

# Exposure to 50-Hz Electric Field and Incidence of Leukemia, Brain Tumors, and Other Cancers among French Electric Utility Workers

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Recent studies on the association between exposure to 50- to 60-Hz fields and cancer carried out among electric utility workers have focused mainly on the magnetic field component of exposure. The authors have investigated tumor risks specifically associated with electric fields, as this exposure is distinct from magnetic fields. The study design is a case-control study nested within a cohort of 170,000 workers employed at Électricité de France-Gaz de France (EDF) between 1978 and 1989. All incident cases of cancer and benign tumor of the brain diagnosed in 1978-1989 among workers before the age of retirement were included. Four randomly selected controls were individually matched to each case by year of birth. The exposure to electric fields was assessed from measurements collected in 850 EDF workers for a full work week. Arithmetic and geometric mean exposures were included in a job-exposure matrix to determine the cumulative exposure of the cases and the controls. Exposures to potentially carcinogenic chemicals found at the workplace were also evaluated through expert judgment. The analysis by site of tumor did not show any increased risk for leukemia (72 cases). An odds ratio of 3.08 (95% confidence interval 1.08-8.74) was observed for all brain tumors (69 cases) for exposure above the 90th percentile (≥387 V/m-year), and there was some indication of a doseresponse relation, although the risk did not increase monotonically with exposure. No confounding from magnetic fields or from other potentially carcinogenic hazards was apparent. The observed association was somewhat stronger after allowing a 5-year latency period before diagnosis (odds ratio = 3.69, 95% confidence interval 1.10-12.43) for exposure above the 90th percentile. However, the risk of brain tumor could not be linked to a specific type of tumor. An unexpected association was also observed for colon cancer, using geometric indexes of exposure, but no other association was seen for any other type of cancer. Our study indicates that electric fields may have a specific effect on the risk of brain tumor, and that this should be taken into account in future analyses on the carcinogenic effects of 50- to 60-Hz fields. Am J Epidemiol 1996;144: 1107-21.

brain neoplasms; case-control studies; colonic neoplasms; electromagnetic fields; leukemia; occupational exposure

Since the early 1980s, many studies have shown an increased incidence or mortality of cancer in occupational groups referred to as "electrical workers." Review papers have shown that the relative risks for leukemia and brain tumors calculated after aggregating the data from these studies were slightly elevated (1-3). It was suggested that electric fields and/or magnetic fields in the extremely low frequency range (50 or 60 Hz for fields produced by electric power systems) assumed to be present at relatively high levels in the work environment of these workers might be responsible for the excess risk of cancer. However, these studies did not include exposure measurements, and the exposure to extremely low frequency fields was simply inferred from the job titles of the study subjects. Recently, studies have been conducted to test more thoroughly the hypothesis of a carcinogenic effect of extremely low frequency fields. These studies have included measurements of exposure to these fields and assessment of exposure to potential carcinogenic confounders, such as benzene or ionizing radiations. Occupational exposure to magnetic fields has been found to be associated with different subtypes of leukemia (4, 5) or with brain tumors (6). In another study, no increased risk was observed with these two

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Abbreviations: CI, confidence interval; EDF, Électricité de France-Gaz de France; ICD-9, International Classification of Diseases, Ninth Revision.

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types of tumor (7). With one exception (8), no study has investigated the role of occupational exposure with regard to electric fields.

At power frequency, electric fields should be distinguished from magnetic fields. An electric field is produced by electric charges and depends on the voltage in the electric conductor, whereas a magnetic field is produced only if these charges are in motion, that is, if the current flows through the conductor (9). Because the exposures to these fields occur under different work situations, the correlations between electric field strength and magnetic field density have been found to be weak in measurement surveys performed among electric utility workers (10, 11). Therefore, the effect of each of these exposures may be analyzed separately in epidemiologic studies. A study examining the risk of cancer in relation to the magnetic field among French utility workers has been published previously in conjunction with two cohorts of Canadian utility workers (5). Besides extremely low frequency fields, another paper has reported the risk of cancer associated with exposure to high frequency transient fields in workers from France and Québec (12). The objective of the present paper is to study the risk of cancer, particularly leukemia and brain tumors, related to 50-Hz electric fields, using the data collected at the French electric utility. In addition, all other sites of cancer are included in an exploratory analysis.

### MATERIALS AND METHODS

### Study population

The study design is a case-control study nested within a cohort of gas and electric utility workers (Électricité de France-Gaz de France (EDF)). This cohort includes all men employed for at least 1 year at EDF in 1978–1989. Among the 170,000 workers included in the cohort, 60 percent were employed in the distribution sector of the company in which the workers may be involved in activities related to both gas and electricity.

### Selection of cases and controls

All men in the cohort whose first diagnosis of tumor was made before the age of retirement in 1978–1989 were included in the group of cases. All cases have been registered at the Social Security department that supervises the health insurance system specific to EDF workers while they are working for the company. The notification of cancer diagnoses to this department is necessary before the insurance benefits can be provided to the worker. All cancers (*International Classification of Diseases*, Ninth Revision (ICD-9), codes 140–208) as well as benign tumors of the brain (ICD-9 code 225) were included, with the exception of squamous and basal cell cancers of the skin (ICD-9 code 173). Diagnoses were reviewed by an oncologist from the original pathology report, and further information was obtained when necessary from the patients' doctors.

After the date of retirement that occurs between 55 and 60 years of age depending on the jobs held at EDF, the worker's health insurance is controlled by the French general system for Social Security, and incident cases of cancer cannot be identified any longer. Therefore, no case of cancer diagnosed after the date of retirement was included in the study.

Controls were individually matched to each case by year of birth. For each case, a set of possible controls was created from the personnel data files. Each set included all workers who had the same year of birth as the case, who were present at EDF, and who never had had a cancer at the date of diagnosis of the matched case. Four controls per case were selected at random from each of these sets.

### Assessment of exposure to electric fields

The assessment of exposure to electric fields was made through a measurement survey carried out among present EDF workers. The objective was to quantify the exposure to electric fields (50 Hz in France) by job category to make a job exposure matrix.

All occupations at EDF were examined and grouped into job categories with similar electric environment. Job grouping was performed by experts chosen among engineers, occupational physicians, and hygienists in the different sectors of the company. Thirty-five job categories were defined in this way and constituted the rows of the job exposure matrix. Electric field exposure measurements were then carried out among EDF workers representative of these 35 job groups.

Measurements of exposure to electric fields were taken with a Positron personal exposure monitor (Positron Industries, Montreal, Québec, Canada) and with the prototype IREQ meter (Institut de Recherche d'Hydro-Québec, Montreal, Québec, Canada) for less than 10 percent of the measurements (13). Each meter was checked and calibrated before use by a worker. The meter was worn on the belt or in a shirt pocket during a full work week, and it recorded the electric field every minute. During work hours, the worker was asked to fill in a diary describing his activities. At the end of the week, measurement data were loaded to a microcomputer for inspection of the exposure profiles and for analysis. Technical problems occurred in about 15 percent of the measurements (e.g., meter out of order, flat battery, meter not worn, etc.) that were then discarded. In total, measurements taken from 850 workers during a full work week were used for estimating the exposure to electric fields. The measurements were taken at different workplaces across the country and at different periods of the year to take regional or seasonal variations into account.

For a given worker, the distribution of electric field values recorded by the meter during work hours was generally highly skewed to the right. Inspection of log-probability plots indicated that the exposure approximately followed a log-normal distribution (14). We used both the arithmetic mean (time-weighted average) and the geometric mean of all these values to summarize the electric field exposure of a worker.

Within a given job, the distribution of mean exposures (arithmetic and geometric) calculated for each worker was also close to a log-normal distribution (14). To summarize the exposure associated with a specific job, we used both the arithmetic mean of the workers' arithmetic means and the geometric mean of the workers' geometric means. Because of the rightskewed distributions of exposure (at the worker and at the job level), the arithmetic mean strongly depends on exposure peaks, whereas the geometric mean is close to the median. These two exposure metrics were included in the job exposure matrix (table 1) and were applied to the analysis of epidemiologic data.

The exposure meter also recorded the exposure to 50-Hz magnetic fields and to high frequency transient fields. These data were collected in the same way as those for electric fields (5, 12).

### Confounders

Occupational exposures to potential carcinogens were evaluated in a separate job exposure matrix, which has been described elsewhere (15, 16). These chemicals were mainly selected from lists 1, 2A, and 2B of the International Agency for Research on Cancer (17). The lists include asbestos, benzene, chlorinated solvents, petroleum solvents, styrene, polyurethane, epoxy resins, coal tars, creosote, herbicides, cutting fluids, mechanical oils, polychlorobiphenyls, hydrazine, cadmium, and coal gasification.

Exposures to chemical agents were assessed through judgment of experts of EDF (engineers, occupational hygienists, occupational physicians) and were reported in the matrix as semiquantitative exposure indexes. Time-weighted average exposures were evaluated from the estimates of exposure intensity and exposure frequency given by the experts for different work tasks. Several time periods were also considered for evaluating past exposures. Ionizing radiations were not included in the job exposure matrix, since the cumulative dose in sieverts could be obtained individually for the cases and for the controls from the EDF surveillance program.

Social class was determined for study subjects based on the first job held at EDF and was coded according to the French classification of social class (18).

## Analysis

In the analysis, we first used the cumulative occupational exposure to electric fields as the exposure metric. Cumulative exposure was calculated from the date of hire to the date of diagnosis for the cases or to the date of diagnosis of the matched case for the controls (reference date). The calculation was made by multiplying the exposure estimate associated with each job held at EDF (read in the job exposure matrix) by the number of years spent in this job and summing over the jobs of the subject's work history. These calculations were made separately for the arithmetic and for the geometric exposure indexes of the matrix. To allow for a latency period before the incidence of cancer, other calculations of cumulative exposures were made by excluding the 5, 10, or 15 years before the reference date. Cumulative exposures to magnetic fields and to potentially carcinogenic chemicals were obtained in the same way.

Statistical analyses were performed independently for each site of cancer using the cases and their matched controls. Conditional logistic regression was used because of the matched design of the study using EGRET software (19). Exact logistic regression was also performed in some analyses with small numbers, using LogXact (20). For electric fields, study subjects were classified into four groups of exposure. To determine exposure cutpoints, we used the 50th, 75th, and 90th percentiles of the cumulative exposure distribution of the cases and the matched controls for each site of cancer. These percentiles were selected a priori before the analysis was conducted. We also examined dose-response relations by fitting models with cumulative exposure to electric fields as a continuous variable and by attributing to each subject the value, in volts per meter-year, of the mean cumulative exposure in his exposure group. The odds ratios associated with an exposure increase of 500 V/m-year (for arithmetic indexes) or 50 V/m-year (for geometric indexes) were then calculated from the coefficients estimated by the models. These values of 500 and 50 V/m-year were approximately equal to the difference between the mean cumulative exposure in the highest  $(\geq 90$ th) and in the lowest (<50th) exposure groups.

For adjusting on occupational hazards other than electric fields, we used models where cumulative exposures were introduced as continuous variables. So-

	No. of workers	Arithmetic mean* (V/m)	95% CI†	Geometric mean‡ (V/m)	95% CI	Geometri SD†
Hydroelectric station < 100 MW						
Foreman	24	10.36	7.60-13.42	2.16	1.67-2.80	1.91
Maintenance mechanics	21	12.08	9.19-18.96	2.45	1.77-3.39	2.14
Electricians and operators	20	12.74	9.70-17.73	2.34	1.77-3 08	1 88
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Hydroelectric station $\geq$ 100 MW	47		10 11 57 17	a / 5		• • • •
Foreman	17	21.33	13.14-57.17	3.15	1.98-5.02	2.66
Maintenance mechanics	26	11.21	7.67-16.90	1.64	1.37–1 97	1.60
Electricians and operators	29	18.63	12.48-29.81	2 45	1.85-3.26	2.18
Nuclear plant						
Mechanics	46	11.46	9.00-14.75	1.67	1.43-1 97	1.75
Plant operators	11	10.84	6.04-36.12	1.36	0.95-1 96	1.84
Electricians	10	11.00	8 10–16.98	1.55	1.31-1.84	1.31
Classical thermoelectric plant						
Mechanics	27	8.10	5.64-14.03	1.32	1.02-1 71	2 00
Plant operators	19	7.58	5 58-12.11	1 34	1.09-1.65	1.58
Electricians	19	18.41	11.78-30.90	2.29	1 91-2.74	1.50
All thermoelectric plants						
Foreman, operators	14	7.58	4.30-15.58	1.30	0.92-1.85	1.96
Foreman, electrician	9	10.28	6.42-20.93	2.26	1.64-3.10	1.63
Instrument, test worker	32	17.72	13 46-25.52	2.30	1 88-2 78	1.75
Transmission						
Foreman	34	21.88	13.72-34.36	2.11	1.71-2.60	1 07
	20	72.16	43.34-204.39			1.87
Lineman, classical	10	174.64		2 15	1.72-2.68	1.66
Lineman, live line	10		87.04-1,214.24	3.78	2.90-4.91	1.53
Lineman, underground cable		56.53	32.83-194.10	1.87	1.38-2.53	1.81
Substation worker	30	236.31	102.64-880.72	2.90	2 01-4.17	2.76
Operators	54	83.10	64.64183.61	2.60	2.19-3.09	1.90
Electric control worker	44	28.89	18.73-40.04	2.43	2.07-2.86	1 73
Telecommunication worker	50	14.20	9.90-16.83	2.43	2.02-2.90	1.92
Safety engineer	13	13.72	8.71-25.96	2.04	1.53-2.72	1.70
Distribution						
Foreman	15	17.00	8.50-37.52	1.98	1.2 <del>9–</del> 3.03	2.33
Lineman, medium voltage	11	121.37	55.37-423.77	3.11	2.27-4 26	1 70
Lineman, low voltage	11	10.95	5.90-26.54	1.32	1.02-1 72	1.56
Lineman underground cable	5	5.68	2.72-52.87	1.00	0.95-1 05	1.06
Lineman, other	43	14.42	8.85-15.66	1.47	1.27-1.71	1.63
Substation worker	21	12.17	7.62-22.74	1.29	1 02-1.64	1.75
Calibration, medium voltage	12	12.00	7.06-22.63	1.81	1 55-2.11	1.32
Electric control worker	11	6.77	4 56-17.08	1 51	1 11-2.06	1.68
Meter readers and installers	10	8.19	6.50-11.03	1.49	1.23~1.80	1.36
Background						
Blue coltar	15	8.38	5.75-15 22	1.54	1.07-2.23	2 07
White collar	102	11.09	8.30-11.89	2 57	2.20-2.99	2.20

TABLE 1. Job exposure matrix, showing arithmetic mean and geometric mean exposures to electric fields by job group among present French gas and electric utility workers

\* Arithmetic mean of the workers' arithmetic mean exposures.

† CI, confidence interval; geometric SD, geometric standard deviation of the workers' geometric means

‡ Geometric mean of the workers' geometric mean exposures.

cioeconomic status was included in the models as a categorical variable on a five-level scale. It was used as an adjustment variable in the site-by-site analysis, since it was associated with the risk for total cancer. Cumulative exposure to electric fields, used in most analyses, is the product of exposure intensity by exposure duration. To separate out the effects of these variables, other models were also fitted using the timeweighted average exposure (i.e., mean exposure over the period of employment, used as an index of exposure intensity) and length of exposure as explanatory variables with an interaction term.

## RESULTS

In total, 1,995 incident cases of tumor occurred during the study period. Work history was missing or incomplete in the personnel data files for 80 cases (4 percent). These cases were excluded from the analysis with their matched controls. Among the 7,658 remaining controls, 90 (1.2 percent) had incomplete work history and were also excluded. The analysis finally includes 1,915 cases and 7,568 controls with complete work history.

The job exposure matrix including both the arithmetic mean and the geometric mean exposures to electric fields with their 95 percent confidence intervals is presented in table 1. The results were close to expectations, with high exposures for both arithmetic and geometric exposures in job groups working with high voltage equipment (transmission linemen, transmission substation workers, medium voltage distribution linemen). Workers in the background exposure groups were divided into blue collar and white collar workers and included people with activities not directly related to electricity production or distribution, for example, clerks or gas workers. Mean exposures close to or even lower than "background" were also observed in some jobs (e.g., low voltage linemen), where work tasks are often carried out outside, far away from the regular wiring of buildings and offices, and with the electric current turned off.

The odds ratios associated with cumulative exposure to electric fields for each tumor site are shown in table 2, using both the arithmetic and the geometric indexes of exposure. Table 2 also shows the odds ratio associated with a 500-V/m-year (arithmetic) or 50-V/ m-year (geometric) increase in exposure, calculated under the assumption of a linear trend between exposure and cancer risk. For all sites combined, the odds ratios in the exposure categories above median were slightly decreased to 0.8 or 0.9. The same tendency was observed for the most frequent sites of cancer, such as the mouth and pharynx, larynx, and lung. For leukemia, the odds ratios for both arithmetic and geometric exposure indexes were below one but not statistically significant. The odds ratios observed for other hematopoietic tumors were close to one. For brain tumors, the odds ratios associated with high cumulative arithmetic exposures were increased and reached the value of 3.08 (95 percent confidence interval (CI) 1.08-8.74) for exposure above the 90th

percentile. An odds ratio of 2.59 (95 percent CI 0.98-6.84) per 500-V/m-year increase in exposure was also calculated under the assumption that the risk increases linearly with exposure, although the odds ratio estimates decrease slightly from the second to the third exposure category. However, the odds ratios for brain tumors associated with cumulative geometric exposures were only weakly elevated, with a nonsignificant odds ratio of 1.63 in the highest exposure group. For melanoma, a nonsignificant odds ratio of 6.80 was observed in the high geometric exposure group, but the odds ratios were close to one for lower exposures. Colon cancer risk was significantly associated with cumulative geometric exposure in the second (odds ratio = 1.97) and the third (odds ratio = 2.62) exposure categories, with a slight decrease for exposure above the 90th percentile (odds ratio = 2.49). The summary odds ratio of 2.77 for a 50-V/m-year increase in exposure was significant. For the other sites of cancer for which there was no previous report of an association with extremely low frequency fields, no clear pattern of association emerged from these data.

To examine in more detail the association of electric field with brain tumors, additional analyses were conducted using the arithmetic indexes of exposure. Leukemia has also been included in these analyses, as it represents another site of cancer of interest a priori. We will also examine the results for colon cancer using the geometric indexes of exposure because of the observed association.

In table 3, the effect of adjustment variables was tested using the likelihood ratio statistic. Different exposure metrics were used for magnetic fields (e.g., cumulative arithmetic, cumulative geometric, timeweighted average exposure), but the results were similar, and table 3 shows the model based on cumulative arithmetic mean exposure to magnetic fields only. For all three sites, adjusting on magnetic fields changed the odds ratios for electric fields only slightly, with a more pronounced effect on the odds ratio in the highest electric field exposure category for brain tumors. However, this odds ratio was at the limit of statistical significance (odds ratio = 2.83, 95 percent CI 0.97-8.28), and the likelihood ratio test indicated no effect of magnetic field exposure on brain tumor risk (p =0.47). For colon cancer, the likelihood ratio test for magnetic fields had a p value of 0.04, indicating that magnetic fields were significantly associated with risk, but no confounding was apparent, with little changes in the odds ratios for electric fields. Also in table 3, other occupational exposures selected in the job exposure matrix among potential risk factors for the specific sites of tumor were included in the model. These

		U	Cumulative	Cumulative arithmetic means	ş				Cumulative	Cumulative geometric means		
Site of cancer	V/m- years†	St o F	ŧ	95% CI‡	Years Years	95% CI	v/m- yearst	A o R	В	95% CI	Ber Ser A	95% CI
All tumore§ (ICD-8‡ codes 140-208, 225)	~277 277-345 346-413 2414	886 454 195	- 0 0 0 88 8 89 0	0.7 <del>9</del> -1.04 0.74-1.04 0.74-1.07	0 88	0 75-1 00	<ul> <li>&lt;46</li> <li>46-63</li> <li>64-76</li> <li>≥77</li> </ul>	1,020 481 173	- 0 88 88 88 88 88 88 88 88 88	0 88-1 12 0.68-0 98 0.66-1 05	0.84	0.711 00
Leukemia (ICD-9 codes 204–208)	<253 253-329 330-401 2402	88 0 0 <del>1</del> 4	1.00 0.96 0.71 0.37	0.45-2 03 0.27-1 92 0.11-1.28	0 40	0 131.24	<42 42–62 63–78 ≥79	5 5 1 1 3 8	1.00 0.76 0.75 0.36	0 36-1.61 0.29-1 93 0.09-1 47	058	0.24-1.36
Other harmatopoletic cancers (ICD-9 codes 200-203)	<194 194-285 286-378 2379	88 19 19 19	1.06 0.89 0.87	0 54-1.89 0 42-2 32 0 35-2.14	0 85	0 35-2 06	8 8 8 8 8 8 8 8 8	8585	1.00 0.92 1.19 1.02	0.49-1.73 0.53-2.67 0.36-2.90	1 07	0 48-2 38
Brain turnors (ICD-9 codes 191, 225)	<238 238-318 319-388 2387	5 8 23 8	1.00 2.47 3.08	0 <del>99 6</del> 16 0.46 - 4 45 1 0 <del>8 -</del> 8 74	2 59	0.98 - 6 84	<37 37–55 56–73 ≿74	81 89 99 99 99 99 99 99 99 99 99 99 99 99	1 25 0	0.50-3 13 0.34-3 14 0 43-6 24	1 32	0.48-3.67
Mouth, pharymx (ICD-8 codes 140149)	~287 287346 347416 2417	5 5 8 8	1 00 0.84 0 69 0 69	0 611 16 0 801 68 0 441 09	0 73	0 48-1 12	<48 48–63 64–75 ≥78	2 8 8 8 8	1 00 0 81 0 37 0 55	0 60-1 11 0 23-0 60 0 32-0.94	0 43	0.28-0 68
Esophagus (ICD-9 code 150)	~298 298-350 351-422 2423	327	1.00 0.72 0.76 0.86	0 39–1 31 0 37–1 54 0 40–1.85	0.89	0 48-1.67	<49 49−63 64−76 ≥77	88 88 89 99 99 99 99 99 99 99 99 99 99 9	1.00 0.82 0.37 0.98	0.47-1 44 0.15-0.94 0.42-2 28	0 63	0.2 <del>8-</del> 1.35
Stormach (ICD-9 code 151)	~287 287-359 360-422 2423	38 5 7 2	1.00 0.76 0.41 0.40	0.36-1 61 0.16-1 04 0.13-1 21	0.32	0 10-1.10	≪49 49—63 64-76 ≿77	₿ <u></u> 68 67 87 87 87 87 87 87 87 87 87 8	0.80 0.80 0.81 0.81	037-171 032-2.03 013-1.77	0 59	0.22-1.60
Colon (ICD-8 code 153)	<305 305-359 360-427 2428	47 31 18	1.00 1.67 1.67	0 922 94 0 813 45 0 834 01	141	0.90-2 21	<50 50-70 282 ≥82	\$ & C 다	1.00 2.62 2.62	1 103.54 1 21-5.68 0 92-6 72	2.77	1.30-5.89
Rectum (ICD-9 code 154)	<279 279–354 355–420 ≥421	8 <u>5</u> 4 4	1.00 1 51 2 12 0.67	071-320 084-533 019-231	0 74	0.27–2 03	48 48-64 85-80 ≥81	ង ដ ដ ទ	1 00 1 28 1 24	0 49-2 32 0 75-5 22 0.33-4.74	151	0 56-4 01
Other digestive (ICD-9 codes 152, 155-159)	<290 290-359 360-429 ≥430	45 55 8	1 00 0.78 1 01 0.71	041149 047219 0291.74	0 78	0 39-1 55	89-80 89-80 89-80	4817	1 00 1 35 0 83 0.76	0 72-2.53 0 38-1 85 0 22-2.67	0 95	0 45-2 01

TABLE 2. Odds ratios associated with cumulative arithmetic and cumulative geometric exposures to electric fields by site of tumor\* among French gas and electric

Larynx (ICD-9 code 161)	~291 291-357 358-421 2422	54 19 15	1.00 1 07 1 19 1 51	0 64-1.79 0 64-2.22 0 74-3.09	1 55	0 74-3.21	<49 49-62 63-73 ≿74	79 09 09 EE	- 1 00 0 28 0 28	0.54-1.53 0 10-0.65 0 39-1.92	0 56	0 26-1.20
Lung (ICD-9 code 162)	<298 298-358 359-419 2420	88 £ £ 8	+ 00 0.89 12 12 12 10 10 10 10 10 10 10 10 10 10 10 10 10	0 64-1.23 0 35-0.83 0 44-1.10	0.67	043-104	<51 51–67 68–78 ≥79	<u>ទី</u> ន	1 00 0 76 0 76 0 76	0.54-1.07 0 40-0.96 0 44-1 31	0.63	0.41-0 99
Other respiratory (ICD-9 codes 160, 163-165)	<ul> <li>254</li> <li>254–325</li> <li>2398</li> <li>2399</li> <li>2399</li> </ul>	4 0 4 4	1 00 0.59 1 95	0 16-2 14 0.17-3 78 0 42-8.95	1 70	0 <del>36 -8</del> .07	<41 41–57 58–74 ≥75	й <del>б</del> <i>ы</i> ю	- 0,0 - 2,2,5,8 8,29,8	0.77-8.28 0 09-4 28 0 30-11.0	1 47	0 37–5.86
Melanoma (ICD-9 codes 172, 190 6)	<226 226-292 233-389 2370	81 0 1 0 1 0 1	1.00 0.68 0.68 0.68	037-405 015-301 002-1.94	0 18	0 02–1.67	<ul> <li>39-50</li> <li>51-67</li> <li>88</li> <li>88</li> </ul>	Ç ∞ 4 0	1 00 1 12 6.80 6.80	0.35-2 79 0.25-5.03 0 73-83 1	2.29	0.47-11 1
Prostate (ICD-9 code 185)	<ul> <li>&lt;326</li> <li>326–388</li> <li>389–427</li> <li>&gt;428</li> </ul>	80 0 <del>4</del>	1 00 0.92 0.25 0 97	0.34-2 48 0 05-1.24 0 24-3 87	0.58	0 08-4 22	66 88 -86 89 -89 89 -89 89 -89	£540	1.70 0.50 0.50	0.46-4.49 0.36-7 89 0 10-2 55	0 84	0 21–3 30
Gentral organs (ICD-9 codes 186-187)	<136 136-227 228-310 2311	4 5 13 22 13	1 2 2 00 2 1 2 2 0 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2	0 57-2 54 0 39-2.64 0 16-1.85	0 49	0.13–1 87	57 55 55 57 55 55 57 55 55 57 57 55 57 5	64 12 7 0 0	0 88 0 42 0 95	0 38-2.02 0 13-1.36 0 23-3.97	<b>28</b> 0	0 20-3.39
Urinary organs (ICD-9 codes 188–189)	~286 288-355 358-417 ≥418	13 14 8 21 15 14 8 21	1 00 0 87 0 94 0 94	0 50-1 52 0 47-1.86 0 49-2.19	5	0 49-2 18	<50 50-64 65-78 ≥79	83 83 52 89	1 00 0 93 0 73 0 57	0 55-1 58 0 36-1 46 0 22-1 45	0 66	0 33-1.31
Unknown primary (ICD-9 codes 196–199)	<295 295-360 361-428 ≿428	49 17 13	23 10 10 10 10 10 10 10 10 10 10 10 10 10	0.33-1 23 0 55-2.47 0 55-2 75	1.31	0 50-3 41	52-71 52-71 288 288	8 £ ⊑ ø	0.67 0.82 0.82 0.82 0.82 0.82 0.82 0.82 0.82	0 722 44 0 412.07 0- 312.68	1 02	0.4 <del>8-</del> 2 12
Other solid turnors (ICD-9 codes 170–175, 192–195)	<190 190-286 287-364 2365	88 t c	0,11 1,21 1,21 1,21 0,4	0 43-2 87 0.37-3 89 0 09-1 73	0 46	0 14-1 46	×8 8 8 8 8 8 8 8 8 8 8 8 8 8 8 8 8 8 8	35 1 1 2 35 6	0.10 0.10 0.70 0.70 0.70	0 20-1.37 0 30-2 65 0 1 <del>9-</del> 2 67	0 81	0 26-2 49
<ul> <li>Odds ratios are adjusted on socioeconomic status.</li> <li>The values shown are the 50th, 75th, and 90th percentilies of the exposure distribution for each stie of cancer</li> <li>The values shown are the 50th, 75th, and 90th percentilies of the exposure distribution for each stie of cancer</li> <li>Codds ratio; CI, confidence interval, ICD-9, <i>International Classification of Diseases</i>, Ninth Revision</li> <li>The cumulative exposure ranged from 8 V/m-year to 5,455 V/m-year (cumulative arithmetic) and from 1.5 V/m-year (cumulative geometric)</li> </ul>	c status. 90th percentiles 2-9, <i>internation</i> a m-year to 5,455	of the exp / Classfic V/m-year	cosure dist ation of Di (cumulativ	ribution for each seases, Nimth Re e artithmetic) and	stte of car evision d from 1.5	ncer V/m-year to 115 \	//m-year (cumula	tive geon	netric)			

TABLE 3.	Odds ratios associated with exposure to electric fields* and adjusted on socioeconomic status (SES), magnetic
fields, and	other risk factors for leukemia, brain tumors, and colon cancer among French gas and electric utility workers,
1978-1989	

Percentiles	No. of	Adjus	ted on SES		d on SES and netic fields	potentia	n SES and other I occupational founders†
	CESES	OR‡	95% Cl‡	OR	95% CI	OR	95% CI
Leukemia							
<50	38	1.00		1.00		1.00	
≥50<75	20	0 96	0.45-2.03	0.95	0.45-2.01	1.11	0.50-2.43
≥75–<90	10	0.71	0 271.92	0.71	0.26-1 91	0.83	0 29-2.38
≥90	4	0.37	0.11-1.28	0.36	0.10-1.26	0.37	0.10-1.40
Likelihood ratio statistic§				0 13 (1	df), <i>p</i> = 0.72	5 66 (5	df), <i>p</i> = 0.34
Brain tumors							
<50	29	1.00		1.00		1.00	
≥50<75	22	2.47	0. <del>99-</del> 6.16	2.51	1.00-6.34	2.29	0.89-5.94
≥75 <b>&lt;9</b> 0	8	1.43	0 46-4.45	1.43	0.45-4.48	1.43	0 45-4.57
≥90	10	3.08	1 08-8.74	2.83	0.97-8.28	2.97	1.00-8.80
Likelihood ratio statistic				0 53 (1	df), <i>p</i> = 0.47	3.51 (	6 df), <i>p</i> = 0.74
Colon cancer							
<50	45	1.00		1.00		1.00	
≥50<75	32	1.97	1 103.54	1.87	1 04-3.37	1.86	1.033 36
≥75–<90	21	2 62	1.21-5.66	2.60	1 20-5.62	2 59	1.20-5.60
≥90	12	2.49	0 92-6.72	2.44	0.90-6.60	2.43	0 90-6.58
Likelihood ratio statistic				3.89 (1	df), <i>p</i> = 0 05	0.09 (1	df), $p = 0.76$

\* Cumulative arithmetic exposure for leukemia and brain tumors; cumulative geometric exposure for colon cancer.

† Leukemia: adjusted on benzene, chlorinated solvents, petroleum solvents, ionizing radiations, and styrene, brain tumors adjusted on benzene, chlorinated solvents, petroleum solvents, ionizing radiations, coal tars, and herbicides; colon cancer: adjusted on ionizing radiations ‡ OR, odds ratio; CI, confidence interval.

§ Calculated as 2(L1 – L2), where L1 is the log likelihood of the logistic model with electric fields and SES, and L2 is the log likelihood of the model with electric fields, SES, and the adjustment factor.

occupational exposures did not confound the association with electric fields, as odds ratios changed only slightly and the likelihood ratio test was not significant.

The odds ratios for subtypes of leukemia and brain tumors are shown in table 4. Leukemias were divided into acute nonlymphoid leukemias and other leukemia subtypes, but none was associated with electric field exposure. For malignant brain tumor (gliomas), the odds ratio was 1.76 (95 percent CI 0.54-5.74) in the highest exposure category, but it was more elevated in the second exposure category (odds ratio = 2.52, 95percent CI 0.93-6.83). Results for benign brain tumors (meningiomas) are also shown in spite of very small numbers. Since there was no case in the reference category, odds ratios are virtually infinite. However, lower limits of 95 percent confidence intervals as calculated from exact methods were below one. In our case series, seven cases (10 percent) were not confirmed histologically but were diagnosed as primary brain tumors, based on other laboratory examinations such as computerized tomography. Excluding these cases and their matched controls from the analysis did not substantially alter the odds ratio estimates for all histologically confirmed brain tumors with exposure

above the 90th percentile (odds ratio = 2.76, 95 percent CI 0.88-8.64) in spite of larger confidence intervals due to smaller numbers of cases. No analysis by histologic subtypes was done for colon cancer because all cases were adenocarcinomas.

In table 5, we analyze the combined effects of exposure intensity and exposure duration on the risk of brain tumor. For exposure intensity, represented by the time-weighted average exposure over the employment period, the cutpoints were 11 V/m (median) and 13 V/m (75th percentile). The relatively small range of exposure variation between these exposure classes is due to the small number of person-years in jobs with high exposure intensity. For length of exposure, cutpoints were 20 years (median) and 25 years (75th percentile). The odds ratios in each cell of the crosstabulation were calculated using exposure intensity below 11 V/m and exposure length below 20 years as the reference group. As seen in table 5, odds ratios increased regularly with the length of exposure in a given level of exposure intensity. Also seen in table 5, an association with exposure intensity was less apparent, as the odds ratio decreased in the medium category of exposure intensity, for all exposure lengths. However, a significant increased odds ratio of 7.18 (95

	Percentiles*	No, of cases	No. of controls	ORt	95% CI†
Leukemia subtypes					
Acute nonlymphoid leukemia‡	<50	18	64	1.00	
	≥50<75	10	42	0.95	0.45-2.01
	≥75<90	4	17	0 71	0.26-1.91
	≥90	2	11	0.36	0.10-1.26
Other leukema§	<50	20	76	1.00	
	≥50-<75	10	28	1.13	0 39-3.25
	≥75–<90	6	26	0.60	0 15-2.51
	≥ <b>9</b> 0	2	21	0.25	0 04–1.51
Brain tumor subtypes					
Malignant brain turnorsII	<50	29	134	1.00	
-	≥50<75	17	48	2.52	0.93-6 83
	≥75–<90	6	27	1.57	0 46–5 39
	≥ <b>90</b>	7	22	1.76	0 54–5.74
Benign brain tumors¶	<50	0	7	1.00	
	≥50<75	5	16	80	0 25 <b>–</b> ∞
	≥75<90	2	15	œ	0.04∞
	≥90	3	2	80	0.61–∞
All histologically confirmed brain tumors	<50	28	133	1 00	
	≥50–<75	19	56	2.20	0.84–5 73
	≥75 <b>&lt;9</b> 0	7	37	1.30	0.33-4 30
	≥ <b>90</b>	8	19	2.76	0 88-8.64

TABLE 4. Odds ratios associated with exposure to electric fields for leukemia and brain tumor subtypes among French gas and electric utility workers, 1978–1989

\* Exposure percentiles are based on the exposure distribution for all leukemia or all brain tumors † OR, odds ratio (adjusted on socioeconomic status and on exposure to magnetic fields); CI, confidence interval

‡ International Classification of Diseases, Ninth Revision, codes 205.0, 205.3, 205.9, 208.0, and 208.9. This group includes mainly acute myeloid leukemia (code 205.0).

§ International Classification of Diseases, Ninth Revision, codes 204.1, 205.1, and 204.0.

I International Classification of Diseases for Oncology, codes M-9400/3, M-9421/3, M-9440/3, M-9441/3, M-9380/3, M9391/3, M-9450/3, and M-9470/3.

International Classification of Diseases for Oncology, code M-9530/0. Results of the lower limit for the confidence interval based on exact logistic regression.

percent CI 1.17-44.22) was observed for exposure intensity greater than 13 V/m and exposure length above 25 years. Similar analysis was conducted for colon cancers. The same pattern appeared for exposure duration that was strongly associated with risk, but no association with exposure intensity was apparent.

The effect of different latency periods was examined by excluding the 5, 10, and 15 years of exposure before diagnosis (table 6). No association was seen for leukemia. For brain tumors, the odds ratio of 3.69 (95 percent CI 1.10-12.43) for exposure above the 90th percentile after excluding the last 5 years before diagnosis was somewhat stronger than with a 10- or 15year latency period. This suggests that the period of exposure most strongly associated with brain tumor risk ranged from 5 to 10 years before diagnosis. For colon cancer, the decrease of the odds ratio from the third to the fourth exposure group was more pronounced for longer latency periods.

### DISCUSSION

A limited number of studies have examined the risk of cancer in relation to occupational exposure to electric fields. In the present study, all cancer sites were studied with a focus on leukemia and brain tumor, for which an association with extremely low frequency fields had been suspected in previous reports. We have observed no association with leukemia, but there was some evidence of an increased risk for brain tumors. An unexpected association was also found between colon cancer and cumulative exposure to electric fields using geometric indexes.

Originally, excess risks of cancer have been reported in occupational groups with potential exposure to both electric and magnetic fields (1-3), but in the absence of exposure measurements, cancer risks could not be attributed to a specific type of extremely low frequency field. Recent studies (4-7) have investigated cancer risks in relation to occupational exposure

Time-weichted						Length	Length of exposure					
exposure		4	<20 yearst			8 N	220-25 yearst			X	225 years	
(m/N)	Cases	Controls	ОН§	85% CI§	Cases	Controls	£	95% CI	Cases	Controls	ቼ	95% CI
<11	14	72	1.00		6	ន	3.35	0.87-12.94	6	ह	3.67	0.66-20.44
211-6139	7	37	0.83	0.30-2.32	ო	ន	1.18	0.25-5.59	4	21	2.79	0.43-17.99
≥13	÷	28	1.74	0.69-4.38	9	ន	2.17	0.53-8.87	9	=	7.18	1.17-44.22

exposure length among brain tumor cases and their controls. years: 50th percentile of

Iwenty-five years: 75th percentile of exposure length OR, odds ratio; CI, confidence interval.

С Ю

time-weighted average exposure.

Eleven V/m: 50th percentile of

75th percentile Thirteen V/m:

of time-weighted average exposure

to magnetic fields, as assessed in large measurement surveys. A comparison of the results on electric fields in the present study with previous findings on magnetic fields among electric utility workers may give some clues on what type of field, if any, is linked to cancer risk.

# Leukemia

The study on magnetic fields carried out in three electric utilities in France and Canada included the present EDF workers (5). It was shown that the incidence of acute nonlymphocytic leukemia was increased for cumulative exposure to magnetic fields above the median (odds ratio = 2.41, 95 percent CI 1.07-5.44), but these results were not concordant among the utilities. This increase was stronger in the cohort of workers of Ontario Hydro, but it was actually attributed to exposure to electric fields in a recent reanalysis of this cohort (8). In the cohort of EDF workers, the association of leukemia with magnetic fields was weak. In a study on magnetic field exposure among Southern California Edison company workers, no increase was observed for hematopoietic tumors, but the number of cancer deaths was small (7). In another study on five US electric power companies by Savitz and Loomis (6), the results for leukemia risk in relation to magnetic fields were essentially negative. Conversely, magnetic fields were associated with chronic lymphoid leukemia in a community-based case-control study carried out in Sweden (4). In total, the findings on leukemia are discordant for magnetic as well as for electric fields, and a conclusion on the type of field preferably associated with leukemia risk, if any, cannot be drawn at the moment.

# Brain tumors

A threefold increased risk was observed for cumulative arithmetic exposure above the 90th percentile (387 V/m-year). Some indication of a dose-response relation was also observed (odds ratio = 2.59, 95percent CI 0.98-6.84 for a 500-V/m-year increase in exposure), but the strength of the association between exposure to electric fields and tumor risk did not increase monotonically. This association was not explained by other potential occupational risk factors of brain tumor in adults including magnetic fields, organic solvents, polycyclic aromatic hydrocarbons, herbicides, and ionizing radiations (21, 22), although little is known about the etiology of this tumor. Because of the absence of a clear association with geometric indexes of exposure, it can be suspected that peak exposures to electric fields, which are correlated with arithmetic indexes, are the most important cause for

TABLE 6. Odds ratios* associated with cumulative exposure to electric fields after allowing for
different latency periods before the diagnosis of cancer, calculated from the date of start of employment
at Électricité de France-Gaz de France to 5, 10, or 15 years before diagnosis (or diagnosis of the
matched case for the controls), 1978–1989

	Latency (years)	V/m-years†	No of cases	OR‡	95% Cは
Leukemia	5§	<215	36	1.00	
	-	215-291	18	0.87	0.40-1.88
		292-351	8 '	0.52	0.18-1.47
		≥352	4	0.35	0.10-1.25
	10	<169	33	1.00	
		169-237	15	0.73	0 32-1.67
		238-296	9	0 80	0 2 <del>9 -</del> 2.21
		≥297	3	0.28	0.07-1.16
	15¶	<120	32	1.00	
		120-181	11	0.53	0.22-1.27
		182-240	11	0.57	0.23-1.42
		≥241	1	0.56	0.05-6.91
Brain tumors	5#	<202	22	1.00	
		202-274	20	3.43	1.25 <del>-9</del> .40
		275-342	9	2.40	0.73-7.90
		≥343	9	3.69	1.10-12.43
	10**	<166	22	1.00	
		166-229	14	1 67	0.67-4.19
		230-294	9	1.79	0.60-5.36
		≥295	7	2.15	0.63-7.26
	15 <del>††</del>	<125	21	1.00	
		125-178	11	1.05	0.41-2.67
		179–243	7	0.83	0.25-2.74
		≥ <b>24</b> 4	5	1.03	0.28-3.72
Colon cancer	5‡‡	<44	45	1.00	
		4461	34	1 57	0.87-2.84
		62-72	20	2.27	1.08-4.77
		≥73	8	1.25	0.433.65
	10§§	<34	46	1 00	
		34-49	31	1.65	0.91-3.00
		5059	21	2.25	1.07-4.72
		≥60	8	1.20	0.41-3.56
	15	<26	41	1.00	
		26-38	30	1.71	0.95-3.08
		39–48	21	2.59	1.24-5.40
		≥49	6	1.16	0.37-3.59

\* Adjusted on socioeconomic status and magnetic field exposure.

+ Exposure cutpoints are the 50th, 75th, and 90th percentiles of the cumulative exposure distribution

(arithmetic indices for leukemia and brain tumors, geometric indices for colon cancer).

‡ OR, odds ratio; CI, confidence interval.

§ Six cases not employed during the period were excluded

Il Twelve cases not employed during the period were excluded.

I Seventeen cases not employed during the period were excluded.

# Nine cases not employed during the period were excluded.

\*\* Seventeen cases not employed during the period were excluded.

†† Twenty-four cases not employed during the period were excluded.

# Three cases not employed during the period were excluded

§§ Four cases not employed during the period were excluded.

IIII Twelve cases not employed during the period were excluded.

the excess risk of brain tumors. We have also investigated the combined effects of exposure intensity (time-weighted average exposure over the employment period) and exposure duration. Although exposure length has shown more consistent effects than has exposure intensity, we were not able to investigate very high time-weighted exposures because of the limited number of workers in highly exposed jobs. However, the results also indicate that relatively high time-weighted exposure ( $\geq 13$  V/m) and long exposure duration ( $\geq 25$  years), when present simultaneously, are associated with a strong elevation of risk. The

hypothesis that both factors should be present to produce an effect may be worthy of further study in other investigations.

The association observed in the present data was not clearly related to the benign (meningiomas) or to the malignant (gliomas) form of the tumor. Most studies among electric workers where the exposure was inferred from the job title have included both tumor types (3, 23–27). In the studies where an analysis by histologic subtype was shown, increased risks for brain tumors have generally been related to astrocytomas or glioblastomas (23–25). Although increased risks for meningiomas have not been reported, firm conclusions are difficult because of small numbers.

In the studies where magnetic field exposure measurements were carried out, results for brain tumors have not been consistent. Magnetic fields were not associated with brain cancers in two studies (4, 7). In the Canada-France study on magnetic fields (5), an elevated nonsignificant odds ratio of 1.95 (95 percent CI 0.76-5.00) was observed for malignant brain tumors in the most exposed group of workers. However, this excess risk was regarded as an artifact by the authors, because it was strongly dependent on the adjustment on socioeconomic status. For benign brain tumors, the odds ratio in the same exposure group was 1.62 (95 percent CI 0.35-7.59). In the reanalysis of Ontario Hydro data, there was also some evidence of an association of brain cancers and benign brain tumors with magnetic fields, but not with electric fields (8). In the most recent US utility workers study (6), an association between exposure to magnetic fields and mortality from malignant brain cancers was observed, and it was stronger for exposure in the previous 2-10 years. Accordingly, we observe that the association with electric fields was stronger for the exposure period preceding the last 5 years before diagnosis than for the exposure period preceding the last 10 years before diagnosis. However, these risk estimates are very unstable, and this should be interpreted with caution. In total, results from all these studies indicate that magnetic fields, or electric fields, or both might be related to brain tumor risk, although no firm conclusion can be drawn from the available evidence.

#### Colon cancer

Colon cancer had never been associated with extremely low frequency field exposure. Hence, the present results should be confirmed by other studies. The association was stronger with the geometric indexes of exposure, but a less consistent association was also seen for arithmetic indexes. In addition, magnetic fields were independently associated with risk. Interestingly, cancers of the rectum also showed a weaker nonsignificant association with electric fields. In previous studies, the most consistent association between colon cancer risk and occupation was that of a protective effect of high physical activity (28). Because white collar workers had both a relatively high geometric mean exposure to electric fields (table 1) and possibly low physical activity at work, we can hypothesize that the observed association with electric fields is, in fact, related to low physical activity. However, physical activity was not evaluated in our study, and further work is needed to confirm this hypothesis.

#### Other sites

Other sites of cancer have rarely been investigated in relation to extremely low frequency fields. We find that cancers of the lung, mouth, and pharynx are negatively associated with some categories of electric field exposure. It has been documented that the blue collar workers, classified in the background exposure group of the matrix (e.g., gas workers, porters, storekeepers), had high mortality from causes of death strongly associated with tobacco smoking and alcohol drinking (29). Because of low exposure to electric fields among these workers, a negative confounding from tobacco and alcohol might explain the apparent decrease in risk for these cancers. Unfortunately, no information on tobacco and alcohol consumption was available, and we could not confirm this hypothesis from the present data. Exposure to electromagnetic fields has also been associated with melanomas in some studies (30-32). We observe an elevated but nonsignificant odds ratio in the high geometric exposure category for this cancer, but this result is isolated, with odds ratios close to one in other exposure groups, and may be due to chance. Associations with breast cancer have also been reported in males (33-35) and in females (36). In our study, breast cancer has been observed in only three men. This number is too small for meaningful analysis, but it was noted earlier that this number is compatible with no increased risk in the cohort of EDF workers in a proportionate incidence analysis (expected number = 3.89) (5). Other hormone-sensitive cancers have been suspected to be related to extremely low frequency fields, based on experimental evidence that these fields induce modifications in melatonin production by the pineal gland (37). Prostate cancer has been suggested as a possible candidate, but our results do not confirm this hypothesis.

#### Methodological issues

Our study has some limitations that should be pointed out. First, only the cases of cancer diagnosed while the worker was still active in the company could be included in the group of cases. An important number of cases diagnosed at the age of 60 years and over could not be included since the incidence of most cancers rises sharply after that age. Thus, in spite of the large study population (1.4 million person-years before the age of retirement), the statistical power was limited for some sites of cancer, and small increased risks may not have been detected.

Unlike magnetic fields, measuring the exposure to electric fields is particularly difficult, because the wearing position of the meter or the posture of the worker influences the values recorded by the monitor. In addition, exposures were not assessed individually for each case and each control but were estimated from a job exposure matrix. Exposure misclassification arises because workers in the same job group do not necessarily have the same exposure. In our measurement data, the within- group variance for electric fields represented 66 percent of the total betweenworker variance. Other authors, using the measurement data on magnetic fields, have defined the lines of the matrix a posteriori, by grouping the jobs as efficiently as possible in order to decrease the withingroup variance (38). We simply used the job categories defined a priori by company experts before the measurements were carried out, because our sampling procedure was not really compatible with rearrangements of job groups, and because the gain in precision would have been only marginal for electric fields (39). Also, we have assumed that past exposures to electric fields were identical to present exposures. This assumption was made because we were able to identify separately the jobs where traditional work techniques were used and the more recent occupations. For example, in the job exposure matrix, we separated mechanics in classic thermoelectric power plants from mechanics in recent thermoelectric nuclear plants. We also separated the "classic" high voltage linemen from the high voltage linemen working on live lines, because this latter technique was introduced in the 1970s. It should also be noted that, in 1960-1980, the distribution current provided to private customers throughout France changed from 110 to 220 V. This shift has likely entailed some additional exposure, but we believe that it was marginal, in any case much smaller than a twofold increase, and that it had little or no effect on the classification into exposure groups. Finally, we did not take into account electric field exposure at home. If the association with disease is real, then exposure outside work participates in the risk burden. We considered that this exposure adds, on average, the same constant value to all subjects, but that it does not affect the values of the odds ratio based

on exposure differences. All of these inaccuracies in exposure assessment may have led to nondifferential exposure misclassification, because the error in assigning exposure is the same for the cases and for the controls. This type of misclassification usually biases the odds ratio toward the null and is therefore not likely to account for the observed associations between exposure and disease. If the association between exposure and disease is real, then misclassification may also have distorted the shape of the dose-response relation (40). Thus, the nonmonotonic dose-response curve observed in our data for brain tumor should not be regarded as a definite argument against a causal association.

Ideally, the choice of exposure indexes should be based on the comprehension of the biologic pathway from exposure to disease. However, no such basis is available for extremely low frequency fields and cancer, and a large number of exposure indexes are virtually available. In this study, we have used two different exposure indexes for electric fields, arithmetic and geometric, which reflect opposite features of the exposure. Because of the right-skewed distribution of electric field values recorded in individual workers, arithmetic means are strongly dependent on very high exposures such as peaks (10). If high infrequent exposures, entailing abrupt increases in exposure levels, were causally linked to cancer, then the arithmetic indexes would be relevant for studying cancer risk. Conversely, geometric means represent a central tendency of exposure close to the median for log-normal exposure distributions (14). If the risk of cancer was related to the repetition of some central and frequent exposure, then the geometric indexes would be more appropriate. These two exposure indexes have been shown to be weakly correlated in exposure measurement surveys carried out among electric utility workers (10, 11), and they were used independently in the present study. Exposure duration is another possibly important parameter that could be linked to increased risk of cancer, in conjunction with the relevant exposure metric. To take duration into account, cumulative exposure was the main exposure metric used in this study. The two components of cumulative exposure, exposure intensity and exposure duration, have also been investigated.

Confounding from other occupational exposures, including magnetic fields, was carefully examined in our study. Based on previous measurement surveys, magnetic field density was weakly correlated with electric field strength among electric utility workers (10, 11). In our study subjects, correlation between cumulative exposures to electric and magnetic fields was moderate (partial correlation adjusted on age = 0.33), and no confounding was actually observed. Adjustments on magnetic field exposure were made in the detailed analyses, but residual confounding due to exposure misclassification remains a possibility. We were also able to examine all major occupational exposures to potentially carcinogenic chemicals at EDF, as well as ionizing radiations. The adjustment on these factors, selected for each site of cancer among the wellestablished or suspected risk factors, did not change importantly the values of the odds ratios for electric fields. Residual confounding from exposures to chemical carcinogens could be suspected in our data, if their evaluation made by experts were inaccurate. However, the same job exposure matrix on chemical carcinogens has been used to analyze the relation between exposure to asbestos and lung cancer (41) and between exposure to benzene and leukemia (manuscript in preparation). In both cases, strong relations between exposure and disease were observed, with a clear dose-response relation. Because of the coherence of these findings with well-established associations, we believe that our exposure estimates are valid and that residual confounding from carcinogenic chemicals is not important in the present results.

We have investigated all sites of tumor in this study. It is therefore remarkable that the main evidence of an association appears for brain tumors, since brain tumors were with leukemia the sites most strongly suspected a priori to be linked with extremely low frequency fields. These results therefore tend to confirm the hypothesis that occupational exposure to 50-Hz electric fields increases brain tumor risk. There was also some indication of a dose-response relation, although inconsistent, since the risk did not increase monotonically with exposure. However, electric fields could not be linked with any particular form of brain tumor, benign or malignant. Conversely, our study does not show any increased risk for leukemia. An unexpected association was also seen for colon cancer, possibly related to confounding from other occupational risk factors, but this result would deserve further attention. If the observed association with brain tumor is real, it implies that electric fields may have their own role in the development of the disease, in conjunction or not with magnetic fields. Electric fields should therefore be taken into account in future analyses of epidemiologic data for testing the associations between extremely low frequency fields and cancer.

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