Prenatal Exposure to EDCs and Developmental and Health Outcomes in a New York City Cohort

Frederica Perera DrPH, PhD

The Columbia Center for Children's Environmental Health
Columbia University
Mailman School of Public Health

CHE Partnership Call
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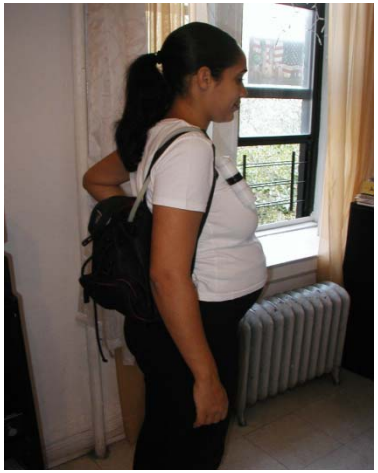
Columbia Center for Children's Environmental Health (CCCEH)

Research Overview



Mission: **Prevention** of childhood neurodevelopmental impairment, asthma, obesity and cancer through early identification of environmental risk factors and **translation** to intervention

Multiple Exposures to EDCs and Outcomes in the CCCEH Cohort

SES/Exposure → Biomarkers → Outcomes

PAH
BPA
Phthalates
CPF
PBDEs
ETS

- Neurodevelopment
- Birth Outcomes
- Obesity/metabolic disorders
- Asthma/Wheeze/Air way inflamm.
- Cancer risk

Multiple Exposures To EDCs and Outcomes in the CCCEH Cohort

SES/Exposure → Biomarkers → Outcomes

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Mechanisms:
- Epigenetics
- MRI

Neurodevelopment

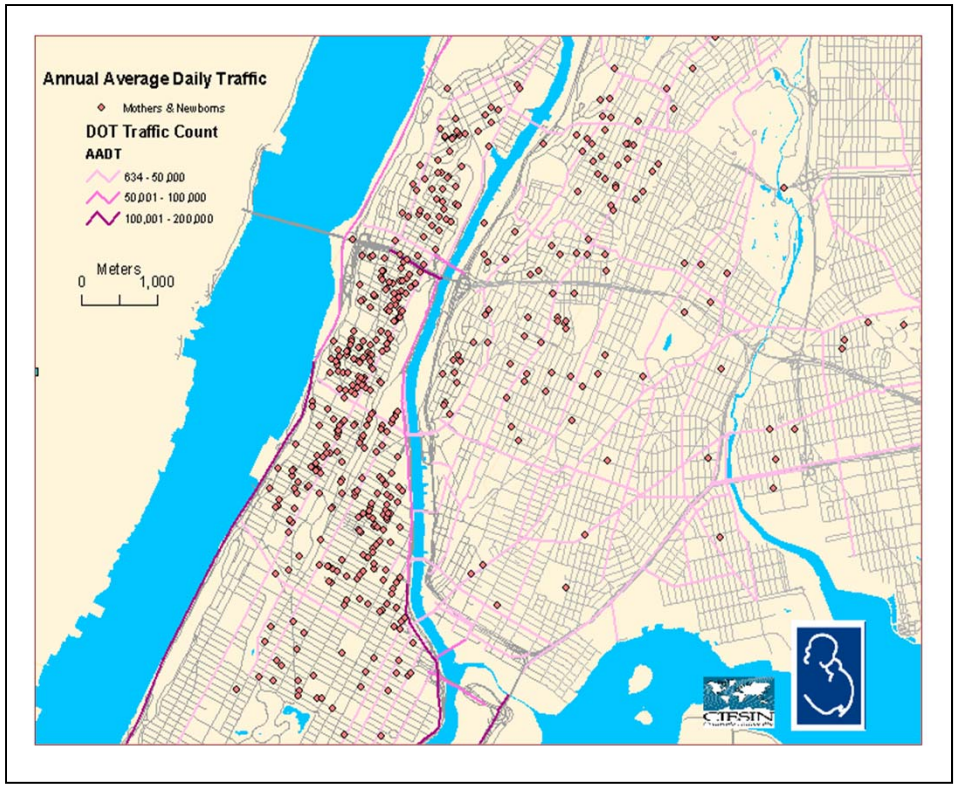
Birth Outcomes

Obesity/metabolic disorders

Asthma/Wheeze/ Airway inflamm.

Cancer risk

CCCEH NYC Cohort Study: 720 Mother-Child Pairs Enrolled

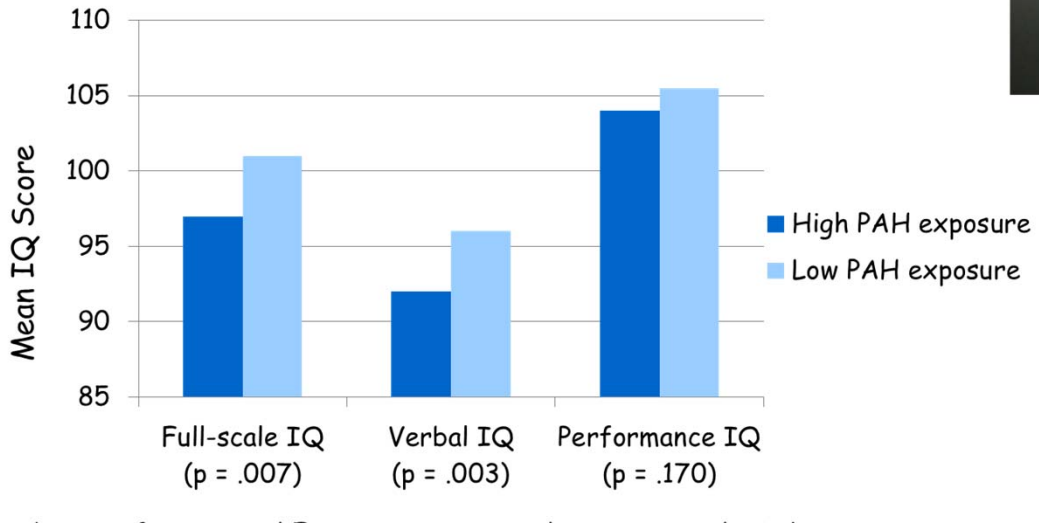


- Mothers non-smoking and healthy, ages 18-35
- African American and Dominican Residents of northern Manhattan and the S. Bronx
- 63.5% of mothers had completed high school education or more
- Mostly low income, on Medicaid
- Recruited during pregnancy: maternal urine and blood collected
- Prenatal personal air monitoring
- Cord blood and placenta collected at birth, blood and urine from children (2 yr-adolescence)
- Follow-up of children through adolescence
- GIS

RESEARCH FINDINGS: PAH

- Prenatal exposure associated with:
  - Developmental delay age 3 (OR= 2.89, 0.01)
  - IQ reduction at age 5 (β=4.31; p=.007)

High prenatal PAH levels associated with reduced full-scale and verbal IQ scores



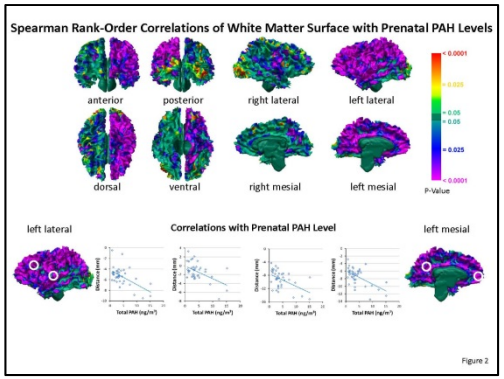
Adjusting for potential confounders

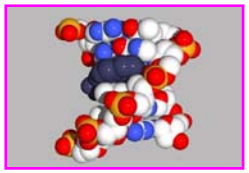
[Perera et al., 2006; 2009; 2012]

RESEARCH FINDINGS: PAH

- Behavioral problems (e.g., anxiety/depression symptoms) ages 6-7
- Prenatal PAH exposure associated with MRI brain changes (age 7-9)

Exposure	Syndrome Scales Anxious /Depressed		
	Exp beta	95% CI	p-value
PAH (high/low) (n=253)	1.45	(1.22, 1.72)	**<0.0001**
Maternal adducts (n=223)	1.23	(1.04, 1.46)	**0.019**
Cord adducts (n=148)	1.46	(1.19, 1.78)	**<0.001**



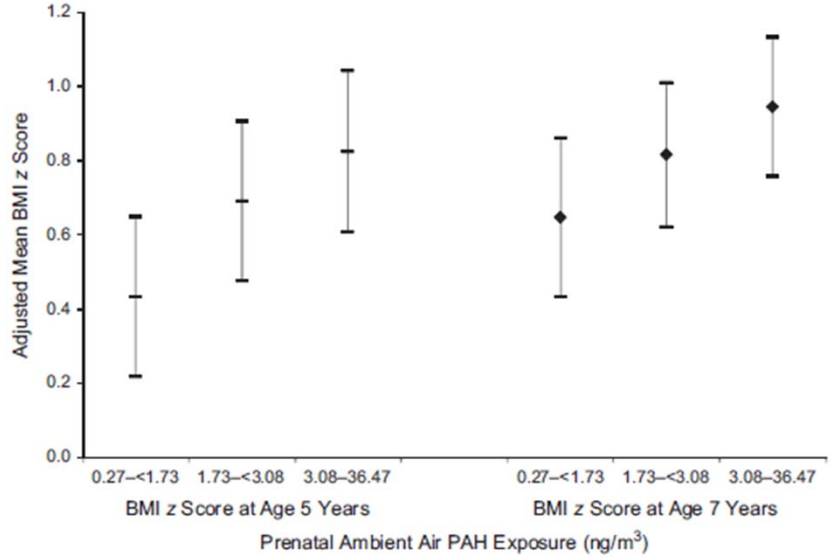


Adjusting for potential confounders

[Peterson et al., submitted, Perera et al., 2012]

RESEARCH FINDINGS: PAH

- Prenatal PAH exposure associated with **obesity** over childhood years



RR=1.79 at age 5;
2.26 at age 7

- High prenatal and high postnatal exposure to PAH (pyrene) associated with **asthma** in children (OR=1.90; 95% CI:1.13-3.20)

- Cockroach allergen and prenatal PAH exposures predict cockroach **allergic sensitization** at ages 5-7

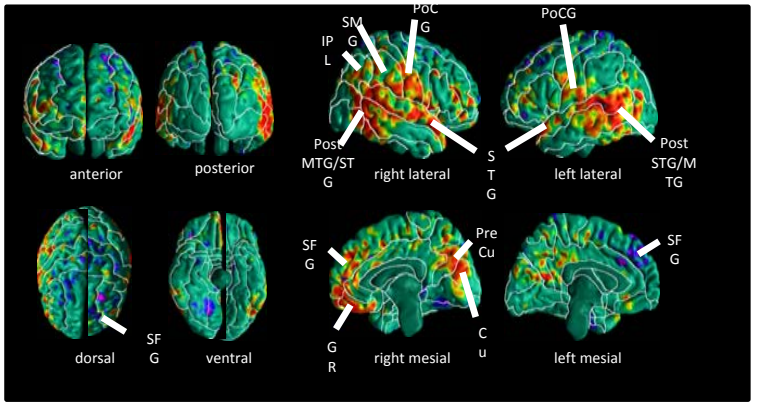
*All analyses adjusting for relevant covariates: environmental co-exposures and social factors

[Rundle et al., 2012; Jung et al., 2012; Perzanowski et al., 2013]

RESEARCH FINDINGS: CPF

- Prenatal CPF exposure associated with reduction in Working Memory at age 7 (p=0.003)

- Brain changes at ages 7-9 (MRI scan) appear to mediate the adverse neurodevelopmental effects of CPF



High CPF exposure associated with enlargement of superior temporal, posterior middle temporal, and inferior postcentral gyri bilaterally, and enlarged superior frontal gyrus, gyrus rectus, cuneus, and precuneus along the mesial wall of the right hemisphere

* All analyses adjusting for relevant covariates

[Rauh et al., 2011, 2012]

Research Findings: Phthalates

- Phthalates associated with **airway inflammation**
  - DEP and BBzP associated with increase in fractional exhaled nitric oxide (FeNO)

- Phthalates associated with **eczema**
  - MBzP with early onset eczema (RR=1.52, p=0.0003)

Metabolites:
- BBzP - butylbenzyl phthalate
- DEP - diethyl phthalate
- MBzP - mono-benzyl phthalate
- MiBP - mono-isobutyl phthalate
- MnBP - mono-n-butyl phthalate

- Phthalates associated with adverse child **mental, motor, and behavioral development**
  - Psychomotor Development Index (PDI) with MnBP and MiBP
  - Mental Development Index (MDI) with MnBP in girls
  - Clinically withdrawn behavior with MnBP

*All analyses adjusting for relevant covariates: environmental co-exposures and social factors

[Just et al., 2012; Whyatt et al., 2011]

RESEARCH FINDINGS: PBDEs

Prenatal Exposure to PBDEs and Neurodevelopment

Julie B. Herbstman,[1] Andreas Sjödin,[2] Matthew Kurzon,[1] Sally A. Lederman,[1] Richard S. Jones,[2] Virginia Rauh,[1] Larry L. Needham,[2] Deliang Tang,[1] Megan Niedzwiecki,[1] Richard Y. Wang,[2] and Frederica Perera[1]

[1]Columbia Center for Children's Environmental Health, Department of Environmental Health Sciences, Mailman School of Public Health, Columbia University, New York, New York, USA; [2]Division of Laboratory Sciences, National Center for Environmental Health, Centers for Disease Control and Prevention, Atlanta, Georgia, USA

Background: Polybrominated diphenyl ethers (PBDEs) are widely used flame retardant compounds that are persistent and bioaccumulative and therefore have become ubiquitous environment contaminants. Animal studies suggest that prenatal PBDE exposure may result in adverse neurodevelopmental effects.

Objective: In a longitudinal cohort initiated after 11 September 2001, including 329 mothers who delivered in one of three hospitals in lower Manhattan, New York, we examined prenatal PBDE exposure and neurodevelopment when their children were 12–48 and 72 months of age.

Methods: We analyzed 210 cord blood specimens for selected PBDE congeners and assessed neurodevelopmental effects in the children at 12–48 and 72 months of age; 118, 117, 114, 104, and 96 children with available cord PBDE measurements were assessed at 12, 24, 36, 48, and 72 months, respectively. We used multivariate regression analyses to evaluate the associations between concentrations of individual PBDE congeners and neurodevelopmental indices.

Results: Median cord blood concentrations of PBDE congeners 47, 99, and 100 were 11.2, 3.2, and 1.4 ng/g lipid, respectively. After adjustment for potential confounders, children with higher concentrations of BDEs 47, 99, or 100 scored lower on tests of mental and physical development at 12–48 and 72 months. Associations were significant for 12-month Psychomotor Development Index (BDE-47), 24-month Mental Development Index (MDI) (BDE-47, 99, and 100), 36-month MDI (BDE-100), 48-month full-scale and verbal IQ (BDE-47, 99, and 100) and performance IQ (BDE-100), and 72-month performance IQ (BDE-100).

Conclusions: This epidemiologic study demonstrates neurodevelopmental effects in relation to cord blood PBDE concentrations. Confirmation is needed in other longitudinal studies.

Key words: biomarkers, children, neurodevelopment, PBDEs, polybrominated diphenyl ethers, prenatal, World Trade Center, WTC. *Environ Health Perspect* 118:712–719 (2010). doi:10.1289/ehp.0901340 [Online 4 January 2010]

Polybrominated diphenyl ethers (PBDEs) are widely used flame retardant compounds applied to a wide array of textiles, building materials, and electronic equipment, including computers and televisions. B are additives rather than chemi to consumer products, they ha pensity to be released into the e (Darnerud et al. 2001). PBDEs a organic chemicals, and some co bioaccumulate; therefore they h ubiquitous contaminants detect environment, in animals, and (Hites 2004; Sjodin et al. 2008b).

A number of toxicologic studie onstrated that exposure to PBDE endocrine-disrupting effects. M studies have focused on thyroid h ruption and a smaller number o of the estrogen/androgen horm [reviewed by Darnerud (2008)]. Ex ruption during critical developme may result in irreversible effects o ating tissue, including the brain (1999). Causal relationships betw exposure to PBDEs and indices of developmental neurotoxicity have been observed in experimental animal models [reviewed by Costa and Giordano (2007)]. Thus, the disruption of endocrine pathways by prenatal exposure to hormonally active environmental chemicals may affect neurodevelopment in children.

Although the association between prenatal exposure to PBDEs and adverse neurodevel-

York University Downtown Hospital, which is within a half-mile of the WTC site. The study methods have been described previously (Lederman et al. 2004). In brief, beginning 12 December 2001 [when institutional review board (IRB) approval was obtained], women were approached in the hospital when they presented for labor and delivery. The women were briefly screened for eligibility, recruited, and enrolled, and they consented before delivery. This study was conducted in accordance with all applicable requirements of the United States (including IRB approval), and all human participants gave written informed consent before participation in this study. Eligible women included those who were between 18 and 39 years of age, reported smoking < 1 cigarette per day during pregnancy, were pregnant on 11 September 2001 (based on their estimated date of conception), and reported no diabetes, hypertension, HIV infection or AIDS, or use of illegal drugs in the preceding year. Not all mothers agreed to have their child followed after birth. For example, some of the Chinese children were to be raised in China [see Supplemental Material, Table 1 (doi:10.1289/ehp.0901340) for follow-up information].

Data collection. Medical records of the mother and newborn were abstracted for information relating to pregnancy, delivery,

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quently delivered at one of three downtown hospitals including Beth Israel, St. Vincent's (and St. Vincent's affiliated Elizabeth Seton Childbearing Center), which are all approximately 2 miles from the WTC site, and New

The findings and conclusions in this report are those of the authors and do not necessarily represent the views of the Centers for Disease Control and Prevention.

The authors declare they have no actual or potential competing financial interests.

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[Herbstman et al., 2010]

RESEARCH FINDINGS: BPA

- Prenatal BPA associated with adverse **neurobehavioral outcomes** at ages 3-5
  - Among boys—high exposure associated with significantly higher CBCL scores on Emotionally Reactive (1.62 times greater) and Aggressive Behavior syndromes (1.29 times greater)
  - Among girls—higher exposure associated with lower scores on all syndromes

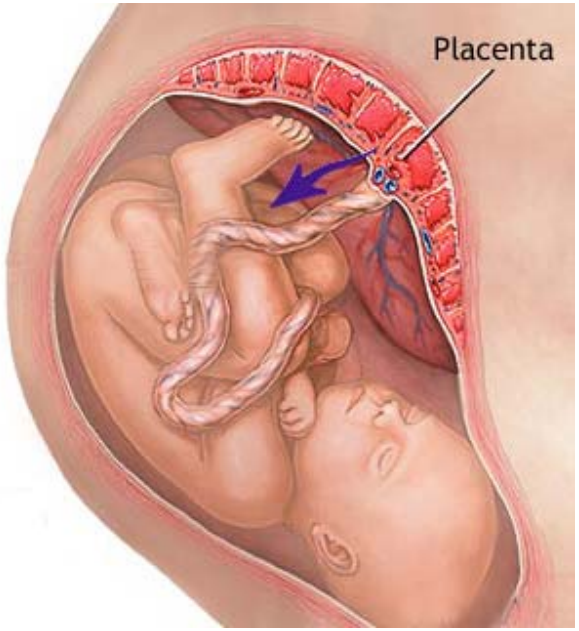
- Postnatal BPA (urinary concentrations) associated with **asthma**
  - BPA at age 3 associated with wheeze at age 5 (OR, 1.4; p=.02) and age 6 (OR=1.4; p=.03)
  - BPA at age 7 associated with wheeze at age 7 (OR, 1.4; p=.04) and FeNO (β = 0.1; p=.02)
  - BPA at ages 3, 5, and 7 associated with asthma (OR, 1.5; p=.005; OR, 1.4; p=.03; and OR, 1.5; p=.04, respectively)

*All analyses adjusting for relevant covariates: environmental co-exposures and social factors

[Perera et al., 2012; Donohue et al., 2013]

Experimental Studies: Effects of Prenatal BPA Exposure on the Developing Brain

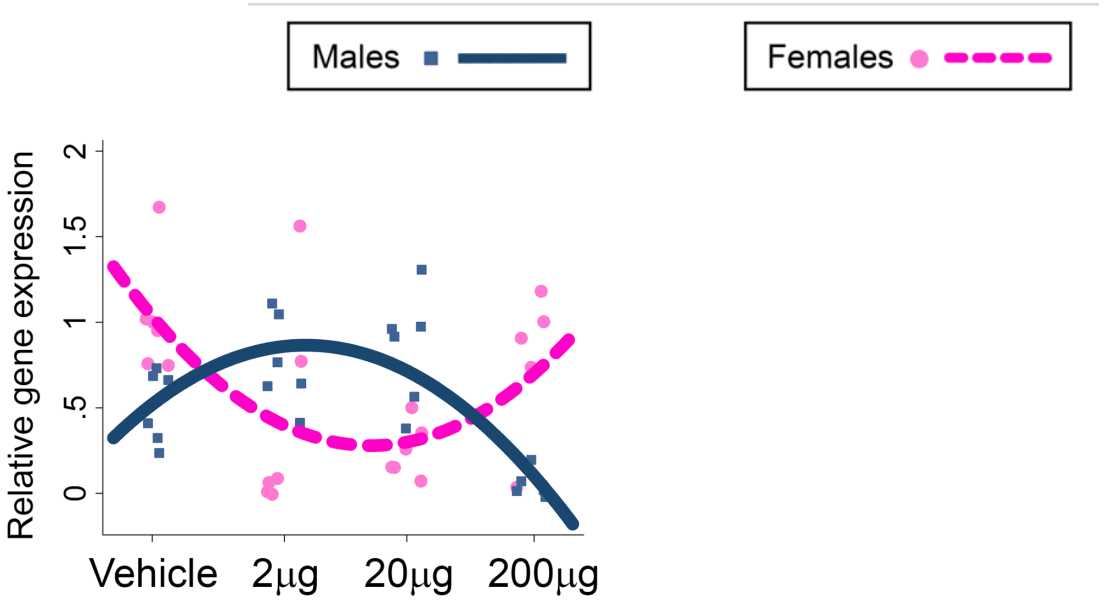
BPA



- Brain development
- Sexual differentiation (BPA)
- Behavior
- Learning

Epigenetic mechanisms?

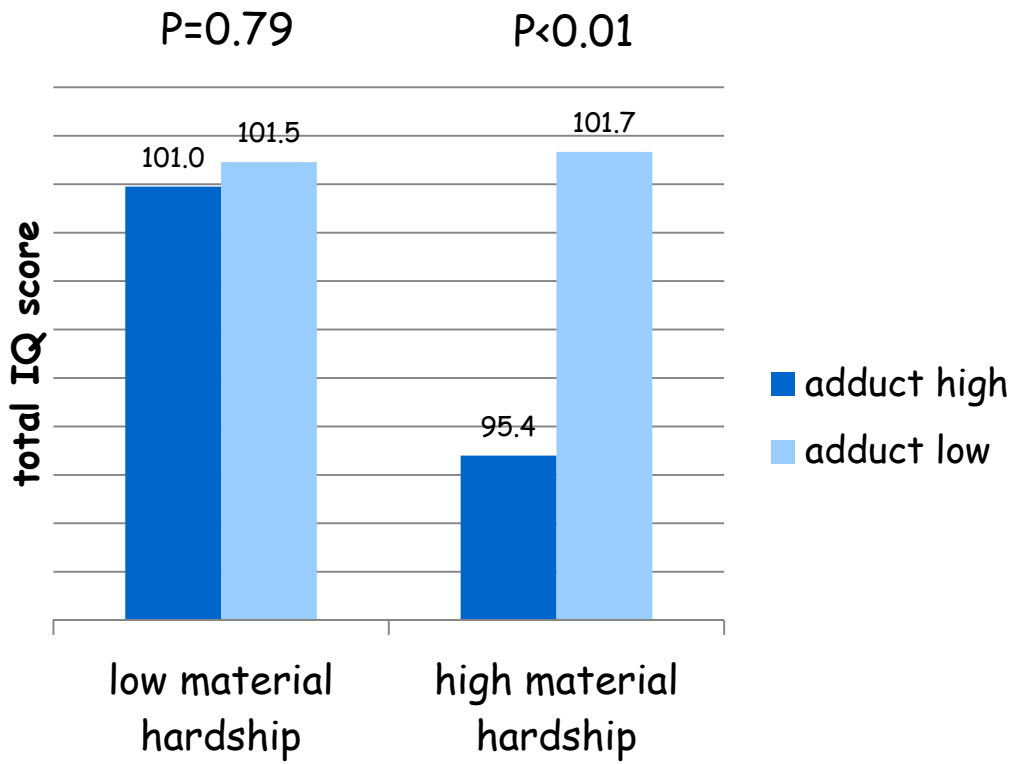
Experimental Studies: Epigenetic and behavioral effects of BPA



- Sex-specific curvilinear effects of gestational BPA exposure on ERa mRNA in the offspring hypothalamus
- Changes in ERa gene expression are associated with changes in DNA methylation also in the offspring hypothalamus
- Changes in ERa gene expression are associated with alteration in social and anxiety-like behavior

[Kundakovic, Champagne et al., 2013]

Social Stressors and Toxic Pollutants Can Interact

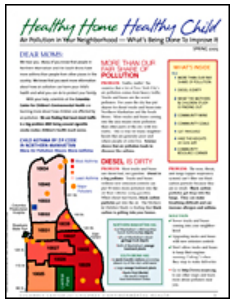


Children with high prenatal exposure (cord adducts) had a lower total IQ score by 6.3 points ($p<0.01$) and a lower working memory score by 9.1 points ($p<0.01$), compared to those with low cord adducts.

[Vishnevetsky et al., submitted]

TRANSLATION OF RESEARCH TO PREVENTION

- The Center's *Healthy Homes Healthy Child Campaign*



- Communication by Center investigators and WEACT to cohort families, the community and policy- makers

- Impact on policy:

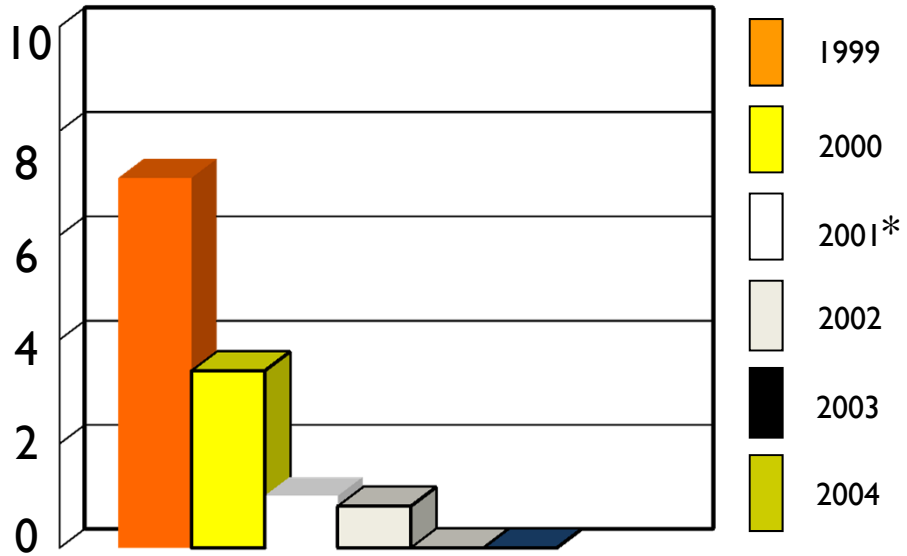
  - Supported reduction of emissions from diesel buses and trucks, cars, and other combustion sources in the City*
  - Supported clean heating fuel policy in NYC
  - Supports clean energy and climate policy
  - Demonstrated benefit of EPA phase-out of residential CPF
  - Prompted passage of Local Law 37, placing New York at the forefront of safer pest control methods in the United States*
  - Demonstrated efficacy of Integrated Pest Management (IPM) interventions in public housing (Kass et al., 2009)

- Brought attention to need for coordinated social and environmental interventions

*Commendation from Mayor Michael Bloomberg, 2009

POLICY RELEVANT RESEARCH

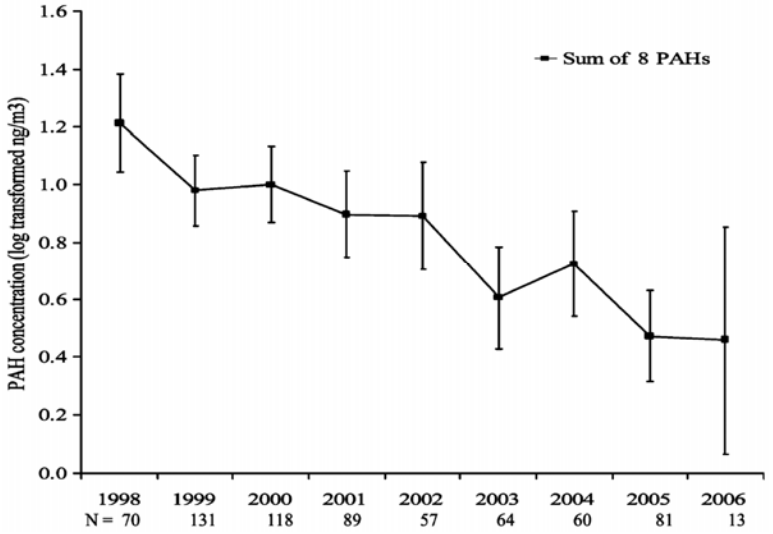
CPF in cord blood (N=395)*
(pg/g)



**EPA Ban on residential use of chlorpyrifos took effect in 2001*

[Whyatt et al., 2003]

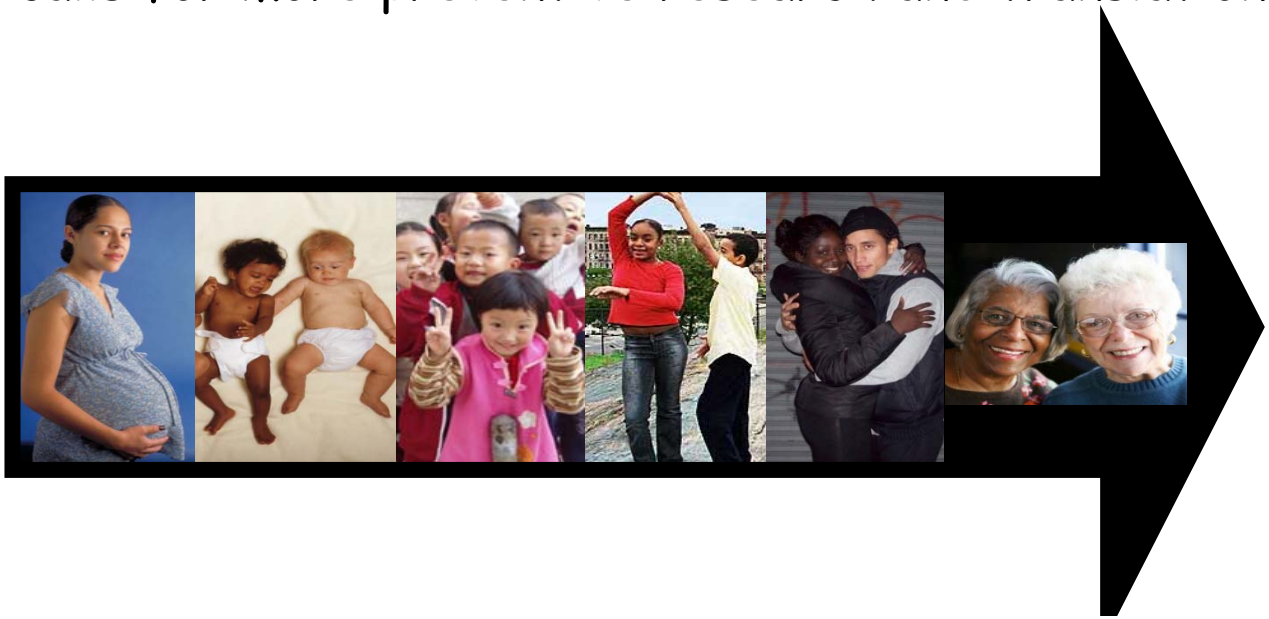
Personal Prenatal Exposure to PAH in the NYC Cohort Declined from 1998 to 2006



[Narvaez, et al. 2008]

Overall Conclusion

- Prenatal and continuing environmental exposures can affect children's health and development with implications for children's ability to learn and their future well-being
- Preventive policies are needed to protect this vulnerable life stage
- Benefits will be seen in childhood and are likely to accrue over the entire life course
- This calls for more preventive research and translation



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