Environmental Research 159 (2017) 444–451

Contents lists available at ScienceDirect

Environmental Research

journal homepage: www.elsevier.com/locate/envres

Livestock and poultry density and childhood cancer incidence in nine states in the USA

Benjamin J. Booth[a,b], Rena R. Jones[a], Mary E. Turyk[b], Sally Freels[b], Deven M. Patel[a], Leslie T. Stayner[b,1], Mary H. Ward[a,*,1]

[a] Occupational and Environmental Epidemiology Branch, Division of Cancer Epidemiology and Genetics, National Cancer Institute, National Institutes of Health, 9609 Medical Center Dr., Room 6E138, Rockville, MD 20850, USA

[b] Division of Epidemiology and Biostatistics, School of Public Health, University of Illinois at Chicago, Chicago, IL, USA

ARTICLE INFO

Keywords:
Childhood cancer
Livestock
Poultry
Farm animals
Agricultural exposures
Environmental epidemiology

ABSTRACT

Background: Parental occupational and childhood exposures to farm animals have been positively associated with childhood brain tumors, whereas associations with childhood leukemia are equivocal. The developing immune system may be influenced by allergen, virus, or other exposures from animal sources, which may contribute to childhood cancer incidence.

Methods: Incident cancers (acute lymphoblastic leukemia [ALL], acute myeloid leukemia [AML], central nervous system [CNS], peripheral nervous system [PNS]) for children aged 0–4 diagnosed between 2003 and 2008 were obtained from nine National Cancer Institute Surveillance, Epidemiology and End Results (SEER) registries and were linked to U.S. Census of Agriculture data from 2002 and 2007 by county of diagnosis. Animal densities (animal units [AU]/km^2; one animal unit is 1000 pounds of animal weight) were estimated for hogs, cattle, chickens (layers and broilers, separately), equine (horses, ponies, mules, burros, donkeys), goats, sheep, turkeys, and total animals. Animal density was examined in models as both continuous (AU per km^2) and categorical variables (quartiles). Animal operation densities (per km^2) by size of operation (cattle, hogs, chickens, sheep) were modeled continuously. Rate ratios and 95% confidence intervals were estimated using Poisson regression.

Results: We found positive associations between AML and broiler chicken densities ($RR_{per\ 10\ AU/km^2}$ = 1.14, 95% CI = 1.02–1.26). ALL rates increased with densities of hog operations (RRper operation/100 km^2 = 1.06, 95% CI = 1.02–1.11). PNS cancer rates were inversely associated with layer chicken density ($RR_{per\ log\ of\ AU/km^2}$ = 0.94, 95% CI = 0.89–0.99). No association was found between any cancer type and densities of cattle, equine, or goats.

Conclusions: Although limited by the ecologic study design, some of our findings are novel and should be examined in epidemiological studies with individual level data.

1. Introduction

Epidemiologic studies of childhood cancer provide some evidence that living on a farm or in agricultural areas is associated with an increased risk of childhood cancer. In Korea, residence in counties with high agricultural intensity was positively associated with increased childhood leukemia mortality rates (Cha et al., 2014). In the United States, the percentage of the county land use in agricultural crops was positively associated with incidence of childhood leukemia, central nervous system (CNS) cancers, and peripheral nervous system (PNS) cancers (Carozza et al., 2008). A case-control study using data pooled from seven countries across three continents (Australia, North America, and Europe) reported that living on a farm during the first six months of life increased the odds of developing childhood brain tumors (CBT) (Efird et al., 2003). Furthermore, two case-control studies found positive associations between living on a farm during childhood, contact with farm animals, and CBT (Efird et al., 2003; Gold et al., 1979).

Hypothesized mechanisms for animal exposures and childhood cancer include exposures to viruses and immune response linked to allergies. Animal viruses, such as avian sarcoma virus, oncornaviruses, papovaviruses, and adenoviruses can cause brain tumors in animals (Copeland et al., 1975; Swenberg, 1977) and positive associations between *Toxoplasma gondii* and CNS tumors have been reported in case-control studies of human adults (Ryan et al., 1993; Schuman et al.,

* Corresponding author.
E-mail address: wardm@mail.nih.gov (M.H. Ward).
[1] Co-senior authors.

http://dx.doi.org/10.1016/j.envres.2017.08.023
Received 9 December 2016; Received in revised form 15 July 2017; Accepted 11 August 2017
Available online 18 September 2017
0013-9351/ Published by Elsevier Inc.

1967). Allergy rates are lower among children with early life exposure to animals (Campo et al., 2006; Ownby et al., 2002) and who live on farms (Riedler et al., 2001; Stein et al., 2016). Lower prevalence of allergic disease among children living on farms or in agricultural areas may be a mechanism for increased risk of CBT and childhood leukemia, because allergy and atopic disease are associated with decreased risk of these cancers (Harding et al., 2008; Roncarolo and Infante-Rivard, 2012; Linabery et al., 2010; Nanni et al., 1996; Schuz et al., 2003; t' Mannetje et al., 2012).

Previous research on animal exposure and childhood cancer has largely employed case-control studies, although registry-based cohorts have also been used to examine associations with parental occupational exposure to animals. Many of these studies did not evaluate relationships separately for specific animal types, which is important because exposures to chemical and biological agents may vary by animal species and animal management practices (Spellman and Whiting, 2007). Most studies of childhood leukemia found no associations with parental or childhood exposure to animals (Keegan et al., 2012; Kristensen et al., 1996; McKinney et al., 2003; Meinert et al., 1996; Rudant et al., 2010; van Steensel-Moll et al., 1985); whereas most studies of CBTs found positive associations with parental or childhood exposure to animals (Christensen et al., 2012; Efird et al., 2003; Holly et al., 1998; Keegan et al., 2013; Kristensen et al., 1996).

Ecologic studies in the United States have evaluated relationships between county-level incidence rates of childhood cancers and the density of specific crop types as a proxy for potential agricultural pesticide exposure (Booth et al., 2015; Carozza et al., 2008). However, densities of animals and animal operations have not previously been studied in relation to childhood cancer. We used county-level data on densities of animals and animal operations to assess relationships with incidence rates of total childhood leukemia, acute lymphoblastic leukemia (ALL), acute myeloid leukemia (AML), CNS cancers, and PNS cancers among children less than five years old, accounting for crop density. Several of the animal types that we examined in our study had not been previously evaluated in relation to childhood cancer.

2. Methods

2.1. Cancer incidence and population data

We obtained cancer incidence data by gender and race (white, black, and other) at the county level for children under the age of five from the Surveillance, Epidemiology, and End Results (SEER) program using SEER*Stat software version 8.1.5 (SEER, 2014). We included nine states with complete case ascertainment from 2003 through 2008 (California, Connecticut, Georgia, Iowa, Kentucky, Louisiana, New Jersey, New Mexico, and Utah). Site codes from the International Classification of Childhood Cancer, third edition (ICCC-3) were used to categorize childhood cancers into total leukemias (ICCC-3 code: 011–015), ALL (011), AML (012), CNS and miscellaneous neoplasms (031 – 036), and neuroblastomas and other PNS cancers (041–042) (Steliarova-Foucher et al., 2005). Inter-censal estimates of county populations by age, race, and sex were obtained from the U.S. Census Bureau and were used as denominators for estimating cancer incidence rates (U.S. Census Bureau, 2010). County-level incidence rates were computed based on residence at the time of cancer diagnosis and county-level population data. Counties with populations greater than 300,000 (N = 48 counties) had few animal operations. We excluded these counties due to their low animal counts and concerns about residual confounding due to urban factors that may be associated with childhood cancer incidence (e.g., specific air pollutants) and that may vary across the study states. After exclusions, data from 541 counties were included in the analysis.

2.2. Animal and operation densities

County-level data on animal inventories and number of animal operations were obtained from the 2002 and 2007 U.S. Department of Agriculture (USDA) National Agricultural Statistics Service (NASS) Census of Agriculture (USDA, 2002, 2007). Inclusion in the Census of Agriculture required that a farm or operation sell or produce at least $1000 in agricultural products. To characterize the time period preceding or overlapping case diagnosis (2003–2008) we averaged the data from the 2002 and 2007 censuses. Counts of animals and operations were available for total cattle (including calves), hogs, chickens (broilers and layers, separately), sheep, goats, turkeys, and equine (horses and ponies; mules, burros, and donkeys). Additionally, the number of operations by size (number of animals per operation) was available for cattle (<500, ≥ 500), layer chickens (1–399, 400-99,999, $\geq 100{,}000$), hogs (<1000, ≥ 1000), and sheep (1–99, 100–999, ≥ 1000). To avoid potential identification of individual operations, the USDA suppressed the number of animals in a county when there were fewer than three operations in a county or when there was an operation that was very large in size compared to other operations in a county (USDA, 2002). However, data were suppressed only for the number of animals, not the number of animal operations.

For counties with missing animal numbers, we imputed five complete datasets for each state in each census period using truncated linear regression. For cattle, hogs, sheep, and layer chickens we used the information on the number of operations by size to impute missing counts within the operation size range. For the other animal types, we used the total number of animal operations of that type to impute suppressed animal counts. We excluded all counties in Iowa, New Jersey, and Utah from our analysis of turkey density because over 45% of the counties had missing data in 2002, 2007, or both years. Further, we did not include turkeys in our calculation of total animal density.

We converted animal counts to animal units (AUs) using the EPA definition, which defines one AU as 1000 pounds based on the average animal weights (Environmental Protection Agency (EPA), 2001). One AU equals one cow, 2.5 hogs, 100 chickens (broilers or layers), 0.5 horses, 10 sheep, 10 goats, one mule, and 55 turkeys. Total land area in km^2 for each county was obtained from the U.S. Census Bureau, 2013 Tiger/LineFile (U.S. Census Bureau, 2013). We computed densities of each animal type and animal operation by dividing the average of the 2002 and 2007 AUs and number of operations by the land area of each county (AU/km^2 and $operation/km^2$, respectively).

2.3. Covariate data

We evaluated factors that have been associated with incidence of one or more childhood cancers and were available for our study counties including population density, urbanicity, population mobility, socioeconomic status, and agricultural crop density. County-level estimates of median household income, educational attainment (percent with at least a bachelor's degree), percent of population with a change of residence within the last five years (from within county, within state, within country, or another country), and percent of residents employed in agriculture (farming, fishing, and forestry) were obtained from the 2005–2009 American Community Survey (U.S. Census Bureau, 2009). Population density was computed by dividing the total population in each county by the total land area. Urbanicity of a county was characterized using the 2003 rural-urban continuum codes created by the USDA (USDA, 2003). The rural-urban continuum categorizes counties into nine levels based on population size, metropolitan designation, and adjacency to metropolitan areas. We also evaluated the proportion of workers in non-metropolitan counties that commute to adjacent metropolitan areas (USDA, 2003).

Data on total harvested acres of cropland by type of crop for each county were obtained from the 2002 and 2007 USDA NASS Census of Agriculture (USDA, 2002, 2007). Estimates of crop acreage were