



Review

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Extremely low-frequency magnetic fields and heart disease

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Extremely low-frequency magnetic fields and heart disease

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The biologically based hypothesis that magnetic fields increase the risk of conditions related to cardiac arrhythmia and acute myocardial infarction but not chronic cardiovascular disease was initially supported by the results of an epidemiologic study. High rates of cardiovascular disease and relatively common exposure to magnetic fields made it an important public health question. Most of the epidemiologic studies that followed showed no effect. In this paper the basis for both this hypothesis and the epidemiologic studies that tested it are presented. It was concluded that the evidence speaks against an etiologic relation between exposure to electric and magnetic fields and cardiovascular disease. This effort represents an interesting case study of a scientific inquiry that has been successfully resolved despite numerous methodological difficulties inherent in research on low-level environmental exposures.

Key terms acute myocardial infarction; case study; electric and magnetic fields; environmental exposure; epidemiologic method.

Concerns about cardiovascular changes resulting from exposure to power-frequency electric and magnetic fields originated from descriptions of symptoms among Russian high-voltage switchyard operators and workers in the 1960s and early 1970s (1, 2). Although these reports were not confirmed (3), more recent investigations focused on direct cardiac effects of exposure to magnetic fields, mostly related to heart rate variability.

On the basis of several lines of evidence, Sastre et al (4) hypothesized an association between exposure to power-frequency magnetic fields and acute cardiovascular disease (CVD). First, a double-blind laboratory investigation found that exposure to intermittent 60-Hz magnetic fields reduced heart rate variability (4). Second, several prospective cohort studies, on (i) the risk of heart disease (5–8), (ii) the overall mortality rate of survivors of myocardial infarction (9–11), and (iii)

the risk of sudden cardiovascular death (12), indicated that reductions in some components of the variation in heart rate increase. Changed heart rate variability reflects changed cardiac autonomic control (13, 14), this phenomenon suggesting a possible mechanism of action of exposure to electric and magnetic fields on the heart. According to this information, Savitz et al (15) postulated that occupational exposure to magnetic fields would increase the risk for cardiac arrhythmia-related conditions and acute myocardial infarction, but not chronic CVD, and conducted an epidemiologic study to evaluate this hypothesis.

This paper presents the basis for this hypothesis and reviews the relevant epidemiologic studies. Furthermore, we provide an overall evaluation of the evidence and a comment on the ability of epidemiology to test a biologically driven hypothesis meaningfully.

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Methods

This systematic review is based on several literature searches. First, an initial Medline search was performed in 2003 for a chapter developed for the Environmental Health Criteria series of the World Health Organization. Second, a search of a database on the health effects of electric and magnetic fields by The Resource Strategies Inc, which includes peer-reviewed literature on the health effects of exposure to electromagnetic fields from 1992 to the present, was done in 2005. Potentially relevant references were identified by examining the title and abstracts of all references obtained from the electronic search, and they were obtained in full for closer examination. We further scrutinized the reference lists of identified papers for further, previously unidentified publications of relevance. All relevant papers published in English in the peer-reviewed literature were included in this review.

Each study was examined for key quality components, such as study type and an ability to detect an association, source (morbidity versus mortality records) of diagnostic information, the specificity of outcome, completeness of follow-up, and representativeness of the population, source (industry, single job title, or complete work history) and quality of exposure assessment (informal assessment, expert assessment through observation or background knowledge, or measurements), and information on and adjustment for known risk factors (particularly smoking and physical activity).

Short-term effects on cardiovascular function

Sastre et al (4) performed studies concerning the heart rate variability of 77 healthy men exposed to 60-Hz magnetic fields of 14.1 μT or 28.3 μT . Decreased alterations in low-frequency (0.04–0.15 Hz) heart rate variability was observed during intermittent exposure to the higher field strength, while no effects occurred at the lower field strengths or when the exposure was continuous. In two other studies on the same issue, heart rate variability was evaluated during intermittent exposure to 28.3 μT magnetic fields (16, 17). In the latter study, three different frequencies were used (16, 40, and 60 Hz). Exposure to 16 Hz was associated with decreased alterations in the spectrum of the heart rate variability. Graham et al (18) also performed studies using a much higher magnetic field (127.3 μT) and both continuous and intermittent exposure. No alterations in heart rate variability were observed under either exposure condition, and the researchers concluded that, when earlier reports were taken into account, direct excitation of the human heart is extremely unlikely during exposure to magnetic fields lower than 127.3 μT .

Another group (19) examined the effects of magnetic fields on heart rate variability in two groups of volunteers. The exposure consisted of 28 μT at 50 Hz (circularly polarized) for 100 or 150 seconds either following or prior to a similar period of sham exposure. An analysis of the spectra of heart rate variability in relation to continuous sinusoidal exposure showed a reduction in the ratio of power in the low band (0.02–0.15 Hz) to the high band (0.16–1.0 Hz). The authors concluded that, despite inconsistencies, these data indicate that short exposures to magnetic fields may influence mechanisms that control heart rate.

Kurokawa et al (20) examined the possibility that exposure to extremely low-frequency alternating magnetic fields may have influenced heart rate variability in 50 healthy volunteers exposed to magnetic fields at frequencies ranging from 50 to 1000 Hz and with flux densities ranging from 20 to 100 μT for periods ranging from 2 minutes to 12 hours. They found no changes in heart rate variability or other parameters and concluded that magnetic fields have no influence on the activity of the cardiovascular autonomic nervous system that modulates heart rate.

A very small study (21) investigated the influence of 50-Hz magnetic fields at strengths from 20 to 500 μT for 30 minutes on nine persons. The results were inconsistent and an apparent *increase* in heart rate variability was observed. However, the authors concluded that the changes could have been associated with the influence of magnetic fields.

The initially positive, albeit inconsistent, results of reduced heart rate variability after exposure to electric and magnetic fields (4, 17) were not reproduced in several subsequent studies with volunteers (18, 20). A multistudy analysis of the different studies previously performed by Graham's team indicated that the decreased heart rate variability occurred when accompanied by increases in physiological arousal, stress, or a disturbance in sleep, such as blood collection, but not otherwise (22, 23).

Long-term effects on cardiovascular function

Several studies have looked at the long-term effects on cardiovascular function in occupationally exposed male workers. Knave et al (24) and Stopps et al (25) found no significant effects on the cardiovascular function (symptoms, blood pressure, electrocardiography) of male workers who were exposed occupationally for more than 5 years to electric fields from 400 kV power lines. Checcucci (26) found no effect on the cardiovascular system of 1200 workers at high-voltage railway substations (1–4.6 kV/m and 4–15 μT). In a health survey of

627 railway high-voltage substation workers, Baroncelli et al (3) found no difference in electrocardiographic findings between exposed and control groups.

Studies of cardiovascular disease

Early studies

Several studies have examined general cardiovascular mortality in relation to exposure to electric and magnetic fields (table 1). A retrospective cohort study of 21 744 men employed in an electrical utility company in the province of Quebec between 1 January 1970 and 31 December 1988 examined the standardized mortality ratio (SMR) for circulatory diseases and exposure to magnetic fields, electric fields, and pulsed electromagnetic fields (27). Unfortunately, all CVD were lumped together as “circulatory diseases”. Exposure information was obtained from a job-exposure matrix constructed for another study (28), and it was based on the last job held in the industry. Among the employees exposed to magnetic fields of $>0.16 \mu\text{T}$, 137 persons died from circulatory diseases [adjusted rate ratio (RR) 0.91, 95% confidence interval (95% CI), 0.73–1.14].

A retrospective cohort study (29) examined cardiovascular death [International Classification of Diseases, revision 9 (ICD-9), 3900–4489] and exposure based on job title and work environment (no measurements). Each employee was assigned to one of seven job categories based on the occupation held for the longest time. Information on mortality was abstracted from death certificates obtained from three public sources and from company records. Using a comparison with the cause-specific mortality rates for the general population in California, these authors observed a significantly reduced standardized mortality ratio of 0.62 (95% CI 0.59–0.65) for CVD mortality for both genders combined. The risk estimates for different occupational categories were very close to each other, and all but the category of meter readers had significantly decreased mortality. In analyses comparing internal occupational groups, using administrative employees as a reference group, mortality from “major cardiovascular” (category not defined) was significantly increased in all of the categories, the highest rate ratio being 1.71 (95% CI, 1.13–2.58) for the “meter reader/field service” category.

Cause-specific mortality was analyzed according to latency and the estimated levels of exposure to 50-Hz electromagnetic fields in a retrospective cohort of Danish electric utility employees (30). A job-exposure matrix was based on expert evaluation and some measurements of job titles and work areas. The individual exposure assignment was based on the characteristics of the first job. The standardized mortality ratio for acute

myocardial infarction (ICD-8 410) was 0.95 (95% CI 0.9–1.0). That for mortality caused by cardiac sclerosis (ICD-8 412) was 0.9 (95% CI 0.8–1.0) on the basis of 300 cases, and that for mortality caused by other heart disorders (ICD-8 394–402, 413, 420–429, 450, and 782) was 0.9 (95% CI 0.8–1.0). No increased mortality was observed for the analysis by time since first employment or categories of estimated exposure to electric and magnetic fields.

Studies of subsets of cardiovascular disease

The first study conducted with the specific aim of testing the hypothesis of an association between occupational exposure to electric and magnetic fields and acute CVD risk was based on an analysis of a retrospective cohort study of utility workers in the United States (15). It included 138 903 men employed for 6 months or more between 1950 and 1986. The exposure categories for electric and magnetic fields were based on 2842 work-shift time-weighted average measurements of magnetic field exposure, and death certificates were obtained for 97% of the deceased. The authors reported a significantly increased risk for mortality from arrhythmia-related conditions and acute myocardial infarction among workers with a long duration of work, with rate ratios of 1.4–1.5 for the longest employment intervals, and with high exposure to magnetic fields, with rate ratios of 1.6–2.4 in the highest exposure category. As postulated, a positive association was found for acute myocardial infarction, but not for chronic CVD. Surprisingly, an inverse association was observed for chronic CVD.

The hypothesis of an association between exposure to electric and magnetic fields and the risk for arrhythmia-related cardiovascular disorders was further addressed in a Danish cohort of utility workers (31) through linkage to the nationwide, population-based Danish Pacemaker Register. The study identified all cases of pacemaker implantation among 24 056 male electric utility workers between 1982 and 2000 and compared this number with the corresponding numbers in the general population. In addition, the data on utility workers were fitted to a multiplicative Poisson regression model in relation to estimated levels of exposure to 50-Hz electromagnetic fields. Overall, the risk was not increased for severe cardiac arrhythmia among employees in the utility companies, with 135 observed cases of men with pacemakers versus 140 expected, yielding a risk ratio of 0.96 (95% CI 0.8–1.1). No clear dose-response pattern emerged with an increasing level of exposure to electric and magnetic fields or duration of employment.

In an attempt to conduct as a close a replication of the work as possible by Savitz et al (15), the same methods and analytical models (32) were applied to the

Table 1. Methods used in the studies of general cardiovascular mortality and morbidity in relation to electric and magnetic fields. (95% CI = 95% confidence interval, ALS = amyotrophic lateral sclerosis, AMI = acute myocardial infarction, CHD = coronary heart disease, CNS = central nervous system, CVD = cardiovascular disease, IHD = ischemic heart disease, MI = myocardial infarction, OR = odds ratio, RR = rate ratio, SIR = standardized incidence ratio, SMR = standard mortality ratio, US = United States)

Study	Study population	Study design	Exposure	Result	Comments
Baris et al, 1996 (27)	Workers employed in electrical company between 1970–1988; total circulatory deaths: 137, no further sub-classification; total cohort 21 744	Cohort; SMR and internal comparisons	Job-exposure matrix	Highest exposure category: SMR 0.63 (95% CI 0.53–0.74), RR 0.91 (95% CI 0.73–1.14)	No information available for known risk factors (tobacco smoking, alcohol consumption or physical activity); no definition of diagnoses, included as “circulatory diseases”, or the extent to which the contributory cause of death was included
Kelsh & Sahl, 1997 (29)	Utility workers, employed 1 year in 1960–1991, followed until 1992; total CVD deaths, not further classified: 1561; total cohort: 40 335	Cohort; SMR and internal comparisons	Certain occupational categories	Total cohort: cardiovascular SMR 0.62 (95% CI 0.59–0.65); linemen, RR 1.42 (95% CI 1.18–1.71)	A clear healthy worker effect could explain the external comparison; no explanation for the increased risk of death from “major cardiovascular disease” for internal comparison
Johansen & Olsen, 1998 (30)	Male utility workers, employed ≥ 3 months in 1990–1993, followed 1974–1993; total death: 3540; AMI: 713; atherosclerosis: 300; total cohort: 21 236	Cohort; SMR	Classification of workplaces based on measurements	High exposure workplace: AMI SMR 1.0 (observed=160)	No information available about known risk factors for cardiovascular disease; exposure assessment based on few measurements and only one job; a possible healthy worker effect, as only external comparisons were used
Savitz et al, 1999 (15)	Male utility workers, employed ≥ 6 months in 1950–1986, followed until 1988; AMI deaths: 4238; arrhythmia-related: 212; atherosclerosis: 142; chronic CHD: 2210; total cohort: 138 903	Cohort; SMR and internal comparisons	Duration of work in jobs with elevated electric and magnetic fields	Highest μ T-year category: MI RR 1.62 (95% CI 1.45–1.82), chronic CHD RR 1.0 (95% CI 0.86–1.77)	No information available for known risk factors; problems in using subtypes of CVD as coded on death certificates, which probably led to misclassification between categories
Johansen et al, 2002 (31)	See Johansen & Olsen, 1998 (30); total pacemaker implants: 135; total cohort: 24 056	See Johansen & Olsen, 1998 (30)	See Johansen & Olsen, 1998 (30)	Highest exposure category: total SIR 1.00 (95% CI 0.6–1.5)	Arrhythmias not associated with pacemaker implantation not included; selection and information bias unlikely due to completeness of Danish Pacemaker Register and the nationwide, compulsory pension fund and the public payroll system and since the information was collected years before the events
Sahl et al, 2002 (32)	Male utility workers in Kelsh & Sahl 1997 (29); AMI deaths: 407; chronic CHD deaths: 369; total cohort: 35 391	See Savitz et al, 1999 (15)	See Savitz et al, 1999 (15)	Highest μ T-year category: AMI RR 0.99 (0.65–1.51); chronic CHD RR 1.19 (95% CI 0.79–1.77)	No information available for known risk factors; however an attempt was made to examine smoking indirectly as a potential confounder; problems in using subtypes of CVD as coded on death certificates; large number of exposed persons made the study more informative than expected on the basis of size alone; carefully duplicated analytic approach of the original investigation
Håkansson et al, 2003 (33)	Swedish twins responding to job questionnaire in 1967 or 1973; AMI deaths: 802; IHD other than AMI: 344; arrhythmia-related: 156; atherosclerosis: 202; total twin cohort: 27 790	Cohort, Cox analysis	Job-exposure matrix	Highest exposure group: AMI RR 1.3 (95% CI 0.9–1.9)	Exposure assessment based on a single question on “main occupation” at one point in time in the past and included persons from the general population with low potential for exposure
Ahlbom et al, 2004 (35)	Male population of Stockholm 1992–1993; 695 incident cases of AMI and 1133 controls	Population-based case-control	Job titles, job-exposure matrix	Highest exposure category: RR 0.57 (95% CI 0.36–0.89)	Population-based, high participation rates and high validity of the AMI diagnosed morbidity; control for blood pressure, serum cholesterol, socioeconomic status, and cigarette smoking; potential for nondifferential recall bias, as information on occupations was based on interviews and misclassification due to a job-exposure matrix from a different study
Sorahan et al, 2004 (36)	Utility workers, employed ≥ 6 months in 1973–1982, followed until 1997; AMI: 3320; arrhythmia: 32; atherosclerosis: 25; chronic CHD: 1552; total CVD deaths: 6802; total cohort: 79 972	Cohort; SMR and internal comparisons	Duration of work in jobs and locations with elevated electric and magnetic fields	Highest μ T-year category: AMI RR 1.03 (95% CI 0.88–1.21); chronic CHD RR 0.92 (95% CI 0.73–1.16)	No information available for known risk factors; problems in using death certificates; exposure assessment, based on individual job histories, job environments, and local sources of magnetic fields which is likely to have reduced misclassification
Mezei et al, 2005 (37)	Sample of deaths in US in 1986 and 1993 collected through death certificates and interviews with proxy respondents; AMI: 2992; arrhythmia: 697; atherosclerosis: 197; chronic CHD: 2,913; other: 34 891	Cases cardiovascular deaths, controls with proxy other causes except ALS, CNS & lymphopoietic cancers	Longest job determined by the interview with proxy; job titles categorized into low, medium and high	Highest exposure category: AMI OR 0.96 (95% CI 0.76–1.22); chronic CHD OR 1.10 (95% CI 0.86–1.41)	Large, but limited by proxy-reported information on exposure and smoking; smoking not a confounder of the MF-CVD association; problems in using death certificates and high potential for exposure misclassification

cohort used by Kelsh & Sahl (29). In this cohort of 35 391 male utility workers in southern California in the United States, with follow-up from 1960 to 1992, 407 deaths from myocardial infarction and 369 deaths from chronic coronary heart disease were identified. For cumulative exposure, with adjustment for socioeconomic factors, no association was observed with mortality from acute myocardial infarction (RR per 1 μ T-year = 1.01, 95% CI 0.99–1.02) or chronic CVD (RR per 1 μ T-year = 1.00, 95% CI 0.99–1.02). When compared with the analysis using SMR measures of effect (29), this study did not find an association between occupational exposure to electric and magnetic fields and a risk of CVD. The reasons for this difference are likely due to methodological differences in that some of the observed changes in risk estimates could have been due to the exclusion of men over 80 years of age in the previous study, the definition used for exposure to electric and magnetic fields based on the usual occupation as opposed to a detailed occupational history, and the different reference groups used in the internal analyses. One group (meter readers) with significantly increased mortality from CVD, but with low exposure to electric and magnetic fields, was assigned to the reference group in Kelsh & Sahl's study (29) but not in that of Sahl et al (32). This procedure was taken because later measurements indicated that this job had low levels of exposure to magnetic fields and to replicate exposure groupings used by Savitz et al (15).

The association between exposure to electric and magnetic fields and mortality from heart disease was examined using data from the Swedish twin registry, including close to 28 000 twins from two different cohorts of twins in Sweden (33). These twins were interviewed in 1967 and 1973, and, at that time, their occupation was recorded. In addition, the interview covered information on smoking, alcohol consumption, level of physical activity, and body mass index. The analyses were based on the primary and contributory cause of death, followed until 1996 with the aid of the previously developed exposure matrix [described in detail by Floderus et al (34)] and adjusted for the previously mentioned risk factors. The results did not show an overall increased risk for arrhythmia-related death or ischemic heart disease, other than acute myocardial infarction or atherosclerosis. A nonsignificantly increased risk for acute myocardial infarction was observed in the highest exposure group (RR 1.3, 95% CI 0.9–1.9, exposure level $>0.3\mu$ T). Since this study was conducted within a twin cohort, a subanalysis that took into account the twin information was conducted. In the analysis the authors observed a larger increase in the risk of acute myocardial infarction and exposure to magnetic fields in genetically susceptible subgroups (ie, among the monozygotic twins, one of whom had previously had an acute myocardial infarction), for which there was no obvious explanation.

A population-based case-control study in Sweden (35), investigating risk factors for acute myocardial infarction in the city of Stockholm included information on occupational exposure to electric and magnetic fields based on job titles 1, 5, and 10 years prior to diagnosis. The analysis was restricted to the 695 cases and 1133 controls with information on job titles. Of these, 595 cases and 949 controls had jobs that were common enough to have been classified according to a previously developed job-exposure matrix (34). The study used two approaches to classify exposure. First, specific individual job titles with presumed elevated exposure to electric and magnetic fields were investigated, and, second, the participants were classified according to a job-exposure matrix. Both analytical approaches revealed risk estimates for acute myocardial infarction below or close to one. Several specific job titles were also analyzed with similar results.

The latest study of utility workers examined a cohort of 83 997 workers employed in the United Kingdom for at least 6 months between 1973 and 1982 and followed from 1973 to 1997 (36). Estimates were obtained for lifetime exposure and exposures accumulated during the most recent 5 years using a comprehensive assessment of occupational magnetic field exposure that considered individual job histories, job environments, and local sources of magnetic fields in individual job locations. Causes of death (both underlying and contributing) from CVD were grouped into the following four categories: (i) arrhythmia-related, (ii) acute myocardial infarction, (iii) atherosclerosis-related, and (iv) chronic or subchronic coronary heart disease. Poisson regression modeling with adjustments for age, gender, calendar time, beginning year of employment, and an indicator for socioeconomic status was used. The relative risk estimates were greater than one only for arrhythmia-related deaths, but the estimates were based on a small number of cases, showed no monotonic trend with increasing exposure, and were not statistically significant (RR per 10 μ T-year 1.1, 95% CI 0.8–1.6).

Mezei et al (37) used death certificates, and proxy-respondent information from the United States. National mortality follow back surveys for 1986 and 1993 were used to determine whether job titles with potential occupational magnetic field exposure were predictive of CVD mortality and whether smoking was a confounder. The cases were those who died from the four defined CVD of interest, and the controls were those who died of all other causes of death, with the exception of diseases with possible associations with magnetic field exposures (amyotrophic lateral sclerosis and malignancies of the lymphopoietic and central nervous systems). Occupational exposure to magnetic fields was assessed on the basis of the longest held job, as determined by the proxy interview. A qualitative magnetic-field-exposure matrix

was developed on the basis of job titles and published exposure measurements. Weighted logistic regression modeling in a case-control design was used to account for the nonrandom, probabilistic sampling method used in the national mortality follow back surveys. Adjustments were made for age, gender, race, work status, level of education, and survey year. Excess was observed for acute myocardial infarction in the medium [adjusted odds ratio (OR) 1.21, 95% CI 1.00–1.47], but not the high (adjusted OR 0.96, 95% CI 0.76–1.22), magnetic field exposure category. Adjustment for smoking behavior did not appreciably change the observed relationship between magnetic field exposure and CVD mortality.

Discussion

The biologically plausible model and initial results from clinical studies provided the impetus to test whether occupational exposure to electromagnetic fields increases the risk for cardiac-arrhythmia-related conditions and acute myocardial infarction. As postulated a priori, Savitz et al (15) observed an increased risk of acute myocardial infarction and arrhythmia-related death, but not from chronic CVD. The only, and limited, support for the original observation comes from a study based on data from the Swedish twin registry (33), which observed a modestly increased risk for acute myocardial infarction. However, other studies specifically designed to test this hypothesis failed to replicate this finding while approaching this hypothesis from different points of view. Two studies attempted to directly replicate the original study in cohorts of electric utility workers (32, 36). One study focused specifically on arrhythmia (32), one study investigated cardiovascular morbidity and provided detailed confounding control (36), and one looked at mortality while controlling for smoking (37).

Three studies were done before the hypothesis on heart rate variability was introduced and were mainly descriptive and did not focus on CVD (27, 29, 30). The finding that consistently fewer cardiovascular deaths occurred among the electric utility workers than would be expected from mortality in the general population illustrates the well-known healthy worker effect, a manifestation of lower-than-average mortality among the working population due to selective employment of fitter and healthier people. The healthy worker effect can lead to masking or an underestimate of a true relationship and should not be interpreted as a beneficial effect of occupational exposure.

Thus only mortality studies [and only two (15, 33)] have reported an association between occupational exposure to electric and magnetic fields and CVD. Studies of CVD that rely on mortality records as the measure

of outcome are limited because the disease under study may not be mentioned at all on the death certificate, and, if noted, the accuracy of the diagnosis may not be correct. It is well known that death certificates do not provide the same quality of outcome measure, as do incidence records, which can be obtained from disease registries or in prospective cohort studies. Problems in using subtypes of CVD as coded on death certificates, which are of uncertain validity and reliability, are particularly evident in the Savitz et al study (15), in which the excess of deaths in acute cardiovascular categories coincided with a deficit of deaths in chronic categories for all exposure groups except the highest group. These problems suggest either specificity of effect or miscoding. In addition, the Savitz et al study could not examine the temporal relation between exposure and outcome in any detail, as the date of diagnosis was unknown, only the date of death. Finkelstein (38) questioned the use of death certificates as a source of information on a diagnosis of loss of autonomic cardiovascular control and pointed out that etiologic conclusions should not be drawn on the basis of using death certificate codes to establish the precise cause of death. A recent study in the United Kingdom found substantial inaccuracy in identifying the cause of death on the death certificates and difficulties in differentiating between acute and chronic cardiac classification (39). The distinction between acute and chronic CVD is especially problematic since, in many instances, acute cardiac events follow long-term cardiovascular changes. Of note are wide variations between the studies reviewed in this report in the number of cases assigned to the different subgroups of CVD. Finally, there are difficulties explaining how the mechanism underlying the transient changes in heart rate variability sometimes seen among healthy young men after exposure to electric and magnetic fields in controlled settings (4, 23) can also explain deaths from arrhythmia and infarction many years after long-term occupational exposure to magnetic fields.

Exposure assessment is a major weakness of epidemiologic studies of electric and magnetic fields and ranges from crude to sophisticated in the studies of CVD. The assignment of exposure has been based on the industry, single job title, or complete work history. Estimates of exposure levels for a given job have been based on informal assessment, expert assessment through observation or background knowledge, or measurements for a sample of workers. The most sophisticated approach involved the creation of a job-exposure matrix and modeling based on a combination of expert evaluation, measurements, and information on job environments and local sources of magnetic fields in individual job locations. In this review, the validity of the exposure assessment did not correlate with the magnitude of the observed effect (eg, two replication

studies with more accurate exposure assessment did not find an effect (32, 36), while the only study that provided some, albeit limited support had very limited quality exposure assessment (33).

While the study by Savitz et al (15) includes the largest cohort, the real power of a study is usually driven by the number of cases in the highest exposure categories. Thus, for example, in a comparative analysis of studies of magnetic fields and cancer in electric utility workers, the Southern California Edison Company cohort (32) contributed more information than would be suggested by its sample size, due to its relatively larger number of cases in higher exposure categories (40).

The inability to control for potentially important lifestyle-related factors that may influence mortality due to CVD, such as smoking and physical activity, also challenges the interpretation of the studies considered. Reassuringly, however, the magnitude of the observed effect did not depend on the ability to control for relevant individual-level data. For example, a study (35) that controlled for potential confounders, in particular blood pressure, serum cholesterol, socioeconomic status, and cigarette smoking, did not observe an increased risk.

In balance, the evidence supporting a relation between occupational exposures to electric and magnetic fields has been overturned by several later studies of different designs with the specific aim of testing this hypothesis. Furthermore, the initial clinical results were not confirmed. We conclude that the evidence speaks against an etiologic relation between occupational exposure to electric and magnetic fields and CVD.

Commentary

This area of investigation was driven by a biologically based hypothesis initially confirmed by an epidemiologic study. Because of the high rates of disease under study and relatively common exposure, it had a potential to be of great public health importance. The epidemiologic studies with rigorous and varied designs that followed showed no effect and, as such, represent an interesting case study of a scientific inquiry that, despite numerous methodologic difficulties inherent in research on the health effects of low-level environmental exposures, has been successfully resolved through continued generation of informative, if not definitive, studies.

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