NIEHS
National Institute of
Environmental Health Sciences

NIEHS & Children's Environmental Health

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National Institute of Environmental Health Sciences

National Birth Defects Prevention Network 15th Annual Meeting

February 29, 2012

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
National Institutes of Health

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NIEHS Mission & Research

NIEHS Mission: reduce the burden of human illness and disability by understanding how the environment influences the development and progression of human disease.

- **The Division of Extramural Research & Training**: plans, directs and evaluates the Institute's grant program which supports research and research training in environmental health.
  - Early life exposures and effects on neurodevelopment, children's health, autism, reproductive health & adult diseases
  - Air pollution, pesticides, endocrine disrupting chemicals, ozone, dioxins, health disparities
  - Basic research and Community Outreach and Translation
- **National Toxicology Program**: evaluates chemicals/agents of public health concern by developing and applying tools of modern toxicology and molecular biology.
  - Reproductive and developmental studies of environmental chemicals
  - Center for the Evaluation of Risks to Human Reproduction (now referred to as OHAT) reports on agents: Acrylamide, BPA, Glycols, Methanol, Phthalates, Soy Formula
- **Division of Intramural Research**:
  - Norwegian Mother and Child Cohort Study (MoBa), early pregnancy, fibroids – epidemiology
  - Basic science of endocrine acting compounds – Laboratory of Reproductive and Developmental Toxicology, Epigenetics

"ENVIRONMENT" Includes:

- Industrial chemicals
- Agricultural chemicals
- Physical agents (heat, radiation)
- By-products of combustion and industrial processes (dioxin)
- Foods and nutrients
- Prescription drugs
- Lifestyle choices and substance abuse
- Social and economic factors



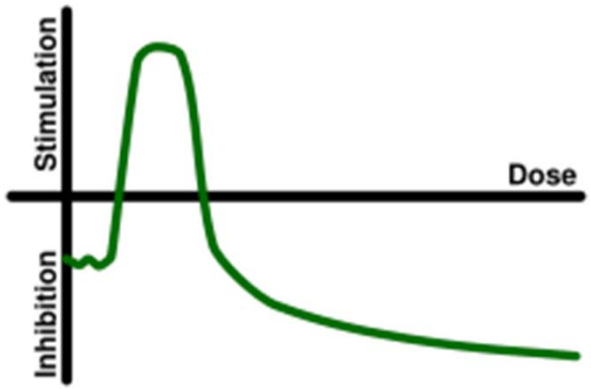

Need for Chemical Testing

- About 12 chemicals (alcohol, lead, mercury, etc.) have been closely associated with human cognitive impairment
- About 100 chemicals have been shown to impair brain development in animal models
- Vast majority of chemicals in commerce are untested for their impacts on neurodevelopment




How Much is Too Much?

- Chemicals, even in low doses, can cause significant, permanent harm to the developing fetus



Early Life Events

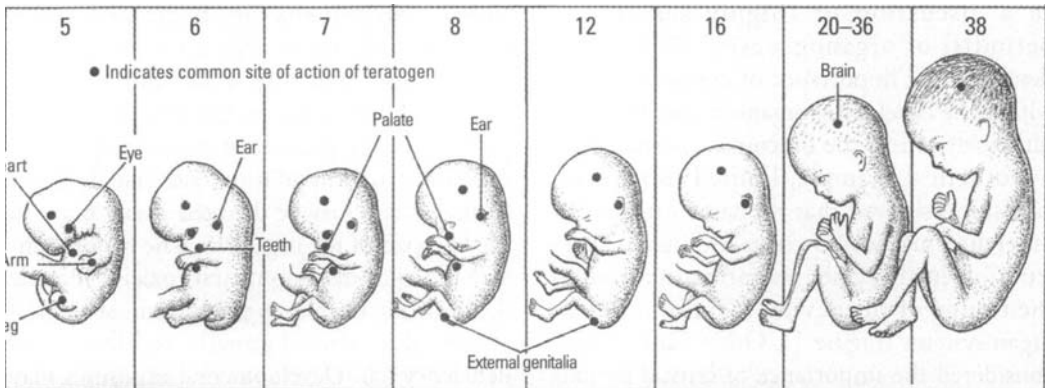
- Normal development is complex
- Exposures in early fetal life can have positive and negative effects on organogenesis
- Establishment of the proper hormonal milieu is essential for proper development
- Within the developmental trajectory there are windows of vulnerability and susceptibility for every organ and system and their interactions
- Turning on and off of genes occurring during development

Overt Effects vs. Functional Changes

- High doses
- Spontaneous abortion
- Stillbirth
- Birth Defects
- Fetal death

- Low doses can cause functional changes
- Effects are at a cellular or molecular level
- Increased susceptibility for disease in later life after additional exposures or aging

Vulnerability of Developmental Period to Environmental Chemicals



- Tissues and organs are forming at different rates
- Immune system is immature during development
- DNA repair not fully functional in all cells
- Liver metabolism lacks the ability to detoxify chemicals
- Blood brain/organ barriers not fully formed
- Epigenetic effects change over development and lifespan

The New Disease Paradigm: Developmental Origins of Disease

- The environment during development.. stress, nutrition, environ
  and drugs:
  - Ca
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  - s

A bad start…lasts a lifetime!
It is likely that all non infectious complex diseases have their origins during development

Developmental Exposures to Environmental Chemicals

- **Teratology**
  - Death
  - Birth Defects
  - Low Birth Weight
  - Functional Changes

Many chemicals will cause all effects depending on the timing and dose!

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Data on developmental exposures and health outcomes (functional changes)

From the NIEHS/EPA Centers for Children's Environmental Health and Disease Prevention

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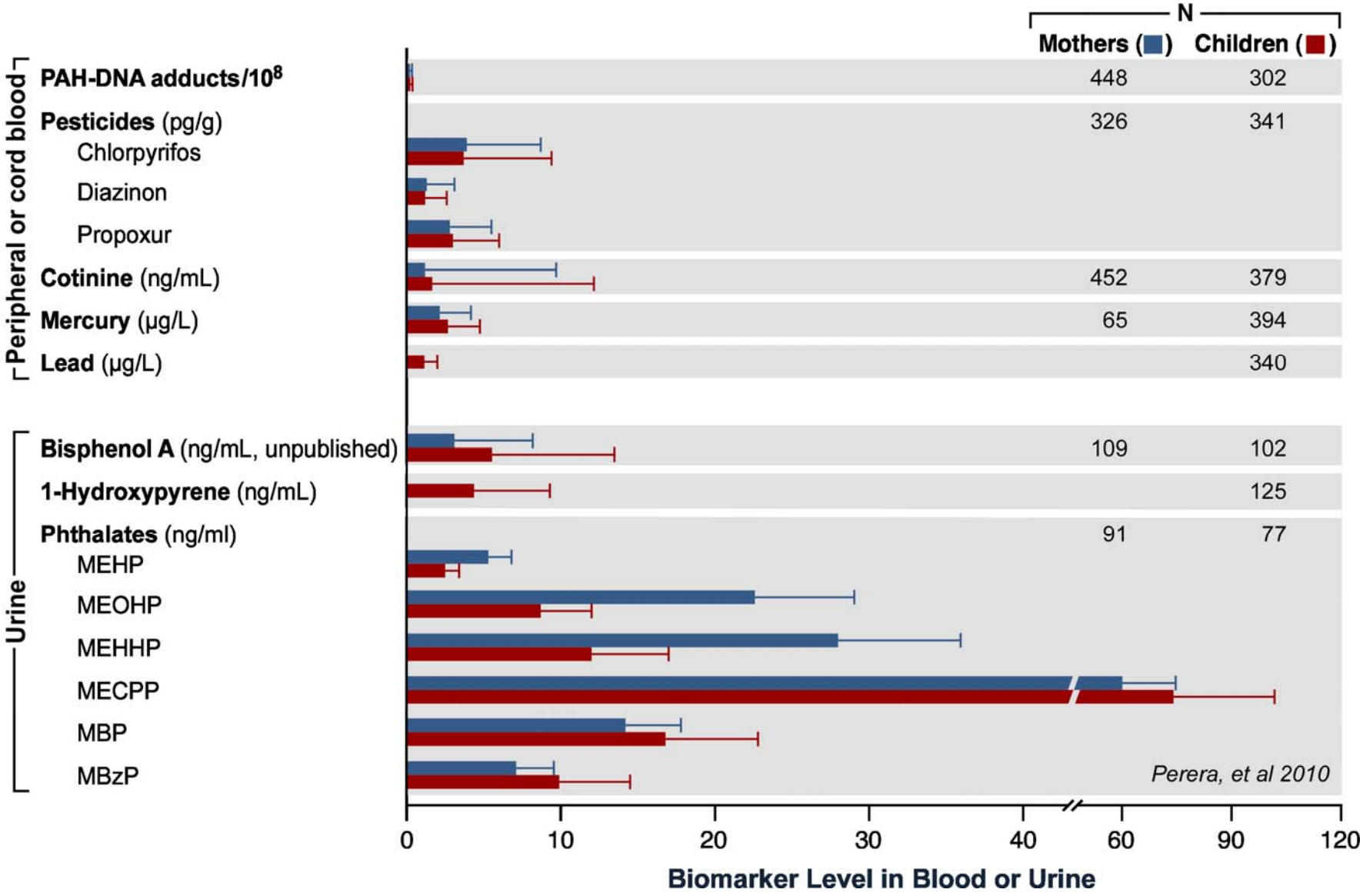
NIEHS/EPA Centers of Children's Environmental Health Research

To establish a national network that fosters communication, innovation and research excellence in Children's Environmental Health with the ultimate goal of reducing the burden of morbidity among children as a result of exposure to harmful environmental agents.

Phthalates and Biomarkers in Mother and Newborn Urines



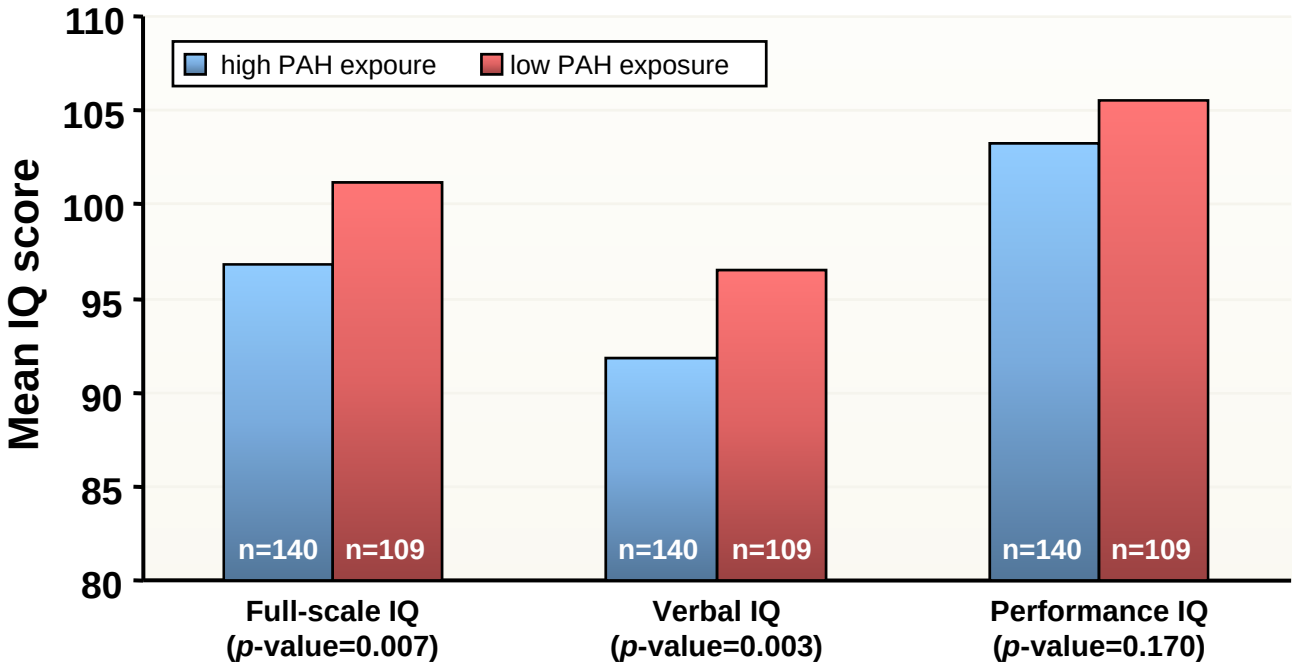
PAH or PAH-DNA adducts associated with:

- Reduction in birth weight and head circumference
- Developmental delays at age 3
- Reduced IQ scores at age 5
- Attentional/behavioral problems through age 7

[Perera et al., 2006, 2009; Edwards et al., 2009., Tang et al., 2008]

Adverse Effects of Prenatal PAHs on Children's IQ

Differences in Full-Scale, Verbal IQ and Performance IQ associated with high prenatal PAH exposure

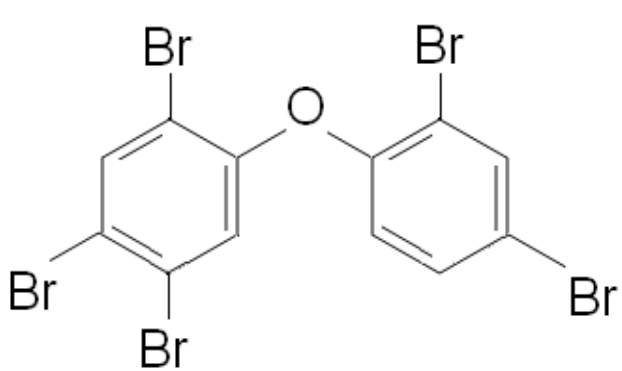


(*n* = 249). Mean IQ levels are adjusted for ETS exposure during pregnancy, gender of child, ethnicity, mother's intelligence (TONI), mother's education, and the quality of the home caretaking environment (HOME).

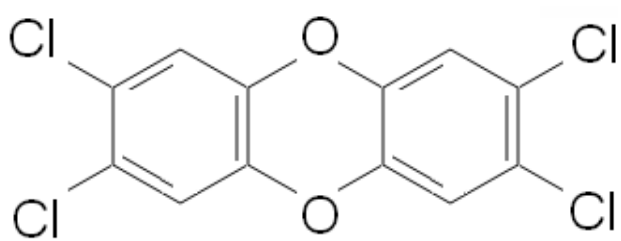
Perera FP, Li Z, Whyatt R, Hoepner L, Wang S, Camann D, Rauh V. Prenatal airborne polycyclic aromatic hydrocarbon exposure and child IQ at age 5 years. *Pediatrics.* 2009; 124(2):195-202

Polybrominated Diphenyl Ethers (PBDEs) – Flame retardants

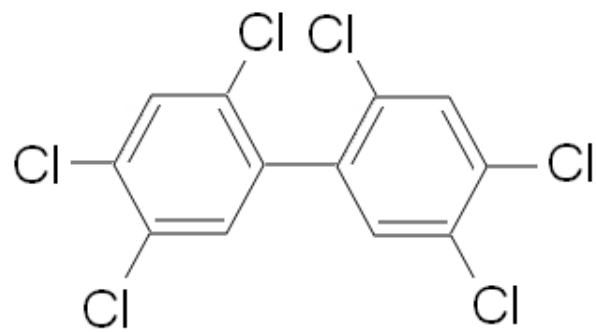
BDE-99



Dioxin



CB-153



- Structurally similar to halogenated carcinogens and PCBs
- PBDEs have been associated with…
  - Developmental neurotoxicity in animals
  - Altered hormone levels in adults
  - Fecundability (*i.e.*, time to pregnancy)

Children in 9/11 cohort with higher levels of PBDEs 47, 99 and 100

in cord blood scored lower on tests of mental and physical development

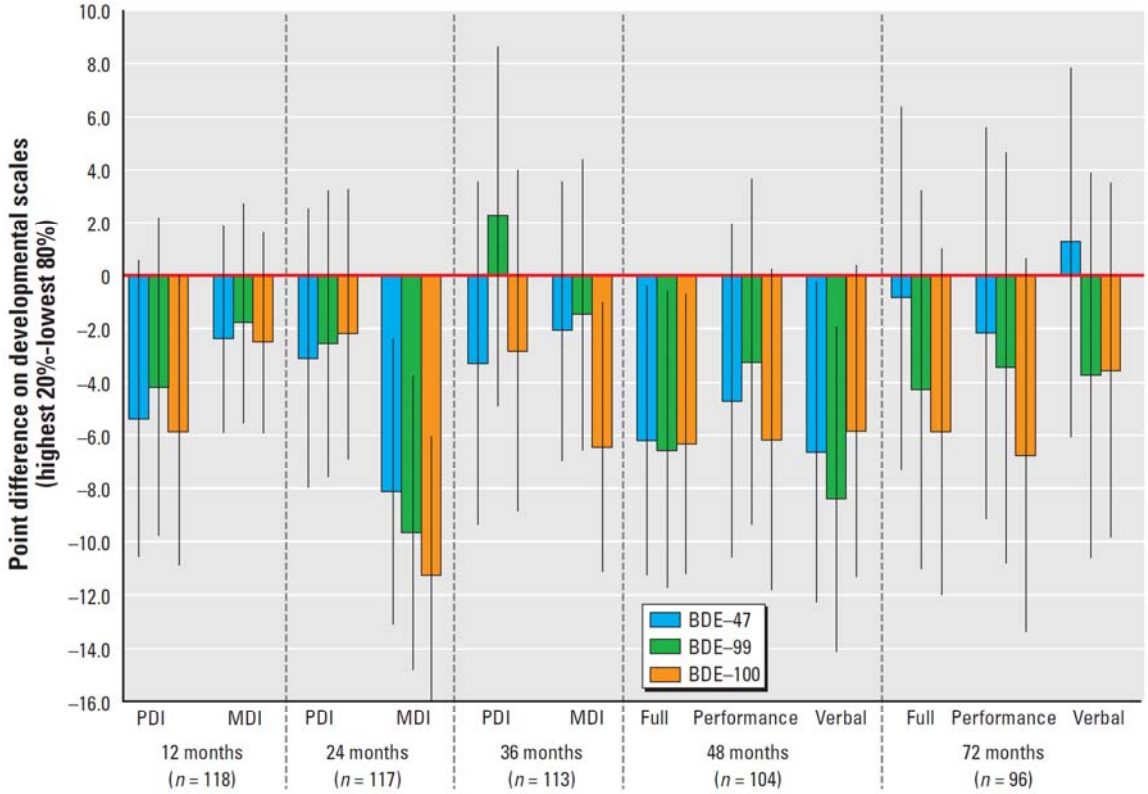


Figure 1. Difference in mean developmental score (and 95% confidence interval around the mean) comparing individuals in the highest quintile (20%) of exposure with those in the lower 80% of BDEs 47, 99, and 100. Mean differences were adjusted for age at testing, race/ethnicity, IQ of mother, sex of child, gestational age at birth, maternal age, ETS (yes/no), maternal education, material hardship, breast-feeding, language, and location of interview.

Herbstman et al. 2010 EHP
Columbia Children's Center

Study Questions

What are the effects of *in utero*/early life exposure to arsenic on children's health:

--immune function/infection

-- developmental pathways

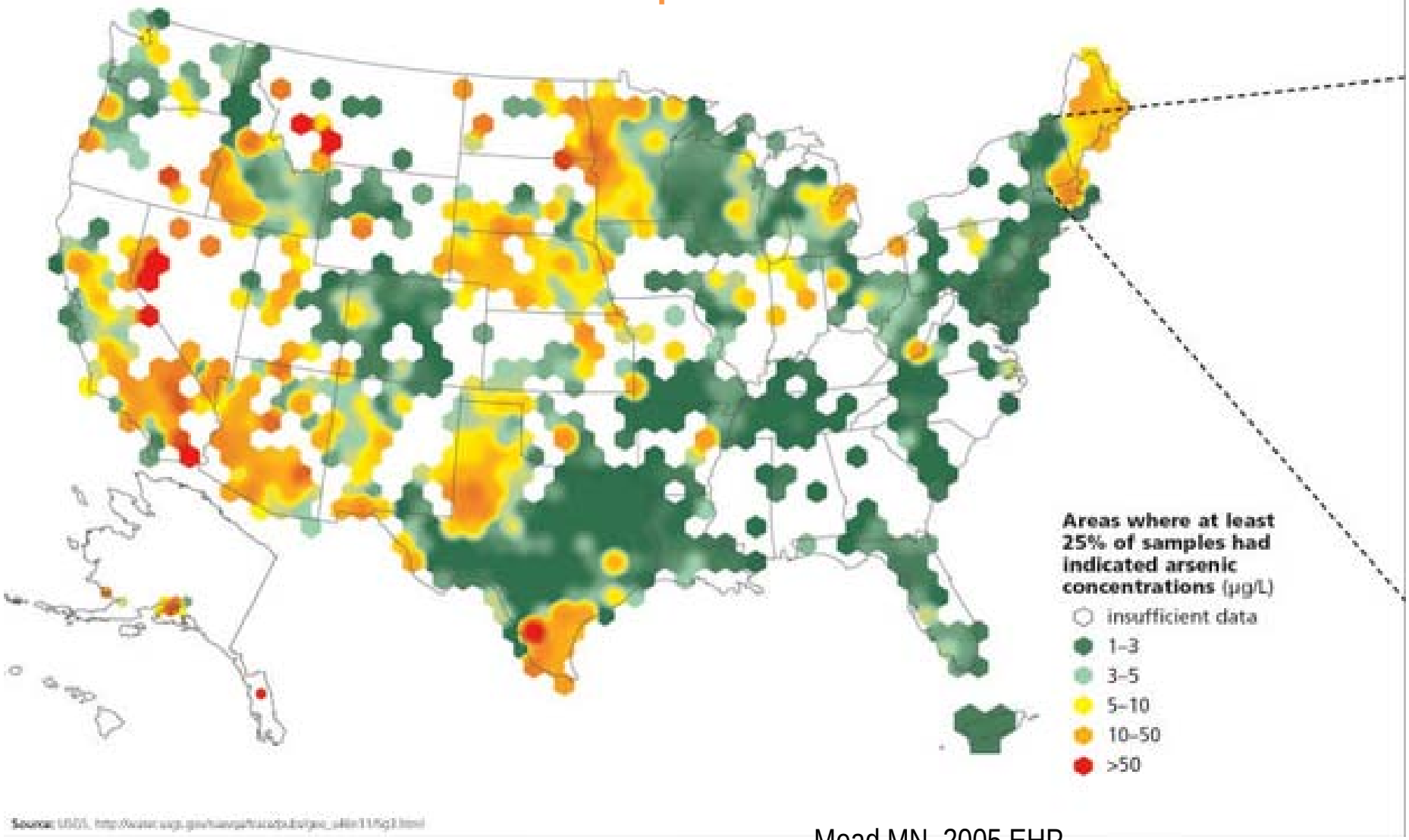
-- birth defects

What are the sources of exposure, in particular via infant diet, rice, rice products?

http://www.dartmouth.edu/~childrenshealth/

Thanks to Margaret Karagas

Arsenic in water samples across the U.S.



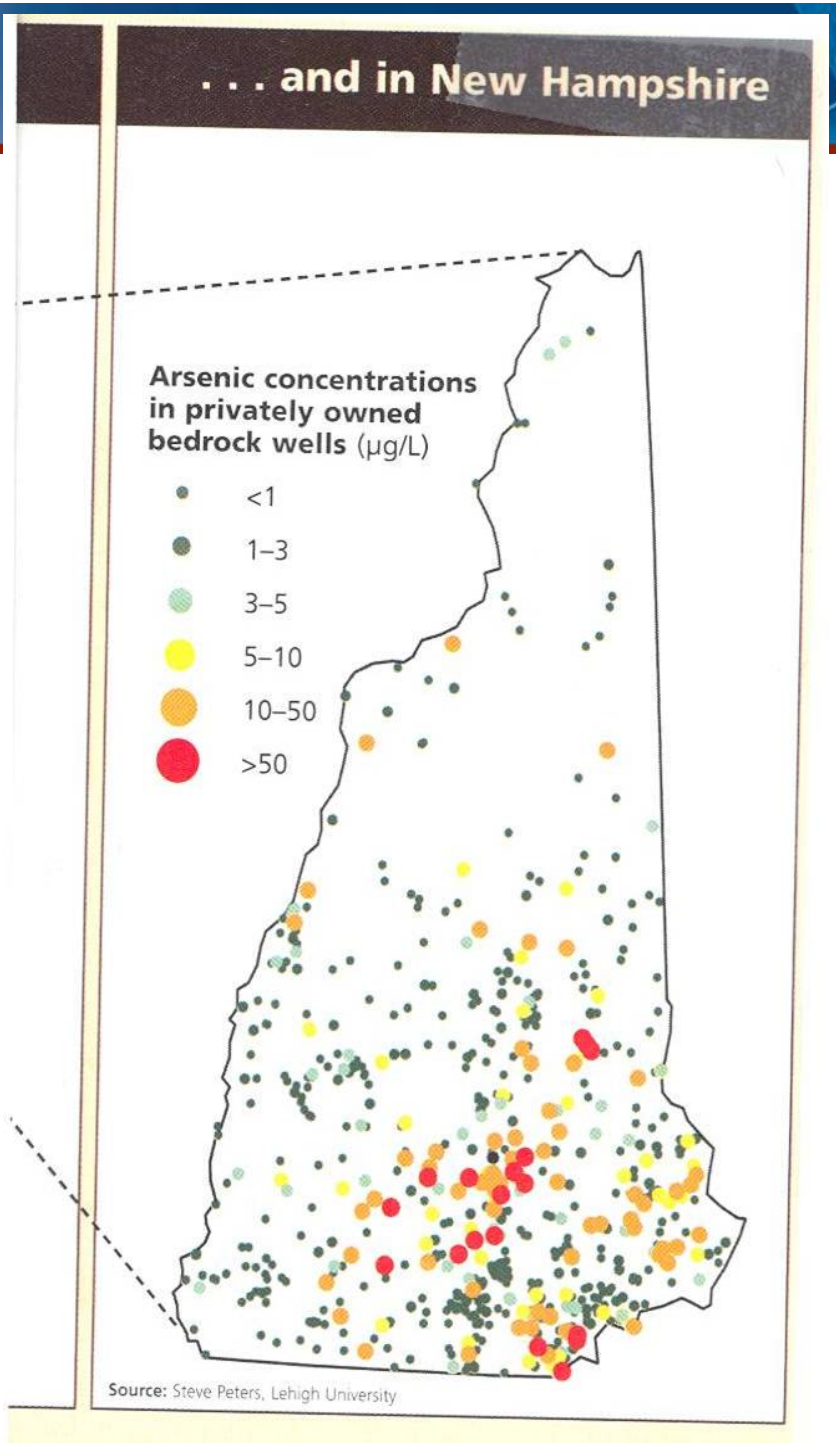
Source: USGS, http://water.usgs.gov/nawqa/hrbp/hrbp_table11/fig11.html

Mead MN, 2005 EHP

Rural Population

>40% use private water systems

>10% wells
>MCL (maximum contaminant level) of 10 ug/L As



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The Children's Environmental Health and Disease Prevention Center at Dartmouth

Dartmouth College, Hanover, New Hampshire

February 28, 2012

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- Project 3
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- Community Outreach
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Project 3: An Integrated Geospaital and Epidemiological Study of Associations Between Birth Defects and Arsenic (As) Exposure in New England

Mission: To integrate geospatial and epidemiological data and characterize the spatial distribution of birth defects in New England in relation to inorganic arsenic.

Few epidemiologic studies exist on the potential teratogenic effects of arsenic in humans. Project 3 will measure the spatial distribution of birth defects and look for high-risk areas. Spatial associations between birth defects and private well drinking water arsenic concentrations will be examined and we will conduct feasibility studies to investigate, at the individual level, the associations between birth defect occurrence, arsenic and other environmental exposures.

Geocoded data on birth defect occurrences will be made available through the New Hampshire Birth Cohort Study. Project 3 will estimate drinking water arsenic exposure using public databases combined with a large data set of private water systems collected through epidemiologic studies in the state in collaboration with the U.S. Geological Survey. Project 3 will test whether conducting a case-control

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Co-Investigator

100%

A Good Start also Lasts a lifetime…

- **Improved Nutrition**
  - Prepregnancy
  - Pregnancy
  - Infancy/childhood
- **Reduced Stress**"Envir
  - Pregnancy
  - Infancy/childhood
- **Reduced Infection**
  - Pregnancy
  - Childhood
- **Reduced exposures to**
  - Prepregnancy
  - Pregnancy
  - Infancy/childhood

Because of the data supporting the developmental basis of disease….
We know what to do and when to do it…to PREVENT DISEASE

Relevant NIEHS Funding Opportunities

Funding Opportunity Announcement Title
Role of Environmental Chemical Exposures in the Development of Obesity, Type 2 Diabetes and Metabolic Syndrome (R01, R21)
Children's Environmental Health Centers (P01) coming soon
Virtual Consortium for Transdisciplinary/Translational Environmental Research (ViCTER) – R01 Competitive Revisions
Mechanisms for Time-Sensitive Research Opportunities (R21, R03)
Unsolicited Research Grants (R01, R21, R03)
Training, Fellowship and Career development awards (Ts, Fs, and Ks)

http://www.niehs.nih.gov/funding/grants/announcements/index.cfm

Relevant Meetings

Meeting Title/Date/Location
EPA & NIEHS Children's Environmental Health and Disease Prevention Centers: Strengthening Network, March 6-7, 2012, NIH, Natcher, Bethesda, MD
Strengthening a Dynamic Environmental Public Health Network for Tomorrow: Partnerships for Environmental Public Health, March 7-8 2012, NIH Natcher, Bethesda, MD
NTP, OHAT, Excess Folic Acid Workshop, June 12-13, 2012, Washington, DC
EPA & NIEHS Children's Environmental Health Center Webinar Series- Second Wednesday of each month at 1 pm EST. Next March 14, 2012 http://www.scgcorp.com/epaniehs2012/

http://www.niehs.nih.gov/news/events/highlight/index.cfm

Questions

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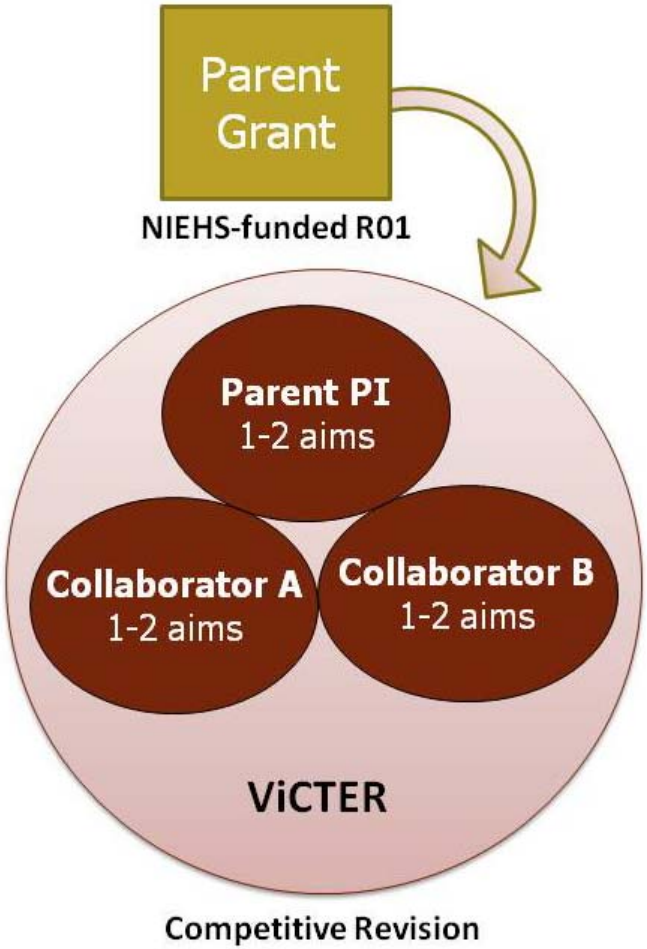
Virtual Consortium for Translational/Transdisciplinary Environmental Research (ViCTER)



- Create new virtual consortium to foster transdisciplinary collaboration and promote translational research efforts in an identified environmental health area
- Accelerate the exchange of knowledge and resources among collaborators
- Expand scope of parent grant through collaborative, synergistic aims → whole is greater than the sum of the parts