

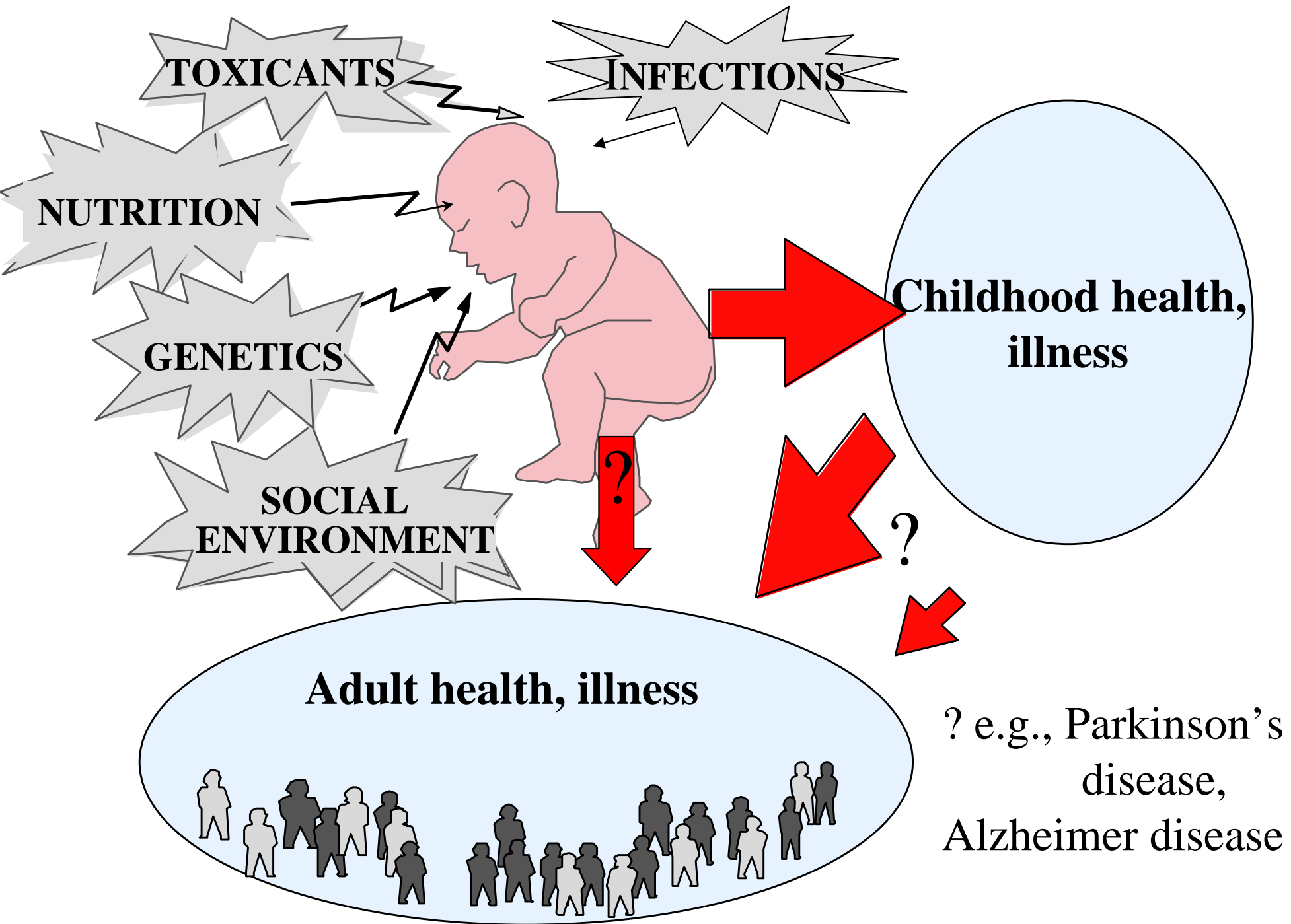
# Environmental Risks to Brain Development

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[www.sehn.org](http://www.sehn.org)

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# The developing brain

- Brain development begins early in fetal life and is not complete for years
- Brain develops under control of neurotransmitters, hormones, other endogenous chemicals **susceptible to alteration by environmental factors**
- Vulnerability extends beyond birth into adulthood

# Cellular Events in Neurodevelopment

Each of these events is subject to disruption by environmental agents

- Division
- Migration
- Differentiation
- Formation of synapses
- Pruning of synapses
- Apoptosis
- Myelination

Active  
throughout  
childhood &  
adolescence



<b>Process</b>	<b>Chemicals associated with disruption: (animal or human data)</b>
proliferation	radiation, ethanol, mercury, organophosphate pesticides
migration	radiation, mercury, ethanol, bisphenol A
differentiation	ethanol, nicotine, mercury, lead, bisphenol A
synaptogenesis	radiation, ethanol, lead, triethyl tin, parathion, PCBs
gliogenesis & myelination	decreased thyroid hormone, ethanol, lead
apoptosis	ethanol, lead, mercury
signaling	ethanol, organophosphate pesticides, mercury, lead, PCBs

# Well-known neurodevelopmental toxicants

- Alcohol – hyperactivity, cognitive deficits
- Nicotine – IQ deficit, learning and attention deficits
- Lead – impaired IQ, learning, attention; hyperactivity, impulsiveness, aggression; failure to complete school, trouble with the law

# Well-known neurodevelopmental toxicants

- Mercury—Impairments of motor skills, attention, visual spatial skills, language, memory
- PCBs—hyperactivity, memory and attention deficits, diminished full scale and verbal IQ (in childhood and pre-teens after fetal exposure)

# Neurotoxic pesticides

- Organophosphates
- Carbamates
- Pyrethroids/pyrethrins
- Organochlorines
- Neonicotinoids

# Organophosphate Pesticide (OP) Effects in Laboratory Animals

- Relatively small single dose on day 10  
(neonatal)
- Permanent changes in brain architecture
- Permanent hyperactivity (Ahlbom, 1995)

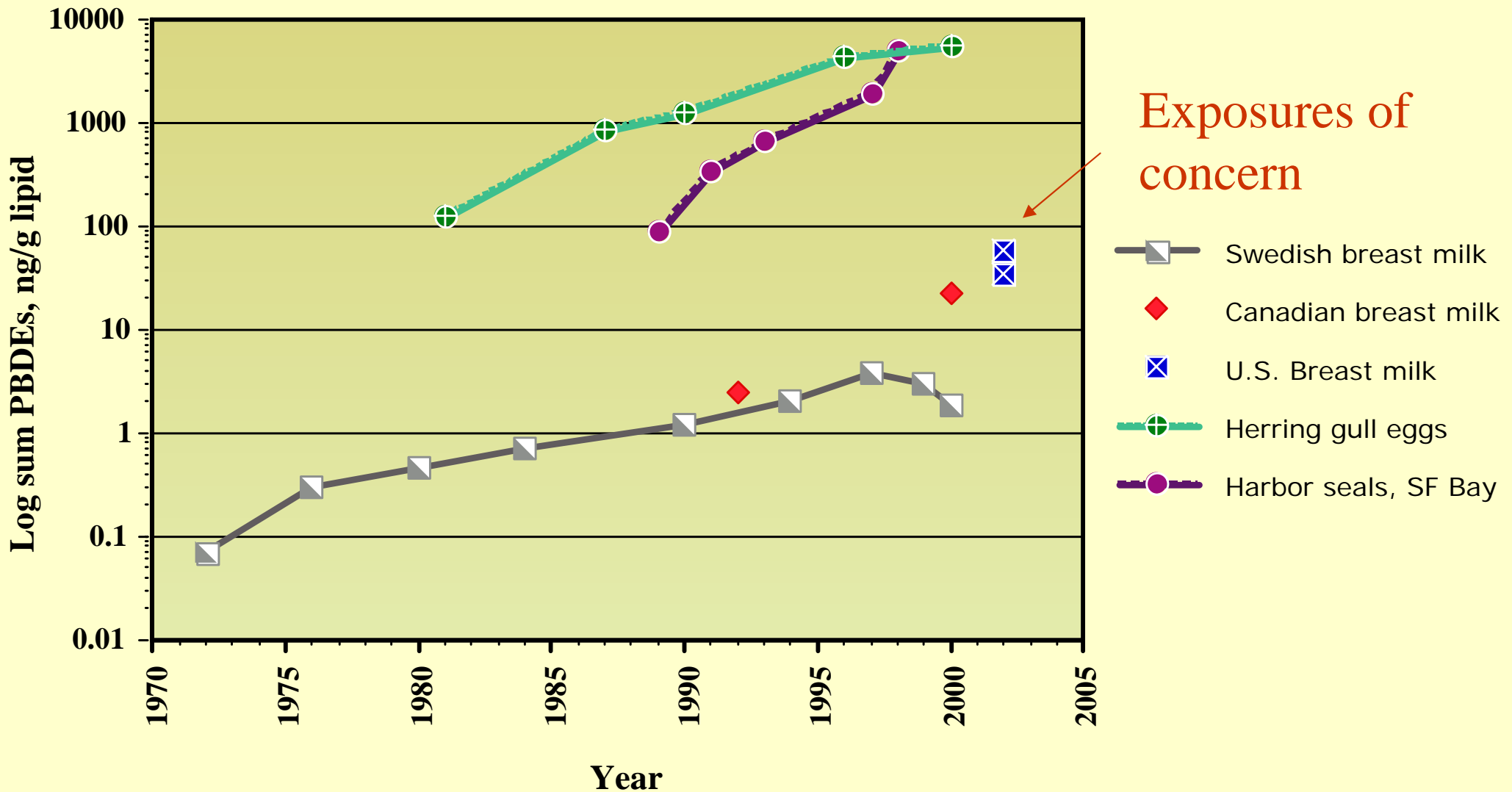
# Organophosphate neurodevelopmental effects—human

- Columbia Univ. study:
  - Prenatal chlorpyrifos exposure associated with 3.5-6 point decrease in 36-month development scores (Bayley MDI and PDI); **most marked in a low-income minority sample**
  - 5 fold increased risk of developmental delay
  - Increased risk of diagnosis of ADHD, attention problems, and PDD (Rauh, et al Pediatrics, 2006)
- Additional studies: CA, Ecuador also show developmental delays associated with OP exposure

# New concerns: Brominated flame retardants

- Added to products to inhibit ignition or spread of flames.
- Over 75 different brominated flame retardants.
- Rodents: Exposure to PBDEs (Penta, Octa, Deca) during critical windows of brain development results in decreased memory and learning (Eriksson, 2001; Viberg, 2003)
- No human neurodevelopmental data

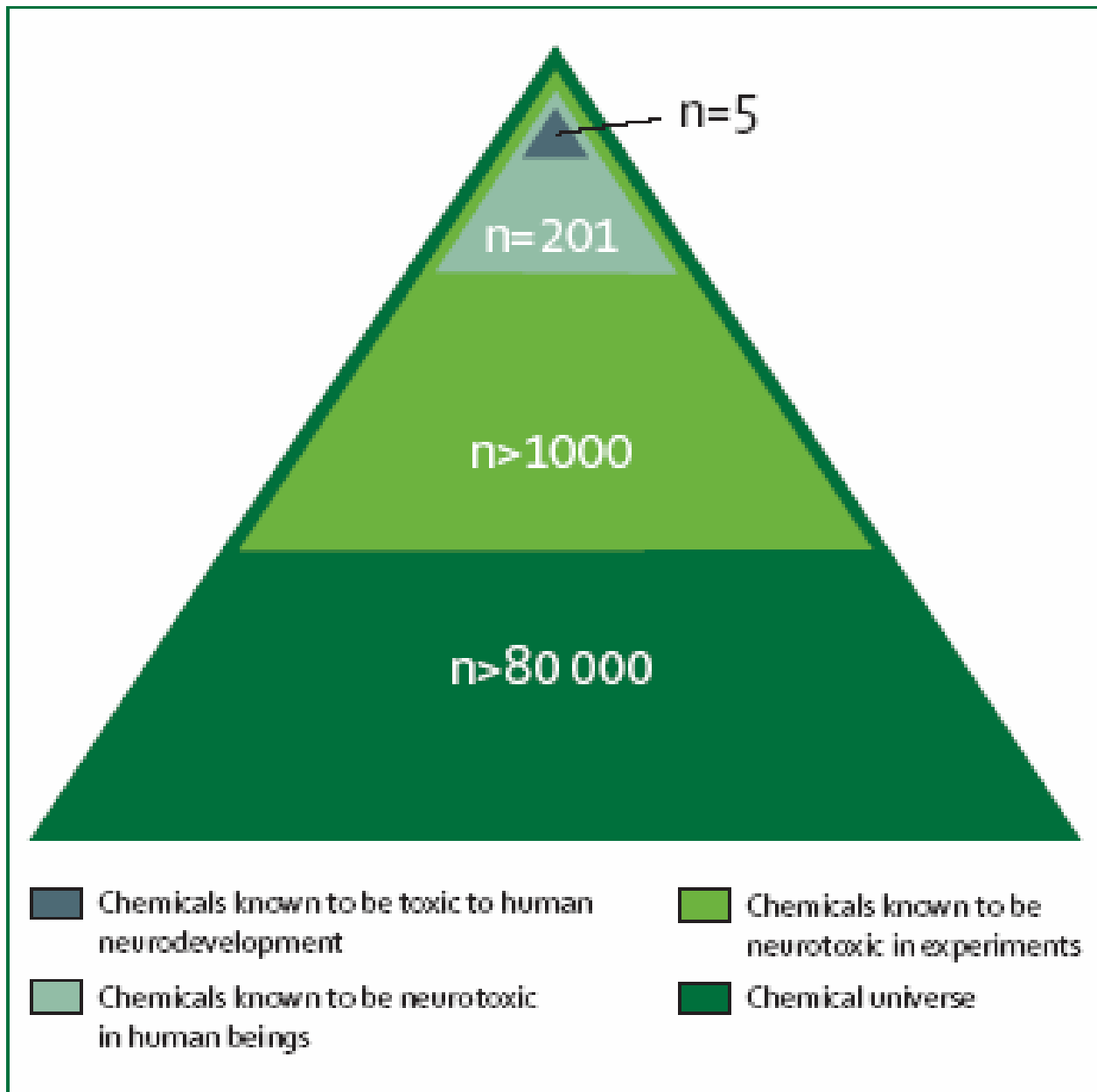
# Human and Wildlife Levels of PBDEs



Source: Hites, 2004; Lunder 2003

# Additional chemicals of concern

- Solvents—toluene, others
- Manganese (soy milk, gasoline additive; DW levels over 300 ppb associated with lower WISC score; rodent and primate studies)
- Arsenic (DW levels above 10 ppb associated with lower WISC score) (Wasserman EHP, 2004)
- Fluoride
- Bisphenol A (interferes with thyroid hormone function)
- Perchlorate
- Many other neurotoxicants



Grandjean, Landrigan. Lancet. 2006

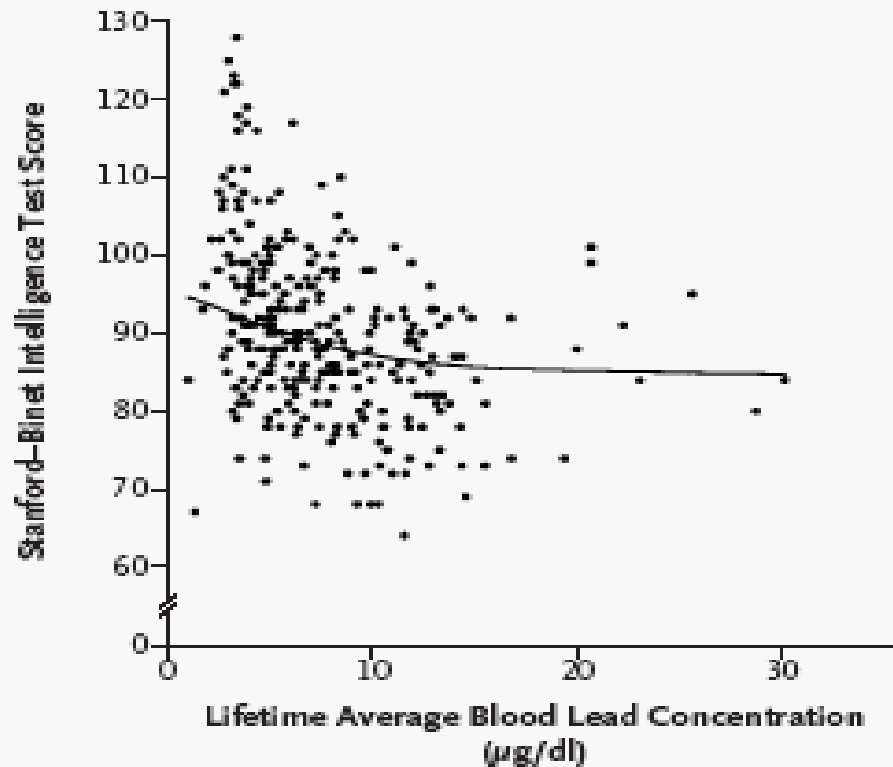
# Interactions

A need for new models and  
approaches to understanding

# Lead

- IQ, learning, attention deficits; hyperactivity, impulsiveness, aggression; failure to complete school, trouble with the law

Canfield, et al  
NEJM, 2003  
348:1517-1526



**Figure 2.** IQ as a Function of Lifetime Average Blood Lead Concentration.

IQ was assessed with use of the Stanford-Binet Intelligence Scale, fourth edition. The line represents the relation between IQ and lifetime average blood lead concentration estimated by the covariate-adjusted penalized-spline mixed model. Individual points are the unadjusted lifetime average blood lead and IQ values. To convert values for lead to micromoles per liter, multiply by 0.0483.

IQ tested at 3 and 5 years; blood lead measured X 7 before age 5

# Nutrition and brain development

- All nutrients are important for normal brain growth and development; some more than others
  - Protein, iron, zinc, iodine, selenium, folate, vitamin A, choline, LC-PU Fatty Acids

# Iron deficiency and brain development

- Iron deficiency: 10% US toddlers, ↑ poverty (?30%), obesity
- Iron deficiency > impaired IQ, auditory discrimination, memory, attention

# Nutrition and lead absorption: interactions

- Lead absorption increased with:
  - Iron-deficient diet
  - Calcium-deficient diet
  - High fat diet
- Iron deficiency up-regulates iron transporters of Fe into the brain; other heavy metals use those transporters

# Socioeconomic status and neurodevelopment

- Adverse socioeconomic conditions independently impair neurodevelopment (this is NOT primarily genetic) (Bradley, Ann R Psych, 2002)

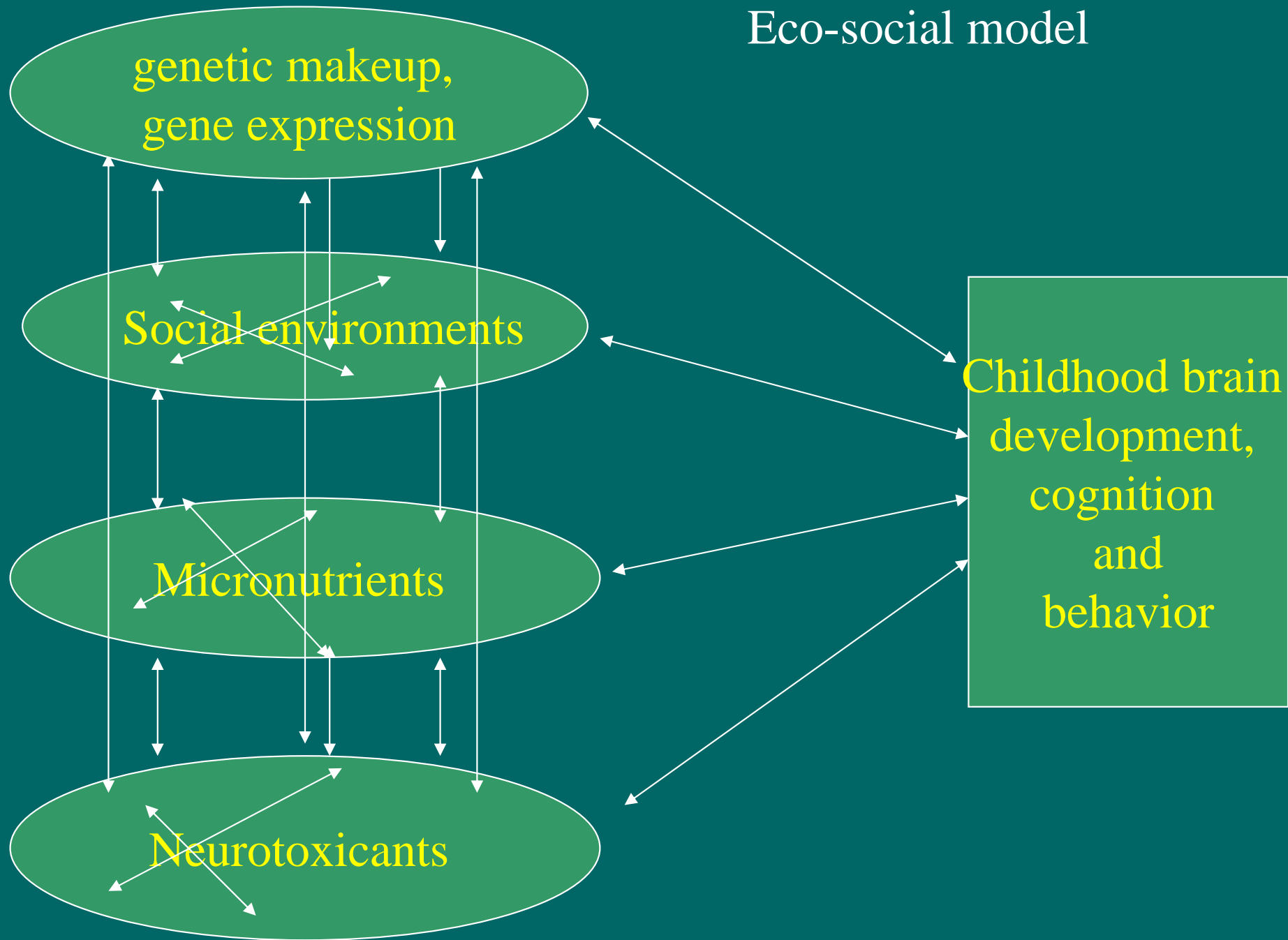
# Intervention studies

- Most interventions require addressing lead reduction, iron repletion, improved social circumstances **collectively** in order to have much beneficial effect.

(e.g., Ruff, EHP, 1996)

- BUT, even then, brain vulnerability outweighs plasticity; i.e., “catch-up” with remediation not as effective as primary prevention

# Eco-social model



# Neurodevelopmental problems

- Learning disabilities alone affect about 7% of children in Canada
- ADHD 5-10% of all Canadian children; Significant number with associated learning disability
- 1 in 160 Canadian children with autism spectrum disorder (ASD); ?? Increase, changes in diagnostic criteria or increased reporting??

# Effects of learning disabilities— in childhood

- Poorer overall health status.
- Less likely to do well in school.
- Less likely to do well in math and/or reading.
- More likely to miss school.
- One-third requires aids, but lack access to them.
- Two-thirds report child's extracurricular activities were reduced because of LD. (LDAC, 2007)

# Effects of learning disabilities— family

- More likely to be caring for the LD child as a single parent.
- More likely that parent has depressive symptoms.
- More likely to be part of a low-income family.

# Effects of learning disabilities— adult aged 30-44

- More likely to still be living with a parent.
- More likely to be unemployed or just not seeking employment.
- Those who are employed earn less.
- More likely to report their mental health status as fair or poor.
- Less likely to handle unexpected problems appropriately.
- More likely to report suicidal thoughts, depression and distress

# Costs of ADHD in US

- Lost productivity attributable to ADHD in US estimated between \$67-116 billion [compared to: drug abuse (\$58 billion) and depression (\$44 billion)]
- High school graduates with the disorder have average annual household incomes nearly \$11,000 lower than those of their non-ADHD counterparts. (Biederman, 2006)

# Summary: Childhood brain development

- Critical sequence—spatial and temporal dimensions
- Vulnerable to disruption by multiple, interacting environmental factors
- Size, timing, duration influence impact
- Susceptibility extends through adolescence; perhaps longer (neurodegenerative diseases)
- Little to no neurodevelopmental data on most chemicals in commerce
- Early life exposures can have long term consequences; individuals, families, society

# Policy responses

- An ethical imperative
- Prevent harm
- Act on early warnings, before definite “proof” of harm (e.g., Canadian Cancer Society)
- Pre-market testing; no data no market
- Seek safer substitutes; reduce exposures
- Multi-disciplinary, cross-agency, “ecological” responses

# Additional resources

- True Cost Clearinghouse  
<http://www.sehn.org/tcc.html>
- Collaborative on Health and the Environment  
[www.healthandenvironment.org](http://www.healthandenvironment.org)
- Greater Boston Physicians for Social Responsibility [www.igc.org/psr](http://www.igc.org/psr)
- A review of hazards of pesticides: Ontario College of Family Physicians:  
<http://www.ocfp.on.ca/>