

Overview of the epidemiologic studies on the health effects of ELF magnetic and electric fields published in the first trimester of 2009.

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1. Reviews

SCIENTIFIC COMMITTEE ON EMERGING AND NEWLY IDENTIFIED HEALTH RISKS SCENIHR: HEALTH EFFECTS OF EXPOSURE TO EMF.

EU Directorate – General for Health & Consumer Protection, 19 January 2009

Extremely low frequency fields (ELF fields)

The few new epidemiological and animal studies that have addressed ELF exposure and cancer do not change the previous assessment that ELF magnetic fields are a possible carcinogen and might contribute to an increase in childhood leukaemia. At present, in vitro studies did not provide a mechanistic explanation of this epidemiological finding.

No new studies support a causal relationship between ELF fields and self-reported symptoms.

New epidemiological studies indicate a possible increase in Alzheimer's disease arising from exposure to ELF. Further epidemiological and laboratory investigations of this observation are needed.

Recent animal studies provided an indication for effects on the nervous system at flux densities from 0.10-1.0 mT. However, there are still inconsistencies in the data, and no definite conclusions can be drawn concerning human health effects.

Very few recent in vitro studies have investigated effects from ELF fields on diseases other than cancer and those available have very little relevance. There is a need for hypothesis-based in vitro studies to examine specific diseases.

It is notable that in vivo and in vitro studies show effects at exposure levels (from 0.10 mT and above) to ELF fields that are considerably higher than the levels encountered in the epidemiological studies (μ T-levels) which showed an association between exposure and diseases such as childhood leukaemia and Alzheimer's disease. This warrants further investigation.

FUTURE NEEDS OF OCCUPATIONAL EPIDEMIOLOGY OF EXTREMELY LOW FREQUENCY ELECTRIC AND MAGNETIC FIELDS: REVIEW AND RECOMMENDATIONS.

Kheifets L, Bowman JD, Checkoway H, Feychting M, Harrington JM, Kavet R, Marsh G, Mezei G, Renew DC, van Wijngaarden E.

Occup Environ Med. 2009; 66 : 72-80.

The occupational epidemiological literature on extremely low frequency electric and magnetic fields (EMF) and health encompasses a large number of studies of varying design and quality that have addressed many health outcomes, including various cancers, cardiovascular disease, depression and suicide, and neurodegenerative diseases, such as Alzheimer disease and amyotrophic lateral sclerosis (ALS). At a 2006 workshop the authors reviewed studies of occupational EMF exposure with an emphasis on methodological weaknesses, and proposed analytical ways to address some of these. They also developed research priorities that they hope will address remaining uncertainties. Broadly speaking, extensive

epidemiological research conducted during the past 20 years on occupational EMF exposure does not indicate strong or consistent associations with cancer or any other health outcomes. Inconsistent results for many of the outcomes may be attributable to numerous shortcomings in the studies, most notably in exposure assessment. There is, however, no obvious correlation between exposure assessment quality and observed associations. Nevertheless, for future research, the highest priorities emerge in both the areas of exposure assessment and investigation of ALS. To better assess exposure, the authors call for the development of a more complete job-exposure matrix that combines job title, work environment and task, and an index of exposure to electric fields, magnetic fields, spark discharge, contact current, and other chemical and physical agents. For ALS, they propose an international collaborative study capable of illuminating a reported association with electrical occupations by disentangling the potential roles of electric shocks, magnetic fields and bias. Such a study will potentially lead to evidence-based measures to protect public health.

DESIGNS AND ANALYSES FOR EXPLORING THE RELATIONSHIP OF MAGNETIC FIELDS TO CHILDHOOD LEUKAEMIA: A PILOT PROJECT FOR THE DANISH NATIONAL BIRTH COHORT.

Greenland S, Kheifets L.

Scand J Public Health. 2009; 37 : 83-92.

Pooled analyses have consistently displayed an association of childhood leukaemia with residential magnetic fields, even after attempting to account for study problems. In light of the serious possibility that the link is indeed causal, a study of possible joint effects (interactions) of magnetic fields and genetic cofactors on childhood leukaemia may be justifiable. Such a study would face serious obstacles of limited numbers for subgroup analysis. To address these obstacles, the authors describe a design and analysis strategy that combines multiphase (multistage) sampling, measurement error modelling, and Bayesian methods for subgroup analysis that incorporate information from earlier pooled analyses. Special attention is given to prior specification, which would be the potentially controversial element. The approach could be pilot tested on data from the Danish National Birth Cohort, but an informative study would require augmenting these data with case-control sampling. Conclusion: The authors conclude that the approach outlined may be of value not only for this topic but also in other studies of effects of rare exposures and genetic factors on rare outcomes.

2. Environmental exposure

A CASE-CONTROL STUDY ON THE ASSOCIATION BETWEEN ENVIRONMENTAL FACTORS AND THE OCCURRENCE OF ACUTE LEUKEMIA AMONG CHILDREN IN KLANG VALLEY, MALAYSIA.

Abdul Rahman HI, Shah SA, Alias H, Ibrahim HM.

Asian Pac J Cancer Prev. 2008; 9: 649-652.

In Malaysia, acute leukemia is the most common cancer among children below the age of 15. A case-control study was here conducted for cases from the Klang Valley, Malaysia, who received treatment at the National University of Malaysia Hospital (HUKM) and Kuala Lumpur General Hospital (GHKL). The main objective was to determine any association with environmental factors.

Case subjects were children aged below 15 years and diagnosed with acute leukemia in HUKM and GHKL between January 1, 2001 and May 30, 2007. Control subjects were children aged below 15 years who were diagnosed with any non-cancerous

acute illnesses in these hospitals. A total of 128 case subjects and 128 control subjects were enrolled in this study. The information was collected using a structured questionnaire and a global positioning system (GPS) device. All factors were analyzed using unmatched logistic regression. The analysis showed that the occurrence of acute leukemia among children was strongly determined by the following factors: family income (odds ratio (OR) 0.19, 95% confidence interval (CI): 0.09-0.42), father with higher social contact (OR 7.61, 95% CI: 3.78-15.4), number of elder siblings (OR 0.36, 95% CI: 0.18-0.77), father who smokes (OR 2.78, 95% CI: 1.49-5.16), and the distance of the house from a power line (OR 2.30, 95% CI: 1.18-4.49). Conclusions: Some socioeconomic, demographic, and environmental factors are strong predictors of the occurrence of acute leukemia among children in Klang Valley, Malaysia. In terms of environmental factors, it is recommended that future housing areas should be developed at least 200 m away from power lines.

RESIDENCE NEAR POWER LINES AND MORTALITY FROM NEURODEGENERATIVE DISEASES: LONGITUDINAL STUDY OF THE SWISS POPULATION.

Huss A, Spoerri A, Egger M, Rössli M; Swiss National Cohort Study.
Am J Epidemiol. 2009; 169: 167-175.

The relation between residential magnetic field exposure from power lines and mortality from neurodegenerative conditions was analyzed among 4.7 million persons of the Swiss National Cohort (linking mortality and census data), covering the period 2000-2005. Cox proportional hazard models were used to analyze the relation of living in the proximity of 220-380 kV power lines and the risk of death from neurodegenerative diseases, with adjustment for a range of potential confounders. Overall, the adjusted hazard ratio for Alzheimer's disease in persons living within 50 m of a 220-380 kV power line was 1.24 (95% confidence interval (CI): 0.80, 1.92) compared with persons who lived at a distance of 600 m or more. There was a dose-response relation with respect to years of residence in the immediate vicinity of power lines and Alzheimer's disease: Persons living at least 5 years within 50 m had an adjusted hazard ratio of 1.51 (95% CI: 0.91, 2.51), increasing to 1.78 (95% CI: 1.07, 2.96) with at least 10 years and to 2.00 (95% CI: 1.21, 3.33) with at least 15 years. The pattern was similar for senile dementia. There was little evidence for an increased risk of amyotrophic lateral sclerosis, Parkinson's disease, or multiple sclerosis.

3. Occupational exposure

A POPULATION-BASED COHORT STUDY OF OCCUPATIONAL EXPOSURE TO MAGNETIC FIELDS AND CARDIOVASCULAR DISEASE MORTALITY.

Cooper AR, Van Wijngaarden E, Fisher SG, Adams MJ, Yost MG, Bowman JD.
Ann Epidemiol. 2009; 19: 42-48.

This cohort study aims to examine cardiovascular disease (CVD) mortality risks among workers in occupations potentially exposed to magnetic fields (MF). Risks for major CVD mortality by potential job-related MF exposure were examined in a sample of U.S. workers from the National Longitudinal Mortality Study using multivariate proportional hazards models. After adjustment for demographic factors, there were no significant excess risks between individuals with medium (0.15 to <0.20 microT), high (0.20 to < 0.30 microT), or very high (\geq 0.30 microT) exposure levels as compared with individuals with background exposure levels of MF (<0.15 microT) for the CVD mortality outcomes. Indirect adjustment for potential confounding by current smoking prevalence did not change the pattern of these results.

Conclusion: This study does not provide evidence for an association between occupational MF exposure and CVD mortality risk.

EXTREMELY LOW FREQUENCY-MAGNETIC FIELDS (ELF-EMF) OCCUPATIONAL EXPOSURE AND NATURAL KILLER ACTIVITY IN PERIPHERAL BLOOD LYMPHOCYTES.

Gobba F, Bargellini A, Scaringi M, Bravo G, Borella P.

Sci Total Environ. 2009; 407: 1218-123.

Extremely Low Frequency-Magnetic Fields (ELF-MF) are possible carcinogens to humans and some data suggest that they can act as promoters or progressors. Since NK cells play a major role in the control of cancer development, an adverse effect on ELF-MF on NK function has been hypothesized. The authors examined NK activity in 52 workers exposed to different levels of ELF-MF in various activities. Individual exposure was monitored during 3 complete work-shifts using personal dosimeters. Environmental exposure was also monitored. ELF-MF levels in the workers were expressed as Time-Weighted Average (TWA) values. NK activity was measured in peripheral blood lymphocytes (PBL). In the whole group the median occupational TWA was 0.21 microT. According to the TWA levels, workers were classified as low exposed (26 subjects, TWA \leq 0.2 microT) and higher exposed workers (26 subjects; TWA $>$ 0.2 microT). In higher exposed workers, a trend to reduce NK activity compared to low exposed was observed, but the difference was not significant. Then the authors selected a subgroup of highest exposed workers (12 subjects; TWA $>$ 1 microT); no difference was observed between low and highest exposed subjects in the main personal variables. Considering both E:T ratios from 12:1 to 50:1 and Lytic Units, a significant reduction in NK activity was observed in the highest exposed workers compared to the low exposed. Multivariate analysis showed a significant negative correlation between exposure and LU, while no correlation was evidenced with other personal characteristics. ELF-MF are considered possible carcinogens, and existing data suggest that they can act as promoters.

Conclusion: Due to the role of NK activity in host defence against cancer, the results obtained in this study in workers exposed to ELF-MF levels exceeding 1 microT are in agreement with this hypothesis, and support the need for further investigation in this field.

EFFECT OF EXTREMELY LOW FREQUENCY MAGNETIC FIELD ON ANTIOXIDANT ACTIVITY IN PLASMA AND RED BLOOD CELLS IN SPOT WELDERS.

Sharifian A, Gharavi M, Pasalar P, Aminian O.

Int Arch Occup Environ Health. 2009; 82: 259-266.

The purpose of this study was to determine a possible relation between exposure to extremely low frequency magnetic field (ELF-MF) and the human antioxidant activity. The total serum antioxidant status (TAS), red blood cells (RBCs) glutathione peroxidase (GPX) and superoxide dismutase (SOD) were measured in 46 spot welders who were occupationally exposed to ELF-MF (magnetic field strength = 8.8-84 microTesla (microT), frequency = 50 Hertz (Hz) and electric field strength = 20-133 V/m). The results were compared with a nonexposed ELF-MF control group. The correlation between magnetic field strength and antioxidant activity in RBCs and plasma was then assessed. No significant differences in TAS levels were observed (P value = 0.065). However, in RBCs of exposed group, a significant decrease in SOD and GPX activities was observed (P value = 0.001 and 0.003, respectively). This decrease was measured as 22 and 12.3%, respectively. Furthermore, a significant negative correlation between SOD/GPX activities and

magnetic field intensity was observed (coefficients of SOD: -0.625, significance: 0.0001 and coefficients of GPX: -0.348, significance: 0.018).

Conclusion: The results of this study indicate that ELF-MF could influence the RBC antioxidant activity and might act as an oxidative stressor. Intracellular antioxidant enzymes such as SOD and GPX were found to be the most important markers involving in this process. The influence of magnetic field on the antioxidant activity of RBCs might occur even at the recommended levels of exposure.

4. Human experimental research

ASSESSMENT OF GENETIC DAMAGE IN PERIPHERAL BLOOD OF HUMAN VOLUNTEERS EXPOSED (WHOLE-BODY) TO A 200 μ T, 60 Hz MAGNETIC FIELD.

Albert GC, McNamee JP, Marro L, Bellier PV, Prato FS, Thomas AW.

Int J Radiat Biol. 2009; 85: 144-152.

In this study, 10 male and 10 female healthy human volunteers received a 4 h whole-body exposure to a 200 μ T, 60 Hz magnetic field. In addition, five males and five females were treated in a similar fashion, but were exposed to sham conditions. For each subject, a blood sample was obtained prior to the exposure period and aliquots were used as negative- (pre-exposure) and positive- [1.5 Gray (Gy) (60)Cobalt ((60)Co) gamma-irradiation] controls. At the end of the 4 h exposure period, a second blood sample was obtained. The extent of DNA damage was assessed in peripheral human blood leukocytes from all samples using the alkaline comet assay. To detect possible clastogenic effects, the incidence of micronuclei was assessed in phytohemagglutinin (PHA)-stimulated lymphocytes using the cytokinesis-block micronucleus assay. There was no evidence of either increased DNA damage, as indicated by the alkaline comet assay, or increased incidence of micronuclei (MN) in the magnetic field exposed group. However, an in vitro exposure of 1.5 Gy gamma-irradiation caused a significant increase in both DNA damage and MN induction.

Conclusions: This study found no evidence that an acute, whole-body exposure to a 200 μ T, 60 Hz magnetic field for 4 hours could cause DNA damage in human blood.

DOES EXPOSURE TO EXTREMELY LOW FREQUENCY MAGNETIC FIELDS PRODUCE FUNCTIONAL CHANGES IN HUMAN BRAIN?

Capone F, Dileone M, Profice P, Pilato F, Musumeci G, Minicuci G, Ranieri F, Cadossi R, Setti S, Tonali PA, Di Lazzaro V.

J Neural Transm. 2009; 116: 257-265.

Using transcranial brain stimulation, the authors studied noninvasively the effect of ELF-MF applied in pulsed mode (PEMFs) on several measures of cortical excitability in 22 healthy volunteers, in 14 of the subjects they also evaluated the effects of sham field exposure. After 45 min of PEMF exposure, intracortical facilitation produced by paired pulse brain stimulation was significantly enhanced with an increase of about 20%, while other parameters of cortical excitability remained unchanged. Sham field exposure produced no effects. The increase in paired-pulse facilitation, a physiological parameter related to cortical glutamatergic activity, suggests that PEMFs exposure may produce an enhancement in cortical excitatory neurotransmission.

Conclusion: This study suggests that PEMFs may produce functional changes in human brain.

5. Exposure assessment

EXPOSURE ASSESSMENT AND OTHER CHALLENGES IN NON-IONIZING RADIATION STUDIES OF CHILDHOOD LEUKAEMIA.

Kheifets L, Oksuzyan S.

Radiat Prot Dosimetry. 2008;132: 139-147.

Studies of electromagnetic fields (EMF) and the development of childhood leukaemia face unique difficulties. EMF are imperceptible, ubiquitous, have multiple sources, and can vary greatly over time and distances. Childhood leukaemia and high average exposures to magnetic fields are both quite rare. Thus, a major challenge in EMF epidemiology is the small number of highly exposed cases and the necessity for retrospective assessment of exposure. Only studies designed to minimize bias while maximizing our ability to detect an association, should one exist, would have a potential to contribute to our understanding. New approaches are needed; the most promising in the extremely low-frequency range involves a study of a highly exposed cohort of children who have lived in apartments next to built-in transformers or electrical equipment rooms. Another promising avenue is an investigation of possible joint effects of environmental exposures and genetic co-factors. An exposure assessment methodology for residential radiofrequency fields is still in its infancy. Rapid changes in technology and exponential increases in its use make exposure assessment more difficult and urgent.

EXPOSURE OF WORKERS TO ELECTROMAGNETIC FIELDS. A REVIEW OF OPEN QUESTIONS ON EXPOSURE ASSESSMENT TECHNIQUES.

Hansson Mild K, Alanko T, Decat G, Falsaperla R, Gryz K, Hietanen M, Karpowicz J, Rossi P, Sandström M.

Int J Occup Saf Ergon. 2009;15: 3-33.

European Directive 2004/40/EC on occupational exposure to electromagnetic fields (EMF), based on the guidelines of the International Commission on Non-Ionizing Radiation Protection, was to be implemented in the Member States of the European Union by 2008. Because of some unexpected problems the deadline was postponed until 2012. This paper reviews some of the problems identified and presents some suggestions for possible solutions based on the authors' experience in assessing occupational exposure to EMF. Among the topics discussed are movement in static magnetic fields, ways to time average extreme low frequency signals, the difference between emission and exposure standards, and ways of dealing with those issues.

6. Leukaemia studies

HOUSEHOLD EXPOSURE TO PAINT AND PETROLEUM SOLVENTS, CHROMOSOMAL TRANSLOCATIONS, AND THE RISK OF CHILDHOOD LEUKEMIA.

Scélo G, Metayer C, Zhang L, Wiemels JL, Aldrich MC, Selvin S, Month S, Smith MT, Buffler PA.

Environ Health Perspect. 2009 ;117: 133-139.

In this case-control study, the authors examined whether the use of paint and petroleum solvents at home before birth and in early childhood influenced the risk of leukemia in children. They based their analyses on 550 cases of acute lymphoblastic leukemia (ALL), 100 cases of acute myeloid leukemia (AML), and one or two controls per case individually matched for sex, age, Hispanic status, and race. We conducted further analyses by cytogenetic subtype. Conditional logistic regression techniques were used to adjust for income. ALL risk was significantly associated with paint exposure [odds ratio (OR) = 1.65; 95% confidence interval

(CI), 1.26-2.15], with a higher risk observed when paint was used postnatally, by a person other than the mother, or frequently. The association was restricted to leukemia with translocations between chromosomes 12 and 21 (OR = 4.16; 95% CI, 1.66-10.4). No significant association between solvent use and ALL risk overall (OR = 1.15; 95% CI, 0.87-1.51) or for various cytogenetic subtypes was found, but a significant association in the 2.0- to 5.9-year age group (OR = 1.55; 95% CI, 1.07-2.25) was observed. In contrast, a significant increased risk for AML was associated with solvent (OR = 2.54; 95% CI, 1.19-5.42) but not with paint exposure (OR = 0.64; 95% CI, 0.32-1.25).

Conclusions: The association of ALL risk with paint exposure was strong, consistent with a causal relationship, but further studies are needed to confirm the association of ALL and AML risk with solvent exposure.

CHILDHOOD LEUKEMIA AND TRAFFIC AIR POLLUTION IN TAIWAN: PETROL STATION DENSITY AS AN INDICATOR.

Weng HH, Tsai SS, Chiu HF, Wu TN, Yang CY.

J Toxicol Environ Health A. 2009;72: 83-87.

To investigate the relationship between traffic air pollution exposure and development of childhood leukemia (14 yr of age or younger), a matched case-control study was conducted using childhood deaths that occurred in Taiwan from 1996 through 2006. Data on all eligible childhood leukemia deaths were obtained from the Bureau of Vital Statistics of the Taiwan Provincial Department of Health. The control group consisted of children who died from causes other than neoplasms or diseases that were not associated with respiratory complications. The controls were pair matched to the cancer cases by gender, year of birth, and year of death. Each matched control was selected randomly from the set of possible controls for each case. Data on the number of petrol stations in study municipalities were collected from the two major petroleum supply companies, Chinese Petroleum Corporation (CPC) and Formosa Petrochemical Corporation (FPCC). The petrol station density (per square kilometer) (PSD) for study municipalities was used as an indicator of a subject's exposure to benzene and other hydrocarbons present in evaporative losses of petrol or to air emissions from motor vehicles. The subjects were divided into tertiles according to PSD in their residential municipality. The results showed that there was a significant exposure-response relationship between PSD and the risk of leukemia development in young children after controlling for possible confounders.

Conclusions: The findings of this study warrant further investigation of the role of traffic air pollution exposure in the etiology of childhood leukemia.

CURED MEAT, VEGETABLES, AND BEAN-CURD FOODS IN RELATION TO CHILDHOOD ACUTE LEUKEMIA RISK: A POPULATION BASED CASE-CONTROL STUDY.

Liu CY, Hsu YH, Wu MT, Pan PC, Ho CK, Su L, Xu X, Li Y, Christiani DC; Kaohsiung Leukemia Research Group.

BMC Cancer. 2009; 9: 15.

Consumption of cured/smoked meat and fish leads to the formation of carcinogenic N-nitroso compounds in the acidic stomach. This study investigated whether consumed cured/smoked meat and fish, the major dietary resource for exposure to nitrites and nitrosamines, is associated with childhood acute leukemia. A population-based case-control study of Han Chinese between 2 and 20 years old was conducted in southern Taiwan. 145 acute leukemia cases and 370 age- and sex-matched controls were recruited between 1997 and 2005. Dietary data were obtained from a questionnaire. Multiple logistic regression models were used in data analyses. Consumption of

cured/smoked meat and fish more than once a week was associated with an increased risk of acute leukemia (OR = 1.74; 95% CI: 1.15-2.64). Conversely, higher intake of vegetables (OR = 0.55; 95% CI: 0.37-0.83) and bean-curd (OR = 0.55; 95% CI: 0.34-0.89) was associated with a reduced risk. No statistically significant association was observed between leukemia risk and the consumption of pickled vegetables, fruits, and tea.

Conclusions: Dietary exposure to cured/smoked meat and fish may be associated with leukemia risk through their contents of nitrites and nitrosamines among children and adolescents, and intake of vegetables and soy-bean curd may be protective.

HOW THE EFFECT OF MATERNAL AGE ON THE RISK OF CHILDHOOD LEUKEMIA CHANGED OVER TIME IN SWEDEN, 1960-2004.

Maule MM, Vizzini L, Czene K, Akre O, Richiardi L.

Environ Health Perspect. 2009; 117: 299-302.

Previous studies on the association between maternal age and risk of childhood leukemia found inconsistent results. The authors aimed to assess whether there is an association between maternal age and risk of childhood leukemia and whether such an association is modified by maternal year of birth. By linking nationwide Swedish registers, they analyzed leukemia incidence among all children between 1 and 5 years of age born between 1960 and 1999. They estimated incidence time trends by child year of birth (overall and stratified by maternal age) and incidence rate ratios (RRs) for maternal age groups stratified by maternal birth cohort. The interaction between maternal age and child year of birth was tested through the likelihood ratio test between nested Poisson regression models. 1,562 leukemia cases were observed. The overall annual percent change (APC) was 1.00 [95% confidence interval (CI), 0.51 to 1.49]. Stratifying by maternal age classes, APCs decreased from 1.66 (0.68 to 2.65) for mothers \leq 24 years to 0.23 (-0.93 to 1.40) for mothers \geq 35 years at delivery. RRs for children born to the oldest with respect to the youngest mothers were 2.42 (1.31 to 4.67), 1.68 (1.00 to 2.72), 1.34 (0.87 to 2.01), and 0.87 (0.46-1.54) for mothers born in 1930-1934, 1940-1944, 1950-1954, and 1960-1964, respectively.

Conclusions: Childhood leukemia risk increased with maternal age for mothers born in the past, whereas maternal age had no effect on this risk for mothers born more recently. This finding may explain the inconsistency of previous studies and suggests that leukemia risk may be related to an environmental factor to which women's exposure has changed over time.