Long-Term Neurotoxic Effects of Early Life Exposure to Tetrachloroethylene-Contaminated Drinking Water

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Overview of Presentation

- Setting of research --- Cape Cod, MA
- How tetrachloroethylene (aka “PCE” or “perc”) contaminated Cape Cod’s drinking water
- Methods and results of birth cohort study
- Context of findings and conclusions
Cape Cod, Massachusetts
About Cape Cod

- 15 towns on “the Cape”
- ~ 200,000 permanent residents
- Mainly White, non-Hispanic
- Small Native American population
- Tremendous population growth since 1970s skewed towards older ages
Source of Drinking Water on Cape Cod

- Main source is groundwater aquifer tapped using shallow wells.
- Local water companies pump and deliver water to homes through pipe distribution system.
- Most homes receive public water; some have private wells.
What is tetrachloroethylene (PCE)?

How does it typically contaminate drinking water?

- Important solvent used in dry cleaning and metal degreasing
- ~650,000 people in US are exposed through work
- Used in small, geographically dispersed, and poorly controlled facilities -- dry cleaners and garages
- Common drinking water contaminant in US
  - 11% of wells
  - 38% of surface water
Unusual source of contamination on Cape Cod

- Source = vinyl liner applied to inside of water distribution pipes
- Introduced in 1969 in response to complaints about metallic taste of water
- Slurry composed of vinyl toluene resin dissolved in PCE was sprayed onto inner pipe surface
- Assumed PCE would disappear in curing process but, because of inadequate drying time, substantial quantities remained and leached into drinking water supplies
Extent of Problem

- Contamination discovered by accident in 1980 when water was tested for other compounds

- 660 miles of vinyl-lined (VL) pipes installed in 91 Massachusetts communities

- 24% installed on Cape Cod because of substantial residential development

- Water tests revealed PCE levels in affected pipes ranging from 1.5 to 7,750 ppb, depending on rate of water flow
Our team has used this “natural experiment” to learn about health effects of PCE in drinking water among individuals exposed during adulthood and in early life.

Birth cohort study of neurotoxic effects stemming from early life exposure.
Neurotoxicity of PCE

- PCE is a recognized animal and human neurotoxin

- Most human research has been conducted among occupationally exposed adults

- Acute exposure: headaches, dizziness, unconsciousness, death from respiratory depression

- Chronic exposure: impairments in memory, attention, vision problems

- Little information on impact of early life exposure especially in community settings

- Only a few small studies of short-term outcomes
Cape Cod Health Study

- Retrospective cohort study to examine long-term neurotoxic effects of early life exposure to PCE in environmental setting
  - Broad view of neurotoxicity: diminished performance on neuropsychological tests, vision problems, structural brain changes, mental illness, and risk-taking behaviors

- Source population: children born from 1969-1983 to women who lived in Cape Cod towns with vinyl-lined pipes

- Study compared two groups:
  - (1) children with early life exposure
  - (2) unexposed children
Cape Cod Health Study

- Subjects identified by cross-matching maternal addresses from birth records with water company records on location and installation year of VL pipes
- Reviewed over 14,000 birth records to identify 1,910 exposed and 1,928 unexposed children
- Mothers and children were traced and invited to participate
Data Collection

Traced mothers and children returned self-administered questionnaires on

- Demographic characteristics, occupational and non-occupational sources of solvent exposure, and other confounding variables
- Bathing habits
- Tap and bottled water consumption
- Drinking water source (private vs. public)
Data Collection

- Children provided information on risk-taking behaviors during teen and adults years
  - Cigarette smoking
  - Alcoholic beverage consumption
  - Illicit drug use -- marijuana, inhalants, crack, cocaine, psychedelics, hallucinogens, club drugs, Ritalin without a prescription and heroin
PCE Exposure Assessment

• Based on leaching and transport model that estimated relative mass of PCE delivered to each residence from prenatal period through child’s fifth birthday

• Three pieces of information needed for determining PCE exposure
  – (1) VL pipe locations
  – (2) Subjects’ residential locations
  – (3) Leaching and transport algorithm
Original Map of Water Pipes
GIS Maps of Water Pipes
Leaching and Transport Algorithm Estimated Annual Mass of PCE Entering the Residence
## Characteristics of Study Population

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Subjects with Prenatal and Early Childhood Exposure N=831</th>
<th>Unexposed Subjects N=547</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current age, mean (sd)</td>
<td>29.2 (3.6)</td>
<td>29.6 (3.8)</td>
</tr>
<tr>
<td>% Female</td>
<td>60.2</td>
<td>60.5</td>
</tr>
<tr>
<td>% White</td>
<td>98.4</td>
<td>98.5</td>
</tr>
<tr>
<td>% College graduate</td>
<td>61.4</td>
<td>61.2</td>
</tr>
<tr>
<td>% Ever had job with solvent exposure</td>
<td>14.8</td>
<td>13.0</td>
</tr>
<tr>
<td>% History of mental illness</td>
<td>24.4</td>
<td>21.4</td>
</tr>
<tr>
<td>% Mother received prenatal care</td>
<td>95.5</td>
<td>95.1</td>
</tr>
<tr>
<td>% Mother smoked cigarettes during gestation</td>
<td>21.9</td>
<td>20.7</td>
</tr>
<tr>
<td>% Mother consumed alcoholic beverages during gestation</td>
<td>36.3</td>
<td>36.8</td>
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</tbody>
</table>
## Findings:
### Frequency of Risk-Taking Behaviors as Teen

<table>
<thead>
<tr>
<th>Risk-Taking Behaviors</th>
<th>Frequency (%)</th>
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</thead>
<tbody>
<tr>
<td>Ever binge drinker (4/5 alcoholic beverages at a time)</td>
<td>35%</td>
</tr>
<tr>
<td>1st drank &lt;=13 years old</td>
<td>19%</td>
</tr>
<tr>
<td>Ever used illicit drugs</td>
<td>55%</td>
</tr>
<tr>
<td>Ever used 2+ major drugs (excl. marijuana)</td>
<td>13%</td>
</tr>
<tr>
<td>Ever used crack/cocaine</td>
<td>9%</td>
</tr>
<tr>
<td>Ever used hallucinogens</td>
<td>18%</td>
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</tbody>
</table>
Findings: Risk-Taking Behaviors

- Highly exposed individuals experienced 30% to 40% increases in risk of using major illicit drugs
  - Risk Ratio for teen use: 1.4  (95% CI: 1.1-1.7)
  - Risk Ratio for adult use: 1.3  (95% CI: 1.1-1.5)

- These increases in risk rose to 50-60% for use of 2+ major drugs
  - Risk Ratio for teen use: 1.6  (95% CI: 1.2-2.2)
  - Risk Ratio for adult use: 1.5  (95% CI: 1.2-2.9)

- Specific drugs for which increases were observed included crack/cocaine, psychedelics/hallucinogens, club/designer drugs, Ritalin without a prescription, and heroin
  - Risk Ratios for specific drugs: 1.4 - 2.1

- 30-60% increases in the risk of certain smoking and drinking behaviors were also seen among highly exposed subjects
Context of Findings

- Biological plausibility for neurotoxic effects:
  - PCE is a small, fat soluble molecule that can cross the placenta and blood brain barrier
  - PCE has high affinity for lipophilic tissues of the CNS

- Mode of action is unknown; possible mechanisms include:
  - Changes in fatty acid profile of brain
  - Loss of myelin
  - Apoptotic neuro-degeneration
# Context of Findings

<table>
<thead>
<tr>
<th>Publication</th>
<th>Exposure</th>
<th>Study Population</th>
<th>Results</th>
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<tbody>
<tr>
<td>Till (2001, Toronto)</td>
<td>Maternal occupational exposure to solvents during pregnancy</td>
<td>Pre-school children N=61</td>
<td>Lower language scores, more behavioral problems</td>
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<tr>
<td>Laslo-Baker (2004, Toronto)</td>
<td>Maternal occupational exposure to solvents during pregnancy</td>
<td>Pre-school children N=32</td>
<td>Lower language scores, more inattention and hyperactivity</td>
</tr>
<tr>
<td>Eskenazi (1988, New Haven)</td>
<td>Maternal occupational exposure to solvents during pregnancy</td>
<td>Pre-school children N=41</td>
<td>No deficits in intellectual ability, memory</td>
</tr>
<tr>
<td>Spector (1999, 2005) NY</td>
<td>Environmental exposure to solvents from nearby dry cleaning facility</td>
<td>Children at daycare center N=40</td>
<td>No impact on cognition or behavior</td>
</tr>
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Conclusions

- Study demonstrates how scientists can take advantage of a unique “natural experiment” to learn about health effects of an environmental pollutant

- Fortuitous circumstances
  - Availability of historical data
  - High prevalence and wide range of PCE exposure levels
  - Little confounding due to irregular contamination pattern

- Challenges
  - Historical exposure assessments → misclassification which may have biased results towards null
  - Little information on social environment, an important determinant of risk-taking behavior
Conclusions

• Newly funded study is examining combined impact of early life exposure to environmental and social stressors on substance use

• PCE remains a common drinking water contaminant, so it’s important to determine its impact on the health of vulnerable populations

• Goal of this research is to provide a sound scientific basis for policy makers to ensure that drinking water supplies are safe for all to consume
References


Thanks to my colleagues.....