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Poultry and Livestock Exposure and Cancer Risk among Farmers in the Agricultural Health Study

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Abstract

Purpose—The purpose of this study is to evaluate cancer risk associated with raising animals as commodities, which is associated with a variety of exposures, such as infectious agents and endotoxins.

Methods—Information was available for 49,884 male farmers in the Agricultural Health Study, who reported livestock and poultry production at enrollment (1993–1997). Cancer incidence data were obtained through annual linkage to state registries. Using Poisson regression analyses, we evaluated whether the number and type of animals raised on the farm impacted cancer risk.

Results—Overall, 31,848 (63.8%) male farmers reported raising any animals. Lung cancer risk decreased with increasing number of livestock on the farm (p-trend=0.04) and with raising poultry (Relative Risk (RR)= 0.6; 95% Confidence Interval (CI): 0.4–0.97). Raising poultry was associated with an increased risk of colon cancer (RR=1.4; 95% CI: 0.99–2.0) with further increased with larger flocks (p-trend=0.02). Risk of non-Hodgkin lymphoma was also elevated in those who raised poultry (RR=1.6; 95% CI: 1.0–2.4), but there was no evidence of increased risk with larger flocks (p-trend=0.5). Raising sheep was associated with a significantly increased risk of multiple myeloma (RR=4.9; 95% CI: 2.4–12.0). Performing veterinary services increased the risk of Hodgkin lymphoma (RR=12.2; 95% CI: 1.6–96.3).

Conclusions—We observed an inverse association between raising poultry and livestock and lung cancer risk and some evidence of increased risk of specific lymphohematopoietic malignancies with specific types of animals and performing veterinary services. Further research into associations between raising animals and cancer risk should focus on identification of etiologic agents.

Keywords

livestock; poultry; cancer; cohort study; agriculture

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Introduction

Animals raised on farms typically fall into two broad categories: poultry, which includes chickens and other birds raised for consumption and for egg production, and livestock, which includes large mammals, such as cattle (beef and dairy), hogs and sheep. Farmers who raise animals have exposures such as endotoxins, viruses, and pesticides that may influence their risk of cancer. Previous studies of individuals occupationally exposed to animals have suggested an increased risk of certain lymphohematopoietic malignancies, which may be related to their exposure to a variety of infectious agents [1]. Farmers, particularly those who raise animals, have been observed to have lower risk of lung cancer [2–3]. Although farmers smoke less than the general population, this does not appear to fully explain the lung cancer deficit. Exposure to endotoxins, which are lipopolysaccharides found in Gram-negative bacterial cell walls, is common in agricultural settings, and may be higher among those who have direct contact with animals or who handle hays and grains, which can be used as feed for animals. [4–6] Endotoxin exposure has been shown to be associated with a decreased risk of lung cancer [7], with inconsistent reports on cancer at other sites. However, cancer risks associated with specific types of farm animals or specific etiologic agents have not been clearly described. The purpose of this study is to evaluate cancer risk at a variety of sites in relation to raising livestock and poultry in a large cohort of occupationally exposed farmers.

Methods

Cohort Description

The Agricultural Health Study (AHS) is a prospective cohort that includes 57,310 licensed pesticide applicators in Iowa and North Carolina. Applicators were recruited and enrolled into the study during 1993 to 1997 when they obtained or renewed their licenses to apply restricted use pesticides. In North Carolina, only private applicators, who are primarily farmers, were recruited, while in Iowa, both private and commercial applicators (n=4,916) were included. Because the focus of this investigation was related to raising animals on the farm, we restricted these analyses to private applicators (farmers). Incident cancers were ascertained through annual linkage to state cancer registries in Iowa and North Carolina and first primary cancers diagnosed from enrollment through December 31, 2007 were included in this analysis. Annually, cohort members were matched to the National Death Index to identify vital status and to current address records of the Internal Revenue Service, motor vehicle registration offices, and pesticide license registries of state agricultural departments to determine whether they continued to reside in Iowa or North Carolina. Person-time was censored at the time of cancer incidence, death, movement out of the state or December 31, 2007, whichever was earlier. The study protocol was approved by the institutional review boards of the National Institutes of Health, the University of Iowa and other contractors.

Exposure assessment

Information about farming activities, including current raising of poultry and livestock, was collected through the completion of a self-administered questionnaire, available at http://aghealth.nci.nih.gov/questionnaires.html. Participants were asked about what major income-producing animals were currently raised on their farms (beef and dairy cattle, hogs, sheep, poultry or eggs) in the last year. They were also asked separately about the number of animals on their farm in the last year. Specifically, farmers were asked about the number of poultry and the number of all non-poultry livestock on their farms. For the purposes of this analysis, we considered anyone who reported raising poultry or eggs for income as having poultry. They were also queried about activities related to raising animals, such as performing veterinary services, butchering, grinding feed and milking cows, as well as

whether or not they worked in swine or poultry confinement areas. Participants also reported on other potential risk factors such as smoking, alcohol consumption, cancer history of first-degree relatives, diet, selected medical conditions, and demographic information.

There are relatively few females with a pesticide license in the AHS cohort (n=1,340) and only 522 who reported raising livestock or poultry on the farm. Of these, a much smaller percentage reported performing tasks related to raising animals than did their male counterparts. For these reasons, we restricted our analysis to male private applicators (n=51,036). Of these, we excluded 1,026 with a cancer diagnosis prior to enrollment and 126 who had missing or zero person-years leaving 49,884 applicators available for analysis. Relative risks (RR) and 95% confidence intervals (CI) were calculated by Poisson regression using SAS v9.1 (Cary, NC). Models were adjusted for age at enrollment (<50, 50–59, 60–69, 70+), smoking history (never, ≤12 pack-years, >12 pack-years), and state of residence (Iowa or North Carolina). We also controlled for pesticides associated with specific cancer types within the AHS. All tests were two-sided and conducted at the 0.05 alpha level. Tests for trend used the midpoint value of each exposure category treated as a continuous variable in Poisson regression models. In primary analyses, we used those who did not report exposure to each animal being studied, including those who reported raising no livestock, as the referent group. However, we also conducted analyses using farmers who did not report raising any animals in the past year as the referent group. We report results for exposures and cancer sites for which there were at least 5 exposed cases.

Results

Overall, 31,848 (63.8%) male farmers reported raising animals of any kind (Table 1). Most farmers raised more than one kind of animal. A total of 3,130 (10.8%) raised poultry, and of these only 783 (25.0%) raised poultry exclusively. Among livestock farmers who were currently raising animals, the most frequent type was beef cattle (n=18,663, 64.3%), followed by hogs (n=16,597, 57.2%). Of the 6,175 farmers who raised more than 1,000 livestock in the last year, 5,730 of them raised hogs (92.7%) and 2,890 raised cattle (46.8%). Farmers who raised animals were less likely to have ever smoked (57% never smokers) than their counterparts who did not raise animals (40% never smokers); thus all risk estimates are adjusted for smoking. Raising poultry was associated with a decreased risk of lung cancer (RR=0.6, 95% CI: 0.4–0.97) (Table 2). There was no evidence of further decreased risk with increasing numbers of poultry, although due to a small number of farmers with very large flocks, (e.g., ≥1,000 birds), we were only able to categorize flock size as <100 (RR=0.6, 95%CI 0.3–1.1) or ≥100 (RR=0.6, 95% CI: 0.3–1.2) birds (Table 3). Conversely, there was an increased risk of colon cancer among farmers who raised poultry (RR=1.4; 95% CI: 0.99–2.0), and an exposure-response association for having more poultry, with risks higher in those with more than 100 birds (RR=1.7, 95% CI 1.0–2.8; p-trend=0.02). There was some evidence of increased risk of Non-Hodgkin lymphoma (NHL) among those who raised poultry (RR=1.6; 95% CI: 1.0–2.4), but no evidence of increasing risk with more poultry (p-trend=0.48). The small number of cases of NHL (n=23) who raised poultry precluded detailed evaluation of NHL sub-types (data not shown). Working in a poultry confinement area was associated with an increased risk of NHL overall (RR=2.1; 95% CI: 1.2–3.7). There was no apparent association between raising poultry or working in a poultry confinement area and cancer at other sites.

Beef cattle were the most common type of livestock raised, and many farmers who raised dairy cattle also raised beef (Table 1). We examined these two types of cattle separately, but also considered them together since many of the exposures may be similar. There was a decreased risk of pancreatic cancer (RR=0.6; 95% CI: 03–0.9) among farmers who raised beef cattle (Table 2). Raising cattle did not appear to be associated with cancer at other sites.

Although there were no statistically significant associations between raising hogs in the last year and cancer at any site, there were suggestive positive associations with prostate cancer (RR=1.1; 95% CI: 0.99–1.2), leukemia (RR=1.3; 95%CI: 0.9–1.9) and multiple myeloma (RR=1.7; 95% CI: 0.96–3.0) (Table 2).

Although the RR for Hodgkin lymphoma for raising hogs was 1.6 (95% CI: 0.6–4.3), there was a significant increased risk among those who worked in hog confinement areas (RR=3.6; 95% CI: 1.2–10.3).

Raising sheep was also associated with a non-significantly decreased risk of lung cancer (RR=0.7; 95% CI: 0.3–1.7) based on 5 cases (Table 2). Based on 7 farmers who raised sheep, there was an increased risk of multiple myeloma (RR=4.9, 95% CI: 2.2–11.1). Permethrin, an insecticide widely used as a dip for sheep, has also been shown in a previous AHS analysis to be associated with increased risk of multiple myeloma. Further control for use of permethrin, however, did not substantively change risk estimates (RR=4.8, 95% CI: 2.1–10.7). Raising sheep was also associated with increased risk of cancers of the pancreas (RR=2.8 95% CI: 2.2–11.1) and brain (RR=2.7; 95% CI: 0.95–7.6).

There were no differences observed in risk estimates for any cancer site or animal type when we considered the referent group to be those with no livestock or poultry exposure; therefore results are reported using those who did not report exposure to each animal being evaluated as the referent group.

There was a significantly decreased risk of lung cancer among those who raised more than 1,000 head of livestock (RR=0.5, 95% CI: 0.3–0.97, p-trend=0.04) (Table 4). We were not able to link this to a specific type of animal as farmers were asked about the number of livestock on their farms and not about the number of specific types and many farmers raised more than one type. There was minimal evidence for an association between cancer and increasing number of livestock. We evaluated other factors associated with raising livestock and poultry, such as frequency of milking cows, grinding feed, butchering and performing veterinary services. The performance of veterinary services was associated with an increased risk of Hodgkin lymphoma based on 17 of the 18 cases who performed these tasks (RR=12.2; 95% CI: 1.6–96.3). Grinding feed on a monthly basis was also associated with increased risk of Hodgkin lymphoma with RR=1.7 (95% CI: 0.97–3.0). There was no evidence of an association with performing these tasks and cancer at any other site.

Discussion

The AHS provided the opportunity to evaluate cancer risks in relation to exposures associated with the rearing of poultry and livestock. In our analyses, we saw a decreased risk of lung cancer among poultry farmers. There was no additional reduction of lung cancer among those with larger numbers of birds. There was a decreasing risk, however, among those who had larger herds of livestock. Other published reports have observed deficits of lung cancer associated with dairy farming [8–9]; however, we did not observe a decrease associated with dairy cattle specifically. Of the types of livestock that we evaluated, only raising sheep was specifically associated with a decreased risk of lung cancer, although the association was not statistically significant. Unfortunately, we could not evaluate the impact of herd size and specific types of livestock since the participants were not asked to provide this information. Decreased risk of lung cancer has been consistently reported among farmers and has often been attributed to lower rates of tobacco use [2]. The decreased risks for lung cancer in our analyses persisted even after control for smoking. Exposure to endotoxins, which are associated with working with animals and handling hays and grains as feed for animals, is a primary hypothesis for the decreased risk of lung cancer among

farmers [7]. There is wide variability in endotoxin exposure levels depending on a number of factors, including the number of animals and the specific conditions in which the animals are kept [10] and amount of time spent with the animals. We were unable to account for these variations in our current analyses. Although early case-control studies conducted in Europe indicated an increased risk of lung cancer among people who had birds as pets [11–13], more recent studies, including those in the United States, have reported either no association or a decreased risk with associated with living with birds [14–15].

We observed a greater risk of NHL among those who raised poultry than among those who did not raise poultry, but no further increase among those who had more poultry on their farm. We also observed an increased risk among those who worked in hog confinements, but not among those who raised hogs. This discrepancy may indicate a spurious association, or it may indicate that there is an exposure specific to working in hog confinements that increases the risk of NHL. We saw no association with any other type of livestock. In a death certificate study, there was an increased risk of NHL mortality among those occupationally exposed to animals [1] although there was no information on specific types of animals. Results from that study also found statistically significant excesses for those with farming-related occupations with animal exposure and not statistically significant associations for non-farming occupations with possible animal exposures. In a death certificate study in Sweden, there was a non-statistically significant increased risk NHL among men who worked as livestock breeders, and among those who worked in dairy production [16]. There is some supporting evidence for our positive association with working in a hog confinement, as three case-control studies that showed increased risk of NHL with raising swine[17] or occupational exposure to pigs [18–19]. Tranah and colleagues also reported an increased risk of NHL among those who had worked with cattle more than five years [19].

In our analysis, we observed a statistically significant increased risk of multiple myeloma associated with raising sheep and a non-significant excess among those who raised hogs, but no evidence of an association with other types of animals. The association with raising sheep did not change with adjustment for use of permethrin, an insecticide used as a sheep dip that has been associated with multiple myeloma in the AHS [20].Multiple myeloma has been associated with farming in numerous studies [21], and there is increased incidence within the AHS [3]. Other studies have reported increased risk of multiple myeloma among those exposed to cattle [18, 22–23] and a meta-analysis of four case-control studies of multiple myeloma [23–26] showed statistically significant increased risk for multiple myeloma associated with raising sheep, horses and dairy cattle [21]. Svec and colleagues also reported increased risk of mortality from multiple myeloma among those who were occupationally exposed to animals, but did not specify the type of animals [1].

We found a non-statistically significant risk of leukemia among those farmers who raised hogs, but no other types of livestock or poultry. A mortality study among workers in a poultry processing plant found an excess risk of death from leukemia [27] and a case-control study showed increased risk of leukemia in those with occupational contact with beef cattle, including higher risks among those with longer duration of exposure [18]. Higher risks of lymphohematopoietic malignancies have been reported among butchers and those working in abattoirs (McLean and Pearce, 2005). However, the types of exposures experienced by workers in a processing plant may be very different than those who are engaged in the raising of chickens or livestock. Controlling for other factors such as performing veterinary services, butchering or coming in contact with animal blood did not change the association with leukemia. Additionally, we only had nine cases of leukemia among those who raised poultry, which may have limited our ability to detect an association.

With only eighteen cases of Hodgkin lymphoma overall, we had limited power to evaluate potential associations between this disease and livestock and poultry. We observed a RR of 1.6 (95% CI: 0.6–4.3) for farmers who reported raising hogs, but a statistically significant increase among those who reported working in a hog confinement. This is consistent with a case-control study that showed increased risk of Hodgkin Lymphoma among those occupationally exposed to pigs [28]. Additionally, we observed an increased risk among those who performed veterinary services. A proportionate mortality study of veterinarians in the United States observed significant excesses of Hodgkin lymphoma [29], and a case-control study based on death certificates indicated an increased risk of Hodgkin lymphoma among veterinarians [1]. The strongest etiologic hypotheses for Hodgkin lymphoma include immune response to infections [30] and individuals performing veterinary activities may have greater exposure to infectious agents than other farmers.

We observed an increased risk of colon cancer for farmers who raised poultry and higher risks among those with more birds. We are unaware of any other literature that has suggested such an association. Colon cancer incidence is generally lower in studies of farmers (Blair and Beane Freeman, 2009). An earlier study evaluating colon cancer and pesticide use in the AHS showed an association between the use of specific pesticides and colon cancer risk (Lee 2007). Controlling for use of these pesticides did not impact the observed risk estimates.

Strengths of this study include its prospective design, and more detailed information on the type and number of animals raised than is available in many other studies. We were able to assess risk for incident cancer cases diagnosed and reported to the state cancer registries. We were able to control for possible confounders for the various cancers, including use of various pesticides and lifestyle factors. Limitations include our inability to fully link the number of livestock to the types of livestock raised. For example, we saw some evidence of an inverse exposure-response with increasing numbers of livestock and lung cancer, but we were unable to attribute this to a specific type of animal because the question on the number of animals was not tied to the specific type of livestock. We do note, however, that most of the farmers with larger number of livestock raised hogs. We were also limited by small numbers to fully evaluate risks among farmers with only one type of livestock and by the fact that farmers were asked about the livestock and poultry that they were currently raising, which may not be indicative of previous exposures. Finally, while raising certain types of livestock may influence cancer risk, the identification of etiologic agents requires more detailed exposure assessment than was possible in this analysis.

Conclusions

We observed a decreased risk of lung cancer among farmers who raised poultry compared to those who did not. We also observed that lung cancer risk decreased with increasing numbers of livestock. These observations are consistent with increased exposure to endotoxins, which have been shown to decrease lung cancer risk and are elevated in agricultural settings, but other factors could be involved. We also observed increased risk of NHL among poultry farmers and increased risk of multiple myeloma among sheep farmers. We also observed an increased risk of Hodgkin lymphoma among those who performed veterinary services and worked in hog confinements. Colon cancer was also increased among poultry farmers, with evidence of an exposure-response trend. Possible exposures from rearing and tending of poultry and livestock have received less attention than chemical exposures in agricultural settings. Our findings indicate that further research into associations between livestock, poultry, and cancer risk are warranted and that they should focus on identification of possible etiologic agents.

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Table 1

Frequency of selected demographic and farm activities among AHS farmers who do and do not raise livestock

	Farmers with no livestock or poultry		Farmers with livestock or poultry		χ^2 p-value
	n	%	n	%	
	18,036	**36.2**	**31,848**	**63.8**	
Age at enrollment					
<35	2690	14.9	6492	20.4	
40–49	6562	36.4	13967	43.9	
50–59	4103	22.7	6511	20.4	
60–69	3332	18.5	3832	12.0	
70+	1349	7.5	1046	3.3	
					p<0.001
State					
Iowa	7085	39.3	23568	74.0	
North Carolina	10951	60.7	8280	26.0	
					p<0.001
Education					
< High school	2418	13.4	2486	7.8	
High school	7459	41.4	15602	49.0	
> High school	6570	36.4	13208	41.5	
					p<0.001
Smoking					
Never	7269	40.3	18262	57.3	
Former	5774	32.0	9024	28.3	
Current	3413	18.9	4362	13.7	
					p<0.001
Type of Livestock					
Poultry			3,130	10.8	
Beef			18,663	64.3	
Dairy			2,784	9.6	
Either Beef or Dairy			20,441	70.4	

	Farmers with no livestock or poultry		Farmers with livestock or poultry		χ^2 p-value
	n	**%**	**n**	**%**	
	18,036	**36.2**	**31,848**	**63.8**	
Hogs			16,597	57.2	
Sheep			1,593	5.5	

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Table 2

Major income producing animals on the farm and risk of cancer among male farmers in the AHS

	Poultry		Beef		Dairy	
Cancer Site	**Number exposed (%)**	**RR 95 %CI**	**Number exposed (%)**	**RR 95 %CI**	**Number exposed (%)**	**RR 95 %CI**
Lung	22 (4.9)	0.63 0.4–0.97	130 (28.7)	1.0 0.8–1.3	17 (4.0)	1.3 0.8–2.0
Pancreas	7 (8.3)	1.1 0.5–2.5	18 (21.4)	0.6 0.3–0.9	6 (3.0)	0.3 0.1–2.2
Colon	36 (10.4)	1.4 0.99–2.0	108 (31.1)	0.9 0.7–1.1	14 (4.1)	1.0 0.6–1.6
Rectum	10 (6.2)	0.7 0.4–1.4	58 (35.8)	1.0 0.7–1.4	4 (2.5)	NA
Renal	9 (6.0)	0.8 0.4–1.5	55 (36.4)	1.1 0.8–1.5	3 (2.0)	NA
Bladder	12 (6.0)	0.8 0.5–1.5	67 (33.5)	1.0 0.7–1.3	6 (3.0)	0.8 0.3–1.7
Prostate	130 (6.9)	1.0 0.8–1.1	705 (37.4)	1.1 0.98–1.2	77 (4.1)	0.9 0.7–1.2
Brain	1	NA	17 (30.4)	0.8 0.4–1.4	2 (3.6)	NA
Melanoma	14 (7.8)	0.9 0.5–1.6	62 (34.4)	0.9 0.7–1.3	7 (3.9)	0.8 0.4–1.6
Oral Cavity	1 (0.09)	NA	35 (32.4)	0.8 0.5–1.2	3 (2.8)	NA
Leukemia	9 (6.4)	0.9 0.5–1.7	47 (33.6)	0.9 0.6–1.2	3 (2.1)	NA
Hodgkin lymphoma	0	NA	9 (50.0)	1.3 0.5–3.4	2 (11.1)	NA
Non-Hodgkin lymphoma	23 (11.4)	1.6 1.0–2.4	75 (37.3)	1.1 0.8–1.4	10 (5.0)	1.1 0.6–2.0
Multiple myeloma	5 (7.2)	1.0 0.4–2.4	19 (27.5)	0.7 0.4–1.2	0	NA
Soft tissue sarcoma	0	NA	6 (37.5)	1.1 0.4–3.0	4 (25.0)	NA

Adjusted for age, state, smoking and education

Table 3

Number of poultry and risk of cancer among male farmers in the AHS

Cancer site	Number of Poultry	n	RR	95% CI	
Lung	None	324	1.0	REF	
	<100	11	0.6	0.3	1.1
	≥100	8	0.6	0.3	1.2
				p-trend=0.10	
Colon	None	252	1.0	REF	
	<100	18	1.3	0.8	2.0
	≥100	16	1.7	1.0	2.8
				p-trend=0.02	
Bladder	None	157	1.0	REF	
	<100	6	0.7	0.3	1.6
	≥100	6	1.2	0.5	2.6
				p-trend= 0.79	
Prostate	None	1427	1.0	REF	
	<100	83	1.1	0.9	1.3
	100–999	14	0.9	0.5	1.4
	≥1,000	27	0.8	0.6	1.2
				p-trend=0.31	
Non-Hodgkin lymphoma		153	1.0	REF	
	<100	13	1.4	0.8	2.5
	≥100	7	1.3	0.6	2.8
				p-trend=0.48	

Adjusted for age, state, smoking and education

Table 4

Number of livestock and risk of cancer among male farmers in the AHS

Cancer site	Number of livestock	n	RR	95% CI	
Lung	None	171	1.0	REF	
	<100	115	1.1	0.9	1.4
	100–999	60	0.9	0.7	1.3
	≥1,000	12	0.5	0.3	1.0
				p-trend=0.04	
Pancreas	None	32	1.0	REF	
	<100	17	0.9	0.5	1.6
	≥100	19	0.7	0.4	0.6
				p-trend=0.32	
Colon	None	128	1.0	REF	
	<100	73	0.9	0.7	1.2
	100–999	61	0.7	0.5	1.0
	≥1,000	26	0.8	0.5	1.3
				p-trend=0.15	
Rectum	None	55	1.0	REF	
	<100	34	1.0	0.6	1.5
	100–999	34	0.9	0.5	1.4
	≥1,000	15	1.0	0.5	1.8
				p-trend=0.72	
Renal	None	50	1.0	REF	
	<100	39	1.2	0.8	1.9
	100–999	31	0.8	0.5	1.3
	≥1,000	10	0.7	0.3	1.4
				p-trend=0.10	
Bladder	None	77			
	<100	41	0.9	0.6	1.3
	100–999	38	0.9	0.6	1.3
	≥1,000	15	0.9	0.5	1.7
				p-trend=0.66	

Cancer site	Number of livestock	n	RR	95% CI	
Brain	None	22	1.0	REF	
	<100	9	0.6	0.3	1.4
	100–999	13	0.7	0.3	1.4
	≥1,000	5	0.6	0.2	1.8
				p-trend=0.43	
Cutaneous melanoma		54	1.0	REF	
	<100	29	0.8	0.5	1.3
	100–999	45	1.2	0.7	1.8
	≥1,000	23	1.4	0.9	2.4
				p-trend=0.09	