ELECTROMAGNETIC FIELDS AND CANCER: HOW ICNIRP HAS DEALT WITH THE ISSUE

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INTRODUCTION

Whether exposure to electromagnetic fields (EMFs) cause cancer has been vigorously debated for many years and has been the most vexing issue with which ICNIRP has had to deal during its short existence. There have been three parts of the electromagnetic spectrum that the issue of cancer has raised: static (0 Hz) magnetic fields, extremely low frequency (ELF) fields (defined as >0 - 300 Hz, but concerns have been raised almost exclusively at the power frequencies of 50/60 Hz), and radiofrequency (RF) fields (300 Hz - 300 GHz). By far the major problems have arisen during the contruction of new high voltage transmission lines and mobile telephone systems. Actions by protest groups concerned with possible health effects, especially with cancer in children, has now reached such a scale that it is costing electrical utilities and communications companies billions of dollars annually world-wide. With such high stakes, ICNIRP has had to be extremely careful in its evaluation of the scientific literature, use valid and defensible methods of literature review, and be completely independent of any special interest groups.

ICNIRP has had to continuously monitor the scientific literature to determine if any studies provide evidence strong enough to warrent a re-evaluation of the guidelines on exposure limits. This has been an increasing problem, particularly in this age of rapid communications (eg INTERNET), where information on new studies is quickly disseminated, evaluated and distributed to various special interest groups around the world who want to know what these studies will mean with respect to standards.

ICNIRP is a collaborator in a the International EMF Project with WHO, the International Agency for Research on Cancer, and many other international and national organizations having responsibility for EMF protection. The objectives of the Project are as follows:

(i) Pool resources of international and national agencies and key scientific institutions in the environmental health domain working on the biological effects of electromagnetic fields.

(ii) Identify gaps in scientific knowledge, provide protocols for the conduct of this research and encourage research in those areas that will lead to better health risk assessments.

(iii) Provide authoritative, independent, scientific, peer-review of the scientific literature, with fully substantiated recommendations.

(iv) Publish an updated EHC monograph giving a health risk assessment using results obtained during the Project on health effects of exposure to static, ELF and RF fields. This monograph would clearly differentiate between well established effects and those requiring further research.

(v) Publish an EHC monograph on risk perception, risk communication and risk management, and public and occupational health policy.

(vi) Publish reports on appropriate topics to assist and support national health programs.

(vii) Use modern efficient means of communicating essential research information and findings which develop during the project.

It should be clearly understood that ICNIRP is a full partner in this Project and that the conclusions on health risk will assist ICNIRP to draft its own guidelines on exposure limits. A more complete description of the Project is available from WHO.

This paper summarises what criteria ICNIRP uses to review the literature, its response to EMF exposure and cancer, and its current position on static, ELF and RF fields.

HOW ICNIRP ASSESSES THE SCIENTIFIC LITERATURE

Scientific studies are in three categories:

(i) ***In-vitro studies*** conducted on isolated components of biological systems such as solutions of molecules (eg DNA), cultures of cells, or pieces of tissue. These studies are important for determining possible mechanisms by which EMF fields interact with biological systems and for identifying appropriate end-points and exposure conditions to be tested in whole animals. Determining mechanisms of interaction is important to give an understanding of how EMF fields act at the molecular or cellular level, and thus allow an extrapolation to the whole animal level. Studying simple systems allows interactions to be detected that may be masked in the complexity of interactions that occur normally at the whole animal level. It is because of this that biological effects found to occur at the molecular or cellular level cannot be assumed to occur at the whole animal level. Thus biological end-points found in-vitro must still be tested *in-vivo.*

(ii) ***In-vivo studies*** are conducted on complete biological systems such as laboratory animals. The great advantage of these studies is that they are conducted under carefully controlled laboratory conditions where all environmental and exposure parameters are kept constant. The only difference between exposed and unexposed animals should be the actual exposure to EMF fields they receive. Since experiments cannot normally be conducted on humans, animal studies are very useful for making health risk assessments related to human exposure. However, when evaluating animal studies, it is important to remember that the results of these studies are only applicable to humans if the effects observed occur in a number of different animal models. This is necessary because one particular animal model may be extremely sensitive to a particular end-point and have characteristics that are not observed in humans.

(iii) ***Human studies*** can be conducted on volunteers in the laboratory or on different populations of people in the living and working environment. Laboratory studies are conducted with the approval of the volunteer, and have the advantage of allowing exposures under strictly controlled conditions (as with animal studies). However the end-points that can be studied are limited. End-points such as cancer and mortality obviously cannot be studied on laboratory volunteers.

Studies on populations are called ***epidemiological studies*** and have the advantage of being non-intrusive. They compare the differences in the incidence of or mortality from some predetermined disease or diseases in populations. Generally one population is exposed to EMF fields and is compared with a population not exposed or at least having a much lower exposure to EMF fields. The major difficulty is to obtain two identical groups in sufficient numbers where the only difference is their exposure. This can become a significant problem when studying rare diseases such as cancer. However, these studies can indicate differences in the incidence of disease; the difficulty then being to attribute this difference to the EMF exposure and not some other factor in the living or working environment that is not detected as a difference between the two groups (eg chemical exposure in the workplace).

Criteria for evaluating scientific studies

When reviewing the scientific literature, certain criteria must be met if claims of a positive or negative effect are to be accepted into the database for conducting a human health risk assessment (Repacholi & Stolwijk 1991):

1) Experimental techniques, methods and conclusions should be as completely objective as possible, using biological systems appropriate to the end-points studied. To safeguard against bias, researchers should use double-blind techniques. Appropriate controls must be used for valid comparison of results. The sensitivity of the experiment must be such that there is a reasonable probability that an effect could be detected if it exists.

2) All data analyses should be fully and completely objective, no relevant data should be deleted from consideration and uniform analytical methods used. Data from experiments within the same protocol should be internally consistent.

3) The published descriptions of the methods should be given in sufficient detail that a critical reader would be convinced that all reasonable precautions have been taken to meet requirements 1 and 2.

4) Results should demonstrate an effect of the relevant variable at a high level of statistical significance using appropriate tests. The effects of interest should ordinarily be shown by a majority of test organisms and the responses found should be consistent.

5) Results should be quantifiable and susceptible to confirmation by independent researchers. Preferably the experiments should be repeated and the results confirmed independently; or the claimed effects should be consistent with results of similar experiments, where the biological systems are comparable.

6) Results should be viewed with respect to previously accepted scientific principles before ascribing them new ones.

While it will not be possible for all the above criteria to be applied to all experiments, these criteria provide a guide when determining what effects are established and can be used in a health risk assessment, and those that merely raise a hypothesis that needs to be tested, or those results which should be considered as preliminary and needing confirmation. Information from the various types of laboratory and human studies, including the limitations in the amount of information they can provide, is also taken into account when conducting health risk assessments.

Assessment of epidemiological studies

Epidemiological demonstration of an association between two variables need not imply causality - both may be due to a common factor. However, establishment of causality is enhanced if (Miller 1986, 1989):

a) the presumed causal event precedes the effect,

b) one rather than multiple cancers are caused by a given exposure; giving specificity of effect,

c) a dose-response relationship exists,

d) there is consistency with other observations on cause and effect,

e) there is the exclusion of concomitant variables, or no alternative explanations,

f) the effect disappears when the cause is removed, and

g) the results are consistent with those from animal experimentation and other human observations.

Not all of these factors can be evaluated or will be true for even the most fully studied effects of an environmental exposure. It is known for example, that ionizing radiation induces various but not all forms of cancer. However, laboratory evidence is normally necessary to support the human studies. In other words, if there is truly a link between exposure to EMF and cancer, one would expect that laboratory studies on animals should show that EMF can cause cancer. If the laboratory studies do not show this and the human studies suggest only a weak association, then most likely there are problems with the human studies and they are not reaching valid conclusions.

What are the factors that must be taken into account when reviewing the epidemiological studies? What problems could affect the validity of associations found in epidemiological studies? There are four factors that could result in false associations in epidemiological studies:

- **inadequate dose assessment:** It is necessary to determine with some reasonable accurately a person's exposure to EMF. If these fields are associated with cancer, what aspect of the field is involved? To date it has been very difficult to gain incites into what should be considered as our concept of "dose" for EMFs.

- **confounders:** Other cancer risk factors could be causing a false association between exposure to EMFs and risk of cancer. Associations between things are not always evidence for causality. Exposure may be associated with a cancer risk other than EMFs. If such an associated cancer risk were identified it would be called a "confounder" of the epidemiological study. An essential part of epidemiological studies is to identify and eliminate possible confounders. Possible confounders may be exposure to herbicides and chemicals such as PCBs, traffic density, socio-economic class and population mobility.

- **inappropriate controls:** The control groups must be selected to match as closely as possible all aspects (age, sex, socio-economic status, occupation etc) of the cancer cases (in a case-control study, which most of the epidemiological study reports are). An inherent problem with many epidemiological studies is the selection of a "control" group that is identical to the "exposed" group for all characteristics related to the disease except the exposure. This is especially difficult for rare disease such as leukaemia and brain cancer where the risk factors are poorly known. An additional complication is that people must consent to be in a "control" in a study, and participation in such studies is known to depend on many factors such as socio-economic class, race and occupation which are linked to differences in cancer rates.

- **publication bias:** Studies reporting positive results are much more likely to be accepted for publication than those with negative results. This would have the effect of skewing any analyses of a number of studies and severely bias meta-analyses that attempt to combine all studies (positive and negative) to investigate trends from a group of studies. Such study groups may erroneously contain more positive studies if negative studies are not published. This can happen because scientific journals are more interested in these for sales and publicity purposes or authors may not feel inclined to publish. Publication bias can thus increase apparent risks. This can effect both epidemiological as well as laboratory studies. Several specific examples of publication bias are known in studies of electrical occupations and cancer (see NRPB 1992). In their review Coleman and Beral (1988) reported the results of a Canadian study that found a RR of 2.4 for leukaemia in electrical workers. However, NRPB (1992) found that further follow-up of the same Canadian workers showed a deficiency of leukaemia (a RR of 0.6), but that this has never been published.

In reviewing the scientific literature, these factors must be taken into account to reach valid, supportable conclusions.

STATIC MAGNETIC FIELDS

There has been increasing concern among workers and the general public that exposure to static magnetic fields may be detrimental to health. This concern has been heightened by the increasing number of sources of exposure to these fields, and the ongoing debate about the possibility that exposure to 50/60 Hz magnetic fields may increase the incidence of cancer, with the implication that static magnetic fields may also be carcinogenic. Concerns have also been expressed because the next generation of train will use static magnetic fields (the magnetic levitation trains). The trains would expose very large numbers of people to quite strong static magnetic fields. In the field of medical diagnosis, magnetic resonance imaging units now expose patients and operators to magnetic fields as strong as 2 T. In the future, magnetic resonance spectroscopy could expose patients to fields up to 10 T.

Static magnetic fields are produced either by permanent magnets or whenever a direct current (DC) flows in a conductor. Direct currents are used to plate metals onto electrodes and so static magnetic fields are produced around the electrolysis tanks. Magnetic fields are not appreciably distorted or attenuated by the human body. However they induce electrical currents in the body wherever there are moving parts (eg heart pumping or the body moving through the magnetic field). Thus, while adverse effects (such as involuntary nerve and muscle stimulation) could occur as a result of these induced currents, the cancer issue still had to be addressed.

ICNIRP completed a thorough review of the available literature on static magnetic fields in conjunction with the World Health Organization (UNEP/WHO/IRPA, 1987) and published a statement on magnetic resonance imaging (INIRC/IRPA, 1991). ICNIRP guidelines on exposure limits to static magnetic fields were published in 1994 (ICNIRP, 1994). No substantiated evidence was found to suggest that exposure to these fields is in anyway carcinogenic.

ELF FIELDS

Many studies have suggested that children exposed to 50/60 Hz magnetic fields, determined by residence near high current electrical installations (high voltage transmission lines, high current distribution lines, pole transformers etc) were at an increased risk of leukaemia or brain tumours. Later studies, using direct measurements and calculations of historical magnetic fields, have also suggested an increased risk of childhood cancer, and an increased carcinogenic risk in workers whose occupations have a higher exposure to magnetic fields.

Childhood epidemiological studies, when considered together, suggest there may be an association between cancer and exposure to 50/60 Hz magnetic fields. However, the average odds ratio for these studies is only of the order of 2.0. These odds ratios are quite small when one compares the odds ratios for cancer induction reported for smoking and X-ray exposure. When the odds ratios are so low, it would be more convincing that a true association exists if there were well conducted and independently confirmed laboratory studies indicating that 50/60 Hz field-exposure of animals or some recognised biological systems would either cause cancer directly or provide reasonable evidence that these fields influence the process of carcinogenesis. It is not necessary that a mechanism be found which would explain how such exposure had a carcinogenic effect, but merely that when the effect was found, it was statistically significant and independently replicated, and that a clear link with human cancer was established. Evidence from the animal studies to support the epidemiological evidence is lacking (Repacholi 1995).

Another major problem with these studies has been the lack of a clearly defined magnetic field measure (no concept of "dose" or the biologically active component of the magnetic field). In addition, many studies have had very low numbers of cases. To determine if a subtle effect exists on the incidence of rare cancers from magnetic field exposure, large numbers of cases and controls are needed. Of great concern has been the lack of consistency between study results. Some studies have suggested an increased leukaemia risk but not brain tumours while others have suggested exactly the opposite or reported no effect on cancer incidence at all. The problems with the 50/60 Hz epidemiological studies has lead to the necessity to conduct large animal studies to determine if indeed magnetic field exposure leads to an increased incidence of cancer.

ICNIRP has had to be very vigilent in this area because of the division of scientific opinion and more recently because of the unfortunate "leak" of a draft report from a National Commission on Radiological Protection and Measurement (NCRP) subcommittee responsible for identifying health effects of ELF fields. Aside from the guidelines on exposure limits to 50/60 Hz fields issued in 1990 (INIRC/IRPA, 1990), ICNIRP reviewed the literature and reaffirmed the guidelines by issue a press release in 1993 (ICNIRP, 1993). ICNIRP is currently reviewing the scientific literature and drafting a set of guidelines that will provide exposure limits for electromagnetic fields from 0-300 GHz.

RADIOFREQUENCY FIELDS

It has also been suggected for many years that exposure to radiofrequency fields may also be associated with an increased incidence of cancer. Most recently ICNIRP has been confronted with concerns of people who find mobile telephone towers built near their home or schools. In addition there is the problem of the use of the mobile telephones themselves. They present an near-field exposure situation not anticipated by the RF guidelines published in 1988 (INIRC/IRPA 1988). In collaboration with WHO, INIRC/IRPA reviewed the RF literature and this was published in 1993 (UNEP/WHO/IRPA 1993). However, the issue of mobile telephones and their base stations resulted in the need to study possible effects from pulsed RF fields. ICNIRP has completed a review and is publishing the statement entitled "Health issues related to the use of hand-held radiotelephones and base transmitters" (ICNIRP 1996). A briefly summary of the reviewe is given below.

No consistent biological effect has been found in molecules or components of body cells exposed to RF fields, other than those effects caused by temperature increases. Researchers in the US reported that modulated microwave exposure of chromosomally abnormal cells which were treated with X-rays and a chemical promoter showed an accelerated rate of change from normal to cancer cells (Balcer-Kubiczek and Harrison 1991). While inconsistencies have been noted between various of these studies, the results are important. However, their implications for carcinogenesis in humans are not clear. This type of study tends to be susceptible to a variety of experimental confounding factors and needs independent confirmation.

Possible effects on DNA and chromosome structure are an important consideration in somatic cells, where such changes could lead to cell death or the development of cancers. If these changes occur in the male or female germ cells, surviving mutations might be passed on to the next generation. A large number of studies have been conducted in various somatic cells (Saunders et al 1991; NRPB 1992, 1993; UNEP/WHO/IRPA 1993) and most have reported a lack of effect on chromosome aberrations and single or double strand breaks in the DNA. Studies on the germ cells also suggests that acute or chronic exposure to RF does not result in increases in mutation or chromosome aberration frequency when the temperature is maintained within physiological limits. Where increased frequencies of chromosomal aberrations have been reported, these studies have not been successfully replicated. Chronic exposure experiments, which are relevant to long term RF exposure from base stations, have not produced any evidence of chromosomal aberrations in rodents exposed to SARs from 1-5 W/kg (UNEP/WHO/IRPA 1993).

In two recent rodent studies, there is the suggestion that RF fields may affect DNA directly. When mice were exposed to 2.45 GHz fields at 1 mW/cm^2 (SAR 1.18 W/kg) for 2 h/d for 120, 150 and 200 days, there was an indication of structural genomic rearrangement in brain and testes cells (Sarkar et al 1994). Lai and Singh (1995) report that rats exposed to pulsed (2 μs pulses, 500 pps) or continuous wave 2.45 GHz fields with SARs of 0.6 or 1.2 W/kg for 2 h increased the number of single stand breaks in brain DNA. Both these papers produce quantitative data subject to sources of inter-trial variation and experimental error such as incomplete DNA digestion (Sarkar et al) or unusually high levels of background DNA fragmentation (Lai and Singh). These experiments should be replicated before the results can be used in any health risk assessment, especially given the weight of evidence suggesting that RF fields are not genotoxic (UNEP/WHO/IRPA1993).

A review of the laboratory studies conducted with WHO (UNEP/WHO/IRPA1993) concluded that RF field exposure is not mutagenic and is therefore unlikely to initiate damage directly to the DNA which would lead to cancer. The evidence for RF exposure causing tumour promotion or progression is not convincing but deserves further investigation.

Epidemiological studies have been conducted to assess the general health patterns and cancer risk among several groups of workers that were occupationally exposed to RF fields. These studies involved radar workers (Robinette et al 1980) and Moscow embassy workers chronically exposed to low-intensity microwaves for surveillance purposes (Lillienfeld et al. 1978). One of the more important studies conducted so far were the large epidemiological studies on Korean War radar technicians exposed to various levels of RF. No adverse health effects were established.

CONCLUSIONS

There is very little evidence to suggest that static fields have an effect on any stage of carcinogenesis. The major animal studies provide little convincing evidence that 50 Hz fields can promote cancer. There is some evidence that 50/60 Hz magnetic fields may be cancer co-promoters in tissues that are in the process of carcinogenesis, but the health impact of such a finding remains unclear.

With respect to whole-body RF exposure, the conclusions of the 1988 IRPA/INIRC guidelines remain valid. However, additional guidance has been given for mobile telephones. The conclusions of the ICNIRP (1996) statement are given below.

1. The results of published epidemiological studies do not form a basis for health hazard assessments of exposure to RF fields, neither can they be used for setting quantitative restrictions on human exposure. They do not provide a basis for hazard assessments in relation to the use of hand-held radiotelephones and base transmitters.

2. Data from laboratory studies relevant to cancer do not provide a basis for limiting exposure to the fields associated with the use of hand-held radiotelephones and base transmitters.

3. Limits for human exposure to the fields associated with the use of hand-held radiotelephones and base transmitters should be those of the INIRC (IRPA/INIRC 1988) for whole body average SAR and those of ICNIRP for localised SAR set out in this document.

4. There is no substantive evidence that adverse health effects, including cancer, can occur

in people exposed to levels at or below the limits on whole body average SAR recommended by INIRC (IRPA/INIRC 1988), or, at or below the ICNIRP limits for localised SAR set out in this document.

5. At the frequencies and power levels involved in the use of hand-held radiotelephones there will be no concern about shocks and burns.

6. The localised SARs in the head associated with the use of hand-held radiotelephones must be assessed for each frequency and configuration used.

7. For hand-held radiotelephones used in occupational situations, ICNIRP recommends that the localised SAR in the head be limited to 10 W kg^{-1} averaged over any 10 g mass of tissue in the head (0.1 W absorbed in any 10 g mass of tissue in the head).

8. For hand-held radiotelephones used by the general public, ICNIRP recommends that the localised SAR in the head be limited to 2 W kg^{-1} averaged over any 10 g mass of tissue in the head (0.02 W absorbed in any 10 g mass of tissue in the head).

9. The use of radiotelephones should be restricted to areas where interference effects are unlikely to occur (for example, well away from hospital intensive care departments and similar locations). Manufacturers of electrical equipment are encouraged to design and manufacture equipment that is insensitive to RF interference.

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