

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

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1. Occupational exposure

OCCUPATIONAL RISK FACTORS FOR NON-HODGKIN'S LYMPHOMA: A POPULATION-BASED CASE-CONTROL STUDY IN NORTHERN GERMANY.

Richardson DB, Terschüren C, Hoffmann W.

Am J Ind Med. 2008; 51 : 258-268.

A population-based case-control study was conducted in which incident cases of high-malignancy NHL (NHL(high)), low-malignancy NHL (NHL(low)), and chronic lymphocytic leukemia (CLL) were ascertained during the period 1986-1998 among men and women aged 15-75 years residing in six German counties; controls were drawn from population registries. Occupational histories were collected and agent-specific exposures were estimated via a job-exposure-matrix. Odds ratios were estimated by conditional logistic regression. RESULTS: A total of 858 cases were included in these analyses. Agricultural workers [odds ratio (OR) = 2.67, 95% confidence interval (CI): 0.99, 7.21] and farmers (OR = 1.98, 95% CI: 0.98, 3.98] had elevated risk of NHL(high). Risk of NHL(low) was elevated among agricultural workers (OR = 2.46, 95% CI: 1.17, 5.16), and among blacksmiths, toolmakers, and machine tool operators (OR = 3.12, 95% CI: 1.31, 7.47). Workers in sales and construction had elevated risks of NHL(high) and NHL(low). Exposure to arsenic compounds, chlorophenols, diesel fuel, herbicides, nitrites/nitrates/nitrosamines, and organic dusts were associated with NHL(high) and NHL(low), while exhibiting little association with CLL. A positive monotonic trend in NHL(low) risk across tertiles of cumulative diesel fuel exposure was observed [P-value for test of linear trend (P) = 0.03].

Workers who were ever employed in jobs judged to involve potential exposure to electromagnetic fields were at a lower risk of NHL(high) (OR = 0.59) and there was no association with NHL(low) (OR = 1.04) and CLL (OR = 1.07).

Conclusions: These findings provide insights into several potential occupational risk factors for NHL and suggest some specific occupational agents for further investigation. Electromagnetic fields seems to be no risk factor.

POPULATION-BASED RESEARCH ON OCCUPATIONAL AND ENVIRONMENTAL FACTORS FOR LEUKEMIA AND NON-HODGKIN'S LYMPHOMA: THE NORTHERN GERMANY LEUKEMIA AND LYMPHOMA STUDY (NLL).

Hoffmann W, Terschueren C, Heimpel H, Feller A, Butte W, Hostrup O, Richardson D, Greiser E.

Am J Ind Med. 2008; 51: 246-257.

The Northern Germany Leukemia and Lymphoma Study (NLL) is a population-based study designed to provide a quantitative basis for investigations into occupational and environmental risk factors for leukemia and lymphoma.

All incident cases of leukemia and lymphoma diagnosed between 1/1/1986 and 12/31/1998 in six counties in Northern Germany were actively ascertained. Controls

were selected from population registries. Use of pesticides, sources of food supply, time spent at home and work, medical and family history were assessed via face-to-face interview. This self-reported information was used in conjunction with direct environmental measurements of pesticides in household dust and electromagnetic fields (EMFs). In addition, geographical information system (GIS) data were used to derive estimates of environmental exposure to pesticides, EMFs associated with transmission lines, and ionizing radiation from routine nuclear power reactor operations. Occupational exposure assessment was based on lifetime work history. For each job, information on branch of industry, company, job description, and duration of employment were ascertained.

Fourteen hundred thirty cases and 3041 controls were recruited. Lifetime residential and workplace histories totaled 49,628 addresses. Occupational exposure to pesticides was reported by 15% of the male participants (women: 16%). Four percent of the men (women: 8%) were occupationally exposed to ionizing radiation for ≥ 1 year over their lifetime. Sixty four percent of the participants had lived in the vicinity (20 km) of a nuclear power plant in operation.

GIS-based exposure to environmental EMF due to high voltage power lines within 50m distance to residences or work places of the study participants was less relevant. The majority of the respective exposures concerned 110 KV high voltage power line. Physical measurements for ELF-EMF were performed in 1935 towns. 3,2% of all 2-hour measurements revealed values above 0,2 μ T. The highest values for 50 Hz magnetic fields were found most often in private work rooms with a PC switched on and in kitchens with electrical appliances turned off.

Conclusions: The NLL illustrates the successful application of innovative methods to simultaneously assess occupational and environmental risk factors for leukemia and lymphoma including radiological hazards and pesticides.

2. Exposure assessment

CURRENT DENSITIES IN A PREGNANT WOMAN MODEL INDUCED BY SIMULTANEOUS ELF ELECTRIC AND MAGNETIC FIELD EXPOSURE.

Cech R, Leitgeb N, Pediaditis M.

Phys Med Biol. 2008; 7:177-186.

The pregnant woman model SILVY was studied to ascertain to what extent the electric current densities induced by 50 Hz homogeneous electric and magnetic fields increase in the case of simultaneous exposure. By vectorial addition of the electric current densities, it could be shown that under worst case conditions the basic restrictions recommended by ICNIRP (International Commission on Non-Ionizing Radiation Protection) guidelines are exceeded within the central nervous system (CNS) of the mother, whereas in sole field exposure they are not. However, within the foetus the induced current densities do not comply with basic restrictions, either from single reference-level electric fields or from simultaneous exposure to electric and magnetic fields. Basic limits were considerably exceeded.

DOSIMETRIC ASSESSMENT OF SIMULTANEOUS EXPOSURE TO ELF ELECTRIC AND MAGNETIC FIELDS.

Leitgeb N, Cech R.

IEEE Trans Biomed Eng. 2008; 55: 671-674.

In the low-frequency range, both electric and magnetic fields interact with biological tissue by inducing intracorporal electric current densities, although ruled by different physical laws and, hence, with different intracorporal orientation and pathways. Presently, standards require a separate assessment of electric and magnetic fields even in the case of simultaneous exposure and, hence, ignore the superposition of intracorporal current densities. Numerical simulations with the Visible Man model show that this can lead to underestimating current densities in the central nervous system (CNS) by up to 29%. While the superposed electric current densities in the CNS still meet the basic restrictions, the situation changes if a fetus with its own CNS requires the same level of protection. When the compliance volume is extended to the trunk, the reference-level electric-field exposure exceeds the basic restrictions by 38%.

Conclusion: Depending on the kind of summation of the vectorial contributions, simultaneous exposure to the 50 Hz-5 kV/m electric field and 100-microT magnetic field may lead to a 2.1-fold to 2.6-fold excess of the basic restriction. While this does not prove noncompliance, it indicates that fetal CNS exposure modeling is needed for clarification.

ELF-MAGNETIC FLUX DENSITIES MEASURED IN A CITY ENVIRONMENT IN SUMMER AND WINTER.

Straume A, Johnsson A, Oftedal G.

Bioelectromagnetics. 2008; 29: 20-28.

Epidemiological studies have indicated a connection between extremely low frequency magnetic flux densities above 0.4 microT (time weighted average) and childhood leukemia risks. This conclusion is based mainly on indoor exposure measurements. The authors therefore regarded it important to map outdoor magnetic flux densities in public areas in Trondheim, Norway. Because of seasonal power consumption variations, the fields were measured during both summer and winter. Magnetic flux density was mapped 1.0 m above the ground along 17 km of pavements in downtown Trondheim. The spectrum was measured at some spots and the magnetic flux density emanated mainly from the power frequency of 50 Hz. In summer less than 4% of the streets showed values exceeding 0.4 microT, increasing to 29% and 34% on cold and on snowy winter days, respectively. The average levels were 0.13 microT (summer), 0.85 microT (winter, cold), and 0.90 microT (winter, snow), with the highest recorded value of 37 microT. High spot measurements were usually encountered above underground transformer substations. In winter electric heating of pavements also gave rise to relatively high flux densities.

Conclusion: There was no indication that the ICNIRP basic restriction was exceeded. It would be of interest to map the flux density situation in other cities and towns with a cold climate.

MAGNETIC EMISSIONS OF ELECTRIC APPLIANCES.

Leitgeb N, Cech R, Schröttner J, Lehofer P, Schmidpeter U, Rampetsreiter M.

Int J Hyg Environ Health. 2008; 211: 69-73.

More than 1000 electric appliances have been investigated regarding their emission of magnetic fields. It was found that complex frequency spectra are common and single

frequency emissions are rare. Since exposure assessment requires frequency-weighted sums, root-mean-square values are not appropriate for comparison with exposure reference levels. It could be shown that they may underestimate emissions up to two orders of magnitude. Analysis of device groups showed a wide span of emission values of up to two orders of magnitude with only weak associations to power consumption. This demonstrates that there is a considerable potential to reduce fields without loss of performance. Exposure to magnetic fields of electric appliances are not negligible in daily life.

Conclusion: Many devices considerably exceeded permitted reference levels and would require a closer analysis to demonstrate conformity with basic limits.

3. Leukemia studies

CHILDHOOD LEUKAEMIA AND POPULATION MOVEMENTS IN FRANCE, 1990-2003.

Bellec S, Baccaïni B, Goubin A, Rudant J, Ripert M, Hémon D, Clavel J.

Br J Cancer. 2008; 98: 225-231.

In a national study, the authors investigated the incidence of childhood leukaemia (CL) over a 14-year period in France in relation to several measures based on the proportion of individuals who changed address between the last two national censuses. A positive association was found with the proportion of migrants who came from a distant place. The further the migrants came, the higher was the incidence of leukaemia, particularly among children aged 0-4 years in 'isolated' communes at the time of diagnosis (RR=1.4, 95% CI: 1.1,1.8 in the highest category of migration distance). Although the role of the population density was less obvious, a more marked association was found above a certain threshold. No association with the proportion of commuters was observed.

POPULATION MIXING, SOCIOECONOMIC STATUS AND INCIDENCE OF CHILDHOOD ACUTE LYMPHOBLASTIC LEUKAEMIA IN ENGLAND AND WALES: ANALYSIS BY CENSUS WARD.

Stiller CA, Kroll ME, Boyle PJ, Feng Z.

Br J Cancer. 2008; 98: 1006-1011.

In this population-based study of acute lymphoblastic leukaemia (ALL) diagnosed among children aged under 15 years in England and Wales during 1986-1995, we analysed incidence at census ward level in relation to a range of variables from the 1991 census, which could be relevant to theories of infectious aetiology. 'Population-mixing' measures, used as surrogates for quantity and diversity of infections entering the community, were calculated from census data on the origins and destinations of migrants in the year before the census. Incidence at ages 1-4 years tended independently to be higher in rural wards, to increase with the diversity of origin wards from which in-migrants had moved during the year before the census, and to be lower in the most deprived areas as categorised by the Carstairs index. This last association was much weaker when urban/rural status and in-migrants' diversity were allowed for. There was no evidence of association with population mixing or deprivation for ALL diagnosed at ages 0 or 5-14 years. The apparent specificity to the young childhood age group suggests that these associations are particularly marked for precursor B-cell ALL, with the disease more likely to occur when delayed exposure to infection leads to increased immunological stress, as predicted by Greaves. The association with diversity of incomers,

especially in rural areas, is also consistent with the higher incidence of leukaemia predicted by Kinlen, where population mixing results in below average herd immunity to an infectious agent.

RISK OF CHILDHOOD LEUKEMIA ASSOCIATED WITH VACCINATION, INFECTION, AND MEDICATION USE IN CHILDHOOD: THE CROSS-CANADA CHILDHOOD LEUKEMIA STUDY.

MacArthur AC, McBride ML, Spinelli JJ, Tamaro S, Gallagher RP, Theriault GP.

Am J Epidemiol. 2008; 167: 598-606.

Current hypotheses consonant with the peak in leukemia incidence in early childhood point to an infectious etiology. The authors examined the effect of postnatal exposures predicted to affect early immune functioning, including childhood vaccinations, illness, medication use, and breastfeeding patterns. Children 0-15 years of age diagnosed with leukemia from 1990 to 1994 and resident within principal cities across Canada were eligible for inclusion. Through pediatric oncology centers and population-based cancer registries, 399 cases were ascertained at the time of diagnosis. For each participating case, an age-, gender-, and area-matched control was randomly selected from government health insurance rolls. Risk factor information was obtained through personal interviews with each child's parents or guardians. Conditional logistic regression was used to calculate odds ratios, with adjustment for potential confounders. Use of immunosuppressant medication by the index child led to a deficit of risk (odds ratio = 0.37, 95% confidence interval: 0.16, 0.84), while vitamin intake was positively associated with leukemia (odds ratio = 1.66, 95% confidence interval: 1.18, 2.33). Breastfeeding for more than 6 months was also protective ($p < 0.05$). Results persisted for cases diagnosed with acute lymphoblastic leukemia and for children diagnosed at 1-5 years of age. These findings suggest a role for early immunologic challenge in the expression of childhood leukemia.

HIGH BIRTH WEIGHT AS AN IMPORTANT RISK FACTOR FOR INFANT LEUKEMIA.

Koifman S, Pombo-de-Oliveira MS; Brazilian Collaborative Study Group of Infant Acute Leukemia.

Br J Cancer. 2008 Feb 12;98(3):664-667.

In this paper, the authors compared the birth weight distribution among 201 infant leukaemia (IL) cases with that of 440 noncancer controls enrolled in Brazil in 1999-2005. Compared with the general population and the stratum 2500-2999 g as reference, IL cases weighing 3000-3999 g presented an odds ratio (OR) of 1.68 (95% CI: 1.03-2.76), and those of 4000 g or more, an OR of 2.28 (95% CI: 1.08-4.75), $P \text{ trend} < 0.01$. Using hospital-based controls, the OR for 4000 g or more, compared to 2500-2999 g, was 1.30 (95% CI: 1.02-1.43) after adjusting for confounders (gender, income, maternal age, pesticide and hormonal exposure during pregnancy). The results suggest that high birth weight is associated with increased risk of IL.

CHILDHOOD LEUKEMIA DEVELOPMENT AND CORRELATION WITH TRAFFIC AIR POLLUTION IN TAIWAN USING NITROGEN DIOXIDE AS AN AIR POLLUTANT MARKER.

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

J Toxicol Environ Health A. 2008; 71: 434-438.

To investigate the relationship between traffic air pollution and development of childhood leukemia (14 yr of age or younger), studies were conducted on a matched cancer case-control cohort using childhood deaths that occurred in Taiwan

from 1995 through 2005. 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 from diseases that were not associated with respiratory complications. The controls were pair matched to the 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. Air quality data for recorded concentrations of nitrogen dioxide (NO₂) from study municipalities for 1995-2005 were obtained as an indicator of a subject's exposure to air emissions from motor vehicles. The subjects were divided into tertiles according to the levels of NO₂ in their residential municipality. The results showed that there was a significant exposure-response relationship between exposure to traffic exhaust pollutants and the risk of leukemia among young children after controlling for possible confounders. The findings of this study warrant further investigation of the role of traffic air pollution in the etiology of childhood leukemia.

ASSOCIATION OF CHILDHOOD LEUKEMIA WITH RESIDENTIAL EXPOSURE TO PETROCHEMICAL AIR POLLUTION IN TAIWAN.

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

Inhal Toxicol. 2008; 20: 31-36.

To investigate the relationship between petrochemical air pollution and childhood leukemia (19 yr of age or younger), the authors conducted a matched case-control study using childhood deaths that occurred in Taiwan from 1995 through 2005. 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 problems. The controls were pair matched to the cases by sex, year of birth, and year of death. Each matched control was selected randomly from the set of possible controls for each case. The proportion of a municipality's total population employed in the petrochemical industry in a municipality was used as an indicator of a resident's exposure to air emissions from the petrochemical industry. The subjects were divided into three levels (< or =25th percentile; 25th-75th percentile; > 75th percentile) according to the levels of the index just described. After controlling for possible confounders, results showed that children who lived in the group of municipalities characterized by the highest levels of petrochemical air pollution had a statistically significant higher risk of developing leukemia than the group that lived in municipalities with the lowest petrochemical air pollution levels. The results of this study shed important light on the relationship between the Taiwan petrochemical industry and human health risks.

RISK OF CHILDHOOD LEUKEMIA ASSOCIATED WITH PARENTAL SMOKING AND ALCOHOL CONSUMPTION PRIOR TO CONCEPTION AND DURING PREGNANCY: THE CROSS-CANADA CHILDHOOD LEUKEMIA STUDY.

Macarthur AC, McBride ML, Spinelli JJ, Tamaro S, Gallagher RP, Theriault G.

Cancer Causes Control. 2008 ;19: 283-295.

As part of a larger case-control study, the authors evaluated risk of childhood leukemia relative to parental self-reported smoking and alcohol consumption. Children 0-14 years of age diagnosed with leukemia between 1990 and 1994 were ascertained through population-based sources at the time of diagnosis. For each participating case, an age, gender, and area-matched control was randomly selected from provincial government health insurance rolls. Risk factor information

was obtained through personal interviews with each child's parents. Conditional logistic regression models were used to examine risk of leukemia associated with parental smoking and drinking.

Maternal alcohol consumption prior to conception (OR = 1.37, 95% CI, 0.99-1.90) and during pregnancy (OR = 1.39, 95% CI, 1.01-1.93) was associated with an excess risk of childhood leukemia, with a positive dose-response trend for increasing weekly consumption ($p < 0.05$). Similar results were observed for children diagnosed with acute lymphoblastic leukemia (ALL). Odds ratios for maternal cigarette smoking before and during pregnancy were consistently elevated above one, but not statistically significant. No relationship was observed with paternal drinking or smoking in the perinatal period.

Conclusions: This study suggests that maternal alcohol drinking before or during pregnancy may contribute to an increased risk of childhood leukemia.

FATHER'S OCCUPATIONAL EXPOSURE TO CARCINOGENIC AGENTS AND CHILDHOOD ACUTE LEUKEMIA: A NEW METHOD TO ASSESS EXPOSURE (A CASE-CONTROL STUDY).

Perez-Saldivar ML, Ortega-Alvarez MC, Fajardo-Gutierrez A, Bernaldez-Rios R, Del Campo-Martinez Mde L, Medina-Sanson A, Palomo-Colli MA, Paredes-Aguilera R, Martínez-Avalos A, Borja-Aburto VH, Rodríguez-Rivera Mde J, Vargas-García VM, Zarco-Contreras J, Flores-Lujano J, Mejía-Arangure JM.
BMC Cancer. 2008; 14; 8:7.

Medical research has not been able to establish whether a father's occupational exposures are associated with the development of acute leukemia (AL) in their offspring. The studies conducted have weaknesses that have generated a misclassification of such exposure. Occupations and exposures to substances associated with childhood cancer are not very frequently encountered in the general population; thus, the reported risks are both inconsistent and inaccurate. In this study, to assess exposure the authors used a new method, an exposure index, which took into consideration the industrial branch, specific position, use of protective equipment, substances at work, degree of contact with such substances, and time of exposure. This index allowed to obtain a grade, which permitted the identification of individuals according to their level of exposure to known or potentially carcinogenic agents that are not necessarily specifically identified as risk factors for leukemia. The aim of this study was to determine the association between a father's occupational exposure to carcinogenic agents and the presence of AL in their offspring.

From 1999 to 2000, a case-control study was performed with 193 children who reside in Mexico City and had been diagnosed with AL. The initial sample-size calculation was 150 children per group, assessed with an expected odds ratio (OR) of three and a minimum exposure frequency of 15.8%. These children were matched by age, sex, and institution with 193 pediatric surgical patients at secondary-care hospitals. A questionnaire was used to determine each child's background and the characteristics of the father's occupation(s). In order to determine the level of exposure to carcinogenic agents, a previously validated exposure index (occupational exposure index, OEI) was used. The consistency and validity of the index were assessed by a questionnaire comparison, the sensory recognition of the work area, and an expert's opinion.

The adjusted ORs and 95% confidence intervals (CI) were 1.69 (0.98, 2.92) during the preconception period; 1.98 (1.13, 3.45) during the index pregnancy; 2.11 (1.17,

3.78) during breastfeeding period; 2.17 (1.28, 3.66) after birth; and 2.06 (1.24, 3.42) for global exposure.

Conclusion: This is the first study in which an OEI was used to assess a father's occupational exposure to carcinogenic agents as a risk factor for the development of childhood AL in his offspring. From these results, the authors conclude that children whose fathers have been exposed to a high level of carcinogenic agents seem to have a greater risk of developing acute leukemia. However, confounding factors cannot be disregarded due to an incomplete control for confounding.

**DNA REPAIR GENE XPD POLYMORPHISMS AND CANCER RISK: A META-ANALYSIS
BASED ON 56 CASE-CONTROL STUDIES.**

Wang F, Chang D, Hu FL, Sui H, Han B, Li DD, Zhao YS.
Cancer Epidemiol Biomarkers Prev. 2008;17: 507-517.

Genetic variations in the XPD gene may increase cancer susceptibility by affecting the capacity for DNA repair. Several studies have investigated this possibility; however, the conclusions remain controversial. Therefore, the authors did a systematic review and executed a meta-analysis to explore the association. From 56 studies, a total of 61 comparisons included 25,932 cases and 27,733 controls concerning the Lys(751)Gln polymorphism; 35 comparisons included 16,781 cases and 18,879 controls in the case of Asp(312)Asn were reviewed. In this analysis, small associations of the XPD Lys(751)Gln polymorphism with cancer risk for esophageal cancer [for Lys/Gln versus Lys/Lys: odds ratio (OR), 1.34; 95% confidence interval (95% CI), 1.10-1.64; for Gln/Gln versus Lys/Lys: OR, 1.61; 95% CI, 1.16-2.25] and acute lymphoblastic leukemia (for Gln/Gln versus Lys/Lys: OR, 1.83; 95% CI, 1.21-2.75) are revealed. Overall, individuals with the Gln/Gln genotype have a small cancer risk compared with Lys/Lys genotype for the reviewed cancer in total (OR, 1.10; 95% CI, 1.03-1.16). Subtle but significant cancer risk was observed for the XPD Asp(312)Asn polymorphism in bladder cancer (for Asp/Asn versus Asp/Asp: OR, 1.24; 95% CI, 1.06-1.46). No significant associations were found for other cancers separately and all the reviewed cancer in total assessed for the Asp(312)Asn polymorphism.

Conclusion: This study suggests that XPD is a candidate gene for cancer susceptibility regardless of environmental factors.