Symposium 2000: Low frequency EMF, Visible Light, Melatonin and Cancer

Summaries of proceedings

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Summary of International Symposium Entitled 'Low Frequency EMF, Visible Light, Melatonin and Cancer'

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The potential relationship of melatonin and cancer has been widely discussed in recent years. Since melatonin is a known oncostatic agent, any factor that depresses its production, secretion or actions in humans may contribute to an increased cancer risk. This was the basis of this symposium inasmuch as light exposure at night unequivocally reduces the nocturnal rise in melatonin levels in the blood. Furthermore, exposure to extremely low frequency electromagnetic fields (EMF) has reported effects on circulating melatonin levels. The EMFs of interest were those to which humans are exposed near transmission lines, electrical appliances, etc. The meeting in Cologne brought together experts from around the world to discuss the state of knowledge in these fields.

Clearly, the incidence of at least certain types of cancer, e.g., breast cancer, has increased substantially with increased industrialization. The implication is that this rise in cancer is somehow related to economic development. One feature that is commonplace throughout the world today is the use of electricity. Indeed, the consumption of electric power increased several 1000-fold during the 20th century. With this increased use there is obviously an increased exposure to light at night (when it would normally be dark) and augmented exposure to EMF. About 10 years ago it was proposed that the rise in cancer incidence may be a consequence of a generalized reduction in melatonin.

The presentation at the Cologne meeting discussed the information in this area in depth. The first day was primarily devoted to considering the interactions of excessive light exposure (or lack of any light exposure, i.e., blindness) on cancer incidence. Clearly, even low light intensities can reduce circulating levels of melatonin in humans. This light pollution limits melatonin production in at least two ways. Firstly, turning on lights at sundown and lights on when we awaken in the morning limits the production of melatonin to the period of sleep, which is often of shorter duration than the period of environmental darkness. This truncates the period during which melatonin is poduced. Likewise, acute exposure to light at night, if of sufficient intensity, suppresses melatonin production.

It was in this context that several presentations discussed the incidence of cancer in profoundly blind (with no light perception) individuals while others considered cancer incidence in humans living at the extremes of latitude where day length and night length vary markedly as a function of season. The results of these reports, considering in view of light suppression of melatonin, generally imply that visual impairment in terms of light perception and winter darkness may contribute to reduced cancer incidence in humans.

The second day of the symposium considered in depth the potential relationship of EMF exposure to melatonin suppression and cancer. These interactions are clearly more enigmatic. While many, but not all, animal studies indicate EMF exposure may suppress melatonin and increase cancer incidence, the results sometimes vary diametrically when seemingly identical studies are performed. Attempts were made to reconcile these different outcomes and there do appear to be some potential explanations which can, and hopefully will, be experimentally tested.

Besides these issues there were excellent presentations regarding alternative explanations (other than EMF exposure) for the alleged increase in cancer incidence in individuals linging in the vicinity of high power lines. Furthermore, a couple of reports summarized, by means of meta-analysis, the outcomes of a large number of epidemiological studies. These studies contributed to our understanding of the complexities of such investigations and pointed out where further studies could be improved.

Overall, I personally found the meeting highly informative and, in discussion with other participants, this opinion was clearly shared by many. The audience and the speakers were multidisciplinary further contributing to an interesting and worthwhile meeting. Unequivocally, the meeting was a major success and helped to clarify and focus an area of research that has, on occasions, been exasperating.

Brief Report of a Conference on Low Frequency Electro-Magnetic Fields, Visible Light, Melatonin and Cancer

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New ideas and new concepts rarely come into the world without long and painful gestation periods. This may be more true at the beginning of the 21st century than at any earlier period of history.

This situation is an inevitable consequence of the success of science, technology and medicine. When science and medicine were relatively unsuccessful and the occupations of the tiniest of minorities within society it was easier to get a hearing for new ideas and easier to get them accepted. Old ideas, because of the limited size of the scientific enterprise, always had limited numbers of supporters. Such supporters often held their views as tenaciously as any modern scientist, but it was not difficult at least to get a hearing for the new. Only relatively limited numbers of people had to be persuaded to change for the new to gain a significant voice. This situation does not hold true now. Every established concept in any field which matters is supported by large numbers of researchers - and often by substantial corporate or state interests - all of whom have a strong vested interest in the broad status quo. Minor improvements in the established concept are lauded excessively as brilliant achievements and disseminated rapidly. Challenges to the established concept which provide quite different sorts of world view as derided are absurd and not worth considering. So many people and so many organisations, both state and private, have so much to lose that radically new concepts are often not heard, let alone accepted.

The possible effects of physical forces on biological phenomena, and particularly on illness, represent such a radical challenge to the established world view. The challenge is to the individual philosophies of both biomedical and physical scientists and also to the vested interests of the state and of private industry. Non-natural physical forces, whether they be internal or external lighting, or the enormous varieties of electromagnetic radiation emanating from domestic and industrial appliances, have been introduced into our world with virtually no testing of the potential adverse or, indeed, beneficial effects on human health. As a crude generalisation, physical scientists have little understanding of biology and biological scientists have little understanding of physics. The idea that physical forces from the environment might have biomedical effects tends to be automatically dismissed by both sides without rational thought. The similar dismissal by state, parastatal and private organisations often follows all-too-rational thought of a non-scientific kind. If physical forces introduced to society by industrialisation have biomedical consequences, these organisations would often rather not know. If such a radical concept were found to be true, the consequences would be literally incalculable.

The forces ranged against a rational discussion are therefore formidable. It is greatly to the credit of Professor Claus Piekarski and Dr. Thomas Erren of the Institute for Occupational and Social Medicine at the University of Cologne that they were able to put together a conference at which the difficult issues of the effects of light and electrical forces on biology and health were discussed in a rational, constructive, enlightened and non-rancorous manner.

The papers fell into three broad groups, those discussing light, those discussing electricity, and those discussing mechanisms. Many papers contained elements of all three areas. Abstracts of the conference papers are available from the organizers and can be viewed at the website http://www.uni-koeln.de/symposium2000 . It is not the function of this overview to provide the details of each individual presentation but rather to generate interest in the meeting so that each interested person can follow up in detail the topics of particular concern.

There could be no doubt in the minds of anyone who attended the conference that the impact of light on biomedical processes is strong and reproducible. Much of the effect, but probably not all, is dependent on melatonin. The transducers are uncertain. They are in the eye and possibly other tissues, but are probably not the receptors usually involved in vision. On the other hand, while none can doubt that light is important, the evidence for its biological actions on cancer, on mental health and on other illnesses remains limited and needs much further research. Tantalising evidence of reduced cancer risk among blind people and those who live north of the Arctic Circle requires replication and study of mechanisms.

There is no such certainty about the biomedical effects of electrical fields. The evidence of effects on biology, particularly in cultured cells where conditions can be rigidly controlled, is looking increasingly solid. But the effects on whole animals and on human health are at present less convincing, perhaps more because of methodological and design problems, and because of preconceived ideas about mechanisms, than because of a lack of effect. In one particularly important presentation, Henshaw pointed out that effects may not be direct effects of electrical fields, but be consequences of charged particles generated by the fields, particles which could carry and precipitate atmospheric chemical pollutants, or infectious agents (like viruses and bacteria which are abundant in the atmosphere), or allergens such as pollens. An important consequence of this concept which has not been considered in the design of any epidemiological studies to date, is that the major impact of electrical forces may not be in the immediate vicinity of power lines, for example, but downwind where these particles of various types may be deposited.

Like any good conference this one generated more questions than answers. Most importantly it left no doubt that there are serious areas of investigation both for basic biology and for human health. They should not be suppressed by a consensus of intellectual, commercial and state interest.

Decisions about Environmental Health Risks: What are the Key Questions and How Does This Apply to Melatonin?

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Two of the key issues involved in the scientific contribution to the assessment of health risks are: 1) "weighing" the evidence to provide some guidance on whether an agent can ever be a health hazard; and 2) conditional on the hazard being real, estimating the "potency" of an agent for a particular hazard outcome. Evaluating the "strength-of-the-evidence" supporting or refuting the possibility of a hazard is a combination of objective, scientific evaluation and subjective, long-term experience in classifying agents. Objective methods, such as laboratory studies that characterize a mechanism involved in a toxic response, or results from statistical tests applied to scientific data, are used routinely as part of the argument for or against accepting a particular toxicity finding. However, less objective criteria, such as study quality, the importance of a finding in laboratory animals with regard to their applicability to humans, sometimes require subjective judgments based upon long-term experience and individual beliefs. To maintain a high level of scientific credibility when identifying potential health hazards, guidelines such as those used by the International Agency for Research on Cancer (IARC Monograph Series) also used by the National Institute of Environmental Health Sciences to evaluate extremely low frequency electromagnetic fields (ELF-EMF)(1) or those described in the US National Toxicology Program’s (NTP) Report on Carcinogens(2) have been developed and applied. These guidelines use a variety of measures to evaluate toxic potential, of which some are described below.

The decision to label an agent as carcinogenic is never a simple binary decision. In the IARC classification scheme, there are five levels of evidence: probably not a human carcinogen, possibly a human carcinogen, probably a human carcinogen, human carcinogen, and not classifiable. The NTP classification scheme refers to inclusion on a list of carcinogenic agents and has only two levels of evidence: (a) reasonably anticipated to be a human carcinogen and (b) known human carcinogen. (There is an assumed third category of not being included in the list if the agent is not a carcinogen or is not classifiable.) The inclusion into categories (a) or (b) depends upon the existence of epidemiological, clinical and mechanistic evidence in humans, laboratory and mechanistic evidence in animals, a reasonable theoretical basis for believing an agent can cause cancer and overall coherence of the data with information about agents with similar action. In each case, the individual studies used to support a finding are judged for their quality and their potential to deliver a misleading interpretation. The strongest category in both the IARC and the NTP classification schemes, (known) human carcinogen, generally requires significant human and animal evidence that the apparent relationship is causal and not simply a statistical association. Strong animal evidence but little human evidence generally leads to classification as a probable human carcinogen or reasonably anticipated to be a human carcinogen.

Based almost entirely on what was presented at the conference, and to stimulate discussion on this issue, the strength of the evidence supporting the melatonin hypothesis was considered. The melatonin hypothesis is complicated because an association of excess cancer with an external factor (e.g., light) that reduces melatonin might be the direct consequence of the reduced level of melatonin per se, or it might be a net effect of the reduction in melatonin and an additional synergistic (or antagonistic) effect of the external agent itself. Both these possibilities have to be considered when evaluating the evidence.

Lack of melatonin can reasonably be anticipated to be a human carcinogen. While the human evidence presented at this conference was suggestive, it did not appear to be sufficiently strong to warrant a conclusion that the link is causal. Clinical case-control studies of melatonin levels in cancer patients and controls displayed a general association with lower melatonin levels in cancer patients, but it was unclear whether the cancer itself or the therapy for these cancers was wholly or partly resposible for the association. The epidemiological data based on people with impaired vision, or individuals in geographic regions with reduced light, did not contribute greatly to resolution of the ambiguity. The strongest evidence appeared to come from laboratory studies with pinealectomized rats in which increased cancer risks were seen.

Light clearly affects melatonin levels; but it was unclear that light at night could affect these levels sufficiently to induce cancer in animals. This observation may be due more to what was not presented at the workshop than due to a lack of such information in the literature.

ELF-EMF has affected melatonin levels in some animal studies and not in others(1). Studies combining ELF-EMF with other chemical carcinogens such as DMBA (7,12-dimethybenzl[a]anthracene) have reported increased cancer risks in some situations but no excess risks in others. This literature appears to contain sufficient evidence to warrant further study, but insufficient evidence to justify either acceptance or rejection of the hypothesis that ELF-EMF affect melatonin and thus eventually affect cancer risks. ELF-EMF studies in humans provide little additional information on cancer risks and melatonin although several clinical studies appear to provide information on changes in melatonin.

"Potency" of an agent refers to the degree to which the agent induces toxicity in humans or animals. In many cases, simple techniques such as identifying exposures that show no significant change in risk are used to define potency. These methods fail to properly use the available information and they are extremely design dependent(3). For hypotheses as complicated as the melatonin hypothesis, mechanism-based mathematical models offer the best tool for evaluating health risks. Models exist(4) for the expression and control of melatonin in animals and humans. These models, linked with other experimental and epidemiological data can account for more of the data than the simpler approaches, and they provide additional mechanistic insight to develop further hypotheses to be studied.

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The International Symposium at the University of Cologne on "Low Frequency EMF, Visible Light, Melatonin and Cancer" was a valuable interdisciplinary conference on a topic of great potential impact on human health and disease in modern, industrialized societies.

The question of whether circadian disruption may account, in part, for the increasing risk of breast cancer worldwide requires intensive examination. Its potential role in a variety of other diseases is also of concern. To conduct meaningful epidemiological studies, it must be determined what exactly is 'circadian disruption' and how can it be measured in people. Measurement should include biological markers, as well as questionnaire-based exposures when biomarkers are not feasible.

Basic scientists are examining the signalling pathways potentially involved in circadian disruption; these begin with the phototransduction of light to a neuronal signal to the SCN. There is then a neuroendocrine transduction from the SCN to the relevant endocrine organs (pituitary, pineal) resulting in changes in circulating levels of hormones such as melatonin and estrogen. These hormonal changes may alter normal mammary tissue development and the potential for malignant transformation. Work on each aspect of this signalling cascade would be relevant to circadian disruption and breast cancer. A better understanding of phototransduction will help in understanding how EMF might also induce circadian disruption.

In order to make rapid progress in understanding all that is required in the cascade from circadian disruption to disease, there must be effective cross-discipline communication and collaboration. To further that goal, the Symposium included basic scientists in mechanisms of phototransduction in the human, and in pineal effects on reproduction in animals as it might pertain to humans. Several scientists who have conducted extensive molecular biological and toxicological studies of melatonin and disease, particularly breast cancer, presented there latest data. At the clinical interface, there was a detailed presentation of a large body of work on melatonin and cancer prognosis after diagnosis. Finally, several epidemiologists presented intriguing results from studies of breast cancer in blind women, and cancer risk in the Arctic.

The Symposium was a significant contribution to the rapidly emerging field of circadian disruption and disease.