

Leukemia in Electric Utility Workers: The Evaluation of Alternative Indices of Exposure to 60 Hz Electric and Magnetic Fields

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Background Epidemiological studies have inconsistently demonstrated a positive relationship between magnetic and/or electric fields and leukemia. Although exposure to both 60 Hz electric and magnetic fields can be characterized in many ways, to date, risk assessment has been performed by using only a limited number of exposure indices.

Methods The associations between adult leukemia and indices of electric and magnetic fields were explored within a nested case-control study of 31,453 Ontario electric utility workers.

Results The percentage of time spent above electric field thresholds of 20 and 39 V/m was predictive of leukemia risk after adjusting for duration of employment and the arithmetic mean exposure to both electric and magnetic fields ($P < 0.05$). Duration of employment was strongly associated with an increased risk of leukemia. Those who had worked for at least 20 years, and were in the highest tertiles of percentage of time spent above 10 and 20 V/m had odds ratios of 10.17 (95% CI = 1.58–65.30) and 8.23 (95% CI = 1.24–54.43), respectively, when compared to those in the lowest tertile. Nonsignificant elevations in risk were observed between indices of magnetic fields and leukemia.

Conclusions Our results support the hypothesis that electric fields act as a promoting agent in the etiology of adult leukemia. Exposure assessment based on alternate indices of electric and magnetic fields should be incorporated into future occupational studies of cancer. *Am. J. Ind. Med.* 37:607–617, 2000. © 2000 Wiley-Liss, Inc.

KEY WORDS: electric fields; magnetic fields; leukemia; exposure assessment; cancer promoter

INTRODUCTION

The possibility that occupational exposure to electric and magnetic fields is associated with an increased risk of leukemia was raised by a series of reports that appeared more than a decade ago [Coleman et al., 1983; McDowall, 1983; Milham, 1982; Wright et al., 1982]. A number of epidemiologic studies of workers have since investigated the association between several cancers, particularly brain

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cancer and leukemia, and exposure to magnetic fields (MF). More recently, the relationship between electric fields (EF) and cancer has come under greater scrutiny [Miller et al., 1996a, b; Guénel et al., 1996; Kheifets et al., 1997]. As a whole, the findings of these studies have been inconsistent, and the hypothesis that magnetic and/or electric field exposures are related to cancer remains controversial.

Magnetic and electric fields are complex entities that can be characterized by their frequency, waveform, polarization, and amplitude [Tenforde and Kaune, 1987]. As a result, there are potentially several different parameters that can be used to define exposure. Studies of cancer and workplace exposures to MF and EF have predominantly relied on the cumulative time weighted average (TWA) based on either the arithmetic or geometric mean exposure to assess risk. Examples of alternative exposure metrics include the proportion of time spent above a specified threshold, standard deviation of field strength, and fluctuations in field strength over successive time intervals.

It is generally accepted that if extremely low frequency fields (ELF) are related to cancer, it is through the promotion stage of the carcinogenic process [Cridland, 1997]. Tumor promoting agents are capable of converting a cancer-initiated cell to a potentially malignant cell and are characterized by the reversibility of their effects, long term exposure and likely require an exposure threshold [Cridland, 1997; Hardell et al., 1995]. The ability of ELF to suppress the secretion of melatonin [Blask, 1990] and to alter the activity of ornithine decarboxylase [Byus et al., 1987], an enzyme intimately involved in cell proliferation, provides support for a cancer promoting effect. Intermittent exposures of electromagnetic fields have also been shown to promote tumors in rodents while no such increase in tumor risk was observed with constant exposures [Beniashvili et al., 1991; Rannug et al., 1994]. Other experimental studies support the theory that ELF serve as tumor promoters [Mevissen et al., 1993, 1996; Baum et al., 1995] whereas others have not [Dees et al., 1996; McLean et al., 1997; Loscher et al., 1994; Lacy-Hubert et al., 1995]. Although *in vitro* and *in vivo* studies support a role for several of these alternate definitions of EF and MF, they have not established which, if any, is the most biologically relevant metric. For these reasons, there is uncertainty about which aspect of electric and/or magnetic fields should be used to evaluate cancer risk in epidemiologic studies.

The evaluation of alternative indices of magnetic field, as they relate to cancer, has been done explicitly in some studies [Floderus et al., 1993; London et al., 1994; Matanoski et al., 1993]. Other work has assessed cancer risk by using cumulative electric and magnetic field exposures based on the geometric and arithmetic mean field strength [Thériault et al., 1994; Miller et al., 1996a; Guénel et al., 1996]. The arithmetic mean is more sensitive to skewed data and is better suited for modeling threshold

effects whereas the geometric mean, which is closely related to the median of the exposure distribution, minimises the influence of outliers.

Previous analyses of this study population have examined the association between these cumulative TWA magnetic and electric field indices and cancer [Miller et al., 1996a; Thériault et al., 1994]. However, correlational analyses of exposure data from this workforce indicates that the use of the arithmetic and geometric means does not adequately characterize the variability of either electric or magnetic field exposures [Villeneuve et al., 1998]. Although a limited number of studies have evaluated the association between alternative indices of magnetic field exposures and risk of cancer in workers, to date, analysis by using comparable indices of electric fields has not been done.

MATERIALS AND METHODS

Study Population

The subjects used in this study consisted of those cases and controls identified within a cohort of Ontario Hydro male employees. The cohort was initially assembled as part of a Tri-Utility Study that also included workers from Quebec and France [Thériault et al., 1994]. As this study population has been described in detail elsewhere [Miller et al., 1996a, b] only a brief description follows. Cases were identified by linking records of the 31,543 Ontario Hydro employees to records of the Ontario Cancer Registry. Leukemia cases that were newly diagnosed in the relevant time period among employees with no less than one year of service were retained and defined by using the International Classification of Diseases (ICD) codes 204–208. The relevant time period for linkage was 1970–1988 for the retirees and 1973–1988 for the active workers. Only the first primary tumor in an individual was eligible, except for previous basal or squamous cancer of the skin.

Controls were randomly selected from the Ontario Hydro employee files after individually matching employees to cases by using the following criteria: same sex (male), year of birth, alive in diagnosis year of case, and no evidence of prior diagnosis of any cancer (including ICD (9) 225) except basal or squamous cancer of the skin. Our results are based on 50 matched sets having a case:control ratio of 1:4.

Evaluation of Exposure to Electric and Magnetic Fields

Measurements of exposures were obtained directly from a sample of employees under usual working conditions by using the Positron #378100 personal exposure monitor (Positron Industries Montreal, Quebec, Canada). This monitor is portable, pocket sized and battery operated, designed to monitor immediate personal environmental

exposure to 50/60 Hz magnetic and electric fields. The Positron monitor used in this study filters the electric and magnetic incoming signals to limit measurements to 60 Hz fields. The monitors were configured to record electric and magnetic fields every minute and were tested and calibrated both before use and at regular intervals during the study. Each reading was assigned according to 16 predefined exposure intervals or bins. The exposure intervals were 0–0.61, 0.61–1.22, 1.22–2.44, ... 5,000–10,000 and >10,000 V/m for electric fields and 0–0.012, 0.012–0.024, 0.024–0.048, ... 100–200, >200 μ T for magnetic fields. Each measure was assigned the value of the midpoint of the interval. The ability of this monitor to differentiate exposures by occupational group and to obtain high compliance has been demonstrated [H  roux, 1991; Deadman et al., 1988].

As part of the exposure assessment in the Tri-Utility Study [Th  riault et al., 1994], field measurements were performed on 895 Ontario Hydro employees that were sampled by job title and work location. Our analyses are based on electric and magnetic field measures obtained from 820 of the original 895 workers. Those workers that were missing either an electric or magnetic field measure were not included in the analyses; these account for most of the 75 workers who were dropped from the previous analysis [Th  riault et al., 1994]. The data for these workers were not used because the monitoring data were suggestive that the monitor was kept close by but not worn; therefore, these data were suitable for magnetic field exposure estimates but not valid for electric field data. There were two worker records that could not be retrieved due to defects that appeared in the discs containing the raw data required to calculate the new metrics.

A job exposure matrix (JEM) was constructed for each of the exposure indices identified in the correlational and principal components analyses [Villeneuve et al., 1998]. As in previous work [Miller et al., 1996a], each JEM was defined by using 17 job titles and 15 worksite locations. For six of the occupational groups (Powerline Maintainers, Meter Readers, Foresters, Truck Drivers, Electrical Inspectors, and Customer Service Representatives) we did not stratify exposure by worksite because workers in these groups spend most of their time away from their designated work location. For the remaining 11 groups, job title and worksite specific means were calculated from the Positron readings obtained from the sampled workers. Where worksite information could not be coded for a subject's work history record, exposure was estimated by using an overall mean calculated for each occupational group.

The exposure for each subject was calculated by multiplying the duration of employment in each work history record by the corresponding entry of the JEM and summing these products up to obtain a cumulative estimate of exposure. Cumulative exposures to electric and magnetic

fields were calculated from date of hire until date of cancer diagnosis, or diagnosis date of the matched case for controls. Average exposures were calculated by dividing the cumulative exposure estimate by the total length of employment. Because cumulative indices of exposure are dependent on length of employment, for each worker's exposure these indices will be correlated with each other. Therefore, to optimize our ability to discriminate risk patterns between exposure metrics considered, we chose to model average exposure indices while adjusting for duration of employment. In other words, our modeling incorporates both components of cumulative exposure, namely intensity and duration. The risk of leukemia was assessed for the following exposure indices:

Exposure indices

Electric fields (V/m)	Magnetic fields (μ T)
Arithmetic mean	Arithmetic mean
Geometric mean	Geometric mean
Standard deviation in field strength	Standard deviation in field strength
Autocorrelation at 5 min lags	Autocorrelation at 5 min lags
Average transition in field strength	Average transition in field strength
Percentage of time spent above: 2.4, 5, 10, 20, 39, 78, 156, 625, and 2500 V/m	Percentage of time spent above: 0.2, 0.8, 3.0, 12.5, and 50 μ T

Risk estimates were adjusted for socioeconomic status by using a five level categorization scheme thought to reflect employee status when first hired. In addition, multivariate models were used to assess the potential confounding influence of other workplace exposures and adjust where deemed appropriate. These confounders included benzene, ionizing radiation, 2,4-D, and 2,4,5-T. These exposure assignments were made blind to case-control status and are described in great detail elsewhere [Miller et al., 1996b].

The data were analyzed with the software SAS (Statistical Analyses System version 6.12) and risks were estimated by using conditional logistic regression that took into account the matched design of the study. Odds ratios and their corresponding 95% confidence intervals were estimated for each exposure index. Indices of average exposure and duration of employment were categorized into tertiles according to the frequency distribution observed in the control population.

A more in-depth analysis of potential threshold effects was examined by estimating the percentage of time spent above specified bin values as defined by the Positron. The lower edges in V/m of the nine bins used were: 2.4, 5, 10,

20, 39, 78, 156, 625, and 2500. Similarly, cut-points used for magnetic fields (μT) were: 0.2, 0.8, 3.0, 12.5, and 50. As before, the percentage of time spent above a specified threshold was defined by both job title and worksite, and was obtained from the appropriate JEM. These threshold exposure indices were entered into a model that already included the arithmetic mean field strength in order to assess whether these indices made a substantial improvement in predicting risk above an index conventionally used. This was formally tested by using the Wald chi-square statistic. Further, the relative roles of duration of employment, arithmetic mean electric and magnetic field exposures, and percentage of time spent above selected thresholds were assessed by calculating standardized coefficients. As outlined by Selvin [1996], this method represents a suitable means to compare factors that have been measured by using different units. Standardized coefficients were calculated by dividing the regression coefficients by their corresponding standard errors.

RESULTS

The relationship between several measures of average exposure to electric fields and leukemia is presented in Table I. Individuals having an arithmetic mean EF exposure

exceeding 13.67 V/m had a significantly increased risk of leukemia (OR = 4.38, 95% CI = 1.33–14.43). With the exception of EF autocorrelations at 5 min lags, an increased risk of leukemia was observed for those in the upper most tertile of all average indices of EF exposure relative to those in the lowest tertile.

Unlike electric fields, no statistically significant increases in leukemia risk were observed with average exposure to magnetic fields (Table II). A nonsignificantly increased risk of leukemia among those in the highest arithmetic mean tertile of MF exposure relative to the lowest was observed (OR = 2.31, 95% CI = 0.66–8.12). Similarly, an elevated risk of leukemia was observed in the highest tertile of magnetic field based on autocorrelations at 5 min lags (OR = 2.46, 95% CI = 0.89–6.78).

A correlation matrix for the variables duration of employment, arithmetic mean electric field exposure, cumulative arithmetic mean electric field exposure, and percentage of time spent above different electric field thresholds is presented in Table III. For the sake of brevity, we have presented correlations for only five of the nine threshold cut-points. Duration of employment was poorly correlated with all exposure indices ($r < 0.45$). Correlations between the average electric field arithmetic mean and the percentage of time spent above various thresholds increased

TABLE I. Risk of Leukemia for Selected Indices of Average Electric Field Exposures, Ontario Electric Utility Workers

Average of electric field exposure (in V/m) ^a	Cases	Controls	Odds Ratio ^b and 95% CI	Odds Ratio ^c and 95% CI
Arithmetic mean				
0–< 8.58	7	70	1.0 —	1.0 —
8.58–< 13.67	18	69	2.20 (0.73–6.62)	2.15 (0.71–6.52)
13.67+	25	60	4.46 (1.35–14.67)	4.38 (1.33–14.43)
Geometric mean				
0–< 1.60	9	73	1.0 —	1.0 —
1.60–< 1.96	20	67	2.12 (0.80–5.64)	2.07 (0.77–5.55)
1.96+	21	59	2.15 (0.80–5.76)	2.18 (0.81–5.85)
Standard deviation				
0–< 26.22	11	76	1.0 —	1.0 —
26.22–< 52.51	16	59	2.09 (0.73–5.99)	2.04 (0.69–6.03)
52.51+	23	64	3.14 (1.01–9.81)	3.08 (0.97–9.80)
Autocorrelation at 5 min lags				
0–< 0.14	18	65	1.0 —	1.0 —
0.14–< 0.17	11	64	0.69 (0.26–1.84)	0.69 (0.26–1.83)
0.17+	21	70	0.85 (0.35–2.18)	0.94 (0.36–2.40)
Average transition in field strength				
0–< 0.87	11	73	1.0 —	1.0 —
0.87–< 0.96	18	58	2.42 (0.83–7.06)	2.37 (0.81–6.94)
0.96+	21	68	2.17 (0.67–7.04)	2.17 (0.67–7.02)

^aCategorized into tertiles according to the distribution of exposure of all controls; the average was calculated by dividing the cumulative exposure for the relevant index by the number of years employed.

^bOdds ratio adjusted for duration of employment, socioeconomic status, year of hire, and exposures to benzene and ionizing radiation.

^cOdds ratio adjusted for duration of employment, socioeconomic status, year of hire, exposures to benzene and ionizing radiation, and arithmetic mean exposure to magnetic fields.

TABLE II. Risk of Leukemia for Selected Indices of Average Magnetic Field Exposures, Ontario Electric Utility Workers

Average magnetic field exposure (in μT) ^a	Cases	Controls	Odds Ratio ^b and 95% CI	Odds Ratio ^c and 95% CI
Arithmetic mean				
0–< 0.22	11	72	1.0 —	1.0 —
0.22–< 0.47	13	62	1.14 (0.29–4.45)	1.10 (0.28–4.28)
0.47+	26	65	2.67 (0.79–8.99)	2.31 (0.66–8.12)
Geometric mean				
0–< 0.074	14	65	1.0 —	1.0 —
0.074–< 0.100	16	73	0.92 (0.37–2.28)	1.12 (0.43–2.93)
0.100+	20	61	1.25 (0.52–3.01)	1.81 (0.66–4.95)
Standard deviation				
0–< 0.43	12	72	1.0 —	1.0 —
0.43–< 1.12	16	59	1.24 (0.37–4.16)	1.20 (0.36–4.06)
1.12+	22	68	1.80 (0.57–5.67)	1.45 (0.44–4.85)
Autocorrelation at 5 min lags				
0–< 0.24	15	69	1.0 —	1.0 —
0.24–< 0.26	6	72	0.35 (0.11–1.09)	0.35 (0.11–1.09)
0.26+	29	58	2.30 (0.99–5.35)	2.46 (0.89–6.78)
Average transition in field strength				
0–< 0.53	16	66	1.0 —	1.0 —
0.53–< 0.62	20	66	0.67 (0.27–1.68)	0.53 (0.20–1.41)
0.62+	14	67	0.38 (0.13–1.15)	0.35 (0.11–1.11)

^aCategorized into tertiles according to the distribution of exposure of all controls; the average was calculated by dividing the cumulative exposure for the relevant index by the number of years employed.

^bOdds ratio adjusted for duration of employment, socioeconomic status at time of hire, year of hire, and exposures to benzene and ionizing radiation.

^cOdds ratio adjusted for duration of employment, socioeconomic status at time of hire, year of hire, exposures to benzene and ionizing radiation, and arithmetic mean exposure to electric fields.

TABLE III. Pearson Correlation Coefficients for Selected Electric Field Exposure Indices, Ontario Electric Utility Workers

	A	B	C	D	E	F	G	H
Duration of employment (A)	1.0							
Cumulative electric field arithmetic mean (B)	0.45	1.0						
Average electric field arithmetic mean (C)	0.15	0.89	1.0					
Percentage of time above 2.4 V/m (D)	0.10	0.32	0.37	1.0				
Percentage of time above 5 V/m (E)	0.04	0.42	0.50	0.88	1.0			
Percentage of time above 10 V/m (F)	–0.01	0.46	0.57	0.78	0.97	1.0		
Percentage of time above 20 V/m (G)	0.07	0.63	0.73	0.68	0.87	0.92	1.0	
Percentage of time above 39 V/m (H)	0.12	0.76	0.87	0.62	0.77	0.83	0.93	1.0

with higher threshold cut-points. For example, the Pearson correlation between the percentage of time spent above 39 V/m and the average arithmetic mean electric field strength was 0.87. Similar correlation patterns were observed with the corresponding indices of magnetic field exposure (Table IV).

The results from modeling the percentage of time spent above selected electric field thresholds in models that also contained the arithmetic mean electric and magnetic field strength and duration of employment are presented in Table V. In all models, duration of employment was independently associated with an increased risk of leukemia ($P < 0.05$).

After controlling for the arithmetic mean electric and magnetic fields, the percentage of time spent above 20 V/m and 39 V/m were significant predictors of leukemia risk ($P < 0.05$). Although significant improvements in model fit were not observed with the other threshold values, the magnitude of the standardized coefficients for these indices exceeded that of the average arithmetic mean electric field strength. This indicates that leukemia risk is more sensitive to exposures above a threshold than to the arithmetic mean.

The percentage of time spent above selected magnetic field threshold values was not associated with leukemia risk above and beyond that accounted for by duration of

TABLE IV. Pearson Correlation Coefficients for Selected Magnetic Field Exposure Indices, Ontario Electric Utility Workers

	A	B	C	D	E	F	G	H
Duration of employment (A)	1.0							
Cumulative magnetic field arithmetic mean (B)	0.37	1.0						
Average magnetic field arithmetic mean (C)	0.16	0.93	1.0					
Percentage of time above 0.2 μ T (D)	0.08	0.62	0.72	1.0				
Percentage of time above 0.8 μ T (E)	0.09	0.72	0.83	0.94	1.0			
Percentage of time above 3.1 μ T (F)	0.14	0.84	0.93	0.82	0.88	1.0		
Percentage of time above 12.5 μ T (G)	0.19	0.92	0.96	0.55	0.70	0.85	1.0	
Percentage of time above 50.0 μ T (H)	0.20	0.93	0.96	0.55	0.69	0.82	0.98	1.0

TABLE V. Standardized Coefficients^a Obtained from the Conditional Logistic Model Containing Terms for Duration of Employment, Percentage of Time Spent Above Electric Field Threshold, and Average Arithmetic Mean Field Exposure

Exposure index ^b	Lower bound of electric field threshold									
	5 V/m		10 V/m		20 V/m		39 V/m		156 V/m	
	Standardized coefficient ^c	P-value ^d	Standardized coefficient	P-value	Standardized coefficient	P-value	Standardized coefficient	P-value	Standardized coefficient	P-value
Average arithmetic mean (magnetic field)	0.24	0.93	0.36	0.72	0.50	0.61	0.72	0.47	0.17	0.87
Average arithmetic mean (electric field)	0.96	0.34	0.69	0.49	-0.23	0.83	-1.23	0.22	-0.93	0.35
Duration of employment	2.09	0.04	2.16	0.03	2.15	0.04	2.11	0.04	1.96	0.03
Percentage of time spent above electric field threshold	1.53	0.13	1.72	0.09	2.03	0.04	2.33	0.02	1.33	0.18

^aThe standardized coefficient was obtained by dividing the regression coefficient by its standard error.

^bExposure indices were modeled simultaneously.

^cStandardized coefficients were adjusted by socioeconomic status and exposures to benzene and ionizing radiation.

^dP-value based on the Wald chi-square test statistic.

employment and the arithmetic mean exposure to electric and magnetic fields (Table VI). As before, length of employment was positively associated with leukemia risk ($P < 0.05$).

Stratified analysis was performed to further evaluate the separate contributions of duration of employment and exposure above electric field thresholds as they relate to leukemia risk (Table VII). For individuals who were employed for less than 20 years, electric field exposures were not associated with leukemia. In contrast, dramatic increases in risk were observed among those with higher electric field exposure who had been employed for at least 20 years. Those in the highest tertile of percentage of time spent above 10 and 20 V/m had odds ratios of 10.17 (95% CI = 1.58–65.30) and 8.23 (95% CI = 1.24–54.43), respectively, when compared to those in the lowest tertile. Less

pronounced risk elevations were observed for the arithmetic electric field mean, and for thresholds up to 5 V/m and above 40 V/m. Additional analyses by period of exposure revealed that the increased risks associated with percentage of time spent above 10 and 20 V/m were more pronounced for exposures received during the first ten years of employment (Table VIII).

DISCUSSION

A two-step approach was adopted to examine the relationship between alternate indices of magnetic and electric field exposure and risk of cancer within Ontario electric utility workers. Initially, we examined how different indices were related to each other by using correlation and principal components analysis [Villeneuve et al., 1998].

TABLE VI. Standardized Coefficients^a Obtained from the Conditional Logistic Model Containing Terms for Duration of Employment, Percentage of Time Spent Above Magnetic Field Threshold and Arithmetic Mean Field Exposure

Exposure index ^b	Lower bound of magnetic field threshold									
	0.2 μ T		0.8 μ T		3.1 μ T		12.5 μ T		50 μ T	
	Standardized coefficient ^c	P-value ^d	Standardized coefficient	P-value	Standardized coefficient	P-value	Standardized coefficient	P-value	Standardized coefficient	P-value
Average arithmetic mean (magnetic field)	−0.79	0.43	−0.70	0.49	−0.16	0.87	1.44	0.15	0.22	0.82
Average arithmetic mean (electric field)	1.94	0.05	1.61	0.11	1.87	0.06	2.44	0.01	2.10	0.04
Duration of employment	2.12	0.03	2.14	0.03	2.09	0.04	2.14	0.03	2.09	0.04
Percentage of time spent above magnetic field threshold	1.43	0.15	1.13	0.26	−0.02	0.98	−1.34	0.18	−0.11	0.91

^aThe standardized coefficient was obtained by dividing the regression coefficient by its standard error.^bExposure indices were modeled simultaneously.^cStandardized coefficients were adjusted by socioeconomic status and exposures to benzene and ionizing radiation.^dP-value based on the Wald chi-square test statistic.

These findings were then used to select a series of indices that form the basis of the cancer risk assessment presented in this paper.

Correlational analysis is an important first step to identify a series of exposure indices that can later be used to perform cancer risk assessment. In particular, the use of indices that are highly correlated with each other will be redundant in an epidemiologic analysis, while low correlations are useful to identify independent components of exposure. The poor correlations observed in the current study between the arithmetic mean electric field and the percentage of time spent above 10, 20, and 39 V/m indicate that the arithmetic mean is a poor surrogate to model effects resulting from exposures at these thresholds. Indeed, the continuous variables representing the percentage of time spent above 20 and 39 V/m were significant determinants of leukemia risk over and above that accounted for by the arithmetic mean electric field exposure. It is a property of lognormal (or positively skewed) data that the correlation between the mean and the proportions above certain thresholds increases as the threshold cut-point increases, and this relationship between exposures in electric utility workers has been observed elsewhere [Sahl et al., 1994; Armstrong et al., 1990]. These points suggest that the arithmetic mean may be suitable to assess health effects that result from exposure above high threshold values, but less proficient for lower field cut-points.

The heterogeneity of exposures between different study populations may lead to the selection of different indices to model risk. For example, Savitz et al. [1994] observed high correlations for job title groups with the time spent above

20 V/m ($r = 0.79$), and 0.2 μ T ($r = 0.87$) and the corresponding arithmetic mean electric and magnetic field strengths. In contrast, Armstrong and colleagues [1990] found that the percentage of time spent above an electric field threshold of 20 V/m was poorly correlated with the arithmetic electric field mean ($r = 0.54$), yet the percentage of time spent above 0.2 μ T was correlated with the arithmetic mean magnetic field ($r = 0.79$). It follows that for some populations, risk assessment by using the arithmetic mean exposure may be suitable to capture increased risks that result from exposures above certain threshold cut-points.

For several reasons, our results support an increased risk of leukemia owing to both increased duration of exposure and exposure above a critical threshold. First, the risk of leukemia was more pronounced when subjects were categorized according to the arithmetic mean exposure rather than the geometric mean. The arithmetic mean, is more sensitive to skewed data, or peak exposures than the geometric mean because the distribution of individual exposures in the Ontario workers is skewed to the right. When average exposure to electric fields and duration of employment were modeled simultaneously, elevations in risk were associated with both increased exposure and duration of employment [data not shown]. Compelling evidence for the relevance of exposures above thresholds comes from modeling the percentage of time spent above selected electric field threshold values while controlling for duration of employment, and the arithmetic mean electric and magnetic field strengths. The percentage of time spent above 20 and 39 V/m were significant predictors of leukemia risk over and above the arithmetic mean electric

TABLE VII. Risk of Leukemia for Selected Indices of Electric Field Exposure, by Length of Employment, Ontario Electric Utility Workers

Electric field exposure index	Employed $\leq$ 20 years Odds ratio and 95% CI	Employed $>$ 20 years Odds ratio and 95% CI
Arithmetic mean (V/m)		
0–< 8.58	1.0	1.0
8.58–< 13.67	0.20 (0.01–3.84)	3.05 (0.60–15.53)
13.67+	0.72 (0.07–7.83)	5.08 (1.00–22.16)
Percentage of time above 2.4 V/m		
0–< 33.32	1.0	1.0
33.32–< 38.17	1.04 (0.10–11.40)	4.25 (0.88–20.25)
38.17+	0.63 (0.08–5.20)	4.21 (0.85–20.87)
Percentage of time above 5 V/m		
0–< 18.20	1.0	1.0
18.20–< 22.29	0.56 (0.03–9.87)	4.21 (0.88–20.25)
22.29+	0.99 (0.07–13.49)	5.24 (1.13–24.21)
Percentage of time above 10 V/m		
0–< 11.19	1.0	1.0
11.19–< 15.27	0.09 (0.01–5.16)	7.96 (1.21–52.25)
15.27+	0.32 (0.01–7.86)	10.17 (1.58–65.30)
Percentage of time above 20 V/m		
0–< 5.88	1.0	1.0
5.88–< 8.82	0.38 (0.03–5.07)	7.73 (1.17–50.92)
8.82+	0.09 (0.01–5.48)	8.23 (1.24–54.43)
Percentage of time above 39 V/m		
0–< 2.80	1.0	1.0
2.80–< 4.78	0.09 (0.01–7.66)	5.60 (1.12–28.10)
4.78+	2.00 (0.10–40.22)	3.17 (0.59–17.15)
Percentage of time above 78 V/m		
0–< 1.26	1.0	1.0
1.26–< 2.25	0.03 (0.00–4.48)	1.76 (0.45–6.82)
2.25+	1.12 (0.06–19.81)	1.70 (0.42–6.91)

^aOdds ratios were adjusted for socioeconomic status, duration of employment, and exposures to benzene and ionizing radiation.

^bCategorized into tertiles according to the distribution of exposure of all controls.

field exposure which is conventionally used to model threshold effects. Similar patterns of risk were observed when threshold measures were modeled with the geometric rather than arithmetic mean field exposures. Finally, when analyses were restricted to subjects who had worked with the utility for at least 20 years, dramatic increases in leukemia risk were observed with the percentage of time spent above 10 and 20 V/m. Elsewhere, no association between electric fields and leukemia was found in workers employed at Electricité de France [Guénel et al., 1996] and in Los Angeles [Kheifets et al., 1997]. Unlike these other studies, our analyses examined exposure metrics other than geometric and arithmetic mean, and the estimates of exposure took into account variations in field strength not only by job title, but also by worksite. The contribution of worksite exposures in risk assessment has been shown to be very important in previous analyses of this study population

[Miller et al., 1996a,b]. In light of our findings of increased risks among those with long term employment, it is also possible that discrepancies between our findings and other studies may be due to a more stable workforce. Historically, there was very little staff turnover at Ontario Hydro and it was common for people to have stayed there over their entire working career.

A few studies have investigated the relation between leukemia and magnetic field exposure indices other than those based on the arithmetic and geometric mean field strength. Floderus and coworkers [1993] found that occupations with frequent or large variations between low and high magnetic field intensities were more common among subjects with chronic lymphocytic leukemia. Similarly, an increased risk of leukemia was observed among workers with long term exposure to intermittent fields and as well as to peak exposures [Matanoski et al.,

TABLE VIII. Risk of Leukemia for Selected Indices of Electric Field Exposure by Period of Exposure Among Ontario Electric Utility Workers Employed for at Least 20 Years

Electric field exposure index	Period of exposure		
	First 10 years of employment	Years 10–< 20 of employment	After 20 years of employment
Arithmetic mean (V/m)			
0–< 8.58	1.0	1.0	1.0
8.58–< 13.67	3.26 (0.54–16.96)	2.98 (0.73–12.23)	2.63 (0.75–9.19)
13.67+	3.55 (0.75–16.94)	2.99 (0.82–10.93)	5.47 (1.37–20.28)
Percentage of time above 2.4 V/m			
0–< 33.32	1.0	1.0	1.0
33.32–< 38.17	5.56 (0.98–32.53)	12.82 (2.57–63.81)	4.11 (1.14–13.28)
38.17+	5.95 (1.01–34.96)	5.75 (1.26–26.18)	4.28 (1.16–12.68)
Percentage of time above 5 V/m			
0–< 18.20	1.0	1.0	1.0
18.20–< 22.29	9.21 (1.10–76.52)	2.04 (0.62–6.75)	3.47 (0.95–9.91)
22.29+	10.94 (1.53–78.12)	3.21 (1.07–9.67)	3.03 (1.01–9.52)
Percentage of time above 10 V/m			
0–< 11.19	1.0	1.0	1.0
11.19–< 15.27	10.48 (1.20–90.98)	1.81 (0.58–5.65)	2.27 (0.83–7.22)
15.27+	14.79 (1.76–124.10)	3.66 (1.14–11.76)	3.05 (1.19–10.18)
Percentage of time above 20 V/m			
0–< 5.88	1.0	1.0	1.0
5.88–< 8.82	9.34 (1.10–79.43)	2.14 (0.66–6.95)	1.33 (0.53–4.25)
8.82+	13.45 (1.58–114.20)	2.27 (0.68–7.58)	2.30 (0.90–8.10)
Percentage of time above 39 V/m			
0–< 2.80	1.0	1.0	1.0
2.80–< 4.78	4.86 (0.90–26.43)	26.90 (2.68–270.10)	4.19 (1.16–11.81)
4.78+	6.32 (1.15–34.74)	17.67 (1.76–177.16)	4.59 (1.07–14.01)
Percentage of time above 78 V/m			
0–< 1.26	1.0	1.0	1.0
1.26–< 2.25	4.88 (0.94–25.19)	3.04 (0.73–12.71)	2.08 (0.45–3.96)
2.25+	3.73 (0.81–17.09)	4.38 (1.18–16.24)	4.01 (0.95–8.74)

^aOdds ratios were adjusted for socioeconomic status, duration of employment, and exposures to benzene and ionizing radiation.

^bCategorized into tertiles according to the distribution of exposure of all controls.

1993]. Exposures above 2.5 μ T were found to be positively related to leukemia risk among Californian electric utility workers [London et al., 1994]. In contrast, no association was observed between a variety of exposure summaries (including peak exposures) and death from leukemia [Sahl et al., 1993]. A Swedish study of magnetic fields and adult leukemia found increased risks of cancer among subjects with high occupational exposures (>0.2 μ T), with more pronounced risks observed among those who also had high residential exposures [Feychting et al., 1997]. The above studies did not measure electric fields, and were, therefore, unable to control for their potential confounding effects. We know of no other study that has performed cancer risk assessment by using alternative indices of electric fields.

This study population was initially assembled as one component of the larger Tri-Utility Study [Thériault et al., 1994] in order to provide sufficient power to identify an odds ratio of two for leukemia risk had that been the true value. Theoretically, therefore, there is limited power to assess statistically significant differences in cancer risk across indices of ELF exposures. However, given that higher risk estimates of leukemia were found in previous analyses [Thériault et al., 1994, Miller, 1996a] than had been predicted in the planning of the study, the study power within the Ontario Hydro data set has proven to be sufficient on its own. Further, the details of exposure information capture several aspects of both electric and magnetic fields, thereby providing a unique opportunity to develop hypotheses for future studies of occupational cohorts.

Another important strength of this study is the detailed information that was collected on occupational confounders. Although individual exposure data were collected for workplace exposures to 2,4-D and 2,4,5-T, these variables were not entered into the final models as they had a negligible impact on the leukemia risk estimates and their inclusion diminished the power of the models by widening the confidence intervals.

The recent investigation of cancer risk within this cohort used job exposure matrices that took into account historical changes in exposure [Miller et al., 1996a]. For those analyses, the development of these job title and site specific historical adjustment factors was complex involving interviews with relevant current and retired supervisory personnel, and a combination of data available from Ontario Hydro archives. These data included peak power loads at a number of specific points in the Ontario Hydro system and overall system data including total energy generated, operating voltages, and total lengths of transmission and distribution circuits. Because historical adjustment factors were only available for the arithmetic and geometric mean 60 Hz electric and magnetic fields, our job exposure matrices were not dependent on calendar period. The inability to take into account historical changes in exposure may result in increased exposure misclassification, thereby limiting our ability to detect associations with other metrics. Indeed, the slope of the cumulative arithmetic mean electric field exposure and risk of leukemia was more pronounced for exposures with historical corrections. Although this suggests that these analyses may underestimate the true risk, this does not imply that the observed patterns of risk may differ. We know of no specific reason why the convexity associated with risk estimates for leukemia across increasing threshold values would no longer persist if historical corrections had been included. Nonetheless, further analyses that examine the role of historical correction factors for exposures on risk estimates, both within this study population and elsewhere, are needed.

By using the same job and worksite categorizations that were employed in previous analyses of this study population [Miller et al., 1996a], it is assumed that these categorizations are suitable for alternative indices. In other words, the categorizations classify exposures into homogeneous groupings. Analysis of the frequency distributions of exposure indices within each job-title and worksite location revealed no bimodal distributions and provided support for this hypothesis.

For most exposure metrics considered, increased risks of leukemia were also observed with both increasing cumulative exposure to electric and magnetic fields [results not shown]. When average exposure to magnetic fields was modeled rather than cumulative exposure, risks were attenuated. This indicates that the increased risk associated with the cumulative measure of magnetic field strength is in

part attributable to its dependence on duration of employment.

It has recently been suggested that failure to consider magnetic field frequencies below 20 Hz that emanate from radial tires may compromise risk estimates obtained from epidemiologic studies [Milham et al., 1999]. As outlined earlier, the personal monitors used in this study were configured to limit exposure assessment to 60 Hz electric and magnetic fields. If exposures below 20 Hz fields are relevant to the biological mechanisms associated with induction of leukemia, our risk estimates for magnetic fields may be understated because of increased exposure misclassification. Nonetheless, the strong associations we observed between leukemia and electric fields would be unaffected by exposures generated from radial tires as radial tires do not produce electric fields.

However, a portion of the Ontario electric utility workers were exposed to lower field frequencies before 1955 as part of the province was powered by electricity at 25 Hz. Given that more pronounced risks were observed among utility workers employed for greater than 20 years, there is a possibility that 25 Hz electric field exposures may have contributed to the increased risk of leukemia. Unfortunately, the sample size available to us did not permit separate analyses among workers who commenced employment before and after the 25 to 60 Hz conversion had taken place.

In summary, the results from our analyses confirm the positive association between leukemia and exposure to electric fields previously observed in this study population [Miller et al., 1996a]. This study uniquely demonstrates that this association is explained by both exposure to electric fields over a prolonged period and exposure above a threshold. After controlling for worker differences in electric field exposures, no significant associations between leukemia risk and magnetic fields were observed. The absence of data relating to historical correction factors may have resulted in an attenuation of risk estimates, in particular, for the arithmetic mean electric field exposures and risk of leukemia. Despite this, our findings support the hypothesis that electric fields may act as promoters in the carcinogenic process. It is recommended that similar analyses be pursued in other study populations that have data on exposure to electric as well as magnetic fields.

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