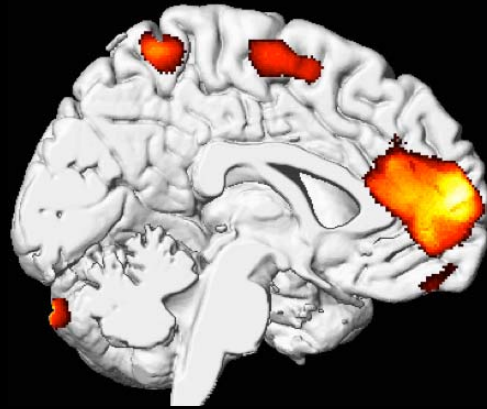
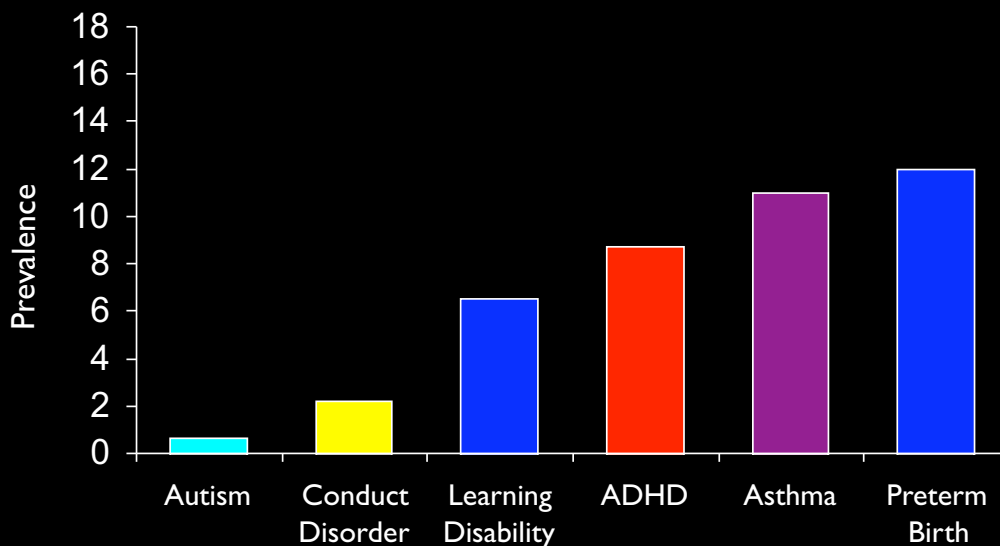


Linking Environmental Toxicants with Learning and Behavioral Problems in Children



Bruce Lanphear, MD, MPH
Child & Family Research Institute, BC Children's Hospital
Faculty of Health Sciences, Simon Fraser University

New Morbidities of Childhood



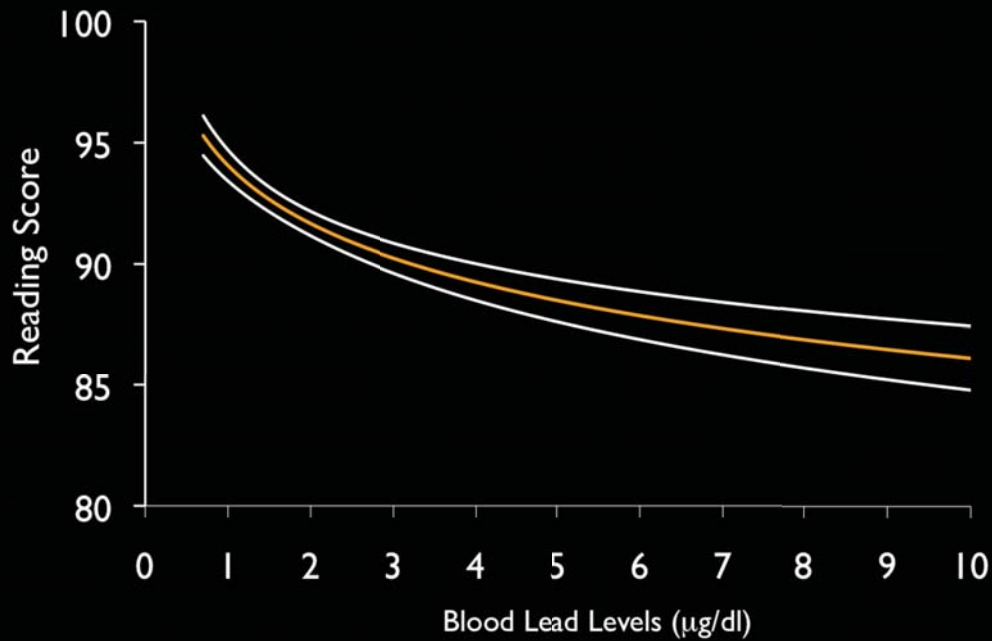
Boyle C, et al. *Pediatrics* 1994;93:399-403; Branum AM, et al. *Paediatr Perinat Epidemiol* 2002;16:8-15; Hedley AA, et al. *JAMA* 2004;291:2847-50. Lanphear BP, et al. *Pediatrics* 2001 e98. Froehlich T, et al. *Arch Ped Adolesc Med* 2007;161:857-864; Braun J, et al. *Environ Health Perspect* 2008;116:956-962.

Environmental Toxicants

- Most recognized toxicants were discovered only as a result of an environmental disaster
- Increasing evidence linking toxicants with cognitive deficits and behavioral problems at levels previously thought to be innocuous or safe
- Increasing evidence linking toxicants with child and adolescent psychopathology

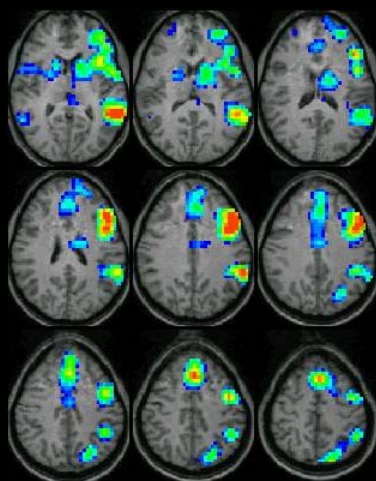
Linking Low-Level Environmental
Toxicants with Learning Abilities

Reading Scores by Blood Lead Levels in US Children, NHANES III, 1998-1994

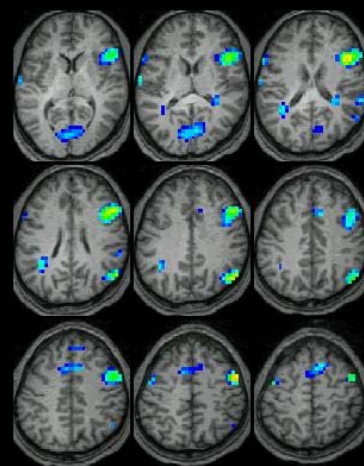


Adapted from Lanphear BP, et al. Public Health Reports 2000;115:521-529

Verb Generation Task by Lifetime Mean Blood Lead Concentration (n=42)



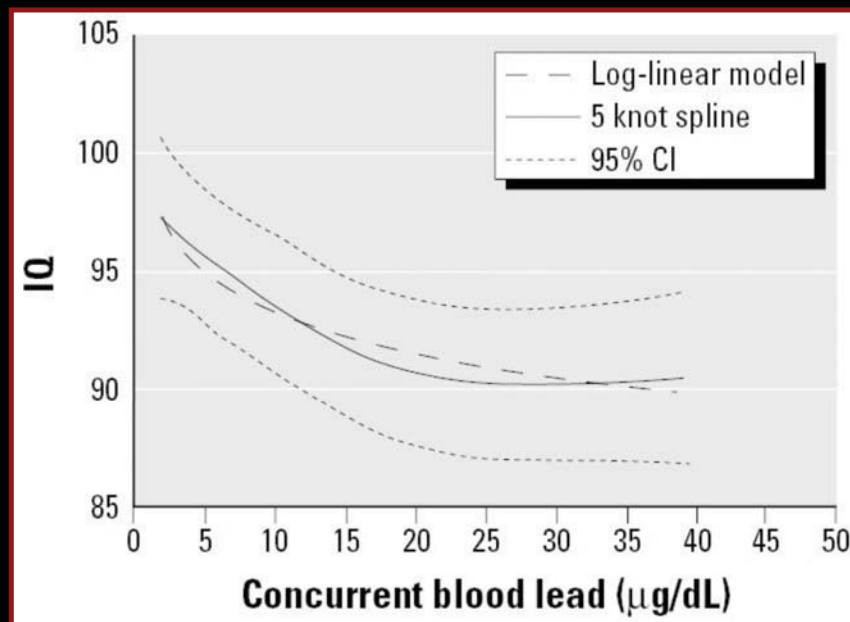
Low Lifetime Mean Blood Lead (7.6 $\mu\text{g/dL}$)



High Lifetime Mean Blood Lead (26 $\mu\text{g/dL}$)

Yuan W, et al. Pediatrics 2006;118:971-977.

The Ongoing Search for a Threshold of Low-Level Lead Toxicity

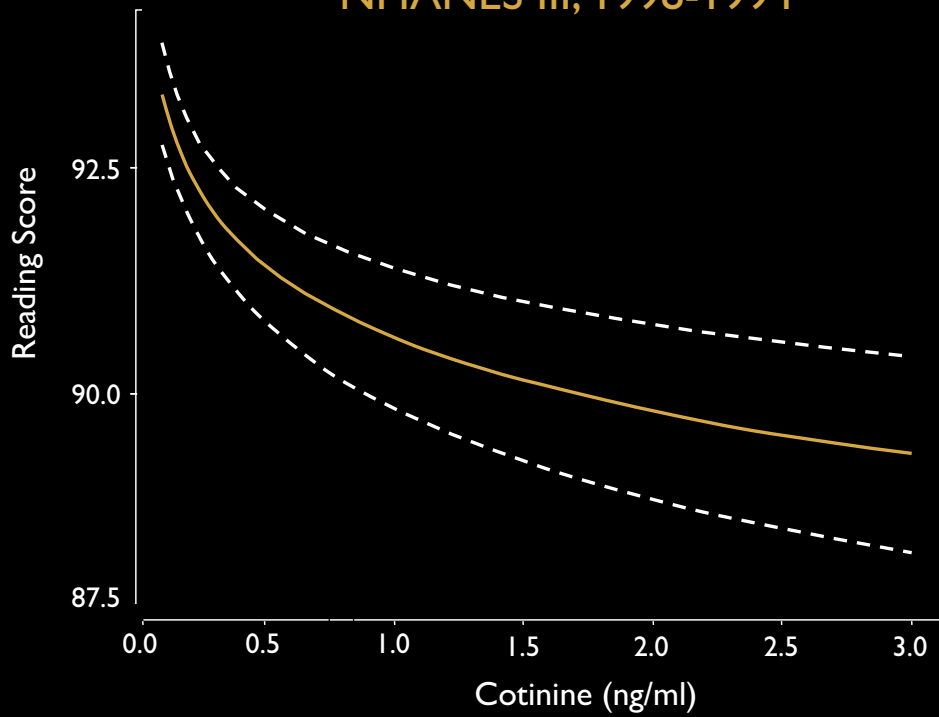


Lanphear BP, et al. *Environ Health Perspect* 2005; 113:894-899.

Research Supporting Adverse Cognitive Effects at Blood Lead Levels < 10 µg/dL

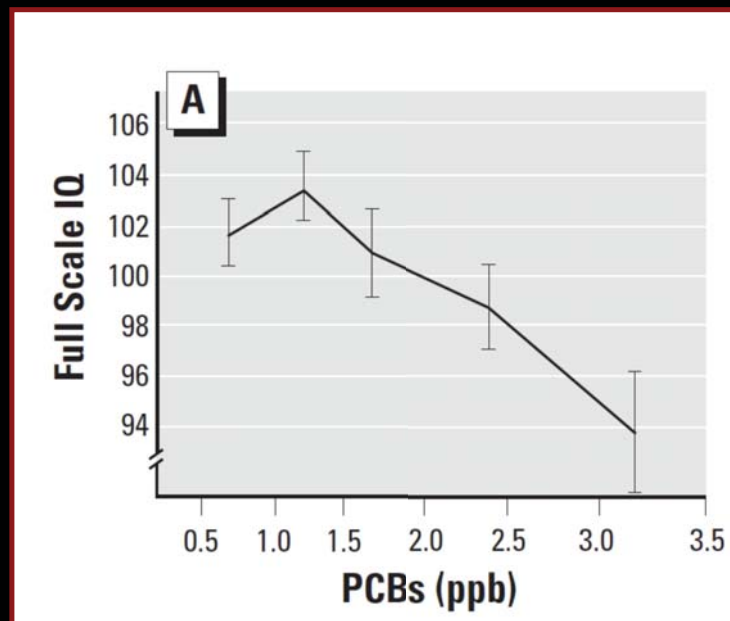
- Fulton M, et al. Influence of blood lead on the ability and attainment of children in Edinburgh. *Lancet* 1987;1:1221-1226.
- Walkowiak J, et al. Cognitive and sensorimotor functions in 6-year old children in relation to lead and mercury levels. *Neurotoxicol Teratol* 1998;20:511-521.
- Lanphear BP, et al. Cognitive deficits associated with blood lead < 10 µg/dl in U.S. children and adolescents. *Public Health Reports* 2000;115:521-529.
- Wasserman G, et al. The Yugoslavia Prospective Lead Study: contributions of prenatal and postnatal lead exposure to early intelligence. *Neurotoxicol Teratol* 2000;22:811-818.
- Sood B, et al. Prenatal alcohol exposure and childhood behavior at age 6 to 7 years: I. dose-response effect. *Pediatrics*. 2001;108:E34.
- Bellinger D, et al. Intellectual impairment and blood lead levels. *N Engl J Med*. 2003;349:500-502.
- Chiodo LM, et al. Neurodevelopmental effects of postnatal lead exposure at very low levels. *Neurotoxicol Teratol* 2004;26:359-371.
- Kordas K, et al. Deficits in cognitive function and achievement in Mexican first-graders with low blood lead concentrations. *Environ Res* 2006;100:371-86.
- Tellez-Rojo MM, et al. Longitudinal associations between blood lead concentrations lower than 10 µg/dL and neurobehavioral development in environmentally exposed children in Mexico City. *Pediatrics*. 2006;118:e323-30.
- Hu H, et al. Fetal lead exposure at each stage of pregnancy as a predictor of infant mental development. *Environ Health Perspect* 2006;114:1730-1735.
- Sarkin PJ, et al. Neuropsychological function in children with blood lead levels below 10 µg/dL. *Neurotoxicology* 2007;28:1170-1177.

Reading Scores by Serum Cotinine in US Children, NHANES III, 1998-1994



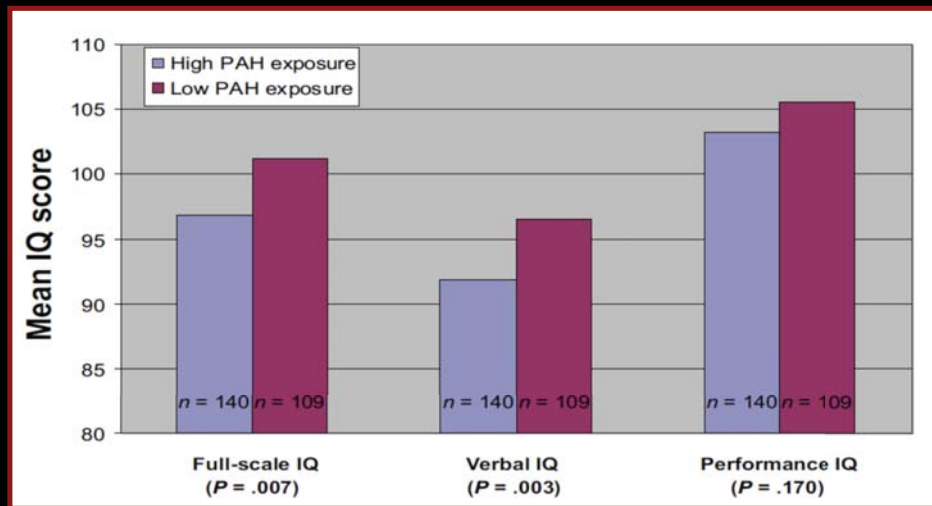
Yolton K, et al. Environ Health Perspect 2005;113:98-103.

Prenatal PCB Exposure and IQ Scores in 9-year old Children, Oswego, NY



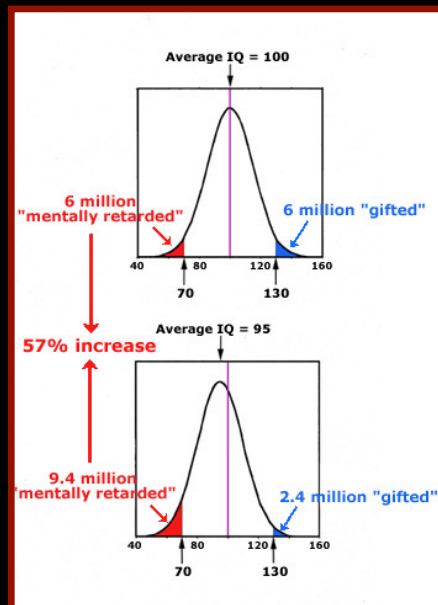
Stewart PW, et al EHP 2008;116:1416-1422.

Differences in IQ Scores among 5-year old Children by Prenatal PAH Exposure



Perera F, et al. Pediatrics 2009;124:e195-e202. Adjusted for prenatal ETS exposure, child's gender, ethnicity, maternal IQ score, maternal education level and HOME Inventory

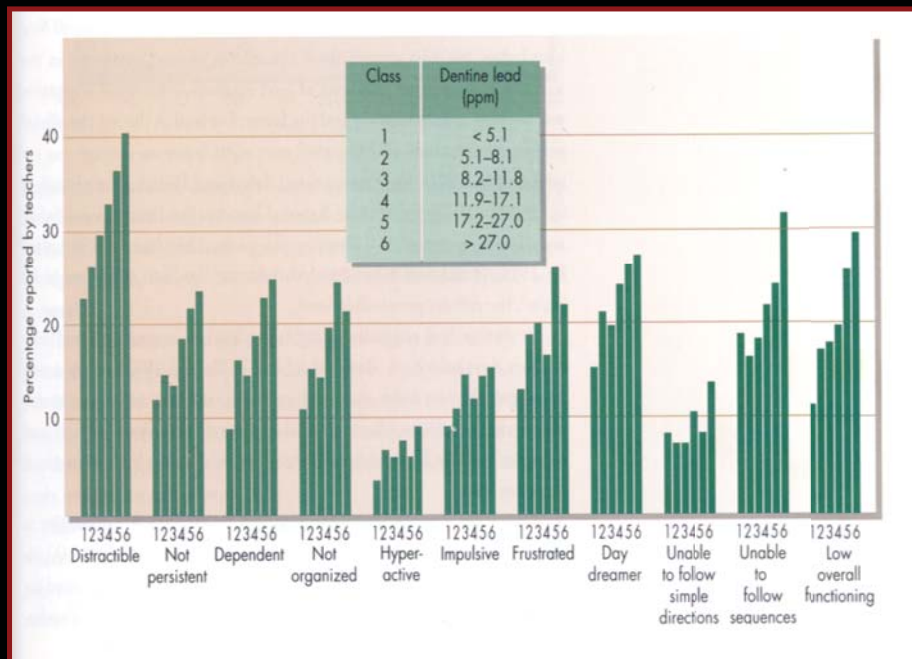
Impact of Reducing IQ by 5 points in US Children



Gilbert S, Weiss B. Neurotoxicology 2006;27:693-701

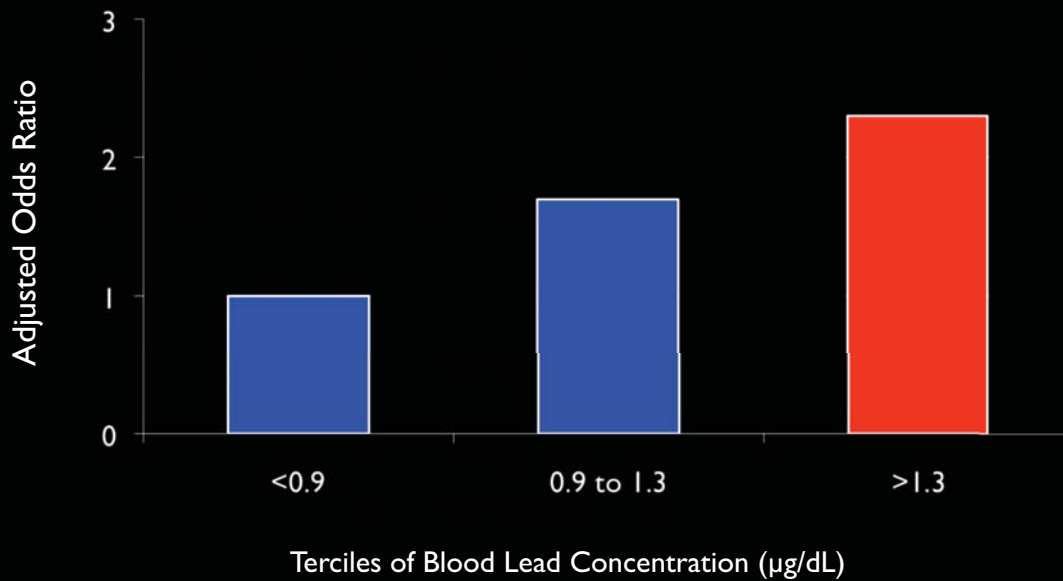
Linking Exposures to Environmental Toxicants with Psychopathology

Lead-associated Behavioral and Emotional Problems in Children by Tooth Lead Concentration



Needleman HL, et al. N Engl J Med 1979;300:689-95.

Risk of ADHD by Blood Lead Levels in US Children, 8 to 15 years, NHANES 2001-2004



Adjusted for child's age, sex, race and ethnicity, preschool, maternal age, birth weight, serum ferritin, poverty-income ratio, prenatal tobacco exposure. Source: Froehlich T, et al. Pediatrics (in press.)

Prenatal Exposure to Tobacco Smoke and Teacher-Rated Behavioral Problems in Children



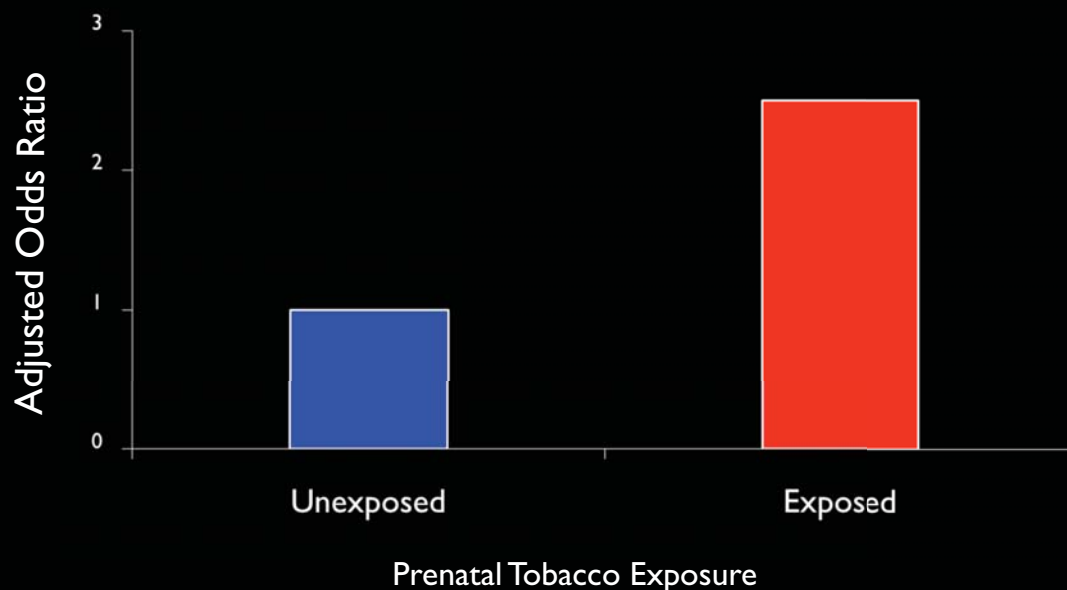
Fergusson DM, et al. Pediatrics 1993;92:815-822.

Case Control Studies of ADHD by Prenatal Tobacco Smoke Exposure

Author (year)	No. Cases	No. Controls	Age of Children	AOR (95%CI)
McIntosh (1995)	130	135	6-13	2.7 (1.1-7.0)
Milberger (1998)	132	139	6-17	4.4 (1.2-15.5)
Mick (2002)	280	242	6-17	2.1 (1.1-4.1)
Langley (2005)*			6-17	2.4 (1.6-3.5)
Schmitz (2006)	100	100	6-18	3.4 (1.2-10)

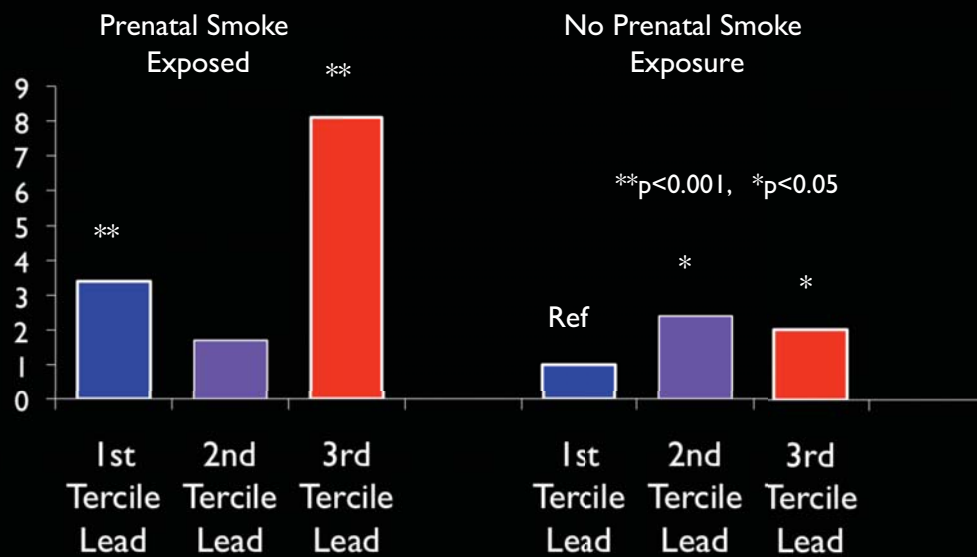
* Pooled analysis

Risk of ADHD by Prenatal Tobacco Exposure in US Children, 8 to 15 years, NHANES 2001-2004



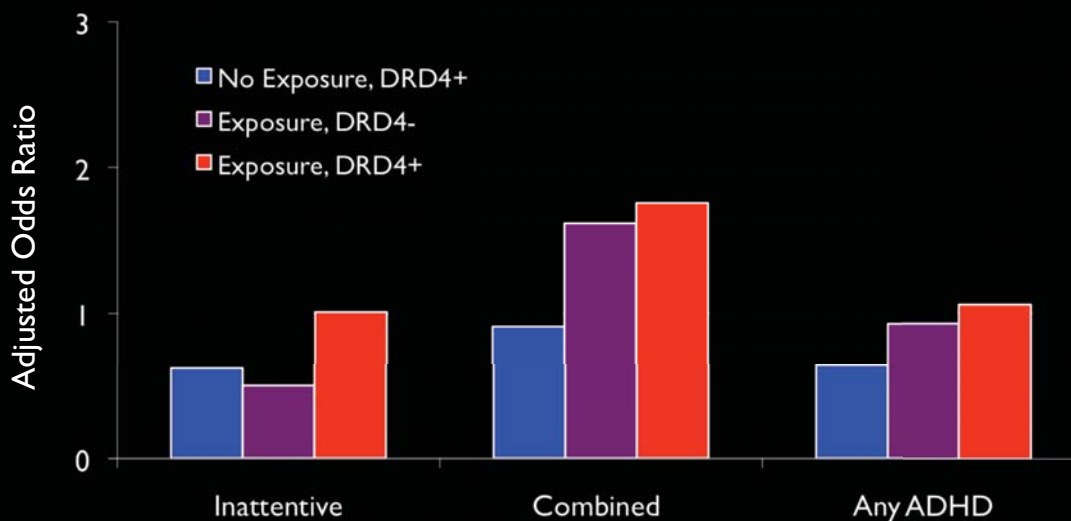
Adjusted for race/ethnicity, sex, age, blood lead level, ferritin level, presence of a smoker in the home, preschool attendance, and insurance. Source: Froehlich T, et al. Pediatrics (in press).

Joint Effects of Lead and Tobacco Exposure on ADHD in US Children NHANES 2001-2004



Adjusted for income, current tobacco exposure, age, sex, race/ethnicity, preschool attendance, maternal age at child's birth, and birthweight. Froehlich T, et al. Pediatrics (in press).

Joint Effects of DRD4 7-Repeat and Prenatal Tobacco Exposure with ADHD in Children

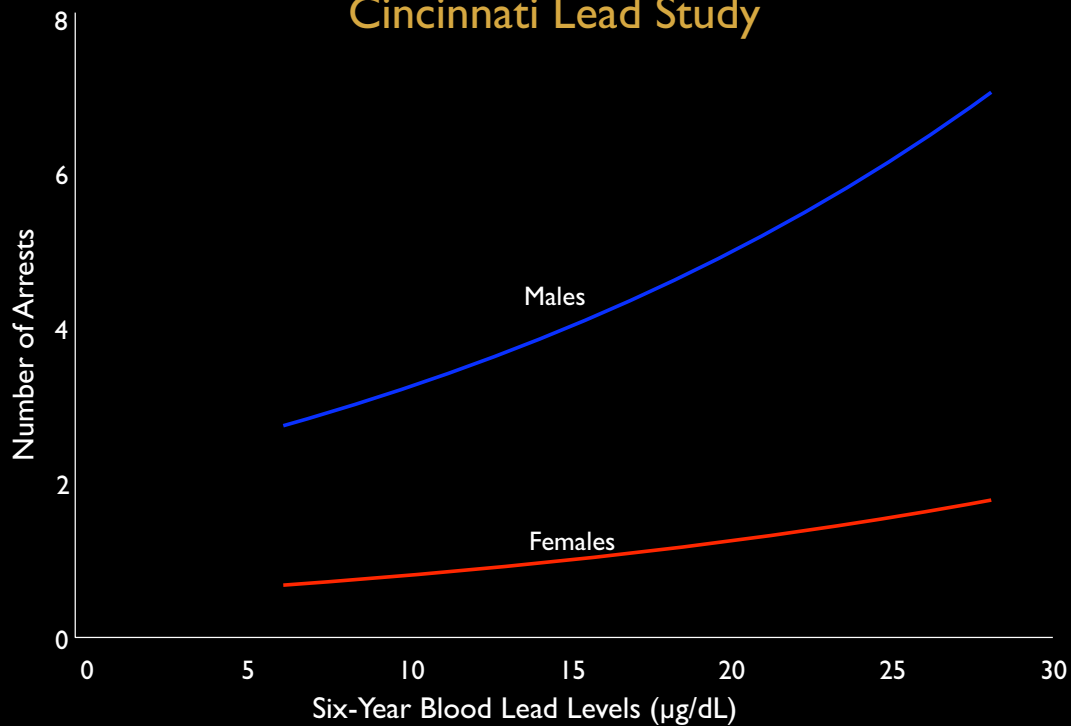


Neuman RJ, et al. Biol Psychiatry 2007;61:1320-1328.

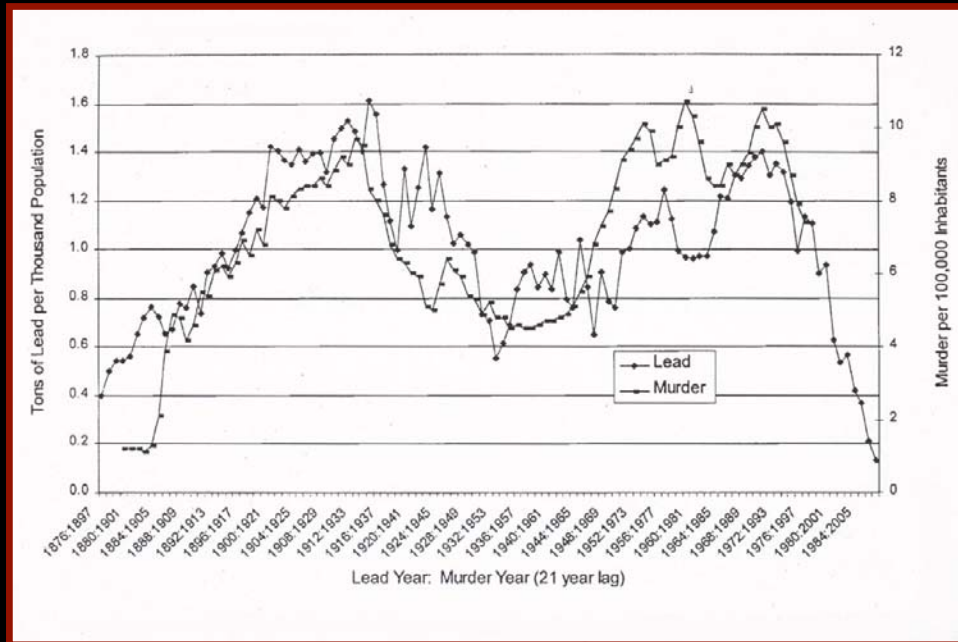
“If causes can be removed, then susceptibility ceases to matter.”

Geoffrey Rose, MD

Number of Arrests by Childhood Lead Exposure: The Cincinnati Lead Study

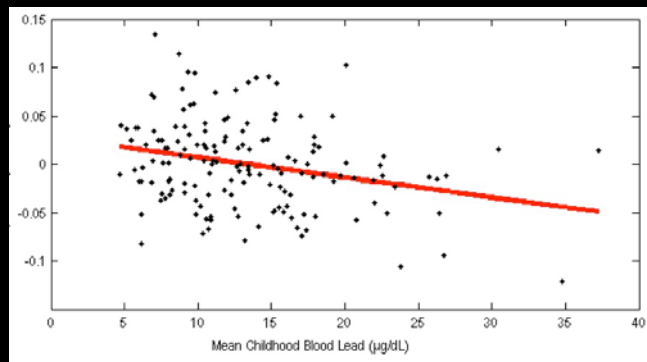
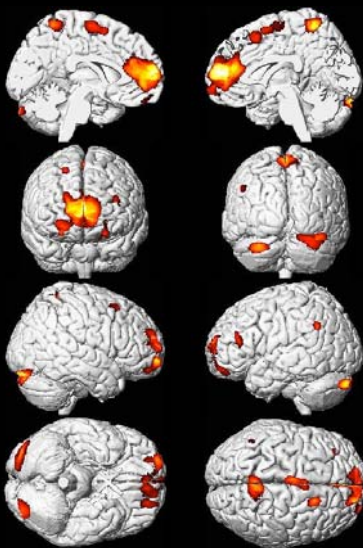


Relationship of Lead Exposure and Murder Rate (/100,000) in the U.S.



Nevin R. Environmental Research 2000;83;1-22.

Reduction in Gray Matter by Childhood Lead Exposure

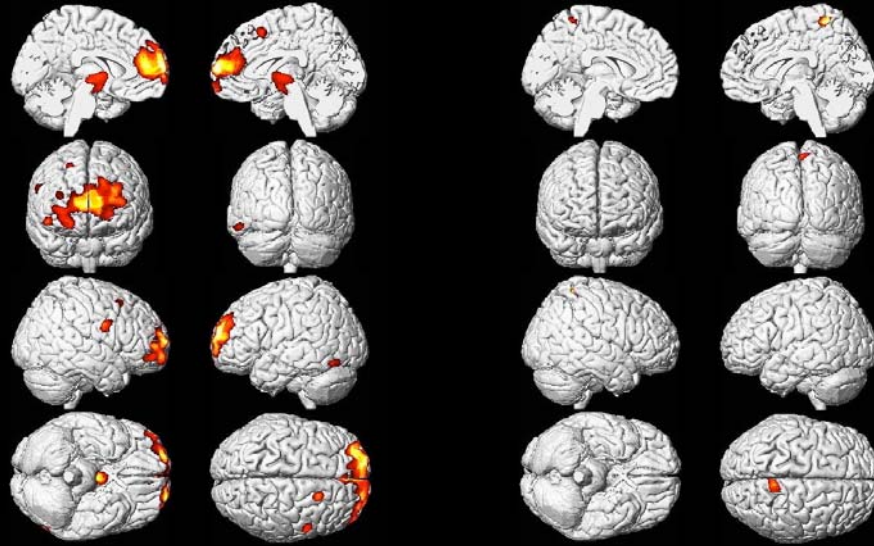


Adjusted for child's age, birth weight. Sex, gestational age, IQ, prenatal tobacco, prenatal alcohol, prenatal marijuana, total intracranial volume, SES and HOME Inventory did not alter results (Cecil K, et al. PLoS Medicine 2008).

Reduction in Gray Matter by Childhood Blood Lead Levels and Subject's Sex

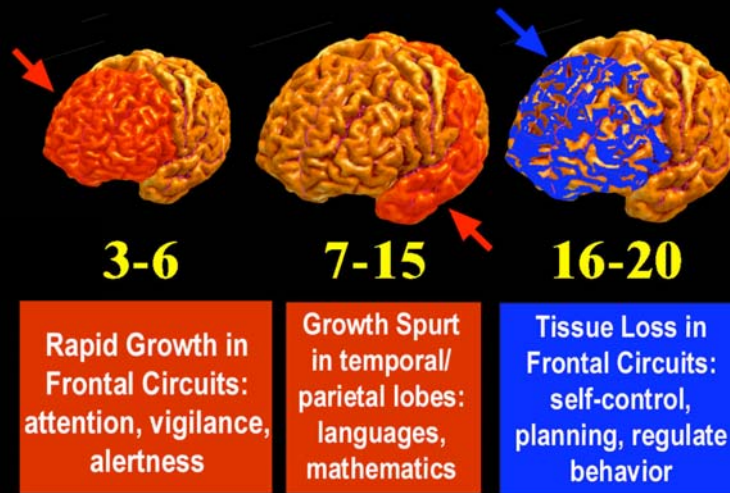
Men (n=83)

Women (n=74)



Adjusted for child's age, birth weight, Sex, gestational age, IQ, prenatal tobacco, prenatal alcohol, prenatal marijuana, total intracranial volume, SES and HOME Inventory did not alter results (Cecil K, Brubaker C, Dietrich KN, et al. PLoS Medicine 2008).

Development of the Brain and Timing of Exposure to Environmental Toxicants

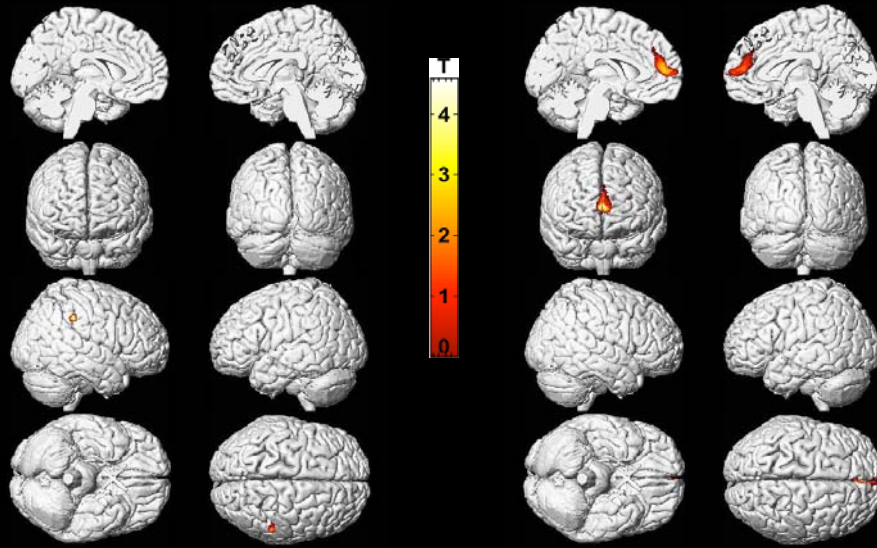


Source: UCLA Lab of Neuroimaging

Developmental Trajectory of Lead Exposure by Gray Matter Deficits

Year 1

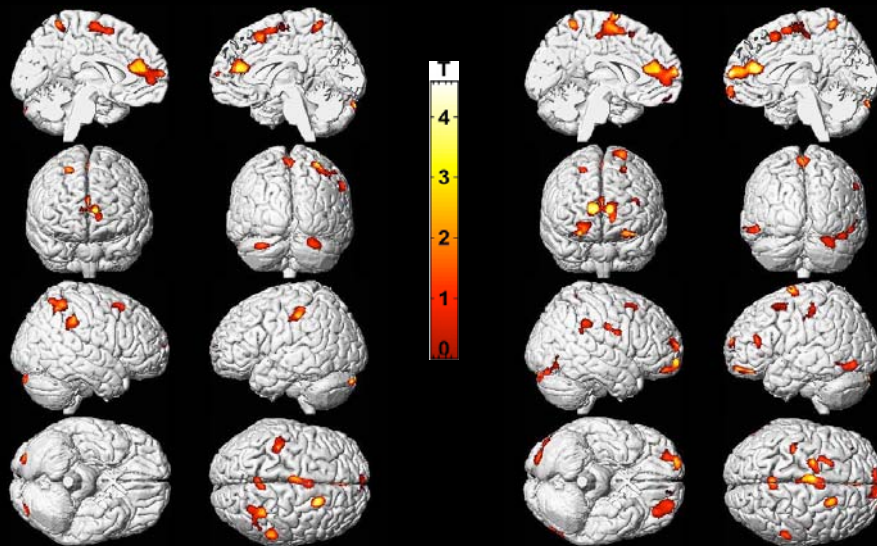
Year 2



Developmental Trajectory of Lead Exposure by Gray Matter Deficits

Year 3

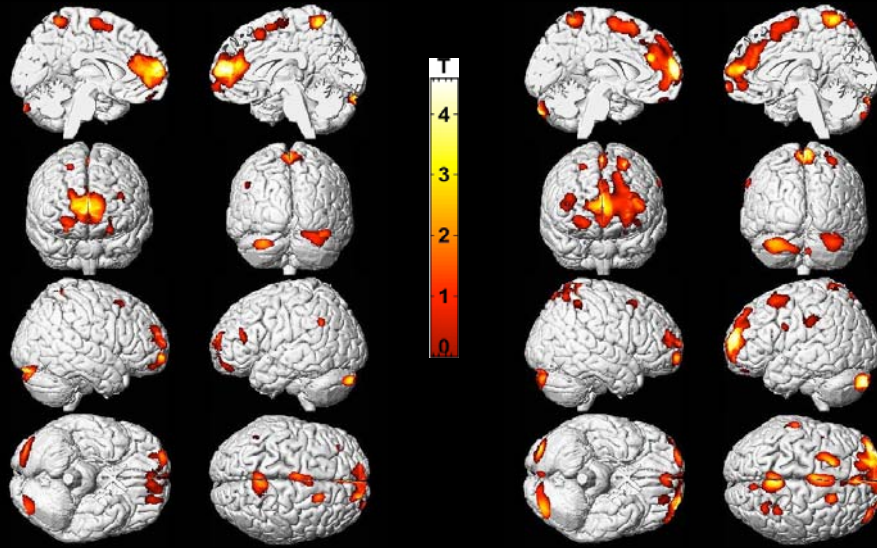
Year 4



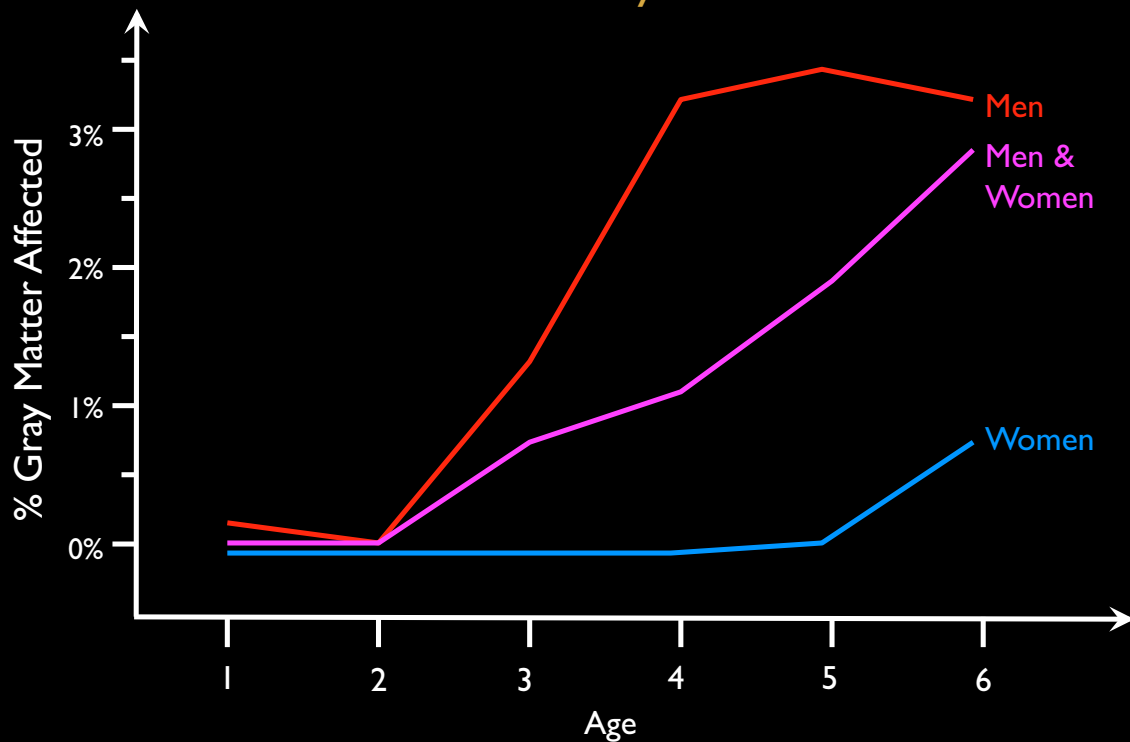
Developmental Trajectory of Lead Exposure by Gray Matter Deficits

Year 5

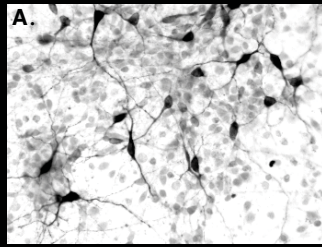
Year 6



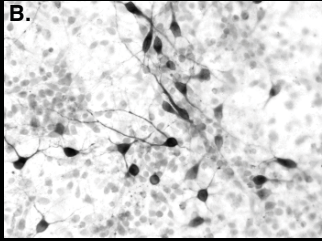
Reduction in Gray Matter by Age of Blood Lead Levels and by Sex



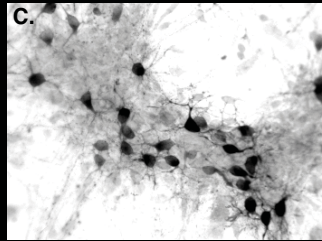
No Lead



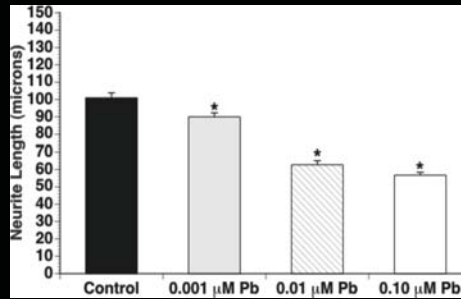
0.001 μM
0.024 $\mu\text{g/dl}$



0.01 μM
0.24 $\mu\text{g/dl}$



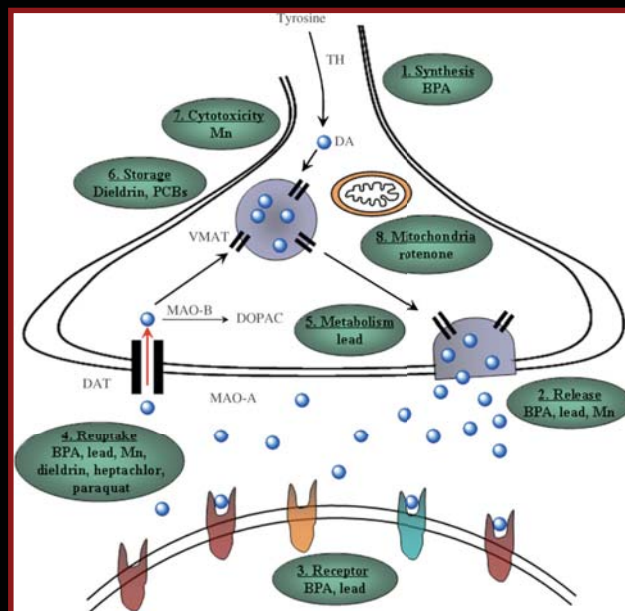
Lead Reduces Neurite Length in Dopaminergic Neurons after 48 Hr Exposure to Lead Acetate



The lowest concentration of lead acetate used (0.001 μM) caused a significant decrease in neurite length that was exacerbated by incubation in higher concentrations of lead (0.01 and 0.10 μM).

Schneider J, et al., *Neurotoxicology and Teratology*, 25 (2003) 555-559.

Dopaminergic Toxicants

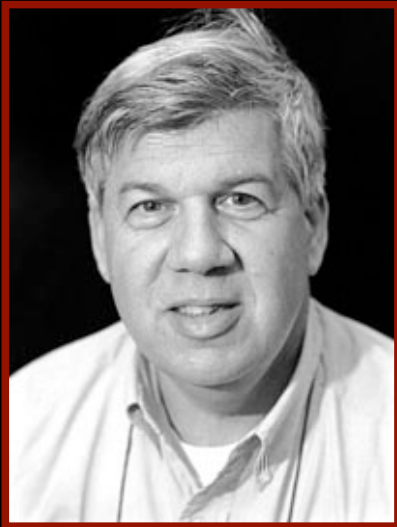


A Pattern of Pathology



The Impact of Toxicants on Human Health

- Increasing evidence that environmental toxicants are toxic at levels previously thought to be safe or innocuous
- Subtle shifts in cognition, behavior, birth weight or physiologic parameters in children are antecedents of disease and disabling disorders in older children and adults
- The effects of environmental toxicants are systemic
- Disease and disability associated with environmental toxicants is preventable



“Few tragedies can be more extensive than the stunting of life, few injustices deeper than the denial of an opportunity to strive or even to hope, by a limit imposed from without, but falsely identified as lying within.”

Stephen Jay Gould