Prenatal PCB & Mercury Exposures & Subsequent Neurobehavioral Development

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Polychlorinated Biphenyls

PCBs
Lipophillic, slowly metabolized
U.S. ban in 1977 but persistent
Exposure: food, soil/sediment, air
Concentrate in fatty tissue (breast milk)

Health Effects:
Probable human carcinogen
Structural teratogen
Growth impairment
Neuromuscular & psychomotor development
Cognition
Behavior
Other:
• Thyroid function
• Immune function
Concentrations of PCBs, dioxins, and pesticides versus location where salmon were grown or purchased

Red = Farmed, Green = Wild, Yellow = Supermarket

(Hites et al. Science 2004)
Mercury (Hg)

• Multiple forms: elemental, inorganic, organic (methylmercury, MeHg)

• Sources of mercury:
  – Natural
  – Industrial
    • Waste incineration
    • Burning of fossil fuels
    • Smelting
    • Medical/lab instrumentation
  – Methylated by bacteria in aquatic environment

• Toxicities of mercury:
  – Neurotoxicity (MeHg)
  – Renal
  – Immune
Study Goals

Assess relation of low level *in utero* PCB and MeHg exposures with prospectively measured:

(1) Growth and maturation
(2) Cognition
(3) *Behavior*
History of New Bedford Study Site

- **1940s-70s**: Discharge of PCB-laden waste
- **1970s**: Contamination discovered in Harbor
- **1977**: PCB production banned in U.S.
- **1979**: Harbor closed to fishing
- **1982**: Harbor on EPA National Priority List
Attention Deficit-Hyperactivity Disorder

- Most common neurobehavioral disorder of children (6-12% worldwide)
- Risk factors poorly understood
- Clinical diagnosis (no specific test)
- Neuroimaging: ↓ brain volume
- Mechanism: “dopamine deficit”
- Deficiencies:
  - vigilance-attention
  - cognitive control (working memory, impulse ctrl)
  - motivation
Study Design

Birth (n=788)

6 months (n=297)

Cognition, growth

Exposure measures, behavior, growth

8 years (n=607)

Cognition, behavior, growth

15 years (in progress)

Cognition, behavior, growth
## Study Population

### CHILD CHARACTERISTICS

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>%</th>
<th>Mean (range)</th>
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</thead>
<tbody>
<tr>
<td>Age at exam (yrs)</td>
<td>51</td>
<td>8 (7-11)</td>
</tr>
<tr>
<td>Male</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>69</td>
<td></td>
</tr>
<tr>
<td>Cape Verdean</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>Other</td>
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</table>

### MATERNAL CHARACTERISTICS

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>%</th>
<th>Mean (range)</th>
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</thead>
<tbody>
<tr>
<td>Age at infant birth</td>
<td>30</td>
<td>27 (17-41)</td>
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<tr>
<td>Smoked during pregnancy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Married when child is school aged</td>
<td>59</td>
<td></td>
</tr>
<tr>
<td>Some college</td>
<td>57</td>
<td></td>
</tr>
<tr>
<td>Breastfed</td>
<td>36</td>
<td></td>
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<tr>
<td>Household income &lt;20,000</td>
<td>21</td>
<td></td>
</tr>
</tbody>
</table>
Distribution of PCB 153 concentration in serum, 10 studies

- U.S./11 Cities (1959-1965)
- U.S./California (1964-1967)
- Netherlands/2 Cities (1990-1992)
- U.S./Massachusetts (1993-1998)
- Denmark/Faroe Islands (1994-1995)
- Canada/Northern Quebec (1995-1998)

\[ \mu g/g \text{ serum lipid} \]

Longnecker et al., Environ Health Perspect, 2003
Outcome: Behavioral Rating Scale

- **Conners Rating Scale – Teachers (CRS-T)**
  - 59 item questionnaire, problem behaviors
  - Used in clinical dx, monitoring, research
  - Analyzed 4 subscales:
    - Conners’ ADHD Index
    - DSM-IV Inattention
    - DSM-IV Impulsivity-Hyperactivity
    - DSM-IV Combined
PCBs & Conners’ Rating Scale (teachers)

Sagiv et al. Am J Epidemiol 2010

Quartiles of Exposure to Sum of 4 PCBs

Relative Risk

Conners’ ADHD

DSM-IV Inattention

DSM-IV Hyperactivity

DSM-IV Combined

RR = 1.76
RR = 1.52
RR = 1.26
RR = 1.79

*p-for-trend <0.05

Slide 12
Maternal Hair Hg & ADHD Behavior at age 8

Summary:
Environmental Contaminants & Behavior in the New Bedford Cohort

↑ADHD-associated behaviors were associated with:
   Prenatal PCBs
   Prenatal MeHg (> 1ppm)

*of note*

↓ADHD-associated behaviors were associated with > 2 servings fish/wk in pregnancy
Collaborators

Channing Laboratory (BWH)
- Chitra Amarasirwardena (MSSM)
- Trace Metals Laboratory

Boston Children’s Hospital
- David Bellinger
- Barry Brazelton
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- Kevin Nugent

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- Marisa Oge
- Sara Orenstein
- Louise Ryan
- Sharon Sagiv (Boston U.)

Emory University
- Paige Tolbert

CDC
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- Larry Needham

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Simon Fraser University
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U. of Rochester
- Sally Thurston