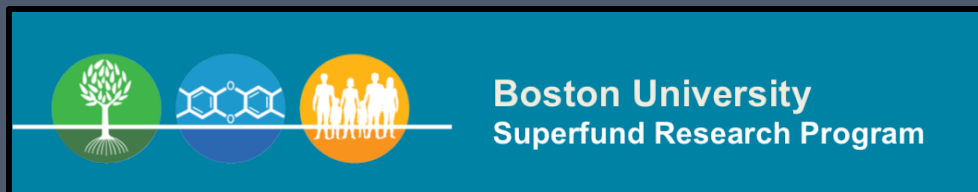


Long-Term Neurotoxic Effects of Early Life Exposure to Tetrachloroethylene-Contaminated Drinking Water

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Overview of Presentation

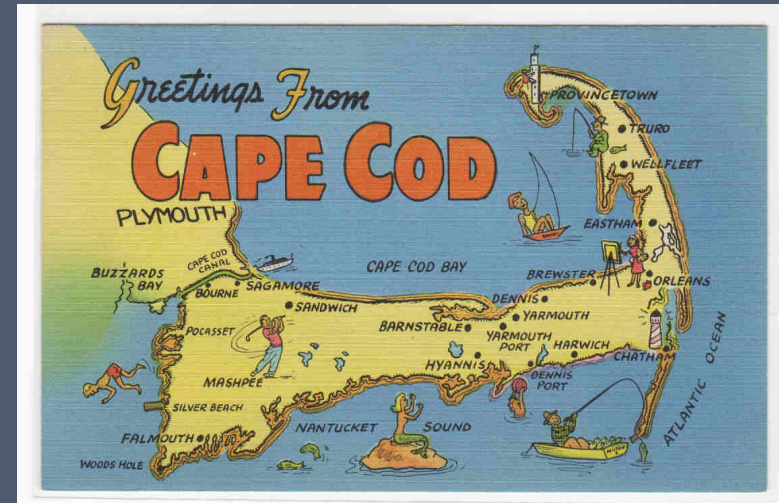
- Setting of research ---Cape Cod, MA
- How tetrachloroethylene (aka “PCE” or “perc”) contaminated Cape Cod’s drinking water
- Methods and results of birth cohort study
- Context of findings and conclusions

Cape Cod, Massachusetts



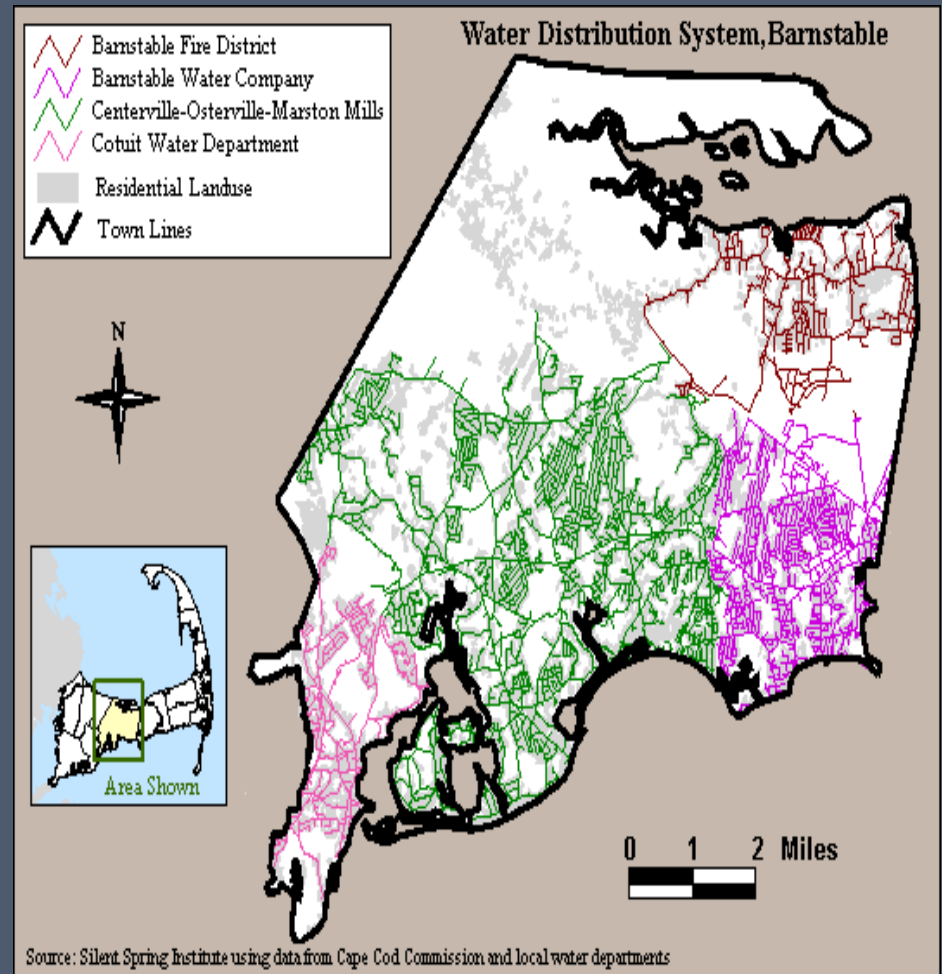
About Cape Cod

- 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 ground water 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

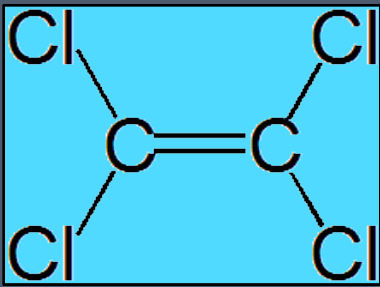


- Source = vinyl liner applied to inside of water distribution pipes
- Introduced in 1969 in response to complaints about metallic taste of water
- Slurry composed of vinyl toluene resin dissolved in PCE was sprayed onto inner pipe surface
- Assumed PCE would disappear in curing process but, because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

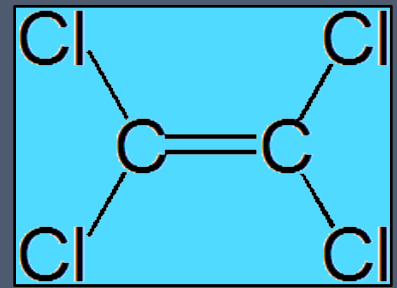
Extent of Problem



- 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 Research



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

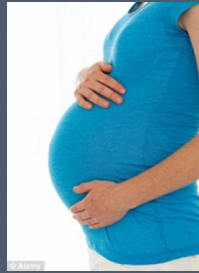


Neurotoxicity of PCE

- 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

STATE OF HAWAII		CERTIFICATE OF LIVE BIRTH			DEPARTMENT OF HEALTH	
				FILE NUMBER	61 10641	
				NUMBER	151	
1a. Child's First Name (Type or print)		1b. Middle Name		1c. Last Name		
BARACK		HUSSEIN		OBAMA, II		
2. Sex	3. This Birth	4. If Twin or Triplet, Was Child Born		5a. Birth Date	Month	Day Year
Male	Single <input checked="" type="checkbox"/> Twin <input type="checkbox"/> Triplet <input type="checkbox"/>	1st <input type="checkbox"/> 2nd <input type="checkbox"/> 3rd <input type="checkbox"/>		August	4,	1961
						5b. Hour
						7:24 P.M.
6a. Place of Birth: City, Town or Rural Location					6b. Island	
Honolulu					Oahu	
6c. Name of Hospital or Institution (If not in hospital or institution, give street address)					6d. Is Place of Birth Inside City or Town Limits? If no, give judicial district	
Kapiolani Maternity & Gynecological Hospital					Yes <input checked="" type="checkbox"/> No <input type="checkbox"/>	
7a. Usual Residence of Mother: City, Town or Rural Location			7b. Island		7c. County and State or Foreign Country	
Honolulu			Oahu		Honolulu, Hawaii	
7d. Street Address				7e. Is Residence Inside City or Town Limits? If no, give judicial district		
6085 Kalaniana'ole Highway				Yes <input checked="" type="checkbox"/> No <input type="checkbox"/>		
7f. Mother's Mailing Address					7g. Is Residence on a Farm or Plantation?	
					Yes <input type="checkbox"/> No <input checked="" type="checkbox"/>	
8. Full Name of Father			9. Race of Father			
BARACK HUSSEIN OBAMA			African			
10. Age of Father	11. Birthplace (Island, State or Foreign Country)	12a. Usual Occupation		12b. Kind of Business or Industry		
25	Kenya, East Africa	Student		University		
13. Full Maiden Name of Mother			14. Race of Mother			
STANLEY ANN DUNHAM			Caucasian			
15. Age of Mother	16. Birthplace (Island, State or Foreign Country)	17a. Type of Occupation Outside Home During Pregnancy		17b. Date Last Worked		
18	Wichita, Kansas	None				
I certify that the above stated information is true and correct to the best of my knowledge.				18a. Signature of Parent or Other Informant		18b. Date of Signature
				Parent <input checked="" type="checkbox"/> Other <input type="checkbox"/>		8-7-61
I hereby certify that this child was born alive on the date and hour stated above.				19a. Signature of Attendant		19b. Date of Signature
				M.D. <input type="checkbox"/> D.O. <input type="checkbox"/> Midwife <input type="checkbox"/> Other <input checked="" type="checkbox"/>		8-8-61
20. Date Accepted by Local Reg.		21. Signature of Local Registrar		22. Date Accepted by Reg. General		
AUG - 8 1961		U.K. Lee		AUG - 8 1961		
23. Evidence for Delayed Filing or Alteration						



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



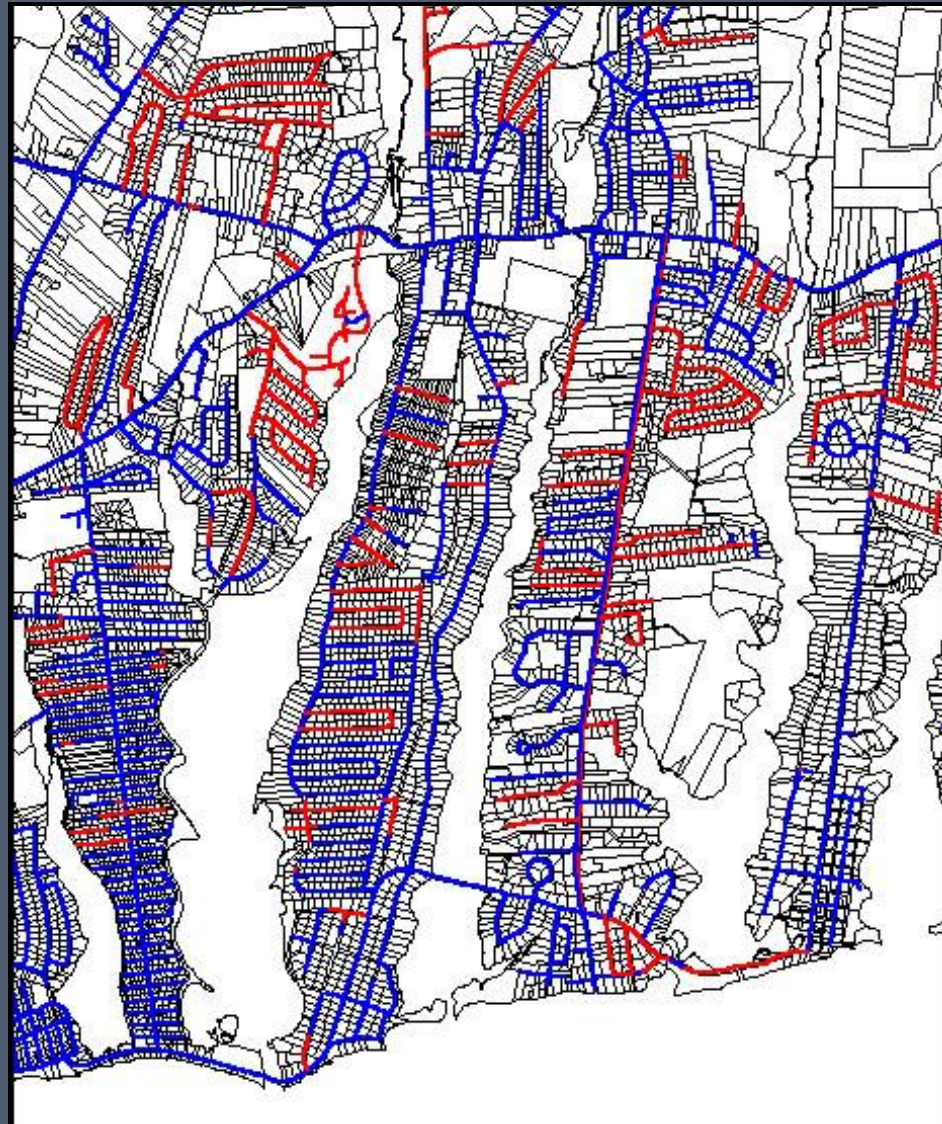
- Children provided information on risk-taking behaviors during teen and adults years
 - Cigarette smoking
 - Alcoholic beverage consumption
 - Illicit drug use --marijuana, inhalants, crack, cocaine, psychedelics, hallucinogens, club drugs, Ritalin without a prescription and heroin



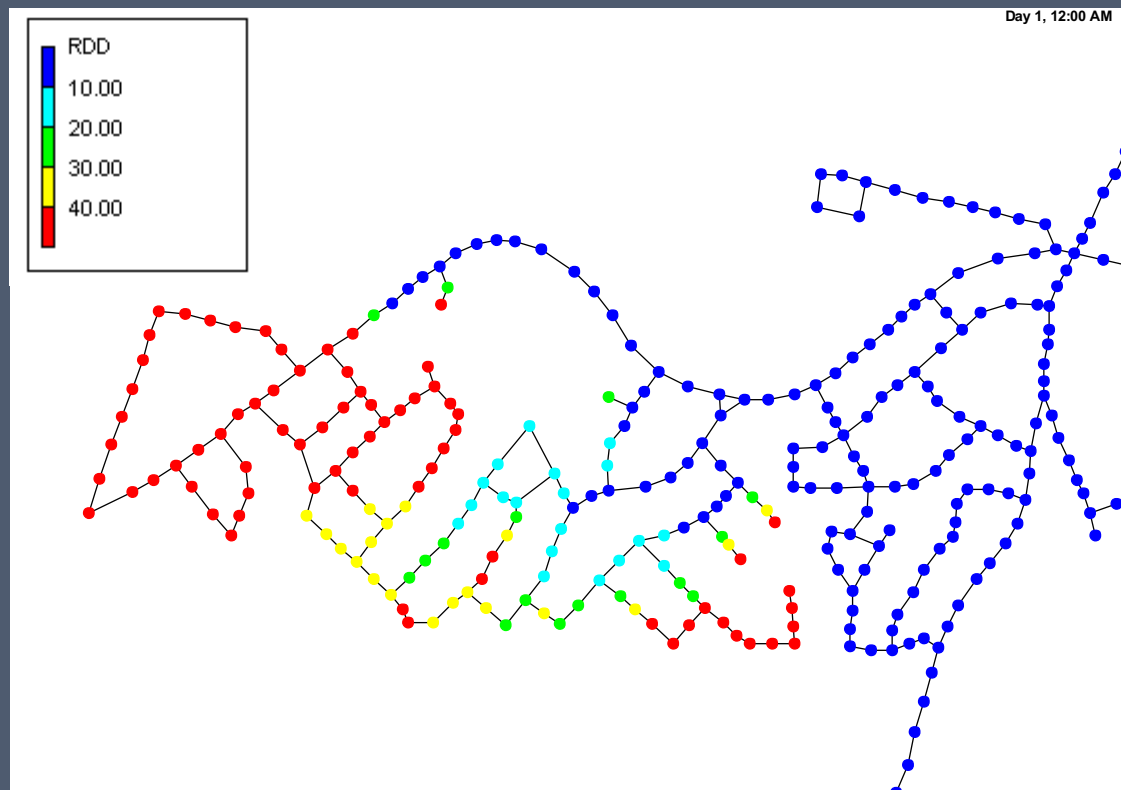
PCE Exposure Assessment

- 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

GIS Maps of Water Pipes



Leaching and Transport Algorithm Estimated Annual Mass of PCE Entering the Residence



Characteristics of Study Population

Characteristic	Subjects with Prenatal and Early Childhood Exposure N=831	Unexposed Subjects N=547
Current age, mean (sd)	29.2 (3.6)	29.6 (3.8)
% Female	60.2	60.5
% White	98.4	98.5
% College graduate	61.4	61.2
% Ever had job with solvent exposure	14.8	13.0
% History of mental illness	24.4	21.4
% Mother received prenatal care	95.5	95.1
% Mother smoked cigarettes during gestation	21.9	20.7
% Mother consumed alcoholic beverages during gestation	36.3	36.8

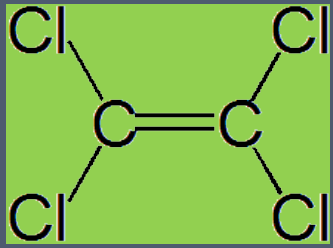
Findings:

Frequency of Risk-Taking Behaviors as Teen

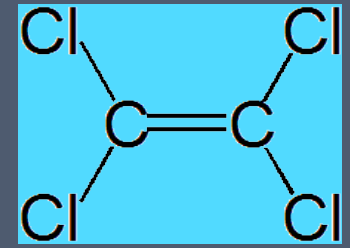
Risk-Taking Behaviors	Frequency (%)
Ever binge drinker (4/5 alcoholic beverages at a time)	35%
1st drank <=13 years old	19%
Ever used illicit drugs	55%
Ever used 2+ major drugs (excl. marijuana)	13%
Ever used crack/cocaine	9%
Ever used hallucinogens	18%

Findings: Risk-Taking Behaviors

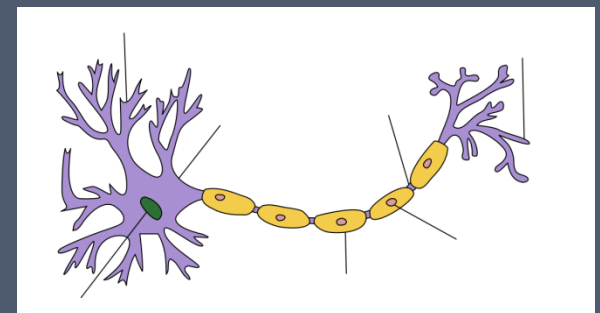
- **Highly exposed individuals experienced 30% to 40% increases in risk of using major illicit drugs**
 - Risk Ratio for teen use: 1.4 (95% CI: 1.1-1.7)
 - Risk Ratio for adult use: 1.3 (95% CI: 1.1-1.5)
- **These increases in risk rose to 50-60% for use of 2+ major drugs**
 - Risk Ratio for teen use: 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

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

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 is a sound scientific basis for policy makers to ensure that drinking water supplies are safe for all to consume

References

- Aschengrau A, Janulewicz P, White R, et al. Long-term neurotoxic effects of early life exposure to tetrachloroethylene-contaminated drinking water. *Ann Global Health* 2016; 82:169-179.
- Aschengrau A, Weinberg J, Janulewicz P et al. Affinity for risky behaviors following prenatal and early childhood exposure to tetrachloroethylene. *Environ Health* 2011; 10: 102.
- Gallagher LE, Webster TF, Aschengrau A. Associations between teenage drug and alcohol use and early life exposure to tetrachloroethylene and alcohol. *Environmental Health* 2017; 16:26.

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