Environmental Threats to Children's Developing Brains

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Perera, 2017.

Outline

- The Problem
- Importance of research
- Some findings from CCCEH
- A call to action: TENDR
- Present threats
- Solutions

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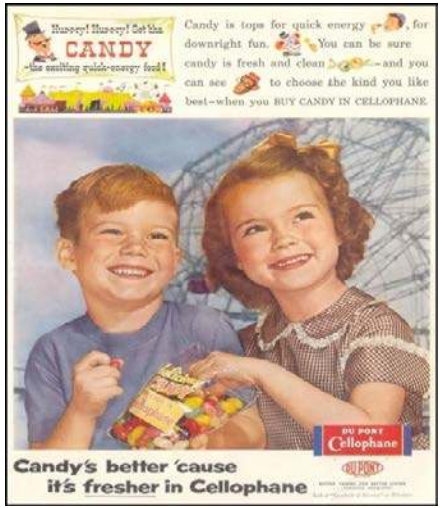
Chemicals and Us



- More than 84,000 chemicals in use today (EPA, 2012)
- Only 20% of chemicals in use have been tested for <u>any</u> early developmental effects (Landrigan and Goldman, 2011); about 200 chemicals documented to be neurotoxic (Grandjean and Landrigan, 2006)

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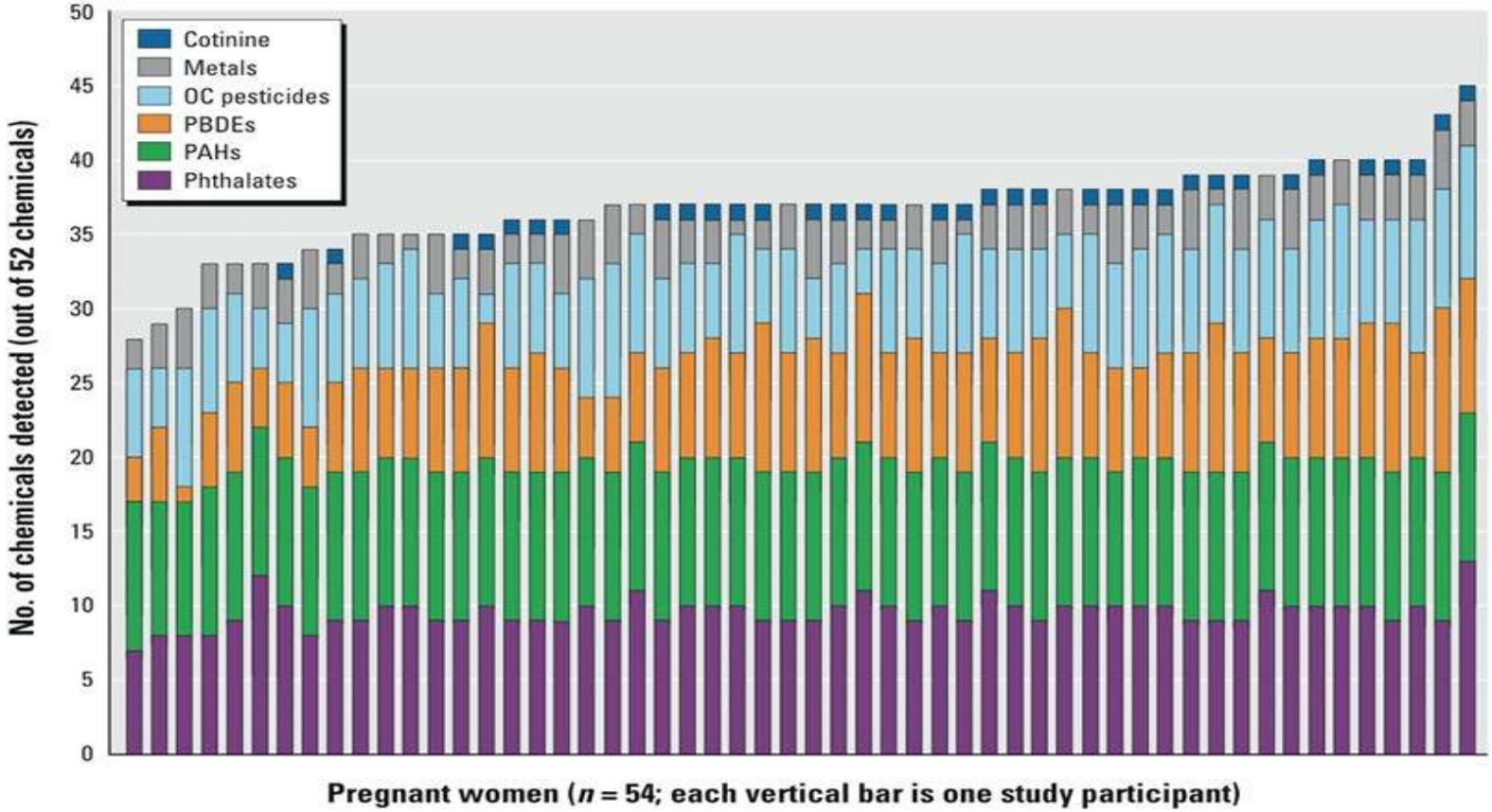
Number of Chemicals (EDCs) Detected by Chemical Class in U.S. Pregnant Women: 43/52 chemicals tested for were detected



(Woodruff et al., 2011)

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Disparities in Exposure and Susceptibility Affecting Low Income Communities and Communities of Color

- Air pollutants (e.g., PAH)
- Pesticides and phthalates, BPA, PBDEs etc. in buildings, food and consumer products
- Poverty-related material hardship, psychosocial stress, and inadequate nutrition

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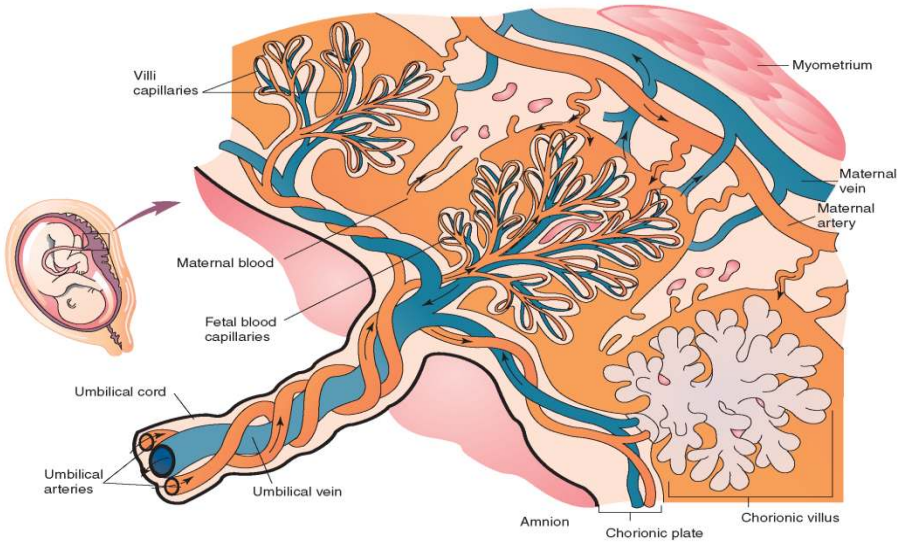
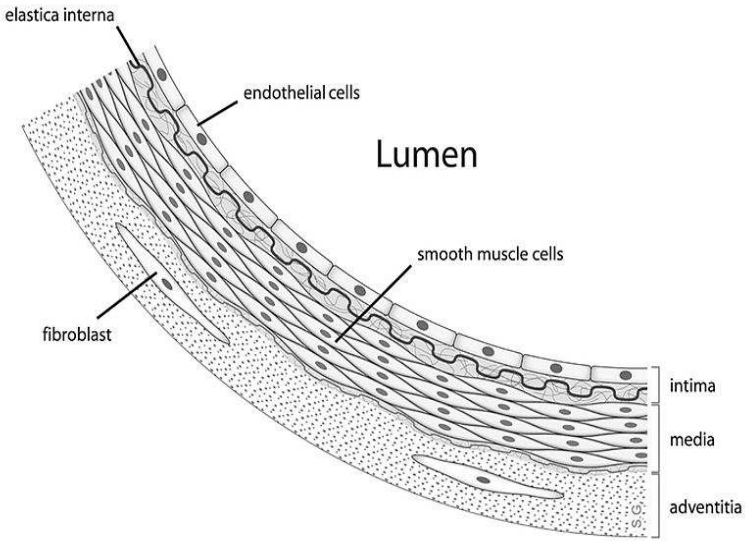
Passage of Chemicals Across Placenta and Blood brain Barrier





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Timing of Maturational Events in Human Brain Development

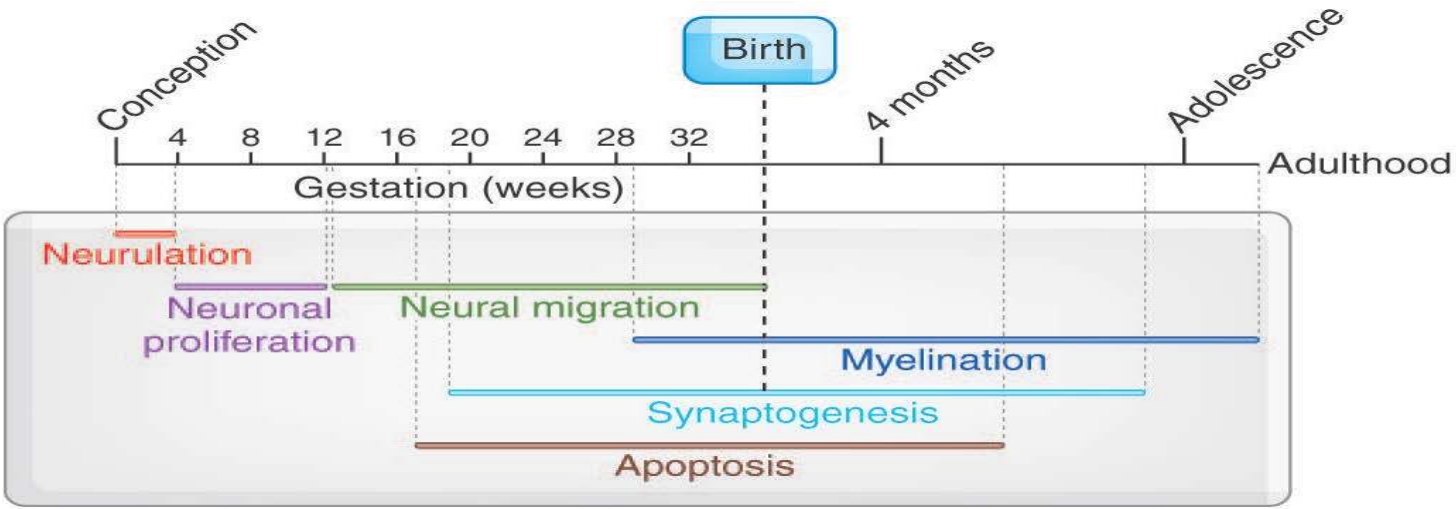

Fig.1. Timing of Maturational Events in Human Brain Development

Giedd J. Brain development, IX: human brain growth. Am J Psychiatry. 1999;156(1):4.

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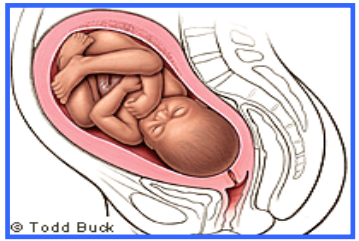
Mechanisms in Increased Susceptibility of the Fetus to Neurotoxicants

- Rapid development of the brain during gestation
- High rate of cell proliferation
- Greater absorption and retention of certain toxicants
- Immature detoxification and repair enzyme systems and immune responses
- High vulnerability to co-exposures to psychosocial stressors
- Many years for longer-latency chronic diseases to develop in later life



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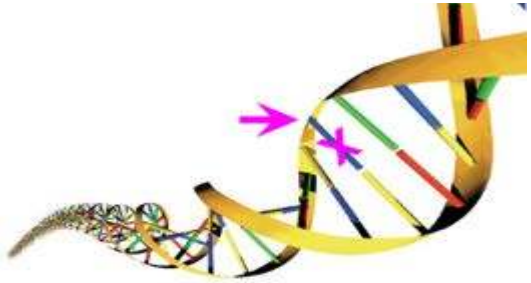
Multiple Mechanisms by Which *In Utero* Exposures Can Affect Fetal Development

- Genotoxicity: DNA damage and mutation
- Oxidative Stress, inflammation
- Epigenetic alterations through methylation changes etc.
- Interference with normal hormonal pathways to disrupt the endocrine system
- Gene-environment interactions
- Interactions with psychosocial stress



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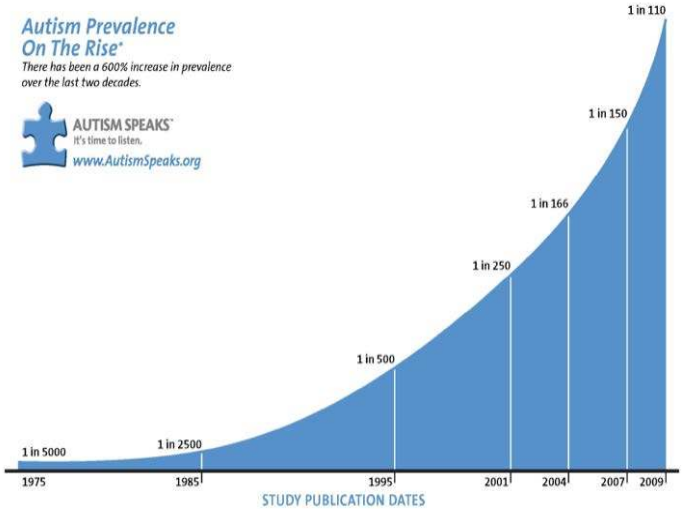
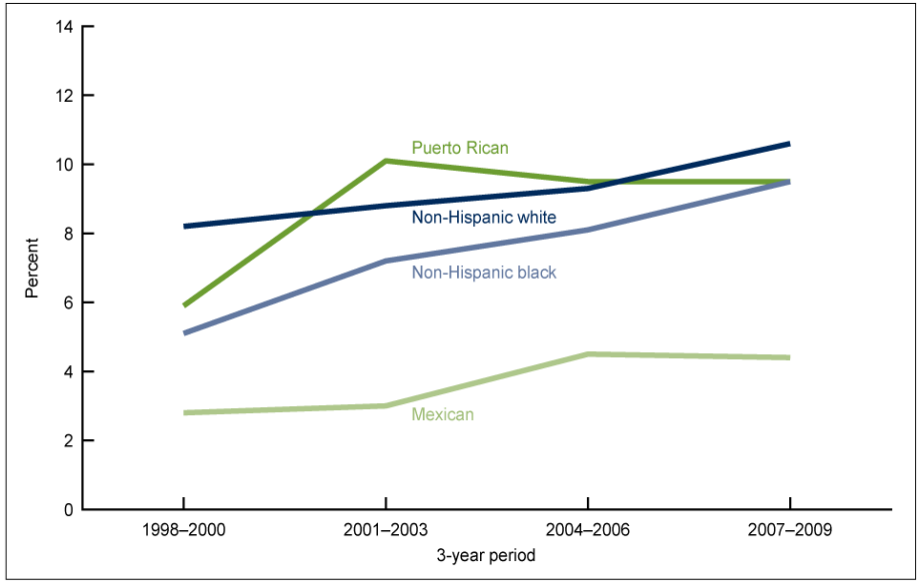
Disturbing Trends



ADHD

Figure 2. Percentage of children aged 5–17 years ever diagnosed with attention deficit hyperactivity disorder, by race and ethnicity: United States, 1998–2009



NOTE: Access data table for Figure 2 at: http://www.cdc.gov/nchs/data/databriefs/db70_tables.pdf#2.
SOURCES: CDC/NCHS, Health Data Interactive and National Health Interview Survey.

One about in 6 U.S. children is affected by a developmental disorder.

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The Growing Burden of Neurodevelopmental Disorders in Children

- 15% of children in the U.S. ages 3 to 17 years affected by neurodevelopmental disorders such as ADHD, learning disorders, or intellectual disability.
- ADHD: 10% prevalence in U.S., annual societal cost $36-$52 billion; annual cost per individual $12,005-$17,458
- 20% global prevalence of child and adolescent mental disorders
- Rates of these conditions have increased in recent decades in U.S. and other countries

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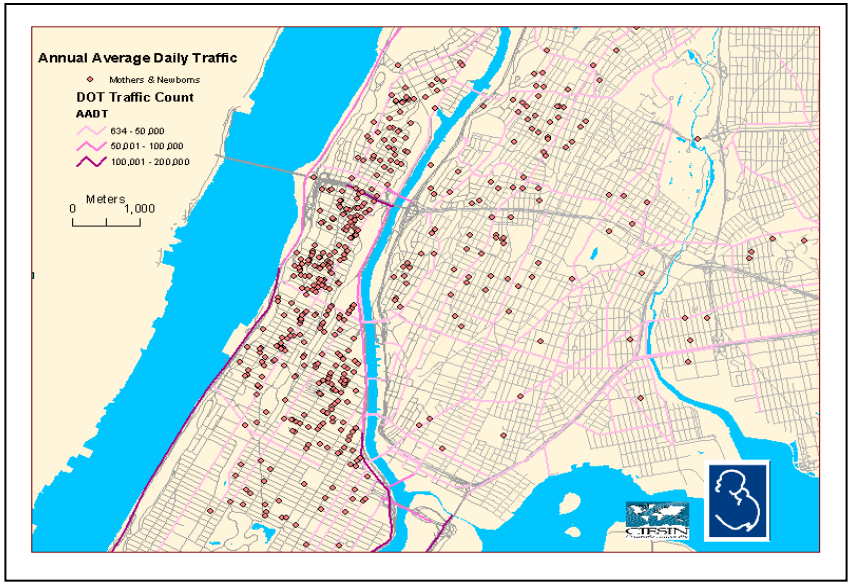
CCCEH NYC Cohort Study: 720 Mother-Child Pairs Enrolled



- Mothers non-smoking and healthy, ages 18-35
- African American and Dominican Residents of N. Manhattan and the S. Bronx
- 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

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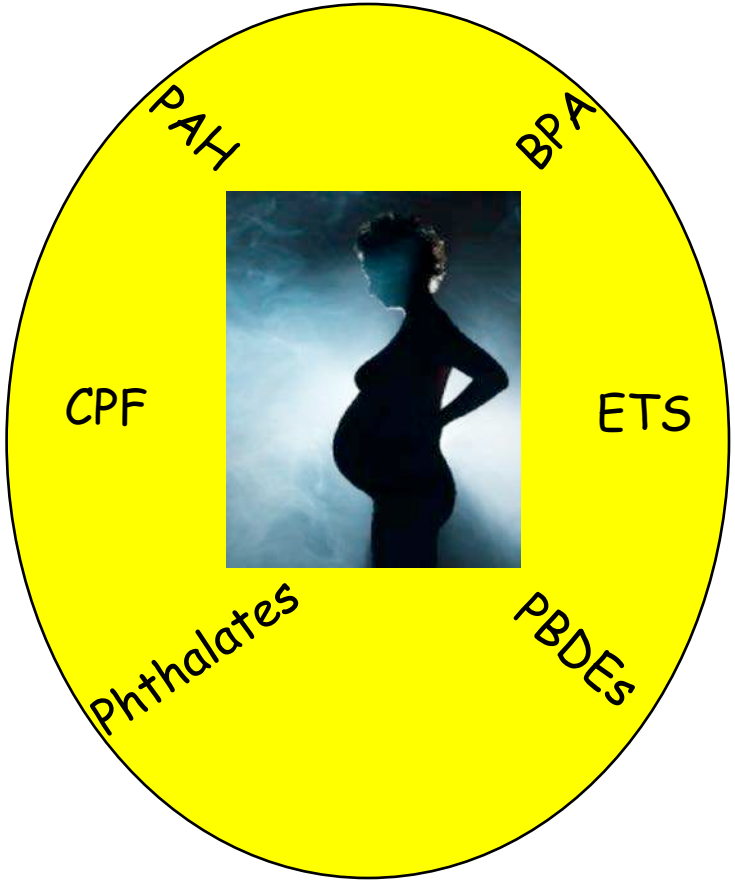
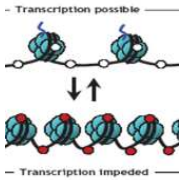
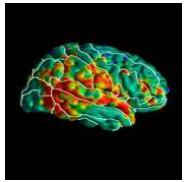
CCCEH: Mothers and Newborns Study in NYC







- Adverse birth outcomes
- **Neurodevelopment** disorders
- Obesity/metabolic disorders
- Asthma
- Increased cancer risk

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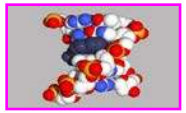
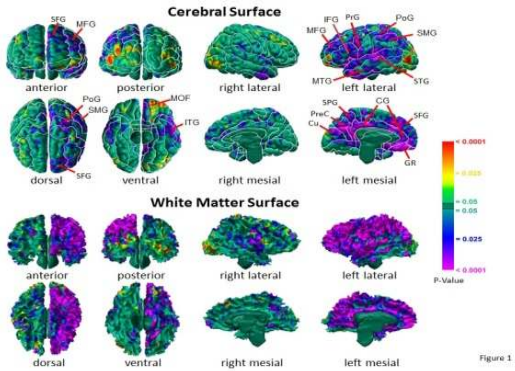
CCCEH: Effects of Prenatal Exposure to PAH Observed in NYC Children*

- Developmental delay (age 3)
- Reduced IQ (age 5)
- Behavioral problems (age 6-7)
- MRI brain changes (age 7-9)
- Symptoms of anxiety/depression and ADHD (age 9)
- Effects on emotional regulation capacity (ages 3-11)
- Interactions between PAH and material hardship





All analyses adjusted for relevant covariates

(Perera et al., 2003, 2004, 2006-2013, 2014; Peterson et al., 2015, Margolis 2017)

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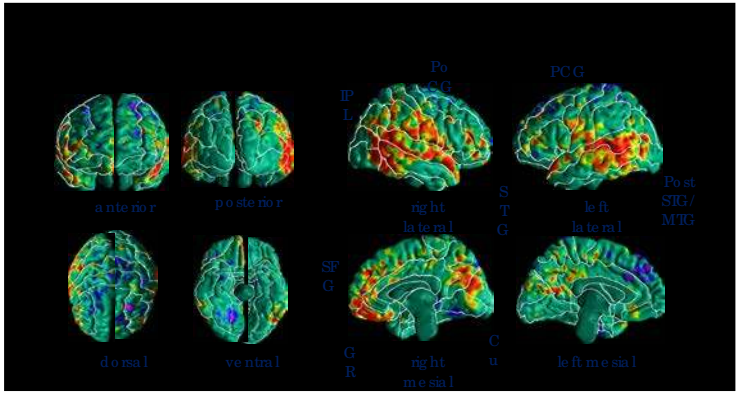
CCCEH Research Findings: Chlorpyrifos

Prenatal CPF associated with:

- Reduction in Working Memory at age 7
- Changes in the structure of the brain measured at age 7-9 (MRI scan)
- These brain changes are distinct from those seen with PAH and appear to explain the adverse neuro-developmental effects of CPF

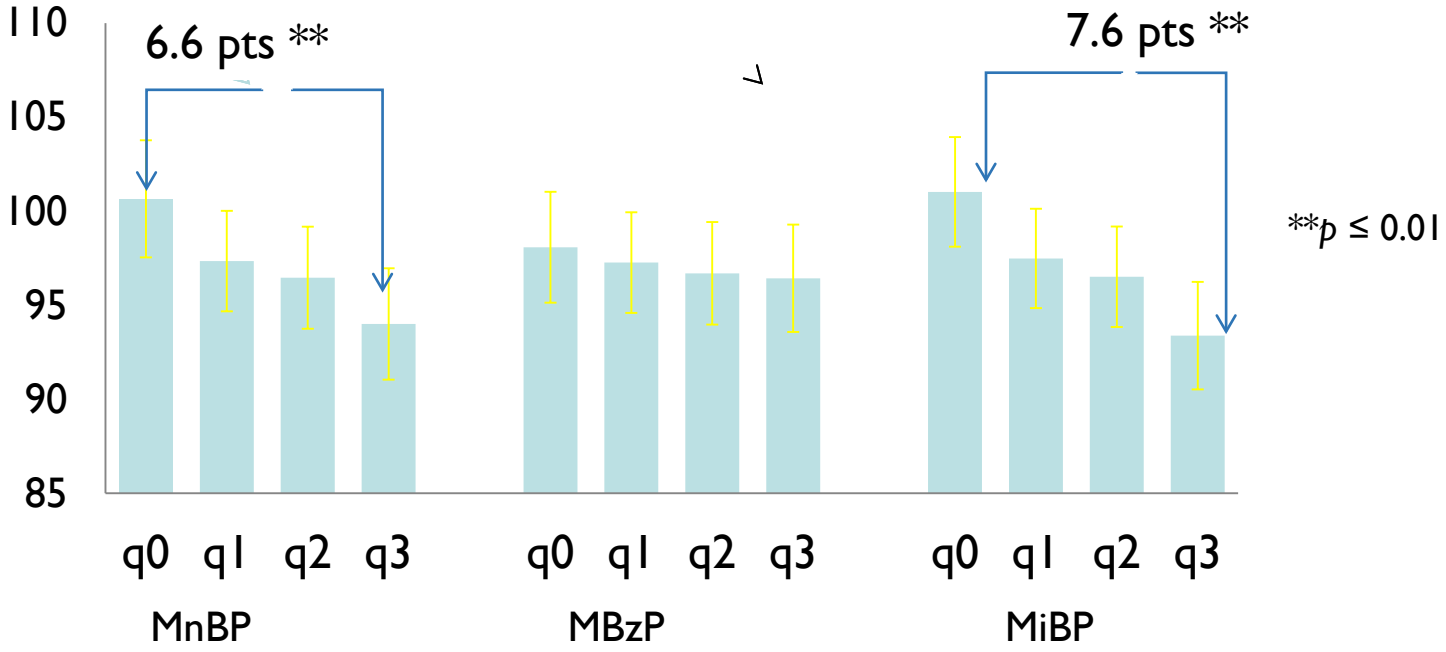


High CPF exposure associated with enlargement of superior temporal, posterior middle temporal, and inferior postcentral gyri bilaterally, and enlarged superior frontal gyrus, gyrus rectus, cuneus, and precuneus along the mesial wall of the right hemisphere

(Whyatt et al., 2004; Rauh et al., 2011, 2012)

Perera, 2017.

CCCEH: Phthalates and Full Scale IQ (age 7) by Quartiles of Maternal Urinary Phthalate Metabolite (n = 328)



(Factor-Litvak, Insel,. Calafat, Liu, Perera, Rauh, Whyatt. 2014)

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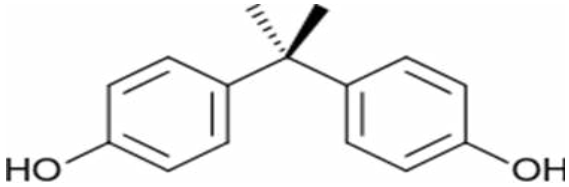
CCCEH: Observed Effects of Prenatal Exposure to BPA



- Neurobehavioral symptoms in cohort children, with differential effects in boys and girls (ages 3-5)
- Internalizing/Externalizing Problems, again with differential effects in boys and girls (ages 7-9)
- Prenatal BPA exposure and anxiety and depression symptoms in boys (age 9)

(Perera et al., 2012, Roen et al., 2015)

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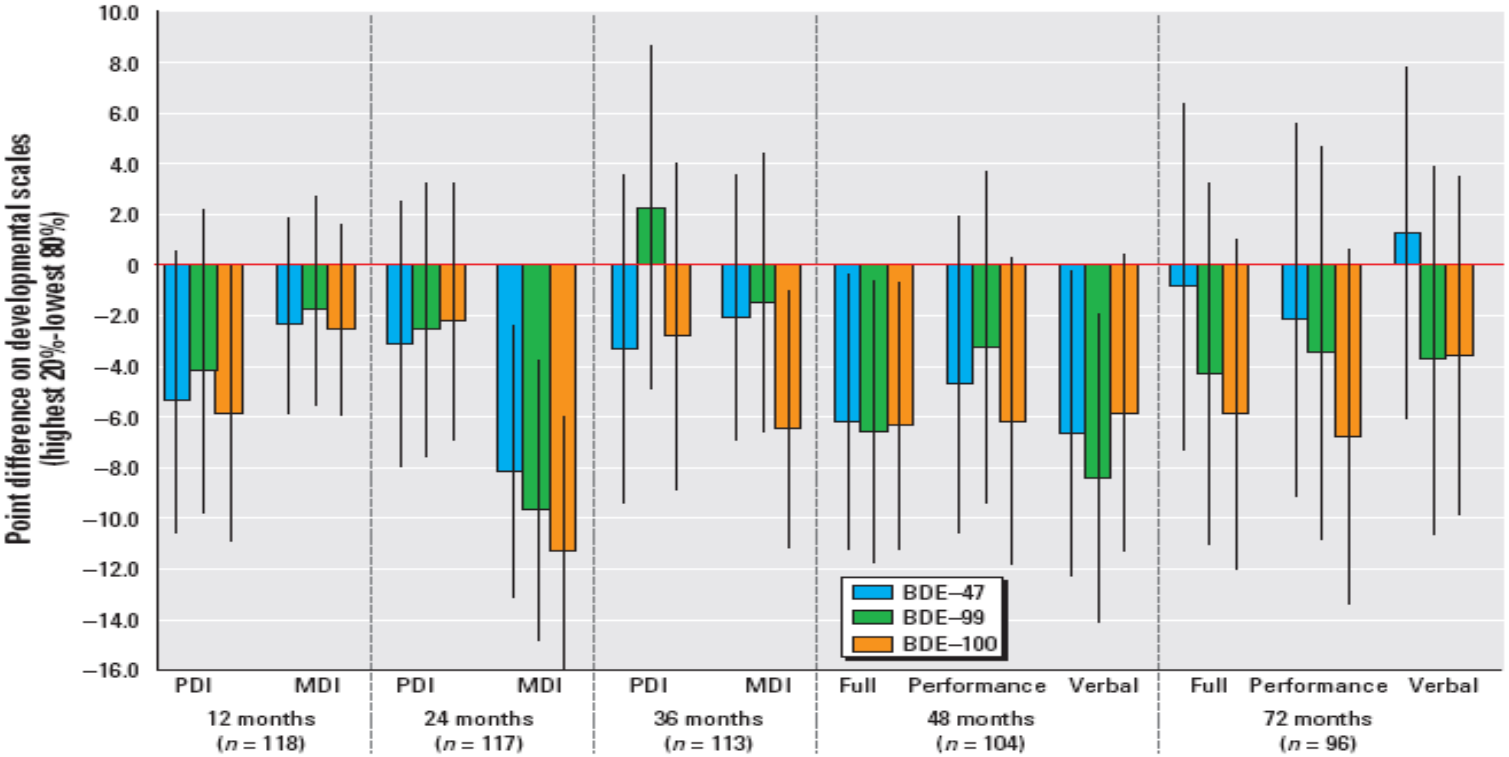
PBDEs: Reduced Mean Developmental Scores (1-3 years): BDEs 47, 99, and 100*



*adjusted for relevant covariates (n=210).

(Herbstman et al., 2010)

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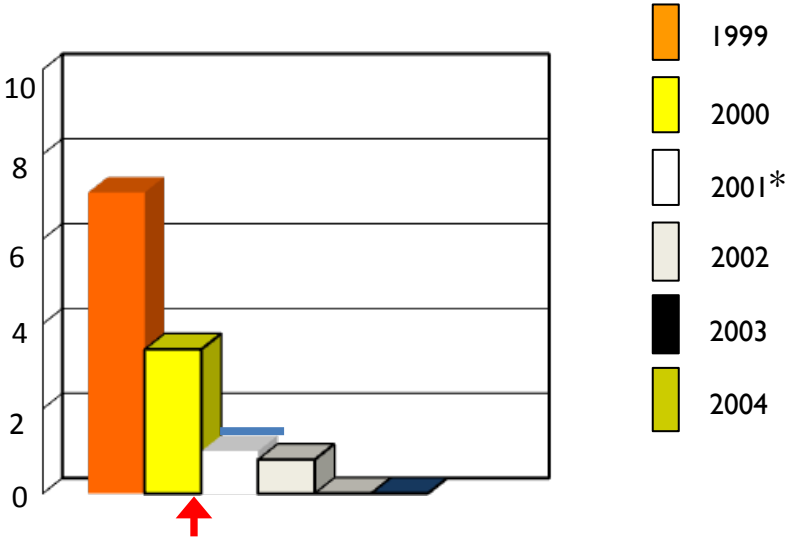
Benefits of Interventions

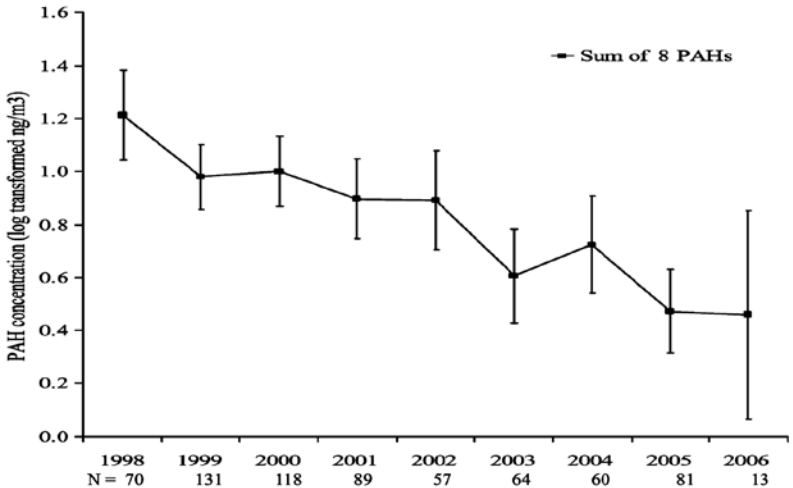
CPF (pg/g) in cord blood (N=395)*



**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)

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Large Economic Benefits of Prevention

- $76.6 billion: costs of childhood illness due to toxic chemicals and air pollutants
- ≥56 billion in 2008 for lead poisoning and prenatal mercury exposure in the U.S.
- 146 billion euros (about $164 billion) each year attributed to prenatal organophosphate pesticide exposure in the European Union
- Health impacts of air pollution and climate change: $361 to $886 billion/year due to U.S. fossil fuel electricity

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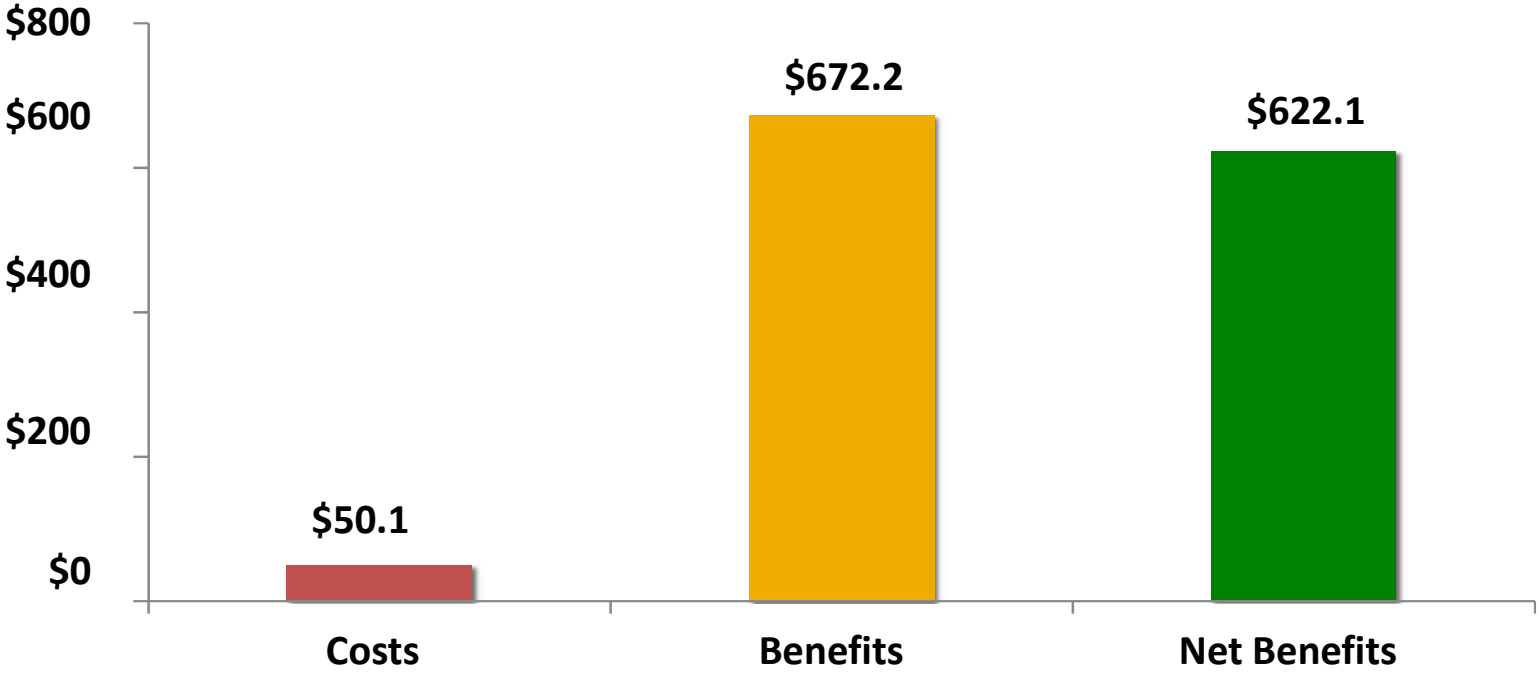
EPA Rules Annual Net Benefits ~$622 billion

Annual Net Benefits of 35 EPA Federal Rules ($ Billions)
Offices of Air; Solid Waste and Emergency Response; Water



Office of Management and Budget. 2016 Draft Report to Congress on the Benefits and Costs of Federal Regulations and Agency Compliance with the Unfunded Mandates Reform Act. Page 10.

(Woodruff, legislative Briefing 2017)

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Project TENDR: Targeting Environmental Neurodevelopment Risks/Consensus Statement

"A Call to Action

"[I]f we are to protect children, we must overhaul how government agencies and business assess risks to human health from chemical exposures, how chemicals in commerce are regulated, and how scientific evidence informs decision-making by government and the private sector."

Prime examples:

- Organophosphate (OP) pesticides
- Polybrominated diphenyl ether (PBDE) flame retardants
- Particulate air pollution
- Lead
- Mercury
- Polychlorinated biphenyls (PCBs)

(EHP, 2016)

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Rollbacks of Rules and Policies Will Directly Harm Children's Health

Less efficient cars

Dirtier power plants

Failure to implement TSCA reform

→ More toxic air pollution (Accelerated climate change)

More chemical contamination

Perera, 2017.

The Wrong Direction

The NEW ENGLAND JOURNAL of MEDICINE

MEDICINE AND SOCIETY

Debra Malina, Ph.D., *Editor*

The Trump Administration and the Environment — Heed the Science

Jonathan M. Samet, M.D., Thomas A. Burke, Ph.D., M.P.H., and Bernard D. Goldstein, M.D.

Science-based policies and regulations have resulted in tremendous gains in environmental quality and reduced the population's exposure to harmful pollutants (Fig. 1). In the United States, the gains have been driven by major laws that were passed and amended by Republican and Democratic administrations alike (Table 1). For example, the 1970 Clean Air Act (CAA), signed by President Richard Nixon, called for a broad array of measures to improve air quality, addressing the major airborne pollutants and their

environment, and through partnership with and delegation to the states. When first implemented, the laws and agency actions were based on a "command and control approach" driven by public demands to clean up visibly polluted air, water, and soil. Detection of additional chemical contaminants in air, water, and biota and scientific evidence of adverse health outcomes led to "risk assessment and management" as an additional approach to environmental control.

The EPA has also faced general challenges

Samet, J. M., Burke, T. A., & Goldstein, B. D. (2017). Trump Administration and the Environment – Heed the Science. The New England Journal of Medicine, 376, 1182-11 doi: 10.1056/NEJMms1615242. http://www.nejm.org/doi/full/10.1056/NEJMms1615242?query=TOC

(Woodruff, 2017, Legislative Briefing)

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The Womb Is No Protection From Toxic Chemicals

The Opinion Pages | OP-ED CONTRIBUTOR

By FREDERICA PERERA JUNE 1, 2017

Until a few decades ago, the popular but falsely reassuring belief was that babies in the womb were perfectly protected by the placenta and that children were just "little adults," requiring no special protections from environmental threats. We now know that a host of chemicals, pollutants

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Conclusions

- Evidence that prenatal exposure to diverse chemicals adversely affect child cognitive and neurobehavioral development
- Evidence of interactions of pollutants with stress due to poverty
- Implications for children's academic performance, lifetime earnings and risk- taking behaviors in adolescence
- Need for multi-faceted interventions to reduce neurotoxic exposures and alleviate stress due to poverty
- Interventions work
- Large benefits of prevention
- This is no time to relax vigilance

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Solutions

- Sustained research, collaborative research (CCEHCs and ECHO)
- Implementation of Toxic Substance Control Act Reform
- Sustainable energy policies
- Market reform: e.g., industry to rely less on the petroleum-based materials used in so many consumer products.
- Common sense (e.g., flame retardants) : *"Where do we really need them? I don't question the need for flame retardants in an airplane, but do we need them in nursing pillows and babies' strollers? Are we putting chemicals in places we don't need them?" (L. Birnbaum, quoted in E. Grossman, Yale environment 360, 2011)*

Perera, 2017.

Colleagues

H. Andrews, K. Burke, D. Evans, J. Herbstman, L. Hoepner, A. Margolis, V. Rauh, A. Rundle, D. Tang, S. Wang, Y. Wang, K. Wheelock, R. Whyatt

WE ACT: P. Shepard

NYSPI/USC: B. Peterson

CDC: A. Calafat, A. Sjodin

Perera, 2017.

Role of Environmental Exposures in Neurodevelopmental Disorders

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Perera, 2017.