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. 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. 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. Although PCE pollution on Cape Cod was eventually resolved by installing bleeder valves, questions remain about the health effects due to past drinking water exposure to PCE and related solvents. 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. Epidemiologic research among adults with job-related exposures have found impairments in cognition, vision, attention, and motor skills. In contrast, studies of early-life exposure are quite limited. Our prior research found diminished visuospatial function, motor skills, and attention and an increase in risk-taking behavior among individuals exposed early in life. 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. 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.”

“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).”

“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.”

“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.”

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...
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. 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.”

“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 sources.”

“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.”

“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.”

“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.”

“PCE exposure levels were estimated only for subjects who had complete geocoded residential histories from birth through age five. This excluded 81 subjects 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.”

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

| Initial Exposure Status | Index Subject | Older Sibling |
|-------------------------|--------------|--------------|
|                         | Exposed      | Unexposed    | Total        |
| Selected                | 1,910        | 1,928        | 5,040        |
| Excluded during enrollment |            |              |              |
| Deceased                | 35           | 40           | 75           |
| Parent refused participation | 199        | 148          | 347          |
| Never located           | 113          | 149          | 262          |
| No response             | 871          | 887          | 1,758        |
| Refused                 | 73           | 78           | 151          |
| Returned questionnaire   | 619          | 626          | 1,245        |
| Percent of located      | 39.6%        | 39.3%        | 39.5%        |
| Excluded during exposure assessment |          |              |              |
| Inadequate residential history | 15        | 37           | 52           |
| Off-Cape address in town with VL/AC pipes | 19        | 27           | 46           |
| Available for analysis  | 585          | 562          | 1,147        |
| Final exposure status   |              |              |              |
| Both prenatal and early childhood exposure | 561      | 160          | 721          |
| Only early childhood exposure | 7       | 42           | 118          |
| Unexposed               | 17           | 360          | 377          |
| Total                   | 585          | 562          | 1,147        |

Statistical Analysis

We evaluated the frequency of unintentional head injuries between exposed and unexposed participants. 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

| Characteristic                                      | Both Prenatal and Early Childhood Exposure (N = 828) | Unexposed (N = 544) |
|-----------------------------------------------------|-----------------------------------------------------|---------------------|
| **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            |
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 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 exposure15 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 2. (Continued) | Both Prenatal and Early Childhood Exposure (N = 828) | Unexposed (N = 544) |
|-----------------------|----------------------------------------|---------------------|
| Characteristic        | 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.
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 and so the resulting nondifferential misclassification should not have biased the RRs.

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. However, a prior validation study showed good concordance between modeled PCE assessments and actual levels in water samples taken in the 1980s, 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). Deaths due to head injuries (mainly from motor vehicle accidents) although infrequent, still represent a significant portion of all deaths, especially for younger age groups. Nonetheless, it is unlikely that these inaccuracies were more common among exposed subjects because most had no knowledge of the PCE contamination episode and so the resulting nondifferential misclassification should not have biased the RRs.

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. On the contrary, two subsequent studies reported more behavior problems and poorer language and motor skills among exposed children. Findings from the latter studies are concordant with neuropsychological test results among members of the current cohort that found diminished visuospatial and motor function among exposed children.

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, 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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