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Residential proximity to industrial facilities and risk of non-Hodgkin lymphoma ☆

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ABSTRACT

Industrial pollution has been suspected as a cause of non-Hodgkin lymphoma (NHL), based on associations with chemical exposures in occupational studies. We conducted a case-control study of NHL in four SEER regions of the United States, in which residential locations of 864 cases and 684 controls during the 10 years before recruitment were used to characterize proximity to industrial facilities reporting chemical releases to the Environmental Protection Agency's Toxics Release Inventory (TRI). For each of 15 types of industry (by 2-digit SIC code), we evaluated the risk of NHL associated with having lived within 2 miles of a facility, the distance to the nearest facility (miles categories of ≤ 0.5, >0.5–1.0, >1.0–2.0, >2 [referent]), and the duration of residence within 2 miles (years categories of 10, 1–9, 0 [referent]), using logistic regression. Increased risk of NHL was observed in relation to lumber and wood products facilities (SIC 24) for the shortest distance of residential proximity (≤ 0.5 mile: odds ratio [OR]=2.2, 95% confidence interval [CI]: 0.4–11.8) or the longest duration (10 years: OR=1.9, 95% CI: 0.8–4.8); the association with lumber facilities was more apparent for diffuse large B-cell lymphoma (lived within 2 miles: OR=1.7, 95% CI: 1.0–3.0) than for follicular lymphoma (OR=1.1, 95% CI: 0.5–2.2). We also observed elevated ORs for the chemical (SIC 28, 10 years: OR=1.5, 95% CI: 1.1–2.0), petroleum (SIC 29, 10 years: OR=1.9, 95% CI: 1.0–3.6), rubber/miscellaneous plastics products (SIC 30, ≤ 0.5 mile: OR=2.7, 95% CI: 1.0–7.4), and primary metal (SIC 33, lived within 2 miles: OR=1.3, 95% CI: 1.0–1.6) industries; however, patterns of risk were inconsistent between distance and duration metrics. This study does not provide strong evidence that living near manufacturing industries increases NHL risk. However, future studies designed to include greater numbers of persons living near specific types of industries, along with fate-transport modeling of chemical releases, would be informative.

1. Introduction

Industrial pollution has been suspected as a cause of non-Hodgkin lymphoma (NHL), based in part on findings from occupational studies in which chemical exposures were related to increased risk of NHL (Hartge et al., 2006), and because NHL rates increased dramatically during the latter half of the 20th century (Clarke and Glaser, 2002), lagging slightly behind expanded industrial production in the United States (US; Alexander, 1952).

Several previous studies have investigated the risk of NHL associated with living near industrial facilities. Self-reported residence within 0.5 mile of any type of industrial facility was

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associated with increased risk of NHL (OR=1.5, 95% CI: 1.1–1.9) in a case-control study conducted in Iowa and Minnesota by Linos et al. (1991). Specific types of industry associated with increased NHL risk (OR > 1.5) for residence within 2 miles were paper (OR=1.5, 95% CI: 0.9–2.4), petroleum (OR=1.5, 95% CI: 0.7–3.2), and stone, clay, and glass industries (OR=1.6, 95% CI: 1.0–2.7). Johnson et al. (2003) conducted a case-control study in Canada in which residential proximity to industry was determined through linkage of residential postal codes to public data on the location of facilities from 1960 to the early 1990s. Increased risk associated with residential proximity to industry was most apparent for follicular lymphoma among women (OR=1.5, 95% CI: 1.1–2.0), and for residence within 0.5 mile of copper smelters (OR=10.8, 95% CI: 1.2–97.5) and sulfite pulp mills (OR=3.7, 95% CI: 1.5–9.4). In a recent study based on Spanish mortality records, in which residential proximity to industry was based on a linkage of industry locations to the centroid of the deceased's municipality of residence, only the paper/pulp industry was associated with increased risk of NHL mortality (RR=1.2, 95% CI: 1.1–1.4; Ramis et al., 2009).

Results from the previous studies, while intriguing, may suffer from recall bias due to self-reported residential proximity to facilities (Linos et al., 1991), or may be affected by non-differential exposure misclassification due to proximity assignment based on residential location as the centroid of a postal code (Johnson et al., 2003) or municipality (Ramis et al., 2009). Our aim was to further investigate whether there is any increase in NHL incidence associated with living near industrial facilities with reported releases of chemicals to the environment. To this end, we conducted a case-control study of the risk of NHL associated with residential proximity to industry in the decade before diagnosis. In our study, we used a more objective source of industry location than that based on recall, and we identified residential location to the street segment or nearest intersection. Industries of *a priori* interest were those with elevated risk estimates in the previous studies, in addition to industries emitting agents that are known or suspected to cause lymphohematopoietic cancers, such as petroleum processing for potential releases of benzene and other solvents, and pulp and paper mills for dioxins releases. Most of the suspicion surrounding these agents derives from studies of exposures in occupation, and the question remains whether environmental exposures, either in the ambient environment or from point sources, cause NHL.

2. Materials–methods

2.1. Study population

The study included participants in a case-control study of NHL, conducted by the National Cancer Institute (NCI) through collaborating centers (Chatterjee et al., 2004). Between July 1998 and June 2000, participants were enrolled from four US Surveillance, Epidemiology, and End Results (SEER) registry areas: the state of Iowa, Los Angeles County, and the metropolitan areas of Detroit, MI and Seattle, WA. The four study sites were chosen to meet the broad aim of the parent study to investigate potential environmental causes of NHL.

Cases included 1321 patients with newly diagnosed NHL of ages 20–74 who did not report HIV infection. Data on case histology were obtained from each local SEER registry and were based on abstracted reports of the diagnosing pathologist. Population controls (n=1057) were identified by random digit dialing (under age 65) and from Medicare eligibility files (65 years and older) and were frequency matched to cases by age, sex, and race. Overall response percentages were 59% and 44% for cases and controls, respectively. Among eligible participants we attempted to contact, 76% of cases and 52% of controls participated in the study. Written informed consent was obtained from each participant prior to interview. A computer-assisted personal interview was administered that contained questions about demographic characteristics, hair coloring, occupational history, pesticide use history, and other exposures. Human subjects review boards approved the study at the NCI and at all participating institutions.

2.2. Residential locations

Global positioning system (GPS) readings were taken outside the current residence for nearly all participants (99%). Interviewers took the measurements 6.1 m (20 ft) away from the home using a 12-channel handheld Garmin GPS12 Personal Navigator (Garmin International, Inc., Olathe, KS). Because approximately 72% of GPS coordinates were collected before the end of selective availability (deliberate corruption of GPS satellite signals by the US Department of Defense resulting in errors of 100 meters or more) on May 1, 2000 (Office of Science and Technology Policy, 2000), GPS coordinates that were discrepant from the geocoded interview address by more than 200 m were corrected using a combination of digital orthophotography, Census Bureau street files, road maps, and driving to the residential location to collect new GPS coordinates (Seattle, Los Angeles, parts of Iowa).

Historic addresses were sought in a residential history section of an interviewer-administered questionnaire. Participants were sent a residential calendar in advance of the interview and were asked to provide the complete address of every home they lived in from birth to the current year, indicating the years they moved in and out. They were also asked to provide information about temporary or summer homes where they lived for a total of 2 years or longer.

Residential street addresses were geocoded using the TeleAtlas' (Lebanon, NH) MatchMaker SDK Professional version 4.3 (October 2002) spatial database of roads and a modified version of a Microsoft Visual Basic version 6.0 program issued by TeleAtlas to match input addresses to the spatial database using an offset of 25 ft from the street centerline. Addresses that were not successfully geocoded were checked for errors using interactive geocoding techniques. Where only a street intersection was available for the residential location (1.3% of residences), we assigned the geographic location of the residence to the middle of the intersection.

2.3. Industrial facility locations

Locations of industrial facilities were obtained from the Risk Screening Environmental Indicators (RSEI) model, version 2.1.2 (USEPA, 2008a). RSEI contains data from the EPA Toxics Release Inventory (TRI; USEPA, 2008b), a program to provide the public with information on releases of toxic chemicals in their communities. TRI reporting requirements began in 1987 and apply to the manufacturing sector (Division D of the Standardized Industrial Classification [SIC] codes: SICs 20–39; OSHA, 2008), plus seven sectors that were not included in our study. Facilities are required to report if they have ten or more full-time employees and either (1) manufacture or process over 25,000 lb of listed TRI chemicals or (2) use more than 10,000 lb of any listed chemical. Facilities report the amount of each type of chemical released or moved off site and information about the facility, including location (latitude and longitude). The RSEI database contains the set of latitude/longitude coordinates deemed to be the 'best'—chosen through a series of tests and checks comparing the facility-reported coordinates, geocoded addresses, results of a major 1996 EPA quality assurance effort, and the EPA's Locational Reference Tables (LRT; USEPA, 2004). RSEI also performs analyses in order to designate a single 'primary' SIC code for each facility (the company's main line of business), where it was not reported as such in the facility's TRI submission.

We included all manufacturing sector facilities (SIC 20–38; we excluded SIC 39—miscellaneous manufacturing industries) reporting on-site chemical releases; off-site facilities that only received chemical transfers were excluded. Each facility was mapped in ArcGIS using the latitude–longitude coordinates provided in RSEI.

2.4. Exposure coding

We constructed metrics for residential proximity to industrial facilities anywhere in the US during a 10-year period prior to each participant's reference year (the diagnosis year for cases or the corresponding reference year for controls). We classified manufacturing facilities according to the primary 2-digit SIC codes (OSHA, 2008). We defined 'proximity' as distance within 2 miles, in order to allow comparison with results from previous studies (Johnson et al., 2003; Linos et al., 1991). Annual exposure status of each participant was determined by measuring the distance between the residence and the nearest facility within a given SIC; the participant was coded as unexposed to that SIC in that year if no facility was present within a 2 mile radius. If a participant lived in more than one residence during the year, the minimum distance to a given SIC was calculated as an average of the distances to the nearest facility from each residence, weighted by the proportion of the year spent at each residence.

Several proximity variables were considered in relation to NHL risk. An indicator variable was created for ever residing within 2 miles of each SIC during the 10-year study period. Indicator variables for ever residing within certain distance increments from each SIC were created, for > 0–0.5, > 0.5–1.0, > 1.0–2.0, and > 2.0 miles (with distances chosen to allow comparison to the previous studies (Johnson et al., 2003; Linos et al., 1991); each person was counted only in the category of the shortest distance they had lived from the SIC. Variables were also created to indicate years of residence within 2 miles of each SIC (0, 1–9, and