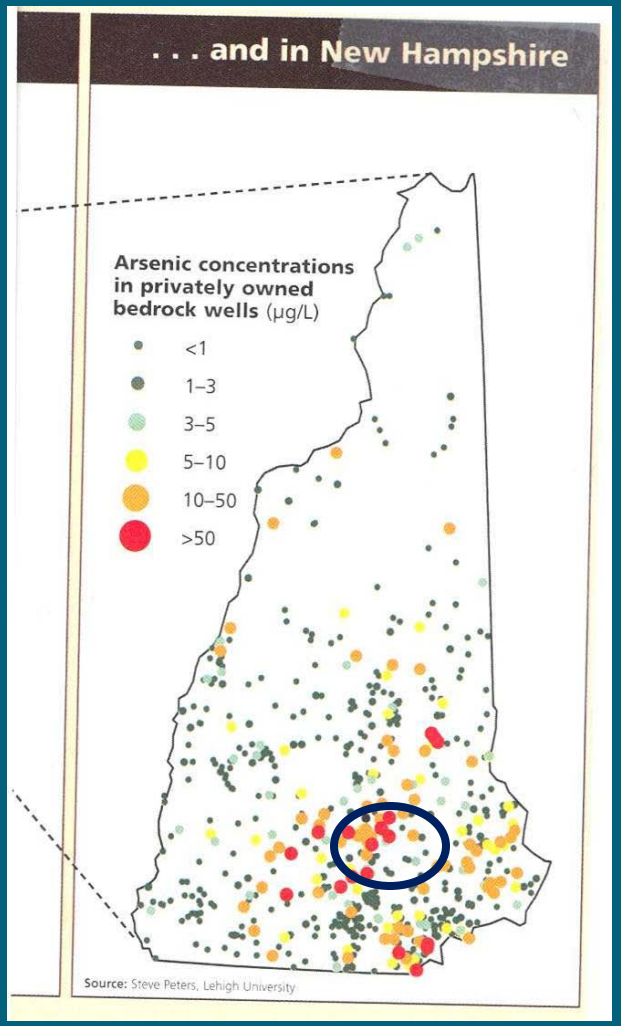

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Eligibility

Pregnant women receiving their routine prenatal care:

- Age 18-45 yrs old
- Private well at home
- Stable residence
  - same residence since last menstruation and same water supply.
  - no plans to move prior to delivery.
- English speaking/mentally competent.

Baseline Information
24-28 weeks gestation

- Self-Administered Questionnaires:
  - Pregnancy history, lifestyle, family, medical history
  - Food frequency questionnaire
  - Three-day food and water intake diary

- Samples:
  - Urine
  - Blood
  - Hair
  - Toenails
  - Tap water (mail back)

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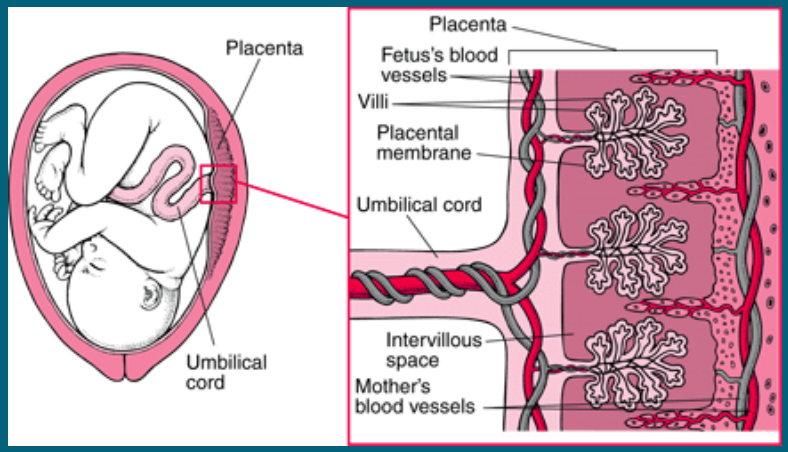
Delivery and Postpartum

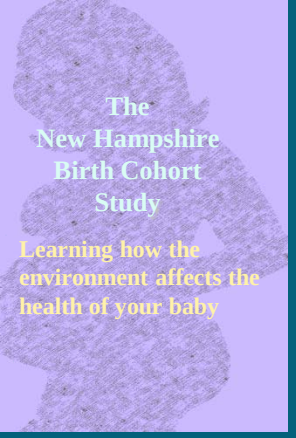
Delivery

- Cord blood sample
- Placenta biopsies
- Meconium

2 weeks post-partum

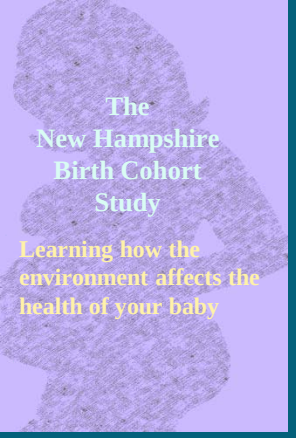
- Follow-up Questionnaire
  - Updated pregnancy information and any changes
- Maternal & infant toenail sample





Biomarkers of Arsenic Exposure in our study

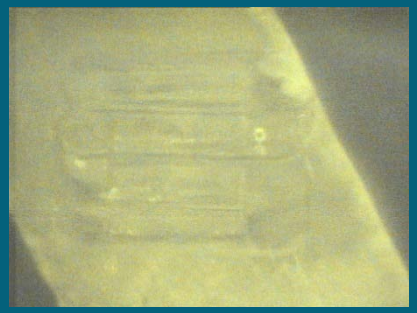
- Nails, maternal and infant
- Urine, maternal
- Blood, maternal and cord
- Placenta
- Meconium



Toenail Arsenic

- Measure of aggregate exposure
- Easily collectable
- Relatively unsusceptible to external contamination
- Measure of inorganic Arsenic

Direct Analysis of solid samples: Laser ablation ICP-MS



<u>Toenail analysis:</u>

- Micro-sampling technique preserves the bulk of sample
- No acid digestion, no 'blank' contamination issues = lower detection limits
- Need to demonstrate LA-ICP-MS arsenic concentration ≈ total nail As

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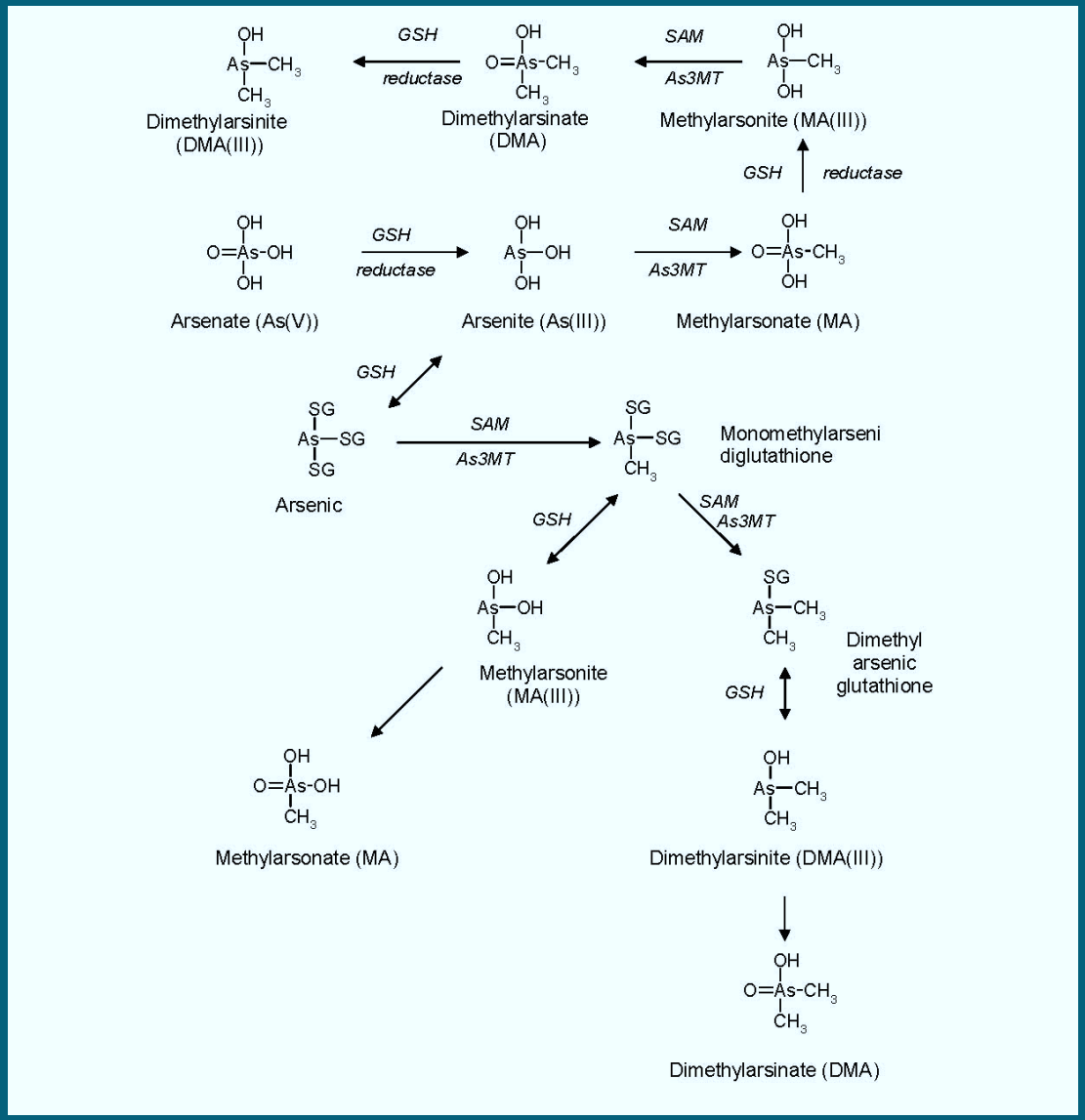
Urinary Arsenic

- Measure of recent arsenic exposure
  - Ingestion experiments by Buchet 1981 indicate half life 39-59 hrs
- Arsenic speciation techniques established

As metabolism ability may be risk factor for iAs-related toxicity



AsIII

↓

AsV

↓

MMA

↓

DMA

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Measuring Arsenic through Trace Element Analysis

- Trace Element Analysis Facility
- High resolution inductively coupled mass spectrometer, with hydride generation (HR-HG-ICPMS)
- Ultratrace detection (0.01 μg/L)
- Clean sample collection, masked QA (r ~ 0.98)
- Arsenic speciation (As+3, As+5)
- Multi-element

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Reducing Risk

What are the routes of arsenic exposure in our population?

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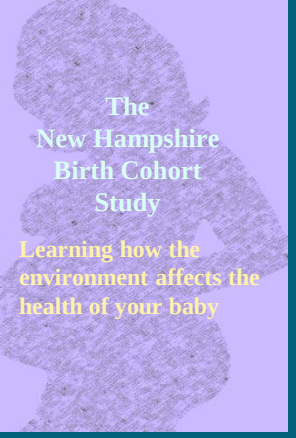
Water: an important potential exposure route in our population



Estimating arsenic intake through well water in our population

- Food frequency questionnaire
- 3-day water consumption history

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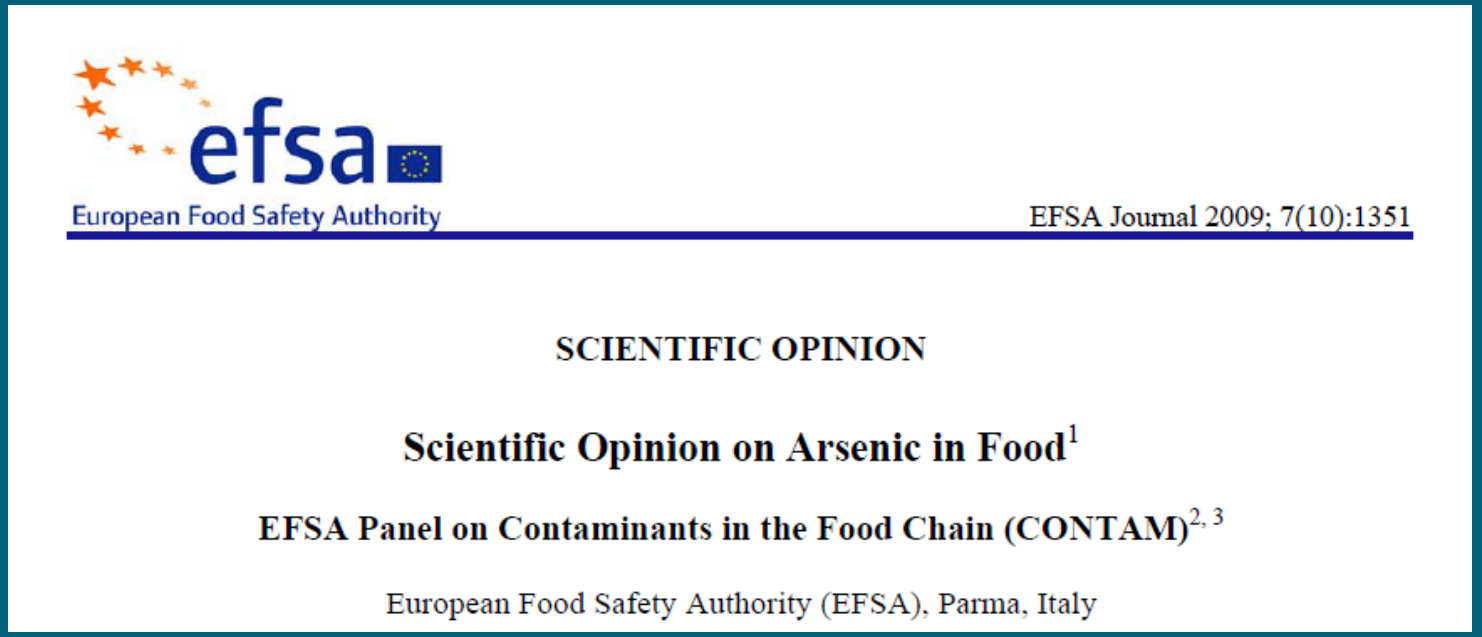
Food: another potential exposure route



efsa

European Food Safety Authority

EFSA Journal 2009; 7(10):1351

SCIENTIFIC OPINION

Scientific Opinion on Arsenic in Food[1]

EFSA Panel on Contaminants in the Food Chain (CONTAM)[2, 3]

European Food Safety Authority (EFSA), Parma, Italy

EFSA Conclusions regarding Arsenic in Food

- Adult intake: 0.13 – 0.56 μg/kg of body weight
- < 3 y children intake: 2-3 x higher than adults
- Main source of exposure: diet
- $BMDL_{01}$: 0.3 – 8 μg/kg of body weight

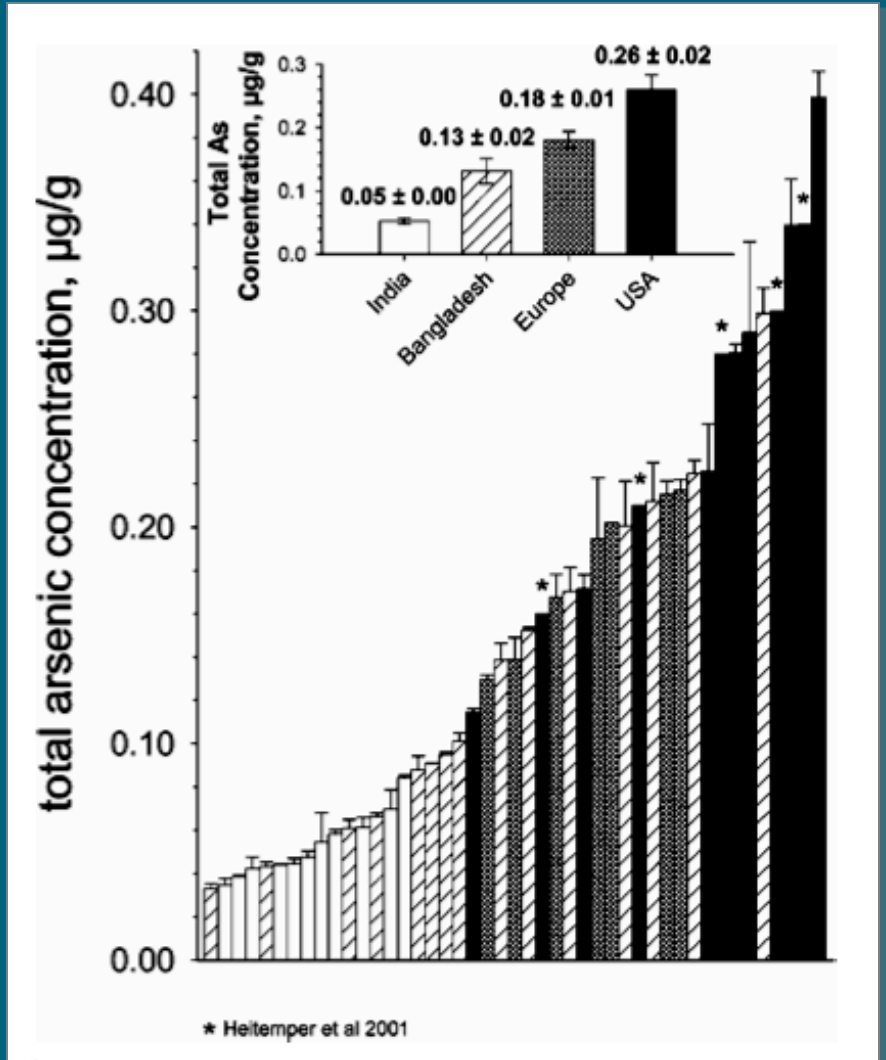
"Dietary exposure to arsenic should be reduced"

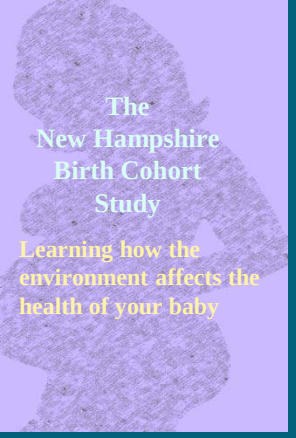
Arsenic in rice

Williams et al ES&T 39: 2005; Meharg et al 2008. Environmental Pollution

"USA long grain rice had the highest mean arsenic level in the grain at 0.26 µg As g^{-1}"

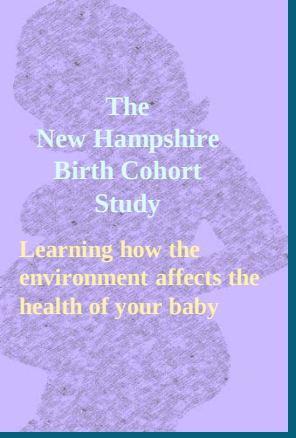
Baby rice and rice cereals also contain arsenic in this range.





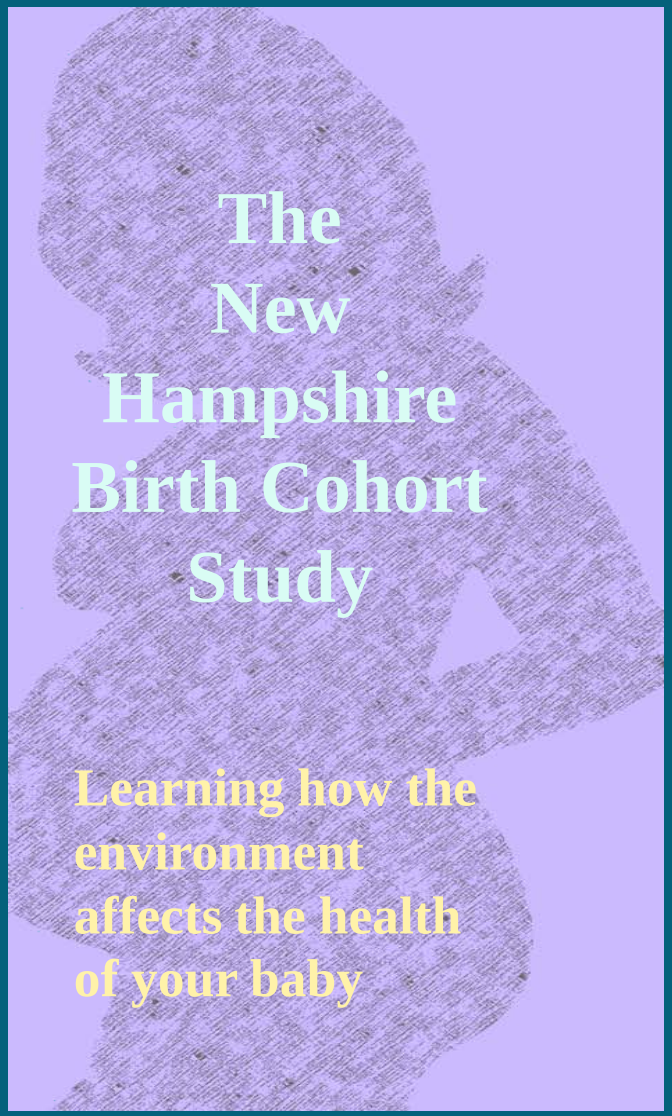
Estimating dietary sources of arsenic in our population

- Food frequency questionnaire
- 3-day water and seafood consumption history



Currently examining foods associated with biomarkers of maternal and fetal arsenic in Birth Cohort Study

Acknowledgements



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Thank You!