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The Precautionary Principle Must Be Guided by EMF Research

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Regulatory action based on the Precautionary Principle is generally guided by the results of epidemiology studies. Even though laboratory research on electromagnetic fields (EMF) has supplied much relevant information and continues to do so, it is often overlooked. Laboratory research has shown that EMF of many frequencies stimulate many biological systems, and at low thresholds of both field strength and duration. It has also shown that EMF stimulate protein synthesis in cells and accelerate electron transfer reactions. In the last few years, important practical insights have been provided by the research on the cellular stress response, where the same specific biological response is induced in cells by both ELF (power frequency) and RF (radio frequency) fields, despite the very different energy levels. Since this protective biological response is not determined by the level of energy absorbed, safety standards based on the best available biological evidence must (1) *recognize non thermal protective responses and* (2) *include cumulative exposures across the EM spectrum.*

Keywords EMF research; EMF safety standards; Precautionary principle.

In the Footsteps of Ross Adey

In this symposium, dedicated to Ross Adey and his contributions to our understanding of the interactions of electromagnetic fields (EMF) with biological systems, I would like to continue a theme he raised in his Preface to the recent REFLEX Project Report (2004). The REFLEX Project, which was funded by the European Union and involved 12 Institutes, found genotoxic effects (i.e., DNA damage) due to ELF and RF fields at relatively low-level exposures. Evidence continues to accumulate about the potential impact of EMF on health, but Ross Adey acknowledged that the question of risk was still open. To help answer the question, he made a plea for more information on mechanisms and exposure metrics

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before embarking on further large epidemiology studies. In his words:

" ... the results obtained neither preclude nor confirm a health risk due to EMF exposure, but they speak in favour of such a possibility."
" ... there should be no more large epidemiological studies on human EMF exposures until essential exposure metrics are established, based on mechanisms of field interactions in tissues."

This article focuses on the results of EMF laboratory research and the insights provided into biological mechanisms and indirectly into the question of risk. I believe we have already learned enough to suggest application of the Precautionary Principle to EMF exposure. It is now also clear that in setting EMF exposure guidelines, we should take into account non thermal biological responses, as well as the effects of cumulative exposure across the EM spectrum.

Role of EMF Laboratory Research

Guidance for EMF policy has come primarily from epidemiology studies of health risks associated with power lines in the case of ELF, and cell phones in the case of RF. In both frequency ranges, the refining of epidemiology studies over the years has helped to clarify the factors involved in health risk. With regard to application of the Precautionary Principle, information about the recognition and responses to previously identified environmental hazards (e.g., smoking), as well as early responses to EMF as a potential hazard, have also provided guidance to public policy.

Laboratory research has provided the background for all of these studies, and particularly for understanding the biological mechanisms that underlie health risk. EMF laboratory research has shown that:

- a wide range of biological systems is affected
- a wide range of frequencies is active
- the thresholds of both field strength and duration are very low
- interference with natural processes (e.g., electron transfer, protein synthesis) is possible
- the molecular mechanisms activated at very low energies are plausible links to disease mechanisms.

It is worth emphasizing that the research on EMF thresholds has shown an unusual sensitivity of cells to ELF frequency fields. Thresholds in the range of 5–10 mG have been reported (Blank and Goodman, 2002), levels that are not very much higher than the usual environmental backgrounds of ~1 mG. Litovitz et al. (1991, 1993), working with the enzyme ornithine decarboxylase, have shown a full response to ELF when cells were exposed to a field for only 10 s duration. The exposure had to be continuous, since gaps in the sine wave resulted in a reduced response. The same group (Mullins et al., 1998) also showed that interference with the sine wave signal in the form of superimposed ELF noise also reduced the response.

These basic research studies on effects of EMF on cellular function have provided the information about biological thresholds and mechanism that can be a basis for a possible health impact (Blank and Goodman, 2004). The epidemiology studies have correlated EMF exposure and health effects on human populations, and have established quantitative dose-response relations. At best, the epidemiology

findings indicate a correlation between EMF exposure and a health effect, and not necessarily a causal relation. It is only EMF laboratory research, leading to information about molecular mechanisms, that can establish the scientific plausibility of effects under particular conditions.

EMF Activates the Stress Response

It has now been shown in many laboratories that EMF stimulates the cellular stress response, a ubiquitous reaction to potentially harmful stimuli where cells start to synthesize stress proteins (e.g., Goodman and Blank, 1998; Kwee et al., 2001; Leszczynski et al., 2002; Shallom et al., 2002; Weisbrot et al., 2003). The same biological response is activated in both ELF and RF ranges, frequency ranges that have very different energies associated with the fields. Therefore, it appears that thresholds for biological processes are not directly related to the energy input.

Protein synthesis occurs only when the two chains of DNA come apart and transfer the code for making a protein to mRNA. The stress response shows that EMF must cause the DNA to come apart even in the weak ELF range. These observations suggest that EMF stimuli could cause greater damage to DNA at more intense and longer exposures. Several experimental studies have reported both single and double strand breaks in DNA after exposure to ELF and RF fields (Lai and Singh, 2004; REFLEX Project Report, 2004).

Stimulation of the cellular stress response, by its very nature, probably indicates damage to DNA. Kultz (2005) actually defines the stress response as a " ... defense reaction of cells to damage that environmental forces inflict on macromolecules.", and he provides evidence from gene analysis that the stress response is a reaction to molecular damage. In a detailed review, Kültz has shown that the genes activated as a group along with stress genes (the "universally conserved proteome") sense and repair damage to DNA and proteins. It should be emphasized that such damage cannot be due to the energy needed to raise temperature, since the stress response can be stimulated by the very weak, non thermal ELF frequencies. In the ELF frequency range, the threshold is at the non thermal level of $\sim 10^{-12}$ W/kg. RF frequency levels that stimulate stress protein synthesis are $\sim 10^{-1}$ W/kg (thermal levels), higher by a factor of $\sim 10^{11}$. This means that a safety standard based on the rate of energy input is unlikely to be protective of anything but thermal damage, and many cellular processes are stimulated long before that level is reached. The energy level at which cellular processes are stimulated by EMF is many orders of magnitude lower (over a billion times lower) than by thermal stimuli (Blank and Goodman, 2004).

The cellular stress response is a fundamental protective response of cells, and it is clearly stimulated by EMF of different energies in the two frequency ranges studied. These results indicate a need to rethink the very basis of setting EMF safety standards. Questions arise immediately about two fundamental aspects of the consensus on safe EMF levels in the environment that are set:

- separately for divisions of EM spectrum rather than for total EMF exposure;
- generally based on temperature rise, determined by Specific Absorption Rate (SAR).

The stress response studies have shown that both criteria are seriously flawed and must be corrected to be brought into line with scientific findings. The SAR-based

threshold that varies along the EM spectrum cannot be a standard for a non thermal biological mechanism, and the cumulative effects of exposure to EMF in more than one frequency range must be considered. EMF background (power lines, radio and TV broadcast, cell phone transmission towers, etc.) includes a wide range of frequencies and is growing. We know that these different transmitters have biological receivers (e.g., DNA) present in all cells that are sensitive to many frequencies. Receivers in the form of enzymes, also present in cells, appear to respond to a more restricted range of frequencies (Blank and Soo, 2001).

EMF and DNA Activation

DNA, the biopolymer that stores and transmits genetic information, must be a very stable polymer. However, DNA is also involved in the continuous protein synthesis that is needed to sustain all living cells. Therefore, the stable biopolymer must also be able to come apart relatively easily to enable biosynthesis to proceed. This usually happens when specialized proteins called transcription factors bind to DNA. However, there is ample experimental evidence that weak ELF fields, as well as more energetic RF fields, both stimulate DNA to start synthesis of stress proteins, as well as other proteins (Leszczynski et al., 2002). In the ELF range, research on the major stress protein, hsp70, has found that the segment of DNA that initiates protein synthesis (called the promoter) has two stimulus-specific domains that cannot be interchanged. The domains have different DNA sequences that respond to two very different physical stimuli, EMF and an increase in temperature (Lin et al., 1999).

In another series of experiments, a DNA sequence from the promoter of an EMF sensitive gene was included in a construct containing a reporter gene, either CAT or luciferase. In each case, the construct proved to be EMF sensitive and responded to an applied ELF field (Lin et al., 2001). The ability to cause EMF sensitivity by transferring EMF-sensitive DNA sequences shows a clear relation between DNA structure and function. Certain DNA sequences are EMF sensitive, and respond to very low energy ELF fields.

The experiments on DNA, together with those on the stress response, suggest that relatively small perturbations can initiate biosynthesis. They also suggest that large perturbations can lead to DNA damage (chain breaks), which if not repaired or eliminated, raise the possibility of initiating carcinogenesis. Because of the low energies needed to cause the perturbations in the ELF range, it is likely that the effects involve electrons, e.g., such as those in the H-bonds that hold the two chains of DNA together. Electrons have very high charge to mass ratio and are most likely to be affected even by weak electric and magnetic fields. The EMF force ($\sim 10^{-21}$ newtons) that activates DNA can move a free electron about the length of a H-bond ($\sim$.3 nm) in 1ns. It is well known that electrons can tunnel such distances in proteins (Gray and Winkler, 2003), and experiments have shown comparable electron movement in DNA (Wan et al., 1999). It has also been shown that EMF accelerate electron transfer in oxidation/reduction reactions (Blank and Soo, 1998, 2003).

A possible scenario for an effect of EMF on DNA is as follows: The two chains of DNA are held together by H-bonds joining the complementary bases of DNA. H-bonds are hydrogens (protons) that are bonded to both chains by electron pairs. They are relatively weak, but the cumulative effect of the large number of H-bonds is strong enough to hold the chains together. If EMF forces displace electrons

in H-bonds, this would lead to local charging and generate forces that overcome the H-bonds and initiate disaggregation of the chains. Studies have shown that biopolymers can be made to disaggregate when the molecular charge is increased (Blank, 1994; Blank and Soo, 1987). Electric fields should have a similar effect since they also exert a force on electrons, and electric fields have been shown to stimulate DNA in HL60 cells (Blank et al., 1992) and in muscle in vivo (Blank, 1995). The genes for the hsp70 stress protein are more likely to be activated since they have been shown to be "bookmarked" on the DNA chain, that is, more exposed to the environmental forces (Xing et al., 2005).

Conclusion

There are good reasons for applying the Precautionary Principle in dealing with the complex environmental issues that have arisen in modern societies. Despite the ambiguities in interpretation and the divergence of EMF safety standards among nations (Foster et al., 2000), some governments have already seen the wisdom of this course of action and have started to implement policies on the basis of the Precautionary Principle. It is important to keep in mind that when we embark on a precautionary course, we must have the best information available. Epidemiology has provided important guidance, but critical scientific information from biological research has indicated that we must correct our course. At the very least, EMF safety standards must take into account non-thermal biological responses and the cumulative exposure across the EM spectrum.

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