Overview of the epidemiologic studies on the health effects of ELF magnetic and electric fields published in the fourth trimester of 2008

Dr. Maurits De Ridder Occupational and Environmental Health Section Ghent University

1. <u>Reviews</u>

EXPOSURE TO ELECTROMAGNETIC FIELDS AND THE RISK OF CHILDHOOD LEUKAEMIA: A REVIEW.

Schüz J, Ahlbom A. Radiat Prot Dosimetry. 2008;132: 202-211.

Extremely low-frequency magnetic fields have been classified as possibly carcinogenic to humans, mainly based on epidemiological studies consistently showing an association between long-term average exposures to magnetic fields above 0.3/0.4 microT and the risk of childhood leukaemia. No mechanism to explain this finding has been established and no support for a causal link emerged from experimental studies. Chance or bias cannot be ruled out with reasonable confidence as an explanation for the observed association. If the association is causal, it explains only a small fraction of childhood leukaemia cases. There were some reports of childhood leukaemia clusters in the vicinity of high-power radio and television broadcast transmitters in studies in Australia and Italy. However, recent large-scale systematic studies in Korea and Germany show no association between exposure to radio frequency electromagnetic fields emitted from broadcast towers and childhood leukaemia risk. Studies on mobile phone use and leukaemia risk in adolescents and young adults may be indicated.

RECENT ADVANCES IN RESEARCH RELEVANT TO ELECTRIC AND MAGNETIC FIELD EXPOSURE GUIDELINES.

Kavet R, Bailey WH, Bracken TD, Patterson RM. *Bioelectromagnetics. 2008; 29: 499-526.*

Limits on exposures to extremely low-frequency electric fields, magnetic fields and contact currents, designated as voluntary guidelines or standards by several organizations worldwide, are specified so as to minimize the possibility of neural stimulation. The limits, which we refer to as guidelines, derive from "basic restrictions" either on electric fields or current density within tissue, or on avoidance of annoying or startling interactions that may be experienced with spark discharge or contact current. Further, the guidelines specify more conservative permissible doses and exposure levels for the general public than for exposures in controlled environments, which most typically involve occupational settings. In 2001 the authors published an update on guideline science. This paper covers more recent developments that are relevant to the formulation and implementation of the next generation of guidelines. The paper deals with neurostimulation thresholds and the relevance of magnetophosphenes to setting guideline levels; dosimetry associated with contact current benchmarked against basic restrictions; tissue and cellular dosimetry from spark discharge; assessment of exposures to high electric fields in realistic situations (e.g., line worker in a transmission tower); a simplified approach to magnetic field assessment in non-uniform magnetic fields; and a quantitative approach to sampling workplace exposure for assessing compliance.

DO ELECTROMAGNETIC FIELDS ENHANCE THE EFFECTS OF ENVIRONMENTAL CARCINOGENS? Juutilainen J.

Radiat Prot Dosimetry. 2008; 132: 228-231.

Epidemiological studies have reported an increased risk of leukaemia in children who are exposed to extremely low-frequency (ELF) magnetic fields (MF), suggesting that ELF MFs may be carcinogenic to humans. No carcinogenic effects have been found in animal studies that have tested ELF MFs alone. Similarly, genotoxicity studies have generally not shown effects from MFs alone. However, ELF MFs have been reported to enhance the effects of known carcinogenic or mutagenic agents in a few animal studies and in several in vitro studies. This paper discusses the findings of studies on such combined effects. The majority of in vitro studies have reported positive findings, which supports the conclusion that MFs of 100 microT or higher interact with other chemical and physical agents. Further studies should address biophysical mechanisms and dose-response relationship below 100 microT. Animal studies designed according to the classical initiation-promotion concept may not be sufficient for studying the cocarcinogenic effects of MFs, and further studies using novel study designs would be useful.

Conclusion: Epidemiological data on the interaction between MFs and other environmental agents are scant and inconclusive, and any further studies may be difficult because of the scarcity of subjects with suitable combined exposures.

CAN DISTURBANCES IN THE ATMOSPHERIC ELECTRIC FIELD CREATED BY POWERLINE CORONA IONS DISRUPT MELATONIN PRODUCTION IN THE PINEAL GLAND? Henshaw DL, Ward JP, Matthews JC. *J Pineal Res. 2008; 45: 341-350.*

Recent epidemiological studies have reported an increased risk of leukemia in adults and children near overhead high voltage powerlines at distances beyond the measured range of the direct electric and magnetic fields. Corona ions are emitted by powerlines, forming a plume that is carried away from the line by the wind. The plume generates highly variable disturbances in the atmospheric electric field of tens to a few hundred V/m on time scales from seconds to minutes. Such disturbances can be seen up to several hundred meters from powerlines. It is hypothesized that these random disturbances result in the disruption of nocturnal melatonin synthesis and related circadian rhythms, in turn leading to increased risk of a number of adverse health effects including leukemia. In support of the hypothesis, it is noted that melatonin is highly protective of oxidative damage to the human hemopoietic system.

Conclusion: A review of electric field studies provides evidence that (i) diurnal variation in the natural atmospheric electric field may itself act as a weak Zeitgeber; (ii) melatonin disruption by electric fields occurs in rats; (iii) in humans, disturbances in circadian rhythms have been observed with artificial fields as low at 2.5 V/m. Specific suggestions are made to test the aspects of the hypothesis.

2. Environmental exposure

CASE-ONLY STUDY OF INTERACTIONS BETWEEN DNA REPAIR GENES (HMLH1, APEX1, MGMT, XRCC1 AND XPD) AND LOW-FREQUENCY ELECTROMAGNETIC FIELDS IN CHILDHOOD ACUTE LEUKEMIA.

Yang Y, Jin X, Yan C, Tian Y, Tang J, Shen X. *Leuk Lymphoma.* 2008; 49 : 2344-2350.

A case-only study was conducted in 123 patients with sporadic acute leukemia (AL). The locations of electric transformers and power lines were noted in each area, and their distances from the houses of the study patients were measured. The intensities of magnetic fields (B) were measured in 66 cases. Unconditional logistic regression analysis was performed adjusting for age, gender, parental education and occupation, indoor and outdoor pesticides use, presence of television sets, refrigerators and microwave ovens in children's rooms and the presence of chemical factories or telecommunication transmitters within 500 m of the houses. The results of the gene-environment analyses revealed that an interaction existed between the XRCC1 Ex9+16 A allele and the presence of electric transformers and power lines within 100 m (Mean B=0.14 microTeslas, microT) of the houses (interaction odds ratio, COR=4.31, 95%CI: 1.54-12.08). The COR for the interaction of XRCC1 Ex9+16A and the presence of these installations within 50 m (Mean B=0.18 microT) of the houses was 4.39 (95%CI: 1.42-13.54).

Conclusion: These results suggest a possible association between electric transformers and power lines and the XRCC1 Ex9+16A allele in patients with childhood AL.

DNA REPAIR GENES, ELECTROMAGNETIC FIELDS AND SUSCEPTIBILITY TO ACUTE LEUKEMIA? Sharma M, Odenike OM. *Leuk Lymphoma. 2008; 49: 2233-2234.*

The approach utilized by Yang You et al. is relatively novel in the sense that although many previous studies have looked at genetic susceptibility to childhood leukemia or environmental exposures to childhood leukemia, there are relatively few studies that have focused on exploring gene-environment interactions. The current report is the first to explore the interaction between DNA repair genes and exposure to EMF, an important objective given the possible link between EMF and childhood leukemia.

There are several limitations to this study, including the fact that this is a case-only study. This approach is increasingly being used for screening for potential gene-environment interactions. It allows the estimation of the interaction effect between the exposure and the genotype, assuming independence between genotype and exposure, and circumvents the challenges that may be encountered in attempting to choose an appropriate control group. A major drawback of the case-only study however, is that it does not allow the direct estimation of the exposure nor of genotype on risk. Another limitation of the current study is the issue of potential recall bias and sampling bias, because only 66 out of the 123 homes involved were visited. It is also unclear why specific SNPs were studied, and others excluded. For example, polymorphisms at codon 399 of the *XRCC1* gene have been associated with an increase in the risk of ALL by other groups; these SNPs were, however, not investigated in this study.

Conclusion: Despite its limitations, the study is certainly hypothesis-generating. The concept that the interaction between an inherited allele in a DNA repair gene and a subtle environmental exposure such as low-frequency EMF could lead to the development of childhood leukemia is biologically plausible, although remains difficult to prove conclusively. Further investigation of this issue would require large case-control studies,

ideally using emerging genomic technologies to examine a wider array of SNPs involving DNA repair genes. The results from these studies would have the potential to provide additional biologic insight into the etiology of acute leukemias, and shape public health policies geared towards prevention of these diseases.

3. Exposure assessment

EXPOSURE TO 50 HZ MAGNETIC FIELD IN APARTMENT BUILDINGS WITH BUILT-IN TRANSFORMER STATIONS IN HUNGARY.

Thuróczy G, Jánossy G, Nagy N, Bakos J, Szabó J, Mezei G. *Radiat Prot Dosimetry. 2008;131: 469-473.*

Exposure to 50 Hz magnetic field (MF) was evaluated in 31 multi-level apartment buildings with built-in step-down transformer stations. In each building, three apartments were selected: one apartment located immediately above the transformer room (index apartment), one located on the same floor and one on a higher floor. The mean value of measured MFs was 0.98 microT in apartments above transformers, 0.13 microT on the same floor, and 0.1 microT in on higher floors. The mean measured MF value was higher than 0.2 microT in 30 (97%) index apartments, 4 (14%) on the same floor as the index apartments and 4 (13%) on higher floors. The corresponding numbers were 25 (81%), 0 and 0, respectively, when 0.4 microT was used as cut-point.

Conclusion: It is concluded that apartments in building with built-in transformers can be reliably classified into high and low-exposure categories based on their location in relation to transformers.

ANALYSIS OF INDIVIDUAL- AND SCHOOL-LEVEL CLUSTERING OF POWER FREQUENCY MAGNETIC FIELDS.

Lin IF, Li CY, Wang JD. Bioelectromagnetics. 2008; 29: 564-570.

This study reports the continuous 8-h monitoring of data on extremely low-frequency magnetic fields (ELF-MF) relating to 14 children and 35 teachers in 11 elementary schools in Northern Taiwan. It was anticipated that the subjects in two of these campuses would have elevated exposure to ELF-MF as a result of their close proximity to high-voltage (161 kilo-Volt, kV) power lines. The results of this analysis reveal that in those schools with high-voltage power lines running through the campuses, the mean ELF-MF exposure level (0.38 +/- 0.51 micro-Tesla (microT), or 0.15, 0.25 and 0.44 microT at the respective 25th, 50th and 75th percentiles) was higher than the mean ELF-MF exposure level for campuses situated far away from such high-voltage power lines (0.14 +/- 0.27 microT, or 0.04, 0.06 and 0.10 microT at the respective 25th, 50th and 75th percentiles). The multi-level analytical technique, which takes individual measurements as the analytical unit, and which also takes into consideration the inter-correlation between measurements from the same individual and/or campus, was also applied to the analysis of the data.

Conclusion: Individual-level and school-level clustering of the measurements, both of which were discernible in this study, should be taken into consideration in any future analysis of data obtained from the continuous monitoring of exposure to ELF-MF.

4. Experimental research

DO NATURALLY OCCURRING MAGNETIC NANOPARTICLES IN THE HUMAN BODY MEDIATE INCREASED RISK OF CHILDHOOD LEUKAEMIA WITH EMF EXPOSURE? Binhi V.

Int J Radiat Biol. 2008; 84: 569-579.

The purpose of this study was to develop the hypothesis that magnetic nanoparticles, found in many organisms and often involved in biological reactions to weak electromagnetic fields (EMF), mediate EMF-induced DNA damage which could result in increased risk of childhood leukaemia and other cancers. An analysis of current research into magnetic nanoparticles was carried out. Physics estimates and the development of the hypothesis that intracellular magnetic nanoparticles chronically change the free radical concentration and can mediate the enhanced rate of DNA damage in hematopoietic stem cells were made.

The properties of magnetic nanoparticles are considered and the naturally occurring magnetic field generated by a magnetic nanoparticle within a cell is calculated to be in the range of about 1-200 millitesla, which exceeds the level of the natural geomagnetic field by orders of magnitude. Experiments are summarized on the biological effects of static magnetic field in this range. It is shown that magnetic nanoparticles can increase the rate of free radical formation by a few percent, in the course of an idealized radical-pair reaction in a cell. A mechanism is discussed that explains how weak alternating magnetic fields, of the order of 0.4 muT, could cause an increase in the rate of leukaemia via millitesla fields produced around superparamagnetic nanoparticles in hematopoietic stem cells.

Conclusion: The postulated presence of magnetic nanoparticles located in hematopoietic stem cells could constitute a cancer risk factor. Superparamagnetic nanoparticles can possibly mediate increased level of leukaemia caused by background exposure to low-frequency weak EMF.

ASSESSING THE POTENTIAL LEUKEMOGENIC EFFECTS OF 50 HZ MAGNETIC FIELDS AND THEIR HARMONICS USING AN ANIMAL LEUKEMIA MODEL.

Bernard N, Alberdi AJ, Tanguy ML, Brugere H, Helissey P, Hubert C, Gendrey N, Guillosson JJ, Nafziger J. *J Radiat Res (Tokyo). 2008; 49: 565-5677.*

To answer the still unresolved question of the possible leukemogenic effects of extremely low frequency magnetic fields (ELF-MFs) and of their harmonics on the incidence of B acute lymphoblastic leukemia in children, the authors used an animal model to explore the possible co-initiating or co-promoting effects of ELF-MFs on the development of leukemia. We used a rat model in which B acute lymphoblastic leukemia is chemically induced by a nitrosurea derivative. From the onset of the chemical treatment, the animals were also exposed to ELF-MFs (100 microT, sinusoidal 50 Hz MFs), with or without harmonics. The experiment was conducted on 280 rats. We compared body weight and survival time, percentage of bone marrow blast cells, cumulative incidence of leukemia and type of leukemia in the unexposed groups and in the groups exposed to 50 Hz MFs, with and without harmonics.

Conclusions: These results showed no significant differences between exposed and unexposed rats for any of these parameters (p > 0.05). Significant changes in the leukemia type obtained after gamma-irradiation of the leukemia model, showed its sensitivity to a physical agent.

Conclusion: These results do not support the hypothesis that ELF-MFs, with or without harmonics, affect the development of B acute lymphoblastic leukemia in children.

5. Leukemia studies

INDOOR RADON AND CHILDHOOD LEUKAEMIA. Raaschou-Nielsen O. *Radiat Prot Dosimetry. 2008; 132: 175-181.*

This paper summarises the epidemiological literature on domestic exposure to radon and risk for childhood leukaemia. The results of 12 ecological studies show a consistent pattern of higher incidence and mortality rates for childhood leukaemia in areas with higher average indoor radon concentrations. Although the results of such studies are useful to generate hypotheses, they must be interpreted with caution, as the data were aggregated and analysed for geographical areas and not for individuals. The seven available case-control studies of childhood leukaemia with measurement of radon concentrations in the residences of cases and controls gave mixed results, however, with some indication of a weak (relative risk < 2) association with acute lymphoblastic leukaemia.

Conclusion: The epidemiological evidence to date suggests that an association between indoor exposure to radon and childhood leukaemia might exist, but is weak. More case-control studies are needed, with sufficient statistical power to detect weak associations and based on designs and methods that minimise misclassification of exposure and provide a high participation rate and low potential selection bias.

INFECTIONS IN EARLY LIFE AND CHILDHOOD LEUKAEMIA RISK: A UK CASE-CONTROL STUDY OF GENERAL PRACTITIONER RECORDS.

Cardwell CR, McKinney PA, Patterson CC, Murray LJ. *Br J Cancer. 2008; 99: 1529-1533.*

The authors investigated infections in early life (diagnosed in general practice) and subsequent risk of childhood leukaemia in the UK General Practice Research Database (GPRD). All children born at GPRD practices and subsequently diagnosed with leukaemia were identified as cases and were individually matched (on year of birth, sex and practice) to up to 20 controls. The final analysis included 162 leukaemia cases and 2215 matched controls. Conditional logistic regression demonstrated no evidence that children with one or more recorded infection in the first year of life had a reduced risk of leukaemia (OR=1.05, 95%CI 0.69, 1.59; P=0.83) or acute lymphoblastic leukaemia (ALL; OR=1.05, 95%CI 0.64-1.74; P=0.84).

Conclusion: This study provides no support for the Greaves hypothesis, which proposes that reduced or delayed exposure to infections in early life increases the risk of childhood ALL.

CHILDHOOD LYMPHOHEMATOPOIETIC CANCER INCIDENCE AND HAZARDOUS AIR POLLUTANTS IN SOUTHEAST TEXAS, 1995-2004. Whitworth KW, Symanski E, Coker AL. *Environ Health Perspect. 2008; 116 : 1576-1580.*

There is increasing interest in the role of air pollutants, including benzene and 1,3-butadiene, in the etiology of childhood cancers. The goal of this study was to assess whether census tracts with the highest benzene or 1,3-butadiene ambient air levels have increased childhood lymphohematopoietic cancer incidence. This ecologic analysis included 977 cases of childhood lymphohematopoietic cancer diagnosed from 1995-2004. The U.S. Environmental Protection Agency's 1999 modeled estimates of benzene and 1,3-butadiene for 886 census

tracts surrounding Houston, Texas were obtained. Poisson regression models were ran by pollutant to explore the associations between pollutant levels and census-tract cancer rates. Models were adjusted for age, sex, race/ethnicity, and community-level socioeconomic status (cSES).

Census tracts with the highest benzene levels had elevated rates of all leukemia [rate ratio (RR) = 1.37; 95% confidence interval (CI), 1.05, 1.78]. This association was higher for acute myeloid leukemia (AML) (RR = 2.02; 95% CI, 1.03-3.96) than for acute lymphocytic leukemia (ALL) (RR = 1.24; 95% CI, 0.92-1.66). Among census tracts with the highest 1,3-butadiene levels, we observed RRs of 1.40 (95% CI, 1.07-1.81), 1.68 (95% CI, 0.84-3.35), and 1.32 (95% CI, 0.98-1.77) for all leukemia, AML, and ALL, respectively were detected No associations between benzene or 1,3-butadiene levels and lymphoma incidence. Results that examined joint exposure to benzene and 1,3-butadiene were similar to those that examined each pollutant separately.

Conclusion: This ecologic analysis suggests an association between childhood leukemia and hazardous air pollution; further research using more sophisticated methodology is warranted.