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1. <u>Reviews</u>

EXTREMELY LOW FREQUENCY ELECTRIC FIELDS AND CANCER: ASSESSING THE EVIDENCE.

Kheifets L, Renew D, Sias G, Swanson J. *Bioelectromagnetics*. 2010; 31: 89-101.

Much of the research and reviews on extremely low frequency (ELF) electric and magnetic fields (EMFs) have focused on magnetic rather than electric fields. Some have considered such focus to be inappropriate and have argued that electric fields should be part of both epidemiologic and laboratory work. This paper fills the gap by systematically and critically reviewing electric-fields literature and by comparing overall strength of evidence for electric versus magnetic fields. The review of possible mechanisms does not provide any specific basis for focusing on electric fields. While laboratory studies of electric fields are few, they do not indicate that electric fields should be the exposure of interest. The existing epidemiology on residential electric-field exposures and appliance use does not support the conclusion of adverse health effects from electric-field exposure. Workers in close proximity to high-voltage transmission lines or substation equipment can be exposed to high electric fields. While there are sporadic reports of increase in cancer in some occupational studies, these are inconsistent and fraught with methodologic problems.

Conclusion: Overall, there seems little basis to suppose there might be a risk for electric fields, and, in contrast to magnetic fields, and with a possible exception of occupational epidemiology, there seems little basis for continued research into electric fields.

IDIOPATHIC ENVIRONMENTAL INTOLERANCE ATTRIBUTED TO ELECTROMAGNETIC FIELDS (FORMERLY 'ELECTROMAGNETIC HYPERSENSITIVITY'): AN UPDATED SYSTEMATIC REVIEW OF PROVOCATION STUDIES.

Rubin GJ, Nieto-Hernandez R, Wessely S. *Bioelectromagnetics. 2010; 31: 1-11.*

Idiopathic Environmental Intolerance attributed to electromagnetic fields (IEI-EMF; formerly 'electromagetic hypersensitivity') is a medically unexplained illness in which subjective symptoms are reported following exposure to electrical devices. In an earlier systematic review, we reported data from 31 blind provocation studies which had exposed IEI-EMF volunteers to active or sham electromagnetic fields and assessed whether volunteers could detect these fields or whether they reported worse symptoms when exposed to them. In this article, we report an update to that review. An extensive literature search identified 15 new experiments. Including studies reported in our earlier review, 46 blind or double-blind provocation studies in all, involving 1175 IEI-EMF volunteers, have tested whether exposure to electromagnetic fields is responsible for triggering symptoms in IEI-EMF. No robust evidence could be found to support this theory. However, the studies included in the review did support the role of the nocebo effect in triggering acute symptoms in IEI-EMF sufferers.

Conclusion: Despite the conviction of IEI-EMF sufferers that their symptoms are triggered by exposure to electromagnetic fields, repeated experiments have been unable to replicate this phenomenon under controlled conditions. A narrow focus by clinicians or policy makers on bioelectromagnetic mechanisms is therefore, unlikely to help IEI-EMF patients in the long-term.

2. Environmental exposure

RISK OF HEMATOLOGICAL MALIGNANCIES ASSOCIATED WITH MAGNETIC FIELDS EXPOSURE FROM POWER LINES: A CASE-CONTROL STUDY IN TWO MUNICIPALITIES OF NORTHERN ITALY.

Malagoli C, Fabbi S, Teggi S, Calzari M, Poli M, Ballotti E, Notari B, Bruni M, Palazzi G, Paolucci P, Vinceti M. *Environ Health.* 2010; 30:9: 16.

Some epidemiologic studies have suggested an association between electromagnetic field exposure induced by high voltage power lines and childhood leukemia, but null results have also been yielded and the possibility of bias due to unmeasured confounders has been hypothesized. The authors studied this relation in the Modena and Reggio Emilia municipalities of northern Italy, identifying the corridors along high voltage power lines with calculated magnetic field intensity in the 0.1-<0.2, 0.2-<0.4, and >=0.4 microTesla ranges. They identified 64 cases of newly-diagnosed hematological malignancies in children aged <14 within these municipalities from 1986 to 2007, and sampled four matched controls for each case, collecting information on historical residence and parental socioeconomic status of these subjects. Relative risk of leukemia associated with antecedent residence in the area with exposure > 0.1 microTesla was 3.2 (6.7 adjusting for socioeconomic status), but this estimate was statistically very unstable, its 95% confidence interval being 0.4-23.4, and no indication of a dose-response relation emerged. Relative risk for acute lymphoblastic leukemia was 5.3 (95% confidence interval 0.7-43.5), while there was no increased risk for the other hematological malignancies.

Conclusion: Though the number of exposed children in this study was too low to allow firm conclusions, results were more suggestive of an excess risk of leukemia among exposed children than of a null relation.

POWER-FREQUENCY MAGNETIC FIELDS AND CHILDHOOD BRAIN TUMORS: A CASE-CONTROL STUDY IN JAPAN.

Saito T, Nitta H, Kubo O, Yamamoto S, Yamaguchi N, Akiba S, Honda Y, Hagihara J, Isaka K, Ojima T, Nakamura Y, Mizoue T, Ito S, Eboshida A, Yamazaki S, Sokejima S, Kurokawa Y, Kabuto M. *J Epidemiol.* 2010;20: 54-61..

The strength of the association between brain tumors in children and residential power-frequency magnetic fields (MF) has varied in previous studies, which may be due in part to possible misclassification of MF exposure. This study aimed to examine this association in Japan by improving measurement techniques, and by extending measurement to a whole week. This population-based case-control study encompassed 54% of Japanese children under 15 years of age. After excluding ineligible targeted children, 55 newly diagnosed brain tumor cases and 99 sex-, age-, and residential area-matched controls were included in the analyses. The MF exposures of each set of matching cases and controls were measured in close temporal proximity to control for seasonal variation; the average difference was 12.4 days. The mean interval between diagnosis and MF measurements was 1.1 years.

The weekly mean MF level was defined as the exposure. The association was evaluated using conditional logistic regression analysis that controlled for possible confounding factors. The odds ratios (95% CI) for exposure categories of 0.1 to 0.2, 0.2 to 0.4, and above 0.4 microT, against a reference category of <0.1 microT, were 0.74 (0.17-3.18), 1.58 (0.25-9.83), and 10.9 (1.05-113), respectively, after adjusting for maternal education. This dose-response pattern was stable when other variables were included in the model as possible confounding factors.

Conclusion: A positive association was found between high-level exposure-above 0.4 microT-and the risk of brain tumors. This association could not be explained solely by confounding factors or selection bias.

HEAVY METAL EXPOSURE IN PATIENTS SUFFERING FROM ELECTROMAGNETIC HYPERSENSITIVITY.

Ghezel-Ahmadi D, Engel A, Weidemann J, Budnik LT, Baur X, Frick U, Hauser S, Dahmen N.

Sci Total Environ. 2010; 408: 774-778.

Risks from electromagnetic devices are of considerable concern. Electrohypersensitive (EHS) persons attribute a variety of rather unspecific symptoms to the exposure to electromagnetic fields. The pathophysiology of EHS is unknown and therapy remains a challenge. Heavy metal load has been discussed as a potential factor in the symptomatology of EHS patients. The main objective of the study was to test the hypothesis of a link between EHS and heavy metal exposure. The authors measured lead, mercury and cadmium concentrations in the blood of 132 patients (n=42 males and n=90 females) and 101 controls (n=34 males and n=67 females). The results show that heavy metal load is of no concern in most cases of EHS but might play a role in exceptional cases.

Conclusion: The data do not support the general advice to heavy metal detoxification in EHS.

3. Occupational exposure

PARENTAL OCCUPATIONAL EXPOSURE TO EXTREMELY LOW FREQUENCY MAGNETIC FIELDS AND CHILDHOOD CANCER: A GERMAN CASE-CONTROL STUDY.

Hug K, Grize L, Seidler A, Kaatsch P, Schüz J. *Am J Epidemiol.* 2010; 171: 27-35.

Extremely low frequency magnetic fields (ELF-MFs) have been classified as possibly carcinogenic to humans by the International Agency for Research on Cancer. The authors investigated, in a population-based case-control study in Germany, if children whose parents were exposed preconceptionally at work to ELF-MFs had an increased risk of developing cancer. Cases aged 0-14 years were ascertained from the German Childhood Cancer Registry. Controls were selected from local resident registration offices. The parental occupational history was recorded in questionnaires and telephone interviews, and preconceptional magnetic field exposure was estimated according to a job-exposure matrix. The analysis included 2,382 controls and 2,049 cases (846 children with acute leukemia, 159 children with non-Hodgkin's lymphoma, 444 children with central nervous system tumors, and 600 children with other solid tumors). Frequency-matched conditional logistic regression models revealed no increased cancer risks in children whose fathers were occupationally exposed to magnetic fields above 0.2 microT. Additionally, there was no evidence for a risk increase at magnetic field levels

exceeding 1 microT. Based on much smaller numbers, maternal occupational exposure was also not related to increased cancer risks.

Conclusion: In this large case-control study, the risk of childhood cancer was not linked to preconceptional parental ELF-MF exposure.

4. Childhood leukaemia studies

RESIDENTIAL PESTICIDES AND CHILDHOOD LEUKEMIA: A SYSTEMATIC REVIEW AND META-ANALYSIS.

Turner MC, Wigle DT, Krewski D. Environ Health Perspect. 2010; 118: 33-41.

The authors conducted a systematic review and meta-analysis of previous observational epidemiologic studies examining the relationship between residential pesticide exposures during critical exposure time windows (preconception, pregnancy, and childhood) and childhood leukemia. Searches of MEDLINE and other electronic databases were performed (1950-2009). Reports were included if they were original epidemiologic studies of childhood leukemia, followed a casecontrol or cohort design, and assessed at least one index of residential/household pesticide exposure/use. No language criteria were applied. Study selection, data abstraction, and quality assessment were performed by two independent reviewers. Random effects models were used to obtain summary odds ratios (ORs) and 95% confidence intervals (CIs). Of the 17 identified studies, 15 were included in the meta-analysis. Exposures during pregnancy to unspecified residential pesticides (summary OR = 1.54; 95% CI, 1.13-2.11; I2 = 66%), insecticides (OR = 2.05; 95%) CI, 1.80-2.32; I2 = 0%), and herbicides (OR = 1.61; 95% CI, 1.20-2.16; I2 = 0%) were positively associated with childhood leukemia. Exposures during childhood to unspecified residential pesticides (OR = 1.38; 95% CI, 1.12-1.70; I2 = 4%) and insecticides (OR = 1.61; 95% CI, 1.33-1.95; I2 = 0%) were also positively associated with childhood leukemia, but there was no association with herbicides.

Conclusion: Positive associations were observed between childhood leukemia and residential pesticide exposures. Further work is needed to confirm previous findings based on self-report, to examine potential exposure-response relationships, and to assess specific pesticides and toxicologically related subgroups of pesticides in more detail.

COMPARISON OF BIRTH WEIGHT CORRECTED FOR GESTATIONAL AGE AND BIRTH WEIGHT ALONE IN PREDICTION OF DEVELOPMENT OF CHILDHOOD LEUKEMIA AND CENTRAL NERVOUS SYSTEM TUMORS.

Sprehe MR, Barahmani N, Cao Y, Wang T, Forman MR, Bondy M, Okcu MF. *Pediatr Blood Cancer.* 2010; 54: 242-9.

High birth weight (HBW) is an established risk factor for childhood acute lymphoblastic leukemia (ALL). The purpose of this study was to evaluate if birth weight (BW) corrected-for-gestational age is a better predictor than BW alone for occurrence of ALL and other malignancies in children. Birth certificate data of 2,254 children with cancer who were younger than 5 years old at diagnosis and registered at Texas Cancer Registry during 1995-2003 were compared to 11,734 age-matched controls. Multivariable logistic regression was used to compare models with BW corrected-for-gestational age and BW alone. Compared to children who were appropriate for gestational age (AGA), children who were large for gestational age (LGA) at birth had a 1.66 times (95% CI 1.32-2.10) higher odds of ALL. Similarly,

children with a BW > or =4,000 g had a 1.5 times (95% CI 1.18-1.89) higher odds for ALL, compared to children who weighed >2,500 and <4,000 g at birth. Using model diagnostics, the model containing BW corrected-for-gestational age was a better predictor than the model with BW alone [Akaike's Information Criterion (AIC) 4,646 vs. 4,658, respectively]. Odds ratios (OR) were similar for LGA children who were <4,000 g and LGA children who were > or =4,000 g (OR = 1.5, 95% CI 0.97-2.5 and OR = 1.67, 95% CI 1.29-2.16, respectively). BW was not an independent risk factor for acute myeloid leukemia or brain tumors.

Conclusion: BW corrected-for-gestational age is a better predictor than BW alone of risk for ALL. Future studies using BW variable should incorporate gestational age in their analyses.