

# A Pilot Case-Cohort Study of Liver and Pancreatic Cancers in Poultry Workers

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**PURPOSE:** To test the hypothesis that exposure to poultry oncogenic viruses that widely occurs occupationally in poultry workers and in the general population, may be associated with increased risks of deaths from liver and pancreatic cancers, and to identify new risk factors.

**METHODS:** A pilot case-cohort study of both cancers within a combined cohort of 30,411 highly exposed poultry workers and 16,408 control subjects was conducted, and risk assessed by logistic regression odds ratios (OR) and proportional hazards risk ratios.

**RESULTS:** New occupational findings were recorded respectively for pancreatic/liver cancers, for slaughtering of poultry (OR = 8.9, 95% confidence interval [CI]: 2.7–29.3)/OR = 9.1, 95% CI: 1.9–42.9); catching of live chickens (OR = 3.6, 95% CI: 1.2–10.9)/OR = 1.0, 95% CI: 0.1–8.5); killing other types of animals for food (OR = 4.8, 95% CI: 1.5–16.6)/OR = 2.0, 95% CI: 0.2–18.2), and ever worked on a pig raising farm (OR = 3.0, 95% CI: 1.0–8.2) for pancreatic cancer only. New non-occupational findings for liver cancer were for receiving immunization with yellow fever vaccine (OR = 8.7, 95% CI: 1.0–76.3); and vaccination with typhoid vaccine (OR = 6.3, 95% CI: 1.1–37.4). The study also confirmed previously reported risk factors for both diseases.

**CONCLUSIONS:** This study provides preliminary evidence that exposure to poultry oncogenic viruses may possibly be associated with the occurrence of liver and pancreatic cancers. Case-control studies nested within occupational cohorts of highly exposed subjects of sufficient statistical power may provide an efficient and valid method of investigating/confirming these findings.

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**KEY WORDS:** Oncogenic Viruses, Pancreas, Poultry, Occupation, Liver, Cancer, Risk Factors.

## INTRODUCTION

Certain viruses naturally infect and cause cancer in chickens and turkeys. They include the avian leukosis/sarcoma viruses (ALSV), reticuloendotheliosis viruses, and Marek's disease virus. Some of these viruses are among the most potent cancer-causing agents known in animals (1). Humans are widely exposed to these viruses from contact with live poultry and their raw products including eggs; from ingestion of raw or inadequately cooked products; or through vaccination with vaccines grown in eggs, such as measles, mumps, influenza, yellow fever, and typhus vaccines (2–7). It has been shown that exogenous ALSV-contaminated yellow fever vaccines caused malignant tumors when injected into chickens (8). Some (9–11) but not all studies (4, 5, 12) have reported the presence of antibodies to these viruses in the sera of poultry workers and

subjects in the general population. It is known that the viruses can infect/transform human cells in vitro (13–15). However, despite these observations, it is not known if they cause cancer in humans, partly because of the lack of analytic epidemiologic studies.

To explore if the development of cancer is associated with exposure to these viruses, we studied mortality in 30,411 workers from 23 poultry slaughtering and processing plants located in seven states in the United States, that were identified from three main sources/cohorts: (1) the United Food and Commercial Workers (UFCW) local union in Baltimore, Maryland; (2) the UFCW local poultry union in Marshall, Missouri; and (3) a UFCW Pension Fund that covered poultry plants in six states (Alaska, Arkansas, Louisiana, Maine, Missouri, and Texas). These workers have one of the highest known human exposures to these viruses. In addition to the poultry workers, the rosters of the Baltimore union and the Pension Fund also contained a total of 16,408 members who worked in various nonpoultry companies located in Maryland, Florida, Illinois, Indiana, Massachusetts, New Jersey, Ohio, Pennsylvania, and Texas.

Excess occurrence of 11 cancer sites, including liver and pancreatic cancers, was observed in the poultry workers (16–20). Accordingly, we conducted a pilot case-cohort

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**Selected Abbreviations and Acronyms**

ALSV = Avian leukosis/sarcoma viruses  
CI = confidence interval  
HR = hazard ratio  
OR = odds ratio

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study of some of the cancers that were in excess in the poultry workers, for the following reasons: (1) to test the hypothesis that exposure to poultry oncogenic viruses may be associated with the increased risks of cancer deaths observed; (2) to obtain preliminary information on possible new risk factors for these diseases not previously reported; and (3) to determine the feasibility of obtaining valid results from a full-scale large case-cohort study that is planned for the immediate future. The study described here is a report of the findings of the case-cohort study for liver and pancreatic cancers. This study, together with those on the underlying three cohorts, are the only studies in the literature that have provided information on the risk of liver and pancreatic cancers associated with occupational exposure to poultry.

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**METHODS**

The source population for this case-cohort study consisted of the 30,411 poultry workers and 16,408 nonpoultry workers, making a total of 46,819 subjects who were members of the UFCW unions anytime between 1949 and 1989. Among this group, 2,915 died during follow-up by the end of 1989. The remaining 43,904 subjects that were alive as of January 1, 1990 constitute the base population for the study reported here, and they were followed up from January 1, 1990 until December 31, 2003. Because no new subjects were added after January 1, 1990, and all subjects lost to follow-up were assumed to be alive at the end of the study, this group of subjects alive as of January 1, 1990 was essentially a closed cohort. Cases consisted of 1,218 subjects in the base population who died of the 11 cancer sites originally observed to be in excess in the poultry workers. However, for the present report, cases were defined as all 49 deaths from liver cancer and 86 from pancreatic cancer that occurred in the base population between January 1, 1990, and December 31, 2003. The comparison group for the liver and pancreas cases was a subcohort that consisted of 1,516 live subjects randomly sampled from the base population, some of whom later died during the study period.

Because this was a feasibility study, exhaustive attempts were not made to identify study subjects or their next-of-kin. Thus, we report here on the first 11 of 49 liver cancer deaths (22%) and 23 of 86 pancreatic cancer deaths

(27%) (cases) whose next-of-kin were traced and provided information over the phone on the deceased cases. Similarly, controls in the pilot study consisted of the first 152 of 1,516 subcohort members (11%) for whom phone interviews were successfully obtained with the same questionnaire either directly (if alive), or through their next-of-kin if deceased. Two of the interviewed cases of pancreatic cancer but none of the liver cases, were also members of the control group of 152 subjects.

The questionnaire was detailed, and had altogether 646 questions that took an average of 40–60 minutes to administer over the phone. It included the usual demographic variables on race, gender, date of birth, and date of death. A detailed list of questions (selected questions shown in the tables) on occupations and industries within each of the following major headings were asked in the questionnaire: (1) occupational poultry-specific exposures—this included a number of tasks carried out by different workers (some were responsible for unloading chickens from trucks, hanging chickens on conveyor lines, others for killing chickens, others for cutting carcasses, packing the chickens, etc.)—workers tend to be assigned to perform one task, but may perform different tasks over the course of their employment at a poultry plant; (2) mixed occupational poultry- and meat-related exposures; (3) working or living on a farm; (4) occupational exposure to seafood; (5) killing food animals other than poultry; (6) applying chemicals at work; and (7) working in occupations and industries outside the poultry and meat industries. Risk associated with each job exposure was calculated for ever/never responses. All questions on specific occupations included dates and duration of employment. However, dose-response results on occupational exposures are not presented because the numbers involved were too few to be meaningful. There were also detailed non-occupational questions on lifestyle, medical history, diet, medication use, family history of medical conditions, radiation exposures, immunizations, and miscellaneous exposures.

To obtain information on the reliability of responses from proxies, the questionnaire was administered to a small subset of seven pairs of live control study subjects and their next-of-kin.

The main analyses consisted of logistic regression and Cox regression in which tobacco smoking and each of newly identified risk factors in the study were individually adjusted for. Adjustment for age, gender, or race individually, did not change the risk estimates to a significant degree in each case, and so adjustment for these variables was dropped. Logistic regression models were initially fit to the data using the SAS PROC LOGISTIC procedure (SAS 9.1, SAS Institute, Cary, NC), and odds ratios (OR) and their associated 95% confidence intervals (CI) estimated. Because the control group was a random sample of the base population, the

**TABLE 1.** Distribution of race, gender, age, and type of worker, of study subjects

	Pancreas cancer cases		Liver cancer cases		Controls	
	Total (n = 86)	Interviewed (n = 23)	Total (n = 49)	Interviewed (n = 11)	Totals (n = 1516)	Interviewed (n = 152)
<b>Race*</b>						
White (%)	51 (58)	18 (78)	33 (63)	10 (91)	1099 (72)	108 (71)
Nonwhite (%)	35 (37)	5 (22)	16 (33)	1 (9)	324 (21)	27 (18)
Unknown (%)	0	0	0	0	93 (6)	19
Total	86	23	49	11	1516	152
<b>Gender</b>						
Female (%)	40 (47)	9 (39)	24 (49)	4 (36)	785 (52)	87 (57)
Male (%)	46 (53)	14 (61)	25 (51)	7 (64)	723 (48)	64 (42)
Unknown (%)	0	0	0	0	8 (1)	1 (1)
Total	86	23	49	11	1516	152
<b>Age<sup>†</sup></b>						
≤50 years (%)	36 (42)	13 (57)	22 (45)	3 (27)	1061 (70)	103 (68)
>50 years (%)	50 (58)	10 (43)	27 (55)	8 (73)	413 (27)	48 (32)
Unknown (%)	0	0	0	0	42 (3)	1 (1)
Total	86	23	49	11	1516	152
<b>Type of worker</b>						
Poultry (%)	55 (64)	14 (61)	33 (67)	4 (36)	898 (59)	113 (74)
Nonpoultry (%)	31 (36)	9 (39)	16 (33)	7 (64)	618 (41)	32 (32)
Unknown (%)	0	0	0	0	0	7 (5)
Total	86	23	49	11	1516	152

\*Race information was not available in union records, and was obtained only from death certificates for deceased or interviewed subjects. Hispanics were classified as whites.  
<sup>†</sup>Age is defined as age at entry into study cohort.

OR obtained were direct estimates of the risk ratio without need for the rare disease assumption (21). In the Cox regression analysis, hazard ratios (HR) (rate ratios) were estimated using the SAS PHREG procedure. Subjects entered the study at the age attained on 01/01/1990 (time variable) and the failure time for formation of a risk set was the age at death of a liver or pancreas cancer case. At failure time, a risk set was formed consisting of the case and all available controls at risk at that time.

## RESULTS

Altogether, 374 of 1218 cases (31%) of all 11 cancer sites of interest were traced, and a telephone interview was successfully obtained for 300 of those traced (80%), 49 and 86 of whom were liver and pancreatic cancers, respectively. Similarly, of 214 of 1516 subjects (14%) in the subcohort that were traced, an interview was obtained for 152 (71%). The distributions of age, race, gender, and percent poultry worker at baseline for interviewed cases and controls are given in Table 1.

A comparison of the responses of the seven live control subjects and those of their next-of-kin showed that of the 245 direct questions with a dichotomous option in the questionnaire (Yes/No), the agreement between the two was 100% for 44% of the questions; 80%–99% for 30% of the questions; 60%–79% for 18% of the questions; and less than 60% for 8% of the questions.

Significantly elevated OR were observed only for the exposures in Table 2. We do not present the HR results because they were very similar to the OR, although they tend to be minimally lower for the most part. In Table 3 and Table 4, we present a detailed listing of OR that were not statistically significant, for pancreatic and liver cancers, respectively. Further comments will not be made on these results other than to note that by and large they are consistent with the results for new and established significant findings in this study.

## Pancreatic Cancer

Poultry jobs pancreatic cancer cases were employed in include: killing chickens; catching live chickens; hanging live chickens; loading live chickens into trucks; wrapping and packing chickens; cutting chickens; chicken truck driver; and unspecified poultry tasks. The interval between first exposure and date of death ranged from 17 years to 32 years (average = 25 years). Duration of employment in poultry jobs was unknown for several cases, but two-thirds (four of six) with known duration worked in poultry jobs for less than 5 years.

As seen in Table 2, the only poultry-related occupational exposures that were significantly associated with pancreatic cancer were slaughtering of chickens at work (OR = 8.9, 95% CI: 2.7–29.3) and catching live chickens at work (OR = 3.6, 95% CI: 1.2–10.9). Nonpoultry occupational exposures that were significantly associated with pancreatic

**TABLE 2.** Significantly increased OR in poultry workers (1990-2003)

	Pancreatic cancer (n = 23) OR (95% CI)*	Liver cancer (n = 11) OR (95% CI)*
Occupational poultry exposures		
Ever kill chickens/birds at work	8.9 (2.7-29.3)	9.1 (1.9-42.9)
Ever catch live chickens/birds at work	3.6 (1.2-10.9)	1.0 (0.1-8.5)
Nonpoultry occupational exposures		
Ever killed other type of animals for food	4.8 (1.5-16.6)	2.0 (0.2-18.2)
Ever worked on pig raising farm	3.0 (1.0-8.2)	—
Ever work where dyes were made or handled	7.5 (1.7-33.9)	—
Medical conditions and treatment		
Pancreatitis	430.0 (8.4-22026)	—
Cirrhosis	6.2 (0.4-104.0)	39.7 (3.2-492.1)
Infectious mononucleosis	—	19.3 (1.1-327.8)
Hepatitis	—	9.9 (1.9-51.3)
Radiation therapy	5.3 (1.8-15.9)	2.3 (0.4-11.7)
Ever receive immunizations for yellow fever	1.4 (0.3-7.2)	8.7 (1.0-76.3) <sup>†</sup>
Ever receive immunizations against typhoid	1.5 (0.4-6.1)	6.3 (1.1-37.4)
Diet		
Bacon	9.5 (1.3-69.2)	—
Peanuts	1.8 (0.7-5.0)	8.2 (2.0-33.7)
Method of meat preparation		
Smoked	5.5 (2.0-15.0)	2.2 (0.6-8.1)
Salted	4.3 (1.5-12.4)	1.9 (0.5-6.9)

CI = confidence interval; OR = odds ratio.

\*Odds ratios adjusted for ever smoking.

<sup>†</sup>Borderline significance.

cancer were: killing food animals other than poultry (OR = 4.8, 95% CI: 1.5-16.6); working on a pig-raising farm (OR = 3.0, 95% CI: 1.0-8.2); and working where dyes were made or handled (OR = 7.5, 95% CI: 1.7-33.9). For non-occupational exposures, pancreatitis (OR = 430.0, 95% CI: 8.4-22026); history of radiation therapy (OR = 5.3, 95% CI: 1.8-15.9); eating a lot of bacon (OR = 9.5, 95% CI: 1.3-69.2); eating meat smoked (OR = 5.5, 95% CI: 2.0-15.0); and eating salted meat (OR = 4.3, 95% CI: 1.5-12.4), were significantly associated with cancer of the pancreas.

The associations between killing chickens at work, catching live chickens at work, and pancreatic cancer persisted with little or no change, after additionally adjusting for each of the nonpoultry occupational and non-occupational exposures listed above that were observed in this study to be significantly associated with the disease (not shown).

### Liver Cancer

The only occupational exposure that was significantly associated with liver cancer was slaughtering of chickens at work

(OR = 9.1, 95% CI: 1.9-42.9). For non-occupational exposures, history of cirrhosis of the liver (OR = 39.7, 95% CI: 3.2-492.1); infectious mononucleosis (OR = 19.3, 95% CI: 1.1-327.8); hepatitis (OR = 9.9, 95% CI: 1.9-51.3); eating a lot of peanuts (OR = 8.2, 95% CI: 2.0-33.7); and vaccination with yellow fever (OR = 8.7, 95% CI: 1.0-76.3) and typhoid (OR = 6.3, 95% CI: 1.1-37.4) vaccines, were significantly associated with cancer of the liver.

The association between killing chickens at work and liver cancer persisted with little or no change, after additionally adjusting for each of the non-occupational exposures listed above that were found to be significantly associated with the disease (not shown).

Poultry jobs held by liver cancer cases include killing chickens, deboning chickens, repairing pallets, and unspecified poultry processing. The interval between first exposure and date of death ranged from 11 years to 45 years (average = 27 years). Of three cases with known duration of employment, two were employed for less than 5 years.

The extreme apparent reduced risk associated with cell phone use for pancreatic cancer is probably an artifact. Most of the controls were alive and thus their use possibly reflects recent use at a time when cell phone use has become widely prevalent in the general population. On the other hand, all the cases were deceased, hence their use more likely reflects use in the more distant past when cell phone use was not as common.

### DISCUSSION

This study identified new and established risk factors for liver and pancreatic cancers. These results are unlikely to be due to bias in selecting subjects into the study for the following reasons: (1) all cases of both cancers were selected for study; (2) the control group was a random sample of the entire cohort; (3) although the proportion of cases and controls traced was low, once traced response rates for providing an interview were high (80% for cases, 71% for controls); and (4) although the distribution of demographic variables was different between interviewed cases and the total number of cases in some instances, none of these variables were found to be significant confounders. There was no evidence of severe recall bias arising from obtaining exposure history of cases (all deceased) from their next-of-kin, whereas live controls were interviewed directly. There was very good to excellent agreement (80% or higher) for 74% of the questions, between responses of a small sample of live controls and those of their respective next-of-kin, and the agreement was less than 60% in only 8% of the questions.

Finally, it should be noted that the majority of subjects in the underlying cohort from which cases and controls in this case-cohort study were selected were poultry workers. Hence

**TABLE 3.** OR results that were not statistically significantly increased—pancreatic cancer

	Exposed (cases/control)	Adjusted OR (95% CI)*
<b>Poultry-specific exposures</b>		
Ever worked as a poultry farmer	3/7	3.5 (0.9–14.8)
Ever worked on poultry farm (not commercial)	5/18	3.0 (0.9–10.2)
Ever worked where poultry feathers were handled	9/37	2.6 (0.8–7.9)
Ever load and unload chickens/birds from trucks	5/18	2.4 (0.8–7.5)
Ever worked in poultry breeding	1/4	2.2 (0.3–20.0)
Ever work loading and unloading chicken or turkey eggs from trucks	2/8	2.0 (0.4–9.9)
Ever drive a vehicle for transporting chicken/birds	2/7	1.9 (0.4–9.8)
Ever work on farm where eggs of chickens/birds produced or laid for commercial purposes	3/12	1.8 (0.4–7.0)
Ever killed chicken/birds outside of work	7/31	1.6 (0.6–4.2)
Ever come in direct contact with blood of chickens/birds at work	10/52	1.3 (0.7–4.4)
Ever spread chicken/bird waste as manure	2/9	1.5 (0.3–7.0)
Ever drive vehicle for transporting chicken/turkey eggs	1/5	1.1 (0.1–10.0)
Ever handled poultry	16/102	0.9 (0.3–2.1)
Ever come into contact with or handled cooked chicken/birds at work	4/34	0.8 (0.3–2.5)
Ever worked in plant where poultry slaughtered	6/32	0.8 (0.2–2.5)
Ever cut raw/chickens/birds at work	8/66	0.7 (0.3–1.7)
Ever work where eggs of chickens/birds were handled	3/29	0.7 (0.2–2.4)
Ever worked on commercial poultry farm	2/17	0.7 (0.1–3.3)
Ever worked in plant where raw poultry processed and packed in plastic (not slaughtered)	10/76	0.7 (0.2–2.1)
Ever wrap raw chickens/birds at work	4/41	0.6 (0.2–2.0)
Ever worked in plant where poultry cooked	4/41	0.6 (0.2–2.3)
Ever pack already wrapped raw chicken/birds	4/42	0.6 (0.2–1.9)
Ever worked where poultry waste was used or handled	3/31	0.6 (0.1–2.2)
Ever come into contact with or handle unwrapped raw chicken/birds at work	7/78	0.4 (0.2–1.1)
Ever handle eggs of chicken/birds at work	2/31	0.4 (0.1–1.8)
Ever worked where poultry was deboned	4/64	0.2 (0.1–0.6)
<b>Exposures associated with killing animals other than poultry</b>		
Ever killed pigs	3/8	2.8 (0.7–11.1)
Ever killed food animals at work such as cows, pigs, sheep	1/6	1.5 (0.2–12.3)
Ever killed cattle	2/9	1.4 (0.3–6.8)
<b>Miscellaneous, mixed poultry and meat exposures</b>		
Ever worked in a stockyard	1/2	2.1 (0.2–22.5)
Ever use wrapping machine for wrapping meat, chicken, or turkey at work	3/21	1.1 (0.3–4.2)
Ever worked as meat cutter (no kill)	5/33	1.0 (0.4–2.9)
Ever worked as a chef or cook	3/27	0.6 (0.2–2.3)
Ever worked in a kitchen	4/29	0.6 (0.2–2.2)
Ever exposed to fumes or smoke while wrapping chickens/meat at work	1/23	0.2 (0.0–1.8)
Ever worked in a restaurant	1/40	0.1 (0.0–0.8)
<b>Occupational farm exposures</b>		
Ever worked on sheep/goat farm	4/9	3.4 (0.9–12.3)
Ever worked on horse farm	5/14	2.3 (0.8–7.2)
Ever worked on dairy farm	3/11	2.3 (0.6–8.7)
Ever worked on cattle farm	7/27	2.0 (0.8–5.5)
Ever worked on commercial mixed (crop and animal) farm	3/9	1.9 (0.5–7.4)
Ever work on commercial animal farm	4/18	1.3 (0.4–4.2)
Ever work on commercial crop farm	3/20	0.8 (0.2–3.1)
<b>Lived on the farm</b>		
Ever lived on a poultry farm as a child	5/24	1.8 (0.6–5.6)
Ever lived on a cattle farm as a child	7/36	1.3 (0.5–3.5)
Ever lived on a horse farm as a child	3/15	1.3 (0.4–4.9)
Ever lived on a farm as a child	12/62	1.2 (0.5–3.0)
Ever lived on a pig farm as a child	4/26	1.2 (0.4–3.8)
Ever lived on a sheep farm as a child	1/7	1.2 (0.2–10.0)
<b>Occupational seafood exposures</b>		
Ever worked on a shellfish farm	2/2	5.8 (0.8–44.2)
Ever worked in fishing or collecting seafood	4/10	2.7 (0.8–9.3)

(Continued)

TABLE 3. (Continued)

	Exposed (cases/control)	Adjusted OR (95% CI)*
Ever handled seafood at work	4/21	1.3 (0.4-4.4)
Ever worked in plant where seafood processed	2/21	0.6 (0.1-2.9)
Pesticide exposures		
Ever applied chemicals on fences at work	1/3	6.7(0.9-48.4)
Ever sprayed chemicals on farm	3/11	2.0 (0.5-7.9)
Ever spray weed killers on farm	1/7	0.9 (0.1-7.6)
Ever sprayed chemicals not on farm (lawns, garden, etc.) as part of work	1/8	0.7 (0.1-5.4)
Occupational exposures outside poultry and meat industries		
Ever worked in textile plant	2/2	5.9 (0.9-39.3)
Ever worked where asbestos was handled	2/6	3.4 (0.8-14.7)
Ever worked where exposed to coal tar, turpentine, naphthalene, natural gas, paraffin, or smoke	3/7	2.9 (0.8-10.7)
Ever worked in forestry	1/1	2.8 (0.2-32.0)
Ever worked in smelter where metals were smelted	2/5	2.3 (0.4-12.8)
Ever worked in dry cleaning	1/3	2.1 (0.2-21.3)
Ever worked in place with exposure to machine oils	6/28	1.9 (0.7-5.3)
Ever worked in plant where lumber was handled	4/11	1.6 (0.5-5.4)
Ever worked where exposure to gasoline, petro, kerosene, or heating fuel occurred	2/9	1.4 (0.3-6.8)
Ever worked as a construction worker	5/22	1.2 (0.4-3.6)
Ever have pets at home	16/99	1.1 (0.4-2.9)
Ever worked with paints at work	3/19	1.1 (0.3-3.6)
Ever worked in a gas station or gasoline storage facility	1/11	1.0 (0.2-4.8)
Ever worked where exposed to sand/dust	3/26	0.8 (0.3-2.8)
Ever worked in an auto mechanic shop	2/16	0.8 (0.2-3.9)
Medical conditions		
Ever been diagnosed with cirrhosis	1/1	6.2 (0.4-104.0)
Ever diagnosed with Parkinson's Disease	1/1	5.6 (0.3-92.9)
Ever diagnosed with small pox	1/2	3.6 (0.3-42.3)
Ever been allergic to skin applications	2/4	2.3 (0.5-12.2)
Ever diagnosed with herpes	1/3	1.5 (0.2-13.9)
Ever had heart burn or indigestion for long periods of time	8/50	1.1 (0.4-2.8)
Ever had blood transfusion	4/27	1.1 (0.3-3.5)
Ever have constipation for long periods of time	4/28	1.1 (0.3-3.4)
Ever been diagnosed with diabetes	5/28	1.1 (0.3-3.6)
Ever hospitalized for an infection	4/21	1.0 (0.3-3.2)
Ever have warts on any part of body	1/49	0.1 (0.0-0.6)
Ever diagnosed with bile/acid problems	5/34	0.8 (0.3-2.4)
Ever had surgery to stomach or bowel	5/46	0.7 (0.3-2.1)
Ever diagnosed with migraines	4/29	0.7 (0.2-2.4)
Ever had cold sores on lip	6/52	0.6 (0.2-1.6)
Ever diagnosed with anemia	2/20	0.6 (0.1-2.9)
Every diagnosed with muscle weakness or paralysis	2/23	0.6 (0.1-2.7)
Ever had occupational allergies	1/10	0.5 (0.1-4.5)
Ever been allergic to any other substances	1/14	0.5 (0.1-3.9)
Ever been allergic to foods	1/10	0.5 (0.1-3.8)
Ever diagnosed with mumps	6/101	0.5 (0.1-1.6)
Ever been allergic to animals	1/15	0.4 (0.1-3.4)
Ever had a head injury	1/16	0.4 (0.1-3.2)
Ever diagnosed with rubella	2/57	0.4 (0.1-1.8)
Ever developed baldness before 40 years of age	3/23	0.4 (0.1-1.6)
Ever been diagnosed as having a peptic ulcer	1/21	0.3 (0.0-2.3)
Ever been allergic to pollen	2/46	0.2 (0.0-0.8)
Ever diagnosed with measles	7/112	0.2 (0.1-0.6)
Ever been allergic to dust	1/34	0.1 (0.0-1.0)
Tobacco use		
Ever smoked cigarettes	19/94	Crude OR = 2.7 (0.9-8.3)
Ever chewed tobacco	1/23	0.3 (0.0-2.0)
Ever smoked pipe	4/12	1.4(0.4-5.5)

(Continued)

**TABLE 3.** (Continued)

	Exposed (cases/control)	Adjusted OR (95% CI)*
Ever lived in same house with someone who smoked tobacco for > 10 years	13/103	0.9 (0.3-2.3)
Ever smoked cigars	3/20	0.8 (0.2-3.0)
Alcohol ingestion		
Ever drank beer	16/71	2.3 (0.8-6.5)
Ever drank liquor	9/42	1.6 (0.6-4.2)
Ever drank wine	7/50	0.6 (0.2-1.8)
Ever been drunk on > 5 occasions	7/53	0.6 (0.2-1.7)
Food consumed		
Ate a lot of pork	21/106	4.0 (0.9-18.1)
Ate a lot of beef	21/122	3.3 (0.4-25.6)
Ate a lot of lamb	3/8	2.9 (0.7-11.9)
Drank coffee for > 1 year	21/110	2.6 (0.5-12.2)
Ate raw eggs at least once every 2 weeks for most life	1/5	2.5 (0.3-24.0)
Ate a lot of nuts	12/73	2.0 (0.7-5.4)
Ate a lot of peanuts	6/34	1.8 (0.7-5.0)
Ate a lot of cheese	19/121	1.8 (0.4-7.7)
Ate a lot of spicy foods	12/61	1.7 (0.7-4.1)
Ate a lot of turkey	11/61	1.5 (0.6-3.7)
Drank a lot of soda	15/96	1.4 (0.5-4.0)
Drank unpasteurized milk at least once every 2 weeks for most of life	4/20	1.4 (0.4-4.6)
Ate freshwater fish from rivers and lakes at least once a month	7/55	0.9 (0.4-2.4)
Ate a lot of seafood	12/83	0.9 (0.4-2.2)
Drank a lot of milk	18/110	0.9 (0.3-2.7)
Ate a lot of fruits	18/128	0.6 (0.2-2.1)
Ate a lot of veggies	22/139	0.5 (0.1-5.4)
Ate a lot of cereal	11/108	0.5 (0.2-1.4)
Mostly prepared own food	14/122	0.5 (0.2-1.4)
Use vitamins at least every week for > 1 year	6/84	0.4 (0.1-1.0)
Ever ingested herbal leaves, drinks, medications at least once a week for > 1 year	1/19	0.3 (0.04-2.7)
Method of cooking meat		
Preferred eating meat barbecued	13/61	2.4 (0.9-6.2)
Drug use		
Ever used hormone replacement therapy or drugs continuously for at least 1 year to control hot flashes	1/16	3.8 (0.1-157.2)
Ever had dye injected for x-ray procedures	5/63	0.7 (0.2-2.2)
Use vitamins at least every week for > 1 year	6/84	0.4 (0.1-1.0)
Ever used steroids at least once every week for > 1 year	0/7	—
Ever have general anesthesia during surgery	11/108	0.4 (0.1-1.2)
Family history or conditions		
Reported cancer in children	4/15	3.6 (0.8-16.1)
Reported cancer in spouse	3/6	1.6 (0.5-5.4)
Reported cancer in parents	7/54	0.7 (0.3-2.3)
Ever treated with radiation for medical condition		
Ever treated with radiation therapy for cancer	7/8	5.4 (0.9-34.3)
Ever treated with radiation therapy for skin/scalp conditions	1/1	2.5 (0.1-50.4)
Ever treated with radiation therapy for arthritis	2/4	1.2 (0.1-10.2)
Immunizations		
Ever receive immunizations against pneumococcal infections	2/17	2.0 (0.5-8.4)
Ever receive immunizations against diphtheria	7/84	1.7 (0.3-8.4)
Ever receive immunizations against typhoid	2/21	1.5 (0.4-6.1)
Ever receive immunizations against yellow fever	1/14	1.4 (0.3-7.2)
Ever receive immunizations against measles	9/80	1.4 (0.4-4.5)
Ever receive immunizations against tuberculosis	6/66	1.3 (0.4-4.5)
Ever receive immunizations against tetanus	13/118	1.3 (0.2-11.2)
Ever receive immunizations against flu	8/83	1.2 (0.4-3.7)
Ever receive immunizations against small pox	9/86	1.2 (0.3-3.9)
Ever receive immunizations against mumps	8/77	1.1 (0.4-3.4)
Ever receive immunizations against rubella	7/78	1.0 (0.3-3.2)

(Continued)

TABLE 3. (Continued)

	Exposed (cases/control)	Adjusted OR (95% CI)*
Other exposures		
Mostly worked in jobs involving heavy physical activity	14/87	1.4 (0.5-3.8)
Mostly worked in sedentary jobs	4/40	0.5 (0.2-1.9)
Swam at least once a month for > 1 year	2/36	0.3 (0.1-1.4)
Regularly performed any exercise	6/104	0.2 (0.1-0.5)
Ever used dye or hair sprays continuously for at least 1 year	2/47	0.2 (0.1-1.0)
Ever owned a cell phone	2/69	0.0 (0.0-0.3)

CI = confidence interval; OR = odds ratio.

\*Adjusted for ever smoking.

the OR given for specific poultry tasks are probably attenuated, because many of those who answered "No" for exposure to a specific poultry task may also be exposed to poultry from performing poultry tasks other than the one in question. Hence essentially, the statistically significant OR associated with killing and catching live poultry simply represent the two activities with the highest risks of pancreatic or liver cancer in poultry plants. Other OR listed in Tables 2-4 may actually be associated with increased risk of these diseases compared to background even though they may not be statistically significant. Also, as seen in Table 1, interviewed controls were more likely to be exposed to poultry than the total number of controls, whereas interviewed liver cancer cases were less likely to be exposed to poultry than the total number of liver cancer cases. The net effect of these imbalances is that again the risk estimates given for poultry-related exposures were further underestimated, especially for liver cancer.

The study identified killing of chickens and catching live chickens at work as independent risk factors for pancreatic and liver cancers, because the risks persisted even after adjusting for each of nonpoultry exposures identified in the study to be significantly associated with these diseases. This is a new and important finding. It is consistent with the observed increased risk associated with killing of food animals other than poultry (Table 2), and with the excess of these cancers observed in the original cohort studies of these poultry workers (16-19). It is also consistent with a similar finding in the pilot case-cohort study of lung cancer in this same cohort (22). Interestingly, a high risk of lung cancer associated with working in the stockyard and killing/dressing departments of abattoirs handling cattle, pigs, and sheep was also observed in another of our studies in the meat industry (23). In the present study, the OR for working in the stockyard were 7.9 (95% CI: 0.6-106.5) and 2.1 (95% CI: 0.2-22.5), for liver and pancreatic cancers, respectively. The association of lung cancer with slaughtering or freshly killed meat has been reported by others (24, 25), not considering several reports of an association between lung cancer and butchers/meat cutters, or working in slaughterhouses, e.g., the report by Fox and Lynge (26).

Working in the stockyard and slaughtering departments of these plants is associated with high exposure to microorganisms present in these animals, including oncogenic viruses. Thus the association observed in this study for liver and pancreatic cancer with killing and catching live poultry suggests that exposure to these viruses could be an important risk factor for these diseases, especially as no other potentially carcinogenic exposures are associated with these activities.

The association between pancreatic cancer and working in a pig-raising farm is new, and its significance is unknown at the moment.

This pilot study showed that the results obtained for established/previously reported risk factors for liver cancer, such as cirrhosis of the liver, infectious mononucleosis, hepatitis, and eating a lot of peanuts (surrogate aflatoxin exposure) are remarkably consistent with the literature (27, 28).

Similarly, the findings in Table 2 for exposure to dyes, pancreatitis, eating a lot of bacon (surrogate for exposure to nitrosamines), and eating meat smoked (polycyclic aromatic hydrocarbon exposure) or salted (exposure to nitrosamines), and in Table 3 for cigarette smoking, are in correspondence with the literature on risk factors for pancreatic cancer (28-30).

Some of the non-occupational significant findings for liver cancer were new (e.g., the increased OR associated with receiving yellow-fever and typhoid vaccines) and are supportive of the oncogenic virus hypothesis. The reasons for these findings are not known. However, both the yellow fever virus and typhoid bacteria demonstrate marked tropism for the liver in the course of infection. Furthermore, before the 1960s, yellow-fever vaccines in use were known to be contaminated with exogenous ALSV (3). Although current yellow-fever vaccines are free of exogenous ALSV, infectious endogenous ALSV have been reported in current vaccines (4, 5, 12). The nonsignificant increased risk of herpes infection (OR = 5.6, 95% CI: 0.6-57.1; not shown in the tables) for liver cancer is consistent with the increased risk associated with infectious mononucleosis that is caused by the Epstein-Barr virus, a herpes virus.

**TABLE 4.** OR results that were not statistically significantly increased—liver cancer

	Exposed (cases/control)	Adjusted OR (95% CI)*
<b>Poultry—specific exposures</b>		
Ever worked in plant where poultry smoked	1/3	15.75 (0.82–301.01)
Ever worked in plant where poultry cooked	3/41	2.0 (0.3–13.0)
Ever worked in plant where poultry slaughtered	4/71	1.6 (0.2–15.4)
Ever come in direct contact with blood of chickens/birds at work	4/52	1.2 (0.3–4.4)
Ever worked on commercial poultry farm	1/17	1.2 (0.1–12.8)
Ever catch live chickens/birds at work	1/16	1.0 (0.1–8.5)
Ever killed chicken/birds outside of work	2/31	0.9 (0.2–4.5)
Ever load and unload chickens/birds from trucks	1/18	0.8 (0.1–6.3)
Ever wrap raw chickens/birds at work	2/41	0.6 (0.1–2.8)
Ever cut raw/chickens/birds at work	3/66	0.5 (0.1–2.0)
Ever worked where poultry waste was used or handled	1/31	0.5 (0.1–4.8)
Ever worked where poultry was deboned	2/64	0.4 (0.1–3.4)
Ever worked where poultry feathers were handled	1/37	0.4 (0.0–4.0)
Ever come into contact with or handle unwrapped raw chicken/birds at work	4/78	0.4 (0.0–3.2)
Ever handled poultry	4/102	0.3 (0.1–1.0)
Ever worked in plant where raw poultry processed and packed in plastic (not slaughtered)	2/76	0.2 (0.0–1.4)
Ever pack already wrapped raw chicken/birds	2/42	0.7 (0.1–3.6)
<b>Miscellaneous, mixed poultry and meat exposures</b>		
Ever worked in stockyard	1/2	7.9 (0.6–106.5)
Ever worked in a kitchen	2/29	1.5 (0.2–9.7)
Ever worked as meat cutter (no kill)	3/33	1.4 (0.4–5.5)
Ever worked as a chef or cook	2/27	1.1 (0.2–5.6)
Ever worked in a restaurant	2/40	0.9 (0.1–5.8)
<b>Exposures associated with killing animals other than poultry</b>		
Ever killed sheep	1/3	5.4 (0.5–56.3)
Ever worked as butcher (killing animals)	1/4	2.9 (0.3–25.9)
Ever killed food animals at work such as cows, pigs, sheep	1/6	2.5 (0.3–22.1)
Ever killed other type of animals for food	1/6	2.0 (0.2–18.2)
Ever killed pigs	1/8	2.0 (0.2–18.3)
Ever killed cattle	1/9	1.9 (0.2–17.7)
<b>Occupational seafood exposures</b>		
Ever handled seafood at work	3/21	2.6 (0.6–10.5)
Ever worked in plant where seafood processed	2/21	1.5 (0.3–7.3)
<b>Lived on the farm</b>		
Ever lived on a cattle farm as a child	2/36	0.7 (0.1–3.3)
Ever lived on a farm as a child	2/62	0.3 (0.1–1.6)
<b>Occupational exposures outside poultry and meat industries</b>		
Ever worked where asbestos was handled	2/6	5.5 (1.0–30.8)
Ever worked in grainery where grains or nuts were stored	1/4	4.2 (0.4–41.9)
Ever worked where exposed to coal tar, turpentine, naphthalene, natural gas, paraffin, or smoke	1/7	1.8 (0.2–15.1)
Ever worked where exposure to gasoline, petro, kerosene, or heating fuel occurred	1/9	1.5 (0.2–13.2)
Ever worked in a gas station or gasoline storage facility	1/11	1.4 (0.2–12.1)
Ever worked as a construction worker	2/22	1.2 (0.2–5.8)
Ever worked in plant where lumber was handled	1/11	1.1 (0.1–9.9)
Ever worked in place with exposure to machine oils	2/28	1.0 (0.2–4.7)
Ever worked in an auto mechanic shop	1/16	0.8 (0.1–7.0)
Ever worked where exposed to sand/dust	1/26	0.5 (0.1–3.8)
<b>Medical conditions</b>		
Ever diagnosed with herpes	1/3	5.6 (0.6–57.1)
Ever been diagnosed as having a peptic ulcer	3/21	2.5 (0.6–10.6)
Ever had blood transfusion	3/27	2.0 (0.5–8.2)
Ever had heart burn or indigestion for long periods of time	5/50	1.9 (0.6–6.5)
Ever have constipation for long periods of time	3/28	1.8 (0.4–7.6)
Ever been diagnosed with diabetes	3/28	1.8 (0.4–7.6)
Ever diagnosed with anemia	2/20	1.6 (0.3–8.0)
Ever diagnosed with migraines	3/29	1.5 (0.4–6.2)
Ever been allergic to feathers	1/9	1.4 (0.2–11.9)

(Continued)

TABLE 4. (Continued)

	Exposed (cases/control)	Adjusted OR (95% CI)*
Ever had occupational allergies	1/10	1.3 (0.2-10.8)
Ever been allergic to foods	1/10	1.2 (0.1-9.8)
Ever had surgery to stomach or bowel	3/46	0.9 (0.2-3.7)
Ever been allergic to any other substances	1/14	0.9 (0.1-7.3)
Ever had a head injury	1/16	0.9 (0.1-7.3)
Ever been allergic to animals	1/15	0.8 (0.1-7.0)
Ever diagnosed with bile/acid problems	2/34	0.7 (0.2-3.6)
Ever diagnosed with muscle weakness or paralysis	1/23	0.6 (0.1-5.3)
Ever hospitalized for an infection	1/21	0.6 (0.1-4.9)
Ever been allergic to dust	2/34	0.6 (0.1-2.7)
Ever diagnosed with chicken pox	5/111	0.5 (0.1-2.5)
Ever diagnosed with rubella	2/57	0.5 (0.1-2.3)
Ever been allergic to pollen	2/46	0.4 (0.1-2.0)
Ever developed baldness before 40 years of age	1/23	0.3 (0.0-2.7)
Ever diagnosed with measles	5/112	0.3 (0.1-1.2)
Ever diagnosed with mumps	3/101	0.3 (0.1-1.5)
Ever been allergic to drug medications	1/39	0.3 (0.0-2.2)
Tobacco use		
Ever smoked pipe	1/12	1.5 (0.2-13.8)
Ever chewed tobacco	2/23	1.4 (0.3-6.8)
Ever lived in same house with someone who smoked tobacco for > 10 years	7/103	0.9 (0.2-3.0)
Ever smoked cigars	1/20	0.8 (0.1-7.1)
Alcohol ingestion		
Ever drank beer	5/71	1.6 (0.4-6.4)
Ever drank liquor	3/42	1.2 (0.3-5.4)
Ever been drunk on > 5 occasions	3/53	1.1 (0.2-6.1)
Ever drank wine	2/50	0.5 (0.1-2.5)
Other		
Mostly worked in sedentary jobs	5/40	3.0 (0.8-11.3)
Ever have pets at home	6/99	0.6 (0.2-2.0)
Mostly worked in jobs involving heavy physical activity	4/87	0.5 (0.1-1.8)
Swam at least once a month for > 1 year	1/36	0.4 (0.1-3.0)
Regularly performed any exercise	3/104	0.2 (0.0-0.7)
Ever used dye or hair sprays continuously for at least 1 year	1/47	0.2 (0.0-1.9)
Food consumed		
Ate a lot of nuts	8/73	6.8 (0.9-51.4)
Ate uncooked food	1/4	4.1 (0.4-39.9)
Ate a lot of lamb	2/8	4.2 (0.8-22.7)
Ate a lot of cereal	9/108	2.7 (0.4-20.0)
Ate a lot of spicy foods	6/61	2.7 (0.7-11.1)
Ate a lot of turkey	5/61	1.4 (0.4-4.9)
Ate a lot of cheese	8/121	1.3 (0.2-10.1)
Ate freshwater fish from rivers and lakes at least once a month	4/55	1.1 (0.3-4.1)
Drank coffee for > 1 year	7/110	0.8 (0.2-3.5)
Ate a lot of chicken	10/133	0.7 (0.1-6.2)
Drank unpasteurized milk at least once every 2 weeks for most of life	1/20	0.7 (0.1-5.6)
Ate a lot of seafood	5/83	0.6 (0.2-2.0)
Drank a lot of soda	5/96	0.5 (0.1-1.7)
Ate a lot of fruits	7/128	0.5 (0.1-2.5)
Use vitamins at least every week for > 1 year	3/84	0.3 (0.1-1.1)
Mostly prepared own food	7/122	0.3 (0.1-1.1)
Ate a lot of veggies	8/139	0.2 (0.0-2.2)
Method of cooking meat		
Preferred eating meat fried	10/110	3.1 (0.4-24.7)
Preferred eating meat smoked	4/35	2.2 (0.6-8.1)
Preferred eating meat barbecued	6/61	2.1 (0.6-7.8)
Preferred eating meat salted	5/52	1.9 (0.5-6.9)
Drug use		
Ever used steroids at least once every week for > 1 year	1/7	2.6 (0.3-24.9)

(Continued)

TABLE 4. (Continued)

	Exposed (cases/control)	Adjusted OR (95% CI)*
Ever had dye injected for x-ray procedures	4/63	1.0 (0.3-3.9)
Ever have general anesthesia during surgery	7/108	0.7 (0.2-2.6)
Use vitamins at least every week for > 1 year	3/84	0.3 (0.1-1.2)
Family history of cancer		
Reported cancer in children	1/6	2.0 (0.2-19.2)
Reported cancer in spouse	2/15	2.4 (0.5-11.5)
Reported cancer in parents	1/54	0.2 (0.0-2.0)
Ever treated with radiation for medical condition		
Ever treated with radiation therapy for skin/scalp conditions	1/1	10.3 (0.6-172.5)
Ever treated with radiation therapy	2/18	2.3 (0.4-11.7)
Immunizations		
Ever receive immunizations against mumps	6/77	3.5 (0.4-30.0)
Ever receive immunizations against diphtheria	7/84	3.2 (0.4-25.7)
Ever receive immunizations against tuberculosis	6/66	2.8 (0.5-14.2)
Ever receive immunizations against pneumococcal infections	1/17	2.6 (0.2-28.7)
Ever receive immunizations against flu	7/83	2.1 (0.4-10.3)
Ever receive immunizations against rubella	6/78	1.7 (0.3-8.9)
Ever receive immunizations against small pox	6/86	1.5 (0.3-7.3)
Ever receive immunizations against measles	5/80	1.5 (0.3-7.3)
Ever receive immunizations against tetanus	8/118	1.3 (0.3-6.8)
Ever receive immunizations against meningococcal infections	1/7	0.9 (0.1-8.2)

CI = confidence interval; OR = odds ratio.

\*Adjusted for ever cigarette smoking.

The study did not have sufficient power to investigate the other potentially carcinogenic exposures in poultry slaughtering and processing plants associated with curing, smoking, and cooking of poultry. It is noted however, that the use of the wrapping machine was not associated with increased risk of either disease.

## CONCLUSIONS

This small study, despite its low statistical power, succeeded in identifying known established risk factors in the literature for both liver and pancreatic cancers. There was no evidence of the occurrence of significant selection/response or recall bias that could have caused artificial elevation of the reported increased risks. Importantly, the study found a possible association between the excess occurrence of liver and pancreatic cancers in poultry workers and workplace activities associated with the highest risk of exposure to poultry oncogenic viruses. The significance of this finding is unknown at this time, because of the preliminary nature of study, especially as it was not possible to adjust completely for important confounders. Effect estimates were imprecise. However, the findings need to be further pursued in other studies, because they may have profound public health implications if later found to be true. Full-scale large case-cohort studies or nested case-control studies of these cancers within occupational cohorts of poultry workers of sufficient statistical power are needed. Such studies will be able to investigate exposures in detail and control for non-

occupational and the other occupational carcinogenic exposures associated with curing, smoking, cooking, and wrapping of poultry in these plants (31-37). These studies will throw more definitive light on this issue, and should be greatly encouraged.

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