Overview of the epidemiologic studies on the health effects of ELF magnetic and electric fields published in the first trimester of 2006 .

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1. **Reviews**

POWER FREQUENCY ELECTROMAGNETIC FIELDS, MELATONIN AND THE RISK OF BREAST CANCER.
Documents of the Health Protection Agency- Series B: Radiation, Chemical and Environmental Hazards, RCE-1, February 2006.

Exposure to power frequency electromagnetic fields (EMFs) is ubiquitous in modern life. The hypothesis that chronic exposure to EMFs may increase the risk of breast cancer, via a reduction in secretion of the hormone melatonin from the pineal gland, was first made almost 20 years ago, and has led to a great deal of research. To review this hypothesis, this report addresses evidence on three issues, namely, whether:

(a) EMFs affect the production or action of melatonin,
(b) melatonin affects the risk of breast cancer,
(c) EMFs affect the risk of breast cancer.

Investigations using cells, animals and humans have not given consistent or convincing evidence that EMF exposure affects melatonin production or action. However, there are deficiencies in the existing research, which leave open the possibility of an effect.

There is stronger evidence that melatonin can inhibit the growth of cancer cells in laboratory culture and in animals. Data on the possible relation of melatonin levels to risk of subsequent breast cancer in humans are limited and inconclusive. Studies investigating the effect of light exposure (which affects melatonin) on breast cancer risk in humans have given some evidence for an association, but left it unclear whether, if there is an association, it is causal in nature.

There is no consistent evidence, from research using cells, animals and humans, that EMF exposure is a cause of breast cancer, nor has any mechanism for such an association been demonstrated.

The report concludes with recommendations for further research.

Conclusion: Overall, the evidence that melatonin, and the timing and extent of light exposure, may affect breast cancer risk is intriguing but inconclusive. In aggregate, the evidence to date does not support the hypothesis that exposure to power frequency EMFs affects melatonin levels or the risk of breast cancer.

CHILDHOOD LEUKEMIA AND RESIDENTIAL MAGNETIC FIELDS: ARE POOLED ANALYSES MORE VALID THAN THE ORIGINAL STUDIES?
Elwood J.M.
Bioelectromagnetics 2006; 27 : 112-118.

The association seen in epidemiological studies between childhood leukemia and magnetic field strength in the child's home has been very important in influencing reviews of international groups and standard setting organizations. This association is usually based on the results of two published pooled analyses, which use

definitions of exposure that differ from those of some the original studies. However, the results and conclusions of the pooled analyses differ from those of the three largest recent studies, which have the most sophisticated methodology and together account for the majority of the exposed cases at high exposure levels in the pooled analyses. These recent studies, using the exposure methods and the cut-off levels set a priori, each concluded that there was little evidence of any association. The pooled analyses, using different exposure measures and different cut-offs, conclude that an association exists at high exposure levels.
Conclusion: It is not clear if the results of the pooled analysis are more valid than those of the recent major studies, although this has been often assumed in influential reviews.

MAGNETIC FIELD EXPOSURE AND CHILDHOOD LEUKAEMIA—MOVING THE RESEARCH AGENDA FORWARD
Röösli M., Künzli N.
Int J Epidemiol. 2006; 35 : 407-408.

An association between childhood leukaemia and exposure to extremely low-frequency magnetic fields (ELF-MF) has been consistently documented in reviews of this field of research. Nevertheless, the relationship remains questionable because the risks were observed at exposure levels where biological effects are not assumed to occur. Animal data have mostly been negative and a plausible and reproducible biological mechanism is still lacking. Studies on adult leukaemia in populations with much higher occupational ELF-MF exposures are inconclusive, though a trend towards an increased risk among highly exposed workers has been noted by the International Commission on Non-Ionizing Radiation Protection. Thus, there is ongoing debate among scientists as to whether the observed statistical association between incidence of childhood leukaemia and exposure to residential ELF-MF is primarily due to bias.

Three main sources of bias have been identified as being potentially important to this field of inquiry: confounding, exposure misclassification, and selection bias. It has previously been shown that confounding due to an unknown, aetiologically relevant correlate of ELF-MF levels (e.g. traffic density) is unlikely to be important in this context. Exposure misclassification is likely to be non-differential and is expected to result in an underestimation of the true exposure–response association.

Mezei and Kheifets' work supports the hypothesis that the observed association between childhood leukaemia and exposure to magnetic fields from power lines is unlikely to be explained by selection bias.

LEUKEMIA ATTRIBUTABLE TO RESIDENTIAL MAGNETIC FIELDS: RESULTS FROM ANALYSES ALLOWING FOR STUDY BIASES.
Greenland S., Kheifets L.
Risk Anal. 2006; 26 : 471-482.

Nearly every epidemiologic study of residential magnetic fields and childhood leukemia has exhibited a positive association. Nonetheless, because these studies suffer from various methodologic limitations and there is no known plausible mechanism of action, it remains uncertain as to how much, if any, of these associations are causal. Furthermore, because the observed associations are small and involve only the highest and most infrequent levels of exposure, it is believed that the public health impact of an effect would be small. The authors present some formal analyses of the impact of power-frequency residential magnetic-field

exposure (as measured by attributable fractions), accounting for our uncertainties about study biases as well as uncertainties about exposure distribution. These analyses support the idea that the public health impact of residential fields is likely to be limited, but both no impact and a substantial impact remain possibilities in light of the available data.

DO EXTREMELY LOW FREQUENCY MAGNETIC FIELDS ENHANCE THE EFFECTS OF ENVIRONMENTAL CARCINOGENS? A META-ANALYSIS OF EXPERIMENTAL STUDIES.
Juutilainen J., Kumlin T., Naarala J.
Int J Radiat Biol. 2006; 82 :1-12.

This paper is a meta-analysis of data from in vitro studies and short-term animal studies that have combined extremely low frequency magnetic fields with known carcinogens or other toxic physical or chemical agents.
The data was analyzed by systematic comparison of study characteristics between positive and negative studies to reveal possible consistent patterns.
The majority of the studies reviewed were positive, suggesting that magnetic fields do interact with other chemical and physical exposures. Publication bias is unlikely to explain the findings. Interestingly, a nonlinear 'dose-response' was found, showing a minimum percentage of positive studies at fields between 1 and 3 mT. The radical pair mechanism (magnetic field effects on recombination of radical pairs) is a good candidate mechanism for explaining the biphasic dose-response seen in the present analysis.

Conclusion: Most of the studies reviewed used magnetic fields of 100 microT or higher, so the findings are not directly relevant for explaining the epidemiological findings suggesting increased risk of childhood leukemia above 0.4 microT. However, confirmed adverse effects even at 100 microT would have implications for risk assessment and management, including the need to reconsider the exposure limits for magnetic fields. There is an obvious need for further studies on combined effects with magnetic fields.

2. Residential exposure

CHILDHOOD LEUKEMIA AND MAGNETIC FIELDS IN JAPAN: A CASE-CONTROL STUDY OF CHILDHOOD LEUKEMIA AND RESIDENTIAL POWER-FREQUENCY MAGNETIC FIELDS IN JAPAN.
Kabuto M., Nitta H., Yamamoto S., Yamaguchi N., Akiba S., Honda Y., Hagihara J., Isaka K., Saito T., Ojima T., Nakamura Y., Mizoue T., Ito S., Eboshida A., Yamazaki S., Sokejima S., Kurokawa Y., Kubo O.
Int J Cancer 2006 [Epub ahead of print]

Residential power-frequency magnetic fields (MFs) were labeled as a possible human carcinogen by the International Agency for Research on Cancer panel. In response to great public concern, the World Health Organization urged that further epidemiologic studies be conducted in high-exposure areas such as Japan. The authors conducted a population-based case-control study, which covered areas inhabited by 54% of Japanese children. They analysed 312 case children (0-15 years old) newly diagnosed with acute lymphoblastic leukemia (ALL) or acute myelocytic leukemia (AML) in 1999-2001 (2.3 years) and 603 controls matched for gender, age and residential area. Weekly mean MF level was determined for the child's bedroom. MF measurements in each set of a case and controls were carried out as closely in time as possible to control for seasonal variation. The association was evaluated using conditional logistic regression models. The odds ratios for children whose bedrooms

had MF levels of 0.4 µT or higher compared with the reference category (MF levels below 0.1 µT) was 2.6 (95% CI = 0.76-8.6) for AML + ALL and 4.7 (1.15-19.0) for ALL only. Controlling for some possible confounding factors did not alter the results appreciably. Even an analysis in which selection bias was maximized did not fully explain the association. Most of the leukemia cases in the highest exposure category had MF levels far above 0.4 µT.

Conclusion: These results provided additional evidence that high MF exposure was associated with a higher risk of childhood leukemia, particularly of ALL.

MAGNETIC FIELD EXPOSURE AND LONG-TERM SURVIVAL AMONG CHILDREN WITH LEUKAEMIA.

Foliart D.E., Pollock B.H., Mezei G., Iriye R., Silva J.M, Ebi KL, Kheifets L, Link MP, Kavet R.

Br J Cancer 2006; 94 : 161-164.

The authors examined the association between magnetic field (MF) exposure and survival among children with acute lymphoblastic leukaemia (ALL) treated at 51 Pediatric Oncology Group centres between 1996 and 2001. Of 1672 potentially eligible children under treatment, 482 (29%) participated and personal 24-h MF measurements were obtained from 412 participants. A total of 386 children with ALL and 361 with B-precursor ALL were included in the analysis of event-free survival (time from diagnosis to first treatment failure, relapse, secondary malignancy, or death) and overall survival. After adjustment for risk group and socioeconomic status, the event-free survival hazard ratio (HR) for children with measurements ≥ 0.3 µT was 1.9 (95% confidence interval (CI) 0.8, 4.9), compared to < 0.1 muT. For survival, elevated HRs were found for children exposed to ≥ 0.3 µT (multivariate HR=4.5, 95% CI 1.5-13.8) but based on only four deaths among 19 children.

Conclusion: While risk was increased among children with exposures above 0.3 µT, the small numbers limited inferences for this finding.

3. Occupational exposure

OCCUPATIONAL EXPOSURE TO POWER FREQUENCY MAGNETIC FIELDS AND RISK OF NON-HODGKIN LYMPHOMA.

Karipidis K.K., Benke G., Sim M., Fritchi L., Yost M., Armstrong B., Hughes A.M., Grulich A., Vajdic C.M., Kaldor J.M., Kricker A.

Occup Environ Med. Published online 21 mar 2006

The purpose of this population-based case control study was to investigate the risk of non- Hodgkin lymphoma (NHL) using a job-exposure matrix (JEM) to assess exposure to occupational magnetic fields at the power frequencies of 50/60 Hz.
The study population consisted of 694 cases of NHL, first diagnosed between 1st January 2000 and 31st August 2001, and 694 controls from two regions in Australia, matched by age, sex and region of residence. A detailed occupational history was given by each subject. Exposure to power frequency magnetic fields was estimated using a population-based JEM which was specifically developed in the United States to assess occupational magnetic field exposure. The cumulative exposure distribution

was divided into quartiles and adjusted odds ratios were calculated using the lowest quartile as the referent group.
For the total work history, the odds ratio (OR) and 95% confidence interval (95% CI) for workers in the upper quartile of exposure was 1.48 (95% CI= 1.02 to 2.16) compared to the referent (p value for trend was 0.006). When the exposure was lagged by 5 years the OR was 1.59 (95% CI = 1.07 to 2.36) (p value for trend was 0.003). Adjusting for other occupational exposures did not significantly alter the results.

Conclusion: These findings provide weak support for the hypothesis that occupational exposure to 50/60 Hz magnetic fields increases the risk of NHL.

OCCUPATIONAL MAGNETIC FIELD EXPOSURE AND THE RISK OF ACOUSTIC NEUROMA.
Forssen U.M., Lonn S., Ahlbom A., Savitz D.A., Feychting M.
Am J Ind Med. 2006; 49 : 112-118.

Acoustic neuroma is the intracranial tumor subtype showing the highest relative risk in relation to ionizing radiation but other environmental risk factors are largely unknown. This study was performed to investigate the effect of power frequency magnetic fields. A total of 793 cases between 1987 and 1999 were identified through the Swedish cancer registry and 101,762 controls were randomly selected from the total population. Information about occupation was obtained from censuses and linked to gender specific job-exposure matrices based on actual measurements of 50 Hz magnetic field exposure.
The authors investigated time-weighted average, peak values, and rate of change of magnetic field exposure considering several different time windows in relation to cancer diagnosis. They found no increases in risks regardless of exposure metric or time window of exposure.

Conclusion: This study is the largest ever on acoustic neuroma and the first study to evaluate this tumor subtype specifically in relation to extremely low frequency magnetic fields. The results do not support the hypothesis that 50 Hz magnetic fields increase the risk of acoustic neuroma.

PHYSICAL ACTIVITY AND MAGNETIC FIELD EXPOSURE IN PREGNANCY.
Savitz D.A., Herring A.H., Mezei G., Evenson K.R., Terry J.W. Jr, Kavet R.
Epidemiology 2006;17 : 222-225.

Peak magnetic field exposure was associated with increased risk of miscarriage in 2 recent studies. Reduced physical activity levels in healthy pregnancies may affect measured exposure and thus bias results.
The authors recruited 100 pregnant women to wear an Actigraph accelerometer and EMDEX magnetic field monitor for a 7-day period. They evaluated the association between physical activity and magnetic field exposure (peaks and time-weighted average) using generalized estimating equations and linear mixed models.
They found a positive association between level of activity and likelihood of incurring elevated exposure in the person-day analysis, most strongly for cutpoints of 16 or 20 mG, for both working and nonworking women among whom odds ratios in the uppermost quartile ranged from 2.1 to 2.6. A positive association was found using person-minutes only among nonworking women.

Conclusion: Physical activity may affect peak magnetic field exposure. If the early nausea and later cumbersomeness of healthy pregnancies leads to reduced physical activity, this could distort measured magnetic field-health outcome associations.

4. Human experimental studies

EFFECTS OF 50 HZ MAGNETIC FIELD EXPOSURE ON HUMAN HEART RATE VARIABILITY WITH PASSIVE TILTING.

Sait M.L., Wood A.W., Kirsner R.L.

Physiol Meas. 2006; 27 : 73-83.

The question of whether power-frequency magnetic fields of strengths relevant to industrial exposure can affect heart rhythm remains controversial. Because the reported effects on heart rate (HR) are so small, procedures which can provoke changes in the sympathovagal balance in a controlled manner may have a greater capacity for identifying subtle field-related changes, if they do exist. The authors have investigated HR and heart rate variability (HRV) spectral indices in 20 volunteers subjected to a tilt from the supine position to 60 degrees , head up. The tilting procedure was carried out under two conditions, field (28 microT resultant, circularly polarized) and sham, in a balanced double-blind design. Subjects were instructed to breathe in time with an audible cue at 2.5 s intervals.

Conclusion: Although the anticipated significant changes in HR and the high frequency (HF), low frequency (LF) and LF/HF ratio (log transformed) occur with tilting, there were no significant differences between corresponding measures with and without exposure to magnetic fields (tilt ln LF/HF ratio 0.94 +/- 0.19 and 0.95 +/- 0.20 for sham and field, respectively). There was also no evidence of a field-related trend in spectral alterations when the time following tilting was divided into three 256 s epochs.

TRANSIENT EFFECT OF LOW-INTENSITY MAGNETIC FIELD ON HUMAN MOTOR CONTROL.

Legros A., Gaillot P., Beuter A.

Med Eng Phys. 2006; [Epub ahead of print]

There is no consensus with respect to how extremely low frequency (ELF) magnetic fields (MF) affect biological systems. However, this information is crucial to establishing new guidelines for: (i) the new design of electronic devices, (ii) working conditions of exposed workers (e.g. electric linepersons), and in a general manner (iii) policies for human risk management. This study evaluates the effect of a sinusoidal 50Hz, 1000muT MF centered at the level of the head on human postural tremor of the index finger, using the wavelet analysis method. In addition to the detection of transient events in tremor time series linked with MF, this method was used to evaluate the differences between MF "on" and "off" conditions and between real and sham exposure in a counterbalanced protocol. Results indicate that neither transient events nor "off-on" or "on-off" MF transition effects were present in the postural tremor time series. Surprisingly, an unexpected significant time dependent decrease in tremor average power was noted along the 20s recordings. Interestingly, this effect was significantly more pronounced in the presence of MF.

Conclusion: These results suggest a relaxing effect of ELF MF on motor control resulting in an attenuation of postural tremor intensity.