

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

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## 1. Reviews

### **THE EFFECTS OF LOW-FREQUENCY ENVIRONMENTAL-STRENGTH ELECTROMAGNETIC FIELDS ON BRAIN ELECTRICAL ACTIVITY: A CRITICAL REVIEW OF THE LITERATURE.**

Carrubba S, Marino AA.

*Electromagn Biol Med.* 2008; 27 : 83-101.

Reports dealing with the stimulus-response relationship between low-level, low-frequency electromagnetic fields (EMFs) and changes in brain electrical activity permit assessment of the hypothesis that EMFs are detected by the body via the process of sensory transduction. These reports, as well as those involving effects on brain activity observed after a fixed time of exposure, are critically reviewed here.

Conclusion: A consistent stimulus-response relationship between EMFs and changes in brain activity has been demonstrated in animal and human subjects. The effects, which consisted of onset and offset evoked potentials, were observed under conditions permitting the inference that the fields were transduced like ordinary stimuli such as light and sound. However, unlike the changes in brain activity induced by these stimuli, the changes induced by EMFs were governed by nonlinear laws. The studies involving attempts to determine whether a period of EMF exposure caused a metabolic effect reflected in pre-exposure/post-exposure differences in brain activity were generally inconclusive.

## 2. Residential exposure

### **RESIDENTIAL MAGNETIC FIELD EXPOSURE AND CHILDHOOD BRAIN CANCER: A META-ANALYSIS.**

Mezei G, Gadallah M, Kheifets L.

*Epidemiology* 2008; 19: 424-430.

The authors conducted a meta-analysis of studies on magnetic field exposure and childhood brain tumors to evaluate homogeneity in the results, to examine reasons for heterogeneity, and to derive a summary effect estimate. Comparison of results from studies of childhood brain cancer and childhood leukemia may also help to assess the potential for selection bias in childhood leukemia studies.

They included results from 13 studies. Using an inverse variance-weighted method, summary effect estimates were calculated separately for distance, wire codes, and measured and calculated magnetic fields. Sensitivity analyses were conducted to assess the influence of individual studies, the potential for selection bias, and the possibility of publication bias. With the exception of wire-code studies, results were compatible with homogeneity across studies. The summary odds ratios (95% confidence intervals) were 0.88 (0.57-1.37) for distance <50 m and 1.14 (0.78-1.67) for calculated or measured magnetic fields above 0.2 microT. For measured or calculated exposures above 0.3 or 0.4 microT, the summary odds ratio was 1.68 (0.83-3.43), with no differences by method of exposure assessment. No single study had a substantial effect on the summary estimates. There was no indication of publication bias.

Conclusions: With the exception of high cut-point analyses (0.3/0.4 microT), where the possibility of a moderate risk increase cannot be excluded, no increase in childhood brain cancer risk was evident for any of the exposure metrics.

**ASSESSMENT OF SELECTION BIAS IN THE CANADIAN CASE-CONTROL STUDY OF RESIDENTIAL MAGNETIC FIELD EXPOSURE AND CHILDHOOD LEUKEMIA.**

Mezei G, Spinelli JJ, Wong P, Borugian M, McBride ML.

*Am J Epidemiol. 2008; 167: 1504-1510.*

The authors evaluated the role of selection bias in the 1999 Canadian case-control study of residential magnetic field exposure and childhood leukemia. They included cases, participating controls, and first-choice nonparticipating controls in their analyses. Exposure was assessed by wire coding, a classification system based on the distribution line characteristics near homes. Although an imperfect measure of magnetic field exposure, wire coding is the only method applicable to nonparticipating subjects. First-choice nonparticipant controls tended to be of lower socioeconomic status than their replacements (non-first-choice participant controls), and lower socioeconomic status was related to higher wire code categories. The odds ratios for developing childhood leukemia in the highest exposure category were 1.6 (95% confidence interval: 1.0, 2.6) when the actual participating controls were used and 1.3 (95% confidence interval: 0.8, 2.1) when the first-choice ideal controls were used, regardless of their participation.

Conclusion: Overall, the authors conclude that, although there is some evidence for control selection or participation bias in the Canadian study, it is unlikely to explain entirely the observed association between magnetic field exposure and childhood leukemia. Inherent problems in exposure assessment for nonparticipating subjects, however, limit the interpretations of these results, and the role of selection bias cannot entirely be dismissed on the basis of these results alone.

**ELECTROMAGNETIC FIELDS PRODUCED BY INCUBATORS INFLUENCE HEART RATE VARIABILITY IN NEWBORNS.**

Bellieni CV, Acampa M, Maffei M, Maffei S, Perrone S, Pinto I, Stacchini N, Buonocore G.

*Arch Dis Child Fetal Neonatal Ed. 2008 ;93: F298-301.*

Incubators are largely used to preserve preterm and sick babies from postnatal stressors, but their motors produce high electromagnetic fields (EMFs). Newborns are chronically exposed to these EMFs, but no studies about their effects on the fragile developing neonatal structure exist. The aim of the study was to verify whether the exposure to incubator motor electric power may alter autonomous nervous system activity in newborns.

Heart rate variability (HRV) of 43 newborns in incubators was studied. The study group comprised 27 newborns whose HRV was studied throughout three 5-minute periods: with incubator motor on, off, and on again, respectively. Mean HRV values obtained during each period were compared. The control group comprised 16 newborns with constantly unrecordable EMF and exposed to changes in background noise, similar to those provoked by the incubator motor.

Mean (SD) total power and the high-frequency (HF) component of HRV increased significantly (from 87.1 (76.2) ms<sup>2</sup> to 183.6 (168.5) ms<sup>2</sup>) and the mean low-frequency (LF)/HF ratio decreased significantly (from 2.0 (0.5) to 1.5 (0.6)) when the incubator motor was turned off. Basal values (HF = 107.1 (118.1) ms<sup>2</sup> and LF/HF = 1.9 (0.6)) were restored when incubators were turned on again. The LF spectral component of HRV showed a statistically significant change only in the second phase of the

experiment. Changes in background noise did not provoke any significant change in HRV.

Conclusion: EMFs produced by incubators influence newborns' HRV, showing an influence on their autonomous nervous system. More research is needed to assess possible long-term consequences, since premature newborns may be exposed to these high EMFs for months.

### **3. Occupational exposure**

#### **OCCUPATIONAL EXPOSURE TO EXTREMELY LOW FREQUENCY ELECTRIC AND MAGNETIC FIELDS AND ALZHEIMER DISEASE: A META-ANALYSIS.**

García AM, Sisternas A, Hoyos SP.

*Int J Epidemiol. 2008; 37: 329-340.*

Among potential environmental risk factors for Alzheimer disease (AD), occupational exposures have received some attention, including extremely low frequency electromagnetic fields (ELF-EMF). A systematic review and meta-analysis of published epidemiological studies on this subject was carried out. The search was concluded in April 2006. Bibliographic databases consulted included PubMed, EMBASE, Cochrane Library and NIOSHTIC2. Pooled estimates were obtained using random-effects meta-analysis. Sources of heterogeneity between studies were explored, as was publication bias.

Fourteen different studies (nine case-control and five cohort studies) accomplished inclusion criteria. All these studies followed standardized criteria for AD diagnosis and most of them obtained quantitative estimates of exposure. Pooled estimates suggest an increased risk of AD from case-control studies (OR(pooled) 2.03; 95% CI 1.38-3.00) and from cohort studies (RR(pooled) 1.62; 95% CI 1.16-2.27), with moderate to high statistical heterogeneity in both cases (respectively,  $I(2) = 58\%$  and  $I(2) = 54\%$ ). Cohort studies showed consistently increased risks for exposed men (RR(pooled) 2.05; 95% CI 1.51-2.80,  $I(2) = 0\%$ ). Evidence of dose-response relationship was not present. Test for publication bias suggests small study effects, mostly for case-control studies.

Conclusions: Available epidemiological evidence suggests an association between occupational exposure to ELF-EMF and AD. However, some limitations affecting the results from this meta-analysis should be considered. More information on relevant duration and time windows of exposure, on biological mechanisms for this potential association and on interactions between electromagnetic fields exposure and established risk factors for AD is needed.

#### **OCCUPATIONAL ELECTROMAGNETIC FIELDS AND LEUKEMIA AND BRAIN CANCER: AN UPDATE TO TWO META-ANALYSES.**

Kheifets L, Monroe J, Vergara X, Mezei G, Afifi AA.

*J Occup Environ Med. 2008 Jun;50(6):677-688.*

The objective of this study was to update past meta-analyses on occupational electromagnetic fields (EMF) and adult brain cancer and leukemia. The authors collected and evaluated all relevant 1993 to 2007 publications. Summary estimates were obtained using various weighting schemes. To explore sources of heterogeneity, study characteristics were examined using regression analysis.

Overall, for new studies, both brain cancer and leukemia showed small increases in risk estimates, 10% and 13%, respectively. Notably, pooled risk estimates were lower than in past meta-analyses, and leukemia subtypes showed no consistent pattern when past and present meta-analyses were compared.

Conclusions: The lack of a clear pattern of EMF exposure and outcome risk does not support a hypothesis that these exposures are responsible for the observed excess risk. Findings were not sensitive to assumptions, influential studies, weighting schemes, publication bias, study characteristics, or funding source.

**CARDIOVASCULAR MORTALITY AND EXPOSURE TO EXTREMELY LOW FREQUENCY MAGNETIC FIELDS: A COHORT STUDY OF SWISS RAILWAY WORKERS.**

Roosli M, Egger M, Pfluger D, Minder C.

*Environ Health.* 2008; 7: 35.

Exposure to intermittent magnetic fields of 16 Hz has been shown to reduce heart rate variability, and decreased heart rate variability predicts cardiovascular mortality. We examined mortality from cardiovascular causes in railway workers exposed to varying degrees to intermittent 16.7 Hz magnetic fields. The authors studied a cohort of 20,141 Swiss railway employees between 1972 and 2002, including highly exposed train drivers (median lifetime exposure 120.5 uT-years), and less or little exposed shunting yard engineers (42.1 uT-years), train attendants (13.3 uT-years) and station masters (5.7 uT-years). During 464,129 person-years of follow up, 5,413 deaths were recorded and 3,594 deaths were attributed to cardio-vascular diseases. We analyzed data using Cox proportional hazards models. For all cardiovascular mortality the hazard ratio compared to station masters was 0.99 (95%CI: 0.91, 1.08) in train drivers, 1.13 (95%CI: 0.98, 1.30) in shunting yard engineers, and 1.09 (95%CI: 1.00, 1.19) in train attendants. Corresponding hazard ratios for arrhythmia related deaths were 1.04 (95%CI: 0.68, 1.59), 0.58 (95%CI: 0.24, 1.37) and 1.30 (95%CI: 0.87, 1.93) and for acute myocardial infarction 1.00 (95%CI: 0.73, 1.36), 1.56 (95%CI: 1.04, 2.32), and 1.14 (95%CI: 0.85, 1.53). The hazard ratio for arrhythmia related deaths per 100 uT-years of cumulative exposure was 0.94 (95%CI: 0.71, 1.24) and 0.91 (95%CI: 0.75, 1.11) for acute myocardial infarction.

Conclusions: This study provides evidence against an association between long-term occupational exposure to intermittent 16.7 Hz magnetic fields and cardiovascular mortality.

**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.* 2008 May 27. [Epub ahead of print]

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 (muT), 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. Exposure assessment**

##### **MEASUREMENTS OF PROFESSIONAL EXPOSURE TO ELF FIELDS IN SOME PRODUCTION AREAS WITHIN THE TERRITORY OF REGIONE CAMPANIA AND COMPARISON WITH THE ACTION VALUES ACCORDING TO 2004/40/CE DIRECTIVE.**

d'Angelo R, Russo E, Attaianese L, Niutta F.  
*G Ital Med Lav Ergon.* 2007; 29 (3 Suppl): 774-776.

The 2004/40/CE Directive (which should be acknowledged within April 30, 2008), introduces the Action values for the prevention of occupational risk related to Extremely Low Frequency-Magnetic Fields (ELF-MF) exposure. In the Regione Campania, the following production areas have been investigated: textiles, industrial graphics, wood, manufacturing and ceramics. We have specifically monitored exposure to ELF magnetic field values for 400 workers belonging to 80 different areas chosen among those for which an exposure could be supposed. Results have been compared to the action values indicated in the 2004/40/CE directive. Used instrumentation includes a Wandel & Goltermann EFA 300 portable field analyser with B-Field Sensor isotropic spectrum analyzer for electric and magnetic field with 5 Hz to 32 kHz bandwidth. Technical rules follow CEI 211-6 Jan-2001. All measurements have been performed in continuous within two working shifts, setting the instrument to make acquisitions every five minutes. Data have been then processed to obtain RMS values of the magnetic field per each work shift. Values found have not shown any exceeding of the action values: more specifically, 90% of values was below it (500 microT) and 70% of the monitored jobs shows an occupational exposure below 0.4 microT, which is the possible threshold proposed for the man chronic effects of ELF magnetic fields based on data coming from some epidemiological studies.

##### **INDOOR TRANSFORMER STATIONS AS PREDICTORS OF RESIDENTIAL ELF MAGNETIC FIELD EXPOSURE.**

Ilonen K, Markkanen A, Mezei G, Juutilainen J.  
*Bioelectromagnetics.* 2008; 29: 213-218.

Transformer stations in apartment buildings may offer a possibility to conduct epidemiological studies that involve high exposure to extremely low frequency magnetic fields (MF), avoid selection bias and minimize confounding factors. To validate exposure assessment based on transformer stations, measurements were performed in thirty buildings in three Finnish cities. In each building, spot measurements in all rooms and a 24-h recording in a bedroom were performed in one apartment above a transformer station (AAT), in one first floor (FF) reference apartment, and one reference apartment on upper floors (UF). The apartment mean of spot measurements was 0.62 microT in the AATs, 0.21 microT in the FF and 0.11 microT in the UF reference apartments. The 24-h apartment mean (estimated from the spot measurements and the bedroom 24-h recording) was 0.2 microT or higher in 29 (97%) AATs, in 7 (25%) FF and in 3 (10 %) UF reference apartments. The corresponding numbers for the 0.4 microT cut-off point were 19 (63%), 4 (14%), and 1 (3.3%). The higher MF level in the FF reference apartments indicates that they should not be considered "unexposed" in epidemiological studies. If such apartments are excluded, a transformer station under the floor predicts 24-h apartment mean MF with

a sensitivity of 0.41 (or 0.58) and a specificity of 0.997 (or 0.97), depending on the MF cut-off point (0.2 or 0.4 microT). The results indicate that apartments can be reliably classified as high and low MF field categories based on the known location of transformer stations.

**MAGNETIC FIELD EXPOSURE IN A NONDESTRUCTIVE TESTING OPERATION.**

Lippert JF, Lacey SE, Kennedy KJ, Esmen NA, Buchanich JM, Marsh GM.

*Arch Environ Occup Health. 2007; 62: 187-193.*

Nondestructive testing is any technique used to inspect the integrity of a manufactured item without diminishing its future usefulness. Magnetic particle inspection is one type of nondestructive testing that uses electromagnetism in the inspection procedure, thus potentially exposing the operator to magnetic fields. During magnetic particle inspection, investigators took peak magnetic field measurements of 8 turbine engine shafts at a turbine engine overhaul and repair center. They recorded 95 peak magnetic field measurements, ranging from < 0.1 to 29.27 mT. The exposure values measured were among the highest reported in the occupational setting. Further work is needed to characterize magnetic field exposures in magnetic particle inspection operations--in particular, by differentiating magnetic field magnitude by current frequency--and to understand exposure as it relates to different types of magnetic particle inspection devices.

## **5. EMF Policy**

***DIRECTIVE 2008/46/EC OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL OF 23 APRIL 2008 AMENDING DIRECTIVE 2004/40/EC ON MINIMUM HEALTH AND SAFETY REQUIREMENTS REGARDING THE EXPOSURE OF WORKERS TO THE RISKS ARISING FROM PHYSICAL AGENTS (ELECTROMAGNETIC FIELDS) (18TH INDIVIDUAL DIRECTIVE WITHIN THE MEANING OF ARTICLE 16(1) OF DIRECTIVE 89/391/EEC).***

The European Parliament and the Council of the European Union

The European Parliament and the Council of the European Union have adopted this directive:

Article 1

In Article 13(1) of Directive 2004/40/EC, the first subparagraph shall be replaced by the following:

"1. Member States shall bring into force the laws, regulations and administrative provisions necessary to comply with this Directive no later than 30 April 2012. They shall forthwith inform the Commission thereof."

***IARC EVALUATION OF ELF MAGNETIC FIELDS: PUBLIC UNDERSTANDING OF THE 0.4-μT EXPOSURE METRIC.***

Bailey WH, Wagner ME.

*J Expo Sci Environ Epidemiol. 2008; 18: 233-235.*

The author reflects on the lack of understanding by the public of the magnetic field exposure metric referenced by 0.4 microTesla. The author explains the meaning of 0.4 microTesla measurements in relation to average calculated values. He says that the use of the metric in epidemiology studies can be best-conveyed to the public using simple analogies like a comparison to diet. He also discussed time-weighted average (TWA) exposure metrics in epidemiologic studies of childhood leukemia.

**OPERATIONAL ASPECTS OF RISK PERCEPTION IN THE ELECTROMAGNETIC FIELDS EXPOSITION.**

Pennarola E, Barletta R, Quarto E, Pennarola R.

*G Ital Med Lav Ergon. 2007; 29(3 Suppl):785-787.*

The increase of electromagnetic fields exposition is being associated with the increase of risk perception in the people exposed due to the uncertainty of the biological and sanitary effects. Research is being carried out on the symptomatology shown by the 45 people living near power-lines in the Benevento area and consequently exposed to electromagnetic fields. The measure of the magnetic and electric field was in the normal range while the people showed most symptoms in the subjective and behavioural sphere. The research findings suggest that risk assessment should take into account the subjectivity of the people exposed as shown in the special questionnaires with the aim of reducing the subjective and behavioural symptomatology for developing a new environmental medicine.

**EVALUATION OF THE OCCUPATIONAL RISK RELATED TO EXPOSURE TO ELECTROMAGNETIC FIELDS ACCORDING TO THE EC DIRECTIVE 2004/40 EC: EXPOSURE DURING PREGNANCY.**

Gobba F, Tavani M, Bianchi N.

*G Ital Med Lav Ergon. 2007; 29(3 Suppl):779-780.*

The EU Directive 2004/40/EC on the minimum health and safety requirements regarding the exposure of workers to the risks arising from physical agents (electromagnetic fields) will introduce the need of an evaluation of the risk related to EMF occupational exposure in pregnancy. Nevertheless, data from research in this field are scarcely conclusive to date. Furthermore knowledge on this risk seems insufficient among OH physicians in Italy. Accordingly, there is an urgent need for further research, and for a diffusion of knowledge among OH physicians on possible risk to pregnancy due to occupational exposure to EMF.

## **6. Leukaemia studies**

**DOMESTIC RADON AND CHILDHOOD CANCER IN DENMARK.**

Raaschou-Nielsen O, Andersen CE, Andersen HP, Gravesen P, Lind M, Schüz J, Ulbak K.

*Epidemiology. 2008; 19: 536-543.*

Higher incidence rates of childhood cancer and particularly leukemia have been observed in regions with higher radon levels, but case-control studies have given inconsistent results. We tested the hypothesis that domestic radon exposure increases the risk for childhood cancer. The authors identified 2400 incident cases of leukemia, central nervous system tumor, and malignant lymphoma diagnosed in children between 1968 and 1994 in the Danish Cancer Registry. Control children (n = 6697) were selected from the Danish Central Population Registry. Radon levels in residences of children and the cumulated exposure of each child were calculated as the product of exposure level and time, for each address occupied during childhood. Cumulative radon exposure was associated with risk for acute lymphoblastic leukemia (ALL), with rate ratios of 1.21 (95% confidence interval = 0.98-1.49) for levels of 0.26 to 0.89 x 10(3) Bq/m<sup>3</sup>-years and 1.63 (1.05-2.53) for exposure to >0.89 x 10(3) Bq/m<sup>3</sup>-years, when compared with <0.26 x 10(3) Bq/m<sup>3</sup>-years. A linear dose-response analysis showed a 56% increase in the rate of ALL per 10(3) Bq/m<sup>3</sup>-years increase in exposure. The association with ALL persisted in sensitivity analyses and

after adjustment for potential confounders. No association was found with the other types of childhood cancer.

Conclusions: This study suggests that domestic radon exposure increases the risk for ALL during childhood but not for other childhood cancers.

#### **DOES PROLONGED BREASTFEEDING REDUCE THE RISK FOR CHILDHOOD LEUKEMIA AND LYMPHOMAS?**

Bener A, Hoffmann GF, Afify Z, Rasul K, Tewfik I.

*Minerva Pediatr.* 2008; 60: 155-161.

Prolonged breastfeeding was shown to reduce the risk of childhood acute leukemia. The aim of the study was to investigate the protective effect of longer breastfeeding on the risk of lymphoid malignancies in children and its dependent socio-economic factors. The study group comprised of 169 patients with acute lymphocytic leukemia (ALL), Hodgkin's (HL) and non-Hodgkin's lymphoma (NHL), age  $\geq$  or  $<$  15 years, and 169 healthy controls, matched to patients by age and sex. Mothers of all study subjects provided information via telephone about the history of breastfeeding and parameters seen as proxies for viral infection. The mean age  $\pm$  SD of cases was 5.44  $\pm$  3.29 years and of control subjects 5.51  $\pm$  3.62 years. The male/female ratio was 1.73. Overall, the mean number of months of breastfeeding in the male patients and controls was 9.1 (95% confidence interval [CI] 7.9-10.4) and 12.1 (95% CI 11.0-13.4), respectively ( $P < 0.001$ ), and in the female patients and controls 8.4 (95% CI 6.9-10.1) and 11.5 (95% CI 10.0-13.0), respectively ( $P < 0.01$ ). In 103 ALL patients, a shorter period of breastfeeding (0-6 months duration), was associated with increased odds ratio (OR) for males (OR=3.1, 95% CI 1.4-6.8) and females (OR=2.2, 95% CI 0.8-6.32) as compared to breastfeeding longer than 6 months. In 103 ALL patients, 32 HL and 34 NHL patients, there were no statistically significant differences in the duration of breastfeeding between the male and female patients and their respective controls. In multivariate analysis, statistically significant risk factors for the development of childhood lymphoid malignancy were: a shorter duration of breastfeeding, lower age and level of education of mother and higher income, larger size of accommodation and birth order in the family.

Conclusion: The current study confirmed that a longer duration of breastfeeding has protective effect against ALL and HL. Additional factors found to be associated with an elevated risk of lymphoid malignancy were low age and low education of mother. All these factors can be related to an increased risk of early childhood infections.

#### **VITAMIN SUPPLEMENT USE AMONG CHILDREN WITH DOWN'S SYNDROME AND RISK OF LEUKAEMIA: A CHILDREN'S ONCOLOGY GROUP (COG) STUDY.**

Blair CK, Roesler M, Xie Y, Gamis AS, Olshan AF, Heerema NA, Robison LL, Ross JA; Children's Oncology Group (COG).

*Paediatr Perinat Epidemiol.* 2008; 22: 288-295.

Vitamin supplements have been proposed for children with Down's syndrome (DS) with claims of improving cognitive abilities, or immune or thyroid function. Several studies have shown decreased levels of zinc in this population. Because children with DS have a 50-fold increased risk of developing acute leukaemia during the first 5 years of life, we explored the relation between child vitamin and herbal supplement use and the risk of leukaemia in a case-control study. During the period 1997-2002, the authors enrolled 158 children with DS aged 0-18 years that were diagnosed with acute lymphoblastic leukaemia (ALL) ( $n = 97$ ) or acute myeloid leukaemia (AML) ( $n = 61$ ) at participating Children's Oncology Group institutions. They enrolled 173 DS children without leukaemia (controls), selected from the cases' primary care clinic and



frequency-matched on age. Data were collected via telephone interviews with mothers of the index child regarding use of multivitamins, zinc, vitamin C, iron and herbal supplements, including age at first use, frequency and duration. Among controls, 57% reported regular multivitamin use ( $\geq 3$  times/week for  $\geq 3$  months) compared with 48% of ALL cases and 61% of AML cases.

Conclusion: The authors found no evidence of an association between children's regular multivitamin use and ALL or AML (adjusted odds ratios [OR] = 0.94 [95% CI 0.52, 1.70] and 1.90 [0.73, 4.91] respectively). There was a suggestion of an increased risk for AML associated with regular multivitamin use during the first year of life or for an extended duration (ORs = 2.38 [0.94, 5.76] and 2.59 [1.02, 6.59] respectively). Despite being the largest study of DS-leukaemia, the sample size was small, resulting in imprecise effect estimates. Future research should include larger sample sizes as well as a full assessment of diet including vitamin supplementation to adequately examine the relation between nutritional status and childhood leukaemia.

**ARE PRE- OR POSTNATAL DIAGNOSTIC X-RAYS A RISK FACTOR FOR CHILDHOOD CANCER? A SYSTEMATIC REVIEW.**

Schulze-Rath R, Hammer GP, Blettner M.

*Radiat Environ Biophys.* 2008; 47: 301-312.

The risk of cancer after diagnostic X-rays received as fetus or during early childhood has been investigated in many studies. The results of recent epidemiological studies are summarized in a present systematic review. The strategies for literature search, inclusion criteria, and items for study quality assessment were defined in the study protocol. All epidemiological case control and cohort studies published in English between 1990 and 2006 that reported at least the size of the study population and risk estimates were included. Results were summarized separately for pre- and postnatal exposure and for each cancer site. Nineteen case control studies and six cohort studies matched the inclusion criteria. No association of leukemia with prenatal exposures was observed in nine case control studies. Heterogeneous results were found for postnatal exposures and leukemia in four studies. No significant effect of pre- and postnatal X-ray exposure was observed for other cancer sites (non-Hodgkin lymphomas, solid tumors and brain tumors). Most studies have limitations in study design, study size, or exposure measurement, and involve very low exposures. These results thus do not contradict previous evidence accumulated since 1956 indicating risk increases associated with prenatal X-ray exposure. Computed tomography is not covered in the studies and needs to be investigated in the future.

**RISK OF CHILDHOOD CANCERS ASSOCIATED WITH RESIDENCE IN AGRICULTURALLY INTENSE AREAS IN THE UNITED STATES.**

Carozza SE, Li B, Elgethun K, Whitworth R.

*Environ Health Perspect.* 2008;116: 559-565.

The potential for widespread exposure to agricultural pesticides through drift during application raises concerns about possible health effects to exposed children living in areas of high agricultural activity. The authors evaluated whether residence in a county with greater agricultural activity was associated with risk of developing cancer in children < 15 years of age. Incidence data for U.S. children 0-14 years of age diagnosed with cancer between 1995 and 2001 were provided by member registries of the North American Association of Central Cancer Registries. The authors determined percent cropland for each county using agricultural census data, and used the overall study distribution to classify agriculturally intense counties. They estimated odds ratios and 95% confidence intervals for all ages and 5-year age groups for total

cancers and selected cancer sites using logistic regression. The study results showed statistically significant increased risk estimates for many types of childhood cancers associated with residence at diagnosis in counties having a moderate to high level of agricultural activity, with a remarkably consistent dose-response effect seen for counties having  $\geq 60\%$  of the total county acreage devoted to farming. Risk for different cancers varied by type of crop.

Conclusions: Although interpretation is limited by the ecologic design, in this study the authors were able to evaluate rarer childhood cancers across a diverse agricultural topography. The findings of this exploratory study support a continued interest in the possible impact of long-term, low-level pesticide exposure in communities located in agriculturally intense areas