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No Association Between Unintentional Head Injuries and Early-Life Exposure to Tetrachloroethylene (PCE)-Contaminated Drinking Water

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Objective: Because of emerging evidence that early-life exposure to the solvent tetrachloroethylene (PCE) has long-lasting neurological consequences, we examined the risk of unintentional head injuries following prenatal and childhood exposure to PCE-contaminated drinking water. **Methods:** Participants provided information on head injuries and other relevant characteristics in a self-administered questionnaire. Exposure to PCE was modeled using a leaching and transport algorithm set in water system modeling software. **Results:** We did not observe any evidence of an increased risk of any type of head injury among exposed participants. **Conclusions:** PCE is a widespread water pollutant. Thus, documenting possible health effects of early-life exposure is vital for ensuring that drinking water regulations adequately protect vulnerable populations.

BACKGROUND

Tetrachloroethylene (PCE) is an organic lipophilic solvent extensively employed in dry cleaning of clothes and degreasing of metals. Regularly found in industrial waste, it can easily evaporate and aerosolize, and may leach into contact solutions, such as drinking water.[1] Before harmful health effects were known, PCE was used to apply a vinyl liner (VL) to asbestos-cement (AC) water distribution pipes in Cape Cod, Massachusetts, to minimize corrosion and complaints about the taste and odor of water flowing through AC pipes.[2] Manufacturers assumed that the PCE would completely evaporate before the installation of the pipes carrying the public drinking water. However, in 1980, state officials discovered that the solvent was seeping from the liner into the water system.[3] Although PCE pollution on Cape Cod was eventually resolved by installing bleeder valves,[3] questions remain about the health effects due to past drinking water exposure to PCE and related solvents.[4–7] Thus, environmental exposure remains a valuable area of scientific inquiry.

Both animal experiments and epidemiological studies provide strong support for neurotoxicity of PCE and other solvents.[1] Epidemiologic research among adults with job-related exposures have found impairments in cognition, vision, attention, and motor skills.[8–10] In contrast, studies of early-life exposure are quite limited.[11–13] Our prior research found diminished visuospatial function, motor skills, and attention and an increase in risk-taking behavior among individuals exposed early in life.[14,15] Because these factors could plausibly increase the likelihood of unintentional injuries, we assessed the occurrence of unintentional head injuries following early-life exposure to PCE-contaminated drinking water.

METHODS

Study Population

We conducted a retrospective cohort study to evaluate the neurotoxicity of early-life exposure to PCE-contaminated drinking water.[14–16] As previously described, ''individuals were eligible for the study if they were born between 1969 and 1983 to married women living on one of eight Cape Cod, Massachusetts, towns known to have some VL/AC pipes on their water distribution system. The exclusion of unmarried women and their children was an approval requirement of the Massachusetts Department of Public Health Privacy and Data Access Office. Eligible individuals were identified by reviewing birth certificates and cross-matching the maternal address and date of birth on the certificate with information collected from water companies on the location and installation year of VL/AC pipes.''[16]

''To efficiently identify subjects who were likely to be exposed or unexposed, we visually inspected maps depicting the pipe distribution network in the vicinity of the birth address. Subjects were tentatively designated as exposed when their birth residence was either directly adjacent to a VL/AC pipe or indirectly adjacent to a pipe connected to a VL/AC pipe with the only possible water flow through VL/AC pipe ($N = 1910$). Subjects who were initially designated as unexposed were randomly selected from the remaining resident births during this time period and frequency matched to exposed subjects on month and year of birth ($N = 1928$).''[16]

''In addition, 1202 older siblings of exposed and unexposed subjects were identified if they were born in Massachusetts during 1969 to 1983. All older siblings were initially considered unexposed during the prenatal period because they were born while the family lived at an apparently unaffected residence. However, the initial exposure status of all subjects was considered tentative until more extensive exposure assessments were completed, as described below.''[16]

''Birth certificates were reviewed to obtain information on the family, including the full names of the subject and parents; the subject's date of birth, birth weight, and gestational duration; and the parents' ages and educational levels at the subject's birth. The study was approved by the Institutional Review Boards of the Massachusetts Department of Public Health and Boston University Medical Center and by the 24A/B/11B Review Committee at the Massachusetts Department of Public Health.''[16]

Follow-Up and Enrollment of Participants

Table 1 describes the follow-up and enrollment process. Ultimately, 40.5% of located subjects returned a self-administered

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At the request of the Commonwealth of Massachusetts, in 1980, Dr Ozonoff was a witness in bankruptcy court in a suit against the Johns-Manville Corporation, manufacturers of the ACVL water mains. He has also, on occasion, testified in personal injury and property damage cases involving exposure to tetrachloroethylene and trichloroethylene. None of the other authors have any conflicts of interest.

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TABLE 1. Selection, Response, and Exposure Status of Subjects

	Initial Exposure Status			
	Index Subject		Older Sibling	
	Exposed	Unexposed	Unexposed	Total
Selected	1,910	1,928	1,202	5,040
Excluded during enrollment				
Deceased	35	40	36	111
Parent refused participation	199	148	80	427
Never located	113	149	70	332
No response	871	887	536	2,294
Refused	73	78	36	187
Returned questionnaire	619	626	444	1689
Percent of located	39.6%	39.3%	43.7%	40.5%
Excluded during exposure assessment				
Inadequate residential history	15	37	29	81
Off-Cape address in town with VL/AC pipes	19	27	50	96
Available for analysis	585	562	365	1,512
Final exposure status				
Both prenatal and early childhood exposure	561	160	110	831
Only early childhood exposure	7	42	85	134
Unexposed	17	360	170	547
Total	585	562	365	1,512

survey that collected data on demographic characteristics, medical and occupational histories, lifestyle factors, residential addresses from birth through early childhood, and history of head injuries.[16] In particular, subjects were asked if they ever had a head injury and, if so, they provided information on the number, year, severity, and other details of each injury. Subjects were also asked about their personal knowledge of the PCE leaching incident and their exposure status.

PCE Exposure Assessment

As explained in a prior report, "a tentative exposure status was assigned to each subject by visually inspecting maps of the pipe distribution network in the area surrounding the birth residence. To determine the final exposure designation, we used a more extensive exposure assessment model to estimate the mass of PCE delivered to each residence from the prenatal period through five years of age."[16]

"The leaching and transport model, which was developed by Webler and Brown for our prior epidemiological studies, estimates the quantity of PCE entering the drinking water using the initial amount of PCE in the liner (based on the pipe diameter and length), the age of the pipe, and the leaching rate of PCE from the liner into the water. Information on the locations, installation dates, and diameters of all VL/AC pipes in the public water supplies was provided by local water departments and the Massachusetts Department of Environmental Protection."[16]

"The transport algorithm requires an estimate of water flow rate and direction, which are functions of the configuration of the pipes and number of water users. The present study incorporated the Webler and Brown algorithm into the publically available source code of EPANET water distribution modeling software that characterizes water flow throughout a town's entire public distribution system. EPANET, which was developed by the US EPA for water monitoring programs, has been also applied in epidemiological studies by others to assess the health effects of drinking water contaminants."[16]

"In the first step of the exposure assessment process, we created geographic information system layers depicting the subject residences, water sources, pipe characteristics, and nodes, which represented points of water consumption along the pipe. Data on the location, installation date, and diameter of VL/AC pipes were obtained from local water companies and the Massachusetts Department of Environmental Protection. The GIS represented the pipe configuration in the period around 1980."[16]

"Next, we used EPANET to simulate the instantaneous flow of water through each town's network and to estimate the annual mass of PCE delivered to each point on the network or node and all subject residences associated with the node. We assumed that all land parcels represented water users, all water users in the network drew the same quantity of water, and water sources did not change over the study period. These assumptions are supported by observations that the study area was mainly composed of residences, and the distribution system changed little between the late 1960s and late 1980s, when some water sources were added to accommodate population growth."[16]

"Only annual PCE exposures were calculated because only move-in and pipe installation years were available. We estimated PCE exposure during the prenatal period by multiplying the annual mass of PCE that entered the subject's residence during their birth year by 9/12. We estimated cumulative exposure during early childhood by summing the estimated mass of PCE that entered their residences from the month and year following birth through the month and year of the fifth birthday. Simple proportions were used to account for partial years."[16]

"PCE exposure levels were estimated only for subjects who had complete geocoded residential histories from birth through age five. This excluded 81subjects because they had inadequate residential histories (Table 1). For practical reasons, another 96 subjects were excluded because at least one of their residences was in an off-Cape town with some VL/AC pipe and our extensive PCE exposure assessments were limited to Cape Cod. Subjects who reported living in a Cape Cod town without any VL/AC pipes ($n = 7$) were assumed to have no PCE exposure at that address because available records indicated little or no PCE contamination of these water sources."[16]

Statistical Analysis

We evaluated the frequency of unintentional head injuries between exposed and unexposed participants.[16] Any PCE exposure and PCE exposure tertiles were examined. Risk ratios (RRs) and 95% confidence intervals (CIs) evaluated the strength and precision

TABLE 2. Distribution of Selected Characteristics of Subjects and Parents by PCE Exposure Status

	Both Prenatal and Early Childhood Exposure ($N = 828$)		Unexposed ($N = 544$)	
Characteristic	***n***	**%**	***n***	**%**
Current age (*n*, mean, SD)	828	29.2 (3.6)	544	29.6 (3.8)
% Female	498	60.1	329	60.5
% White race	815	98.4	536	98.5
Current educational level				
High school graduate or less	126	15.2	67	12.3
Some college	192	23.2	143	26.3
Four-year college grad or higher	509	61.5	333	61.2
Missing	1	0.1	1	0.2
Currently employed				
Yes	716	86.5	484	89.0
No	91	11.1	54	9.9
Missing	20	2.4	6	1.1
Current marital status				
Single	271	32.7	156	28.7
Married or cohabitating	534	64.5	371	68.2
Other	20	2.4	13	2.4
Missing	3	0.4	4	0.7
History of vision problems				
Yes	496	59.9	361	66.4
No	332	40.1	183	33.6
History of ADD/ADHD				
Yes	59	7.1	42	7.7
No	764	92.3	497	91.4
Missing	5	0.6	5	0.9
Drank alcoholic beverages as teen				
Yes	624	75.4	400	73.5
No	192	23.2	135	24.8
Missing	12	1.4	9	1.7
Drank alcoholic beverages as adult				
Yes	668	80.7	434	79.8
No	148	17.9	107	19.7
Missing	12	1.4	3	0.6
Used marijuana as teen				
Yes	448	54.1	288	52.9
No	371	44.8	252	46.3
Missing	9	1.1	4	0.7
Used marijuana as adult				
Yes	510	61.6	317	58.3
No	305	36.8	224	41.2
Missing	13	1.6	3	0.6
Used major illicit drugs as teen				
Yes	223	26.9	118	21.7
No	598	72.2	419	77.0
Missing	7	0.8	7	1.3
Used major illicit drugs as adult				
Yes	288	34.8	160	29.4
No	529	63.9	379	69.7
Missing	11	1.3	5	0.9
Ever had job with solvent exposure				
Yes	123	14.9	71	13.1
No	685	82.7	458	84.2
Missing	20	2.4	15	2.8
Ever had hobby with solvent exposure				
Yes	699	84.4	459	84.4
No	123	14.9	79	14.5
Missing	6	0.7	6	1.1
Mother's age at subject's birth [*n*, mean (SD)]	828	27.2 (4.7)	459	27.5 (4.4)
Father's age at subject's birth [*n*, mean (SD)]	828	29.8 (5.7)	544	29.8 (5.3)
Mother's educational level at subject's birth				
High school graduate or less	325	39.3	178	32.7
Some college	242	29.2	188	34.6
Four year college grad or Higher	260	31.4	177	32.5
Missing	1	0.1	1	0.2
Father's occupation at subject's birth				
White collar	419	50.6	254	46.7

TABLE 2. (*Continued*)

Characteristic	Both Prenatal and Early Childhood Exposure ($N = 828$)		Unexposed ($N = 544$)	
	n	%	*n*	%
Blue collar	274	33.1	170	31.3
Other	125	15.1	112	20.6
Missing	10	1.2	8	1.5
Mother received prenatal care during subject's gestation				
Yes	792	95.7	517	95.0
No	4	0.5	0	0.0
Missing	32	3.9	27	5.0
Mother smoked cigarettes during subject's gestation				
Yes	182	22.0	113	20.8
No	481	58.1	327	60.1
Missing	165	19.9	104	19.1
Mother consumed alcohol during subject's gestation				
Yes	302	36.5	199	36.6
No	359	43.4	241	44.3
Missing	167	20.2	104	19.1
Number of older siblings				
0	348	42.0	259	47.6
1	287	34.7	163	30.0
2+	192	23.2	119	21.9
Missing	1	0.1	3	0.6
Mother had occupational exposure to solvents				
Yes	75	9.1	51	9.4
No	572	69.1	378	69.5
Missing	181	21.9	115	21.1
Mother separated, divorced, or widowed after child's birth				
Yes	51	6.2	32	5.9
No	777	93.8	512	94.1
Subject's birth weight (*n*, mean, SD)	820	3,444 (506)	497	3,413 (535)
Subject's gestational age (*n*, mean, SD)	788	40.1 (2.5)	513	39.9 (2.4)

ADD/ADHD indicates attention deficit disorder/attention deficit hyperactivity disorder.

of the relationship between early-life PCE exposure and subsequent head injuries. Generalized estimating equation (GEE) analyses accounted for the correlation of head injuries between siblings.[17,18]

Stratified analyses assessed whether the association between PCE exposure and head injuries was modified by substance use. In addition, adjusted analyses evaluated potential confounding by demographic characteristics, risk factors for head injuries, and other sources of solvent exposure. Potential confounders were controlled individually. Because none altered the crude RRs by at least 10%, unadjusted findings are reported.

RESULTS

Exposed and unexposed participants had similar social and demographic features (Table 2). There was no evidence of an increased risk among PCE-exposed participants for any type of unintentional head injury, including those requiring a doctor's visit, involving loss of consciousness or a concussion; or those stemming from a motor vehicle accident or recreational activity (Table 3). There was also no evidence that exposure was related to traumatic brain injuries, although the number of subjects with this history was quite small ($N = 4$ exposed and 6 unexposed subjects). We also did not find any evidence of a dose–response relationship with increasing PCE exposure or any evidence that substance use modified the association between early-life PCE exposure and head injuries (data not shown). The age at head injuries requiring a doctor's visit spanned from infancy to 37 years. The median age in each group was 15.0 years and about 41% sustained head injuries when they were 18 years or older. The crude associations were unchanged when numerous potentially confounding variables were controlled.

DISCUSSION

Unintentional head injuries, particularly those resulting in traumatic brain injury, are a significant public health problem[19,20] and so it is important to understand both their proximate and distant causes. Although PCE is a recognized neurotoxicant that impairs cognition, vision, attention, and motor skills among adults,[8–10] these findings suggest that early-life exposure to PCE-contaminated drinking water does not increase the incidence of unintentional head injuries later in life.

There are however several important limitations to this analysis. First was missing information on contextual factors that increase the likelihood of sustaining head injuries such as concurrent alcohol and illicit drug use and the failure to use seatbelts while riding in motor vehicles or helmets while engaging in sports.[21–23] The hypothesis that substance use could mediate the association between PCE exposure and head injuries is supported by analyses from the current cohort showing an increased risk of substance use among those with early-life PCE exposure[15] and a modest increase in the risk of head injuries (ie, RRs 1.2 to 1.4) among participants reporting a history of substance use, irrespective of their PCE exposure history. Thus, it will be important for future studies to collect detailed information on concomitant behaviors that may have contributed to the injury.

Another shortcoming of the present study was the use of self-reported information on head injuries with likely under-reporting of

TABLE 3. Prenatal and Early Childhood Exposure to Tetrachloroethylene and Risk of Head Injuries

Outcome	Exposure Category/ Percentile	% Yes (*n*/*N*)	Crude Risk Ratio (95% CI)	GEE Risk Ratio (95% CI)
Any head injury	Any	26.9 (223/828)	0.9 (0.8–1.1)	0.9 (0.8–1.1)
	≥67th	28.8 (79/274)	1.0 (0.8–1.3)	1.0 (0.8–1.3)
	33rd to <67th	26.8 (75/280)	0.9 (0.7–1.2)	0.9 (0.7–1.2)
	>0 to <33rd	25.2 (69/274)	0.9 (0.7–1.1)	0.9 (0.7–1.1)
	None	28.7 (156/544)	1.0 (—)	1.0 (—)
Head injury involving doctor or hospital visit	Any	23.8 (189/794)	0.9 (0.8–1.1)	0.9 (0.8–1.1)
	≥67th	26.1 (69/264)	1.0 (0.8–1.3)	1.0 (0.8–1.3)
	33rd to <67th	22.6 (60/265)	0.9 (0.7–1.1)	0.9 (0.7–1.1)
	>0 to <33rd	22.6 (60/265)	0.9 (0.7–1.1)	0.9 (0.7–1.1)
	None	26.1 (137/525)	1.0 (—)	1.0 (—)
Head injury involving loss of consciousness	Any	11.5 (79/684)	1.0 (0.7–1.3)	1.0 (0.7–1.4)
	≥67th	12.9 (29/224)	1.1 (0.7–1.6)	1.1 (0.7–1.7)
	33rd to <67th	11.6 (27/232)	1.0 (0.6–1.5)	1.0 (0.6–1.5)
	>0 to <33rd	10.1 (23/228)	0.8 (0.5,1.3)	0.8 (0.5–1.4)
	None	12.0 (53/441)	1.0 (—)	1.0 (—)
Head injury involving a concussion	Any	12.3 (85/690)	0.8 (0.6–1.1)	0.8 (0.6–1.2)
	≥67th	14.8 (34/229)	1.0 (0.7–1.5)	1.0 (0.7–1.5)
	33rd to <67th	10.5 (24/229)	0.7 (0.5–1.1)	0.7 (0.5–1.1)
	>0 to <33rd	11.6 (27/232)	0.8 (0.5–1.2)	0.8 (0.5–1.2)
	None	14.9 (68/456)	1.0 (—)	1.0 (—)
Head injury during motor vehicle accident	Any	3.4 (21/626)	0.7 (0.4–1.3)	0.7 (0.4–1.3)
	≥67th	4.4 (9/204)	0.9 (0.4–2.1)	0.9 (0.4–2.1)
	33rd to <67th	2.4 (5/210)	0.5 (0.2–1.3)	0.5 (0.2–1.3)
	>0 to <33rd	3.3 (7/212)	0.7 (0.3–1.7)	0.7 (0.3–1.7)
	None	4.7 (19/407)	1.0 (—)	1.0 (—)
Head injury during recreational activity	Any	4.3 (27/632)	0.9 (0.5–1.6)	0.9 (0.5–1.6)
	≥67th	3.9 (8/203)	0.8 (0.4–1.9)	0.8 (0.4–1.9)
	33rd to <67th	5.1 (11/216)	1.1 (0.5–2.3)	1.1 (0.5–2.3)
	>0 to <33rd	3.8 (8/213)	0.8 (0.4–1.8)	0.8 (0.4–1.8)
	None	4.7 (19/407)	1.0 (—)	1.0 (—)

95% CI, 95% confidence interval; GEE, generalized estimating equation.

minor injuries, especially those occurring at a young age. Nonetheless, it is unlikely that these inaccuracies were more common among exposed subjects because most had no knowledge of the PCE contamination episode[16] and so the resulting nondifferential misclassification should not have biased the RRs.[24]

Misclassification of PCE exposure was also probable because our modeled assessments required many assumptions about the water distribution system and could not integrate relevant behaviors (such as bathing practices) because of inadequate recall.[16] However, a prior validation study showed good concordance between modeled PCE assessments and actual levels in water samples taken in the 1980s,[25] suggesting that the degree of exposure misclassification was small.

Still another limitation was the relatively small sample size stemming from the low proportion of participants who completed the survey. Although this likely reduced the statistical power of the analysis, we do not believe that it resulted in selection bias, mainly because participants and nonparticipants had similar characteristics. Furthermore, the frequency of deaths among participants was relatively low and similar across compared groups (Table 1).[16] Deaths due to head injuries (mainly from motor vehicle accidents) affected only eight individuals.

We do not believe that any epidemiological study has previously investigated the occurrence of head injuries following early-life solvent exposure. Most studies have focused on other neurotoxic effects of solvent mixtures (including PCE) among adults with workplace exposures. Impairments in cognition, motor function, and vision, and mood changes have been observed in these investigations.[8–10,26–32] The small number of studies investigating workplace exposure to PCE alone present conflicting findings. A few studies have reported lower test scores for attention and executive function,[8] while others have reported no harmful neurological consequences, except for impaired visuospatial skills.[9,33]

Three small studies have previously investigated neurodevelopmental outcomes among young children whose mothers worked with solvent mixtures during their pregnancies. A 1988 study reported no meaningful effect cognition.[11] On the contrary, two subsequent studies reported more behavior problems and poorer language and motor skills among exposed children.[12,13] Findings from the latter studies are concordant with neuropsychological test results among members of the current cohort that found diminished visuospatial and motor function and attention among subjects with early-life exposure to PCE-contaminated drinking water.[14]

In summary, the findings from the current study do not support the hypothesis that there is an elevated risk of unintentional head injuries following early-life exposure to PCE-contaminated drinking water. However, numerous limitations should be taken into account when interpreting these findings. As PCE remains a widespread pollutant of surface and ground water supplies,[34] documenting the presence of any adverse health effects stemming from early-life exposure is vital for ensuring that U.S. drinking water regulations adequately protect vulnerable populations such as pregnant women and their children.

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