

**A Case-control Study of
Multiple Myeloma in
Decatur, Illinois**

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Abstract

Background: A cancer cluster investigation that was conducted in ZIP code 62521 of the city of Decatur in Macon County, Illinois, showed a statistically significant excess of multiple myeloma cases for residents of the study area from 1986 through 1992. The cases did not cluster in any one neighborhood within ZIP code 62521, but followed the distribution of the population within the entire study area. When current occupations and industries were assessed, eight of the 13 cases had an occupation with the potential for exposure to substances known to be associated with multiple myeloma. To determine whether cases, who were residents of Decatur, Illinois, were more likely to have worked in an industry or occupation whose exposures are associated with the development of multiple myeloma and whether cases were more likely to have been long-term residents of the city of Decatur, Illinois, a case-control study was conducted.

Method: A case-control study was designed with two controls selected for each case. Controls were matched to the case by sex and year of birth (\pm five years). Cases and controls were interviewed on residential status and occupational history for the last 35 years, medical history, use of medications and hair dyes, exposure to chest and dental X-rays, and radiation therapy.

Results: Fifty-eight percent of the cases agreed to participate in the study and participation rates varied by ZIP code, age, and gender. One factor found to be statistically significant was living on a farm during one's lifetime. However, none of the cases was a farmer, suggesting that cases might have lived on a farm in their childhood. In addition, the trend for increasing length of residence IN Decatur and increasing risk of multiple myeloma was significant.

Conclusion: Although the study results did not provide evidence to support an occupational risk factor for multiple myeloma in Decatur, it was not possible to exclude the possibility that environmental factors may have an influence on multiple myeloma in the Decatur area.

A Case-control Study of Multiple Myeloma in Decatur, Illinois

INTRODUCTION

Results of a cancer cluster investigation conducted in ZIP code 62521 of the city of Decatur in Macon County, Illinois, showed a statistically significant excess of multiple myeloma cases for residents of the study area from 1986 through 1992.¹ The cases did not cluster in any one neighborhood within ZIP code 62521, but rather followed the distribution of the population within the entire study area.

Little is known about the causes of multiple myeloma except that it occurs more often among the aged. Other factors reported to be associated with the disease include ionizing radiation, genetic susceptibility, immunosuppressive diseases, and occupational exposure.²⁻¹³ When current occupations and industries were assessed, eight of the 13 cases had an occupation with the potential for exposure to substances known to be associated with multiple myeloma. Because of these findings, a case-control study of multiple myeloma was conducted to determine whether cases, who were residents of Decatur, Illinois, were more likely to have worked in an industry or occupation with exposures known to be associated with the development of multiple myeloma and whether cases were more likely to have been long-term residents of the study area after controlling for other known risk factors for myeloma.

METHODS

Case Definition and Recruitment

All cases of multiple myeloma (International Classification of Diseases - Oncology, 2nd edition, M-code-9732) diagnosed among residents of the city of Decatur, Illinois (ZIP codes 62521, 62522, 62523, 62524, and 62526), from 1986 through 1992 were identified through the population-

based Illinois State Cancer Registry (ISCR). Case reports were received from all Illinois hospitals, federal hospitals, and central registries of other states where some Illinoisans travel for cancer care. Case reporting completeness for Illinois was estimated to be 90 percent during the study period.¹⁴

Protocol for the study was developed by staff of the Illinois Department of Public Health's divisions of Epidemiologic Studies and Environmental Health. For all eligible cases, permission was sought from the attending physician prior to contacting the patient or family for an interview. Eligible cases were contacted by letter to introduce the study and to invite participation. These cases were asked to provide a telephone number and to sign an informed consent form, mailing both to the Illinois Department of Public Health (IDPH) in a prepaid envelope. If cases did not respond after three mailing attempts, a telephone contact was made to enlist cases willing to participate in the study. Telephone numbers of these cases were obtained by searching local telephone directories or contacting directory assistance.

Control Definition and Recruitment

Two controls were sought for each case in the study. Controls for living cases were selected from a list of licensed drivers provided by the Illinois Secretary of State's Department of Motor Vehicles. A list of deceased individuals, whose next-of-kin could be used for controls, were obtained from IDPH death certificate files. Controls, who were residents of ZIP codes composing the city of Decatur (62521, 62522, 62523, 62524, and 62526), were matched to the case by sex and year of birth (± 5 years).

Similar to the cases, matched controls were contacted by letter to introduce the study and invite participation. Controls were asked to provide a telephone number and to sign an informed consent form, and to mail to IDPH in a prepaid envelope. If controls did not respond after three

mailing attempts, a telephone contact was made to enlist controls willing to participate in the study. Controls were excluded if they had been diagnosed with any lymphatic or hematopoietic cancer.

Data Collection

A revised questionnaire, using a prototype from a previous Surveillance, Epidemiology, End Results (SEER) study on multiple myeloma, was administered to all subjects by telephone. The interview took approximately 15 to 20 minutes and included questions on residential status and occupational history for the last 35 years, medical history, use of medications or hair dyes, exposure to chest and dental X-rays, and radiation therapy. Each matched control was recruited and interviewed after the case interview was completed.

Data Management and Analysis

A visual review of each questionnaire was performed to detect any missing values or errors in the data before duplicated data entry using a FoxPro 2.0 database program. Occupation and industry information was coded using the 1970 U.S. Bureau of the Census index of industries and occupations and the Census's standard coding procedures.¹⁵ Occupation codes were categorized into seven broad groups: 1) professional and technical workers; 2) farmers; 3) managers, officials, and proprietors; 4) sales and clerical workers; 5) service workers; 6) craftsmen and operatives; and 7) laborers. In the same manner, industry codes were assigned to one of eight groups: 1) agriculture; 2) construction; 3) manufacturing; 4) transportation; 5) wholesale; 6) finance; 7) services; and 8) public administration.

Odds ratios (OR) and 95 percent confidence intervals (95 percent CI) for each occupation and industry category were calculated and compared with all other occupations and industries combined. For each occupation and industry category, subjects never employed in that occupation and industry

composed the referent group.

We grouped length of residence into fewer than 11 years, 11 to 15 years, 16 to 20 years and 21 years or more. ORs were calculated for cases and controls and for each covariate included in the study: education level, smoking history, military service, use of hairdyes, X-ray exposure, benzene exposure, occupational exposure to radiation, mammography, specific disease conditions, anti-seizure medications, and lawn treatment with chemicals. Multiple logistic regression was not performed due to small numbers.

The study design was a case-control study with two controls selected for each case. Based on the 48 cases diagnosed from 1986 to 1992, a statistically significant result with a 20 percent chance of a type II error ($\beta=0.20$) and a 5 percent chance of a type I error ($\alpha=0.05$), and a relative risk ranging from 3.0 to 4.5 with an exposure rate of 10 percent to 50 percent, was possible to detect.

RESULTS

Twenty-eight of the 48 eligible cases agreed to participate in the study, a participation rate of 58 percent. A total of 56 controls were also enrolled. Table 1 shows the number and percentage of participating and non-participating cases by age, gender, and vital status. Forty-six percent of participating cases were still alive and 54 percent were deceased. Live cases were more likely to participate in the study (65 percent) than were informants for deceased cases (54 percent). Cases, ages 45 to 54, were more likely to participate than those in older age groups. Female cases were more likely to participate than male cases. None of these differences between participating and non-participating cases was statistically significant.

Table 2 shows the number and percentage of participating and non-participating cases and controls by ZIP code of residence. Cases in ZIP code 62526 were more likely to participate (81

percent) than were cases from ZIP code 62521 (52 percent). Participation rates in ZIP code 62521 differed between cases (52 percent) and controls (31 percent). Rates of participation in ZIP code 62526 also differed between cases (81 percent) and controls (22 percent).

Table 3 shows the results of univariate analyses. The trend for increasing length of residence in Decatur and increasing risk of multiple myeloma was significant ($p=0.02$). There was a significant difference in the mean length of residence between cases (29.2 years) and controls (24.4 years) ($p<0.0000001$). However, the occupation and industry categories were not found to be associated with the risk of multiple myeloma. A history of living on a farm was statistically significant (OR=3.2, 95 percent CI, 1.2-8.3). Another factor that approached statistical significance was ZIP code of residence (62526 *cf.* other ZIPs) (OR=2.9, 95 percent CI, 0.9-8.5). In addition, none of the other factors that were included in the interview were associated with the risk of multiple myeloma.

DISCUSSION

The exact cause of multiple myeloma (MM) is unknown. Both environmental and genetic factors may contribute to its development. Several studies of Japanese atomic bomb survivors, U.S. radiologists, radium dial workers, and nuclear power plant workers have suggested that radiation exposure might be a predisposing factor in the development of malignant plasma cell clones.^{2,4-5,16-17} Occupational factors found in farming and in heavy metal, rubber manufacture, benzene and other chemicals, wood, leather, and petroleum industries are also considered to be serious risks.^{3,6-7,8-13,18} In addition, an elevated risk for MM has been associated with home and occupational exposure to hair dyes in some North American cohorts.¹⁹⁻²⁰ Disease conditions, such as allergy-related conditions, rheumatoid arthritis, and diabetes, also have been associated with the occurrence of

multiple myeloma.⁶ Occasional geographic clusters of multiple myeloma have occurred. However, only few specific associations have been observed consistently with the disease. Results have been inconsistent across studies and considerable uncertainty still remains concerning the role of occupation in the etiology of MM. In addition, while MM is also known to cluster geographically, residential status has never been considered to be a predisposing factor in the development of the disease.

The purpose of this case-control study was to provide explanations for the excess of multiple myeloma cases observed in Decatur ZIP code 62521 on a population basis.¹ Factors of particular concern were occupation and location and length of residence in Decatur.

No occupation or industry groups appeared to be at higher risk for multiple myeloma. Living on a farm during one's lifetime was found to be statistically significant. Multiple myeloma has been associated with farming in previous studies so the finding of increased risk with a history of farm residence was not surprising. However, none of the cases was a farmer, suggesting that cases might have lived on a farm in their childhood. If there was a causative agent for the multiple myeloma attributable to living on farms as children, this would indicate an extremely long latency period between exposure and occurrence of multiple myeloma. An alternative explanation might be that the causative exposure on farms might be acting as an inducer and later in life the cases were exposed to a promoter that triggered the neoplastic process.

The trend for increasing risk with increasing length of residence was also found to be significant. If an environmental factor was contributing to the occurrence of multiple myeloma in the area, both length of residence and geographic location would be expected to vary with the disease status. Only the trend for length of residence was found to be significant. However, a limitation of

the study was the poor participation rate by both cases and controls. Only 58 percent of cases agreed to participate in the study. Low response rates can cause substantial bias in study results as participants may differ extensively from individuals who refuse to participate. Participation rates varied by ZIP code. While 56 percent of eligible cases of multiple myeloma were residents of ZIP code 62521, participation rates for this ZIP code were lower when compared with participation rates for ZIP code 62526 (52 percent and 81 percent, respectively). However, participation rates for controls were higher for ZIP code 62521 (31 percent) than for ZIP code 62526 (22 percent).

In conclusion, it was not possible to exclude the possibility that environmental factors may have an influence on multiple myeloma in the Decatur area.

REFERENCES

1. Illinois Department of Public Health. Incidence of Cancer in ZIP Code 62521 of Decatur, Illinois, 1988-1992. Division of Epidemiologic Studies. Springfield, Illinois. August 1994.
2. Boice JD, Morin MM, Glass AG, Friedman GD, Stovall M, Hoover RN, Fraumeni JF. Diagnostic X-ray procedures and risk of leukemia, lymphoma, and multiple myeloma. *JAMA*. 1991;265:1290-4.
3. Cuzick J, DeStavola B. Multiple myeloma - A case control study. *Br J Cancer*. 1988;57:516-520.
4. Darby SC, Kendall GM, Fell TP, *et al*. A summary of mortality and incidence of cancer in men from the United Kingdom who participated in the United Kingdom's atmospheric nuclear weapons tests and experimental programmes. *Br Med J*. 1988;296:322.
5. Matanoski GM, Seltser R, Sartwell PE, *et al*. The current mortality rates of radiologists and other physician specialists: Specific causes of death. *Am J Epidemiol*. 1975;101:199.
6. Riedel D, Pottern LM. The epidemiology of multiple myeloma. In Barlogie E. (ed) Hematology/Oncology Clinics of North America - *Multiple Myeloma*, Vol 6. Philadelphia: W.B. Saunders Company, 1992.
7. Boffetta P, Stellman, SD, Garfinkel L. A case-control study of multiple myeloma nested in the American Cancer Society prospective study. *Int J Cancer*. 1989;43:554-9.
8. Demers PA, Vaughan TL, Koepsell TD, Lyon JL, Swanson GM, Greenberg RS, Weiss NS. A case-control study of multiple myeloma and occupation. *Am J Ind Med*. 1993;23:629-39.
9. Eriksson M, Karlsson M. Occupational and other environmental factors and multiple myeloma: A population based case-control study. *Br J Ind Med*. 1992;49:95-103.

10. McLaughlin JK, Malaker HSR, Weiner JA *et al.* Multiple myeloma and occupation in Sweden. *Arch Env Health.* 1988;43:(1):7-10.
11. Milham S. Leukemia and multiple myeloma in farmers. *Am J Epidemiol.* 1971;94(4):307-310.
12. Pearce NE, Smith AH, Fisher DO. Malignant lymphoma and multiple myeloma linked with agricultural occupations in a New Zealand cancer registry-based study. *Am J Epidemiol.* 1985;12(2):225-237.
13. Pearce NE, Reif JS. Epidemiologic studies of cancer in agricultural workers. *Am J Ind Med.* 1990;18:133-148.
14. Howe HL, Lehnher M, Derrick L (eds). *Cancer Incidence in North America, 1988-1992.* North American Association of Central Cancer Registries. Sacramento, CA. April 1996.
15. Bureau of Census. *Alphabetical Index of Industries and Occupations.* 1990 Census of Population and Housing. U.S. Department of Commerce. U.S. Government Printing Office, Washington DC.
16. Higami Y, Shimokawa I, Iwasaki K. *et al.* Incidence of multiple myeloma in Nagasaki City, with special reference to those subjects to atomic bomb exposure. *Jpn J Cancer Clin.* 1990;36:157.
17. Stebbings JH, Lucas HF, Stehney AF. Mortality from cancers of major sites in female radium dial workers. *Am J Ind Med.* 1984;5:435.
18. Decoufle P, Blattner WA, Blair A. Mortality among chemical workers exposed to benzene and other agents. *Environ Res.* 1983;30:16.
19. Brown LM, Everett GD, Burmeister LF, Blair A. Hair dye use and multiple myeloma in

- white men. *Am J Pub Health*. 1992; 82(12):1673-1674.
20. Zahm SH, Weisenburger DD, Babbitt PA, Saal RC, Vaught JB, Blair A. Use of hair coloring products and the risk of lymphoma, multiple myeloma and chronic lymphocytic leukemia. *Am J Pub Health*. 1992;82:990-997.
21. Kosaka M, Okagawa K, Miyamoto Y, Goto T, Saito S. Geographic clustering of myeloma in Tokushima. *Int J Hem*. 1991;54:405-409.

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Table 1. Number and percent of Participating and Nonparticipating Cases by Age, Gender and Vital Status

	Participating (n=28)		Nonparticipating (n=20)		TOTAL
	n	%	n	%	
Age					
15-45	0	0.0	2	100.0	2
45-54	6	85.7	1	14.3	7
55-64	3	50.0	3	50.0	6
65-74	11	61.1	7	38.9	18
75+	8	53.3	7	46.7	15
Gender					
Male	13	54.2	11	45.8	24
Female	15	62.5	9	37.5	24
Vital Status					
Alive	13	65.0	7	35.0	20
Dead	15	53.6	13	46.4	28

Source: Illinois Department of Public Health, Division of Epidemiologic Studies, 1996.

Table 2. Number and Percent of Participating and Nonparticipating Cases and Controls by ZIP Code of Residence

ZIP CODE	CASES					CONTROLS				
	Participating		Non participating		TOTAL	Participating		Non participating		TOTAL
	n	%	n	%		n	%	n	%	
62521	14	51.9	13	48.1	27	33	30.6	75	69.4	108
62522	1	20.0	4	80.0	5	9	23.1	30	76.9	39
62525	0	-	0	-	0	1	50.0	1	50.0	2
62526	13	81.3	3	18.8	16	13	22.4	45	77.6	58
TOTAL	28	58.3	20	41.7	48	56	27.1	151	72.9	207

Source: Illinois Department of Public Health, Division of Epidemiologic Studies, 1996.

Table 3. Distribution of All Covariates Among Cases with Multiple Myeloma and Among Control Subjects

Characteristics	CASES (N=28)		CONTROLS (N=56)		OR	95%CI
	n	%	n	%		
Age						
<55	6	21.4	9	16.1	1.0	
55-64	3	10.7	12	21.4	0.4	0.0-2.4
65-74	11	39.3	17	30.4	0.9	0.2-4.2
75+	8	28.6	18	32.1	0.7	0.1-3.0
					$\chi^2=0.02$	p=0.8
Gender						
Male	13	46.4	26	46.4		
Female	15	53.6	30	53.6		
Highest level of education completed						
No HS/Some HS	8	28.6	15	26.8	1.0	
HS Grad	9	32.1	15	26.8	1.1	0.3-4.4
Some College/Tech	4	14.3	14	25.0	0.5	0.1-2.6
College Grad	2	7.1	6	10.7	0.6	0.1-4.9
Grad School	4	14.3	5	8.9	1.5	0.2-9.4
Unknown	1	3.6	1	1.8	-	-
					$\chi^2=0.01$	p=0.9
Hispanic ethnicity						
Yes	0	0.0	0	0.0	-	-
No	27	96.4	55	98.2		
Farm resident						
Yes	17	60.7	17	32.7	3.2	1.2-8.3
No	11	39.3	35	67.3	1.0	
Current smoker						
Yes	10	35.7	23	42.6	0.7	0.3-1.9
No	18	64.3	31	57.4	1.0	
Past smoker						
Yes	9	69.2	14	58.3	1.6	0.4-6.7
No	4	30.8	10	41.7	1.0	

Table 3. Distribution of All Covariates Among Cases with Multiple Myeloma and Among Control Subjects

Characteristics	CASES (N=28)		CONTROLS (N=56)		OR	95%CI
	n	%	n	%		
Have served in the military						
Yes	5	19.2	8	14.3	1.4	0.4-4.9
No	21	80.8	48	85.7	1.0	
Have served in Japan						
Yes	1	3.8	0	0.0	-	-
No	25	96.2	56	100.0		
Ever used hair dye						
Yes	6	25.0	15	30.0	0.8	0.2-2.3
No	18	75.0	35	70.0	1.0	
Used semi-permanent hair dye						
Yes	3	33.3	5	55.6	0.4	0.05-2.7
No	6	66.7	4	44.4	1.0	
Used permanent hair dye						
Yes	4	36.4	6	60.0	0.4	0.06-2.2
No	7	63.6	4	40.0	1.0	
Exposure to dental X-rays						
Less Frequently	9	33.3	21	45.7	1.0	
At least yearly	7	25.9	14	30.4	1.2	
At least every 5 years	6	22.2	11	23.9	1.3	
Don't Know	5	18.5	10	21.7	-	
					$\chi^2=0.15$	$p=0.7$
Exposure to chest X-rays						
Less Frequently	8	28.6	25	44.6	1.0	
At least yearly	8	28.6	8	14.3	3.1	
At least every 5 years	8	28.6	15	26.8	1.7	
Don't Know	4	14.3	8	14.3	-	
					$\chi^2=0.9$	$p=0.3$
Occupational exposure to radiation						

Table 3. Distribution of All Covariates Among Cases with Multiple Myeloma and Among Control Subjects

Characteristics	CASES (N=28)		CONTROLS (N=56)		OR	95%CI
	n	%	n	%		
Yes	0	0.0	1	1.8	-	-
No	28	100.0	55	98.2		
Exposure to benzene						
Yes	1	5.9	6	16.2	0.3	0.03-2.9
No	16	94.1	31	83.8	1.0	
# times/year mammography(Women)						
0	2	25.0	1	7.1	1.0	
1	4	50.0	13	92.9	0.1	0.-3.2
2	1	12.5	0	0.0	-	-
3	1	12.5	0	0.0	-	-
Diagnosed with allergy						
Yes	5	20.8	10	19.6	1.1	0.3-3.6
No	19	79.2	41	80.4	1.0	
Diagnosed with asthma						
Yes	1	4.2	5	9.4	0.4	0.04-3.8
No	23	95.8	48	90.6		
Diagnosed with diabetes						
Yes	2	7.7	8	14.5	0.5	0.1-2.5
No	24	92.3	47	85.5	1.0	
Diagnosed with hepatitis						
Yes	0	0.0	3	5.4	-	-
No	28	100.0	53	94.6		
Diagnosed with mononucleosis						
Yes	0	0.0	2	3.6	-	-
No	28	100.0	54	96.4		
Diagnosed with rheumatoid arthritis						

Table 3. Distribution of All Covariates Among Cases with Multiple Myeloma and Among Control Subjects

Characteristics	CASES (N=28)		CONTROLS (N=56)		OR	95%CI
	n	%	n	%		
Yes	3	12.0	9	17.3	0.6	0.2-2.6
No	22	88.0	43	82.7	1.0	
Took antiseizure medications						
Yes	0	0.0	1	1.8	-	-
No	28	100.0	55	98.2		
Diagnosed with tuberculosis						
Yes	2	7.1	0	0.0	-	-
No	26	92.9	56	100.0		
Ever employed						
Yes	26	92.9	50	90.9	1.3	0.2-7.2
No	2	7.1	5	9.1	1.0	
Occupational groups						
Professional/Technical	5	19.2	15	28.8	0.5	0.2-1.8
I	0	0.0	1	1.9	-	-
Farmers	1	3.8	4	7.7	0.5	0.5-4.5
Managers	7	26.9	11	21.2	1.3	0.5-4.0
Sales/Clerical	3	11.5	7	13.5	0.8	0.2-3.5
Service	5	19.2	7	13.5	1.5	0.4-5.3
Craftsmen	5	19.2	7	13.5	1.5	0.4-5.3
Production Workers						
Industry groups						
Agriculture	0	0.0	3	5.8	-	-
Construction	2	7.7	0	0.0	-	-
Manufacturing	9	34.6	17	32.7	1.1	0.4-2.8
Transportation	3	11.5	5	9.6	1.2	0.3-5.5
Wholesale	4	15.4	9	17.3	0.9	0.2-3.1
Finance	0	0.0	3	5.8	-	-
Services	8	30.8	12	23.1	1.2	0.4-3.5
Public Admin	0	0.0	3	5.8	-	-
Length of residency in Decatur						

Table 3. Distribution of All Covariates Among Cases with Multiple Myeloma and Among Control Subjects

Characteristics	CASES (N=28)		CONTROLS (N=56)		OR	95%CI
	n	%	n	%		
>10	1	3.6	12	21.4	1.0	
11-15	1	3.6	7	12.5	1.7	0.0-77.2
16-20	6	21.4	5	8.9	14.1	1.0-
>20	20	71.4	32	57.1	7.5	416.6
						0.9-166.2
					$\chi^2=4.97$	p=0.02
(Mean)	28	29.2 years	56	24.4 years	F statistic 122.2	p=<0.0000
Lawn treated with chemicals						
Yes	14	50.0	17	30.4	2.2	0.8-5.8
No	12	42.9	32	57.1	1.0	
ZIP of residence						
62521	14	50.0	33	58.9	0.7	0.2-1.9
other ZIPs	14	50.0	23	41.1	1.0	
62526	13	46.4	13	23.2	2.8	0.9-8.5
other ZIPs	15	53.6	43	76.8	1.0	

Source: Illinois Department of Public Health, Division of Epidemiologic Studies, 1996.

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