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Cancer among farmers

A review

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BLAIR A, MALKER H, CANTOR KP, BURMEISTER L, WIKLUND K. Cancer among farmers: A review. *Scand J Work Environ Health* 11 (1985) 397—407. During the performance of routine tasks farmers may come in contact with a variety of substances, including pesticides, solvents, oils and fuels, dusts, paints, welding fumes, zoonotic viruses, microbes, and fungi. Because some of these substances are known or suspected carcinogens, the epidemiologic literature regarding cancer risks concerning farmers has been reviewed. Farmers had consistent deficits for cancers of the colon, rectum, liver, and nose. The deficits for cancer of the lung and bladder were particularly striking, presumably due to less frequent use of tobacco among farmers than among people in many other occupational groups. Malignancies frequently showing excesses among farmers included Hodgkin's disease, leukemia, non-Hodgkin's lymphoma, multiple myeloma, and cancers of the lip, stomach, prostate, skin (nonmelanotic), brain, and connective tissues. The etiologic factors that may contribute to these excesses in the agricultural environment have not been identified. Detailed, analytic epidemiologic studies that incorporate environmental and biochemical monitoring are needed to clarify these associations.

Key terms: analytic epidemiology.

Farming is a physically demanding occupation that requires varied skills. Farmers routinely perform tasks normally associated with other occupations; for example, they repair machinery, weld, apply pesticides, paint, and operate heavy equipment. In doing so, farmers may come in contact with a number of potentially hazardous chemical and biological agents, including pesticides, solvents, fuels and oils, dusts, zoonotic viruses, microbes, and fungi (58), some of which are known or suspected carcinogens. In addition the use of power tools and mechanized equipment and the tending of livestock place farmers at increased risk of accidental death or injury (15, 53, 68).

Despite these potential hazards, overall mortality among farmers is less than that among the general population (38, 43, 63) and many other occupations, including some white-collar groups. Lower mortality rates for ischemic heart disease among farmers than among other occupational groups have been reported from England and Wales (38), Australia (63), and the United States at the national (43), county (21), and state (74) level. Despite low mortality from all causes combined, surveys of occupational groups and studies of specific tumors suggest that farmers may have elevated incidence and mortality rates for certain cancers. A thorough review of the epidemiologic literature may help focus attention on agricultural factors that pose a carcinogenic risk to farmers. Some findings are also relevant to the general public, since many chemicals used by farmers (eg, insecticides, herbicides, paints, and solvents) are also used by other segments of the population.

Materials and methods

We have assembled findings from epidemiologic studies and broad occupational surveys of cancer mortality and morbidity among farmers from industrialized countries around the world. Table 1 details the occupational surveys included in this review, while tables 2—5 present observed and expected numbers and ratios from these surveys by cause. The statistical significance of the ratios of the observed and expected numbers in tables 2—5 was assessed with the use of the ratio of a Poisson variable to its expectation following the procedure of Bailar & Ederer (4). In order to summarize data from broad occupational surveys, we have grouped the cancers into three categories according to their pattern of risk among these populations. Cancers that occur among farmers more frequently than expected (risk ratios >1.0) in at least two-thirds of the surveys are in the high-risk category, while those that are not elevated or elevated in less than one-third of the surveys are in the low-risk category. The remaining cancer sites with elevated risks among farmers in more than one-third but less than two-thirds of the studies form the intermediate category.

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Table 1. Description of the occupational mortality and morbidity studies surveyed.

Geographic location of study	Data base	Years	Total number of white male subjects	Number of malignant neoplasms among farmers	Age range (years)	Mortality/ incidence index[a]	Occupation	Reference
United States, Washington State	Death certificates	1950—1979	429 926	4 654	≥20	PMR	Usual	Milham (65)
United States, California	Death certificates	1951—1961	200 000	1 956	≥20	PMR	Latest	Petersen & Milham (73)
The Netherlands	Death certificates	1931—1935	23 318	2 801	All ages	PMR	Latest and previous	Versluys (89)
United States, Iowa	Death certificates and census	1971—1978	All white men	Not given	20—64	SMR	Usual	Pomrehn et al (74)
	Death certificates	1971—1978	121 101	6 402	≥20	PMR	Usual	Burmeister (16)
United States	Death certificates and census	1950	All white men	5 165	20—64	SMR	Usual	Guralnick (43)
United States, veterans	Veterans with life insurance	1954—1970	293 458	824	31—84	SMR	Usual	Walrath et al (90)
England and Wales	Death certificates and census	1970—1972	550 297	Not given	15—64	SMR	Latest	Fox & Goldblatt (38)
Canada	10 % census sample	1965—1969	415 201	75	All ages	SMR	Current	Howe & Lindsay (51)
Australia	Death certificates and census	1968—1978	All men	Not given	30—64	SRR	Usual	McMichael & Hartshorne (63)
Denmark	Death certificates and census	1970—1975	1 401 967	1 012	20—64 (1970)	SMR	At census (1970)	Danmarks Statistik (25)
Sweden[b]	Death certificates and census	1961—1970	3 738 861	6 593	≥15 (1960)	SMR	At census (1960)	.
United States, Massachusetts	Death certificates	1971—1973	34 879	183	≥20	MOR	Usual	Dubow & Wegman (30)
Sweden[c]	National Swedish Cancer-Environment Register	1961—1979	3 738 861	28 226	≥15 (1960)	SIR	At census (1960)	.
United States, Roswell Park	Hospital register	1956—1965	6 434 + unknown number of referents	275	≥15	OR	Lifetime occupational history	Decoufle et al (26)
United States, Third National Cancer Survey	10 % interview survey of all incident cancer cases	1969—1971	3 539	109	≥15	OR	Usual	Williams et al (94)
British Columbia	Death certificates	1950—1978	254 901	4 602	≥20	PMR	Usual	Gallagher et al (39)

[a] PMR = proportionate mortality ratio, SMR = standardized mortality ratio, SRR = standardized risk ratio, MOR = mortality odds ratio, SIR = standardized incidence ratio, OR = odds ratio.
[b] Data from the linked register between the Death Cause Register (1961—1970) and the census of 1960 (82).
[c] Data from the linked register between the National Swedish Cancer Register (1961—1979) and the census of 1960 (93).

Results

Tables 2—6 display the risks for selected diseases among farmers from various countries. The studies are grouped according to design (ie, proportionate mortality, cohort, or case-referent). Although risks vary from population to population, certain patterns occur.

Mortality from all causes, arteriosclerotic heart disease, and all cancer is low among farmers. Specific cancers that fall into the low-risk category for farmers include those of the colon, rectum, liver, nose, lung, and bladder. Each survey showed a deficit for cancers of the lung and bladder, presumably due to the less frequent use of tobacco by farmers than by other occupational groups (21, 63, 84, 85). In Sweden, for example, in the early 1960s about 30 % of farmers smoked in comparison to nearly 50 % of the general population (22). These figures would imply a relative risk of about 0.6 for lung cancer among farmers, on the assumption of a 10-fold relative risk for smoking (3). The consistent deficits for cancers of the colon

may be related to high levels of physical activity among farmers (40). Reasons for the low risk of cancers of the rectum, liver, and nose are not clear.

Malignancies commonly high among farmers include Hodgkin's disease, multiple myeloma, and cancers of the lip, stomach, prostate, skin (nonmelanotic), brain and connective tissue. The remaining cancers [ie, non-Hodgkin's lymphoma, leukemia, and cancers of the skin (melanoma), esophagus, pancreas, testis and kidney] show a generally inconsistent pattern. Leukemia, non-Hodgkin's lymphoma, and cancers of the skin (melanoma) and pancreas show relative risks greater than 1 in more than 50 % of the surveys.

The observed numbers of specific cancers were small in a few surveys, and cancers with fewer than three cases or deaths were dropped from consideration in table 6. Despite this restriction, the risk pattern in table 6 is nearly identical to that in tables 2—5. Cancers commonly high among farmers (ie, elevated risk in two-thirds of the eligible surveys) in the restricted evaluation included Hodgkin's disease, multiple myeloma, leukemia, and cancers of the lip, stomach, prostate, skin (nonmelanotic), brain and connective tissue. The relative risks for these sites were usually less than 1.5, except for cancer of the lip, for which five of six studies had relative risks greater than 1.5. For the other cancers in the commonly high category, the proportion of the studies with relative risks less than 1.1 was 8 % for stomach, 33 % for prostate, 20 % for nonmelanotic skin, 38 % for brain, and 20 % for connective tissue cancer and 33 % for Hodgkin's disease, 17 % for multiple myeloma, and 22 % for leukemia. Sites generally not elevated in this restricted set of studies included cancer of the esophagus, colon, rectum, liver, nose, lung, and bladder.

The risks among farmers are not exceptionally high for most cancers, and many elevations did.not achieve statistical significance. The proportion of studies reported in table 6 with statistically significant elevations in relative risks by specific cancer was lip (43 %), stomach (58 %), prostate (33 %), skin (40 %), brain (0 %), connective tissue (0 %), Hodgkin's disease (0 %), multiple myeloma (43 %), and leukemia (22 %). The consistent excesses for specific cancers across these broad surveys prompted us to conduct a detailed review of the literature for further information on the sites of particular interest, ie, those in the commonly high category.

Leukemia

Of studies investigating the association between farming and cancer, leukemia has received the most attention.

Table 2. Mortality from all causes, heart disease, and cancer among farmers from various countries.

Country[a]	All causes		Arteriosclerotic heart disease		All cancer	
	N[b]	Risk	N[b]	Risk	N[b]	Risk
I. Proportionate mortality ratios (risk = PMR)						
United States, Washington (65)	..	..	11 315	0.98*	4 654	0.95*
United States, California (73)	..	..	4 792	1.00	1 956	0.98
United States, Iowa (16)	..	..	..	..	6 402	0.97*
The Netherlands (89)	..	..	..	..	2 801	1.00
British Columbia (39)	..	..	11 100	1.01	4 602	0.94*
II. Standardized mortality ratio (risk = SMR)						
United States (43)	36 273	0.83*	8 648	0.69*	5 165	0.77*
United States, veterans (90)	4 489	0.92*	1 797	0.91*	824	0.90*
United States, Iowa (74)	..	0.93*	..	0.92*	..	0.89*
England and Wales[c](38)	10 041	0.91*	..	0.82	..	0.92
Canada (51)	331	0.88*	..	..	75	0.87
Denmark (25)	3 283	0.67*	1 087	0.68*	1 012	0.67*
Australia (63)	..	0.90*	..	0.86*	..	..
Sweden (82)	32 151	0.82*	10 252	0.78*	6 593	0.85*
III. Standardized incidence ratios (risk = SIR)						
Sweden (93)	..	..	..	..	28 205	0.92*
IV. Case-referent studies (risk = odds ratio)						
United States, Roswell Park (26)	..	..	..	..	..	..
United States, Third National Cancer Survey (94)	..	..	..	..	..	..
United States, Massachusetts[d] (30)	..	..	..	..	181	0.78*
Percentage of surveys showing excess (with number excessive/total in parentheses)	0 (—/18)		10 (1/10)		0 (—/14)	
Risk category[e]	Low		Low		Low	

[a] Reference in parentheses.
[b] For the proportionate and standardized mortality ratios N = number of deaths among the farmers; for the case-referent studies N = number of farmers among the cases.
[c] Farmers, foresters, and fishermen.
[d] Risk determined from the mortality odds ratio.
[e] Low = cancer occurrence not elevated or elevated in less than one-third of the surveys.
* $p \leq 0.05$.

Table 3. Risk of cancer of the lip, esophagus, stomach, colon, rectum, liver, and pancreas among farmers from various countries. (Numbers and risks connected with a broken line are figures for the included group of cancer sites)

Country[a]	Cancer sites													
	Lip		Esophagus		Stomach		Colon		Rectum		Liver		Pancreas	
	N[b]	Risk	N[b]	Risk	N[b]	Risk	N[b]	Risk	N[b]	Risk	N[b]	Risk	N[b]	Risk
I. Proportionate mortality ratios (risk = PMR)														
United States, Washington (65)	21	1.56	82	0.83	573	1.18*	428	0.88*	203	0.94	91	1.02	323	1.09
United States, California (73)	3	1.30	55	1.23	210	1.12	188	0.98	93	0.92	13	0.77	139	1.17
United States, Iowa (16)	20	1.62	95	0.74*	338	1.14*	1 064	----------		1.03	54	0.90	416	1.07
The Netherlands (89)	25	1.87*	171	0.92	1 566	1.23*	163	0.78*	166	0.90	159	1.06	17	0.52*
British Columbia (39)	17	1.91*	68	0.59*	672	1.19*	389	0.84*	..	..	..	..	334	1.05
II. Standardized mortality ratio (risk = SMR)														
United States (43)	..	..	..	..	763	0.89*	647	----------		0.69	..	..	..	..
United States, veterans (90)	..	..	9	0.61	60	1.07	87	0.71*	32	0.79	19	0.83	60	1.03
England and Wales[c] (38)	..	..	..	1.13	..	0.97	..	1.20	..	1.00	..	..	..	1.02
Canada (51)	..	..	2	1.10	15	1.77	4	0.53	4	1.16	..	..	3	0.57
Denmark (25)	343	----------												0.72*
Australia (63)	..	..	..	..	..	0.96	..	0.81*	..	0.84*	..	..	..	0.91
Sweden (82)	9	1.9	87	0.61	1 601	1.08*	459	0.74*	386	0.90	30	0.50*	464	0.80*
III. Standardized incidence ratio (risk = SIR)														
Sweden (93)	777	1.63*	246	0.71*	3 399	1.10*	1 850	0.80*	1 624	0.96	411	0.61*	1 021	0.88*
IV. Case-referent studies (risk = odds ratio)														
United States, Roswell Park (26)	..	..	6	1.00	22	1.67*	33	----------		0.58*	..	..	..	..
United States, Third National Cancer Survey (94)	..	..	2	1.03	4	0.49	15	1.24	6	0.77	..	..	5	1.05
United States, Massachusetts[d] (30)	..	..	..	..	..	..	7	2.33	..	..	..	..	5	1.37
Percentage of surveys showing an excess (with number excessive/total in parentheses)[e]	100	(7/7)	33	(4/12)	71	(10/14)	25	(3/12)	10	(1/10)	29	(2/7)	57	(8/14)
Risk category[f]	High		Intermediate		High		Low		Low		Low		Intermediate	

[a] Reference number in parentheses.
[b] For the proportionate and standardized mortality ratios N = number of deaths among the farmers; for the case-referent studies N = number of farmers among the cases.
[c] Farmers, foresters, and fishermen.
[d] Risk determined from the mortality odds ratio.
[e] Does not include a study if the figures given are for a group of sites.
[f] High = cancer occurrence more frequent among farmers than expected (risk ratio > 1.0) in at least two-thirds of the surveys, low = cancer occurrence not elevated or elevated in less than one-third of the surveys, intermediate = cancer occurrence elevated in more than one-third but less than two-thirds of the studies.
* $p \leq 0.05$.

Studies in the United States from Washington (64), California (35), Nebraska (10, 12), Iowa (18, 28), Wisconsin (11), and Illinois (14), as well as from British Columbia (39) and Tasmania (41), suggest that farmers are at higher risk of leukemia than many other occupations. The study from Tasmania (41) also noted increased relative risks for myeloproliferative and lymphoproliferative disorders among persons employed in rural industries (not further described). Not all studies, however, have shown this association. An initial report on leukemia incidence in Olmsted County, Minnesota, suggesting that farmers were at high risk (61), was not confirmed in a more detailed, case-referent study (62).

Recent studies have attempted to identify specific agents or farm practices related to leukemia risk. In death-certificate case-referent studies (10, 11, 18), the risk of leukemia was the greatest among farmers born after 1900 and/or dying before 65 years of age, a phenomenon suggesting that more recent agricultural practices may be associated with an increase in risk. A link with oncogenic viruses has also been suggested. This hypothesis is particularly appealing since an infectious virus has been established as the primary agent in bovine lymphoma and because human exposure may occur through contact with infected animals and/or from the use of unpasteurized milk (37). Although the virus can cross species barriers (47), there is no serologic evidence that it can be transmitted to humans (29, 80). Furthermore, findings from ecological comparisons between the distribution of cattle populations and the occurrence of human leukemia are inconsistent (7, 55, 57, 96). No such association was noted in geographic studies from Sweden (57), Russia (55), and the United States (7), nor did studies in Wisconsin (11) and New York (81) find evidence of increased risk among dairy farmers in comparison to that among other farmers. On the other hand, the frequency of bovine leukemia in areas in Poland (96) correlated positively with leukemia rates among humans, and Donham et al (28) found elevated rates of acute lymphatic leukemia among Iowa men from counties where dairying was an important agricultural activity. The rates for acute lymphatic leukemia were the highest among persons from Iowa counties where dairy herds were known to be infected with the bovine leukemia virus. Burmeister et al (18) also reported higher risks for unspecified lymphatic leukemia among Iowa farmers from dairying counties. In summary, despite some suggestive findings, the weight of serologic and epidemiologic evidence gives little support to a role for bovine leukemia viruses in the etiology of human leukemia.

Other zoonotic viruses, such as that involved in fowl leukosis, have been considered possible etiologic agents

Table 4. Risk of melanotic and nonmelanotic skin cancers and cancer of the prostate, testis, kidney, bladder and brain among farmers from various countries. (Numbers and risks connected with a broken line are figures for the included group of cancer sites)

Country[a]	Cancer sites													
	Melanoma		Non-melanotic skin		Prostate		Testis		Bladder		Kidney		Brain	
	N[b]	Risk	N[b]	Risk	N[b]	Risk	N[b]	Risk	N[b]	Risk	N[b]	Risk	N[b]	Risk
I. Proportionate mortality ratios (risk = PMR)														
United States, Washington (65)	16	0.73	48	1.25	842	1.02	9	0.88	213	0.87*	89	0.89	69	1.11
United States, California (73)	16	1.26	30	1.55*	304	1.07	5	1.37	86	0.86	44	1.07	18	0.88
United States, Iowa (16)	105	----------	----------	1.13	1 138	1.10*	..	..	274	0.92	178	1.08	111	1.10
The Netherlands (89)	69	----------	----------	1.70	132	0.88	..	..	56	0.78	10	0.73	..	..
British Columbia (39)	..	..	..	..	764	1.13*	..	..	215	0.97	..	..	..	..
II. Standardized mortality ratio (risk = SMR)														
United States (43)	..	..	..	..	263	0.88*	..	..	165	0.73*	..	..	223	0.97
United States, veterans (90)	..	..	..	..	120	1.06	..	..	20	0.50*	21	0.80	27	1.04
England and Wales[c] (38)	..	..	..	1.19	..	1.22	..	..	..	0.70	..	..	..	0.99
Canada (51)	..	..	..	..	6	1.16	..	..	..	..	..	..	4	1.77
Denmark (25)	..	..	..	..	140	----------	----------	----------	----------	----------	----------	0.73*	..	..
Australia (63)	..	..	..	..	..	..	..	..	..	0.75*	..	..	..	..
Sweden (82)	92	1.06	28	1.29	1 066	0.96	39[d]	0.90	165	0.66*	240	0.85*	164	1.03
III. Standardized incidence ratio (risk = SIR)														
Sweden (93)	383	0.85*	1 690	1.07*	6 839	1.06*	128	0.95	1 297	0.73*	1 080	0.86*	856	1.06
IV. Case-referent studies (risk = odds ratio)														
United States, Roswell Park (26)	6	3.11*	43	0.76	26	1.52	5	1.14	19	0.57*	6	1.49	2	6.53
United States, Third National Cancer Survey (94)	..	..	..	..	37	1.52*	1	2.00	6	0.65	1	0.56	1	1.73
United States, Massachusetts[e] (30)	..	..	..	..	..	..	..	..	..	..	78	1.83	..	..
Percentage of surveys showing excess (with number excessive/total in parentheses)[f]	60 (3/5)		83 (5/6)		77 (10/13)		50 (3/6)		0 (—/14)		40 (4/10)		73 (8/11)	
Risk category[g]	Intermediate		High		High		Intermediate		Low		Intermediate		High	

[a] Reference number in parentheses.
[b] For the proportionate and standardized mortality ratios N = number of deaths among the farmers; for the case-referent studies N = number of farmers among the cases.
[c] Farmers, foresters, and fishermen.
[d] Cancer of the testis and other genital organs.
[e] Risk determined from the mortality odds ratio.
[f] Does not include a study if the figures given are for a group of sites.
[g] High = cancer occurrence more frequent among farmers than expected (risk ratio > 1.0) in at least two-thirds of the surveys, low = cancer occurrence not elevated or elevated in less than one-third of the surveys, intermediate = cancer occurrence elevated in more than one-third but less than two-thirds of the studies.
* $p \leq 0.05$.

in human leukemia (47). The epidemiologic evidence to support this hypothesis is mixed. Milham (64) used death certificates from Washington and Oregon in a case-referent approach and reported a significantly elevated risk for leukemia and multiple myeloma among poultrymen, and unspecified lymphatic leukemia was elevated among Iowa farmers from counties with a large poultry industry (18). These reports suggest that oncogenic viruses (fowl leukosis) may be involved. Associations between leukemia and poultry production were not seen in other studies however (10, 75).

In several studies (10, 11, 12, 18) the subjects were stratified according to agricultural characteristics of their county of residence to uncover farm-related factors associated with the risk of leukemia. Although no single agricultural factor has been consistently associated with leukemia risk, correlations with insecticide use were noted in Nebraska (10, 12) and Wisconsin (11), with herbicide use in Iowa (18), and with corn production in Nebraska (10) and Iowa (18). Several studies have attempted to correlate specific histological types of leukemia with farm practices. Acute and chronic lymphatic and acute unspecified were the cell types most strongly associated with farming in Nebraska (10, 12) and Iowa (18, 28), while chronic myeloid leukemia showed the strongest association among Wisconsin farmers (11). In Iowa (18) unspecified lymphatic leukemia was elevated among farmers from heavy soybean-producing counties, while in Nebraska (12) acute lymphatic leukemia and acute and chronic myeloid leukemia were associated with corn production.

Other lymphatic and hematopoietic cancers

Other hematopoietic malignancies have not been as extensively studied as leukemia with regard to the role of agricultural factors. In California, farm residence was associated with leukemia mortality, but no association was found with non-Hodgkin's lymphoma, Hodgkin's disease, or multiple myeloma (35).

Cantor (19), using a death-certificate case-referent approach similar to that employed in studies of leukemia (10, 11, 18), found that Wisconsin farmers from heavy fertilizer-, herbicide-, and insecticide-using counties had increased risks of non-Hodgkin's lymphoma. The association between non-Hodgkin's lymphoma and farming in Wisconsin was stronger

Table 5. Risk of cancer of the nose, lung, and connective tissue and of non-Hodgkin's lymphoma, Hodgkin's disease, multiple myeloma, and leukemia among farmers from various countries. (Numbers and risks connected with a broken line are figures for the included group cancer sites)

Country[a]	Cancer sites													
	Nasal		Lung		Connective tissue		Non-Hodgkin's lymphoma		Hodgkin's disease		Multiple myeloma		Leukemia	
	N[b]	Risk	N[b]	Risk	N[b]	Risk	N[b]	Risk	N[b]	Risk	N[b]	Risk	N[b]	Risk
I. Proportionate mortality ratios (risk = PMR)														
United States, Washington (65)	9	0.63	646	0.79*	25	1.52	72	1.01	38	1.07	78	1.25	225	1.07
United States, California (73)	..	..	167	0.64*	8	1.21	36	0.81	20	1.34	22	1.00	97	1.15
United States, Iowa (16)	..	..	1 466	0.78*	56[c]	1.08	208	1.14*	47	1.22	133	1.27*	332	1.10
The Netherlands (89)	..	..	63	0.41*	..	..	..	..	..	..	..	..	..	..
British Columbia (39)	14	1.78	742	0.66*	..	..	102	0.99	..	..	68	1.03	219	1.22*
II. Standardized mortality ratio (risk = SMR)														
United States (43)	..	..	728	0.55*	..	..	348	0.89*	348	----------		0.89*	333	1.16*
United States, veterans (90)	..	..	144	0.83*	..	..	..	..	..	..	..	..	55	1.13
England and Wales[d] (38)	..	..	..	0.84	..	..	..	1.12[e]	..	1.03	..	..	..	..
Canada (51)	..	..	19	0.69	..	..	3	0.62	3	----------		0.62	1	0.33
Denmark (25)	..	..	234	0.44*[f]	..	..	..	..	128	----------				1.03
Australia (63)	..	..	..	0.73*	..	..	..	..	..	..	..	..	..	..
Sweden (82)	10	0.60	453	0.45*	26	0.86	135	1.02	98	0.98	198	1.11	338	0.92
III. Standardized incidence ratio (risk = SIR)														
Sweden (93)	87	0.87	1 224	0.46*	216	1.04	208	1.04	267	1.04	611	1.29*	1 066	1.01
IV. Case-referent studies (risk = odds ratio)														
United States, Roswell Park (26)	..	..	..	..	..	..	19	0.59*	19	0.59*	2	0.41	7	0.58
United States, Third National Cancer Survey (94)	5	0.89	51	0.69*	..	..	1	2.15	1	1.50	1	1.17	2	0.56
United States, Massachusetts[g] (30)	..	..	15	0.79	..	..	..	..	..	..	7	3.09*	..	..
Percentage of surveys showing excess (with number excessive/total in parentheses)[h]	20 (1/5)		0 (—/15)		80 (4/5)		55 (6/11)		75 (6/8)		78 (7/9)		64 (7/11)	
Risk category[i]	Low		Low		High		Intermediate		High		High		Intermediate	

[a] Reference number in parentheses.
[b] For the proportionate and standardized mortality ratios N = number of deaths among the farmers; for the case-referent studies N = number of farmers among the cases.
[c] Connective tissue and bone cancer.
[d] Farmers, foresters, and fishermen.
[e] Lymphosarcoma only.
[f] Cancer of the respiratory system.
[g] Risk determined from the mortality odds ratio.
[h] Does not include a study if the figures given are for a group of sites.
[i] High = cancer occurrence more frequent among farmers than expected (risk ratio > 1.0) in at least two-thirds of the surveys, low = cancer occurrence not elevated or elevated in less than one-third of the surveys, intermediate = cancer occurrence elevated in more than one-third but less than two-thirds of the studies.
* $p \leq 0.05$.

among decedents born more recently and among those less than 65 years of age than among those dying at older ages. Mortality from non-Hodgkin's lymphoma in New Zealand showed a similar age pattern (72). In Iowa, however, the risk of non-Hodgkin's lymphoma was greater among farmers born before 1890 or dying after age 65 (17) and among farmers residing in counties where herbicide usage was high and in counties where chickens, hogs, and dairy products were major commodities. Results from case-referent studies in Sweden are consistent with the association between herbicide use and non-Hodgkin's lymphoma in Iowa and Wisconsin. In the Swedish study herbicide exposure was associated with a fivefold risk of Hodgkin's disease and non-Hodgkin's lymphoma (45). Most herbicide exposures in the Swedish study were farm-related. Prior to this report, Hodgkin's disease had not previously been linked to farming in general or to specific agricultural exposures (44).

Multiple myeloma has been associated with farming in Washington and Oregon (64), Wisconsin (20), Iowa (17), and Texas (1). In Wisconsin, farmers born before 1906 or dying after age 65 were at the highest risk (20), but no such pattern was discernable among Iowa farmers (17). In New Zealand the risk of multiple myeloma was greater among farmers under 65 years of age (72). In Wisconsin and Iowa, however, farmers residing in counties with heavy herbicide and insecticide use or with large chicken inventories were at higher risk than farmers residing elsewhere. Particularly striking was the elevated risk among Wisconsin farmers from heavy insecticide-using counties who were born after 1906. This was the only situation in the Wisconsin study where the relative risk for farmers born more recently was higher than those born earlier. Farmers born during this recent time period are more likely to have engaged in modern, chemical farming than farmers born earlier. In New Zealand (72) farmers in general were at higher risk of non-Hodgkin's lymphoma and multiple myeloma than other occupations. There was no association for dairy or other livestock farmers.

Soft-tissue sarcomas

Since many farmers use herbicides, Swedish reports

Table 6. Surveys with three or more deaths or cases per cancer site among farmers.[a]

Cancer site	Number eligible	Number with risk >1.0[b]	Number with risk ≥ 1.5[b]	Number with risk > 1.0 and < 1.1[b]	Number with statistically significant elevations[b]	Number with statistically significant deficits[b]
Lip	7	7 (100)	6 (86)	— (0)	3 (43)	— (0)
Esophagus	9	1 (11)	— (0)	— (0)	— (0)	3 (33)
Stomach	12	10 (83)	2 (17)	1 (8)	7 (58)	1 (8)
Colon	10	2 (20)	1 (10)	— (0)	— (0)	5 (50)
Rectum	9	1 (11)	— (0)	— (0)	— (0)	— (0)
Liver	7	2 (29)	— (0)	2 (29)	— (0)	2 (29)
Pancreas	12	7 (58)	— (0)	5 (42)	— (0)	4 (33)
Melanoma	5	3 (60)	1 (20)	— (0)	1 (20)	1 (20)
Nonmelanotic skin	5	4 (80)	1 (20)	1 (20)	2 (40)	— (0)
Prostate	12	9 (75)	2 (17)	4 (33)	4 (33)	1 (8)
Testis	5	2 (40)	— (0)	— (0)	— (0)	— (0)
Kidney	9	4 (44)	1 (11)	2 (22)	1 (11)	2 (22)
Bladder	12	— (0)	— (0)	— (0)	— (0)	7 (58)
Brain	8	6 (75)	1 (12)	3 (38)	— (0)	— (0)
Nose	5	1 (20)	1 (20)	— (0)	— (0)	— (0)
Lung	13	— (0)	— (0)	— (0)	— (0)	11 (85)
Connective tissue	5	4 (80)	1 (20)	2 (20)	— (0)	— (0)
Non-Hodgkin's lymphoma	9	4 (44)	— (0)	3 (33)	— (0)	2 (22)
Hodgkin's disease	6	4 (67)	— (0)	2 (33)	1 (17)	1 (17)
Multiple myeloma	7	6 (86)	1 (17)	1 (17)	3 (43)	— (0)
Leukemia	9	7 (78)	— (0)	2 (22)	3 (33)	— (0)
All cancer	12	— (0)	— (0)	— (0)	— (0)	9 (75)

[a] Publications not providing number of cases not included.
[b] Percentage in parentheses.

of an increased risk of soft-tissue sarcoma among farmers and foresters with herbicide exposure are of particular interest (33, 46). The high proportionate mortality ratio for this cancer among Washington farmers (65) and the occurrence of soft-tissue sarcomas among industrial populations exposed to herbicides (24, 70, 97) raise further concerns. However, in a New Zealand case-referent study of soft-tissue sarcomas, in which most of the exposed persons were farmers, the relative risk was elevated, but less than 2 (79). Reports are not yet available from ongoing case-referent studies of soft-tissue sarcoma in the United States that specifically focus on agricultural exposures.

Lip cancer

The excess risk of lip cancer among farmers in six surveys evaluating this site is consistent with the known association with outdoor occupations (54, 59, 60). In one study of discharges from veteran's hospitals in the United States, 27 % of the lip cancer patients, but only 8 % of the referents, were farmers (54). Solar radiation is considered to play the major etiologic role in this excess.

Nonmelanotic skin cancer

As with cancer of the lip, excess mortality from nonmelanotic skin cancer among farmers (16, 26, 48, 65) is consistent with epidemiologic findings implicating ultraviolet radiation as the major etiologic factor (32, 36).

Stomach cancer

In addition to the surveys in tables 2—5, elevated mortality from stomach cancer among farmers has been reported in Kansas (49), Iowa (17), New York (56), and Ireland (78). In Iowa (17) farmers born before 1900 and residing in cattle- and corn-producing counties were at higher risk, while stomach cancer patients from the Roswell Memorial Park Institute showed an association with exposure to grain dusts (56). These findings may be confounded by social class since the risk of stomach cancer is inversely related to socioeconomic status (13). Diet is also thought to play a major role in the origin of stomach cancer, and studies indicate that a high intake of complex carbohydrates or salted food and a low intake of fresh fruits and vegetables are consistently related with high risk (69). This pattern closely parallels the diet of many nonmetropolitan families that emphasizes breads and potatoes rather than fresh fruit and vegetables (88).

There is also evidence that high nitrate intake, either from food or from water, is associated with stomach cancer. The problems caused by high nitrates are examined in detail in a report published by the National Academy of Sciences in the United States (71). Some salient facts from the report are as follows: (i) important sources of nitrates include leaching and surface runoff from croplands, (ii) agricultural watersheds have the highest nitrogen export rates, and (iii) fertilizer was the largest single anthropogenic input of fixed nitrogen into water in the contiguous United States in 1975. The two areas of highest use are the corn belt and the central valley of California. In addition several

reports (2, 50, 76, 98) have concluded that positive correlations exist between stomach cancer and nitrates in drinking water and high consumption of salt-preserved foods, presumably high in nitrate and perhaps in sodium nitrite.

In addition nitrates may interact with common herbicides such as atrazine to produce n-nitrosamine, a known mutagen. Atrazine has a low basicity, and therefore the chemical environment of the stomach may offer a suitable site for n-nitrosamine formation from ingested atrazine in drinking water (95).

Prostatic cancer

Cancer of the prostate is associated with farming occupations in several of the large surveys of occupational groups (16, 26, 65, 94). The positive correlation between county mortality rates for prostatic cancer and chicken inventory (6) is consistent with the excess mortality noted among Washington poultrymen (65). A review of occupation and industry on death certificates from the Alameda and San Francisco counties in California indicated that gardeners and groundskeepers and persons in horticultural services (which included farmers) had elevated risks for prostate cancer (34). However, a case-referent interview study of prostate cancer in Minnesota did not find farmers to be at high risk (77). In Iowa (17) prostate cancer risk was greater among farmers born before 1900 and dying at older ages. This risk was not associated with any particular agricultural commodity, nor have other studies revealed compelling associations with specific agricultural agents.

Brain cancer

Mortality from cancer of the brain and central nervous system was elevated among farmers in Minnesota (23) and among Washington ranchers, dairymen, and poultrymen (65). Children from Maryland with brain cancer were more likely to have lived on farms than children without cancer (42). Previous contact with insecticides was more common among children with brain tumors than among reference children. These differences may be partially due to selective recall, since reported exposure to insecticides did not differ between children with brain cancer and children with other tumors. In an Italian study (67), glioma patients worked in agriculture more often than referents. This association was particularly evident among those first engaged in agricultural work after 1960 and those who worked for more than 10 years; these findings suggest that modern agricultural chemicals which became commonplace in the 1960s may be involved. A report of higher levels of organochlorine compounds in adipose tissue from glioblastoma patients than from noncancer referents (87) also supports the association between pesticides and brain cancer. Although the etiology of brain cancer is not well understood, these findings, plus reports of brain cancer among petroleum workers (86), suggest that exposure to certain chemicals may play a role.

Studies of related occupations

The mortality experience of veterinarians is of interest because of exposures they have in common with farmers, particularly to insecticides and zoonotic viruses. Elevated mortality from cancers of the lymphatic and hematopoietic system, brain and central nervous system, and skin (9) among veterinarians raises suspicion that exposures common to both groups may be involved. The increased relative frequency of skin cancer among veterinarians is confined to practitioners specializing in large animals, in accord with their presumed greater exposure to sunlight. Mortality from brain cancer was found to be excessive among all types of veterinarians (small animal, large animal) and nonpractitioners such as regulators and meat inspectors and is, therefore, not likely due to occupational exposures, but rather may reflect the quality of medical care received by professional groups. The leukemia excess is probably linked to x-ray exposure, since the excess is mostly confined to veterinarians who practiced during the 1950s and 1960s, a period when there was rapid growth in diagnostic radiography without adequate attention to safety procedures (9). The role of zoonotic animal viruses in the origin of leukemia is possible, but unlikely, since we have no information to suggest that the level of contact of veterinarians with supposedly infectious animal agents has varied appreciably over the past several decades. In conclusion, although the cancer mortality pattern among veterinarians resembles that of farmers, it is unlikely that common environmental agents are involved, except for cancer of the skin.

Approximately 65 % of all pesticides used in the United States in 1976 (74 % of the herbicides, 59 % of the insecticides, and 39 % of the fungicides) were used by farmers (31). Twenty-five percent may have been applied by commercial applicators (52), who may have considerable contact with pesticides. Studies of pesticide applicators suggest that these workers may experience high risks for certain cancers, particularly cancer of the lung (5, 8), which is not excessive among farmers. Slight excesses of leukemia have also been reported among some pesticide-exposed populations (8, 27, 83), but other studies have failed to uncover significant excesses (66, 91, 92). None of the studies had the statistical sensitivity necessary to detect significant elevations in leukemia and other cancers less common than lung cancer.

Discussion

Epidemiologic studies suggest that farmers, despite their generally favorable overall mortality experience, have elevated risks for cancers of the lymphatic and hematopoietic system, stomach, prostate, brain, lip,

skin, and connective tissue. The evidence is strongest for cancer of the lip, for which heavy exposure to ultraviolet radiation undoubtedly plays a predominant role. The epidemiologic evidence for an association between farming and lymphatic and hematopoietic tumors is intriguing. Potential biases related to diagnostic practices and the quality of medical care must, however, be considered for several of the cancers commonly high among farmers. Less sensitive diagnostic practices and a limited availability of medical care in rural areas may result in an underascertainment of leukemia and cancers of the brain and prostate. Such bias would, however, tend to understate the risk of these cancers among farmers. Although studies to evaluate the level of ascertainment among farmers apparently, have not been attempted, two recent investigations comparing characteristics of prostate cancer in Iowa farmers and nonfarmers have been completed. An unpublished review of records of 800 histologically confirmed prostate cancer cases referred to University of Iowa hospitals between 1966 and 1978 indicated that the diagnosis of prostate cancer by a screening examination was less frequent for farmers (4 %, 9 %, 19 %) than for nonfarmers (10 %, 16 %, 20 %) among those aged 75, 65—74, and 50—64 years, respectively. The stage of diagnosis was localized less among farmers for each of the three age groups. Although these results were not statistically significant within each age group, they do suggest that ascertainment is lower among farmers. Another study from the Iowa Health Registry (1971—1978) on stage of diagnosis of prostate cancer indicated that fewer farmers than nonfarmers were diagnosed at stage I. The stage at diagnosis was localized in 64.3 % of 1 564 farmers, compared to 69.5 % of 2 693 nonfarmers. This difference is statistically significant ($p < 0.01$).

Specific agents that might contribute to the excesses of certain cancers among farmers have yet to be identified. The identification of such agents is difficult because farm work involves exposure to a wide variety of potentially hazardous agents for which details on duration and intensity are generally unavailable. Epidemiologic evidence for the role of oncogenic animal viruses is weak and consists primarily of sporadic reports of leukemia excesses among certain farm populations. No serologic evidence of human infection from such viruses has been found. Heavy pesticide use may account for some excess risk of cancer among farmers. The excess of leukemia among farmers suggests a link with pesticide exposure in view of the suggestion of an increased risk of leukemia among pesticide applicators and producers and case reports of pesticide-related aplastic anemia and chromosome aberrations. Although certain chemicals associated with modern agriculture are suspect, analytic studies are now needed to clarify associations between farm work and particular cancers and to identify the specific etiologic agents. These studies should include an assessment of exposure through ambient air monitoring, patch tests for skin exposures and biochemical monitoring of levels of suspect agents or their metabolites in body fluids or tissues.

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