

COMMENTARY

Health effects of magnetic fields generated from power lines: new clues for an old puzzle

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Summary. Thirty years ago, Nancy Wertheimer and Ed Leeper published the first report on the association between childhood cancer and “electrical current configuration” of houses in Denver, Colorado. In 2001 the International Agency for Research on Cancer defined 50-60 Hz magnetic fields as “possibly carcinogenic to humans” because of the “limited evidence” of carcinogenicity of residential exposure relatively to childhood leukemia. With respect to health effects other than cancer, namely neurodegenerative disorders, miscarriage, subtle differences in the timing of melatonin release, altered autonomic control of the heart, and changes in the number of natural killer cells, some open questions still remain. Several authors recommended further investigation of the possible long-term effects of magnetic fields, focussing on populations experiencing high exposure levels. In this frame a research team of ISS searched for a suitable location to implement an epidemiological study aimed at a wide range of outcomes for which *a priori* hypotheses could be formulated. The recently published findings of this project showed an increase of primary and secondary malignant neoplasms, ischaemic disease and haematological diseases. Future studies should thus address the most exposed sectors of the population, take into account different outcomes (all neoplasms, neurodegenerative diseases, immunological disorders, specific cardiovascular effects) and follow research protocols that enable subsequent pooled analyses. A precautionary approach may provide the frame for decision making where the available resources for environmental remediation be prioritatively allocated to worst-off situations.

Key words: magnetic fields, epidemiological studies, public health.

THREE DECADES OF INVESTIGATIONS AND SOME OPEN QUESTIONS

Thirty years ago, Nancy Wertheimer and Ed Leeper [1] published the first report on the association between childhood cancer and “electrical current configuration” of houses in Denver, Colorado. Prior to this study, concern for electrical and magnetic fields generated from power frequency (50-60 hertz, corresponding to “ELF” – Extremely Low Frequency fields) exposure, had been confined to their possible neurobehavioural effects, following case-reports of electrical substation workers in the former Soviet Union [2]. The Wertheimer-Leeper study prompted a number of investigations aimed at evaluating the carcinogenicity of electrical and magnetic fields generated by power lines, domestic appliances and industrial installations. The first overall WHO evaluation [3] stated that the reported neurobehavioural, haematological and cardiovascular adverse health effects were not adequately confirmed. It was concurrently

clear that the rationale for properly evaluating the possible health impact of ELF fields was partly based on the awareness of the large size of the exposed population, and further studies were warranted.

The “second generation studies” were characterized by a remarkable methodologic refinement in terms of case ascertainment, exposure assessment, control of confounding and sample size. Besides leading to more valid and precise findings, this major scientific commitment resulted in increased comparability between adopted study protocols, which lead to meta-analyses and, more interestingly, to the possibility of pooled analyses of the original data at least for the childhood leukemia studies [4, 5]. The latter two papers reached the conclusion that a significant increase of childhood leukemia was detectable in dwellings characterized by levels of magnetic induction exceeding 0.3-0.4 microtesla (μT). The carcinogenicity of ELF fields was evaluated in 2001 by the International Agency for Research on Cancer (IARC), that defined 50-60 Hz mag-

netic fields as “possibly carcinogenic to humans” because of the “limited evidence” of carcinogenicity of residential exposure with respect to childhood leukemia [6].

Recently, a comprehensive review document by WHO confirmed the IARC evaluation, and stated that some open questions remain with respect to health effects other than cancer, namely neurodegenerative disorders, miscarriage, subtle differences in the timing of melatonin release, an altered autonomic control of the heart, and changes in the number of natural killer cells [7].

FOCUSSING ON HIGHLY EXPOSED COMMUNITIES

In this frame, an aspect deserving particular relevance should be addressed: several authors and working groups recommended further investigations of the possible long-term effects of magnetic fields, focussing on populations experiencing high exposure levels.

Firstly, the authors of the aforementioned pooled analyses of childhood leukaemia studies emphasized the need to design future studies in order to observe a sufficiently high number of subjects experiencing exposures to magnetic flux density higher than 0.3-0.4 μT [4, 5]. Then, the International Commission on Non-Ionizing Radiation Protection recommended that future studies be of high methodological quality, of sufficient size, and with sufficient numbers of highly exposed subjects [8]. Finally, the recent document by WHO [7] mentions the lack of a clear contrast between high and low exposure categories among the critical points of exposure assessment in epidemiological studies on electrical and magnetic fields.

Interestingly enough, support to the recommendation to focus on highly exposed groups was provided by the findings of studies on neurodegenerative, reproductive and immunological outcomes, that indicated possible adverse effects at exposure levels of the same order of magnitude of those suggested by the childhood leukaemia studies [7, 9].

These consistent observations may be regarded as converging on a core concept of epidemiology, the notion of “high risk groups”. The original definition comes from occupational epidemiology “Groups of human beings for whom current or past exposures to carcinogens exceeding background levels can be demonstrated or suspected, even if not ascertained” and it was subsequently applied in environmental epidemiology by US scientists investigating populations living close to waste dumping sites. It was then shown that individuals are exposed to different levels of chemicals and the exposure distribution may typically be described as log-normal, showing

a bell shape with a strong asymmetry represented by its right tail, with a decreasing number of subjects exposed to an increasingly high level of the agent of interest. This distribution may subsume a substantial lack of risk (or a moderate risk) for the majority of the population, together with a small proportion of subjects experiencing exposure levels corresponding to those which are associated to ascertained or possible adverse health effects; for a review of these aspects, the reader is referred to [10] and the cited reference list.

Exposure to ELF magnetic fields in the general population shows somehow similar patterns. According to WHO, magnetic flux density geometric means in dwellings range between 0.025 and 0.07 μT in Europe and between 0.055 and 0.11 μT in the USA [7]. On the basis of five extensive exposure surveys, it was estimated that approximately 4-5% of the general population experiences arithmetic mean exposures above 0.3 μT and that the median exposure of just 1-2% of the population is above 0.4 μT [11]. Estimates based on exposures of controls in case-control studies show that 0.5-7.0% have arithmetic mean exposures above 0.3 μT and 0.4-3.3% have geometric mean exposures above 0.4 μT [7]. For Italy, the only available figures are those from Anversa *et al.* [12] and Petrini *et al.* [13]; these authors estimate that 0.26-0.43% of the Italian population is exposed to average magnetic flux density levels above 0.3 μT , and 0.20-0.35% are exposed to levels above 0.4 μT , taking into account magnetic fields generated by high-voltage power lines.

In light of the aforementioned scientific literature, including the recommendations to concentrate future studies on populations experiencing high levels of exposure to ELF magnetic fields (orientatively, in the range of one up to few μT), a research team of ISS searched for a suitable location to implement an epidemiological study aimed at a wide range of outcomes for which *a priori* hypotheses could be formulated [14, 15]. The study was then realized in the district of Longarina, in Ostia Antica (Rome municipality), partly built under a 60 kV power line. Long-term measurements in the dwellings and theoretical evaluations showed that the main source of magnetic fields is the 60 kV electric line and that there are some dwellings with time-weighted average (TWA) exposure levels above 1 μT . The study cohort includes the subjects resident in the area corresponding to a distance of 100 m from the line, for any period of time since 1954 (the year when the first houses were built) through the end of 2003, the year of cohort enumeration. Cohort members were categorized by exposure levels and duration of residence in the area. Mortality and morbidity were investigated [16, 17]. The re-

cently published findings of the morbidity study, which considered a wide range of outcomes, including non fatal conditions, showed an increase of primary and secondary malignant neoplasms, ischaemic disease and haematological diseases. The increase of primary malignant neoplasms had been anticipated in the mortality study. In both studies, these increases were concentrated in the subcohort closest to the electric line, thus exposed to highest level of magnetic field, and in the subjects who lived in the area for longest periods of time.

An independent support to the indication of studying highly exposed populations comes from some studies that appeared in the literature in the last two years, subsequently to the publication of WHO Environmental Criteria.

RESEARCH DEVELOPMENT HEALTH AND THE RECENT SCIENTIFIC DEBATE

A recent pooled analysis of case-control studies, performed in four countries (Canada, Germany, UK, USA) on childhood leukaemia and ELF magnetic fields, confirmed the association, finding a statistically significant increase (Odds Ratio (OR)=1.93; 95% Confidence Interval (CI): 1.11-3.35) in children exposed to magnetic fields at levels higher than 0.4 μT with respect to those exposed to below 0.1 μT . The analysis did not support the study hypothesis that night-time bedroom measurements may provide a more appropriate exposure evaluation than previously used 24-48 hour measurements [18].

Some authors suggested that genetic susceptibility to leukaemia may modify the effect of magnetic field exposure, namely that the magnetic fields may have a causal role in the aetiology of leukaemia among a genetically susceptible children subgroup. Mejia-Arangure *et al.* [19] observed a significant increase of childhood acute leukaemia among Down syndrome subjects resident in dwellings with levels of magnetic flux density over 0.6 μT (OR= 3.7; 95% CI: 1.05-13.3). The researchers hypothesized that the magnetic fields may act as cancer promoters or progressors. The hypothesis of interaction between genotype and environmental exposure to magnetic fields was investigated by a case-only study in 123 patients with sporadic acute leukaemia. The results show that residence at a distance below 100 m from electric transformers and power lines may be considered a risk factor for the development of acute leukaemia in children with XRCC1 Ex9p16A genotype [20]. These findings suggest that modification of genetic susceptibility in vulnerable subjects may be involved in the effect of extremely low frequency magnetic fields, since inadequately repaired DNA damage and

chromosome breaks might ultimately lead to the initiation and progression of disease.

It can be stated that these studies provide new evidence on the pathogenesis of leukaemia in children exposed to magnetic field. Furthermore, in the last two years, some studies about ELF magnetic fields exposure and non neoplastic diseases were published.

A national register based study published in 2008 on mortality from neurodegenerative diseases and residential magnetic field exposure (a topic regarded by WHO as "high priority" for future research) shows increase of risk for Alzheimer's disease in the Swiss population resident within 50 m from 220-380 kV power lines, with a dose-response relation for duration of residence. A similar pattern is found for senile dementia, but no risk is shown for Parkinson's disease and amyotrophic lateral sclerosis (ALS) [21].

The increased risk for Alzheimer's disease in subjects residentially exposed to high levels of ELF magnetic fields has been confirmed by Garcia and colleagues in a meta-analysis that investigates fourteen studies based in the occupational setting. The increased risk had been consistently seen for men occupationally exposed to above 0.5 μT [22].

An interesting study has been published in 2009 on magnetic fields and natural killer cells (NK), one of the issues regarded as an "open question" by WHO. The NK cells play an important role in the control of cancer development and a relationship between ELF fields exposure and their activity and number has been hypothesized. The study considered workers exposed to different levels of ELF fields; significant reduction of NK activity and of Lytic Units number were observed in workers exposed to above 1 μT , with respect to those exposed to below 0.2 μT . The authors conclude that their results suggest that occupational exposure to ELF levels exceeding 1 μT may induce a reduction of NK activity, in agreement with the hypothesis that ELF fields could act as promoters or progressors of cancer [23].

While the aforementioned studies on childhood leukemia, neurodegenerative disorders and immunological response provide some support to the issue of investigating highly exposed populations, the recent literature on cardiovascular disease does not offer new hints. A literature review by McNamee *et al.* [24], based on both epidemiological and laboratory studies, defines the current evidence as largely inconclusive. The WHO indication of a substantial lack of association between cardiovascular disease and ELF magnetic fields, with the "open question" of a possible altered autonomic control of the heart, remains the most accurate evaluation.

Finally, three recently published papers suggest new approaches for future studies in order to clarify the health impact of magnetic fields.

The first paper takes into account the multifactoriality of carcinogenesis, proposing a case-control study on leukaemia and non-Hodgkin's lymphoma, whose design takes into account both occupational and environmental exposures to a wide range of potential risk factors and confounding factors. The study is currently in progress [25].

The second paper specifically addresses leukaemia and it indicates as a priority the study of highly exposed children who live in apartments next to built-in transformers or electrical equipment rooms. The authors also emphasize the investigation of joint effects of ELF environmental exposure and genetic co-factors. In particular, regarding exposure assessment, they indicate the need to identify unexposed children with a more specific procedure, in order to avoid "false negatives", and to focus on assignment of subjects to different exposure categories rather than on the absolute value of exposure levels [26].

The most recent article, finally, encourages the use of pooled analyses of data sets from multiple occupational cohort studies rather than meta-analyses of the study findings. Indications of an increased risk for some diseases associated with occupational ELF exposure are recognized, even if the evidence is regarded as weak or inconsistent. Misspecification of exposure metrics is regarded as a cause of underestimation of risk. ALS is considered the highest priority in terms of outcome [27].

TRANSLATING RESEARCH FINDINGS INTO PUBLIC HEALTH PRACTICE

The reasons for aiming at a thorough appraisal of the health impact of 50-60 Hz magnetic fields, as it has been discussed in this paper, are essentially two: the ubiquitous and still increasing occurrence of electrical lines and appliances, and the consolidation of the scientific evidence of a range of adverse health effects observed in the highly exposed sectors of the population. Future studies should thus address these sectors of the populations, take into account different outcomes (all neoplasms, neurodegenerative disease, immunological disorders, specific cardiovascular effects), and follow research protocols that enable subsequent pooled analyses.

In order to successfully achieve these goals, the first step is to link information about the network of power lines with population and health data on a geographic information system. The identification of spatial "corridors" along the lines characterized by estimated levels of exposure (obtained by modelling current load and geometric characteristics of the conductor) may lead to mortality and morbidity figures specific by exposure category. A national database of administrative units close to high tension power lines has been realized in England by Briggs *et al.* [28]. The authors, though, have used a buffer of 600 meters on both sides of the lines, which may result in considerable dilution of exposure. Since magnetic fields generated by power lines may determine an appreciable increase of exposure levels only in a relatively narrow corridor, not exceeding in most instances 30-40 meters on both sides of the line, the possibility to adopt a microgeographical study design based on aggregate data requires the use of high resolution population databases. Alternatively, a cohort approach should be used, with geocoding of residence and ascertainment of health outcomes at the individual level. Both ecological and cohort studies provide information on all health outcomes of interest, while case-control studies, addressing one endpoint, appear to be less needed in this stage.

The approach that has been briefly depicted requires the integration of environmental and health data, coherently with the recommendations for multidisciplinary research in environmental health provided by the international scientific community [29], especially compelling according to some authors who refer to the notion of "precautionary research" [30]. This approach, furthermore, may contribute to public health action by fostering its interaction with scientific research: public health officers may in fact more actively search highly exposed populations in the communities where they serve, and scientists may be asked to apply their research methods to suitably selected settings. The precautionary attitude that has been extensively recommended to empower public health may then provide a frame for decision making where the available resources for environmental remediation be prioritatively allocated to worst-off situations [31].

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