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LEUKEMIA AND FARM PRACTICES IN IOWA[1]

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Death certificate analyses of 1675 white, male Iowans over age 30 years who died of leukemia in 1964–1978 were completed. Each case was matched to two controls on age (within two years) at death, county of usual residence and year of death. Consideration of usual occupation, as recorded on the death certificate, resulted in an odds ratio for leukemia mortality among farmers of 1.24 ($p < 0.05$). The highest odds ratios for farmers were observed in those born after 1890, those dying after 1970, and those dying at age 65 years or younger. Odds ratios for farmers were also elevated in counties with high soybean and corn production per acre for those born between 1890 and 1900. For those born after 1900, odds ratios for farmers were increased in counties with the greatest numbers of egg-laying chickens and the largest number of acres treated with herbicides. The types of leukemia causing elevated mortalities in Iowa farmers were chronic lymphatic and unspecified lymphatic. Mortality from unspecified lymphatic leukemia was associated with corn per acre, number of milk cows and number of egg-laying chickens.

agricultural workers' diseases; death certificates; leukemia; mortality

During the past two decades, several studies (1–6) have concluded that farmers are subject to increased mortality from leukemia. The studies have been based on a wide range of geographic areas, including Great Britain (5), the entire United States (1, 6) and the western United States (2–4). Of particular concern are the upper midwestern states because of the importance of farming in these states and because of the identification of high-rate leukemia mortality counties in this area (6).

More recent studies (7) have continued to indicate that leukemia mortality rates are elevated in the midwestern states. Although mortality from all cancers was lower in Iowa farmers, leukemia was one of six cancers with statistically significant elevated mortality (8). A study of Nebraska death certificates by Blair and Thomas (9) also indicated an increased mortality from leukemia in farmers. The Nebraska study is extremely important since it attempts to identify farming practices associated with leukemia. The farming practice in Nebraska most strongly associated with leukemia mortality on a county basis is corn production.

In contrast to the suggestion that farming practices peculiar to corn production may be associated with leukemia, the possibility that dairy farming may be associated with leukemia has also been suggested (10–16). Not all epidemiologic studies evaluating the association of dairy cattle and leukemia have been positive, however (17, 18). Therefore, further research to identify suspected farming practices is necessary.

Because of its high corn and dairy pro-

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duction, Iowa provides an excellent opportunity to compare the association of suspected farming practices with leukemia. Iowa ranked first in corn production by state in 1950 and 1960, compared to fifth in 1950 and third in 1960 for Nebraska (19, 20). Although Iowa's dairy production (number of cows and heifers two years old and over kept for milk) did not rank as high nationally (fifth in both 1950 and in 1960) as did corn production, it is much higher than that of Nebraska (19th and 18th in 1950 and 1960, respectively). It may be that Nebraska's dairy production is not sufficiently large to allow any association with leukemia mortality to be detected; therefore, the Iowa death certificate study was completed to determine which farming practices are associated with leukemia mortality rates.

Materials and methods

The methods utilized in the Nebraska study were duplicated whenever possible to assure comparability of the two studies. The Nebraska study was based on deaths in 1957–1974, whereas the Iowa study was based on deaths 1964–1978. The following steps, however, are common to the two studies:

1) The records of all white males, aged 30 years or more at time of death from leukemia as classified by the Seventh (code 204) and Eighth (codes 204–207) Revisions of the International Classification of Diseases (ICD) (21, 22), were abstracted from computer listings.

2) For each leukemia death (1675 in Iowa compared to 1084 in Nebraska), two nonleukemic deaths were selected as controls. The controls were matched by county of usual residence, age at death (± two years) and calendar year of death. When more than two eligible controls were identified for a case, the two controls included in the study were selected randomly. Only white males were included in both studies.

3) The usual occupation indicated on the Iowa death certificate was coded according to the 1960 Census (23) for the years 1964–1970 and according to the United States Bureau of Labor (24) for 1971–1978. The entire Nebraska study was based on occupations defined by the Bureau of the Census. However, both studies combined all "non-farmer" occupations.

4) Farm owners, tenants and laborers were all considered "farmers."

Iowa counties were ranked according to 1949 crop and livestock production provided by the Iowa Crop and Livestock Reporting Service and by pesticide usage provided by the 1964 agricultural census (25), which is the only year for which pesticide usage data are available. Crop and livestock production figures from 1949 were used to provide a 15-year lag period from time of production until the first year included in the death certificate analyses. However, agricultural production in Iowa counties has changed very little during the past three decades. Spearman rank correlation coefficients for Iowa counties ordered for each of the major agricultural production figures in 1949 and 1974 were highly significant ($p < 0.001$).

The geographic distributions of the highest producing 33 counties (of 99 counties) for selected commodities are indicated in figure 1. Ratios of production of the median county in the highest producing 33 counties to the median county in the lowest producing 66 counties ranged from 1.52 for acres in oats to 3.49 for acres in soybeans.

Estimated relative risks and associated confidence intervals were computed as suggested by Miettinen (26). All computations utilize the matching of two controls to each case.

Results

Heart disease, stroke and circulatory disease accounted for 43.5 per cent of the control deaths in Iowa (compared to 54.2

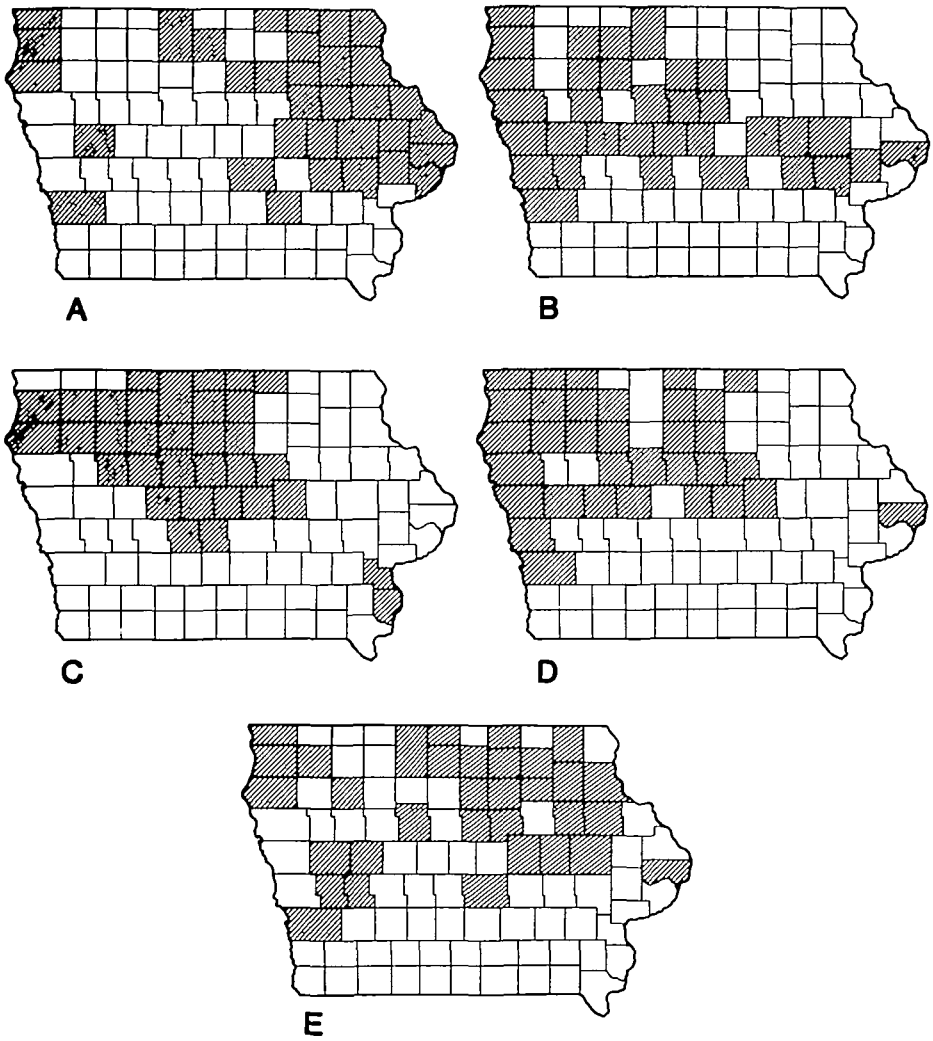

FIGURE 1. Geographic distributions of highest producing 33 Iowa counties for selected agricultural production characteristics A, milk cows; B, corn, C, soybeans, D, herbicides; E, egg-laying chickens.

per cent in Nebraska). Cancer deaths other than leukemia totaled 18.9 per cent in Iowa (compared to 10.3 per cent in Nebraska).

The distributions of usual occupation for both cases and controls are quite similar in Iowa and Nebraska (table 1). Also similar are the elevated risks of leukemia mortality for farmers. An odds ratio of 1.25 (95 per cent confidence limits of 1.05 and 1.49) was computed for Nebraska. The odds ratio for farming in Iowa was 1.24 with 95 per cent confidence limits of 1.09 and 1.42.

Table 2 summarizes the odds ratios for leukemia mortality computed for separate strata according to year of birth, year of death and age at death. Iowa farmers born after 1890 and those whose age at death was less than or equal to 65 years have odds ratios significantly greater than 1. These results are similar to those found in Nebraska where farmers born after 1900 and those aged 65 years or less

TABLE 1

Distributions of usual occupation, by death certificate analysis, of leukemia deaths and matched controls, white males over 30 years of age, resident in Nebraska dying 1957–1974, and resident in Iowa dying 1964–1978

Occupational group	Cases				Controls			
	Iowa		Nebraska		Iowa		Nebraska	
	No	%	No	%	No	%	No	%
Teachers	17	1 0	9	0.8	37	1 1	12	0.6
Engineers, scientists	49	2 9	25	2.3	64	1 9	66	3 0
Farmers	661	39.5	433	39.9	1184	35.3	781	36 0
Clerks, salespersons	116	6.9	84	7.7	230	6.9	163	7 5
Carpenters, woodworkers	89	5.3	31	2.9	183	5 5	52	2.4
Printers	12	0 7	3	0.3	8	0.2	9	0 4
Machinists, mechanics	71	4.2	33	3.0	162	4 8	77	3 6
Laborers	116	6.9	49	4 5	298	8 9	126	5 8
No occupation listed	5	0 3	65	6.0	19	0.6	161	7.4
Other	539	32.2	352	32 5	1165	34 8	721	33 3
Total	1675		1084		3350		2168	

TABLE 2

Odds ratios for leukemia mortality in white, male Iowa farmers over 30 years of age, according to year of birth, year of death and age at death, 1964–1978

Stratum	Cases		Controls		Odds ratio	95% CL*
	No. of farmers	% Farmers	No of farmers	% Farmers		
Year of birth						
1869–1889	166	49 7	392	52 0	0 89	0 67–1 18
1890–1900	290	47 2	488	39 9	1 36	1 10–1 68
1901–1947	205	28 2	304	22 2	1 39	1 11–1 73
Year of death						
1964–1970	344	40 4	640	37 6	1 15	0 96–1 39
1971–1978	317	38 5	544	33 0	1 36	1 11–1 66
Age (years) at death						
≤65	116	24 1	166	18 5	1 36	1 02–1 80
≥66	545	45 7	1018	41 5	1 21	1 04–1.41

* CL, confidence limits.

at death had increased odds ratios. The odds ratio for farming was also elevated for those dying after age 65 years in Iowa, whereas it was not elevated in Nebraska. The odds ratio for years of death in 1971–1978 was elevated in Iowa; however, the odds ratio for the years of death 1957–1965 was markedly higher in Nebraska.

As noted in table 2, the greatest risk for leukemia mortality in Iowa farmers appears to be in those born after 1890. Therefore, analyses stratified by counties according to selected county production figures were completed by year of birth of the cases. The results are summarized in table 3.

As might be expected from the low odds ratio for Iowa farmers in those born before 1890 (table 2), there are no significantly elevated risks in this cohort. Soybeans per acre and corn per acre are associated with increased leukemia mortality risks among farmers for those born from 1890 to 1900. However, neither association is statistically significant for those born after 1900. The relatively low livestock producing counties have increased odds

TABLE 3

Odds ratios for leukemia mortality in white, male Iowa farmers over 30 years of age, according to selected county crop and livestock production, 1964–1978

Production categories by counties	Year of birth (of case)					
	Before 1890		1890–1900		After 1900	
	Odds ratio	95% CL*	Odds ratio	95% CL	Odds ratio	95% CL
Soybeans/acre						
33 highest	0.672	0.415–1 088	1 594	1 129–2.250	1 405	0 979–2 016
Others	1.032	0.727–1 465	1 233	0 940–1.616	1.376	1 038–1.824
Corn/acre						
33 highest	0 831	0 554–1.247	1 634	1.168–2 285	1.384	0.980–1.954
Others	0.947	0 638–1.406	1.201	0.912–1.582	1.389	1 039–1.857
Milk products sold						
33 highest	0 906	0 586–1.401	1.187	0.835–1 685	1.302	0.926–1.829
Others	0.877	0.605–1 271	1.474	1 126–1.929	1 454	1.084–1.950
Cattle						
33 highest	0.969	0.632–1 485	1.287	0.921–1.798	1.231	0.879–1.722
Others	0.831	0.570–1.213	1.414	1.072–1.864	1.522	1.131–2.049
Hogs						
33 highest	0 782	0.512–1 193	1 246	0.873–1.778	1.400	1.006–1.949
Others	0 987	0.675–1.446	1.429	1.095–1 865	1 376	1.019–1.857
Milk cows						
33 highest	0.954	0 623–1 461	1 171	0 827–1 658	1 446	1.027–2.035
Others	0.841	0 576–1.228	1 490	1 136–1.953	1.345	1 004–1.802
Egg-laying chickens						
33 highest	1.105	0.683–1.788	0.954	0.659–1.380	1 532	1.053–2.229
Others	0.792	0.557–1 125	1.627	1.250–2 118	1.314	0.997–1.732
Fertilizer						
33 highest	1 260	0.786–2 018	1.089	0.767–1.548	1.340	0.929–1.934
Others	0 730	0 512–1.042	1.548	1 183–2.026	1.414	1 070–1.870
Insecticides						
33 highest	0.731	0.420–1 271	1.323	0 922–1.900	1.129	0.762–1.673
Others	0.954	0.686–1 327	1.381	1.061–1.797	1.526	1.166–1.998
Herbicides						
33 highest	0 767	0 462–1.273	1 104	0 773–1.575	1 595	1 105–2.301
Others	0.951	0.676–1.337	1.528	1.171–1.994	1 278	0.966–1.691

* CL, confidence limits.

ratios. None of the agricultural production figures evaluated in Nebraska led to increased risk among farmers in the 1890–1900 cohort.

It is for those born after 1900 that the Iowa and Nebraska studies have the greatest inconsistencies. The odds ratios for farmers in Nebraska were significantly greater than 1 in those counties with the highest production of corn, cattle and hogs and highest number of acres treated with insecticides. None of these farming practices were associated with leukemia mortality in Iowa. Only acres treated with herbicides and egg-laying chickens per county were statistically significant at the 5 per cent level.

The odds ratios for Iowa farmers for specific leukemia cell types are summarized in table 4. Only those dying in 1968–1978 are included in table 4 since the ICD Seventh Revision (used prior to 1968) may not separate acute lymphatic and acute myeloid leukemias. Both chronic lymphatic and unspecified lymphatic leukemias cause increased mortality in Iowa farmers. The odds ratios for chronic lymphatic leukemia are elevated in those born after 1890 (table 5). Although the odds ratios for unspecified lymphatic leukemia are greater than 1 for each birth cohort, none is statistically significant, due in part to small numbers in each cohort.

Odds ratios for chronic and unspecified leukemias according to county agricultural production figures associated with combined leukemia types are summarized in table 6. Chronic lymphatic leukemia is elevated in both the high and low producing counties for the five county characteristics investigated. The strongest associations, both in magnitude of the odds ratios and differences in the high and low producing counties, are with soybeans per acre and acres treated with herbicides. Unspecified lymphatic leukemia mortality in farmers is associated with corn per

TABLE 4

Odds ratios for leukemia mortality in white, male Iowa farmers over 30 years of age for specific leukemia types, 1968–1978

Leukemia type	ICD No	Cases		Controls		Odds ratio	95% CL*
		No of farmers	% Farmers	No of farmers	% Farmers		
Acute lymphatic	204 0	28	28 9	69	35 6	0.68	0 37–1.23
Chronic lymphatic	204.1	132	45 8	207	35.9	1.70	1 22–2.38
Unspecified lymphatic	204 9	64	51.2	102	40 8	1 66	1 03–2 68
Acute myeloid	205 0	86	30.7	168	30.0	1.04	0 74–1.48
Chronic myeloid	205.1	46	32 6	90	31.9	1 04	0.65–1 65
Unspecified myeloid	205.9	36	36.7	80	40 8	0.80	0.45–1.41
Chronic myeloid	206 0	10	32.3	19	30.1	1.07	0 44–2.59
Leukemia unspecified	207 9	31	41.3	60	40.0	1.07	0.58–1 97

* CL, confidence limits.

TABLE 5

Odds ratios (ORs) for leukemia mortality in white, male Iowa farmers over 30 years of age for selected leukemia types and year of birth, 1968–1978

Leukemia type	ICD No	Year of birth					
		Before 1890		1890–1900		After 1900	
		OR	95% CL*	OR	95% CL	OR	95% CL
Chronic lymphatic	204.1	1.00	0.54–1 85	2.03	1 24–3 10	1 80	1 09–2.97
Unspecified lymphatic	204.9	1.58	0 65–4 54	2 30	0 97–6.97	1 25	0.64–2.55

* CL, confidence limits.

TABLE 6

Odds ratios (ORs) for leukemia mortality in white, male Iowa farmers over 30 years of age, according to selected leukemia types and selected county crop and livestock production, 1968–1978

County characteristics	Leukemia type	Highest 33 counties		Other counties	
		OR	95% CL*	OR	95% CL
Soybeans/acre	Chronic lymphatic	2.21	1.33– 3 66	1 39	0 97–2 00
	Unspecified lymphatic	0.62	0.25– 1.52	2 49	1 38–4.48
Corn/acre	Chronic lymphatic	1 34	0.87– 2.06	1.94	1 29–2 92
	Unspecified lymphatic	4.63	1.82–11 74	1 00	0 56–1.80
Milk cows	Chronic lymphatic	1.19	0.76– 1.85	2 10	1 41–3.14
	Unspecified lymphatic	4 94	1 96–12 47	0 94	0 52–1 70
Egg-laying chickens	Chronic lymphatic	1 36	0.82– 2.25	1 80	1 25–2 59
	Unspecified lymphatic	2 47	1 03– 5.92	1 37	0.77–2 45
Herbicides	Chronic lymphatic	1.89	1.16– 3 08	1 50	1 03–2 18
	Unspecified lymphatic	1.21	0 51– 2 85	1.90	1 07–3.37

* CL, confidence limits

acre, number of milk cows and egg-laying chickens.

DISCUSSION

Mortality from several types of cancer has been shown to be elevated in farmers (2, 8). These include stomach, prostate and lip cancer, as well as lymphomas and multiple myeloma. However, leukemia is perhaps the cancer most consistently associated with farming during the past 30 years (1–9). Therefore, it is incumbent upon epidemiologists not merely to repeatedly demonstrate that such an association exists, but to diligently search for reasons for the association.

The Nebraska study of Blair and Thomas (9) represents an attempt to identify such reasons or farming practices. Previous epidemiologic evidence has associated dairy farming with leukemia mortality in farmers (10–16). The Nebraska study is particularly important since it implicates corn production with leukemia in those born after 1900, rather than any measure of dairy production.

The results of the Iowa study lend some support to those found in Nebraska. The odds ratios for farmers based on the high producing counties are statistically significant for only corn and soybean production for those born from 1890 to 1900. Apparently, soybean production in Nebraska is not sufficient to be evaluated for association with leukemia mortality in farmers; however, the association of corn production with leukemia mortality in both states indicates that modern farming

practices used in corn production may be a cause of the higher leukemia mortality rates in farmers. This possibility is given credence by the fact that corn production is implicated only in those born after 1890 in Iowa and after 1900 in Nebraska. In addition, the number of acres treated with herbicides in Iowa and the number of acres treated with insecticides in Nebraska are associated with leukemia mortality in farmers born after 1900. These results also tend to implicate modern farming practices as possible causes of leukemia. There is no evidence linking leukemia mortality in farmers with corn production, use of herbicides or use of insecticides in either state for those born before 1890.

The fact that the number of egg-laying chickens is associated with increased leukemia mortality in farmers was not anticipated from the results of the Nebraska study. However, Milham's study (4) of Washington and Oregon death certificate data did indicate that a statistically significant association existed between farming and leukemia mortality, and that the greatest excess of leukemia mortality was in poultry farmers.

Analyses by type of leukemia indicate that chronic and unspecified lymphatic leukemias cause increased mortalities in Iowa farmers. Thus, it appears that it is the lymphatic leukemias that are of greatest concern. Sixty-three per cent of incident acute lymphatic leukemias in Iowa males in 1969–1979 occurred in individuals under age 30 years. Consequently, relatively few (table 4) acute lymphatic deaths in those over age 30 years were included in this study.

Analyses by leukemia type are also of importance because of strong associations of unspecified lymphatic leukemia with number of dairy cows and corn production per acre by county. Donham et al. (14) showed significant association between acute lymphatic leukemia incidence in Iowa and dairy farming. As noted above, acute lymphatic leukemia mortalities were of limited number in this study; however, it is of importance to note the continued evidence of association between dairy farming and lymphatic leukemia. Since corn per acre was also highly associated with unspecified lymphatic leukemia mortality, any elements common to both corn and dairy production are worthy of further investigation.

Many agricultural innovations that have greatly increased corn production, such as extensive use of hybrids and pesticides, have been introduced since World War II. One that is particularly important is commercial fertilizer usage, increased from 8,425,000 tons in the United States in 1930 to 18,400,000 tons in 1950 (27).

The amount of nitrogenous fertilizer applied has added to the agricultural runoff problem (28). This problem is exacerbated by the fact that the nitrogenous waste of dairy animals is much greater than that of other common farm livestock (28). Although highly speculative, one mechanism of increasing the risks for farmers for leukemia and other cancers is contamination of shallow farm wells and farm ponds. This research, of course, offers no direct evidence that shallow wells might contribute to increased farmer mortality from leukemia. However, studies such as this and that of Blair and Thomas (9) are important since they go beyond identification of farming as a risk function and attempt to identify farming practices and specific mechanisms that must be closely studied if the cancer risks of farmers are to be decreased.

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