Little Things

The Impact of Toxic Chemicals on the Developing Brain

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OHSU Psychiatry Grand Rounds
Brain-based Disorders in Children

Factors that Impact Brain Development

- Sex
- Nutrition
- Toxic Stress
- Preterm Birth
- Toxic Chemicals
- Built Environment
- Maternal Depression
- Genetic Susceptibility
- Preschool Attendance
Environmental Disasters
... are just the tip of the iceberg
Vulnerability of the Developing Brain

- The blood brain barrier isn’t fully formed; it is more permeable to toxic chemicals
- Rapidly growing cells are often more vulnerable to toxins than slowly growing cells
- Brain growth occurs over a longer duration than other organs
- The fetus and child may lack enzymes to detoxify contaminants
- Young children often more heavily exposed to contaminants than older children and adults
Little Things Matter

The impact of toxins on the developing brain
Prenatal PCB Exposure and IQ Scores in 9-year old Children, Oswego, NY

Impact of Air Pollution on the Developing Brain

No Acceptable Level?
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).

Tobacco Exposure and Birthweight

ETS Ban
ETS Ban

15% Reduction PTB

-151 grams

-0.5 week

ADHD
Lead Exposure and Motor Activity in Mice

**Figure 4.** Effects of lead on motor activity (counts/hr) of 30- to 150-day-old mice given 5 mg/ml lead acetate before and after weaning. Results are for the second hour of measurement with each point representing the mean ± S.E.M. for 5–16 animals. Differences between controls (solid line) and treated are significant at \( P < 0.001 \).

**Figure 5.** Effects of drugs on motor activity (counts/hr) in control and treated mice. Open bars represent predrug baselines in both groups. Results are expressed as means ± S.E.M. of at least seven animals. Differences in response to all drugs between control and treated mice were significant at \( P < 0.001 \). Data of Silbergeld and Goldberg (15).

Behavioral and Emotional Problems of Lead Exposure

<table>
<thead>
<tr>
<th>Class</th>
<th>Dentine Lead (ppm)</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>&lt;1.1</td>
</tr>
<tr>
<td>2</td>
<td>5.1 to 8.1</td>
</tr>
<tr>
<td>3</td>
<td>8.2 to 11.8</td>
</tr>
<tr>
<td>4</td>
<td>11.9 to 17.1</td>
</tr>
<tr>
<td>5</td>
<td>17.2 to 27.0</td>
</tr>
<tr>
<td>6</td>
<td>&gt;27.0</td>
</tr>
</tbody>
</table>

Lead Exposure and ADHD in United States Children, NHANES

Lead and Tobacco Exposure and ADHD in United States Children, NHANES

Tooth Lead Levels and Criminality

No. of Arrests by Childhood Lead Exposure
The Cincinnati Lead Study

Gray Matter Loss 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, PLoS Medicine, et al. 2008).
Reduction in Gray Matter by Childhood Blood Lead Levels and Subject’s Sex

Men (n=83)  

Women (n=74)
Risk of Conduct Disorder by Blood Lead Concentration in US Children, 8 to 15 years, NHANES 2001-2004

Lead Exposure and Homicides in United States

Nevin R. Environmental Research 2000:83;1-22
Cause or Cure?
Pesticide Exposure, Folate and Autism

Schmidt R, et al. EHP 2017
https://doi.org/10.1289/EHP604
Pesticide Exposure, Folate and Autism

Schmidt R, et al. EHP 2017
https://doi.org/10.1289/EHP604
Gestational Air Pollution (PM$_{2.5}$) Exposure and Development of Autism


<table>
<thead>
<tr>
<th>Source</th>
<th>Adjusted Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>This study</td>
<td></td>
</tr>
<tr>
<td>Becerra et al, 10 2013</td>
<td></td>
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<tr>
<td>Guxens et al, 19 2016</td>
<td></td>
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<tr>
<td>Raz et al, 13 2015</td>
<td></td>
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<tr>
<td>Raz et al, 16 2017</td>
<td></td>
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<tr>
<td>Talbott et al, 15 2015</td>
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<td>Volk et al, 12 2013</td>
<td></td>
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<tr>
<td>Meta-analyses</td>
<td></td>
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<tr>
<td>Flores-Pajot et al, 8 2016</td>
<td></td>
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<tr>
<td>Lam et al, 7 2016</td>
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</tbody>
</table>
Limitations

• Prospective cohorts with biomarkers of exposure to toxic chemicals are typically modest in size

• Measures of exposures to toxic chemicals are imperfect

• Failure to account for variety of other risk factors or test for modification (e.g., folate status)

• Challenging to infer causal association from observational studies
The Prevention Paradox

The majority of disease and disability occurs in those who are at low to moderate risk
### The Prevention Paradox

The table below illustrates the impact of different blood lead levels on the estimated IQ points lost among children.

<table>
<thead>
<tr>
<th>Blood Lead Level</th>
<th>No. of Children in Distribution</th>
<th>Average IQ Loss</th>
<th>Estimated IQ Points Lost</th>
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<tbody>
<tr>
<td>12.7 Million</td>
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<td>0.3</td>
<td>4.7 Million</td>
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<tr>
<td>5.7 Million</td>
<td></td>
<td>0.9</td>
<td>5.7 Million</td>
</tr>
<tr>
<td>9.3 Million</td>
<td></td>
<td>1.6</td>
<td>3.1 Million</td>
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<tr>
<td>0.5 Million</td>
<td></td>
<td>6.1</td>
<td>3.1 Million</td>
</tr>
<tr>
<td>Current Reference Value = 5 μg/dL</td>
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Neurotoxicity of Industrial Chemicals

Lessons from the FDA
If we didn’t evolve with it …

avoid it.
How to Avoid Exposures to Toxic Chemicals

- Eat fresh, organic and unpackaged foods; avoid canned foods
- Minimize use of pesticides around the home
- Avoid cosmetics, fingernail polish and lotions
- Support bans on smoking in public places and cosmetic pesticides
- Support efforts to update chemical management policies and reduce industrial pollutants
“We can’t live in a state of perpetual doubt, so we make up the best story possible and we live as if the story were true.”

Daniel Kahneman