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Review Article

Is Epidemiology Implicating Extremely Low Frequency Electric and Magnetic Fields in Childhood Leukemia?

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Abstract

We have reviewed epidemiological studies examining the association between residential exposure to extremely low frequency electric and magnetic fields (ELF-EMF) and childhood leukemia. We have excluded studies focusing on electrical appliances, because it is difficult to consolidate transient exposure from multiple sources and equally difficult to control information bias. We have identified 24 studies of residential exposure to ELF-EMF and childhood leukemia. About half of these studies were reported as positive and the remaining as null. For each of the studies reported as positive, however, one or more sources of bias could not be confidently excluded. Moreover, studies which were methodologically more sound, or benefited from high quality registry data, were more frequently null than other investigations. We conclude that the empirical evidence in support of an association between ELF-EMF and childhood leukemia is weak.

Key words: ELF-EMF, childhood leukemia, extremely low frequency electric and magnetic fields, epidemiology

Introduction

A working group of the respected International Agency for Research on Cancer (IARC) was recently convened to evaluate possible carcinogenic hazards to human beings from exposures to static and extremely low frequency (ELF) electric and magnetic fields (EMF). The relevant monograph has not been published yet, but it has been stated in the official IARC internet site (http://www.iarc.fr) that "ELF-EMF were evaluated as *possibly carcinogenic to humans* (Group 2B), based on the statistical association of higher level residential ELF-EMF and increased risk for childhood leukemia". In the absence of an acceptable scientific explanation for carcinogenicity of these fields, the epidemiological evidence has been intensively scrutinized. Most meta-analyses have indicated that ELF-EMF are not associated with forms of cancer other than childhood leukemia. Many meta-analyses, however, have suggested that exposure to ELF-EMF is associated with childhood leukemia with a relative risk of approximately 1.5. Meta-analyses are an effective tool in summarizing randomized controlled trials, but their utility in observational research has not been universally accepted (1, 2). Their usefulness may be further challenged in situations where exposure metrics and conditions vary substantially among studies, as it happens with ELF-EMF in epidemiological research.

In this review, we have critically evaluated the studies that have examined the association between residential exposure to ELF-EMF *from power lines* and childhood leukemia. For each study, four of the authors of this review made independent evaluations, whereas the senior author amalgamated the individual reports. Clearly, no epidemiological study is perfect. Our criticism, therefore, should be interpreted as an attempt to reconcile the absence of biomedical evidence linking ELF-EMF to cancer and the occasional epidemiological reports suggesting that an association between these fields and childhood leukemia may exist.

Basic studies

The first paper reporting that ELF-EMF was causally related to childhood leukemia was published by Wertheimer and Leeper (3) who reported an excess of electrical wiring configurations suggestive of high current-flow near the homes of children who developed cancer, as compared to the homes of control children in Colorado. The authors, among themselves, have subsequently published more than fifteen papers claiming that ELF-EMF cause, in addition to childhood leukemia, childhood brain tumors, many forms of adult onset cancers, fetal growth retardation and fetal losses. There are several reasons why the Wertheimer and Leeper study (3) is difficult to interpret. The study did not meet modern methodological standards for planning, implementing, analyzing and reporting epidemiological investigations. In order to assess

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exposure, the authors used only wiring codes that categorize homes by visible features of nearby electrical power lines (e.g., thickness) and by the proximity of the homes to these lines. Although critically important for the avoidance of bias and easy to accomplish, the assignment of wire codes to the homes of cases and controls was not done "blindly," that is, after masking the case or control status of the homes. Moreover, the control selection procedure was so complicated and so inadequately presented, that it has eluded critical scrutiny.

Fulton et al. (4) studied 119 leukemia patients and 240 controls, using as proxy ELF-EMF exposure a wire code scheme similar to that introduced by Wertheimer and Leeper (3). The authors found no relation of ELF-EMF fields to childhood leukemia. Their work, however, has been criticized because cases were confined to residentially stable patients diagnosed or treated in a major Rhode Island hospital, whereas controls came from among all the residents of this small state.

McDowall (5) undertook a study in East Anglia. They followed up nearly 8,000 persons, identified as living in the vicinity of electrical transmission facilities, and reported that overall mortality was lower than expected and no evidence of major health hazards emerged. The study was designed and analyzed as a cohort investigation, and thus has superior inherent methodological advantages against selection and information bias. The weakness of the study is that by addressing overall mortality from all causes it had limited statistical power to examine associations of proximity to electricity transmission facilities with any particular cancer type, in this instance childhood leukemia. Nevertheless, no excess risk for leukemia overall was evident in this study.

A large case-control study of subjects aged 0 to 18 years was undertaken by Tomenius in Sweden (6). The data of this study with respect to childhood leukemia suggest either the absence of an association with ELF-EMF or the existence of an *inverse* association, depending on the choice of ELF-EMF exposure measure. The study has several advantages, including the population-based design and the use of population controls in a satisfactory way, as well as the undertaking, for the first time in an epidemiological investigation, of actual magnetic field strength measurements. The study has been criticized for using a high cut-point of 0.3 microtesla (3 milliGauss) for distinguishing ELF-EMF exposed from unexposed units, thus sharply reducing the prevalence of exposed units and the power of the study. This is not, however, a criticism aiming at validity and, in fact, it may be unfair to criticize a study for a choice that nobody knows, even now, whether it is right, wrong, or irrelevant (if ELF-EMF have no carcinogenic potential). A more serious criticism is that the paper did not, as it should, focus on numbers of cases and controls, but on counts of dwellings, with individuals who have lived in more than one dwelling over-represented in the analysis.

Savitz and his colleagues (7) undertook a large case-control study in which all Denver residents aged 0–14 years who were diagnosed with any form of cancer between 1976 and 1983 were included as cases. In addition to establishment of wire codes, the authors have measured electric and magnetic fields, during periods of low and high electricity consumption in the houses of cases of childhood cancer and controls. Attention was directed to the residence at birth, the residence two years prior to diagnosis and the residence at diagnosis. The study has the hallmark of the expertise of the authors. However, more than 1000 comparisons had to be undertaken, because 4 different exposures, each with 4 or 5 levels, were evaluated at 3 points in time, for 3 different types of house occupancy, for 7 different disease entities. On the basis of chance alone at least 50 would be expected to indicate statistically significant differences or associations at the P~0.05 level. In fact the statistically significant results were markedly fewer and inconsistent. For childhood leukemia in general, the relative risk (and P-value) were: for magnetic fields under low electricity consumption, using 2 milliGauss as cut-off, 1.9 (P~0.22); for magnetic fields under high electricity consumption using the same cut-off 1.4 (P~0.45), and; for electric fields under high electricity consumption using 12 V/m as cut-off, 0.8, i.e. the association was inverse. Even the modest elevations can be explained by unavoidable control selection bias. Nearly 60% of the residential controls in this study did not respond to the request for interviews. In general, persons of very low socioeconomic status are particularly difficult to identify, contact and recruit as controls by the random digit telephone dialing technique used in the Savitz study. Very low socioeconomic status in crowded inner city neighborhoods is associated with proximity to electrical lines and, accordingly, to high current wire codes. A deficit of controls of very low socioeconomic status would thus create an apparent excess of cases of low socioeconomic status and an apparent association of childhood leukemia with low socioeconomic status and with various correlates of this status, including proximity to power lines.

Coleman and his colleagues (8) have undertaken a case-control study of both adult and childhood leukemia in relation to residential proximity to electricity supply equipment in south-east England. This study has been criticized because the 84 childhood leukemia cases could only be compared with 141 controls affected with other types of childhood cancer. This may not be a serious drawback, however, because there is a consensus that childhood cancer types other than leukemia are not associated EMF. By considering as evidence for high ELF-EMF exposure residence within 50 meters from local transformer substations, which are equivalent to the pole-mounted transformers in the USA, the authors found a small and statistically non-significant risk elevation for childhood leukemia [relative risk 1.5 with 95% confidence interval (CI) 0.7 to 3.4; P~0.30].

Myers and colleagues (9) undertook a case-control study in England to examine the occurrence of childhood cancer in relation to the proximity of overhead power lines to a child's home address at birth and to the *calculated* magnetic field at the address. Using 50 meters as a cut-off gave a relative risk of 1.1 for childhood leukemia (P~0.80) and calculated magnetic field generated similar results. The study was adequately designed, but had limited statistical power, because of low prevalence of "highly exposed" individuals.

In a case-control study by London and her colleagues (10), the relation between residential exposure to electric and magnetic fields and risk of leukemia was investigated among children up to 10 years old in Los Angeles County, California. The study assessed ELF-EMF exposure at an "etiological period" that started at conception and ended at diagnosis for infants, six months before diagnosis for children less than two years old, and one year before diagnosis for older children. ELF-EMF were ascertained through wire codes, spot measurements and, for the first time in an epidemiological investigation, through 24-hour magnetic field measurements in the children's bedroom. There was essentially no association of childhood leukemia with spot measurement of either magnetic or electric fields. More importantly, there was no association with 24-hour measurements of magnetic fields, even though these measures were *a priori* considered the optimal metric. There was, however, a statistically significant positive association with wire codes and the pattern was very similar to that noted in the Savitz study (7). This is not really surprising, since controls in both of these studies were mostly chosen by random digit telephone dialing. This procedure can lead to under-representation of controls of low socioeconomic status, who are more likely to live close to electrical wires in their crowded neighborhoods. In summary this study, though expertly designed, provides little, if any, support to the hypothesis that measured magnetic fields affect the risk of childhood leukemia and casts serious doubts on the interpretability, in biologic terms, of the occasionally observed associations with wire codes.

In a case-control study conducted in Mexico city by Fajardo-Gutierrez and colleagues (11), the association between risk of childhood leukemia and living close to EMF generating sources, like electric transformers, high electric voltage distribution or transmission lines and electric substations was examined. A statistically significant positive association between ELF-EMF and childhood leukemia was reported. The study, however, presents serious methodological problems. The authors indicate that all study subjects were visited at home. Yet, surprisingly, exposure to ELF-EMF sources was not based on actual inspection of the surroundings, but relied on interviews. The authors acknowledge in the discussion section that this procedure is likely to introduce information bias. The results section and the tabulations are also problematic, because EMF sources are considered “in general” when they are within certain distances (an understandable approach) and then after “adjustment for distance” (a questionable procedure).

The study by Lin and Lee (12) is not an analytical epidemiological investigation, but relies on an inherently weak ecological design. Taipei City and Taipei County have several districts and each of these districts has a large population (frequently more than 100,000) and many elementary school campuses. In five of these districts at least one elementary school is passed over by a “high power transmission line”—but clearly, very many other elementary schools in these five districts are not. It would have been logical to compare the pupils in the exposed schools with those in the unexposed schools for different patterns of occurrence of childhood leukemia. Instead the authors compare the incidence of childhood leukemia in each of the five index districts with the Taiwan-wide incidence of this disease, as if all the elementary school pupils in the five districts were exposed to these high power transmission lines. The standardized incidence ratio (equivalent to adjusted relative risk) turned out to be higher than 1 in three of the districts and lower in the other two, an unremarkable finding. Indeed, given the likely better ascertainment of childhood leukemia in the five index districts compared to routine cancer registry data for Taiwan as a whole, it is surprising that not all five standardized incidence ratios were higher than 1.

Coghill et al. (13) measured ELF-EMF fields between 2000 h and 0300 h in the bedplaces of 56 children with leukemia and 56 controls. Mean ELF electric field levels in case homes were significantly higher (P<0.01) than those in control homes. By contrast, no significant case-control differences were found with respect to ELF magnetic fields. The authors advance the hypothesis that if ELF-EMF somehow increase the risk of childhood leukemia they may accomplish this not through magnetic fields but through electric fields. It has generally been assumed that electric fields are unlikely to be involved because, in contrast to magnetic fields, they are readily shielded by walls and other materials standing between the ELF-EMF source and the individuals at risk. There is very little in the literature in support of this hypothesis, but it is also true that most studies have focused, explicitly or implicitly, on magnetic fields. This study is conceptually intriguing, but has shortcomings that the authors discuss very objectively. These shortcomings cover both questionable sampling strategies and technical problems with the instruments used.

Michaelis and colleagues (14) studied 129 children with leukemia and 328 controls, by measuring several aspects of ELF magnetic field exposure, including 24 h measurements in the children’s bedroom. Advantages of this study are the technical expertise in the measurement of magnetic fields and the large sample size. The study, however, has also serious limitations, including non-cooperation by 20% of cases and 30% of controls and, more importantly, unblinded assessment of exposure. Moreover, the authors have neglected to control for an important confounding variable that could probably explain the apparent positive, albeit non-significant, association of childhood leukemia with *some* of the ELF-EMF metrics used in this study. Thus, cases were more frequently living in multiple-apartment houses than controls, and median ELF-EMF levels tend to be higher in these houses than in single or double-family houses. This condition can create typical positive confounding that has not been controlled for.

In a case-control investigation undertaken by Petridou and colleagues in Greece (15), residential proximity to electrical power lines of different voltage in relation to childhood leukemia were studied in a group of 117 cases of childhood leukemia and 202 controls. No significant trends of childhood leukemia risk with increasing exposure levels were noted, nor were there statistically significant elevations of disease risk at the higher exposure levels in each measure of exposure. Among the weaknesses of the study are the moderate study size and the use of hospital, rather than population-based, controls. Among the strengths of the study are the minimal refusal proportions on the part of both cases and controls, and the ascertainment of exposure through a mechanism that was both objective and blind as to case/control status of the study participants.

In a large case-control study of childhood leukemia in five Canadian provinces by McBride and colleagues (16), several exposure metrics were used, including 48-hour personal ELF-EMF measurements, wire coding and residential measurements. No significant positive association with any exposure metric was found and, indeed, personal ELF-EMF measurements were non-significantly inversely associated with childhood leukemia risk.

In another case-control study of childhood leukemia undertaken in Ontario, Canada, by Green and colleagues (17), measurements of magnetic fields were undertaken and three different classification schemes of wire coding were assigned to each residence. The authors indicate that their findings do not support an association between leukemia and proximity to power lines with high current configuration, although elevated leukemia relative risk estimates for selected groups of children, using selected exposure metrics, were noted.

A nationwide case-control study of childhood leukemia in New Zealand by Dockerty and colleagues (18, 19) included measurements of electric and magnetic fields in children’s homes. According to the authors there was no significant association between leukemia and the time-weighted average of the 50 Hz magnetic or electric fields in the bedroom and living room combined, although a risk elevation in the highest category of the mean measured bedroom magnetic field was noted in one of the multiple comparisons undertaken.

In a population-based case-control study of acute childhood leukemia by Schuz and colleagues (20), residential magnetic fields were measured over 24 hr. The study covered the whole of the former West Germany. Though the 24-hour median magnetic fields were only weakly related to childhood leukemia, a significant association was seen with respect to magnetic field exposure during the night—a *post hoc* choice. Moreover, the results were based on small numbers of exposed children

In a small Italian study by Bianchi and colleagues (21), exposure to magnetic fields was not directly measured, but estimated using line load data and the distance between subjects' homes and the nearest power line. A significant increase in risk for leukemia in exposed subjects was reported based on a small number of exposed subjects.

The 18 basic studies reviewed so far suffer from one or more of the following problems: small study size, poor identification of study base, questionable control selection procedure, inadequate safeguards against selection bias, sub-optimal ascertainment of exposure to EMF, or *post hoc* selection of the principal exposure variable. Of the 18 studies, ten have been reported as positive, although statistical significance with respect to a metric identified in advance was not always reached.

Methodologically stronger studies

At the time of the completion of this review (December 2001), 6 epidemiological studies on ELF-EMF in relation to childhood leukemia were considered as more important, although there can be no guarantee that all of them have generated valid results. Four of them were undertaken in Scandinavian countries that possess superior population registries allowing valid sampling, whereas the other two were sophisticated investigations undertaken under the auspices of the USA National Cancer Institute and the UK Childhood Cancer Group. These 6 studies are evaluated, in some detail, below.

Feychting and Ahlbom (22–24) undertook a case-control study in Sweden. The study covered all 39 leukemia cases under age 16 years who had lived on a property located within 300 meters of any of the 220 and 400 kV power lines in Sweden during the period 1960–1985. Controls were selected at random from the underlying population. Exposure was assessed by spot measurements and by calculations of the magnetic fields generated by the power lines, taking distance, line configuration, and load into account. Information about historical loads on the power lines was used to calculate the magnetic fields for the year closest in time to diagnosis. When historical calculations were used as exposure assessment for childhood leukemia with cut-off point at 0.1 and 0.2 microtesla (μT), the estimated relative risk increased over the two exposure levels and was estimated at 2.7 (95% CI 1.0–6.3) for 0.2 μT or over; p for trend=0.02.

The study by Feychting and Ahlbom (22–24) received wide publicity before the actual paper was published. The study has several advantages, but also inconsistencies, both internal and in comparison to other Swedish studies. These inconsistencies have been pointed out in a letter to Science (25) from which the comments that follow are drawn.

The study by Feychting and Ahlbom has examined residential exposure in relation to childhood leukemia, but also in relation to adult leukemia and brain tumors in both children and adults. The previously reviewed study by Tomenius (6) has examined residential exposure in relation to childhood tumors (mainly brain tumors and leukemia) and another Swedish study by Floderus et al. (26, 27) has focused on occupational ELF-EMF exposure in relation to leukemia and brain tumors in adults. Thus, in these major Swedish studies, childhood leukemia, childhood brain tumors, adult brain tumors, adult lymphocytic leukemia and adult myeloid leukemia have each been examined in relation to ELF-EMF by two of the studies. The results of the two relevant studies were not similar for any of the cancer sites or types—in fact in every instance the findings pointed to opposite directions. For childhood leukemia, a positive association was reported by Feychting and Ahlbom (22–24), but an inverse association is evident in the Tomenius study (6); for childhood brain tumors, a positive association was found by Tomenius (6), but in the data of Feychting and Ahlbom (22–24) the association is, if anything, inverse; for adult brain tumors, an increased risk was found by Floderus et al. (26, 27), but a declining trend with increasing exposure may be noted in the results of Feychting and Ahlbom (22–24); for adult lymphocytic leukemia, the risk appears to increase in the study by Floderus et al. (26, 27), but seems to decline with exposure in the investigation by Feychting and Ahlbom (22–24); and for adult myeloid leukemia there is a positive association in the study by Feychting and Ahlbom (22–24), whereas in the study by Floderus (26, 27) the association is, if anything, inverse. It may be concluded that the undeniable superior quality of Swedish data bases does not guarantee valid results in every particular investigation, especially when the number of subjects is limited, as it was in the Feychting and Ahlbom study. For each pair of studies dealing with the investigated cancer sites or types, at least one of the studies, and conceivably both, have generated incorrect results.

The study by Feychting and Ahlbom (22–24) has evaluated both calculated and actually measured magnetic fields. There was no association between actually measured magnetic fields and childhood leukemia. Moreover, more cases of childhood leukemia than the 39 observed would have been expected in the study population, even if the incidence of the disease in this population were no higher than in Sweden in general. This contradicts the hypothesis that magnetic fields cause childhood leukemia, because the study population consisted of children living within 300 meters from 220 and 400 kV power lines. It appears reasonable that these children, whether living within 30 meters or 300 meters from these EMF sources, would frequently, in their daily activities, find themselves very close to these EMF sources. Notwithstanding the renowned competence of the investigators and the high quality of the Swedish data bases, the results of this investigation appear internally and externally inconsistent.

A study with design similarities to the previously described Swedish investigation (22-24) was undertaken in Denmark by Olsen and his colleagues (28). The Danish study has also the advantage of using the entire country population, which allows a more straightforward presentation. Exposure to magnetic fields was based on calculations. Cut-off points were *a priori* set for high exposure at 0.25 μT, and for moderate exposure between 0.1 μT and 0.24 μT. Based on very small numbers, the relative risk for those moderately exposed was 0.5 (95% CI 0.1 to 4.3) and for those highly exposed 1.5 (95% CI 0.3 to 6.7). The lack of an exposure-response pattern or a statistically significant elevation among "highly exposed" children suggest that EMF are unrelated to childhood leukemia. The authors also point out that between 1945 and 1990 the incidence of leukemia in Denmark has remained essentially stable, whereas electricity consumption has increased about 30-fold over the same period.

A study undertaken in Finland by Verkasalo and colleagues (29) has some design similarities to the Swedish study (22–24) and the Danish study (28) previously reviewed, but its cohort design makes it superior. Among 134,800 children aged less than 20 years and living within 500 meters of overhead power lines, 35 cases of childhood leukemia were observed over a 20-year period, whereas more, i.e. 38, were expected. Exposure to ELF-EMF was also calculated using an appropriate computer program. The relative risk was 0.89 with 95% CI 0.6 to 1.3 among the 127,500 children exposed to less than 0.20 μT (32 childhood leukemia cases), and 1.6 with 95% CI 0.3 to 4.5 among the 7,300 children exposed to 0.20 μT or more (3 cases of childhood leukemia). The lack of an exposure-response pattern or a statistically significant elevation among "highly exposed" children provide little, if any, support to the hypothesis that EMF are related to childhood leukemia.

Tynes and Haldorsen undertook a nested case-control study of childhood leukemia in Norway (30). Several metrics were used to assess exposure to ELF-EMF. For calculated time-weighted average exposure to magnetic fields from birth to diagnosis, the odds ratio for childhood leukemia in the high exposure category, which was defined as 0.14 μT or higher, was lower than the null value of 1. When 0.2 μT were used as cut-off, the odds ratio was 0 with wide confidence interval. The authors have carefully considered the strengths and the power limitations of their study before concluding that their data provide no support for an association between EMF and childhood leukemia.

Because the four studies in the Scandinavian countries have important design similarities, we have undertaken a meta-analysis using the standard procedure which is applied for the summarization of published data. The overall relative risk was derived from the weighted average of the logarithm of relative risk of individual studies. The weight for each study was taken to be proportional to the inverse variance of the logarithm of the respective relative risk. The variance, which is the square of the standard error, was derived from the reported confidence interval. We have calculated the 95% CI of the summary relative risk by taking the inverse sum of weights as the variance of the logarithm of the summary relative risk. In essence, this procedure "weights" each contributing study by the precision of the corresponding relative risk. The results are summarized in the text table below.

Table 1 Meta-analysis of the childhood leukemia results of 4 methodologically advanced ELF-EMF studies undertaken in Scandinavian countries

Country	Reference	Exposed cases*	Relative risk	95% CI
Sweden	22	7	2.7	1.0–6.3
Denmark	28	3	1.5	0.3–6.7
Finland	29	3	1.6	0.3–4.5
Norway	30	4	0.8	0.3–2.4
Overall		17	1.6	0.9–2.8

* 0.2 μT for the Swedish and Finnish studies; 0.25 μT for the Danish study; 0.14 μT for the Norwegian study.

The overall evidence from these Scandinavian studies provides little or no support for an association of EMF exposure to childhood leukemia. This is not simply because the overall relative risk is not significantly different from the null value of 1 (P~0.12), but also because the summary relative risk is elevated largely under the influence of the Swedish study which has serious shortcomings previously described.

Linet and her colleagues have noted that previous investigations found associations between childhood leukemia and surrogate indicators of exposure to magnetic fields, that is wire codes, but not between childhood leukemia and actual measurements of residential magnetic fields. Thus, they undertook a major case-control study of the main form of childhood leukemia, that is acute lymphoblastic leukemia, in children under 15 years of age (31). Magnetic fields were measured for 24 hours in each case patient or control's bedroom, whereas additional spot magnetic field measurements were undertaken in other rooms and a computer algorithm assigned wire code categories. There was no association of childhood leukemia with wire code categorization (relative risk between the highest and the lowest wire code category was 0.88, with 95% CI 0.48 to 1.63). Moreover, in this large study there was no statistically significant association between childhood leukemia and summary time-weighted average residential magnetic field levels (relative risk between exposures higher than 0.200 μT and less than 0.065 μT was 1.24, with 95% CI 0.86 to 1.79). The authors concluded that there was little evidence in their data that measured magnetic fields or high wire code categorization are associated with the risk of childhood leukemia.

This is an important study (31) that, under the constrains imposed by the lack of population-based registries, meets most of the contemporary methodological standards for the epidemiological investigation of ELF-EMF in relation to childhood cancer. Most of the previously published studies that have claimed to link residential ELF-EMF exposure to childhood leukemia relied on wire codes or on calculated fields that reflect a similar philosophy. In this large, sophisticated, adequately controlled for recognizable potential confounders and statistically powerful study by Linet et al. (31), the results *with respect to wire codes* are reassuringly and convincingly null. With respect to measured magnetic fields, the findings of Linet et al. are equivocal, but there is little else in the published literature to support this association. Moreover, no cut-off point in any of the analyses with respect to any of the exposure measures reaches a statistically significant, or even suggestive, P-value. Thus, the results of this study argue strongly against a causal link between ELF-EMF exposure and childhood leukemia.

The UK Childhood Cancer Study (32, 33) was a large population-based case-control investigation covering the whole of England, Wales and Scotland. Exposure to ELF-EMF relied on actual measurements, as well as on distances from high voltage lines and electric substations. The authors found no evidence that either proximity to electrical installations or the magnetic field levels these installations produce are associated with increased risk of childhood leukemia. Indeed, most relative risk estimates were below the null value of 1.

Among the above discussed six methodologically stronger studies, five have been reported as negative and they were all published in major medical journals. Only one of these studies (22) was reported as positive and this study has been criticized for internal and external inconsistencies.

Discussion

In this review, we have focused on childhood leukemia, the only form of cancer for which there is still controversy as to its possible link to ELF-EMF. Moreover, we have not reviewed studies concerning exposures to electric appliances, because such exposures are difficult to consolidate or to dissociate from information bias.

Among the basic studies, those reported as positive were, as a rule, focusing on wire codes rather than actual measurements. Wire codes, however, or measurements of similar philosophy, were found to be unrelated to childhood leukemia in the major USA (31) and UK studies (32, 33). Nevertheless, the positive associations that have been reported with various metrics of ELF-EMF should be explained in methodological terms before ELF-EMF can be acquitted of any suspicion of being component causes in even a minority of childhood leukemia cases. Several such methodological factors need to be considered, including the following:

• The multiple comparison process frequently implemented by authors of many studies, coupled with the tendency of all authors to report a positive rather than a negative finding.

• Residual confounding that may be unavoidable because very few risk factors for childhood leukemia have been identified.

• The difficulty of avoiding selection bias in countries lacking the population-based resources available to Scandinavian investigators.

• The scarcity of highly exposed individuals that asymmetrically facilitates documentation of a significant excess, but not a significant deficit, of cases (if one case is expected under the null hypothesis, no deficit can ever be significant).

• The underestimation of the chance variation and of the width of the confidence intervals in observational research (34–36).

• The fact that when there is in fact no association between a particular exposure (ELF-EMF) and a certain disease (childhood leukemia), it takes only a few biased large studies to create a significant elevation of relative risk in a meta-analysis, because the unbiased studies converge to the null relative risk of 1.

The relation of wire codes or, more rarely, other metrics of ELF-EMF exposure with childhood leukemia is likely to have been generated by bias that has found its way, as it frequently does, in even well designed epidemiological investigations. A positive association between ELF-EMF and childhood leukemia is not supported by the diverging time trends of electricity consumption and childhood leukemia incidence. During the last 50 years, electricity consumption has increased about 30-fold, whereas the incidence of childhood leukemia in countries with long-standing, reliable cancer registration statistics, notably the Scandinavian countries, has increased only slightly, if at all. Virtually all investigators agree that the ascertainment of true relevant exposure in EMF studies is subject to considerable random misclassification that systematically underestimates any relevant association. Thus, the relative risk linking ELF-EMF to childhood leukemia, had it been truly elevated, should in fact be much higher than the empirically derived relative risk estimates. Exposure to ELF-EMF is almost universal in industrialized nations and electrical power consumption has increased exponentially in this century. If a rapidly increasing and widespread exposure were strongly and etiologically linked to childhood leukemia, we would be witnessing a major and expanding epidemic of childhood leukemia, which is by no means evident. Ecological correlations (including time trends) are, of course, difficult to interpret. Nevertheless, it is important to remember that widespread exposures characterized by high relative risk estimates can generate strong ecological correlations.

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