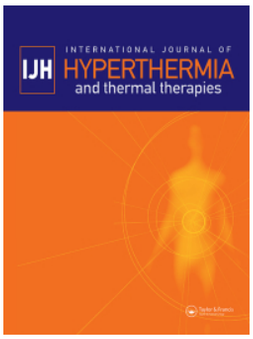

International Journal of Hyperthermia

ISSN: 0265-6736 (Print) 1464-5157 (Online) Journal homepage: informahealthcare.com/journals/ihyt20

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**To cite this article:** L. Kheifets, M. Repacholi & R. Saunders (2003) Thermal stress and radiation protection principles, International Journal of Hyperthermia, 19:3, 215-224, DOI: 10.1080/0265673031000090693

**To link to this article:** https://doi.org/10.1080/0265673031000090693

INT. J. HYPERTHERMIA
VOL. 19, NO. 3 (MAY–JUNE 2003), pp. 215–224

Taylor & Francis
healthsciences

# Thermal stress and radiation protection principles

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(*Received 14 January 2003*)

Exposure to radiofrequency (RF) fields can occur in residential, occupational and medical settings. Since many technologies use RF fields, it is important to fully investigate their effects on the human body. Since the demonstrated effect of RF exposure is heating, it is important to critically evaluate studies of elevated temperature effects on the human body, from the cellular and tissue level to the whole body level, including potential effects on the susceptible groups such as the very young and the very old. WHO convened a Workshop in the Spring of 2002 on the subject of Adverse Temperature Levels in the Human. The goal of the workshop was to evaluate most recent data useful for the development of science-based RF exposure limits. This paper outlines radiation protection principles that underline such an evaluation. It discusses the quality of literature needed for sound scientific reviews, provides the hierarchy of scientific evidence used to establish effects, distinguish between biological effects and adverse health consequences and indicates how evidence is evaluated. In addition, criteria for determining the most sensitive effects, the value of an effect that has a dose-response and methods of extrapolation are also described. Finally, the need to account for scientific uncertainty in the formulation of guidance on exposure is discussed.

*Key words:* Radiofrequency fields (RF), radiation protection principles, scientific uncertainty, guideline setting, risk assessment, thermal stress.

## 1. Introduction

The World Health Organization (WHO) established the International Electromagnetic Fields (EMF) Project in 1996 to provide an international response to key concerns related to health effects resulting from EMF exposure. Since many developing technologies use radiofrequency (RF) fields, it is important that their effects on the human body be fully investigated.

Exposure to RF fields can occur in residential, occupational and medical settings. Common human-made sources of RF fields include: monitors and video display units (3–30 kHz), AM radio (30 kHz–3 MHz), industrial induction heaters (300 kHz–3 MHz), RF heat sealers, medical diathermy (3–30 MHz), FM radio (30–300 MHz), mobile telephones, television broadcast, microwave ovens, radar, satellite links and microwave communications (3–30 GHz).

Use of mobile phones has grown dramatically. In many countries, over half the population uses these phones already and the market is still growing rapidly. The industry predicts that there will be as many as 1.6 billion mobile phone subscribers world-wide in the year 2005. Because of this, increasing numbers of mobile base stations have had to be installed. Base stations are low-powered radio antennae that

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*International Journal of Hyperthermia* ISSN 0265–6736 print/ISSN 1464–5157 online 
http://www.tandf.co.uk/journals
DOI: 10.1080/0265673031000090693

communicate with users' handsets. In early 2000, there were ~20 000 base stations in operation in the UK and ~82 000 cell sites in the US, with each cell site holding one or more base stations. Even though RF exposure from telecommunications facilities is generally less than from radio or TV broadcasting, concern over this wide spread exposure, especially among the young and the elderly, has been growing.

Occupational RF exposures occur in workers engaged in a number of industrial processes, particularly dielectric heaters used for wood lamination and the sealing of plastics and industrial induction heaters. Relatively high levels of exposure to RF fields can occur to workers in the broadcasting, transport and communications industries when they work in close proximity to RF transmitting antennae and radar systems. An important sub-set of these workers is military personnel.

Medical exposures can come from medical diathermy equipment to treat pain and inflammation, electrosurgical devices for cutting and welding tissues and from diagnostic equipment such as Medical Resonance Imaging (MRI).

## 2. Existing guidance

The International Commission on Non-Ionizing Radiation Protection (ICNIRP) has developed guidelines on exposure limits for EMF that can be applicable internationally. The rationale for establishing their limits has been published[1]. In the RF range, exposure limits (basic restrictions) are provided in terms of whole body and localized specific absorption rate (SAR), together with derived reference levels for power density and electric and magnetic field strength. ICNIRP basic restrictions for whole body exposure are set for both occupational ($0.4\,W\,kg^{-1}$) and for general public exposure ($0.08\,W\,kg^{-1}$) over the frequency range 100 kHz–10 GHz. For localized exposure in this frequency range, the basic SAR limit is $10\,W\,kg^{-1}$ averaged over any 10 g mass of tissue in the head or trunk for occupational exposures and $2\,W\,kg^{-1}$for general public exposure. In the limbs, the basic SAR limit for occupational exposures is 20 and $4\,W\,kg^{-1}$ for general public exposure. Occupational restrictions are envisaged to apply over an 8-h working day, 5 days per week; restrictions for members of the public apply over a 24-h period, 7 days a week. All the SAR values are averaged over any 10 g mass of tissue and time-averaged over any 6 min period.

These levels are based on the following summary. ICNIRP[1], in which it was noted that the experimental evidence available at the time indicated:

> that the exposure of resting humans for ~30 min to EMF producing a whole-body SAR of between 1–4 $W\,kg^{-1}$ results in a body temperature increase of less than 1°C. Animal data indicate a threshold for behavioural responses in the same SAR range. Exposure to more intense fields, producing SAR values in excess of 4 $W\,kg^{-1}$ can overwhelm the thermoregulatory capacity of the body and produce harmful levels of tissue heating. Many laboratory studies with rodent and non-human primate models have demonstrated the broad range of tissue damage when either partial-body or whole-body heating produces temperature rises in excess of 1–2°C[2]. The sensitivity of various types of tissue to thermal damage varies widely, but the threshold for irreversible effects in even the most sensitive tissues is greater than 4 $W\,kg^{-1}$ under normal environmental conditions. These data form the basis for an occupational exposure restriction of 0.4 $W\,kg^{-1}$, which provides a large margin of safety for other limiting conditions such as high ambient temperature, humidity or level of physical activity. (p. 507)

It was further argued that:

> Data on human responses to high-frequency EMF that produce detectable heating have been obtained from controlled exposure of volunteers and from epidemiological studies on workers exposed to sources such as radar, medical diathermy equipment and heat sealers. They are fully supportive of the conclusions drawn from laboratory work, that adverse biological effects can be caused by temperature rises in tissue that exceed 1°C. Epidemiological studies on exposed workers and the general public have shown no major health effects associated with typical exposure environments. Although there are deficiencies in some of the epidemiological work, such as poor exposure assessment, the studies have yielded no convincing evidence that typical exposure levels lead to adverse reproductive outcomes or an increased cancer risk in exposed individuals. This is consistent with the results of laboratory research on cellular and animal models, which have demonstrated neither teratogenic nor carcinogenic effects of exposure to athermal levels of high-frequency EMF. (p. 508)

An additional safety factor was included for members of the public because:

> The occupationally exposed population consists of adults who are generally exposed under known conditions and are trained to be aware of potential risk and to take appropriate precautions. By contrast, the general public comprises individuals of all ages and of varying health status and may include particularly susceptible groups or individuals. Both laboratory data and the results of limited human studies[3] make it clear that thermally stressful environments and the use of drugs or alcohol can compromise the thermoregulatory capacity of the body. In many cases, members of the public are unaware of their exposure to EMF. Moreover, individual members of the public cannot reasonably be expected to take precautions to minimize or avoid exposure. It is these considerations that underlie the adoption of more stringent exposure restrictions for the public than for the occupationally exposed population. (p. 508)

Thus, data on short-term acute effects produced by small increases in temperature have thus far been shown to be the earliest detectable changes (most sensitive effect) that could potentially lead to adverse health consequences and so form the threshold level for current international standards. Long-term, low-level RF exposure has not been established to produce any effects adverse to health. In the ICNIRP[1] guidelines, a reduction factor of 10, from the exposure level producing the most sensitive effect, is used to determine the limits for occupational exposure. A further reduction of 5, making a total reduction of 50 from the level of the most sensitive effect, is used to determine the exposure limits for the general public.

## 3. The WHO workshop

Since the main effects of the exposure of humans to RF radiation is heating, it is of particular importance to critically evaluate information relating elevated temperature effects on the human body, from the cellular and tissue level to the whole body level. This would include heating of the embryo and foetus as well as thermally sensitive organs in the body. In order to provide this information, WHOs EMF Project convened a Workshop on Adverse Temperature Levels in the Human Body from 21–22 March 2002 at WHO headquarters in Geneva.

The purposes of the Workshop were to:

- present state-of-the-science information on the effects of elevated temperature and times of exposure on mammalian cells and tissues, the foetus, sensitive organs (e.g. eye, skin, brain and testes) and the whole body;
- define the combined elevated temperature and exposure times causing adverse effects in biological systems;

- prepare a written report on the persuasiveness of the data for recommendations for maximal permissible temperature elevations in tissues and organs in human beings and make such recommendations if appropriate; and
- provide information useful for development of RF exposure standards.

This paper outlines radiation protection principles which underline such an evaluation. It discusses quality of literature needed for sound scientific reviews, provides the hierarchy of scientific evidence used to establish effects, distinguishes between biological effects and adverse health consequences and indicates how evidence is evaluated. In addition, criteria for determining the most sensitive effects, the value of an effect that has a dose-response and methods of extrapolation are also described. Finally, the need to account for scientific uncertainty in the formulation of guidance on exposure is discussed.

## 4. Establishing adverse effects

### 4.1. *Quality of literature used for reviews*

Peer-reviewed scientific literature forms the basis for establishment of adverse health effects. Although the rigour of peer-review varies widely among scientific journals, and the process cannot assure scientific quality, peer-reviewed studies are generally of higher quality and usually provide basic information needed for the assessment of study quality. For studies to be useful to health risk assessments, they must be of high scientific quality with clearly-defined hypotheses, estimates should be given of the ability of the study to detect small effects (the study power) and protocols that are consistent with good scientific practice should be used[4]. Quality assurance procedures should be included in the protocol and monitored during the study.

While peer review adds confidence in the study results, additional review is necessary to evaluate study design, conduct an analysis of each report and to compare these with the results of other studies. Peer-reviewed reports not published in scientific journals can also be included. However, conference abstracts are of little value as they generally receive no prior peer-review, contain sparse information and cannot be considered as the final outcome of an experiment until all results are available and properly analysed.

Study techniques, methods and conditions should be as unbiased as possible. Methodology and biological systems should be appropriate to end points studied. Safeguards such as double blind techniques should be employed. Within every study there should be appropriate corresponding controls. The sensitivity of the study should be adequate to ensure a reasonable probability that an effect would be detected, if it indeed exists.

Data analyses should be comprehensive, no relevant data deleted from consideration and appropriate analytical methods used. Data from experiments within the same study should be internally consistent, within normal statistical variability. Where data are reported as ratios, the underlying data should be reported as well or available for in-depth analysis.

### 4.2. *Health risks and biological effects*

The existence of biological effects from EMF exposure may be established when research results are independently replicated or supported by related studies. This is further strengthened when:

- There is agreement with accepted principles or results lead to new and coherent scientific principles;
- The underlying mechanism of action on the biological system is understood; and
- A dose–response relationship can be determined.

Extrapolating from biological effects to possible adverse human health consequences is not an easy step. Biological effects can be defined as any measurable changes in a biological system in response, for example to an EMF field, but not all effects will necessarily be hazardous. WHO defines health as the state of complete physical, mental and social well being and not merely the absence of disease or infirmity[5]. Thus, deciding whether biological changes have adverse health consequences depends on whether they affect the mental, physical or social well-being of exposed people, either in the short- or the long-term. In this regard, the context of the exposure might be important. For example, transient perception of the field and/or relatively low level heating may be entirely inconsequential in most cases, but might reduce the effectiveness of a worker performing a cognitively demanding task, such as air traffic control. Exposures that engender the normal thermoregulation of skin vasodilation and sweating may be innocuous in healthy people, but may pose a severe risk to elderly people who may have inadvertently become dehydrated in hot weather. Localized heating at levels below the threshold for acute damage might be considered acceptable for one or a few exposures, but in a context where exposure might be repeated daily, the possibility of chronic changes occurring after years of exposure must be considered. Similarly, functional changes resulting from localized heating that might be harmless in the short-term might be debilitating in the longer term.

### 4.3. *Exposure scenarios*

Following on from the above, it might be helpful to consider the application of limits on exposure in the context of various 'generic' exposure scenarios. Occupational limits are often envisaged to apply over an 8-h working day, 5 days a week. The workforce may include people with minor health problems receiving medication of various types and pregnant women, in which case there is the health both of the worker and her developing child to consider. An example might be someone working with a RF sealer/welder or adventitiously exposed by a nearby RF source. Appropriate limits on exposure would be expected to allow for the repeated exposure and for physical work in hot environments. However, such limits may be relaxed for exposures of short duration, such as climbing past a 'live' RF antenna during maintenance work, where the worker has been deemed fit and a full work/environment heat assessment has been carried out.

With regard to members of the public, restrictions on exposure are expected to apply 24 h per day, 7 days per week. Typical exposure scenarios would include living in proximity to powerful RF sources such as TV and radio towers, mobile phone and other communication systems and radar stations. Generally, such exposures are physiologically trivial, orders of magnitude below current guidance levels. In addition, mobile phone handsets act as relatively small RF sources. The general population can be considered to include people of all stages of health, from those supremely fit, to those, often-elderly people, in the terminal stages of illness. With regard to the latter, such individuals, e.g. with a chronic heart condition,

may nevertheless be mobile. Appropriate limits need to consider the sensitivity of these sub-groups.

4.4. *Hierarchy of scientific evidence*

The body of evidence is always considered as a whole, based on the weight of evidence approach and incorporating different lines of scientific enquiry. As radiation protection is ultimately aimed at protecting human health, protective limits, where possible, should be derived from human data, using the animal and cellular data only to provide insight into biological principles and mechanisms. The relationship between exposure and short-term biological effects can sometimes be evaluated from human laboratory studies, whereas data on long-term human effects can only be derived from epidemiological studies. However, in spite of their direct relevance, the results of epidemiological studies may, in themselves, not provide sufficient evidence of causal relationships without supportive data from experimental studies, especially when the suggested risks are small. This is because bias or confounding can more easily explain small risks.

Studies carried out at the cellular level are usually used to investigate mechanisms of interaction with EMFs but are not generally taken alone as evidence of effects *in vivo*. There are a number of reasons for this: cells in culture are removed from the normal constraints of growth *in vivo*, the culture medium is usually supplemented with serum to enable the cells to grow, and quite often, cell lines used are derived from various types of cancer because of their ability to grow in culture for long periods of time. Because they are relatively inexpensive and rapid, cellular studies are often used as a pre-screen to identify agents that are suitable for entry into long-term testing on animals or in human studies[6].

Animal studies are frequently based on experiments using inbred strains of mice or rats. The advantage of such studies compared to *in vitro* data is that they provide information concerning the interaction of EMFs with living systems which display the full repertoire of body functions, such as immune responses, cardiovascular changes, behaviour, etc., in a way that cannot always be achieved with cellular studies. Individual animals of inbred strains are genetically identical, thus ensuring a relative consistency of response to the agent in question. Animal models based upon genetic manipulation in order to represent certain human diseases have further increased the value of animal studies to reveal potential adverse health effects. Animal studies are, thus, usually a more powerful experimental tool than cellular studies in this context, but are expensive and time-consuming.

Extrapolation of this information to humans, however, cannot be expected *a priori* to be straightforward, since there are obvious differences. Example differences include life span, physiology, metabolism, the proliferative capacity of different tissues, DNA repair capacity and many other variables. In this context, the thermoregulatory and cardiovascular responses to heat in humans are substantially different from those of typical laboratory animals. On the other hand, at a molecular level, there are many similarities between processes in animals and human and, for example, animal studies have been very useful in helping unravel the sequence of genetic events in the development of a number of human cancers and in the growth and development of the embryo and foetus. To be sufficiently powerful, testing of potential hazard for many chemicals are done at levels of exposure that are several orders of magnitude above typical human exposures. Such studies are not feasible for EMF exposures.

Generally, animal studies can be expected to provide qualitative information regarding potential outcomes, but the data would not be extrapolated quantitatively to give estimates of risk[7]. Risk estimates applicable to the development of guidance are more properly derived from human studies. IARC[8], however, note that, with regard to cancer specifically: 'in the absence of adequate data on humans, it is biologically plausible and prudent to regard agents and mixtures for which there is sufficient evidence of carcinogenicity in experimental animals as if they presented a carcinogenic risk to humans' (p. 17). IARC also notes that the possibility that a given agent may cause cancer through a species-specific mechanism that does not operate in humans should also be considered.

Experimental studies using volunteers are, for ethical reasons, naturally restricted to the investigation of transient physiological phenomena that, in the controlled conditions of a laboratory, can be determined to be harmless. The advantages of volunteer experiments are that they indicate the likely response of other humans exposed under similar conditions. Disadvantages of volunteer studies include the relative harmlessness of the possible effects that can be investigated, the often-short duration of exposure and follow-up, the small number of subjects usually examined and that the subjects are usually screened for fitness and, therefore, may not reflect the responses of potentially more susceptible members of society. Within this limited context, however, volunteer studies can give valuable insight into the physiological effects of human exposure to an agent. In contrast, information regarding possible effects on morbidity and/or mortality comes from epidemiological studies.

Epidemiology is observational rather than experimental in nature. In contrast to controlled studies in which subjects are randomized to receive, say, a treatment or a placebo, epidemiologists cannot influence who does or does not receive an exposure. Consequently, epidemiological studies may be affected by bias (i.e. systematic errors in the design or conduct of the study) or confounding (i.e. spurious findings due to the effect of a variable that is correlated with both the exposure and disease under study). Epidemiologists generally attempt to address these problems by choosing an appropriate form of study and by conducting and analysing the study well. However, not all studies are equally good and it is important to review their strengths and weaknesses. While epidemiologic investigations are difficult to conduct and they can be subject to confounding and bias, they offer unique advantages. In particular, epidemiologic studies permit the evaluation of the consequences of an environmental exposure or other factor in the precise manner in which it occurs in human populations, i.e. under usual rather than artificial conditions of exposure. Thus, epidemiology does not require extrapolation between species. Moreover, because epidemiologic research is conducted in natural settings, it may permit the study of the joint influence of multiple factors on disease occurrence while taking into account the defence mechanisms of the individual. Equally important, extrapolation from high doses to low doses as is usual in animal studies is not necessary because in epidemiologic studies it is often possible to examine an exposure within the relevant dose range.

Clinical experience, although failing to fulfil the quality criteria given above for human health studies, may, nevertheless, provide complementary information. Anecdotal reports in themselves do not provide a basis for the assessment of risk, because of their inherent poor control and possible observational bias. They may, however, provide an indication of the need for further investigation or advice.

4.5. *Hierarchy of severity*

Death is clearly the most severe biological end-point considered in this context. Deaths from heat stroke and, predominately in the elderly, from heat-induced coronary thrombosis are considered by Donaldson *et al.*[10] dealing with cardiovascular responses to heat. At a cellular level, however, the possible induction of cancer by elevated tissue temperatures is discussed by Dewhirst *et al.*[2] Otherwise, the avoidance of acute heat-induced cell death and tissue necrosis provides an extreme upper limit on the effects of localized temperature in various body tissues. This information would clearly be of value, for example, in the investigation of accidental overexposures. More generally, restrictions on occupational and public exposure would seek to avoid cumulative damage from repeated sub-acute-threshold exposures and the functional changes induced by increased temperatures in cell and tissue physiology that might lead to chronic adverse health effects. Lepock[11] discusses the fundamental changes in cellular proteins and function that occur with elevated temperature. Dewhirst *et al.*[3] review concepts of thermal dose and thresholds for both sub-acute and acute thermal damage to normal tissues in this issue.

The potentially adverse effects of heat on the development of the embryo and foetus are also of great importance in this context; an abnormality induced in pregnancy can affect the whole life of the unborn individual. The central nervous system has been identified as critically sensitive to heat-induced developmental abnormalities. Edwards *et al.*[12] critically examines the extent to which thresholds for these effects have been established in humans.

For localized tissue heating, the extent of the temperature elevation experienced depends to a large extent on the ability of the blood circulation to dissipate excess heat. This, in turn, depends on the intrinsic vascularity of the tissue and the localized and whole-body circulatory responses to heat. Effects of whole body and localized heating on the central nervous system are discussed by Sharma[13].

Cardiovascular responses to heat are considered by Donaldson *et al.*[10] Generally, compared to many animals, humans are exceptionally well adapted to dissipate excess heat; in addition to a well developed ability to sweat, which in humans can be produced over most of the body surface, the dynamic range of blood flow rates in the skin is much higher than in other species. A corollary of the ability to dissipate heat is a lower tolerance of excursions in core temperature. Physiological effort to dissipate excess heat is maximal at $\sim$39_C[14] and is dependent on adequate hydration. Occupational limits on work in hot environments typically seek to minimize physiological strain and heat-related disorders. For members of the public, consideration should be given to those, such as the elderly, who may be very susceptible to increased heat loads and those whose ability to lose heat is compromised by medication and other factors.

Finally, the ability to reason (one's cognitive ability) also sets humans apart from other members of the animal kingdom. Increasingly, in society, people work in jobs requiring astute mental processing. In many cases, the safety of others depends on the mental alertness of the operator. An example cited above was that of an air traffic control operator. Hancock and Vasmatzidis[15] consider the adverse effect of heat on cognitive performance for different task categories.

Many forms of EMF find application in medical practice, often at exposure levels that are much greater than normal population exposure levels. Thermal and EMF exposures of patients lie outside the scope of exposure limits for workers and mem-

bers of the public, as the risk/benefit considerations are very different in these circumstances.

## 5. Protection of human health and scientific uncertainty

The existence of established EMF effects form the basis and rationale for current exposure standards or guidelines. However, while scientific research is continuing, in some situations the data are not sufficient to allow the definite evaluation of potential adverse human health effects related to EMF exposure. Various approaches to protection have been suggested to deal with uncertainty. In recent years, increased reference has been made to cautionary policies and in particular the Precautionary Principle.

The Precautionary Principle is mentioned in international law and is the basis for European environmental legislation. The exact definition of the Principle and the range of actions invoked or suggested by the Principle have varied. Within Europe, the European Commission has taken a leading role in fostering discussion on the use of the precautionary principle, principally through the publication of a 'Communication from the Commission on the precautionary principle'[16]. Here the reference of application is again to the environment, but the EC clearly states that this cannot be interpreted as applying only to the environment.

The use of the Precautionary Principle is a risk management tool, whereas the development of EMF exposure safety standards or guidelines based on established health effects involves a proper risk analysis. Use of the Precautionary Principle should complement rather than undermine exposure guidelines. Components of the Principle that would enhance this complementarity would be the proportionality (measures should not be disproportionate to the desired level of protection), the degree to which the Principle is based on the science (requiring an evaluation of risk research) and the provisional nature of measures pending further acquisition of scientific data. These have been described by the European Commission[16] and it's application to EMF in Foster *et al.*[17], WHO[18] and Kheifets *et al.*[19]

## 6. Concluding remarks

The WHO Workshop on Adverse Temperature Levels in the Human Body reviews the evidence for the detrimental effects of heat on the tissues, organs and functions of the human body, weighting the evidence as described above and providing consideration of scientific uncertainty in the evaluation of the health effect data. Consideration is given to the potential consequences of heating in healthy people and in those more susceptible to excess heating such as the very young and the elderly.

The results of the Workshop should be useful for the development of science-based RF exposure limits. This review is timely in view of the use of the older scientific literature on thermal effects used for developing the levels of short-term acute effects thresholds in the international guidelines.

## References

1. ICNIRP. International Commission on Non-Ionizing Radiation Protection. Guidelines for limiting exposure to time varying electric, magnetic and electromagnetic fields (up to 300 GHz). *Health Phys* 1998; 74: 494–522.
2. Dewhirst MW, Lora-Michiels M, Vigilanti BL, Dewey WC, Repacholi M. Carcinogenic effects of hyperthermia. *Int. J Hyperthermia* 2003; 19: 236–251.

3. Dewhirst MW, Vigilante BL, Lora-Michiels M, Hanson M, Hoopes PJ. Basic principles of thermal dosimetry and thermal thresholds for tissue damage from hyperthermia. *Int J Hyperthermia* 2003; 19: 267–294.
4. Michaelson SM, Elson EC. Modulated fields and 'window' effects. In: Polk C, Postow E, eds, Biological effects of electromagnetic fields. Boca Raton, FL: CRC Press, 1996; 435–533.
5. Repacholi MH, Cardis E. Criteria for EMF health risk assessment. *Radiat Protect Dosim* 1997; 72: 305–12.
6. WHO. Preamble to the Constitution of the World Health Organization as adopted by the International Health Conference, New York, 19–22 June, 1946; signed on 22 July 1946 by the representatives of 61 States (Official Records of the World Health Organization, no. 2, p. 100) and entered into force on 7 April 1948.
7. AGNIR. ELF electromagnetic fields and the risk of cancer. *Report of an Advisory Group on Non-ionising Radiation*. Docs NRPB, 12(1), Chilton, NRPB, 2001.
8. UNSCEAR. Biological effects of pre-natal irradiation. Annex C. In: *United Nations Scientific Committee on the Effects of Atomic Radiation, Genetic and Somatic Effects of Ionising Radiation. UNSCEAR Report to the General Assembly with Scientific Annexes*. New York: United Nations, 1986; 263–366.
9. IARC. *Monograph Volume 80: Non-ionizing Radiation. Part I: Static and Extremely Low Frequency (ELF) Electromagnetic Fields*. Lyon: IARC, 2002.
10. Donaldson GC, Keatinge WR, Saunders RD. Cardiovascular responses to heat stress and their adverse consequences in healthy and vulnerable human populations. *Int J Hyperthermia* 2003; 19: 225–235.
11. Lepock JR. Cellular effects of hyperthermia: relevance to the minimum dose for thermal damage. *Int J Hyperthermia* 2003; 19: 252–266.
12. Edwards MJ, Saunders RD, Shiota K. Effects of heat on embryos and foetuses. *Int J Hyperthermia* 2003; 19: 295–324.
13. Sharma HS, Hoopes PJ. Hyperthermia induced pathophysiology of the central nervous system. *Int J Hyperthermia* 2003; 19: 325–354.
14. Rowell, LB. Cardiovascular aspects of human thermoregulation. *Circ Res* 1983; 52: 367–379.
15. Hancock PA, Vasmatzidis I. Effects of heat stress on cognitive performance: the current state of knowledge. *Int J Hyperthermia* 2003; 19: 355–372.
16. EC. *Communication from the Commission on the Precautionary Principle* COM, 2000; 1.
17. Foster KH, Vecchia P, Repacholi MH. Science and the precautionary policy. *Science* 2000; 288: 979–81.
18. WHO. Electromagnetic fields and public health: mobile telephones and their base stations. *WHO Fact Sheet* 193, June 2000; www.who.int/emf
19. Kheifets L, Hester G, Banerjee G. The precautionary principle and EMF: implementation and evaluation. *J Risk Res* 2001; 4: 113–25.