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Exposure to tetrachloroethylene-contaminated drinking water and time to pregnancy

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ABSTRACT

Background: The synthetic solvent tetrachloroethylene (PCE), commonly used in dry cleaning operations, is a human neurotoxicant and carcinogen. However, its effect on reproduction is poorly understood, as prior studies have been limited to small occupational cohorts. We examined the association between PCE exposure from contamination of the public drinking water supply and time-to-pregnancy (TTP) in a cohort of mothers from Cape Cod, Massachusetts.

Methods: The Cape Cod Family Health Study is a retrospective cohort study designed to examine the reproductive and developmental health effects of exposure to PCE-contaminated drinking water. Our analysis included 1565 women who reported 3826 planned pregnancies from 1949 to 1990. Women completed self-administered questionnaires that ascertained TTP for each of her pregnancies, regardless of the outcome, as well as residential history and demographic information. We utilized EPANET water distribution system modeling software and a leaching and transport model to assess PCE exposure for each pregnancy. We used log-binomial regression models to estimate relative risks (RR) and 95% confidence intervals (CI), adjusting for potential confounders. We performed a probabilistic bias analysis to examine the effect of outcome misclassification on our results.

Results: Any cumulative PCE exposure before pregnancy was associated with a 15% reduction in risk of TTP > 12 months (RR = 0.85, 95% CI: 0.70, 1.03). However, women with the highest average monthly PCE exposure around the time of the pregnancy attempt (≥ 2.5 g) had increased risk of TTP > 12 months (RR = 1.36, 95% CI: 1.06, 1.76).

Conclusions: We found little evidence for long-term, cumulative adverse effects of PCE exposure on TTP, but high levels of PCE exposure around the time of the pregnancy attempt were associated with longer TTP. These associations may be underestimated due to the exclusion of unsuccessful pregnancy attempts from our study population, and may be biased by outcome and exposure misclassification given the long-term recall of TTP and use of a leaching and transport model to estimate PCE exposure.

1. Introduction

Tetrachloroethylene (perchloroethylene; PCE) is a synthetic, volatile organic solvent used in dry cleaning solutions, textile processing, and metal degreasing operations (Environmental Protection Agency, 2012). The primary routes of exposure in the general population are vapor inhalation from conventionally dry-cleaned fabrics and contaminated soil, and ingestion of contaminated water (Environmental Protection Agency, 2012; Sherlach et al., 2011). PCE distributes widely throughout the body, with the highest concentration in adipose tissue due to its lipophilic nature, and has a half-life of approximately 96 days (Environmental Protection Agency, 2012). PCE is a well-recognized animal and human neurotoxicant (Environmental Protection Agency, 2012) and carcinogen (Agency for Toxic Substances and Disease Registry, 1997; International Agency for Research on Cancer, 2014); however, its effects on reproduction are poorly understood. In rodent studies, PCE and the related solvent trichloroethylene (TCE) have adversely affected fertilization (Berger and Horner, 2003; Wu and Berger, 2007; Xu et al., 2004) and semen quality (Beliles et al., 1980). Epidemiologic studies conducted almost exclusively among dry cleaning

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workers have found evidence that dry cleaning work or suspected occupational PCE exposure is associated with increased risk of poor semen quality (Chia et al., 1996; Eskenazi et al., 1991b; Tielemans et al., 1999), infertility (Eskenazi et al., 1991a; Rachootin and Olsen, 1983), and longer time-to-pregnancy (TTP) (Sallmen et al., 1998, 1995).

From 1968 through 1980, public water departments throughout the New England region of the United States installed vinyl-lined asbestos-cement (VL/AC) water pipes on an as-needed basis to solve taste and odor problems. The liner was painted onto the inner surface of the pipes in a slurry of vinyl toluene resin (Piccotex™) and PCE. The manufacturer recommended that 48 h lapse to allow the liner to dry before shipping the pipes for distribution; it was assumed that most of the PCE would evaporate by the time of shipment (Demond, 1982). However, in 1980, government officials discovered that high levels of PCE persisted in the liner and had been slowly leaking into the public drinking water supply for over a decade. Approximately 660 miles of VL/AC pipes were installed in Massachusetts, with a large proportion in the Cape Cod region (Larson et al., 1983). PCE levels on Cape Cod ranged from 1,600-7750 μg/L in low-flow areas and 1.5–80 μg/L in medium- and high-flow areas (Demond, 1982). Current United States Environmental Protection Agency (US EPA) drinking water regulations set the maximum PCE contaminant level at 5 μg/L (U.S. Environmental Protection Agency, 2009). Because replacing the VL/AC pipes was prohibitively expensive, officials began a program of regular flushing and bleeding in 1980 to remediate the problem. This exposure scenario constitutes a type of natural experiment because the irregular installation pattern of VL/AC pipes resulted in neighboring households with vastly different contaminant levels (Aschengrau et al., 2016). PCE exposure levels were, in some instances, substantially higher than those typically seen in non-occupational populations. Levels of other drinking water contaminants were low (Swartz et al., 2003).

In the present analysis, we examined the association between PCE exposure through contaminated drinking water and TTP in a cohort of women from Cape Cod who had successfully conceived.

2. Materials and methods

2.1. Study design and selection of study population

The Cape Cod Family Health Study is a retrospective cohort designed to examine the association between exposure to PCE-contaminated drinking water and reproductive and developmental health. Study methods have been described in detail elsewhere (Aschengrau et al., 2008). Briefly, in 2002, we identified women who gave birth from 1969 to 1983 while residing in a Cape Cod town with documented VL/AC distribution pipes. We visually inspected water pipe distribution maps in the vicinity of the maternal address at birth to identify exposed and unexposed births. We classified 1492 women as exposed because they either lived adjacent to a VL/AC pipe or the only possible water flow to the residence was through a VL/AC pipe. We selected a comparison group of 1704 unexposed women so that their offspring were frequency-matched to those of the exposed women based on the birth month and year. Initial exposure status was considered preliminary; we later conducted a more detailed exposure assessment, described below (see “PCE exposure assessment”).

We successfully traced 91.2% of exposed and 92.0% of unexposed women. We mailed introductory letters and self-administered questionnaires to all traced participants from 2002 to 2003. Self-administered questionnaires collected information on demographic characteristics, residential history, water consumption and bathing habits, medical history, and reproductive history, including detailed information about each of their pregnancies (live births, still births, miscarriages, induced abortions, and ectopic pregnancies).

Women initially classified as exposed and unexposed had similar response rates (64.3% and 63.8%). Non-participants were younger (mean age 26.0 vs. 27.5 years) and less educated (11.3% vs. 3.6% did not graduate from high school), but were similar with respect to race (96.2% white in both groups) and year of pregnancy (54.7% vs. 56.0% births between 1979 and 1983); these differences were observed for both exposed and unexposed women (Aschengrau et al., 2008, 2009a).

All participants provided informed consent. The institutional review boards of Boston University Medical Center and the Massachusetts Department of Public Health approved the study protocol.

2.2. Geocoding of residential addresses

On self-administered questionnaires, women reported detailed information on each of their Cape Cod residences from 1969 through 1990, including exact street address, nearest cross street, calendar years of occupancy, and drinking water source. Throughout the study period, 29.5% of women did not move, whereas 31.7% of women moved once and 38.8% of women moved more than once. The 5324 reported addresses were incorporated into a geographic information system (GIS) using ArcGIS 8.1. Geocoding to a latitude and longitude was conducted without knowledge of exposure or pregnancy history. The majority of addresses were successfully geocoded to a parcel of land (87.6%) or the nearest reported cross street or the middle of the street in instances where street number was missing (9.6%). We were unable to geocode the remaining 2.7% of addresses, and pregnancies associated with these addresses were excluded from the analysis.

2.3. PCE exposure assessment

We refined our PCE exposure assessment using a leaching and transport model developed by Webler and Brown for our prior epidemiologic studies (Aschengrau et al., 2003; Webler and Brown, 1993). This model estimates the amount of PCE entering the drinking water using the initial PCE loading in the pipe liner (estimated using the pipe dimensions), the age of the pipe, and the leaching rate of PCE from the pipe into the water (Demond, 1982). We incorporated the Webler and Brown algorithm into EPANET water distribution system modeling software to account for water flow and direction, which are functions of the water system geometry and the number of water users. This software was developed by the US EPA and simulates the instantaneous flow of water throughout the entire public water distribution system in a town (Rossman, 1994). It has been used to assess exposure to drinking water contaminants in several epidemiologic studies (Aral et al., 1996; Gallagher et al., 1998; Maslia et al., 1996; Reif et al., 2003).

We created a GIS schematic, which represented the pipe configuration present around 1980, a year that is likely to be representative of the water distribution system during the study period. We included water source locations, nodes (points of water consumption), and pipe characteristics obtained from local water companies and the Massachusetts Department of Environmental Protection. EPANET software was used to model the flow of water through thousands of pipe segments in order to estimate the quantity, or mass, of PCE delivered to each participant's residence. We assigned each geocoded residence to the closest node on the water distribution system. We assumed that each residence drew the same quantity of water and that the water sources did not change over the study period. We calculated annual PCE exposure for each woman for every year from 1949 through 1990. Annual exposure was zero before 1969 and during years when women lived in residences with private wells or in a town without documented VL/AC pipes.

2.4. Assessment of time to pregnancy

On self-administered questionnaires, women reported how long it took for them to conceive each of their planned pregnancies. Response choices were < 3 months, 3–6 months, 7–12 months, or > 12 months.