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1. Residential exposure

RESIDENTIAL MAGNETIC FIELDS EXPOSURE AND CHILDHOOD LEUKEMIA: A POPULATION-BASED CASE-CONTROL STUDY IN CALIFORNIA.

Kheifets L, Crespi CM, Hooper C, Cockburn M, Amoon AT, Vergara XP. *Cancer Causes Control. 2017 Sep 12.*

The authors conducted a large records-based case-control study of childhood leukemia risk and exposure to magnetic fields from power lines in California. The study included 5,788 childhood leukemia cases (born in and diagnosed in California 1986-2008) matched to population-based controls on age and sex. Magnetic fields at birth addresses were calculated using geographic information systems, aerial imagery, historical information on load and phasing, and site visits.

Based on unconditional logistic regression controlling for age, sex, race/ethnicity, and socioeconomic status using subjects geocoded to a basic standard of accuracy, a slight risk deficit was reported in two intermediate exposure groups and a small excess risk in the highest exposure group (odds ratio of 1.50 (95% confidence interval [0.70, 3.23])). Subgroup and sensitivity analyses as well as matched analyses gave similar results. All estimates had wide confidence intervals.

Conclusions: This large, statewide, record-based case-control study of childhood leukemia in California does not in itself provide clear evidence of risk associated with greater exposure to magnetic fields from power lines, but could be viewed as consistent with previous findings of increased risk.

2. Human experimental studies

FUNCTIONAL BRAIN MRI IN PATIENTS COMPLAINING OF ELECTROHYPERSENSITIVITY AFTER LONG TERM EXPOSURE TO ELECTROMAGNETIC FIELDS. Heuser G, Heuser SA.

Rev Environ Health. 2017 Sep 26;32(3):291-299.

Over the years the authors have seen an increasing number of patients who had developed multi system complaints after long term repeated exposure to electromagnetic fields (EMFs). These complaints included headaches, intermittent cognitive and memory problems, intermittent disorientation, and also sensitivity to EMF exposure. Regular laboratory tests were within normal limits in these patients. The patients refused to be exposed to radioactivity. This of course ruled out positron emission tomography (PET) and single-photon emission computed tomography (SPECT) brain scanning. This is why the authors ordered fMRI brain scans on these patients. They hoped to document objective abnormalities in these patients who had often been labeled as psychiatric cases.

Ten patients first underwent a regular magnetic resonance imaging (MRI) brain scan, using a 3 Tesla Siemens Verio MRI open system. A functional MRI study was then performed in the resting state using the following sequences: A three-dimensional, T1-weighted, gradient-echo (MPRAGE) Resting state network. The echo-planar imaging (EPI) sequences for this resting state blood oxygenation level dependent (BOLD) scan were then post processed on a 3D workstation and the independent component analysis was performed separating out the various networks. Arterial spin labeling. Tractography and fractional anisotropy.

All ten patients had abnormal functional MRI brain scans. The abnormality was often described as hyperconnectivity of the anterior component of the default mode in the medial orbitofrontal area. Other abnormalities were usually found. Regular MRI studies of the brain were mostly unremarkable in these patients.

Conclusions: The authors propose that functional MRI studies should become a diagnostic aid when evaluating a patient who claims electrohypersensitivity (EHS) and has otherwise normal studies. Interestingly, the differential diagnosis for the abnormalities seen on the fMRI includes head injury. It turns out that many of our patients indeed had a history of head injury which was then followed sometime later by the development of EHS. Many of these patients also had a history of exposure to potentially neurotoxic chemicals, especially mold. Head injury and neurotoxic chemical exposure may make a patient more vulnerable to develop EHS.

3. Exposure assessment

EXPOSURE MODELLING OF EXTREMELY LOW-FREQUENCY MAGNETIC FIELDS FROM OVERHEAD POWER LINES AND ITS VALIDATION BY MEASUREMENTS. Bürgi A, Sagar S, Struchen B, Joss S, Röösli M. Int J Environ Res Public Health. 2017 Aug 23;14(9).

A three-dimensional model for calculating long term exposure to extremely lowfrequency magnetic fields from high-voltage overhead power lines is presented, as well as its validation by measurements. For the validation, the model was applied to two different high-voltage overhead power lines in Iffwil and Wiler (Switzerland). In order to capture the daily and seasonal variations, each measurement was taken for 48 h and the measurements were carried out six times at each site, at intervals of approximately two months, between January and December 2015. During each measurement, a lateral transect of the magnetic flux density was determined in the middle of a span from nine measurement points in the range of ±80 m. The technical data of both the lines as well as the load flow data during the measurement periods were provided by the grid operators. These data were used to calculate 48 h averages of the absolute value of the magnetic flux density and compared with modelled values.

Conclusions: The highest 48 h average was 1.66 μ T (centre of the line in Iffwil); the lowest 48 h average was 22 nT (80 m distance from the centre line in Iffwil). On average, the magnetic flux density was overestimated by 2% (standard deviation: 9%) in Iffwil and underestimated by 1% (8%) in Wiler. Sensitivity analyses showed that the uncertainty is mainly driven by errors in the coordinates and height data. In particular, for predictions near the centre of the line, an accurate digital terrain model is critical.

4. Leukaemia studies

PARENTAL OCCUPATIONAL EXPOSURE TO BENZENE AND THE RISK OF CHILDHOOD CANCER: A CENSUS-BASED COHORT STUDY. Spycher BD, Lupatsch JE, Huss A, Rischewski J, Schindera C, Spoerri A, Vermeulen R, Kuehni CE; Swiss Paediatric Oncology Group; Swiss National Cohort Study Group. *Environ Int. 2017 Nov;108:84-91.*

The objective of this study was to examine whether parental occupational exposure to benzene is associated with an increased cancer risk in a census-based cohort of children.

From a census-based cohort study in Switzerland, the authors included children aged <16years at national censuses (1990, 2000). They retrieved parental occupations reported at census and assessed exposure to benzene using a job exposure matrix. Incident cancer cases were identified through record linkage with the Swiss Childhood Cancer Registry. Cox proportional-hazards models were fitted to assess associations between exposures and the following outcomes: any cancer, leukaemia, acute lymphoid leukaemia (ALL), acute myeloid leukaemia (AML), lymphoma, non-Hodgkin lymphoma, central nervous system (CNS) tumours, and glioma. Models were adjusted for a range of socio-economic, perinatal and environmental factors.

Analyses of maternal (paternal) exposure were based on 9.0 (13.2) million person years at risk and included 1004 (1520) cases of cancer, of which 285 (438) had leukaemia, 186 (281) lymphoma, 227 (339) a CNS tumour. Maternal exposure was associated with an increased risk of childhood leukaemia (hazard ratio 1.73, 95% Cl 1.12-2.67) and ALL (1.88, 1.16-3.04). Little evidence of an association for other outcomes or for paternal exposure was found. Adjusting for potential confounders did not materially affect the results.

Conclusions: This nationwide cohort study suggests an increased risk of leukaemia among children whose mothers were exposed to benzene at work.

RESIDENTIAL EXPOSURE TO ULTRAVIOLET LIGHT AND RISK OF PRECURSOR B-CELL ACUTE LYMPHOBLASTIC LEUKEMIA: ASSESSING THE ROLE OF INDIVIDUAL RISK FACTORS, THE ESCALE AND ESTELLE STUDIES.

Coste A, Hémon D, Orsi L, Boniol M, Doré JF, Faure L, Clavel J, Goujon S. *Cancer Causes Control. 2017 Aug 2.*

In a previous nationwide ecological study based on 20 years of registration and 7,443 cases of acute lymphoblastic leukemia (ALL), the authors reported a positive association between residential solar ultraviolet (UV) light at diagnosis and childhood precursor B-cell acute lymphoblastic leukemia (PBC-ALL).

The present study investigated the influence of suspected individual risk factors for ALL on the association between UV and PBC-ALL, and evaluated this association at the residence at birth.

Individual data collected by interviews in the ESCALE (2003-2004) and ESTELLE (2010-2011) nationwide case-control studies, which included 1,511 cases of leukemia

aged less than 15 years and 3,102 population controls, were analyzed. Municipalities of residences at birth and at diagnosis/interview were extracted and assigned UV radiation exposure from the EUROSUN database. The potential confounders or effect modifiers considered were strongly suspected risk factors for ALL that were available in the ESCALE and ESTELLE studies.

UV exposure at diagnosis was associated with PBC-ALL (OR = 1.27 [1.08-1.48]) for UV > 105.5 J/cm2 compared to UV \leq 105.5 J/cm2. Considering exposure to UV at birth rather than at diagnosis/inclusion yielded almost identical results as both variables were strongly correlated. Taking into account the suspected ALL risk factors did not affect this association in the pooled study.

Conclusions: These findings suggest that the previous observation of an ecological association between residential UV radiation exposure at diagnosis and PBC-ALL was not confounded or modified by individual risk factors, and that the critical exposure time window may be prenatal.

SPATIAL CLUSTERING OF CHILDHOOD LEUKAEMIA WITH THE INTEGRATION OF THE PAEDIATRIC ENVIRONMENTAL HISTORY.

Cárceles-Álvarez A, Ortega-García JA, López-Hernández FA, Orozco-Llamas M, Espinosa-López B, Tobarra-Sánchez E1, Alvarez L. *Environ Res. 2017 Jul;156:605-612.*

Leukaemia remains the most common type of paediatric cancer and its aetiology remains unknown, but considered to be multifactorial. It is suggested that the initiation in utero by relevant exposures and/or inherited genetic variants and, other promotional postnatal exposures are probably required to develop leukaemia. This study aimed to map the incidence and analyse possible clusters in the geographical distribution of childhood acute leukaemia during the critical periods and to evaluate the factors that may be involved in the aetiology by conducting community and individual risk assessments.

The authors analysed all incident cases of acute childhood leukaemia (<15 years) diagnosed in a Spanish region during the period 1998-2013. At diagnosis, the addresses during pregnancy, early childhood and diagnosis were collected and codified to analyse the spatial distribution of acute leukaemia. Scan statistical test methodology was used for the identification of high-incidence spatial clusters. Once identified, individual and community risk assessments were conducted using the Paediatric Environmental History.

A total of 158 cases of acute leukaemia were analysed. The crude rate for the period was 42.7 cases per million children. Among subtypes, acute lymphoblastic leukaemia had the highest incidence (31.9 per million children). A spatial cluster of acute lymphoblastic leukaemia was detected using the pregnancy address (p<0.05). The most common environmental risk factors related with the aetiology of acute lymphoblastic leukaemia, identified by the Paediatric Environmental History were: prenatal exposure to tobacco (75%) and alcohol (50%); residential and community exposure to pesticides (62.5%); prenatal or neonatal ionizing radiation (42.8%); and parental workplace exposure (37.5%) CONCLUSIONS: This study suggests that environmental exposures in utero may be important in the development of childhood leukaemia. Due to the presence of high-incidence clusters using pregnancy address, it

is necessary to introduce this address into the childhood cancer registers. The Paediatric Environmental History which includes pregnancy address and a careful and comprehensive evaluation of the environmental exposures will allow us to build the knowledge of the causes of childhood leukaemia.