ELSEVIER

REVIEW

Breast Cancer and Electromagnetic Fields—A Review

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PURPOSE: Several statements have been issued to the effect that no consistent, significant link has been demonstrated between cancer and electromagnetic fields (EMF). However, there continues to be much interest in a possible association with breast cancer, in part because breast cancer risk is substantially higher in industrialized countries than in other areas, and electric power generation and consumption is one of the hallmarks of industrialized societies. In 1987, Stevens proposed a biological mechanism whereby two products of electric power generation, EMF and light at night, might contribute to mammary carcinogenesis through inhibition of melatonin.
METHODS: We conducted a comprehensive review of the epidemiologic literature and hypothesized mechanisms pertaining to EMF exposure and the risk of breast cancer, in order to assess whether or not there was evidence to suggest a link between EMF and breast cancer.
RESULTS: Some occupational epidemiological studies have demonstrated an increased incidence of breast cancer among mainly male electrical workers. It has been difficult to study women, as few are employed in these types of occupations. In all, there have been eleven occupational studies related to breast cancer in women, and statistically significant risk ratios have been observed: 1.98 for premenopausal women in occupations with high EMF exposure in one study, 2.17 in all women who worked as telephone installers, repairers, and line workers in another study, and 1.65 for system analysts/programmers, 1.40 for telegraph and radio operators, and 1.27 for telephone operators in a third study. However, six of the studies did not find any significant effects and two found effects only in subgroups. The results of the eight studies of residential exposure and four electric blanket studies have been inconsistent, with most not demonstrating any significant association. However, this might be attributed, at least to some extent, to difficulties in assessing residential exposure in these studies, as well as other methodological considerations.
CONCLUSIONS: The biologic plausibility of an association between EMF and breast cancer, coupled with suggestive data from occupational studies and unexplained high incidence rates of breast cancer, suggests that further investigation of this possible association is warranted.
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INTRODUCTION

Over the past 3–4 years, several statements have been issued regarding the health effects of electromagnetic fields (EMF). The Council of the American Physical Society declared that "the scientific literature and the reports of reviews by other panels show no consistent, significant link between cancer and power line fields" (1). The National Research Council's Committee on the Effects of Electromagnetic Fields on Biological Systems echoed these sentiments by stating that "based on a comprehensive evaluation of published studies relating to the effects of power-frequency electric and magnetic fields on cells, tissues, and organisms (including humans), the conclusion of the committee is that the current body of evidence does not show that exposure to these fields presents a human-health hazard" (2). These conclusions have been misinterpreted in some media reports as meaning that exposure to EMF is *not* a human health hazard. While conclusive evidence is lacking, however, various studies have indeed suggested that exposure to power-

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Selected Abbreviations and Acronyms

EMF = electromagnetic fields
ALL = acute lymphocytic leukemia
SIR = standardized incidence ratio
SMR = Standardized Mortality Rate

frequency electric and magnetic fields may increase the risk of cancer, and specifically of breast cancer (3–12).

EMF are produced by electric transmission and distribution lines, electric appliances (such as air conditioners, microwave ovens, heaters, refrigerators, televisions, computers, electric clocks, electric blankets, blenders, mixers, hair dryers), and even by the earth and its atmosphere. The hypothesis for their association with breast cancer is based on experimental evidence that light and extremely low frequency EMF affect melatonin production by the pineal gland, thus influencing mammary carcinogenesis in laboratory studies (13–15). This biologic plausibility of an association between EMF and breast cancer, coupled with unexplained high incidence rates of breast cancer in some industrialized, urban areas, suggests that further investigation is warranted. The purpose of this paper is to review the relevant information pertaining to EMF and breast cancer to provide a perspective on this issue.

EPIDEMIOLOGIC STUDIES OF EMF AND CANCER

Prior to the late 1970s, EMF were not suspected of being harmful or of having major biological effects. It was not until 1979 that a case-control study by Wertheimer and Leeper on electrical wiring configurations and childhood cancer stimulated interest in this issue (3). The study reported that children with cancer were more likely than control children to live in homes near electric wires which the authors believed to carry large levels of active current. Since that time, other studies have also shown associations between an increased risk of certain childhood cancers and residence near power lines (16–19).

Some studies have shown an increased risk of brain cancer in children of electrical workers (20–23). A comprehensive review of studies of childhood cancer and residential exposure to magnetic fields was completed by Wartenberg (24). Based upon this review, he concluded that there was a preponderance of positive studies with statistically significant positive results, more than would be expected by chance. When the studies were pooled, the average risks for leukemia, lymphoma, and nervous system cancers were all positive, with the risks for leukemia and nervous system cancers being statistically significant. When the studies were stratified by exposure metric (wire coding and distance, spot measurements, and historical calculations), all average risks were in the positive direction; however, risk of leukemia was statistically significant only when assessed with wire codes and distance and with historical calculations, and risks of lymphoma and nervous system cancers were not significant with any of the exposure metrics. Wartenberg himself pointed out several limitations to these studies. First, no study could possibly monitor a subject's exposure 24 hours a day from conception to diagnosis, and it is not even clear at this time which aspect of magnetic field exposure, i.e., peak magnetic field strength, average magnetic fields, variability of magnetic fields, etc., is most relevant to cancer.

An interesting finding was the disparity of results based on exposure metric. However, less than 50% of subjects agreed to spot measurements in studies that offered the option, which raises issues of validity for these studies. Other limitations included the possible presence of unadjusted confounding and the possible influence of bias. An updated meta-analysis of residential magnetic fields and childhood leukemia by Wartenberg, which used a variety of statistical methods to determine the reliability of the results and publication bias, found a consistent, weak positive association between living within close proximity of power lines and childhood leukemia (25). Wartenberg suggested that future studies should include individuals residing close to power lines with high-current configurations.

In a large, comprehensive case-control study by Linet and coworkers, the odds ratio (OR) for the risk of childhood acute lymphoblastic leukemia (ALL) associated with residential magnetic field levels of 0.200 uT or greater was 1.24 (95% confidence interval (CI) 0.86–1.79)), whereas at levels of 0.300 uT or more, the OR was 1.72 (95% CI 1.03 - 2.86) (26). The study did not find an association between childhood ALL and the highest wire-code category, which is the category believed to have the greatest potential exposure. This study had several advantages over previous studies of childhood leukemia: magnetic fields were measured within 24 months after the date of diagnosis as opposed to years or decades in other studies; it had a larger sample size; homes of non-respondents were wire coded; the residential mobility was similar for cases and controls; the interviewers and wire coders were masked as to case-control status; the measurement protocol was carefully evaluated; meters were calibrated; and there was good quality control of interviewers and measurements. The findings and an editorial that accompanied the article, which called for an end to further EMF research, were not without controversy (27). Many subsequent letters to the editor questioned the study's conclusions and the editorial's opinion (28–34).

Most studies exploring the possible link between EMF and adult cancers have been based on occupational exposures. Of these, a number of studies have reported an increased risk of leukemia among electrical workers (35–40). The first found the association in electricians, power station workers, and aluminum workers (35). Wright and coworkers reported that power linemen were almost six times as likely to develop acute leukemia as men working in non-electrical occupations (36), whereas Pearce and coworkers found a five-fold increased risk in radio and television repairmen and an eight-fold increased risk of leukemia in electronic equipment assemblers (37). In a study of over 5000 leukemia cases, Linet found that power line workers had nearly double the observed number of cases of chronic lymphocytic leukemia when compared to the expected number for that employment category (38). Richardson and coworkers found a three- to four-fold increase in acute myelogenous leukemia among workers exposed to EMF, but these estimates were imprecise and were only significant when arc welding was excluded (39).

A study of over 4000 cancer cases among Canadian and French electric power utility workers found nearly a 2.5-fold increased risk of acute non-lymphoid leukemia and a more than three fold increase for acute myeloid leukemia (40). This study, however, did not find an association with brain cancer, unlike a number of similar studies that reported such a relationship (41–43). Finally, a large historical cohort mortality study by Savitz and Loomis suggested a link between magnetic field exposure and brain cancer, but not leukemia, among electrical utility workers (44).

EMF AND BREAST CANCER

Laboratory Evidence

The risk of breast cancer is substantially higher in industrial urban areas, such as northern Europe and North America, than in less developed areas, such as Africa and Asia (13, 14). Electric power generation and consumption is one of the hallmarks of industrialized societies. In 1978, Cohen and coworkers suggested that lower production of melatonin by the pineal gland would increase circulating levels of estrogen, stimulate the proliferation of breast tissue, and could lead to breast cancer (45). Cohen and coworkers hypothesized that environmental lighting may be a factor that would lead to lower melatonin production.

In 1987, Stevens proposed a biological mechanism whereby two products of electric power generation, EMF and light at night, might contribute to mammary carcinogenesis (13). The mechanism involves estrogen, the common thread that ties together many breast cancer risk factors. Melatonin, a hormone secreted by the pineal gland, plays an important role in inhibiting estrogen production. According to Stevens and coworkers, this biological mechanism has three aspects, including light effects on melatonin, EMF effects on melatonin, and melatonin effects on breast cancer (14, 46). The published evidence regarding light effects on melatonin indicates that light of sufficient intensity can suppress the normal nocturnal melatonin rise in humans in a qualitatively similar way to that observed in other mammals, and that this effect varies substantially among individuals and by wavelength of light (46–51). The effect appears to be dose-dependent, with the brighter the light, the greater the reduction of circulating melatonin, ranging from minimal suppression at 200 lux to maximal suppression at 3000 lux (52). However, it is unclear whether the usual ambient light levels at night (or even brief exposure to bright lights at night) affect melatonin in a significant proportion of individuals. In addition, it is unclear whether daily exposure to artificial lighting during the day can affect melatonin rhythms (46).

Regarding the effects of EMF on melatonin, most of the laboratory studies have demonstrated a suppression of melatonin in laboratory animals (53–62). However, three studies found no effect and this, coupled with the absence of data on humans, certainly raises some question regarding an association (63–65). At least one on-going study is utilizing portable meters to measure EMF exposure and assess melatonin in order to address the effects of EMF on melatonin in humans, by measuring the primary melatonin metabolite 6-sulfatoxymelatonin (6-SMT) in the urine (46).

Finally, regarding melatonin effects on breast cancer, manipulation of melatonin levels in laboratory animals through melatonin injection has led to decreases in chemically- (both DMBA and N-nitro-N-methylurea) induced mammary tumor development, while pinealectomy has had the opposite effect (66–67). However, these findings do not define how melatonin may affect breast cancer at the cellular level. Other experiments have revealed the oncostatic effect of melatonin in certain subclones of MCF-7 breast cancer cells (46). In some animal experiments, melatonin has been shown to affect levels of estrogen and prolactin. Little evidence of melatonin effects on breast cancer in humans exist at this point.

If EMF are associated with breast cancer, one question is whether they operate as inducers, promoters, or in another role. No mutagenic activity has been demonstrated for EMF, making an inducer role unlikely (13). A number of other possible mechanisms have been proposed whereby exposure to EMF might lead to breast cancer (68). One is that EMF would lower melatonin levels, which would lead to increased estrogen levels and stimulation of turnover of the breast epithelial cells at risk (13). The fact that early menarche, late menopause, and nulliparity are risk factors for breast cancer supports this hypothesis, as each of these factors results in a longer period for proliferation of breast epithelial stem cells. Another possibility is that the EMF would lower melatonin levels, which in turn would release existing cancer cells from a quiescent state (68). This effect might be termed progression. The mechanism with the shortest expected latency period would be an EMF-induced disruption of melatonin's oncostatic action (14). In support of this mechanism, one laboratory reported that a 12 mG, 60-

Hz magnetic field could reverse the growth inhibition of MCF-7 mammary cancer cells by melatonin in vitro (69). In summary, the direct laboratory evidence, a further discussion of which can be found in work by Stevens and coworkers, should be pursued and considered, as it provides direct support for the biological rationale for studying a possible influence of EMF exposure on the risk of breast cancer in women (14, 46).

Occupational Epidemiologic Studies

Male Breast Cancer. The results from a number of occupational epidemiological studies in men have suggested a possible association between male breast cancer and electrical occupations (9, 70–73), whereas two other studies have not (74, 75). A New York study found a standardized incidence ratio (SIR) of 6.5 for breast cancer in male telephone company technicians with a mean daily exposure of 2.5 mG (70). In a multi-center case-control study of 33 cases of male breast cancer in the U.S., an OR of 1.8 was found among electricians, telephone linemen, electric power workers, and communications and radio workers (9). Similar associations were seen in a Norwegian study where the SIR for breast cancer among all occupations with potential exposure was 207 (71). In this study, breast cancer risk was most pronounced among men working in electric transport, with a SIR of 396. A case-control study was conducted using death registration data from the 24 states that began reporting occupational data on death certificates in 1985 (72). There were 250 breast cancer cases among men over age 19 who died from the disease between 1985 and 1989. Four of these cases had electrical occupations listed on their death certificates, which was the number expected. However, three of these cases were less than 65 years of age, and this was more than twice the expected number for this age group (OR 2.2 (95% CI 0.6–7.8)).

Among telephone workers, the one observed case was nine-times the expected number, but the CI spanned from 0.9 to 88.7. A study among all Swedish men, 20–64 years of age and employed in 1960, compared railway workers, a group known to have high EMF exposure, to the rest of the population (73). The follow-up was divided into two periods, 1961–1969 and 1970–1979, because the number of men employed as railway workers had decreased more than 50% since 1960, perhaps implying that the exposure may have been discontinued for many of these workers in the second time period. Three cases of breast cancer were detected among engine drivers and conductors between 1961 and 1969, with a relative risk (RR) of 4.9 (95% CI 1.6–15.7); and four cases were observed among all railway workers during the same time period, with a RR of 4.3 (95% CI 1.6–11.8). This study also detected an increase in pituitary tumors for these workers, a finding the authors felt may help to better understand the mechanism involved, since this gland is involved in the production of hormones, such as prolactin. However, a case-control study of 71 cases of male breast cancer reported to the New York State Tumor Registry between 1979 and 1988 and 256 healthy male controls found no increased risk of breast cancer with occupational exposure to EMF (OR = 0.7, 95% CI 0.3–1.9) (74). In addition, a cohort study of causes of death among 2190 dockyard workers in Genoa, Italy found that two individuals died from breast cancer, but neither of them worked in occupations where exposure to high levels of EMF would be expected (75).

Female Breast Cancer. Data on female breast cancer and similar occupational exposures are sparse, because of the small numbers of women employed in jobs with high levels of EMF exposure. Results of available studies are presented in Table 1. There have been two studies of breast cancer and EMF in both male and female workers (76, 77). A cohort study was performed comparing the Swedish population classified in the 1960 census as working in the electronics or electrical manufacturing industry (exposed) and the general working population (not exposed) (76). No increase was seen for breast cancer in males or females. However, the method used to categorize a person into categories of exposed and non-exposed was very broad, and could have lead to misclassification. No information was available on the number of breast cancer cases who were exposed and not exposed. In Denmark, a cohort that was between 20 and 64 years of age in 1970, was followed from 1970 to 1987 (77). Each person was classified by his or her industry and occupation in 1970, and each industry-occupation group was categorized for potential exposure to magnetic fields above the threshold of 0.3 μT, as well as for intermittent or continuous exposure. No increase in breast cancer risk was seen in women, and only a slight increase was seen in men.

Two studies specifically evaluated the issue of breast cancer and occupational exposure among female workers in the U.S. (10, 78). These studies combined pre-menopausal and post-menopausal women. Loomis and coworkers compared 27,882 women whose underlying cause of death was breast cancer with 110,949 control women who died from causes other than leukemia and brain cancer from 1985 to 1989 (10). The authors found that female electrical workers had excess mortality from breast cancer as compared with women in other occupations, with the highest mortality being seen in telephone installers, repairers, and line workers. These analyses were adjusted for age, race, and SES (measured by occupational code). However, another analysis of the same database, with an additional year of deaths (1984–1989), yielded more equivocal results, i.e., no consistent relationship between probability of exposure and breast cancer in white women, and a modest association in black women (78). Although these analyses were similarly ad-

TABLE 1. Summary of occupational studies and breast cancer in females

Reference and location	Study type and time period of study	Occupational categories	Number of cases/controls	Risk Ratios
Vagero and Olin (76) (1983) Sweden	Cohort study of the Swedish population, cancer cases accrued using the Swedish Cancer Environment Registry from 1961–1973	Classified in the 1960 census as working in the electronics or electrical manufacturing industry	Numbers not reported for breast cancer specifically. Compared to the general population	Not significant for both males and females
Guenel et al. (77) (1993) Denmark	Cohort of 2.8 million Danes, aged 20–64 years in 1970, cases accrued through the Danish Cancer Registry, 1970–1987	Codes based on published studies and a few field measurements. (0) no exp to fields. (1) probable exp to intermittent magnetic fields higher than 0.3 μT. (2) probable exp to continuous magnetic fields higher than 0.3 μT	Number of breast cancer cases intermittently exposed = 1526 women and 23 men. Number of cases continuously exposed = 55 women and 2 men. Compared to the economically active population	Obs/Exp for intermittent exposure Females = 0.96 (95% CI = 0.91–1.01) Males = 1.22 (0.77–1.83) For continuous exposure, Females = 0.88 (0.68–1.15) Males = 1.36 (0.16–4.91)
Loomis et al. (10) (1994) USA	Case-control, mortality study, 1985–1989 in 24 states that include occupation on the death certificate	Death certificate data, 3-digit occupational code used to classify women who had worked in electrical occupations	27882 cases (68 exposed) 110,949 controls (199 exposed) Controls were women who died of any cause except leukemia and brain cancer	OR = 1.38 (95% CI 1.04–1.82) for all electrical workers OR = 2.17 (95% CI = 1.17–4.02) for telephone installers, repairers, and line workers
Cantor et al. (78) (1995) USA	Case-control, mortality study, 1984–1989 in 24 states that include occupation on the death certificate	Same database as Loomis, et al, with 1 more year of data. An industrial hygienist rated occupational titles for level and probability of exposure as none, low, medium, high, or unknown. Probable VDT use was also estimated	White cases: 29,397 (11,229 exposed) White controls: 102,955 (41,108 exposed) Black cases: 4112 (1977 exposed) Black controls: 14,839 (7436 exposed)	Whites, med level: OR = 1.10 (1.03–1.2) med prob*: OR = 1.14 (1.05–1.3) high prob*: OR = 1.09 (1.02–1.2) Blacks: med level OR = 1.29 (1.1–1.5) med prob*: OR = 1.29 (1.06–1.6) high prob*: OR = 1.28 (1.10–1.6) No ↑ risk for probable VDT use.
Tynes et al. (79) (1996) Norway	Norwegian Telecom cohort of female radio and telegraph operators working at sea between 1920 and 1980 (n = 2619) linked to the Cancer Registry of Norway (1961–1991). Nested case-control study for breast cancer	Spot measurement were taken on the ship (at the operator's desk). ELF levels were similar to normal work places in Norway, and the background levels in the radio room were comparable to levels in Norweigian homes. Also studied shift work	50 breast cancer cases matched with four to seven controls from the Telecom cohort, alive at time of diagnosis and matched on year of birth (± one year), and for women born before 1920, ± five years (259 controls)	SIR (compared with national female population) for breast cancer = 1.5 (1.1–2.0). For ages 50–54, SIR = 2.5 (1.3–4.3) For women ⩾ 50 yrs old, significant trend for duration of employment categorized by none, 0–3.2 yrs, and 3.2–14.6 yrs (p = 0.02) and amount of shift work categorized by none, low, and high (p = 0.01)
Coogan et al. (11) (1996) USA	Large population-based case-control study, April 1988–December 1991	Interview data, "usual occupation" as the basis for occupational exposure (job exposure matrix, industrial hygienist)	6,888 cases and 9,529 controls, less than 74 years old from Maine, Wisconsin, Massachusetts, and New Hampshire, newly diagnosed between 4/88 and 12/91. Controls: driver's license and HCFA	Potential for high exposure All: OR = 1.43 (95% CI = 0.99–2.09) Premenopausal: OR = 1.98 (1.04–3.78) Postmenopausal: OR = 1.33 (0.82–2.17) Mainframe operators: OR = 1.79 (1.03–3.11)
Fear et al. (81) (1996) England	Data collected during 1981–1987 as part of national cancer registration, and including only those with valid occupational information (29% or 119,227 women)	Job titles from cancer registry forms categorized into job groups using the 1980 Classification of Occupations (OPCS, 1980)	83 cases ages 20–74	Proportional registration ratio: All registrations with an adequately described occupation other than electrical workers were the standard for comparison) = 89 (95% CI = 79–112)

(*continued*)

TABLE 1. *Continued*

Reference and location	Study type and time period of study	Occupational categories	Number of cases/controls	Risk ratios
Kelsh et al. (82) (1997) USA	Occupational cohort of employees of the Southern California Edison Company between 1960 and 1991 (9788 women). Cancer cases accrued through death certificates	Occupational information accrued from company personnel records, categorized into seven groups according to different work activities and environment	26 cases ages 20–79	SMR for breast cancer in employees vs the general population: 0.80 (0.52–1.17). SMR for linemen/service appliance occupations was 3.57 (0.05–19.87), 13 cases. SMR for service/labor occupations was 3.03 (0.34–10.94), 2 cases. SMR for internal cohort analyses (using administrative/technical/clerical occupations as the referent): service/labor occupations 0.65 (0.14–2.92) SMR for internal cohort analyses linemen: 0.13 (0.02–0.89).
Coogan et al. (80) (1998) USA	Large population-based case-control study in Upper Cape Cod, Massachusetts, 1983–1986	Interview data, complete occupational history, occupations coded to 1980 Bureau of the Census 3-digit occupational codes as the basis for occupational exposure (job exposure matrix, industrial hygienist)	259 cases and 738 controls, from five Upper Cape Cod towns in Massachusetts, newly diagnosed between 1983–1986. Controls: random digit dialing and HCFA	Potential for high exposure: High EMF-job: OR = 1.2 (95% CI = 0.4–3.6) Medium EMF-job: OR = 0.9 (95% CI = 0.5–1.7)
Johansen et al. (83) (1998) Denmark	Nationwide cohort of Danish electric utility company employees between 1908 and 1993 (5871 women), cancer cases accrued through the Danish Cancer Registry from date of first employment or April 1, 1968 whichever came last to the date of death, emigration, or 12/31/93 whichever came first	Job exposure matrix for combination of 25 job titles and 19 work areas, each assigned an average level of exposure during a working day, categorized as background (< 0.09 μT), low (0.1–0.29 μT), medium (0.30–0.99 μT), high (⩾ 1.00 μT), and unknown	96 breast cancer cases	SIRs (compared with national incidence rates): < 0.1 μT: SIR = 1.3, 63 cases 0.1–0.29 μT: SIR = 0.3, 2 cases 0.3–0.99 μT: 0 cases ⩾ 1.00 μT: SIR = 1.0, 1 case unknown: SIR = 1.3, 30 cases Overall SIR = 1.08 (95% CI = 0.9–1.3), 96 cases
Pollan et al. (12) (1999) Sweden	Women employed during the 1970 census, lived in Sweden during the 1960 census, and alive and > 24 years old as of 1/1/71. A total of 1,101,669 women aged 25–64 followed up for 19 years. Cases accrued through the Swedish cancer environment registry	Occupations reported in 1970 which involved more than 200 women and at least 10 observed breast cancer cases	19,284 breast cancer cases aged 26–64 years. Expected number of cases calculated using age and time period-specific reference rates. RR calculated using all other occupations, and other occupations in same group as reference	Electrical engineers: SIR = 149 (88, 236) RR (all other occupations) = 1.40 (0.88, 2.23) System analysts, programmers: SIR = 179 (115, 267) RR (all other occupations = 1.65 (1.11, 2.46) Telegraph and radio operators: SIR = 147 (106, 197) RR (all other occupations) = 1.40 (1.04, 1.88) Telephone operator: SIR = 128 (109, 150) RR (all other occupations) = 1.27 (1.08, 1.48)

* Probability of occupational exposure to extremely low frequency electromagnetic fields (none, low, medium, high).

justed for age and SES, the methods used to define exposure status differed between the two studies.

Loomis and coworkers used death certificate information on usual occupation and industry to classify women into a group of electrical occupations presumed to entail elevated exposures, as defined by aggregating Census bureau occupation codes (10). In addition, a separate group included another seven occupations with larger numbers of female workers that were judged to have potential for above background exposure. All of the remaining occupations were aggregated to form a single reference group of unexposed. In the study of Cantor and coworkers, however, an expert industrial hygienist rated each of the U.S. Census Code occupational titles for level and probability of exposure to extremely low frequency fields (78). This method led to many more cases and controls being classified as having at least low or medium levels of exposure. Thus, the study was able to determine risks for different levels of exposure, unlike the study of Loomis, and coworkers, where exposure was more of a yes/no variable. Furthermore, the disparate results between the two studies might suggest that there is a greater increased risk of breast cancer in women with electrical occupations than with other occupations with EMF exposure.

Coogan and coworkers used data from a population-based study of 6888 breast cancer cases and 9529 randomly selected controls to determine whether women whose usual occupation involved exposure to higher than background 60-Hz magnetic fields had a higher risk of breast cancer than unexposed women (11). This study, unlike the Loomis and coworkers' study which relied on death certificates, actually involved a 25-minute telephone interview that obtained information regarding a woman's "usual" occupation. There was an increased risk in women with potential for high exposure, but no increased risk for women with potential for medium or low exposure (11). The risk among pre-menopausal women in the high exposure group was higher than the risk among post-menopausal women with high exposure. However, this study relied exclusively on data on usual occupation, without information regarding length of employment and non-occupational exposures, thereby underestimating total historical exposure to magnetic fields (15). As a result, there is likely to have been some non-differential exposure misclassification, which would have reduced the odds ratios towards the null and thus reduced or masked an association.

A Norwegian study explored breast cancer incidence in female radio and telegraph operators with potential exposure to light at night, radio frequency (405 KHz-25 MHz), and, to some extent, extremely low frequency fields (50 Hz) (79). The SIR for breast cancer in this cohort, compared with the Norwegian female population, was increased, especially for those aged 50–54 years. Analysis of a nested case-control study within the cohort for breast cancer in women 50 years and older showed significant trends for duration of employment and amount of shift work. The shift work finding is interesting, as shift work may affect pineal function, and in turn may be associated with the risk of breast cancer (5). The rate ratio for the incidence of breast cancer among radio and telegraph operators born after 1935, using Poisson regression analysis adjusted for age, calendar year, year of first birth, and fertility factors, was 1.5 (95% CI (1.0, 2.1)) (79).

The Upper Cape Cod Incidence Study (80) included an in-person interview with a complete occupational history of all full-time jobs held for at least one year from age 18 on. Each job was categorized into three levels according to potential for exposure to "higher-than-background" 60-Hz magnetic fields (high, medium, and no exposure) based on the judgment of an industrial hygienist and the probability of working in close proximity to a source with high or medium magnetic field exposure. No increased breast cancer risk was seen for women with high or medium occupational magnetic field exposure compared to women with no exposures to occupational or residential magnetic fields (proximity to transmission lines, slept with electric devices, or had electric heating). Analyses of cohorts of electrical workers in England, California, and in Denmark found no increase in either incidence (81, 82) or mortality (83) of female breast cancer. Several important limitations to these studies include that only 29% of women had enough information on occupation to be included in the analysis (81) and limited information was available on confounders (81–83). One of the job exposure matrices used estimated exposures partly by 24-hour measurements taken in 1993 for 129 employees in six Danish utility companies (83). A recent cohort study of the Swedish population who were employed in 1970 and followed through 1989 found elevated SIRs and RRs (using all occupations or other occupations in the same occupational group as the comparison) for system analysts or programmers, telegraph and radio operators, and telephone operators (12). There weren't enough women employed as electricians, or wire and line workers to be considered for analysis. Breast cancer confounders could not be adjusted for in this study, however, the authors state that the risk estimates in studies that adjusted for such factors have found no change in risk estimates.

Residential Epidemiologic Studies

As seen in Table 2, there have been a few studies of residential EMF exposure and breast cancer, but with inconsistent results. A British study, based on 7631 individuals who lived either within 50 meters of any electrical installation or within 30 meters of an overhead power cable at the time of the 1971 Census, aimed to determine if living close to power lines was related to an increase in mortality (84). The mortality rates for this group between 1971 and 1983 were compared to the general population rates, and the Standardized Mortality Rate (SMR) was 106.

A cancer mortality study was conducted of individuals who lived at least five consecutive years in Limmel, The Netherlands from 1956 to 1981, and were followed from 1961–1987 (85). High exposure was defined as living in a home within a 100-meter radius of a substation or power lines, and low exposure was defined as living farther than 100 meters. Magnetic field measurements confirmed that the average exposures in the homes within 100 meters (magnetic field intensity ranged from 1.0 to 11.0 mG) were higher than in the homes outside 100 meters (magnetic

TABLE 2. Summary of residential studies and breast cancer in females

Reference and location	Study type and time period of study	Method of exposure assessment	Number of cases/controls	Risk Ratios
McDowall (84) (1986) East Anglia region of England	Cancer mortality study, 1971–1983	A sample of 7631 individuals living within 50 meters of any electrical installation or within 30 m either side of an overhead power cable at the time of the 1971 Census	22 deaths due to breast cancer. Compared to the general population rates	SMR for breast cancer: 106 (95% CI = 66–160) SMR for living within 0–14 meters 37 (1–206), 1 case 15–34: 122 (61–239), 11 cases 35–50: 110 (53–202), 10 cases
Wertheimer and Leeper (6,8) (1987) Colorado	Case/control study, matched, cancer deaths between 1967 and 1975 and prevalent cases diagnosed 5 years prior to 1979	Wire coding	87 pairs where cases show higher potential for alternating electromagnetic field exposure than the controls, and 53 pairs where the reverse is true	C-ratio 164 ($p \leqslant 0.01$)
NYSDOH (89) (1992) Nassau and Suffolk Counties, NY	Breast cancer incidence rates (age-adjusted) by census tracts, 1978–1988, comprising 17,131 breast cancer cases	Exposed: living in a census tract containing 138kV transmission lines, at time of breast cancer diagnosis	Incidence rates (age-adjusted) of breast cancer, by Nassau and Suffolk county, 1978–1988. Nassau 103.6 Suffolk 93.8 Both 99.2	Incidence rates (age-adjusted) of the Area Exposed Not-exposed Nassau 105.2 102.3 Suffolk 99.4 89.0 Both 102.9 96.1 The exposed CT's had slightly higher average income rates and localized staging of breast cancer
Schreiber et al. (85) (1993) The Netherlands	Cancer mortality study, retrospective cohort, Limmel residents 1956–1981 (any 5 consecutive years), follow-up through the Dutch population registry 1961–1987	High exposure group: lived in a home within a 100 m radius of a substation or power lines. Low exposure group: lived further than 100 m	14 breast cancer deaths in Limmel, compared to the general Dutch population	SMR for breast cancer for Limmel: 115 (95% CI = 63–193), 14 cases SMR for high exposure: 96 (31–223), 5 cases SMR for low exposure: 128 (58–243), 9 cases
Verkassalo et al. (88) (1996) Finland	Nationwide cohort study (record linkage), 1970–1989	Calculations of annual magnetic fields between 1970 and 1989 at all structures located within 500 meters of 110 kV, 220 kV, and 400 kV overhead power lines. Cumulative exposure was calculated by summing the products of residential magnetic field (in μT) and number of years of such exposure	1229 observed number of breast cancer cases; expected number of cases calculated by multiplying the number of person years for the category of exposure (< 0.20; 0.20–0.39; 0.40–0.99; 1.00–1.99; ⩾ 2.00 μT years) by the corresponding incidence of cancer in the Finland, by age (5-year age period) calendar period (1974–1981; 1982–1990), and social class	SIR (95% CI) for cumulative exposure < 0.20 μT SIR = 1.05 (0.98–1.12), 945 cases 0.20–0.39 μT SIR = 1.06 (0.88–1.25), 130 cases 0.40–0.99 μT SIR = 0.89 (0.71–1.10), 87 cases 1.00–1.99 μT SIR = 1.22 (0.89–1.64), 44 cases ⩾ 2.00 μT SIR = 0.75 (0.48–1.13), 23 cases Incidence rate ratio (95% CI) per 1 μT year increase in exposure = 0.95 (0.88–1.02)
Li et al. (86) (1997) Taiwan	Case-control study, 1990–1992. Controls were persons with cancers of sites other than those previously suspected of being associated with magnetic fields	Exposure defined as distance to the nearest transmission lines using utility maps and the average and maximum residential magnetic fields were calculated. Measurements were taken at 407 residences for validation	1980 breast cancer cases diagnosed between 1990 and 1992 and 1880 matched controls on date of birth (±5 years) and date of diagnosis (±6 months)	No increase in breast cancer risk seen for proximity to transmission lines or calculated electromagnetic fields

(*continued*)

field intensity ranged from 0.2 to 1.5 mG). It was decided to use distance instead of actual measurements to classify the homes, because if the latter were used, more detailed measurements would have been needed. There were only 14 deaths due to breast cancer during this time period, of which five were in the high exposure category and nine were in the low exposure category. The effects of confounding factors were not investigated in this study.

TABLE 2. *Continued*

Reference and location	Study type and time period of study	Method of exposure assessment	Number of cases/controls	Risk Ratios
Feychting et al. (87) (1998) Sweden	Case-control study nested within a cohort, 1960–1985	Study population defined as a cohort who had lived within 300 meters of 220- or 400-kV power lines in Sweden at any time between 1960 and 1985, for at least one year. Magnetic field exposure estimated through calculations of the magnetic fields generated by the power lines before diagnosis	699 female breast cancer cases diagnosed between 1960 and 1985, and 699 controls matched on age (±5 years), residence in the same parish (location) during the year of case diagnosis, and residence near the same power line as the case	For calculated magnetic fields ⩾ 2 μT, RR = 1.0 (95% CI = 0.7–1.5) For calculated magnetic fields ⩾ 2 μT and < 50 years old, RR = 1.8 (95% CI = 0.7–4.3) For ER+ and fields ⩾ 1μT RR = 1.6 (95% CI = 0.6–1.1) For ER+, fields ⩾ 1 μT, and < 50 years old: RR = 7.4 (95% CI = 1.0–178.1)
Coogan et al. (80) (1998) USA	Large population-based case-control study in Upper Cape Cod, Massachusetts, 1983–1986	Exposed group defined as lived in home with electric heat. Exposed group defined as any residence between 1943 and 1986 within 500 ft (152 meters) of a transmission line or substation	259 cases and 738 controls, from five Upper Cape Cod towns in Massachusetts, newly diagnosed between 1983 and 1986. Controls: random digit dialing and HCFA	Ever lived in home with electric heat: OR = 0.7 (95% CI = 0.4–1.2) Residential proximity to transmission lines and substations: OR = 1.5 (95% CI = 0.6, 3.3)

A case-control study in Taiwan was carried out between 1990 and 1992 consisting of 1980 breast cancer cases and 1880 controls with cancers of sites other than those previously suspected of being associated with magnetic field exposure (cancers of the hematopoietic and reticuloendothelial systems, skin, ovary, fallopian tube, and broad ligament) and matched to cases on date of birth ± 5 years and date of diagnosis ± 6 months (86). Exposure was defined as distance to the nearest transmission lines using utility maps; the average and maximum residential magnetic fields were estimated using a software package. Measurements were taken at 407 residences for validation of these estimates. No increase in breast cancer risk was seen for women: 1) who lived within 0–49 meters or within 50–99 meters of a transmission line, as compared to those who lived at least 100 meters away; 2) with calculated residential EMF levels between 0.1 and 0.2 μT or > 0.2 μT, as compared to those with < 0.1 μT; or 3) with residential EMF levels in the 95th percentile (0.59 μT) or the 99th percentile (2.34 μT), as compared to those with levels < 0.1 μT. All analyses were adjusted for age at diagnosis, year of diagnosis, and an index of urbanization; no information on other breast cancer risk factors was obtained from study participants. No cumulative exposure index could be estimated since only residence at time of diagnosis was known.

Wertheimer and Leeper found an increase in breast cancer in women with high-current power-line configurations near their homes, as compared to matched controls (C-ratio of 164, $p < 0.01$), which was more pronounced in pre-menopausal women than in post-menopausal women (6, 8). In a study conducted in Oregon, Morton hypothesized that housewives in homes with electric heating had higher risks of certain cancers, including breast cancer (7). One area (Eugene, Oregon) exhibited an increase in cancer mortality for a number of cancers, including breast cancer, in housewives compared to employed women, while the other area did not. A difference between the two areas was that Eugene had inexpensive electric power, and therefore its residents were more likely to have electric heating than those of the other area. Morton proposed further study to determine if the higher EMF exposure might account for the higher cancer mortality.

A case-control study of breast cancer in a cohort of women in Sweden (87) found for calculated magnetic field levels of 0.2 μT or greater, the overall RR estimate was 1.0, but for women younger than 50 years of age at diagnosis the RR was 1.8. When stratified by estrogen receptor-positive breast cancer (obtained for women diagnosed between 1980-1985 only) and using the exposure cutoff of 0.1 μT or greater, the RR was 1.6. Among estrogen receptor-positive women younger than 50 years at diagnosis (an unmatched analysis was done due to small numbers), the RR was 7.4, however, this estimate was unstable because it was based on only six exposed cases and one exposed control.

The Upper Cape Cod Incidence Study described earlier also included an assessment of residential magnetic field exposure (80). The in-person interview included a residential history between 1943 and 1986 and questions on the

TABLE 3. Summary of electric blanket usage and breast cancer in females

Reference and location	Study type and time period of study	Method of exposure assessment	Number of cases/controls	Risk Ratios
Vena et al. (91) (1991) NY	Case-control study, 1987–1989	Electric blanket use	Postmenopausal breast cancer cases: 382,439 controls (driver's license and HCFA files)	OR = 0.89 (95% CI = 0.66–1.19), users of electric blankets compared to nonusers.
Vena et al. (92) (1994) NY	Case-control study, Nov. 1986 to April 1991	Electric blanket use	Premenopausal breast cancer cases: 290, and 289 controls (driver's license)	OR = 1.18 (95% CI = 0.83–1.68) for electric blanket users compared to nonusers.
Coogan et al. (80) (1998) USA	Large population-based case-control study in Upper Cape Cod, Massachusetts, 1983–1986	Exposed group defined as ever use of "an electric blanket, electric heating pad, electric mattress pad, or electric water bed heater"	259 cases and 738 controls, from five Upper Cape Cod towns in Massahusetts, newly diagnosed between 1983 and 1986. Controls: random digit dialing and HCFA	Regularly slept with electric heating device OR = 1.0 (95% CI = 0.7–1.4)
Gammon et al. (90) (1998) USA	Large population-based case-control study of women diagnosed between May 1, 1990 and December 31, 1992 in Seattle and New Jersey (women under 45 years of age only), and Atlanta, GA (women under 55 years of age)	Exposed group defined as regular use of electric blankets, electric mattress pads, or heated water beds where regular use was not defined. Info asked on whether used to warm the bed; total number of years of use and number of months per year used	2170 cases and 1987 controls frequency matched to cases on 5-year age groups and geographic area. Controls: random digit dialing and HCFA	Ever use of electric blankets, mattress pads, or heated water beds among women < 45: OR = 1.01 (95% CI = 0.86–1.18) Ever use of electric blankets, mattress pads, or heated water beds among women ages 45–54: OR = 1.12 (95% CI = 0.87–1.43)

use of electric heat. No increased risk in breast cancer was seen for women who used electric heat in any of their residences compared to women who did not have any occupational or residential magnetic field exposures. Participants residing within 500 ft (152 meters) of transmission lines or substations were considered exposed. A slight increase in breast cancer risk was seen for women who lived in close proximity to transmission lines and substations compared to women with no occupational or residential magnetic field exposure. A record-linkage study of the Finnish population that calculated SIRs for breast cancer (and other cancers) in five categories of cumulative exposure to residential power lines (defined a priori) between 1970 and 1989 found no relationship with breast cancer after adjustment for age and social class (88). Finally, some preliminary work by the New York State Department of Health suggested that a slight increase in age-adjusted incidence rates between 1978 and 1988 existed for Long Island women living in census tracts with 138 kV electric transmission lines, as compared to those living in tracts without 138 kV lines (89). Of note are the findings that the census tracts with 138 kV lines had slightly higher average levels of income and higher localized staging of breast cancer than the tracts without these lines.

Residential Studies of Electric Blanket Usage. A population based case-control study in three regions of the United States in younger women included questions on electric blanket use in their in-person interview (90). There was no risk associated with ever having used electric blankets, mattress pads, or heated water beds among women under age 45 or among women aged 45–54 years. There were no differences in risk with duration of use; with whether the appliance was used only to warm the bed or used throughout the night; when stratified by menopausal status; with the cases' hormone receptor status or stage of disease; or with inclusion of potential breast cancer risk factors that were associated with electric blanket use. The limitations of this study were that electric blanket use and breast cancer was not a primary hypothesis of the study; information on the age or make of electric blankets was not collected; and other sources of EMF exposure were not investigated.

The Upper Cape Cod Incidence Study described earlier also included an assessment of electric blanket use (80). The in-person interview included a question on whether the participant regularly slept "using an electric blanket, an electric heating pad, an electric mattress pad, or electric water-bed heater." If the response was yes, then further questions on total years of use were asked. No increase in breast cancer risk was seen for women who regularly used electric heating devices when compared to women with no occupational or residential magnetic field exposure. In another study, Vena and coworkers found no association between electric blanket use and post-menopausal breast cancer (91). However, they believed that the possible EMF-effects on melatonin, cell growth, and proliferation might be more relevant to pre-menopausal women than to post-menopausal women. Although they conducted another study to include pre-menopausal women, no association was found (92). Wertheimer and Leeper re-analyzed the data from these two studies of electric blankets and found that women who used electric blankets throughout the night were 2–3 times as likely to have breast cancer than women who used them only to warm the bed (93). However, Vena and coworkers responded that the association disappeared when women using electric blankets throughout the night were compared to women who never used them (94).

Comment

The differences in methodology among studies, especially concerning EMF exposure measures, makes it difficult to interpret their results. Furthermore, the interpretation of the associations between wire codes and cancer remains problematic. In 1989, Savitz and coworkers reviewed the methodological issues involved in the study of EMF and cancer (95). They concluded that the research up to that point fell short of providing conclusive evidence for a causal association. They pointed to the variety and ubiquity of sources of EMF in the environment, which make exposure assessment difficult. Residential exposure assessment was generally performed using wire coding. However, increasing evidence suggested that wire coding was imperfectly related to average magnetic fields in the home. Savitz and coworkers recommended that potential confounders should be more vigorously evaluated as possible causes of spurious positive results seen in some studies. These sentiments were echoed by the scientists in Loscher's laboratory, who also pointed to uncertain magnetic field exposure conditions and inadequate examination of possible confounding exposures as the major problems with these epidemiologic studies (96).

From an updated review of these methodologic issues, it appears that EMF exposure assessment continues to be a major concern (97). A major limitation of spot EMF measurements is their assumed inability to reflect long-term exposure, because of short-term fluctuations in magnetic fields. However, since a study found significant short- and long-term stability in spot measurements, it is possible that the value of spot measurements has been underestimated (98). Although 24-hour measurements should be more highly correlated with long-term average exposures, they have failed to show a stronger association with cancer than wire codes. The lack of a gold standard, based on historical measurements over extended time periods, makes it difficult to determine which type of data should be collected to better reflect cumulative EMF exposures. Thus, the inconsistency of the results of the residential studies could largely be due to the variability in measuring exposure, and therefore the issue of exposure assessment needs to be carefully addressed in the planning of future EMF studies.

Additional problems pointed out by Savitz are potential bias resulting from control selection and potential confounding (97). For example, studies using random-digit dialing (RDD) to identify controls may be subject to biases, due to the differential inclusion of people of low SES in cases and controls. If lower SES is associated with higher magnetic field exposure, a common perception that has never been proven, one could speculate that the RDD method (which could yield proportionally fewer low SES controls relative to the cases) would, therefore, bias the odds ratios upward. This issue is probably less of a concern for breast cancer and EMF studies (since most did not obtain their controls through RDD) than for some childhood cancer studies. As to potential confounding, in the study by Coogan and coworkers, the case and control groups had very similar distributions of demographic variables, including age, parity, and having a usual occupation outside the home vs. being a housewife (11, 15). Furthermore, multivariate adjustment for a host of variables including age, state, body mass index, benign breast disease, family history of breast cancer, age at menarche, parity, age at first birth, education, and alcohol consumption changed the RRs only slightly, as did exclusion of subjects who were never employed outside the home.

CONCLUSIONS

This review opened with statements by the Council of the American Physical Society and the National Research Council indicating that the current body of evidence does not show that exposure to power-frequency EMF poses a risk to human health (1, 2). Regarding breast cancer, however, the role of EMF as a potential environmental risk factor has not been adequately explored. The few studies dealing with occupational exposure to EMF and breast cancer have suggested a possible relationship. Although the handful of studies that evaluated residential exposure to EMF have not shown any consistent link to breast cancer (80, 84–92), the limitations in assessing long-term exposures do not allow any firm conclusions. Furthermore, the EMF-breast cancer link through melatonin is not only biologically plausible, but has been repeatedly verified in laboratory settings (13, 14, 46). Even though the oncogenic mechanism through which EMF might operate is unclear, a number of plausible mechanisms involving melatonin are being entertained (68); these should not be dismissed simply because current knowledge does not allow us to classify EMF as initiator or promoter, following the traditional two-stage model for carcinogenesis (99).

In a review of EMF exposure and cancer, Heath concluded that "the weakness and inconsistent nature of epidemiologic data, combined with the continued dearth of coherent and reproducible findings from experimental laboratory research, leaves one uncertain and rather doubtful that any real biologic link exists between EMF exposure and carcinogenicity" (100). These statements may not completely reflect the current status of knowledge on the possible association of EMF and breast cancer. Although experimental evidence exists, there have not been enough well-designed epidemiologic studies focusing specifically on this disease. It is certainly true that an EMF-breast cancer link has not been established conclusively. Only further research can determine whether or not EMF is associated with breast cancer.

Considering the incomplete knowledge of breast cancer risk factors and the importance of the disease as a public health problem, it seems justified to follow available leads; the ever increasing amounts of EMF in our environment should only bolster the argument. Therefore, research into a potential EMF-breast cancer link is certainly warranted, and the possibility of an association should not be discounted. In conclusion, the following excerpt from the National Research Council seems to echo these sentiments (101): "Countering the claim that epidemiologic studies have gone as far as they can in addressing the potential role of exposure to electric and magnetic fields in cancer etiology, it is quite likely that, at least in the near term, only further epidemiologic research can more strongly implicate or exonerate magnetic fields. That is not to argue for simply conducting more studies to reach consensus, but rather to design studies, some of a purely methodologic nature, that can address the specific gaps in our understanding." We agree with this conclusion.

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